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All topics related to diseases of the skin, hair, and nails, with special emphasis on technologies for information exchange, education, and clinical care
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Original Paper

Association Between VDR and CYP24A1 Polymorphisms, Atopic Dermatitis, and Biochemical Lipid and Vitamin D Profiles in Spanish Population: Case-Control Study

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Abstract

Background: Atopic dermatitis (AD) is the most prevalent inflammatory skin disorder, characterized by impaired epidermal barrier function and an altered immune response, both of which are influenced by vitamin D deficiency. Single-nucleotide polymorphisms (SNPs) in *VDR* and *CYP24A1* have been previously associated with AD.

Objective: We sought to characterize the associations between the *VDR* and *CYP24A1* polymorphisms and the vitamin D and lipid biochemical profile in children diagnosed with AD.

Methods: A total of 246 participants (143 patients with AD and 103 healthy controls) were enrolled in this study. Genotyping for polymorphisms in *VDR* (rs2239185, rs1544410, rs7975232, rs2238136, rs3782905, rs2239179, rs1540339, rs2107301, rs2239182, and rs731236) and *CYP24A1* (rs2248359 and rs2296241) was performed by allele-specific polymerase chain reaction using integrated fluidic circuit technology. Serum levels of calcium, phosphorus, and vitamin D were measured, and the biochemical lipid profile was determined.

Results: Among *VDR* SNPs, rs2239182 exerted a protective effect against the development of AD, whereas rs2238136 was identified as a risk factor for AD. The GCC haplotype (rs2239185-G, rs1540339-C, and rs2238136-C) appeared to protect against the development of AD. rs2239182-CC was associated with higher 25(OH)D concentrations, whereas rs2238136-TT, rs2239185-GA, and rs2248359-TT were present in a large proportion of patients with serum vitamin D deficiency. rs2239185-AA, rs2239182-CC, and rs1540339-CC were associated with higher serum total cholesterol; rs2239182-TT was associated with lower low-density lipoprotein cholesterol; and rs2239182-TC with lower high-density lipoprotein cholesterol. Both *CYP24A1* SNPs (rs2296241-AA and rs2248359-TT) were associated with higher high-density lipoprotein cholesterol levels.

Conclusions: The *VDR* SNP rs2238136 is a risk factor for AD and other SNPs in *VDR* and *CYP24A1*, which may lead to alterations in biochemical parameters that influence the risk of AD. Our findings highlight the complex genetic basis to AD and indicate that interrelationships between different genetic factors can lead to alterations in vitamin D metabolism or lipid profiles, which in turn may influence the development of AD.

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KEYWORDS

VDR; CYP24A1; atopic dermatitis; dermatology; vitamin D; lipid; dermatitis; biochemical; biochemistry; genomics; polymorphism; SNP; Spanish; inflammatory; skin disorder; epidermal; immune; deficiency; children; youth; calcium; phosphorus; risk factor; genetic; development; genotyping; genotype

Introduction

Atopic dermatitis (AD) is the most prevalent inflammatory skin disorder, characterized by impaired epidermal barrier function and an altered immune response; it is caused by a combination of genetic and environmental factors [1-3]. Vitamin D influences both these processes, and several studies have demonstrated an association between 25 OH vitamin D deficiency and AD [4-6], suggesting that vitamin D supplementation may help ameliorate AD severity [7]. However, other authors have highlighted the scarcity of evidence supporting a beneficial effect of vitamin D supplementation in patients with AD [8,9].

The effects of vitamin D deficiency are the consequence of low serum concentrations, mainly due to insufficient sun exposure together with inadequate dietary intake. However, alterations in proteins involved in vitamin D metabolism may also contribute to vitamin D deficiency. Vitamin D receptor (VDR) is an intracellular hormone receptor that specifically binds 1,25(OH)2D3 and mediates its effects. It is encoded by the vitamin D receptor gene (*VDR*; 12q13.11, OMIM#601769), which contains 11 exons and spans approximately 75 kb. Exons 2 and 3 are involved in DNA binding, and exons 7-9 are involved in binding to 1,25(OH)2D3. Using mutation analysis, some authors characterized arg18/arg22, *VDR* residues immediately N-terminal of the first DNA-binding zinc finger, as vital for contact with the general transcription factor II B. Variations in *VDR* (MIM*601769) may alter 1,25(OH)2D3 responsiveness in inflammatory conditions and stimulate the proliferation of T lymphocytes and cytokines [10]. Several studies [11-16] and a recent meta-analysis [17] have described associations between AD and single-nucleotide polymorphisms (SNPs) in *VDR*, although most of these studies only evaluated the impact of the classical FokI (rs2228570), BsmI (rs1544410), ApaI (rs7975232), and TaqI (rs731236) *VDR* polymorphisms.

1,25(OH)2D3 activity also depends on the function of certain enzymes responsible for its endogenous metabolism in keratinocytes and lymphocytes, such as the enzyme 1,25-dihydroxyvitamin D3-24-hydroxylase (encoded by *CYP24A1*, MIM*126065). Vitamin D 24-hydroxylase, encoded by *CYP24A1* (20q13.2, OMIM#126065), is a mitochondrial enzyme responsible for inactivating vitamin D metabolites through the C-24 oxidation pathway. 1,25-(OH)2D3 induces the 24-hydroxylase, whereas hypocalcemia, through increased parathyroid hormone, suppresses this enzyme. The presence of certain SNPs in *CYP24A1* have also been associated with atopic diseases such as AD and asthma [16]. 1,25(OH)2D3 has a short time of action because it induces its own inactivation through the positive regulation of the CYP24A1 enzyme, which carries out the metabolic processes that produce the different products of higher polarity and the loss of hormonal activity. CYP24A1 is located in the inner mitochondrial membrane and is expressed in various tissues at low concentrations, with high capacity to be rapidly activated in response to 1,25(OH)2D3 levels. Particularly, in the liver, this enzyme is not expressed. CYP24A1 activation is not exclusively produced by 1,25(OH)2D3; induction by other compounds such as lithocholic acid, retinoic acids, and pregnane X receptor ligands and by prolonged treatment with different groups of antimicrobial, antituberculosis, and anticonvulsant drugs, among others, has also been demonstrated. CYP24A1 participates in the metabolism of both 25-hydroxy vitamin D3 and 1,25(OH)2D3, although it is more closely linked to the latter [18].

Vitamin D deficiency may also underlie metabolic syndrome, especially during infancy. It has been proposed that in patients with AD, alteration of the lipid profile and the consequent appearance of metabolic syndrome, especially in childhood, may be a consequence of 25 OH vitamin D deficiency due to insufficient serum levels, receptor (VDR) hypofunction, or dysregulation of enzymes involved in its metabolism (CYP24A1) [16,19-21].

In this study, we sought to assess associations between the *VDR* and *CYP24A1* polymorphisms and the 25 OH vitamin D and lipid biochemical profile in children diagnosed with AD.

Methods

Study Population

We conducted a case-control pilot study of patients aged between 2 months and 14 years who fulfilled the following criteria: AD at the time of inclusion, skin phototype 2-4, Mediterranean phenotype, and born to parents of Spanish origin. Participants were recruited between January 2011 and December 2012 in the Departments of Dermatology and Paediatric Allergy of the San Jorge Hospital (Huesca, Spain), primary care centers in Huesca city, and the Dermatology Department of the Niño Jesús Hospital (Madrid, Spain). These patients were initially recruited for other studies previously published by our group [22,23]. Participants in the control group were recruited at the University Hospital Miguel Servet (Zaragoza, Spain), being apparently healthy individuals, and by using the following exclusion criteria: family history of atopy or allergic diseases; symptoms of atopic eczema, asthma, or hay fever; and allergies to food, pollen, or other environmental allergens (eg, animals).

AD severity was scored using the Scoring Atopic Dermatitis (SCORAD) index [24,25] and classified as mild (SCORAD <15), moderate (SCORAD 15-40), or severe (SCORAD >40) [26]. Personal history of atopic diseases, including asthma and allergic rhinitis, was also recorded.

Ethics Approval

This study was approved by the Aragon Ethical Committee for Clinical Research (PI08/81). Written informed consent was obtained from all participants, or their guardians, before inclusion.

Genomic Studies

Genomic DNA was obtained from peripheral blood leukocytes extracted from ethylenediaminetetraacetic acid whole blood samples using the QIAamp DNA Blood Mini Kit (QIAGEN) and an automated EZ1 biorobot (QIAGEN). Both cohorts were genotyped for the *VDR* (rs2239185, rs1544410, rs7975232, rs2238136, rs3782905, rs2239179, rs1540339, rs2107301, rs2239182, and rs731236) and *CYP24A1* (rs2248359 and rs2296241) polymorphisms.

SNP genotyping was performed using the commercial FlexSix Genotyping integrated fluidic circuit kit (Fluidigm). This method is based on allele-specific polymerase chain reaction detection using an integrated fluidic circuit.

Biochemical Studies

Calcium (mg/dL), total cholesterol (mg/dL), high-density lipoprotein (HDL) cholesterol (mg/dL), triglycerides (mg/dL), and phosphorus (mg/dL) serum concentrations were measured by spectrophotometric methods, and 25(OH)D (ng/mL), immunoglobulin E (UI/L), and parathyroid hormone (pg/mL) by immunochemiluminescence using an automated AU5400 and UniCel DxI 800 (Beckman Coulter), respectively. While acknowledging that the gold standard for vitamin D metabolites is liquid chromatography-mass spectrometry, immunochemiluminescent assays are the most widely used clinically. Low-density lipoprotein (LDL) cholesterol (mg/dL) were calculated by the Friedewald equation.

Data Analyses

Descriptive statistics for quantitative values were expressed as the mean and SD, according to the data distribution. Categorical variables were presented as frequencies and percentages. Chi-square or Fisher exact tests were used to assess associations between the *VDR* and *CYP24A1* polymorphisms and AD and AD-associated variables, including the SCORAD index and associated atopic diseases. The association between genotypes or alleles and AD was assessed by calculating the odds ratio (OR) and 95% CIs. Allele and genotype frequencies were calculated by direct counting, and the chi-square test was used to compare frequencies between cases and controls. The Hardy-Weinberg equilibrium was tested in both groups using the chi-square goodness-of-fit test. The level of statistical significance was set at $P<.05$. Statistical analyses were performed using SPSS version 19 (IBM Corp) and R software (haplo.stats package; R Foundation for Statistical Computing).

Results

The clinical characteristics of the study population is described in Table 1.

Genotype distributions of *VDR* and *CY24A1* SNPs in the control and AD groups are summarized in Multimedia Appendix 1. rs7975232 and rs2107301 were among the SNPs initially proposed for evaluation but were later excluded as they failed to meet Hardy-Weinberg equilibrium criteria. Genotype frequencies for global (TOT, n=2504), European (EUR, n=503), and Iberic populations (IBS, n=107), based on 1000 Genomes Project phase 3 populations, are also presented for the sake of comparison [27].

Table 2 summarizes the association between AD and SNPs. For each SNP, the results for the 5 genetic models (codominant, dominant, recessive, overdominant, and additive) are shown. Statistically significant associations were observed for 2 polymorphisms in *VDR*: rs2239182, which was identified as a protective factor; and rs2238136, which was identified as a risk factor. No significant associations were observed for the remaining polymorphisms analyzed.

The presence of rs2239182-C/C in the codominant model exerted a protective effect, reducing the risk of AD by 66% (OR 0.34, 95% CI 0.13-0.87; *P*=.03), whereas the presence of allele C in the dominant model reduced the risk by 58% (OR 0.42, 95% CI 0.18-0.90; *P*=.03). Moreover, rs2238136 was identified as a risk factor for AD in the codominant, dominant, and overdominant models (*P*=.02, .02, and .02, respectively). These data indicate that in the overdominant and codominant models, the risk of AD increases 2.94- and 3.09-fold, respectively, in patients with the rs2238136-C/T genotype. In the dominant model, the presence of one T allele increased the risk of AD 2.7-fold (OR 2.70, 95% CI 1.24-6.15; *P*=.02).

The association between the *VDR* and *CYP24A1* genotypes and the severity of AD and other atopic diseases is shown in Table 3. We observed no significant association between any of the SNPs analyzed and the severity of AD (SCORAD index) or other atopic diseases, such as asthma or rhinitis.

The association between AD and specific combinations of alleles and haplotypes in selected SNPs is shown in Table 4. rs2238136, rs2239185, and rs1540339 were selected owing to their presence in intronic regions of *VDR* that encode transcription factors. rs2239182, rs2107301, and 2239179 are located in the same intronic region (between exons 4 and 5) and were therefore selected given the possibility that these SNPs are in linkage equilibrium. Finally, haplotypes corresponding to combinations of SNPs in *CYP24A1* were also analyzed (Table 4). Significant associations were observed only for the GCC haplotype (rs2239185-G, rs1540339-C, and rs2238136-C), which appeared to exert a protective effect, reducing the risk of AD by 49% (OR 0.511, 95% CI 0.232-0.939; *P*=.04).

The associations between SNP genotypes and serum levels of calcium phosphorus and vitamin D (Table 5) and lipid profile (Table 6) were also analyzed, considering cases and controls as a single cohort. The data showed that 25(OH)D concentrations were higher in individuals with the rs2239182-CC versus the rs2239182-TT genotype (28.10 ± 8.80 vs 24.80 ± 8.70 ng/mL; *P*=.03), whereas vitamin D levels were lower in individuals with the rs2238136-TT genotype than the rs2238136-CT or rs2238136-CC genotype (21.82, 27.06, and 29.04 ng/mL, respectively; *P*=.046; Table 5).

rs2239185-GA and rs2248359-TT were present in a large proportion of patients with serum 25 OH vitamin D deficiency (42.31% and 56.52%, respectively) compared with alternative genotypes. The presence of a T allele in rs2239179 was associated with lower levels of phosphorus compared with the CC haplotype (5.11 vs 6.75 mg/dL; *P*=.04) (Table 5).

rs2239185-AA, rs2239182-CC, and rs1540339-CC were associated with higher total cholesterol concentrations; rs2239182-TT was associated with lower LDL cholesterol; and rs2239182-TC with lower HDL cholesterol. Both *CYP24A1* SNPs (rs2296241-AA and rs2248359-TT) were associated with higher HDL cholesterol levels (Table 6).

Table 1. Clinical characteristics of the study population (N=246).

Characteristics	AD[a] cases	Controls
Group size, n	143	103
Age (years), mean (SD)[b]	5.43 (3.98)	8.93 (5.81)
Sex (male/female)[c], n	73/70	57/46
Severity (SCORAD[d] index), n (%)		
Mild[e]	69 (48.3)	—[f]
Moderate[g]	61 (42.7)	—
Severe[h]	13 (9)	—
Asthma, n (%)	44 (34.6)	—
Rhinitis, n (%)	28 (22)	—
Asthma+rhinitis, n (%)	21 (16.5)	—

[a]AD: atopic dermatitis.
[b]*P*<.05.
[c]*P*=.50.
[d]SCORAD: Scoring Atopic Dermatitis.
[e]Mild: <15.
[f]Not available.
[g]Moderate: 15-40.
[h]Severe: >40.

Table 2. Association between the VDR and CYP24A1 polymorphisms and atopic dermatitis.

SNP[a]/model	Overall, n (%)	Control, n (%)	Atopic dermatitis, n (%)	OR[b] (95% CI)	*P* value[c]	*P* value[d]
rs731236						
Codominant	191	77	114			N/A[e]
A/A	81 (42.4)	37 (48)	44 (38.6)	N/A	N/A	.35
G/A	75 (39.3)	25 (33)	50 (43.9)	1.64 (0.82-3.34)	.17	N/A
G/G	35 (18.3)	15 (20)	20 (17.5)	1.09 (0.47-2.64)	.84	N/A
Dominant	191	77	114			N/A
A/A	81 (42.4)	37 (48)	44 (38.6)	N/A	N/A	.33
G/A-G/G	110 (57.6)	40 (52)	70 (61.4)	1.44 (0.76-2.71)	.26	N/A
Recessive	191	77	114			N/A
A/A-G/A	156 (81.7)	62 (81)	94 (82.5)	N/A	N/A	.89
G/G	35 (18.3)	15(19)	20 (17.5)	0.87 (0.39-1.98)	.73	N/A
Overdominant	191	77	114			N/A
A/A-G/G	116 (60.7)	52 (68)	64 (56.1)	N/A	N/A	.21
G/A	75 (39.3)	25 (32)	50 (43.9)	1.59 (0.84-3.10)	.16	N/A
Additive	0.77 (0.74)	0.72 (0.78)	0.79 (0.72)	1.13 (0.74-1.73)	.56	.57
rs1544410						
Codominant	188	71	117			N/A
C/C	67 (35.6)	27 (38)	40 (34.2)	N/A	N/A	.77
C/T	83 (44.2)	29 (41)	54 (46.2)	1.25 (0.64-2.45)	.51	N/A
T/T	38 (20.2)	15 (21)	23 (19.7)	1.03 (0.46-2.37)	.94	N/A
Dominant	188	71	117			N/A
C/C	67 (35.6)	27 (38)	40 (34.2)	N/A	N/A	.71
C/T-T/T	121 (64.4)	44 (62)	77 (65.8)	1.18 (0.64-2.18)	.60	N/A
Recessive	188	71	117			N/A
C/C-C/T	150 (79.8)	56 (79)	94 (80.3)	N/A	N/A	.96
T/T	38 (20.2)	15 (21)	23 (19.7)	0.91 (0.44-1.93)	.81	N/A
Overdominant	188	71	117			N/A
C/C-T/T	105 (55.9)	42 (59)	63 (53.9)	N/A	N/A	.58
C/T	83 (44.2)	29 (41)	54 (46.2)	1.24 (0.68-2.27)	.48	N/A
Additive	0.85 (0.73)	0.83 (0.76)	0.85 (0.72)	1.05 (0.70-1.57)	.83	.83
rs2239185						
Codominant	202	89	113			N/A
A/A	65 (32.2)	29 (32)	36 (31.9)	N/A	N/A	.52
G/A	77 (38.1)	30 (34)	47 (41.6)	1.24 (0.57-2.68)	.59	N/A
G/G	60 (29.7)	30 (34)	30 (26.6)	0.79 (0.36-1.77)	.57	N/A
Dominant	202	89	113			N/A
A/A	65 (32.2)	29 (33)	36 (31.9)	N/A	N/A	>.99
G/A-G/G	137 (67.8)	60 (67)	77 (68.1)	1.02 (0.51-1.99)	.96	N/A
Recessive	202	89	113			N/A
A/A-G/A	142 (70.3)	59 (66)	83 (73.5)	N/A	N/A	.41
G/G	60 (29.7)	30 (34)	30 (26.6)	0.71 (0.36-1.41)	.32	N/A

SNP[a]/model	Overall, n (%)	Control, n (%)	Atopic dermatitis, n (%)	OR[b] (95% CI)	*P* value[c]	*P* value[d]
Overdominant	202	89	113			N/A
A/A-G/G	125 (61.9)	59 (66)	66 (58.4)	N/A	N/A	.41
G/A	77 (38.1)	30 (34)	47 (41.6)	1.38 (0.72-2.71)	.33	N/A
Additive	0.97 (0.78)	1.02 (0.82)	0.95 (0.77)	0.89 (0.60-1.33)	.58	.59
rs2239182						
Codominant	205	85	120			N/A
T/T	69 (33.7)	24 (28)	45 (37.5)	N/A	N/A	.04[e]
T/C	90 (43.9)	38 (45)	52 (43.3)	0.47 (0.20-1.08)	.08	N/A
C/C	46 (22.4)	23 (27)	23 (19.2)	0.34 (0.13-0.87)	.03[e]	N/A
Dominant	205	85	120			N/A
T/T	69 (33.7)	24 (28)	49 (40.8)	N/A	N/A	.046[e]
T/C-C/C	136 (66.3)	61 (72)	71 (59.2)	0.42 (0.18-0.90)	.03[e]	N/A
Recessive	205	85	120			N/A
T/T-T/C	159 (77.6)	62 (73)	97 (80.8)	N/A	N/A	.24
C/C	46 (22.4)	23 (27)	23 (19.2)	0.64 (0.33-1.25)	.19	N/A
Overdominant	205	85	120			N/A
T/T-C/C	115 (56.1)	47 (55)	68 (56.7)	N/A	N/A	.96
T/C	90 (43.9)	38 (45)	52 (43.3)	0.95 (0.54-1.66)	.85	N/A
Additive	0.89 (0.74)	0.99 (0.75)	0.82 (0.73)	0.73 (0.50-1.07)	.10	.11
rs1540339						
Codominant	198	82	116			N/A
C/C	76 (38.4)	32 (40)	44 (37.9)	N/A	N/A	.82
T/C	82 (41.4)	35 (43)	47 (40.5)	0.99 (0.51-1.95)	.99	N/A
T/T	40 (20.2)	15 (18)	25 (21.6)	1.27 (0.55-3.03)	.58	N/A
Dominant	198	82	116			N/A
C/C	76 (38.4)	32 (39)	44 (37.9)	N/A	N/A	.94
T/C-T/T	122 (61.6)	50 (61)	72 (62.1)	1.08 (0.58-1.99)	.81	N/A
Recessive	198	82	116			N/A
C/C-T/C	158 (79.8)	67 (82)	91 (78.5)	N/A	N/A	.66
T/T	40 (20.2)	15 (18)	25 (21.6)	1.27 (0.60-2.83)	.54	N/A
Overdominant	198	82	116			N/A
C/C-T/T	116 (58.6)	47 (57)	69 (59.5)	N/A	N/A	.90
T/C	82 (41.4)	35 (43)	47 (40.5)	0.92 (0.50-1.69)	.78	N/A
Additive	0.82 (0.75)	0.78 (0.73)	0.84 (0.76)	1.11 (0.74-1.66)	.62	.62
rs2239179						
Codominant	193	80	113			N/A
T/T	84 (43.5)	36 (45)	48 (42.5)	N/A	N/A	.43
T/C	86 (44.6)	32 (40)	54 (47.8)	1.27 (0.64-2.53)	.50	N/A
C/C	23 (11.9)	12 (15)	11 (9.7)	0.66 (0.24-1.87)	.43	N/A
Dominant	193	80	113			N/A
T/T	84 (43.5)	36 (45)	48 (42.5)	N/A	N/A	.90
T/C-C/C	109 (56.5)	44 (55)	65 (57.5)	1.10 (0.58-2.09)	.77	N/A

SNP[a]/model	Overall, n (%)	Control, n (%)	Atopic dermatitis, n (%)	OR[b] (95% CI)	*P* value[c]	*P* value[d]
Recessive	193	80	113			N/A
T/T-T/C	170 (88.1)	68 (85)	102 (90.3)	N/A	N/A	.39
C/C	23 (11.9)	12 (15)	11 (9.7)	0.59 (0.23-1.57)	.28	N/A
Overdominant	193	80	113			N/A
T/T-C/C	107 (55.4)	48 (60)	59 (52.2)	N/A	N/A	.40
T/C	86 (44.6)	32 (40)	54 (47.8)	1.39 (0.73-2.67)	.32	N/A
Additive	0.68 (0.67)	0.71 (0.73)	0.67 (0.65)	0.93 (0.58-1.48)	.75	.76
rs3782905						
Codominant	206	87	119			.62
C/C	113 (54.9)	47 (54)	66 (55.5)	N/A	N/A	N/A
C/G	74 (35.9)	30 (34)	44 (37)	1.04 (0.57-1.91)	.89	N/A
G/G	19 (9.2)	10 (11)	9 (7.6)	0.64 (0.24-1.74)	.38	N/A
Dominant	206	87	119			.95
C/C	113 (54.9)	47 (54)	66 (55.5)	N/A	N/A	N/A
C/G-G/G	93 (45.2)	40 (46)	53 (44.5)	0.94 (0.54-1.65)	.84	N/A
Recessive	206	87	119			.47
C/C-C/G	187 (90.8)	77 (89)	110 (92.4)	N/A	N/A	N/A
G/G	19 (9.2)	10 (11)	9 (7.6)	0.63 (0.24-1.66)	.35	N/A
Overdominant	206	87	119			.83
C/C-G/G	132 (64.1)	57 (66)	75 (63)	N/A	N/A	N/A
C/G	74 (35.9)	30 (34)	44 (37)	1.11 (0.62-2.00)	.72	N/A
Additive	0.54 (0.66)	0.57 (0.69)	0.52 (0.64)	0.88 (0.58-1.34)	.56	.57
rs2238136						
Codominant	178	74	104			N/A
C/C	95 (53.4)	50 (68)	45 (43.3)	N/A	N/A	.02[e]
C/T	69 (38.8)	18 (24)	51 (49)	3.09 (1.34-7.73)	.008[e]	N/A
T/T	14 (7.9)	6 (8)	8 (7.7)	1.44 (0.37-7.41)	.62	N/A
Dominant	178	74	104			N/A
C/C	95 (53.4)	50 (68)	45 (43.3)	N/A	N/A	.02[e]
C/T-T/T	83 (46.6)	24 (32)	59 (56.7)	2.70 (1.24-6.15)	.01[e]	N/A
Recessive	178	74	104			N/A
C/C-C/T	164 (92.1)	68 (92)	96 (92.3)	N/A	N/A	>.99
T/T	14 (7.9)	6 (8)	8 (7.7)	0.92 (0.24-4.62)	.91	N/A
Overdominant	178	74	104			N/A
C/C-T/T	109 (61.2)	56 (76)	53 (51)	N/A	N/A	.02[e]
C/T	69 (38.8)	18 (24)	51 (49)	2.94 (1.30-7.24)	.009[e]	N/A
Additive	0.58 (0.63)	0.41 (0.64)	0.64 (0.62)	1.92 (1.00-3.71)	.05	.06
rs2296241						
Codominant	192	100	92			N/A
A/A	66 (34.4)	39 (39)	27 (29)	N/A	N/A	.63
G/A	87 (45.3)	44 (44)	43 (47)	1.39 (0.50-3.88)	.53	N/A

SNP[a]/model	Overall, n (%)	Control, n (%)	Atopic dermatitis, n (%)	OR[b] (95% CI)	*P* value[c]	*P* value[d]
G/G	39 (20.3)	17 (17)	22 (24)	1.75 (0.51-6.33)	.38	N/A
Dominant	192	100	92			N/A
A/A	66 (34.4)	39 (39)	27 (29)	N/A	N/A	.53
G/A-G/G	126 (65.6)	61 (61)	65 (71)	1.50 (0.59-3.90)	.40	N/A
Recessive	192	100	92			N/A
A/A-G/A	153 (79.7)	83 (83)	70 (76)	N/A	N/A	.67
G/G	39 (20.3)	17 (17)	22 (24)	1.46 (0.49-4.57)	.50	N/A
Overdominant	192	100	92			N/A
A/A-G/G	105 (54.7)	56 (56)	49 (53)	N/A	N/A	.98
G/A	87 (45.3)	44 (44)	43 (47)	1.12 (0.46-2.73)	.81	N/A
Additive	0.88 (0.74)	0.79 (0.73)	0.95 (0.74)	1.34 (0.73-2.46)	.34	.35
rs2248359						
Codominant	193	96	97			.89
C/C	68 (35.2)	33 (34)	35 (36)	N/A	N/A	N/A
C/T	76 (39.4)	36 (38)	40 (41)	1.05 (0.34-3.17)	.92	N/A
T/T	49 (25.4)	27 (28)	22 (23)	0.79 (0.23-2.73)	.71	N/A
Dominant	193	96	97			>.99
C/C	68 (35.2)	33 (34)	35 (36)	N/A	N/A	N/A
C/T-T/T	125 (64.8)	63 (66)	62 (64)	0.94 (0.34-2.53)	.90	N/A
Recessive	193	96	97			.83
C/C-C/T	144 (74.6)	69 (72)	75 (77)	N/A	N/A	N/A
T/T	49 (25.4)	27 (28)	22 (23)	0.77 (0.26-2.31)	.64	N/A
Overdominant	193	96	97			.95
C/C-T/T	117 (60.6)	60 (63)	57 (59)	N/A	N/A	N/A
C/T	76 (39.4)	36 (38)	40 (41)	1.16 (0.44-3.08)	.77	N/A
Additive	0.90 (0.78)	0.94 (0.80)	0.87 (0.77)	0.90 (0.49-1.64)	.72	.73

[a]SNP: single-nucleotide polymorphism.

[b]OR: odds ratio.

[c]*P* value (comparison with the null model).

[d]*P* value for the null model.

[e]Statistically significant (*P*<.05).

Table 3. Association between the VDR and CYP24A1 polymorphisms and the severity of atopic dermatitis, asthma, rhinitis, and asthma+rhinitis.[a]

SNP[b]	Atopic dermatitis severity	Asthma	Rhinitis	Asthma+rhinitis
rs731236	.84	.36	.23	.12
rs1544410	.56	.79	.21	.10
rs2239185	.32	.21	.17	.12
rs2239182	.44	.30	.18	.15
rs1540339	.86	.43	.12	.14
rs2239179	.42	.80	.21	.35
rs3782905	.10	.29	.71	.22
rs2238136	.82	.52	.25	.55
rs2296241	.54	.66	.90	.78
rs2248359	.97	.69	.21	.32

[a]*P* value is shown for each group. Atopic dermatitis severity is based on Scoring Atopic Dermatitis (SCORAD). This table only corresponds to the codominant model for each SNP, regardless of whether this model is the best fit for the distribution.

[b]SNP: single-nucleotide polymorphism.

Table 4. Haplotypes for combination of selected polymorphisms.

SNP[a] 1	SNP 2	SNP 3	F[b]	OR[c] (95% CI)	*P* value
rs2239185	rs1540339	rs2238136	N/A[d]	N/A	N/A
A	C	C	0.262	1	N/A
A	C	T	0.090	0.830 (0.270-2.546)	.74
A	T	C	0.091	0.474 (0.175-1.279)	.14
A	T	T	0.072	2.882 (0.634-13.097)	.17
G	C	C	0.208	0.511 (0.232-0.939)	.04[e]
G	C	T	0.032	0.686 (0.240-2.409)	.57
G	T	C	0.166	0.933 (0.441-1.974)	.86
G	T	T	0.079	1.252 (0.411-3.812)	.69
rs2239182	rs2107301	rs2239179	N/A	N/A	N/A
C	G	C	0.347	1	N/A
C	A	C	0.010	80.403 (80.285-80.521)	<.001
C	G	T	0.087	0.752 (0.323-1.754)	.51
T	A	T	0.284	1.555 (0.726-3.334)	.26
T	G	T	0.267	1.053 (0.539-2.059)	.88
rs2248359	rs2296241	N/A	N/A	N/A	N/A
T	A	N/A	0.398	1	N/A
C	A	N/A	0.138	1.620 (0.552-4.751)	.38
C	G	N/A	0.398	1.108 (0.546-2.247)	.78
T	G	N/A	0.065	0.904 (0.189-4.323)	.90

[a]SNP: single-nucleotide polymorphism.

[b]F: haplotype frequency.

[c]OR: odds ratio.

[d]N/A: not applicable.

[e]Statistically significant (*P*<.05).

Table 5. Association between the VDR and CYP24A1 polymorphisms and selected calcium phosphorus metabolism and vitamin D–related analytes.

SNP[a]/genotype	25(OH)D (ng/mL), mean (SD)	*P* value	25(OH)D >30 ng/mL (%)	25(OH)D 20-29 ng/mL (%)	25(OH)D <20 ng/mL (%)	*P* value	Calcium (mg/dL), mean (SD)	*P* value	Phosphorus (mg/dL), mean (SD)	*P* value	PTH[b] (pg/mL), mean (SD)	*P* value
rs731236												
G/G	28.35 (12.28)	N/A[c]	28.57	33.33	38.10	.44	9.79 (0.59)	N/A	5.34 (1.24)	N/A	28.67 (16.17)	N/A
G/A	27.81 (11.20)	.86	24.07	35.19	40.74	N/A	9.84 (0.50)	.69	5.01 (0.65)	.69	24.38 (14.34)	.30
A/A	28.05 (12.82)	.92	18.18	52.27	29.55	N/A	9.78 (0.57)	.99	5.97 (5.10)	.39	29.55 (17.15)	.82
rs1544410												
T/T	29.51 (11.10)	N/A	16.67	41.67	41.67	.23	9.83 (0.55)	N/A	4.98 (0.84)	N/A	29.06 (16.98)	N/A
C/C	29.35 (13.74)	.96	14.63	51.22	34.15	N/A	9.89 (0.55)	.65	5.42 (1.18)	.59	28.06 (15.62)	.82
C/T	26.42 (10.55)	.28	31.03	32.76	36.21	N/A	9.71 (0.54)	.33	5.68 (4.80)	.37	27.43 (16.37)	.69
rs2239185												
G/G	29.60 (14.91)	N/A	20.00	46.67	33.33	.049[d]	9.75 (0.58)	N/A	4.89 (0.86)	N/A	27.14 (16.42)	N/A
A/A	27.45 (9.15)	.47	13.89	55.56	30.56	N/A	9.78 (0.55)	.83	5.85 (5.03)	.26	26.94 (14.88)	.96
G/A	27.49 (11.93)	.44	30.77	26.92	42.31	N/A	9.84 (0.56)	.53	5.35 (1.11)	.60	29.52 (17.75)	.59
rs2239182												
C/C	28.10 (8.80)	N/A	20.83	37.50	41.67	.48	9.84 (0.49)	N/A	5.18 (0.47)	N/A	28.57 (14.76)	N/A
T/T	24.80 (8.70)	.03[d]	25.00	47.73	27.27	N/A	9.69 (0.57)	.37	4.93 (0.71)	.82	29.03 (17.86)	.94
T/C	30.00 (13.50)	.26	20.69	34.48	44.83	N/A	9.85 (0.52)	.98	5.77 (4.35)	.58	27.33 (15.20)	.83
rs1540339												
T/T	25.61 (10.01)	N/A	24.00	44.00	32.00	.80	9.90 (0.50)	N/A	5.06 (0.74)	N/A	25.53 (12.72)	N/A
C/C	28.90 (13.65)	.27	25.53	34.04	40.43	N/A	9.87 (0.54)	.86	6.11 (5.19)	.31	27.42 (14.51)	.73
T/C	28.27 (10.91)	.36	20.00	46.00	34.00	N/A	9.70 (0.56)	.21	5.09 (0.72)	.98	28.49 (18.11)	.58
rs2239179												
C/C	27.35 (7.60)	N/A	18.18	45.45	36.36	.45	9.89 (0.64)	N/A	6.75 (7.12)	N/A	28.30 (15.29)	N/A
T/T	26.99 (9.89)	.93	18.75	50.00	31.25	N/A	9.73 (0.54)	.22	5.11 (0.75)	.04[d]	26.86 (17.90)	.73
T/C	28.97 (14.05)	.68	27.12	32.20	40.68	N/A	9.80 (0.51)	.46	5.11 (0.75)	.03[d]	28.92 (15.17)	.88
rs3782905												
C/C	29.90 (9.88)	N/A	22.22	33.33	44.44	.21	9.86 (0.45)	N/A	5.00 (0.67)	N/A	26.03 (13.97)	N/A
C/G	26.92 (12.59)	.51	32.61	32.61	34.78	N/A	9.82 (0.57)	.72	6.10 (5.51)	.15	27.50 (15.48)	.73

SNP[a]/genotype	25(OH)D (ng/mL), mean (SD)	*P* value	25(OH)D >30 ng/mL (%)	25(OH)D 20-29 ng/mL (%)	25(OH)D <20 ng/mL (%)	*P* value	Calcium (mg/dL), mean (SD)	*P* value	Phosphorus (mg/dL), mean (SD)	*P* value	PTH[b] (pg/mL), mean (SD)	*P* value
C/C	29.70 (12.21)	.96	14.29	45.71	40.00	N/A	9.74 (0.56)	.30	5.11 (0.82)	.88	29.57 (17.44)	.38
rs2238136												
T/T	21.82 (11.46)	N/A	50.00	37.50	12.50	.14	9.81 (0.66)	N/A	5.79 (1.74)	N/A	28.96 (15.27)	N/A
C/T	27.06 (9.85)	.18	20.75	47.17	32.08	N/A	9.90 (0.55)	.65	5.22 (0.91)	.10	29.06 (14.94)	.99
C/C	29.04 (10.26)	.046[d]	19.15	34.04	46.81	N/A	9.73 (0.53)	.69	5.25 (0.71)	.12	24.21 (13.41)	.39
rs2296241												
G/G	28.85 (13.97)	N/A	18.18	54.55	27.27	.10	9.33 (0.84)	N/A	8.94 (12.02)	N/A	38.05 (10.43)	N/A
A/A	31.54 (8.26)	.58	14.29	14.29	71.43	N/A	9.59 (0.44)	.22	4.86 (0.48)	.05	32.42 (15.21)	.36
G/A	26.62 (12.75)	.62	25.00	45.00	30.00	N/A	9.71 (0.51)	.07	5.03 (0.76)	.06	30.71 (17.67)	.24
rs2248359												
T/T	27.82 (11.60)	N/A	43.48	0.00	56.52	.007[d]	9.72 (0.48)	N/A	5.02 (0.78)	N/A	36.43 (16.64)	N/A
C/C	29.24 (17.95)	.81	18.07	48.19	33.73	N/A	9.30 (0.80)	.06	7.82 (10.17)	.18	33.88 (10.92)	.71
C/T	29.30 (10.96)	.80	11.76	52.94	35.29	N/A	9.63 (0.44)	.67	4.78 (0.66)	.90	30.27 (17.24)	.31

[a]SNP: single-nucleotide polymorphism.

[b]PTH: parathyroid hormone.

[c]N/A: not applicable.

[d]Statistically significant (*P*<.05).

Table 6. Association between the VDR and CYP24A1 polymorphisms and selected lipid analytes.

SNP[a]/genotype	Cholesterol (mg/dL), mean (SD)	*P* value	LDL[b]-cholesterol (mg/dL), mean (SD)	*P* value	HDL[c]-cholesterol (mg/dL), mean (SD)	*P* value	Triglycerides (mg/dL), mean (SD)	*P* value
rs731236								
G/G	171.22 (29.50)	N/A[d]	108.60 (28.86)	N/A	52.42 (12.14)	N/A	83.22 (41.04)	N/A
G/A	168.54 (31.48)	.69	106.74 (29.41)	.81	52.77 (12.89)	.91	79.59 (55.10)	.76
A/A	162.17 (25.26)	.18	99.57 (27.37)	.26	52.54 (9.73)	.97	74.21 (50.49)	.45
rs1544410								
T/T	170.26 (24.58)	N/A	104.50 (24.24)	N/A	53.70 (12.76)	N/A	79.71 (40.48)	N/A
C/C	163.48 (25.51)	.29	100.02 (27.26)	.54	53.70 (10.50)	>.99	74.52 (48.66)	.64
C/T	166.60 (32.16)	.56	107.30 (29.96)	.70	51.71 (11.61)	.50	78.55 (54.30)	.92
rs2239185								
G/G	160.71 (23.63)	N/A	98.69 (22.29)	N/A	53.75 (9.55)	N/A	78.08 (54.82)	N/A
A/A	176.78 (33.68)	.04[e]	112.98 (33.50)	.06	53.69 (12.16)	.98	74.44 (37.65)	.75
G/A	166.04 (27.54)	.37	101.06 (26.51)	.74	51.41 (12.23)	.43	82.05 (57.35)	.71
rs2239182								
C/C	175.97 (26.76)	N/A	113.83 (28.55)	N/A	57.68 (11.79)	N/A	69.92 (29.82)	N/A
T/T	156.37 (26.51)	.009[e]	98.22 (25.90)	.02[e]	52.73 (12.45)	.08	80.45 (55.17)	.31
T/C	166.30 (28.78)	.09	104.27 (26.77)	.15	51.63 (9.59)	.03[e]	77.18 (48.93)	.46
rs1540339								
T/T	158.26 (22.55)	N/A	96.33 (20.72)	N/A	52.09 (13.04)	N/A	89.63 (59.93)	N/A
C/C	171.58 (30.87)	.04[e]	108.44 (31.12)	.10	53.12 (11.77)	.73	73.63 (46.83)	.16
T/C	164.70 (28.06)	.30	103.48 (27.68)	.33	53.02 (10.43)	.76	74.66 (46.86)	.18
rs2239179								
C/C	177.07 (23.27)	N/A	109.16 (25.11)	N/A	57.18 (15.64)	N/A	82.67 (37.52)	N/A
T/T	162.59 (27.57)	.08	100.68 (26.66)	.37	51.48 (11.98)	.14	80.10 (52.39)	.86
T/C	168.03 (30.59)	.27	107.50 (30.38)	.86	52.63 (9.67)	.24	76.58 (52.48)	.68
rs3782905								
G/G	168.27 (23.06)	N/A	104.48 (21.22)	N/A	53.67 (14.65)	N/A	75.33 (32.11)	N/A
C/G	169.19 (26.91)	.91	104.96 (22.69)	.96	54.82 (10.33)	.76	73.74 (42.84)	.90
C/C	164.15 (29.37)	.60	103.07 (30.00)	.87	52.58 (11.15)	.76	76.35 (46.56)	.93
rs2238136								
T/T	168.33 (40.99)	N/A	109.70 (46.48)	N/A	52.00 (18.19)	N/A	100.22 (44.92)	N/A
C/T	165.28 (26.98)	.78	104.77 (25.96)	.70	51.74 (11.82)	.96	76.46 (55.76)	.22
C/C	166.97 (31.15)	.90	104.33 (30.19)	.68	52.65 (11.19)	.90	79.71 (51.44)	.28
rs2296241								
G/G	160.08 (27.36)	N/A	104.75 (31.55)	N/A	48.00 (11.75)	N/A	88.50 (46.87)	N/A
A/A	163.56 (27.81)	.70	102.58 (19.48)	.86	61.50 (8.83)	.048[e]	88.00 (49.27)	.98
G/A	162.31 (18.36)	.79	95.11 (12.89)	.46	52.57 (12.59)	.51	103.96 (64.99)	.45
rs2248359								
T/T	163.82 (28.39)	N/A	110.87 (24.42)	N/A	70.33 (6.66)	N/A	101.45 (55.99)	N/A
C/C	159.50 (23.03)	.63	98.12 (21.07)	.39	52.25 (9.74)	.02[e]	82.75 (46.58)	.38
C/T	162.06 (20.49)	.85	94.52 (19.82)	.31	46.40 (10.71)	.005[e]	114.82 (65.83)	.54

[a]SNP: single nucleotide polymorphism.
[b]LDL: low-density lipoprotein.
[c]HDL: high-density lipoprotein.
[d]N/A: not applicable.
[e]Statistically significant (P<.05).

Discussion

Previous studies have reported associations between the development of AD and certain SNPs such as *FokI* (rs2228570), *BsmI* (rs1544410), *ApaI* (rs7975232), and *TaqI* (rs731236) [11-15]. Contradicting some of those findings, a recent meta-analysis found that only rs1544410 and rs731236 were associated with the development of AD and asthma [17]. In this study, we found an association between AD and a total of 12 selected SNPs (10 in *VDR* and 2 in *CYP24A1*). Although a previous study analyzed 13 SNPs in *VDR*, only the association with asthma was investigated [28]. Therefore, ours is one of the most extensive studies performed to date in terms of the number of SNPs analyzed in these 2 genes implicated in AD.

Although our findings do not support the association between AD and classic SNPs described in the literature (rs1544410 and rs731236), we observed a significant association between AD and the polymorphisms rs2238136 and rs2239182. Both SNPs correspond to intronic regions of *VDR*, and none have been previously described as risk factors for AD.

Given their impact on keratinocyte proliferation and differentiation in the epidermal layer, SNPs in genes involved in vitamin D metabolism may be important genetic risk factors for the development of AD [29]. Our data suggest that altered vitamin D metabolism due to the presence of genetic variants influences the pathogenesis of AD. In this way, we identified rs2239182 and the GCC haplotype (rs2239185-G, rs1540339-C, and rs2238136-C) as protective factors and rs2238136 as a risk factor.

rs2238136 is located in an intronic region between exons 1 and 2 of *VDR*. Although no clinical information regarding the functionality of the encoded protein is reported in the consulted databases (ClinVar, Ensembl, PubMed, and ClinGen), the location of this SNP in a transcription factor binding region (GATA1) suggests that it could regulate gene expression and alter protein function. SNP databases (ClinVar and Ensmbl) contain no information about the association between this SNP and AD. Therefore, this is the first study to provide evidence supporting an association between rs2238136 and AD.

rs2239182 is also located in an intronic region (between exons 5 and 6 of *VDR)*. It is mentioned in 18 studies cited in ClinVar and 22 in Ensmbl, but none report any association with AD. Because ours is the first study investigating this association, we cannot compare our findings with those of previously published studies.

According to the severity of AD, we were unable to establish any association with the analyzed SNPs. The paucity of studies investigating this association underlines the need for further research in this area.

The prevalence of overweight, obesity, and dyslipidemia is higher in children with AD [23]. Moreover, 25 OH vitamin D deficiency may contribute to the development of hypertension, diabetes, hypertriglyceridemia, and obesity [30-32]. For this reason, we investigated the influence of 25 OH vitamin D deficiency and of SNPs in genes implicated in vitamin D metabolism (*VDR* and *CYP24A1*) on lipid parameters. rs2239185-AA, rs2239182-CC, and rs1540339-CC were associated with higher serum concentrations of total cholesterol, rs2239182-TT with a higher LDL cholesterol levels, and rs2239182-TC with lower HDL cholesterol levels. In all cases, cholesterol levels in the AD group were within the normal range; the observed difference were therefore quantitative, but unlikely to affect the individual's health.

This study shows how the complicated genetic environment and interrelationships between different genetic factors influence the development of AD and of alterations in vitamin D metabolism or lipid profiles (Figure 1).

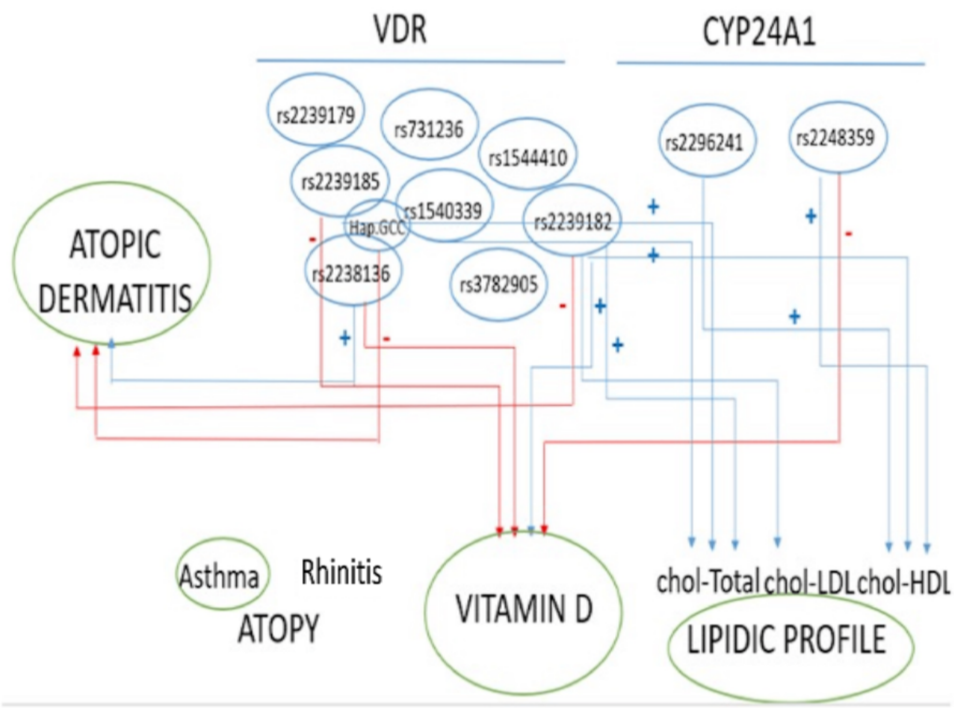
A global survey in 18 countries [33] revealed that AD affects around 20% of children, a substantial proportion of the pediatric population, although prevalence and severity varied across age groups and countries. Among the countries in Europe, Germany had the lowest prevalence (8.4%) and the Southern European countries of Spain and Italy had the highest prevalence (18.6% and 17.6%, respectively). A study led by Guttman-Yassky and Krueger [34] established, for the 6-7 years age group, an overall prevalence of 7.9%, and 6.2% in Spain. For the 13-14 years age group, the estimated prevalence was of around 15%. When stratified by sex, AD prevalence varied between male and female individuals, but no clear trend was observed. The estimation of prevalence by residential setting revealed that those living in rural areas had a lower prevalence of AD relative to urban or suburban settings.

It is well known that climate conditions have an influence in AD. Low temperatures and increased time spent indoors in warmth and low humidity increase the prevalence of AD. Increased ultraviolet radiation is inversely related to the prevalence of AD, as it exerts a protective effect because of its anti-inflammatory properties and increased production of vitamin D. The relief of Spain is characterized by being quite high, with an average altitude of 660 m above sea level. The varied orography of Spain, as well as its geographical location, in the middle latitudes of the temperate zone of the northern hemisphere means that the country has a remarkable climatic diversity. Thus, we pass from places with mild temperatures, around 15 °C, to others that exceed 40 °C in summer, and from places with a humid oceanic climate with annual rainfall of more than 2500 mm to places with a Mediterranean desert climate that do not exceed 200 mm per year. The thermal amplitude is greater in the interior of the Meseta, where it sometimes reaches 20 °C, whereas in places like the Canary

Islands, this amplitude is smaller, and between the warmest and the coldest month, there is barely a variation of 5 °C.

There are other social determinants that affect in some way AD. The prevalence of AD has been found to increase with increasing socioeconomic status. The higher the socioeconomic status of parents, the higher the allergic sensitization and atopy in their children, probably related to the lower reduction in allergen exposure due to living in a better sanitary environment. Moreover, exposure to factors such as air pollution, tobacco, stress, or alcohol has been associated with a higher prevalence of AD.

Figure 1. Summary of the main findings and associations between VDR and CYP24A1 polymorphisms and the variables analyzed. VDR: vitamin D receptor.



25 OH vitamin D deficiency is a major health problem worldwide, especially in industrialized countries. As it is a problem that affects the general population, being not limited to atopic patients, public authorities have begun to promote safe sun exposure habits to maintain adequate 25 OH vitamin D serum concentrations. Our study evaluates, for the first time, the relationship between the *VDR* and *CYP24A1* polymorphisms and parameters related to phosphocalcic and vitamin D metabolism. Our findings shed light on the importance of genetic background, and not just exogenous VD intake, on the physiopathology of diseases in which this vitamin is implicated.

Some limitations of our study should be noted. First is the sample size. In addition, the patient and control cohorts were not exactly matched for age, weight, or height. This discrepancy could influence biochemical parameters. However, the reference values used in this study were equivalent across the age ranges of the population studied. Second, participants were recruited in the Departments of Dermatology and Paediatric Allergy of the San Jorge Hospital (Huesca, Spain), primary care centers in Huesca city, and the Dermatology Department of the Niño Jesús Hospital (Madrid, Spain). For this reason, the sample is not very representative of the whole country; ideally, more areas of Spain would have been covered during patient recruitment. According to the selection of patients, it must be noted that the high prevalence of AD complicates the process, as patients classified as healthy controls could feasibly become atopic over time. In addition, the generalizability of the findings is in some way compromised, because the study population included only Spanish individuals, and the genetic associations could be influenced by ethnicity. Finally, AD is a very heterogeneous disease in which the interplay between genomic changes associated with mutations in the key barrier and immune genes and a spectrum of environmental factors play a fundamental role in the pathogenesis. To make it more complex, recent studies indicate the importance of epigenetic alterations in the development of the disease. Epigenetic modifications are mainly mediated by DNA methylation, histone acetylation, and the action of specific micro-RNAs. It has been determined that the epigenome in patients with AD differs from the one observed in healthy individuals. This applies especially to the genes regulating immune responses and inflammatory processes, genes of the innate immunity, and those encoding the structural proteins of the epidermis [35].

In conclusion, these findings show how a complex genetic backdrop and interrelationships between different genetic factors influence alterations in vitamin D metabolism and lipid profiles and may contribute to the development of AD. We identified the SNP rs2238136 in *VDR* as a risk factor for AD and show that other SNPs in *VDR* and *CYP24A1* may lead to alterations in biochemical parameters and influence the risk of AD.

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Authors' Contributions

RG-T, AH-M, and YG-C drafted and critically reviewed the manuscript with literature research. ES-R, SI-A, and JP-F contributed to data collection and literature search. NGR helped to draft the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Genotype distributions of VDR and CY24A1 single nucleotide polymorphisms in the control and atopic dermatitis groups. Comparison with frequencies in populations in the 1000 Genomes Project.
[DOCX File , 21 KB - derma_v6i1e39567_app1.docx]

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Abbreviations

AD: atopic dermatitis
HDL: high-density lipoprotein
LDL: low-density lipoprotein
OR: odds ratio
SCORAD: Scoring Atopic Dermatitis
SNP: single nucleotide polymorphism
VDR: vitamin D receptor gene

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Original Paper

A Digital Self-help Intervention for Atopic Dermatitis: Analysis of Secondary Outcomes From a Feasibility Study

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Abstract

Background: Atopic dermatitis (AD) is a common inflammatory skin disease characterized by dry skin, eczematous lesions, and an often severe pruritus. The disease may have a negative effect on quality of life and is also associated with symptoms of anxiety and depression. Few individuals with AD receive any form of behavioral intervention. Behavioral interventions for AD are potentially efficacious but need to be constructed so that they are safe, credible, and user-friendly. We have previously reported on a feasibility study that demonstrated that a self-management version of a digital intervention based on cognitive behavioral therapy (CBT) for AD can potentially be effective in reducing AD symptoms. The aim of this secondary report was to further examine treatment feasibility and preliminary effects on dermatological quality of life, itching sensations, depressive symptoms, and perceived stress.

Objective: This is a secondary report on intervention credibility, usability, adverse events, and preliminary effects on secondary measures of a self-management digital intervention for atopic dermatitis.

Methods: In total, 21 adults with AD, recruited nationwide in Sweden, were assessed by telephone, and used the digital intervention for 8 weeks. Participants were also assessed directly afterward and 3 months after the end of the intervention. There was no therapist guidance. Feasibility indicators included intervention credibility, usability, and possible adverse effects. Other measures included preliminary effects on dermatological quality of life, itching sensations, depressive symptoms, and perceived stress.

Results: The intervention was regarded as credible and no serious adverse events were reported. System usability was, however, found to be below the predetermined cutoff for acceptable usability. Preliminary effects at 3-month follow-up were in the moderate to large range for dermatological quality of life (Cohen d=0.89, 95% CI 0.18-1.56), itching sensations (Cohen d=0.85, 95% CI 0.15-1.52), depressive symptoms (Cohen d=0.78, 95% CI 0.1-1.45), and perceived stress (Cohen d=0.75, 95% CI 0.01-1.36).

Conclusions: This 8-week self-management digital CBT-based intervention was, together with telephone calls before and after, a feasible intervention for participants with AD. Preliminary effects were promising and should be explored further in a randomized controlled trial. Intervention usability was, however, rated below cutoff scores. Efforts should be made to improve written material to increase usability.

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KEYWORDS

atopic dermatitis; eczema; pruritus; cognitive behavioral therapy; CBT; dermatitis; skin; dermatology; self-management; self-guided; self-help; digital health; digital intervention; stress; depressive; depression; mental health

Introduction

Up to 10% of adults have the inflammatory skin disease—atopic dermatitis (AD) [1]. AD is characterized by dry skin, rash, and itch. Treatment is aimed at decreasing inflammation in the skin and preventing symptoms. Treatment consists mainly of emollients, but when the skin is inflamed, this must be complemented with anti-inflammatory treatments, such as topical corticosteroids or calcineurin inhibitors. In more severe cases, additional treatments with UV light, systemic immunomodulators, and biological treatments are needed [1]. Extradural symptoms, such as depression and anxiety disorders are common, and psychiatric comorbidity has been found to increase in correlation with more severe eczema [2]. One study on a UK sample found that 40% of people with AD had a depression- or anxiety-related diagnosis compared to 17% of people without AD [3]. Stress and negative emotions can lead to increased scratching and skin tearing behavior. Scratching, in turn, can lead to skin damage, thus increasing inflammation—a process described as the "vicious circle of itch" [4]. Furthermore, people with AD tend to avoid situations associated with itching or other skin-related symptoms. This can lead to avoidance of important activities and, further, a decreased quality of life [5].

Cognitive behavioral therapy (CBT) for AD has been tentatively evaluated, with a focus on coping, habit reversal, and stress management, with mixed or uncertain effects [6]. We have previously developed a CBT protocol where exposure is the main treatment component. Exposure is a gradual and controlled approach to emotionally charged experiences that tend to be avoided to prevent short-term discomfort and negative emotions [7]. People with AD tend to avoid situations that they would want to experience but might trigger symptoms [5]. The purpose of exposure is to go against the initial discomfort and do what one wants in one's life, despite the presence of symptoms or negative emotions. This exposure-based treatment was tested in a pilot study and a randomized controlled trial [8,9]. In the latter study, the treatment was delivered as a therapist-guided web-based intervention, and the results indicated moderate to large effects on eczematous symptoms and secondary measures [9]. Web-based CBT uses a similar approach to conventional CBT, usually with written feedback and guidance from a therapist [10]. However, there is a limited supply of clinical psychologists, especially those with the knowledge of AD, and to our knowledge, psychologists are not commonly found in dermatological care. An intervention without therapist support could have advantages in terms of accessibility and implementation [11]. For a self-management intervention to be as effective as its therapist-guided equivalent, it needs to be designed such that it compensates for the many potential functions of the therapist. A solid clinical process including monitoring as well as the access to well-written material and design that makes the intervention easy to use are all proposed methods to achieve this end [12]. Based on the comprehensive and therapist-guided intervention by Hedman-Lagerlöf et al [8], we developed a new self-management intervention where substantial revisions were made to adapt the treatment to a format not requiring therapist guidance [13]. The treatment material was substantially shortened, the interface streamlined, and automated messages were used to encourage participants to engage in the treatment. In a preliminary comparison, we described the differences between the 2 versions of digital CBT for AD and present some data supporting the new revised version being preliminary effective in reducing the severity of AD symptoms (69% of responders on 3-month follow-up), as well as having acceptable treatment satisfaction ratings and being associated with acceptable indicators of intervention adherence (65% of participants returned at least 5 out of 8 homework assignments) [13].

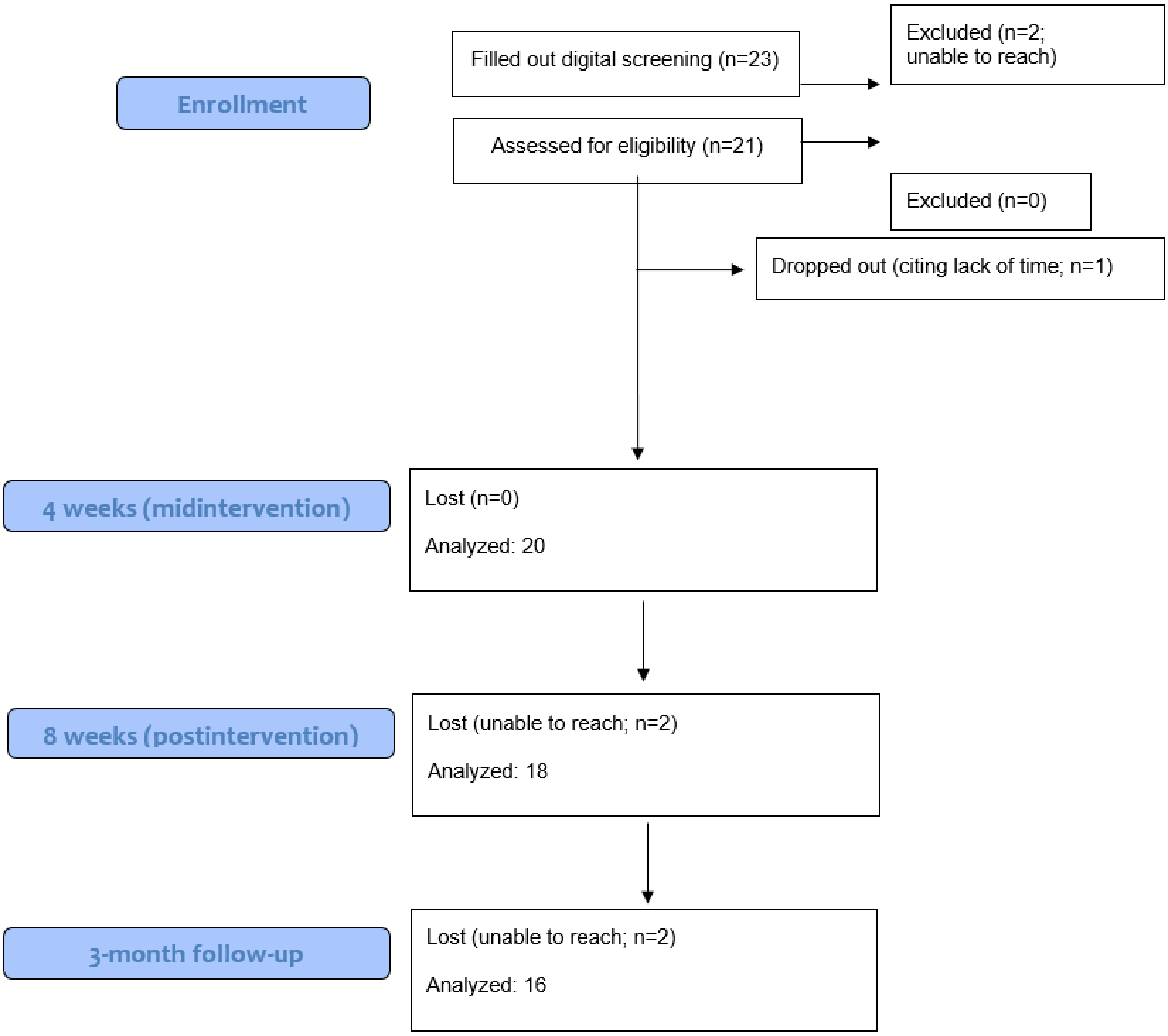
Our aim of this secondary report is to further examine the credibility, usability, and adverse events of the new self-management digital intervention for AD and present the preliminary effects on secondary measurements related to quality of life in AD and other related problems.

Methods

Recruitment

In line with earlier similar feasibility trials [14-16] that had included 12 participants or more, we aimed to recruit at least 16 participants, to compensate for potential attrition. Eventually, 21 participants (20 female; mean age 42.5, SD 16 years) were recruited nationwide through advertisements on social media, included in the study, and started on treatment. One person dropped out, 2 were lost to postmeasurement, and 2 more were lost to 3-month follow-up. Inclusion criteria were being aged 16 years or older with a self-reported AD diagnosis. Exclusion criteria were having a disease or condition with immediate treatment priority before AD. Potential participants were screened through telephone interviews. All individuals who were interviewed were subsequently included in the study. Participants were also called after the intervention period. The purpose of the second telephone call was not to collect data, but rather for the benefit of participants who had the opportunity to summarize their experience and ask questions to the study psychologists. Recruitment started March 15, 2021, and the last 3-month follow-up assessment was collected August 20, 2021. The study flowchart is shown in Figure 1.

Figure 1. Study flowchart based on the Consolidated Standards Of Reporting Trials 2010 flow diagram.



Intervention

The intervention was administered on a secure website designed to resemble a mobile app. Participants read education material and used CBT-based tools. The education material starts with a short introduction to AD, and then mainly consists of how psychological and behavioral factors interact with the disease, as well as instructions on how to perform treatment exercises. The intervention content was a shortened and optimized self-management version of the therapist-guided digital CBT for AD used in the earlier described randomized controlled trial [9]. The intervention content was optimized by study psychologist DK, with the help of psychologists MK and BL. LL, a dermatologist, and NL, a psychiatrist, served as consultants. The main components were mindfulness training and exposure, same as in the original intervention, which were presented as the “Mindfulness tool” and the “Exposure tool” in the treatment [13]. These tools helped participants carry out exercises in their everyday life. A central mindfulness exercise included neutrally observing bodily sensations, such as itchiness, in a highly focused state, without attempting to judge or change any experiences. Exposure exercises are highly individualized but focus on going against unhelpful avoidance behaviors, to help participants gain more flexible behaviors. Two examples could be voluntarily putting on a woolen sweater without scratching or going to a party despite having facial eczema. The participants could gain inspiration from fictive patient examples throughout the intervention. The intervention was especially focused on exposure to an itching sensation, with scratching prevention. After performing treatment exercises, participants evaluated them with help of the program tools. Administration of the intervention was handled by DK, which included assigning treatments in the digital platform and monitoring for any automatic notices or warnings in the system—the latter indicating that participants experienced difficulties. Please see the previously reported quality improvement study for a detailed comparison of the current self-management version of the intervention, compared to the original therapist-guided version [13].

Ethical Considerations

Study dermatologists LL and MB were consulted in the development of exercises, in order to ensure that they were safe and relevant. This study was approved by the Swedish Ethical Review Authority (2020-05702) on January 19, 2021.

Measures

Overview

In addition to the measures presented below, please see Kern et al [13] for participant adherence as measured by the number of finished homework assignments, outcomes on AD severity measured with the Patient-Oriented Eczema Measure (POEM) [17], and intervention satisfaction measured with the Client satisfaction questionnaire [18].

Feasibility Measures

Intervention credibility was measured at the 4-week midassessment with a 5-item version of the Credibility/Expectancy Questionnaire [19]. Therein, users are asked to rate their expectations with questions such as “How successful do you think this treatment will be in reducing your symptoms?” and “How confident would you be in recommending this treatment to a friend?” The scale consists of 11-point items (0-10), yielding a score of 0-50 points in total, with higher scores reflecting higher treatment credibility. A total score of ≥30 points, reflecting the average responses to be in the upper half of the credibility ratings, is considered to indicate adequate treatment credibility [19].

Usability was measured post assessment with the System Usability Scale [20]. Therein, users are asked to rate their experience by responding to items such as “I think I would like to use this system frequently” and “I found the system unnecessarily complex.” The scale consists of ten 5-point items relating to usability, with a score range from 0-100, with higher scores reflecting better system usability and a score of ≥70 points considered to indicate acceptable usefulness [21].

Participants were also asked about any adverse effects at the end of treatment, using a self-report questionnaire where participants were asked if they have had any adverse events since the start of treatment. If they, responded with “yes,” they were asked to describe that adverse event in free text. This questionnaire is not published.

Outcome Measures

The Dermatology Life Quality Index [22], which measures AD-specific quality of life, ranges from 0 to 30, with a higher score indicating a lower quality of life. The authors of the scale suggest the following cutoffs: 1=no impact on quality of life, 2-5=slight impact, 6-10=moderate impact, 11-20=very large impact, and 21-30=extremely large impact.

The Peak Pruritus Numerical Rating Scale [23] measures itching sensations in the last 24 hours and uses a scale from 0=no itch to 10=worst possible itch. In this study, we only measured perceived average itch, but the scale can also be used for the worst itch during the 24 hours.

The 9-item Patient Health Questionnaire [24], measures depressive symptoms with a range from 0-27. The authors suggest cutoffs at 5 (possible depression) and 15 (probable depression).

The Perceived Stress Scale [25] measures general experience of stress using 14 items, with a range of 0-40. The authors suggest cutoffs at 0-13 (low stress), 14-26 (moderate stress), and 27-40 (high perceived stress).

Participants were asked about subjective improvement, using the Subjective Assessment Questionnaire, with a range of 0-6, using corresponding statements ranging from “much declined” to “much improved.” This type of scale is often used for other somatic conditions and has been found to be useful and valid [26].

All outcomes, collected on the web, have been frequently used in clinical practice and in several studies and have all been found to be valid and reliable.

Statistical Analysis

Descriptive statistics were used to present observed data. Dependent samples *t* tests were performed with SPSS for Windows (version 27.0; IBM Corp). Data were analyzed per protocol. Effect sizes of within-group changes were calculated using Cohen *d* and presented with 95% CIs. Both postassessment and 3-month follow-up effect sizes were compared to the baseline preassessment effect size.

Representative Quotes

In the final module of the intervention, participants had the opportunity to summarize and comment on their experience with this intervention in writing. To illustrate some of the general tendencies of participant feedback, 4 quotes were chosen by author DK. Two quotes were considered positive and 2 were considered negative. They were chosen to represent general tendencies, without any qualitative research method. The quotes were translated from Swedish.

Results

Feasibility Measures

Participants’ demographic characteristics are summarized in Table 1. Please see Table 2 for the credibility and usability of the intervention. Credibility (measured using the Credibility/Expectancy Questionnaire) was rated above the cutoff; that is, participants on average rated the intervention as acceptably credible. However, usability (measured using the System Usability Scale) was rated below the cutoff of acceptable system usability at 67 points, whereas the suggested cutoff is 70. Regarding the safety of the intervention, no serious adverse effects were reported, although some participants described a temporarily increased itching sensation in relation to exposure exercises. No participant reported a subjective deterioration of AD symptoms based on the POEM [17].

Table 1. Participants' characteristics at screening (N=21).

Characteristics	Values
Age (years), mean (SD; range)	42.5 (16; 21-62)
Gender, n (%)	
Males	1 (4)
Females	20 (96)
Eczema severity, n (%)	
Mild	3 (14)
Moderate	5 (24)
Severe	9 (43)
Very severe	4 (19)
Education level, n (%)	
Secondary school	6 (28)
University	13 (61)
Other	2 (11)
Living with a partner (yes), n (%)	14 (66)
Self-reported comorbidities (n=16), n (%[a])	
Allergy	5 (20)
Asthma	2 (10)
Fatigue	1 (5)
Panic disorder	1 (5)
Atopic keratoconjunctivitis	1 (5)
Reactive arthritis	1 (5)
Endometriosis	1 (5)
Alopecia universalis	1 (5)
Glaucoma	1 (5)
Osteoarthritis	1 (5)
Thalassemia	1 (5)

[a]Percentage of the total study population (N=21).

Table 2. Participant involvement, credibility, and usability of the intervention.

Measurement	Score
Returned homework assignments (n=8), mean (SD)	5.51 (2.38)
Credibility/Expectancy Questionnaire score, mean (SD; 95% CI)	33.0 (12.4; –28.66 to 94.66).
System Usability Scale score, mean (SD; 95% CI)	66.9 (16.8; –22.03 to 150.03)
Serious adverse events, n	0

Outcome Measures

Results on outcomes and preliminary effects are summarized in Table 3. At postintervention, the outcomes showed significant improvements with small to moderate effect sizes. One exception was itching sensations, which failed to show significance. At 3-month follow-up, all outcomes were significant, with moderate to large effect sizes. On average, participants reported a score of 4, indicating a slight subjective improvement in adequate relief. Out of 18 participants at postintervention, 4 reported slight improvement, 7 reported moderate improvement, 1 person reported great improvement, and 6 reported no improvement. Participants who were not considered responders by POEM typically reported no subjective change.

In Figure 2, the levels of AD severity at different assessment points are illustrated, based on the previously published outcomes on the POEM of this study [13].

Table 3. Outcomes and preliminary effects.

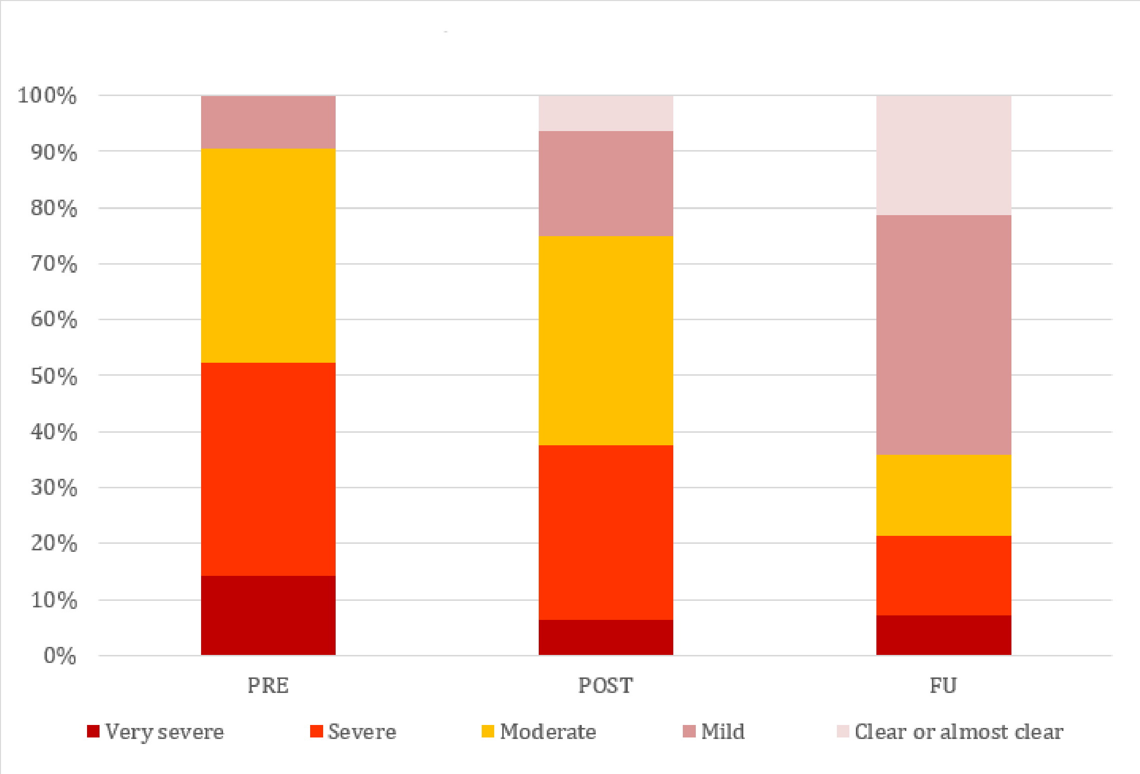
Measure	Changes from preintervention		
	Score, mean (SD)	*P* value	Effect size (95% CI)
Dermatology Life Quality Index			
Preintervention	13.8 (8.3)	Reference	N/A[a]
Postintervention	8.5 (7.9)	.049[b]	0.66 (–0.00 to 1.3)
3-month follow-up	7 (7)	.01[b]	0.89 (0.18 to 1.56)
Peak Pruritus Numerical Rating Scale			
Preintervention	5.6 (2.6)	Reference	N/A
Postintervention	4.7 (2.7)	.28	0.36 (–0.3 to 0.98)
3-month follow-up	3.4 (2.6)	.01[b]	0.85 (0.15 to 1.52)
9-item Patient Health Questionnaire			
Preintervention	8.3 (6.0)	Reference	N/A
Postintervention	3.8 (4.2)	.001[b]	0.87 (0.19 to 1.52)
3-month follow-up	3.9 (5.2)	.003[b]	0.78 (0.1 to 1.45)
Perceived Stress Scale			
Preintervention	18.7 (9.6)	Reference	N/A
Postintervention	10.7 (6.9)	<.001[b]	0.91 (0.27 to 1.62)
3-month follow-up	12.2 (9.2)	.003[b]	0.75 (0.01 to 1.36)
Subjective Assessment Questionnaire			
Postintervention	4.1 (1.3)	—[c]	—

[a]N/A: not applicable.

[b]A significant change from preintervention values.

[c]Not determined.

Figure 2. Levels of severity based on the self-rated Patient-Oriented Eczema Scale reported by Kern et al [13]. FU: 3-month follow-up; POST: postintervention; PRE: preintervention.



Participant Quotes

We present 4 quotes from participants, as shown in Textbox 1.

Textbox 1. Participant quotes.

Regarding exposure (positive):

> *I am most definitely going to continue to do as I please, without letting my eczema control me […] I will continue to approach uncomfortable feelings and situations, even though it's really hard. But it's worth it because I am not plagued as much by the itch anymore.*

Regarding exposure (negative):

> *I believe that the tool isn't user friendly, as I find it difficult to navigate. I also feel that these exercises would do more for people with milder eczema than I have.*

Regarding mindfulness (positive):

> *It is very important that I continue to practice mindfulness. Scratching is the worst trigger of eczema for me, but mindfulness helps me with the difficult task not to scratch.*

Regarding mindfulness (negative):

> *It was a lot of work to fill out the mindfulness diary, but it was unclear to me what purpose it would serve. Furthermore, I thought some of the exercises were too long at 15-20 minutes.*

Discussion

Principal Results

Our aim was to evaluate the feasibility of a web-based psychological self-management intervention for AD, based on an earlier therapist-guided and more comprehensive version. Treatment credibility was acceptable, and no serious adverse events were reported. System usability, however, was rated 3 points below the cutoff. The intervention preliminarily showed moderate to large effects on AD-related quality of life, itching, depressive symptoms, and perceived stress up to 3 months after the intervention. Overall, these results indicate that it is feasible to attempt this intervention on a larger scale. However, as system usability was, on average, rated to be below the cutoff, efforts should be made to improve system usability before carrying out a larger study. We believe that the best way to improve usability is to rework the written material, with additional and very clear instructions on how to use the tools. Based on participant feedback, participants should be better informed of the purpose of using each aspect of the mindfulness and exposure tools. However, it is also important to note that 50% of participants rated usability above the cutoff. In relation to previous research, this study supports the notion that self-guided interventions can be well-liked and useful to people with AD, if the intervention is well designed and a clinical context is provided [12].

Limitations

There was only 1 male participant, which could imply that there is a gender-related difference in interest in this type of treatment for AD. This also implies that if there is a gender-related difference in the feasibility of this intervention, we would not have been able to find it. In addition, the effects reported are only preliminary, the sample size was small, and the intervention group was not compared to a control group. The increases in effects from postintervention to 3-month follow-up in this study is notable and could be due to external factors. Moreover, the placebo effect is assumed to be prominent in all types of interventions studies on AD and could have played a role in this study [27]. One additional external factor could be seasonal variations, as 3-month follow-up data were collected in late summer because AD symptoms are known to decrease during the summer in regions with temperate climate, such as Sweden [28].

Comparison With Prior Work

Psychological treatment with the aim to decrease symptoms of AD is a relatively novel idea, and the results supports the use of CBT with mindfulness and exposure for AD, similar to previous studies [5,9]. In comparison to previous interventions, this intervention is characterized by its brief content, unguided and internet-delivered format, and focus on mindfulness and exposure.

Conclusions

The results of this study showed the intervention to be acceptable, potentially effective, and safe. Considering these preliminary results, we believe that it would be feasible to conduct a randomized controlled trial, with the self-management intervention being compared directly against the therapist-guided intervention. This is conditional to the written material being improved to offer better guidance to the mindfulness and exposure tools, as the usability was below the cutoff. Future studies should attempt to recruit more male participants so that any potential gender differences in treatment preference and response could be explored. A further consideration for future research is to investigate the feasibility of this method to adapt psychological treatments for disorders other than AD.

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Authors' Contributions

DK designed the study and the intervention, drafted the manuscript, and carried out the statistical analysis. BL designed the study and the intervention, and contributed to the development of the manuscript. LL contributed to the design of the intervention and the manuscript. MB and EH-L conceptualized the study and contributed to the development of the manuscript. NL conceptualized and designed the study and contributed to the development of the manuscript. MK conceptualized the study, designed the study and the intervention, and was the principal investigator. All authors critically reviewed and revised the manuscript.

Conflicts of Interest

BL owns shares in DahliaQomit, which specializes in web-based services for symptom assessment outside the submitted work, and licenses a cognitive behavioral therapy manual for irritable bowel syndrome, with royalties received from Pear Therapeutics.

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Abbreviations

AD: atopic dermatitis
CBT: cognitive behavioral therapy
POEM: Patient-Oriented Eczema Measure

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Original Paper

Prescribing Patterns of Dupilumab for Atopic Dermatitis in Adults: Retrospective, Observational Cohort Study

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Abstract

Background: Atopic dermatitis (AD) is a common inflammatory disease caused by a type 2 T helper cell–mediated immune response to environmental antigens. Approximately 1 in 5 patients with AD presents with moderate to severe disease, and treatments approved by the Food and Drug Administration include emollients, topical glucocorticoids, and calcineurin inhibitors. Dupilumab, a fully human monoclonal antibody, improves AD via inhibition of interleukin-4 and interleukin-13.

Objective: Our aim was to characterize the prescribing patterns of dupilumab for AD in adults at a large university-affiliated health system.

Methods: A retrospective, observational cohort study was conducted using electronic data from the Observational Health Data Sciences and Informatics database, assessing data from the University of Colorado Medical Campus and its affiliates. The outcome measured was the prevalence of dupilumab prescribed for adults with AD (n=6421), between March 28, 2013, and March 28, 2021. We assessed whether the characteristics of patients who received dupilumab were different from those who did not. Each patient characteristic was assessed using a univariate logistic regression with the binary outcome of receiving or not receiving dupilumab.

Results: We found a population prevalence of 5.6% (6421/114,476) for AD. In our cohort, Black patients with AD were more than twice as likely to have received dupilumab compared to White patients (odds ratio 2.352, 95% CI 1.58-3.39). Patients with a diagnosis of atopic neurodermatitis were approximately twice as likely to have received dupilumab compared to those with other diagnostic variants of AD (odds ratio 1.87, 95% CI 1.01-3.22).

Conclusions: Our results demonstrate that both patient racial characteristics and specific AD diagnoses were associated with variations in dupilumab prescription patterns.

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KEYWORDS

dupilumab; atopic dermatitis; systemic treatment; biologics; monoclonal antibody; prescribing patterns; dermatitis; adults; disease; immune response; data; inflammatory; immune; dermatology; dermatologist; eczema; Dupixent; asthma; nasal polyp; chronic sinusitis; eosinophilic; neurodermatitis

Introduction

Atopic dermatitis (AD) is a chronic inflammatory disease that affects US children and adults, with a reported prevalence of 10%-13% and 7%, respectively [1-4]. Higher disease severity is associated with lower quality of life, worsened mental status, and higher use of health care resources [1,5]. This includes emergency department visits and hospitalizations as well as increased pharmaceutical and outpatient costs [6-8]. Consequently, effectively treating patients with AD has substantial clinical and economic implications.

Assessing the severity of AD is determined by the number of sites involved (eg, head and neck, upper extremities, or trunk and lower extremities), the lesion characteristics (eg, erythema, edema or papulation, and lichenification), as well as reported symptoms. Patients who have 10%-29% bodily involvement with notable signs of inflammation are classified as having moderate disease, and those with greater or equal to 30% bodily involvement are considered to have severe disease. This classification is important in the diagnosis and treatment of AD, thereby affecting therapeutic outcomes [9]. Treatment of AD with a systemic immunomodulating agent is indicated when the disease is considered moderate to severe [10]. A variety of systemic agents, including cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, and systemic steroids, are used in practice without strict guidelines or recommendations to guide treatment choices [10,11]. In March 2017, dupilumab became the first biologic drug approved for the treatment of AD in adults, and in May 2020, it gained approval for use in children aged 6 years and older. Dupilumab blocks the interleukin (IL)-4 alpha receptor, inhibiting IL-4 and IL-13 signaling and preventing the release of type 2 cytokines that promote inflammation in AD [12]. Compared with the aforementioned systemic immunomodulating agents, dupilumab may be more effective as a long-term maintenance therapy and has the advantage of an overall improved side-effect profile, with no required drug-specific laboratory monitoring [11]. However, access to this immunomodulator may be limited by its novelty and cost (depending upon the dose, up to US $59,000/year for patients without insurance) [13].The disease burden of AD disproportionately affects non-Hispanic Black patients; the source of this disparity is multifactorial. Although the specific gene-environment interactions in the pathophysiology of AD are unknown, many factors—such as differences in environmental pollution, contact with tobacco smoke, hygiene practices, access to health care, diet, and exposure to disease—likely play a role [4,14,15]. Loss of function mutations in the filaggrin gene is linked with an increased risk of developing AD, oftentimes leading to persistent disease. Filaggrin loss-of-function mutations are less common in Black patients compared to White patients, yet Black patients are still more likely to experience persistent disease [16,17]. In addition, Black patients have lower skin ceramide/cholesterol ratios, attenuated T helper 1 and T helper 17 immunophenotypes, and higher serum immunoglobulin (Ig) E levels, which predisposes to skin breakdown, dysregulated immunity, and increased inflammation [18,19]. Despite higher AD disease severity and increased health care needs, Black patients are less likely to receive outpatient dermatologic care [3,20-22]. A prior investigation reporting on race- and ethnicity-related disparities in the treatment of AD found that Black patients had statistically significant lower odds of receiving dupilumab compared to White patients [23]. Previous research has also shown that Black patients with psoriasis are less likely than White patients to receive biologic treatment, independent of demographic or socioeconomic factors and comorbidities [24,25].

Data related to the prescription patterns of dupilumab for AD are needed to inform health equity and decision-making in everyday practice.

Methods

Ethical Considerations

The Colorado Multiple Institutional Review Board determined that this research did not involve human subjects, and therefore, was exempt from ethics approval.

Data Source

We performed a retrospective, observational cohort study of adult patients treated for AD, using electronic data from the University of Colorado Anschutz Medical Campus and its affiliates (hospital wards and outpatient clinics) via Health Data Compass (HDC), an electronic health data warehouse [26]. Records of patients who visited any of the institution's facilities from January 1, 2010, to March 28, 2021, were pulled from HDC and remained in the format of the Observational Health Data Sciences and Informatics (OHDSI) Observational Medical Outcomes Partnership common data model. Data extracted included demographics, prescription history, diagnosis history, and visit details.

Study Design and Study Population

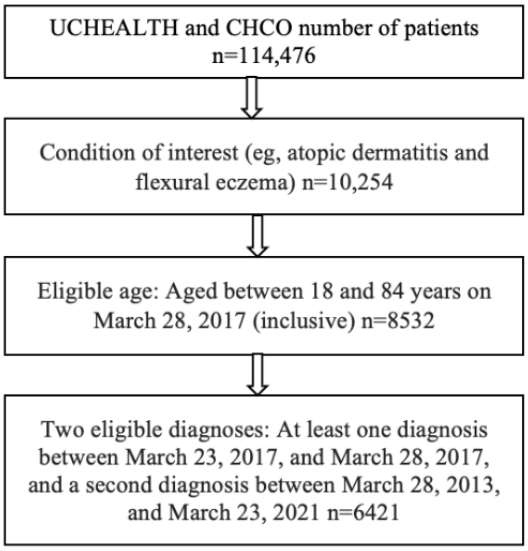
The outcome of interest was the prevalence of dupilumab prescribed for AD, stratified by patient characteristics. The study cohort, consisting of individuals with specific AD diagnoses and various dupilumab prescription types, was developed using the OHDSI Atlas cohort and concept set tools (Table 1). All study participants were between the ages of 18 and 85 years as of March 28, 2017, with a diagnosis of AD, as defined by at least two encounter diagnoses of AD (Figure 1). The drug of interest was any prescription order of dupilumab (200 mg or 300 mg syringe or pen). Records included were those of ordered medications. Information regarding fulfilment for this study was not used, nor did we include orders external to our institution. Included dupilumab prescriptions were required to have a start date on or after March 28, 2017, and to have occurred following a diagnosis of AD. Prescriber data, including their medical credential and practice setting, were not analyzed.

Table 1. Concept set for diagnosis of atopic dermatitis, displaying *International Classification of Diseases, Tenth Revision* (*ICD-10*) source codes that map to the included Observational Medical Outcomes Partnership concept IDs.

Concept ID	Concept code	Concept name	Class	Domain	Vocabulary
45601213	L20.84	Intrinsic (allergic) eczema	5-character billing code	Condition	*ICD-10-CM*[a]
45596150	H60.54	Acute eczematoid otitis externa	5-character nonbilling code	Condition	*ICD-10-CM*
45581716	H60.549	Acute eczematoid otitis externa, unspecified ear	6-character billing code	Condition	*ICD-10-CM*
45572269	L30.1	Dyshidrosis (pompholyx)	*ICD-10* code	Condition	*ICD-10-CM*
45572263	L20.83	Infantile (acute, chronic) eczema	5-character billing code	Condition	*ICD-10-CM*
45567351	L20.89	Other atopic dermatitis	5-character billing code	Condition	*ICD-10-CM*
45562535	L30.0	Nummular dermatitis	*ICD-10* code	Condition	*ICD-10-CM*
45557698	L20	Atopic dermatitis	*ICD-10* hierarchy	Condition	*ICD-10-CM*
45557486	H60.542	Acute eczematoid otitis externa, left ear	6-character billing code	Condition	*ICD-10-CM*
45557485	H60.541	Acute eczematoid otitis externa, right ear	6-character billing code	Condition	*ICD-10-CM*
45552974	L20.82	Flexural eczema	5-character billing code	Condition	*ICD-10-CM*
45548191	L20.9	Atopic dermatitis, unspecified	*ICD-10* code	Condition	*ICD-10-CM*
45547951	H60.543	Acute eczematoid otitis externa, bilateral	6-character billing code	Condition	*ICD-10-CM*
45533637	L20.8	Other atopic dermatitis	*ICD-10* code	Condition	*ICD-10-CM*
35208498	L30.1	Dyshidrosis (pompholyx)	4-character billing code	Condition	*ICD-10-CM*
35208497	L30.0	Nummular dermatitis	4-character billing code	Condition	*ICD-10-CM*
35208450	L20.9	Atopic dermatitis, unspecified	4-character billing code	Condition	*ICD-10-CM*
1569766	L20.8	Other atopic dermatitis	4-character nonbilling code	Condition	*ICD-10-CM*
1569765	L20	Atopic dermatitis	3-character nonbilling code	Condition	*ICD-10-CM*
1418386	L30.100	Dyshidrosis (pompholyx)	*ICD-10* code	Condition	*ICD-10-CM*
1418385	L30.1	Dyshidrosis (pompholyx)	*ICD-10* code	Condition	*ICD-10-CM*
1418384	L30.000	Nummular dermatitis	*ICD-10* code	Condition	*ICD-10-CM*
1418383	L30.0	Nummular dermatitis	*ICD-10* code	Condition	*ICD-10-CM*
1418239	L20.900	Atopic dermatitis, unspecified	*ICD-10* code	Condition	*ICD-10-CM*
1418238	L20.9	Atopic dermatitis, unspecified	*ICD-10* code	Condition	*ICD-10-CM*
1418237	L20.806	Newborn skin eczema (machine translation)	*ICD-10* code	Condition	*ICD-10-CM*
1418236	L20.805	Diffuse neurodermatitis (machine translation)	*ICD-10* code	Condition	*ICD-10-CM*
1418235	L20.804	Baby eczema (machine translation)	*ICD-10* code	Condition	*ICD-10-CM*
1418234	L20.803	Atopic neurodermatitis (machine translation)	*ICD-10* code	Condition	*ICD-10-CM*
1418233	L20.802	Allergic eczema (machine translation)	*ICD-10* code	Condition	*ICD-10-CM*
1418232	L20.801	Neurodermatitis (machine translation)	*ICD-10* code	Condition	*ICD-10-CM*
1418231	L20.800	Other atopic dermatitis	*ICD-10* code	Condition	*ICD-10-CM*
1418230	L20.8	Other atopic dermatitis	*ICD-10* code	Condition	*ICD-10-CM*
1418227	L20	Atopic dermatitis	*ICD-10* hierarchy	Condition	*ICD-10-CM*

[a] *ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification.*

Figure 1. Flowchart of included patients. UCHEALTH: University of Colorado Health; CHCO: Children's Hospital Colorado.



Statistical Analysis

We assessed whether the characteristics of patients with AD who received dupilumab were different from those who did not. Each patient characteristic was gathered based on AD-associated billing and nonbilling codes. These codes were based on the *International Classification of Diseases, Tenth Revision* and are listed in Table 1. The characteristics were then assessed using a univariate logistic regression, with the binary outcome of receiving dupilumab or not receiving dupilumab (Table 2). The resulting *P* values associated with multilevel categorical characteristics (eg, race and diagnosis) were corrected for multiple testing using the False Discovery Rate (Benjamini-Hochberg correction) method. Reference levels included White race, non-Hispanic ethnicity, female sex, and AD as the first eligible diagnosis.

Table 2. Summary statistics—overall and by patients who did and did not receive dupilumab.

User prevalence	Did not receive (n=6172)	Received (n=249)	Overall (N=6421)
Age (years), mean (SD)	53.3 (17.9)	51.4 (16.7)	53.2 (17.9)
Age (years), median (min, max)	54.0 (22.0, 89.0)	52.0 (22.0, 87.0)	54.0 (22.0, 89.0)
Sex, n (%)			
Female	3532 (57.2)	146 (58.6)	3678 (57.3)
Male	2621 (42.5)	102 (41)	2723 (42.4)
Missing	19 (0.3)	1 (0.4)	20 (0.3)
Race, n (%)			
American Indian and Alaska Native	20 (0.3)	1 (0.4)	21 (0.3)
Asian	246 (4)	11 (4.4)	257 (4)
Black or African American	397 (6.4)	34 (13.7)	431 (6.7)
Multiple race	161 (2.6)	6 (2.4)	167 (2.6)
Native Hawaiian and other Pacific Islander	12 (0.2)	0 (0)	12 (0.2)
White or Caucasian	4912 (79.6)	179 (71.9)	5091 (79.3)
Other	340 (5.5)	13 (5.2)	353 (5.5)
Missing	84 (1.4)	5 (2.0)	89 (1.4)
Ethnicity, n (%)			
Hispanic	563 (9.1)	20 (8)	583 (9.1)
Non-Hispanic	5491 (89)	226 (90.8)	5717 (89)
Missing	118 (1.9)	3 (1.2)	121 (1.9)
Diagnosis, n (%)			
Atopic dermatitis	3050 (49.4)	213 (85.5)	3263 (50.8)
Atopic neurodermatitis	107 (1.7)	14 (5.6)	121 (1.9)
Flexural eczema	758 (12.3)	5 (2)	763 (11.9)
Nummular eczema	1120 (18.1)	6 (2.4)	1126 (17.5)
Vesicular eczema	1137 (18.4)	11 (4.4)	1148 (17.9)

Results

Summary statistics gathered based on the *International Classification of Diseases, Tenth Revision* billing codes are provided in Table 2. There were 249 dupilumab prescriptions among 6421 patients. Our cohort had a mean age of 53.2 (SD 17.9) years and was composed of mostly non-Hispanic (n=5491, 89%), White (n=4912, 79.3%), and female (n=3532, 57%) patients. The most common recent diagnosis was a general diagnosis of atopic dermatitis (n=3263, 50.8%), followed by vesicular eczema (n=1148, 17.9%), nummular eczema (n=1126, 17.5%), flexural eczema (n=763, 11.9%), and lastly, atopic neurodermatitis (n=12, 1.9%). Among those who received dupilumab, the mean age was 51.4 (SD 16.7) years and 58.6% (n=146) were female. Every patient who received a prescription had either multiple prescriptions, prescriptions for quantities greater than 1, or received refills. The majority of patients were White (n=179, 71.9%), followed by patients identifying as Black or African American (n=34, 13.7%) and “Other” races (n=13, 5.2%). Among the most common recent diagnoses, 85.8% (n=213) were general diagnoses of AD, and the remaining were diagnoses of atopic neurodermatitis (n=14, 5.6%), flexural eczema (n=5, 2.2%), nummular eczema (n=6, 2.2%), or vesicular eczema (n=11, 4.1%).

We assessed whether the proportion of patients who received dupilumab was different based on patient characteristics. Each patient characteristic (Table 3) was assessed using logistic regression with the binary outcome of receiving dupilumab or not receiving it. The *P* values associated with multilevel categorical characteristics (eg, race or diagnoses) were corrected for multiple testing using the False Discovery Rate (Benjamini-Hochberg correction) method. Reference levels included white race, non-Hispanic ethnicity, female sex, and AD as the first eligible diagnosis.

In our cohort, Black patients were approximately twice as likely to have received dupilumab for AD compared to White patients (odds ratio 2.352, 95% CI 1.58-3.39). Similarly, those diagnosed with atopic neurodermatitis were about twice as likely to have received dupilumab compared to those who were diagnosed with AD (odds ratio 1.87, 95% CI 1.01-3.22). Conversely, those with other eczema diagnoses, including flexural eczema, nummular eczema, or vesicular eczema, were less likely to have received dupilumab compared to those with a most recent diagnosis of atopic neurodermatitis.

Table 3. Univariate analysis by patient characteristics.

Variable	Odds ratio (CI)	*P* value
Age (per 10-year increase)	0.944 (0.879-1.013)	.11
Sex		
Male	1.00 (reference)	—[a]
Female	0.941 (0.726-1.217)	.65
Race		
American Indian or Alaska Native	—	—
Asian	1.228 (0.622-2.183)	.86
Black or African American	2.352 (1.583-3.397)	<.001
Multiple Race	1.024 (0.398-2.15)	.96
Native Hawaiian or Other Pacific Islander	—	—
White or Caucasian	1.00 (reference)	—
Other	1.05 (0.564-1.791)	.96
Ethnicity		
Non-Hispanic or Latino	1.00 (reference)	—
Hispanic or Latino	0.863 (0.526-1.340)	.54
Diagnoses		
Atopic dermatitis	1.00 (reference)	—
Atopic neurodermatitis	1.87 (1.01-3.22)	.03
Flexural eczema	0.0945 (0.0335-0.207)	<.001
Nummular eczema	0.0767 (0.0302-0.158)	<.001
Vesicular eczema	0.139 (0.0708-0.243)	<.001

[a]Not applicable.

Discussion

Principal Findings

We found that patient racial characteristics as well as specific eczema diagnoses were associated with different frequencies of dupilumab prescriptions.

Specifically, our results suggest that patients who reported their race as African American or Black were more likely to have received a dupilumab prescription compared to White patients in our health care system. This result is surprising, as previous research demonstrated less outpatient dermatologic care and fewer biologic prescriptions among the population of Black patients with AD [27,28].

Our study also revealed that patients with a diagnosis of atopic neurodermatitis were twice as likely to be prescribed dupilumab compared to patients with a diagnosis of AD. The term “neurodermatitis” refers to localized, circumscribed patches of lichenified skin that are commonly associated with itching. This term is increasingly being used to describe skin eruptions associated with anxiety [29].

Our study also revealed that patients with specific AD diagnoses, such as flexural eczema, nummular eczema, and vesicular eczema, are less likely to receive dupilumab than those with general AD, without further specification. One possible explanation may be that patients with certain subtypes of AD respond well to more conservative, first-line therapies (ie, topical corticosteroids, emollients, and topical calcineurin inhibitors) [30].

Limitations

Although the study results provide novel insights pertaining to the prescribing practices of dupilumab, there are important limitations. Data capturing patients’ insurance status and type of insurance at the time of visit would have been useful to provide further clarity regarding prescribing relationships; unfortunately, our HDC data warehouse only has the current insurance status and type available from our electronic health record system. Furthermore, the type of health care provider prescribing dupilumab as well as their specific sector of medical employment were not analyzed. Additional studies evaluating the background of the clinicians prescribing dupilumab may provide a better understanding of these unique prescription patterns.

Conclusions

We found that Black patients and patients diagnosed with atopic neurodermatitis were approximately twice as likely to have received dupilumab compared to White patients and those with a diagnosis of AD, respectively. Future studies may consider exploring possible factors contributing to the dupilumab prescription patterns we discovered, such as AD disease severity as a potential contributing factor and the role of insurance type in dupilumab prescribing frequency. Investigating similar trends among other OHDSI network sites might also be beneficial in elucidating the trends noted among our study population and would contribute to the generalizability of the results. Furthermore, there is little existing data regarding the treatment of AD in the pediatric demographic—additional research would allow clinicians to provide evidence-based care to this population subset.

Conflicts of Interest

RD is editor in chief of the *JMIR Dermatology*, an editor for *Cochrane Skin*, a dermatology section editor for UpToDate, a social media editor for the *Journal of the American Academy of Dermatology (JAAD)*, and a Cochrane council cochair. TES is an editorial board member at large for *JMIR Dermatology*. RD receives editorial stipends (*JMIR Dermatology*), royalties (UpToDate), and expense reimbursement from Cochrane. TES receives fellowship funding from Pfizer, Inc. All other authors declare no conflicts of interest.

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Abbreviations

AD: atopic dermatitis
HDC: Health Data Compass
IL: interleukin
OHDSI: Observational Health Data Sciences and Informatics

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Original Paper

The Comparison of Sun Protection Factor 30 Persistence Between Inorganic and Organic Sunscreen in Swimmers: Double-blind Randomized Clinical Trial

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Abstract

Background: Long-term sun exposure is one of the risks faced by outdoor swimmers and can cause sunburn. Using sunscreen is one way to prevent sunburn; however, physical activity can trigger sweat, friction, and water washing that can interfere with sunscreen efficacy and decrease its sun protection factor (SPF). Sunscreens are classified into inorganic and organic based on their filter. Organic sunscreen has a better bond to the skin than inorganic sunscreen, which forms a barrier above the skin layer that makes removing it easier. Organic sunscreen lasts longer than inorganic sunscreen when used in physical activities, but it has a limited spectrum, is more photolabile, and is more allergenic.

Objective: This study aims to evaluate the persistency of SPF 30 between inorganic and organic sunscreens on the back area after 1.5 hours of swimming.

Methods: This study is a randomized, split-body, double-blind clinical trial to evaluate the persistency of SPF 30 of the inorganic versus organic sunscreens in swimmers. Randomization was done to allocate the participants into treatment groups. Each participant received inorganic and organic sunscreen treatments applied to the back area. The research participants were swimmers from the Cikini swimming pool and Bina Taruna swimming pool, both in Jakarta, Indonesia.

Results: A total of 22 swimmers were enrolled in this study. The analysis showed no significant difference between the SPF of the two sunscreens before swimming (P=.22). After swimming, the SPF levels of both sunscreens decreased: the inorganic sunscreen decreased from a median of 27 (range 23-47) to 12.3 (range 8-19), and the organic sunscreen decreased from a median of 30 (range 24-47) to 9.9 (range 6-19), which was statistically significant (P<.001). When comparing the SPF of inorganic and organic sunscreens after swimming, there was a statistically significant difference in the decrease in SPF levels between the two groups (P=.02), which indicated a better SPF persistence for inorganic sunscreens when compared to organic sunscreens.

Conclusions: There was a decrease in the SPF levels of inorganic and organic sunscreens after 1.5 hours of swimming, with better persistence in inorganic sunscreens compared to organic sunscreens.

Trial Registration: ClinicalTrials.gov NCT04618536; https://clinicaltrials.gov/ct2/show/NCT04618536

International Registered Report Identifier (IRRID): RR2-10.2196/42504

(JMIR Dermatol 2023;6:e41633) doi:10.2196/41633

KEYWORDS

inorganic sunscreen; organic sunscreen; outdoor pool; sun protection factor; swimmer; sun protection; sunscreen; sun exposure; sunburn; prevention; efficacy; skin care; dermatology

Introduction

In Indonesia, swimmers commonly train about five times a week for 1.5 hours per day at outdoor or indoor pools. Training occurs in the morning or evening, where the UV index usually ranges from 1 to 4 [1]. Swimmers who train in outdoor pools are exposed to humidity, hot and cold weather, windy conditions, and long-term sun exposure or UV radiation [2]. These exposures can cause various skin disorders such as sunburn [3,4].

For sunburn prevention, protection from the sun is needed and can be achieved in several ways, one of which is by using sunscreen [5,6]. There are two types of sunscreens based on their filters, specifically, organic and inorganic. Organic sunscreen absorbs and prevents UV light from entering the epidermis. Meanwhile, inorganic sunscreen works by reflecting and scattering radiation [5,7,8]. Previous trials have shown that organic sunscreens had better bonding properties to the skin layer than inorganic sunscreens. Meanwhile, inorganic sunscreens tend to form layers on the skin's surface so they can be removed easily [7,8]. This study aimed to evaluate the persistence of sunscreen with sun protection factor (SPF) 30 used by swimmers after 1.5 hours of training.

Methods

Ethics Approval

This clinical trial has received ethics approval from the Ethical Committee Faculty of Medicine Universitas Indonesia (ID 20-09-1037).

Study Design

This randomized, split-body, double-blind, noninferiority, and multicenter clinical trial was done from August to December 2020. This clinical trial has been registered into ClinicalTrials.gov with the identifier NCT04618536. The primary objective of this clinical study is to compare the persistency of the SPF between inorganic and organic sunscreens after 1.5 hours of swimming in the athlete population. The difference in the SPF before and after swimming was measured and compared. The SPF was quantified using a minimal erythema dose (MED) test conducted over 2 days. Irradiation was conducted on the first day, and 24 hours after irradiation, the result was collected. Furthermore, we assessed the SPF value based on the in vivo method conducted before swimming using an MED as the primary objective. This trial also aims to know the decreased level of SPF after swimming for 1.5 hours and which type of sunscreen provides higher persistence.

Recruitment

Swimmers were recruited from Millenium Aquatic swimming club, which practice at the Cikini swimming pool, and Bina Taruna swimming club, which practice at the Bojana Tirta swimming pool, both in Jakarta, Indonesia.

Participants

The inclusion criteria of this study were as follows:

- Female or male swimmers aged 18-40 years who practice swimming at least three times a week for 1.5 hours in the morning or evening
- Willing to consent to being a research participant
- Does not have skin diseases
- Does not have a history of allergies to sunscreens

Conversely, the exclusion criteria applied for this study were as follows:

- The existence of skin lesions in the test area
- Undergoing phototherapy treatment
- Using drugs with photosensitivity as a side effect
- Having a history of malignancy
- Showing photosensitivity reactions or disease affected by UV rays, direct sunlight exposure to the test area within 24 hours before the study, or during the study period
- Absence of erythema response 24 hours after the radiation test
- Erythema that occurs in the entire test area box within 24 hours after the radiation test

Randomization and Masking

Computer-based randomization was done to allocate the participants into treatment groups. The split-body method was conducted on the same person to collect the data. Each participant received both inorganic and organic sunscreens simultaneously on the right or left (by random) of the back area. Treatment was allocated by numbering the research participants (1 being the right back area and 2 being the left back area). We used a computer-based randomization method to determine which side of the back area and type of sunscreen should be given [9]. The allocation data for each participant was placed in a sealed opaque envelope. Both the research participants and the researchers, but not the statistician, were unaware of the type of sunscreen that was be applied. The research assistant applied the sunscreen. Researchers were responsible for carrying out the irradiation test and assessment. At the end of data collection, a randomization code was revealed by a statistician who was not involved in the sampling process.

Sunscreen

This study used inorganic and organic sunscreens made by PT Paragon Technology and Innovation with the formulation adjusted according to the research needs. Both sunscreens are made in the form of oil in water emulsion with the addition of a film-forming layer. The inorganic and organic sunscreens have the same base ingredients but different filters: titanium dioxide and zinc oxide for inorganic sunscreen, and diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, ethylhexyl triazone, ethylhexyl salicylate, and methylene bis-benzotriazolyl tetramethylbutylphenol for the organic sunscreen.

Procedure

A COVID-19 prevention protocol was carried out to prevent the spread of the pandemic by using masks, face shields, handwashing, general physical examination, and social distancing of at least 1 meter during data collection. The general cleaning of tools and tool calibration were done for each research participant. Before data collection began, we conducted a preliminary study to identify the value of broadband UV-B (BB-UVB) MED on various skin types and interreviewer reliability tests to ensure the production of high-quality data during research. After the consent was obtained from the research participants, we performed history taking, physical examination, and documentation. Two sessions were held 1 week apart: the first session for primary data collection (skin type and identification of any skin lesion) and the second session for randomizing the participant and providing the treatment as stated in Figures 1 and 2.

Figure 1. Procedure of research at the first session.

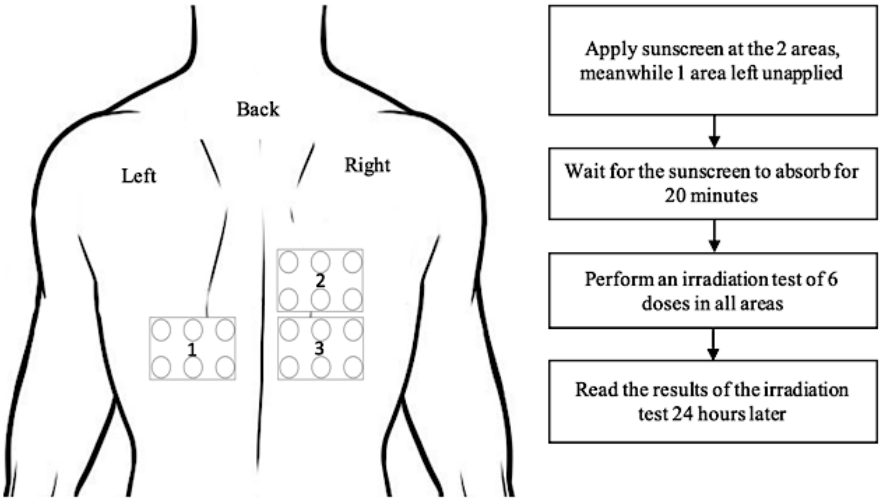
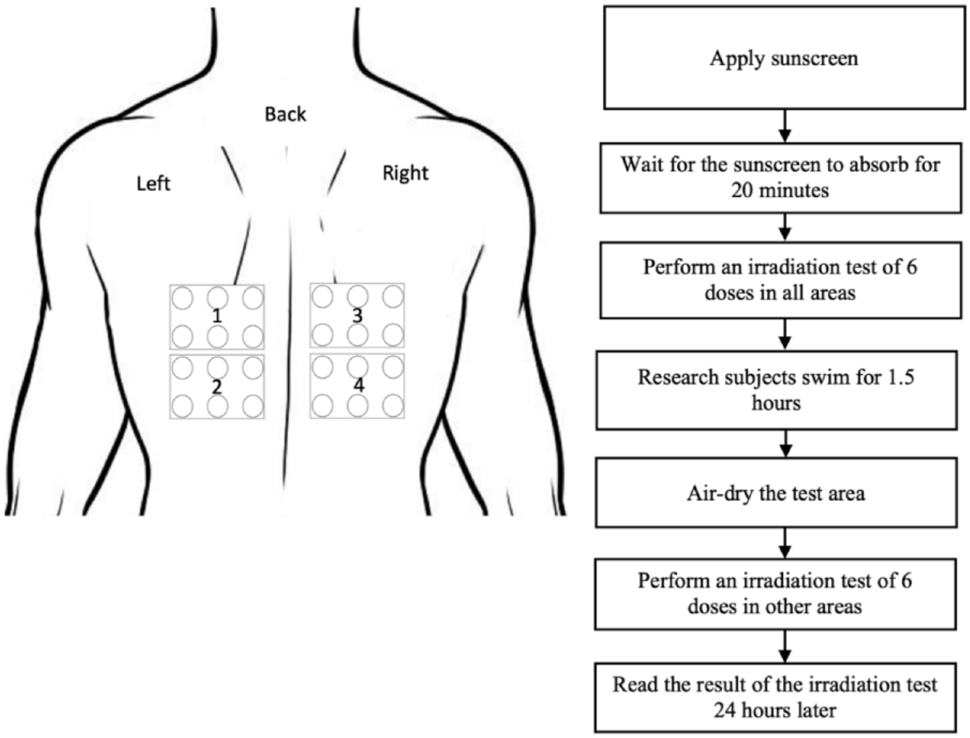


Figure 2. Procedure of research at the second session.



At the first meeting, we marked the back of the swimmers with three areas. At the second meeting there were four areas marked. Each area is 40 cm^2 and marked with a perforated sticker. The sunscreen was applied at a dose of 2 mg/cm^2 using a 1 cc syringe for each area. Afterward, the sunscreen was spread using gloves, starting with circular and then followed by horizontal and vertical movements with light pressure for 35 seconds. The irradiation test was done 20 minutes after sunscreen application, using a metal halide UV-enhanced lamp BB-UVB in the active spectrum of 290-320 nm (The Daavlin Lumera). The MED values were calculated 24 hours after the test. The SPF of each sunscreen was compared before and after the swimming period. Swimming activities occurred in the morning or evening when the UV index was in the 0-2 range. Sunscreens used in this study were creams (oil in water emulsion) with a film-forming layer. Sunscreens were made by PT Paragon Technology and Innovation. If there were any severe side effects, the study would have been discontinued, such as anaphylactic reactions. Research participants who experienced any side effects were excluded from the study, but their development will be followed until they recover.

Statistical Analysis

The minimum estimated sample size was calculated using the difference in the average decrease in SPF levels that is considered significant based on the clinical judgment set by the researchers as 5. A total of 22 participants in the experimental and control groups were estimated to be needed to reject the null hypothesis that the population means of the experimental and control groups are equal, with a probability (power) of 0.9. The type I error probability associated with this null hypothesis test is 0.05. The collected data were analyzed using SPSS version 20.0 (IBM Corp) software in descriptive and inferential analysis. The persistency of the organic and inorganic sunscreens' SPF was assessed using the MED, stated in mJ/cm^2. The SPF was calculated from the ratio between MED in protected and unprotected skin areas and persistence of SPF, stated in index units. The persistency of SPF was defined as the lowest differences of SPF before and after 1.5 hours of swimming. We used a 1-sided CI approach in the statistical methods. The mean difference in SPF will be no different if the *P* value for the paired *t* test or Wilcoxon test is >.05 and the upper limit of the CI does not exceed 4 SPF.

Results

Initially, the research was planned to include only Millenium Aquatic swimmers from one swimming pool, namely, the Cikini swimming pool. However, some research participants could not attend the sampling session due to the pandemic conditions, so we added swimmers from the Bina Taruna swimming club who practice at another location, namely, the Bojana Tirta swimming pool. This research took place from August to December 2020, and the enrollment of the participants ended when the minimum sample size was achieved. Of the 25 swimmers from both swimming clubs, 22 were included in the study based on the inclusion and exclusion criteria. A total of 14 swimmers came from the Millenium Aquatic swimming club and 8 from the Bina Taruna swimming club (Figure 3).

This study's demographic distribution showed that participants were mostly male, had Fitzpatrick skin types III and IV, were unmarried, and had an undergraduate education. The median age of participants was 22 (range 19-28) years, and 64% (n=14) of the participants were Millenium Aquatic members (Table 1). Swimmers had an average training session six times per week starting at 6 AM (based on Jakarta, Indonesia time). As many as 27% (n=6) of the participants had a history of sunburn when exposed to UV radiation. We also analyzed the temperature, pH, osmolarity, and conductivity differences between the two swimming pools (Table 2).

Figure 3. The flowchart for participant enrollment, assignment, allocation, follow-up, and analysis for the split-body interventions. SPF: sun protection factor.

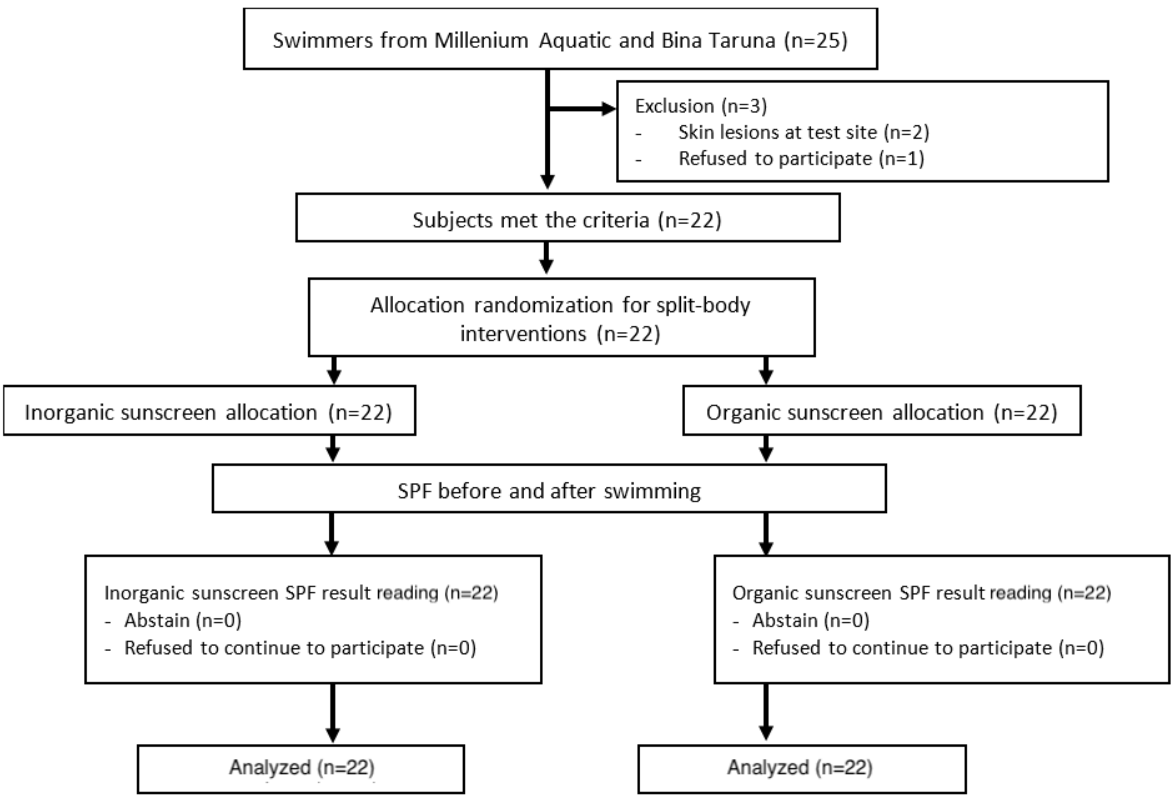


Table 1. Clinical characteristics of research participants (N=22).

Characteristics	Values
Age (years), median (range)	22 (19-28)
Gender, n (%)	
Male	12 (54)
Female	10 (46)
Swimming club, n (%)	
Millenium Aquatic	14 (64)
Bina Taruna	8 (36)
Marital status, n (%)	
Yes	1 (5)
No	21 (95)
Education, n (%)	
High school	10 (46)
Undergraduate	12 (54)
Skin type, n (%)	
Type III	13 (59)
Type IV	9 (41)
MED[a] based on skin type (mJ/cm^2), mean (SD)	
Type III	107.23 (20.51)
Type IV	131.33 (29.38)
MED based on swimming club (mJ/cm^2), mean (SD)	
Millenium Aquatic athletes	106.86 (19.28)
Bina Taruna athletes	135 (29.70)
Frequency of swimming practice per week, n (%)	
Less than 6 times	10 (46)
More than 6 times	12 (54)
History of skin disease, n (%)	
Yes	4 (18)
No	18 (82)
History of skin cancer, n (%)	
Yes	0 (0)
No	22 (100)
History of allergies, n (%)	
Yes	4 (9)
No	18 (91)
History of red skin after sun exposure, n (%)	
Yes	6 (27)
No	16 (73)
History of skin complaints after sun exposure, n (%)	
Yes	5 (23)
No	17 (77)
Current skin disease, n (%)	

Characteristics	Values
Yes	3 (14)
No	19 (86)
History of drug consumption, n (%)	
Yes	0 (0)
No	22 (100)
Sport beside swimming, n (%)	
Yes	9 (41)
No	13 (59)

[a]MED: minimal erythemal dose.

Table 2. Swimming pool profiles.

	Cikini swimming pool	Bojana Tirta swimming pool
Temperature (°C), mean (SD)	28.5 (0.6)	29.4 (0.9)
pH, mean (SD)	8.4 (0.3)	7.6 (0.2)
Osmolarity (ppm), median (range)	469 (105-506)	187.5 (180-195)
Conductivity (μS/cm), median (range)	952.5 (404-1013)	432 (390-455)

After swimming, the SPF levels decreased in both sunscreens, namely, the SPF of the inorganic sunscreens decreased from a median of 27 (range 23-47) to 12.3 (range 8-19), and the SPF of the organic sunscreens decreased from a median of 30 (range 24-47) to 9.9 (range 6-19; Table 3). The decrease in the SPF levels in each group of sunscreens was statistically significant (*P*<.001). Based on the analysis results, there was no significant difference in the SPF of the two sunscreens on the research participants before swimming. When we compared the SPF of the inorganic and organic sunscreens after swimming, there was a difference in the decrease in SPF levels between the two groups. This difference was statistically significant (*P*=.02) and indicated that the inorganic sunscreen had a better SPF persistence than the organic sunscreens (Table 4). No serious adverse events or other harms were encountered during this study.

Table 3. Comparison of sun protection factor (SPF) in each sunscreen group after swimming.

	Before swimming, median (range)	After swimming, median (range)	*P* value
SPF of inorganic sunscreen[a]	27 (23-47)	12.3 (8-19)	<.001
SPF of organic sunscreen[a]	30 (24-47)	9.9 (6-19)	<.001

[a]Data analyzed using Wilcoxon test.

Table 4. Comparison of sun protection factor (SPF) between inorganic and organic sunscreen before and after swimming.

	Type of sunscreen (SPF), median (range)		*P* value
	Inorganic	Organic	
Before swimming[a]	27 (23-47)	30 (24-47)	.22
After swimming[a]	12.3 (8-19)	9.9 (6-19)	.02

[a]Data were analyzed using Wilcoxon test.

Discussion

Principal Results

The participants of this study had a median age of 22 years and consisted of more male swimmers (n=12, 54%) than female swimmers (n=10, 46%). Differences in age, height, and weight determined the variability of distance, style, and time of the swimmers. The participants in this study had similar ages to other studies, namely, the average age of female swimmers compared to male swimmers was 22.7 and 23.2 years, respectively [10]. A cross-sectional study in the United States in 2016 and 2017 showed that sunburn was significantly higher in young adults (aged 18-29 years; *P*<.001), especially for those with a previous history of sensitive skin [11]. A study conducted on 246 participants in Spain, involving various athletes from water sports aged 16-30 years showed no significant difference between the sexes regarding habits for sun protection [12]. Qualitative research has stated that women use sunscreen more often and protect themselves from the sun more than men because they have a higher knowledge about skin cancer and feel more at risk of developing cancer. Men tend to think of using sunscreen only when they are at the beach, while women think sunscreen is a daily necessity and must be applied before leaving the house [13].

The number of participants who practiced in the Cikini swimming pool (n=14, 64%) was more than in the Bojana Tirta swimming pool (n=8, 36%). The frequency of exercise was generally more than six times per week for 54% (n=12) of the participants. Almost all research participants started swimming exercises before 8 AM (Jakarta, Indonesia time). A total of 54% (n=12) of the participants had a bachelor's degree. The Fitzpatrick skin type of the research participants was mostly type III and type IV. A history of skin diseases and allergies was rarely found in the study participants. None of the study participants had a history of skin cancer or routine drug use. More than 70% of the research participants had no complaints after sun exposure. More than 50% of the research participants did sports other than swimming, such as running, cycling, futsal, and soccer. These findings suggest an increased risk of greater exposure to UV radiation for swimmers.

The characteristics of the water in swimming pools, such as pH, temperature, conductivity, and osmolarity, play a role in influencing water quality. Based on the World Health Organization recommendations, swimming pools must have specific physicochemical parameters to ensure that the water does no harm. Our findings show that both swimming pools were in accordance with the guideline [14,15].

Fitzpatrick divides skin type based on the response to sun exposure, namely, burning and tanning. Influencing factors of this skin type include genetic predisposition and habits that increase UV radiation exposure, sunbathing activities, and the use of sunscreen [16]. This study showed that MED was greater in skin type IV after 24 hours of exposure to unprotected skin than type III. The MED values were higher in skin types IV-VI because of the higher levels of eumelanin, which makes it appear darker. Low MED values in skin types I-III cause the skin to be prone to inflammation, be more sensitive, burn easily, and increase the risk of skin cancer [17]. Another study showed a strong correlation between the MED and Fitzpatrick skin type (correlation coefficient 0.5-0.69). However, the discrimination value of Fitzpatrick's skin type is poor, which can lead to different skin types having the same MED value [18].

Sunscreens are classified according to their filter, namely, organic and inorganic. Organic sunscreens change the conformation of molecules to prevent UV radiation from reaching the skin, while inorganic sunscreens reflect and scatter light [19]. This study used diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, ethylhexyl triazone, ethylhexyl salicylate, methylene bis-benzotriazolyl tetramethylbutylphenol, and bis-ethylhexyloxyphenol methoxyphenyl triazine as organic filters. These components are photostable and well-dispersed oil-soluble filters in aqueous phase emulsions, producing higher SPF values. This can be seen from the organic SPF value of the sunscreen when it has not been used for swimming [5].

Inorganic filters used in this study were titanium dioxide and zinc oxide. Both are metal oxide particles that have long been used as filters in sunscreens and are efficient and photostable. Because both are metal oxide particles, these filters must be coated with an inert substance. Silicon dioxide, dimethicone, and triethoxycaprylylsilane were used as an inert substance to coat the inorganic filter. This coating aims to stabilize the titanium dioxide and zinc oxide so that they do not react when exposed to UV [5,20]. The use of silicone and its derivatives in this sunscreen can increase the resistance of emulsion preparations due to their hydrophobic nature [21,22]. This study used sunscreen in the form of cream (oil in water emulsion) with the addition of a film-forming agent. Isododecane and trimethylsiloxysilylcarbomoyl pullulan are film-forming materials based on silicone polymers. Polymers provide a water-resistant effect, contributing to an increase in SPF levels, and affect the sensory effects of sunscreen formulations. The purpose of adding polymers is to increase water resistance and increase SPF levels. The addition of polymers will add a layer on top of the sunscreen in the form of a hydrophobic barrier so that the sunscreen layer cannot bind to water and becomes more challenging to wash off. The hydrophobic and water-resistant sunscreen layers that adhere to the skin's surface have the potential to withstand constant hygroscopic pressure and help maintain the integrity of the skin barrier. This underlies the resistance of both sunscreens in the study after swimming [23-25].

Limitations

The data collection was initially planned in one swimming pool. However, due to the COVID-19 pandemic, a limited number of swimmers were available, which resulted in an insufficient sample size. We had to add more swimmers who practiced at another swimming pool. It is assumed that the effectiveness of the sunscreens has been affected due to the differences in the characteristics of the two swimming pools, namely, the temperature, pH, osmolarity, and conductivity.

Comparison With Prior Work

This research is the first double-blind randomized clinical trial to compare sunscreen filters under actual conditions in skin types III and IV. Based on our literature review, there has been no study like this before. Hopefully the research results can be used to develop further inorganic sunscreens for swimming or other sports.

Conclusions

In conclusion, there was a decrease in the SPF levels of inorganic and organic sunscreen after swimming for 1.5 hours, whereas the SPF persistence of the inorganic sunscreen was better than the organic sunscreen.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
CONSORT checklist.
[PDF File (Adobe PDF File), 144 KB - derma_v6i1e41633_app1.pdf]

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Abbreviations

BB-UVB: broadband UV-B
MED: minimal erythema dose
SPF: sun protection factor

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Original Paper

User Experiences in a Digital Intervention to Support Total Skin Self-examination by Melanoma Survivors: Nested Qualitative Evaluation Embedded in a Randomized Controlled Trial

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Abstract

Background: Melanoma is a relatively common cancer type with a high survival rate, but survivors risk recurrences or second primaries. Consequently, patients receive regular hospital follow-up, but this can be burdensome to attend and not optimally timed to detect arising problems. Total skin self-examination (TSSE) supports improved clinical outcomes from melanoma via earlier detection of recurrences and second primaries, and digital technology has the potential to support TSSE. Recent research with app-based interventions aimed at improving the well-being of older adults has found that they can use the technology and benefit from it, supporting the use of digital health care in diverse demographic groups. Thus, the Achieving Self-directed Integrated Cancer Aftercare (ASICA) digital health care intervention was developed. The intervention provided melanoma survivors with a monthly prompt to perform a TSSE as well as access to a dermatology nurse who provided them with feedback on photographs and descriptions of their skin.

Objective: We aimed to explore participants' attitudes, beliefs, and experiences regarding TSSE practices. Furthermore, we explored how participants experienced technology and how it influenced their practice of TSSE. Finally, we explored the practical and technical experiences of ASICA users.

Methods: This was a nested qualitative evaluation within a dual-center randomized controlled trial of the ASICA intervention. We conducted semistructured telephone interviews with the participants during a randomized controlled trial. The participants were purposively sampled to achieve a representative sample with representative proportions by age, sex, and residential geography. Interviews were transcribed verbatim and analyzed using a framework analysis approach applied within NVivo 12.

Results: A total of 22 interviews were conducted with participants from both groups. In total, 40% (9/22) of the interviewed participants were from rural areas, and 60% (13/22) were from urban areas; 60% (13/22) were from the intervention group, and 40% (9/22) were from the control group. Themes evolved around skin-checking behavior, other people's input into skin checking, contribution of health care professionals outside ASICA and its value, ideas around technology, practical experiences, and potential improvements. ASICA appeared to change participants' perceptions of skin checking. Users were more likely to report routinely performing TSSE thoroughly. There was some variation in beliefs about skin checking and using technology for health care. Overall, ASICA was experienced positively by participants. Several practical suggestions were made for the improvement of ASICA.

Conclusions: The ASICA intervention appeared to have positively influenced the attitudes and TSSE practices of melanoma survivors. This study provides important qualitative information about how a digital health care intervention is an effective means of prompting, recording, and responding to structured TSSE by melanoma survivors. Technical improvements are required, but the app offers promise for technologically enhanced melanoma follow-up in future.

Trial Registration: ClinicalTrials.gov NCT03328247; https://clinicaltrials.gov/ct2/show/NCT03328247?term=ASICA&rank=1

International Registered Report Identifier (IRRID): RR2-10.1186/s13063-019-3453-x

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KEYWORDS

mobile apps; melanoma; early detection of cancer; qualitative interviews; cancer survivorship

Introduction

Melanoma is a cancer of the melanocyte or pigment cell of the skin. It is the fifth most common cancer in the United Kingdom, with >16,000 diagnoses conducted annually [1,2]. Melanoma accounts for 1% of all cancer-related deaths in the United Kingdom, equaling 2300 deaths annually [2]. Although melanoma can be fatal, the relative survival rate at 5 years is high, almost 90% in Scotland, with equivalent rates across the United Kingdom [3]. Once treated, there is a high chance of recurrence as well as the development of new primary melanoma [4]. Therefore, follow-up of patients with melanoma is very important. The high chance of recurrence, combined with high survival rates, leads to a large cohort of patients who require continued surveillance. This has led to patient care after melanoma becoming burdensome to both health services and patients [5].

Melanoma follow-up is largely based on regular hospital appointments where patients are physically examined. In addition, most guidelines recommend that patients perform the total skin self-examination (TSSE) in the intervals between hospital appointments [6-9]. Studies have shown that 62% of melanomas are first identified by patients themselves, with early detection being the key to improving clinical outcomes [9,10]. Regular TSSE by patients is thought to lead to earlier detection of melanoma [10,11]. However, the rate of skin checking after melanoma is similar to that of the general population as a whole, despite it being widely recommended [12].

Technology has become commonplace in daily life and is recognized as a potential solution to health care challenges, especially in rural areas [13-15]. A recent narrative review, including 15 studies of digital rural health care interventions, reported positive outcomes for patients and health care professionals, supporting their feasibility and potential [16]. In the United Kingdom, 55% of the population in the ≥65 age group owns a smartphone, and this number increases to 96% in younger groups [17], indicating that a high percentage of the population is familiar with this type of technology. Indeed, recent research with app-based interventions aiming to improve the well-being of older adults has found that both can use the technology and benefit from it [18,19]. Qualitative interviews undertaken with melanoma survivors suggest that, with appropriate training, smartphone apps offer an acceptable means to promote TSSE between routine follow-up appointments [20]. In a recent review in the United States, the authors reported the presence of 632 downloadable apps related to dermatology [21]. Of these, 94 focused on aiding people in monitoring, diagnosing, and treating skin conditions, such as skin cancer, providing evidence that a digital approach to management is not uncommon [21]. However, although smartphone apps can be helpful in cancer management, there is still a requirement for validation of their safety and utility [22,23].

The Achieving Self-directed Integrated Cancer Aftercare (ASICA) intervention aims to prompt, support, record, and respond to TSSE conducted by survivors of melanoma, and the development has been fully described elsewhere [20,24]. The intervention was delivered via a tablet and included access to personalized skin maps, as well as feedback from a dermatology nurse practitioner (DNP) on worrisome skin lesions. Using ASICA led to improvements in the participants' well-being and TSSE adherence [25]. ASICA use also led to earlier detection and treatment of some relevant skin problems [26]. A detailed analysis of adherence suggested 3 patterns of adherence (close adherence, partial adherence, and nonadherence), as described in previous digital health adherence studies [27-29].

Qualitative studies can complement the quantitative data produced by randomized controlled trials (RCTs) by granting detailed insights into how participants have experienced the trial and intervention [30]. For the ASICA trial, a nested qualitative evaluation was conducted to facilitate understanding of how participants experienced the ASICA intervention and to attempt to explain the change in mechanisms underpinning the observed trial outcomes. In this nested study, we aimed to gather information on how the intervention and its underpinning technology could be improved ahead of the next stage of development and implementation, should ASICA be shown to have a positive impact on patient outcomes. In this nested qualitative evaluation, interviews were conducted with a representative sample of the participants in the ASICA trial. The interviews also formed part of the user-centered design approach, where users participated in every step of a product's development to fully meet the needs of the users. The first aim of the study was to explore attitudes, beliefs, and TSSE practices in people treated for melanoma who had participated in the ASICA trial. The second aim of the study was to explore how users of ASICA experienced the technology and how it influenced their practice of TSSE. Third, we wanted to determine how ASICA users believed the intervention could be improved [24].

Methods

Study Design

This was a nested qualitative evaluation within a multicenter RCT of the ASICA intervention. Briefly, the ASICA intervention was an iteratively developed evidence-based app intervention to support and improve TSSE adherence and practice by people previously treated for melanoma using tablet-based technology. The app, hosted on Android tablets, uses animated instructional videos and monthly prompts to support TSSE. The app's features included an individual digital skin map and a facility to send electronic reports of any skin concerns, including photographs, to a remote DNP. The DNP was a specialist nurse with expertise in clinical dermatology who reviewed the submitted information and assessed the patient.

Semistructured telephone interviews were guided by a predefined topic schedule (Multimedia Appendix 1). First, they explored the prior experiences of TSSE by trial participants, as well as their orientation toward technology, including its role in their health care and TSSE specifically. Furthermore, those who had experienced the ASICA intervention were asked about their practical experiences of the intervention and their views on how it might be improved. The app evaluation questions in the interview schedule were informed by a validated evaluation tool for health care apps [31]. This questionnaire was not presented to interview participants for completion during the trial; instead, its component questions were used as an aide-mémoire for the interviewer during the interviews.

Sampling Strategy

The aim was to recruit approximately 10% of trial participants (intervention and control), up to a maximum of 30 participants across both sites. Purposive sampling was used when inviting participants to ensure the acquisition of multiple viewpoints representing the demographic range of the participants in the trial. The sampling sought representative proportions by age, sex, and residential geography. Age was chosen because it is a parameter that could influence familiarity with technology and its use to monitor one's health [32]. Sex was used because it may influence adherence to health-checking behaviors [32]. Geography was chosen because the travel burden to attend follow-up appointments is well recognized for rural cancer survivors and, in theory, could influence an individual's willingness to engage with telemedicine consultations [15]. The pool for potential participants in the nested qualitative evaluation was determined from those individuals who consented to be contacted for a subsequent interview at the point of recruitment. Demographic data supported a sampling framework to ensure that invitees represented the full range of age, sex, and rurality of trial participants. We also ensured that we recruited both intervention and control group participants for interviews. Because participants in the control group had not experienced the ASICA intervention, these interviews focused on their personal experiences of and orientation toward monitoring their skin during the study year.

Recruitment

Eligible participants for the interview had completed 12 months in the ASICA trial, had not withdrawn from the trial, and had consented to be contacted for further research. Recruitment was carried out in 2 tranches, with a 6-month interval between the initiation of the ASICA trial in Aberdeen (March 2018) and Cambridge (November 2018). Potential interviewees were sent an invitation letter, a consent form, and a patient information leaflet describing the qualitative study. Participants who returned signed and correctly completed consent forms were contacted via telephone or email to arrange a suitable time for a call from one of the project interviewers for a telephone interview. All participants were given the opportunity to ask questions and seek further explanations of the qualitative study before proceeding. Recorded verbal consent was obtained before the start of each interview.

Data Collection

The first tranche of telephone interviews with the Aberdeen participants (intervention and control) was conducted in April 2019. The second tranche of interviews with the Cambridge participants was conducted in November 2019. The sequential geographical interviewing pattern reflects the fact that recruitment was completed in Aberdeen sometime before that in Cambridge. The interviews were digitally recorded, anonymized, and transcribed verbatim by a professional transcribing service.

Data Analysis

A preliminary thematic analysis was conducted on a sample of the Aberdeen interviews conducted in May 2019. Subsequently, all completed interviews were analyzed using a framework approach between April and July 2020 [33]. Professional transcriptions were uploaded to NVivo 12 (QSR International) for analysis [34]. Framework analysis was adopted because of its structured approach and for its utility in applied health research with well-defined questions and structured data, and in enabling comparison between several cases at once [35]. The first analytical step involves immersion. All transcripts were read and reread in sequence to enable familiarization with the data. This was particularly important because the analyst had not conducted or transcribed the interviews. A third reading identified the main themes and subthemes that were applied to the data and used to develop the initial analytical framework, which was checked, adapted, and agreed upon by the authors. Because the main analysis was completed by an analyst who had not conducted the interviews, the decision that data saturation had been reached was not straightforward. The pragmatic view was that, because similar themes were repeated in the Aberdeen and Cambridge interviews, the sample size was sufficient to capture the most important issues from the perspective of participants. A second analyst independently read and coded 3 interviews (approximately 10% of the sample) using the framework. Subsequent discussions enabled further minor adjustments and refinement of the framework. The final framework is available in Multimedia Appendix 2.

Subsequently, each interview transcript was coded in NVivo 12. All relevant data were sorted into identified themes and subthemes. The data were charted and interpreted thematically. Data from different respondents were compared, and an overview summarizing the data from each theme was created. Special consideration was given to the influence of individual demographics on their experiences, feelings, opinions, and suggestions for improvement. Finally, a full thematically structured narrative account supported by tabulated illustrative quotes was produced.

Ethics Approval

For the ASICA study, ethics approval was given by the National Research Ethics Service Grampian Ethics committee on April 28, 2017 (reference number 17/NS/0040), and all participants gave written informed consent. This qualitative substudy received further ethics approval from the North of the Scotland Research Ethics Committee in February 2019 (reference number 17/NS/0040). This study was approved by the National Health System Grampian Research and Development in March 2019. All methods were carried out in accordance with Good Clinical Practices and the research governance and quality assurance policies and procedures of the University of Aberdeen.

Results

Sample Demographics

Of the 240 trial participants, 212 (88.3%) had consented to be contacted for further study. Invitations were sent to 32 participants (20 Aberdeen and 14 Cambridge), of whom 22 (13 Aberdeen and 9 Cambridge) replied that they were willing to participate in a telephone interview. Therefore, 22 telephone interviews, ranging in duration from 10 to 45 minutes, were completed and transcribed. In total, 60% (13/22) of the interviewed participants were in the intervention group, and 40% (9/22) were in the control group. The mean age of the participants was 56.3 (SD 14.7) years. In total, 45% (10/22) of the interviewees were female, and 55% (12/22) were male; 40% (9/22) of the interviewed participants were from rural areas, and 60% (13/22) were from urban areas. In total, 5% (1/22) of the interviewees lived in the second indices of multiple deprivation quintile, 10% (2/22) in the third quintile, 32% (7/22) in the fourth quintile, and 53% (12/22) in the fifth quintile. During coding, 6 main themes emerged: skin-checking behavior; friends and family; other health professionals; ideas around technology; "nuts and bolts"—practical experience of the ASICA trial; and finally, ASICA: the app impact, design, and usability. See Multimedia Appendix 2 for the full framework, themes, and subthemes.

Theme 1: Skin-Checking Behavior

How Often and How Thoroughly Participants in Both Intervention and Control Groups Checked Their Skin During the ASICA Trial

More than three-quarters of the participants interviewed stated that they regularly examined their skin. Of those who did not, only 1 was in the ASICA intervention group. It appeared that living alone was a potentially determining factor, as well as not having someone to encourage, remind, and help them check awkward or difficult-to-see areas of the body. Individuals living alone tended to await for regular hospital follow-up appointments, feeling that they were sufficient for monitoring their condition. Those who regularly checked their skin mentioned a variety of approaches. The most common method was an unstructured look over. This idea ran through most interviews with participants, stating that it was part of the daily routine to "keep an eye" (Female, 49 years, control) on things:

> *I have a quick check to see there's no other strange things happening and there isn't.* [Male, 76 years, control]

> *I mean I do keep an eye on it, I don't know if you would class it as examining.* [Female, 48 years, control]

Almost 90% of the intervention group stated that they used ASICA to aid skin checking, and most reported following the instructions provided, which were designed to facilitate high-quality skin examination. Two participants in the intervention group stated that they no longer used the app to check their skin; however, 1 described using what it had taught them initially to continue checking their skin using their own tablet:

> *Well I use the app, just look at the pictures and then look at the, look at the bits on my, bits on my skin, I usually get my husband to look at my back, backs of my legs and down my back and that.* [Female, 47 years, intervention]

> *The ipad is quite good at taking pictures close up as well, so that's what we used, I find it a lot easier [than the study tablet], and it moves a lot easier to touch.* [Male, 54 years, intervention]

It was generally apparent from the interviews that skin checking was widely occurring and valued, but that the thoroughness and effectiveness of checking varied between individuals. All but 1 ASICA user reported making a conscious effort to check their skin regularly in a structured way, and approximately one-third stated that they had communicated concern about the study DNP using the app. Together, this suggests that ASICA can appropriately support skin checking, although further research is required to confirm this. Notably, 2 participants in the control group reported having used technology to digitally enhance their own skin checking and were tracking areas of concern with photos stored on their mobile phones.

Timing of Participants From Both Intervention and Control Groups Checking Their Skin

Although there were variations in how often and how thoroughly people checked their skin, the contexts in which the checks were conducted were consistent. Almost all mentioned checking their skin when they showered, with washing being a near-universal prompt:

> *If I've had a shower or whatever, I'll sort of look, does that look different, or does it not.* [Female, 47 years, intervention]

The app users stated that the monthly reminders were useful prompts to remember to perform a structured skin check:

> *Every month I get a reminder to, to go over it on the app and check from top to toe.* [Male, 61 years, intervention]

Not only did the participants in the intervention group mention that the trial was triggering them to check skin but also a participant in the control group stated that taking part in the trial had influenced her to change her perceptions and personal practice with respect to skin checking.

The questionnaire probably acted as a reminder for me to do a little bit more. [Female, 49 years, control]

Views About Knowledge and Skills Required to Perform a Skin Check From Both Intervention and Control Groups

Although all participants in the intervention group had received training on how to perform a TSSE as part of the intervention, reports of having received training to conduct TSSE in the past as part of usual care varied between individuals and study sites. Overall, 4 of the 6 Cambridge participants reported having received TSSE training, whereas only 3 of the 14 Grampian participants had received TSSE training before joining the study. Some participants had skin checking explained and demonstrated to them by a specialist, such as a nurse or a physician:

> *Fairly good instructions, and usually from the nurses more than the doctors, but on the skin checks I've had through the NHS, they, they've been quite good in terms of tutorials, so I'm quite happy in terms of what I'm looking at.* [Female, 39 years, control]

Less than one-quarter of the participants reported having received a leaflet explaining TSSE, whereas several participants reported no knowledge or education about TSSE.

> *I'll just have a look, but no, never been told, whatever the, never been verbally told, there was a leaflet sometime back.* [Male, 51 years, control]

> *I haven't been taught by anybody. I've been doing it for so long, I just know.* [Male, 49 years, control]

Beliefs About Skin Checking in Both Intervention and Control Groups

The value people placed on skin checking varied among individuals, but some dismissed its value, and it appeared to be rarely considered an active health improvement practice:

> *How do you learn to check your skin, you just look!* [Female, 76 years, control]

The relationship between previous melanoma and current health did not appear to be acutely perceived; only 1 participant mentioned previous melanoma when asked about their general health. Some participants' opinions and beliefs about skin checking appeared to change after using the ASICA app:

> *I would just say you're, you're far more aware of it, checking your skin and stuff now as what you ever, maybe more so now, than what I was previous.* [Male, 54 years, intervention]

Overall, for members of the intervention group, using the ASICA app appeared to increase positive attitudes toward and frequency of practice of TSSE.

Feelings About Skin Checking in Both Intervention and Control Groups

Although it was possible that frequent skin checking could function to increase or heighten worries about melanoma recurrence, there was little evidence within the transcripts that feelings and emotional responses to skin checking were especially powerful. For most, it appeared to be a straightforward and nonemotive practice.

Of those who did, some respondents in both the intervention and control groups expressed a lack of confidence in their own ability to correctly self-check and identify changes that may be indicative of recurrence, suggesting that they saw this as a health professional's role. This view tended to be expressed more by younger respondents:

> *I feel more happier if there's someone told me that, you know, everything is right with my skin, and that's the words coming from the specialist, and not me after checking my skin on the app, so you know.* [Male, 39 years, intervention]

One intervention group participant suggested that before using ASICA, their skin checking had been an ad hoc activity to reassure themselves when they became worried about something. Another intervention participant implied that ASICA worked well for them, but only because they were already confident in their ability to check their skin. None of the participants stated that they felt the need to use the tablet provided for skin checks more regularly than once a month:

> *[Before starting using the ASICA app] I just kind of tended to keep an eye on things generally, you know, without kind of saying, oh I must do it this week or whatever, I just do it whenever, whenever it came to mind, but quite often I would say, because I was kind of worried about it.* [Female, 47 years, intervention]

Theme 2: Family and Friends' Input Into Skin Checking—Opinions From Both Intervention and Control Groups

Previously, one of the perceived difficulties with skin checking was that it was difficult to perform thoroughly alone. Not all participants received regular help with skin checking, although approximately three-quarters did:

> *The bit I can't see is my back, so my husband checks that for me regularly.* [Female, 53 years, intervention]

Views on the absolute necessity of having assistance varied. Two participants perceived themselves as being unable to complete effective TSSE, particularly when checking their backs, without the support of another person. In contrast, other 2 mentioned completing it alone (eg, using a mirror), and 1 saw no barrier to other people doing the same. Clearly, individual experiences, circumstances, and capabilities were influential in determining attitudes toward this aspect of skin checking:

> *I find quite difficult, well I, well I sometimes don't get that all done actually, when I'm on my own, no.* [Female, 73 years, intervention]

> *The most difficult is the scalp, because you obviously can't see that, so but I've got short hair, so it's not too bad, the rest you can pretty much do yourself, with a mirror.* [Female, 62 years, intervention]

Theme 3: Input of Health Professionals Outside the ASICA Trial—Experiences From Both Intervention and Control Groups

The involvement of health care professionals outside the trial varied according to the demographic and health status of the interviewees. Some had been attending scheduled melanoma follow-up appointments in the hospital during the study period, others had completed follow-up appointments and had seen only their general practitioner as required, whereas others had received no health professional contact at all:

> *They're remarkably busy as, as you would expect and so I was discharged from dermatology and advised that if I had any concerns that I would, should see my GP.* [Female, 49 years, control]

Participants generally perceived difficulties and barriers to obtaining appointments for their skin in both primary and secondary care:

> *She had to refer me to a GP which, and she, and I had to wait three weeks to see the GP.* [Female, 73 years, intervention]

Two interviewees discussed having a lack of confidence in their GP's expertise on skin and the corresponding ability to reassure them when concerns arose. However, overall, approximately half reported that they were highly satisfied with the care they were receiving. Approximately a quarter of the participants expressed a preference for receiving specialist care rather than care from a GP:

> *Prefer to speak with the, some kind of professionals, someone like a dermatologist, than just checking myself, because you know, if you see your, your body on a daily basis, it's difficult notice that any changes or something is going on, especially on the back of my body.* [Female, 48 years, control]

Theme 4: Ideas Around Technology From Both Intervention and Control Groups

Participants in the sample were relatively experienced in using technology, with more than three-quarters of the participants saying that they used digital devices and apps every day. Most older participants were already familiar with technology and did not perceive it as a barrier to participation because they reported receiving good training at the start of the study. Two participants who were not as keen on using technology in health care were from the control group, both female, rurally based, and aged >70 years. Both appeared relaxed about their skin and viewed ongoing structured skin checking and follow-up as potentially burdensome and stressful:

> *I don't know, I don't know if it's an app or not. Well I mean, I've got two apps on my phone today. One of which works and one doesn't yet.* [Female, 76 years, control]
>
> *Oh gosh, daily, many, many times a day.* [Female, 48 years, control]

The use of other skin-checking apps was rare, and most participants were unaware of their existence. One participant in the control group had used another skin-checking app but found it ineffective; however, using ASICA intrigued them. Previous experience of using digital technology specifically for health care was limited within the sample, but there was a general agreement that technology offered promise for more efficient care in the future. One described ASICA as "like a real innovation" (Male, 39 years, intervention).

However, there were contrasting views on the direction of the influence of technology on health care in the future. Generally, younger participants and those from rural settings expressed the most enthusiasm. One participant perceived efficiencies of care, whereas another clearly felt that technology could not substitute for personal face-to-face care:

> *We use mobile technology and phones and apps so much these days, I think it's the way to go. It prevents you sort of wasting the GP's time.* [Female, 62 years, intervention]
>
> *I don't rely...on the ASICA thing to actually keep me ... up to date, if I've got a, really concern, I would contact the hospital. Think it's nice as a backup, but when it comes to actually examining moles that could be cancerous I think that still needs to be done by [specialist], when they check me, they're using a specialist eye glass.* [Female, 53 years, intervention]

Confidentiality and data protection are clearly important considerations when using technology to deliver health care although, notably, only 1 of the interviewees directly volunteered concerns about confidentiality. The concern was about their own device security rather than data misuse:

> *I wouldn't want any images being stored and easily accessible on my device, so happy if it's all kind of encrypted and locked away by passwords, so that would be a big deal for me in terms of where any data was stored...no problem with it being uploaded to external storage, but I would have an issue with it being stored locally.* [Female, 39 years, control]

When asked about the qualities that effective digital health care apps should possess, participants reported that they should be coherent and consistent in purpose, straightforward, uncomplicated, and easy to use. It was also said that it is important that apps contain enough information for them to be used effectively, and that they signpost the user to further help if needed.

Theme 5: "Nuts and Bolts"—the Practical Experience of the ASICA Trial—Opinions of the Intervention Group Only

Participants in the intervention group who had used the ASICA app reported few technical problems. Most importantly, there did not appear to be any particular issues experienced and associated with a single demographic characteristic. One significant issue was that 1 participant stated that they had not received monthly prompts through SMS text messages (ID: *11018, male, 39 years, int*). Furthermore, 2 participants reported that some photographs appeared missing from their digital skin maps. The hardware provided (Samsung Galaxy tablets) did appear to have created technical problems with slow functioning and charging difficulties. The operating system of the tablet was identified as a barrier to its use:

> *The Samsung app's a bit slow and cumbersome and just not quite up to speed really is what the ipad is.* [Female, 62 years, intervention]

Another issue expressed was the tablet's camera, a key requirement of ASICA for reporting. Just under a quarter of the intervention group interviewed submitted poor quality photos [26], hindering interpretation and assessment of the photographed lesion by the Dermatology Nurse Practitioner. This then required the submission of further photos, usually from their smartphones, to enable the assessment to be completed:

> *They didn't get a good enough picture using the tablet, and so when, the guy phoned me back the next day, he said can you use your smart phone to take a picture, and then send through, because just because the, what he could see, like I'm not really sure what I'm looking at.* [Female, 48 years, intervention]

In general, most participants viewed participation in the ASICA trial positively. Many expressed interest in participating as having an altruistic intent to improve care for others rather than to expect a personal benefit.

Theme 6: ASICA—Impact, design, and usability—What Did the Intervention Group Think?

Feelings About Using ASICA

In the ASICA trial, the primary outcomes measured in both groups were psychological well-being and quality of life measured using the melanoma worry scale, Hospital Anxiety and Depression Scale, and EQ-5D [29]. A mixture of views was expressed on these points by the ASICA users interviewed here and are found in subsequent sections.

Two participants indicated an initial increase in concern when they began using ASICA but suggested that this decreased as they continued to use it. Another participant stated that the app did not change their worry level but suggested that this may not have been the case if they did not have regular access to specialists as part of the ongoing scheduled melanoma follow-up. In contrast, some participants reported finding that they became less anxious when they started using ASICA and were positive about the app, enabling people who are likely to worry about the opportunity for greater reassurance compared with less structured alternatives. Importantly, it did not seem that the arrival of email or text prompts reminding participants to perform a TSSE led to an increase in anxiety:

> *I think having the app kind of brought it back for a while, and I think looking at the pictures didn't really help that, to start with, but I kind of came okay again, with kind of regularly using it.* [Female, 47 years, intervention]
>
> *I don't worry too much, because I am still under the hospital.* [Female, 53 years, intervention]

Barriers to and Facilitators of Engaging With ASICA

It appeared that those who had completed follow-up and were no longer receiving regular hospital appointments, especially liked using ASICA. One reported that it gave them a sense of "no longer being off the radar." Conversely, 1 intervention group participant said they relied on and engaged less with ASICA after being initially enthusiastic, because they still had ready access to a dermatologist and felt they were receiving enough input from them. ASICA users also reported that it was more convenient to use the app to submit concerns about their skin, rather than having to travel and park at the hospital to attend outpatient appointments. There was a sense from some, however, of a certain unwillingness to completely trust the ability of the app to detect something as serious as cancer. Another respondent underlined that the validity of ASICA had not been proven because it was novel and untested. For this individual, the concern was mitigated by the safety net of still being in formal follow-up. The interviews were completed before the COVID-19 pandemic; therefore, it was not possible to determine whether the experience of the pandemic had an influence on participants' views.

Areas for ASICA Improvement

The layout, design, and functionality of the app were generally well-received, and only a few participants offered feedback for improvement. The addition of a skip button to prevent skin-checking instructional videos from playing in full each time was mentioned by 2 participants as a time-saving measure. Furthermore, the ability to pinch and zoom on skin map digital photos and clearer orientation is also recommended. The largest area of feedback was that the app should be made available for different operating systems and devices, specifically Apple, so that future users could use the app on their own devices rather than the 17.8-cm tablets, which were reported to be awkward to use by some:

> *You have to watch all the videos before you can just go into actually doing the, the, putting in your data, and that, so and that drives me mad.* [Female, 48 years, intervention]
>
> *I hate that ruddy bit of kit I'm supposed to sort of keep in communication with you, it's a Samsung thing, I'm an Apple man, so I hate the damn thing, so that gets me frustrated, because I don't understand.* [Male, 86 years, intervention]

Discussion

Summary of Main Findings and Comparison With the Literature

Melanoma follow-up is extensively practiced and, in recent years, has become more important because improved treatments mean that detecting new primaries and recurrences at an early stage offers the best outcomes for people with melanoma [36]. There is growing evidence on the value of TSSE as part of follow-up and how it is perceived and best performed by patients [37].

This nested qualitative evaluation showed a range of experiences, behaviors, beliefs, and feelings among people previously treated for melanoma with respect to their skin, skin checking, and technology in improving TSSE awareness, practice, and quality. Most participants stated that they checked their skin regularly but that using the ASICA intervention increased the frequency and consistency of checking and supported a more systematic approach to their skin-checking practices. Most participants did not believe that ASICA had changed their feelings around skin checking, but it had raised their awareness and changed their own skin-checking behaviors for the better. Some ASICA users reported that the intervention improved their confidence regarding when and how they checked their skin.

Few participants managed skin checking alone, and opinions on the role of health professionals in satisfactory skin checking were mixed. Interestingly, follow-up and melanoma care by GPs were viewed positively in a study in the United Kingdom, in contrast to some negative views expressed here [38]. GP follow-up has been previously viewed as a low-tech solution to the challenge of increasing melanoma follow-up burden. Now, perhaps, ASICA, with its facility of rapid access to a remote dermatology specialist, offers a more elegant solution consistent with the priorities of melanoma survivors. Participants in this study valued specialist input and the opportunity to contact a specialist during scheduled follow-ups.

A systematic review of 15 studies further identified reassurance from qualified professionals as reducing worry [39]. This was also found in the present data, with participants feeling reassured that a specialist nurse practitioner reviewed their submitted concerns and images. The added dimension in this study was that anxiety may peak when commencing TSSE (declining thereafter as skin checking becomes more routine), a point that could be borne in mind when developing training and preparing people to undertake TSSE. In contrast, several participants viewed the app as a means of providing rapid reassurance when concerns arose.

Several studies have demonstrated that there is anxiety after melanoma around attendance at follow-up appointments [40]. Our qualitative data consolidate the findings of an earlier qualitative study that identified structured skin checking as a reassurance technique for those who experienced anxiety following a melanoma diagnosis [41]. These investigators also suggested that low self-confidence about skin checking was a barrier to achieving this benefit; therefore, our respondents' view that ASICA improved their confidence in performing TSSE is very encouraging [41]. Overall, the use of ASICA did not appear to result in adverse psychological effects. Some participants suggested that ASICA temporarily and briefly increased their anxiety about skin checking at the start, but that this has settled over time with regular use.

This study was conducted before the onset of the COVID-19 pandemic and its disruptive effects on all aspects of cancer care. However, even then, participants were almost universally well-disposed to technology becoming an integral part of their health care, with the caveat that personal interaction can be an element of high-quality care. Most saw the potential of digital technology and the likelihood that it will be increasingly used to facilitate health care in the future.

Participants had mainly positive experiences of using the ASICA intervention and made several useful suggestions to improve usability and functionality. With the user experience in mind and aiming for an app that meets the needs of melanoma survivors that are using it, these suggestions will be incorporated into the newest version of the ASICA prototype. The hardware provided had perceived limitations, with several participants reporting issues with the camera (providing images of poor clarity) and the operating system (slow functioning and charging difficulties). There was no capacity to make adjustments during the trial. All feedback has been noted, and an updated prototype is currently being developed. The unwieldy 17.8-cm tablet was perceived by some as a major barrier to using ASICA effectively and may have contributed to lower adherence for some [27]. Adherence to the intervention was explored in a further paper [27] and it was found that baseline depression, anxiety, and low confidence (also highlighted here) predicted adherence. The means of improving adherence will be a major focus of future work.

Travel and distance have previously been recognized as barriers to participating in and benefiting from melanoma follow-up, whereas having a life partner has been cited as an important source of support for successfully completing a TSSE [39,42]. In this context, the positive views expressed by our rural participants are encouraging and support the prevailing view that remote health care represents an effective way to meet the challenges of geography in the future.

Finally, age did not appear to be a barrier to the adoption of ASICA, with older users generally reporting that it was easy to use and that the training prepared them well. This suggests that older people are sufficiently familiar with technology, and that the design of ASICA avoids an age-adoption barrier [24].

Strengths and Limitations

Nesting qualitative interviews within the main ASICA trial enabled an in-depth exploration of participants' beliefs about their experiences with skin checking, use of technology, and the ASICA app. It also provided access to participants who were actively thinking about and engaged with TSSE to provide qualitative data that would facilitate understanding of the quantitative results of the ASICA trial. The ASICA app was initially field-tested with 19 participants and then revised for the current trial according to the participants' feedback [24]. The results provide invaluable insights into how digital health care is perceived and experienced by these users, which is very important given the likely increasing role of technology in delivering dermatology care in the future National Health System.

Of the 240 ASICA participants, 221 (92%) consented to be contacted for the interview. There were no striking demographic differences between the participants who consented to be interviewed and those who declined to participate. However, we recognize that this substudy has the potential for selective recruitment bias. This nested qualitative evaluation sample size of 22 participants represented almost 10% of the total number of participants in the ASICA trial. This sample was purposefully selected to include a range of demographics from 2 UK sites, with locations further assessed to assure representation of both urban and rural participants. This sampling method ensured an enhanced representativeness. Including participants from both the intervention and control groups enabled a further dimension of understanding in the analysis, enabling the attitudes and experiences of those who had experienced the intervention to be compared.

In contrast, the sample was, on average, relatively well-educated and affluent, with an underrepresentation of participants from deprived backgrounds. This is important because individuals from deprived backgrounds are likely to face more challenges in adopting digital health care [43,44] and should be given higher priority for digital health care research. There is also the possibility of volunteer bias, because those agreeing to be interviewed were likely to be interested in technology. This may be reflected in the generally positive tone of the data, along with detailed infrastructural frustrations.

Importantly, there are likely to be differences between participants who did and did not fully engage with the ASICA intervention over the course of the trial. Such differences are both theoretically and clinically relevant, indicating, respectively, who is least likely to engage with the intervention provided and who is least likely to benefit as a result. It was not possible within this qualitative study to capture the experiences of those who did not fully engage with the intervention, as these participants were the least likely to provide consent to participate in an additional interview. This issue could be explored in the future by analyzing TSSE adherence data collected during the ASICA trial to identify the characteristics of those who did not engage.

The interviews were conducted on 2 tranches by 2 different interviewers. The transcripts from both sets of interviews were then analyzed by a third researcher with support from a senior qualitative researcher and senior clinical researcher. We believe there are limitations and strengths of this approach, which is similar to the accepted practice of secondary analysis of qualitative data [45]. This enabled the data to be considered from different disciplinary perspectives and also provided an objective and consistent interpretation of the written factual data. However, this approach clearly precludes any interpretation based on a recollection of the emotional tone during particular interviews. This limitation was somewhat mitigated by FR spending considerable time immersed in the data over 3 detailed readings. Furthermore, the ongoing involvement of all members of the research team ensured agreement with the emerging themes and overall interpretation. The layered approach to the study also reduced individual researcher bias. In the context of the responses from ASICA users, this has given quite a clear sense, with respect to ASICA, of what worked well, what did not, and what needed to change.

This nested qualitative evaluation study embedded within an RCT provided findings that complement the main trial findings. With the caveat of some practical issues (mainly relating to a suboptimal digital interface as currently configured), ASICA was positively received by users who found it helpful and that it improved attitudes toward the frequency and thoroughness of a TSSE. Some participants reported an initial upswing in anxiety related to using the ASICA, but this subsequently settled over time. The system was effective and viewed positively in general, with some constructive suggestions made for improvement. The study provides important qualitative information that a digital health care intervention is an effective means of prompting, recording, and responding to structured TSSE by melanoma survivors. Furthermore, it appears that ASICA has the potential to improve future aftercare for melanoma survivors. However, the limitations of the proposed technology must be recognized. It currently works better than others. However, we have a good basis for further work to develop our prototype to enable a wider demographic range of melanoma survivors to benefit maximally.

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Data Availability

The data sets generated and analyzed during this study are not publicly available because of concerns about the potential for individual participants to be identified from the data and the scope of the ethics approvals received. However, data may be available from the corresponding author upon reasonable request and subject to appropriate safeguards.

Authors' Contributions

PM conceived the study with intellectual contributions from FR, NW, SH, HM, JA, and LC. NW and SH conducted interviews with project management support from LC. FR analyzed the data with inputs from PM and HM. PM and FR wrote the manuscript, with comments on drafts from NW, SH, HM, JA, and LC. MN helped with the analysis, interpretation, writing, and drafting of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Achieving Self-Directed Integrated Cancer Aftercare qualitative study topic schedule.
[DOCX File , 38 KB - derma_v6i1e39544_app1.docx]

Multimedia Appendix 2
Framework.
[DOCX File , 17 KB - derma_v6i1e39544_app2.docx]

Multimedia Appendix 3
CONSORT-eHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 1231 KB - derma_v6i1e39544_app3.pdf]

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Abbreviations

ASICA: Achieving Self-Directed Integrated Cancer Aftercare
DNP: dermatology nurse practitioner
RCT: randomized controlled trial
TSSE: total skin self-examination

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Original Paper

Refusal of Retreatment With Topical 5-Fluorouracil Among Patients With Actinic Keratosis: Qualitative Analysis

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Abstract

Background: Actinic keratosis (AK) is a common premalignant skin lesion, and topical 5-fluorouracil (5-FU) is commonly used in field-directed therapy. However, 5-FU is associated with frequent local skin reactions.

Objective: This study aimed to qualitatively assess experiences among patients with AK who refuse retreatment with 5-FU.

Methods: Semistructured interviews were conducted with 10 adult participants who had received treatment with 5-FU for AK between January 1, 2017, and January 1, 2020, and refused future treatment with 5-FU. Results were analyzed using qualitative research methods.

Results: Although most participants had low concern upon having received a diagnosis of AK, most felt that treatment is very important. When initiating treatment with 5-FU, most cited recommendation by their health care professionals as the primary motivator and initially had low concern regarding treatment. The side effects associated with treatment were physically and psychosocially burdensome for most participants and led to temporary lifestyle adjustments. After treatment, most did not believe that their health care provider prepared them for treatment or were unsure. While half of the participants felt that 5-FU helped treat AKs, half were either unsure, due to premature discontinuation, or did not think that 5-FU treated their AKs.

Conclusions: 5-FU is one of the most commonly prescribed treatments for AKs, yet most patients experienced both a physical and psychosocial burden with the treatment. Inability to assess efficacy due to premature discontinuation secondary to 5-FU–related reactions is common, and shared decision-making, navigating treatment options, and taking into account patient preferences may be critical to help assure better adherence and outcomes. Although our study was limited by input from participants who refused future treatment with 5-FU, most stated that they would still continue to seek treatment for AKs in the future and would consider other topical treatments, especially if associated with a milder tolerability profile.

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KEYWORDS

actinic keratosis; solar keratosis; topical 5-fluorouracil; fluorouracil; topical treatment; cancer; carcinoma; neoplasm; oncology; pharmacotherapy; pharmacological; malignant; malignancy; tolerability; adherence; preference; opinion; attrition; attitude; perception; qualitative; skin; dermatology; lesion

Introduction

Actinic keratosis (AK) is a common premalignant lesion clinically presenting as a scaly, red papule on sun-exposed areas of the skin [1]. AKs are treated using a variety of different treatment modalities to prevent progression to invasive squamous cell carcinoma [2]. Treatments can either be lesion-directed (for limited lesions) or field-directed therapies that target areas of skin with multiple AKs and clinical evidence of field cancerization [2].

Topical 5-fluorouracil (5-FU) is a commonly used field-directed therapy to treat AK [2]. It blocks DNA synthesis by inhibiting thymidylate synthetase, which targets the rapidly growing dysplastic cells involved in AK pathogenesis and causes the cells to undergo apoptosis [3]. Topical 5-FU may also be the most efficacious field-directed treatment for AK according to a network meta-analysis [4]. While topical 5-FU is commonly used to treat AKs, many patients experience adverse effects, especially burdensome local skin reactions (LSRs), including inflammatory erythema, scaling, crusting, swelling, erosion, and localized pain [3,5]. LSRs are seen in up to 90% of patients [5]. These can be bothersome and can interfere with activities of daily living and social engagements, leading to a negative impact on quality of life [6].

Adverse effects, frequent dosing, and prolonged duration of treatment can lead to poor adherence, early discontinuation of treatment, and may deter patients from future retreatment with 5-FU [5]. Few studies have assessed adherence to topical 5-FU, and LSRs may discourage patients from seeking treatment for future AKs; some patients refuse to use 5-FU a second time, potentially increasing the risk of malignant transformation [5,7]. Moreover, there is limited literature assessing patient experience with 5-FU treatment. Previous studies using interventions, such as educational videos, to improve patient satisfaction have also not been successful [8]. To further characterize the adverse effects of topical 5-FU and its impact on future use, we qualitatively assessed patient experience among those who stated they would refuse future treatment with 5-FU.

Methods

Recruitment

Participants who received a clinical diagnosis of AK (ICD10: L57) and had received treatment with 5-FU between January 1, 2017, and January 1, 2020, were identified through a retrospective review of patients from the Atrium Health Wake Forest Baptist Dermatology Clinic. Potential participants were contacted for assessment, and telephone interviews were conducted with 10 participants who refused future treatment with 5-FU. Multiple reports analyzing patient cohort sizes in qualitative research have suggested the utility of a small sample size, particularly among homogenous populations, such as ours, to address the research question. Specifically, certain commentators have suggested a sample size of 10 to be adequate to sample among a homogenous population [9,10]. Participant recruitment was additionally terminated once thematic saturation was achieved. Each participant received a unique identification code as “Pt#.”

Interviews

Data were collected through audio-recorded semistructured interviews. Interviews lasted between 7 and 33 minutes. Participants were asked about details regarding 5-FU use (indication, dose, duration, outcome, and condition response), medication regimen details (additional medications taken), impact that treatment has had on patient life, and adverse effects experienced. Every participant was asked 22 core questions (Textbox 1). Additional questions were asked to clarify or expand upon responses.

Textbox 1. Interview questionnaire listing the questions asked during semistructured interviews with the study participants.

1. Can you please tell me how you felt when you were diagnosed with actinic keratosis (AK)?
2. How important to you is receiving the proper treatment?
3. Why do you consider treatment important/not important?
4. Please, tell me about your previous experiences with treatment—if you had any?
5. When receiving treatment, did you get any support? From whom? Did it help?
6. Have you previously (in the past) discontinued your treatment for AK? Why?
7. Please, tell me about your experience of using the topical 5-fluorouracil (5-FU) cream?
8. What made you use the medications?
9. How did you feel about the 5-FU treatment?
10. Can you tell me about the challenges you experienced?
11. Did you have any concerns about the treatment? Can you describe them for me?
12. Did the use of 5-FU help treat your AKs?
13. How did the 5-FU affect your everyday life? In particular, has this affected social activities or your job responsibilities?
14. How did the 5-FU treatment make you feel about your appearance?
15. What effects did taking the medicine have on you?
16. Can you describe your side-effects? (When did they occur? How long did they last? Which one was the worst? Did anything make the side effects better?)
17. How did you feel during that time?
18. Were you prepared by your health care provider to manage the side effects? Can you describe how that affected you?
19. Did the side effects cause you to stop the treatment?
20. Did the side effects outweigh the benefits of treating your AK?
21. In the future, would you be willing to try other topical treatments for AK? Why/why not?
22. In the future, would you seek treatment for AK? Why/why not?

Method of Analysis

The semistructured participant interviews were recorded, carefully reviewed, and then transcribed verbatim upon conclusion of participant interviews. Results were then analyzed using both descriptive statistics and a qualitative research method. The interview transcriptions were initially reviewed by study team members (RS, SM, and SRF) and then coded by 2 members of the study team (RS and SM). Preliminary codes were initially identified using open coding and collaborative analysis. The codes were then clustered in accordance with categories, and themes were then used for further data refinement per conventional qualitative analysis as described in literature [11]. Representative quotations were extracted for illustrative purposes. NVivo (version 11; QSR International) software was used to analyze data and aid in data management.

Ethical Considerations

This study received ethics approval from the Wake Forest University of Health Science's institutional review board (IRB00077121).

Results

Overview

A total of 1276 potential participants were identified (mean age 68 years, 69% male, and all of them were White). All of the 10 participants included in this study identified as male and were White (mean age 66 years, range 39-89 years). Participant interviews revealed 4 major themes centered on how participants felt and their concerns about a diagnosis of AK, motivation to start 5-FU treatment, experience during treatment and perception of preparation, and how treatment affected perception of AK and future care.

Participants' Concerns and Input When Diagnosed With AK

There was low concern among most participants upon having received a diagnosis of AK, although some were shocked or unhappy with their diagnosis. While most were not overly concerned regarding their diagnosis, almost all participants considered treatment very important, and most specifically cited the underlying carcinogenic etiology of the lesion as the reason for the criticality of treatment. Other less commonly stated reasons for concern included general health concerns and embarrassment associated lesion appearance (Table 1).

Table 1. Representative quotes exemplifying participant reactions to their diagnosis of actinic keratosis and their initial motivation to use topical 5-fluorouracil cream.

Theme	Quote
Concern and input when diagnosed with actinic keratosis	• *Well, I don't want to have this disease or any other if I can help it. And of course they want to remove it if I had it….I think I was shocked to hear the word cancer associated with my health.* [Pt #2] • *I've had them for years and I treated them in the past. And so it was just something that from time to time I will treat them to so they don't get any worse.* [Pt #5] • *I have known people to die of skin cancer at an alarming rate. If you were to ask me what I know most of them to die from, cancer would be probably in the top five.* [Pt #6]
Motivation to start topical 5-fluorouracil treatment	• *No, I didn't have any concerns. I mean you're talking to someone who about always trusted my doctors to give me medication that was going to be what I needed and that it would work and never imagined that there would be you know a shortfall in quality of what I got.* [Pt #2] • *It was just the doctor's recommendation initially.* [Pt #3] • *No, not really. I trusted the physician that was prescribing and I read did some research on myself.* [Pt #7]

Patient Motivation to Start 5-FU Treatment

When participants were asked why they initiated therapy with 5-FU, almost all stated the recommendation by their health care provider (HCP) as the reason. Moreover, almost all participants stated they had no or very low concern at the time 5-FU was recommended and prescribed by their HCP. Trust in the prescribing HCP was a pervasive subtheme that participants mentioned to explain the lack of concern. Most participants had received prior interventions for their AKs, and only 3 participants stated they had never received any previous treatment for AK. Among the treatments referred, cryosurgery and other surgical interventions were the most common. Photodynamic therapy and treatment with another topical medication were also referenced. Only one participant stated having previously discontinued treatment for AK (Table 1).

Experience During Treatment and Perception of Preparation

Almost all participants experienced difficulty during treatment with 5-FU, specifically due to symptoms from 5-FU–related adverse effects. Pain or burning at the site of the application was most commonly reported by participants. Other common adverse effects that caused patient difficulty during treatment included red or inflamed skin, peeling, sloughing, and flaking of the skin, and blistering of the skin at the site of application. Most participants stated that symptom onset occurred within days of 5-FU application and resolved within days to 2 weeks after application cessation. However, there was a particular subset of participants who reported residual effects of the medication for months after application cessation (Table 2).

Treatment with 5-FU also was associated with a negative impact on participant self-perception. Particularly, many participants stated they felt self-conscious or embarrassed while receiving treatment, particularly in those who experienced visible inflammation in their skin with associated blistering or peeling of the skin at the site of application. The treatment, and associated visible symptoms, also caused a pervasive impairment in the social activities of participants, although most stated that the treatment itself did not physically limit them from completing daily activities. A subset of the participants also experienced impaired sleep during treatment (Table 2).

When asked regarding challenges faced while on treatment, most participants referenced 5-FU–associated pain and an overall lifestyle adjustment they had to make while on therapy. Specifically, participants stated issues with application of the medication, especially around bedtime to avoid smearing of contents, and preparation for their social appearance (Table 2).

Overall, all participants felt they were not adequately prepared by their HCP on what to expect while on treatment and few were also unsure whether their HCP had adequately informed them before treatment. During treatment, participants reported that they either received support from their family and their physician or their staff, from just their family, or just from their physician or staff. Some participants, however, stated that they received no support while on treatment (Table 2).

Table 2. Representative patient quotes regarding treatment experience and preparation.

Theme	Quote
Experience during treatment	• *It made me look very sick. Cause my face and arms were extremely red. And at times had blisters on them.* [Pt #1] • *It was difficult because it was painful and unsightly….if I were to say bad, that would mean to me very, very painful.* [Pt #2] • *[Which side effect that you described earlier was the worst sir?] Probably burning, tingling sensation on the scalp. Much similar to say, a sunburn feeling.* [Pt #8] • *You get that fluorouracil cream, you get diagnosed with getting whatever that treats … and, um, it was terrible… So I mean, I'm happy for treatment, but it's hard, some hard treatment.*[Pt #9]
Symptom timeline	• *I'd say at least five, four to five days. That's when I noticed it starting to turn red, it stinged, it peeled. At the end of the treatment, my last day that I used it just seemed like stayed red for a long time. And I would I would say approximately a good month before it ever started diminishing and then vanished probably within that next month, just real slow.* [Pt #5] • *Probably within 12 to 24 hours at first application. [And how long did they last?] They probably stopped about 3-4 days after my last application.* [Pt #8] • *It starts itching and burning. So those were some side effects. High levels of pain once you get into the, you know, it started hurting probably past the itching and burning phase, you know day five to seven, and at night, you know at night I get home and you know I think it was I was reapplied on it twice a day. I can't remember but I remember it hurts when you go to bed. So you have sometimes have trouble sleeping, because of the pain and you don't want to move too much. You know put your face on a pillow like the last thing you want to do.* [Pt #9]
Daily activities and psychosocial impact	• *It made me look very sick. Cause my face and arms were extremely red. And at times had blisters on them.* [Pt #1] • *I think it did dramatically. Yeah, when you can't sleep at night that's pretty serious. I think I was retired at the time. So it didn't affect my job responsibilities, but it's certainly affecting my everyday life because I was just miserable.* [Pt #3] • *I didn't let it affect me in any way, I went on and did everything that I needed to do. You know, there was there were times it probably caused me to not get decent sleep, but other than that, you know, it was painful. Nobody knew about it. I didn't tell anybody or let anybody know or let it inhibit anything I needed to do. And I have a high tolerance for pain, which is a whole other story.* [Pt #4] • *Well it didn't make me feel good. If my skin is blistered, and I can't go out with friends and everything and then obviously it doesn't make me feel real good.* [Pt #7] • *It was hard when I used it. Yeah, I mean, just like anything else, you look like a zombie... People probably stare at me, you know? But it's, it's I guess it's all how you take it. You know, I've had so many hard things that it doesn't, you know, I just kept doing... I mean, socially, I probably went out less and did things less just, I don't want to have to have that conversation.* [Pt #9]
Challenges while on treatment	• *It starting to turn red, it stinged, it peeled. At the end of the treatment, my last day that I used it just seemed like stayed red for a long time. And I would I would say approximately a good month before it ever started diminishing and then vanished probably within that next month, just real slow.* [Pt #5] • *It's just that it's a commitment on my part whenever I started it, that I would not be venturing out in public too much because it does look like a leper or something. I mean, it's like more like leprosy.* [Pt #7] • *Well there was a period of time where I would have very little exposure outside. Generally, it said it was recommended that I should do it in the winter. It set strict adherence to not going out in sunlight, to touch my skin. Applying it twice a day and made sure I wore gloves when I put it on so as not to get it, you know rubbing my eyes for example or any mucosal membrane. And then also using pillow cases such that I didn't have to be concerned about the pillowcases becoming discolored or damaged that type of thing. When I applied it before bedtime.* [Pt #8] • *Only one thing that's good about it is it's easy to put on. But after you put it on it starts... I mean you can't touch it. You know after a few days your face is so tender, and I only put on my face that's why I keep talking about my face, but so tender you definitely ain't going in the sunshine. It's like a Marvel movie the way it just burns when you get in the sun. It's crazy. And then once your face, my face started swelling up to the point where I was having, I couldn't chew or having trouble just talking, couldn't smile. A smile on my face was gonna crack open. Those are some of the basic challenges, I guess. And itching and burning, of course, I mean, the whole time.* [Pt #9]
Level of preparedness	• *Well, I think the entire staff, the dermatology department were very supportive, you know, not just the doctors but the nurses.* [Pt #2] • *No, I didn't get any support. It was like the job that I had was to survive it.* [Pt #4] • *No, they didn't mention anything like that. It didn't bother me with my doctor. I mean, it just didn't work for me. I don't know. I'll tell him when I go back.* [Pt #10]

How 5-FU Treatment Affected Patient Perception of AK and Future Care

Participants stated having mixed feelings while receiving treatment with 5-FU. While some stated treatment was fine or a minor convenience, other participant responses included feeling self-conscious. Including those who stated that treatment was a minor inconvenience, more participants felt uncomfortable and self-conscious during treatment with 5-FU. Particularly, of the participants who felt uncomfortable and self-conscious, some stated that treatment was very difficult for them (Table 3).

Table 3. Representative quotes regarding patient perception of treatment success and satisfaction.

Theme	Quote
Convenience of treatment	• *I do remember they were saying a lot of it was pre-cancer. And that's what this particular drug was supposed to do, so you know, deal with. So it was it was sort of, I had to do something that was difficult. And so how I felt about it.* [Pt #2] • *Well, generally I felt great, because I didn't you know, this was is like putting a Band-Aid on and you got some underneath the Band-Aid that hurts real bad. And you do everything you got to do you just keep doing it. You know it didn't inhibit anything that I did at all. Because I just got going I wouldn't let it slow down the things I had to do.* [Pt #4] • *Like crap. That would be the mental side, the physical side, not so bad.* [Pt #7] • *It wasn't... let's put it this way it was a minor annoyance. And at times you, by focusing on other things in life I didn't even really pay much attention.* [Pt #8]
Perception of treatment effectiveness	• *Short answer, no. The full answer is somewhat partially in some areas, like my neck is significantly improved over what it was. And there's very small areas there. Down my chest on either side of my sternum, on the left side, there's very little, but there's a rim that that runs probably a four inch line with little very small spots of it left. On the right side there are larger spots over a wider area, and the area below my breasts at the bottom of my sternum on the right hand side there's a fairly significant area that's kind of appeared afterwards.* [Pt #4] • *Yes, it definitely works. It's just a question of whether that is the best solution.* [Pt #7] • *It only provided very, very short-term results and would need to have to be repeated frequently.* [Pt #8] • *It's 50/50. It's as much as you can take, because it ends up...you're going to have to do something. So either I took as much as I could and I said you know whatever's next I have to take next because I couldn't finish.* [Pt #9]
Patient satisfaction with treatment	• *In the long run, of course, I'm happy that the doctor seems to believe that it helped, and I trust doctors, you know.* [Pt #2] • *Well, the positive effects were that it treated the cancer. I mean, for me it's hard though because I wore glasses. On my face and anywhere my glasses touched, I had to wear like a like a napkin, on my nose bridge. And I mean, putting it on every day and wash my face and there's a constant burning that goes with it that kind of affects your behavior just by your attitude. You kind of like get tired of that burning. And then it starts swelling and you can't move your face from the people staring at you and everything else. It's a, I mean it's a process. You know? It's a difficult process to go through.* [Pt #9]
Likelihood to seek future treatment	• *Well, of course, I'd be willing to this I was told that the side effects were much more minimal. Then the ones in the fluorouracil. I'm not interested in going through that again.* [Pt #4] • *I think if a dermatologist recommended another way of treating it, I would definitely look into other ways, yes.* [Pt #5] • *I would consider it depending on the ease of use, as well as a discussion about effectiveness.* [Pt #8] • *I said yes, I would be willing to try after consulting with my doctor. But if it's going to do the same thing the other cream done, I'm not interested.* [Pt #10]

There were mixed responses from participants about whether treatment with 5-FU helped treat AK. Half of the participants believed that 5-FU helped treat their AKs, while the other half of the participants were not sure or stated that it did not help. Inability to assess treatment responses due to premature discontinuation of 5-FU was a particular subtheme. Specifically, 4 participants stated that side effects from 5-FU use caused them to stop treatment (Table 3).

Although some participants were satisfied with treating AK owing to its potentially carcinogenic nature, mental health impairment and lifestyle inconvenience were other particular subthemes. There was a pervasive belief among participants that it was either difficult to assess or the benefits of treatment were not worth the side effects associated with 5-FU (Table 3).

Despite all participants stating that they would refuse future treatment with 5-FU for AK, most stated that their experience with 5-FU would not deter them for seeking future alternative treatment, and they would be open to other topical treatments, specifically if associated with fewer side effects (Table 3).

Discussion

Principal Findings

All patients in our cohort refused future retreatment with 5-FU. Despite an overall low concern when diagnosed with AK, most participants believed that treatment was important. There are multiple treatment options for AKs, including both surgical and field-directed treatments, and cryosurgery and 5-FU are the most commonly prescribed therapies [2,12]. While cryosurgery is intended to treat isolated or a few lesions, topical treatments, such as 5-FU, are more efficacious to treat both clinical and subclinical AKs [2,12,13]. However, 5-FU is associated with frequent LSRs, and patients with a greater number of AKs at baseline may be predisposed to severe LSRs [14,15].

Most participants stated that they had had low concern with therapy before initiating treatment and trusted the recommendation of their HCP. However, after completing treatment, most participants stated that they were either unsure or were not adequately prepared by their HCP. Moreover, there were mixed responses regarding the efficacy of 5-FU treatment. Specifically, many participants did not believe that treatment helped their AKs. Inability to assess effectiveness due to premature discontinuation secondary to 5-FU–related adverse events (AEs) was also a common theme. There was a pervasive theme that the side effects associated with treatment were not worth the benefits.

Altogether, participants experienced both physical and psychosocial burden secondary to topical 5-FU treatment. During treatment, 5-FU–associated pain or burning, erythema, peeling, sloughing, and flaking caused difficulty to participants. Particularly, 5-FU–associated reactions had a negative impact on participant self-perception and caused feelings of self-consciousness and embarrassment. Social impairment during treatment, secondary to 5-FU–associated LSRs, was another common theme. Although treatment did not prevent participants' abilities to complete daily activities, it led to lifestyle changes and limitations. Sleep impairment and prevention of 5-FU smearing onto bedsheets was a notable subtheme.

Limitations

Our study was limited by input from participants who refused future retreatment with 5-FU, potential recall bias, and lack of an objective measure of treatment burden. Still, most stated that they would still continue to seek alternative treatment for AKs in the future and would still be open to other topical treatments, especially if associated with a better safety and tolerability profile than 5-FU. Nonadherence to treatment is a major cause of treatment failure. Particularly, up to 50% of dermatology patients may be nonadherent to treatment regimens [16]. Ineffective communication about treatment-related AEs may predispose patients to poor adherence [16,17]. Prescription of a topical steroid as needed may also help decrease the burden of intolerable skin irritation secondary to 5-FU [18]. Shared decision-making with patients after discussing the benefits and risks of medicines, in addition to therapeutic options, and appropriate counseling may increase adherence and improve patient outcomes [19,20].

Conclusions

Most participants believed that AK is important to treat and had low concern regarding 5-FU at baseline. During treatment, participants experienced both physical and psychosocial burden secondary to topical 5-FU treatment. Although our study was limited by input from participants who refused future treatment with 5-FU, many did not believe that treatment helped their AKs, and inability to assess effectiveness due to premature discontinuation secondary to AE was a common theme. Most stated that they would continue to seek alternative treatment for AKs in the future. Nonadherence is a major cause of treatment-resistant disease. Shared patient-physician decision-making focusing on the benefits and risks of treatment, realistic expectations, therapeutic alternatives, and counseling may increase adherence and improve outcomes.

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Conflicts of Interest

SRF has received research and speaking or consulting support from a variety of companies including Galderma, GSK/Stiefel, Almirall, Leo Pharma, Baxter, Boeringer Ingelheim, Mylan, Celgene, Pfizer, Valeant, Taro, Abbvie, Cosmederm, Anacor, Astellas, Janssen, Lilly, Merck, Merz, Novartis, Regeneron, Sanofi, Novan, Parion, Qurient, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate, and National Psoriasis Foundation. He is the founder and majority owner of www.DrScore.com and founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment.RS and SM have no conflicts to disclose.

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Abbreviations

5-FU: topical 5-fluorouracil
AE: adverse event
AK: actinic keratosis
HCP: health care provider
LSR: local skin reaction

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Original Paper

Recommendations From a Chinese-Language Survey of Knowledge and Prevention of Skin Cancer Among Chinese Populations Internationally: Cross-sectional Questionnaire Study

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Abstract

Background: There is a paucity of studies assessing awareness and prevention of skin cancer among Chinese populations.

Objective: The aim of the study is to compare attitudes and practices regarding skin cancer risks and prevention between Chinese Asian and North American Chinese populations and between Fitzpatrick scores.

Methods: A cross-sectional, internet-based, 74-question survey in Chinese was conducted focusing on Han Chinese participants internationally. The survey included Likert-type scales and multiple-choice questions. All participants were required to read Chinese and self-identify as being 18 years or older and Chinese by ethnicity, nationality, or descent. Participants were recruited on the internet over a 6-month period from July 2017 through January 2018 via advertisements in Chinese on popular social media platforms: WeChat, QQ, Weibo, Facebook, and Twitter.

Results: Of the 113 completed responses collected (participation rate of 65.7%), 95 (84.1%) were ethnically Han Chinese, of which 93 (96.9%) were born in China and 59 (62.1%) were female. The mean age of these 95 participants was 35.8 (SD 13.3) years; 72 (75.8%) participants were born after 1975. Few but more North American Chinese reported that Chinese Asian populations received annual skin checks (4/30, 4.2% vs 0/65, 0%; P=.009) and believed that their clinician provided adequate sun safety education (13/30, 43.3% vs 15/65, 23.1%; P=.04). Participants with higher Fitzpatrick scores less frequently received sun safety education from a clinician (4/34, 11.8% vs 22/61, 36.1%; P=.02). More participants with lower Fitzpatrick scores used sunscreen (41/61, 67.2% vs 16/34, 47.1%; P=.05), but alternative sun protection use rates are similar across groups.

Conclusions: Cultural differences and Fitzpatrick scores can affect knowledge and practices with respect to sun protection and skin cancer among social media–using Chinese Asian and North American Chinese communities based on respondent demographics. Most participants in all groups understood that people of color have some risk of skin cancer, but >30% of all groups across regions and Fitzpatrick scores are unaware of current skin protection recommendations, receive insufficient sun safety education, and do not use sunscreen. Outreach efforts may begin broadly with concerted public and private efforts to train and fund dermatologists to perform annual total body skin exams and provide more patient education. They should spark community interest through mass media and empower Chinese people to perform self-examinations and recognize risks and risk mitigation methods.

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KEYWORDS

skin cancer; basal cell carcinoma; squamous cell carcinoma; melanoma; people of color; skin of color; risk and prevention; photoprotection; sun protection; sunscreen; prevention; cancer risk; cancer prevention; Chinese Asian; Chinese; Asian; North American Chinese; Fitzpatrick score; cultural difference; awareness; education

Introduction

Skin cancer is a global health issue. Among people of color (POC), the outcomes are far worse than that of the general population [1-8]. This poorer outcome has been associated with delay in diagnosis due to the failure of the medical community and patients to recognize the distinct risks [4,5,9-11] and signs [4,11-15] of skin cancer in non-White populations.

China is the most populous country with approximately 1.4 billion people; Han Chinese is the largest ethnic group native to China, making up 92% of the Chinese population and 19% of the global population. Despite the attention to skin in the market for skin products and treatments among Chinese consumers, skin cancer incidence rates continue to increase in Chinese populations [14,16-23].

One study noted that, between 2004 and 2011, the overall incidence of melanoma in China increased from 0.4/100,000 to 0.48/100,000 [21]. A study of long-term trends of skin malignant melanoma in China between 1990 and 2019 reported annual incidence net drifts of 3.523% and 3.779% for males and females, respectively [23]. In tandem with China's rapidly aging population, the age-standardized incidence rate of melanoma in China has increased as well [23], increasing by 110.3% from 1990 to 0.9/100,000 in 2017 [17]. Among the Chinese population of Hong Kong, between 1990 and 1999, the incidence of basal cell carcinoma increased from 0.32/100,000 to 0.92/100,000, and the incidence of squamous cell carcinoma from 0.16/100,000 to 0.34/100,000 [14]. In Singapore, between 1968 and 2016, the age-standardized incidence rate of cutaneous basal cell carcinoma among ethnically Chinese people increased from 2.7/100,000 to 6.9/100,000 [22].

Nonetheless, compared to the wealth of research on skin cancer risks, incidence, awareness, and prevention among Western White and people of color populations [24-29], there is a paucity of publications concerning that of Chinese populations. A recent review paper reported the identification of only 9 papers across numerous Western and Chinese English-accessible databases that studied knowledge, attitudes, beliefs, and behaviors related to skin cancer and sun protection in China [30]. In Chinese, a limited collection of peer-reviewed and non–peer-reviewed research has been published in the past decade [31-37]. Chinese people internationally are often [8,10,28,38]—but not always [16,27,39]—grouped into Asian and East Asian categories for studies related to skin cancer rates and behavioral risks, impeding extrapolation for subgroups. Only 2 studies were identified comparing the perspectives on the risks of skin cancer among specific ethnic Chinese populations from different sociocultural backgrounds [38,40].

In this study, international Han Chinese perspectives on skin cancer were recruited through social media and anonymously surveyed in simplified Chinese. Trends and gaps in knowledge of risk factors and preventative measures were identified and used to determine necessary educational measures for developing future interventions with patients, educators, and providers.

Methods

Participant Recruitment

Participants were recruited on the internet over a 6-month period via advertisements in Chinese on popular social media platforms: WeChat (Tencent Holdings Limited), QQ (Shenzhen Tencent Computer System Co, Ltd), Weibo (Sina Corporation), Facebook (Meta Platforms, Inc), and Twitter (Twitter, Inc). All participants were required to read Chinese and self-identify as being 18 years or older and Chinese by ethnicity, nationality, or descent. No financial compensation was provided.

Survey Details

An internet-based survey was adapted into Chinese from an English survey used in previous studies for assessing current knowledge and management of skin cancer in English-speaking populations [41-44]. The survey contained 74 questions in Chinese (Multimedia Appendix 1) and took approximately 30 minutes to complete. The University of Central Florida Institutional Review Board approved the Chinese-adapted version. Participants completed the survey on SurveyMonkey cloud-based software (SVMK Inc). Survey contents and results are reported in English.

Data Analysis and Visualization

Data analysis and visualization were completed in Excel (Microsoft Corporation) and R (R Foundation for Statistical Computing). Comparisons with chi-square and Fisher exact tests were made—for query responses with all counts 10 or greater and at least 1 less than 10—between responses by Chinese participants in Asia (group 1) versus those of Chinese participants in North America (group 2), and by those with modified Fitzpatrick scores ≤14 (modified Fitzpatrick group 1 [FG1]) versus those with modified Fitzpatrick scores ≥15 (modified Fitzpatrick group 2 [FG2]).

Due to the relative homogeneity in ethnicity, hair color, and eye color among ethnically Chinese people, scores were determined as a summation of points from questions modified to be more specific to skin phototyping for Chinese skin types [45] and more granular than the conventional Fitzpatrick scoring system:

1. How dark is your skin normally? (0=albino; 7=very dark brown)
2. How dark do you get if you tan? (0=albino; 7=very dark brown)
3. How easy is it for your skin to tan? (0=never tans; 7=always tans)
4. How easy is it for your skin to sunburn? (0=always sunburns; 7=never sunburns)

Since the maximum possible score was 28, half of the maximum (14) was chosen to be the dividing value between FG1 and FG2. In short, participants in FG1 had paler skin or experienced more sensitivity to burning than their FG2 counterparts.

Ethical Considerations

This study has been reviewed and exempted by UCF institutional review board (IRB No. SBE-17-12900).

Results

The response rate was 113 of 172 (65.7%). Of this subset, 95 (84%) participants were of Han Chinese ethnicity. Only the results from fully completed surveys by Han Chinese participants are reported to reduce cross-cultural confounding factors. Participant demographics and history of skin cancer are summarized in Table 1. Of note, 93 (98%) of respondents were born in China, while 64 (67%) currently live in China. Comparisons between responses from different geographical locations are shown in Table 2. A modified Fitzpatrick scale was used to determine whether the variable darkness of the skin among Chinese contributes to skin cancer risks and perception in Table 3. Among all participants, 37 (39%) reported not using any sunscreen; the primary cited reasons for not doing so are summarized in Table 4. The use of alternatives options to sunscreen are shown in Table 5 (participants could select more than one option as listed).

Table 1. Participant demographics and history of skin cancer (n=95).

Characteristic	Participants, n (%)
Han Chinese ethnicity	95 (100)
College or higher degree	66 (70)
Born in China	93 (98)
Born after 1975, residence in Asia	54 (57)
Born after 1975, residence in North America	18 (19)
Geographical region of residence	
China	64 (67)
Other Asian countries	1 (1)
United States	26 (27)
Canada	3 (3)
Australia	1 (1)
Other countries (unspecified)	1 (1)
History of precancerous and cancerous lesions	1 (1)

Table 2. Skin cancer knowledge and preventative measures between regions. Survey responses from Han Chinese are displayed, and responses are separated for comparison into 2 groups based on the participants' region of residence: Asia (group 1) and North America (group 2). The sample sizes from other geographical regions were too small for statistical analysis.

Category	Han, n (%)	Group 1, n (%)	Group 2, n (%)	*P* value
Group size	95 (100)	65 (100)	30 (100)	N/A[a]
Skin cancer risk in Chinese less than White people	73 (77)	46 (71)	27 (90)	.06
No skin cancer risk in Chinese	10 (11)	9 (14)	1 (3)	.16
POC[b] can get skin cancer	86 (91)	58 (89)	28 (93)	.78
Can identify melanoma as a type of skin cancer	57 (60)	42 (65)	15 (50)	.18
Have not read about the latest skin care recommendations	82 (86)	56 (86)	26 (87)	>.99
Interested but do not know how to get resources for recommendations	35 (37)	27 (42)	8 (27)	.18
Know that sunscreen protects from skin cancer	65 (68)	42 (65)	23 (77)	.34
Level of concern about skin cancer in lifetime				.83
Do not worry	39 (41)	26 (40)	13 (43)	
Mild to moderate	50 (53)	34 (52)	16 (53)	
Serious	6 (6)	5 (8)	1 (3)	
Likelihood of seeing clinician for new skin lesion				.84
Never	8 (8)	5 (8)	3 (10)	
Unlikely	29 (31)	21 (32)	8 (27)	
Likely to very likely	58 (61)	39 (60)	19 (63)	
Clinician discussed risks of tanning	2 (2)	1 (2)	1 (3)	.53
Clinician discussed skin cancer risks	6 (6)	4 (6)	2 (7)	>.99
Received annual skin check	4 (4)	0 (0)	4 (13)	.009
Received sun safety education from clinician	26 (27)	19 (29)	7 (23)	.63
Felt clinician gave adequate sun safety education	28 (30)	15 (23)	13 (43)	.04
Sunbathe to tan	6 (6)	2 (3)	4 (13)	.08
Uses sunbeds or tanning booths	0 (0)	0 (0)	0 (0)	>.99

[a]N/A: not applicable.

[b]POC: people of color.

Table 3. Skin cancer knowledge and preventative measures between Fitzpatrick groups. Survey responses from Han Chinese are separated for comparison into 2 groups based on the participants' Fitzpatrick scores: those with modified Fitzpatrick score ≤14 (modified Fitzpatrick group 1 [FG1]) and those with modified Fitzpatrick score ≥15 (modified Fitzpatrick group 2 [FG2]).

Category	FG1, n (%)	FG2, n (%)	*P* value
Group size	61 (100)	34 (100)	N/A[a]
Skin cancer risk in Chinese less than White people	48 (79)	25 (74)	.62
No cancer risk in Chinese	5 (8)	5 (15)	.49
POC[b] can get skin cancer	55 (90)	31 (91)	>.99
Can identify melanoma as a type of skin cancer	37 (61)	20 (59)	.86
Have not read about the latest skin care recommendations	52 (85)	30 (88)	.77
Interested but do not know how to get resources for recommendations	24 (39)	11 (32)	.50
Know that sunscreen protects from skin cancer	47 (77)	18 (53)	.02
Level of concern about skin cancer in lifetime			.75
Do not worry	23 (38)	16 (47)	
Mild to moderate	34 (56)	16 (47)	
Serious	4 (7)	2 (6)	
Likelihood of seeing clinician for new skin lesion			.30
Never	3 (5)	5 (15)	
Unlikely	19 (31)	10 (29)	
Likely to very likely	39 (64)	19 (56)	
Clinician discussed risks of tanning	2 (3)	0 (0)	.32
Clinician discussed skin cancer risks	5 (8)	1 (3)	.54
Received annual skin check	3 (5)	1 (3)	>.99
Received sun safety education from clinician	22 (36)	4 (12)	.02
Felt clinician gave adequate sun safety education	18 (30)	10 (29)	.99
Sunbathe to tan	4 (7)	1 (3)	.65
Uses sunbed or tanning booth	0 (0)	0 (0)	>.99

[a]N/A: not applicable.

[b]POC: people of color.

Table 4. Reasons for not using sunscreen. The proportion of respondents who denied using sunscreen and their cited reasons are tabulated. Participants were only able to select one reason for not using sunscreen. *P* values were calculated for Asia (Group 1) versus North America (Group 2) with *P* value A and Fitzpatrick score ≤14 (modified Fitzpatrick group 1 [FG1]) versus Fitzpatrick score ≥15 (modified Fitzpatrick group 2 [FG2]) with *P* value B.

Category	Han (n=95), n (%)	Group 1 (n=65), n (%)	Group 2 (n=30), n (%)	*P* value A	FG1 (n=61), n (%)	FG2 (n=34), n (%)	*P* value B
Do not use sunscreen	37 (39)	27 (42)	10 (33)	.45	20 (33)	18 (53)	.05
No need to use sunscreen[a]	10 (27)	6 (22)	4 (40)	.83	7 (35)	3 (17)	.24
Inconvenient to use sunscreen	11 (30)	8 (30)	3 (30)		3 (15)	8 (44)	
Choose other means of sun protection	2 (5)	2 (7)	0 (0)		1 (5)	1 (6)	
Do not know how to use sunscreen correctly	1 (3)	1 (4)	0 (0)		1 (5)	0 (0)	
Other reasons	13 (35)	10 (37)	3 (30)		8 (40)	6 (33)	

[a]Percentages in this category are based on the "do not use sunscreen" numbers.

Table 5. Sun protection aside from sunscreen. Methods other than sunscreen used to protect against UV exposure outdoors are detailed. Some respondents have overlaps between categories as well as with sunscreen usage. *P* values were calculated for group 1 versus group 2 (*P* value A) and FG1[a] versus FG2[b] (*P* value B).

Category	Han (n=95), n (%)	Group 1 (n=65), n (%)	Group 2 (n=30), n (%)	*P* value A	FG1 (n=61), n (%)	FG2 (n=34), n (%)	*P* value B
Wide-brimmed hats or long-sleeve clothing	58 (61)	39 (60)	19 (63)	.76	40 (66)	18 (53)	.23
Sunglasses	59 (62)	35 (54)	24 (80)	.02	36 (59)	23 (68)	.41
Umbrella	48 (51)	38 (59)	10 (33)	.02	34 (56)	14 (41)	.17

[a]FG1: modified Fitzpatrick group 1.

[b]FG2: modified Fitzpatrick group 2.

Discussion

Overview

Skin lightening is a multibillion dollar industry among Chinese people. Despite Chinese culture's well-known and generally strong preferences for whiter, lighter-toned skin [46-48], limited research has been done on Chinese knowledge and practices with respect to sun protection and skin cancer.

Given that skin cancer incidence rates and mortality continue to increase among Chinese people [14,16-19,49], it is imperative to understand and identify optimal strategies to synergize with consumer interests for effective UV radiation protection. This study is the first to compare Chinese attitudes and practices between Chinese Asian and North American Chinese populations as well as between modified Fitzpatrick scores.

In this study, most participants were Han Chinese, which is consistent with Chinese ethnic demographics. Most participants were born in China after 1975 (Table 1), the year when a generational paradigm shift was instituted, altering from traditional to modern Chinese culture and economics. Thus, our findings and recommendations are more focused on the perspectives and knowledge of younger generations who are more highly educated and actively use and were recruited through social media.

Consistent with the participants' age distribution, only one of the participants had a history of precancerous or cancerous lesions (Table 1). The incidence rate of skin cancer increases with age across races [2,18,50,51], and Chinese patients are more likely to be diagnosed with skin cancer after 40-60 years of age [17,52].

On the Risks Factors of Race and Ethnicity

While participants across all groups predominantly (>89%) believe that POC can get skin cancer, most participants believe that Chinese people are less at risk than Caucasian people (Tables 2 and 3). North American Chinese people may believe more often than their Chinese-Asian counterparts in a lower skin cancer risk (*P*=.06, Table 2). However, there is no significant difference between FG1 and FG2.

The potential significance of geographic location could be linked to experience bias. The higher awareness of skin cancer by Chinese people in North America may be related to living in heterogenous communities, wherein non-Asian counterparts are subject to skin cancer. Nonetheless, there is consistent recognition across regions and Fitzgerald scores that skin color does not guarantee immunity to skin cancer.

On Knowledge of Melanoma and Skin Care

Knowledge about skin cancer is limited in Chinese communities; only 50.0%-64.4% of participants can define melanoma as a type of skin cancer (Tables 2 and 3). Neither modified Fitzpatrick score nor geographical location yielded statistically significant differences in this lack of knowledge.

Group 1 and group 2 have read the latest skin care recommendations at comparable rates (*P*>.99, Table 2). Acquiring knowledge of skin cancer risk may be more associated with interest and motivation as opposed to resource access (Tables 2 and 3).

On Interest and Clinical Care Related to Skin Cancer

Across location and modified Fitzpatrick score groups, 37.7%-47.1% of respondents in each group lacked concern regarding the risk of skin cancer in their lifetime (Tables 2 and 3).

While most participants are either likely or very likely to see a clinician for a new lesion, participants consistently reported low rates of annual skin checks; significantly more annual skin checks occured in North America than in Asia (*P*=.009, Table 2). This rate does not appear to be affected by the modified Fitzpatrick score (Table 3).

Most Chinese people across all groups had neither received sun safety education from their clinicians nor were generally satisfied with the education when provided (Tables 2 and 3). However, within these findings, significantly more North American Chinese people felt satisfied with the education provided (*P*=.04, Table 2). Furthermore, significantly more participants in FG1 than in FG2 received sun safety education from clinicians (*P*=.02, Table 3).

On Tanning Practices

While no participants used sunbeds, outdoor sun tanning practices were more popular among North American Chinese than Chinese Asian people (*P*=.08, Table 2), which would be in agreement with the existing literature [38]. Consequently, Western clinicians should recognize this behavior and be proactive in initiating sun safety discussions with ethnically Chinese people living in North America. In Asia, the monitoring of trends should continue, and dedicated educational programs on sunbathing and tanning should be proactively implemented.

On Sun Protection Practices

Sunscreen use was reported in 47.1%-67.2% of participants across locations and modified Fitzpatrick score groups (Tables 2-4). Participants in FG1 may use sunscreen more frequently than their counterparts in FG2 (*P*=.05, Table 4).

Nonetheless, a sizeable minority do not use sunscreen. Efforts are needed to confirm that these individuals are using other forms of UV protection, including hats, umbrellas, and sunglasses; in this study, 35 (37%) of all 95 Han Chinese participants stated that they used no forms of UV protection at all (Table 4). It is furthermore pertinent to conduct additional surveys to confirm that sunscreen is being applied at appropriate time intervals and in appropriate volumes.

No significant differences concerning the lack of sunscreen use were found between group 1 and group 2 nor FG1 and FG2 (Table 4), suggesting similar viewpoints between groups.

It is worthwhile to note that some people reported a lack of knowledge on correct sunscreen use (Table 4). Perhaps sunscreen manufacturers could add to their products QR codes linked to instructional videos for proper sunscreen applications [53].

In terms of alternative methods for sun protection, group 1 and group 2 used wide-brimmed hats and long-sleeve clothing at similarly high rates (39/65, 60% vs 19/30, 63%, Table 5). Use of sunglasses for sun protection had a much higher proportion (35/65, 54% vs 24/30, 80%) in group 2 than in group 1 (*P*=.02, Table 5). This statistically significant difference is understandable due to the popularity of sunglasses in North American 20th century culture [54]. Although sunglasses are growing in popularity, their use remains minimal for sun protection in Asia [30,55-57]. On the other hand, "sun umbrellas" use among Chinese-Asian people, especially Chinese-Asian women, is frequently used to maintain a white complexion [30,55-58].

Between FG1 and FG2, protective clothing, sunglasses, and umbrella use rates were similar between the groups (Table 5). As such, modified Fitzpatrick scores are less likely to affect sun protection practices beyond sunscreen.

Closing the Educational Gap

It is imperative to educate and motivate Chinese communities to intervene in the growing severity of diagnoses and incidence of skin cancer. Given the similarities in responses between groups, it is not unreasonable to begin with a standard guide translated into various languages and methodology for addressing skin cancer knowledge and behavior between clinicians and Chinese patients in various languages. Effective dissemination of educational messages can be achieved via social media and other forms of mass media [30,59]. Additional research should be conducted to identify viewpoints shared among participants and develop effective media-based outreach for skin cancer prevention campaigns, which may be accomplished using a method like that of Shi et al [60].

Moreover, Chinese communities have expressed interest in skin exams and increased breadth and depth of sun safety education. Efforts should be made in dermatology residency programs internationally to emphasize skin cancer risks, signs, and symptoms among all skin types, including Chinese; review specific techniques for skin protection to aid in patient education; and train residents to complete total body skin exams (TBSEs). We recommend that annual TBSEs should be conducted by a dermatologist.

Current screening guidelines confound this recommendation—the US Preventative Services Task Force states that there is insufficient evidence to determine the effectiveness of visual skin exam screenings in US patients without obvious related signs or symptoms [61]; however, the methods behind this recommendation have been extensively critiqued [62], and notably, the conclusions are based on data inclusive of primary care clinicians alongside dermatologists without a direct means of comparison between screening accuracy [61]. Organizations' recommendations for other regions vary from no recommendations to self-examination twice a year for specific high-risk populations to 2-year intervals for all individuals from the age of 35 years onward [63,64]. Nevertheless, emerging data demonstrate that TBSEs conducted by dermatologists are low-cost and efficacious as a screening tool for detecting skin cancer [65], and they detect skin cancer at significantly higher rates than partial skin exams; for malignant melanoma, it is suggested that a dermatologist-conducted TBSE is 23.5 times more likely to identify a lesion than a Pap smear to identify a cervical cancer lesion [66].

Differences in health care systems provide another challenge to implementing TBSEs. In China, traditional Chinese medicine (TCM) is practiced alongside Western medicine, each with its own set of diagnostics, interpretations, therapeutics principles, and treatments [67,68]. Different logic systems are in place, including for cancer, with some analogous language and principles [69]. Both forms of medicine recognize the value of preventative medicine through early detection and treatment [67-69]; this shared perception should be used to adequately reach out to Chinese communities in China and abroad that preferentially rely on TCM. Collaboration with TCM universities to reconcile and integrate knowledge related to skin cancer risks, prevention, and screening into their curriculum and improve the cultural competency of allopathic clinicians to provide parallels to TCM concepts will improve the care and patient education of TCM patients [68,70-74].

Furthermore, China's multitiered health care system is intended to coordinate between primary health care with general practitioners and secondary and tertiary health care at hospitals, with more complex levels of care and with more resources available at higher-tiered hospitals. Currently, there is limited use of primary health care services in China and preferential use of hospitals for medical services [75]. The type of first-visit hospitals and socioeconomic status have also been shown to significantly impact the time for diagnosis of melanoma [76]. In addition to ongoing reform efforts, one method to address these limitations would be to fund annual TBSEs by dermatologists as a part of routine primary care, which would lessen the financial burden and incentivize more patients to receive timely screenings.

Supplementarily, self-examination techniques should be taught through private and public health organizations to be conducted at regular intervals appropriate to individuals' genotypic, phenotypic, and environmental risk levels; all communities should be encouraged to seek clinical evaluation for lesions identified by tools such as the ABCDE rule (asymmetry, border irregularity, color nonuniformity, diameter >6 mm, and evolution) or the "ugly duckling" sign. Resources for POC to recognize their risks of malignancy and methods to protect against UV radiation—such as how to properly apply sunscreen—should be commonplace, and some examples can be found on the American Academy of Dermatology [77], American Cancer Society [78], and other organization websites. *Mind the Gap*, an extensive open-source handbook, compiles clinical signs in black and brown skin [79], and such efforts further aid in broadening the understanding and awareness among patients, educators, and clinicians. A selection of sun safety and skin cancer–related resources are available within China from government and nongovernment sources, some of which are highlighted in Multimedia Appendix 2 [80].

For the individual patient, culture, phenotypes, and lifestyles can significantly influence responses to upon all steps of the process, from information intake to application. Thus, all these factors ultimately should be considered in individualized educational programs and clinicians' care for Chinese patients both in Asia and in North America.

Limitations and Future Directions

Aside from the limitations of recall bias for survey-based research, future comparisons of groups by demographics of sex, age, and level of education would elucidate further stratifications of attitudes and practices and may provide suggestions for tailoring educational programs more specifically for individual patients [19,30,55,81]. While these demographic data were collected, distributions were insufficient to make meaningful inferences, except that our findings and recommendations from this study are primarily directed toward Chinese populations that use Chinese-language social media. At the time of surveying, Chinese-Asian participants on average were 32.1 years of age, 7.5 years younger than their North American Chinese participants at 40.6 years of age. Although this age difference is a limitation of our study, individuals of these groups are not void of skin cancer risks. Future studies with other languages, as discussed below, will better encapsulate younger populations.

Contextual exposure to UV radiation was not accounted for as part of this study. Though it certainly influences practices for sun protection and the risk of skin cancer, everyone has noninsignificant exposure risks to UV radiation. Among melanoma cases, the most common subtypes in China are acral and mucosal, followed by superficial spreading [6,64,82]. While UV radiation damage is primarily identified as the etiology of superficial spreading and has only been associated with a subset of mucosal and acral melanomas [82-84], reduction of risk against UV-induced damage overall would relieve the disease burden of skin cancer among the large population of Chinese people worldwide.

We consequently plan to expand our survey questions and recruit more participants to gain further insight concerning awareness of, exposure to, and behavior related to vocational and avocational exposure risks to UV radiation effects on skin health [36,37,85-88]. We then plan to develop community-specific best-practice recommendations adapted from existing methods [89] to mitigate these exposure risks. These include occupational and public health policies for communication, training, and protective equipment, and encourage use of the materials by making them conveniently accessible based on survey responses. Depending on the responses, for various situations, we will recommend different interventions such as onboarding training, protective clothing appropriate to the climate and conditions, shade structures, and sunscreen dispensers placed in locations frequented by workers in a certain industry; based upon the findings of Walkosz et al [89], these types of interventions likely will reduce the incidence of sun damage. Regular targeted free awareness-raising and screening events following the structure detailed by programs such as the American Academy of Dermatology "SPOT Skin Cancer" initiative [90,91] would also benefit populations associated with an identified high risk of skin cancer.

Given the population size of Han Chinese and the diaspora across the globe, new surveys will capture additional demographics and clarify regional geographical differences in cancer incidence and burdens within different Chinese provinces [17,92]. Maintaining the criteria of Chinese ethnicity while including different translations of the survey would provide better insight into the effects of geographical and cross-cultural differences. Thus, surveys should be available in both traditional and simplified Chinese, as well as languages of countries that currently have the largest overseas Chinese populations, including but not limited to English, Russian, Spanish, French, Italian, Indonesian, Thai, and Malay [93].

Furthermore, we will collaborate with more Chinese dermatology researchers and clinicians to expand our outreach. The collaboration would facilitate the surveying of more older participants who were born prior to 1975, allowing us to compare viewpoints between generations.

Conclusions

In conclusion, our Chinese-language survey was used to assess and compare Han Chinese attitudes and practices related to skin cancer risks and prevention. We identified manifestations of cultural differences between Chinese Asian and North American Chinese communities that use social media, and we determined that opinions and behaviors among Han Chinese people may differ by modified Fitzpatrick score.

From our findings, we proposed several aims for educational programs by clinicians and health care organizations in Asia and North America for the largest ethnic group in the world. Through a collective and adaptive effort across all levels of health care, knowledge and practices with respect to sun protection and skin cancer among Chinese populations globally can be improved to reduce morbidity and mortality among this subset of POC.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Survey questions in Chinese as seen by participants and English translation of questions.
[DOCX File , 83 KB - derma_v6i1e37758_app1.docx]

Multimedia Appendix 2
Select highlights of sun safety and skin cancer–related resources from China.
[DOCX File , 20 KB - derma_v6i1e37758_app2.docx]

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Abbreviations

FG1: modified Fitzpatrick group 1
FG2: modified Fitzpatrick group 2
POC: people of color
TBSE: total body skin exam
TCM: traditional Chinese medicine

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Original Paper

Acceptability of a Hypothetical Reduction in Routinely Scheduled Clinic Visits Among Patients With History of a Localized Melanoma (MEL-SELF): Pilot Randomized Clinical Trial

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Abstract

Background: After treatment for a localized melanoma, patients attend routinely scheduled clinics to monitor for new primary or recurrent melanoma. Patient-led surveillance (skin self-examination with patient-performed teledermoscopy) is an alternative model of follow-up that could replace some routinely scheduled visits.

Objective: This study aims to assess the acceptability of a hypothetical reduction in routinely scheduled visits among participants of the Melanoma Self Surveillance (MEL-SELF) pilot randomized clinical trial of patient-led surveillance (intervention) versus usual care (control).

Methods: Patients previously treated for localized melanoma in New South Wales who were participating in the MEL-SELF pilot randomized clinical trial were asked to respond to a web-based questionnaire at baseline and after 6 months on trial. We used mixed methods to analyze the data. The main outcome of interest was the acceptability of a hypothetical reduction in routinely scheduled visits for melanoma surveillance.

Results: Of 100 randomized participants, 87 answered the questionnaire at baseline, 66 answered the questionnaire at 6 months, and 79 provided a free-text explanation at either time point. At 6 months, 33% (17/51) of the control group and 35% (17/49) of the intervention group indicated that a hypothetical reduction in routinely scheduled visits with all melanoma doctors was at least slightly acceptable (difference in proportions –1%, 95% CI –20% to 17%; P=.89). Participants suggested that prerequisites for a reduction in routinely scheduled visits would include that sufficient time had elapsed since the previous diagnosis without a new primary melanoma or recurrence, an unscheduled appointment could be made at short notice if the patient noticed something concerning, their melanoma doctor had suggested reducing their clinic visit frequency, and patients had confidence that patient-led surveillance was a safe and effective alternative. Participants suggested that a reduction in routinely scheduled visits would not be acceptable where they perceived a very high risk of new or recurrent melanoma, low self-efficacy in skin self-examination and in the use of technologies for the patient-led surveillance intervention, and where they had a preference for clinician-led surveillance. Some patients said that a partial reduction to once a year may be acceptable.

Conclusions: Some patients may be receptive to a reduction in routinely scheduled visits if they are assured that patient-led surveillance is safe and effective.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12616001716459; https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371865&isReview=true; ClinicalTrials.gov NCT03581188; https://clinicaltrials.gov/ct2/show/NCT03581188

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KEYWORDS

melanoma; surveillance; medical overuse; teledermatology; pilot; clinical visit; treatment; clinics; monitoring; self-examination; online questionnaire; diagnosis; patient; safe; effective

Introduction

Patient-led surveillance has the potential to replace some routinely scheduled clinic visits after treatment of primary localized melanoma [1-3], offering a more sustainable model of follow-up care [4]. We recently completed a pilot randomized clinical trial (RCT) to assess the safety, feasibility, and acceptability of patient-led surveillance compared to clinician-led surveillance [5]. As part of the pilot trial, we asked participants about the acceptability of a hypothetical reduction in routinely scheduled clinics.

Methods

Overview

The Melanoma Self Surveillance (MEL-SELF) pilot RCT included patients previously treated for localized melanoma (stages 0, 1, and 2) who owned a smartphone, had a skin check partner to assist with skin self-examination (SSE), and were attending a routinely scheduled follow-up. Participants were recruited from specialist and primary care clinics in New South Wales, Australia. Participants were randomized (1:1) to 6 months of patient-led surveillance (intervention: reminders to perform SSE, patient-performed dermoscopy, teledermatologist assessment, and fast-tracked unscheduled clinic visits, in addition to usual care) or usual care (control). The pilot trial protocol is provided in Multimedia Appendix 1.

Prior to randomization, potential participants were provided with a participant information statement that included information about the patient-led surveillance intervention (Textbox 1). Participants assigned to the control group did not experience any components of the patient-led surveillance intervention.

In a web-based survey at baseline and at 6 months (delivered via REDCap [Research Electronic Data Capture]; Vanderbilt University [6,7]), participants were asked questions about the acceptability of a hypothetical reduction in routinely scheduled clinic visits at baseline and 6 months (Multimedia Appendix 2 [6,7]). For the quantitative analysis, we undertook an intention-to-treat analysis of outcomes at 6 months. We undertook an exploratory subgroup analysis by American Joint Committee on Cancer substage (AJCC; melanoma in situ, AJCC 0 compared with invasive melanoma, or AJCC 1-4). We used standard formulas to estimate the *P* values. We undertook statistical analysis using RStudio 2022.2.2.485 (RStudio, PBC). For the qualitative analysis of free-text answers, we used content analysis of free-text explanations to group them into themes. Two authors inductively developed codes and themes from the data.

Textbox 1. Text from participant information statement provided to all participants about the patient-led surveillance intervention.

"Most melanomas are detected by patients or their family members between scheduled visits; even more might be detected if patients are trained in total body skin self-examination (SSE). The objective of this study is to investigate whether a Smartphone App with videos showing how to perform skin self-examination and teledermoscopy (taking close up photographs of your skin using your phone) may lead to performing skin self-examination more regularly and increases confidence in doing this compared to standard education to learn about skin self-examination from a booklet alone (usual care)."

"If you are in the 'intervention' group you will also receive:

- A dermatoscope (this device allows you to take magnified images of skin lesions under polarized light for electronic transmission to a specialist) to attach to a smartphone and work in conjunction with a Smartphone App. A dermatologists will review the reports and images you submit in the app within 3 working days (if not the study coordinator will notify you with information on the delay). The dermatologist will then provide you with a clinical recommendation after they review your images.

- Written and video instructions on how to use the dermatoscope and the associated Smartphone App.

- Email and SMS text reminders every 2 months to perform self-examination on the Smartphone App and to complete a survey. The skin checker survey will also provide you with instructional videos on guided total skin self-examination and electronic reporting."

Ethics Approval

This study was approved by the Sydney Local Health District Ethics Committee (HREC/15/RPAH/593). All participants provided informed consent. The reporting of this study followed the CONSORT-EHEALTH (Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Telehealth) guidelines [8].

Results

Overview

This study was conducted from November 1, 2018, to January 17, 2020. Of the 100 trial participants, 87 answered questions at baseline, and 66 answered at 6 months (Table 1 and Multimedia Appendix 3). In addition, 71 participants provided a free-text explanation for their answers at baseline, and 56 provided this at 6 months.

Table 1. Effects of the intervention on the acceptability of a hypothetical decrease in routinely scheduled visits at the 6-month follow-up.[a,b]

	Control (n=51), n (%)		Intervention (n=49), n (%)		Total (N=100), n (%)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Acceptability of a decrease in scheduled visits with all melanoma doctors (specialists and GP[c])						
Not acceptable	21 (41)	19 (37)	23 (47)	13 (27)	44 (44)	32 (32)
Slightly/somewhat acceptable	19 (37)	14 (27)	16 (33)	15 (31)	35 (35)	29 (29)
Very/completely acceptable	4 (8)	3 (6)	4 (8)	2 (4)	8 (8)	5 (5)
Acceptability of a decrease in scheduled visits with GP						
Not acceptable	13 (25)	9 (18)	11 (22)	9 (18)	24 (24)	18 (18)
Slightly/somewhat acceptable	18 (35)	17 (33)	20 (41)	17 (35)	38 (38)	34 (34)
Very/completely acceptable	13 (25)	10 (20)	12 (24)	4 (8)	25 (25)	14 (14)
Acceptability of a decrease in scheduled visits with melanoma specialist						
Not acceptable	22 (43)	18 (35)	21 (43)	15 (31)	43 (43)	33 (33)
Slightly/somewhat acceptable	16 (31)	14 (27)	18 (37)	13 (27)	34 (34)	27 (27)
Very/completely acceptable	6 (12)	4 (8)	4 (8)	2 (4)	10 (10)	6 (6)

[a]Percentages may not sum to 100 owing to rounding.

[b]Missing data at baseline for 7 (14%) participants in the control group and 6 (12%) participants in the intervention group and at follow-up for 15 (29%) in the control group and 19 (39%) in the intervention group.

[c]GP: general practitioner.

Quantitative Analysis

We measured the acceptability of a hypothetical reduction in routinely scheduled visits with all melanoma doctors on a 5-point Likert scale. After dichotomizing this outcome (not acceptable vs slightly/some/very/completely acceptable), there was no difference between the randomized groups in the acceptability of reducing routinely scheduled visits at 6 months, with 33% (17/51) of participants in the control group and 35% (17/49) of participants in the intervention group indicating that a hypothetical reduction was at least slightly acceptable (difference in proportions –1%, 95% CI –20% to 17%; *P*=.89).

Among all 100 participants, 34% (95% CI 25%-44%; *P*=.002) indicated that a reduction in routinely scheduled visits was at least slightly acceptable, with 5% (95% CI 2%-11%; *P*<.001) indicating it was very or completely acceptable and 29% (95% CI 20%-39%; *P*<.001) indicating it was slightly or somewhat acceptable. On the other hand, 32% (95% CI 23%-42%; *P*<.001) indicated that a reduction in routinely scheduled visits overall would not be acceptable (there was no response from 34%, [34/100] of participants for this question at 6 months).

These proportions were also similar for patients with melanoma in situ compared to patients with invasive melanoma in the exploratory subgroup analysis. At 6 months, 31% (11/36) of participants with melanoma in situ and 36% (23/64) with stage 1 or 2 melanoma indicated that a hypothetical reduction in scheduled visits was at least slightly acceptable (difference in proportions –5%, 95% CI –24% to 14%; *P*=.59). More detailed results on this exploratory subgroup analysis are presented in Multimedia Appendix 4.

Qualitative Analysis

The free-text explanation responses were similar across the randomized arms and indicated a number of broad themes as to when a reduction would (Textbox 2) and would not be acceptable (Textbox 3).

Textbox 2. Circumstances in which a reduction in routinely scheduled visits would be acceptable (note, general practitioner [GP] in Australia is equivalent to primary care physician in North America).

Sufficient time had passed without any subsequent new melanomas

- "I would potentially be more comfortable monitoring it without their supervision as I get further from my surgery without any repeats." (015_control_6months)
- "If there has been no further problems or issues l can see no reason why they cannot be reduced." (034_control_6months)
- "Maybe go to yearly check with specialist if nothing found on next visit which is this Month/ October." (095_control_6months)
- "Acceptable as I am presently on 6 monthly checks that will be completing in March 2020 as it will be 5yrs since having my lesion removed. Will continue own skin examinations and visit GP if there is anything abnormal." (017_intervention_6months)

Timely access to a specialist facilitated by teledermatology and fast-tracked clinic visits

- "If there are any problems or issues develop prior to you next scheduled visit, l can make an appointment see my GP or specialist." (034_control_6months)
- "but if anything worries me I photo and email or book a short notice check." (064_control_6months)
- "It would be acceptable provided if any issues the moles etc could be emailed, photos sent etc for confirmation they are ok." (061_control_baseline)
- "I feel fewer scheduled visits would be ok if you are reassured it is ok to call with concerns and you can be guaranteed to be seen within a short time frame (1-2 weeks)." (072_control_6months)
- "I think knowing that I have access to them with concerns (not waiting too long for an appointment) I would feel ok with this." (072_contol_baseline)

Confidence in alternative to scheduled visits with or without digital technology

- "In the longer-term future if I was confident there were other ways of checking, I'd be very happy to go less. But don't have confidence in my GP (they just send me to Melanoma specialist) or in my own detection skills." (066_control_baseline)
- "Fewer follow up visits introduces an amount of uncertainty - unless good instructions are provided about using an I-phone to discover any problem areas." (085_intervention_baseline)
- "Only if given tools/devices that I would be confident in self-examination." (100_control_baseline)
- "I'm more confident in checking self." (059_control_6months)
- "If I had confidence in technology reducing risk." (089_control_baseline)
- "Provided my examinations were satisfactory in early detection it would remove anxiety and thus less unnecessary visits." (064_control_baseline)
- "I like the idea of a specialist yearly check, but very happy to do in between checks by myself with added technology to help. But if technology is good, maybe no scheduled checks, then." (070_control_baseline)
- "With the digital technology I am a little more confident of picking up a melanoma early." (011_intervention_6months)

Advice from the patient's treating doctor that a reduction in visits was safe and that they were suitable for patient-led surveillance

- "Due to the quantity of moles I have, I find regular personal checking and doctor checking helpful for my treatment, I am also willing to use the mole scope process to reduce doctor's visits if I am deemed suitable." (025_intervention_6months)
- "Only acceptable if specialist/doctor gave strong assurance that reduced visits were appropriate." (085_intervention_6months)

Textbox 3. Why a reduction in routinely scheduled visits would not be acceptable.

Reassurance from being checked by physician with specialist expertise

- "Specialist knowledge practised daily is expertise that should be lifesaving. In my opinion there is no substitute for this type of medical examination. Therefore, I would not reduce my medical check frequency." (030_control_6months)
- "Whilst confident I could spot a change, I would still like reassurance of a specialist." (088_intervention_baseline)
- "They are the experts in their fields, not me. I can see, what I think are changes to moles, but they know and when you have had Melanoma you want to be sure." (026_control_baseline)
- "The expert eye of the specialist would be missed." (043_control_6months)
- "I like the reassurance of regular specialist visits. I have so many moles it is hard to keep track with certainty. Do not visit GP for skin checks, only the specialist." (088_intervention_6months)
- "I regard my annual check-up as a 'safety net' of sorts and get some assurance from having a specialist observe my skin for any changes/concerns." (096_intervention_baseline)
- "Having had two melanomas, I feel comfort in having my skin routinely checked by a specialist. I am comfortable checking my own skin and am happy to raise concerns if needed, but I would want to continue with my routine scheduled visits." (062_intervention_baseline)

Perceived very high risk of a subsequent melanoma

- "No circumstances would be acceptable to me, I have a very huge number of dysplastic nevi and had 2 melanomas removed and an area of moles pre melanoma removed. Due to the large number, I feel regular scheduled visits must continue." (003_intervention_6months)
- "I'm a high-risk melanoma patient after having 4 melanomas removed. I will always see my specialist 1 to 2 times per year for the rest of my life." (081_control_6months)
- "One needs regular scheduled visits to keep on top of health issues, especially as one ages." (049_control_6months)
- "Because of family history I would not feel confident having myself or other family members check my skin - especially in areas that I can't see on my body." (031_intervention_6months)
- "I adopt a 'belts and braces' approach. Any missed chance could be fatal for me." (030_control_baseline)

Low confidence in their ability to undertake thorough skin self-examination and detect a concerning lesion

- "The anxiety of not having regular appointments in case I have missed something in my checks." (045_intervention_6months)
- "Prefer regular check-ups with my melanoma specialist as I'm not confident enough with my own recognition." (022_intervention_6months)
- "Not confident enough at present that I can recognise a melanoma." (008_control_6months)
- "I would like to be active in the process and take responsibility, but I don't feel comfortable - I am an anxious person and I feel inadequately prepared to monitor it solely on my own." (015_control_baseline)
- "I would worry I would miss something in my checks and then the longer between doctor visits the more advanced the melanoma becomes." (045_intervention_baseline)

Need for minimum annual clinic review

- "I only see the Melanoma clinic 1 per year now so I would not like to go any less than this. Once per year is not onerous." (014_control_6months)
- "I need the reassurance that I get from a yearly visit with the specialist" (063_control_6months)
- "I see a specialist now every 12 months (last 4 years every 6 months). Every 12 months is not an issue, and it gives me the confidence that I am being examined by a professional." (004_control_baseline)
- "It's always nice to know that an expert will look at your skin at least once per year, even if you yourself are highly conscientious in checking your own skin." (093_control_6months)
- "I am on yearly checks now, reducing this may make me worry more that something may be missed." (071_intervention_baseline)

Circumstances in Which a Reduction in Routinely Scheduled Visits Would Be Acceptable

Trial participants reported prerequisites for a reduction in routinely scheduled visits to be acceptable. These included sufficient time had passed without any subsequent new melanomas, if patients could access expert advice from their specialist via teledermatology and in-person checks could be arranged quickly, if the patient had confidence that patient-led surveillance using digital technology was effective for them personally (answers from control patients were hypothetical in nature, but intervention patients reported that after using the intervention, they were more confident that digital technology tools could help them identify a melanoma early), and if they were reassured that a reduction in routinely scheduled visits was safe and suitable for them.

Why a Reduction in Routinely Scheduled Visits Would Not Be Acceptable

Other trial participants provided explanations for why a reduction in routinely scheduled visits would not be acceptable to them. These included patients who perceived or felt that they were at very high risk of developing a subsequent melanoma; patients who valued the expertise of their specialist and felt reassurance from being checked by a physician with specialist expertise, even if they were confident in SSE; and patients with low confidence in their ability to undertake thorough SSE and detect a concerning lesion. Some patients also said that they were attending annually scheduled reviews and that a further reduction would not be acceptable; others who were attending more frequently said that a partial reduction to annual visits may be acceptable but not any less frequent.

Why Reduction in Routinely Scheduled Primary Care Visits May Have Been More Acceptable Than a Reduction in Scheduled Specialist Visits

Some participants expressed an explicit preference for being checked by their specialist skin doctor (dermatologists and primary care physicians with training in skin cancer) over their local primary care physician, explaining that they had trust in the expertise of their specialist. Other patients explained that only their specialist, not their local primary care physician, played a significant role in their melanoma care (Textbox 4).

Textbox 4. Why reduction in routinely scheduled primary care visits may have been more acceptable than a reduction in scheduled specialist visits (note, general practitioner [GP] in Australia is equivalent to primary care physician in North America).

GP not involved in patient's melanoma care

- "I only go to GP for suture removal. I do monitor my skin and if an issue comes up, I contact the melanoma clinic." (061_control_6_months)
- "With my family history I have annual check. But if anything worries me I photo and email or book a short notice check. My GP says I'm in the best hands and doesn't get too involved." (064_control_6_months)
- "My GP is happy to leave these inspections to my skin Dr." (008_control_baseline)
- "I never consult my GP for skin concerns." (063_control_baseline)
- "I only see my GP when necessary and this isn't connected with my skin examinations." (002_intervention_6_months)
- "Do not visit GP for skin checks, only the specialist." (088_intervention_6_months)
- "I have routine specialist check annually and feel this should continue. Following Molescope photo submission I have been advised to get a mole checked urgently - GP did not want to touch it..." (013_intervention_6_months)

Trust in skin specialist over GP

- "GPs are good however I think you need to have found a GP that you are confident in and have a good relationship with that you can leave the office with either a plan or similar level of confidence that you leave a Dermatologist office with." (072_control_6_months)
- "...don't have confidence in my GP (they just send me to Melanoma specialist) or in my own detection skills." (066_control_baseline)

Discussion

In this pilot trial of 100 patients randomized to patient-led surveillance or usual care, we found no difference between randomized groups in the acceptability of a reduction in routinely scheduled visits. At 6 months after randomization, 34% reported that a reduction would be at least slightly acceptable, 32% reported that a reduction would not be at all acceptable, and 34% did not respond to the question. Among those identifying that a reduction in routinely scheduled visits could be acceptable, a number of prerequisites were identified: sufficient time without a new primary melanoma or recurrence; an unscheduled appointment could be made at short notice if the patient noticed something concerning; their melanoma doctor advised that reducing visit frequency was suitable for them; and they had confidence that an alternative method of surveillance, such as patient-led surveillance, was a safe and effective alternative to usual care.

Our findings agree with previous reports that while some patients may be willing to reduce the frequency of routinely scheduled visits if this is recommended by their clinician [1], many patients, and especially high-risk patients, may be reluctant to do so [9]. The frequency of routinely scheduled clinic visits varies across settings and clinicians and is often influenced by local clinical culture [10,11]. The "less is more" approach [12] aims to deimplement or deadopt inappropriate health care, including that which is untested [13-15]. This may be difficult when the potentially inappropriate care is the usual and expected care and if the new intervention requires learning complex, technical skills that differ significantly to those of the existing health care [13]. Other barriers to deimplementation include patient fear and anxiety, and overestimation of the effectiveness of usual health care by both patients and clinicians [16]. Patients at risk of a new primary or recurrent melanoma may experience reassurance from routine visits, even if it may be otherwise unnecessary. Less contact with their specialist skin doctor may also potentially weaken their patient-doctor relationship [13].

For some patients, taking on more responsibility for surveillance may be empowering and lead to improved clinical and psychological outcomes, especially if they also have an effective skin check partner to support them [17]. Others may not want to take on this responsibility and prefer to continue with their usual routinely scheduled clinic visits [1,9].

Study limitations include missing data (34% [34/100] did not complete the 6-month questionnaire) and unknown generalizability of the trial population. Patients are more likely to be receptive to decreases in visit frequency if there is clear evidence that alternative models of surveillance are safe and effective and that these alternatives do not mean a reduction in care but rather higher value care [10]. A larger MEL-SELF RCT that is currently underway will generate further evidence on the acceptability of a reduction in routinely scheduled visits when undertaking patient-led surveillance [18].

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Melanoma Self Surveillance (MEL-SELF) pilot randomized clinical trial protocol.

[PDF File (Adobe PDF File), 727 KB - derma_v6i1e45865_app1.pdf]

Multimedia Appendix 2

Survey questions relating to hypothetical reduction in routinely scheduled clinic visits.

[DOCX File , 17 KB - derma_v6i1e45865_app2.docx]

Multimedia Appendix 3

Flow of participants: Melanoma Self Surveillance (MEL-SELF) pilot randomized clinical trial.

[DOCX File , 96 KB - derma_v6i1e45865_app3.docx]

Multimedia Appendix 4

Exploratory subgroup analysis by American Joint Committee on Cancer substage.

[DOCX File , 16 KB - derma_v6i1e45865_app4.docx]

Multimedia Appendix 5

CONSORT-EHEALTH (V 1.6.1) - Submission_Publication Form.

[PDF File (Adobe PDF File), 1270 KB - derma_v6i1e45865_app5.pdf]

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Abbreviations

AJCC: American Joint Committee on Cancer substage
CONSORT-EHEALTH: Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Telehealth
MEL-SELF: Melanoma Self Surveillance
RCT: randomized clinical trial
REDCap: Research Electronic Data Capture
SSE: skin self-examination

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Original Paper

Crowdsourcing Skin Demarcations of Chronic Graft-Versus-Host Disease in Patient Photographs: Training Versus Performance Study

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Abstract

Background: Chronic graft-versus-host disease (cGVHD) is a significant cause of long-term morbidity and mortality in patients after allogeneic hematopoietic cell transplantation. Skin is the most commonly affected organ, and visual assessment of cGVHD can have low reliability. Crowdsourcing data from nonexpert participants has been used for numerous medical applications, including image labeling and segmentation tasks.

Objective: This study aimed to assess the ability of crowds of nonexpert raters—individuals without any prior training for identifying or marking cGHVD—to demarcate photos of cGVHD-affected skin. We also studied the effect of training and feedback on crowd performance.

Methods: Using a Canfield Vectra H1 3D camera, 360 photographs of the skin of 36 patients with cGVHD were taken. Ground truth demarcations were provided in 3D by a trained expert and reviewed by a board-certified dermatologist. In total, 3000 2D images (projections from various angles) were created for crowd demarcation through the DiagnosUs mobile app. Raters were split into high and low feedback groups. The performances of 4 different crowds of nonexperts were analyzed, including 17 raters per image for the low and high feedback groups, 32-35 raters per image for the low feedback group, and the top 5 performers for each image from the low feedback group.

Results: Across 8 demarcation competitions, 130 raters were recruited to the high feedback group and 161 to the low feedback group. This resulted in a total of 54,887 individual demarcations from the high feedback group and 78,967 from the low feedback group. The nonexpert crowds achieved good overall performance for segmenting cGVHD-affected skin with minimal training, achieving a median surface area error of less than 12% of skin pixels for all crowds in both the high and low feedback groups. The low feedback crowds performed slightly poorer than the high feedback crowd, even when a larger crowd was used. Tracking the 5 most reliable raters from the low feedback group for each image recovered a performance similar to that of the high feedback crowd. Higher variability between raters for a given image was not found to correlate with lower performance of the crowd consensus demarcation and cannot therefore be used as a measure of reliability. No significant learning was observed during the task as more photos and feedback were seen.

Conclusions: Crowds of nonexpert raters can demarcate cGVHD images with good overall performance. Tracking the top 5 most reliable raters provided optimal results, obtaining the best performance with the lowest number of expert demarcations required for adequate training. However, the agreement amongst individual nonexperts does not help predict whether the crowd has provided an accurate result. Future work should explore the performance of crowdsourcing in standard clinical photos and further methods to estimate the reliability of consensus demarcations.

(JMIR Dermatol 2023;6:e48589) doi:10.2196/48589

KEYWORDS

graft-versus-host disease; cGVHD; crowdsourcing; dermatology; labeling; segmentation; skin; medical image; imaging; feasibility; artificial intelligence

Introduction

Chronic graft-versus-host disease (cGVHD) is the leading cause of nonrelapse long-term morbidity and mortality in patients after allogeneic hematopoietic cell transplantation [1]. Skin is the earliest and most commonly affected organ [2]. Changes in cutaneous manifestations are used to evaluate treatment efficacy and disease progression, assessed by the affected surface area involvement. The National Institutes of Health (NIH) Skin Score is the primary outcome measure in major clinical trials. It is a composite score derived from assessment of the body surface area of erythema (categorical approximation), moveable sclerosis, and nonmoveable sclerosis, combined with a functional and symptomatic assessment [3,4]. The clinical trial for the first Food and Drug Administration–approved (2017) cGVHD treatment, ibrutinib, had a minimum of 25% body surface area erythema as an inclusion criterion [5]. In practice, surface area is estimated by visual assessment using either the Wallace rule of nines, Lund and Browder chart, or palmar units [6]. However, visual assessment of cGVHD suffers from low reliability. Mitchell et al [7] found that the threshold for defining change exceeding measurement error was 19%-22% of the entire body surface area for erythema. This poses a significant barrier to improving patient care through accurate tracking of disease severity and is compounded by the low availability of expert dermatologist evaluation [8].

A recent multicenter cohort study showed that for erythema-type cGVHD, percentage body surface area involvement was a better predictor of mortality than the categorical NIH cGVHD Skin Score [8]. Automated analysis of body surface area from photographs by artificial intelligence (AI) image analysis has shown promise, with a recent study finding that 77% of AI demarcations were scored as clinically acceptable by a board-certified dermatologist across more than 300 photos [9]. Further development of such engineering solutions is greatly hampered by the cost and difficulty of collecting expert demarcations for large numbers of photographs for training and validation.

Crowdsourcing data from a large number of nonexpert participants has been widely used for many medical applications [10,11], including bioinformatics [12], histology image labelling and cell segmentation [13-15], demarcating organs and regions of disease in both 2D and 3D radiology images [16,17], and combining crowd opinions with AI models for improving the severity scoring of diabetic retinopathy [18]. Recent work has also shown expert-level crowd performance for identifying some features of pigmented skin lesions in dermoscopic images, which comprise high magnification, narrow field of view cross-polarized photos of the skin surface [19].

Our study aimed to assess the ability of a crowd of nonexpert raters to demarcate photos of cGVHD-affected skin, which could provide a scalable solution for demarcating large numbers of patient photos for AI training. Cutaneous cGVHD often presents as complex areas of erythema and surface changes with ill-defined borders. This demarcation task typically requires significant training and is known to exhibit high variability even among experts [7]. To study the effect of training and feedback on crowd performance, we split raters into 2 groups (high and low feedback) that each received a different amount of ground truth feedback during data collection.

Methods

Materials

Patient characteristics are given in Table 1. The patient cohort had an age range of 21-72 (median 58, IQR 46-66) years and were photographed at 6 to 4520 days post–hematopoietic cell transplantation (median 1092, IQR 266-1724 days). Cutaneous cGVHD presented as erythema for 7 patients, sclerosis for 7 patients, and both erythema and sclerosis for 9 patients.

We took 360 3D photographs of the skin of 36 patients with cGVHD using a handheld commercial stereoscopic camera (Vectra H1, Canfield Scientific). This stereoscopic camera provides a cross-polarized flash and ranging lights to improve the consistency of photographic conditions between body sites and patients. It also enables accurate ground truth markings of affected skin areas directly on the 3D surface, which can generate multiple 2D views of the same skin from different angles to more closely emulate standard clinical photography. From each 3D photo, a set of 2D images were created from different viewing angles using Vectra Analysis Module software (Canfield) following an automated scripting protocol, as described in previous work [9,20]. Defining the original camera view as an angle of 0 degrees, we rotated the skin surface through combinations of 0 degrees, +15 degrees, and -15 degrees along the horizontal and vertical axes to create multiple views of the same skin area under identical photographic conditions. Table 2 shows how the photo set was split into photos for training and feedback (7 angles per photo) and photos for testing crowd performance (9 angles per photo). We refer to the training set as the “ground truth provided” set and the test set as the “ground truth withheld” set (Table 2). In total, the full set consisted of 3000 2D images for demarcation by the crowd, with the test set consisting of 711 ground truth withheld images with cGVHD-affected skin (per ground truth).

Table 1. Race, gender, ethnicity, and Fitzpatrick skin types of patients involved in the study.

Characteristic	Patients (n=36)
Race, n (%)	
American Indian or Alaska Native	0 (0)
Asian	0 (0)
Black or African American	3 (8)
Native Hawaiian or Other Pacific Islander	0 (0)
White	33 (92)
Gender, n (%)	
Man	26 (72)
Woman	10 (28)
Ethnicity, n (%)	
Hispanic or Latino	0 (0)
Not Hispanic or Latino	36 (100)
Fitzpatrick skin type, n (%)	
I	0 (0)
II	8 (22)
III	24 (67)
IV	1 (3)
V	1 (3)
VI	2 (7)
Age (years), median (IQR)	58 (46-66)
Time since transplant (days), median (IQR)	1092 (266-1724)

Table 2. Distribution of photos and patients between the feedback (ground truth provided) and analysis (ground truth withheld) sets. For each stereoscopic photo, 9 images from different angles were produced.

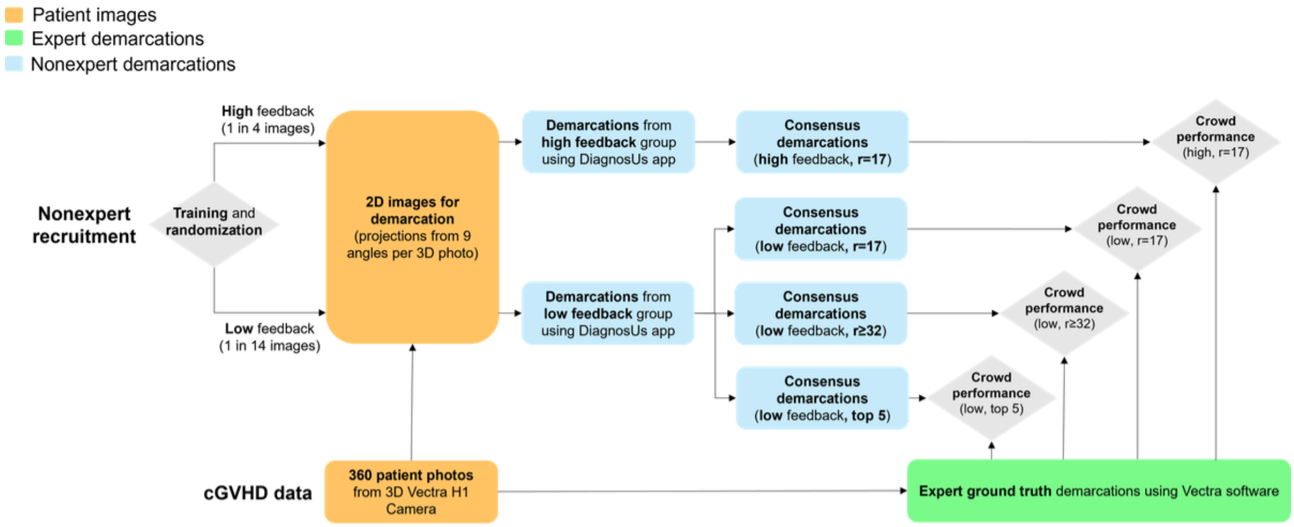
Data category	Ground truth provided set	Ground truth withheld set
cGVHD[a]-affected		
Photos (n=179), n (%)	100 (56)	79 (44)
Patients (n=25), n (%)	19 (76)	22 (88)
cGVHD-unaffected		
Photos (n=181), n (%)	20 (11)	161 (90)
Patients (n=23), n (%)	18 (78)	22 (96)
Total		
Photos (n=360), n (%)	120 (33)	240 (67)
Patients (n=36), n (%)	31 (86)	34 (94)

[a]cGVHD: chronic graft-versus-host disease.

Study Design

A flowchart of the study design is shown in Figure 1. Patient photos were first demarcated by a trained expert to provide the ground truth. A crowd of nonexperts were then recruited through the Centaur Labs' DiagnosUs app and randomized into low and high feedback groups after training. Crowd demarcations were gathered for each image, which were combined into separate consensus demarcations for each crowd. Performance was assessed by comparing the consensus demarcations to the expert ground truth.

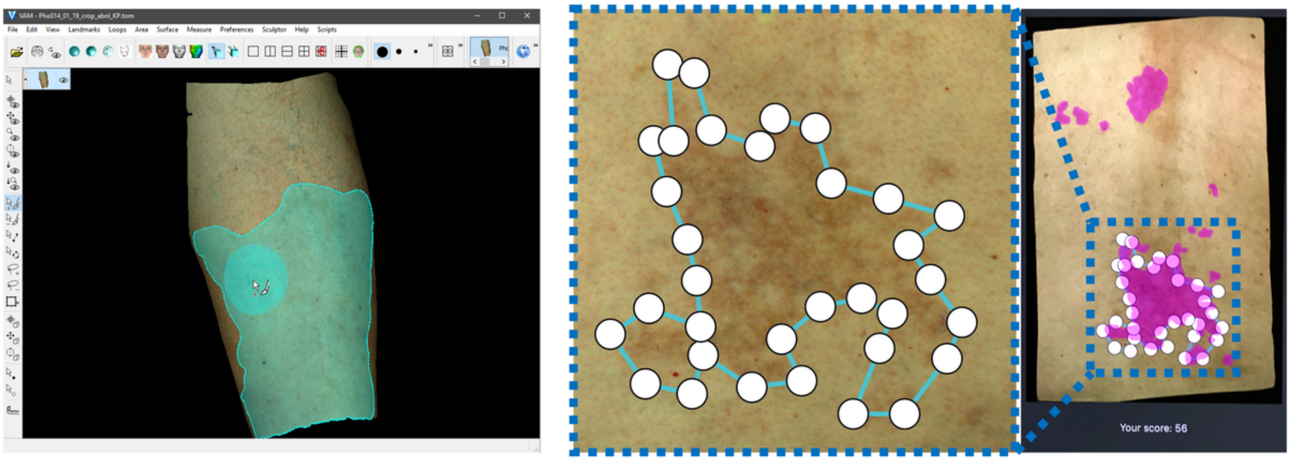
Figure 1. Flowchart of the study design. cGVHD: chronic graft-versus-host disease; r: rater.



Ground Truth Demarcations

A single expert (KP) provided ground truth demarcations of cGVHD-affected skin following an extensive training program [21], which were reviewed by a board-certified dermatologist (ERT) for accuracy. Affected skin areas were demarcated on the 3D skin surface using Vectra Analysis Module software (Figure 2a). The skin surface could be rotated and zoomed in 3D space, with affected skin areas demarcated using a paintbrush tool. This allowed us to create the most accurate demarcations of affected skin from the visual appearance alone. These ground truth areas were used for training the crowd through visual feedback and evaluating their performance.

Figure 2. Annotation interfaces used for (A) ground truth demarcations using the Vectra Analysis Module and (B) crowd demarcations using the DiagnosUs app, including ground truth feedback during training.



(a) Vectra Analysis Module interface (b) DiagnosUs app interface

Crowd Training and Data Collection

The DiagnosUs app gamifies medical image demarcation tasks, creating time-limited competitions with leaderboards and prizes to incentivize engagement. Only 2D images are supported through the app and its mobile interface, necessitating the use of projected images of the skin surface. The interface uses the touch screen of a mobile device for demarcating areas using nodes, which outline the desired shape (Figure 2b). Multiple nontouching areas can be marked on a single image if needed, and node positions can be adjusted after placing before the final submission.

We used 8 images to train all raters before they began the demarcation task (Figure 3). For each training image, the rater was first shown the unmarked image with corresponding text by the expert dermatologist describing what features they should look for (Table 3). Upon submitting their demarcation, the rater was then shown the expert ground truth and their accuracy score. Training was completed once all 8 training images had been adequately marked. Each rater was randomly assigned to the high or low feedback group. No knowledge of the different groups or their assignments were communicated to the raters.

We held 8 24-hour competitions for data collection, with each user asked to demarcate 200 randomly selected images from the full set of 3000. Cash prizes were offered for each competition based on performance ranking, and all 200 images needed to be demarcated to be eligible for a given competition. Images were split into those for which the ground truth may be provided for feedback and quality assurance and those for which the correct answer was entirely withheld. Crowd performance was assessed on the 711 images of affected skin for which the ground truth was entirely withheld (never released to Centaur Labs). Raters in the high feedback group received feedback on 1 out of every 4 cases, while those in the low feedback group received feedback on 1 out of every 14 cases. For each image, we recorded the first 17 rater (r) opinions in both the high and low feedback groups, denoted as "r=17". To test if a larger crowd could overcome the expected performance drop from less training feedback, data collection was extended for the low feedback group up to 32-35 demarcations per image, denoted as "r≥32". Finally, the effect of tracking only the most reliable raters was examined. The performance of individuals was tracked on the images for which the ground truth was provided (ground truth provided set in Table 2), and the 5 best performers for each image in the ground truth withheld set were selected in the low feedback group, denoted as the "top 5" group.

Figure 3. The 8 images used for training the crowd during study enrollment. Ground truth demarcations of cGVHD-affected skin are shown in green. The corresponding text descriptions of each disease presentation are given in Table 3. cGVHD: chronic graft-versus-host disease.

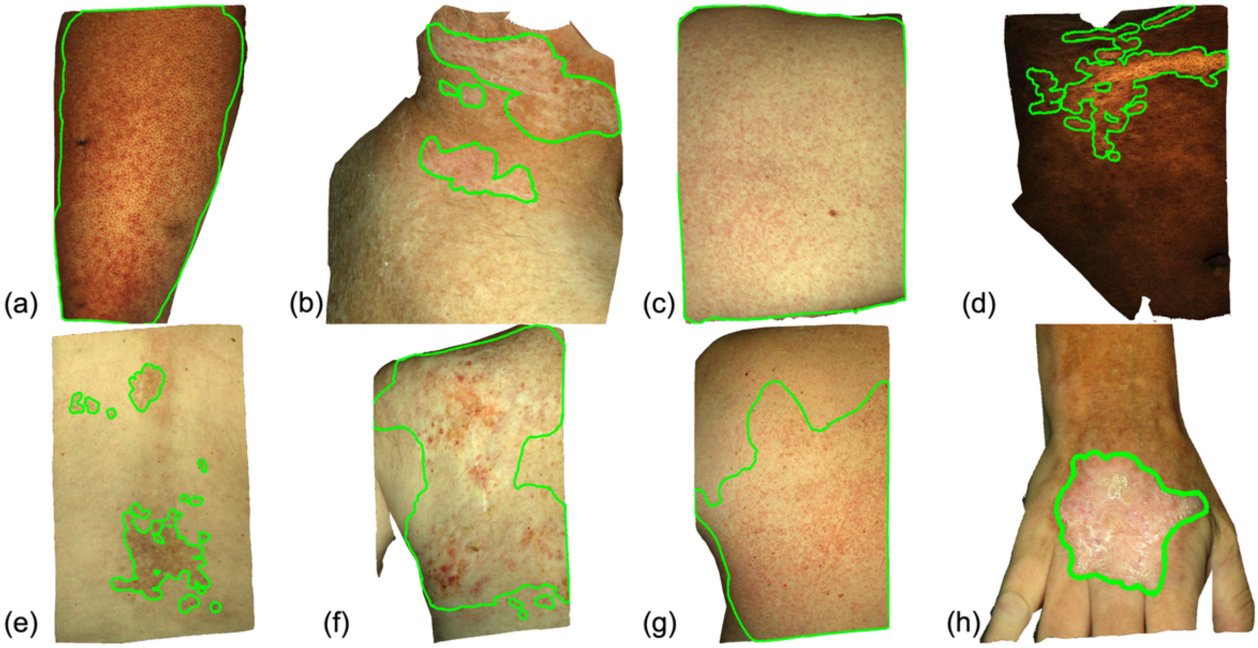


Table 3. Text descriptions provided for each of the 8 training images shown in Figure 3.

Image[a]	Description
(a)	On the anterior left thigh, there are numerous diffuse erythematous macules and papules coalescing into patches and plaques. When large areas of the skin are affected by cGVHD[b], visual comparison to healthy skin can be difficult.
(b)	On the right, posterior neck of a patient with sun damage, there is a large scaly, hypopigmented patch with erythematous borders.
(c)	On the back, there are diffuse, erythematous papules that coalesce into a plaque in the central, left portion of the image. This is an example of a morbilliform eruption, which can be caused by cGVHD. The entirety of the skin image may be affected by cGVHD, as in this example, so careful attention must be paid to all areas shown.
(d)	On the right upper quadrant of the abdomen, there is a well-defined hypopigmented patch. As skin tones vary between patients, visual comparisons should be made with unaffected regions on each image when possible.
(e)	On the back, there are several well-defined, hyperpigmented patches consistent with post-inflammatory changes that can occur in cutaneous cGVHD.
(f)	cGVHD may present as a large area of sclerosis with superimposed areas of color and texture changes.
(g)	On the back, there are numerous diffuse erythematous macules and papules. Areas of rash may be ill-defined, so care must be taken to examine the skin in detail. The annotation boundaries should be carefully placed to encompass all high certainty regions of affected skin.
(h)	On the dorsum of the right hand, there is a single well-defined, scaly erythematous plaque.

[a]Image letters correspond to the panels in Figure 3.

[b]cGVHD: chronic graft-versus-host disease.

Crowd Consensus Demarcations

We constructed 4 different sets of consensus demarcations from the 4 constructed crowds (r=17 from the high feedback group and r=17, r≥32, and top 5 from the low feedback group). Each crowd's consensus demarcation for an image was calculated by simple majority vote. For a given image, each pixel was labelled with the number of raters who marked it as affected. The consensus demarcation consisted of all pixels labelled by the plurality of raters (50% or more) in the crowd being analyzed, following the standard majority vote method [22]. The final consensus mask provides a binary label for every pixel in the image, being either cGVHD-affected skin or cGVHD-unaffected skin. The consensus demarcation for each crowd was considered their best estimate of cGVHD-affected skin for the given image.

Agreement Measures

Crowd demarcations were analyzed only for photos for which the ground truth was never provided to any of the app users. We used 2 metrics: the Dice coefficient and the surface area error. To measure spatial overlap, we used the machine vision metric of the Dice coefficient [23], which ranges from 0 for no overlap to 1 for perfect agreement. For context, a recent study of 3 nonexperts who underwent an extensive 4-month training program for demarcating cGVHD led by a board-certified dermatologist were found to achieve a median Dice of 0.75 (IQR 0.68-0.84) when compared to the expert [21]. While commonly used for comparing demarcations in many medical imaging tasks, use of the Dice metric alone has been shown to be inadequate for capturing training effects for cGVHD skin demarcations [21]. Therefore, we also calculated the surface area error, which represents the absolute difference in the percentage of skin area marked by the crowd compared to the ground truth. For example, if the ground truth demarcation covered 10% of the skin area and the crowd marked 25%, then the surface area error is 15%. This performance measure of skin area estimation parallels the scoring accuracy measures often used for in-person clinical assessment [7].

Learning Effects

The effect of feedback and experiential learning on the performance of the crowd was examined by tracking the performances of individual raters over the first 100 images with cGVHD-affected skin as the ground truth.

Ethical Considerations

This study was performed using nonidentifiable photographs under Vanderbilt University institutional review board exemption 191042.

Results

Demarcating cGVHD-Affected Skin

Combined across all 8 competitions, a total of 291 raters were recruited, with 130 (45%) assigned to the high feedback group and 161 (55%) to the low feedback group, 111 (38%) of which contributed to the low r=17 crowd. This produced a total of 133,854 individual demarcations, including 54,887 (41%) from the high feedback group and 78,967 (59%) from the low feedback group.

The subset of photos for which no ground truth was shown to any user included 79 photos from 22 patients with cGVHD-affected skin per the completely withheld ground truth (Table 2). To avoid the possibility that a user might have somehow seen the solutions to their delineation task for a particular patch of skin, we assessed the performance of the crowd on these 711 images (9 angles per photo) only. Figure 4a shows the crowd performance by Dice. The high feedback r=17 crowd and low feedback top 5 crowd were not significantly different according to a Mann-Whitney *U* test (*P*=.64), with a Dice coefficient of 0.8. Compared to the high feedback crowd, both the low r=17 and low r≥32 crowds were significantly different, with Dice coefficients of 0.7. Figure 4b shows the surface area error for each group. The high feedback and low feedback top 5 crowds had a surface area error of 9%, but the other 2 low feedback crowds were significantly different at 11%.

Figure 5 shows examples of inconsistencies observed across the crowds. Figure 5a shows consistent demarcation of highly affected areas by both the high and low top 5 crowds; however, there was poor identification of subtle surface changes, which were also marked in the expert ground truth. Figure 5b demonstrates an instance where the high feedback crowd failed to identify abnormal changes while the low top 5 crowd identified 75% of the abnormal skin area. Figure 5c highlights an instance of high variability between images from different angles of same skin region in the low top 5 crowd, where 2 images show good agreement with the ground truth, but the third image consensus predicted no affected skin. In all cases, we also noted the sharp edge and lower specificity of areas marked by the crowd. This is likely due to the mobile interface providing lower fidelity for marking complex shapes as compared to the Vectra Analysis Module software used for marking the ground truth (Figure 2).

Figure 4. Performance of crowd groups for demarcating images with cGVHD-affected skin per ground truth using the (A) Dice coefficient and (B) surface area error. Each point represents the majority vote mask for a single image (711 images in total). Whiskers indicate 1.5 × IQR. Mean values are shown indicated by the dashed red line. cGVHD: chronic graft-versus-host disease; r: rater.

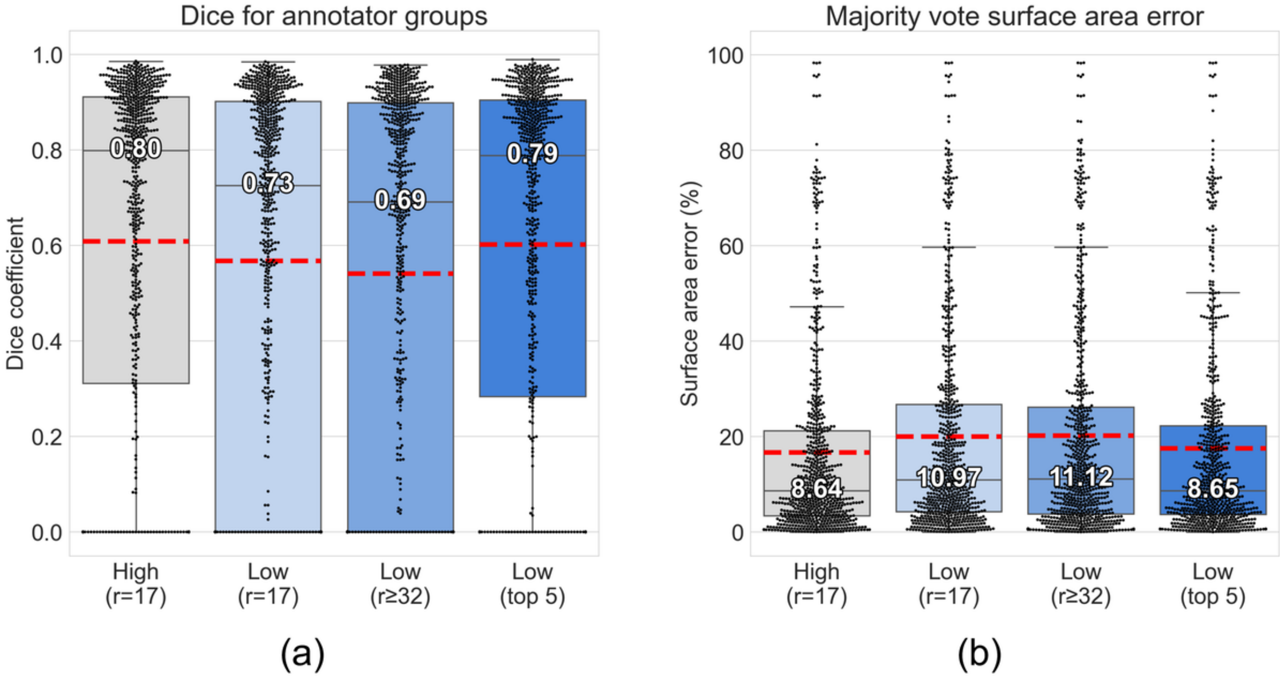
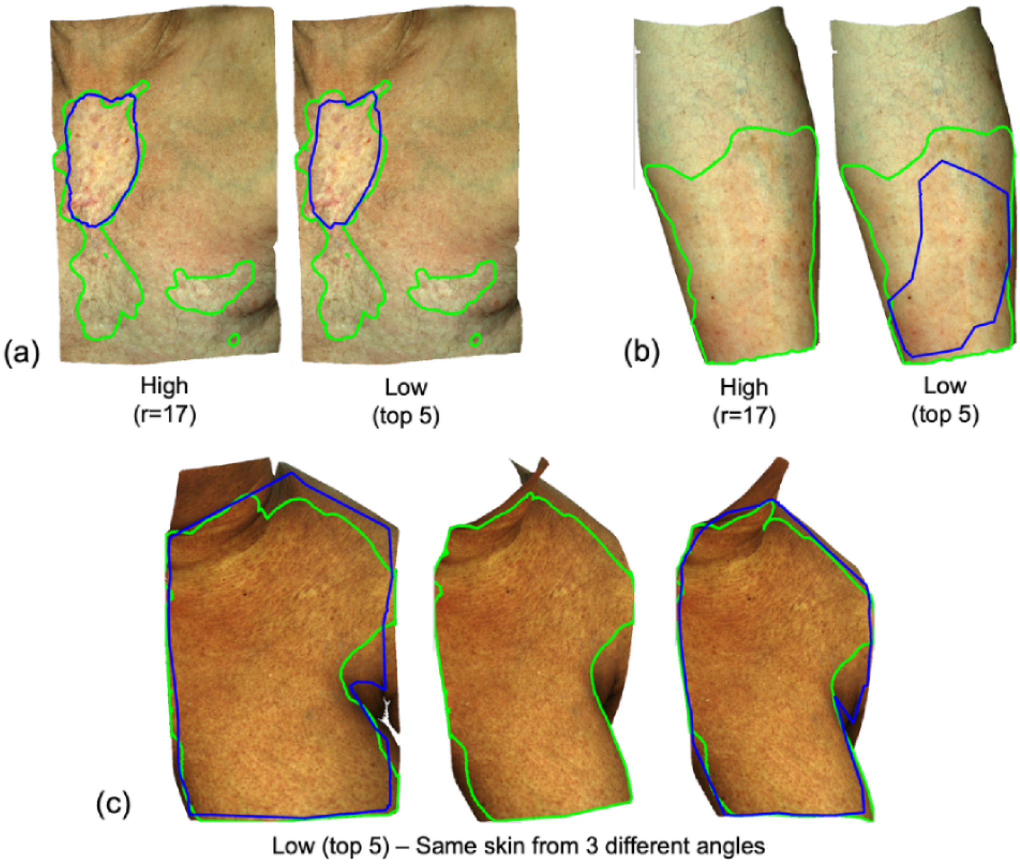


Figure 5. Example demarcations from the crowd (blue) versus ground truth (green). (A) Consistent demarcation of highly affected areas by crowds assembled from both the high and low feedback groups, but both missed areas of subtle surface changes. (B) The high feedback crowd failed to identify abnormal changes while low feedback top 5 crowd identified 75% of abnormal skin areas. (C) High variability between images of the same skin region viewed from different angles by the low feedback top 5 crowd. cGVHD: chronic graft-versus-host disease; r: rater.



Reliability of Demarcations

Despite good median performance of the different crowds across the full set, we observed a number of high error images in all groups (Figure 4b). Because the expert ground truth was available in 3D on our unique photo set but crowd annotation was done in 2D, we were able to test the performance of the crowd on the same area of skin under identical photographic conditions from different viewing angles. Figure 6 shows the surface area error for the low feedback top 5 crowd for each of the 9 projected images from each 3D photo, ordered by descending median error. We observe outlier images with significant errors in both high and low median error photos. The set of individual raters contributing to the consensus demarcation will vary between images, suggesting that interrater variability could contribute to the inconsistent reliability across images of the same skin.

To test if there was an observable association between the level of disagreement and the accuracy of the crowd demarcations, Figure 7 shows correlation plots of the surface area error of the consensus mask for a given photo against the SD of the crowd's estimate of surface area for that photo. We found no significant correlation between the variability of individual raters and the accuracy of the consensus mask, with a near-zero coefficient of determination for simple linear regression in all groups. Therefore, the level of disagreement between raters cannot be used as a measure of reliability for this task.

Figure 6. Per-photo surface area error for the low feedback group (top 5 raters). 3D photo IDs are ordered by decreasing median error. The shaded area shows the range of error between 2D projections for each 3D photo.

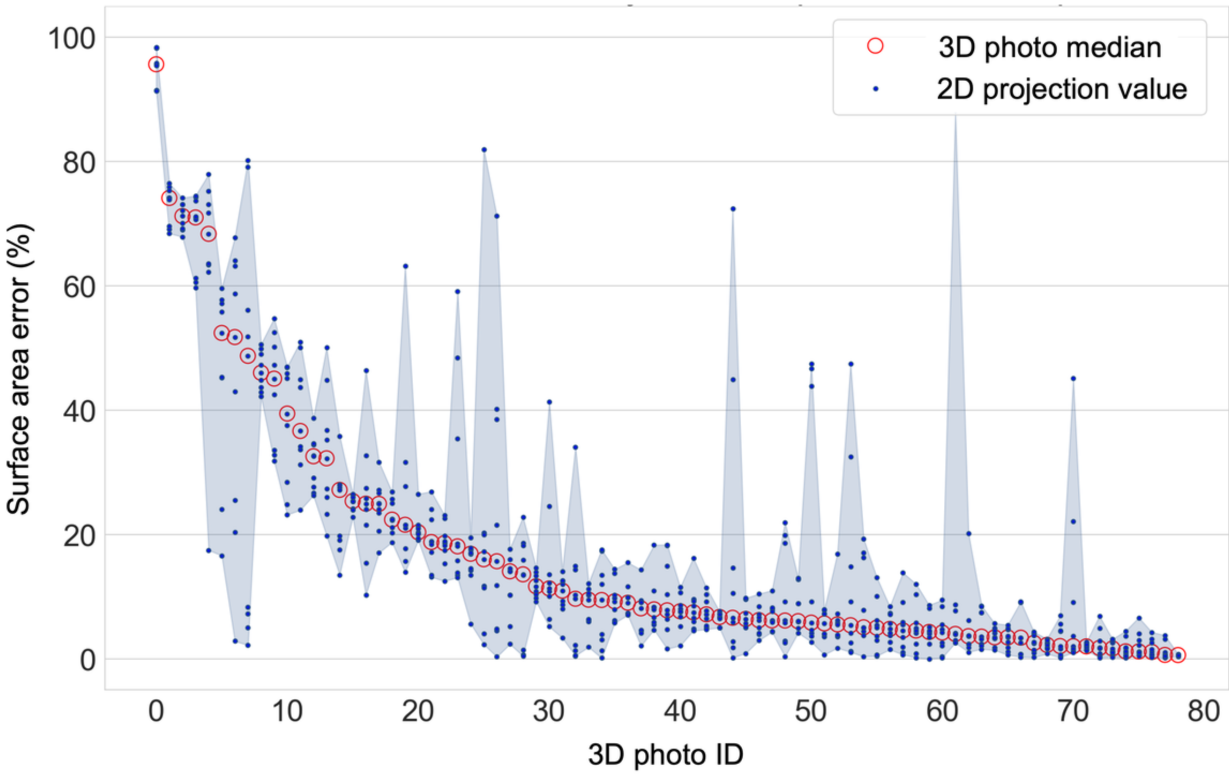
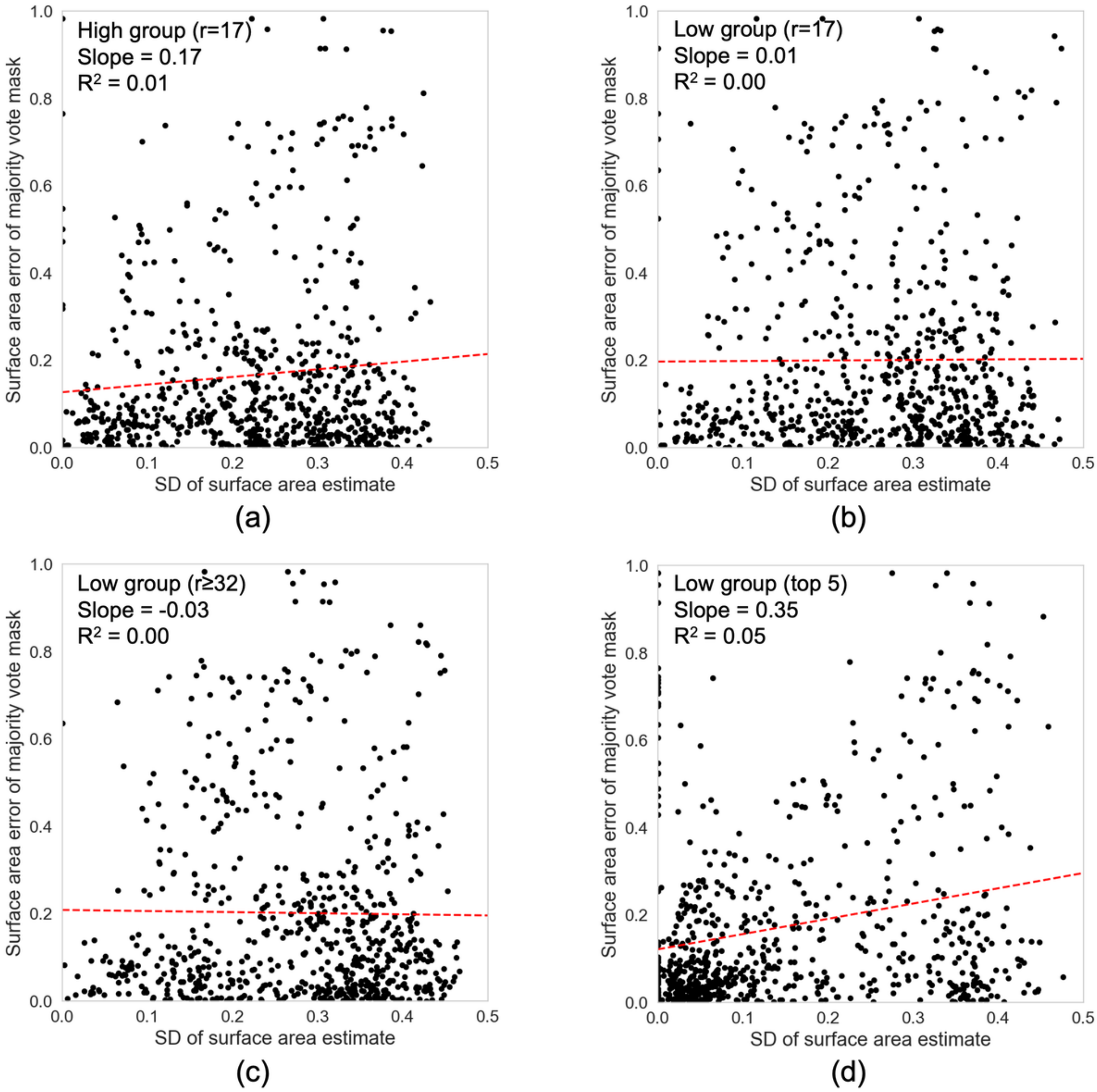


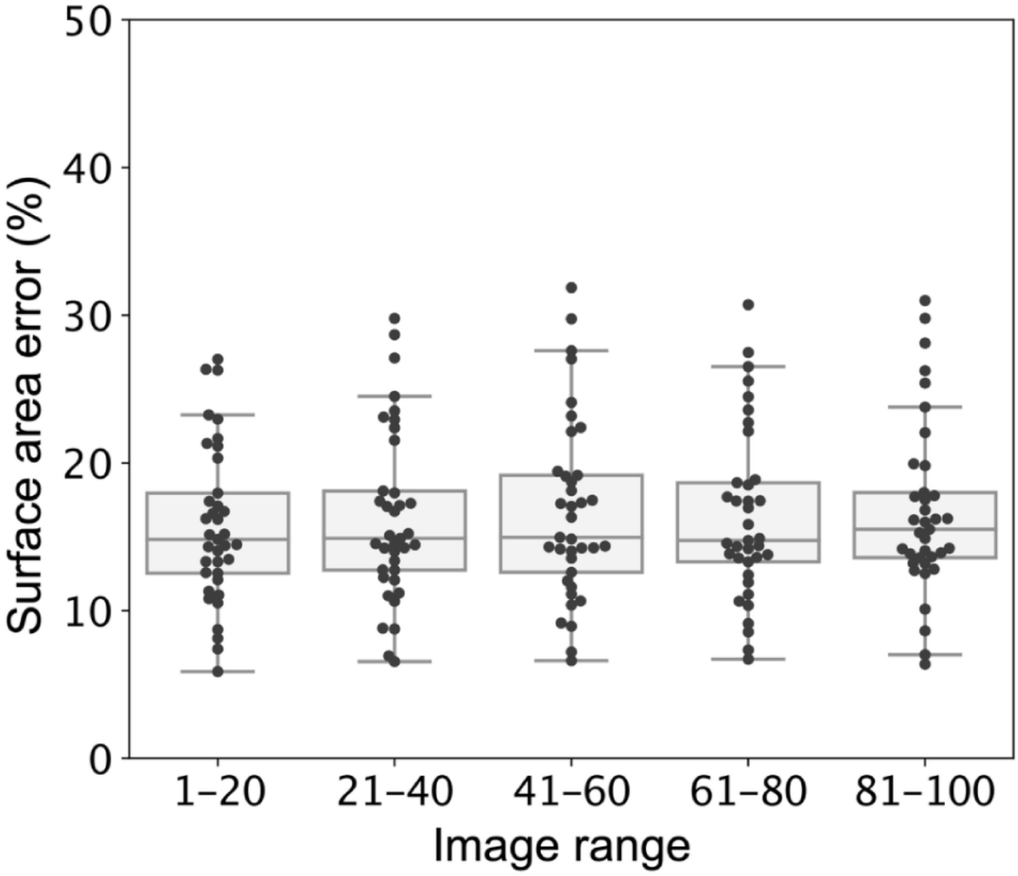
Figure 7. Surface area error of the majority vote mask versus the SD of surface area estimates for each photo. Slope and coefficient of determination (R_2) for the linear regression fit (red dashed line) are also given.



Performance Over Time

The effect of training on performance was examined by tracking the performance of all raters over the first 100 affected skin photos that they marked for which the ground truth was never shown. A total of 37 raters met this criterion. The mean performance over time for each eligible rater is shown in Figure 8, with no increase in performance seen over the first 100 images marked. Similar results on minimal training effects have been reported in other crowdsource studies [17].

Figure 8. Surface area error of individual raters in successive groups of affected images. Error is displayed for all 37 raters who marked at least 100 affected images. Each point is the mean error for a given user for the group of 20 photos in the stated image range.



Discussion

Principal Findings

A crowd of nonexpert raters was able to achieve good overall performance for segmenting cGVHD-affected skin with minimal training. The median surface area error was less than 12% for all crowds. The low feedback r=17 crowd performed slightly poorer than the high feedback crowd, with a 2% to 3% increase in surface area error. Recruiting more raters to the low feedback group for a larger crowd (r≥32) did not improve performance relative to the original low feedback crowd (r=17). However, tracking the top 5 most reliable raters from the low feedback group for each image was able to recover almost identical performance to the high feedback crowd. We believe this is due to individuals within the crowd likely having different skill levels for the assigned task, as has been noted in similar crowdsource studies [22]. We therefore recommend tracking rater performance to ensure the most reliable individuals contribute to the consensus demarcations. This optimal strategy will yield the best crowd performance while lowering the required number of expert demarcations for training.

High variability between different angles of the same skin area were observed, raising concerns for the reliability of the consensus demarcation for any given image with an unknown ground truth. Higher variability between raters for a given image was not found to correlate with lower performance of the crowd consensus demarcation and cannot therefore be used as a measure of reliability. Finally, no significant learning was observed during the task as more photos and feedback were seen.

Limitations

A limitation of our study was the lack of diversity in skin types. Our cohort was dominated by lighter skin tones; 32 patients had Fitzpatrick skin type III or lower, while only 4 patients had skin types IV and higher. Despite the good overall performance of the crowd, further study is needed to disentangle the possible sources of disagreement that were observed and develop methods to mitigate these effects.

Future Work

We have demonstrated the potential utility of employing a crowd of nonexpert raters for demarcating cGVHD-affected skin in patient photos. Next steps should explore if this performance is maintained when applied to standard clinical photos, where lighting conditions, imaging distances, and photo quality may be more variable than the more standardized set used here. In addition, further methods of estimating the reliability of the consensus demarcations should be explored to provide more robust quality assurance and filter out high error outliers. Future studies using more extensive training techniques and a unified interface for crowd and expert demarcations will also be important for establishing nonexperts' understanding of the complex task and methods to minimize potential sources of variability. Accurately recognizing active disease is a major clinical concern, with even expert dermatologists commonly disagreeing on whether a skin area is erythematous or hyperpigmented [24]. New technologies, such as hyperspectral imaging, have shown promise for addressing this limitation in clinical practice [25]. The ability of the crowd to differentiate between disease types should also be explored in future studies given the good overall performance for recognizing cGVHD-affected skin.

Ultimately, the application of crowdsourcing could offer a scalable solution for labelling large sets of images for the training of automated AI algorithms. The effect of training with a larger volume of lower quality demarcations versus a smaller number of expert demarcations, as reported previously [9], also warrants future investigation.

Conclusion

We have shown that a crowd of nonexpert raters is capable of delineating surface areas of cGVHD-affected skin (9%-11% surface area error) better than the current clinical standard (19-22% [7]). Crowd demarcation therefore offers a practical solution for accurately demarcating large databases of patient photos, which is a crucial unmet need for training reliable AI image analysis methods. Such methods could provide a clinically meaningful improvement to the current standard given that body surface area has been shown to be a better predictor of mortality than the NIH cGVHD Skin Score [8].

Acknowledgments

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Conflicts of Interest

EPD is the chief executive officer of Centaur Labs and holds shares in the company. KM is an employee of Centaur Labs.

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Abbreviations

AI: artificial intelligence
cGVHD: chronic graft-versus-host disease
NIH: National Institutes of Health
r: rater

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Original Paper

Dermatologists' Perceptions of the Use of Teledermatology in Managing Hidradenitis Suppurativa: Survey Study

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Abstract

Background: The field of teledermatology has expanded tremendously and has been used for conditions including hidradenitis suppurativa (HS). However, due to the sensitive location of lesions, HS may be considered less suitable for teledermatology.

Objective: We sought to assess dermatologists' experiences and perceptions toward using teledermatology for HS relative to atopic dermatitis (AD) as a comparison.

Methods: A survey was disseminated electronically to practicing dermatologists in the Asia-Pacific region between February and June 2022. Differences in attitudes and perceptions between HS and AD were compared using random-effects ordered logistic regression, controlling for demographics.

Results: A total of 100 responses were obtained comprising of 76 (81.7%) dermatologists and 17 (18.3%) dermatology trainees; 62.6% (62/98) of physicians were uncomfortable with using teledermatology for HS. Multivariable regression confirmed increased perceived challenges with managing HS using teledermatology compared to AD. These challenges include the need for photography of hard-to-reach or sensitive areas (odds ratio [OR] 4.71, 95% CI 2.44-9.07; *P*<.001), difficulties in accurate assessment of severity (OR 2.66, 95%CI 1.48-4.79; *P*=.001), and inability to palpate lesions (OR 2.27, 95% CI 1.23-4.18; *P*=.009).

Conclusions: This study confirms the relative reluctance of dermatologists to use teledermatology for HS and complements existing data showing mixed levels of willingness from patients. The use of teledermatology for HS may need to be optimized to overcome these challenges, including increasing security features, selection of patients with milder or limited diseases, and selecting patients with an established and strong doctor-patient relationship.

(JMIR Dermatol 2023;6:e43910) doi:10.2196/43910

KEYWORDS

teledermatology; telehealth; telemedicine; hidradenitis suppurativa; atopic dermatitis; dermatitis; skin; dermatology; perception; experience; attitude; opinion; dermatologist; health care professional; health care provider; acceptance; adoption; COVID-19

Introduction

With the COVID-19 pandemic, there has been a rapid adoption of teledermatology on a global scale. A large survey study by the American Academy of Dermatology Teledermatology Task Force subgroup assessed the effects of COVID-19 on teledermatology among American Academy of Dermatology members, illuminating dermatologists' sentiments toward different teledermatology modes as well as their opinions regarding reimbursement, perceived barriers, and anticipated future use [1].

Hidradenitis suppurativa (HS) is a condition that has been managed with teledermatology [2-4]; however, unique barriers and considerations may be present due to the sensitive sites and nature of skin lesions. Although several studies have explored the willingness and concerns of patients with HS toward teledermatology, the perceptions of dermatologists in this regard remains relatively unexplored.

Methods

Procedures

An electronic questionnaire was disseminated to members of the Asia Pacific Hidradenitis Suppurativa Foundation through a central email blast and word of mouth. Responses were gathered from February to June 2022. Inclusion criteria included any current practicing dermatologist (in private and public sectors) or dermatology trainee. Exclusion criteria included dermatologists who were not actively practicing and health care practitioners who were not yet officiated under a dermatology training program.

The survey questioned opinions toward using teledermatology to manage HS. To differentiate concerns specific to HS and those relating to teledermatology in general, perceptions were compared with atopic dermatitis (AD), a common chronic inflammatory dermatosis that has been managed over teledermatology. Several questions from this survey drew reference from the Likert-scale questions in the study by Kennedy et al [1]. Physician demographics, such as age, gender, and practice type, were also collected. Responses were anonymous and collected using a secure platform (FormSG).

Descriptive findings were summarized by frequency (percentages). Attitudes of physicians toward using teledermatology for HS and AD were summarized according to the extent of agreement (ie, strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree). For simplicity of data representation, the groups were reduced to "agree," "neutral," and "disagree." Associations between demographics and attitudes toward teledermatology for HS were evaluated by multivariable ordered logistic regression. The proportional odds assumption was assessed by approximate likelihood-ratio test via a generalized ordered logistic regression. Attitudes toward teledermatology between HS and AD were compared by random-effects ordered logistic regression, with adjustment for demographics. Age was treated as a continuous variable and analyzed at 5-year unit intervals. All statistical analyses were conducted using Stata/SE (version 17.0; StataCorp LLC). All statistical tests were 2-sided with a 5% significance level.

Ethics Approval

This study was approved by the National Health Group institutional review board (DSRB 2021/00632). Respondents were not compensated for participating in this study.

Results

In total, 100 responses were obtained, comprising of 76 (81.7%) dermatologists and 17 (18.3%) dermatology trainees. There was an equal representation of male and female genders (n=52, 52% males). The majority of physicians (n=70, 70%) were between 30-45 years of age, and 88 (86.3%) physicians practiced in parts of the Asia-Pacific region. More than half of the surveyed physicians (n=64, 64%) worked in public institutions (Table 1).

A minority of respondents (38/98, 38.8%) agreed or strongly agreed that there were comfortable using teledermatology to manage HS. The majority (62/98, 62.6%) disagreed or strongly disagreed that they would be comfortable using teledermatology to replace their usual physical HS consultations; only 30/98 (30.6%) perceived their patients with HS to be receptive toward teledermatology (Table 2).

Physician age influenced perceived comfort with using teledermatology for HS. Older physicians tended to express difficulties with accurate assessment of disease severity for HS over teledermatology (for every 5 year increment of age, there was an increased OR of 1.30, 95%CI 1.01-1.67; P=.045) and concerns that patients may not be familiar with using teledermatology for HS (for every 5 year increment of age, there was an increased OR of 1.37, 95%CI 1.05-1.80; P=.02; Table S1 in Multimedia Appendix 1).

Figure 1 and Figure 2 show the distribution of responses regarding the perceptions toward use of teledermatology for HS and AD, respectively. For both HS and AD, the greatest reported barriers toward the use of teledermatology were difficulties with assessing disease severity and inability to palpate lesions. In contrast, unfamiliarity of physicians followed by unfamiliarity of patients with teledermatology were the least reported barriers.

Multivariable regression confirmed increased perceived challenges with managing HS using teledermatology compared to AD even after controlling for physician demographics. These challenges include the following: (1) ensuring privacy when examining sensitive body areas (OR 2.75, 95%CI 1.36-5.56; P=.005); (2) photography of hard-to-reach or sensitive areas (OR 4.71, 95% CI 2.44-9.07; P<.001); (3) accurate assessment of severity (OR 2.66, 95%CI 1.48-4.79; P=.001); (4) ability to palpate lesions (OR 2.27, 95% CI 1.23-4.18; P=.009); and (5) visualization of lesions clearly over teledermatology (OR 3.59, 95% CI 1.86-6.96; P<.001; Table 3).

Table 1. Demographics of survey respondents.

Characteristics	Values, n (%)
Age (years)	
30-35	26 (26)
36-40	24 (24)
41-45	20 (20)
46-50	10 (10)
51-55	2 (2)
56-60	8 (8)
61-65	4 (4)
66-70	4 (4)
>70	2 (2)
Gender	
Male	52 (52)
Female	48 (48)
Type of practice	
Public or restructured	64 (64)
Private hospital	10 (10)
Private clinic (solo)	13 (13)
Private clinic (group)	13 (13)
Current role	
Dermatologist	76 (81.7)
Dermatology trainee	17 (18.3)

Table 2. Physician views toward using teledermatology to manage hidradenitis suppurativa (HS).

Questionnaire items	Strongly disagree, n (%)	Disagree, n (%)	Neither agree nor disagree, n (%)	Agree, n (%)	Strongly agree, n (%)
I would feel comfortable using teledermatology to manage HS.	6 (6.1)	26 (26.5)	28 (28.6)	28 (28.6)	10 (10.2)
I would feel comfortable with using teledermatology to replace my usual consults for HS.	22 (22.2)	40 (40.4)	25 (25.3)	9 (9.1)	3 (3)
I think my patients with HS are generally technologically savvy.	4 (4.1)	22 (22.5)	51 (52)	14 (14.3)	7 (7.1)
I think my patients with HS would be receptive to being seen over teledermatology.	6 (6.1)	28 (28.6)	34 (34.7)	23 (23.5)	7 (7.1)
The keenness of my patient with HS to do a teledermatology would increase my willingness to do a teledermatology consult.	6 (6.1)	12 (12.2)	29 (29.6)	37 (37.8)	14 (14.3)

Figure 1. Challenges faced by physicians when using teledermatology for hidradenitis suppurativa.

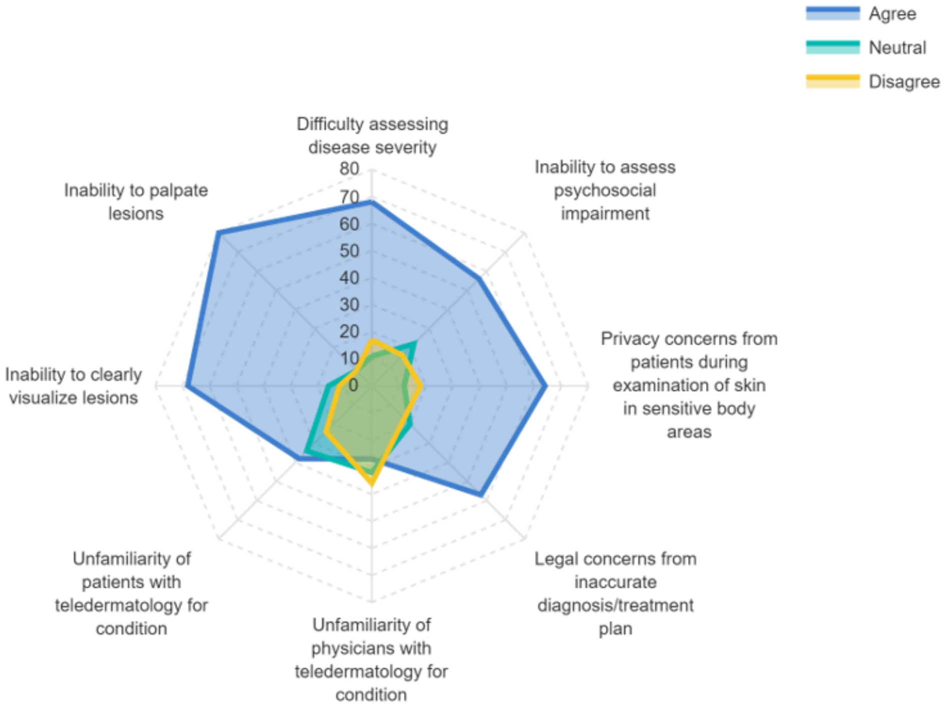

Figure 2. Challenges faced by physicians when using for atopic dermatitis.

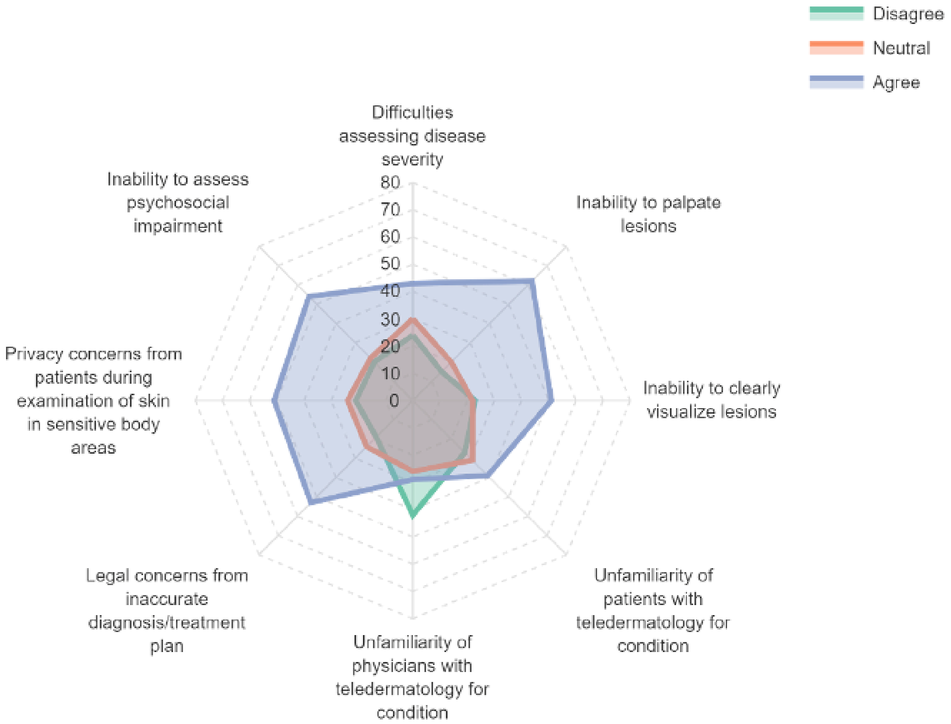

Table 3. Comparison of attitudes toward teledermatology between hidradenitis suppurativa (HS) and atopic dermatitis (AD). Italicized *P* values are significant.

HS vs AD	Univariable		Multivariable[a]	
	Unadjusted OR[b] (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
It is difficult for patients to photograph or video hard-to-reach or sensitive areas	4.25 (2.28-7.94)	<.001	4.71 (2.44-9.07)	*<.001*
It is difficult for physician to accurately assess disease severity	2.72 (1.54-4.81)	.001	2.66 (1.48-4.79)	*.001*
Unable to palpate lesions over teledermatology	2.37 (1.30-4.32)	.005	2.27 (1.23-4.18)	*.009*
Unable to visualize lesions clearly over teledermatology	3.30 (1.75-6.20)	<.001	3.59 (1.86-6.96)	*<.001*
Concerns that patients may not be familiar with using teledermatology for condition	1.36 (0.73-2.54)	0.34	1.61 (0.83-3.12)	0.16
Concerns that physicians may not be familiar with using teledermatology for condition	1.24 (0.69-2.22)	0.47	1.22 (0.67-2.21)	0.51
Concerns about litigation regarding inaccurate diagnosis or treatment plan	1.39 (0.74-2.59)	0.30	1.41 (0.74-2.68)	0.30
Concerns about privacy issues arising in patients when examining skin in sensitive body areas	3.03 (1.51-6.06)	.002	2.75 (1.36-5.56)	*.005*
Inability to properly assess psychosocial state and impairment experienced by patients	1.68 (0.87-3.24)	0.12	1.71 (0.87-3.37)	0.20

[a]Age group, gender (female vs male), practice (private vs public), and role (trainee vs dermatologist) were adjusted in the multivariable analyses.
[b]OR: odds ratio.

Discussion

Principal Findings

Compared to other chronic, debilitating dermatological conditions—such as acne and AD, which have been managed via telemedicine during the COVID-19 pandemic—the role of teledermatology services for patients with HS has not been well characterized.

HS is unique compared to other chronic dermatological conditions due to its propensity for skin lesions that involve deeper layers of skin and of largely intimate body areas. This highlights the need for an independent investigation into the barriers to teledermatology for HS.

Our study findings confirm that the use of teledermatology for patients with HS lacks strong traction among dermatologists. We further demonstrate that a significant proportion of physicians were reluctant to have teledermatology completely replace their routine face-to-face visits and were ambivalent toward perceived willingness of patients to be managed over teledermatology. This reluctance was more apparent in older physicians who perceived more difficulties with accurate assessment of disease severity and had concerns that patients with HS may not be familiar with the technology. This echoes the findings of Choi et al’s [5] mixed methods study on the use and perceptions of teledermatology in 942 Asian patients, which showed that age (or youth) was independently associated with greater willingness to use teledermatology. Our study shows that age is a common factor influencing individuals’ (be it physician or patient) willingness to engage in teledermatology.

Furthermore, the apparent reluctance portrayed by physicians in this study could be associated with time period bias. During the peak of the COVID-19 pandemic, when there were strict lockdowns, teledermatology was positioned as one of the few available means to obtain a health consult. In comparison, a year after the onset of the COVID-19 pandemic, when this survey was conducted, many health care systems have seen a gradual lifting of physical isolation policies, allowing physical consultations to take place. The overall willingness of health care providers to practice teledermatology revealed in those studies may therefore have been overinflated [5-7].

We found significant differences in attitudes and perspectives for physicians in terms of using teledermatology to manage HS compared to AD, with overall increased tendency for physicians to experience difficulty in managing HS compared to AD. Most concerns revolved around perceived difficulty for patients with HS in photographing or videoing hard-to-reach or sensitive areas and physician-reported difficulties with accurate assessment of disease severity for HS compared to AD—consistent with existing literature expounding the challenges faced by dermatologists when providing teledermatology for HS [3,8]. With AD being one of the commonest chronic skin conditions, priority for the optimization of teledermatology for its diagnosis and management has enabled more widespread use with provisions for in-person appointments with dermatologists for most of the severe cases [9,10]. In recent years, studies have also given support to the use of telemedicine in treating patients with AD [11-14]. In comparison, the complex nature of HS management has impeded more rapid use of teledermatology. Andriano et al [15] highlighted that those patients with HS who were satisfied with teledermatology tended to have mild disease and were less likely to require office visits for acute flare management. It is likely that physicians would think alike and may be more cautious in their overall outlook of the usefulness of teledermatology for patients with a more severe HS.

Finally, this study raises significant clinical considerations for the use of teledermatology in patients with HS, particularly as the COVID-19 pandemic evolves and the need for strict physical isolation and social distancing is reduced. Ambivalence of physicians regarding uptake suggests a need to continually optimize teledermatology to ensure sustainability. We suggest that physicians could more strongly consider offering such services to patients with quiescent or mild HS (ie, Hurley stage I, International Hidradenitis Suppurativa Severity Score System score 1-3); patients with less HS involvement in intimate body areas; patients who are more willing to share documentation, if required, of affected body areas; and patients who already have an established and strong doctor-patient relationship with their HS provider. The use of teledermatology for HS is also helpful in circumstances of surges in outpatient and inpatient attendances, where physical clinical space is limited. The use of specialized, secure telehealth platforms may boost physicians' confidence to manage HS and patient's assurance of data security; this includes the telehealth module from the Epic Systems Corporation (or EPIC)—a largely nationwide, secure clinical records platform used in Singapore. Cultural barriers require navigation, as examination of sensitive body parts (such as genitalia) over teledermatology might still be challenging in more conservative regions [16-18]. This echoes the findings by Okeke et al [8], who suggest that the act of requesting for patient representation via technology—be it for patient-submitted photographs or real-time video examination of HS-affected skin in teleconsultations, where physician-patient rapport is harder to establish—could generate significant patient unease. Difficulties with navigating cultural barriers, coupled with the restoration of face-to-face consults as the region emerges from the pandemic, may impede robust teledermatology uptake for HS in the Asia-Pacific region.

Learning from previously published literature and cautionary messages for practicing physicians could streamline the teledermatology practice for patients with HS. In his study of 41 patients with HS who were being treated over teledermatology, Patel [19] has described that the center's approach was to request images of HS-affected skin only when deemed "essential," such as prior to urgent commencement of adalimumab. Patel further stressed the importance of clinical face-to-face assessment, advising the need to handle photographic or video evaluation sensitively due to the high prevalence of anxiety and depression in the affected patient. We suggest that it would be reasonable to first assess the likely severity of HS in patients who are managed over teledermatology, through sensitive history taking—triaging patients who may require urgent commencement of biologics or conversion to face-to-face consultations to assess flare symptoms and those who have previously tried other forms of treatment and have failed to respond. Assessing patients' level of psychoemotional concerns (such as anxiety, depression, and body dysmorphism) may also help physicians select suitable modes of teledermatology consults, be it hybrid, video- or telephone-based, or other modes.

Although many studies have exhorted the benefits of teledermatology, we recommend that physicians need to remain vigilant about the nuances of this practice and continue to refine the service for HS with the above-suggested patient profiles and caveats.

Strengths of this study include a fairly large sample size, including global respondents, with a predominance of respondents from the Asia-Pacific region. The inclusion of a compactor condition (ie, AD) provided a reference with which perceptions toward teledermatology use in HS could be compared.

Limitations of this study include inability to assess true response rates (as the survey was disseminated to respondents who had the option of further eligible colleagues) and potential response bias. Teledermatology as a term is also broad and encompasses various modalities (eg, videos; telephone calls; as well as store and forward modalities, which use electronically stored health information, including patient photographs, for clinical decision-making asynchronous to the patient encounter). Further questionnaires could investigate differential perceptions and comfort with regard to various modalities. There is also limited generalizability of findings to the Asia-Pacific region.

Conclusions

Our study suggests that dermatologists in Asia find HS difficult to manage via teledermatology, especially in comparison to AD. However, teledermatology in this region may be considered useful in selected settings. Physicians' efforts should be focused on streamlining patient selection and optimizing consult environments for patients with HS.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Association between demographics and attitudes of physicians towards teledermatology for hidradenitis suppurativa.

[DOCX File , 18 KB - derma_v6i1e43910_app1.docx]

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Abbreviations

AD: atopic dermatitis
HS: hidradenitis suppurativa
OR: odds ratio

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Review

Demographic Data Associated With Digital Inequity Reported in Patient-to-Provider Teledermatology Studies in the United States From 2011 to 2021: Scoping Review

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Abstract

Background: Patient-to-provider teledermatology relies on a patient's access to technology to ensure a successful visit. However, access to broadband internet and technology varies across populations in the United States—leading to the digital divide. While teledermatology has been recognized as a model to improve access, little is known about how often demographic data associated with digital inequity are captured in studies.

Objective: Given the expansion of teledermatology over the past decade, we sought to determine how often demographic data associated with digital inequity are reported in patient-to-provider teledermatology studies.

Methods: A scoping literature review search was conducted using the search term *teledermatology* in the following databases: PubMed, Embase, and the Cochrane Database of Systematic Reviews. All studies published between December 31, 2011, and December 31, 2021, that evaluated patient-to-provider teledermatology were eligible.

Results: In total, 1412 publications describing teledermatology were identified, of which 46 met the inclusion criteria. Race or ethnicity was the most frequently reported demographic characteristic (28/46, 61%). However, only 41% (19/46) of studies were representative of race or ethnicity, defined as including >20% nonwhite participants. Studies rarely reported the number of participants greater than 65 years of age (14/46, 30%), preferred language (9/46, 20%), income (6/46, 13%), highest level of education (5/46, 11%), or access to a device (4/46, 9%). Studies conducted after the onset of the COVID-19 pandemic were significantly more likely to report preferred language (9/25, 36% vs 0%; P=.002) and appeared more likely to report other demographic data associated with digital inequity, without reaching statistical significance (P>.05).

Conclusions: Demographic data associated with digital inequity are rarely reported in patient-to-provider teledermatology studies to date. These studies frequently lack adequate representation of racial and ethnic minorities. With increased calls for equitable representation in dermatology studies, future teledermatology studies can improve the reporting of race and ethnicity and consider demographic data associated with digital inequity as an important criterion in research design.

(JMIR Dermatol 2023;6:e43983) doi:10.2196/43983

KEYWORDS

teledermatology; equity; inequity; scoping review; digital divide; dermatology; racial minority; ethnic minority; digital inequity; patient care; COVID-19

Introduction

Unlike traditional in-person care, patient-to-provider teledermatology relies on a patient's access to a compatible device and broadband internet to ensure a successful visit. However, access to broadband internet and technology varies across populations in the United States—creating what is referred to as the digital divide [1,2]. Populations less likely to report a broadband internet subscription include those with less formal education or lower income, racial and ethnic minorities, persons greater than 65 years of age, and residents of rural communities [3].

Demographics that report less access to broadband internet and technology recorded lower telehealth utilization rates during the COVID-19 pandemic. For instance, older age and persons who reported a non-English language as their primary language were associated with fewer completed telemedicine visits [4-6]. Inequity in access to telemedicine care exists. However, it is unknown whether demographic data associated with digital inequity are frequently reported in teledermatology studies.

Demographic data associated with digital inequity should be included in patient-to-provider teledermatology studies to ensure conclusions that reflect all populations. We conducted a scoping review of patient-to-provider teledermatology studies conducted in the United States to characterize how often patients vulnerable to the digital divide are represented. Given the expansion of teledermatology during the COVID-19 pandemic, we also compared how often demographic data associated with digital inequity were reported in studies conducted prior to and after the declaration of the pandemic.

Methods

Study Design

A scoping review search was performed on PubMed, Embase, and the Cochrane Database of Systematic Reviews from December 31, 2011, through December 31, 2021. We used the search term *teledermatology*. This study is registered with the International Prospective Register of Systematic Reviews (CRD42022325030) and followed the relevant portions of the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist.

Eligibility Criteria

Studies were included if they evaluated an asynchronous or synchronous model of patient-to-provider teledermatology. Both quantitative and qualitative studies evaluating teledermatology were included to represent the broad scope of research. Only studies conducted in the United States were included. No restrictions were placed on the age or gender of study participants. Telephone-based studies were excluded as these encounters involve separate technology and resources unrelated to measures of broadband connectivity and access to a device.

Article Selection and Data Extraction

Two reviewers (PI and JM) sequentially evaluated titles, abstracts, and then the full text of all publications based on the inclusion criteria. Studies were assessed based on whether they reported demographic data associated with digital inequity as described in a national report by the Pew Research Center [3]. These included participant income, highest level of education, race or ethnicity, number of participants greater than 65 years of age, and residents of rural communities [3]. Studies were defined as unrepresentative of race and ethnicity if they included less than 20% nonwhite participants, consistent with the methodology of a previous study by Chen et al [7].

Data Analysis and Synthesis

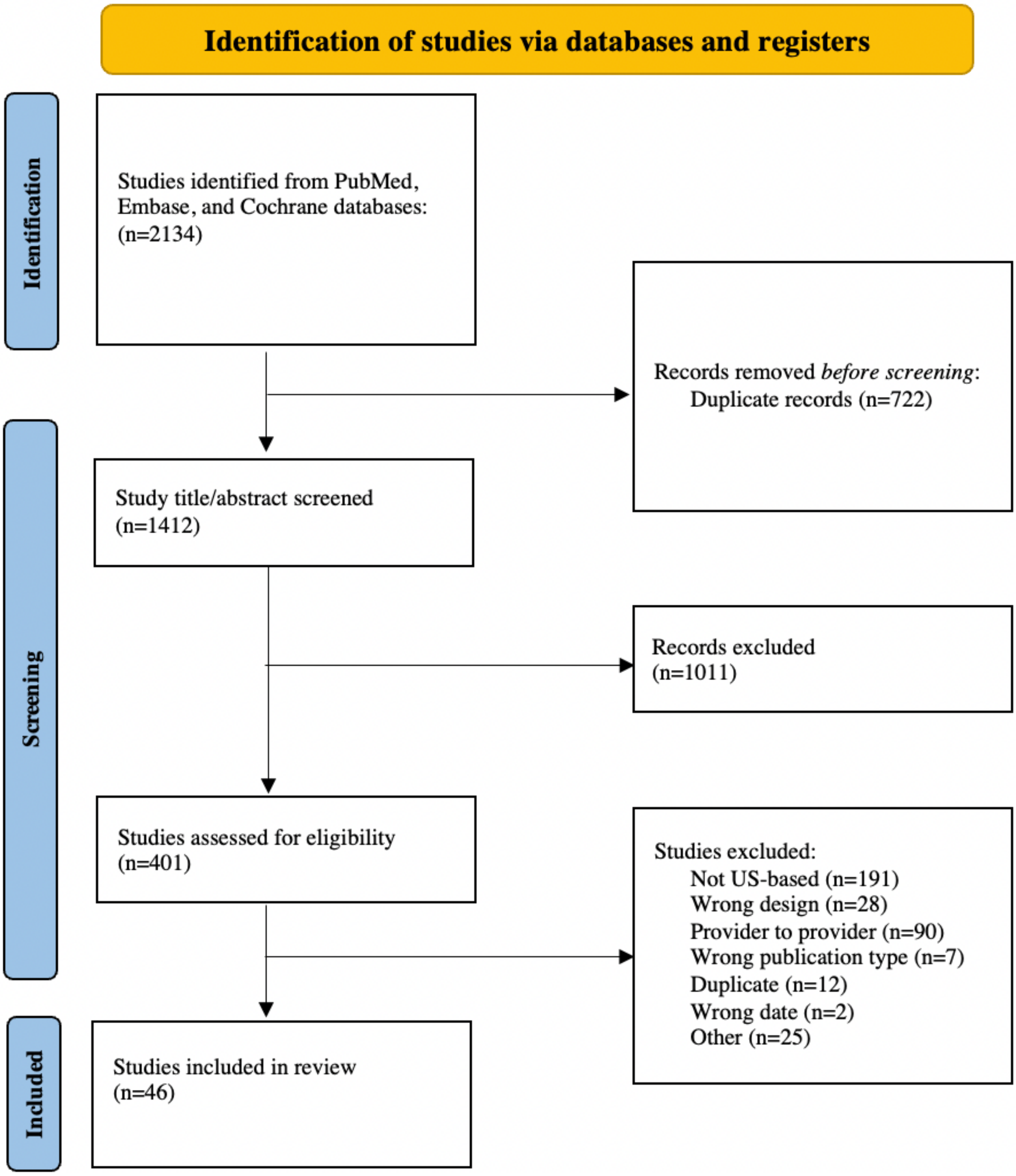
The primary outcome was the frequency of reported demographic characteristics associated with digital inequity. The secondary outcome was the likelihood of reporting demographic characteristics associated with digital inequity in studies conducted prior to versus during the COVID-19 pandemic. The Fisher exact test was used to analyze the secondary outcome. Analysis was performed using Stata software (version 17.0; StataCorp LLC). $P<.05$ was considered statistically significant.

Results

Selection of Articles

Among 1412 potential studies, 46 satisfied the inclusion criteria [8-53]. Figure 1 shows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart illustrating the publication selection process. The full list of included studies and general study characteristics are presented in Multimedia Appendix 1.

Figure 1. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart for publication selection.



Demographic Data Associated With Digital Inequity

Demographic data associated with digital inequity reported in patient-to-provider teledermatology studies are presented in Table 1. Studies most often reported race or ethnicity (28/46, 61%), but a representative sample was present in only 41% (19/46). Of 46 studies, 14 (30%) reported the number of participants greater than 65 years of age. Studies infrequently reported preferred language, income, highest level of education, or access to a device (Table 1). No studies reported participant-reported internet quality or the number of rural residents included.

Table 1. Demographic data reported in patient-to-provider teledermatology studies.

Characteristic reported	Studies (N=46), n (%)
Race or ethnicity	28 (61)
Representative of racial and ethnic minorities[a]	19 (41)
Number of participants >65 years of age	14 (30)
Preferred language	9 (20)
Income	6 (13)
Highest level of education	5 (11)
Access to a device	4 (9)
Internet quality	0 (0)
Number of rural residents	0 (0)

[a]Studies were representative of racial and ethnic minorities if they included >20% nonwhite participants.

Demographic Data Reported and COVID-19

Demographic data reported in patient-to-provider teledermatology studies conducted before (n=21) and after (n=25) the declaration of the COVID-19 pandemic are presented in Table 2. Studies conducted after the onset of the COVID-19 pandemic appeared more likely to report race or ethnicity, number of participants older than 65 years, income, highest level of education, and access to a device, without reaching statistical significance. Studies conducted during the COVID-19 pandemic were significantly more likely to report the participant's preferred language (9/25, 36% vs 0%; P=.002). Studies conducted before and after the declaration of the COVID-19 pandemic were representative of racial and ethnic minorities at comparable rates.

Table 2. Demographic data reported in patient-to-provider teledermatology studies conducted before and after the declaration of the COVID-19 pandemic.

Characteristic reported	Studies conducted before COVID-19 (n=21), n (%)	Studies conducted after COVID-19 (n=25), n (%)	*P* value
Race or ethnicity	11 (52)	17 (68)	.22
Representative of racial and ethnic minorities[a]	9 (43)	10 (40)	.54
Number of participants >65 years of age	4 (19)	10 (40)	.11
Preferred language	0 (0)	9 (36)	.002
Income	2 (10)	4 (16)	.42
Highest level of education	1 (5)	4 (16)	.23
Access to a device	1 (5)	3 (12)	.37

[a]Studies were representative of racial and ethnic minorities if they included >20% nonwhite participants.

Discussion

Principal Findings

The findings of this study highlight that demographic data associated with digital inequity are infrequently included in patient-to-provider teledermatology studies. With the explosion of telemedicine during the pandemic, our study noted a promising trend toward the inclusion of patient demographic information associated with digital inequity regarding race or ethnicity, participants older than 65 years, income, highest level of education, and access to a device. Preferred language was the only demographic characteristic that was significantly more likely to be reported in teledermatology studies following the pandemic onset. Even so, an overall lack of reporting of demographic data associated with digital inequity persisted.

Demographic Data Associated With Digital Inequity

Demographic data associated with digital inequity may be an indicator of the likelihood to complete teledermatology visits. Patients greater than 65 years of age, those who reported a non-English language as their primary language, and participants with lower income were less likely to complete teledermatology visits compared to their counterparts [5,6,8,9]. Other studies noted patients older than 65 years and those reporting lower income were less satisfied with the visit experience [10-12]. Demographic data associated with digital inequity should be reported more often to inform inclusive research design and ensure generalizable conclusions.

The deficiencies in racial and ethnic representation identified in this review are consistent with those reported in dermatology clinical trials over the past decade [7]. It is critical to capture race and ethnicity data in patient-to-provider teledermatology studies as Black race and Latinx ethnicity were associated with lower use of video-based telemedicine during the pandemic [4]. Future teledermatology studies can improve the reporting of race and ethnicity and should consider this important criterion in research design.

Demographic Data Reported and COVID-19

Our study noted a trend toward the inclusion of demographic data associated with digital inequity in studies conducted after the COVID-19 pandemic compared to before. Dermatologists quickly adopted and expanded their teledermatology programs at the onset of the pandemic [54]. The sheer increase in the volume of care due to a lack of access to alternatives and improved reimbursement likely drove a wider demographic reach in the patient population. This trend coincides with increased calls for equitable inclusion in dermatology studies [55] and studies highlighting how teledermatology may exacerbate digital inequity [4,56-60]. As a result, lack of access combined with increased awareness of social inequities in care possibly encouraged researchers to be more intentional in seeking broader demographic variables to ensure their teledermatology programs represented underserved and underrepresented communities. Despite the positive trend, reporting of inclusive demographic data is insufficient to date and can be improved upon in future research design.

Limitations

This study is limited in its design. The studies included in our review had variable primary outcomes. Of note, our study did not determine whether a study's primary outcome correlated with the inclusion of demographic data associated with digital inequity. It is also possible that studies captured demographic data associated with digital inequity in their methods but did not report these findings. This trend is consistent with medical studies' failure to report sociodemographic variables consistently [61]. Studies will be unable to correct health inequity if these variables are not reported more consistently [61]. Lastly, this study only reflects demographic reporting trends in studies conducted in the United States.

Conclusion

This study highlights the need for equitable representation of racial and ethnic minorities and improved reporting of demographic data associated with digital inequity in patient-to-provider teledermatology studies over the past decade. With increased calls for equitable representation in dermatology studies, future teledermatology studies can improve reporting of race and ethnicity and consider the inclusion of demographic data associated with digital inequity an important criterion in research design. Professional and telehealth societies can help drive change by creating guidelines that reflect the value of reporting demographic data associated with digital inequity. Continued research and education can increase awareness of the digital divide's impact on patient care and help optimize teledermatology's potential to serve vulnerable populations.

Conflicts of Interest

None declared.

Multimedia Appendix 1

General characteristics of included studies.

[DOCX File , 21 KB - derma_v6i1e43983_app1.docx]

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Abbreviations

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

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Original Paper

Teledermatology for Enhancing Skin Cancer Diagnosis and Management: Retrospective Chart Review

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Abstract

Background: Skin cancer rates are at all-time highs, but the shortage of dermatologists compels patients to seek medical advice from general practitioners. A new referral pathway called the Suspected Skin Cancer (SSC) service was established to provide general practitioners in Waikato, New Zealand, with rapid diagnosis and treatment advice for lesions suspicious for skin cancer.

Objective: The aim of this study was to assess the quantity, quality, and characteristics of referrals to the SSC teledermatology service during its first 6 months.

Methods: A retrospective chart review of all referrals sent to the SSC teledermatology service during the first 6 months of its operation was conducted. Time to advice, diagnoses, diagnostic discordance, adherence to advice, and time to treatment were recorded. Diagnostic discordance between general practitioners, dermatologists, and pathologists was calculated.

Results: The SSC service received 340 referrals for 402 lesions. Dermatologists diagnosed 256 (63.7%) of these lesions as benign; 56 (13.9%) were histologically confirmed as malignant, including 19 (4.7%) melanomas. The overall discordance between referrer and dermatologist on specific and broad (ie, benign or malignant) diagnoses for 402 lesions was 47% and 26% (κ=0.58, SD 0.07), respectively; 44% and 26% (κ=0.61, SD 0.15) between referrer and pathologist; and 18% and 12% (κ=0.82, SD 0.12) between dermatologist and pathologist. The mean time between referral submission and receiving advice was 1.02 days. The average time to action (eg, excision) was 64.8 days.

Conclusions: An electronic referral system can be an effective form of teledermatology for providing prompt diagnosis and management advice for benign and malignant skin lesions.

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KEYWORDS

teledermatology; melanoma; keratinocyte cancer; basal cell carcinoma; BCC; squamous cell carcinoma; SCC; referral and consultation; dermoscopy; telemedicine; skin cancer; diagnosis; management; treatment; skin lesion

Introduction

The global incidence of melanoma and keratinocyte skin cancers is increasing, and New Zealand is home to one of the highest rates of skin cancer in the world [1,2]. However, there is a severe shortage of dermatologists to diagnose and manage these conditions [3]. At the time of this study, only 2 full-time equivalent public dermatologists were employed to serve over 400,000 residents living in the Waikato region of New Zealand.

As a result, most patients with skin disorders consult general practitioners (GPs), who provide over 85% of dermatological consultations but possess inferior diagnostic accuracy compared with dermatologists [3,4].

This diagnostic uncertainty of nonspecialists drives unnecessary referrals to dermatologists and the needless excision of benign lesions. Teledermatology, a form of telemedicine consisting of remote consultations with a dermatologist, can mitigate this by providing easier, faster access to a dermatologist's opinion. It reduces waiting times, produces cost savings, and leads to satisfied patients [5-7]. This is especially important for patients with skin cancer, especially melanoma, because early intervention is linked to reduced costs and better outcomes [8].

New Zealand has offered a publicly funded teledermoscopy service known as the Virtual Lesion Clinic (VLC) since 2010. At the VLC, nurses record a targeted history and take dermoscopy images of skin lesions, which are important for lesion referrals to dermatology [6,8-10]. This high-quality diagnostic service allows for faster management of skin cancers, but its disadvantages include long waiting times for imaging, requiring patient travel to an imaging centre, and the lack of integration with GP and hospital electronic medical records.

In July 2017, the existing web-based electronic referral system was adapted to include an alternative option for GPs, the Suspected Skin Cancer (SSC) pathway, a new teledermatology service created based on data fields from the British Primary Care Commission's Quality Standards for Teledermatology [11].

Referrers to the SSC pathway are asked to attach regional, close-up, and dermatoscopic images of up to 5 lesions of concern. In addition, optional, free, and web-based or in-person training in lesion photography and dermoscopy was made available. Unlike VLC referrals, SSC referrals and responses are retained in the patients' medical records.

The referral is viewed by a consultant dermatologist using a high-quality monitor. The standard referral triage form was modified to allow the dermatologist to select a diagnosis from a menu of International Classification of Diseases-10 codes and to provide advice. Treatment recommendations may include no action, excise, perform a diagnostic biopsy, prescribe a specified medication, cryotherapy, refer to the plastic surgical service, rerefer to the Suspected Skin Cancer service after an interval of time or with better images, or refer to the nurse-led teledermoscopy service for expert imaging. The referrer remains responsible for patient care.

Methods

Ethical Considerations

The objectives of this pilot study were to assess the quantity, quality, and characteristics of referrals to the Suspected Skin Cancer teledermatology service during its first 6 months. As a service review, it was exempt from requiring approval by a New Zealand Ministry of Health's Health and Disability Ethics Committee.

Overview

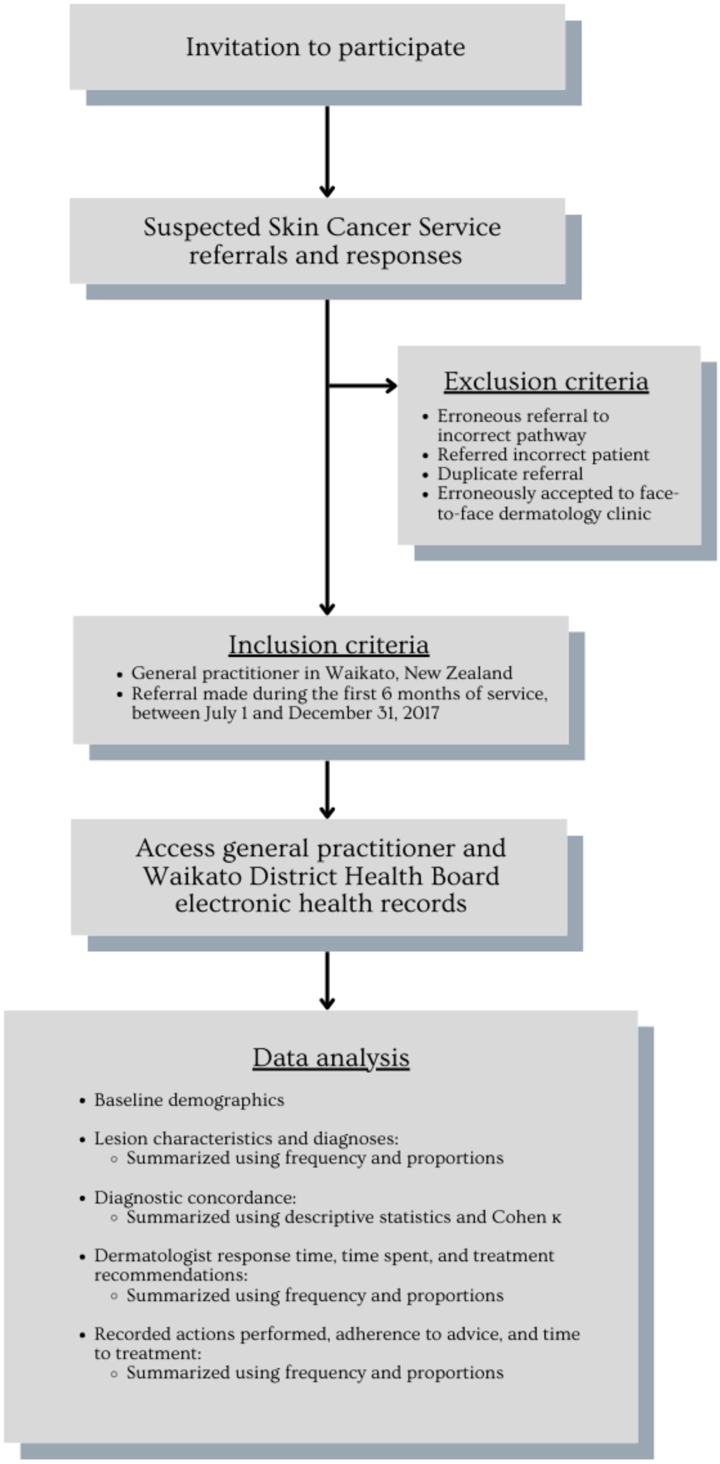
We conducted a retrospective chart review of all patients referred to the SSC service between July 1 and December 31, 2017, using electronic health records at Waikato Hospital, formerly known as the Waikato District Health Board, and summarized GP electronic records. Lesion outcomes were followed until July 31, 2018. Exclusion criteria included erroneous referral to the incorrect pathway, referral of the incorrect patient, duplicate referral, or erroneous acceptance to face-to-face dermatology clinic (Figure 1).

Referrals and responses to referrals, dermatology clinic letters, summarized primary care records, and histology reports were used to determine the referrer's diagnosis for each lesion, the dermatologist's diagnosis for each lesion, the pathologist's diagnosis of biopsied or excised lesions, lesion details, the dermatologist's recommendations, and the dermatologist's response time. The dermatologist's time spent responding was determined for a sample of referrals.

Diagnostic concordance was based on the specific diagnosis made and by the broad diagnostic category (ie, benign or malignant). For each lesion, the referrer's presumptive diagnosis was compared to the dermatologist's diagnosis. For lesions that were biopsied or excised, referrer and dermatologist diagnoses were compared to the pathologist's diagnosis, respectively. Nonconcordance indicated that the different physicians disagreed upon the diagnosis. Partial concordance was noted when either the referrer or the dermatologist provided multiple diagnoses, one of which was concordant. Concordance could not be calculated when images were inadequate for diagnosis, when the dermatologist did not give a diagnosis, or when the dermatologist noticed an additional significant lesion in a photograph that the referrer did not deliberately mention in the referral. Concordance based on broad diagnostic category (ie, benign or malignant) was quantified using the Cohen , a measure of interrater agreement that accounts for the possibility of agreement occurring by chance.

For many cases, limited access to summarized GP electronic records was possible, and thus adherence to the dermatologist's advice (the action) could be estimated. The actions evaluated included the prescription of a specific medication or biopsy of the lesion. The time from the date of referral to the date of the action was calculated.

Figure 1. Study flowchart.



Results

Overview

A total of 350 referrals were received between July 1 and December 31, 2017. Of those, 8 were excluded due to referral error, and 2 were excluded due to pathway allocation error. Outcomes of the referrals were followed until July 31, 2018, and so the observation period was 7-13 months after the referral.

Referrals

There were 340 referrals for 402 unique lesions in 310 individual patients (Table 1). There was an average of 1.2 lesions per referral (range 1-4 lesions). A total of 26 patients were referred multiple times, with 11 patients being referred for the same lesion and 18 patients being referred for a different one.

When the referrers provided images that were suboptimal in number or quality (42/340, 12.4% of referrals), the dermatologist offered suggestions about how to improve the quality of future referrals.

Table 1. Patient characteristics.

Suspected Skin Cancer service characteristics	Values
Referrals, n	340
Patients, n	310
Lesions, n	402
Gender, n (%)	
Male	135 (43.5)
Female	175 (56.5)
Age (years), median (SD; range)	62.9 (19.6; 0.9-99.5)
Ethnicity, n (%)	
European	290 (93.6)
Māori, Samoan, or Tongan	24 (7.7)
Asian	6 (1.9)
Mixed	9 (2.9)
Not available	1 (0.3)

Lesion Location

Lesions were most often located on the face (110/402, 27.4% of all lesions), back (77/402, 19.2%), leg (52/402, 12.9%), or thorax (52/402, 12.9%). Lesions were less often located on the arm (34/402, 8.5% of all lesions), other parts of the head and neck (15/402, 3.7%), foot (15/402, 3.7%), or hand (14/402, 3.5%).

Time to Advice

The time to advice was calculated as the time from receipt of the referral to the dermatologist's response. The average and median time to advice was 1.02 days and 0.84 days, respectively, and the range was 0.01-4.90 days.

A random sample revealed that the dermatologist took 6 minutes on average to complete a teledermatology consultation (n=10).

Diagnostic Concordance

The diagnoses made by the referrer, the dermatologist, and, when applicable, the pathologist, were noted and compared for each lesion (Table 2).

Diagnostic concordances were determined for the specific diagnosis (eg, melanoma and seborrheic keratosis) and for the broad diagnostic category (ie, benign or malignant; Table 3). The overall discordance between the referrer and the dermatologist on specific and broad diagnoses for 402 lesions was 47% and 26% (κ=0.58, SD 0.07), respectively; 44% and 26% (κ=0.61, SD 0.15) between referrer and pathologist; and 18% and 12% (κ=0.82, SD 0.12) between dermatologist and pathologist. Histopathological data were missing for 11 suspected skin cancers that were recommended for excision.

Referrers made the same specific diagnosis as the dermatologist for 150 (37.3%) of the 402 lesions. Of the 103 lesions where referrers and dermatologists disagreed on whether the lesion was benign or malignant, 96 (93%) lesions were diagnosed by the dermatologist as benign, and 6 (6%) lesions were diagnosed by the dermatologist as malignant.

Of the 77 lesions the referrer diagnosed as melanoma, the dermatologist diagnosed 16 (20.8%) as melanoma, 25 (32.5%) as melanocytic nevus, and 14 (18.2%) as seborrheic keratosis.

Of the 82 lesions the referrer diagnosed as basal cell carcinoma, the dermatologist diagnosed 33 (40.2%) as basal cell carcinoma, 14 (17.1%) as squamous cell carcinoma, 6 (7.3%) as actinic keratosis, 5 (6.1%) as seborrheic keratosis, 3 (3.7%) as benign melanocytic nevus, and 8 (9.8%) as other benign lesions.

Of the 62 lesions the referrer diagnosed as squamous cell carcinoma, the dermatologist diagnosed 24 (38.7%) as squamous cell carcinoma, 11 (17.7%) as actinic keratosis, 16 (25.8%) as basal cell carcinoma, and 7 (11.1%) as a different benign lesion.

Diagnostic discordance between the referrer and pathologist was observed in 18 excised lesions, of which 9 (50%) were given a benign diagnosis by the referrer whereas the other 9 (50%) were given a malignant diagnosis by the referrer. Discordance between dermatology and pathology was observed in 8 lesions (Table 3).

Table 2. Diagnoses of referred lesions.

Lesions	Referrer diagnosis[a]		Dermatologist diagnosis[a]		Pathologist diagnosis[b]	
	n	Ratio[c] (%)	n	Ratio[c] (%)	n	Ratio[c] (%)
Malignant	235	56.0	130	33.7	56	74.7
Melanoma	77	18.3	25	6.5	19	25.3
Basal cell carcinoma	82	19.5	59	15.3	26	34.7
Squamous cell carcinoma	62	14.8	44	11.4	11	14.7
Merkel cell carcinoma	0	0	1	0.3	0	0
Not specified	14	3.3	0	0	0	0
Benign	185	44.2	256	66.3	19	25.3
Melanocytic nevus	96	22.9	101	26.2	3	4.0
Vascular lesion	8	1.9	24	6.2	0	0
Other inflammatory lesion	6	1.4	17	4.4	3	4.0
Other nonmelanocytic benign lesion	50	11.9	109	28.2	13	17.3
Not specific	25	6.0	5	0	0	0
Total	420	100	386	100	75	100

[a]In some cases, multiple diagnoses were made for one lesion. Each diagnosis was counted.

[b]Pathologists only diagnosed lesions that were excised or biopsied.

[c]The ratio is the number of diagnoses of a particular category compared to the total number of diagnoses given.

Table 3. Diagnostic concordance.

Diagnosis	GP[a] vs dermatologist	GP vs pathologist	Dermatologist vs pathologist
Specific diagnosis, n (%)			
Concordant	150 (37.3)	35 (50.7)	46 (69.7)
Nonconcordant	189 (47.0)	30 (43.5)	12 (18.2)
Partially concordant	28 (7.0)	4 (5.8)	8 (12.1)
Unable to calculate	35 (8.7)	0 (0)	3 (4.3)
Broad diagnosis			
Concordant, n (%)	235 (58.5)	46 (66.7)	53 (76.8)
Nonconcordant, n (%)	103 (25.6)	18 (26.1)	8 (11.6)
Partially concordant, n (%)	31 (7.7)	5 (7.2)	5 (7.2)
Unable to calculate, n (%)	33 (8.2)	0 (0)	3 (4.3)
Cohen κ	0.58	0.61	0.82

[a]GP: general practitioner.

Adherence to Advice

Primary care records showed that the patient's GP followed the dermatologist's treatment recommendations for 74.1% (140/189) of the lesions for which the dermatologist recommended action. The SSC dermatologists recommended excision for 78 lesions, of which 60 (76.9%) were excised and another 11 (13%) were on the waiting list for excision surgery at the end of the study period. An additional 3 (3%) lesions were excised that did not receive a dermatologist's recommendation for excision. Of the 402 lesions, 63 (15.7%) lesions were excised, 35 (8.7%) lesions were prescribed medication, 11 (2.7%) lesions underwent shave or punch biopsy, and 7 (1.7%) were treated with cryotherapy; moreover, 2 (0.5%) lesions were referred to the plastic surgery department for assessment, and 1 (0.2%) lesion was followed up by the GP, as recommended. Referrals with poor image quality led to a recommendation that the GP refer to the VLC or refer again to the Suspected Skin Cancer pathway with higher-quality photographs (46/340, 13.5% of referrals), and this recommendation was followed for 29 lesions (29/46, 63.0%).

For 4 (4/189, 2%) lesions where actionable advice was given, the advice was partially followed—the GP either prescribed a similar medication to that recommended, prescribed only some of the medications recommended, or took longer to rephotograph the lesion than recommended. In 4 (4/189, 2%) cases, data about prescriptions, excisions, or cryotherapy were missing.

In 41 (41/189, 22%) cases where the teledermatologist provided actionable advice, the limited access to primary care records indicated that the recommended advice may not have been followed. Some referrals to the plastic surgery department did not lead to the recommended excision (4/58, 6.9%). Data for prescriptions were missing in 10 (10/36, 27.7%) cases where the dermatologist recommended treatment with medication. We found data indicating patient noncompliance with treatment recommendations (3/189, 1.6% of lesions where actionable advice was given), lesion regression (2/189, 1.1% of lesions), and patient death (1/310, 0.32% of patients).

Time to Treatment

The average time from the date of the Suspected Skin Cancer referral to the date the action was performed, if any, was 64.8 days (SD 73.1 days; n=144 lesions acted upon; Table 4). The average time from the Suspected Skin Cancer referral to excision performed by different specialties was 108.3 days for plastics (SD 71.9 days; n=42), 43.9 days for GPs (SD 89.1 days; n=17), 61.1 days for dermatology (SD 48.8 days; n=2), and 75.23 days for oncology (n=1). When lesions were recommended to be treated by medication, the median time from Suspected Skin Cancer referral to being prescribed the medication was 2.4 days.

Table 4. Time to action by action performed (in days).

Variable	Time to action (days)			
	Average	Median	Minimum	Maximum
Excision (n=67)	88.6	67.9	2.4	374.5
Prescribe (n=35)	12.6	2.4	0[a]	153.6
Rerefer (n=23)	58.8	32.4	0.4	268.2
Biopsy (n=11)	70.7	25.2	8.2	178.6
Cryotherapy (n=7)	60.9	43.3	1.2	182.4
Follow-up by GP[a] (n=1)	83.3	83.3	83.3	83.3

[a]GP: general practitioner; some of the recommended prescriptions were already prescribed at a recent GP visit before the dermatologist advice was received.

Discussion

Principal Results

The Suspected Skin Cancer pathway is an adaptation of a New Zealand public hospital electronic referral system and is intended to expedite the early diagnosis and treatment of skin cancers by increasing access to dermatology advice. We have shown that this form of store-and-forward teledermatology can provide fast and accurate support to primary care physicians when they have any diagnostic or treatment uncertainty about a skin lesion. All referrals were assessed within 5 working days, and many were assessed within a few hours. Whereas the routine wait time for a face-to-face first specialist assessment at the Waikato Hospital's dermatology outpatient clinic is 120 days, the average time to advice was only 1.02 days via the SSC service, with clear implications for faster and increased access to dermatology advice.

Referrers were almost 5 times as likely to proffer a diagnosis of melanoma compared with the dermatologists for the same lesion. We suspect the Suspected Skin Cancer pathway significantly reduced the number of unnecessary excisions and needless referrals for benign lesions, consequentially saving patients anxiety, expense, and risk of complications. The majority of lesions suspected to be melanoma by the dermatologists were confirmed histologically, which is consistent with our previous research that demonstrated the diagnostic equivalence of teledermatology to in-person evaluations [8]. Referrers were also 2.5 times more likely to diagnose lesions as basal cell carcinoma or squamous cell carcinoma compared with the dermatologists. As almost half of the specific diagnoses made by the referrer were discordant with the dermatologists' diagnoses, GPs and their patients would benefit from timely access to teledermatology.

The Suspected Skin Cancer pathway shifts some of the patient care burden to primary care. An electronic referral to a specialist service is normally a quick process, as many fields are automatically populated from the practice management system's database, and care of the patient is handed over to another service, but the responsibility of care for a teledermatology patient is retained by the GP. Most referrers followed the advice given by the dermatologist.

Limitations

It should be noted that lesions diagnosed as benign by dermatologists were not followed further to verify stability, and this is a limitation of this study.

Although the Suspected Skin Cancer pathway is a free service, referrers need time and equipment—a dermatoscope, a camera, and a secure data transfer method—for referrals to have the appropriate details. Equipment burden can be lessened by obtaining a dermatoscope that can attach to a smartphone, thus eliminating the need for a separate camera. We estimate that referrers typically spend 10 to 15 minutes to complete the referral form, including capturing and uploading images. The patient may also incur costs for additional visits to their GP clinic for imaging and follow-up.

Comparison With Prior Work

Our previous research reported that referrers greatly value the educational component of a teledermatology consultation, especially because it is often offered within hours of making the referral [12]. The dermatologist's work of assessing electronic referrals is time-tabled and offers an important opportunity to train dermatology registrars and medical students in teledermatology, teledermatoscopy, and skin cancer identification and treatment.

By reducing the time to diagnosis and retaining management of some cases in primary care, teledermatology often expedites treatment compared to traditional face-to-face encounters. For example, the average time from Suspected Skin Cancer referral to excision in primary care was less than half of that for lesions excised by the plastic surgery service. Increasing the availability of teledermatology services in conjunction with bolstering GP capacity to provide treatment for skin lesions will promote better care for patients, especially in areas with a lack of dermatologists.

Conclusions

In conclusion, our adaptation of an electronic referral system to provide a teledermatology service has improved patient access to dermatology and has promoted early identification and treatment of skin cancer. It has the potential to reduce waiting lists for in-person appointments and surgery, to expand access to the accurate diagnosis and appropriate management of skin lesions, and to improve productivity.

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Authors' Contributions

All authors contributed significantly to the design of the research study, interpretation of the data, drafting, and critical revision of this work. All authors have reviewed and approved the final version for submission.

Conflicts of Interest

None declared.

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Abbreviations

GP: general practitioner
SSC: Suspected Skin Cancer
VLC: Virtual Lesion Clinic

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Original Paper

General Practitioners' Perspectives About Remote Dermatology Care During the COVID-19 Pandemic in the Netherlands: Questionnaire-Based Study

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Abstract

Background: The COVID-19 pandemic affected the delivery of primary care and stimulated the use of digital health solutions such as remote digital dermatology care. In the Netherlands, remote store-and-forward dermatology care was already integrated into Dutch general practice before the COVID-19 pandemic. However, it is unclear how general practitioners (GPs) experienced this existing digital dermatology care during the pandemic period.

Objective: We investigated GPs' perspectives about facilitators and barriers related to store-and-forward digital dermatology care during the COVID-19 pandemic in the Netherlands, using a sociotechnical approach.

Methods: In December 2021, a web-based questionnaire was distributed via email to approximately 3257 GPs who could perform a digital dermatology consultation and who had started a digital consultation (not necessarily dermatology) in the previous 2 years. The questionnaire consisted of general background questions, questions from a previously validated telemedicine service user satisfaction questionnaire, and newly added questions related to the pandemic and use of the digital dermatology service in general practice. The open-ended and free-text responses were analyzed for facilitators and barriers using content analysis, guided by an 8-dimensional sociotechnical model.

Results: In total, 71 GPs completed the entire questionnaire, and 66 (93%) questionnaires were included in the data analysis. During the questionnaire distribution period, another national lockdown, social distancing, and stay-at-home mandates were announced; thus, GPs may have had increased workload and limited time to complete the questionnaire. Of the 66 responding GPs, 36 (55%) were female, 25 (38%) were aged 35-44 years, 33 (50%) were weekly platform users, 34 (52%) were working with the telemedicine organization for >5 years, 42 (64%) reported that they used the store-and-forward platform as often during as before the pandemic, 61 (92%) would use the platform again, 53 (80%) would recommend the platform to a colleague, and 10 (15%) used digital dermatology home consultation. Although GPs were generally satisfied with the digital dermatology service, platform, and telemedicine organization, they also experienced crucial barriers to the use of the service during the pandemic. These barriers were GPs' and patients' limited digital photography skills, costs and the lack of appropriate equipment, human-computer interface and interoperability issues on the telemedicine platform, and different use procedures of the digital dermatology service.

Conclusions: Although remote dermatology care was already integrated into Dutch GP practice before the pandemic, which may have facilitated the positive responses of GPs about the use of the service, barriers impeded the full potential of its use during the pandemic. Training is needed to improve the use of equipment and quality of (dermoscopy) images taken by GPs and to inform GPs in which circumstances they can or cannot use digital dermatology. Furthermore, the dermatology platform should be improved to also guide patients in taking photographs with sufficient quality.

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KEYWORDS

teledermatology; teledermoscopy; dermatology; dermoscopy; telemedicine; telehealth; remote care; general practitioner; GP; general practice; family physician; COVID-19; questionnaire; perspective; mobile phone

Introduction

Background

The COVID-19 pandemic had a major impact on the access and delivery of primary care owing to social distancing and other public health measures, such as lockdowns or stay-at-home mandates [1]. This unprecedented crisis forced health care organizations to consider innovative ways to plan and deliver their care remotely [2] and led to substantial changes in health care delivery. One of those changes has been the rapid growth and uptake of digital health solutions such as telemedicine [3,4], including the use of remote digital dermatology care [5-7]. Digital dermatology allows general practitioners (GPs), the patient's first point of contact, to digitally contact the patient or to consult a remote dermatologist for advice [8-11]. Digital dermatology is suitable for web-based assessment of skin lesions because it provides a digital representation of the skin. Moreover, this type of service has enabled Dutch GPs to continually provide dermatology care to patients while minimizing the number of (unnecessary) conventional face-to-face consultations (in dermatology or GP practice) and the risk of exposure to SARS-CoV-2.

The Netherlands is one of the few countries where an integrated remote digital dermatology service in GP care has been operating, integrated, and fully reimbursed since 2006 [12]. Therefore, it was expected that GPs could smoothly apply the service in their work practices during the COVID-19 pandemic. However, how the pandemic subsequently influenced the existing digital dermatology care delivery and affected the Dutch GP work processes remains unknown.

The digital dermatology service cannot be adequately evaluated in isolation from the organizational context in which it is implemented. Organizational factors such as the lack of adequate training and technological support, existing and new policies, leadership and change management, and communication needs can hinder the adoption and implementation of digital health tools [13,14]. Moreover, digital dermatology is used in a complex health system that consists of numerous interconnected components (eg, technological elements and social human system aspects) that interact and must work together to positively contribute to the delivery of such a service [15,16]. Digital services affect the work processes of health care providers and the way in which they deliver care to patients. Ideally, such telemedicine service should be seamlessly incorporated into the provider's day-to-day work processes [13], but achieving that goal requires insight into the aspects that affect GPs' satisfaction and the continued use of the service.

Sociotechnical models provide a framework to focus on a broad range of factors that influence the use and adoption of health IT and incorporate technical and nontechnical factors [17]. In other words, the entire implementation process and evaluation of a digital innovation includes the interactions among the technical, social, workflow, and organizational factors. These factors are closely interrelated and are crucial for understanding the complex picture of health care innovations [18].

Objective

To evaluate health care providers' experiences with store-and-forward telemedicine services from a contracted telemedicine organization perspective and to assure telemedicine service quality, we previously developed and validated the Store-and-Forward Telemedicine Service User-satisfaction Questionnaire (SAF-TSUQ) [19]. However, this questionnaire does not focus on the interrelations between aspects from a broad sociotechnical perspective. A sociotechnical framework can be used to enhance the analysis of open-ended questions and to model the interrelated aspects of digital dermatology care. In addition, such a framework can be used to identify the sociotechnical facilitators and barriers that influenced GPs regarding the use of remote digital dermatology care during the pandemic. These findings on GPs' perspectives about digital dermatology care can be used to support future sustainable use of this service in daily practice.

Therefore, in this study, the following research questions were answered:

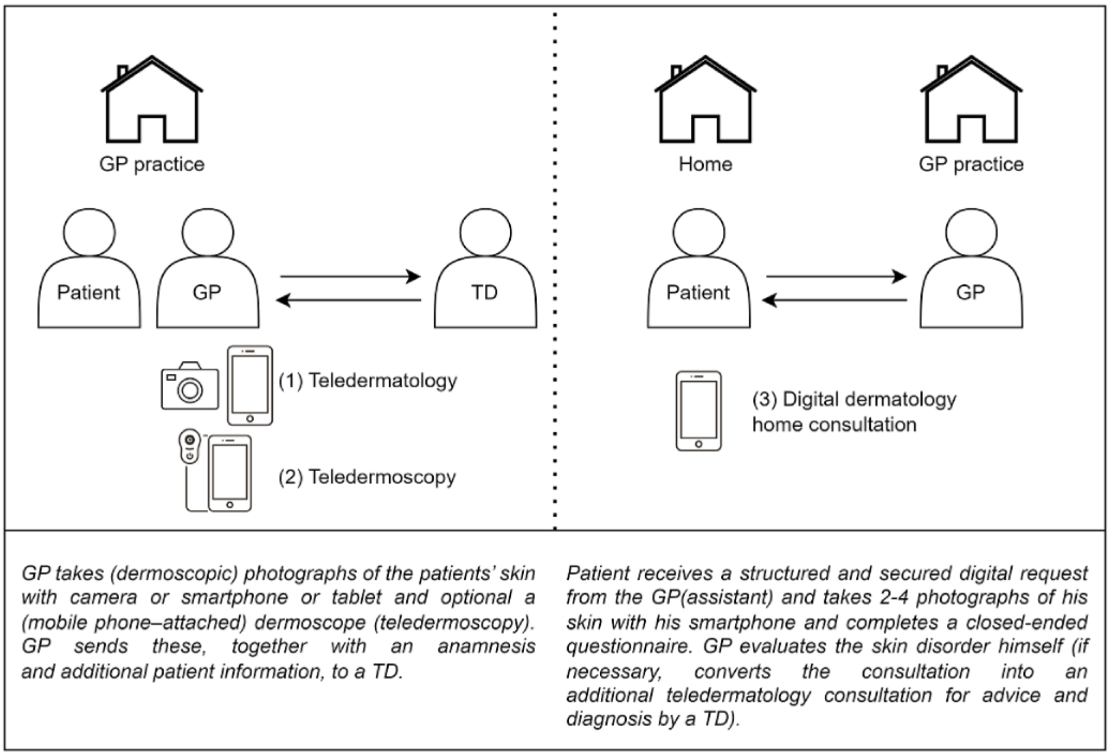
1. How do Dutch GPs experience the remote dermatology care service quality, based on the SAF-TSUQ questionnaire from a contracted telemedicine organization perspective?
2. Which facilitators and barriers do GPs experience in remote dermatology care from a sociotechnical perspective?

Methods

Overview

Ksyos [20] is one of the largest health care organizations in the Netherlands that facilitates three types of remote store-and-forward digital dermatology care: (1) teledermatology, (2) teledermoscopy, and (3) dermatology home consultation (Figure 1). Ksyos-affiliated health care providers acknowledge and approve that Ksyos monitors the quality of its telemedicine services and conducts scientific research when they register for an account on the Ksyos telemedicine platform. The Amsterdam University Medical Center (location: Academic Medical Center) performed this study in collaboration with Ksyos. Data collection for this study was conducted between December 2021 and March 2022 by a researcher (ET).

Figure 1. Teledermatology, teledermoscopy, and digital dermatology home consultation process. GP: general practitioner; TD: teledermatologist.



Ethical Considerations

The Medical Ethical Commission of the Amsterdam University Medical Center granted a waiver stating that the study did not require additional approval.

Participants

Ksyos invited all affiliated GPs (approximately 3257 GPs) to complete the questionnaire. These GPs were able to perform a store-and-forward digital dermatology consultation and had started a digital consultation request (not necessarily dermatology) between October 2019 and September 2021, and their email addresses were known. Owing to outdated email addresses or accounts, we were unable to determine the exact number of invited GPs.

Procedure

The questionnaire invitation email included a personalized URL link to an anonymous web-based questionnaire tool called LimeSurvey. The URL link was deactivated when the questionnaire was completed, to prevent multiple participation. It was impossible to link this URL to the provided responses. Owing to technical issues in the email tool, it was impossible to send multiple invitation emails to GPs registered with the same general GP practice email address. If this was the case, the email tool chose only 1 recipient.

After 1 week, nonresponding GPs received a reminder email. Participation was voluntary, and GPs could unsubscribe via email. In total, 4 gift cards worth €50 (US $53.65) were raffled among all responding health care providers in a large study.

Questionnaire Instrument

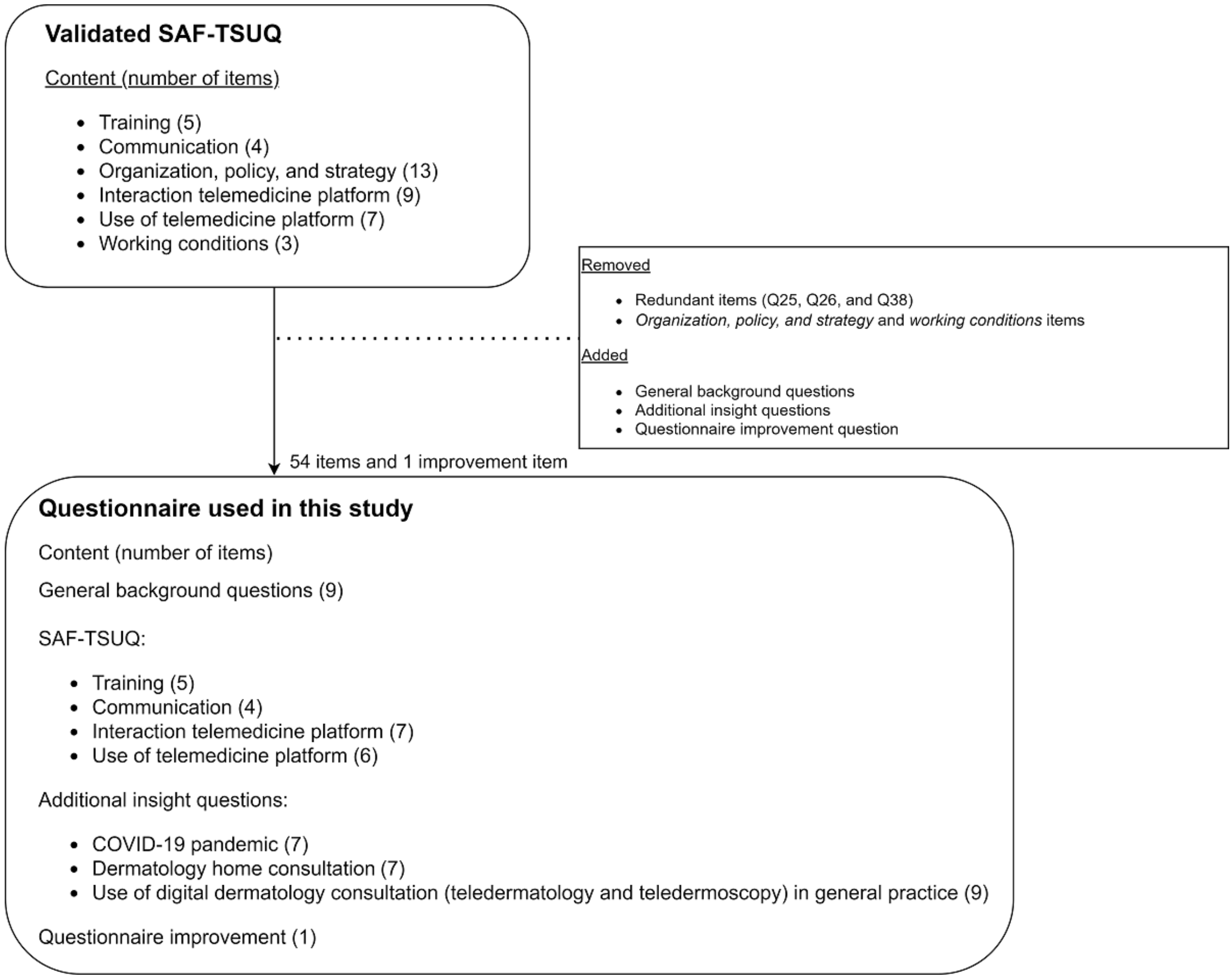
The web-based GP questionnaire (Multimedia Appendix 1) was available in Dutch only and consisted of 54 open-ended and closed-ended questions. The questionnaire included general background questions, questions from the validated SAF-TSUQ questionnaire [19], and newly added insight questions related to the pandemic and use of digital dermatology care in general practice (Figure 2). The SAF-TSUQ questions evaluated the service quality as experienced by GPs from a contracted telemedicine organization perspective, whereas in-depth insight questions were added to evaluate digital dermatology care as experienced by GPs from a broad sociotechnical perspective.

Answers to the SAF-TSUQ questions were recorded on a 5-point Likert scale (range: 1=strongly disagree to 5=strongly agree) and the nonsubstantive options, "I do not know" and "not applicable." Overall, 3 redundant items of the original SAF-TSUQ were discussed with a quality manager at Ksyos and were removed beforehand. In addition, the questions related to "organization, policy, and strategy" and "working conditions" were excluded because during the validation of the original SAF-TSUQ questionnaire among all health care providers, the Dutch GPs frequently reported that these questions were not applicable to them in the Dutch context. Furthermore, the newly added questions related to the pandemic were formulated based on questions that emerged out of interest from the researchers during the COVID-19 pandemic. The other additional in-depth insight questions were related to the use of teledermatology, teledermoscopy, and digital dermatology home consultation in general practice (Figure 2). These questions were also specifically formulated for this study and focused on training and image quality, as these factors are often mentioned as barriers to telemedicine use [21-23].

For some of the closed-ended questions, GPs were prompted in an open-ended follow-up question to explain why they chose a specific answer category. At the end of each section, a separate textbox was presented for additional free-text comments.

Furthermore, 1 final open-ended feedback question was included to gather any feedback or suggestions from GPs for improvement of the questionnaire. All questions (except the additional free-text comments and open-ended follow-up questions) were mandatory. A GP resident and a GP reviewed the newly added questions and options in advance. Then, 2 researchers (ET and Femke van Sinderen) evaluated the questionnaire's technical operation, and a data management consultant (Miranda Roskam-Mul) externally reviewed the questionnaire's technical operation.

Figure 2. Questionnaire instrument. General background questions: for example age, sex, the frequency of telemedicine platform use, years of experience with telemedicine platform, self-reported computer skills, and technology adoption. COVID-19 pandemic questions: the frequency of telemedicine platform use, experiences and lessons learned with teledermatology, teledermoscopy, and digital dermatology home consultation. Dermatology home consultation questions: general practitioners' (GPs) experiences with digital dermatology home consultation (ie, image quality with patients as photographers and needed improvement, which skin conditions and population are suitable for digital dermatology home consultation, and other patient-GP delivery modalities used). The use of digital dermatology consultation in general practice questions: reasons for (not) performing a digital dermatology consultation, the photographer of the (dermoscopic) photographs, the dermatologist feedback received about the quality of the photographs, suggested improvements to optimize photograph quality, GPs' confidence in teledermatology and teledermoscopy use, and the extent of image training received. SAF-TSUQ: Store-and-Forward Telemedicine Service User-satisfaction Questionnaire.



Data Analysis

This study excluded the responses of GPs who responded that they did not use digital dermatology consultation in the Ksyos platform and did not consent in the questionnaire to anonymously process their answers for scientific purposes. Furthermore, incomplete questionnaires, vague or incomprehensible free-text or open-ended responses, and comments that related to a care path other than dermatology were excluded from data analysis. Incomplete questionnaires were excluded, as this was the only way to prevent the inclusion of questionnaires submitted by the same GP.

Descriptive statistics were used to analyze the single-choice, multiple-choice, and Likert scale responses, using numbers and percentages (R software, version 4.0.3; R Foundation for Statistical Computing) [24].

Overall, 2 researchers (ET and Bibiche Groenhuijzen) independently read all open-ended and free-text responses line by line and applied *(thematic)* content analysis to get a deep understanding of the issues GPs experience when using remote digital dermatology care. The sociotechnical model was developed by Sittig and Singh [25] to identify the sociotechnical issues that arise during the design, development, implementation, use, and evaluation of health IT within complex health care systems. We applied their model to group the open and free-text responses into 8 interrelated dimensions: (1) hardware and software; (2) clinical content; (3) human-computer interface; (4) people; (5) workflow and communication; (6) internal organizational policies, procedures, and culture; (7) external rules, regulations, and pressures; and (8) system measurement and monitoring.

During axial coding, 1 coder (Bibiche Groenhuijzen) applied a subcode for each answer, and main codes were formulated (LWP and Bibiche Groenhuijzen) and assigned to each subcode. Most answers were short; however, some answers contained more detailed information and were assigned to multiple codes. The codes were applied to categorize the open-ended responses systematically and to compare the data with other similar parts of the data set. The second coder (ET), a Ksyos expert, assigned a subcode and main code to each response and, if necessary, added additional subcodes. After coding the first few responses, an informative meeting between the researchers (ET and Bibiche Groenhuijzen) was conducted to discuss how coding proceeded till then and any uncertainties about the process and definitions of the codes. Then, the second coder (ET) finalized the coding. This second coder had access to the list of predefined subcodes and main codes but was blinded to the previous codes assigned to free-text and open-ended responses by the first coder. Both researchers (ET and Bibiche roenhuijzen) classified the responses as facilitating, impeding the use of digital care, or neutral and assigned a sociotechnical dimension of the 8-dimensional model by Sittig and Singh [25] to the responses.

Finally, responses that were coded differently or assigned to a different dimension were discussed until consensus was reached (ET and Bibiche Groenhuijzen). Several iterations were conducted to reach consensus in assigning codes to responses and to modify the descriptions of the original 8 sociotechnical dimensions in the telemedicine context (Table 1). Finally, based on this complete analysis, we extracted the facilitators of and barriers to digital dermatology care from the 8 sociotechnical dimensions.

Table 1. Definitions based on the 8-dimensional sociotechnical model by Sittig and Singh modified to the telemedicine context [25,26].

Sociotechnical dimension	Definition in the model
Hardware and software	All technical remarks about the hardware and software used on the (teledermatology) consultation platform, for example, the ease of use of the photography equipment, uploading images, and interoperability issues.
Clinical content	All remarks about the structured, unstructured, textual, or numeric data; information; and knowledge that are stored on the (teledermatology) consultation platform. Also remarks about (the feedback received from the dermatologist about) the quality of images in the consultation or the quality of responses of the dermatologist.
Human-computer interface	All remarks about the software's interaction with the user, for example, about the platform layout or front-end features.
People	All remarks about individuals who interact with the platform or related to training and learnability.
Workflow and communication	All remarks about how teledermatology is used in the workflow, impact on workload, tasks required to provide appropriate care, and communication with the telemedicine organization.
Internal organizational policies, procedures, and culture	All remarks about structures, policies, financial aspects, and procedures of the telemedicine organization that influence technology management.
External rules, regulations, and pressures	All remarks about external forces outside the telemedicine organization that facilitate or impede efforts to design, implement, use, and evaluate technology and remarks indicating that the use has changed owing to the COVID-19 pandemic.
System measurement and monitoring	All remarks about platform availability, its use by stakeholders, its effectiveness, and associated intended and unintended consequences. This dimension also includes comments in which participants indicate that the COVID-19 pandemic had no effect.
Not able to code	All remarks that were not sufficiently specific or not comprehensive to be assigned to a dimension. Remarks about the questionnaire itself are also included in this dimension.

Results

Participant Characteristics

Of 3257 GPs, 40 (1.23%) GPs were retired, no longer worked in the GP practice, no longer used their email address, were absent for a long time, or unsubscribed themselves from the study. Overall, 71 GPs indicated performing digital dermatology consultations and completed the entire questionnaire. If all these remaining 3217 GPs received and read the email, this would indicate a response rate of 2.21% (71/3217); however, it is possible that several emails were not delivered or read; therefore, the response rate could not be determined and might be underestimated.

Of the 71 GPs, 5 (7%) did not provide consent for the use of their data for scientific purposes and were therefore excluded. Table 2 presents the background characteristics of the remaining 93% (66/71) of the GPs. Of the 66 GPs, most GPs were female (n=36, 55%), aged between 35 and 44 years (n=25, 38%), weekly platform users (n=33, 50%), working with the telemedicine organization for >5 years (n=34, 52%), and reported themselves as early majority adopters (n=44, 67%) with good computer skills (n=30, 45%).

Table 2. Background characteristics of the responding GPs[a] (n=66).

Characteristics	GPs, n (%)
Age range (years)	
18-24	0 (0)
25-34	2 (3)
35-44	25 (38)
45-54	17 (26)
55-64	19 (29)
≥65	3 (5)
Sex	
Male	30 (45)
Female	36 (55)
Frequency of use	
Daily	10 (15)
Weekly	33 (50)
Monthly	19 (29)
A few times in a year	4 (6)
Never	0 (0)
Working with telemedicine organization	
<6 months	0 (0)
6-12 months	1 (2)
1-3 years	14 (21)
3-5 years	17 (26)
5-10 years	22 (33)
>10 years	12 (18)
Use of other telemedicine care pathways[b]	
Cardiology	38 (58)
Laboratory requests	5 (8)
Mental health	15 (23)
Ophthalmology	31 (47)
Pulmonology	6 (9)
Sleep	30 (45)
Self-reported computer skills	
Poor	2 (3)
Sufficient	20 (30)
Good	30 (45)
Excellent	14 (21)
Adopter category	
Innovators	3 (5)
Early adopters	9 (14)
Early majority	44 (67)
Late majority	10 (15)
Laggards	0 (0)

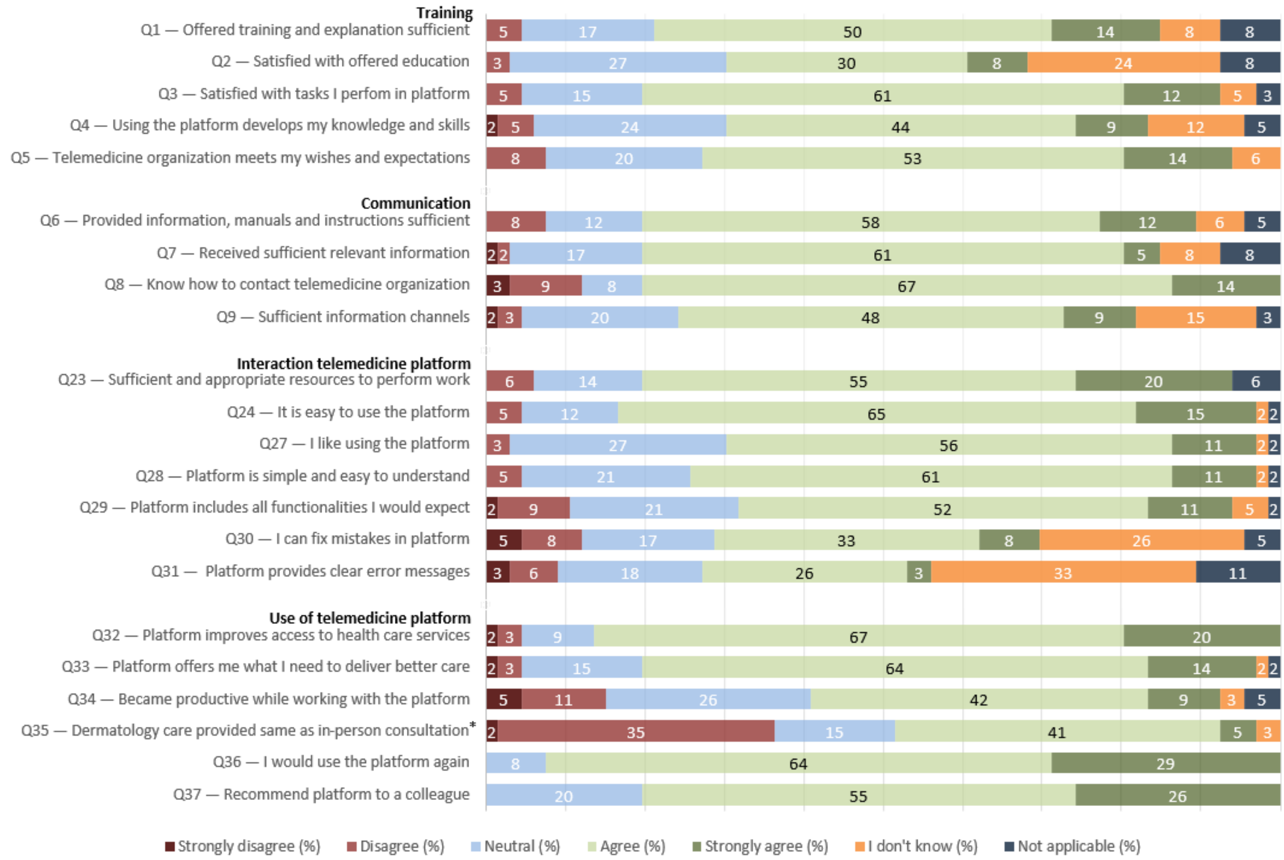
[a]GP: general practitioner.

[b]The total response percentage exceeds 100% because multiple responses were allowed.

Responses to SAF-TSUQ

The responding GPs were positive about training, communication, the use of, and interaction with the telemedicine platform (Figure 3). Almost all GPs would use the platform again (61/66, 92%) and recommend it to a colleague (53/66, 80%). Most GPs (42/66, 64%) found the training and explanation offered by the telemedicine organization as sufficient to be able to use the platform in their daily practice. However, one-third (21/66, 32%) of the GPs were not familiar with the options for additional or continuing education offered by the telemedicine organization. Overall, the results of the SAF-TSUQ show opportunities for improvement regarding interaction with the platform (eg, missing functionalities or the lack of knowledge about how to rectify or avoid mistakes). Notably, more than one-third (24/66, 36%) of GPs disagreed that the digital dermatology care provided with the telemedicine platform can be considered as a replacement of an in-person dermatology consultation.

Figure 3. Store-and-Forward Telemedicine Service User-satisfaction Questionnaire responses to the training, communication, interaction, and use statements. *Additional explanation in the questionnaire—by this question, we meant that a digital consultation can replace a regular consultation.



Responses to Additional Insight Questions

Closed-ended responses to the additional insight questions are presented in Table 3. Most GPs (42/66, 64%) reported that they used the telemedicine platform approximately as often during the first COVID-19 wave as in the period before the COVID-19 pandemic, whereas 23% (15/66) of the GPs used the telemedicine platform more often. Of the 66 GPs, 46 (70%) GPs used the telemedicine platform at the time of this study as often as before the pandemic, and 16 (24%) GPs used the platform more frequently. Of the 66 GPs, 40 (61%) had (strongly) positive experiences with the use of digital dermatology during the pandemic. Almost all GPs (60/66, 91%) received sufficient support to provide digital care. Of the 66 GPs, 63 (95%) took the (dermoscopic) photographs during a teledermatology or teledermoscopy consultation themselves. Of the 66 GPs, only 30 (45%) received training or instructions about taking (dermoscopic) photographs from the telemedicine organization, 7 (11%) took an (additional) imaging course (eg, dermoscopy and medical imaging), and 13 (20%) gained experience in taking (dermoscopic) images in daily practice. Of the 66 GPs, 25 (38%) GPs did not receive any training or instruction, and 15 (60%) of them did not judge this training or instruction as necessary. Of the 66 GPs, 60 (91%) felt (strongly) confident and 5 (8%) felt "neutral" confident in determining the patient's treatment policy after a teledermatology or teledermoscopy consultation (based on the advice and diagnosis received from the dermatologist). GPs primarily use digital dermatology consultations to prevent physical referrals of their patients to a dermatologist (54/66, 82%).

Table 3. GPs'[a] responses to additional insight questions (n=66).

Questions and response options	GPs, n (%)
Platform use during the first COVID-19 wave[b] compared with before the COVID-19 pandemic	
Less often	9 (14)
Approximately as often	42 (64)
More often	15 (23)
Not applicable	0 (0)
Current[c] platform use compared with that during the period before the COVID-19 pandemic	
Less often	3 (5)
Approximately as often	46 (70)
More often	16 (24)
Not applicable	1 (2)
Received sufficient support to provide digital care during the COVID-19 pandemic	
Yes	60 (91)
No	6 (9)
Experiences regarding consultations in digital dermatology care pathway during the COVID-19 pandemic	
Strongly negative	0 (0)
Negative	3 (5)
Neutral	18 (27)
Positive	32 (48)
Strongly positive	8 (12)
Not applicable	5 (8)
Reasons for using digital dermatology in daily practice[d]	
Preventing physical referrals	54 (82)
Unable to determine a differential diagnosis	46 (70)
Treatment is unsuccessful	41 (62)
Receiving additional advice	40 (61)
Lower costs for the patient	27 (41)
Long waiting times in hospitals	21 (32)
At the request of the patient	8 (12)
Suspicion of malignancy	3 (5)
Doubts about the size of the deviation	3 (5)
Emergencies	1 (2)
Prevent physical consultation in practice owing to crowds or SARS-CoV-2 infection of a patient	1 (2)
Used digital dermatology home consultation	
Yes	10 (15)
No	56 (85)
Experiences regarding digital dermatology home consultation (n=10)	
Strongly negative	0 (0)
Negative	1 (10)
Neutral	1 (10)
Positive	7 (70)
Strongly positive	1 (10)

Questions and response options	GPs, n (%)
Quality of the photographs taken by patients (n=10)	
Always poor	0 (0)
Usually poor	1 (10)
Sometimes good, sometimes poor	5 (50)
Usually good	4 (40)
Always good	0 (0)
Age preference for digital dermatology home consultation (n=10)	
No age preference at all	6 (60)
Solely for babies	1 (10)
Solely for children aged <12 years	1 (10)
For babies, toddlers, and adults	1 (10)
Any patient with a smartphone	1 (10)

[a]GP: general practitioner.

[b]The first COVID-19 wave was defined as the start of the pandemic (March 2020 to May 2020).

[c]At the time of this study (December 2021 to March 2022).

[d]The total response percentage exceeds 100% because multiple responses were allowed.

Of the 66 GPs, 10 (15%) used digital dermatology home consultation and 80% (8/10) of them were (strongly) positive about their experiences. These GPs perceived digital dermatology home consultation as specifically suitable for skin conditions with red discoloration (10/10, 100%), birthmarks (3/10, 30%), bumps (7/10, 70%), wounds (7/10, 70%), and diaper rash (8/10, 80%). GPs had no evident age preference for which patients digital dermatology home consultation is the most appropriate. In addition, GPs reported divergent experiences with the quality of photographs taken by patients.

Qualitative Analysis of Free-Text and Open-Ended Responses

Overview

The 66 GPs provided a total of 385 answers to the open-ended questions. Furthermore, they provided 100 and 35 additional free-text answers in the separate textboxes at the end of each section and the last questionnaire improvement question, respectively. After the exclusion of the no responses (116/520, 22.3%) and not applicable (dermatology) responses (22/520, 4.2%), a total of 324 responses to the open-ended questions and 58 free-text responses remained. Overall, 12.3% (47/382) of the remaining responses contained additional information, and after splitting these into 2 or 3 responses, this resulted in 436 remarks for the qualitative data analysis. Then, 2 researchers (ET and Bibiche Groenhuijzen) mapped these remarks across all 8 sociotechnical dimensions. No third reviewer was needed to reach an agreement between the 2 raters. Most remarks (97/413, 23.5%) were assigned to the *clinical content* dimension, followed by *system measurement and monitoring*, *internal organizational policies*, *procedures*, *and culture*, and *people* (Table 4).

Table 4. Exemplary quotes of open-ended and free-text remarks for each of the 8 dimensions of the sociotechnical model by Sittig and Singh [25].

Dimension	Facilitating quotes (%)	Neutral quotes (%)	Impeding quotes (%)	Exemplary relevant quotes
Hardware and software (n=38)	2 (5)	2 (5)	34 (89)	• "The conversion lens on the phone for dermoscopic photographs does not meet the quality of the photographs that we had previously with the dermoscope. I often hear from dermatologists that they cannot interpret the photographs properly and patients still have to go to the specialist." [ID 1625][a] • "Uploading photographs [from my phone to my desktop] takes a lot of time and often has to be done again because the amount of MBs is exceeded." [ID 1376][a] • "Teledermoscopy remains difficult, 'every phone [requires] a new [dermoscopy] attachment.'" [ID 1259][a]
Clinical content (n=97)	24 (25)	42 (43)	31 (32)	• "Many skin problems, spots, and rashes can often be easily assessed via [a] photograph." [IDs 1637 and 1804][b] • "Fast responses, good content and practical responses from specialists with clear and adequate diagnoses and treatment advice." [IDs 109, 1373, 1479, and 1344][b] • "Images [taken by patients] are often not sharp enough, bad lightning, wrong distance." [DHC[c]; ID 1638][a] • "I find the quality and sharpness of the patient's photographs extremely poor. For example, [there is] only a detailed image or [the image is] too out of focus. I prefer to take my own photographs and send them in with an adequate anamnesis." [DHC; ID 1373][a]
Human-computer interface (n=16)	1 (6)	3 (19)	12 (75)	• "Only allow patients to send in a [dermatology home] consultation when all photographs have been taken and loaded." [DHC; ID 1691][d] • "Less change in well-intentioned updating of layout." [ID 1660][a] • "The patient found it [dermatology home consultation] extremely difficult and user unfriendly." [DHC; ID 1692][a]
People (n=65)	8 (12)	51 (78)	6 (9)	• "[I learned] which questions are suitable for teleconsultation." [ID 1710][b] • "The learning capacity [of digital dermatology consultation] is strong. I notice that the number of consultations has decreased, partly due to the learning curve of comparable consultations." [ID 1692][b] • "The patient's photography skills are on average poor (and so are the photographs)." [DHC; ID 1257][a] • "The patient is not trained how [to take photographs]." [DHC; ID 1692][a]
Workflow and communication (n=13)	3 (23)	4 (31)	6 (46)	• "Patients like [digital consultations] for a while but then want to be seen [physically] again. However, there is an increase in e-consultations that is partly extra and possibly better care, but certainly no relief from work." [ID 1188][a]
Internal organizational policies, procedures, and culture (n=78)	1 (1)	66 (85)	11 (14)	• "[I take photographs] with my own camera on [my] smartphone. That [camera] is fine. Only the attachment no longer fits and is no longer supplied unfortunately. Another stand-alone USB version would be possible, but it costs quite a lot. A little discount through [the telemedicine organization] (win-win) would have been nice...It is a pity that [the telemedicine organization] does not invest so much in teledermatology anymore. Devices used to be 'free' if you performed enough [consultations]. Now that is no longer the case, I perform fewer [consultations]. Because the attachment no longer fits. I think that we both benefit less from that. Then I just refer to the dermatologist." [ID 1363][a] • "Offer better phones as was common practice 4 years ago. This is an extra incentive to use the dermatology service and guarantees quality of the photo cameras." [ID 1349][a]

Dimension	Facilitating quotes (%)	Neutral quotes (%)	Impeding quotes (%)	Exemplary relevant quotes
External rules, regulations, and pressures (n=21)	11 (52)	5 (24)	5 (24)	• "Digital care where I [as GP] seek secondary care [dermatologist] for advice has not been increased. Digital care where I was able to come to a solution together with the patient has been increased." [ID 1692][b] • "[We] already used teledermatology and teledermoscopy, but [we] have also started to digitally assess [patients'] skin conditions ourselves." [ID 1540][b] • "Before [the pandemic] we did not allow patients to send in pictures; that has naturally crept in during the COVID-19 pandemic; this with a satisfying result." [DHC; ID 1366][b] • "Digital dermatology was already an absolute winner before the COVID-19 pandemic. [Digital dermatology was used] less [often] during [the] COVID-19 [pandemic] because patients [were] preferably not [seen] live in [GP] practice, so spots had to wait." [ID 1257][d] • "[Digital dermatology] can lead to risky contacts at less than 1.5 meters." [ID 1257][a]
System measurement and monitoring (n=85)	56 (66)	27 (32)	2 (2)	• "Quick and easy for the patient, without [physical] referral with a long waiting time." [ID 1667][b] • "[Digital dermatology consultations are] a great way to communicate with [a] dermatologist." [ID 1362][b] • "It is nice to have [the patient] observed remotely and to be able to keep the patient out of the hospital." [IDs 1313 and 1710][b]
Not able to code (n=23)	N/A[e]	N/A	N/A	N/A

[a]Impeding quote.

[b]Facilitating quote.

[c]DHC: digital dermatology home consultation.

[d]Neutral quote.

[e]N/A: not applicable.

Facilitators

During the pandemic, GPs found digital dermatology care to be reliable, fast, and time efficient (accelerates care delivery). GPs experienced substantive good, practical, and fast responses from the specialists, including adequate diagnoses and treatment recommendations for their patients with skin lesions. GPs found it positive that they themselves remained responsible for the care of their patients. Overall, 26% (17/66) of the GPs indicated that digital care and digital dermatology consultations (partly) replaced physical consultations of their patients in primary and secondary care. A GP reported that he temporarily requested a few more teleconsultations in dermatology during the pandemic, but this number dropped after some time. GPs expressed that they learned from the feedback provided by teledermatologist and for which patient symptoms a teleconsultation is beneficial. Furthermore, a GP reported that the number of digital dermatology consultations that he requested to a dermatologist has decreased because he learned from the feedback from similar previous consultations.

Barriers

Limited Digital Photography Skills of Patients and GPs

The first barrier that GPs encountered relates to the limited digital photography skills of GPs and their patients. GPs reported to receive poor or nonassessable photographs from their patients because their patients have poor photography skills as they are not specifically trained in how to take photographs of their skin lesion. More specifically, GPs reported that patients provided skin photographs that were not sharp (when zoomed in), lacked proper details, were blurry or had poor lighting, were taken from a wrong distance, and did not always have good shades of color. In particular, overview, detailed, and magnified photographs of patients' skin lesions were not optimal, or patients provided an insufficient number of photographs. GPs reported that good web-based support and an understandable guide are needed to ensure good quality of photographs taken by patients; otherwise, their ignorance about how to take pictures will lead to many additional, time-consuming questions from patients to the GP. GPs expressed the need for a quality warning system if images uploaded by a patient are incomplete and not with sufficient quality.

Furthermore, approximately half (35/66, 53%) of the GPs indicated that they received complimenting or constructive feedback from a dermatologist about the quality of their photographs. Although most GPs (42/66, 64%) were positive about the provided training, they suggested additional (web-based) training options such as short video instructions as refreshers, practice sessions about photographing skin lesions with their own (dermoscopy) equipment, and advice about using the mobile phone camera. Others do not consider training as necessary to use the service.

Lack of Appropriate Up-to-Date Imaging Equipment and Equipment Costs

The second barrier relates to the lack of up-to-date, appropriate, digital dermatology imaging equipment and equipment costs. In the past, the telemedicine organization offered up-to-date, free-of-charge equipment to GPs in exchange for performing a minimum number of digital dermatology consultations, but they do not provide this equipment anymore. Nowadays, technology develops rapidly and GPs must purchase the latest off-the-shelf equipment themselves. GPs reported that especially dermoscopes are very expensive and that the provision of digital dermatology imaging equipment by the telemedicine organization is an extra incentive to use the service. GPs missed an appropriate mobile phone–attached dermoscope or had troubles with using the outdated attachment and reported that their photographs were not with sufficient quality with the current conversion lens.

Human-Computer Interface and Interoperability Issues

The third barrier relates to the human-computer interface and interoperability issues on the telemedicine platform. Interface issues included platform usability issues, strict validation on capitalization of address data, linking new user accounts, and changing layout. Interoperability issues included difficulties in uploading all patient information (eg, medical history, medication, and address) from the GP Information System (*Dutch: Huisarts Informatie Systeem*) into the digital dermatology consultation and vice versa in loading relevant patient data back from the digital consultation into the GP Information System. Furthermore, for teledermatology and teledermoscopy, most GPs take images with their mobile phones and upload these images via an app into the digital dermatology consultation form. Subsequently, on their computer, they complement the digital dermatology consultation form and send it to a teledermatologist. This process is time-consuming and complex; therefore, GPs prefer to start the digital dermatology consultation on their phones and directly send the consultation request and the images from their phone to a dermatologist.

Different Use Procedures

The fourth encountered barrier is that GPs have various reasons to use or to not use the service. Of the 66 GPs, 5 (8%) GPs reported no threshold for use at all, whereas other GPs experience thresholds for use. For example, if a patient has >1 skin abnormality, they have to create a new consultation for each abnormality. Another threshold for use is if they are not able to upload the images. Other reasons for a GP to not request a digital dermatology consultation are when an in-person visit or treatment or biopsy in the hospital is required anyway, or when in their opinion, a digital dermatology consultation is not indicated. In addition, GPs do not perform teledermatology when the patient prefers a physical consultation or disagrees with a digital consultation, for atypical or pigmented nevi for which skin inspection by touch is required for a correct diagnosis, for unclear skin abnormalities, for common skin lesions, or for urgent skin problems such as suspicion of melanoma or malignancy (36/66, 55%). In the latter possibly malignant cases, GPs perform a biopsy themselves or refer the patient to a dermatologist. However, 6% (4/66) of the GPs indicated to apply digital dermatology care for emergencies and lesions that are suspected to be malignant.

Questionnaire Improvement

Only 4 suggestions for improving the questionnaire were given and 2 support questions were asked. The remaining GPs had no comments or were satisfied with the questionnaire.

Discussion

Principal Findings

Overall, GPs had positive experiences with remote digital dermatology care during the COVID-19 pandemic. However, despite these positive perspectives, important barriers of the digital dermatology service were revealed regarding GPs' and patients' limited digital photography skills, costs and the lack of appropriate imaging equipment, human-computer interface and interoperability issues, and different use procedures.

Comparison With Previous Studies

Most GPs (46/66, 70%) in our study used the telemedicine platform approximately as often at the time of this study as before the pandemic. In contrast, the Netherlands Institute for Health Services Research (*Dutch: Nederlands instituut voor onderzoek van de gezondheidszorg* [NIVEL]) reported that 52% of Dutch GP practices intensified their teleconsultation contacts with medical specialists during the first COVID-19 wave, but GPs from these practices considered this only as a slight increase in teleconsultation use [27,28]. Furthermore, studies in other countries showed that dermatologists saw an increase in the number of remote dermatology consultations that they assessed during the pandemic in comparison with that during the prepandemic period [29,30]. Possible reasons for this lack of growth in teleconsultations requested by GPs in our study were, first, the service was already successfully implemented before the pandemic and, second, during the pandemic, patients were not only avoiding hospital care but also GP care. Teledermatology and teledermoscopy had the potential to reduce the number of physical referrals to hospitals but also required the patients to visit the GP's practice with possible physical contact at <1.5 m (4.9 feet). Patients were still hesitant to physically contact a GP because of the risk of exposure to the virus [1,31]. As a complementary service to the conventional face-to-face dermatology consultation in GP practice, digital dermatology home consultation, which was already in practice, took off. With this service, patients could take the photographs themselves with their own mobile phone or smartphone device and send these photographs securely to the GP for assessment without waiting time, physical contact, and the risk of contamination in GP practice. Therefore, a new group of complaints related to skin disorders that were normally handled physically by the GPs in their practice was submitted digitally by the patient. This meant that the pandemic had changed the spectrum of skin disorders managed and the profile of patients. Digital dermatology consultation was no longer used by GPs solely for difficult-to-assess skin complaints but also for easy-to-assess skin complaints sent in by patients that were usually assessed in GP practice. However, digital dermatology home consultation requires that patients have the appropriate equipment and technical literacy to engage the service on their own. Despite that most patients had access to a mobile phone or smartphone [32], they were not trained to take photographs of their skin condition. Therefore, GPs in our study reported images of mostly inadequate quality taken by patients. This shows that the external pressure of the pandemic pushed the use of remote dermatology care by (new and untrained) people; however, the fact that these users had insufficient knowledge about the requirements for taking appropriate photographs led to problems with the clinical assessment of the photographs. Future studies could investigate whether the skin disorders in the remote store-and-forward digital dermatology care population changed in comparison with the prepandemic period.

A Spanish study during the pandemic confirmed that patients had limited photography skills [33]. They found that only half (52.1%) of the images captured by patients and directly sent to the dermatologist were of adequate quality. Furthermore, in approximately one-fourth of these cases, poor image quality of these patient-submitted images was the reason why the teledermatologist could not provide a diagnosis. A prepandemic American study showed that a slightly higher percentage (62.2%) of the images sent by a patient to a dermatologist via teledermatology were with sufficient quality, whereas dermatologists perceived only half of the total images as having sufficient quality for decision-making [34].

Besides the remarks of GPs in our study about the photography skills of the patients, GPs also reported that they received constructive or complimentary feedback from dermatologists about the quality of their photographs. Previous studies about image quality of photographs taken in primary care for digital dermatology consultation also have demonstrated diverse results [10,35-39]. Poor photograph quality in these studies was, similar to our study, caused by out-of-focus images or missing overview or dermoscopic images of a patient's skin lesions. Digital dermatology consultations can be performed using current technologies, but many of the pictures are of unacceptable quality, and the training of health care providers and patients in taking images should thus be considered [21]. In the Dutch GP training curriculum, GPs are, in general, not trained to use digital services [40]. Only 5% (3/66) of GPs in our study indicated that they received training for taking (dermoscopic) photographs in their GP training curriculum. Owing to this lack of training in the GP curriculum, the telemedicine organization (Ksyos) organizes personal training sessions about the use of the digital dermatology service for all newly operating GP practices. Despite this introductory training, only about half (30/66, 45%) of the GPs in our study reported that they opted for this training or instruction about taking (dermoscopic) photographs from the telemedicine organization. This indicates that GPs did not experience this introductory training as an official education or instruction moment but solely as an installation or demonstration. In addition, a few GPs in our study took a (follow-up) imaging course. Although most GPs were satisfied with the training they received or indicated that they felt no need for (additional) training, many photograph quality issues were revealed in our study. This shows that training of people influences the quality of the images captured during a remote dermatology consultation. Furthermore, more than one-third (25/66, 38%) of the GPs used the telemedicine platform monthly or only a few times in a year. Such a long interval between uses might dilute their acquired skills and knowledge [41]. Therefore, our results suggest that GPs need continuous web-based and good practice training sessions and video instructions as refreshers (eg, instructions to refresh their knowledge about the use of the equipment to capture images and how to use the platform). We propose that these training sessions are accredited by the European Accreditation Council for Continuing Medical Education, which might stimulate GPs across Europe to participate in training sessions and to use digital dermatology services [42]. Furthermore, (video) instructions about how to obtain adequate photographs and an understandable, straightforward, step-by-step (web-based) guide for GPs and patients should be provided by the telemedicine organization to mitigate the image quality barrier in the future.

In addition, our results showed that the quality of the (dermoscopic) images was not only dependent on the photography skills of the patients and GPs but also on the imaging devices used in daily practice. These equipment issues related, among others, to the (outdated) mobile dermoscope attachments that were not compatible with GPs' new phones. Problems with their imaging equipment can limit GPs from using this equipment or continuing digital dermatology care [11]. Furthermore, a study conducted 10 years ago with the same Dutch teledermoscopy platform already reported equipment issues regarding failing or empty camera batteries and attaching and detaching the dermoscope [41]. Although technology and imaging equipment have developed enormously in recent years, GPs reported that the lack of appropriate up-to-date imaging equipment and equipment costs still hindered their digital dermatology use. Although most GPs own a self-purchased appropriate smartphone device and off-the-shelf dermoscopy attachments are available for a few hundred euros or US dollars, GPs in our study reported that they would appreciate it and consider it as an incentive if imaging equipment would be offered for free by the telemedicine organization. Costs to purchase the imaging equipment was also mentioned in other teledermatology and teledermoscopy studies as a barrier [43-45]. These findings show that the internal organizational policies regarding equipment influence the availability of appropriate hardware and software by GPs and that the lack of use of appropriate equipment directly influences the ability to clinically justify teledermatologists' advice based on the images. Therefore, solutions for purchasing or hiring up-to-date adequate imaging equipment for GP practices should be considered by telemedicine organizations.

Besides the issues with photography skills and the equipment, the human-computer interface and interoperability issues with the telemedicine platform might have influenced GPs' intentions of using the digital dermatology negatively. These platform-related issues should be taken into account by the telemedicine organization and might require technological improvements because GPs also reported about missing functionalities in our study. The human-computer interface should be specifically optimized based on the clinical information needs that teledermatologists and GPs have in the digital dermatology decision-making context. For example, the

Ksyos digital dermatology platform does not verify whether the photograph's quality is sufficient or whether the correct number of images are attached. As suggested by GPs in the open-ended questions, quality validation in the consultation platform is needed that allows patients and GPs to only send digital dermatology consultations when all photographs have been taken and uploaded and are with sufficient quality. Such a quality validation step on the platform could warn the user if the uploaded photographs are incomplete or of inadequate quality and could request the GP directly to retake the images. In addition, image quality checklists or guidelines for taking (dermoscopic) images implemented on the platform can instruct GPs and patients to take photographs with sufficient quality [46,47]. Furthermore, a study in the United States showed promising results with an automated machine learning algorithm that evaluates dermatology image quality and provides, if necessary, specific recommendations and guidance to patients about how to improve the quality of their images [48]. Su et al [49] launched a feedback algorithm with "smart phrases" that induces patients to retake images if the latest images were of insufficient quality. Such algorithms might also improve the quality of the submitted images in the Dutch digital dermatology platform over time.

In our study, two-thirds (42/66, 64%) of the GPs agreed that the dermatology care provided through the digital dermatology platform was the same as that in an in-person dermatology visit, meaning that digital consultation could replace regular in-person consultation. This percentage is consistent with a telemedicine study in the United States, where 63% of the physicians responded that the web-based telemedicine quality of care during the pandemic was generally similar to that of in-person care [50]. However, the sociotechnical analysis in our study showed that GPs had different perspectives and reported divergent reasons for when and for which skin conditions and patients they can or cannot apply the digital dermatology service instead of an in-person visit. Furthermore, this variety in GPs' answers about when they (think they can) apply the service suggest that it is not always clear to GPs which skin conditions are (not) suitable for a digital dermatology consultation. Training by the telemedicine organization and during GP education programs is needed to better instruct GPs when to use and not use the service.

Most GPs in our study responded that they would use the telemedicine platform again (61/66, 92%) and would recommend the platform to a colleague (53/66, 80%). Studies in other countries also show high GP satisfaction with and acceptance levels for digital dermatology care [35,45]. GPs in our study responded that they learned from practical experience (after repeated use of the platform) and the teledermatologist provided feedback, which facilitated the use of the service. This learning curve can be seen as a personal motivator for GPs to apply digital dermatology consultation [11]. Furthermore, this learning curve, in combination with the telemedicine experience level of the GPs before the pandemic, could also have stabilized the number of digital dermatology consultations during the pandemic. In addition, GPs in our study were satisfied with the time-efficient and adequate responses of the dermatologists. A scoping review by Osman et al [51] confirmed that primary care providers' perspectives about facilitators of digital consultations include obtaining timely responses from specialists and establishing knowledge.

Finally, Dutch GPs generally use digital dermatology consultations to prevent physical referrals, if they are unable to determine a differential diagnosis, if the treatment was unsuccessful, or to receive additional advice from the dermatologist. French GPs also use digital dermatology consultation mostly to resolve diagnostic doubts [52]. Furthermore, approximately two-thirds of these French GPs used the service before the pandemic owing to long waiting times for face-to-face dermatology visits, and one-third of the GPs used the service for emergencies [52]. In our study, approximately one-third (21/66, 32%) of the Dutch GPs mentioned long dermatology waiting times as reason for use, and only 2% (1/66) of the GPs used digital dermatology for emergencies. Thus, both Dutch and French GPs indicate that the use of digital dermatology accelerates contact with dermatologists. Table 5 shows the sociotechnical considerations for remote digital dermatology.

Table 5. Sociotechnical considerations for remote digital dermatology.

Barriers	Recommendations for future
GPs'[a] and patients' limited digital photography skills	• Accredited, continuous, web-based, and good practice training sessions and video instructions as refreshers for GPs (eg, recap about the use of the imaging equipment and the platform) • (Video) instructions for GPs and patients about how to obtain adequate photographs • Understandable, straightforward, step-by-step guide for GPs and patients
Costs and the lack of appropriate imaging equipment	• Solutions for the availability of appropriate imaging equipment (eg, purchasing or hiring up-to-date equipment)
Human-computer interface and interoperability issues	• Quality validation in the teledermatology platform that verifies whether the photograph's quality is sufficient and whether the correct number of images are taken and uploaded • Implementing image quality checklists and guidelines about taking (dermoscopic) images
Different use procedures	• Policy development about the use of the teledermatology service • Training of GPs (by the telemedicine organization and during GP education programs) when they can or cannot use the teledermatology service

[a]GP: general practitioner.

Strengths

The first strength of this study was the unique opportunity to evaluate GPs' perspectives and their experienced facilitators and barriers related to the digital dermatology consultation service during the COVID-19 pandemic, as the service had already been integrated into Dutch general practice before the pandemic. These insights are essential to maintain and optimize the quality of digital dermatology services to the needs of the GPs and to stimulate continuous use of the service in the future. The second strength of this study was the use of a sociotechnical model for the interpretation of the data, which has also been used in other telemedicine and telehealth evaluations [26,53,54]. This subsequently allowed us to identify the GPs' experienced facilitators and barriers related to digital dermatology care. The added value of this model was that it provided insight into the interrelations between the sociotechnical aspects obtained using the SAF-TSUQ and the additional open-ended insight questions. This model has shown that changes and barriers in one of these sociotechnical aspects directly influence the other aspects.

Limitations

The first limitation of this study is that the questionnaire was distributed to GPs affiliated with the telemedicine organization who performed a store-and-forward consultation between October 2019 and September 2021. In doing so, we excluded GPs working with other telemedicine organizations, GPs who chose not to use the service during the pandemic, or GPs who were less comfortable with using the service. However, the main aim of this study was to assess GPs' perspectives about 3 types of digital dermatology consultation in the Netherlands. Future studies should expand upon the use of digital dermatology care during the COVID-19 pandemic from the perspectives of other involved stakeholders, such as dermatologists and patients.

The second limitation is that the study data were only collected for 1 already existing Dutch store-and-forward digital dermatology service, even though this service has been implemented nationwide. This may limit the generalizability of our findings to other (Western European) countries that have implemented digital dermatology services, which are still in the preliminary stages. In many countries, teledermatology was not reimbursed before the pandemic, which has driven providers away from practicing teledermatology consultations [6]. Although the telemedicine contexts may differ in other countries, our results also provide general facilitators and barriers that apply to the adoption and implementation of digital dermatology consultation in preliminary stages or other contexts. Future research could involve a more extensive study that would allow us to examine what contextual and other factors (eg, age, the number of years of practice, and the type of practice) influence GPs' perceptions and use of remote dermatology services.

The third limitation is that our study was questionnaire based, with the typical limitations of incomplete responses and low response rates. The questionnaire was administered at the end of 2021, when a COVID-19 mandated national lockdown, social distancing, and stay-at-home mandates were announced. We assume that the low participation rate might be owing to GPs' limited time and increased workload. We tried to increase the response rate by sending 1 reminder via email but did not want to burden GPs in such a hectic time.

Conclusions

Remote dermatology care was already integrated into Dutch GP practice before the pandemic, which may have facilitated the positive responses of GPs to the use of the service. However, barriers impeded the full potential of its successful use by GPs during the pandemic and may limit the continuity of the service in GP practices in the future. The training of GPs is needed to effectively use the imaging equipment and to guarantee adequate quality of taken (dermoscopy) images. Furthermore, GPs should be trained when (not) to use the digital dermatology service. In addition, the remote dermatology platform should be improved to guide patients in taking photographs with sufficient quality. The identification of these barriers provides insights to telemedicine organizations, health institutions, and policy makers to guide digital dermatology implementation and sustainability.

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Authors' Contributions

ET and LWP were involved in the study design and conception, design of the questionnaire, and analysis and interpretation of the questionnaire data. ET was also involved in the distribution of the questionnaire and data acquisition. ET drafted the first manuscript version, and LWP was involved in writing the manuscript from the first version onward. CK and MWJ were further involved in critical revision of the manuscript. All authors approved the final version of the manuscript.

Conflicts of Interest

ET is a PhD researcher at the Amsterdam University Medical Center and employed by Ksyos. All other authors declare no other conflicts of interest.

Multimedia Appendix 1
Web-based questionnaire sent to general practitioners and the English translation.
[DOCX File , 125 KB - derma_v6i1e46682_app1.docx]

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Abbreviations

GP: general practitioner
NIVEL: Nederlands instituut voor onderzoek van de gezondheidszorg (the Netherlands Institute for Health Services Research)
SAF-TSUQ: Store-and-Forward Telemedicine Service User-satisfaction Questionnaire

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Original Paper

Rapid Expansion of a Teledermatology Web Application for Digital Dermatology Assessment Necessitated by the COVID-19 Pandemic: Retrospective Evaluation

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Abstract

Background: The COVID-19 pandemic necessitated a change in the provision of outpatient care in dermatology.

Objective: A novel, asynchronous, digital consultation platform was codeveloped with 2 National Health Service dermatology teams to improve access and enhance choice in outpatient care.

Methods: The rollout of the platform was accelerated during the initial COVID-19 lockdown, and its wider use across 2 Scottish health boards was retrospectively evaluated. Integrated with the hospital booking system and electronic patient record, the platform provides an alternative to face-to-face consultations, using information and images submitted by the patients.

Results: In total, 297 new patient consultations and 108 return patient consultations were assessed, and 80% (324/405) of the images submitted were of satisfactory quality. The consultations were, on average, 3 minutes shorter than equivalent face-to-face interactions, and a total of 5758 km of patient travel was avoided. Outcomes included web-based reviews (66/405, 16.3%), face-to-face reviews (190/405, 46.9%), biopsies (46/405, 11.4%), discharge (89/405, 22%), and other treatments or investigations (14/405, 3.5%). High levels of patient satisfaction (92/112, 82.1%) were reported.

Conclusions: Digital dermatology assessments are now included in the choices for consultation types that are available to patients, helping to augment service capacity during pandemic recovery.

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KEYWORDS

dermatology; asynchronous; outpatient; consultation; teledermatology; telehealth; telemedicine; consultation; digital health; eHealth; digital consultation; dermatologist; skin; return patient; digital assessment; online platform

Introduction

Dermatologists have been identified as “behind the curve” in digital innovation [1]. Prior to the pandemic, teledermatology had not been used as a consultation method in outpatient clinics within Scotland. Although lesion photo triage was available in a limited number of health boards, its primary purpose was for enhanced referral triage, and it required patients to have face-to-face contact with a clinical photographer. Pandemic restrictions necessitated a reduction in face-to-face consultations, with priority given to essential cancer and emergency services. To provide continuing patient care, existing outpatient models were redesigned to enable the use of store-and-forward asynchronous teledermatology. In comparison with synchronous real-time teledermatology (primarily video consultations), asynchronous teledermatology involves electronically transmitting clinical details and images to a clinician for review at a different time and location [2]. This method was preferred, as it has been widely reviewed, has the potential to improve clinical efficiency [3-5], provides flexibility and convenience to both clinicians and patients, and confers environmental benefits through reduced travel and carbon emissions [6]. Asynchronous teledermatology also permits the uploading of higher-quality images of specific lesions by patients. This is preferable to relying on lower-resolution videos and avoids the potential pitfalls of slow internet connection speeds, which are issues in the case of synchronous teledermatology [7].

A government-sponsored initiative sought to fund innovative solutions for use in modern health care settings. Dermatology, with its high volumes of outpatient consultations, was identified as an area with development potential, and software companies were asked to pitch their ideas for novel digital systems to improve health care efficiency. Through this, an asynchronous teledermatology platform was developed collaboratively by dermatology teams from 2 Scottish health boards (National Health Service [NHS] Forth Valley and NHS Greater Glasgow and Clyde) and a digital agency [8]. NHS Forth Valley serves a diverse geographical area in the heart of Scotland, and NHS Greater Glasgow and Clyde is the largest NHS organization in Scotland and one of the largest in the United Kingdom. Clinicians' and patients' views were taken into account when designing the system to make it user-friendly at both ends of the interface.

The platform allows patients to submit information and photographs of their skin condition, which are then assessed by a clinician. Afterward, the patients receive a response, and a summary of the consultation is sent to primary care and stored on the patients' electronic records.

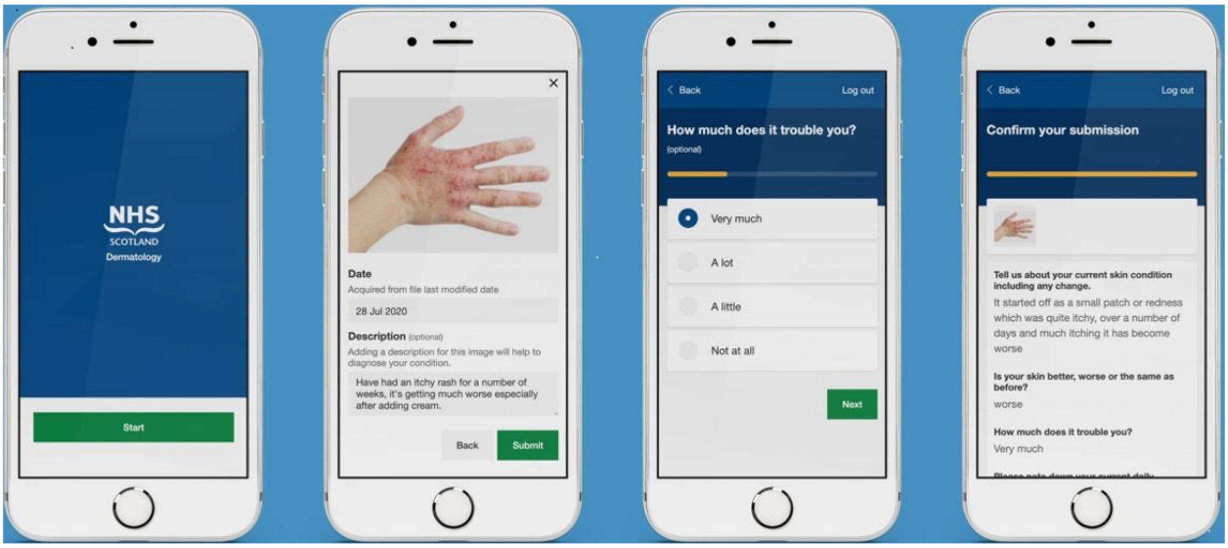
Although the platform was originally designed for follow-up consultations, the challenges posed by the COVID-19 pandemic lockdown prompted its more widespread use, including for new consultations. We therefore evaluated its feasibility as a consultation platform, with respect to efficiency, patient satisfaction, and its use as a diagnostic or triage tool.

Methods

Overview

The real-time capture of data was undertaken as part of a cross-sectional evaluation of 405 digital assessments performed from March to June 2020 across 2 Scottish health boards (NHS Forth Valley and NHS Greater Glasgow and Clyde). Patients referred from primary care urgently with suspected skin cancer, in addition to urgent general dermatology referrals, were triaged for their suitability for this system and offered a digital assessment. Patients were invited to register and provide consent within the platform. They then had 5 days to upload 1 to 4 images and answer 6 questions about their presentation (Figure 1).

Figure 1. Patient interface. Patients are invited to register for the web-based platform via email. They can upload up to 4 images of their skin and are prompted to answer 6 questions about their presentation.



The application developed for this study provides bespoke clinician and patient interfaces. The clinicians' individual dashboard allows them to view submissions from their assigned patients; if more information is needed, a direct request can be made to patients via the built-in messaging system. The clinician then sends a response with their diagnosis and management plan. A PDF summary is automatically sent to the primary care clinician, and a copy is stored on the electronic patient record.

Following each digital assessment, clinicians were asked to complete a standardized questionnaire, detailing the diagnosis, image quality, outcome, and time taken to complete the response (recorded by a stopwatch). The equivalent appointment length for a face-to-face consultation was stated by the clinician to permit comparison with conventional work patterns. Patient feedback was formally collated via a web-based survey of their user experience. This included specific questions on the ease of use, need for technical support, quality of care provided, travel time saved, and overall experience with the web-based platform.

Ethics Approval

As the new system was introduced as part of service development (albeit in an accelerated way due to the pandemic), any evaluation of its acceptability and effectiveness would be considered a service evaluation or clinical audit. This means that the evaluation would not be considered NHS research and therefore had no need of either an NHS Research Ethics Committee review and opinion, or of NHS R&D approval from the participating Health Boards. The policy that service evaluations/audits do not require either NHS Research Ethics Committee review or NHS R&D approval dates back to the introduction of the Research Governance Framework (RGF) released in 2005. This was rolled over to the UK Policy Framework for Health and Social Care Research which superseded the RGF in October 2017 and was therefore applicable during the COVID-19 pandemic.

Results

During the 11 weeks of the first national lockdown, 405 digital assessments were completed for 394 patients (Table 1). Of the 405 assessments, 297 (73.3%) were for new referrals, while 108 (26.7%) were return consultations. Patient ages ranged from 1 to 98 (mean 48) years, with 30.7% (121/394) aged older than 60 years, and parents of 12 children successfully completed digital assessments. Two-thirds of patients used a smart device, with the remainder using a PC or laptop (263/394). Further, 80% (324/405) of submitted images were considered of satisfactory quality by the assessing clinician, 41 patients under the government's shielding program (identifying patients at the highest risk of COVID-19) received outpatient care from the safety of their home, and 218 consultations were carried out by a clinician working from home, highlighting the potential for digital dermatology assessments to provide a flexible alternative to traditional working patterns.

Table 1. Distribution of diagnoses (lesions vs inflammatory dermatoses).

Diagnoses	Distribution, n
Lesions	292
Benign naevus	80
Actinic keratosis or Bowen disease	37
Seborrheic keratosis	33
Atypical naevus	29
Basal cell carcinoma	21
Solar lentigo	12
Vascular lesion	10
Squamous cell carcinoma or keratoacanthoma	7
Benign nail lesion	7
Viral wart	7
Dermatofibroma	4
Melanoma	3
Lentigo maligna	2
Other benign lesion[a]	26
Unknown diagnosis	10
Postbiopsy or photodynamic therapy review	4
Inflammatory dermatoses	113
Psoriasis	44
Eczema or seborrheic dermatitis	33
Acne or rosacea	9
Nodular prurigo or lichen simplex	4
Urticaria	3
Lupus	3
Vasculitis	2
Infective (tinea or impetigo)	2
Folliculitis	2
Postinflammatory hyperpigmentation	2
Indeterminate rash	2
Other inflammatory dermatoses[b]	7

[a]Other benign lesions included Spitz naevus, clear cell acanthoma, glomus tumors, epidermoid cysts, sebaceous hyperplasia, and chondrodermatitis nodularis helicis.

[b]Other inflammatory dermatoses included panniculitis, lichen planus, pyoderma gangrenosum, necrobiosis lipoidica, dermatitis herpetiformis, pemphigus foliaceus, and telangiectasia macularis eruptiva perstans.

Of the 405 assessments, 292 (72.1%) concerned lesions, with the majority (241/292, 82.5%) referred for suspected cancer. Of these 292 lesions, 21 (7.2%) were booked for a web-based review, 139 (47.6%) were booked for a face-to-face review, 46 (15.8%) were directly booked for surgery, 81 (27.7%) resulted in discharge, and 5 (1.7%) were referred for photodynamic therapy. The remaining 113 (27.9%) assessments were for inflammatory dermatoses. Of these dermatoses, 45 (39.8%) were recommended for a web-based follow-up, 51 (45.1%) were recommended for a face-to-face review, 8 (7.1%) resulted in discharge, and 9 (8%) were referred for further investigations or treatments (Table 2). The majority of those needing a face-to-face review (137/190, 72.1%) were scheduled for a routine follow-up, although 27.9% (53/190) did require an urgent one-stop review for the confirmation of lesion diagnosis (including patients whose submitted images were unsatisfactory).

Table 2. Outcomes for digital assessments during lockdown.

	Outcomes, n (%)
Overall outcomes (N=405)	
Further web-based review	66 (16.3)
Face-to-face review	190 (46.9)
Direct to biopsy	46 (11.4)
Discharged	89 (22)
Other treatments or investigations (phototherapy, patch testing, and PDT[a])	14 (3.5)
Outcomes for lesions (n=292)	
Further web-based review	21 (7.2)
Face-to-face review	139 (47.6)
Direct to biopsy	46 (15.8)
Discharged	81 (27.7)
Other treatments or investigations (PDT)	5 (1.7)
Outcomes for inflammatory dermatoses (n=113)	
Further web-based review	45 (39.8)
Face-to-face review	51 (45.1)
Direct to biopsy	0 (0)
Discharged	8 (7.1)
Other treatments or investigations (phototherapy and patch testing)	9 (8)

[a]PDT: photodynamic therapy.

Additional information was acquired in 1 health board regarding histological diagnoses in 42 patients who were directly referred for biopsy or surgery following their assessment. This showed that 3 melanomas and 8 nonmelanoma skin cancers had been identified and treated.

Consultations in 1 health board were timed by using a stopwatch. The mean time for a total of 312 timed digital assessments was 10 minutes, whereas equivalent face-to-face consultations averaged 13 minutes. The time saving of digital consultations points to efficiency gains as well as the potential to increase available capacity and free up face-to-face appointments for those with complex care needs.

Feedback surveys indicated that satisfaction was high, with 82.1% (92/112) of respondents across both boards reporting ease of use. Further, 42% (47/112) reported that they would have normally needed to take time off work to attend a face-to-face appointment, while 21% (24/112) would have needed to travel for greater than 30 minutes to reach their hospital. Patient comments were generally positive, with many reporting that the reduced need for travel and time off work was a key benefit. Some patients reported technical difficulties, of which many have been subsequently improved after further development of the software. Newly referred patients were more likely to report that they would like more open dialogue with a clinician. Avoiding unnecessary hospital visits reduces the carbon footprint of the NHS and its contribution to the current climate emergency. During this evaluation, a total of 5758 km of patient travel was avoided through the use of digital assessments. This is equivalent to avoiding 719 kg of vehicle carbon dioxide emissions.

Discussion

Principal Findings

The COVID-19 pandemic has seen a paradigm shift in medical consultations, with telemedicine expanding rapidly to replace face-to-face interactions and reduce infection risk. A US institution reported a reduction in in-person visits to 1% of the prepandemic visit volume, with asynchronous consults accounting for 1 in 5 of all visits early in the pandemic [9]. Further, a questionnaire answered by dermatologists from 49 countries has confirmed the increased use and first-time adoption of teledermatology during the pandemic [10]. Improved patient access and staff productivity are also cited as reasons for continued use after pandemic lockdowns. We report the successful implementation of a digital assessment platform that has minimized face-to-face interactions, although we recognize that certain patients find digital assessment challenging, and others may prefer a real-time video or face-to-face consultation. Patients with established chronic dermatoses and those requiring a review of systemic therapies may be the most suited to digital assessment. We have been surprised by the utility of the platform in triaging and assessing skin lesions. Although this consultation platform demonstrates time savings per consultation, it did generate more review consultations. We recognize that patients requiring ongoing follow-up in dermatology would benefit from a mix of face-to-face and web-based consultations. The digital platform, which has now been evaluated and implemented in a third health board (NHS Grampian), is available for procurement by other health boards across the country.

Although we acknowledge that the pandemic necessitated travel restrictions, the system would ordinarily confer significant environmental benefits and improved convenience for patients. The greater adoption of digital consultations within high-footfall specialties, such as dermatology, could confer significant reductions in the carbon footprint of health care while also enabling patients to access flexible and convenient specialist assessments [11].

To date, over 3500 appointments have been completed, with more than 2500 occurring during mandated lockdown periods. This resulted in 150 hours of clinician time saved, representing a significant improvement in efficiency. The pandemic represents a paradigm shift in working patterns, and the digital solution reported herein, which is supported by dermatology patients and clinicians, is now supporting pandemic recovery. Interest in the platform has also been expressed by other specialties, including rheumatology, gastroenterology, and orthopedics.

Conclusions

The novel store-and-forward asynchronous digital platform we describe offers an additional choice for providing outpatient care. The integration of the platform with the hospital booking system and patient record improved the efficiency and convenience of use. Digital consultations were typically shorter than conventional consultations, but around 50% (190/405, 46.9%) of patients did require a subsequent face-to-face review. The potential convenience for patients (eg, avoiding the need for travel and, beyond lockdown, avoiding the need to leave work or arrange childcare) was highly valued. Patients with a known diagnosis requiring follow-up may be the most suitable for the platform, but our experience indicates the potential utility of digital assessments for lesions and presentations of new dermatoses. An asynchronous digital platform complements phone, video, and conventional face-to-face consultations in offering choices in patient care, but it should only be offered within an integrated service.

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Conflicts of Interest

None declared.

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Abbreviations

NHS: National Health Service

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Original Paper

Acceptance of Telemedicine Compared to In-Person Consultation From the Providers' and Users' Perspectives: Multicenter, Cross-Sectional Study in Dermatology

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Abstract

Background: Teledermatology is currently finding its place in modern health care worldwide as a rapidly evolving field.

Objective: The aim of this study was to investigate the acceptance of teledermatology compared to in-person consultation from the perspective of patients and professionals.

Methods: This multicenter, cross-sectional pilot study was performed at secondary and tertiary referral centers of dermatology in Switzerland from August 2019 to January 2020. A customized questionnaire addressing demographics and educational data, experience with telemedicine, and presumed willingness to replace in-patient consultations with teledermatology was completed by dermatological patients, dermatologists, and health care workers in dermatology.

Results: Among a total of 664 participants, the ones with previous telemedicine experience (171/664, 25.8%) indicated a high level of overall experience with it (patients: 73/106, 68.9%, dermatologists: 6/8, 75.0%, and health care workers: 27/34, 79.4%). Patients, dermatologists, and health care workers were most likely willing to replace in-person consultations with teledermatology for minor health issues (353/512, 68.9%; 37/45, 82.2%; and 89/107, 83.2%, respectively). We observed a higher preference for telemedicine among individuals who have already used telemedicine (patients: $P<.001$, dermatologists: $P=.03$, and health care workers, $P=.005$), as well as among patients with higher educational levels ($P=.003$).

Conclusions: This study indicates that the preference for teledermatology has a high potential to increase over time since previous experience with telemedicine and a higher level of education were associated with a higher willingness to replace in-patient consultations with telemedicine. We assume that minor skin problems are the most promising issue in teledermatology. Our findings emphasize the need for dermatologists to be actively involved in the transition to teledermatology.

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KEYWORDS

acceptance; patient; physician; satisfaction; teledermatology

Introduction

Teledermatology is finding its place in modern health care worldwide as a rapidly evolving field. Telemedicine is defined as the use of telecommunication technology to provide clinical health care from a distance [1]. Due to its visual character, dermatology is regarded as a particularly suitable telemedicine application [2-4]. The individual attitude toward teledermatology has favorably changed within the last 10 years, as reported in a recent survey of British dermatologists [5]. During the COVID-19 pandemic, remote consultations have markedly increased in importance [6]. However, a prerequisite for widespread adoption of telemedicine is that it must favorably compete with in-person consultations on several objective measures, including effectiveness [7,8], availability [9,10], and costs [11]. During the COVID-19 pandemic, video- and audio-only visits were reimbursed even at the same rate as face-to-face visits in the United States [12]. A current debate in the United States on whether telemedicine increases spending and whether it improves patient outcomes leads to an unclear future for telemedicine [12], whereas France extends its tele-expertise funding even after the pandemic [13].

Nowadays, teledermatology is accepted as a valid tool and gains popularity in many countries [2,14]. Of paramount importance is also the acceptance and overall experience among patients as users and physicians as providers. Thus, telemedical services can benefit from provider- and user-friendly adaptations to implement and further develop this growing medical sector. Also, the World Health Organization has recently recognized and accepted that telemedicine is an important tool to allow health care access in remote areas and underserved communities [15]. The worldwide use of teledermatology is highest in Europe and North America, whereas regions with poor geographical distributions of doctors appear to be underrepresented [2]. Various studies reveal high levels of user satisfaction in teledermatology over the last 2 years [14]. However, common barriers reported by dermatologists include low reimbursement, concerns about government regulations, and liability [16].

Various studies suggest that dermatologists may achieve comparable accuracy in diagnosis and management with teledermatology in comparison to classical in-person visits [17-22]. The target group benefiting most from teledermatology seems to be rather older, immobilized patients with chronic wounds, as well as patients with treatment monitoring of inflammatory and infectious dermatoses [1,19,23]. Teledermatology bears enormous potential for being less stressful and saving time and money, especially for immobilized patients living in rural regions far away from health care centers [1]. Certain prerequisites and concerns of telemedicine include the implementation of appropriate devices and the technical skills involved in their handling, data safety, and diagnostic reliability [5]. Further arising concerns are the lack of a patient-physician relationship due to the remote nature of the procedure and insufficient follow-up [24,25]. Anxiety about being photographed is another reported reason for patients' dissatisfaction with teledermatology [26]. Patients' acceptance seems to be often neglected in current studies addressing this topic [1].

For several decades now, various models have been developed and used to investigate the use and acceptance of IT [27]. The "technology acceptance model" (TAM) is still one of the most popular theories to analyze the perception and factors influencing the acceptance of a novel technology [28]. First developed by Davis in 1986, the central goal of TAM was to increase the usage of IT by promoting its acceptance [29]. Thus, knowledge of the factors that contribute to acceptance is essential for this purpose. After being validated several times, the TAM model has been improved and adapted in 2000 (TAM 2), focusing on the "perceived usefulness," and 2008 (TAM 3), focusing on the "perceived ease of use." Venkatesh et al [30] validated a new model called the "unified theory of acceptance and use of technologies" (UTAUT), which is based on the conceptual similarities of 8 different models. The UTAUT model states that the intention to use a technology can be divided into "performance expectancy," "effort expectancy," "social influence," and "facilitating conditions" [30]. The use of the most recent model version, UTAUT2, has been validated in several studies and is an important theoretical approach [31-34].

Given the sparse current data about the combination of users' and providers' overall experience with teledermatology, the aim of this study was to investigate the acceptance of telemedicine from different perspectives. By focusing on 3 target groups (patients, physicians, and health care workers) and asking physicians and health care workers about their patients' views for the first time, we identified a research gap in dermatology. Further, to identify the acuity and severity of skin problems for which patients, health care workers in dermatology, and dermatologists would be willing to replace in-person consultations with telemedicine, we analyzed individual differences influencing satisfaction with telemedicine. In this study, we intended to focus on the practical value for practitioners and health policy makers which is why we used study-specific questionnaires and not validated ones.

Methods

Study Design and Participating Population

This multicenter, cross-sectional study was conducted at 1 secondary and 2 tertiary referral centers for dermatology in Switzerland. We applied a customized questionnaire from August 1, 2019, to January 31, 2020, at the Department of Dermatology of the University Hospitals of Basel and Zurich and at the Cantonal Hospital of Aarau. The questionnaire was offered to all patients aged 18 years and older at check-in and anonymously completed in the waiting room before the appointment with the dermatologist at the mentioned centers. We also sent an adapted version of the questionnaire to all dermatologists and medical staff (nurses and secretaries) at these hospitals (henceforth referred to as "health care workers") to be completed at any time. The questionnaire was also applied to other physicians who do not work in dermatology; however, these data were not included in this study. Overall, 70.6% (512/725) of the patients, 72.6% (45/62) of the dermatologists, and 68.6% (107/156) of the health care workers responded to the questionnaire. Exclusion criteria were language barriers, cognitive impairment, and a lack of informed consent.

Study Procedures and Questionnaire

We designed the questionnaire in German to assess individual characteristics and telemedicine-related aspects in patients (see questionnaire Q-A in Multimedia Appendix 1), as well as in physicians and health care workers (see questionnaire Q-B in Multimedia Appendix 2). A total of 12 questionnaire items were identical across cohorts. The questionnaire addressed demographics, educational, and economic data (currency was converted from Swiss Francs to Euros [1.0 CHF=1.0 Euro, July 4, 2022]), as well as aspects of individual experience with and opinion about telemedicine. Here, we only assessed the presumed willingness to replace in-person consultation and the overall experience with telemedicine, as well as their associations with individual characteristics. The 4 different categories of acuity and severity (minor, severe, acute, and chronic) were defined as the subjective, individual judgment of each participant for the acuity and severity of skin diseases. Other aspects of the questionnaire will be published later. Depending on the question, possible answers were either binary (yes/no), multiple choice, visual analog scales (VASs) with scores from 0-10, or free text.

Data Analysis

We reported the proportions of primary answers and investigated the differences in the questionnaire answers related to the previous use of telemedicine (Q-A #12a, Q-B #5), additional in-person consultation to the telemedicine (Q-A #15, Q-B #8), media for telemedicine (Q-A #14, Q-B #7), overall experience with telemedicine consultation (Q-A #16, Q-B #9), presumed willingness to replace in-person consultation with telemedicine (Q-A #19, Q-B #11), preference for telemedicine or in-person consultation (Q-A #17-18, Q-B #10), and individual differences (Q-A #0-2, Q-B #0-2) across the 3 different cohorts (here defined as patients, physicians, and health care workers). Differences in proportion of answers across cohorts were explored with chi-square tests, with Monte-Carlo resampling with 10,000 iterations if the frequency in any cell was less than 5. Differences in answers for presumed willingness to replace in-person consultation with telemedicine across cohorts were evaluated for different severities (minor and severe) and acuities (chronic and acute) of skin problems. Differences in answers for preference for telemedicine or in-person consultation across individual differences were evaluated for each cohort separately. Differences in age were explored with the Kruskal-Wallis test. *P* values were adjusted for multiple comparisons using the false discovery rate (FDR) for each analysis separately. All analyses were performed through R (versions 3.6.2 and 4.2.0; The R Foundation) and Python version 3.7.6 (Python Software Foundation).

Ethics Approval

The study was approved by the Northwest and Central Switzerland Ethics Committee (2019-00523) and was registered with ClinicalTrials.gov (NCT04495036). The study was conducted in full compliance with the Declaration of Helsinki (1964) and Good Clinical Practice was maintained throughout the study.

Results

Patient Demographics

A total of 512 dermatological patients (mean age 49.5, SD 17.9 years; 239/512, 46.7% women), 45 dermatologists (mean age 34.1 SD 8.5 years; 32/45, 71.1% women) and 107 health care workers (mean age 38.6, SD 13.0 years; 88/107, 82.2% women) completed the questionnaire (a total of 664 individuals). Information about nationality, place of residence, monthly salary, highest level of education, work experience, and previous use of telemedical services for patients, physicians, and health care workers is summarized in Table 1.

Table 1. Characteristics and telemedicine-related aspects of the study population (N=664). "A currency exchange rate of Euro €1=US $1.093 is applicable."

Characteristics	Patients (n=512), n (%)	Dermatologists (n=45), n (%)	Health care workers (n=107), n (%)
Gender			
Female	239 (46.7)	32 (71.1)	88 (82.2)
Male	268 (52.3)	13 (28.9)	18 (16.8)
N/A[a]	5 (1)	0 (0)	1 (0.9)
Nationality			
Swiss	425 (83)	27 (60.0)	84 (78.5)
Other	84 (16.4)	17 (37.8)	21 (19.6)
N/A	3 (0.6)	1 (2.2)	2 (1.9)
Place of residence			
Urban (>100,000 inhabitants)	88 (17.2)	35 (77.8)	30 (28)
Urban (10,000-100,000 inhabitants)	146 (28.5)	5 (11.1)	26 (24.3)
Rural (<10,000 inhabitants)	278 (54.3)	5 (11.1)	50 (46.7)
N/A	0 (0)	0 (0)	1 (0.9)
Monthly salary (in Euros)			
≤2000	59 (11.5)	N/A	N/A
2000-5000	164 (32)	N/A	N/A
5000-8000	136 (26.6)	N/A	N/A
≥8000	97 (18.9)	N/A	N/A
N/A	56 (10.9)	N/A	N/A
Highest level of education			
Primary and secondary school	52 (10.2)	N/A	N/A
Apprenticeship	204 (39.8)	N/A	N/A
High school diploma	69 (13.5)	N/A	N/A
University or college degree	166 (32.4)	N/A	N/A
N/A	21 (4.1)	N/A	N/A
Medical occupation			
Resident in dermatology	N/A	29 (64.4)	N/A
Board certification in dermatology	N/A	16 (35.6)	N/A
Work experience (years)			
≤5	N/A	19 (42.2)	25 (23.4)
5-10	N/A	17 (37.8)	22 (20.1)
10-20	N/A	4 (8.9)	24 (22.4)
20-30	N/A	4 (8.9)	21 (19.6)
≥30	N/A	1 (2.2)	12 (11.2)
N/A	N/A	0 (0)	3 (2.8)
Already used telemedicine (as a patient)?			
Yes	123 (24)	9 (20)	39 (36.4)
No	382 (74.6)	36 (80)	68 (63.6)
N/A	7 (1.4)	0 (0)	0 (0)
Already used teledermatology?			
Yes	23 (18.7)	N/A	N/A

Characteristics	Patients (n=512), n (%)	Dermatologists (n=45), n (%)	Health care workers (n=107), n (%)
No	92 (74.8)	N/A	N/A
N/A	8 (6.5)	N/A	N/A
Already worked as a teledermatology provider?			
Yes	N/A	19 (29.7)	4 (3.7)
No	N/A	45 (70.3)	73 (68.2)
N/A	N/A	0 (0)	30 (28)
Health insurance based on telemedicine			
Yes	64 (12.5)	6 (13.3)	17 (15.9)
No	51 (10)	3 (6.7)	20 (18.7)
N/A	397 (77.5)	36 (80)	70 (65.4)
Daily internet use (in hours)			
≤1	209 (40.8)	7 (15.6)	39 (36.4)
1-2	160 (31.2)	22 (48.9)	36 (33.6)
2-3	58 (11.3)	9 (20)	19 (17.8)
3-4	26 (5.1)	3 (6.7)	7 (6.5)
>4	38 (7.4)	4 (8.9)	3 (2.8)
N/A	21 (4.1)	0 (0)	3 (2.8)

[a]N/A: not applicable or did not answer.

Overall Experience With Telemedicine Consultation

Considering only individuals who reported having already used telemedicine (henceforth referred to as "telemedicine users"; Q-A #12a, Q-B #5, Table 1) and having an in-person consultation for the same medical problem (Q-A #15, Q-B #8), telemedicine was used before rather than after an in-person consultation by 84.4% (54/64) of the patients, 83.3% (5/6) of the dermatologists, 92.3% (24/26) of the health care workers and we observed no differences across cohorts (χ^2=1.1; *P*=.70).

Considering only previous telemedicine users (Q-A #12a, Q-B #5, Table 1), the overall experience with telemedicine from patients' perspective within all 3 target group was rated as either "very good" or "good" by 68.9% (73/106) of the patients, 75.0% (6/8) of the physicians, and by 79.4% (27/34) of the health care workers (Q-A #16, Q-B #9, Table 2) and we observed no differences across cohorts (χ^2=7.3; *P*=.50, Table 2), excluding the "not applicable/did not answer" responses. We also report information about media used for telemedicine counselling in Table S1 in Multimedia Appendix 3 (Q-A #14, Q-B #7).

Table 2. Overall experience with use of telemedicine from the patients' perspective within the 3 target groups. The *P* value did not include the "not applicable/did not answer" responses.

Rating	Patients' perspective (n=120), n (%)	Patients' perspective within dermatologists (n=9), n (%)	Patients' perspective within health care workers (n=39), n (%)	*P* value
Very good	18 (15)	2 (22.2)	6 (15.4)	.50
Good	55 (45.8)	4 (44.4)	21 (53.8)	.50
Regular	25 (20.8)	1 (11.1)	6 (15.4)	.50
Bad	6 (5)	0 (0)	1 (2.6)	.50
Very bad	2 (1.7)	1 (11.1)	0 (0)	.50
N/A[a]	14 (11.7)	1 (11.1)	5 (12.8)	.50

[a]N/A: not applicable or did not answer.

Presumed Willingness to Replace In-Person Consultation With Telemedicine for Different Acuities and Severities of Skin Problems

Considering all respondents, they reported that they could consider replacing the in-person consultation with telemedicine for minor skin problems (patients: 353/512, 68.9%; dermatologists: 37/45, 82.2%; and health care workers: 89/107, 83.2%), but not for severe (patients: 30/512, 5.9%; dermatologists: 4/45, 8.9%; and health care workers: 7/107, 6.5%), acute (patients: 122/512, 23.8%; dermatologists: 22/45, 48.9%; and health care workers: 39/107, 36.4%), and chronic skin problems (patients: 120/512, 23.4%; dermatologists: 19/45, 42.2%; and health care workers: 37/107, 34.6%; Q-A #19, Q-B #11, Table 3).

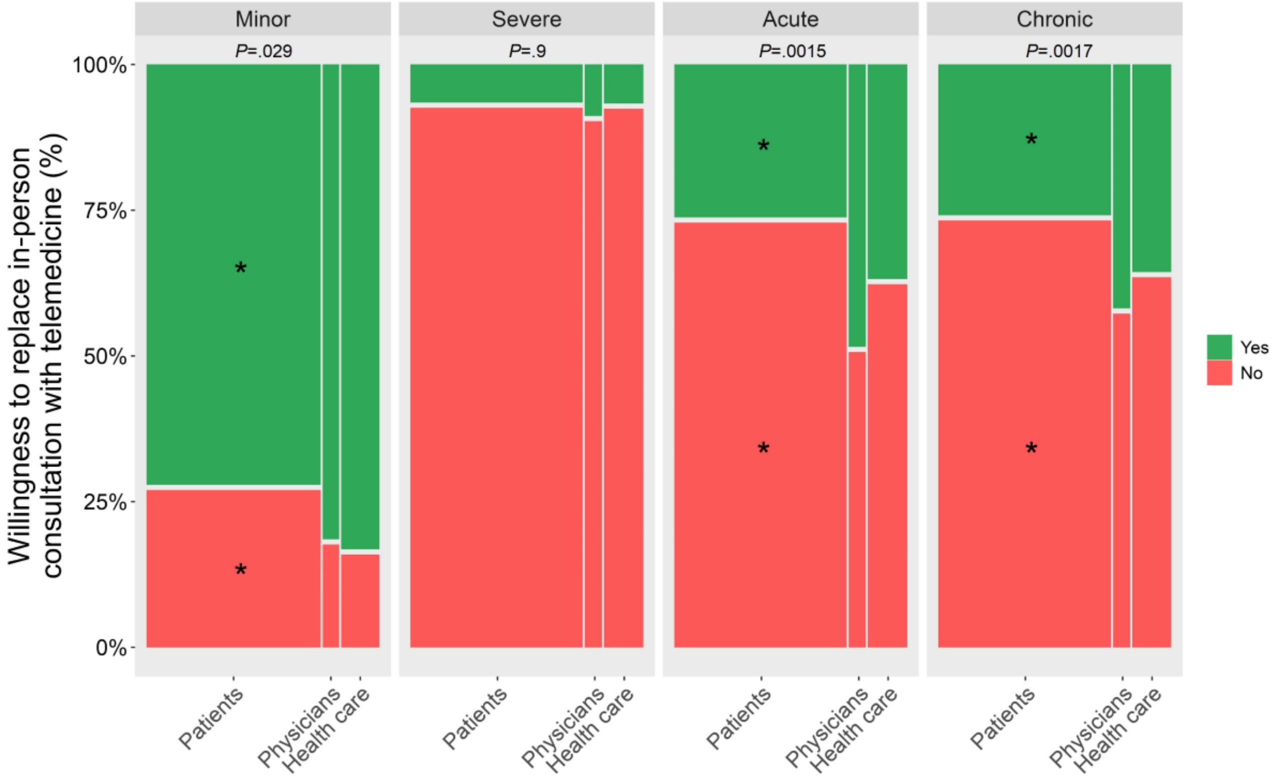
We observed differences across cohorts in the responses when individuals were asked if they could consider replacing in-person consultation with telemedicine for minor (χ^2_2=7.09; P=.04), acute (χ^2_2=12.95; P=.008), and chronic (χ^2_2=8.12; P=.03) skin problems, but not for severe skin problems. Nonresponses (not applicable or did not answer) have not been included in statistical tests (Q-A #19, Q-B #11, Table 3, Figure 1). Post hoc analyses revealed a lower presumed willingness to replace in-person consultation with telemedicine for minor and chronic skin problems among patients compared to other cohorts. Furthermore, post hoc analyses also revealed a higher presumed willingness to replace in-person consultation with telemedicine for acute skin problems among physicians compared to other cohorts.

Table 3. Presumed willingness to replace in-person consultation with telemedicine across cohorts for different severities and acuities of skin problems. Nonresponses were excluded from statistical tests.

Severity and acuity of skin problem and willingness to replace in-person consultations with telemedicine	Patients (n=512), n (%)	Dermatologists (n=45), n (%)	Health care workers (n=107), n (%)	*P* value
Minor problem				.04
No	132 (25.8)	8 (17.8)	17 (15.9)	
Yes	353 (68.9)	37 (82.2)	89 (83.2)	
N/A[a]	27 (5.3)	0 (0)	1 (0.9)	
Severe problem				.90
No	427 (83.4)	41 (91.1)	97 (90.7)	
Yes	30 (5.9)	4 (8.9)	7 (6.5)	
N/A	55 (10.7)	0 (0)	3 (2.8)	
Acute problem				.008
No	339 (66.2)	23 (51.1)	66 (61.7)	
Yes	122 (23.8)	22 (48.9)	39 (36.4)	
N/A	51 (10.0)	0 (0)	2 (1.9)	
Chronic problem				.03
No	340 (66.4)	26 (57.8)	66 (61.7)	
Yes	120 (23.4)	19 (42.2)	37 (34.6)	
N/A	52 (10.2)	0 (0)	4 (3.7)	

[a]N/A: not applicable or did not answer.

Figure 1. Presumed willingness to replace in-person consultation with telemedicine across cohorts for different severities and acuities of skin problem. Green and red areas represent the presumed willingness to replace in-person consultation with telemedicine ("yes") or not ("no"), respectively. *P* values for the chi-square tests are given on top of the plots. * Asterisks represent significant pairwise comparisons in post-hoc analyses (*P*<.05) following chi-square tests, corrected for multiple comparisons using the false discovery rate (FDR) method.



Preference for Telemedicine or In-Person Consultation

Considering all respondents (ie, including individuals with no previous experience with telemedicine), the reported preference as a patient for telemedicine or in-person consultation (Q-A #17, Q-B #10) across skin problems and several individual characteristics for all cohorts is shown in Table S2 in Multimedia Appendix 3.

Analyzing the cohorts separately, we observed differences in preference for telemedicine or in-person consultation (or no preference) with patient age (Q-A #0.1; *P*=.01) and physician age (Q-B #0.1; *P*=.02) (Table S2 in Multimedia Appendix 3, Figure 2). Post hoc analysis showed that the age of those who reported preferring in-person consultation was higher than the age of those who reported no preference, with no difference between in-person consultation and telemedicine. In addition, we observed that patients' preferences for telemedicine or in-person consultation were different across education levels (χ^2=24.6; *P*<.001; Q-A #0.5, Figure 3). Post hoc analysis indicated a higher preference for telemedicine in patients with university degrees compared to other levels of education.

Figure 2. Preference for telemedicine or consultation across patients' age. Patients' preference for in-person consultation is associated with higher age compared to individuals who reported no preference, with no difference in the preference between in-person consultation and telemedicine. The asterisk represents a significant difference following posthoc analysis, corrected for multiple comparisons using the false discovery rate (FDR) method.

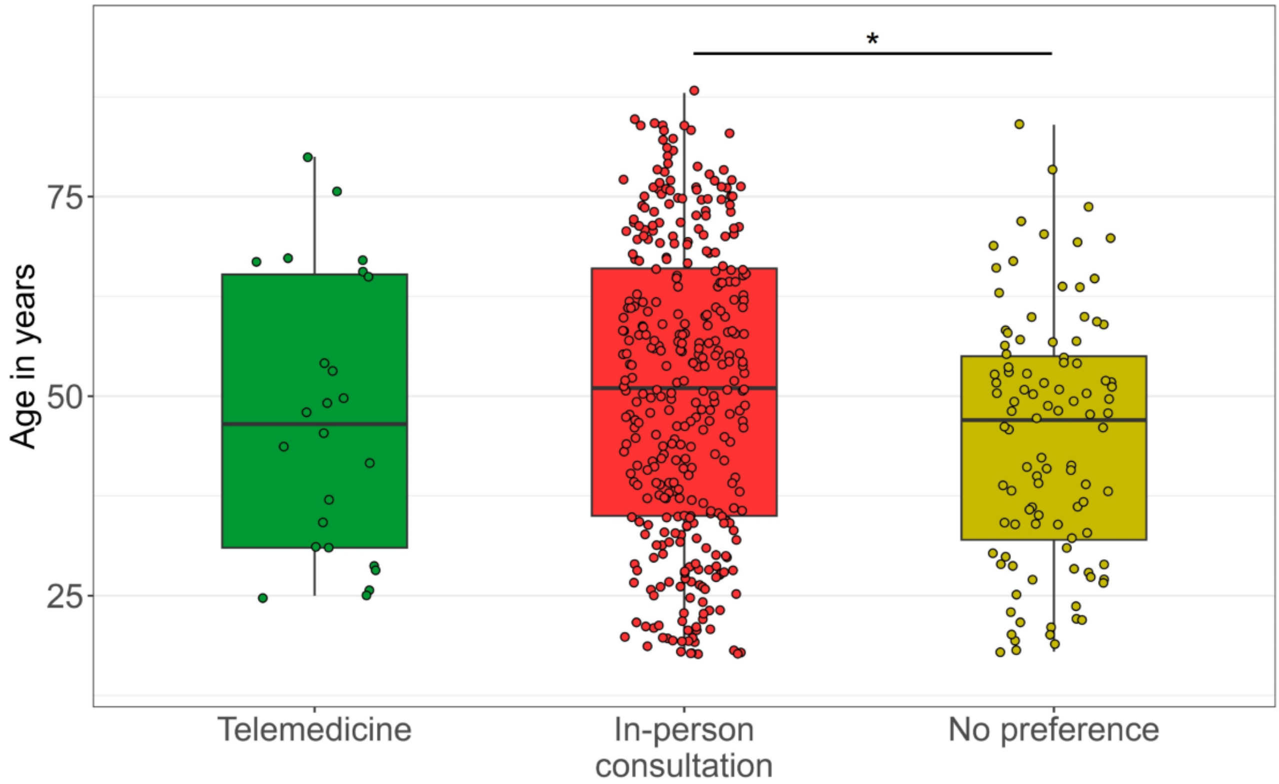
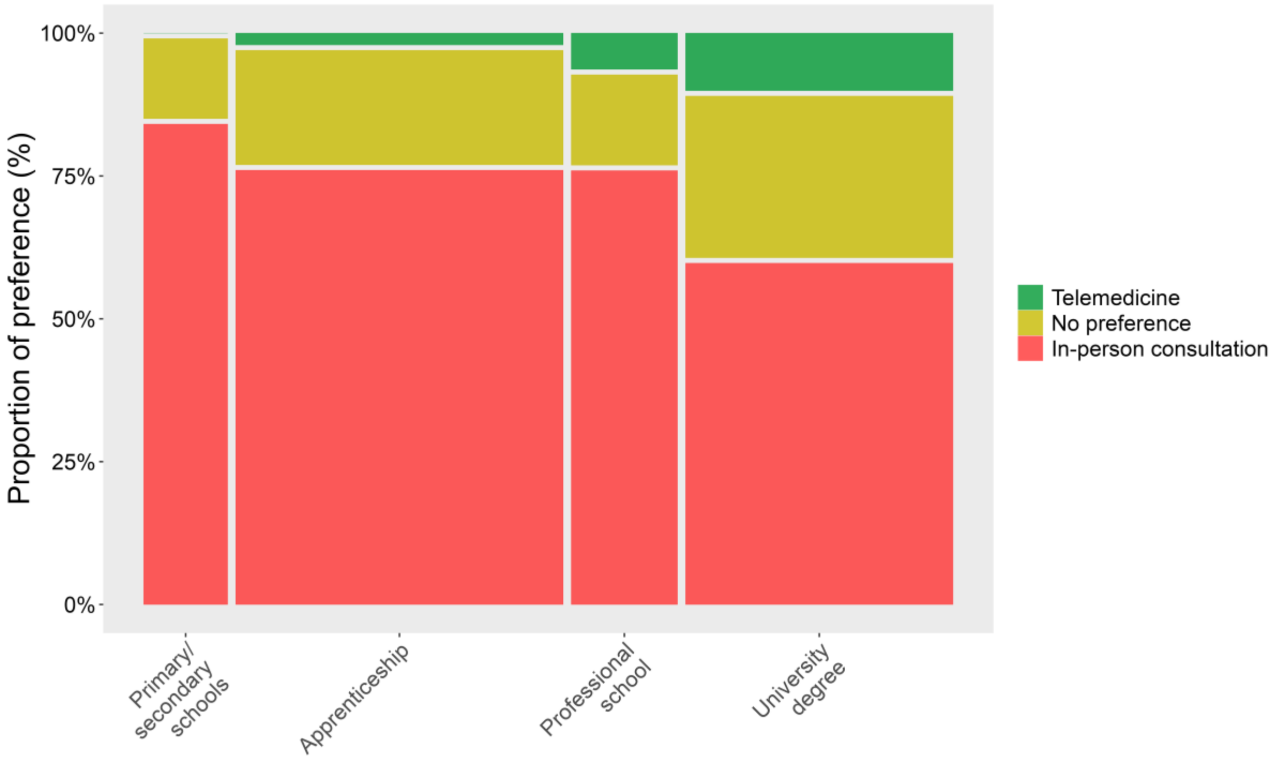
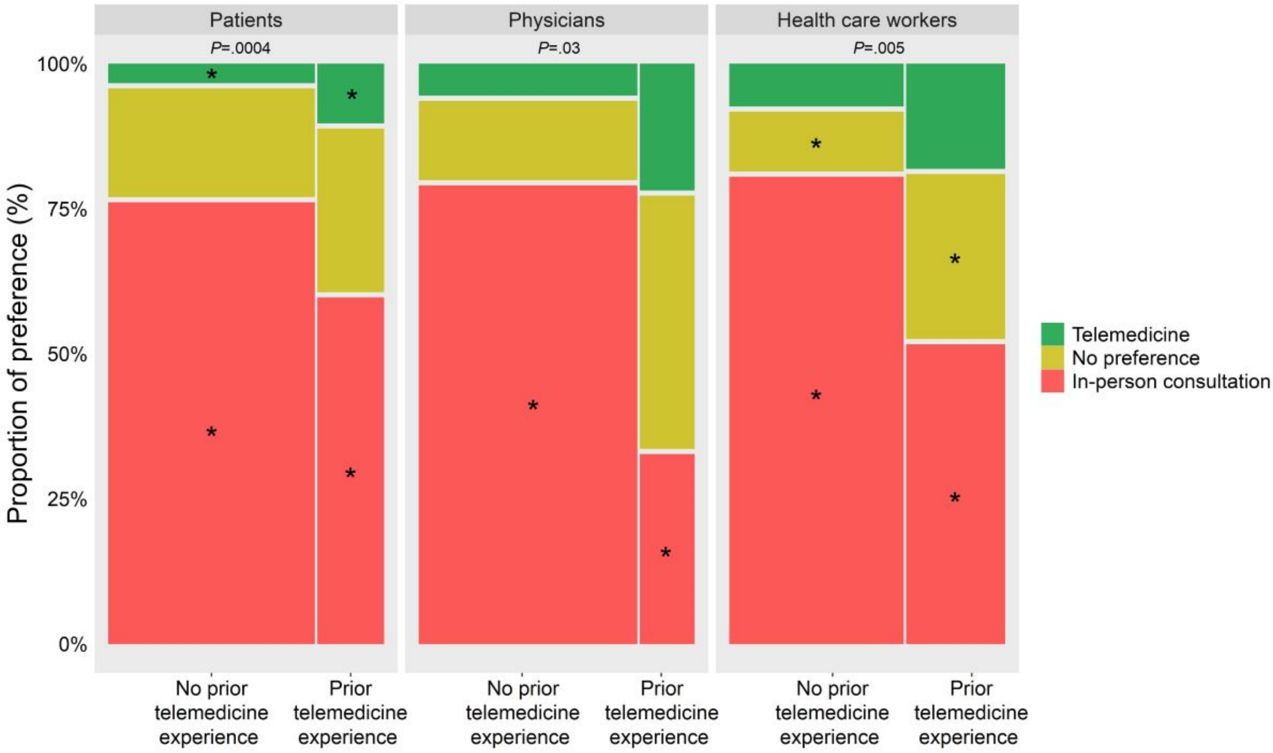


Figure 3. Association between patients' highest education level achieved and preference for telemedicine or in-person consultation: higher preference for telemedicine among patients with university degree. Asterisks represent significant pairwise comparisons following posthoc analysis, corrected for multiple comparisons using the false discovery rate (FDR) method.



Furthermore, we observed that the preference of patients (χ^2_2=15.6; *P*<.001), dermatologists (χ^2_2=7.87; *P*=.03), and health care workers (χ^2=10.3; *P*=.005) for telemedicine depended on their previous telemedicine experience (Q-A #12a, Q-B #5, Figure 4). Post hoc analyses indicated that, with previous telemedicine experience, there is a higher preference for telemedicine and lower preference for in-person consultation among patients; a higher preference for in-person consultation among physicians; and a higher reporting of no preference and lower preference for in-person consultation among health care workers. We observed no other differences in preference for telemedicine for the other considered individual characteristics, for either the cohorts analyzed separately (Table S2 in Multimedia Appendix 3) or for patients currently using telemedicine (Table S3 in Multimedia Appendix 3).

Figure 4. Higher preference for telemedicine over in-person consultation depended on previous telemedicine experience of patients, physicians, and health care workers. *P* values for chi-square tests are shown on top of the plots. Asterisks represent significant pairwise comparisons in posthoc analyses, corrected for multiple comparisons using the false discovery rate (FDR) method.



Discussion

Overview

Understanding the population's current attitudes toward telemedicine is highly relevant to optimizing the transition to teledermatology. We found that individuals who have previously used telemedicine reported a high level of overall experience with it. Patients, health care workers, and physicians reported that they would consider replacing in-person consultations with telemedicine for minor health issues. We observed a higher preference for telemedicine among patients with higher levels of education and among individuals who had previous experience with telemedicine.

Overall Experience With Telemedicine Consultation

This study revealed high overall experience among all individuals with their use of telemedicine (between 68.9% and 79.4%), which is consistent with previous studies [35-37]. However, satisfaction with telemedicine is controversial. In a comparative study with 121 patients, only 44% of them reported satisfaction with telemedicine, while 10% of them reported dissatisfaction [38]. Despite the relevance of better understanding the perspectives of medical staff and nonmedical staff, this study is the first to examine the physicians and health care workers' level of overall experience with telemedicine from their perspective as patients, to the best of our knowledge.

The COVID-19 pandemic has triggered a new era in telemedicine with an immense increase in applications within various medical fields [39,40], as telemedicine has minimized the hazard of direct exposure to individuals during the pandemic. A Brazilian study identified that the posture toward telemedicine of physicians as providers was positively influenced and significantly increased from 18.5% before the pandemic to 63.6% during the COVID-19 period [41]. Furthermore, over 70% of patients at New York University Langone Health reported being satisfied with live-interactive teledermatology during the pandemic in 2020 [42]. Our findings indicate that the overall experience with telemedicine in the Swiss-German population was already comparably high before the pandemic. We further postulate that our findings on the level of overall experience should now be even higher than reported here, as pandemic conditions have further strengthened telemedicine services.

Presumed Willingness to Replace In-Person Consultation With Telemedicine for Different Acuities and Severities of Skin Problems

In the context of teledermatology, we found that the presumed willingness to replace in-person consultation with telemedicine depends on the severity and acuity of the skin problem. Most patients, physicians, and health care workers favored replacement for minor skin problems. We observed that, among the cohorts analyzed, the highest level of acceptance for telemedicine for acute and chronic skin problems was among physicians. Most participants would not consider replacing in-person consultations with telemedicine for severe skin issues.

Previous studies have suggested that in-person consultations cannot generally be replaced by telemedicine [43,44]. The identification of the most suitable indications for telehealth versus traditional consultations is crucial for maintaining patients' safety and satisfaction. The COVID-19 pandemic has transformed the health care system through a sudden expansion of telemedicine for nonurgent and urgent care [40]. Data from the pandemic period showed an increase of 683% in teledermatology usage in the United States, particularly for urgent care [45]. Even during the pandemic, the patients preferred in-person consultations over telemedicine for severe conditions [45], which is consistent with our pre–COVID-19 findings.

On the other hand, a systematic review indicated that, for particular situations, telemedicine can adequately replace in-person consultation [46]. The willingness to use telemedicine after the pandemic was reported by many studies [46]. One study reported that only a minority of patients (36%) consider that telemedicine is not appropriate to replace in-person consultations [47]. We suggest that teledermatology services should take into account the acuity and severity of skin problems in the future and thereby focus on the diagnoses best handled with telemedicine.

Preference for Telemedicine or In-Person Consultation

Our data indicate that patients, physicians, and health care workers with experience in telemedicine and patients with a higher educational level showed a higher preference for telemedicine. As expected, older patients and physicians favored in-person consultations.

Our findings imply that one of the main problems telemedicine is facing is trust among new patients. We observed that a first experience with telemedicine influences one's attitude toward it positively. As we detected that there is somehow a barrier to the first use of telemedicine, some acclimatization needs to occur [48]. In a previous study with 184 teledermatology patients, telemedicine experience was also associated with a higher odds ratio of preferring teledermatology in the future [49]. Also, during the COVID-19 pandemic, first-time teledermatology patients in the United States reported being less satisfied with telemedicine communication [36].

Furthermore, we also observed that a high preference for telemedicine was associated with a higher educational level. We suggest that the finding is related to the increased attitude of highly educated individuals to inform themselves about new technologies and to have sufficient technical skills [50].

This study indicates that older patients and physicians prefer in-person consultations over telemedicine. An American study with >600 participants reported that patients older than 66 years of age preferred in-person consultation and follow-up during the COVID-19 pandemic [42]. In fact, another study indicated higher satisfaction rates with telemedicine among patients younger than 56 years of age and without suspected cancer [51]. While studies focusing only on teledermatology generally report higher levels of satisfaction, direct comparative studies of in-person consultations and telemedicine report mixed outcomes [26,51-56]. Consistent with our findings, a questionnaire-based survey among 720 patients in Saudi Arabia during the COVID-19 pandemic showed that older age (over 40 years), lower education levels, and first-time experience were associated with poor-to-average satisfaction with telemedicine [57].

We identified factors associated with a lower preference for teledermatology: older age, lower education, and no experience with telemedicine. As teledermatology becomes more prominent, these cohorts may develop disparities in care. Therefore, we propose that the following steps should be considered to increase acceptance of teledermatology: minimization of technical barriers by simple handling of the telemedical offers as well as increasing the attractiveness of the first telemedicine consultation through reduced waiting time and cost savings.

Despite technological improvements, such as increased access to mobile phones and high-resolution screening, the latest studies about satisfaction with teledermatology revealed that patients and dermatologists still prefer in-person examinations [51,58]. We speculate that this reluctance to use telemedicine may be related to accessibility skills and previous knowledge about telemedicine. Future assessments could be designed to guide us in handling teledermatology as a screening tool.

The era of telemedicine has also opened new horizons for rapid digital professional exchange of expertise between physicians of different specialties and the ability to obtain a second opinion [13,59,60]. Tele-expertise is cost-effective as patients can reduce doctor -patient contact with a specialist [61]. Remote areas and the pandemic have taught us that tele-expertise alongside teledermatology is of high importance because access to primary care is limited, especially in these scenarios [62]. Future studies focusing on the challenges, integration, and quality of tele-expertise in relation to telemedicine are needed.

Limitations

This study has some limitations. First, there was a low number of dermatologists and health care workers since we predefined the centers. This is also the reason why sample size was not beforehand determined, but we aimed to maximize the sampling given our time and site predefinitions. While this study might be minimally representative of the dermatologists' perspective in German-speaking Switzerland working at massive health care centers, it may be difficult to generalize the findings to a larger population of medical professionals. We suggest that data for dermatologists should be viewed with caution when interpreting the emerging patterns. Second, our findings may not be generalizable outside of Switzerland. However, as our results were consistent with related literature, we speculate that it is likely that our findings can be reproduced in similar cultures. Third, the results might have been influenced by confounders, such as dermatologists being mostly women and living in large cities. Thus, we cannot really conclude if the differences are due to their gender, profession, and place of residence. Further research assessing the acceptance of teledermatology in a larger study population, especially also in countries with a geographically challenging health care situation and including the distinction between live-interactive and store-and-forward applications will help to better understand the impending value of telemedicine. Due to a lack of usage of nonvalidated scales to measure the variables, our results' value might be less important in scientific research but has a higher impact on clinical daily routines and health policy makers.

Conclusions

This study indicates that acceptance and preference for teledermatology have a high potential to increase over time as they depend on experience with telemedicine. Acclimatization is needed for new users and providers. We assume that minor skin problems are the most promising field for teledermatology, and thus we suggest focusing on them for further development. This study indicated that within the 3 target groups, 65.4% to 80% of individuals were overchallenged with the question of whether their insurance covers telemedicine services. This finding provides a relevant insight for health policy makers and health insurance managers. The reimbursement of telemedicine services is not yet regulated evenly within countries and globally which reflects the ongoing debate of its acceptance. There is a high need to expand telemedicine and teledermatology in order to provide access to medicine and care for patients globally. We provide new insights into the telemedicine situation in German-speaking Switzerland and emphasize the need for dermatologists to be actively involved in the transition to teledermatology. Future studies integrating well-established models such as UTAUT2 are required to focus on an in-depth view of the different target groups after the outbreak of the pandemic.

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Authors' Contributions

LVM (lead) and JTM (supporting) are responsible for the conceptualization of this study. LVM (lead), ASJ, MS, LG, SM, RB, CG, AAN, and JTM (all supporting) played a role in the data curation. GSPP (lead), MLN, LVM and JTM (supporting) undertook the formal analysis. LVM (lead), ASJ, MS, LG, SM, RB, CG, AAN, JTM (all supporting) carried out the investigation. LVM (lead), LG and JTM (supporting) participated in methodology. LVM (lead) is responsible for project administration. LVM and JTM played an equal role in the supervision of this study. GSPP (lead), LVM and JTM (supporting) carried out the visualization. LVM (lead), GSPP and JTM (supporting) participated in writing the original draft. LVM, ASJ, GSPP, MS, LG, SM, RB, MLN, CG, AAN, and JTM (all equal) carried out the writing, review, and editing of this manuscript. All authors have contributed and approved the published version of the manuscript.

Conflicts of Interest

CG is founder of the teledermatology platform derma2go. AAN holds shares in the teledermatology company Derma2Go. LVM has served as advisor and received speaking fees and participated in clinical trials sponsored by Almirall, Amgen, BMS, Celgene, Eli Lilly, MSD, Novartis, Pierre Fabre, Roche, and Sanofi. AAN declares being a consultant and advisor and receiving speaking fees and grants and served as an investigator in clinical trials for AbbVie, Almirall, Amgen, Biomed, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, GSK, LEO Pharma, Janssen-Cilag, MSD, Novartis, Pfizer, Pierre Fabre Pharma, Regeneron, Sandoz, Sanofi, and UCB. JTM is and has served as advisor and received speaking fees and participated in clinical trials sponsored by AbbVie, Almirall, Amgen, BMS, Celgene, Eli Lilly, LEO Pharma, Janssen-Cilag, MSD, Novartis, Pfizer, Pierre Fabre, Roche, Sanofi, and UCB. ASJ, GSPP, MS, LG, SM, RB, and MLN have no conflicts of interest to declare.

Multimedia Appendix 1
Supplementary Figure 1: Questionnaire about telemedicine for patients in dermatology (Q-A).
[DOCX File , 40 KB - derma_v6i1e45384_app1.docx]

Multimedia Appendix 2
Supplementary Figure 2: Questionnaire about telemedicine for healthcare workers in dermatology and dermatologists (Q-B).
[DOCX File , 35 KB - derma_v6i1e45384_app2.docx]

Multimedia Appendix 3
Supplemantary Tables: (Tables S1-3).
[DOCX File , 50 KB - derma_v6i1e45384_app3.docx]

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Abbreviations

FDR: false discovery rate
TAM: technology acceptance model
UTAUT: unified theory of acceptance and use of technologies
VAS: visual analogue scale

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Viewpoint

The Importance of Gender-Neutral Terminology in Risk Evaluation and Mitigation Strategy Programs: A Call to Action

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Abstract

The use of risk evaluation and mitigation strategy (REMS) programs is frequently required for prescriptions with potentially teratogenic effects, especially in the field of dermatology. Among these REMS programs, the most well-known example is isotretinoin, an oral retinoid that uses the iPLEDGE system. iPLEDGE has strict regulations and a lengthy approval process, and until recently, patients were grouped into 3 categories: male, female, or female of reproductive potential. This strict grouping has posed problems in the medical community, especially for gender-diverse individuals where their perceived gender conflates with their assigned grouping causing patient-specific distress. The distinction between gender—a multifactorial perception of identity—and biological sex is addressed under new iPLEDGE guidelines. Dermatologists now register patients under one of 2 categories: patients who can become pregnant and those who cannot become pregnant. This change simultaneously improves the accessibility to isotretinoin among gender-diverse individuals, while limiting prescription barriers. Despite initial success being limited due to lengthy system conversions, a registration process based on reproductive potential ultimately enhances iPLEDGE's goal to prevent potential birth defects. We propose that other REMS programs follow the standard set by the iPLEDGE system, including those for the medications thalidomide, acitretin, and mycophenolate mofetil, all of which currently have a similar taxonomy to that of the old iPLEDGE system. Implementing the standardization of gender-neutral terminology can maximize enrollment and minimize distress. Current and ongoing refinement of iPLEDGE and other REMS is needed to build protocols solely around the prevention of birth defects without regard to sex or gender.

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KEYWORDS

iPLEDGE; REMS; evaluation and mitigation strategy; gender dysmorphia; transgender patients; call to action; oral retinoid; medical community; gender; identity; biological sex; accessibility; barrier; gender diversity; quality of care; treatment

Introduction

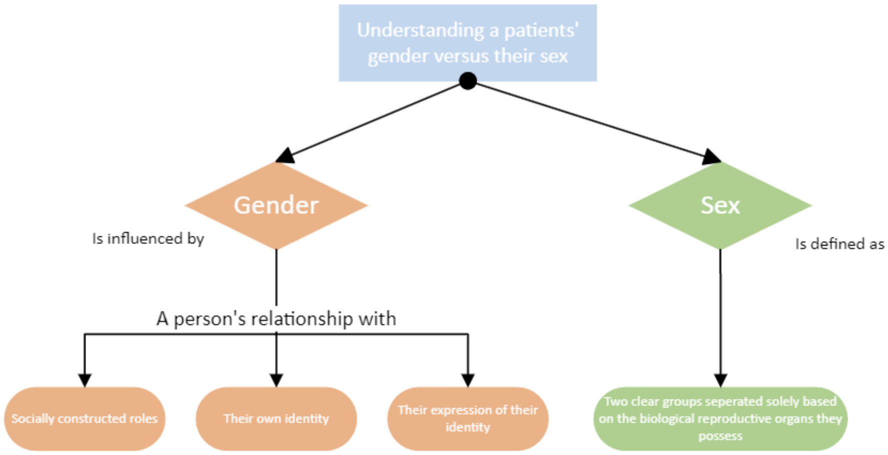
Risk evaluation and mitigation strategy (REMS) programs in dermatology should clarify how they define gender and biological sex to appropriately focus on patients' reproductive potential and risk for birth defects (Table 1). Specifically, REMS programs should adopt proper gender-neutral terminology. While several teratogenic prescriptions are monitored by REMS programs, isotretinoin, an oral retinoid used for acne treatment is likely the most well-known. Regulated by iPLEDGE, isotretinoin prescription originally required patients to register under one of 3 categories: male, female, or female of reproductive potential [1]. This classification system posed problems as providers were required to categorize patients of gender-diverse backgrounds into limited categories. For example, transgender males with intact uteruses and ovaries might have been categorized as females of reproductive potential. In some cases, patients have forgone treatment because improper categorization conflicted with their gender identity [2].

Medical care providers may conflate gender and biological sex. Growing awareness and inadequate terminology for transgender patients have led to changes. In December 2021, the Food and Drug Administration streamlined the iPLEDGE process and introduced gender-neutral terminology, allowing for the separation of a patient's biological sex from their gender identity (Figure 1). Dermatologists now register patients under one of 2 categories: patients who can become pregnant and those who cannot become pregnant [3,4]. This change may improve access to isotretinoin for transgender candidates such as transmasculine patients with an increased predisposition for acne secondary to exogenous testosterone therapy [5]. A registration process based on reproductive potential ultimately enhances iPLEDGE's goal to prevent potential birth defects.

Table 1. Definitions of key terms.

Keyword	Definition
Gender	Socially constructed characteristics of women, men, girls, and boys, which define their identity
Sex	A set of biological attributes in humans and animals
Gender incongruence	Gender identity that is different from a person's biological sex
Gender-diverse	Gender identity that demonstrates a diversity of expression beyond the binary framework
Transgender	Denoting or relating to a person whose gender identity does not correspond with the sex registered to them at birth
Transmasculine	A person who was registered as female at birth but whose gender identity is characterized or aligned with masculinity
Transfeminine	A person who was registered as male at birth but whose gender identity is characterized or aligned with femininity
Female of reproductive potential	A person who is capable of giving birth to offspring

Figure 1. Flowchart breaking down the differences between gender and identity.



Conclusions

Though recent changes to iPLEDGE do not resolve population-specific concerns faced by gender-diverse individuals, it is nonetheless a pivotal step in transgender patient care—an additional step that other REMS programs have yet to adopt. Prescription medications including thalidomide, acitretin, and mycophenolate mofetil still use a similar taxonomy to the old iPLEDGE system, with patient groupings of male, female, or female of reproductive potential [6,7]. Nevertheless, overall prescription prevalence and increasing associations of skin disease with exogenous hormone therapy indicate a potential area for the use of updated REMS terminology [8]. Future standardization of gender-neutral terminology can maximize patient enrollment, minimize distress, and prevent teratogen exposure. The revision of iPLEDGE categories with gender-neutral terminology reveals continued inadequacies; ongoing effort is needed to build REMS protocols solely around the prevention of birth defects, without regard to sex or gender.

Conflicts of Interest

RD is the editor-in-chief of *JMIR Dermatology* but had no role in the selection of this paper for publication. TES is an editorial board member-at-large of *JMIR Dermatology* but did not participate in the review or editorial oversight of this paper. DS is a social media editor for *JMIR Dermatology*.

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Abbreviations

REMS: risk evaluation and mitigation strategy

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Original Paper

Psychodermatological Disorders in Patients With Primary Psychiatric Conditions: Cross-Sectional Study

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Abstract

Background: Psychodermatological disorders (PDs) and their associations with mental health problems are one of the most frequent research themes in dermatology outpatient settings. Surprisingly, very few studies have been conducted to evaluate PDs among patients with primary psychiatric conditions. As such, the relationship between preexisting psychiatric conditions and comorbid PDs is underrepresented in the literature.

Objective: This study examined the prevalence and distribution of PDs among adults with primary psychiatric conditions and determined their association with underlying psychiatric diagnoses.

Methods: We conducted a cross-sectional analysis at a tertiary health care facility in southwestern Nigeria. Comorbid PDs were identified and classified using preexisting classification systems. A bivariate analysis was conducted to determine the association between PDs and underlying psychiatric conditions. The level of statistical significance was set at $P<.05$.

Results: The study included 107 patients with mental health disorders, of whom 64 (59.8%) were female. The mean age of the patients was 40.73 (SD 13.08) years. A total of 75 (75/107, 70%) patients had at least one comorbid PD. The prevalence of PDs was highest in patients with affective disorders (15/20, 75%) and least in those with schizophrenia (45/66, 68%). PDs associated with delusions or hallucinations and somatoform symptoms were 9 and 13 times more frequent in patients with anxiety disorders compared to those with other psychiatric conditions (P=.01; odds ratio [OR] 9.88, 95% CI 1.67-58.34 and P=.003; OR 13.13, 95% CI 2.34-73.65), respectively. In contrast, patients with schizophrenia were significantly less likely to be diagnosed with dermatoses resulting from delusions or hallucinations (P=.002; OR 0.04, 95% CI 0.00-0.75). A weak but significant negative association was also found between psychophysiological PDs and anxiety disorders (φ=–0.236; P=.02).

Conclusions: This study provides important insights into the overwhelming burden of psychodermatological conditions in patients with mental health disorders and specific associations with underlying psychiatric diagnosis.

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KEYWORDS

affective disorders; anxiety, stress-related, and somatoform disorders; primary dermatological disorders with psychiatric co-morbidity; primary psychiatric disorders with dermatologic manifestations; primary psychiatric psychodermatoses; psychocutaneous disorders; psychophysiological disorders; schizophrenia

Introduction

Psychodermatological disorders (PDs) are a heterogeneous group of skin conditions that are significantly associated with mental disorders. Dermatoses that fall into this category often have a significant negative impact on mental health or may also run a clinical course that is determined by the primary psychiatric or psychological disorder. On one hand, skin conditions can precipitate serious psychiatric illness in individuals without preexisting mental health problems [1,2], while on the other hand, primary psychiatric conditions such as trichotillomania present primarily with skin complaints. In the latter scenario, the skin conditions may be the sole manifestation of the underlying psychiatric conditions, and the patient may present first to the dermatologist. Very often, however, the relationship between skin conditions and mental health is bidirectional, complex, and incompletely understood [1,3,4]. A vicious cycle in which psychological factors trigger or aggravate skin conditions and the exacerbated dermatoses induce further psychological problems is a characteristic finding of typical PDs.

Many studies have shown that the burden of psychological and psychiatric problems among patients with dermatological conditions is high and that there are significant relationships between anxiety, depression, and various PDs that have a serious impact on therapeutic results [5-9]. While the majority of research has focused on determining the link between primary skin conditions and the psychiatric or psychological factors that exacerbate or complicate them, very few studies have examined the connection between preexisting psychiatric conditions and comorbid PDs [10,11]. Consequently, existing data on PDs frequently demonstrate a bias toward primary dermatological disorders with psychiatric comorbidities (PDDPCs), while other PDs are underrepresented and their relationships with major psychiatric conditions are underresearched.

The aim of this study was to explore psychodermatological conditions among a sample of patients with mental health disorders receiving care at a mental health clinic in southwestern Nigeria. The specific objectives were to (1) determine the prevalence and pattern of PDs in patients with primary psychiatric conditions and (2) determine the sociodemographic and illness-related factors that are associated with PDs among the study population.

Methods

Overview

This was a cross-sectional hospital-based study conducted among patients with primary psychiatric conditions receiving care at the outpatient mental health clinics of the Obafemi Awolowo University Teaching Hospitals Complex in southwestern Nigeria.

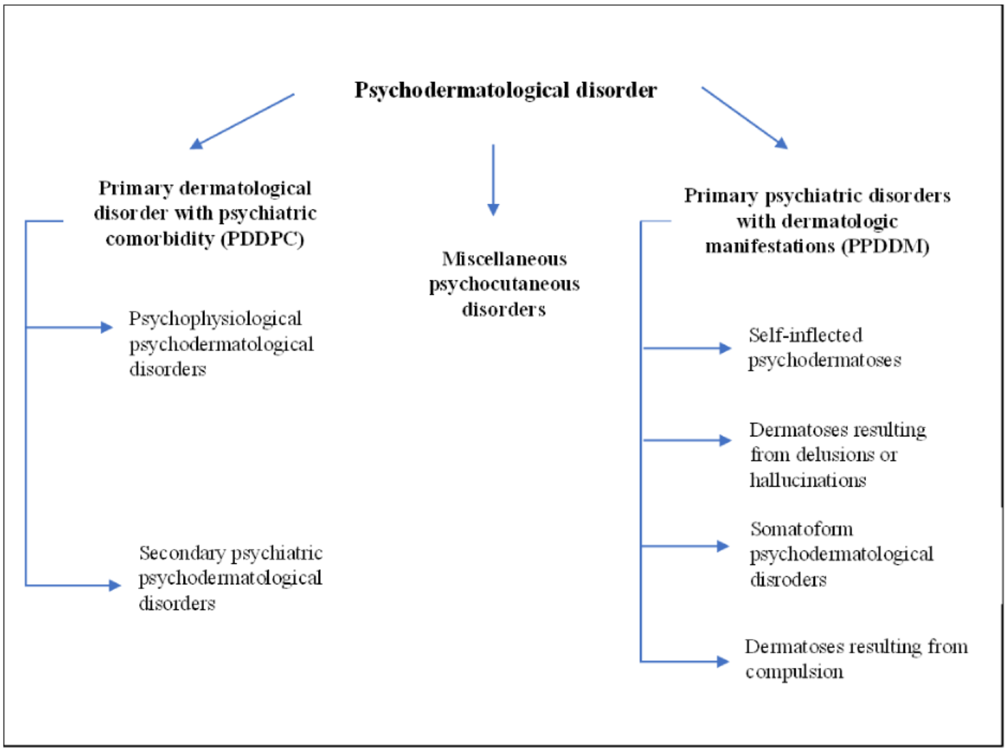
Recruitment and Data Collection

Adults with primary psychiatric conditions diagnosed using Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria by an experienced psychiatrist were recruited consecutively between January and April 2017. Psychiatric diagnoses were categorized into three main groups, as follows: (1) the affective disorders group, comprising patients with major depressive disorders, those with bipolar affective disorders, and those with manic episodes; (2) the anxiety and somatoform disorder group, comprising patients diagnosed with generalized anxiety disorders, those with unspecified anxiety disorders, those with social anxiety disorders, and those with somatoform disorders; and (3) the schizophrenia group, under which patients with either schizophrenia or schizotypal disorders were grouped.

Skin conditions were classified as either psychodermatological or nonpsychodermatological. Psychodermatological conditions, which comprised dermatoses that have significant associations with mental health, were further separated into 3 main categories guided by underlying pathophysiologic mechanisms and preexisting classification systems [12-16]. These include PDDPCs, primary psychiatric disorders with dermatologic manifestations (PPDDM), and miscellaneous PDs [12-15]. The classification system proposed by Koo and Lee [17] was adapted to further classify the PDDPCs into psychophysiological and secondary psychiatric PDs, while miscellaneous disorders comprised dermatoses caused by psychotropic medications or substance use disorders [2,15,17,18]. Figure 1 outlines the algorithm for the classification of PD in this study.

All the study participants gave both written and verbal informed consent before being recruited into the study. Patients with mental health disorders with chronic debilitating systemic conditions such as uncontrolled diabetes mellitus, chronic renal disease, advanced heart failure, retroviral disease, and malignancies were excluded from the study. Unstable mental health state and pregnancy were additional exclusion criteria.

Figure 1. Algorithm for the classification of psychodermatological disorders.



Sociodemographic and Clinical Characteristics of the Study Population

A data pro forma administered by the researchers was used to document relevant information, including sociodemographic, medical, and drug history, from all the participants. Information regarding the underlying mental health diagnosis and treatment was obtained from the patients' medical records. A whole-body clinical examination for skin conditions was performed on all the recruited participants, and clinical findings were documented in the data pro forma. The diagnosis of skin conditions was mostly clinical. To support or confirm the clinical diagnosis, investigations such as skin scraping for fungal studies, woods lamp examination, and skin biopsy for histology were performed when needed.

Prevalence of PDs and Association With Psychiatric Conditions

The participants were categorized into 3 groups based on their psychiatric diagnosis: schizophrenia; affective disorders; and anxiety, stress-related, and somatoform disorders. Psychodermatological dermatoses were noted for each patient within their respective diagnostic groups to determine prevalence, and comparisons were made between groups using appropriate statistical tests of association.

Data Analysis

Data entry and analysis were performed using SPSS software (version 21; IBM Corp). A univariate analysis was performed to summarize the demographic characteristics of the participants. Categorical variables of interest were recoded as dichotomous variables (with exception of level of education) and analyzed using bivariate statistical tests. The Fisher exact test and likelihood ratio were used in place of the chi-square test in cases where the chi-square assumption was violated. Symmetry and measure of association between the variables were performed using phi and odds ratio, respectively. The level of statistical significance was set at .05.

Ethical Considerations

This study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics and Research Committee of the Obafemi Awolowo University Teaching Hospitals Complex (national and international registration numbers NHREC/27/02/2009a and IRC/IEC/00045553, respectively) before the commencement of the study.

Results

Sociodemographic and Clinical Characteristics of the Study Population

A total of 107 patients with mental health disorders participated in the study. The major categories of psychiatric diagnosis in the study population were schizophrenia (66/107, 61.7%), anxiety and related disorders (21/107, 19.6%), and affective disorders (20/107, 18.7%). Comorbid substance use disorders were diagnosed in 13 (12.1%) participants and were most prevalent in patients with affective disorders. Females outnumbered males by a ratio of 1.49:1. These are presented in Table 1.

There was no significant age or gender disparity among the various categories of psychiatric conditions. However, patients with schizophrenia were significantly less well-educated compared with other groups of psychiatric conditions (P=.04). Patients with schizophrenia were also significantly more likely to be treated with antipsychotic drugs compared to those with affective disorders, anxiety disorders, or somatoform disorders.

Table 1. Comparison of sociodemographic variables and clinical characteristics of the different groups of psychiatric conditions.

Demographics	Schizophrenia (n=66)	Affective disorders (n=20)	Anxiety, stress-related, and somatoform disorders (n=21)	*P* value
Age (years), mean (SD)	39.52 (11.62)	39.3 (13.74)	45.91 (15.9)	.13
Sex, n (%)				.32
Female	42 (64)	9 (45)	13 (62)	
Male	24 (36)	11 (55)	8 (38)	
Marital status, n (%)				.005
Single	37 (56)	11 (55)	5 (24)	
Married	18 (27)	9 (45)	13 (62)	
Separated, divorced, and widowed	11 (17)	—[a]	3 (14)	
Education, n (%)				.04
No formal education	3 (4)	—	—	
Primary	9 (14)	5 (25)	4 (19)	
Secondary	32 (48)	3 (15)	6 (29)	
Tertiary	22 (33)	12 (60)	11 (52)	
Comorbid substance use disorder, n (%)				.87
No	58 (88)	17 (85)	19 (90)	
Yes	8 (12)	3 (15)	2 (10)	
Type of treatment, n (%)				<.001
Nonpharmacological	1 (2)	5 (25)	11 (52)	
Antipsychotics	65 (98)	15 (75)	10 (48)	
Dermatological disorder, n (%)				
Psychodermatological disorder	45 (68)	15 (75)	15 (71)	.83
Reported or sought treatment for skin conditions	12 (27)	9 (60)	11 (73)	.002

[a]Not applicable.

Prevalence of PDs and Association With Psychiatric Conditions

The pattern and distribution of PDs are presented in Table 2, while Table 3 shows the association between PDs and primary psychiatric conditions in the study population. A total of 75 (70.1%) out of 107 participants had at least one comorbid PD. Although the proportion of patients with PDDPCs (47/107, 43.9%) exceeded that with PPDDMs (42/107, 39.3%), PPDDMs were the overall most frequently diagnosed group of PDs, accounting for 61 of the 129 (47.3%) different psychodermatological diagnoses in the study population. Neurotic excoriation, followed by psychogenic pruritus and onychophagia, were the 3 most frequent PPDDMs in this study, while delusion of parasitosis (5/107, 4.7%) was among the least frequent.

The total prevalence of PDs did not differ significantly between groups of psychiatric conditions. However, significant associations were found between some psychiatric conditions and comorbid PDs. Compared to patients with either schizophrenia or affective disorders, patients with anxiety disorders were significantly more likely to be diagnosed with PPDDMs resulting from delusions or hallucinations and somatoform disorders (*P*=.01; odds ratio [OR] 9.88, 95% CI 1.67-58.34 and *P*=.003; OR 13.13, 95% CI 2.34-73.65), respectively. They were also significantly less likely to be diagnosed with PDDPCs (OR 0.24, 95% CI 0.07-0.76), particularly psychophysiological dermatoses (OR 0.18, 95% CI 0.04-0.81). On the other hand, patients with schizophrenia demonstrated a moderate negative association with a diagnosis of PPDDMs resulting from delusions or hallucinations (*P*=.002; φ=–0.309). Following binary regression analysis, female sex was the only significant predictor of both PPDDM and PDDPC, while obesity was predictive of PDDPCs (Table S4 in Multimedia Appendix 1).

Table 2. Relative frequency and distribution of psychodermatological disorders (PDs) among patients with psychiatric conditions.

	Schizophrenia (n=45), n (%)	Affective disorder (n=15), n (%)	Anxiety, stress-related, and somatoform disorders (n=15), n (%)	Total (n=75), n (%)
Primary dermatological disorders with psychiatric comorbidities				
Psychophysiological dermatoses				
Seborrheic dermatitis	11 (24)	5 (33)	1 (6)	17 (22)
Acne vulgaris	11 (24)	4 (26)	1 (6)	16 (21)
Atopic dermatitis	0 (0)	1 (6)	0 (0)	1 (1)
Hyperhidrosis	1 (2)	0 (0)	0 (0)	1 (1)
Urticaria	1 (2)	0 (0)	0 (0)	1 (1)
Secondary psychiatric PDs				
Alopecia	9 (20)	2 (13)	1 (6)	12 (16)
Ichthyosis	4 (8)	0 (0)	0 (0)	4 (5)
Vitiligo	2 (4)	1 (6)	1 (6)	4 (5)
Other chronic eczemas	1 (2)	2 (13)	0 (0)	3 (4)
Primary psychiatric disorders with dermatologic manifestations				
Self-inflicted dermatoses				
Neurotic excoriation	11 (24)	2 (13)	4 (26)	17 (22)
Onychophagia	6 (13)	0 (0)	1 (6)	7 (9)
Acne excoriee	1 (2)	0 (0)	1 (6)	2 (2)
Dermatitis artefacta	1 (2)	0 (0)	0 (0)	1 (1)
Disorders resulting from delusions or hallucinations				
Delusion of parasitosis	0 (0)	1 (6)	4 (26)	5 (6)
Body dysmorphia	0 (0)	1 (6)	0 (0)	1 (1)
Somatoform disorders				
Cutaneous pain syndromes	2 (4)	0 (0)	4 (26)	6 (8)
Venereophobia	0 (0)	0 (0)	1 (6)	1 (1)
Disorders resulting from compulsion				
Psychogenic pruritus	11 (24)	1 (6)	2 (13)	14 (18)
Lichen simplex chronicus	3 (6)	2 (13)	2 (13)	7 (9)
Miscellaneous PDs				
Cutaneous stigmata of substance use disorders	3 (6)	0 (0)	1 (6)	4 (5)
Antipsychotic induced pigmentary changes	3 (6)	1 (6)	0 (0)	4 (5)
Other cutaneous adverse drug reactions	0 (0)	1 (6)	0 (0)	1 (1)

Table 3. Association between psychodermatological disorders and primary psychiatric conditions.

Psychodermatological disorder	Affective disorders (n=20)			Anxiety, stress-related, and somatoform disorders (n=21)			Schizophrenia (n=66)		
	Patients, n (%)	*P* value	OR[a] (95% CI)	Patients, n (%)	*P* value	OR (95% CI)	Patients, n (%)	*P* value	OR (95% CI)
PDDPC[b]	11 (55)	.26	1.73 (0.65-4.61)	4 (19)	.01	0.24 (0.07-0.76)	32 (48)	.23	1.63 (0.73-3.62)
Psychophysiological dermatoses	9 (45)	.16	2.03 (0.750-5.99)	2 (10)	.02	0.18 (0.04-0.81)	23 (35)	.39	1.46 (0.62-3.44)
Secondary psychiatric	5 (25)	.44	1.28 (0.410-3.99)	2 (10)	.11	0.33 (0.07-1.52)	16 (24)	.39	1.55 (0.58-4.18)
PPDDM[c]	5 (25)	.15	0.45 (0.150-1.35)	12 (57)	.06	2.49 (0.94-6.58)	25 (38)	.71	0.86 (0.39-1.91)
Self-inflicted dermatoses	2 (10)	.11	0.33 (0.070-1.53)	4 (19)	.47	0.78 (0.23-2.58)	18 (27)	.13	2.19 (0.79-6.08)
Dermatoses resulting from delusions or hallucinations	2 (10)	.31	2.31 (0.392-13.57)	4 (19)	.01	9.88 (1.67-58.34)	—[d]	.01	0.04 (0.00-0.75)
Somatoform disorders	—	.22	0.26 (0.014-4.78)	5 (24)	.003	13.13 (2.34-73.65)	2 (3)	.07	0.23 (0.04-1.22)
Dermatoses resulting from compulsion	3 (15)	.41	0.68 (0.178-2.56)	4 (19)	.61	0.96 (0.28-3.21)	14 (21)	.60	1.31 (0.48-3.57)
Miscellaneous psychodermatological disorders	2 (10)	.46	1.50 (0.280-8.05)	1 (5)	.51	0.56 (0.07-4.85)	5 (8)	.64	1.04 (0.24-4.56)
Adverse effects of medications	1 (5)	.65	1.09 (0.115-10.33)	—	.33	0.34 (0.02-6.48)	4 (6)	.36	2.58 (0.28-23.93)
Cutaneous manifestation of substance use disorders	—	.43	0.45 (0.023-8.766)	1 (5)	.59	1.38 (0.14-14.01)	3 (5)	.50	1.91 (0.19-18.95)

[a]OR: odds ratio.

[b]PDDPC: primary dermatological disorder with psychiatric comorbidity.

[c]PPDDM: primary psychiatric disorder with dermatologic manifestations.

[d]Not available.

Discussion

Background

This study demonstrates a high burden of PDs among patients with mental health disorders. There are significant gaps in the scientific literature on PDs in the context of primary psychiatric conditions. Most data on PDs are derived from the general population or dermatology outpatient settings and have consistently demonstrated a high prevalence of comorbid psychiatric symptoms among patients with diverse dermatological conditions [5-7,19-21].

Prevalence of PDs

We recorded a high (75/107, 70%) prevalence of PDs in this study, with more than half (54/107, 50.46%) of the population having multiple PDs. The exact prevalence of PDs in those with primary psychiatric conditions is uncertain due to limited research, a lack of standard classification system, and underdiagnosis [18,22]. Nevertheless, previous studies highlight the significant burden of psychiatric problems among patients with dermatological conditions [21-23]. Our findings echo this, underscoring the substantial relationship between dermatological and psychiatric conditions.

Pattern of PDs in Patients With Mental Health Disorders

PDDPCs are commonly diagnosed noninfectious dermatoses in patients with mental health disorders [24-26]. This study found that 43.9% (47/107) of patients had at least one PDDPC. Comparable rates were reported among patients with dermatological conditions seeking psychodermatological consultations in Singapore (31.6%) [27] and patients with psychiatric conditions in Morocco (34.3%) [18]. The most frequent PDDPC was seborrheic dermatitis, affecting 17 of 107 (15.9%) patients. This is consistent with earlier reports of a high prevalence of seborrheic dermatitis in patients with mental health disorders [18,24] and may be linked to seborrhea induced by psychotropic medications.

The prevalence and pattern of secondary psychiatric conditions in this study mirror observations among patients with mental health disorders in Morocco, where alopecia and vitiligo were the most frequent secondary PDDPCs [18]. A similar prevalence of hair loss (14.9%) was also reported among patients with mental health disorders in India [28]. In contrast to research conducted among patients with dermatological conditions [29], the incidence of alopecia seems remarkably higher in patients with mental health disorders. This may be related to the impact of psychological stress and psychotropic medications on hair growth [30,31].

PPDDMs comprise dermatoses whose complex etiology is rooted in pathological psychological processes. The significant association between PPDDMs and primary psychiatric conditions is corroborated by our research findings, in which more than a third (42/107, 39.3%) of patients with mental health disorders were diagnosed with PPDDMs. A comparable prevalence of PPDDMs (22%) among patients with mental health disorders was reported by Barrimi et al [18] in Morocco. However, lower rates have also been documented by various authors, ranging from 5.4% among patients with mental health disorders in Nepal [32] to 8.7% in an Egyptian study [25]. Differences in the nomenclature and categorization systems adopted by various authors researching PDs may be responsible for these variations.

The least common PDs in this study were miscellaneous PDs, primarily encompassing cutaneous reactions to psychotropic drugs and skin signs of substance use disorders, which both occurred in 4% (4/107) of the study population. This corresponds with the 2%-5% prevalence documented for adverse reactions to psychiatric medications in the literature [33-35]. However, skin manifestations of substance abuse are rarely mentioned in studies documenting skin conditions in patients with mental health disorders [32,36].

Relationship Between Psychiatric Conditions and PDs

Affective Disorders and PDs

The prevalence of PDs, especially PDDPCs, was highest in patients with affective disorders compared with other psychiatric conditions (Table S5 in Multimedia Appendix 2). While this contrast lacked statistical significance in this study, previous investigators have reported a significant association between PDDPCs, specifically psychophysiological disorders, and affective disorders [6,24,37,38]. The pathophysiological mechanism connecting PDs and affective disorders may be related to disrupted allostasis [39]. This occurs when persistent psychological and physical stress from long-standing skin conditions overwhelms normal homeostatic mechanisms and initiates pathological processes that are detrimental to mental health. Conversely, persistent psychological stress and emotional conflicts can trigger neuroimmunological and hormonal mediators capable of inducing pathological changes in the skin [40,41]. In either situation, a vicious chain of events that is characteristic of psychophysiological disorders is established, in which skin conditions cause psychological distress, which in turn exacerbates preexisting dermatoses.

Anxiety, Stress-Related, and Somatoform Disorders

In this study, patients with anxiety, stress-related, and somatoform disorders had the lowest prevalence of PDDPCs and were less likely to be diagnosed with psychophysiological dermatoses. (φ=–0.236; P=.02). This contrasts with dermatology outpatient findings that often associate anxiety disorders with PDs [23]. Possible explanations for the negative association between anxiety disorders and PDDPCs in this study could be the influence of psychotropic medications. Furthermore, the heightened inclination of patients with anxiety disorder in this study to seek treatment for their skin complaints could have played a role in the reduced prevalence and negative correlation of anxiety with PDDPCs.

PPDDMs resulting from delusions, hallucinations, and somatoform disorders, unlike PDDPCs, showed a strong association with anxiety disorders. Patients with anxiety disorders were 13 times more likely to be diagnosed with somatoform disorders and 9 times more likely to have PPDDMs from delusions or hallucinations, compared to schizophrenia or affective disorders. Notably, 4 (80%) out of 5 cases of delusion of parasitosis and 5 out of 7 cases of somatoform disorders were identified in patients with anxiety disorders. Although delusions of parasitosis have been previously linked to anxiety disorders [42], most researchers have presented differing associations with various psychiatric conditions [36,43,44]. Consequently, the exact relationship between delusional parasitosis and specific comorbid psychiatric conditions remains controversial. Further studies are required to better understand the conditions in relation to underlying psychiatric conditions.

Schizophrenia and PDs

Patients with schizophrenia had the lowest prevalence of PDs. However, self-inflicted dermatoses like neurotic excoriations and secondary psychiatric dermatoses such as alopecia were more common in patients with schizophrenia than in those with other psychiatric conditions. Reports of self-inflicted dermatoses in patients with schizophrenia are uncommon [45-47]. Rather, most studies demonstrate an association between self-inflicted dermatoses and major depression, obsessive-compulsive disorder (OCD), and anxiety disorders [46,48-50]. The higher prevalence of self-inflicted dermatoses among patients with schizophrenia in this study, therefore, contradicts popular findings in the literature. However, considering the recent reclassification of self-inflicted dermatoses within the OCD spectrum [51] and previous reports of high comorbidity of OCD with schizophrenia [52,53], our findings may indicate a potential underdiagnosis of coexisting OCD in the group of patients with schizophrenia.

In this study, schizophrenia had a significant negative relationship with delusion of parasitosis (φ=–0.309; P=.001), which is at variance with earlier reports [36,54-56]. This could be due to the effects of antipsychotics on delusional symptoms because, compared to the cohort of patients with the highest frequency of delusion of parasitosis (patients with anxiety disorder) in this study, patients with schizophrenia were significantly more likely to be treated with antipsychotics (P<.001).

Conclusions

This study provides important insights into the overwhelming burden of psychodermatological conditions in patients with mental health disorders and specific associations with underlying psychiatric diagnosis. Noteworthy is the significant association between anxiety disorders and PPDDMs due to delusions or hallucinations and somatoform disorders. The relationship between PDs and psychiatric conditions in patients with mental health disorders differs from reports of studies conducted among patients with dermatological conditions. Larger studies conducted among patients with mental health disorders are, however, required to confirm these findings.

Study Limitations

There are some limitations to this study that can affect the degree to which our findings can be extrapolated to the general population. First is the relatively small sample size and relatively lower proportions of patients with anxiety and affective disorders. Second is the lack of representation of some other major categories of psychiatric conditions in the study population, and finally, the lack of a control group comprising patients without mental health disorders to enable the comparison of the burden and pattern of PDs between patients with and without psychiatric conditions.

Authors' Contributions

AA was the lead researcher; she conceived the research idea and developed the study protocol. Other authors listed contributed to the result collection, analysis, discussion, and writing of the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Logistic regression analysis for predictors of Psychodermatological Disorders.
[DOCX File , 19 KB - derma_v6i1e47769_app1.docx]

Multimedia Appendix 2
Comparison of the frequency and pattern of psychodermatological disorders among the major groups of major psychiatric conditions.
[DOCX File , 17 KB - derma_v6i1e47769_app2.docx]

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Abbreviations

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition
OCD: obsessive-compulsive disorder
OR: odds ratio
PD: psychodermatological disorder
PDDPC: primary dermatological disorder with psychiatric comorbidity
PPDDM: primary psychiatric disorder with dermatologic manifestations

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Original Paper

Analyzing the Predictability of an Artificial Intelligence App (Tibot) in the Diagnosis of Dermatological Conditions: A Cross-sectional Study

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Abstract

Background: Artificial intelligence (AI) aims to create programs that reproduce human cognition and processes involved in interpreting complex data. Dermatology relies on morphological features and is ideal for applying AI image recognition for assisted diagnosis. Tibot is an AI app that analyzes skin conditions and works on the principle of a convolutional neural network. Appropriate research analyzing the accuracy of such apps is necessary.

Objective: This study aims to analyze the predictability of the Tibot AI app in the identification of dermatological diseases as compared to a dermatologist.

Methods: This is a cross-sectional study. After taking informed consent, photographs of lesions of patients with different skin conditions were uploaded to the app. In every condition, the AI predicted three diagnoses based on probability, and these were compared with that by a dermatologist. The ability of the AI app to predict the actual diagnosis in the top one and top three anticipated diagnoses (prediction accuracy) was used to evaluate the app's effectiveness. Sensitivity, specificity, and positive predictive value were also used to assess the app's performance. Chi-square test was used to contrast categorical variables. P<.05 was considered statistically significant.

Results: A total of 600 patients were included. Clinical conditions included alopecia, acne, eczema, immunological disorders, pigmentary disorders, psoriasis, infestation, tumors, and infections. In the anticipated top three diagnoses, the app's mean prediction accuracy was 96.1% (95% CI 94.3%-97.5%), while for the exact diagnosis, it was 80.6% (95% CI 77.2%-83.7%). The prediction accuracy (top one) for alopecia, acne, pigmentary disorders, and fungal infections was 97.7%, 91.7%, 88.5%, and 82.9%, respectively. Prediction accuracy (top three) for alopecia, eczema, and tumors was 100%. The sensitivity and specificity of the app were 97% (95% CI 95%-98%) and 98% (95% CI 98%-99%), respectively. There is a statistically significant association between clinical and AI-predicted diagnoses in all conditions (P<.001).

Conclusions: The AI app has shown promising results in diagnosing various dermatological conditions, and there is great potential for practical applicability.

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KEYWORDS

artificial intelligence; AI-assisted diagnosis; machine learning; neural network; deep learning; dermatology; mobile; application; app

Introduction

Background

Artificial intelligence (AI) is "the scientific understanding of the mechanisms underlying thought and intelligent behaviour, and their exemplification in machines" [1]. It aims to reproduce properties similar to human cognition [2-4]. A subset of AI where computer programs learn from experience without any definitive coding instructions is known as machine learning (ML) [1].

It may become crucial in the future for every member of the medical community to have a thorough understanding of AI, as it could be the catalyst for the transformation of health systems to increase productivity and effectiveness, providing versatility for universal health coverage, hence introducing a rudimentary change in the way we practice medicine [5,6].

The majority of diagnoses in dermatology are made primarily on visual pattern recognition and mainly depend on morphological traits. Its comprehensive clinical, dermatoscopic, and dermatopathological picture database makes it perfect for using AI image recognition skills for assisted diagnosis [1,2,7].

AI can prove to be an important tool in the screening and early diagnosis of skin cancers, thus improving the quality of care [4,8-10]. It has also been used in diagnosing and assessing various inflammatory conditions, pigmentary diseases, and hair disorders [4,9-11]. Opportunities for AI in dermatology include the potential to robotize redundant assignments, streamline tedious undertakings, improve spectator dependability issues, and eventually extend the diagnostic toolbox of dermatologists [11].

The manifestation of dermatological conditions in various forms, the lack and uneven distribution of competent dermatologists, and the need for prompt and precise diagnosis necessitate the need for an automated computer-aided diagnosis [12]. In lower-income nations like India, where there is a significant gap between the availability and demand for facilities and where the cost of health care is high, AI is especially helpful. As pandemics such as COVID-19 cannot be foreseen, it can be a noteworthy alternative for patients and doctors to use online consultations during these periods.

About the Tibot AI App

The Tibot AI app, which is owned by Polyfins Technology Inc, was analyzed in this study. This app aims to raise awareness about skin conditions among users, categorize various skin conditions in terms of criticality, and encourage users to seek medical advice from a skin care specialist for proper treatment whenever needed. The patient's data is safeguarded using numerous firewalls, and the users have complete control over the encrypted data. Upon sharing a photo on the app and answering a couple of questions about the skin lesion, it uses ML to break down images, inspect and compare them with similar images from its memory, and predict the most probable diagnoses.

The following are the 12 categories of skin conditions tracked by the AI app: acne and rosacea; alopecia; benign and suspicious tumors; eczema; immunological skin disorders; pigmentary disorders; psoriasis; skin infestation; and bacterial, fungal, and viral infections. The specific skin conditions tracked by the app in each category are listed in Multimedia Appendix 1. Many other apps working on a similar principle are available, and appropriate research to determine their reliability is necessary.

Objective

This study analyzes the predictability of the Tibot AI app in the identification of dermatological diseases as compared to a dermatologist.

Methods

Study Design and Participant Inclusion Criteria

This observational cross-sectional study included participants of all ages consulting the dermatology outpatient department in a tertiary care facility. The skin disorders were grouped according to the categories put forward by the AI app and included acne; alopecia; benign and suspicious tumors; eczema; immunological skin disorders; pigmentary disorders; psoriasis; skin infestation; and bacterial, fungal, and viral infections. Patients with conditions warranting further evaluation, who had been treated earlier, or who were unwilling to allow their photographs to be used were excluded from this study.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethical Committee of BLDE (Deemed to be University; IEC/No. 09/2021 and 22/01/2021). Informed consent was obtained from all participants involved in the study.

Methodology

A detailed history was taken, a clinical examination of the patients was performed, and a clinical diagnosis was established by an expert dermatologist. Using a smartphone camera of 12MP, images of the skin lesions were taken in confidence in a room with adequate lighting and uploaded onto the Tibot iOS app. Certain questions put forward by the app regarding the demographic profile of the patient and those pertaining to the site and duration of lesions, associated symptoms, and their intensity were answered. For every skin condition, three diagnoses were predicted by the app based on probability, and these were compared with the clinical diagnosis.

Statistical Analysis

Percentages were used to offer a descriptive analysis of various skin problems. The efficacy of the AI app was assessed based on its potential to predict the actual diagnosis in the top one and top three anticipated diagnoses. Sensitivity, specificity, and positive predictive value (PPV) were also evaluated. Data analysis was performed using JMP Pro 16 software Version 16 (SAS Institute). Chi-square test was used to contrast categorical variables. $P<.05$ was considered statistically significant.

Results

Participant Characteristics

A total of 600 patients were included in the study. The majority of the patients belonged to the age group of 20-29 years (n=167, 27.8%), with a male preponderance (n=339, 56.5%). Clinical conditions included viral infections (n=111, 18.5%), alopecia (n=89, 14.8%), fungal infections (n=88, 14.7%), pigmentary disorders (n=87, 14.5%), acne and rosacea (n=73, 12.2%), psoriasis (n=47, 7.8%), benign tumors (n=28, 4.7%), eczema (n=24, 4%), immunological disorders (n=20, 3.3%), skin infestation (n=16, 2.7%), suspicious tumors (n=11, 1.8%), and bacterial infections (n=6, 1%).

Performance of the AI App

The mean prediction accuracy for the anticipated top three diagnoses of the AI software was 96.1% (95% CI 94.3%-97.5%) and 80.6% (95% CI 77.2%-83.7%) for the precise diagnosis. The precision of diagnoses in the top three and top one predictions, known as prediction accuracy, was analyzed in each skin condition. Prediction accuracy (top one) was 97.7% for alopecia and 91.7%, 88.5%, and 82.9% for acne, pigmentary disorders, and fungal infections, respectively. Prediction accuracy (top three) was 100% for alopecia, benign tumors, eczema, and suspicious tumors (Table 1).

The AI app’s sensitivity and specificity were found to be 97% (95% CI 95%-98%) and 98% (95% CI 98%-99%), respectively.

The confusion matrix between AI-anticipated top diagnoses and actual diagnoses, along with sensitivity (top one) and PPV for individual skin conditions, is depicted in Figure 1. The sensitivity (top three) for alopecia, eczema, and benign and malignant tumors was 100%. The PPV for pigmentary disorders and alopecia was 96% and for acne and viral infections 91% and 90%, respectively. Table 2 depicts the sensitivity, PPV, and specificity of the AI app in the diagnosis of individual skin conditions. There was a statistically significant association between clinical diagnosis and predicted top diagnosis in all the conditions (*P*<.001). Figure 2 shows clinical photographs of various skin conditions with actual and predicted diagnoses.

Table 1. Prediction accuracy of the artificial intelligence app in top one and top three predictions in various skin conditions.

Skin conditions	Prediction accuracy (95% CI), %	
	Top one	Top three
Acne and rosacea	91.7 (82.9-96.9)	98.6 (92.6-99.9)
Alopecia	97.7 (92.1-99.7)	100 (95.9-100)
Bacterial infection	50 (11.8-88.1)	83.3 (35.9-99.6)
Benign tumor	71.4 (51.3-86.8)	100 (87.7-100)
Eczema	75 (53.3-90.2)	100 (85.8-100)
Fungal infection	82.9 (73.4-90.1)	96.5 (90.4-99.3)
Immunological skin disorder	75 (50.9-91.3)	95 (75.1-99.9)
Pigmentary disorder	88.5 (79.9-94.3)	98.8 (93.8-99.9)
Psoriasis	70.2 (55.1-82.7)	91.4 (79.6-97.6)
Skin infestation	68.7 (41.3-88.9)	93.7 (69.8-99.8)
Suspicious tumor	81.8 (48.2-97.7)	100 (71.5-100)
Viral infection	63 (53.4-72)	94.5 (88.6-97.9)

Figure 1. Confusion matrix of actual diagnosis versus artificial intelligence–predicted top diagnosis along with sensitivity and positive predictive value for individual skin conditions. Dark blue cells represent true positives.

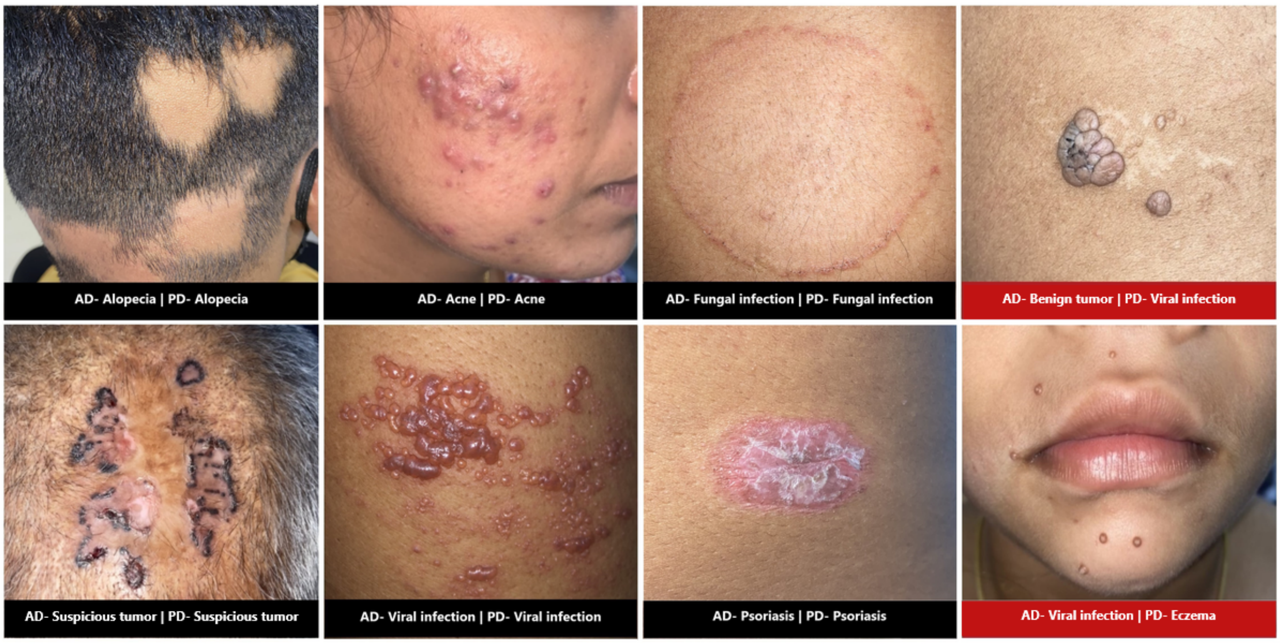
		Actual diagnosis													
		Acne and rosacea	Alopecia	Bacterial infections	Benign tumors	Eczema	Fungal infections	Immunological skin disorders	Pigmentary disorders	Psoriasis	Skin infestation	Suspicious tumors	Viral infections	Total	PPV
Predicted diagnosis	Acne and rosacea	67	1	0	0	0	0	0	3	0	0	0	3	74	91%
	Alopecia	0	87	0	1	0	2	0	0	0	0	0	1	91	96%
	Bacterial infections	1	0	3	0	0	0	0	0	0	0	0	3	7	43%
	Benign tumors	0	0	0	20	0	0	1	3	0	0	0	5	29	69%
	Eczema	0	0	2	1	18	9	3	1	5	3	0	7	49	37%
	Fungal infections	1	1	0	1	2	73	0	0	3	0	0	10	91	80%
	Immunological skin disorders	2	0	0	0	0	1	15	2	6	0	2	8	36	42%
	Pigmentary disorders	2	0	0	0	0	0	0	77	0	1	0	0	80	96%
	Psoriasis	0	0	0	0	3	2	0	0	33	0	0	0	38	87%
	Skin infestation	0	0	0	0	1	0	0	0	0	11	0	3	15	73%
	Suspicious tumors	0	0	0	2	0	0	0	0	0	0	9	1	12	75%
	Viral infections	0	0	1	3	0	1	1	1	0	1	0	70	78	90%
	Total	73	89	6	28	24	88	20	87	47	16	11	111	600	
	Sensitivity	92%	98%	50%	71%	75%	83%	75%	89%	70%	69%	82%	63%		

Table 2. The sensitivity, PPV, and specificity of artificial intelligence software for the diagnosis of various dermatoses.

Skin conditions	Sensitivity (95% CI), %		PPV[a] (95% CI), %	Specificity (95% CI), %
	Top one	Top three		
Acne and rosacea	92 (83-97)	99 (93-99)	91 (82-95)	99 (97-99)
Alopecia	98 (92-99)	100 (96-100)	96 (89-98)	99 (98-99)
Bacterial infection	50 (12-88)	83 (36-99)	43 (17-77)	99 (98-99)
Benign tumor	71 (51-87)	100 (88-100)	69 (53-82)	98 (97-99)
Eczema	75 (53-90)	100 (86-100)	37 (28-47)	95 (92-96)
Fungal infection	83 (73-90)	97 (90-99)	80 (72-87)	96 (94-98)
Immunological skin disorder	75 (51-91)	95 (75-99)	42 (30-54)	96 (95-98)
Pigmentary disorder	89 (80-94)	99 (94-99)	96 (89-99)	99 (98-99)
Psoriasis	70 (55-83)	91 (80-98)	87 (73-94)	99 (98-99)
Skin infestation	69 (41-89)	94 (70-99)	75 (50-89)	99 (98-99)
Suspicious tumor	82 (48-98)	100 (72-100)	75 (48-91)	99 (98-99)
Viral infection	63 (53-72)	95 (89-98)	90 (81-95)	98 (97-99)

[a]PPV: positive predictive value.

Figure 2. Clinical images of various skin conditions with actual and artificial intelligence–predicted diagnoses. AD: actual diagnosis; PD: predicted diagnosis.



Discussion

Principal Findings

In this study, we have analyzed the diagnostic precision of the Tibot AI app for a variety of dermatological disorders as compared to that of a dermatologist. The app works on the principle of a convolutional neural network (CNN), which breaks down images into numerical forms and compares them with similar images from its own memory to predict the probable diagnosis [4,8].

This study included the maximum number of patients with infections, alopecia, and pigmentary disorders. The app's mean prediction accuracy was 96.1% (95% CI 94.3%-97.5%) for identifying and predicting the diagnosis in the top three predictions and 80.6% (95% CI 77.2%-83.7%) for the exact diagnosis. The prediction accuracy (top 1) was 97.7%, 91.7%, 88.5%, and 82.9% for alopecia, acne, pigmentary disorders, and fungal infections, respectively. The prediction accuracy (top 3) was 100% for alopecia, eczema, and benign and suspicious tumors. The PPV was 96% for alopecia and pigmentary disorders and 91%, 90%, and 87% for acne, viral infections, and psoriasis, respectively.

Comparison With Previous Studies

A study done by Patil et al [4] assessed the Tibot AI app in 398 patients. The study showed that the mean prediction accuracy of the app was 60.7% for the precise diagnosis and 85.2% to predict the actual diagnosis in the anticipated top three. A better mean prediction accuracy of 96.1% and 80.6% was demonstrated in our study in the top three and top one predictions, respectively. The comparison of the prediction accuracy (top three) and PPV of this study and their study is depicted in Table 3. The prediction accuracy in individual skin conditions was also significantly better in our study. The PPV was comparable in most of the conditions. The sensitivity of the AI app was 86% in their study as compared to 97% in our study, whereas the specificity was 98% in both studies. Suspicious tumors were not included in their study.

AI has an active learning process that allows the app to expand the database, ultimately improving the predictive accuracy and diagnostic ability [4]. The better results in our study could be attributed to this nature, along with software updates of the app and variations in the quality of the pictures uploaded. By submitting clinical images and responding to a few key questions pertaining to the location, duration, and intensity of the associated symptoms of the lesions, these dermatoses are evaluated. The different visual manifestations of the same disorder among various patients and the subjective nature of symptoms can be attributed to the discrepancy in accuracy.

A study conducted by Wu et al [13] assessed a CNN model in diagnosing inflammatory skin conditions such as psoriasis, atopic dermatitis, and eczema. The model was trained based on 4740 clinical images. The overall accuracy of the application was 95.8%, with a sensitivity of 94.4% and a specificity of 97.2%. The accuracy for psoriasis was 89.46% and for atopic dermatitis and eczema 92.57%. In our study, the app showed a prediction accuracy (top one) of 75% and 70.2% for eczema and psoriasis, respectively.

Fujisawa et al [14] assessed a CNN that was trained using a data set of 4867 images in classifying skin tumors into benign and malignant as compared to board-certified dermatologists. The overall classification accuracy was 76.5%, with a sensitivity of 96.3% and a specificity of 89.5%.

A study on the classification of skin cancer using deep neural networks was published by Esteva et al [15]. They trained a CNN using 129,450 clinical pictures comprising 2032 distinct illnesses. This app diagnosed melanomas and keratinocyte carcinomas with an overall accuracy of 72.1%, with a comparable or better efficacy than 21 dermatologists.

Han et al [16] developed an automated classification system for 12 established benign and malignant dermatoses using 19,398 images. The CNN performed comparably to 16 dermatologists. For all conditions, the average sensitivity and specificity were 85.1% and 81.3%, respectively.

Our study included 39 skin tumors, of which 11 were suspicious and 28 were benign. For suspicious tumors, the prediction accuracy (top one) and PPV were 81.8% and 75%, respectively, while for benign tumors, it was found to be 71.4% and 69%, respectively. The prediction accuracy (top three) and sensitivity for both were 100%. Although these conditions ideally require histopathological confirmation, the tumors included in this study were clinically apparent.

Table 3. Comparison of the prediction accuracy and PPV of artificial intelligence software in this study and the study by Patil et al [4].

	Current study, %		Study by Patil et al [4], %	
	Prediction accuracy	PPV[a]	Prediction accuracy	PPV
Acne and rosacea	98.6	91	84	87.5
Alopecia	100	96	100	100
Bacterial infection	83.3	43	78.9	78.9
Benign tumor	100	69	71.4	83.3
Eczema	100	37	91.7	94.3
Fungal infection	96.5	80	95.6	90
Immunological skin disorder	95	42	88.9	42.1
Pigmentary disorders	98.8	96	75	75
Psoriasis	91.4	87	73.7	82.3
Skin infestation	93.7	73	63	94.4
Suspicious tumor	100	75	—[b]	—
Viral infection	94.5	90	26.7	80

[a]PPV: positive predictive value.

[b]Suspicious tumors were not included in their study.

Nomenclature and Inception of AI

AI is a broad scientific discipline dedicated to developing programs that display properties of human intellect and encompasses ML and deep learning [3,6,17,18]. ML includes various approaches that enable algorithms to learn from data without explicit programming [1,10,17]. A supervised, semisupervised, or unsupervised learning process can be used. A subtype of ML called deep learning incorporates artificial neural networks that mimic the structure of biological neural networks in the brain [1,8].

Artificial neural networks or neural networks are flexible mathematical models that identify complex nonlinear relationships in large data sets. They are arranged in three layers—input, hidden, and output. A “deep” neural network has three or more concealed layers. The input layer receives relevant data, which is then processed through multiple layers of hidden algorithmic processes, where each layer detects some feature within the input [1,5,8,11]. A special category of artificial neural networks known as CNNs includes three types of layers—convolution, pooling, and fully connected [8,18].

Since the dawn of time, man has relied on machines to help him live and simplify his existence. Inferential statistics are used in the medical field to confirm or refute hypotheses that have been developed via observation and analysis of the patients. AI expands on this strategy by recognizing patterns that are difficult for humans to notice [5]. Although AI in dermatology was focused on pigmented skin lesions and melanoma detection initially, newer algorithms have since been developed with a wide range of applications, including collecting images, decoding, evaluation, report generation, and strategizing for follow-up [11,17].

Limitations

The limitations of our study include a lack of standardization of images with respect to focus, angle, and lighting, and the inability to record skin type. Assessment of various Fitzpatrick skin types is required to corroborate the findings. Regarding the composition of study participants, the majority had infections, alopecia, pigmentary disorders, and acne. Although AI recognition of skin tumors in this study is feasible, further studies with more participants are required, as a small sample size has less validity.

Currently, AI in dermatology, including the Tibot app, can only recognize a group of explicit skin diseases with a lack of a specific diagnosis [2,11]. To construct the ideal app, close collaboration among multidisciplinary experts in the domains of computer science, biomedicine, and medicine is essential [2,19]. There are unresolved legal, ethical, privacy, and liability issues associated with AI diagnosis that might hinder regulatory approval [2,3,11,18,20]. Another hurdle that AI faces is public trust and acceptance as people struggle to understand the decision-making process of AI, referred to as a black box [11,18,20]. A particular issue that is understudied in the existing research on the principles of using AI in health services is the absence of explicit and unique descriptions of the notions used to construct the algorithms, as well as how their core concept may be translated into machine code and subsequently interpreted by doctors [21]. Dermatology, being primarily a visual specialty, is also a tactile one [2]. Therefore, predicting the diagnosis based solely on 2D photographs is difficult. These are some of the drawbacks of AI in dermatology.

The AI Conundrum

This new era of AI-augmented practice has its fair share of skeptics and supporters. While AI might seem threatening to dermatologists' diagnostic skill set, it is important to remember that AI can only provide a probability of broad diagnoses and certainly not the treatment nor can it provide humanistic care. To achieve the utmost potential of AI, developers must strive to create algorithms that represent a variety of patient populations, ensure that the output is ultimately comprehensible, prospectively validate its performance, provide doctor-patient interaction when necessary, and demonstrate authenticity to the regulatory bodies.

Conclusion

The Tibot AI app has shown encouraging results in diagnosing various dermatological conditions. There is great potential for practical applicability, although further improvement is required for its implementation in clinical practice. Its greatest strength is the ability to learn independently without human intervention.

AI is by no means an equivalent to the correspondence between doctors and patients neither can it offer medical care or human touch, but it is an important aid to dermatologists and patients. The public's lack of inclination to adopt a contentious technology will be the biggest barrier to its general acceptance. While it is helpful in broadly categorizing diseases, detailed knowledge of the subject and its implementation in the correlation of various diseases will still be needed for fine-grained diagnosis and further management. Rather than succumbing to the fear of a dystopian future where AI replaces dermatologists, it is imperative that we should embrace it and incorporate it into patient care paradigms.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Specific skin conditions tracked by the artificial intelligence application in each clinical category.

[DOCX File , 17 KB - derma_v6i1e45529_app1.docx]

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Abbreviations

AI: artificial intelligence
CNN: convolutional neural network
ML: machine learning
PPV: positive predictive value

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Original Paper

An mHealth App (eSkinHealth) for Detecting and Managing Skin Diseases in Resource-Limited Settings: Mixed Methods Pilot Study

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Abstract

Background: In sub-Saharan Africa, the disease burden from skin diseases, including skin-related neglected tropical diseases (skin NTDs), is extremely high. These diseases often are overlooked due to limited access to health care stemming from, for example, remote geographical locations and a lack of experts. To address these gaps, we developed a mobile health app, eSkinHealth, which is a field-adapted platform to serve as a portable electronic patient chart and for teledermatology.

Objective: The purpose of the study is to evaluate the usability and effectiveness of the app in rural Côte d'Ivoire for diagnosing and managing skin NTDs and other skin diseases.

Methods: A 2-arm trial with local health care providers and patients with skin diseases was implemented over a 3-month period. The providers were assigned to an intervention receiving the eSkinHealth app or control with usual care. Four nurses and 8 community health care workers participated in each arm. The training was provided on the use of the app to the intervention arm only, while both arms were trained on skin diseases. For the usability study, we evaluated our approach with the System Usability Scale (SUS) and in-depth interviews. For the effectiveness study, our primary outcome was to evaluate the detection and management of 5 skin NTDs as our targeted diseases, namely, Buruli ulcer, leprosy, lymphatic filariasis, scabies, and yaws, using the eSkinHealth app. Procedures of our methods were reviewed and approved by the institutional review board of the Ministry of Health and by Tulane University.

Results: The mean age of our participants (providers) was 40.5 and 42.5 years for the intervention and control arms, respectively, and all were male (n=24). The average SUS scores taken from the intervention arm at baseline, the midpoint (6 weeks), and the end of study (12 weeks) were 72.3 (SD 11.5), 72.3 (SD 12.4), and 86.3 (SD 10.8), respectively. All participants interviewed, including 4 dermatologists and program managers, were satisfied with the app. Especially community health care workers felt empowered by being equipped with the tool. A total of 79 cases of skin NTDs were reported in the intervention arm as compared to 17 cases in the control arm (P=.002). Besides the skin NTDs, more skin diseases and conditions were reported from the control than from the intervention arm (P<.001). However, 100 cases (66%) were not given any particular diagnosis in the control arm and were documented only as a "dermatosis." In the intervention arm, 151 cases (72.9%) were diagnosed within the eSkinHealth platform, and the remaining were diagnosed on-site by dermatologists.

Conclusions: The study provided evidence for the usability and effectiveness of the eSkinHealth app embedded into our surveillance approach to improve the detection and management of skin NTDs and other skin diseases in Côte d'Ivoire and, furthermore, is expected to contribute to knowledge on mobile health approaches in the control of skin diseases in resource-limited settings.

Trial Registration: ClinicalTrials.gov NCT05300399; https://clinicaltrials.gov/ct2/show/NCT05300399

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KEYWORDS

dermatology; developing countries; digital health tool; LMICs; low- and middle-income countries; skin; teledermatology; eHealth application; skin disease; digital health intervention; health platform; system usability

Introduction

The prevalence of skin diseases is extremely high in sub-Saharan Africa [1-7]. These diseases are most often overlooked due to a lack of local specialists and a lack of experience among Western specialists looking at darker skin [8,9]. Sometimes, it is also because of geographical barriers to accessing health care or the health-seeking behavior of patients and their families that they do not usually visit health care facilities for skin lesions [8]. However, if left untreated, even some of the most common skin diseases could have severe complications (eg, scabies could lead to rheumatic fever and nephropathy, as well as often debilitating physical, social, and mental effects that may deprive one of educational and social opportunities) [10,11]. Furthermore, some diseases, including leprosy, Buruli ulcer, lymphatic filariasis, and other skin infections, lead to lifelong disabilities and deformities if not diagnosed and treated early [10,12]. These skin infections that prevail in low- and middle-income countries (LMICs) are members of the skin-related neglected tropical diseases (skin NTDs) listed by the World Health Organization (WHO) and targeted for disease control globally. Concurrently, more than 1 billion individuals worldwide are known to be affected or at risk for skin NTDs [13]. In particular, recently, integration within the skin NTDs has been promoted in order to strengthen the disease control of this set of diseases [14-16]. The health system built upon this approach is also expected to benefit not only skin NTDs but other skin diseases that are prevalent in LMICs [13,14].

Observation of the skin could be very informative. Without undergoing invasive examinations requiring special skills and equipment, many skin diseases could be diagnosed with just a sufficient patient history and examination of the skin. This is well suited to field settings in LMICs. Photos of the skin lesions could serve as an alternative to direct observation and, if of sufficiently good quality, could allow for the diagnosis to be made on-site or remotely. Telemedicine for dermatology, or teledermatology, is currently an emerging field taking advantage of this unique feature of skin diseases. A few attempts at teledermatology have been made in sub-Saharan African countries and have shown promising results [17-19]. These previous efforts have faced a number of challenges that we plan to overcome with the proposed work, which has the following features:

- A field-adapted mobile health (mHealth) app that could provide direct diagnostic and management assistance to health care workers in a remote setting: There is no novel tool to support teledermatology, especially in LMICs where internet accessibility and connection quality are challenges. It is also of note that photos alone are often not adequate to make a correct diagnosis, as outlined previously by Resneck et al [20]. Although clinical photos offer essential information, they need to be accompanied by some clinical information to make a more accurate diagnosis. Furthermore, such a tool needs to be optimized for use on the skin of people of color, given that the diagnosis of several skin conditions on skin type IV and darker remains a challenge [21,22].
- A platform for storage of longitudinal patient records for improved follow-up: We have been conducting active surveillance for skin diseases in Côte d'Ivoire [2]. After providing a diagnosis, the patients need to be followed up, especially as most skin diseases are chronic in nature; this is an ethical obligation in medicine. However, there is a lack of skills and expertise in dermatology to pursue this, which is a universal situation in most LMICs [23]. Our field is no exception, and it has been challenging to follow up with our patients without making repeated field visits, which are often a long distance from city centers [24]. In addition, this lack of capability to follow up with patients is partly due to a lack of a system to document patient records. A platform that stores serial photo documentation of the clinical course could guide health care practitioners, both on-site and remotely, to provide better care.
- A platform for the formal collection and automatic organization of clinical and image data of the skin: Currently, teledermatology is mostly done on platforms without any formal framework for the collection or organization of data [19,25]. There is a need for developing such a platform both for direct patient care and epidemiologic purposes, especially for the organization of

clinical photos, which is a cumbersome task if done manually. Patient information management is another challenge in developing a successful teledermatology system, ensuring that patient privacy is fully protected. Nowadays, social networking sites such as WhatsApp and Facebook are sometimes used for teledermatology [19,25-27], but these informal platforms need to be used with care, considering patient privacy. If there is a platform that addresses these gaps, this could further support data analysis and quality control.

In summary, with targeted training, a technology-assisted decision support system, and a telemedicine network, local health care workers could be leveraged to enhance the diagnosis and management of these conditions as well as support health care managers in quality control. If an mHealth app that overcomes these current gaps and weaknesses is developed, this could serve as a breakthrough in managing skin diseases in LMICs.

This project is built upon a previous project for the development of a prototype smartphone or tablet app for skin diseases, which we named the eSkinHealth app [28]. This app is aimed at on-site and remote diagnosis, monitoring, clinical decision support, and geographic mapping of skin diseases adapted for use in LMICs and for skin type IV and darker. Through the lifecycle of this project, we aim to develop a powerful and comprehensive but easy-to-use mHealth app that could be used for the diagnosis and management of all types of skin conditions, especially focused for use in LMICs.

Methods

Study Design

We conducted a pilot trial with 2 arms over a 3-month follow-up in rural villages in Côte d'Ivoire, where multiple skin NTDs are coendemic. A mixed methods approach was used to evaluate the usability and effectiveness of the eSkinHealth app in the early detection and case management of skin diseases. We selected 5 skin NTDs, namely Buruli ulcer, leprosy, lymphatic filariasis, scabies, and yaw, as our primary target diseases to evaluate our approach.

Recruitment Procedure

We selected 8 primary health centers (PHCs) in Sinfra Health District with multiple skin NTD coendemicities as our study sites. Sinfra Health District is located in a central district of the country, with a population of 283,971 in 2021. We selected the PHCs based on the number of cases of our target skin NTDs in the past 3 years, the population size of the catchment area, geographical distribution, and access. Using the information, we matched the PHCs (primarily those with similar sizes) and divided them equally into intervention and control arms. Targeted patients included individuals with skin conditions who accessed the selected PHCs for diagnosis and treatment of their conditions.

Participant Inclusion or Exclusion Criteria

Two groups of eligible participants were defined as below.

Eligible Patients With Skin Conditions

Eligible patients in selected PHCs were defined as those who were clinically suspected or diagnosed with skin NTDs (Buruli ulcer, leprosy, lymphatic filariasis, scabies, and yaws) or other skin conditions. Patients were excluded if they were unable to provide consent for the study or reside outside of the target site.

Eligible Health Care Providers

Eligible local health care providers included nurses or community health care workers (CHWs) who were 18 years or older, working at PHCs or within the catchment area of the selected PHCs in Côte d'Ivoire, able to read and speak fluent French, willing to participate in the pilot study for the 3-month study duration and use a provided tablet with the eSkinHealth app if they were assigned to the intervention arm, and able to consent to participate in the study. Ineligible local health care providers were defined as those who were planning to leave the job within the study period and had difficulty operating mobile devices.

A total of 4 nurses and 8 CHWs were selected to participate in the study for each arm. One nurse per PHC was selected, while for CHWs, the number was chosen based on the population of the catchment area of the PHC. All participants were formally enrolled only after signing the informed consent form.

Intervention

The eSkinHealth app has 2 main functions: to serve as a portable electronic medical record and a platform for teledermatology when users are in need of support from a remote specialist. The current prototype of the eSkinHealth app is made up of 6 primary screens: patient ID and demographics, symptom list, basic symptom information, clinical notes, photo list, and evolution list [28]. The content of these screens has been developed based on our previous field surveys [2] and the research team's experience in managing dermatological patients. We have built-in some special features within each screen. They are as follows:

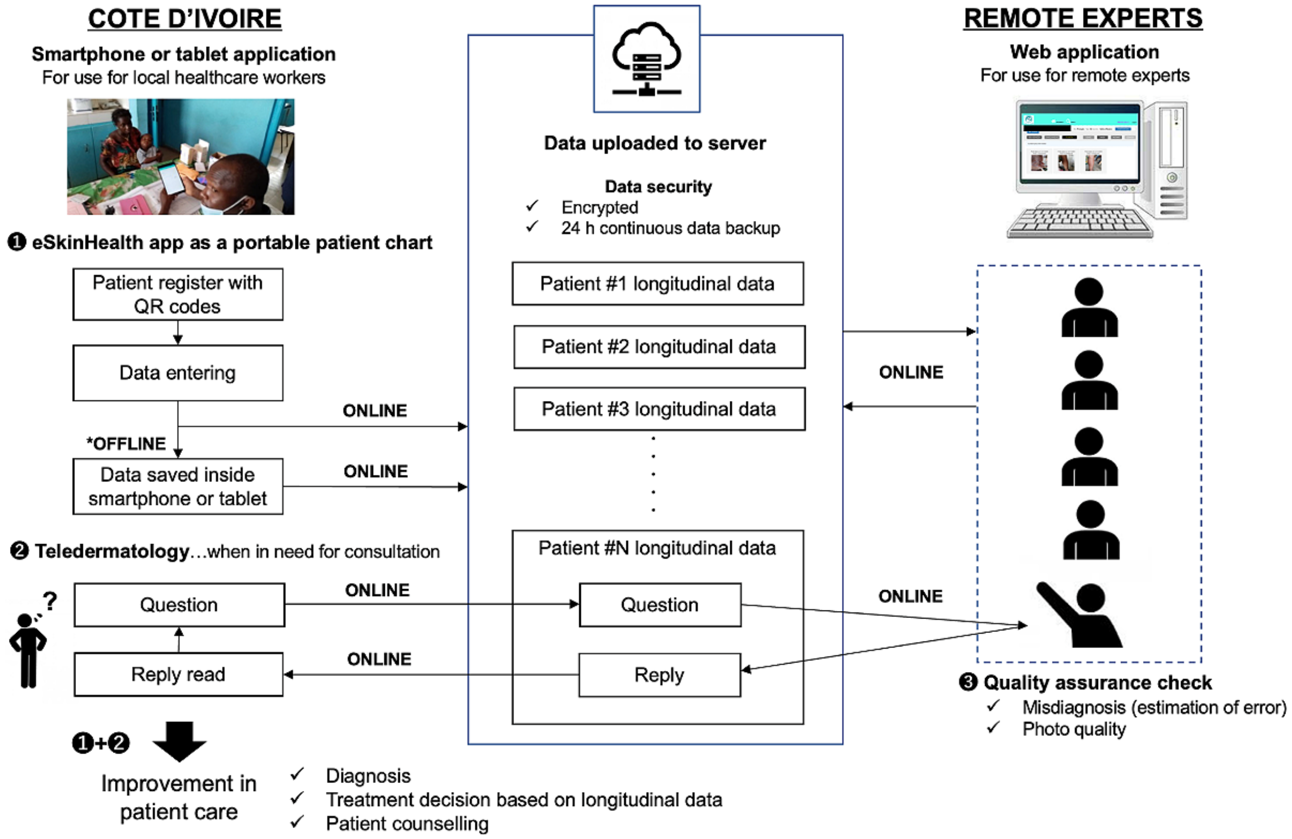
1. The "patient ID and demographics" screen allows for the entry of basic background information, including age, sex, occupation, and educational level. Automatic calculations are embedded for BMI and mid-upper arm circumference, allowing assessment of the patient's nutritional status.
2. Patients may present with multiple skin conditions, and these could be organized and managed under the "symptom list" screen. When a diagnosis is entered, it appears on this screen.
3. In the "basic symptom information" screen, important information needed in diagnosing a skin disease is provided in a drop-down menu, so it is not missed and is easy to enter.
4. Physical examination results of a 1-day visit could be entered in the "clinical notes" screen. One of the unique functions that we included here is the itchiness and pain visual scales, whereby patients themselves could touch the screen and indicate how they are experiencing these sensations each time.
5. Clinical photos could be taken, which are automatically organized in the "photo list" screen.

6. Lastly, if patients are to return to the clinic, the evolution of their condition could be seen at a glance in the “evolution list” screen, allowing comparison with previous presentations.

This app is not a disease-specific tool and is fit for use with a wide range of skin conditions. Other special features of the app include patient information security using QR codes. Patients are issued a QR code on their first visit. When they present it to a local health care provider with a device running the app during follow-up visits, it allows access to their records, making their health records secure and portable.

The eSkinHealth app is currently available for Android tablets with an OS version above 9.0. In the project, we used the Lenovo Tab M10 FHD Plus ZA5V0274JP. In addition, we have a web-based platform for the app to manage the case and facilitate a consultation with a remote health care provider. The app does not require a constant internet connection. Patient visits can be conducted, and all necessary information can be entered offline. When the users have access to the internet, the app synchronizes with the platform via our database server, transmitting and retrieving data (Figure 1). The platform includes the following additional functionalities: data overview, search function, and graphical display of data.

Figure 1. Data flow of the eSkinHealth app.



Usability Study

We conducted a 3-month pilot trial to evaluate the usability of eSkinHealth. Local health care providers in the intervention arm were provided with a tablet with eSkinHealth installed and a Wi-Fi router and were trained on how to use the app by study staff. All local health care providers, irrespective of intervention or control arm, were provided with training on the screening and management of important skin diseases, including our target 5 skin NTDs. We then applied a questionnaire survey to investigate the usability of the eSkinHealth app [29]. As for usability, the questionnaire surveys used the System Usability Scale (SUS), developed and validated by Brooke [30,31]. We used the French-language version of SUS (Multimedia Appendix 1). Furthermore, we conducted several semistructured, in-depth interviews with:

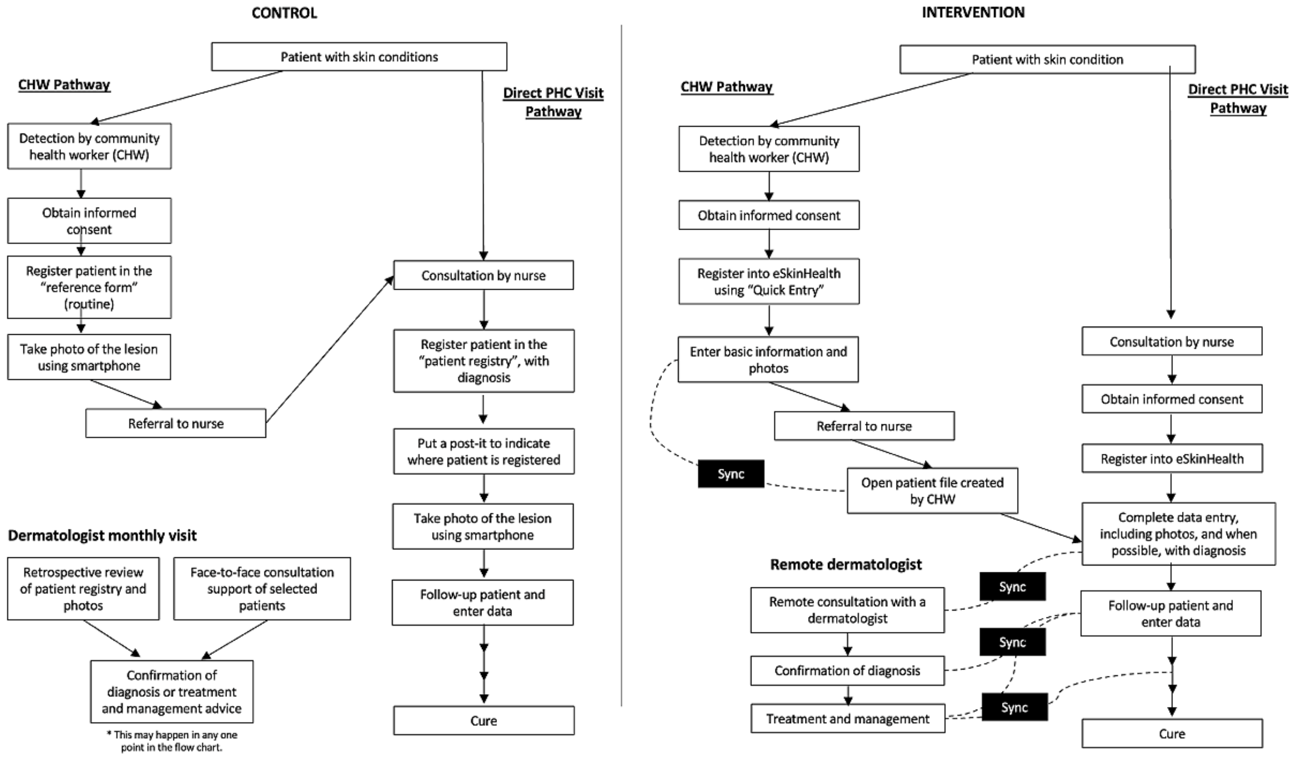
- Users (ie, local health care providers) to gather feedback on their experience, perceived value, and willingness to use the eSkinHealth app and identify the obstacles and challenges faced in the implementation of the mobile apps; and
- Dermatologists and program managers to collect and further examine their opinions about the feasibility, advantages, and disadvantages of adopting the eSkinHealth app by local health care providers already involved in the delivery of primary health care.

Topic guidelines for these interviews are provided in Multimedia Appendix 2.

Effectiveness Study

This study involved the same local health care providers who participated in the usability study above. The patient flow for the trial is provided in Figure 2. The CHWs were instructed to register patients when they detected a suspicious case of skin NTDs or any skin conditions seemingly of importance and refer them to their designated PHCs. Patients suspected of having the targeted skin NTDs (Buruli ulcer, leprosy, lymphatic filariasis, scabies, and yaws) and other skin conditions who provided informed consent during consultation at PHC throughout the trial period were enrolled by the nurses and registered on the eSkinHealth app platform. The nurses were instructed to enter clinical data at the time of the initial visit and every follow-up until cure in the eSkinHealth app, including photos of skin lesions. The data were uploaded when connected to the internet and integrated into 1 database server. When they needed a consultation, a request was sent to remote dermatologists affiliated with the project, either in the cities of Abidjan or Bouaké, and advice or clinical confirmation was provided. Dermatologists were instructed to review registered cases periodically and provide their assessment and recommendations wherever possible.

Figure 2. Patient flowchart for the 3-month pilot project of eSkinHealth app. CHW: community health care workers; PHC: primary health center.



As for the control arm, the number of cases with skin diseases was retrieved from the patient consultation registry booklet issued by the Ministry of Health and from the WHO skin NTDs reporting forms [25]. The CHWs were provided with paper reference forms and were instructed to refer any suspicious cases of skin NTDs or any skin conditions seemingly of importance to their designated PHCs. All participants in the control arm were also equipped with smart tablets or phones and were instructed to take photographs of skin lesions and create and organize them in an electronic folder labeled with patient names and IDs. All cases of skin NTDs were diagnosed and managed following the national standard guidelines.

For monitoring purposes, monthly field visits were made by the study team during the study period. During the visits, additional training on dermatology and, for the intervention arm, technical assistance on the usage of the app was provided. On request, face-to-face consultations with patients with skin conditions were performed.

Outcome Measurement

For the usability study, we used a validated questionnaire, the SUS, to assess the usability of the app and portal. The outcome measurement was an average score of SUS. Bangor et al [32] found that the SUS was highly reliable (α=.91) and useful over a wide range of interface types [33,34]. The SUS consists of 10 statements with responses in the form of a 5-point Likert scale (eg, 1: strongly disagree; 5: strongly agree). According to Bangor and Miller [33], a SUS score above 68 would be considered above average. In addition, a SUS score above 80 is considered excellent and places the product in the top 10% of products tested [35]. We assessed the usability at baseline, the midpoint (6 weeks), and the end of the study (12 weeks). Semistructured, in-depth interviews were performed at the end of the study.

For the effectiveness study, differences in the number of cases diagnosed and followed up between the intervention group (diagnosis with the app) and the control group (usual care) were measured as the primary outcome.

Data Collection

For the usability study, all survey data were obtained by study staff. Semistructured, in-depth interviews were all conducted in French, lasted between 10 and 20 minutes, and were held in private spaces either outside or inside the PHC or at the district hospital. All participants gave informed consent for voice-recording their interviews. All interviews were conducted by 2 staff members trained in and experienced in qualitative research. For the effectiveness study, the data collected using the eSkinHealth app were used.

Analysis

Statistical analyses were performed using Stata software (version 16; StataCorp). The threshold for statistical analyses was set at $P<.05$ in a 2-tailed test. We summarized the baseline data by group assignment using descriptive statistics: means and SDs were used for continuous data with a normal distribution, medians and IQRs for skewed data, and percentages for categorical data. As for our primary outcome, we compared the number of patients diagnosed between the control and intervention groups using the chi-square test. Qualitative data were first transcribed and translated verbatim from French into English by a translator. They were then imported into the MAXqda software (version 20.4.2; VERBI GmbH) and coded (25 codes in total). Two researchers (RRY and AY) were responsible for coding all interviews. The frequency of the coded segments and relations between the segments were examined, resulting in identifying 6 main themes. All researchers checked for consistency, similarity, and diversity within and across groups and themes that we all agreed upon.

Ethics Approval

The procedures of our methods have been reviewed and approved by the institutional review board (IRB) of the Ministry of Health, Côte d'Ivoire (No. IRB000111917) and by Tulane University (IRB 2020-2054-SPHTM). This study is registered at ClinicalTrials.gov (2020-2054). Informed consent was obtained in French, which is the official language of Côte d'Ivoire. In cases where a participant only spoke a local language, a member of our study team translated the informed consent form verbally to obtain consent. Our informed consent descriptions included consent for the primary data collection and secondary analyses of research data, including the use of images of skin lesions. No compensation was offered to patients, as the study's aim was to support routine health care practices with minimal or no harm.

For storage of data registered in the eSkinHealth app, we have been using the Simple Storage Service (S3) storage of the Amazon Web Service server, which offers a safe, secure, highly durable storage infrastructure with continuous backups, regulated under the US Health Insurance Portability and Accountability Act. Only the study team and those registered with the eSkinHealth app system (nurses and CHWs) had access to the data. Access to data in eSkinHealth is regulated by user levels, meaning that, for example, nurses and CHWs can only view patient data designated to their PHC or catchment area. All paper documentation, including the signed consent forms, was stored in a secure cabinet, and access was available only to the study staff approved by the IRB. All data were deidentified during analysis.

Results

Table 1 provides characteristics of local health care providers recruited to the study by each arm. Their mean ages were 40.5 and 42.5 years for the intervention and control arms, respectively, and all were male. Educational backgrounds differed for CHWs, but the distribution was the same between the 2 arms. All participants were familiar with and used cell phones or tablets on a daily basis, while the frequency of use of computers varied between individuals.

SUS was applied to 12 users of the eSkinHealth app in the intervention arm, and the results are shown in Table 2. The average scores at baseline, the midpoint (6 weeks), and the end of the study (12 weeks) were 72.3 (SD 11.5), 72.3 (SD 12.4), and 86.3 (SD 10.8), respectively.

The in-depth semistructured interviews were conducted with 20 participants from both arms: 5 nurses (3 from intervention, 2 from control) and 15 CHWs (7 from intervention, 8 from control). In addition, we invited 2 dermatologists and 2 program managers (district and national levels) for the interviews.

Two of the 3 nurses (66%) and 4 of the 7 CHWs (57%) in the intervention arm felt that it was initially a challenge to "manipulate" the app and also provide a diagnosis of skin lesions, and this challenge was overcome with time. The main difficulty faced with the app was over synchronization of data to the server due to poor internet connectivity in some study areas. Besides synchronization, no significant challenges or difficulties were mentioned.

> *The only problem I faced was the synchronization one...But with your [study team's] support, finally we are able to manipulate easily. Now I go quicker in synchronizing. It used to take more time but now within three minutes I can synchronize.* [CHW No 1-7, intervention]

Concerning the smart tablets, 2 CHWs of the 10 individuals (20%) in the intervention arm complained that the tablet was "big and heavy." One nurse and one CHW (20%) requested a flash function for the camera "because during the night it's difficult to take photos" (our tablets did not have flash embedded in their cameras). One nurse (10%) pointed out that the quality of photographs taken with tablets was poorer compared to smartphones.

All 3 nurses in the intervention arm (100%) were satisfied with the app because they can be in contact with dermatology specialists when encountering cases that are difficult to diagnose by messaging them and getting support. For the CHWs, 5 out of 7 (71%) mentioned that they were satisfied with the project, and their satisfaction came from being equipped with a tablet and an app. It created self-confidence in their job and also supported their increasing reputation in their communities.

> *Really! With this tablet, it made my work as a CHW easier. With this tablet, I am well known in my working area. My practice improved because now I can use the device which was given to me. I can register and synchronize myself. Also, I can now stand before a patient and speak [feel more confident]. In the past, I could not stand before a patient and speak to him without tension. Before I got the tablet, I did some referrals [to PHCs] but it was not with insurance. Knowing that I have the tablet, I can refer more people with more insurance about what I am doing.* [CHW No 1-4, intervention]

> *There is a change [to my practice] because in the past we used to work without any guidance, but now*

that we have the tablets, everybody comes to us. Now we take their photos and we send. Sometimes they come to us and ask: "where is my photo you took last time". When we open the tablet and show them the photos, then they trust us. [CHW No 1-11, intervention]

One nurse and 2 CHWs (30%) mentioned the benefit of portability of the app. With the app, they had the mobility to go see patients in their communities.

We are no more obliged to transport our register to conduct diagnosis. Everywhere we have the tablet, we can consult patients. [Nurse No 1-9, intervention]

Table 1. Characteristics of local health care providers in the study (N=12).

	Intervention	Control
Age (years), mean (SD)	40.5 (8.6)	42.5 (10.2)
18-29, n (%)	1 (8.3)	0 (0.0)
30-39, n (%)	5 (41.7)	6 (50.0)
40-49, n (%)	4 (33.3)	3 (25.0)
50 years or older, n (%)	2 (16.7)	3 (25.0)
Sex, n (%)		
Male	12 (100.0)	12 (100.0)
Female	0 (0.0)	0 (0.0)
Educational background, n (%)		
Primary school	3 (25.0)	3 (25.0)
Junior high school	4 (33.3)	4 (33.3)
Senior high school	1 (8.3)	1 (8.3)
University or graduate school	4 (33.3)	4 (33.3)
Occupation, n (%)		
Community health worker	8 (66.7)	8 (66.7)
Nurse	4 (33.3)	4 (33.3)
Working periods, n (%)		
Less than 1 year	2 (16.7)	1 (8.3)
1-5 years	2 (16.7)	1 (8.3)
6-10 years	5 (41.7)	4 (33.3)
More than 10 years	3 (25.0)	6 (50.0)
Frequency of use of cell phones/tablets, n (%)		
Every day	12 (100.0)	12 (100.0)
A few times per week or less	0 (0.0)	0 (0.0)
Frequency of use of computers, n (%)		
Every day	3 (25.0)	3 (25.0)
A few times per week	1 (8.3)	1 (8.3)
A few times per month	0 (0.0)	0 (0.0)
A few times per year	1 (8.3)	1 (8.3)
Never	7 (58.3)	7 (58.3)

Table 2. Results with System Usability Scale (SUS) scores (n=12)

System Usability Scale	Baseline, mean (SD)	Week 6, mean (SD)	Week 12, mean (SD)
I think that I would like to use this system frequently.	4.00 (0.00)	4.17 (0.94)	4.50 (0.80)
I found the system unnecessarily complex.	1.33 (0.65)	1.83 (1.53)	1.25 (0.87)
I thought the system was easy to use.	3.83 (0.72)	4.42 (0.67)	4.58 (0.79)
I think that I would need the support of a technical person to be able to use this system.	3.25 (1.82)	2.75 (1.77)	1.58 (1.38)
I found the various functions in this system were well integrated.	4.42 (1.17)	4.58 (0.79)	4.67 (0.65)
I thought there was too much inconsistency in this system.	1.25 (0.62)	2.25 (1.42)	1.25 (0.87)
I would imagine that most people would learn to use this system very quickly.	4.00 (1.35)	3.33 (1.56)	3.25 (1.77)
I found the system very cumbersome to use.	2.92 (1.51)	2.08 (1.56)	1.50 (1.24)
I felt very confident using the system.	4.42 (1.00)	3.75 (1.77)	4.67 (0.65)
I needed to learn a lot of things before I could get going with this system.	4.00 (1.48)	2.42 (1.68)	1.58 (1.38)
SUS score[a]	72.3 (11.5)	72.3 (12.7)	86.3 (10.8)

[a]Calculating SUS score: X = Sum of the points for all odd-numbered questions – 5; Y = 25 – Sum of the points for all even-numbered questions; SUS score = (X + Y) × 2.5.

All dermatologists and program managers interviewed (4/4, 100%) described the benefits of having the app to support nurses working in the very peripheral areas, allowing them to know the conditions of patients who are living hundreds of kilometers away, as most dermatologists are "concentrated in big cities." They all voiced the opinion that it has enabled capacity building for those nurses and CHWs and strengthened their ability to screen, diagnose, and treat skin diseases.

> *The app enable us to be close to our patients. We are far physically but close to them virtually with this application.* [Dermatologist No 1]

All participants at all levels (24/24, 100%) felt the benefits of the project in general. All nurses, including those from the control arm (5/5, 100%), voiced that the project benefited them in providing a better and more accurate diagnosis rather than just writing down "dermatosis" when they see skin conditions, ultimately benefiting their patients. They showed appreciation for training them on basic skin diseases, not only the targeted skin NTDs. In addition, several participants (6/24, 25%) mentioned that they had observed behavioral changes in community members and that more people were coming out to disclose their skin diseases, which they used to hide before the project.

> *When you make an accurate diagnosis, it's for the benefit of the patients. The patient are at the core of our activities. It's the patient who gains. We, in return are satisfied.* [Nurse No 1-12, intervention]

> *With the training in dermatology, now in my village, I'm known as a dermatologist. This is already a success in my job.* [Nurse No 2-1, control]

> *Dermatology is an area that I love but since I am not equipped, I could not do well. The project is welcome because it enabled us to go deeper and to know new things. We learnt basic skin lesions which are at the beginning of dermatology. It enabled us to learn more and to treat more disease than the five targeted ones.* [Nurse No 2-2, control]

During the study period, a total of 207 and 311 patients with skin conditions were recruited in the intervention and control arms, respectively. In the intervention arm, their mean age was 31.9 (SD 22.3), and 37.2% were female. In the control arm, their mean age was 20.1 (SD 18.6), and 46% were female. The composition of skin diseases registered by intervention and control arms is provided in Tables 3 and 4. A significant difference was observed in the number of cases of skin NTDs between the intervention and control arms, that is, 79 and 17 cases, respectively (P=.002; Table 3). Moreover, when the number of cases of skin NTDs in which dermatologists either made or confirmed diagnosis was compared between the intervention and the control arms, the difference was further widened by almost 10-fold (P<.001). One case of mycetoma, which is a skin NTD not well documented in Côte d'Ivoire and was outside our target skin NTDs, was diagnosed in the intervention arm with the remote support of a dermatologist. Proportions of child and female cases with confirmatory diagnoses of skin NTDs in the intervention arm are provided in Multimedia Appendix 3. Besides the skin NTDs, more skin diseases and conditions were reported from the control arm than from the intervention arm (P<.001; Table 4). However, 100 cases (66%) were not given any particular diagnosis or description of a condition in the control arm and were documented only as a "dermatosis." For a total of 320 cases that were registered from both intervention and control arms, 53 different diagnoses and conditions were indicated. This list is provided as Multimedia Appendix 4.

In the intervention arm, a total of 151 cases (72.9%) were diagnosed on the eSkinHealth platform. The median number of days from entry to diagnosis by remote dermatologists was 21 (IQR 25%-75%, 16-63) and the average was 34.9 (SD 25.5) days. The diagnosis of 54 cases (26.1%) was supported on-site by dermatologists during field visits due to any reason, including upload failure of images to the server, at the time of reviewing the patient file. Three cases in the intervention arm were diagnosed from the results of a skin biopsy performed during the field monitoring visit (lichen planus, pyogenic granuloma, and atheroma). In the control arm, the diagnosis of 20 patients (6.4%), among whom 3 patients had skin NTDs, was confirmed by dermatologists during the monitoring field visit; 11 patients (3.5%) were referred to the district general hospital; the rest were nonconfirmed.

Results on the comparison of diagnoses by nurses in the intervention arm against those by dermatologists are shown in Table 5. The overall diagnosis rate of skin NTDs by nurses was 62%, with the highest for yaws (with the use of a rapid diagnostic kit) followed by scabies.

Table 3. Number of cases of skin diseases, intervention versus control—skin-related neglected tropical diseases (skin NTDs).

	Intervention				Control				Total cases confirmed, n (%)
	Confirmed[a]	Suspected	Subtotal	Confirmed cases among all cases, %	Confirmed[a]	Suspected	Subtotal	Confirmed cases among all cases, %	
Buruli ulcer	26	0	26	100	1	2	3	33.3	29 (93.1)
Leprosy	11	0	11	100	1	0	1	100	12 (100)
Lymphatic filariasis	4	0	4	100	0	0	0	N/A[b]	4 (100)
Mycetoma	1	0	1	100	0	0	0	N/A	1 (100)
Scabies	34	0	34	100	0	6	6	0	40 (85.0)
Yaws	3	0	3	100	6	1	7	85.7	10 (90.0)
Total	79	0	79	100	8	9	17	47.1	96 (88.5)

[a]Includes cases either diagnosed or confirmed by dermatologists.

[b]N/A: not applicable.

Table 4. Number of cases of skin diseases, intervention versus control—skin diseases and conditions besides skin-related neglected tropical diseases (skin NTDs).

	Intervention	Control	Total
Registered with diagnosis or condition[a], n	126	194	320
Registered only as "dermatosis," n	2	100	102
Total, n	128	294	422
With diagnosis or condition, %[a]	98.4	66.0	74.6

[a]Includes both confirmed and suspected diagnosis.

Table 5. Number of cases of skin-related neglected tropical diseases (skin NTDs) diagnosed by nurses and additionally diagnosed by dermatologists.

Disease	Cases diagnosed by nurses, n	Additional diagnoses by dermatologists, n	Diagnosis rate by nurses, %
Buruli ulcer	13	13	50.0
Leprosy	4	7	36.4
Lymphatic filariasis	2	2	50.0
Mycetoma	0	1	0
Scabies	27	7	79.4
Yaws	3	0	100
Total	49	30	62.0

Among all registered patients (n=207) in eSkinHealth, 59 cases (28.5%) were detected by the CHWs and were referred to the nurses. For the control arm, this was unclear as instructions on using referral paper forms were not followed. Alternatively, photographs of skin lesions were taken for 92 patients and 58 patients by CHWs and nurses using smartphones or tablets provided to them, respectively. Through reviewing these 2 image sets, at least five cases were photographs of the same patients, suggesting that these cases were referred from CHWs to nurses. Although the images were taken, the participants in the control arm did not organize the photographs with patient information as instructed, and further assessment of the images was therefore not possible, resulting in a high number of non-confirmed cases.

In the intervention arm, 24 of 207 patients (11.6%) had 1 follow-up (this excludes the first visit), 11 patients (5.3%) had 2 follow-ups, and 3 patients (1.4%) had 3 follow-ups entered by the nurses. This data was not available for the control arm.

Discussion

Principal Findings

This paper reported on a 3-month pilot trial to evaluate the usability and effect of the eSkinHealth app for the early detection and management of skin NTDs and other skin conditions in remote communities in sub-Saharan Africa. This app has been our invention, and to our knowledge, there is currently no other mHealth app of the kind that is developed for the collection of clinical data on skin diseases that can be used both online and offline, making it fit for use in LMICs. We found that our app was appreciated by most users, as shown by the high SUS scores as well as our interview results. On the other hand, while the app is developed to be capable of offline usage, the difficulty was still felt with the poor internet connectivity when uploading and retrieving data.

While our SUS scores were rated "excellent" for all 3 time points, they significantly increased during the intervention, jumping from a mean of 72.3 both at baseline and week 6 to 86.3 at the end of the project. This could be showing that the time needed to get accustomed to the system was around 2 to 3 months. We do not necessarily consider this to be overly long, as the usage of the app involves a behavioral change in their daily practice, and usually behavioral change takes time [36]. This being the case, we still need to make efforts to improve our system to increase usability and feasibility. In addition, although one of the major functions and expectations of the app was for it to be used for following up on patients, only a limited proportion of patients (18.3%) had more than one follow-up. While not enough time has elapsed for most patients to require follow-up and to assess this, it may also be an indication that this function was not well understood by our participants. Moreover, when participants were asked why follow-up data were not taken, oftentimes their replies were that "patients did not come back." Losses in follow-up rates in LMICs, especially in sub-Saharan Africa, for any condition are known to be high due to multiple factors [37-39]. There is potential for mHealth tools and telemedicine systems to fill this gap [40].

The benefits of using the app were shown by the higher number of targeted skin NTDs diagnosed in the intervention arm as compared to the control arm. However, it was interesting to see that more patients with skin diseases and conditions were documented in the control arm, which may be demonstrating the high prevalence of skin diseases in these communities, supporting previous reports [1-7]. Or, it could also be that with the decision-support provided by the eSkinHealth app, the patients seen by providers in the intervention arm were more likely to be screened out. Although we did not explicitly hear about the workload of entering data into the eSkinHealth app, the lower number of cases in the intervention arm for the overall number of skin diseases could possibly also be explained by the felt need for extra time in seeing a patient and entering their data in the system. During this pilot study, we did not measure the time required to register each patient, which should be considered for our future studies. Nevertheless, while there were more patients registered in the control arm, one-third of them were only documented as "dermatosis" compared to only 2 undiagnosed cases in the intervention arm, which was a significant change in their practice between the 2 arms; with the intervention, patients were now provided with their diagnosis. This was also described by our participants during their interviews.

Some users of the app voiced difficulties with "synchronization," or the uploading or retrieving of data. This was mainly due to 2 factors: the location of the users and the data size of the images. The issue was mostly experienced by the same users living in more remote rural areas with poor network connectivity. Poor or no connection to network services has been one of the major challenges shared across projects aiming at implementing mHealth strategies in LMICs [19,41,42]. In our study, sometimes changing the network service improved their synchronization. Nonetheless, most times, text data were able to be transmitted to the server, but the major challenge was with images, as they require a larger bandwidth. This limited the remote diagnosis by dermatologists and therefore had a considerable impact on the overall project outcome. The size of each image was 2080 × 1560 pixels. There is no universally accepted standard for image sizes for teledermatology, and recommendations vary between guidelines and reports [43-45]. On the other hand, there is a report that states that a minimal image size can be 768 × 512 pixels, and above this does not substantially improve the results [46]. Therefore, 1 option for us is to decrease the size of the images to make them more transmissible, but this requires careful consideration. This may limit us, for example, in the accuracy of diagnosis and future usage of the collected images. Although there is ever-increasing connectivity globally, there are still challenges to overcome in the settings of LMICs, and there is a constant need to think about how we can overcome them.

Dermatologists supported 27% of cases in the intervention arm for diagnosis on-site during monitoring visits. One reason for this was the absence of images owing to the abovementioned issue of synchronization, and images were absent for making remote consultations. Or sometimes, images taken by local health care providers were of poor quality to make a diagnosis. There was no function where dermatologists could indicate these issues during the time of this pilot project, and therefore, unfortunately, we were unable to calculate the number of cases that fell into these categories. This is currently being addressed. Yet another reason for an on-site diagnosis was due to the nature of the disease. Subcutaneous conditions such as atheroma and lipoma are difficult to diagnose remotely through regular photographic images, and these conditions tended to be diagnosed on-site. This observation is supported by previous studies showing that teledermatology with regular photographs is useful for superficial lesions but is limited otherwise [47].

Indeed, we observed definite advantages of using the app and the platform established around it in the management of skin diseases at our study sites compared to not using it. A timely and accurate diagnosis of both skin NTDs and other locally prevalent skin diseases has potential benefits beyond what can be quantified during the brief period of this study's implementation. These can include the prevention of disabilities and a better understanding of disease epidemiology. It is also a very scalable intervention that would ultimately leverage scarce in-country dermatologists and international dermatologists to supplement and complement local health care workers. We also observed that our participants improved their knowledge of dermatology over time while using the app, which we plan to measure in our future project. It is a limitation of this study that we were unable to provide accurate data for the control arm, while simultaneously representing the advantages of using the app. While we did train our participating providers in the control arm to take photographs and organize them so that we could compare the 2 arms, this was not pursued adequately to make valid comparisons between the 2 arms. Involving CHWs in our approach was effective, as they are the ones who are the closest to patients, as has also been demonstrated in previous studies [42]. We observed that the referral pathway created by the eSkinHealth app worked, with close to 30% of cases diagnosed being those that were connected from CHWs to PHCs. If CHWs can be empowered and involved more, for instance by being equipped with the app, this may contribute to the control of skin diseases, including skin NTDs, to a large extent. In a systematic review that investigated involving CHWs in the delivery of primary health care services through the use of mHealth tools, it was found that not only did mHealth tools change how CHWs delivered care, but they also led to new forms of positive engagement and relationships with people in their communities, creating self-confidence [42]. Similar findings were observed among the CHWs in our study.

Through our study, one case of mycetoma, which is listed as one of the skin NTDs but was outside of our target diseases, was identified. This was because we were unaware that the disease existed at our study sites. This indicates that diseases such as mycetoma are being missed and remain unreported due to a lack of awareness. Moreover, 6 cases of snakebites were reported from the control arm. Snakebite is not a disease grouped as a skin NTD, but it is one of the NTDs recently added to the WHO NTD list in 2017. While its occurrence and management differ largely from those grouped as skin NTDs, snakebites also manifest as skin lesions and, therefore, can potentially be part of an integrated approach for skin NTDs. It is important that efforts are made to gain a better understanding of the epidemiology, ideally in combined efforts to save resources and time, to support the implementation of effective and efficient disease control measures for these diseases [14]. Our integrated training on dermatological conditions not limited to skin NTDs was highly welcomed by local health care providers, and this kind of approach should be promoted with relevant diseases in the community.

A report of some conditions that were not part of the set menu of skin diseases included in the eSkinHealth app allowed us to consider further improvements. Fifteen cases of sexually transmitted diseases (STDs) (5 females and 10 males) were reported from the control arm and one (secondary syphilis) from the intervention arm, which was a critical finding of this study. Although we do not know their exact diagnosis, this result indicated that this set of diseases existed in the communities but was not registered in eSkinHealth. This may also imply that it is difficult to obtain patient consent for registering them on the digital platform and taking photographs of their private body parts. Meanwhile, patients with hydroceles and hernias involving male genital areas were registered, and so it is suspected that it is not only about the body parts that patients become hesitant about disclosing their disease. There is much stigma and discrimination around STDs, and their disease burden in these communities is largely hidden [48-50]. This needs to be addressed in some way or other, however, which may be a difficult area for a digital health tool to intervene in.

Limitations

We acknowledge several limitations of our study. First, although the app can be used offline, an internet connection is required for certain functions. Poor internet connectivity affected our results and hindered the assessment of its true effectiveness. For instance, some patients underwent diagnosis on-site by dermatologists rather than through the app during our monitoring visits. Furthermore, some of the benefits of the project outlined here may have come from the monitoring visits that were made by the study team and therefore cannot solely be attributed to the effectiveness of the app. However, it was important that we paid these monitoring visits to support our participants in using the system and to follow our study protocol. Second, all our participants were male. Usually, nurses working in PHCs in these remote communities are mostly male because females tend not to volunteer to be placed in such areas as it involves some duties traditionally not done by women in this setting, such as traveling to difficult-to-reach villages on motorbikes. Some diseases may have been missed due to this gender imbalance among our participants, such as STDs in females. Lastly, this is a pilot trial involving 8 PHCs in 1 health district, and therefore, the study findings may not be generalizable to other health districts in Côte d'Ivoire. We believe that additional research is needed to further evaluate the usability and effectiveness of the eSkinHealth app, taking the learnings from this pilot study into account as it launches and becomes more widely used.

Conclusions

The burden of skin diseases in LMICs is often neglected, as many are not considered fatal. It is in LMICs and marginalized communities that mHealth tools could be most useful and valuable [40]. This study examined the usability and effectiveness of the eSkinHealth app to improve the early detection and case management of skin NTDs and other skin conditions, which provided promising results. It is also portable, and therefore, it can be used in remote communities in LMICs where infrastructure is usually very poor. We plan to further test our app in a wider region of sub-Saharan African countries. Furthermore, given the importance of improving the early detection and case management of skin NTDs in LMICs, our study results provide a compelling rationale for infectious disease policymakers and decision makers regarding mHealth interventions for skin NTDs in these settings.

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Data Availability

The data sets generated or analyzed during this study are available from the corresponding author on reasonable request.

Conflicts of Interest

None declared.

Multimedia Appendix 1

System Usability Scale (French version) used in the study.

[PDF File (Adobe PDF File), 107 KB - derma_v6i1e46295_app1.pdf]

Multimedia Appendix 2

Topic guidelines fro semistructured in-depth interviews.

[PDF File (Adobe PDF File), 18 KB - derma_v6i1e46295_app2.pdf]

Multimedia Appendix 3

Number of child and female cases of skin-related neglected tropical diseases confirmed in the intervention arm.

[PDF File (Adobe PDF File), 23 KB - derma_v6i1e46295_app3.pdf]

Multimedia Appendix 4

Skin diseases and conditions reported besides skin-related neglected tropical diseases (intervention vs. control).

[PDF File (Adobe PDF File), 45 KB - derma_v6i1e46295_app4.pdf]

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Abbreviations

CHW: community health care worker
IRB: institutional review board
LMIC: low- and middle-income country
mHealth: mobile health
NTD: neglected tropical disease
PHC: primary health center
Skin NTD: skin-related neglected tropical disease

SUS: System Usability Scale
WHO: World Health Organization

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Original Paper

A Mobile Health App for Facilitating Disease Management in Children With Atopic Dermatitis: Feasibility and Impact Study

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Abstract

Background: Inadequate control of atopic dermatitis (AD) increases the frequency of exacerbations and reduces the quality of life. Mobile health apps provide information and communication technology and may increase treatment adherence and facilitate disease management at home. The mobile health app, Atopic App, designed for patients and their caregivers, and the associated web-based patient education program, Atopic School, provide an opportunity for improving patients' and caregivers' engagement and adherence to the management of AD.

Objective: This noninterventional, observational study aimed to explore the feasibility and potential impact on the management of AD in children by caregivers using the Atopic App mobile health app.

Methods: The patient-oriented eczema measure (POEM) and numerical rating scale for the grading of pruritus were used as severity scores (scale range: 0-28). The artificial intelligence model of the app was used to assess the severity of AD based on the eczema area and severity index approach. The deidentified data enabled the analysis of the severity of AD, treatment plan history, potential triggers of flare-ups, usage of available features of the app, and the impact of patient education.

Results: During a 12-month period, of the 1223 users who installed the app, 910 (74.4%) registered users were caregivers of children with AD. The web-based Atopic School course was accessed by 266 (29.2%) caregivers of children with AD, 134 (50.4%) of whom completed the course. Usage of the app was significantly more frequent among those who completed the Atopic School program than among those who did not access or did not complete the course (P<.001). Users who completed a second POEM 21 to 27 days apart exhibited a significant improvement of AD severity based on the POEM score (P<.001), with an average improvement of 3.86 (SD 6.85) points. The artificial intelligence severity score and itching score were highly correlated with the POEM score (r=0.35 and r=0.52, respectively).

Conclusions: The Atopic App provides valuable real-world data on the epidemiology, severity dynamics, treatment patterns, and exacerbation-trigger correlations in patients with AD. The significant reduction in the POEM score among users of the Atopic App indicates a potential impact of this tool on health care engagement by caregivers of children with AD.

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KEYWORDS

atopic dermatitis; eczema; Atopic App mobile health application; artificial intelligence; dermatitis; dermatology; skin; disease management; child; children; pediatric; pediatrics; feasibility; mHealth; mobile health; app; apps; applications; applications

Introduction

Atopic dermatitis (AD) ranks highest among all skin disorders as a cause of lost disability-adjusted life-years in patients worldwide [1]. Poor medication adherence is a major barrier to treatment success in AD and results from various underlying causes, including forgetfulness, medication side effects, complex dosing regimens, cost barriers, a lack of understanding about the importance of the medication, and disruptions to daily activities [2,3]. Addressing these barriers often requires a multidisciplinary approach involving health care providers, parents, and the child, which is very time-consuming and imposes an additional barrier. A number of solutions have been offered to date to address barriers for poor medication adherence, such as patient education, medication simplification, and telemedicine. Research investigating action plans as educational tools for managing pediatric AD or teledermatology revealed that the effectiveness of these measures was either unexamined or considered insignificant [4,5], with a notable absence of reports on how treatment simplification impacts patients' adherence. In a systematic review of 11 studies exploring the therapeutic adherence of mobile apps, 7 studies confirmed that use of the mobile app increased treatment adherence [6]. The use of mobile apps in AD is still uncommon, and few of these have been scientifically studied; existing studies have mainly demonstrated a given app's feasibility and involved small numbers of users [7,8].

The use of artificial intelligence (AI) in mobile health apps for the management of AD involves machine learning algorithms and data analysis techniques to assist in various aspects of AD care. AI in these apps may help with tasks such as assessing the severity of AD, providing personalized treatment recommendations, predicting flare-ups, and enhancing the overall management and monitoring of the condition. AI-driven features aim to improve patients' and caregivers' involvement in the treatment process and to improve adherence.

The Atopic App was developed following a series of 20 in-depth interviews with dermatologists, allergists, adult patients with AD, and parents of children with AD that aimed to identify difficulties in the management of AD in home settings. The app uses a numerical rating scale for grading the severity of pruritus [9] and the patient-oriented eczema measure (POEM) [10] as a global severity score.

AI can assist in tailoring treatment plans for individuals with atopic eczema by analyzing patient data, including lifestyle factors, environmental conditions, and treatment responses. Attempts to develop accurate automated measurements of eczema severity using images have shown promising results. While impressive accuracy was achieved in the diagnosis and assessment of the severity of AD [11-13], to reap the technological benefits in remote patient monitoring and self-management, there is a need to validate the results of AI models on the images taken by patients in home settings.

Our app's AI model was designed to evaluate the severity of AD using the eczema area and severity index (EASI) method. This AI severity estimation model was embedded into the Atopic App for the analysis of images taken by users at home.

The AI severity model was previously trained on publicly available digital images on the internet. An image search was conducted based on the keywords "eczema" or "atopic dermatitis" and reviewed by 2 certified dermatologists. Only images that were unequivocally considered representative of AD were used for the AI training. The affected area was marked by the dermatologists using the Computer Vision Annotation Tool (Intel) [14]. The images were split into training and testing sets. A HarDNet model [15] was trained to recognize skin versus nonskin, skin with signs of AD, and each sign along with the severity. The images were augmented using the *albumentations* library [16,17] and shrunk to 384 × 384 pixels prior to feeding to the model [17]. The intersection over union was used as a loss function [15].

The Atopic App [18] is available as a free download in the App Store and Google Play for patients with AD and their caregivers. A Chabot-guided onboarding process includes completion of the POEM questionnaire, acquisition of clinical photographs and the numerical rating scale for the severity of itch [19], transcription of action plans [20] prescribed by a treating physician, documentation of suspected triggers of exacerbations, and patient education by the web-based Atopic School program [21].

The purpose of this noninterventional, observational study was to assess the feasibility of the Atopic App mobile health app in terms of in-app retention and engagement, the accuracy of the AI algorithm, the impact on patients' adherence, and subsequent disease severity in children with AD.

Methods

Ethical Considerations

The Institutional Helsinki Committee concluded that the research satisfied the criteria for exemption from additional review and a waiver for informed consent. All collected data were deidentified.

Study Design

The study participants were users of the app who downloaded the free Atopic App between May 2021 and April 2022 and declared that they are parents or caregivers of a child with AD. The collected demographic data included the date of birth and gender of the person with AD.

The app reminded users to submit a subsequent POEM on the seventh day after completion of the previous POEM by daily push notifications until the form was submitted again.

AI severity scores were calculated for the images taken by users of the mobile app as follows: (1) the percentage of skin affected by AD on the image was calculated as a percentage of the number of pixels classified by the model as skin with signs of AD out of all pixels classified as skin on the image, (2) the percentage of the affected skin was converted into an area score from 0 to 6 based on the EASI scoring method, (3) the severity of each of the EASI categories was averaged for each image based on the number of pixels representing different severities, and (4) the final severity score was calculated for each image by multiplying the area by the severity score. The resulting severity scores ranged from 0 to 72.

Statistical Analysis

The collected data were extracted using SQL queries from PostgreSQL tables and further refined with Python scripts [22]. The data were then analyzed using paired *t* tests, Mann-Whitney U tests, Wilcoxon signed-rank tests, Pearson correlations, and multiple regression.

For evaluation of patients' adherence, the app users were divided into 3 groups. Cohort 1 included users who did not register for the Atopic School, cohort 2 included users who registered but did not complete the program, and cohort 3 included users who completed the program. Atopic School was considered completed if users scored ≥80% of correct answers in a quiz at the end of each of the following program sections: AD basics, skin care in AD, management of flares, and triggers of exacerbation.

AI accuracy in the determination of AD severity was determined using multiple regression analysis of POEM scores and AI-estimated severities from the submitted images. Only cases that had images obtained and submitted by users in the preceding 0 to 6 days were included in the analysis. Correspondingly, each POEM record was matched with an average AI severity and itch score recorded over the course of the 0 to 6 days preceding the POEM completion for a given user.

The following data were included in the multiple linear regression analysis of the relationship between POEM scores and independent variables: age, gender, recorded medications, recorded triggers, AI AD severity score, and itch score. An *F* test was used as a measure of a model's accuracy on a data set.

To assess the impact of the app in a real-world context, POEM scores were categorized into 5 severity levels [23]: clear or almost clear (scores 0-2), mild (scores 3-7), moderate (scores 8-16), severe (scores 17-24), and very severe (scores 25-28).

Results

During the 12-month period from May 2021 to April 2022, 1223 people downloaded the app. Of these, 888 (72.6%) were parents of a child with AD, 224 (18.3%) were adults with AD, and 111 (9.1%) were other caregivers of patients with AD. In total, 910 (74.4%) registered users were caregivers of children with AD; of these children with AD, 494 (54.3%) were boys and 416 (45.7%) were girls. The age distribution of the registered children with AD is presented in Figure 1.

The period between the first and the last launch of the app ranged from 0 to 366 days, and 165 (18%) users used the app for more than 4 weeks. Of the 910 users who were caregivers of children with AD, the web-based Atopic School patient education course was accessed by 266 (29.2%) users, of which 132 (49.6%) did not complete the course (cohort 2) and 134 (50.4%) did complete the course (cohort 3). The remaining 644 (70.8%) users did not register for the education course (cohort 1). Users who completed the education course used the app twice as frequently during the 3 months after the installation of the app compared to those who did not take the education course ($P<.001$).

The POEM was completed at least once by 775 (85.2%) of the users who were caregivers of children with AD. The median POEM score at the time of registration in the application was 10 (IQR 6-14; range 0-28). The distribution of severity as measured by POEM score is presented in Figure 2.

A total of 51 users completed a subsequent POEM 21 to 27 days apart from the first POEM. There was a statistically significant difference ($P<.001$) between the first and subsequent POEM scores. A decrease in the POEM score was observed for 36 (70.6%) users, while 3 (5.9%) users showed no difference and 12 (23.5%) users reported an increase in the subsequent POEM score (Figure 3). The average decrease in the POEM scores was 3.86 points ($P=.001$, Wilcoxon signed-rank test; Figure 4). A prominent shift from the more severe categories to the milder categories based on the POEM scores was observed from day 1 to days 21-27 (Table 1).

A total of 3385 photos were taken by 364 (40%) users. Of these, the data from 204 (56%) users were considered complete and were included in the multiple linear regression analysis to assess the relationship between POEM scores and several independent variables. Data from the remaining 160 (44%) users were excluded from the analysis because these users did not provide corresponding POEM scores after taking their photos. The AI severity and itching scores were highly significant predictors of POEM score ($P<.001$), while the presence of triggers ($P=.14$), medication records ($P=.18$), age ($P=.29$), and gender ($P=.95$) were weak predictors of POEM score, as expected. An *F* test was used as a measure of the model's accuracy on the data set (multiple R=0.58, $F_{6,294}=25.2529$, $P<.001$).

The AI severity score and itching score were highly correlated with the POEM score for photos taken during the 7 days leading up to and including the day of POEM completion ($r=0.35$ and $r=0.52$, respectively) (Figures 5 and 6). Conversely, age, gender, medications, and triggers were not significantly correlated with POEM scores (Table 2).

Among the 910 caregivers of children with AD, 330 (36.3%) documented prescribed action plans, which included using emollients (n=301, 91.2%), topical medication (n=126, 38.2%), and systemic medication (n=69, 20.9%). Topical corticosteroids were included in the action plans of 25.5% (n=84) of patients, while topical calcineurin inhibitors were included in 13.0% (n=43) of patients. Oral antihistamines were the most common systemic medication in children with AD (n=53, 16%). Systemic anti-inflammatory drugs were not prescribed in the action plans of any patient.

At least 1 potential trigger was suspected by 443 (48.7%) users (Table 3).

Figure 1. Age distribution of children with atopic dermatitis cared for by users of the Atopic App.

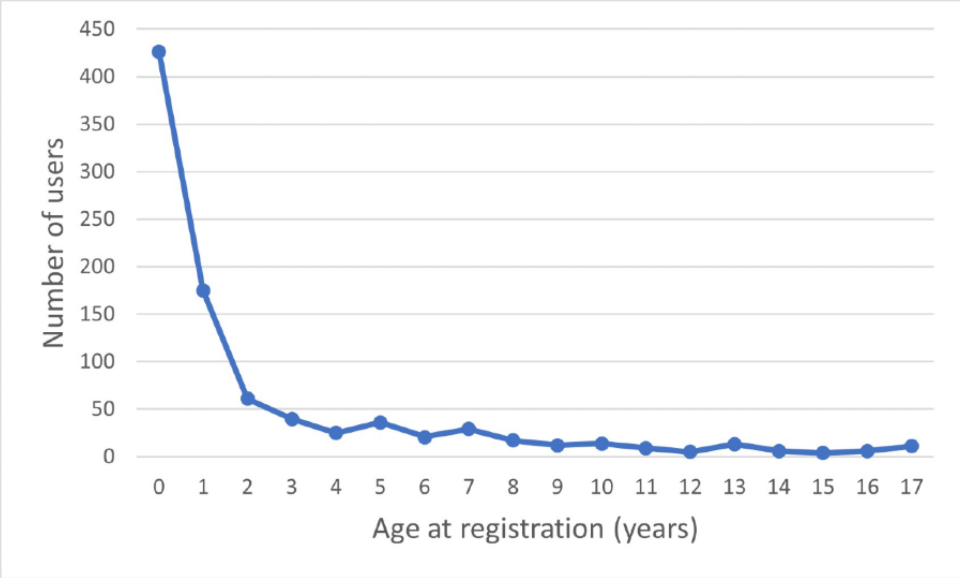

Figure 2. POEM score of children with atopic dermatitis cared for by users of the Atopic App at the time registration. POEM: patient-oriented eczema measure.

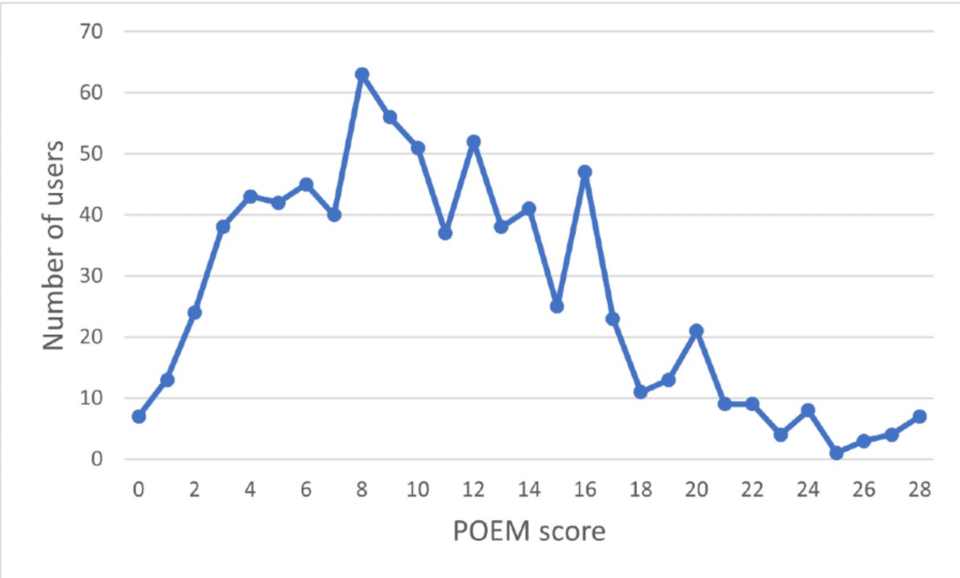

Figure 3. Change in POEM scores from day 1 to day 21-27 by user percentiles. POEM: patient-oriented eczema measure.

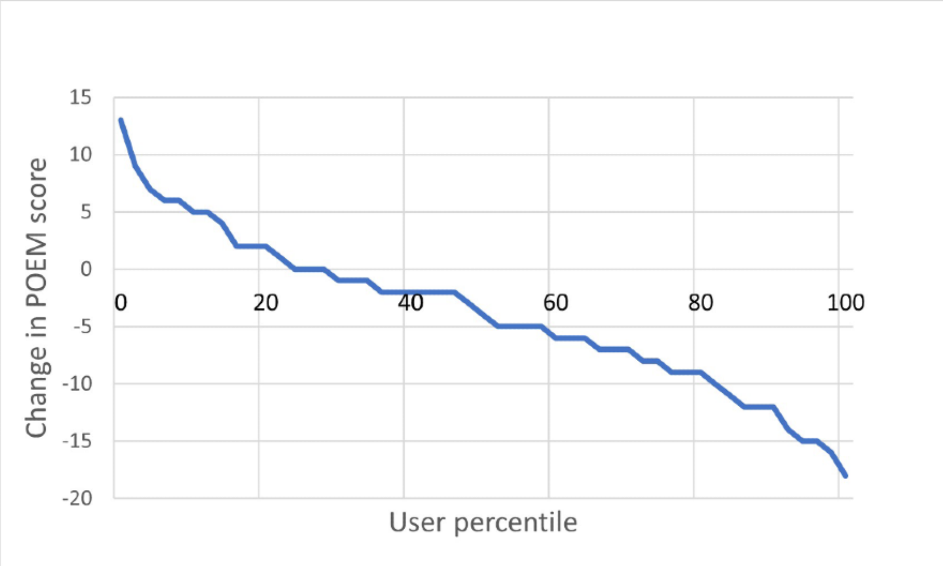

Figure 4. Distribution of POEM Scores at Day 1 and Days 21-27. The error bars represent the minimum and maximum values excluding outliers. POEM: patient-oriented eczema measure.

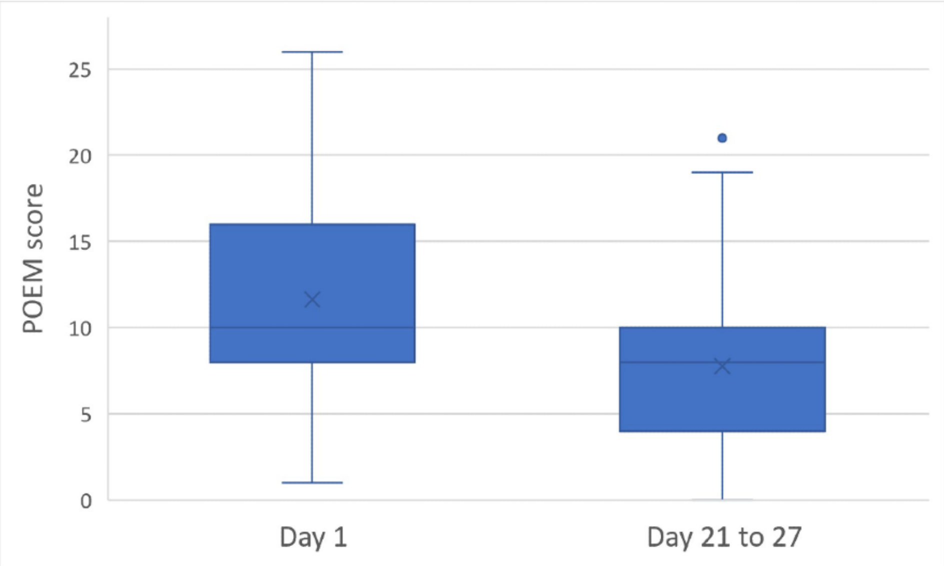

Table 1. A shift in severity categories based on patient-oriented eczema measure scores on day 1 and days 21 to 27.

Severity	Day 1, n	Days 21 to 27, n
Clear or almost clear	2	7
Mild	10	18
Moderate	31	22
Severe	7	4
Very severe	1	0

Figure 5. Normalized correlation between POEM and severity scores of AD predicted by AI. AD: atopic dermatitis; AI: artificial intelligence; POEM: patient-oriented eczema measure.

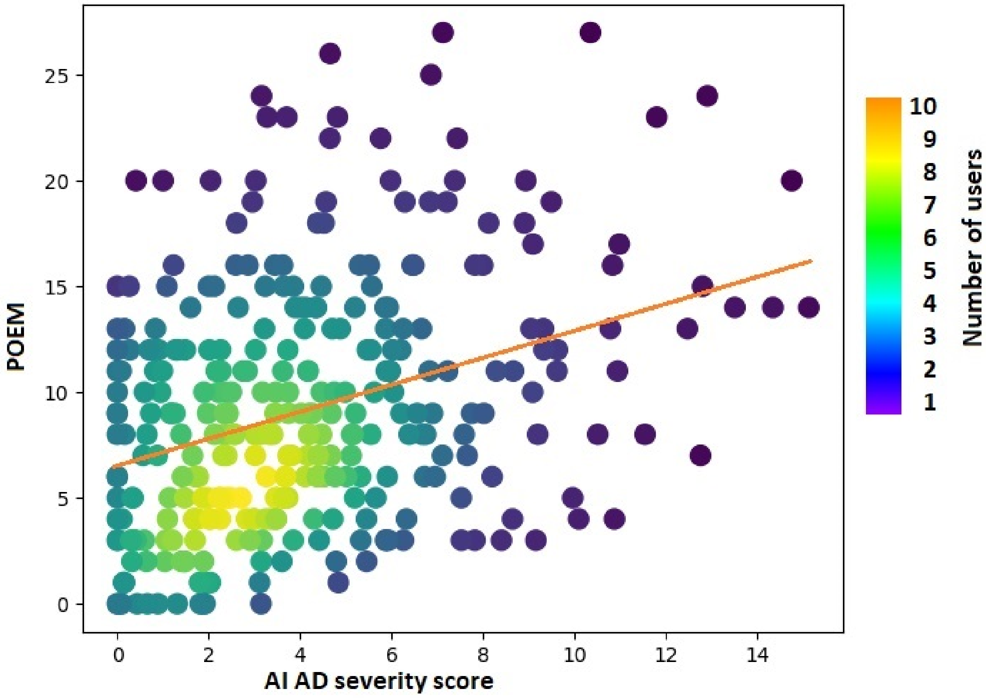

Figure 6. Normalized correlation between POEM and itch scores. POEM: patient-oriented eczema measure.

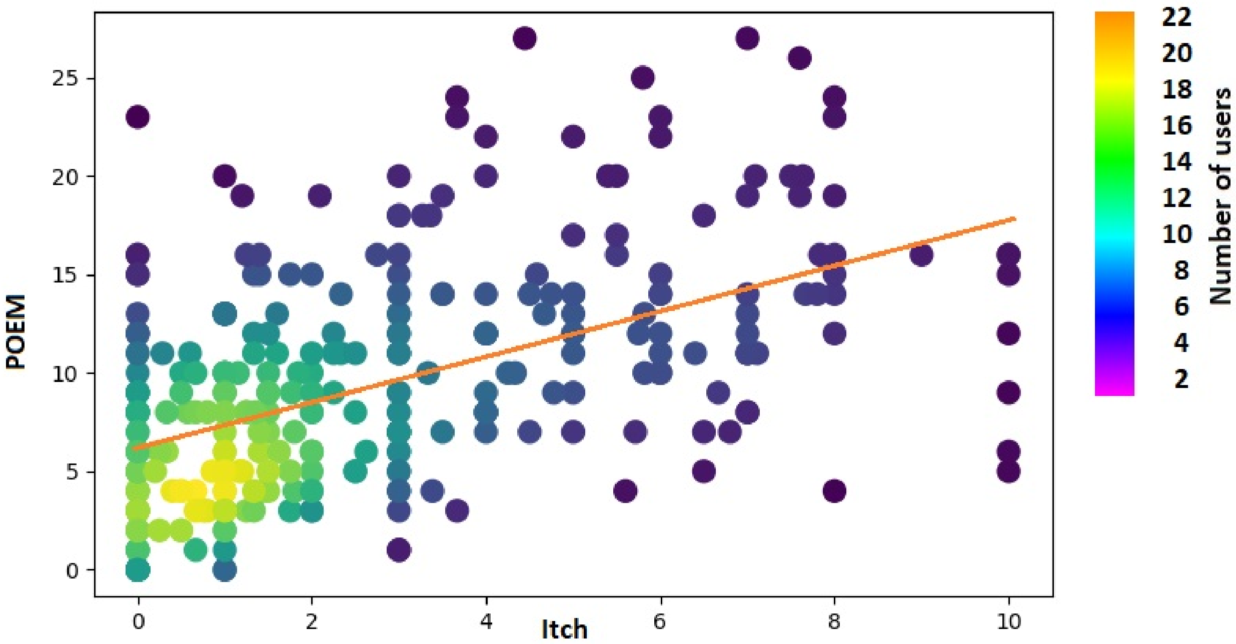

Table 2. Correlation coefficients between patient-oriented eczema measure scores and each independent variable.

Variable	*r*
Age	0.08
Gender	0.01
Recorded medications	0.11
Recorded triggers	–0.02
Average itching score	0.52
Average AI[a] AD[b] severity prediction score	0.35

[a]AI: artificial intelligence.

[b]AD: atopic dermatitis.

Table 3. Prevalent triggers suspected by users of the Atopic App.

Trigger	Users who added the trigger (n=443), n (%)
Dry air	275 (62.1)
Cow’s milk	195 (44)
Dust	191 (43.1)
Sweating	181 (40.9)
Pets	174 (39.3)
Heat	154 (34.8)
Stress	149 (33.6)
Detergents	141 (31.8)
Chicken eggs	138 (31.2)
Viral or bacterial diseases	102 (23)
Soap	80 (18.1)
Cereals	80 (18.1)
Synthetic clothing	74 (16.7)
Fish	73 (16.5)
Nuts	71 (16)
Cleaning products	58 (13.1)
Peanut	55 (12.4)
Seafood	47 (10.6)
Wool clothing	46 (10.4)
Tobacco smoke	46 (10.4)

Discussion

Principal Findings

There is a growing list of AD-related mobile apps [8]. Only a few of these are designed for bidirectional communication between patients or caregivers and the app, and they primarily focus on assessing the severity of the disease. The most important feature required for the development of mobile apps for caregivers of children with AD is an educational functionality, including knowledge of the disease, management of symptoms, medication usage, and triggers [8]. Unlike other mobile apps for AD management, the Atopic App contains Chabot-directed instruction of proper use of the app’s features and targeted education for enhancing adherence in the management of AD. The Atopic App also includes the basic features found in other apps. Other exceptional features of the app include its associated web-based patient-education program (Atopic School), AI assessment of severity, integration of action plans, and its ability to identify personal trigger factors for AD exacerbations.

Currently, there are no publications on the usability, acceptability, or impact of any of these apps in patients with AD or their caregivers, resulting in an inability to compare feasibility findings using our app to other available mobile health apps for AD. The most recent studies on mobile apps for AD focused on the burden of the disease as determined by itch score, quality of sleep, and energy or stress levels and involved a small number of users that precluded assessment of the clinical significance and impact of the app [7,24].

This study reports on the largest cohort of mobile app users in the management of AD. The similar correlations between POEM and itch scores and between POEM and AI severity scores indicate the usefulness and accuracy of the AI algorithm of the Atopic App in predicting AD severity.

The real-life impact demonstrated by the increase in the clear or almost clear POEM score category between day 1 and days 21 to 27 indicates that patients whose caregivers repeatedly used the app experienced a complete or nearly complete resolution of their symptoms, possibly related to improved engagement and adherence rates for prescribed treatments during the period of the study.

Environmental factors, like ambient climate conditions, dust, food allergens, pets, and clothing, can significantly impact AD flare-ups. The relevance of environmental factors can vary from person to person. Identifying and managing these triggers on an individual basis is essential for effectively controlling AD symptoms—this aspect of the management of AD was facilitated by the Atopic App.

The incorporation of novel technology has the potential to improve patients' engagement and therapy adherence. It has been advised that easily implementable interventions should encourage parents and older children to take photographs and use clinician-designed apps that can deliver regular portable reminders with written plans of treatment regimens [20,25]. Documentation of prescribed action plans on the app may have improved treatment adherence, leading to an improvement in disease severity, at least among those users who had recorded sequential POEM scores in this study.

Nonadherence to therapy has been associated with poor therapeutic outcomes [26]. To improve adherence, health care providers are expected to motivate patients and their parents to adhere to treatment through appropriate patient-tailored education programs [27]. Clinical studies exploring the effects of mobile apps indicate that they promote treatment adherence [6].

Access to smartphones among adults is almost universal, and mobile app usage is also growing substantially, with adolescents representing the fastest growing sector to adopt smartphone technology [28].

Limitations of the Study

There are multiple inherent limitations in studies that explore mobile health apps as auxiliary tools for optimizing outcomes in chronic diseases, including selection bias, a lack of control groups, unknown external confounding factors, and short observation periods.

Several user-driven factors affected the computation of the AI severity score, such as the distance between a smartphone camera and the affected skin, illumination conditions, and reporting bias, including selection of the area photographed. These factors, which potentially represent an obstacle for the reproducibility and comparability of AI severity estimations, should be addressed in the future by incorporating automated control over the illumination and distance during the process of photographing and providing clear instructions for the user.

The real-life impact demonstrated by the shift toward a milder severity of disease correlated with more frequent usage of the app may represent self-selection bias of a subset of highly motivated caregivers whose engagement and adherence levels may not be representative of the broader population of caregivers of children with AD. Additionally, there were possible obstacles for Atopic School attendance and completion that will be addressed in updated versions of the app. These include the lack of regular prompts to sign up for Atopic School and engage with the educational content and the dual registration process, whereby after initial registration within the app, logging in to the Atopic School course required a separate registration that demanded an additional effort and may have posed a barrier.

Conclusion

The Atopic App is a valuable source of real-world data on the epidemiology, severity dynamics, treatment patterns, and exacerbation-trigger correlations in patients with AD. The Atopic App is a promising tool that can help increase the health care engagement of patients with AD and their caregivers. Addressing the limitations of this study in newer versions of the Atopic App can improve the feasibility and impact of the mobile health app for managing AD in children by caregivers.

Conflicts of Interest

SL is an employee of AvantaTrading Ltd. AZ and NM have no conflict of interest to declare.

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Abbreviations

AD: atopic dermatitis
AI: artificial intelligence
EASI: eczema area and severity index
POEM: patient-oriented eczema measure

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Original Paper

Epidemiology and Perception of Acne Among Adolescents in Jos, Nigeria: Cross-Sectional School-Based Study

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Abstract

Background: Adolescents who make up a vast majority of the secondary school population are at a stage at which they are largely affected by acne. This condition, which is widely visible and easily recognized by peers, has numerous misperceptions surrounding it, which may influence attitudes toward people affected by it. There is a paucity of information on the prevalence of acne and how adolescents in Jos, Nigeria, view the condition.

Objective: This study aimed to determine the prevalence of acne, perceived risk factors, and the accuracy of self-report among adolescents in Jos, Nigeria. The study also sought to understand perceptions surrounding acne in this age group.

Methods: This descriptive cross-sectional study was conducted among adolescents attending private and public secondary schools in Jos, Nigeria. In total, 482 students were recruited through a multistaged stratified random sampling method. A self-administered semistructured questionnaire was used to collect information on history of acne, perceptions of causes, and the attitude toward those who have the condition. All participants were examined for the presence of acne. Univariate, bivariate, and multivariate analysis were conducted using SPSS (version 26; IBM Corp).

Results: The self-reported prevalence of acne was 44% and that upon clinical examination was 55%. Self-report showed a moderate degree of agreement with clinical diagnosis (Cohen κ=57.3%; *P*<.001). Predictive factors for the presence of acne in general were age of ≥15 years (odds ratio [OR] 1.79, 95% CI 1.12-2.87; *P*=.02), being in a private school (OR 2.17, 95% CI 1.38-3.42; *P*=.001), and being in a senior secondary class (OR 2.14, 95% CI 1.32-3.47; *P*=.002). The female gender (OR 3.03, 95% CI 1.64-5.61; *P*=.001) and religion (OR 3.24, 95% CI 1.27-8.24; *P*=.02) were predictive for acne only among adolescents aged <15 years, while a positive family history was predictive in those aged ≥15 years (OR 2.04, 95% CI 1.15-3.61; *P*=.02). A distinct perception and attitude pattern surrounding acne was observed, as a significant proportion (84/131, 64.1% vs 47/131, 35.9%; *P*=.02) of those who related acne to a biological phenomenon had acne themselves; however, the belief that acne is caused by skin lightening practices was significantly more common in those without acne (19/28, 67.9%) than in those with acne (9/28, 32.1%; *P*=.01). One-fourth of the adolescents (n=122, 25.3%) had no idea of the possible causes of acne.

Conclusions: Though acne is a prevalent skin condition among Nigerian adolescents, many misperceptions and unfavorable attitudes surround acne and persons affected by the condition. Our findings have revealed the need to work with the school health program to educate the general adolescent population about acne, to refer and manage teenagers with acne.

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KEYWORDS

prevalence; predictors; misconception; perception; groundnuts; pimples; teenagers; acne; dermatology; Nigeria; acne vulgaris; comedone; papule; pustule; nodule; cyst; blackhead; whitehead

Introduction

Acne vulgaris is a disease of the pilosebaceous units of the skin of the face, neck, chest, shoulders, and back. The condition typically starts at puberty and is induced by abnormal follicular keratinization, excessive sebum production, *Propionibacterium acnes* colonization, and localized inflammation. In addition to the typical lesions of comedones, papules, pustules, nodules, and cysts, there may be scarring and postinflammatory hyperpigmentation [1,2]. According to the Global Burden of Disease study [2], the estimated global prevalence of acne in 2010 was 9.38%, and acne ranked as the eighth most prevalent skin condition worldwide.

Few conditions exist where there is significant prevalence of acne across countries and cultural groups. Reported prevalence varies in accordance with age groups and is influenced by the different methods used in studies. Identification of acne by experts through clinical examination in certain studies have revealed a prevalence almost equivalent to the total number of adolescents examined [3-5]. Studies based on adolescent self-report have also reported substantial prevalence rates (49.8%-83.4%) [6-8]. Self-report by affected individuals has shown some validity as fair to good agreement with experts' diagnosis has been demonstrated, albeit insufficient for both treatment and research purposes [9-11].

The etiology of acne is multifactorial, and diet has frequently been implicated as a risk factor in acne occurrence and severity. High-glycemic-index foods, including those with high carbohydrate and sugar content, combined with low intake of vegetables and high intake of dairy products have been associated with the occurrence or severity of acne [12,13]. These factors are known to be individualized and influenced by genetics; thus, family history has also been identified as a predisposing factor [1]; other commonly documented factors are heat and humidity, overweight, use of skin and hair care products such as pomades [14,15]. Furthermore, there are many acne-related beliefs held with little supporting evidence, which influence health-seeking behaviors and attitudes toward persons with acne [8,16]. Inadequate awareness of acne has also been linked to stigma, discrimination, low self-esteem, depression, and suicidal thoughts in affected adolescents who are still undergoing physical and psychological maturation. Thus, taking into account adolescents' knowledge of acne is useful in developing approaches to health education and management [17-19].

Studies have reported that the prevalence of acne in adolescents and youths in Nigeria is between 30% and 90.7%, with documented associated factors possibly unique to those regions where the studies were conducted—mostly Southern Nigeria [4,8,12,20]. For instance, Jos, seated on a plateau that has cooler weather with food items cultivated and consumed that are unique to the state, may have a distinct epidemiology of acne among its adolescents. This study, therefore, aimed at ascertaining the prevalence of acne among adolescents in Jos, Nigeria, associated factors, and the reliability of self-report when compared to clinical diagnosis. An additional goal of the study was to document adolescents' perceptions about the causes and attitudes toward persons with acne.

Methods

Overview

Jos is the capital of state of Plateau in North-Central Nigeria, with a significantly cooler temperature than that in other states in Nigeria. It is the center of cultivating vegetables and tubers, which are distributed to other parts of the country. Many settlements in Jos are characterized by persons of similar religion or tribe with their distinctive cultures. Schools are, therefore, influenced by this pattern, such that their populations reflect that of the host community. Furthermore, access to schools in the country is largely based on socioeconomic status as students from poorer homes attend public schools with lower funding while children from families of upper socioeconomic class, who can afford private schools, attend private schools [21].

This cross-sectional study was conducted among adolescents at 4 secondary schools in 2 Local Government Areas (LGAs) of Jos Metropolis within a 4-week period, between September and October 2022. Multistage random sampling was used to select 482 students in the schools in Jos North and Jos South LGAs (1 private and public secondary school in each LGA). The eligibility criteria for schools were that they were coeducational day schools with all 6 class years—the first 3 years termed as junior secondary and the last 3 as senior secondary. Participants were chosen from a sampling frame of each school, which included every class throughout the school using a predetermined sampling interval.

Information regarding demographic characteristics, first-degree family history of acne, perceptions regarding the causes of acne, and the impression that study participants have of others with acne were collected using self-administered questionnaires. All participants had their anthropometric measures (weight and height for BMI calculation) taken and examined privately for acne by a pediatric dermatologist. Participants with a BMI of <18.5 were classified as undernourished; those with a BMI of 18.5 to 24.9 as normal, and those with a BMI of ≥25 as overnourished. All forms of acne (inflammatory and noninflammatory) were recorded as "Acne present." Data collected were entered into SPSS Statistics for Windows (version 26.0; IBM Corp).

Data were tabulated as frequency and percentage values, while numeric variables were presented as means. The Pearson chi-square test and Fisher exact test were used to analyze the association between categorical groups, and multinomial logistic regression was performed to explore the relationship between the predictor variables and the presence of acne. Odds ratios (ORs) with 95% CIs were used to state the measure of relationship between variables. A *P* value of <.05 was determined to be the level of statistical significance.

Ethical Considerations

The study was approved by the Research and Ethical Committee of the Jos University Teaching Hospital, Jos (JUTH/DCS/IREC/127/XXX1/2750). Permission was sought from each school, and written informed consent was obtained from the guardians or parents of the students prior to their involvement. Participation was voluntary, and each student could withdraw from the study at any time.

Results

Respondent Demographic Characteristics

Of 482 students selected and provided consent forms for their parents or guardians, 14 of them refused to consent, did not have capacity to fully understand and fill in the questionnaire, or were absent, so they were replaced by the next student on the list whose parents or guardians had provided consent.

The age range of the participants (9-21, mean 14.6, SD 2.2 years) was wider than expected in Nigerian secondary schools (11-17 years). There were more female (292/482, 60.6%) than male students. The general ratio of male and female students was 1:1.5; however, the male:female ratio in public schools (1:2.1) was higher than that in private schools (1:1.2). Students' BMI ranged from 12.9 to 29.9 (mean 19.5, SD 3.1) with only 24 of 482 (5.0%) being overnourished (having overweight and obesity) and 189 (39.2%) being undernourished (Table 1).

Table 1. Frequency distribution of the characteristics of the study participants (N=482).

Characteristics	Participants, n (%)
Gender	
Female	292 (60.6)
Male	190 (39.4)
Age group (years)	
<15	228 (47.3)
≥15	254 (52.7)
Religion	
Christianity	377 (78.2)
Islam	105 (21.8)
School	
Private	242 (50.2)
Public	240 (49.8)
Tribe	
Other tribes	153 (31.7)
Plateau indigenes	329 (68.3)
Class	
Junior secondary class	257 (53.3)
Senior secondary class	225 (46.7)
Nutritional status	
Underweight or undernourished	189 (39.2)
Normal	269 (55.8)
Overnourished (having overweight and obesity)	24 (5)
Family history of acne	
No	180 (37.3)
Yes	302 (62.7)

Acne Prevalence by Self-Report and Examination

Only over one-third (n=188, 39%) of respondents said that they experienced acne in the past, while less than half (n=213, 44.2%) of the respondents self-reported having acne at the time of the study, while on clinical examination, more than half (n=265, 55%) of them were found to actually have acne.

There was an 88% chance of adolescents properly stating when acne was absent because only 12% of self-reported cases of acne were false positive (specificity). The sensitivity of self-report compared to that of clinical diagnosis was 70.6%, with 78 (29.4%) participants who self-reported having no acne at the time of the study actually deemed as having acne upon clinical diagnosis (false negative). The negative predictive value was 71%, and the positive predictive value was 87.8%.

On assessing the presence of acne, a weighted κ of 57.3% (P<.001) indicates moderate consistency between the adolescents' self-report and examination by a pediatric dermatologist. Table 2 summarizes the prevalence of acne by self-report and on clinical examination, and Table 3 compares the accuracy of adolescents' self-reports of acne to their clinical diagnoses.

Table 2. Prevalence of acne by self-report and clinical examination (N=482).

Presence of acne	Participants, n (%)
Do you currently have acne (self-report)?	
Yes	213 (44.2)
No	269 (55.8)
History of acne in the past (irrespective of current status)	
Yes	188 (39)
No	294 (61)
Having acne on clinical examination	
Yes	265 (55)
No	217 (45)

Table 3. Comparison of the accuracy of adolescents' self-report of acne with that of their clinical diagnosis (N=482).

Self-report of acne	Acne by examination, n (%)	
	Present	Absent
Yes	187 (70.6)	26 (12)
No	78 (29.4)	191 (88)

Characteristics Associated With the Presence of Acne

Multinomial logistic regression was used to analyze the relationship between certain characteristics and the presence of acne (Table 4). Five variables were found to be predictive of the presence of acne: age of ≥15 years (OR 1.78, 95% CI 1.11-2.86; *P*=.02), female gender (OR 1.80, 95% CI 1.19-2.71; *P*=.01), identifying as Christian (OR 2.1, 95% CI 1.10-4.01; *P*=.02), studying at a private school (OR 2.17, 95% CI 1.38-3.42; *P*=.001), and being in a senior secondary class (OR 2.14, 95% CI 1.32-3.47; *P*=.002).

Table 4. Multinomial logistic regression of factors associated with the presence of acne.

Factors	Adjusted odds ratio (95% CI)	*P* value
Age group (years)		.02[a]
<15	1 (reference)	
≥15	1.78 (1.11-2.86)	
Gender		.01[a]
Male	1 (reference)	
Female	1.80 (1.19-2.71)	
Religion		.02[a]
Muslim	1 (reference)	
Christian	2.10 (1.10-4.01)	
Tribe		.55
Plateau Indigenous	1 (reference)	
Others	1.19 (0.68-2.08)	
School type		.001[a]
Public	1 (reference)	
Private	2.17 (1.38-3.42)	
Class		.002[a]
Junior secondary	1 (reference)	
Senior secondary	2.14 (1.32-3.47)	
Known family history		.09
Yes	1 (reference)	
No	0.7 (0.47-1.11)	
BMI status		
Underweight	1 (reference)	N/A[b]
Normal	2.15 (0.57-6.13)	.15
Overweight	1.31 (0.48-3.56)	.60

[a]Significant at *P*<.05.

[b]N/A: not applicable.

When separated into 2 major groups based on age, of 95 of 228 (41.7%) adolescents younger than 15 years had acne, and 170 of 254 (66.9%) adolescents aged 15 years and older were found to have acne. School type and class remained predictive of the presence of acne in both age groups. The female gender (OR 3.03, 95% CI 1.64-5.61; *P*=.001) and religion (OR 3.24, 95% CI 1.27-8.24; *P*=.02) were predictive for acne only in adolescents aged <15 years, while positive family history was predictive in those aged ≥15 years (OR 2.04, 95% CI 1.15-3.61; *P*=.02; Table 5).

Table 5. Factors associated with the presence of acne in different age groups.

	Participants aged <15 years		Participants aged ≥15 years	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Gender		<.001[a]		.68
Male	1 (reference)		1 (reference)	
Female	3.03 (1.64-5.61)		1.13 (0.62-2.06)	
Religion		.02[a]		.39
Muslim	1 (reference)		1 (reference)	
Christian	3.24 (1.27-8.24)		1.52 (0.58-4.00)	
Tribe		.32		.85
Plateau Indigenous	1 (reference)		1 (reference)	
Others	1.46 (0.69-3.06)		1.09 (0.45-2.63)	
School		.03[a]		.01[a]
Public	1 (reference)		1 (reference)	
private	2.08 (1.08-4.01)		2.50 (1.28-4.85)	
Class		.03[a]		.02[a]
Junior	1 (reference)		1 (reference)	
Senior	2.42 (1.11-5.28)		2.06 (1.1-3.88)	
Known Family History		.84		.02[a]
Yes	1 (reference)		1 (reference)	
No	1.06 (0.59-1.93)		2.04 (1.15-3.61)	
BMI				
Underweight	1 (reference)	N/A[b]	1 (reference)	N/A
Normal	1.44 (0.79 -2.63)	.24	3.30 (0.88-12.36)	.08
Over-nourished	1.42 (0.18-11.06)	.74	1.58 (0.48-5.20)	.45

[a]Significant at $P<.05$.

[b]N/A: not applicable.

Perception and Attitudes Related to Acne

When asked what they thought causes acne, a large proportion of respondents (122/482, 25.3%) reported having no idea about the causes of acne. Factors believed to be risk factors of acne, as cited by the study participants, were eating groundnuts or peanuts (n=132, 27.4%), eating other dietary items (n=46, 9.5%), acne being a natural or biological phenomenon (n=131, 27.2%), using skin care products or cosmetics (n=45, 9.3%), using skin lightening products (n=29, 6%), health and hygiene (n=66, 13.7%), weather (n=29, 6%), and others (n=17, 3.5%).

Interestingly, participants with acne had significantly different perceptions surrounding acne from those without acne. A larger proportion of adolescents (84/131, 64.1%; *P*=.02) perceived that acne was due to a biological phenomenon. Among those who perceived acne as being caused by skin lightening practices, 19 of 28 (67.9%, *P*=.01) did not have acne. When asked to express their opinions of acne in individuals in 1 word, respondents chose the following: unattractive, not bad, ugly, matured, developed, unhygienic or not clean, unhealthy, pitiable, awful, nasty, overweight, and unhappy people. When these perceptions were grouped together as favorable or unfavorable attitudes, participants without acne had significantly less favorable attitudes toward those with acne than did those with the condition themselves (27.3% vs 72.7%; *P*=.04). In addition, 132 (27.4%) participants also believed acne to be contagious (Table 6).

Table 6. Perceptions of the causes of acne and attitudes toward individuals with acne.

Perceived causes of acne or pimples	Acne clinical on examination		Chi-square (*df*)	*P* value
	Present	Absent		
Eating groundnuts or peanuts			2.3 (1)	.13
Mentioned	80 (60.6)	52 (39.4)		
Not mentioned	185 (52.9)	165 (47.1)		
Consuming other foods (greasy or fatty foods, milk, eggs, beans, sugary items, and soft drinks)			0.7 (1)	.39
Mentioned	28 (80.9)	18 (39.1)		
Not mentioned	237 (54.4)	199 (45.6)		
Biological or natural phenomenon (maturity, period or premenstrual, or familial)			6.1 (1)	.02[a]
Mentioned	84 (64.1)	47 (35.9)		
Not mentioned	181 (51.6)	175 (48.4)		
Skin-related (using skin care products, cosmetics, and skin type)			0.5 (1)	.82
Mentioned	24 (53.3)	21 (46.7)		
Not mentioned	241 (55.1)	196 (44.9)		
Skin lightening practices or bleaching			6.3 (1)	.01[a]
Mentioned	9 (32.1)	19 (67.9)		
Not Mentioned	256 (56.4)	198 (43.6)		
Health and hygiene (dirt, poor hygiene, or disease)			3.2 (1)	.07
Mentioned	28 (44.4)	35 (55.6)		
Not mentioned	237 (90.2)	182 (43.4)		
Environmental factors (weather and heat)			0.17 (1)	.68
Mentioned	17 (58.6)	12 (41.4)		
Not mentioned	248 (54.7)	208 (45.3)		
Others (sex, drugs, hormone intake, insects bites, smoking, face-touching, shaving, stress, cloths, bed-wetting, and chalk-dust)			0.34 (1)	.56
Mentioned	14 (60.9)	9 (3.7)		
Not mentioned	251 (54.7)	209 (45.3)		
Perception of persons with acne (single response)			6.5 (2)	.04[a]
Favorable	32 (72.7)	12 (27.3)		
Unfavorable	76 (51.4)	72 (48.6)		
No response	157 (54.1)	133 (45.9)		

[a]Significant at $P<.05$.

Discussion

Principal Findings

This is one of the few studies conducted in North-Central Nigeria, and, to the best of our knowledge, the only one in Jos to investigate the prevalence of (by self-report and clinical examination) and perceptions surrounding acne in adolescents.

We found that 265 of the 482 (55%) study participants had acne, implying that despite differences in geography, culture, and lifestyle, acne vulgaris is as prevalent among adolescents in Jos as it is in other regions of Nigeria and globally [4-8,20]. The prevalence in Jos is higher than that in Ilorin, another town in North-Central Nigeria, where 40.1% of secondary school students reportedly had acne [20], but lower than that in Kaduna (North West Nigeria), where 90.7% secondary school students reportedly had acne [8]. The huge disparity in prevalence between the Kaduna study and our study could result from the fact that occurrence and severity of acne increase with advancing age and development, and the mean age of our study participants was lower than that of those in the Kaduna study (14.6 vs 16.1 years). Bagatin et al et [3] reported a similar pattern to a greater degree in Brazil where acne was universal in teenagers older than 14 years, such that analysis of associated factors had to be restricted to only those aged 10-13 years.

While expert diagnosis through clinical examination is the gold standard, self-report in our study still revealed a significant prevalence of 44%, which was similar to that reported by Ražnatović Đurović et al [6] (49.8%) among adolescents aged 14-17 years in Montenegro. The self-report rate in our study was lower than that determined through clinical diagnosis (44% vs 55%). A similar pattern was observed in a study among final-year female medical students in Jeddah, Saudi Arabia, when self-evaluation was contrasted with a doctor's examination (83.4% vs 98%) and in Kaduna, Nigeria (59.4% vs 90.7%) [7,8]. Despite the difference between the 2 methods in our study, self-reports agreed fairly well with the expert's diagnosis with the specificity higher than the sensitivity (88% vs 70.6%). This implies that the accuracy of adolescents' recognition of when they did not have acne was higher than that when they had acne, which is consistent with that reported in other studies [7,9]. This is expected as our study participants are not trained observers with a capacity for identifying all forms of acne lesions. Also, acne in certain regions, such as the posterior trunk, may not be visible. Still, the condition is so commonplace that 7 of 10 adolescents reported it correctly. In contrast, among Egyptian adolescents, a higher prevalence of acne was determined through self-report than through an experts' diagnosis (34.7% vs 24.4%) [22]. Higher self-reports of acne and other skin disorders in general have been linked to the availability of resources in health systems, exposure to information, and increased self-awareness, although the experiences of adolescents in our setting may differ [23]. This demonstrates the limitations of self-report and supports the case for dermatologists' participation in education for and management of prevalent skin conditions of children and adolescents within the school health program [9-11,22].

It was not unexpected to find older adolescents to be almost twice as likely than younger adolescents to have acne, as this condition occurs more frequently with advancing age or maturity [8,11]. Furthermore, older, more mature adolescents are likely to be in higher classes, consequently having an older age (OR 1.78, 95% CI 1.11-2.86; *P*=.02) as well as being in a senior class (OR 2.14, 95% CI 1.32-3.47; *P*=.001) were predictive of the presence of acne [24]. The female gender was only predictive of the presence of acne in younger adolescents (OR 3.03, 95% CI 1.64-5.61; *P*=.001) probably because female individuals in early adolescence attain puberty earlier than male individuals, but by the older adolescent stage, male individuals will have caught up, thus eliminating any gender difference in acne prevalence in older adolescents as seen in this study. This is in agreement with the findings of Anaba et al [25], where a higher acne prevalence was found among female individuals. This, however, differs from studies by Bagatin et al [3] and Yahya et al [8] where prevalence was higher in male individuals. Generally, adolescents in private schools were more likely to have acne (OR 2.17, 95% CI 1.38-3.42; *P*<.001) than those in public schools and it remained consistently so across age groups, as observed by Tayel et al [22] in Egypt and Okoro et al [24] in Southern Nigeria. School type is known to be determined largely by socioeconomic status, which also influences lifestyle, diet, and stress levels and affects acne [22,24].

The relationship between religious practices and acne has scantily been explored, though some studies have suggested that the hijab worn by female students, which covers the scalp and part of the face, increases the likelihood of acne on the forehead and hairline [26]. Our results did not align with this finding, as Christian adolescents had a significantly higher prevalence of acne (OR 2.1, 95% CI 1.10-4.01; *P*=.02) than those of the Islamic faith, although the hijab is the predominant Muslim female attire even in school uniforms. While the exact reason is unknown, there may be underlying genetic and lifestyle-related differences between the 2 religious groups. This highlights the contribution of the frequent face washing during ablution in acne control. Muslims wash the face with water as much as 5 times a day. While water alone may be insufficient in controlling the underlying factors of acne formation, it may remove some surface impurities such as dirt, sweat, and some oil from the surface of skin, preventing pore blockage that is implicated in the etiology of acne [27]. This hypothesis may need further exploration. Familial predisposition of acne has been documented in various studies [1,12]. We, however, found that family history was predictive of acne only in older adolescents but not in younger adolescents (OR 2.04, 95% CI 1.15-3.61; *P*=.02), which could be attributable to possible response bias, as older adolescents are more likely to be aware of their family's history of acne or be observant of first-degree family members with acne than are younger adolescents. Recent systematic reviews have shown an increased risk for acne among individuals with overweight or obesity in relation to those with a normal BMI or with underweight [1,14]. This pattern was not observed in our study but adolescents who were undernourished consistently had a lower prevalence of acne than those with a normal or overnourished nutritional status, the difference was not significant across both age groups.

Diet featured prominently as a perceived risk factor for acne among our study participants, with opinions similar to those of other reports; this refers to items such as chocolates, greasy foods, milk, eggs, and sugary drinks [6,8,13,14]. Eating peanuts, which are commonly called groundnuts across Nigeria, was the most frequently cited associated factor for acne in our study irrespective of the presence of acne. This was also reported by Aiyedun et al [28] in South West Nigeria. The widespread strong belief that intake of nuts in general will result in acne outbreaks has little evidence in support [1,13,16]. Groundnuts are a staple food in the Northern Nigeria and are consumed in a variety of ways; the corollary of this misperception in a resource-poor setting like ours is that adolescents may avoid this important and inexpensive source of protein used in a variety of snacks, soups, and meals, which is needed in a study population like ours, in which a sizable proportion of individuals (39%) had underweight. Any denial of nutrient-rich foods because of erroneous beliefs would further compromise growth and development in this age group [29].

Unlike Ražnatović Đurović et al [6], who found no difference in the perceptions of aggravating and ameliorating factors of acne between adolescents with and those without acne in Montenegro, we found some differences in perceptions surrounding acne between the 2 groups [6]. There was a higher proportion of individuals who linked acne with a biological phenomenon (puberty, maturity, menstruation, or genetic or familial factors) among participants with acne than in those without clinically diagnosed acne. On the contrary, perceptions that seem judgmental were expressed to a significantly higher extent by those without acne, such as associating the presence of acne with the use of skin lightening products, which is a practice largely disapproved of by society. The perception may not be completely unfounded as the use of topical steroids is associated with a form of acne and has become increasingly common in young persons in Nigeria [8,20].

The view that some adolescents have of persons with acne being filthy or unhygienic has been reported in other studies where the dark color of an open comedone caused by keratin oxidation was interpreted as dirt [1]. It has been demonstrated that these misconceptions add to the psychological burden of acne and are linked to obsessional face washing or persistent use of medicated soaps, which can irritate the skin [8,20].

The significantly lesser positive attitudes or perceptions held by people without acne (27.3% vs 72.7%; *P*=.04) depict how persons not affected by a particular condition may have less tolerant or favorable opinions of those with the condition. Other studies have reported that this attitude usually underlies poor social behaviors toward persons with acne, affecting mental health, which may be explored in adolescents with acne in Jos.

Limitations

The study's' limitations include the possibility of recall and response bias. The data could also have been skewed by the higher proportion of female participants. The relationship between severity and the variables may be investigated for a better knowledge of the epidemiology of acne.

Conclusions

Despite these limitations, our study suggests that acne is prevalent in adolescents in Jos, and there were a variety of misconceptions and unfavorable perceptions of the condition within this age group. This highlights the need for appropriate health education inculcated in school health programs, including services and referral by dermatologists. Additional research on the effects of acne on adolescents and their treatment-seeking behavior will also help to understand the burden of acne in our settings.

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Authors' Contributions

RA conceptualized, designed, and supervised the study; collected, ensured the integrity of, statistically analyzed, and interpreted the data; and drafted and critically revised the manuscript for intellectual content. HY collected and analyzed data and critically revised the manuscript. Q-AVO collected the data and critically revised the manuscript. All authors were involved in the revision of the manuscript and approval of the final version.

Conflicts of Interest

None declared.

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Abbreviations

AOR: adjusted odds ratio
LGA: Local Government Area
OR: odds ratio

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Original Paper

Mucocutaneous Manifestations Among HIV-Infected Patients in Madagascar: Cross-Sectional Study

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Abstract

Background: More than 90% of HIV-infected patients present with at least one mucocutaneous manifestation during the course of their disease. Insufficient data are available regarding dermatologic findings among HIV-infected patients in Madagascar.

Objective: This study aimed at evaluating the spectrum of mucocutaneous manifestations and their relationship with CD4 cell counts in HIV-infected patients in Madagascar.

Methods: A cross-sectional study on HIV-positive patients attending the Department of Infectious Diseases in the University Hospital of Antananarivo in Madagascar was conducted from January 2013 to March 2020. HIV-positive patients older than 18 years and receiving antiretroviral therapy as well as those awaiting antiretroviral therapy commencement were included.

Results: Among 328 patients enrolled in this study, 167 (51%) presented with at least one type of mucocutaneous lesion. Oral candidiasis was the most common presentation, followed by seborrheic dermatitis and Kaposi sarcoma. Decreases in CD4 cell counts were substantially correlated with oral candidiasis, syphilis, and condyloma acuminatum.

Conclusions: According to our findings, oral candidiasis, syphilis, and condyloma acuminatum may serve as clinical indicators for predicting the immune status of patients. As HIV infection progressed and immune function declined, an increase in cutaneous manifestations was observed.

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KEYWORDS

HIV infection; mucocutaneous manifestations; oral candidiasis; HIV; cross-sectional study; lesion; mucocutaneous; dermatitis; sarcoma; syphilis; immune; useful; disease

Introduction

In Madagascar, the prevalence of HIV infection in the general population increased from 0.02% to 0.25% between 1989 and 2018. High prevalence of HIV was found among key populations in Madagascar, with rates of 14.8% in men who have sex with men, 8.4% in injecting drug users, and 5.6% in sex workers [1,2]. In 2019, an estimated 13% of people living with HIV (PLWH) in Madagascar had access to antiretroviral therapy (ART). Although the number of people with access to ART had increased, 1400 individuals died from AIDS-related diseases [3].

HIV infection is commonly associated with various mucocutaneous manifestations that can be present in all situations. Mucocutaneous disorders develop in more than 90% of HIV-infected individuals at some point during the course of their illness [4]. The epidemiologic profile of dermatologic illnesses related to HIV varies among countries. Prevalence reported by Asian [5,6] and African studies [7,8] ranged from 52.5% to 96%. The spectrum of dermatologic illnesses related to HIV has also changed since the introduction of highly active ART [9].

The purpose of this study was to describe the epidemiology and the clinical spectrum of mucocutaneous manifestations in HIV-positive patients attending the Department of Infectious Diseases in the University Hospital of Antananarivo in Madagascar.

Methods

Ethics Approval

This study was approved by the Ethics Commission of the University Hospital of Antananarivo in Madagascar (23-CHUJRB/CE). Confidentiality was maintained. Patients provided written informed consent to allow their medical records data to be used in research and their case details to be published.

Procedure

A cross-sectional study was conducted in HIV-positive patients (men and women aged ≥18 years) seeking care at the Department of Infectious Diseases at the University Hospital of Antananarivo in Madagascar from January 2013 to March 2020. Patients receiving ART and those awaiting ART commencement were included.

Data on the mode of infection, duration of disease, the nearest level of CD4 cell counts (within the last 2 months) at the time of diagnosis of a specific skin condition, treatment regimen, and any prior dermatological history were considered. Physical examination of patients was conducted by dermatologists. Dermatoses were primarily diagnosed clinically, with additional support from mycological, histological, and hematological testing, as necessary.

Statistical Analysis

Statistical analysis was performed with Epi Info software (version 3.5.4; Centers for Disease Control and Prevention). Categorical data were compared using the chi-square test, and the student *t* test (2-tailed) was used to analyze continuous variables. The level of statistical significance was set at $P<.05$. Regression analysis was performed to assess the relationship between the number of dermatoses and CD4 cell counts.

Results

Among the 345 HIV-positive patients seen during the study period, 7 were excluded due to incomplete data, and an additional 10 declined participation. As a result, a total of 328 patients were included in the study, of whom 215 (65.5%) of them were male. A total of 168 (51%) patients presented with at least one dermatological disease. Among these 168 patients, 130 (77.3%) were receiving ART. Of the total 328 participants, 123 (37%) patients in the age group of 30-39 years were affected by HIV. The median age was 41 (IQR 27-52) years. Among the 328 participants, the primary mode of HIV transmission was heterosexual in 272 (83%) individuals, whereas the number of men who have sex with men was 30 (9.1%). In terms of occupation, 104 (32%) patients worked in the commerce sector, 37 (11.2%) were housewives, 26 (8%) were students, and 8 (2.4%) were health care professionals. The average duration of HIV infection was 9.8 (SD 6.2) years. Additionally, 160 (48.7%) patients had a low level of education.

A total of 231 dermatoses were identified in 168 HIV-infected patients. Among these patients, 117 (69.6%) had one type of dermatoses, while 41 (24.4%), 8 (4.7%), and 2 (1.1%) presented with 2, 3, and 4 types of dermatoses, respectively. Infectious dermatoses affected half of the participants, with 111 (66%) patients presenting with fungal infections, which were the most prevalent, followed by viral infections in 35 (20.8%) patients and bacterial infections in 17 (10%) patients. The most common fungal infection was oral candidiasis, while herpes zoster (Figure 1) and syphilis were the most common viral and bacterial infections, respectively. Additionally, 10 (5.9%) of 168 patients presented with condyloma acuminatum (Figure 2).

Noninfectious dermatoses affected 61 (36.3%) of the 168 patients. Among the noninfectious dermatoses, inflammatory dermatoses was the most prevalent, with seborrheic dermatitis being the main condition observed in 27 (11.6%) patients. Regarding neoplastic diseases, 16 patients presented with Kaposi sarcoma (8 men and 8 women), with 6 patients in the age group of 30-39 years (Figure 3). No case of other types of skin tumors was seen. Toxidermia (Figure 4) was observed in 7 patients, 2 of whom were induced by ART and the other 5 were attributed to antituberculosis drugs and trimethoprim-sulfamethoxazole. Exanthematous rash, the most common type of drug eruption, was seen in 6 cases. Additionally, 1 case of acute generalized exanthematous pustulosis was observed.

Table 1 shows a list of the most common dermatologic diagnoses encountered in this study, with the corresponding mean CD4 cell counts.

The mean CD4 cell count for all patients was 190 (SD 32) cells/mm^3. LTCD4 was less than 200 cells/mm^3 in 139 (83%) of 168 patients who had skin manifestations. The mean CD4 cell count of patients with cutaneous manifestations (119, SD 40 cells/ mm^3) was significantly lower than the mean CD4 cell count of those without manifestations (262, SD 65 cells/mm^3; $P<.05$).

Of the 328 PLWH in this study, 259 (79%) were receiving ART. Among them, 251 (77%) were receiving a fixed-dose combination of 2 nucleoside reverse transcriptase inhibitors and nonnucleoside reverse transcriptase inhibitors. However, 47 (18%) of the 259 patients had not initiated treatment. Of the 8 PLWH, 2 (3%) who were treated by 2 nucleoside reverse transcriptase inhibitors associated with protease inhibitors were pregnant.

Among the infectious dermatoses, oral candidiasis ($P=.001$), syphilis ($P=.002$), and condyloma acuminatum ($P=.03$) showed statistically significant associations with the CD4 count (<200 cells/mm^3). The association of dermatoses with CD4 cell counts is shown in Table 2.

CD4 cell counts were inversely proportional to the number of dermatoses presented by PLWH—as the CD4 cell counts increased, the number of dermatoses decreased (Figure 5). A strong negative correlation was identified, with a correlation coefficient of –0.39.

Figure 1. Hemorrhagic and extensive herpes zoster.

Figure 2. Anal condylum acuminatum.

Figure 3. Kaposi sarcoma affecting lower limbs.

Figure 4. Lyell syndrome induced by antiretroviral therapy.

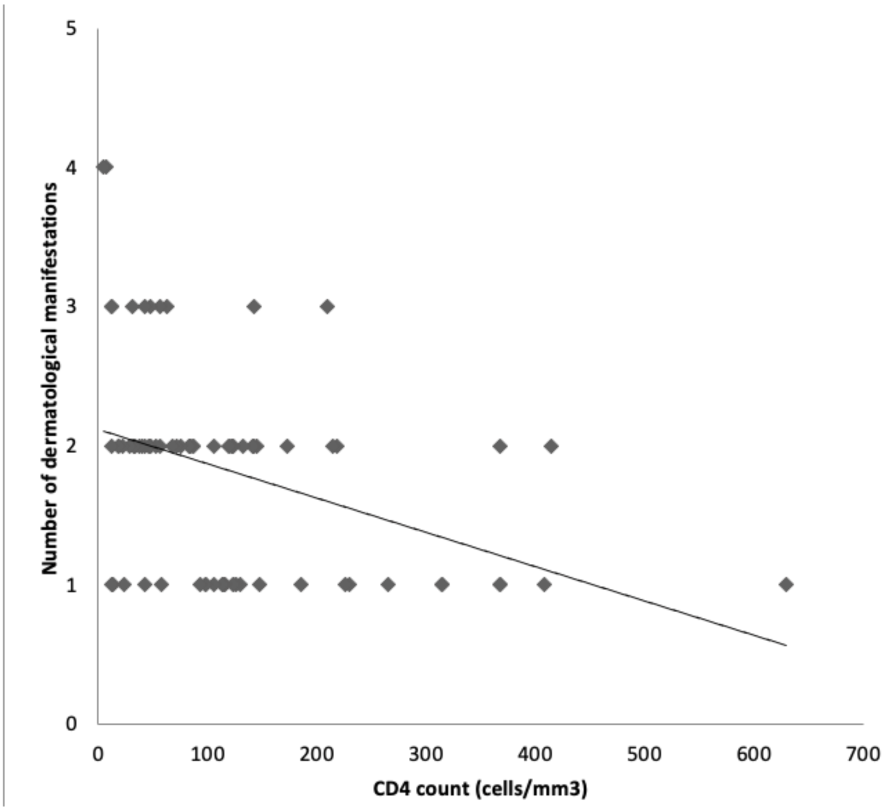
Table 1. The most common dermatologic diagnoses among HIV-positive patients, along with the corresponding mean CD4 cell counts.

Dermatologic diagnoses	Participants (n=231), n (%)	CD4 count (cells/mm^3), mean (SD)
Infectious diseases		
Oral candidiasis	111 (48.2)	97 (80)
Herpes zoster	12 (5.2)	164 (70)
Syphilis	11 (4.7)	187 (98)
Genital herpes	10 (4.3)	105 (79)
Condyloma acuminatum	10 (4.3)	217 (101)
Molluscum contagiusum	2 (0.86)	78 (31)
Pustulosis	2 (0.86)	226 (57)
Furunculosis	3 (1.30)	186 (61)
Noninfectious diseases		
Kaposi sarcoma	16 (6.9)	68 (43)
Seborrheic dermatitis	27 (11.6)	88 (49)
Prurigo	13 (5.6)	106 (71)
Toxidermia	7 (3)	163 (78)

Table 2. Association of dermatoses with CD4 cell counts.

Dermatologic diagnoses	CD4<200 cells/mm^3 (n=186), n (%)	CD4≥200 cells/mm^3 (n=24), n (%)	*P* value
Oral candidiasis	103 (55.3)	8 (33.3)	.001
Herpes zoster	9 (4.8)	3 (12.5)	.33
Genital herpes	8 (4.3)	2 (8.3)	.66
Syphilis	6 (3.2)	5 (20.8)	.002
Condyloma acuminatum	6 (3.2)	4 (16.6)	.03
Kaposi sarcoma	16 (8.6)	0 (0)	.29
Seborrheic dermatitis	26 (13.9)	1 (4.1)	.23
Prurigo	12 (6.4)	1 (4.1)	.57

Figure 5. The number of dermatoses according to CD4 cell counts. CD4 cell counts were inversely proportional to the number of dermatoses presented by people living with HIV, with a strong negative correlation between these two parameters (correlation coefficient –0.39).



Discussion

Principal Findings

The prevalence of mucocutaneous manifestations in patients with HIV was 51% in our study. The mean CD4 cell count (119 cells/µl) of patients with cutaneous manifestations was significantly lower than the mean CD4 cell count of those without manifestations. Oral candidiasis was the most prevalent of infectious dermatoses and was associated with a mean CD4 count of 97 cells/mm^3. Seborrheic dermatitis was the most prevalent of noninfectious dermatoses. The prevalence of mucocutaneous manifestations in HIV-infected patients found in this study is close to that among Korean patients (55.6%), reported by Kim et al [5]. This observed similarity may be contributed to changes in the prevalence of cutaneous disorders associated with the introduction of ART. Previous studies have found dermatological manifestations to be less prevalent in patients treated by ART compared with those who did not receive ART [10,11]. However, comparing the prevalence of mucocutaneous manifestations in HIV-infected patients is challenging due to differences in study designs and the socioeconomic status of patients included in different studies.

The mean age of our study participants was 36.5 (SD 19.1) years. This finding is consistent with results reported by Josephine et al [12] for patients in Cameroon (mean age 37.2 years) and Atadokpede et al [13] for patients in Benin (mean age 37.8 years). According to data from the 4th Demographic and Health Survey in Madagascar conducted in 2008-2009 [14], some factors may contribute to the early age of HIV infection among the participants in this study, including low levels of education, lack of access to health care services and AIDS education, as well as low condom use, particularly among young people aged 15-19 years.

Patients with cutaneous manifestations had a significantly lower mean CD4 cell count (119 cells/µl) compared to patients without signs of cutaneous manifestations (262 cells/µl; *P*<.05). Our results are consistent with those reported by Lahoti et al [15] from India and Li et al [6] from China.

Among the infectious dermatoses, oral candidiasis (*P*=.001), syphilis (*P*=.002), and condyloma acuminatum (*P*=.03) showed statistically significant correlations with CD4 cell counts. Several authors reported the association of oral candidiasis with low CD4 cell counts [1,16,17]. In addition, Veldhuijzen et al [18] have demonstrated a relationship between low CD4 cell counts, increased HPV infection rates, and the development of anogenital warts. However, Azfar et al [19] were unable to show a relationship between skin manifestations and CD4 cell counts. These discrepancies in the results may be attributed to variations in sample sizes, disease stages, infection routes, and regional patterns of the reported.

A negative correlation was found between CD4 cell counts and the number of dermatoses seen in PLWH. This finding suggests that the number of mucocutaneous diseases related to HIV infection should be considered among the key clinical indicators for the prediction of underlying immune status and disease progression. Asian and Indian studies have reported similar results [20,21].

Oral candidiasis was found to be the most prevalent infectious dermatoses, associated with a mean CD4 count of 97 cells/mm^3.

Our result is consistent with results reported in previous studies [8,22], which have also reported a high prevalence of oral candidiasis in PLWH, ranging from 36% to 88%. A statistically significant correlation was found between a CD4 count <200 cells/mm^3 and the frequency of oral candidiasis (*P*<.001). Our results are consistent with those reported by Monsel et al [8] from Senegal, Ghate et al [23] from India, and Suryana et al [24] from Indonesia. This indicates that the presence of fungal infections is a predictor of advanced immunosuppression in HIV infection.

Among 231 dermatological diagnoses, seborrheic dermatitis was found to be the most prevalent of noninfectious dermatoses, presented by 27 (11.73%) patients. Our result is consistent with the findings reported by Claasens et al [25] in South Africa. A high frequency of seborrheic dermatitis (40%-80%) associated with HIV infection was reported before the use of highly active ART [26]. However, studies conducted in the ART era in China, India, and the United States have reported low prevalence rates of seborrheic dermatitis [9,27,28].

Human herpes virus type 8 (HHV-8) is the causative agent of Kaposi sarcoma. The seroprevalence of HHV8 in Africa ranged from 2% to 100% depending on the regions [29]. Kaposi sarcoma was presented by 16 (6.95%) patients in our study, with a mean CD4 count of 68 cells/mm^3. Ranaivo et al [30] reported lymphedema of the upper limb as a revealing symptom of Kaposi sarcoma associated with HIV infection. Environmental factors may also influence the onset of this disease. Similar to what is observed in other African countries, our study confirms the occurrence of Kaposi sarcoma in the advanced stages of immunosuppression. However, Kaposi sarcoma is relatively rare among the US population and Asians due to the lower seroprevalence of HHV8 in these populations [9,31].

Another important skin problem observed in our study was prurigo, which was present in 13 (5.65%) cases and associated with a mean CD4 count of 106 cells/mm^3. In African populations, prurigo has been linked to arthropod bites and poor socioeconomic conditions [13,32]. Our study showed that prurigo was predictive of advanced immunosuppression.

Herpes zoster was seen in 12 (5.21%) patients, with a mean CD4 count of 164 cells/mm^3. ART has been shown to reduce the incidence of herpes zoster in adults with HIV, presumably because of immune restoration [33]. Herpes zoster can occur in adults with HIV at any CD4 lymphocyte cell count, but the risk of disease is higher with CD4 counts <200 cells/mm^3. Several studies have also reported that the risk of herpes zoster is increased in the 6-month period immediately after initiation of ART [34,35].

Toxidermia was observed in 7 (3.10%) patients among our study population, with benign drug eruptions accounting for 6 of these toxidermia cases. Our result is close to those reported in South Africa by Claasens [25]. However, Asian studies in the ART era have reported higher prevalence rates for drug eruptions, ranging from 10% to 17% [6,9,20]. The mean CD4 count of these patients was 163 cells/mm^3. This finding is consistent with the results reported by Goh et al [20] in Singapore and Hagos et al [36] in Eritrea, which demonstrated that a low CD4 cell count was associated with adverse drug eruptions.

Conclusions

Our study provides data on the epidemiology and spectrum of mucocutaneous diseases in patients with HIV infection attending the Department of Infectious Diseases at the University Hospital of Antananarivo in Madagascar. Oral candidiasis, seborrheic dermatitis, and Kaposi sarcoma were found to be the most prevalent dermatoses. Among 328 participants included, toxidermia was observed in 7 (3.1%) patients. Oral candidiasis, syphilis, and warts showed potential as useful clinical indicators for predicting the immune status of the patients.

Acknowledgments

All authors meet the International Committee of Medical Journal Editors criteria for authorship, take responsibility for the integrity of the work as a whole, and have given their approval for this manuscript to be published.

Conflicts of Interest

None declared.

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Abbreviations

ART: antiretroviral therapy
HHV-8: human herpes virus type 8
PLWH: people living with HIV

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Original Paper

Rapid Web-Based Recruitment of Patients With Psoriasis: Multinational Cohort Study

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Abstract

Background: Wide-ranging patient recruitment not restricted to the location of the investigator will provide a better representation of the patient population in clinical studies.

Objective: Our goal was to assess the feasibility of a broad web-based recruitment strategy in an 8-week observational study of 500 study participants with psoriasis and healthy controls from locations remote from the investigator and to assess the cost associated with each participant.

Methods: A decentralized team in Denmark recruited patients with psoriasis and healthy controls using Google and Facebook advertisements and posts to Facebook groups. All individuals were screened via the internet, and patients diagnosed with psoriasis were included. Questionnaires regarding itch and sleep were completed by both groups at inclusion, week 4, and week 8.

Results: During a 2-week recruitment period, 12,887 unique advertisement views were registered, and 839 participants were enrolled, of which 507 completed the study (220 with psoriasis and 287 healthy controls) with a retention rate of 60.4%. Participants were recruited from 11 different countries on 4 separate continents, mainly from the United States, Canada, and the United Kingdom. The recruitment rate was 59.9 participants per day, and the conversion rate was 57.2%. Recruitment costs were US $13 per enrolled participant and US $22 per participant completing the study.

Conclusions: It is feasible and rapid to recruit a large number of participants from locations different from the investigator and to retain patients in an observational study with no visits to a clinical site at low costs.

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KEYWORDS

web-based recruitment; remote recruitment; conversion rate; recruitment rate; psoriasis; population; dermatologist; derma; itchy skin; Insomnia Severity Index; ISI; Pittsburgh Sleep Quality Index; PSQI; Dermatology Life Quality Index; DLQI; quantile-quantile plot; Q-Q plot; dermatology

Introduction

Recruitment of study participants is considered to be one of the most difficult aspects of the clinical research process [1]. More than 3 out of 4 patients do not enroll in a given trial due to structural and clinical barriers [2]. Moreover, a disproportionate number of participants from higher socioeconomic classes are typically enrolled [3]. Globally, more than 80% of trials fail to meet the timeline for enrolling participants leading to the addition of study sites or extension of the respective study [3,4], and 30% of phase-3 trials are terminated due to enrollment difficulties [5].

In particular, recruitment of an insufficient number of participants in studies with rare diseases is a challenge. Internet advertising, especially through Facebook, has resulted in efficient enrollment of large numbers of individuals with rare diseases, compared to recruitment through government and academic websites, patient advocacy groups, and health care providers [6]. This indicates that internet communication advances provide new opportunities to assemble individuals with rare diseases to web-based patient registries from wide geographic areas for research. A larger and broader recruitment not restricted by geography will likely also provide a better representation of the patient population. In a review from 2020 [7], Facebook was the most used social media platform for recruiting study participants through web-based platforms for clinical trials.

Other benefits of web-based recruitment include lower cost and bigger outreach. Web-based recruitment costs are lower compared with in-person recruitment methods [8-10], and web-based recruitment may enable outreach to populations otherwise challenging to enroll [9-11].

The aim of this observational study was to assess the feasibility of a broad web-based recruitment not restricted by the location of the investigator. We aimed to recruit 500 study participants, including patients with psoriasis and healthy controls, and to assess the cost associated with each participant recruited via the internet.

Methods

Study Design and Participants

A team based in Copenhagen, Denmark, recruited patients with psoriasis and healthy controls located primarily in the United States, Canada, and the United Kingdom to an 8-week observational feasibility study using Facebook ads, Google Search AdWords, and posts to Facebook groups (Multimedia Appendix 1). Inclusion criteria were age >18 years and self-reported physician's diagnosis of psoriasis. Healthy controls were individuals without a psoriasis diagnosis. Participants did not receive any compensation for participation.

Data Collection

After signing up with contact information, participants received a screening and demographic questionnaire, including questions regarding age, gender, nationality, English language proficiency, comorbidities, if they suffered from itchy skin, medications (which medication they take and how often they take them), height, and weight. Patients with psoriasis were asked to estimate the percentage of body area affected by psoriasis, the number of years they have been living with psoriasis, self-rated severity of psoriasis (ie, mild, moderate, or severe), and the type of psoriasis they have (the full questionnaire could be viewed in Multimedia Appendix 2).

Validated questionnaires were adapted to Google Forms for data collection. All participants were asked to complete a baseline questionnaire scoring Insomnia Severity Index (ISI) [12], Pittsburgh Sleep Quality Index (PSQI) [13], and 5-D Itch Scale (5DIS) [14]; patients with psoriasis were furthermore asked to complete the Dermatology Life Quality Index (DLQI) questionnaire [15]. The same questionnaires were to be completed again after week 4 and week 8.

Recruitment, Retention, and Costs

The recruitment rate was calculated as the number of participants enrolled in the study on average per day of the active recruitment period. The conversion rate was calculated as the percentage of participants screened who proceeded to be enrolled in the study. The retention rate was calculated as the percentage of participants filling out all the given questionnaires after enrollment.

The budget for advertisements on Google and Facebook was used to calculate the cost per unique view on the website, completed sign-ups, completed baseline questionnaires, and participants completing the entire study.

Clinical End Points and Statistical Analysis

To assess the correlations between sleep quality, life quality, and itch in the psoriasis group, the total scores from each questionnaire (ie, PSQI, ISI, 5-DIS, and DLQI) were used. When comparing participants with itch, those responding "no itch" were assigned a total score of 5, since this is the equivalent response on the questionnaire. To test for time or group effect for each questionnaire outcome, a linear mixed effects model, presented in an ANOVA table, was applied; the time category was considered as the within-subjects factor, and the psoriasis versus healthy controls groups were treated as the between-subjects factor; the interaction between the group variable and time variable was also assessed to determine if there was a significant change between people living with psoriasis and healthy controls over time. The linear mixed effects models were fitted by a restricted maximum likelihood with the lmer function from the lme4 R package. Visual inspection of quantile-quantile plots and residual plots was performed to reveal any obvious deviations from normality or homoscedasticity. Wilcoxon signed-rank test was conducted to compare average itch scores in good and poor sleepers. The participants were categorized into groups based on their sleep quality: poor sleep (PSQI>5) and good sleep (PSQI≤5) [13]. Statistical analysis was performed using the computing environment R (version 3.6.2; R Core Team).

Ethics Approval

This study was carried out in accordance with the principles expressed in the Declaration of Helsinki, and the regional ethical committee for the capital region of Denmark was consulted prior to its initiation, which waived the need for ethics approval, as it is a noninterventional questionnaire study (VEK protocol 16025688).

Results

Recruitment, Retention, and Costs

Participants were recruited during 2 weeks in September 2016, and data collection was finalized in January 2017. In just 14 days, 12,887 individuals clicked on the ads; 1466 completed the sign-up and screening processes, of which 839 completed the baseline questionnaire and were enrolled in the study. Participants were recruited from 11 different countries on 4 separate continents. The recruitment rate was 59.9 participants per day, and the conversion rate was 57.2%.

Of the 839 participants enrolled, 507 completed the 12-week study: 220 in the psoriasis group and 287 in the control group, with a retention rate of 60.4%.

Study participants were predominantly female and came from multiple different geographical locations (Table 1).

The total budget for recruitment was US $11,226 (equivalent to DKK 74,840 on September 1, 2016) [16], translating to US $13.24 per enrolled participant and US $22.1 per participant completing the study (Figure 1).

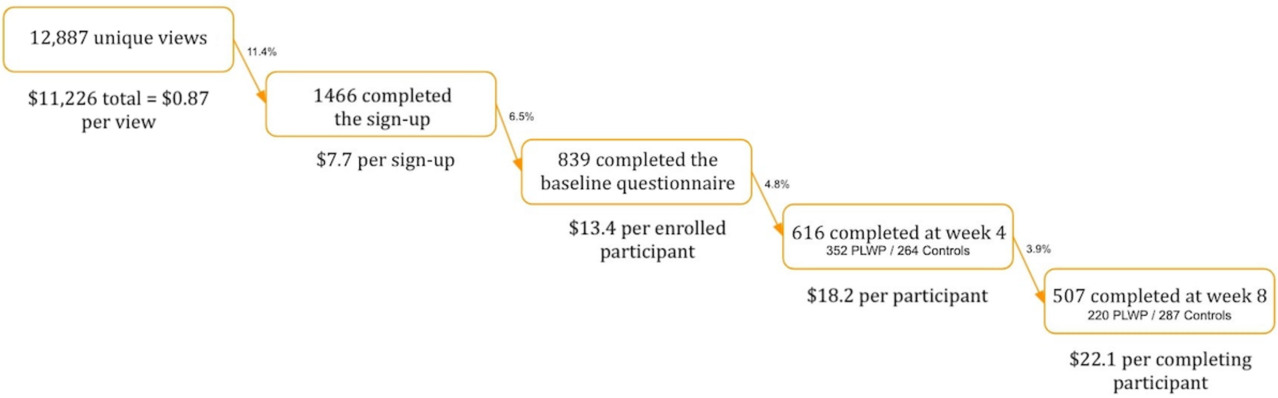
Table 1. Participant characteristics.

Characteristics	Healthy controls (n=287)	Patients with psoriasis (n=220)	*P* value
Age (years), mean (IQR)	39 (23-55)	49 (38-58)	<.001
Gender, n (%)			.4
Female	208 (72)	158 (72)	
Male	76 (26)	62 (28)	
Other	3 (1)	0 (0)	
Country, n (%)			.05
United Kingdom	119 (41)	91 (41)	
Canada	93 (32)	80 (36)	
United States	36 (13)	27 (12)	
Ireland	36 (13)	14 (6.4)	
Other[a]	3 (1)	8 (3.6)	
Living with psoriasis (years), mean (IQR)	N/A[b]	18 (6-30)	
Comorbidities, n (%)			
Any	178 (62)	145 (66)	.4
None	109 (38)	75 (34)	.4
Depression	91 (32)	61 (28)	.3
Eczema	20 (7)	18 (8.2)	.6
Self-perceived severity of psoriasis, n (%)			N/A
Moderate	N/A	126 (57)	
Mild	N/A	64 (29)	
Severe	N/A	30 (14)	

[a]Other countries: Denmark, Iran, Italy, Mauritius, New Zealand, and South Africa.

[b]N/A: not applicable.

Figure 1. Recruitment, retention, and cost. The currency is in US dollars. PLWP: people living with psoriasis.



Clinical End Points

There were no differences in sleep quality and sleep disturbance between patients with psoriasis and healthy controls over time, assessed with the PSQI questionnaire (Table 2 and Figure 2).

Moreover, perceived insomnia severity (based on ISI) was not different between groups, but there was a statistically significant decrease in insomnia severity over time within both groups (P=.003; Table 2 and Figure 3).

Self-assessed itch, reported with the 5-DIS, showed a statistically significant difference between the psoriasis group and the healthy controls (P<.001), while there was no statistically significant change over time (Figure 4).

In addition, there was a statistically significant positive correlation between itch and poor sleep in the psoriasis group and the control group (Figure 5), although patients with psoriasis with good sleep generally reported more itchiness, with a median score of 13.5 (IQR 10.8-15.5), compared to the controls with poor sleep, who had a median score of 11.3 (IQR 5.0-14.7).

There was a moderate correlation between itch and quality of life, as assessed with DLQI (r=0.51; Figure 6).

Table 2. ANOVA table with P values for the fixed effects (ie, time, group, and interaction) for different outcome measures from the questionnaires.

Outcome measure	Time effect		Group effect		Interaction effect	
	F value	*P* value	*F* value	*P* value	*F* value	*P* value
PSQI[a]	1.26	.28	2.37	.12	.024	.98
ISI[b]	5.96	.003	.12	.73	.51	.60
5DIS[c]	1.46	.23	148.75	<.001	.18	.84

[a]PSQI: Pittsburgh Sleep Quality Index.

[b]ISI: Insomnia Severity Index.

[c]5DIS: 5D Itch Scale.

Figure 2. Difference in sleep quality scores between the psoriasis group and the control group over time. (A) Pittsburgh Sleep Quality Index (PSQI) total scores (y-axis) over 3 time points grouped by controls (blue) and patients with psoriasis (yellow). No statistically significant differences were observed. (B) Boxplot of PSQI scores (y-axis) grouped by controls (blue) and patients with psoriasis (yellow). No statistically significant differences were observed.

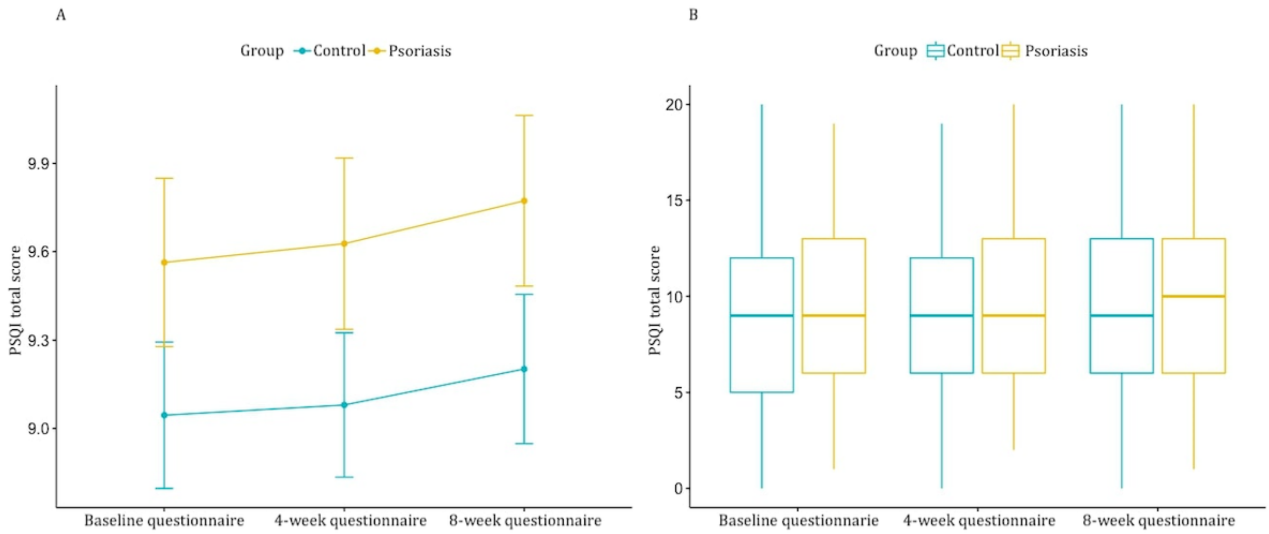


Figure 3. Difference in insomnia scores between the psoriasis group and the control group over time. (A) The mean Insomnia Severity Index (ISI) total scores (y-axis) over time in the control group (blue) and the psoriasis group (yellow). (B) Boxplot of the ISI total scores (y-axis) over time for the control group (blue) and the psoriasis group (yellow).

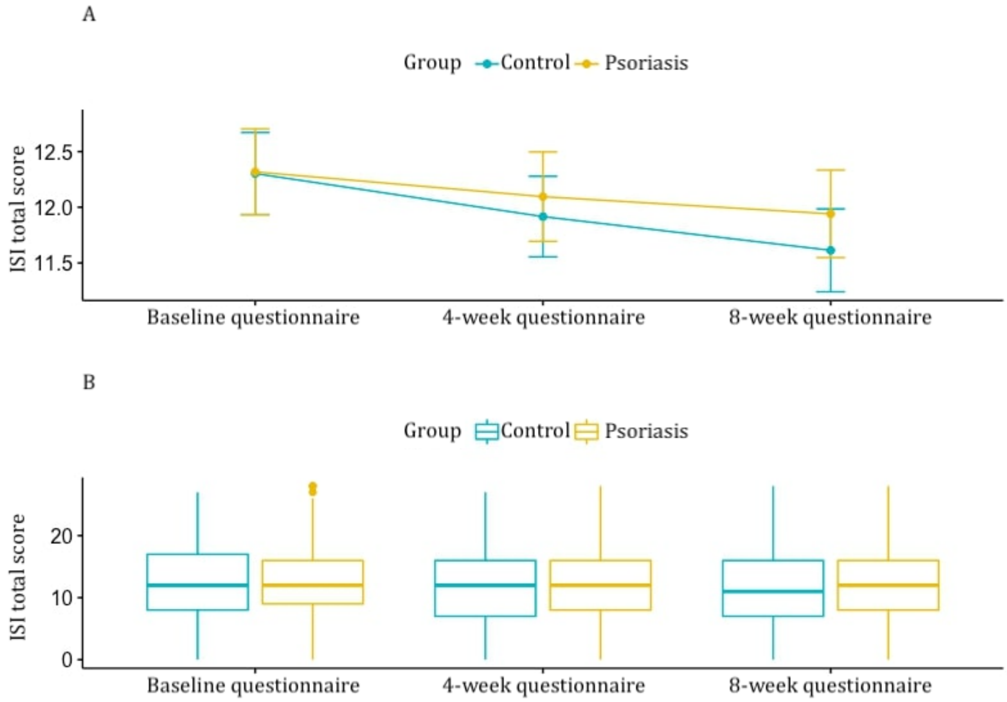


Figure 4. Difference in itch between the psoriasis group and the control group over time. (A) The mean 5D Itch Scale (5DIS) total score (y-axis) over time in the control group (blue) and the psoriasis group (yellow). (B) Boxplot of 5DIS total scores (y-axis) over time (x-axis) for both groups.

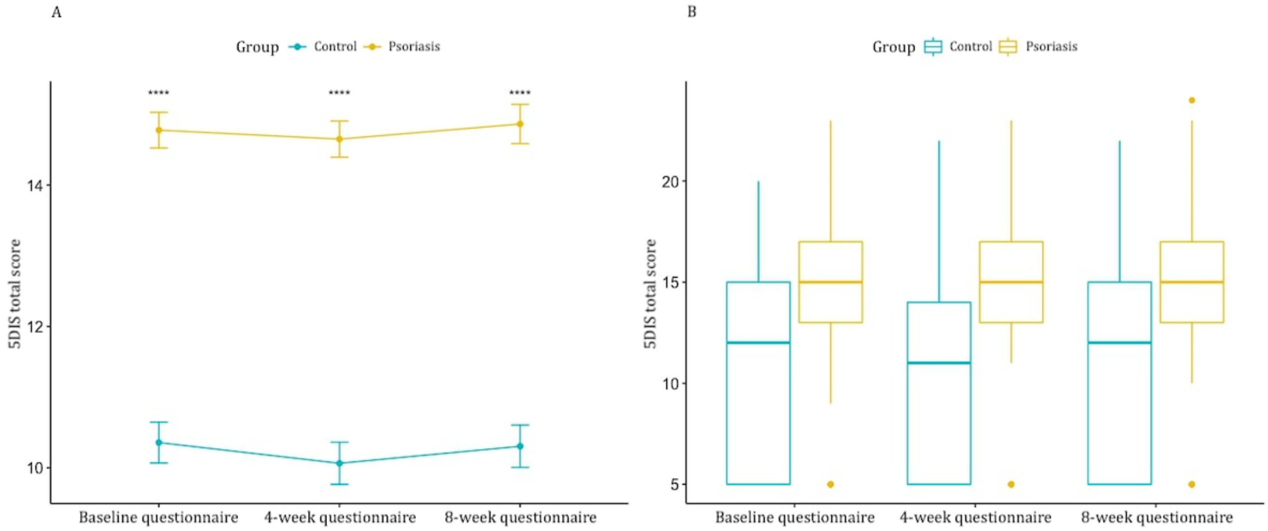


Figure 5. Boxplot of the 5D Itch Scale (5DIS) total score (y-axis) between controls and patients with psoriasis, grouped by the Pittsburgh Sleep Quality Index (PSQI) global score sleep quality. Adhering to the PSQI global score, poor sleep is defined as a score of 5 or more (blue), while good sleep is defined as a score lower than 5 (yellow).

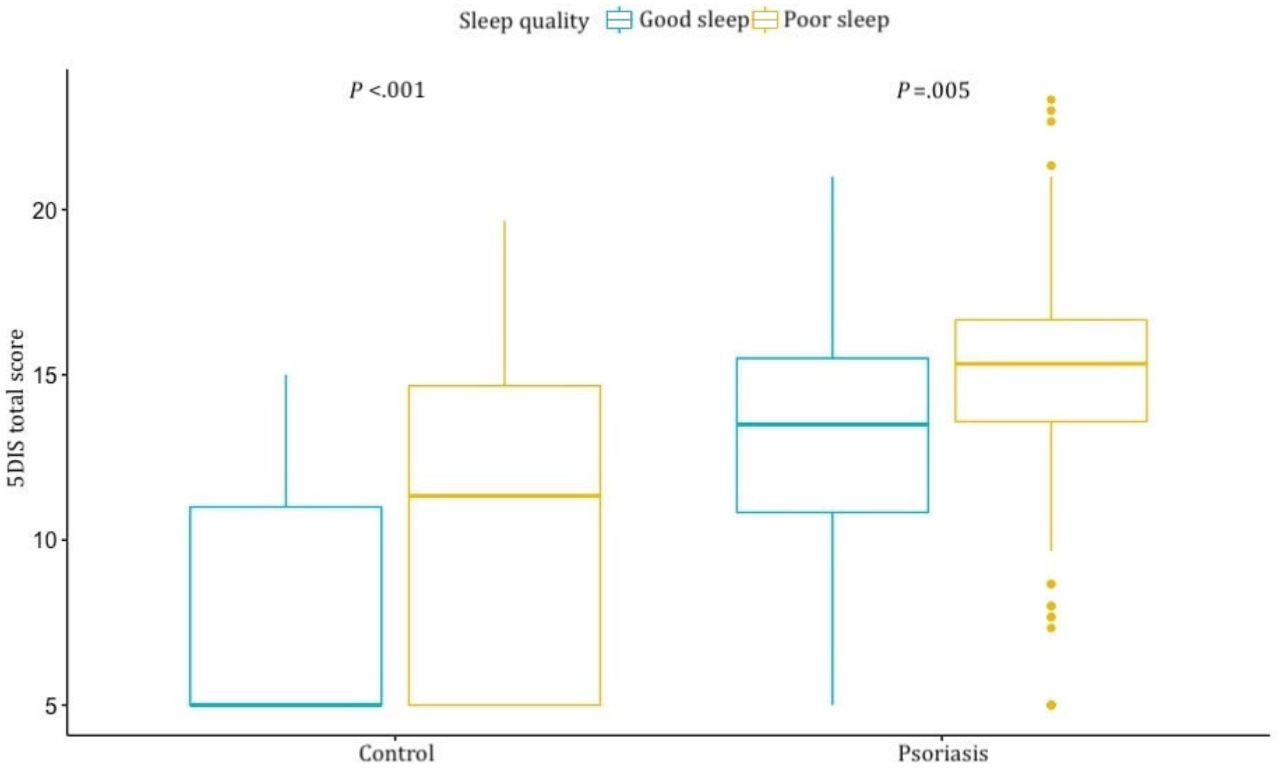
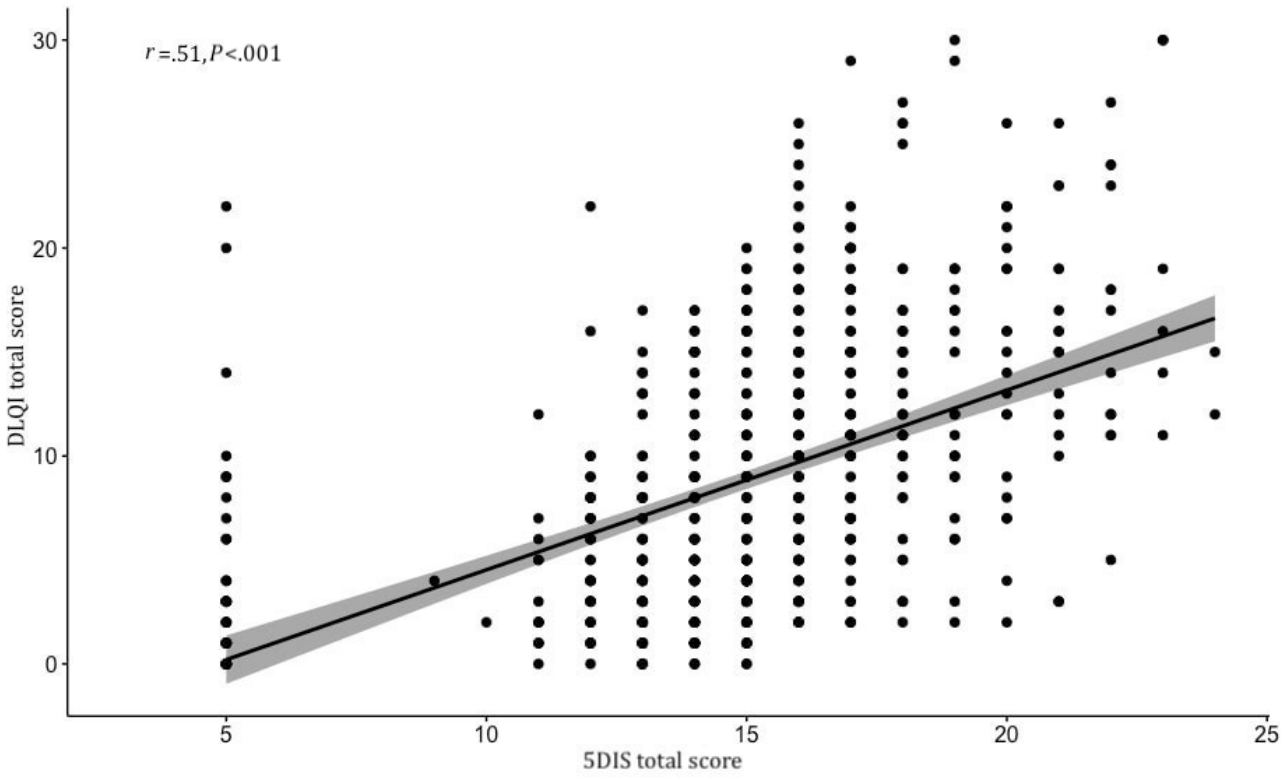


Figure 6. Impaired quality of life as a function of itch. Dermatology Life Quality Index (DLQI) total score is a function of the 5D Itch Scale (5DIS) total score.



Discussion

Principal Findings

In just 2 weeks, we recruited 1466 participants from several countries into an 8-week observational study of psoriasis. The conversion rate was 58%, and the retention rate was almost 60%, meeting the goal of 500 participants with a total of 507 participants completing the entire study. It is not uncommon to experience dropout rates as high as 70% in longitudinal studies [17], and considering the lack of in-person visits and the extensive study design with time-consuming questionnaires for study participants over the course of 8 weeks, our figures were surprisingly high. We managed to recruit participants from 11 different countries on 4 separate continents, offering a huge potential for representative and generalizable data.

In a recent systematic review and meta-analysis assessing cost-effectiveness of web-based and in-person recruitment strategies in 23 studies, the median cost per participant enrolled via the internet was US $72, while the median cost per enrollee for in-person recruitment was US $199 [10]. Although the study designs and the eligibility criteria for study participants varied tremendously, the cost per enrolled participant in this study was US $13, making it an extremely cost-effective approach. Pricing for Google Ads and Facebook Ads also varies over time, making it difficult to compare cost-effectiveness.

Although our clinical end points served as retention catalysts in this feasibility study, the questionnaires also offered information on sleep quality or insomnia, itch, and for patients with psoriasis, quality of life. We were able to show statistically significant differences in itch between patients with psoriasis and healthy controls, a common characteristic of psoriasis [18]. We also found that sleep quality as assessed by the total score in the ISI questionnaire improved from baseline to week 4 and from week 4 to week 8. In previous studies, the ISI was only moderately correlated with the PSQI [19], which could explain the lack of similar changes over time in the PSQI total score. Lower sleep quality is associated with other comorbidities, such as depression [20]; however, the 2 groups did not show a statistically significant difference in this parameter.

Even though this study was conducted in 2016, the general methods for web-based patient recruitments have not changed drastically, Facebook still being the most commonly used social media recruitment platform [7]. TikTok and other more recent platforms tend to cater to younger audiences not usually enrolled in clinical studies [21,22].

Study Limitations

There are several limitations in this study. With the potential of heterogenous and generalizable data, collected using web-based recruitment, it is important to mention the potential opposite effect. A recent study from 2022 by Li et al [23] investigating recruitment and retention within different incentive structures in the United States found certain characteristics related to higher retention rates. Overall, older participants showed higher retention rates. In a subgroup, where participants were recruited from advertisements in social media and web-based newspapers, ethnicity (non-Hispanic White), education level (college or higher) and income level (<US $49,999) showed longer retention. These findings suggest the necessity of finding other methods in retaining a more diverse study population.

Another limitation of our study is that we did not assess how demographic data of study participants pertained to study outcomes, such as recruitment and retention. One notable difference from Li et al [23] is that we did not offer monetary incentives. This may likely affect the demographic characteristics of the study population, especially regarding income levels. Future studies should evaluate whether their recruitment outcomes are related to participant demographics.

Given the self-reported design of this study, one limitation relates to our secondary, clinical outcomes. There is a possibility of recruiting patients without a clinically validated psoriasis diagnosis. There is also the possibility of a selection bias toward patients having more severe psoriasis than is representable in the standard population. Although patients were asked whether they were clinically diagnosed by a certified physician, the self-perceived severity of their diagnosis, and the treatment options they used, there was no way to verify this information.

One major limitation to web-based recruitment is selection bias. In our study, focusing on psoriasis and sleep quality, the healthy controls most likely had an interest in sleep quality, and that presented a possible bias. Another limitation was thought to be related to age, with the hypothesis that older people, being less digitally savvy, would not sign up because of the fully remote digital design of the study. However, the median age in the psoriasis group was 49 years, while it was 39 years in the healthy control group; given the bimodal peaks of psoriasis onset being 20-30 and 50-60 years of age, the age group in this study was representative.

The observational design of this study also offers limitations when compared to decentralized clinical trials with interventional elements. Comparing the number of sign-ups to the completion of the questionnaires, it is possible that the easy sign-up process might lead to higher dropout rates later in the study.

Conclusions

In conclusion, we managed to enroll and retain more than 500 study participants not restricted by geography for a duration of 8 weeks in this feasibility study. This represents a promising strategy for recruitment of patients with rare diseases and to furthering better representation of study participants. Future studies should investigate the feasibility of web-based recruitment in clinical trials without geographical restrictions and explore the characteristics of study populations recruited through this method.

Acknowledgments

The authors would like to thank Morten Krarup Kristensen and Alexander Almegaard who contributed to the conduct of the study.

Conflicts of Interest

ZA and SFT have no conflicts of interest in regard to this study. ZDH, API, JRZ, and ADA were employed by Studies&Me A/S at the time the study was conducted. Studies&Me A/S is a virtual contract research organization specializing in decentralized clinical trials and digital recruitment of subjects for clinical trials. This does not alter our adherence to the journal's policies. Furthermore, JRZ was employed by Future-Brain Aps when the manuscript was being written; there are no conflicts of interest, as they do not specialize in recruitment strategies.

Multimedia Appendix 1
Google AdWords.
[DOCX File , 14 KB - derma_v6i1e44405_app1.docx]

Multimedia Appendix 2
Sign-up questionnaire.
[DOCX File , 15 KB - derma_v6i1e44405_app2.docx]

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Abbreviations

5DIS: 5D Itch Scale
DLQI: Dermatology Life Quality Index
ISI: Insomnia Severity Index
PSQI: Pittsburgh Sleep Quality Index

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Corrigenda and Addenda

Correction: Brachioradial Pruritus Due to Cervical Spine Pathology

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Related Article:

Correction of: https://derma.jmir.org/2022/3/e39863

(JMIR Dermatol 2023;6:e55896) doi:10.2196/55896

In “Brachioradial Pruritus Due to Cervical Spine Pathology” (JMIR Dermatol 2022;5(3):e39863) the authors noted one error.

The term “pruritis” was used instead of "pruritus" in several instances across the manuscript. This term was changed within the Keywords section, along with four other locations as follows:

The first sentence of the "Case" section was present as:

> *A 70-year-old female patient with no past medical history presented to the outpatient spine clinic with a 2-year history of intermittent pruritis predominantly along the bilateral dorsolateral forearm.*

And will now appear as:

> *A 70-year-old female patient with no past medical history presented to the outpatient spine clinic with a 2-year history of intermittent pruritus predominantly along the bilateral dorsolateral forearm.*

The fifth line under "Case" appeared as:

> *The patient reported no prior dermatological diseases, familial pruritis, or trauma to the spine or extremities.*

And will now be changed to:

> *The patient reported no prior dermatological diseases, familial pruritus, or trauma to the spine or extremities.*

The final line of the "Discussion" section previously appeared as:

> *This case is unique given that our patient presented with solely pruritis and without any history of pain related to her cervical spine pathology.*

And will now be changed to:

> *This case is unique given that our patient presented with solely pruritus and without any history of pain related to her cervical spine pathology.*

Finally, the title was presented as:

> *Brachioradial Pruritis Due to Cervical Spine Pathology*

And will now appear as:

> *Brachioradial Pruritus Due to Cervical Spine Pathology*

The correction will appear in the online version of the paper on the JMIR Publications website on December 29, 2023 together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

Submitted 28.12.23; this is a non–peer-reviewed article;accepted 28.12.23; published 29.12.23.

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Original Paper

Evolution of a Project to Improve Inpatient-to-Outpatient Dermatology Care Transitions: Mixed Methods Evaluation

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Abstract

Background: In-hospital dermatological care has shifted from dedicated dermatology wards to consultation services, and some consulted patients may require postdischarge follow-up in outpatient dermatology. Safe and timely care transitions from inpatient-to-outpatient specialty care are critical for patient health, but communication around these transitions can be disjointed, and workflows can be complex.

Objective: In this 3-phase quality improvement effort, we developed and evaluated an intervention that leveraged an electronic health record (EHR) feature, known as SmartPhrase, to enable a new workflow to improve transitions from inpatient care to outpatient dermatology.

Methods: Phase 1 (February-March 2021) included interviews with patients and process mapping with key stakeholders to identify gaps and inform an intervention: a SmartPhrase table and associated workflow to promote collection of patient information needed for scheduling follow-up and closed-loop communication between dermatology and scheduling teams. In phase 2 (April-May 2021), semistructured interviews—with dermatologists (n=5), dermatology residents (n=5), and schedulers (n=6)—identified pain points and refinements. In phase 3, the intervention was evaluated by triangulating data from these interviews with measured changes in scheduling efficiency, visit completion, and messaging volume preimplementation (January-February 2021) and postimplementation (April-May 2021).

Results: Preintervention pain points included unclear workflow for care transitions, limited patient input in follow-up planning, multiple messaging channels (eg, EHR based, email, and phone messages), and time-inefficient patient tracking. The intervention addressed most pain points; interviewees reported the intervention was easy to adopt and improved scheduling efficiency, workload, and patient involvement. More visits were completed within the desired timeframe of 14 days after discharge during the postimplementation period (21/47, 45%) than the preimplementation period (28/41, 68%; P=.03). The messaging workload also decreased from 88 scheduling-related messages sent for 25 patients before implementation to 30 messages for 8 patients after implementation.

Conclusions: Inpatient-to-outpatient specialty care transitions are complex and involve multiple stakeholders, thus requiring multifaceted solutions. With deliberate evaluation, broad stakeholder input, and iteration, we designed and implemented a successful solution using a standard EHR feature, SmartPhrase, integrated into a standardized workflow to improve the timeliness of posthospital specialty care and reduce workload.

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KEYWORDS

care transition; discharge planning; inpatient; outpatient; follow-up; teledermatology; dermatology; consultative dermatology

Introduction

Changes in health care financing, including adoption of diagnosis-related groups, have had a negative effect on coverage and reimbursement for inpatient dermatological care [1-3]. In response, inpatient dermatological care has shifted from dedicated dermatology wards to consultative services [1,3-5]. Thus, patients with dermatologic disorders are admitted to inpatient services attended by nondermatologist providers, and in-hospital dermatological care is provided by consulting dermatologists. Some consulted patients may require postdischarge follow-up dermatological care provided in outpatient clinics. Coordination of transitions requires close collaboration between multiple stakeholders, including the primary inpatient team, dermatology team (dermatologists and residents), clinic staff, and patients, to plan, schedule, and execute follow-up care [6].

Care transition workflows are complex with multiple stakeholders. Poor coordination has wide-ranging impacts from frustration to complications resulting in suboptimal health, excess cost, and hospital readmissions [2,7]. Timeliness of transitions is associated with higher follow-up visit attendance [8], but structural and organizational barriers and communication deficits contribute to gaps in coordination [9,10]. Shifting transitions from siloed, disease-centric care to integrated, patient-centered care [11,12] can improve health outcomes, readmissions, costs, and patient satisfaction [13]. Nurse-led transition support can help patients and caregivers navigate the health system but is resource intensive and may not be feasible in all situations [14]. Easy-to-use, rapidly deployable solutions are needed to support effective and timely care transitions from inpatient consultations to outpatient specialty care.

Widespread outpatient teledermatology use has allowed greater flexibility for scheduling dermatology patients [15-17]. However, concerns regarding communication, timely follow-up, and excessive workload remain among clinicians and staff, prompting this quality improvement (QI) project. In this study, we described our efforts to improve dermatology care transitions in three phases: (1) redefining the problem and solution development; (2) exploring preintervention pain points and adapting the solution; and (3) evaluating the intervention and identifying persisting challenges.

Methods

Study Setting and Patients

Stanford Medicine's Dermatology Department (Bay Area, California) has 13 outpatient clinics with 16 subspecialties and provides 2 inpatient consultative services in a quaternary hospital: general dermatology and supportive dermato-oncology, a service for oncology patients with dermatological complications. A total of 5 dermatologists and rotating residents (2 per month) provide inpatient consultations to >1500 inpatients per year and outpatient follow-up care. Approximately 40% of patients who receive an inpatient dermatology consultation require postdischarge dermatology follow-up; many are affected by complex, high-risk skin conditions; are immunocompromised; and have multidisciplinary inpatient care teams. Care transitions also involved scheduling staff, including front office scheduling staff, new patient coordinators (NPCs), and their managers.

QI Process, Data Collection, and Analysis

Phase 1: Redefining the Problem and Solution Development

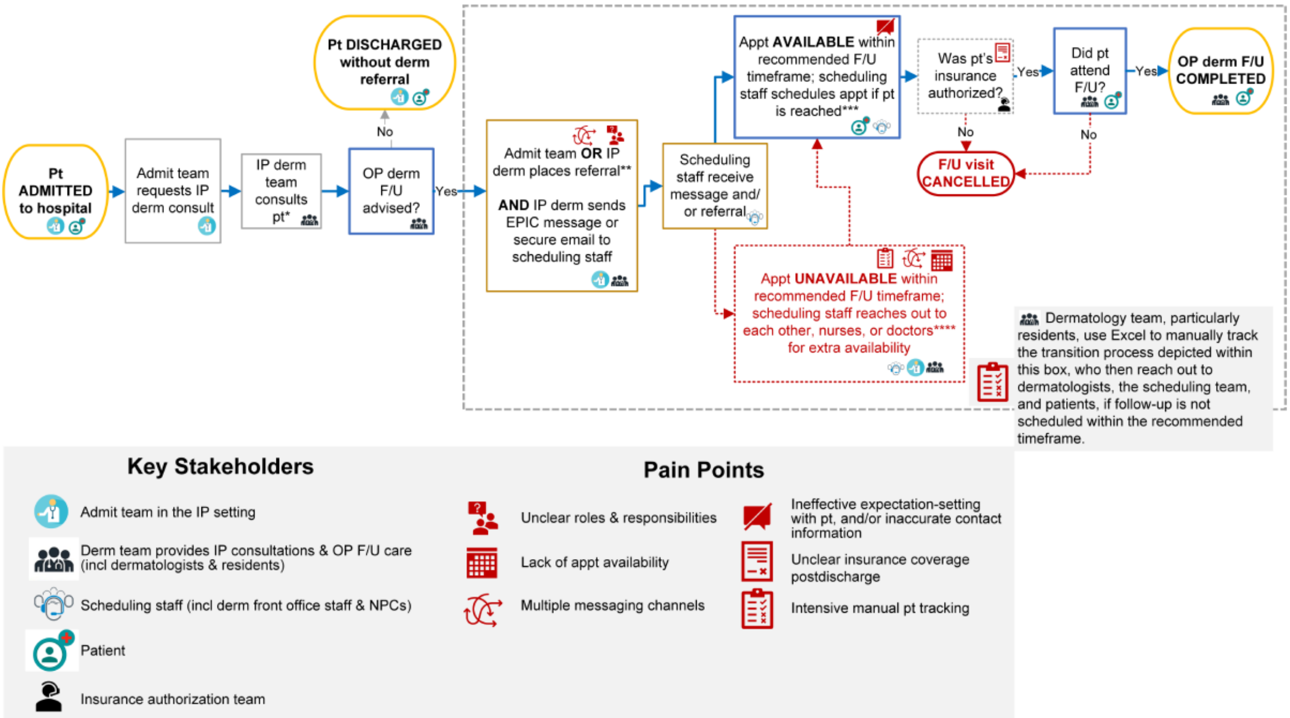
Current State

In February 2021, clinical leaders (MAA, JMK, BYK, and AC) met with scheduling staff and insurance authorization representatives to understand concerns regarding inpatient-to-outpatient care transitions. These insights were combined with informally collected anecdotal experiences of dermatologists and residents in the preintervention process map (Figure 1). In brief, the preintervention workflow had the following steps:

1. Admitting team (eg, general medicine) requested a dermatology consultation.
2. Inpatient dermatology team (dermatologists and residents) conducted a consultation with the patient and would determine if outpatient follow-up is needed.
3. The admitting team or dermatology team would place the referral. A member of the dermatology team would also contact the scheduling staff via electronic health record (EHR)–based message and a secure email or telephone call.
4. Scheduling staff would receive the message, identify the correct work queue, and contact the patient to schedule an appointment.
5. The dermatology team, primarily residents, would monitor the patients' EHR to determine if patient was scheduled for follow-up, had insurance approval, and completed follow-up visit. Resident would contact the scheduling staff via EHR-based message and a secure email or telephone call if any step of the process fell through.

Key pain points included (1) multiple and inconsistent communication channels (eg, EHR-based messages, emails, and phone calls), (2) unclear roles and responsibilities, (3) burdensome workload for dermatology and scheduling teams, and (4) intensive manual tracking of the process to schedule follow-ups. These pain points may be exacerbated in the consultative context; the inpatient dermatology team consults for numerous services, such as medicine, surgery, intensive care, and obstetrics and gynecology, resulting in many workflows to navigate. Furthermore, skin issues will often not completely resolve by discharge, despite the dermatology consultative team following up with patients closely throughout their hospitalization. Thus, patients may benefit from outpatient skin-directed follow-up; enabling this care faces substantial barriers. In particular, patients’ dermatologic diagnoses may often be unrelated to their primary reason for hospitalization, which may result in a deprioritization (by both patients and providers) of skin issues after discharge.

Figure 1. Preintervention (ie, baseline) process mapped using insights from schedulers, insurance authorization, dermatologists, and residents in phase 1 and redefining the problem and solution development of a quality improvement project aiming to improve timeliness of transitioning patients from inpatient-to-outpatient dermatology and reduce workload. *Inpatient dermatology consult completed in person or via e-consult. **Could occur pre or postdischarge. If before, scheduling team may wait to initiate scheduling until patient is discharged. ***Patient contacted by phone up to three times and sent a mailed letter. ****Dermatology team, particularly residents, manually track patient transitions in Excel who reached out to dermatologists, scheduling staff, and patients if follow-up not scheduled within the recommended timeframe. Admit: Admitting; Appt: Appointment; Derm: dermatology; F/U: follow-up; incl: including; IP: inpatient; NPC: new patient coordinator; OP: outpatient; pt: patient.



Patient Perspectives

Phase 1 also included formative qualitative interviews conducted to understand patients’ and caregivers’ experiences with inpatient-to-outpatient dermatology care transition and elucidate their needs. A total of 14 patients and 1 caregiver were interviewed; methods and patient characteristics can be found in Multimedia Appendix 1.

Patients were satisfied with discharge plans and communication with their dermatologists; however, issues persisted around 3 themes: communication and expectation setting during discharge planning; dermatology team support and postdischarge teledermatology; and care coordination and prioritization for medically complex patients. Multimedia Appendix 2 contains supporting quotations. Notably, patients who experienced serious, nondermatological medical events had limited recall of interactions with dermatology. Consequently, for some patients, the necessity of dermatology follow-up was unclear, but caregivers could provide indispensable support. Prioritizing other health issues and coordinating dermatology care with other teams also impacted follow-up success. Nevertheless, patients who followed up with dermatology were generally satisfied with their follow-up coordination experience, even if delayed. They appreciated the dermatology team’s accessibility during transition, facilitated for some patients by teledermatology and direct provider messaging. Despite not all patients following up via video and some still preferring in-person visits, most agreed that video visits are convenient, easy, and provide better access. In fact, almost all patients expressed interest in future video visits, although concerns remained around photo or video quality.

Intervention Development

The developed intervention included a SmartPhrase (also known as a dot phrase), a flexible Epic EHR feature that creates templates (eg, fillable statement or table) that can be integrated into patient notes, referrals, or discharge instructions by typing a period and short phrase [18]. On the basis of the patient interviews and informal data collection with inpatient dermatologists, dermatology residents, NPCs, front office schedulers, nurses, and insurance representatives, a team drafted a SmartPhrase form that addressed the main pain points. In particular, the SmartPhrase addressed schedulers’ request for more information, including recommended follow-up timeline, preferred patient contact information, and preferred provider for scheduling and requests for overbooking. Including the reason for follow-up and follow-up timeline was particularly important for confirming patient’s understanding of the importance of follow-up. Patients’ perspectives prompted the inclusion of a field to indicate whether a video visit would be an acceptable option. To address the patients’ perspective that their dermatologic condition was not always their priority, the SmartPhrase was completed with the patient at the bedside to explain the importance of follow-up to the patient and caregiver. The team shared the SmartPhrase with residents and incorporated their feedback before integrating it into Epic.

The SmartPhrase (Table 1) prompted dermatologists to obtain and document pertinent patient information necessary for scheduling follow-up care in the new workflow:

1. Dermatology team (dermatologists and residents) engages in shared decision-making with patients and caregivers during an inpatient consultation.
2. Dermatology team obtains the necessary information to schedule follow-up and documents in the SmartPhrase during inpatient consultation.
3. Dermatology team submits an “as soon as possible (ASAP)” referral for outpatient care that includes completed SmartPhrase.
4. NPCs receive the referral. NPCs keep new patient referrals in their work queue and forward return patient referral to the front office scheduling staff.
5. Scheduling team, NPCs and front office scheduling staff, facilitate correct and timely scheduling of follow-up visits with patient.
6. Scheduling team connects with dermatology team about patients who decline follow-up or cannot be reached to determine the next steps.

The intervention, the SmartPhrase and associated workflow, was activated on March 22, 2021. Dermatologists (n=5), rotating residents (2 per month), and 15 scheduling staff received group verbal training with written documentation describing the workflow and SmartPhrase use from an improvement leader. A total of 13 scheduling staff, including front office scheduling staff and NPCs and their 2 managers, were also trained.

Table 1. Content of developed electronic health record–based SmartPhrase table, a key component of the associated workflow, that prompted predischarge conversations with the patient to capture and document necessary patient information to schedule follow-up for patients transitioning from inpatient-to-outpatient dermatology care. At the top of the SmartPhrase table, there were two notes that emphasized steps in the workflow: (1) "PLEASE MARK ALL INPATIENT REFERRALS AS PRIORITY: ASAP" and (2) "PLEASE PLACE THIS DOT PHRASE INTO THE COMMENTS SECTION OF THE REFERRAL." The first statement was added after initial implementation and was based on early feedback from dermatologists, residents, and scheduling staff.

SmartPhrase component and generalizable drop-down menu options	Example of content within an ASAP[a] referral for outpatient follow-up care
Patient name on file	
[Patient name from patient's electronic health record]	Jane Doe
Date of birth on file	
[Patient date of birth from patient's electronic health record]	00/00/0000
Patient ID	
[Patient ID from patient's electronic health record]	00000000
REASON FOR REFERRAL: Patient recently admitted to hospital, seen by inpatient derm[b] team, needs outpatient dermatology follow-up for: (Reason for derm DC[c] referral: 45,992)	
SCAR[d] (SJS[e] or TEN[f], DRESS[g], AGEP[h])	SSTI[i]
Blistering dermatitis (PV[j], BP[k], Linear IgA[l], etc)	—[m]
GVHD[n]	—
Chemo[o] or immunotherapy-related rash	—
Vasculitis	—
Connective tissue disease (lupus, DM[p], etc)	—
Neutrophilic dermatosis (PG[q], sweets[r], etc)	—
SSTI	—
Skin exam	—
Other[s]	—
IS THIS A NEW OR RETURN PATIENT (New or return patient: 46914)	
New	Return
Return	—
TIME REQUESTED FOR FOLLOW-UP: (Time requested for derm appt: 46001)	
1-3 days	2 weeks
1 week	—
2 weeks	—
1 month	—
2 months	—
Next available (nonurgent follow-up)	—
Discharge clinic VV only (gen[t] derm): Wednesday AM	—
Discharge clinic CC[u] only (SDO[v])—Tuesday PM	—
[Insert specific date]	—
VISIT TYPE REQUESTED: (Visit type requested: 46002)	
No preference	Video visit
In person	—
Video visit	—
E-consult	—
Other[s]	—

SmartPhrase component and generalizable drop-down menu options	Example of content within an ASAP[a] referral for outpatient follow-up care
LOCATION PREFERRED: (Location of derm follow-up: 46003)	
[Drop-down list of outpatient dermatology clinics]	Clinic name
PROVIDER PREFERRED: {Provider preferred for derm follow-up: 46006)	
[Drop-down list of dermatology providers]	Provider name
INTERPRETER NEEDED FOR SCHEDULING AND VISIT: (Interpreter Needed: 46005)	
Yes	Yes
No	—
PREFERRED LANGUAGE SPOKEN: (Preferred Language: 46006)	
English	Spanish
Spanish	—
Mandarin	—
Russian	—
Vietnamese	—
Other[s]	—
BEST CONTACT NUMBER OR WHO TO CONTACT TO SCHEDULE: (Best contact: 46007)	
[Text box]	123-345-5678 James Doe (spouse)

[a]ASAP: as soon as possible.
[b]derm: dermatology.
[c]DC: discharge.
[d]SCAR: severe cutaneous adverse reactions.
[e]SJS: Stevens-Johnson syndrome.
[f]TEN: toxic epidermal necrolysis.
[g]DRESS: drug reaction with eosinophilia and systemic symptoms.
[h]AGEP: acute generalized exanthematous pustulosis.
[i]SSTI: skin soft tissue infection.
[j]PV: Pemphigus vulgaris.
[k]BP: bullous pemphigold.
[l]IgA: immunoglobin A.
[m]Clinicians were to select the relevant options from the SmartPhrase for each individual patient. For the provided example, 1 option was selected from each SmartPhrase component.
[n]GVHD: graft-versus-host disease.
[o]Chemo: chemotherapy.
[p]DM: dermatomyositis.
[q]PG: yogerma gangrensoum.
[r]sweets: Sweet syndrome, also called acute febrile neutrophilic dermatosis.
[s]Clinicians could indicate other options using a free text box.
[t]gen: general.
[u]CC: continuity clinic.
[v]SDO: supportive dermatology-oncology.

Phase 2: Exploring Preintervention Pain Points and Adapting the Intervention

Semistructured interviews were conducted to further understand phase 1 pain points and inform early adaptations to the intervention. Clinicians and staff who had worked with the preintervention and postintervention workflows were invited via email (with 2 reminders) to participate in 30-minute phone interviews between April and May 2021. A total of 15 interviews were held by EASG or AA with 5 of 5 dermatologists, 5 of 5 residents, and 6 of 13 schedulers. Interviews were audio recorded and lasted for 30 to 60 minutes. Interviews informed both phases 2 and 3.

Data were analyzed, deductively and inductively, using a multiphase analysis approach that leveraged rapid analytic procedures to extract early themes, consensus coding of transcripts, and a matrix analysis [19]. In brief, EASG and AA summarized individual interview transcripts independently, reviewed summaries, had consensus discussions, and consolidated summaries into a matrix to identify themes and compare across interviewees. Identifiable information was removed from transcripts to maintain anonymity.

Phase 3: Evaluating the Intervention and Identifying Persisting Challenges

Overview

Mixed methods were used to evaluate the impact and sustainability of the intervention, the SmartPhrase and associated workflow. Specifically, qualitative interview data, scheduling data, and EHR messaging data were triangulated and consolidated and interpreted in parallel.

Perceptions of the Intervention's Early Impact and Its Sustainability

The semistructured interviews explored interviewees' perceptions of the early impact of the intervention on follow-up timeliness, workflow and workload, its potential sustainability, and persisting challenges for phase 3 (see phase 2 for methods and analysis).

Timeliness of Follow-up

The impact of the intervention on the timeliness of scheduling, completion of follow-up, and messaging workload was assessed by comparing two periods: (1) preimplementation (January 1 to February 28, 2021) and (2) postimplementation (April 1 to May 31, 2021). March 2021 was excluded, as the SmartPhrase was enabled on March 22, 2021. Data were extracted for all patients who received an inpatient dermatology consultation, were discharged from the hospital (ie, inpatient, observation, and emergency department [ED] encounters) within 1 of the 2 evaluation periods, and were expected to need an outpatient follow-up dermatology visit, that is, hospitalization had current procedural terminology codes indicating potential need for follow-up care (Multimedia Appendix 3). Follow-up visits scheduled and completed within 90 days of discharge were included; those scheduled or completed more than 90 days postdischarge were unlikely to be related to the hospitalization. Outcomes included (1) proportion of patients completing a follow-up visit within 90 days postdischarge, (2) proportion of patients completing a follow-up visit within 14 days postdischarge (postdischarge goal of department), and (3) days from inpatient discharge to completed follow-up. Descriptive statistics are reported. *P* values were calculated using chi-square tests for categorical outcomes and 2-tailed *t* tests for continuous outcomes.

Staff Messaging

EHR-based messaging volume data, specifically in-basket messaging in Epic [20], was used as a proxy for communication workload, as it was a commonly used and measurable. Sent messages were extracted for 5 inpatient dermatologists and 8 dermatology residents (2 per month) involved in inpatient care during the 2 periods. Of 13 scheduling staff, 12 schedulers sent messages during the preimplementation period and 11 schedulers during the postimplementation period. Messages related to scheduling patients who received an inpatient consultation and completed an outpatient follow-up visit within 90 days of discharge were identified using a keyword search (Multimedia Appendix 4). A total of 2 outcomes are reported for the two periods: (1) number of follow-up patients associated with staff messages and (2) number of in-basket messages sent.

Ethics Approval, Informed Consent, and Participation

This project received a nonresearch determination from the Stanford University institutional review board (IRB-60382). Interviewees provided verbal informed consent before the initiating the interview and recording, and all responses were kept confidential and anonymous. Detailed interview notes were taken when participants declined to be recorded.

Results

Phase 2: Exploring Preintervention Pain Points and Refining the Intervention

Overview

Interviewees reported that the preintervention workflow had a high risk for communication errors, delays, losing patients to follow-up, and potentially adverse patient outcomes. Unclear roles and responsibilities, multiple messaging channels, limited patient input, and intensive manual tracking of patients were identified as local barriers. Lack of appointment availability and insurance authorization issues were important structural barriers. Supporting quotes are in Tables 2 and 3. Barriers were overlaid onto the original process map (Figure 2).

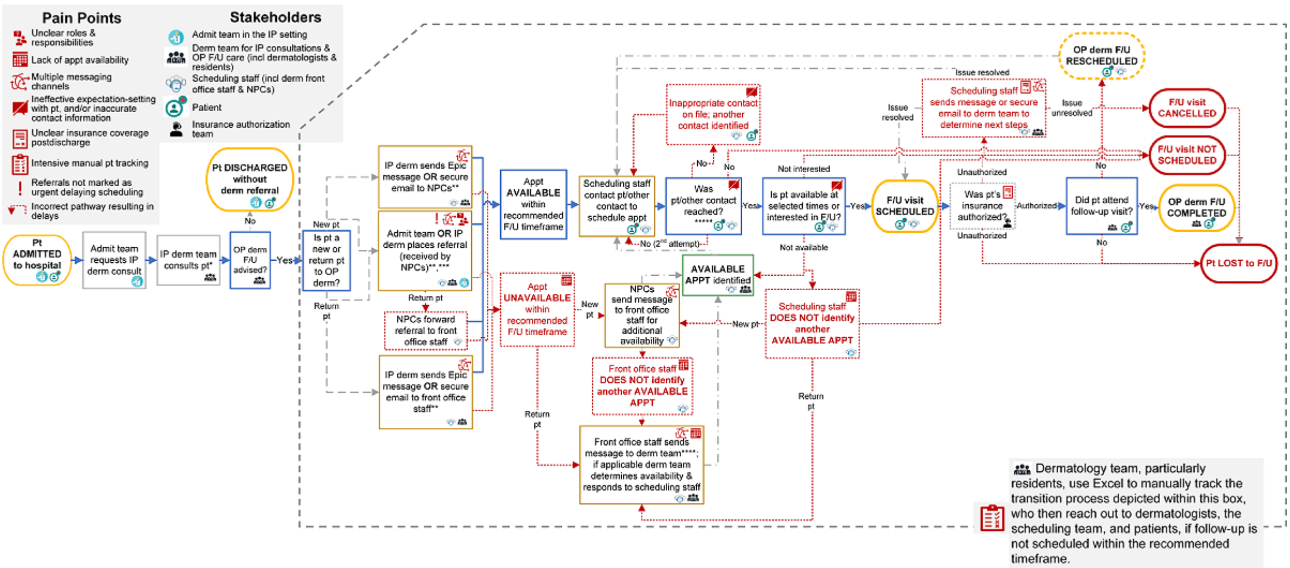
Table 2. Exemplary quotes from interviews with dermatologists, residents, and scheduling staff describing preintervention pain points related to the preintervention scheduling workflow for transitioning recently discharged patients to outpatient dermatology for follow-up care and associated workload lacking a standard process.

Theme: preintervention scheduling workflow lacked a standard process	Exemplary quotes
Overall perceptions	• "...our gut feeling was that it didn't work. We're always so nervous that something falls through the cracks, and we don't know about it" (dermatologist). • "...before the SmartPhrase the system was just based on messaging and it was just a lot of work for everyone. I think that things fell through the cracks as well there" (resident). • "...a lot of backend work that I just don't think is that efficient, because it's never actually solving the problem. It's like, we're just kind of patching things up, patient by patient, making sure one person doesn't falls through the cracks. But we're just not able to account for everybody that way" (dermatologist).
Unclear roles and responsibilities	• "There's so many residents, and we're rotating so much, that you have to have a really well set up system that everyone's involved in. Otherwise, things will for sure fall through the cracks" (resident). • "...wasn't honestly that clear whether it was the primary team that was sending the referral or whether we would send the referral [...] sometimes we were having the primary team send the referral. Then you would be reaching out to the medicine [admitting] team, like, 'Hey, could you please put the referral?' But I think just because I knew that I could send in the referral and it saves them a step, I would usually just do it anyway. I just felt like it was more work to have them do it. And I know they're busy as well" (resident).
Multiple messaging channels	• "...sometimes residents would message through Epic® and then sometimes it would be through email. So, it wasn't always consistent where these messages 'lived.' And then sometimes the messaging would actually take place in the referral itself. So, there were just so many different places for us to keep track of" (dermatologist). • "...I look at my schedule an unhealthy number of times every day" (dermatologist). • "...they are all small tasks but then when you're seeing two to four or five new patients a day, and then discharging a similar number, it adds up, doing those messages and referrals and trying to keep track" (resident). • "I would send the referral to, and then would send a staff message as well, to the front office staff...patient was admitted for this reason, we might follow up. I will try to specify the timeframe and if there was a specific provider. But I obviously wasn't always including every detail that they might need to help set the appointment" (resident). • "...it's very important that when creating the referral...that the appointment is marked urgent. That's the most important thing to make sure that the patients are scheduled in a timely manner" (scheduler).
Limited patient and caregiver input	• "...patients oftentimes have complex medical problems...the fact that they have a lot going on, it would be easy for them to not prioritize their skin issues" (resident). • "...we need to ask the patient if they want an appointment because we actually were getting a bunch of patients scheduled, who then canceled same day or just no-showed, because they actually didn't want follow-up. [...] it's just very important to...engage the patient in that decision" (dermatologist).
Intensive patient tracking	• "...we probably micromanage it. We won't let go until something's happened. So I think that feeling of worry that something is going to fall through the cracks led us to all universally micromanage more and send a lot of messages, want to see the confirmation if a patient doesn't show then go back and ask, and then resend referrals again, and have schedulers call" (dermatologist). • "...sometimes patients are anticipated to be discharged and then the resident will send the message to the staff, put in the referral and then the patient ends up having another reason for the stay in the hospital longer than what we anticipated. So by the time the schedulers call, the patients are still admitted in the hospital and so they're not able to appropriately gauge when would be a reasonable time to schedule the patient" (resident).

Table 3. Exemplary quotes from interviews with dermatologists, residents, and scheduling staff describing preintervention pain points related to structural barriers for transitioning recently discharged patients to outpatient dermatology for follow-up care and associated workload.

Theme: structural barriers	Exemplary quotes
Limited appointment availability	• "...they are all small tasks but then when you're seeing two to four or five new patients a day, and then discharging a similar number, it adds up, doing those messages and referrals and trying to keep track" (resident). • "...for every message that we send asking for a patient to be seen in follow-up within a couple of weeks, I think almost 100% of them, we then get a message back saying, 'Please advise on where to schedule? There are no openings'" (dermatologist). • "...one thing I've noticed that has been quite effective is, if the patient is going to be following with the attending that is seeing the patient, sometimes attendings pull up their calendar in the room and pick a date that day, and let the patient know. Then coordination becomes much more straightforward..." (resident).
Insurance authorizations	• "...a patient can get scheduled for a visit regardless of their insurance status, whether or not they should go because they have to pay out of pocket is another story, but the lack of authorization doesn't prevent scheduling teams from putting them on the schedule at a slot" (dermatologist). • "...why can't the process for insurance authorizations start when the patient's still in the hospital? Why can't we identify that we may encounter problems when they're still in the hospital as opposed to waiting until they're discharged?" (dermatologist).
Early implementation problems	• "If they just mark it as urgent and then just put like hospital or ED discharge in the title, then we know that that's a priority when we're scanning, especially right now, the front desk we're short. So, we're not able to get to messages like we were before. So, marking it as urgent and just kind of giving us a heads up. It lets us know that those need to be a priority and worked on first" (scheduler). • "...there's a lot of lack of trust in the process. We've piloted different things in the past that stick around for a little bit, and then you're back to normal again, so I always feel this sense of really needing to have ownership over it and closely monitoring to make sure it's happening" (dermatologist).

Figure 2. Expanded preintervention (ie, baseline) map informed by insights from scheduling and dermatology team through semistructured interviews in phase 2, exploring preintervention pain points and refining the intervention, of a quality improvement project aiming to improve timeliness of transitioning patients from inpatient-to-outpatient dermatology and reduce workload. *Inpatient dermatology consult completed in person or via e-consult. **Could occur pre or postdischarge. If before, scheduling team may wait to initiate scheduling until patient is discharged. *** If referral not marked as urgent, could result in a 1-2 week scheduling delay. ****Dermatology team, particularly residents, manually track patient transitions in Excel, who reached out to dermatologists, scheduling staff, and patients if follow-up not scheduled within the recommended timeframe. *****Patient contacted by phone up to two times and sent a mailed letter.Admit: Admitting; Appt: Appointment; Derm: dermatology; F/U: follow-up; incl: including; IP: inpatient; NPC: new patient coordinator; OP: outpatient; pt: patient.



Unstandardized Preintervention Workflow

Unclear Roles and Responsibilities

Residents felt responsible for care transitions, but they were unsure whether the admitting (ie, nondermatology) or consulting dermatology team was responsible for initiating a referral for outpatient follow-up (Table 2). Consequently, several residents found it easier to submit referrals themselves with a separate message to schedulers and consulting dermatologist. When urgent, some residents also called patients directly or sent additional staff messages to accelerate the process. However, residents rotate monthly, creating opportunities for inconsistencies in workflow and to lose patients during transitions. Residents also did not have role in outpatient dermatology during their 1-month inpatient dermatology rotation. In contrast, other academic dermatology programs have created discharge clinics where residents can provide follow-up care to achieve care continuity [21].

Multiple Messaging Channels

Scheduling relied heavily on back-and-forth messaging among interviewees through various channels, including referrals, in-basket messaging, and email (Table 2). Communication channels used depended on who initiated the referral, whether the patient was considered a new or return patient to the outpatient dermatology clinic, and whether the request was marked with "ASAP"; referrals not marked with "ASAP" were deprioritized with patient outreach occurring within 1 to 2 weeks, delaying care. Within this complex process (Figure 2), referrals were occasionally sent to the wrong staff members, and routinely lacked sufficient information were sent to schedule patients requiring further messaging among the team.

Limited Patient and Caregiver Input

Even with timely and adequate information, schedulers struggled to reach and schedule patients, as patients were unaware of the need or reason for follow-up care (Table 2). Clinicians recognized this may be especially challenging for complex patients juggling many medical issues. Engaging patients and caregivers in shared decision-making predischarge and gauging their interest or ability to attend a follow-up appointment was considered necessary to accommodate patients, improve response to schedulers' phone calls, and decrease the number of patients who decline or miss follow-up. This may be particularly challenging in the context of consultative dermatology. Although the inpatient dermatology team closely followed most patients during their hospitalization, there was high variability exposure to each patient and their caregivers. There may be variability in the prioritization of dermatological conditions and follow-up care depending on other health conditions and their admitting care team.

Intensive Patient Tracking

Scheduling and dermatology team lacked closed-loop communication; the dermatology team rarely knew whether patients were scheduled for follow-up, leading to persistent worry about losing patients (Table 2). Primarily residents, but also dermatologists, manually kept lists of patients discharged to monitor scheduling activities and follow-up status. This required repeatedly checking the EHR and messaging other scheduling and dermatology team members. Discharge delays further disrupted scheduling of follow-up, but residents only knew of these delays through this tracking and they "probably micromanage[d] it" (dermatologist).

Structural Barriers

Limited Appointment Availability

The lack of appointment availability within the desired time frame also contributed to additional messaging (Table 3). When suitable timeslots were not available, extra messages were sent between scheduling staff and clinicians to find additional availability (Figure 2). All interviews considered this process burdensome. Timeliness of follow-up care was considered more important than ensuring continuity of care, but some schedulers and residents believed scheduling with the consulting dermatologist is easier, as the dermatologist could suggest specific timeslots or allow overbooking. The limited appointment availability is particularly challenging for high-volume specialties, including dermatology, that receive referrals from a variety of sources with various urgency.

Insurance Authorizations

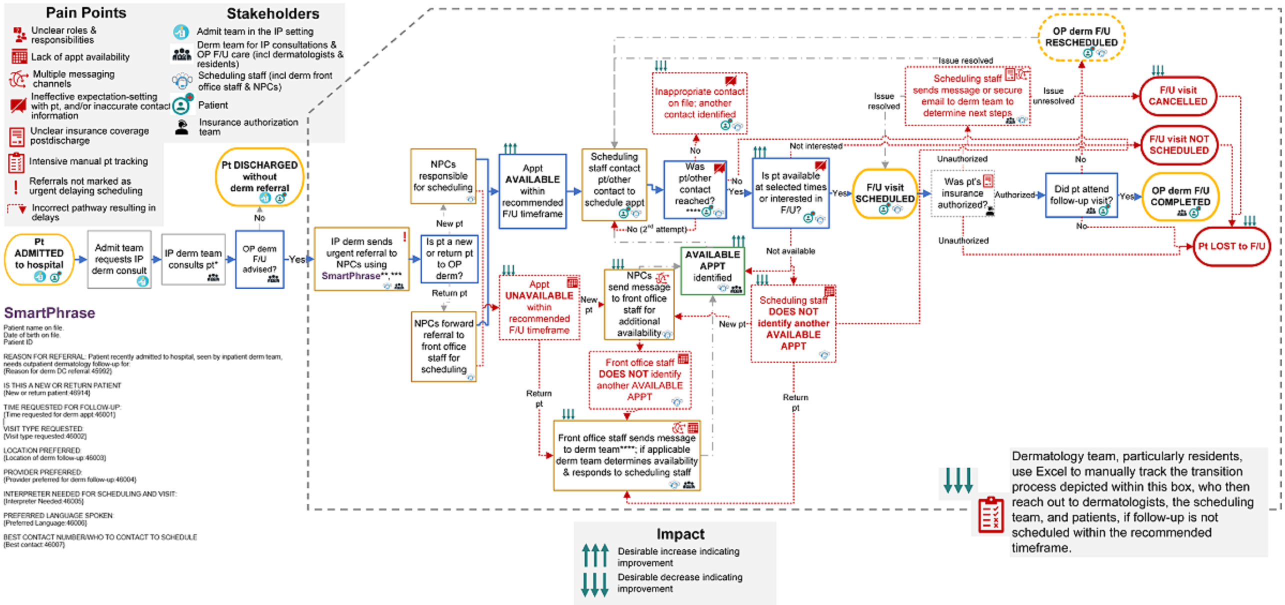
According to the dermatology team, "...a patient can get scheduled for a visit regardless of their insurance status" (dermatologist), but insurance authorization could disrupt and delay follow-up plans (Table 3). Thus, obtaining approval before discharge could facilitate appropriate follow-up care plan.

Early Implementation Problems and Resulting Intervention Adaptations

In the first weeks of implementation, intervention vulnerabilities included unforeseen staffing shortages and referrals not marked as "ASAP," a key step in submitting the referral with the SmartPhrase (Table 3). These contributed to scheduling delays and one anecdotally reported readmission. Consequently, manual tracking of patients continued as the dermatology team was uncertain whether the new workflow worked as intended.

Within the first month, early inconsistencies were addressed by onboarding and training the weekend and overnight dermatology residents on the intervention. Early on, the SmartPhrase was being used inconsistently because of failure to update weekend residents and overnight residents of the new workflow (Table 3). Furthermore, referrals were not being marked as "ASAP," which was identified as a crucial step to ensure the referral was processed urgently. As a response, the SmartPhrase was edited to include text that emphasized that all inpatient referrals need to be marked "ASAP" (Table 1). This information was also included in monthly email reminders to all residents rotating onto the inpatient service (as well as those covering weeknights and on weekends), inpatient handbook for clinicians and residents, verbal sign-out by residents, and yearly introductory presentation for residents. Table 1 presents the final SmartPhrase, and Figure 3 displays the workflow.

Figure 3. Process map for intervention, a SmartPhrase and associated workflow, developed using insights from schedulers, dermatologists, and residents through semistructured interviews, scheduling data, and messaging data. Data were collected in phase 2, exploring preintervention pain points and refining the intervention, and phase 3, evaluating the intervention and persisting challenges, of a quality improvement project aiming to improve timeliness of transitioning patients from inpatient-to-outpatient dermatology and reduce workload. *Inpatient dermatology consult completed in person or via e-consult. **Could occur pre or postdischarge. If before, scheduling team may wait to initiate scheduling until patient is discharged. *** If referral not marked as urgent, could result in a 1-2 week scheduling delay. ****Dermatology team, particularly residents, manually track patient transitions in Excel, who reached out to dermatologists, scheduling staff, and patients if follow-up not scheduled within the recommended timeframe. *****Patient contacted by phone up to two times and sent a mailed letter.Admit: Admitting; Appt: Appointment; Derm: dermatology; F/U: follow-up; incl: including; IP: inpatient; NPC: new patient coordinator; OP: outpatient; pt: patient.



Phase 3: Evaluating the Intervention and Persisting Challenges

Overview

During the pre- and postimplementation periods, 114 and 120 patients, respectively, received an inpatient consultation from the dermatology team, were discharged from the hospital, and potentially needed follow-up (Figure 4). Qualitative themes (supporting quotes in Table 4) and quantitative data were triangulated and are presented in subsequent sections.

Figure 4. Number (percentage) of patients who received inpatient dermatology consultation and potentially needed were scheduled for and completed their outpatient postdischarge follow-up and number (percentage) of patients identified in staff and clinician messages related to inpatient-to-outpatient care transitions before and after implementation of an intervention are reported. The intervention, a SmartPhrase and associated workflow, was implemented as part of a quality improvement project aiming to improve timeliness of transitioning patients from inpatient-to-outpatient dermatology and reduce workload.

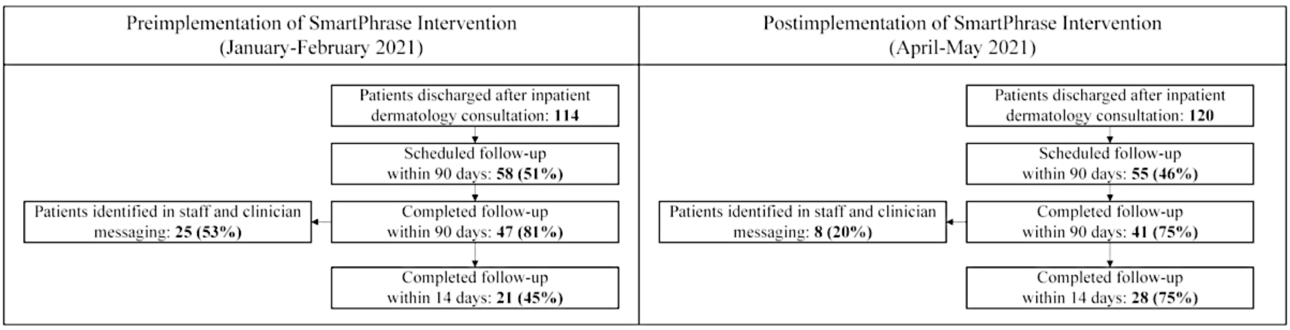


Table 4. Exemplary quotes from interviews with dermatologists, residents, and scheduling staff perceptions of intervention to improve the timeliness of transitioning recently discharged patients to outpatient dermatology for follow-up care and associated workload.

Theme: evaluating the intervention	Exemplary quotes
Timeliness of scheduling and follow-up	• "...just one system, one process that we now have. So, instead of multiple emails being sent, staff messages being sent, there is just one unified way to do it. So, I think that makes it much easier for residents" (dermatologist).
Messaging workload	• "...there's just more information that's built into the SmartPhrase right off the bat, so there's less need for messaging back and forth between the schedulers, residents, faculty members and nursing staff" (dermatologist). • "...the SmartPhrase does decrease workload in terms of hours, our time spent on documentation and administrative tasks. [...] one of the biggest areas that can lead to burnout is the documentation burden, so I think SmartPhrases definitely help with that" (resident). • "[Before the introduction of the discharge SmartPhrase] closing the loop did not happen. I think that's the biggest change is making the physicians aware of when the patient will be scheduled and that they are on the schedule" (scheduler).
Clinical burden	• "...for the handful that I've dealt with this week that needed follow up, I still feel like I've been pretty involved in making sure they're on the schedule" (dermatologist). • "There's just more time and mental energy to spend on urgent items, clinical direct care...but also the exhaustion of worry about going back...that finally took me out of my worry sphere. [...] the ability to not worry about that has been tremendously helpful because that even goes beyond the physical time we spend in the chart...that constant worry in the back of your head that maybe it's still not done has been eliminated" (dermatologist). • "I don't really see a big difference as far as the number of staff messages. I just think the efficiency and communication is better with the SmartPhrase and closing the loop, because once you send out the message to the referring physician and the doctor that you're scheduling with, that's just where it ends" (scheduler). • "Maybe a little bit improved [my wellbeing], but very minimally. [...] it's just a small fraction of our workload as a consult resident. That it just doesn't proportionally have that much effect" (resident).
Integrating patient and caregiver input	• "They're [patients] involved from the beginning, we usually have it at bedside to get their preferences. And then part of the discharge checklist is we clarify their preference for care, whether they want it to be in person or video, sort of a timeline, the preferred contact method..." (resident). • "...it's very helpful when you put [in the SmartPhrase]...the best person to contact for the patient because sometimes it's not the patient. Sometimes it's the patient's husband. It's the daughter. It's the long-term rehabilitation facility, so that makes it really helpful for us to know who's the primary person to contact to get the patient scheduled" (scheduler).

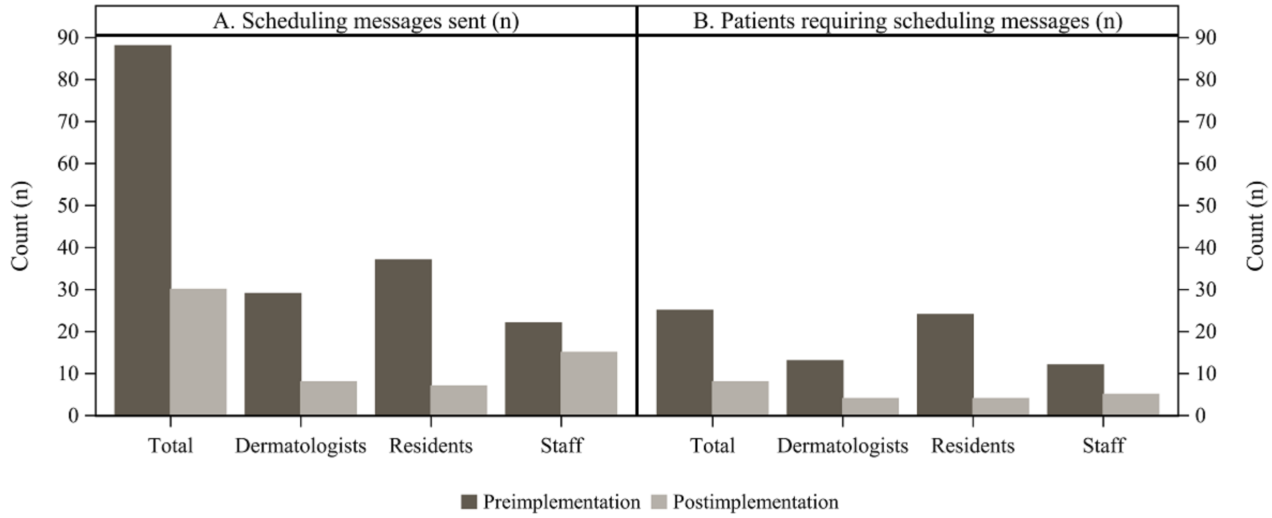
Timeliness of Scheduling and Follow-up

The intervention was well-accepted by all interviewees (Table 4). The dermatology and scheduling teams were familiar with the SmartPhrase feature, as it has been used to create other templates used in their daily practice. The intervention was reported to be easily adopted and facilitated efficient scheduling of discharged patients for outpatient follow-up. However, the intervention did not substantially impact the proportion of patients with scheduled or completed follow-ups. The proportion of patients scheduled for a follow-up visit with a 90-day postdischarge period did not improve, 50.9% (58/114) preimplementation period versus 45.8% (55/120) postimplementation period (*P*=.44; Figure 4), nor did the proportion of patients with completed follow-up visits within the same timeline (47/58, 81% vs 41/55, 75%, respectively; *P*=.41). The overall time from hospital discharge to follow-up completion decreased slightly, but not significantly, from before the implementation to after the implementation (mean 20.4, SD 19.3 to mean 17.8, SD 20.8 days; *P*=.55). However, the proportion that completed their follow-up visit within 14 days of discharge significantly increased from 45% (21/47) to 68% (28/41), before the implementation to after the implementation, respectively (*P*=.03).

Messaging Workload

The volume of messages related to care transitions decreased after intervention; dermatology and scheduling teams sent a total of 88 messages before the implementation and 27 messages after the implementation (Figure 5A). The group sending the most messages also shifted; before the implementation, almost half of the messages were sent by residents, whereas in the postimplementation period, the majority of the messages were sent by schedulers (Figure 5A). Furthermore, messages were also sent for fewer patients; of the patients who completed follow-up within 90 days of discharge, 53% (25/47) of patients were associated with messages before the implementation and 20% (8/41) of patients were associated with messages after the implementation (Figure 5B). This aligned with interviewee perceptions that completed SmartPhrases provided the schedulers with sufficient information to schedule a follow-up and reduced back-and-forth messaging and time spent in the EHR (Table 4).

Figure 5. (A) Total number of messages sent by dermatologists, residents, and staff per patient and (B) total number of patients who completed a follow-up visit within 90 days of discharge and required messaging to schedule their visit and prior pre- and postimplementation of the intervention, a SmartPhrase and associated workflow, for a quality improvement project aiming to improve timeliness of transitioning patients from inpatient-to-outpatient dermatology and reduce workload.



Clinical Burden

Perceived impact of the intervention on clinical burden was mixed among dermatology and scheduling staff (Table 4). The standardized workflow, reduced messaging, and more consistently closing the communication loop when a follow-up was scheduled were perceived to reduce burden. Most dermatologists and residents reported that the intervention allowed them to shift their focus onto more pressing needs and brought a sense of relief and improved well-being. However, 1 dermatologist and 1 resident did not note differences in workload because of additional back-and-forth messaging during early implementation.

Integrating Patient and Caregiver Input

The intervention prompted the inpatient dermatology team to engage patients and caregivers in bedside shared decision-making before discharge to obtain necessary information for scheduling. Interviewees reported that this resulted in more accurate and detailed information that facilitated scheduling and minimized delays (Table 4). Clinicians were also prompted to discuss the importance and purpose of follow-up with patients and caregivers, which was helpful to schedulers as "...patients are informed about the referrals...so they expect us to call them" (scheduler).

Sustainability and Persistent Challenges

The perceived and actual benefits of this easy-to-use intervention (Figure 3) led all interviewees to believe that it was sustainable (supporting quotes in Multimedia Appendix 5). However, interviewees reported persisting challenges: (1) inconsistent timing of when to initiate scheduling effort (ie, before or after discharge); (2) lack of process for tracking patients with missed follow-ups; (3) follow-up reason not always documented in the SmartPhrase (Table 1); (4) lack of systematic training for new residents and scheduling staff, roles with frequent turnover, and compromising trust; (5) lack of a dedicated coordinator to own and manage care transitions; and (6) hesitation to fully trusting the intervention. The best timing of scheduling activities is dependent on patient discharge from inpatient settings, but the inpatient dermatology team was not always involved in discharge decisions nor notified about delays. Structural barriers also remained, including continued lack of appointment availability within the recommended follow-up timeline and postdischarge insurance denials leading to cancelations and delays.

Discussion

Principal Findings

Transitioning patients from inpatient consultation services to outpatient dermatology for follow-up is a complex process. Dermatology and scheduling teams reported undue burden owing to several pain points: lack of standardized workflow; limited patient and caregiver involvement in predischarge planning; and burdensome, manual tracking of patients through their transition. Patients were generally satisfied with the transition process but identified persisting issues around communication and expectation setting during discharge planning and care coordination and prioritization, especially for medically complex patients. Identified issues and pain points were partially addressed by the intervention, a SmartPhrase and associated workflow, by prompting the inpatient dermatology team to collect information needed for scheduling at bedside and standardizing the communication between the dermatology and scheduling teams. The intervention was widely accepted, was easy to use, reduced the workload, and increased the proportion of patients receiving follow-up within the desired 14-day postdischarge timeline. Fewer patient transitions required EHR scheduling–related messaging, and messaging workload shifted from residents to the scheduling team. Although the intervention was viewed as sustainable, local and system-level challenges to effective care transitions remain.

Comparisons With Previous Literature and Implications

Burnout among clinicians and health care workers has been identified as a consequence of intensive EHR use, including documentation, inbox messaging, and other tasks that increase mental load and time spent caring for patients [22-24]. These activities were plentiful in the preintervention workflow at the present organization, which contributed to stress and worry among team members. The flexibility and accessibility of the SmartPhrase feature in the Epic EHR allowed rapid development of a stakeholder-informed template that consolidated patient information needed for scheduling follow-ups into a standard referral. Almost all clinicians, residents, and scheduling staff reported at least some improvement in their workload, stress, and well-being after implementation, which aligned with the decrease in messaging seen after the implementation. Other studies have also found that when strategically used, the SmartPhrase is easy to use and a rapidly deployable solution for projects with short timelines and limited resources needing to consolidate documentation, streamline communication, and decrease workload [25,26].

Providing patients with timely access to follow-up care after hospitalization has many documented benefits to the patient and health care system [27-31]. Research has shown that faster postdischarge follow-up may prevent readmissions and mortality in irritable bowel syndrome, heart failure, and Hospital Readmissions Reduction Program's priority conditions, such as acute myocardial infarction and pneumonia [27-30]. Although this QI project did not increase the proportion of patients receiving follow-up or average time between discharge and follow-up visit, the proportion of patients receiving dermatology follow-up care within the desired 14-day postdischarge timeline was 68% after the intervention. This is similar to a reported proportion of patients accessing any ambulatory follow-up 14 days after hospitalization (50%-67%) [32-34] and 30 days after an ED visit (71%) [35] related to a variety of concerns and greater than the proportion of patients with heart failure seeking follow-up care 30 days after the ED visit (23%) [36]. This suggests that the intervention addressed preintervention concerns around prioritization or deprioritization and (lack of) awareness of dermatological issues, which are important for adherence to care plans, including follow-up visits [35,37]. However, gaps remain in the coordination of postdischarge dermatological care. Baseline clinical factors and social risk factors [29,31,38] have been shown to be related to follow-up attendance and benefits but were not explored here because of the small sample size. We were also unable to explore if follow-up care completion or timing was impacted by a patient's specific dermatological diagnosis, and dermatology conditions vary widely in urgency, timeline of treatment, and thus appropriate timing of follow-up. Further investigation is needed to understand how to tailor follow-up recommendations to patient factors and dermatologic diagnosis and to develop patient-centered workflows that promote appropriate and timely postdischarge care.

Challenges in care transitions persist, but this mixed methods evaluation enabled the identification of the next steps for improvement [2,7,39-42]. In particular, it was recommended that the inpatient dermatology team should obtain additional information, such as best time to call and follow-up purpose, at bedside and clarifying the workflow for when discharge is delayed or when a patient cancels, reschedules, or misses their follow-up. Offering teledermatology could also help patients receive timely follow-up care [17]. Systematic onboarding of new clinicians, residents, and staff members are also needed to sustain the intervention. The current intervention heavily relies on team members in roles with high turnover and frequent shifts in roles or responsibilities, specifically residents and scheduling staff. Other research suggests that a dedicated owner of the process, such as a care coordination team [42,43] or discharge clinic [21], is effective. However, these are resource-intensive solutions and may not resolve the pervasive problem of lack of appointment availability. Dedicated timeslots allotted for discharged patients in each clinician's schedule or a "discharge clinic" may somewhat help [21]. However, interviewees worried that they would give patients less flexibility. Further exploration of such interventions is warranted.

Limitations

There are several limitations to this evaluation. First, this single-center study may not be generalizable, although some of the identified pain points, such as poorly defined roles and responsibilities and nonstandard communication channels, have been previously reported [39-42]. Second, we were unable to accurately identify all patients needing follow-up care and SmartPhrase use, as these were not documented in unique, extractable data fields during this study. Thus, the denominator for the study is not precise, but there is no reason to expect that there was systematic difference in identification of patients with current procedural terminology codes between the 2 periods. These issues have been resolved by the institution's EHR team since the completion of this study. Third, only in-basket messaging data were available, which were the most common, but not the only, channel for communication (eg, email, phone, and instant messaging). Finally, because of limited resources, we were unable to capture patient perspectives during implementation.

Conclusions

A well-accepted, easy-to-use intervention, the SmartPhrase and associated workflow, improved the proportion of patients receiving follow-up dermatology care within 14 days of discharge but did not impact the proportion of patients scheduled or completing follow-up within 90 days of discharge. It also facilitated efficient scheduling of discharged patients with substantial reduction in staff messaging, alleviating the scheduling burden; clinicians, residents, and scheduling staff reported less stress and improved well-being. The SmartPhrase can be adjusted based on user experience, making it flexible for long-term sustainability. The multipronged approach to evaluate this intervention not only informed the QI project but also provided a foundation for future efforts, which will be applied to address the remaining challenges around care transitions. We found that a simple stakeholder-informed solution can be created and implemented quickly with a standard EHR figure that results in a positive impact; this approach could be easily applied to care transitions beyond dermatology.

Acknowledgments

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Data Availability

The data that support these findings are available from the corresponding author on reasonable request.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Description of qualitative methodology and participating patients and caregivers that elucidated experiences with inpatient-to-outpatient dermatology care transitions.
[PDF File (Adobe PDF File), 75 KB - derma_v6i1e43389_app1.pdf]

Multimedia Appendix 2
Findings and exemplar quotes from patient (n=14) and caregiver (n=1) interviews organized by theme.
[PDF File (Adobe PDF File), 74 KB - derma_v6i1e43389_app2.pdf]

Multimedia Appendix 3
Current procedural terminology (CPT) codes that were associated with inpatient dermatology consult and provider that were used to identify patients who had an inpatient consult with dermatology and who may need follow-up care in outpatient dermatology. Inpatient dermatology consultations were identified with the following CPT codes for both in-person consults and e-consults (primarily offered during pandemic) linked to a dermatologist during an inpatient encounter. As clinician recommendation on follow-up need or timeline could not be reliably extracted from the electronic health record, it was assumed that patients who received an inpatient dermatology consultation associated with these CPT codes may have needed follow-up care.
[PDF File (Adobe PDF File), 9 KB - derma_v6i1e43389_app3.pdf]

Multimedia Appendix 4
Keywords used to identify clinician and staff sent messages related to transitioning patients from inpatient care to outpatient follow-up care in dermatology.
[PDF File (Adobe PDF File), 10 KB - derma_v6i1e43389_app4.pdf]

Multimedia Appendix 5
Exemplary quotes from interviews with dermatologists, residents, and scheduling staff describing persisting challenges postimplementation of a SmartPhrase-enabled workflow to improve timeliness of patient transitions from inpatient-to-outpatient dermatology care and associated messaging workload.
[PDF File (Adobe PDF File), 68 KB - derma_v6i1e43389_app5.pdf]

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Abbreviations

ASAP: as soon as possible
ED: emergency department
EHR: electronic health record
NPC: new patient coordinator
QI: quality improvement

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Original Paper

Prescribing Patterns of Oral Antibiotics and Isotretinoin for Acne in a Colorado Hospital System: Retrospective Cohort Study

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Abstract

Background: Guidelines established by the American Academy of Dermatology recommend oral antibiotics as first-line therapy for mild, moderate, and severe acne. However, it is recommended to minimize the duration of oral antibiotic use, and there is increasing support for other systemic agents for acne.

Objective: We sought to characterize the use of oral antibiotics and isotretinoin for the treatment of acne in the pediatric and young adult population aged 10 through 20 years and the adult population aged 21 to 45 years from 2011 to 2019.

Methods: We conducted a retrospective, observational cohort study using electronic data from the enterprise data warehouse of the University of Colorado Anschutz Medical Campus and its affiliates, with data in the format of the Observational Health Data Sciences and Informatics (OHDSI) Observational Medical Outcomes Partnership (OMOP) common data model. Categorical values (sex, race, and ethnicity) were compared using chi-square tests, and continuous variables (age) were compared using 2-tailed *t* tests.

Results: Our cohort of 15,704 patients was composed of mostly White (12,776/15,704, 81.4%), non-Hispanic or Latino (13,307/15,704, 84.7%), and female (11,093/15,704, 70.6%) patients. Among the 4605 male patients in the eligible cohort, 1810 (39%) received an oral antibiotic treatment, in comparison to 3109 (28%) of the 11,093 eligible women ($P<.001$). Among the 4605 men who were eligible for treatment with isotretinoin in this population, 988 (21.5%) received a course of isotretinoin, compared to only 10.4% (1159/11,093) eligible women ($P<.001$). Male patients were 1.67 times more likely to have received an antibiotic prescription (odds ratio [OR] 1.67, 95% CI 1.55-1.79) and over twice as likely to have received an isotretinoin prescription (OR 2.34, 95% CI 2.13-2.57) than female patients.

Conclusions: Minocycline was the most frequently prescribed antibiotic for the treatment of acne in this study cohort. From 2015 to 2019, there was no significant change in the number of antibiotic prescriptions over time. Men were significantly more likely to receive both oral antibiotics and isotretinoin than female patients. Multiple factors could be contributing to this discrepancy, including the burden of iPLEDGE, additional systemic treatment options for female patients, and the difference in acne severity

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across sexes. We could not determine the difference in severity of acne between male and female patients in our cohort, and further research is needed to ascertain the variation across sexes.

(JMIR Dermatol 2023;6:e42883) doi:10.2196/42883

KEYWORDS

acne; antibiotics; databases; guidelines; isotretinoin; prescribing; retinoids

Introduction

Acne is a common and debilitating medical condition, particularly among adolescents and young adults [1-3]. Guidelines established by the American Academy of Dermatology (AAD) recommend systemic antibiotics as first-line treatment for mild, moderate, and severe inflammatory acne, in combination with topical retinoids and benzoyl peroxide [1]. Monotherapy with systemic antibiotics is not recommended, and it is suggested that patients be re-evaluated every 3 to 4 months to limit antibiotic use to the shortest duration possible to avoid bacterial resistance [1]. In addition to promoting resistance, long-term oral antibiotic use has been associated with a number of adverse events, including microbiome disruption and pharyngitis, as well as possible associations with inflammatory bowel disease (IBD) and obesity [4,5]. Several studies have analyzed the prescription patterns of acne treatments [4-9]. This study investigated oral antibiotic and isotretinoin use for acne in a Colorado hospital system between 2011 and 2019.

Methods

Data Source

We performed a retrospective, observational cohort study of patients treated for acne using electronic data from Health Data Compass, the enterprise data warehouse of the University of Colorado Anschutz Medical Campus and its affiliates, and from Children's Hospital Colorado [10]. Data were obtained in the format of the Observational Medical Outcomes Partnership (OMOP) common data model from the Observational Health Data Sciences and Informatics (OHDSI) network. OHDSI is an interdisciplinary collaborative composed of an international network of researchers and health databases. The OMOP common data model was chosen for this study to facilitate future collaboration and expansion of this study to other sites within the OHDSI network and because of its methods library, which facilitates both large-scale implementation of observational study designs and large-scale data analytics. The cohort and outcome phenotype code and analytic code are available on GitHub [11].

Study Design and Study Population

Outcomes of interest were the type of oral antibiotic therapy prescribed for patients with acne diagnoses. All study subjects were aged between 10 and 45 years as of January 1, 2015, with a diagnosis of acne defined by at least 2 diagnoses of acne, as represented by select OHDSI concept IDs (Multimedia Appendix 1). While a variety of acne diagnoses fell into our inclusion criteria phenotype, only the following appeared in our population: acne, acne conglobata, acne varioliformis, excoriated acne, and tropical acne. Antibiotic start date was on or after January 1, 2015, occurring on or after any diagnosis of acne, with at least one year of follow-up from the first oral antibiotic prescription index date. Prescriptions for oral liquid or suspension forms were excluded. Similar data were collected regarding prescriptions for isotretinoin.

In an attempt to exclude antibiotics prescribed for reasons other than acne, the minimum antibiotic dose required was a prescription quantity of 28 or more, unless determined by the physician authors (MJA, TES) consensus to represent an equivalent quantity (eg, prescriptions for packs containing multiple doses).

Statistical Analysis

We assessed the prevalence of antibiotics and isotretinoin prescriptions for the treatment of acne according to age and sex. Categorical values (sex, race, and ethnicity) were compared using chi-square tests, and continuous variables (age) were compared using 2-tailed *t* tests. All tests were evaluated at the P=.05 significance level. R (version 3.6.0; R Core Team) was used for all summaries and figures. We assessed whether the proportion of patients who received medication was different based on sex using an unadjusted logistic regression model with the binary outcome of receiving or not receiving medication.

Ethical Considerations

This study is exempt from institutional review board assessment under category four of the University of Colorado Exempt Research Guidelines [12].

Results

Among a total of 15,704 patients who were identified as meeting the inclusion and exclusion criteria for our outcome of interest, a total of 4920 patients received antibiotic prescriptions (Table 1).

Our cohort had a mean age of 22.3 (SD 8.6) years, and was composed of mostly (12,776/15,704, 81.4%), non-Hispanic or Latino (13,307/15,704, 84.7%), and female (11,093/15,704, 70.6%) patients (Table 1). The most common diagnosis was acne: International Statistical Classification of Diseases and Related Health Problems (ICD) code 1569798 (15,668/15,704 99.8%).

There were statistically significant differences in age, sex, and race when comparing those who did and did not receive an antibiotic prescription; however, the magnitude of the differences in age and race was very small and not clinically meaningful (Table 1). Of the patients who received antibiotics, 63.2% (3109/4920) were female. However, men were more likely than women to receive a prescription for antibiotics (1810/4605, 39% vs 3109/11,093, 28%; *P*<.001).

Findings were similar when comparing those who did and did not receive an isotretinoin prescription. Differences in age, sex, and race were all statistically significant, but only sex was associated with a clinically meaningful difference between patients with and without isotretinoin treatment (Table 2). Men were more likely than women to receive a prescription for isotretinoin (988/4605, 21.5% vs 1159/11,093, 10.4%; *P*<.001).

Using an unadjusted logistic regression model with the binary outcome of receiving medication or not, we were able to assess the odds of receiving antibiotics or isotretinoin based on sex (Table 3). Our results suggest that male patients were 1.67 times more likely to have received an antibiotic prescription than female patients (odds ratio [OR] 1.67, 95% CI 1.55-1.79) and over twice as likely (OR 2.34, 95% CI 2.13-2.57) to have received an isotretinoin prescription than female patients.

The most prescribed antibiotic was minocycline, followed by doxycycline (Figure 1). Minocycline was also the most prevalent initial antibiotic prescribed for every year captured in this analysis, followed by doxycycline (Figure 2). Figure 2 also illustrates a slow rise in doxycycline prescription prevalence starting in 2013 and a slow decline in minocycline prescriptions starting in 2013. Some antibiotic prescriptions may have been missed, particularly in the years 2011-2014, where the total count of antibiotics for these data points was much lower than in the period 2015-2019 (Table 4). However, when looking at the total amount of antibiotic prescriptions over time from 2015-2019, there is no significant observable change in the use of oral antibiotics over this time period (Table 4).

Table 1. Cohort demographics.

User prevalence by antibiotics	No antibiotic prescribed (n=10,784)	Antibiotic prescribed (n=4920)	All participants (N=15,704)
Age (years), mean (SD)	22.9 (8.5)	21.1 (8.5)	22.3 (8.6)
Sex, n (%)			
Female	7984 (74)	3109 (63.2)	11,093 (70.6)
Male	2795 (25.9)	1810 (36.8)	4605 (29.3)
Missing	5 (0)	1 (0)	6 (0)
Race, n (%)			
American Indian or Alaska Native	39 (0.4)	15 (0.3)	54 (0.3)
Asian	305 (2.8)	108 (2.2)	413 (2.6)
Black or African American	291 (2.7)	93 (1.9)	384 (2.4)
Native Hawaiian or Other Pacific Islander	17 (0.2)	8 (0.2)	25 (0.2)
White	8708 (80.7)	4068 (82.7)	12,776 (81.4)
Missing	1424 (13.2)	628 (12.8)	2052 (13.1)
Ethnicity, n (%)			
Hispanic or Latino	920 (8.5)	417 (8.5)	1337 (8.5)
Non-Hispanic or Latino	9195 (85.3)	4112 (83.6)	13,307 (84.7)
Missing	669 (6.2)	391 (7.9)	1060 (6.7)
Diagnosis, n (%)			
Acne	10,761 (99.8)	4907 (99.7)	15,668 (99.8)
Acne conglobate	6 (0.1)	2 (0)	8 (0.1)
Acne varioliformis	5 (0)	6 (0.1)	11 (0.1)
Excoriated acne	9 (0.1)	4 (0.1)	13 (0.1)
Tropical acne	3 (0)	1 (0)	4 (0)

Table 2. User prevalence among isotretinoin recipients.

User prevalence by isotretinoin	None (n=13,555)	Received medication (n=2148)
Age (years), mean (SD)	22.8 (8.7)	19.6 (6.6)
Sex, n (%)		
Female	9934 (73.3)	1159 (54)
Male	3617 (26.7)	988 (46)
Missing	5 (0)	1 (0)
Race, n (%)		
American Indian or Alaska Native	51 (0)	3 (0.1)
Asian	373 (2.8)	40 (1.9)
Black or African American	349 (2.6)	35 (1.6)
Native Hawaiian or Other Pacific Islander	23 (0.2)	2 (0.1)
White	11,010 (81.2)	1766 (82.2)
Missing	1750 (12.9)	302 (14.1)
Ethnicity, n (%)		
Hispanic or Latino	1182 (8.7)	155 (7.2)
Non-Hispanic or Latino	11,521 (85)	1786 (83.1)
Missing	853 (6.3)	207 (9.6)
Diagnosis, n (%)		
Acne	13,524 (99.8)	2144 (99.8)
Acne conglobata	5 (0)	3 (0.1)
Acne varioliformis	10 (0.1)	1 (0)
Excoriated acne	13 (0.1)	0 (0)
Tropical acne	4 (0)	0 (0)

Table 3. Odds ratio of receiving medication by sex.

Outcome	Odds ratio[a] (CI)	*P* value
Antibiotics	1.7 (1.5-1.8)	<.001
Isotretinoin	2.3 (2.1-2.6)	<.001

[a]Reference level is female.

Figure 1. Frequency of prescription for each antibiotic.

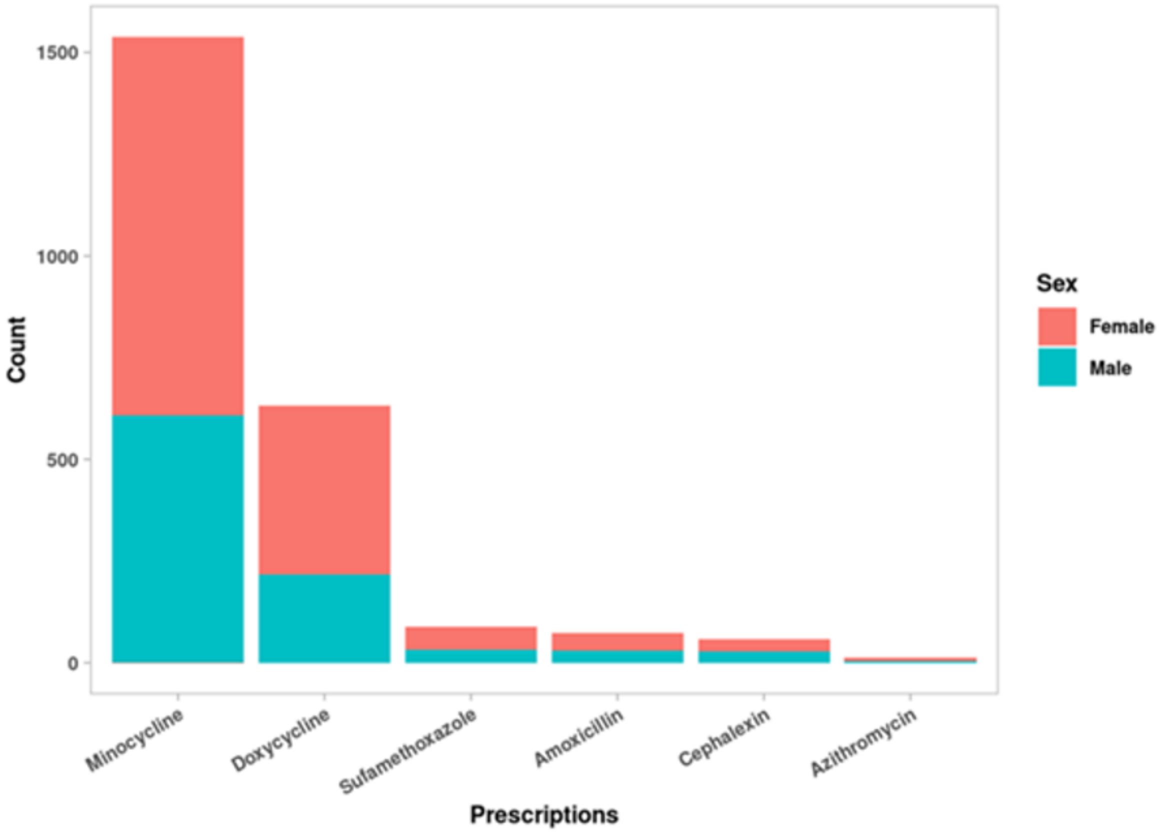

Figure 2. First antibiotic prescription over time by proportion.

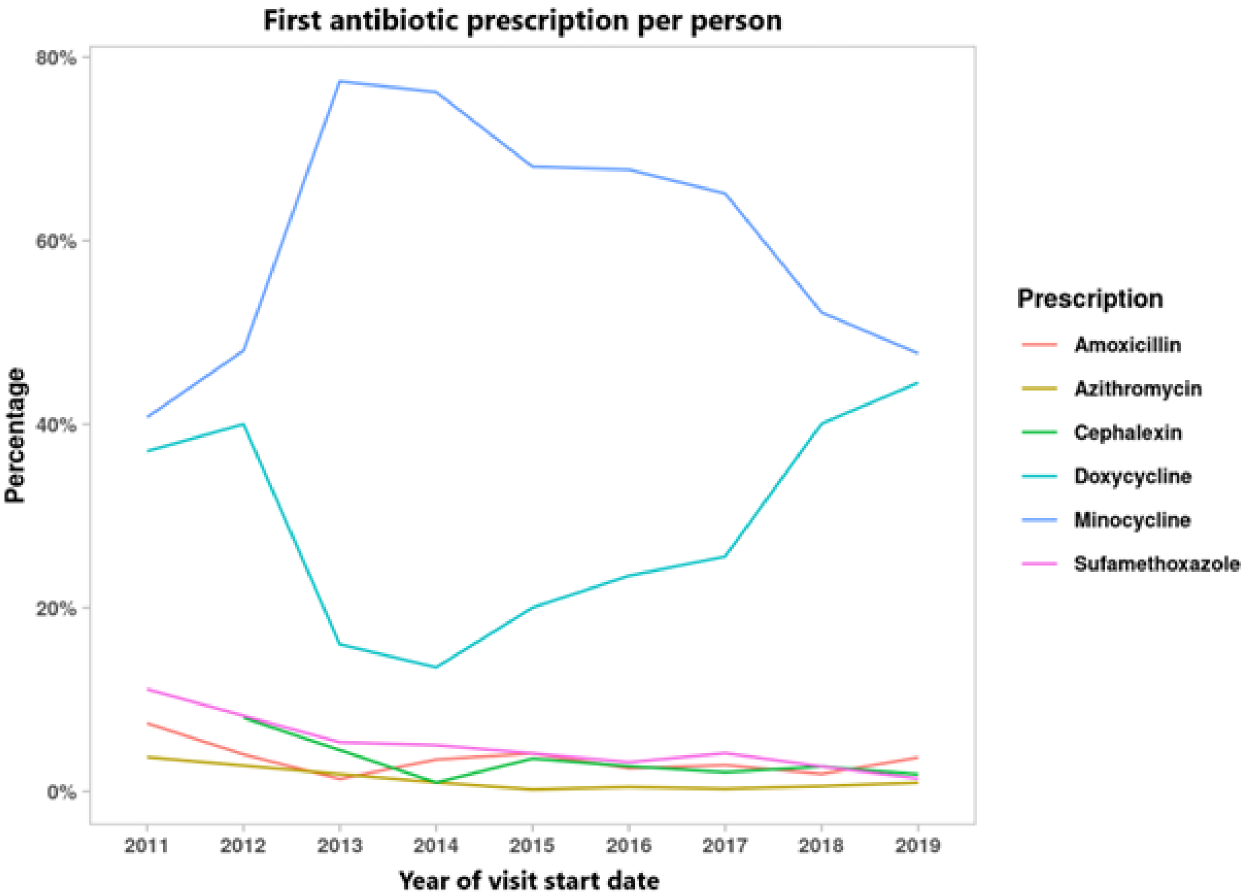

Table 4. Antibiotic prescriptions over time. Some antibiotic prescriptions may have been missed, particularly in the years 2011-2014.

Year	Prescriptions, n
2011	71
2012	136
2013	242
2014	735
2015	1763
2016	1867
2017	1781
2018	1808
2019	1509

Discussion

Overview

We characterized oral antibiotic use for acne treatment in a Colorado hospital system. Among 15,704 patients, we found that male patients were more likely than female patients to receive both antibiotic and isotretinoin prescriptions for acne. Among the eligible recipients of prescriptions for acne, there were 11,093 eligible female patients (70.6%) and 4605 eligible male patients (29.3%). However, among recipients of antibiotics, only 28% (3109/11,093) of female patients received prescriptions, compared to 39% (1810/4605) of male patients. Similarly, among recipients of isotretinoin prescriptions, only 10.4% (1159/11,093) of eligible female patients received prescriptions, compared to 21.5% (988/4605) of male patients. Male patients were 1.67 times as likely to receive antibiotics for acne and over twice as likely to receive isotretinoin for acne compared to female patients.

Previous research on the health burden of acne has revealed that women with acne demonstrate greater self-consciousness of their appearances and are more likely to seek care due to an increased subjective rating of severity [13]. Thus, female patients may seek care for less severe forms of acne compared to male patients, leading to a lower likelihood of being prescribed systemic medications for acne. Another potential explanation for this discrepancy could be that female patients have access to other systemic acne treatment options that male patients do not, namely, oral contraceptive pills (OCPs) and spironolactone [1,14-16]. This study did not include an analysis of antiandrogen medication.

Other studies suggest acne severity could be significantly higher in male patients, thus necessitating the need for systemic treatment [17]. However, further research is needed regarding the severity of acne presentations in male versus female patients, as we did not have this data and cannot say for certain that the female patients in our cohort had a less severe presentation compared to male patients.

The discrepancy in isotretinoin prescriptions may also reflect the increased burden of iPLEDGE, an FDA risk management program, on women capable of bearing children. In its initial introduction, iPLEDGE was associated with an initial 30% decrease in isotretinoin prescriptions for both men and women [18]. The system has requirements for patients, prescribers, pharmacies, and wholesalers. For women looking to start isotretinoin, iPLEDGE requires 2 negative pregnancy tests before starting therapy, monthly pregnancy tests during therapy, use of 2 forms of contraception during therapy, and use of 2 forms of contraception the month before and after therapy [19,20]. A 2013 pharmacy prescription claims–based study found that the overall number of isotretinoin prescriptions across all ages and sexes decreased after iPLEDGE implementation, with a greater decrease among women [19]. The extra requirements of iPLEDGE for women could be a dissuading factor, as they may be unable or unwilling to comply with the stringent contraception and testing requirements or may be considering pregnancy.

This study builds upon previous literature analyzing trends in antibiotic and isotretinoin prescriptions in dermatology (Table 5). In a large, retrospective study using OptumInsight data from 2004 to 2013, authors looked at prescribing patterns among dermatologists and nondermatologists for the treatment of acne [21]. They found a significant increase in spironolactone prescriptions for acne throughout that time period [21]. A separate retrospective OptumInsight study using data from 2007 to 2017 aimed to identify potential disparities in acne treatment and found that female patients were less likely than male patients to be prescribed both isotretinoin and oral antibiotics [6]. In addition, a retrospective population-based cohort study in British Columbia also found that individuals treated with isotretinoin were more likely to be male [5].

Minocycline was the most prescribed initial antibiotic and the most prevalent antibiotic in every year of data captured in this analysis (Figures 1 and 2). Beginning in 2013, doxycycline, the second most prevalent initial antibiotic, began a slow increase in prevalence, while minocycline prevalence began slowly declining. It is not completely clear why this trend occurred, as there is no overall clinical difference in efficacy between minocycline and doxycycline [22]. Side effects, such as an increased risk of lupus erythematous with minocycline, and patient and physician perceptions regarding the costs of the 2 drugs may have affected prescription patterns [22-25].

Table 5. Previous studies evaluating oral antibiotics and isotretinoin prescription patterns.

Studies	Total participants, N	Age (years)	Location	Period	Oral antibiotics OR[a,b] (95% CI)	Oral antibiotics male to female ratio	Isotretinoin OR[a] (), 95% CI	Isotretinoin male to female ratio	Duration of oral antibiotic therapy (days), mean (type of prescriber)
This study	15,700	22.3	Colorado, United States	2011-2019	1.67 (1.55-1.79)	1.39	2.34 (2.13-2.57)	2.14	__[c]
Barbieri et al [4]	79,600	12-22	United Kingdom	2003-2013	—	—	—	—	Nondermatologist: 175
Al-husayen et al [5]	1,500,000[d]	12-29	British Columbia, Canada	1997-2008	—	—	—	1.17	—
Barbieri et al [6]	30,000	15-35	United States	2007-2017	1.12 (1.06-1.18)	1.93	2.44 (2.10-2.95)	4.33	—
Barbieri et al [7]	572,600	15-27	United States	2004-2014	—	—	—	—	Dermatologist: 192; nondermatologist: 213
Straight et al [21]	16,500	32.6	United States	2008-2010	—	—	—	—	Dermatologist: 122; nondermatologist: 134

[a]Reference level is female.

[b]OR: odds ratio.

[c]Not available.

[d]Population based cohort (participants not confined to patients diagnosed with acne).

In contrast to this study, a cross-sectional analysis of antibiotic prescribing patterns among dermatologists from 2008 to 2016 found a decrease in antibiotic prescriptions for acne during that time [8]. We found no significant change in antibiotic prescription frequency in our cohort.

Limitations

We used ICD codes, established by the Global Burden of Disease Study and validated by an international panel of skin disease experts, to determine the appropriate OHDSI acne concept IDs [26]. Some diagnoses may have been missed or inappropriately classified and were therefore not included in this study.

Similarly, some antibiotic prescriptions may have been missed, particularly in the years 2011-2014, where the total count of antibiotics for these data points was much lower than in the period 2015-2019. We used antibiotics cited in previous acne literature, and antibiotics not commonly prescribed for the treatment of acne or that are available over the counter were not captured [4,21]. Patients prescribed antibiotics for acne without an acne diagnosis would also have been missed, as would patients who were given a prescription for acne for a shorter time period than 28 days. We could also have potentially included patients who were on long-term antibiotics or isotretinoin for a reason other than acne, despite having 2 diagnoses of acne. Other data limitations include missing information on insurance, severity of disease, treatment duration, and prescription refills.

Conclusions

In our sample, male patients were 1.67 times more likely to have received an antibiotic prescription and over twice as likely to have received an isotretinoin prescription than were female patients. These findings could be attributed to the fact that female patients may seek treatment for less severe acne, resulting in fewer systemic therapy prescriptions. Further research is needed regarding the severity of acne presentations in male versus female patients, as we did not have this data and cannot say for certain that the female patients in our cohort had a less severe presentation compared to male patients. Side effect profiles and additional systemic treatment options for male patients (OCPs and spironolactone) may also play a role in this discrepancy between sexes.

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Conflicts of Interest

RPD is deputy chair of the American Academy of Dermatology DataDerm Data Governance Committee and a Cochrane Council Co-Chair. RPD is also Editor-in-Chief of *JMIR Dermatology* at the time of this publication. TES received salary from Pfizer (grant 25B1519; principal investigator Stanca Birlea) and the National Institutes of Health (grant 2T32AR00741136A1; principal

investigator Dennis Roop). TES served as an editorial board member-at-large for *JMIR Dermatology*. MJA received a fellowship salary from Pfizer (independent grants 65894351 and 58858477; principal investigator RPD). JSB has received consulting fees from Dexcel Pharma.

Multimedia Appendix 1
Acne diagnosis concept set.
[DOCX File , 13 KB - derma_v6i1e42883_app1.docx]

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Abbreviations

AAD: American Academy of Dermatology
OHDSI: Observational Health Data Sciences and Informatics
OMOP: Observational Medical Outcomes Partnership
IBD: inflammatory bowel disease
ICD: International Statistical Classification of Diseases and Related Health Problems
OCP: oral contraceptive pill

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Original Paper

Evaluating the Impact of a Cream Containing Horse Placental Extract on Eye Corner Wrinkles in Healthy Women: Single-Blind Comparative Study

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Abstract

Background: Placental extract has been mostly used in skin care for cosmetic purposes. However, the use of various placental extracts has been limited due to the lack of established and effective application methods.

Objective: In this study, we investigated the antiwrinkle effect of a cream formulation—LNC wrinkle eye cream (LNC-EC)—containing horse placental extract as the main ingredient.

Methods: A total of 24 healthy women, aged 37-54 years, with wrinkle grades 1-3, were treated with LNC-EC for 2 weeks. The cream was applied on one-half of the participants' faces, and the results were compared with the untreated half of the face.

Results: Visual inspection, using the wrinkle grade standard, showed that the area treated with LNC-EC had a significantly lower wrinkle grade than the untreated area when comparing before and after the application of LNC-EC. In addition, replica analysis showed a significant reduction in both the maximum wrinkle width and the number of wrinkles in the LNC-EC–treated area in comparison to the untreated area before and after the application. These results suggest that LNC-EC has an antiwrinkle effect on the corners of the eyes based on parameters like the maximum wrinkle width and the number of wrinkles.

Conclusions: LNC-EC, with horse placental extract as its main ingredient, was shown to be effective in improving wrinkles at the eye corners, presumably due to a reduction in the maximum wrinkle width and the number of wrinkles. Interpretation of the results is limited because this study was conducted only in the intervention group. A randomized controlled trial with a placebo control group is necessary to verify the antiwrinkle effects of horse placental extract.

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KEYWORDS

wrinkle; horse placental extract; corner of the eyes; eye corner; wrinkle grade standards; skin replica analysis; crow's feet; laugh lines; lateral canthal lines; canthal line; dermis; epidermis; nasolabial fold; cheek; forehead; under eye; dynamic wrinkle; static wrinkle; wrinkle fold; dermatology; dermatologist; skin; women; skin care; effective; cream; face; design; effect; eye; optician; ophthalmologist

Introduction

Skin aging is influenced by both internal (changes in hormonal status and local immune system [1]) and external (ultraviolet exposure and effects of the regulation of the hypothalamic-pituitary-adrenal axis [1,2]) factors. The human face is constantly exposed to the outside world, influencing personal impressions [3]. Various age-related facial changes are noticeable [4], particularly periorbital area changes [5]. The skin around the orbits is thinner compared to other parts of the face [6]; wrinkles tend to form at eye corners because of frequent movements, such as blinking and facial expressions [7].

Dermatologically, placental extracts have been reported to enhance epidermal protection by promoting keratinocyte proliferation, increasing antibacterial peptide expression (eg, defensins), reducing cell damage from fine particulate matter, supporting the growth of epidermal indigenous bacteria, and inhibiting cellular aging during 5-bromo-2’-deoxyuridine induction [8,9]. Although the effectiveness of placental extracts in skin care, especially in improving wrinkles, has been reported [10,11], their practical remains undetermined due to variations in extraction and administration methods, including dosing and application, across different studies. To assess the efficacy of placental extracts, we investigated their impact on eye-corner wrinkles in healthy participants during the drier winter months.

Methods

Materials and Clinical Study

The LNC wrinkle eye cream (LNC-EC; Japan Bio Products Co) was used.

This randomized, single-blind clinical trial was conducted from January 20 to February 3, 2022, in Kirei Testing Labo Co, Ltd. We established a single group to compare the untreated and treated sites in the same participant. Randomization was performed to reduce bias.

Ethics Approval

This study was reviewed and approved by the Kirei Testing Laboratory Ethics Committee on January 18, 2022 (ID 22000134) and registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN000051646). The participants signed an informed consent, which included the study purpose, methods, confidentiality, and the right to withdraw. Confidentiality was ensured. Study procedures were conducted according to the World Medical Association’s Helsinki Declaration and its amendments.

Participants and Setting

The inclusion criteria were as follows: healthy Japanese women aged ≥20 and <59 years at the time of consent, women with wrinkle grades 1 to 3 at both eye corners, and women with skin classified as Fitzpatrick type III or IV. Exclusion criteria included the following:

- Women with markedly different wrinkle grade scores (specifically, a difference ≥ +/–1) between the left and right eye corners
- Women whose skin at the evaluation site had inflammation, trauma, contusion, pimples, warts, blemishes, or traces of diseases like atopic dermatitis or urticaria that may affect study results
- Women continuously using skin care products, cosmetics, quasi-drugs, or health foods claiming or emphasizing similar efficacy as the test product (reduction of fine lines and wrinkles caused by dryness) at the evaluated area
- Women who had undergone or planned to undergo cosmetic procedures on the evaluation site or elsewhere during the study period
- Women who changed their skin care products or started using new basic cosmetic or sunscreen products on the evaluation site within the past 4 weeks
- Women exposed to excessive ultraviolet radiation (eg, prolonged outdoor work, exercise, swimming, or leisure activities) within the past 4 weeks or planning such activities during the study
- Women participating in another study at enrollment or during the planned study duration
- Women receiving hormone replacement or any other treatments for various medical conditions at enrollment or during the study
- Women currently undergoing dermatological treatment
- Women with a history of serious diseases involving glucose and lipid metabolism; liver and renal function; cardiac, cardiovascular, respiratory, endocrine, immune, and neurological systems; or psychiatric disorders
- Women working night or a combination of day and night shifts
- Women with a history of alcohol and drug dependence
- Women who take alcohol, vitamin B_{12}, or melatonin for sleeping
- Women at risk of developing allergies to cosmetics and food or who have developed skin rashes or other skin problems due to cosmetics within the past year
- Pregnant or lactating women at the time of consent or those planning to become pregnant during the study
- Women using mosaics, eye tapes, or other double-eyelid-shaping products that cannot be removed for testing
- Women who had eyelash extensions and could not tolerate the solvent used during the replica collection
- Participants deemed ineligible for any reason by the supervising physician or investigator

If any information rendering them ineligible was identified during the study, they were excluded from the analysis. A total of 24 participants were selected for the study through visual assessment based on the wrinkle grade standard (8 grades: 0-7). Informed consent was obtained from all participants. Furthermore, a consultation service was established at a medical institution to address any health-related enquiries.

Test Product Application

Test products were randomly assigned to participants using the half-face method on symmetrical areas of the face, with no apparent bias in the left-right distribution [11]. Participants were instructed to apply the test product (0.5 g) to one-half of the face both in the morning and at night, consistently at the same time, and to continue applying the product until the final measurement date.

Wrinkle Measurement Using Wrinkle Grade Standards

Photographic and visual assessments were conducted in accordance with the guidelines for evaluating antiwrinkle products, as authorized by the Japanese Cosmetic Science Society. Trained experts, proficient in wrinkle evaluation, assigned participants an 8-point wrinkle grade score using the wrinkle grade evaluation criteria and photographs provided by the Japanese Society of Cosmetic Science and Technology [12].

Wrinkle Measurement Using Skin Replica Analysis

Skin replicas of the target site (10 × 10 mm or larger) were made and analyzed using a replica analysis system (ASA-03RXD; ASH, Japan) to calculate the wrinkle area and volume ratios, maximum wrinkle depth and width, average wrinkle depth, and the number of wrinkles [13].

Statistical Analysis

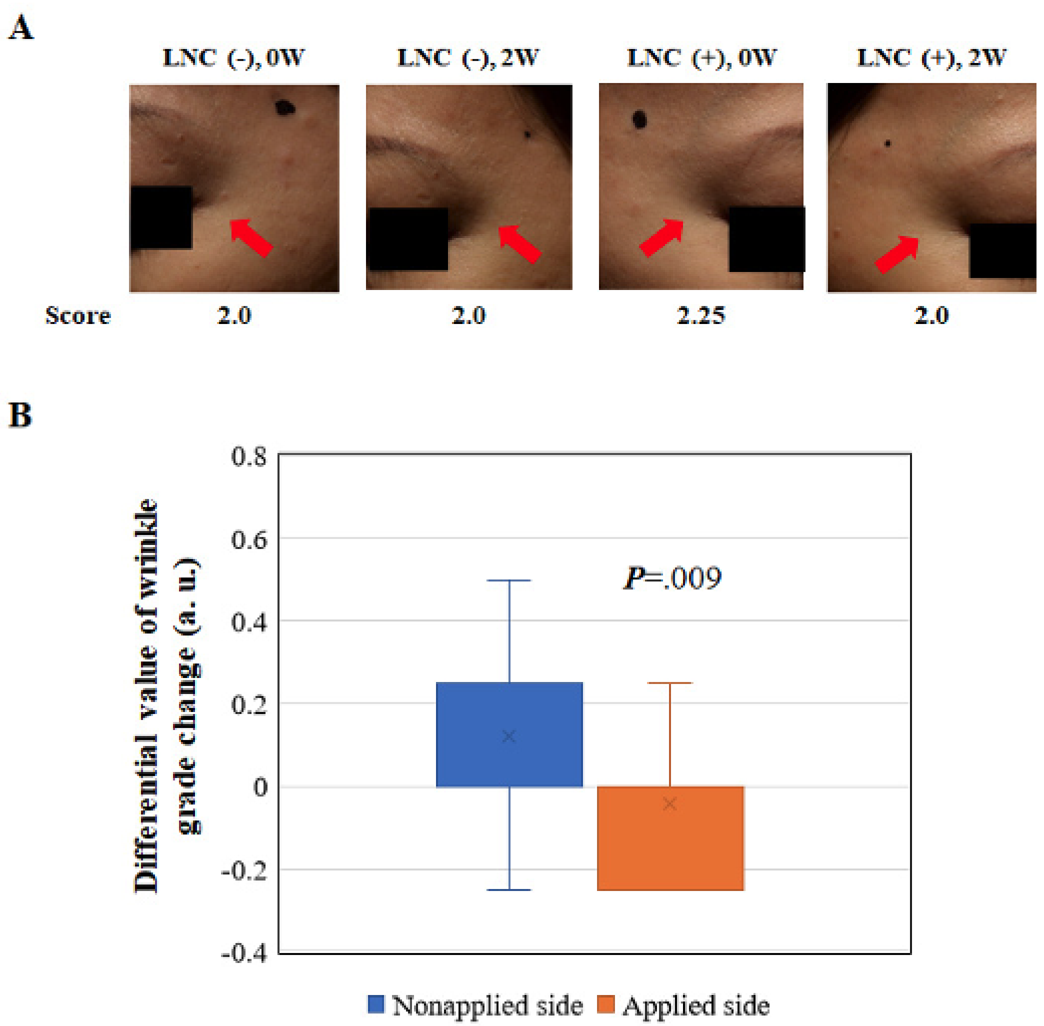
The untreated and treated sides were compared by calculating the change (Δ) at 2 weeks (baseline scores minus 2-week scores, reported as the mean change from baseline for a parameter). Skin replica analysis was performed using a statistical software program built into the replica analysis system (ASA-03RXD; Nihon Ash Co, Ltd). For each clinical parameter, the groups were compared using the Wilcoxon signed rank test and a paired 2-tailed *t* test (*P*=.05) for wrinkle and replica analysis, respectively, to determine statistically significant differences in improvement between the untreated and treated sides.

Results

LNC-EC Effects on Skin Wrinkles According to Wrinkle Grade Standards

The wrinkle grade on the treated side was 2.25 at baseline but decreased to 2.0 after 2 weeks of use, resulting in less noticeable wrinkles. On the untreated side, the grade remained at 2.0 from baseline to the end of the 2-week period (Figure 1A). A significant difference was observed when subtracting the pretest from the posttest assessment value based on the wrinkle grade standard (Figure 1B).

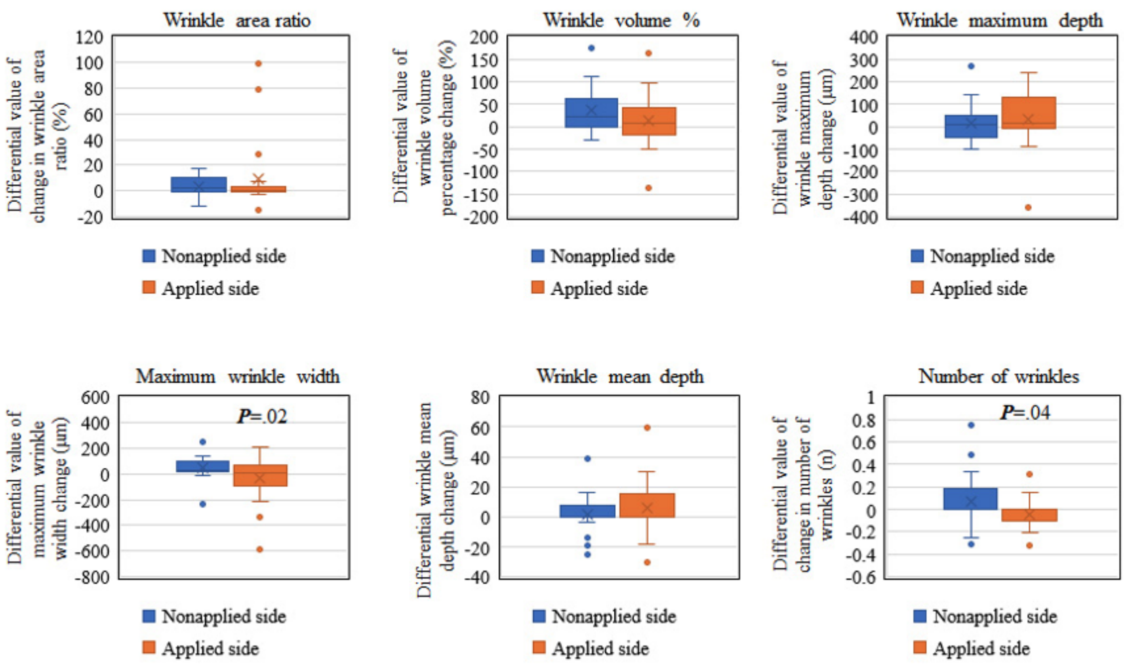
Figure 1. Assessment based on the wrinkle grading standards. (A) Representative example comparing the untreated and treated sides with LNC wrinkle eye cream before (baseline) and after 2 weeks of treatment. Photographs illustrate the improvement in facial wrinkles. Arrows indicate the specific areas of interest. (B) Box plot representation of the differential value of wrinkle grade change (arbitrary unit: a. u.) between the untreated and treated sides with LNC eye cream before (baseline) and after 2 weeks of treatment.



LNC-EC Effects on Skin Wrinkles Based on Skin Replica Analysis

No significant differences were observed in pre- and posttest results for wrinkle area ratio, wrinkle volume percentage, maximum wrinkle depth, and wrinkle mean depth. Meanwhile, a significant difference was detected in pre- and posttest results for maximum wrinkle width and the number of wrinkles (Figure 2).

Figure 2. Box plot representation of the differential value of various parameters between the nonapplied and applied sides of the skin when using LNC wrinkle eye cream, both before (0 weeks) and after 2 weeks of treatment.



Discussion

Principal Findings

In this study, LNC-EC was applied to healthy participants for 2 weeks to verify its cosmetic effects. Both wrinkle grade evaluation and replica analysis demonstrated its antiwrinkle effects at the eye corners. The replica analysis revealed a reduction in the maximum width and the number of wrinkles. These results suggest that horse placental extract has cosmetic benefits.

Wrinkles can result from external factors like dryness due to decreased temperature and humidity as well as internal factors related to reduced moisture retention due to aging. This study was conducted during winter when temperature and humidity levels are at their lowest. Consequently, external factors could potentially compromise the barrier function of each skin layer. The stratum corneum's barrier function weakens during winter due to smaller corneocytes compared to summer [14]. Epidermal dryness leads to structural changes causing shallow wrinkles, so preventing dryness is crucial in improving wrinkles. Horse placental extract enhances skin barrier function by promoting the growth of *Staphylococcus epidermidis* and antimicrobial peptide expression in human epidermal keratinocytes [8]. Furthermore, aged human keratinocytes exhibit increased stratifin expression, suppressing filaggrin and serine palmitoyltransferase involved in epidermal moisturization [15]. Horse placenta extract reduces stratifin expression in aged human cultured epidermal cells [9], suggesting that strengthening the skin barrier with this extract may help prevent worsening wrinkles.

Ultraviolet B stimulates epidermal keratinocytes, resulting in the release of inflammatory cytokines (interleukin [IL]-1α, IL-6, and tumor necrosis factor-α), which stimulate dermal fibroblasts and keratinocytes to increase matrix metalloproteinase (MMP)-1, MMP-3, and MMP-9—enzymes that degrade collagen and elastic fibers, causing wrinkles [16]. Horse placenta extract suppresses IL-6 expression, which increases with age, in cultured aged human epidermal cells [9]. This suggests that the extract may indirectly mitigate the worsening of wrinkles by preventing increased MMP expression. Considering these factors, LNC-EC's antiwrinkle effects in this study likely result from the placental extract's various biological activities.

Conclusions

LNC-EC appears effective in improving the appearance of eye-corner wrinkles, presumably by reducing their maximum width and number. No adverse events associated with LNC-EC application were observed during the study, indicating its safety for use.

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Authors' Contributions

TW analyzed and interpreted the data, and she wrote the first draft of the manuscript. KT interpreted the data. EH analyzed and interpreted the data and wrote the paper. All authors read and approved the final manuscript.

Conflicts of Interest

All authors are employees of Japan Bio Products Co, Ltd.

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Abbreviations

IL: interleukin

LNC-EC: LNC wrinkle eye cream
MMP: matrix metalloproteinase

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Original Paper

The Effect of Remote Digital Services on Health Care Inequalities Among People Under Long-Term Dermatology Follow-Up: Cross-Sectional Questionnaire Study

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Abstract

Background: Given the expansion of remote digital dermatology services from the National Health Service, particularly during the COVID-19 pandemic, there is a need for methods that identify patients at risk of digital exclusion to guide equitable representation in service co-design processes and tailor remote services to the needs of their patient population.

Objective: This quality improvement project aims to inform the redesign of remote services to optimally support the ongoing needs of patients with chronic skin diseases, ensuring that the services are tailored to patients' digital health literacy requirements.

Methods: We profiled the digital health literacy of 123 people with chronic skin conditions who require long-term surveillance in 2 specialist clinics (London, United Kingdom) using the Multidimensional Readiness and Enablement Index for Health Technology (READHY) questionnaire alongside the Optimizing Health Literacy and Access (Ophelia) process for hierarchical cluster analysis.

Results: The cluster analysis of READHY dimensions in responding participants (n=116) revealed 7 groups with distinct digital and health literacy characteristics. High READHY scores in groups 1 (n=22, 19%) and 2 (n=20, 17.2%) represent those who are confident with managing their health and using technology, whereas the lower-scoring groups, 6 (n=4, 3.4%) and 7 (n=12, 10.3%), depended on traditional services. Groups 3 (n=27, 23.3%), 4 (n=23, 19.8%), and 5 (n=8, 6.9%) had varying digital skills, access, and engagement, highlighting a population that may benefit from a co-designed dermatology service.

Conclusions: By identifying patient groups with distinguishable patterns of digital access and health literacy, our method demonstrates that 63.8% (n=74) of people attending specialist clinics in our center require support in order to optimize remote follow-up or need an alternative approach. Future efforts should streamline the READHY question profile to improve its practicality and use focus groups to elicit strategies for engaging patients with digital services.

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KEYWORDS

dermatology; health literacy; digital health literacy; digital literacy; skin; chronic; cluster analysis; innovation; eHealth literacy; dermatologists; telehealth; dermatologist; telemedicine; remote care; service; services; quality improvement

Introduction

Technological advances alongside the COVID-19 pandemic have driven remote digital dermatology service adoption across the National Health Service (NHS). Such services include application-based patient-initiated follow-up, where people initiate an appointment, as required, using their devices [1]. Our hospital department (London, United Kingdom) provides several specialist clinics for people under long-term dermatology follow-up. Considering many of these patients are not locals, a digital patient-initiated follow-up service may be an efficient and cost-effective alternative. However, this may widen inequities by disadvantaging digitally excluded individuals, including the estimated 10 million UK residents who have unequal access and capacity to use technologies that are essential for participating in society fully [2]. Specific patient-reported barriers associated with remote dermatology include low technology use, poor telephone facilities, and difficulty with photo sharing [3-5].

NHS England suggests several actions to mitigate digital exclusion, including creating guidance that measures teledermatology referral suitability [6]. Dermatology literature provides sparse information on the most appropriate measure. However, 1 way to determine this suitability is by measuring patients' health technology readiness (how prepared and willing one is to use health technology) using the Multidimensional Readiness and Enablement Index for Health Technology (READHY) questionnaire [7]. In addition to exploring the mechanisms behind readiness, such as the motivation to engage with digital services, this tool identifies those at risk of digital exclusion [7]. Co-design with this population would provide the essential user-centered approach needed to develop a tailored service [8].

This study documents the initial steps of a quality improvement project, whereby we profile the health technology readiness of people for whom we plan to use digital services in the dermatology outpatient setting, aiming to use these data to optimize service design.

Methods

Recruitment

We invited consecutive people receiving long-term dermatology follow-up at 2 specialist clinics in our department—organ transplant recipient skin cancer surveillance (OTS) and biologics monitoring for chronic inflammatory skin disorders (BioM).

The READHY questionnaire is a validated tool based on the concept of digital health literacy, self-management, and social support using 13 related scales from the eHealth Literacy Questionnaire (7 scales) [9], Health Literacy Questionnaire (2 scales) [10], and Health Education Impact Questionnaire (4 scales) [11]. This tool assesses health technology readiness using 65 statements that participants respond to using a 4-point Likert scale (1=strongly disagree and 4=strongly agree). By averaging the scores for the responses to each question of a given scale, each scale is given an overall rating [7].

Authors (HM, AUP, and ZH) verbally administered the READHY questionnaire in the BioM (February-March 2022) and OTS (July-October 2021) clinics by telephone or in person, with assistance where required. Additional questions were asked to acquire demographic data, including age, gender, and ethnicity. People who could not understand basic spoken English were excluded.

Analysis

In addition to descriptive statistics, the READHY responses and demographic data were subjected to cluster analysis using the Optimizing Health Literacy and Access (Ophelia) process [9]. Based on the principle of health equity, the Ophelia process recognizes that a population is not homogenous and there are subgroups within a population that may have different strengths and challenges, especially since health literacy or health technology readiness is a multidimensional concept. Hence, cluster analysis, a statistical method to identify subgroups based on a set of variables, is recommended. Following the Ophelia process protocol, a hierarchical cluster analysis using the Ward method, based on the 13 scale scores of the READHY tool, was undertaken. This helps to identify the strengths and challenges of subgroups among survey participants to foster the development of tailored actions to support the use of the service. People who did not answer at least 1 piece of demographic data were excluded from this analysis.

Ethical Considerations

This work forms part of a quality improvement project and was approved by the local Quality Improvement Team (137292). Patients were invited to participate and provided informed verbal consent. The data was anonymized. No compensation was provided.

Results

Demographics

Of the 163 people (BioM: n=35, 21.5%; OTS: n=128, 78.5%) we invited to participate, 23 (66.5% response rate) out of 35 people from the BioM clinic and 100 (77.3% response rate) out of 128 people from the OTS clinic completed the questionnaire. There were 4 reasons for nonparticipation (40/163, 24.5%). Of the 163 people invited, 21 (12.9%) did not answer our telephone call, 14 (8.6%) declined our invitation, 3 (1.8%) did not telephone back, and 2 (1.2%) did not have sufficient English language skills. The final cohort (Table 1) consisted of 48 (BioM:OTS=11:37) women and 66 (BioM:OTS=12:54) men with a median age of 58.6 (IQR 50.2-66.6; BioM:OTS=52.6, IQR 38.9-60.1:60.1, IQR 51.7-67.6) years.

Table 1. Demographics of people included in this quality improvement project[a].

Demographics	All (n=123), n (%)	Group 1 (n=22), n (%)	Group 2 (n=20), n (%)	Group 3 (n=27), n (%)	Group 4 (n=23), n (%)	Group 5 (n=8), n (%)	Group 6 (n=4), n (%)	Group 7 (n=12), n (%)
Age group (years)								
21-29	2 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	1 (8.3)
30-39	7 (5.7)	3 (13.6)	2 (10)	0 (0)	0 (0)	0 (0)	0 (0)	2 (16.7)
40-49	17 (13.8)	4 (18.2)	5 (25)	5 (18.5)	2 (8.7)	0 (0)	0 (0)	1 (8.3)
50-59	34 (27.6)	6 (27.3)	6 (30)	11 (40.7)	6 (26.1)	1 (12.5)	0 (0)	4 (33.3)
60-69	35 (28.5)	6 (27.3)	3 (15)	6 (22.2)	11 (47.8)	6 (75)	1 (25)	2 (16.7)
70-79	17 (13.8)	3 (13.6)	4 (20)	3 (11.1)	3 (13)	1 (12.5)	1 (25)	2 (16.7)
80 or older	2 (1.6)	0 (0)	0 (0)	1 (3.7)	0 (0)	0 (0)	1 (25)	0 (0)
Not answered	9 (7.3)	0 (0)	0 (0)	1 (3.7)	1 (4.3)	0 (0)	0 (0)	0 (0)
Gender								
Men	67 (54.5)	15 (68.2)	11 (55)	15 (55.6)	12 (52.2)	6 (75)	1 (25)	7 (58.3)
Women	48 (39)	7 (31.8)	9 (45)	12 (44.4)	11 (47.8)	1 (12.5)	3 (75)	5 (41.7)
Prefer not to say	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Not answered	8 (6.5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)	0 (0)	0 (0)
Ethnicity								
Asian or British Asian	9 (7.3)	3 (13.6)	2 (10)	2 (7.4)	1 (4.3)	0 (0)	0 (0)	1 (8.3)
Black, African, Caribbean, or Black British	9 (7.3)	0 (0)	3 (15)	1 (3.7)	1 (4.3)	1 (12.5)	0 (0)	3 (25)
White	95 (77.2)	19 (86.4)	14 (70)	23 (85.2)	21 (91.3)	7 (87.5)	4 (100)	7 (58.3)
Mixed or multiple ethnicity groups	2 (1.6)	0 (0)	0 (0)	1 (3.7)	0 (0)	0 (0)	0 (0)	1 (8.3)
Prefer not to say	1 (0.8)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Not answered	7 (5.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Marital status								
Married	73 (59.3)	13 (59.1)	14 (70)	20 (74.1)	17 (73.9)	6 (75)	1 (25)	2 (16.7)
Divorced	7 (5.7)	1 (4.5)	1 (5)	2 (7.4)	0 (0)	0 (0)	1 (25)	2 (16.7)
Widowed	5 (4.1)	0 (0)	1 (5)	1 (3.7)	2 (8.7)	0 (0)	1 (25)	0 (0)
Never married	15 (12.2)	5 (22.7)	0 (0)	2 (7.4)	1 (4.3)	1 (12.5)	1 (25)	5 (41.7)
Separated	5 (4.1)	1 (4.5)	3 (15)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8.3)
Engaged	2 (1.6)	1 (4.5)	0 (0)	0 (0)	1 (4.3)	0 (0)	0 (0)	0 (0)
Partner	2 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)	0 (0)	1 (8.3)
Not answered	14 (11.4)	1 (4.5)	1 (5)	2 (7.4)	2 (8.7)	0 (0)	0 (0)	1 (8.3)
Education								
Primary school	1 (0.8)	0 (0)	0 (0)	0 (0)	1 (4.3)	0 (0)	0 (0)	0 (0)
Secondary school (up to 16 years)	36 (29.3)	6 (27.3)	7 (35)	5 (18.5)	12 (52.2)	2 (25)	1 (25)	3 (25)

Demographics	All (n=123), n (%)	Group 1 (n=22), n (%)	Group 2 (n=20), n (%)	Group 3 (n=27), n (%)	Group 4 (n=23), n (%)	Group 5 (n=8), n (%)	Group 6 (n=4), n (%)	Group 7 (n=12), n (%)
College or university (ie, bachelor's degree)	35 (28.5)	11 (50)	2 (10)	11 (40.7)	1 (4.3)	5 (62.5)	2 (50)	3 (25)
Higher or further education (ie, A-levels)	24 (19.5)	2 (9.1)	5 (25)	7 (25.9)	6 (26.1)	1 (12.5)	0 (0)	3 (25)
Postgraduate degree	10 (8.1)	2 (9.1)	4 (20)	1 (3.7)	1 (4.3)	0 (0)	1 (25)	1 (8.3)
Prefer not to say	5 (4.1)	0 (0)	1 (5)	1 (3.7)	2 (8.7)	0 (0)	0 (0)	1 (8.3)
Not answered	12 (9.8)	1 (4.5)	1 (5)	2 (7.4)	0 (0)	0 (0)	0 (0)	1 (8.3)
Household income (£)[b]								
Up to 17,499	24 (19.5)	3 (13.6)	7 (35)	2 (7.4)	5 (21.7)	0 (0)	2 (50)	5 (41.7)
17,500-29,999	13 (10.6)	3 (13.6)	1 (5)	2 (7.4)	3 (13)	1 (12.5)	1 (25)	2 (16.7)
30,000-39,999	6 (4.9)	0 (0)	1 (5)	1 (3.7)	2 (8.7)	2 (25)	0 (0)	0 (0)
40,000-49,999	9 (7.3)	2 (9.1)	0 (0)	4 (14.8)	2 (8.7)	0 (0)	0 (0)	1 (8.3)
50,000 and over	32 (26)	10 (45.5)	5 (25)	9 (33.3)	2 (8.7)	4 (50)	0 (0)	2 (16.7)
Not answered	39 (31.7)	4 (18.2)	6 (30)	9 (33.3)	9 (39.1)	1 (12.5)	1 (25)	2 (16.7)

[a]People who did not answer 1 or more demographic questions were excluded from the cluster analysis.

[b]1 £=US $1.22.

Outcomes

The mean READHY domain scores followed a similar trend in both clinics (Figure 1), with higher scores for self-monitoring, support, and health understanding and lower scores for emotional distress, suitability, and technology for processing health information. The most notable difference in domain responses occurred in "skills and technique acquisition," where the OTS group scored higher.

A total of 116 people were eligible for the cluster analysis, which revealed 7 groups (Table 1 and Figures 2 and 3). The higher READHY scores in groups 1 (n=22, 19%; median age 56.2, IQR 45.8-65.3 y; men:women=15:7) and 2 (n=20, 17.2%; median age 54.5, IQR 45.5-66.2 y; men:women=11:9) represented those confident with managing their health and using technology, although people in group 2 reported somewhat higher emotional distress. Conversely, groups 6 (n=4, 3.4%; median age 69.5, IQR 29.5-79.5 y; men:women=1:3) and 7 (n=12, 10.3%; median age 54.5, IQR 39.5-64.5 y; men:women=7:5) were low-scoring populations dependent on traditional services with limited access to and engagement with prospective remote care. Accompanying their low digital health literacy, group 7 members felt less supported, more emotionally distressed, and with a lower sense of control. Groups 3 (n=27, 23.3%; median age 56.8, IQR 50.9-65.3 y; men:women=5:4), 4 (n=23, 19.8; median age 62.2, IQR 55.3-67.2 y; men:women=9:5), and 5 (n=8, 6.9%; median age 64.5, IQR 61.2-67.8 y; men:women=6:1) consisted of well-supported individuals possessing some experience with digital services. However, each group had varying levels of access to, interest in, and skills in using technology for health management.

Figure 1. Mean READHY domain scores as per clinic. READHY: Multidimensional Readiness and Enablement Index for Health Technology.

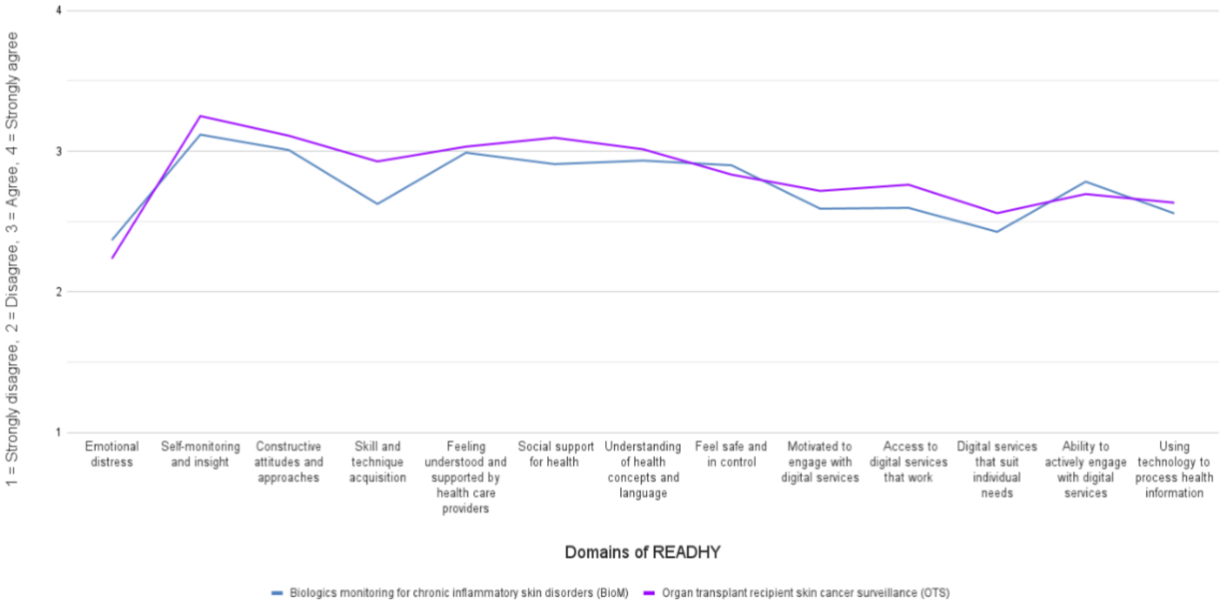


Figure 2. Mean READHY domain scores as per cluster analysis. READHY: Multidimensional Readiness and Enablement Index for Health Technology.

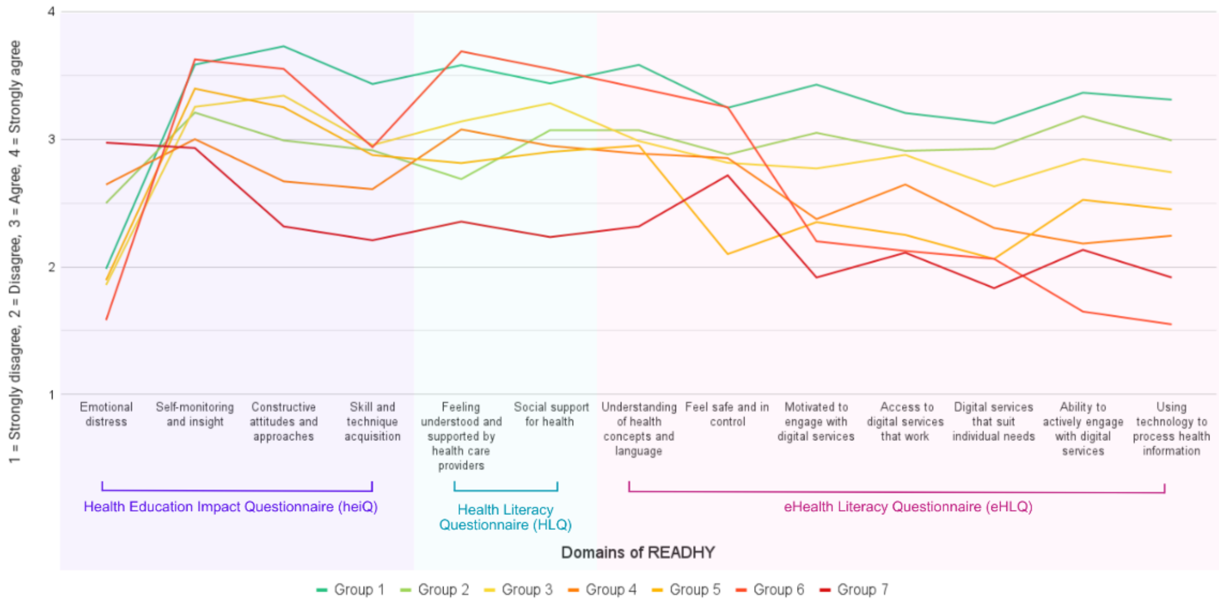
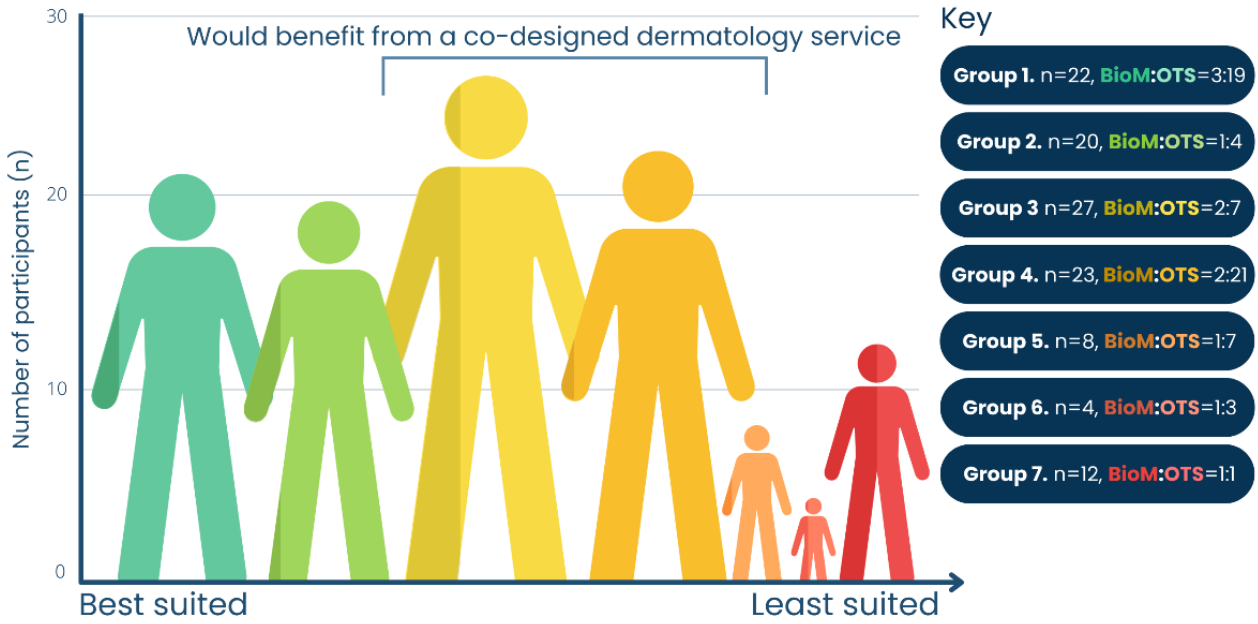


Figure 3. Patient groups (1-7) based on hierarchical cluster analysis of demographics and READHY scores. BioM: biologics monitoring for chronic inflammatory skin disorders; OTS: organ transplant recipient skin cancer surveillance; READHY: Multidimensional Readiness and Enablement Index for Health Technology.



Discussion

Principal Findings

We use a method in a cohort of people receiving long-term dermatology follow-up revealing that 63.8% (74/116) of these individuals belong to groups 3 to 7, which are characterized by lower health technology readiness and are vulnerable to digital exclusion. However, members of groups 3 to 5 have moderate health technology experience, alongside support in the community, highlighting a population that may use a co-designed dermatology service. Additionally, lower readiness was not associated with any specific demographics. It is, therefore, essential to evaluate health technology readiness when developing remote dermatology services to recognize those that may already safely benefit from technology (groups 1 and 2), require targeted support (groups 3 to 5), or need alternative care provision (groups 6 and 7).

Stratifying health technology readiness has only ever been successfully conducted outside of a dermatological setting, such as in an outpatient irritable bowel disease clinic [12]. Furthermore, there is minimal literature exploring user suitability for digital dermatology care. eHealth literacy has, however, previously been assessed by Stege et al [13] in a population of patients with skin cancer. Stege et al [13] report greater eHealth literacy in younger, well-educated participants, though we are unable to determine from their data the proportion of their participants who are at risk of digital exclusion. Our comparative lack of demographic trends may be due to the broad inclusion criteria for the cluster analysis and limited sample size.

Unexpectedly, most of our cohort fell within groups 1 to 4, with group 1 being the third largest cluster overall. This skew of our population toward profiles with higher health technology readiness could be explained by the upskilling of the public during the COVID-19 pandemic, thus improving their confidence with digital tools. Nielsen et al [12] and Thorsen et al [14] document a similar skew, although this is minimal in Thorsen et al [14] perhaps due to the data collection that occurred in 2018, before the previously mentioned upskilling.

Limitations

The limitations include using direct data collection alongside self-reported demographics. Social desirability bias may affect our findings since participants may not want to reveal information that is more sensitive. Indeed, the 31.7% (39/123) of eligible participants who did not disclose their household income supports this notion. Next, despite an acceptable response rate, sample selection bias is likely present since we used a highly comprehensive measure of health technology readiness and a translator was absent, excluding non-English speakers and those with low literacy. Finally, the generalization of our findings to the wider population requiring long-term dermatology follow-up is limited as we surveyed only 2 clinics. Clinical interviews and focus groups with people who are frequently difficult to engage in will need to be a part of future work to elicit their opinions about digital health interventions. Furthermore, streamlining the READHY question profile would likely improve its practicality in busy clinical settings.

Conclusions

In summary, through a preliminary exploration of READHY, we demonstrate that 63.8% (74/116) of people attending specialist clinics in our center need at least some support to optimize remote digital follow-up. This proportion is likely to vary considerably across centers and patient populations. However, it is paramount that clinicians consider such information to guide equitable representation in service co-design processes and tailor remote services to the needs of their patient population.

Conflicts of Interest

None declared.

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Abbreviations

BioM: biologics monitoring for chronic inflammatory skin disorders
NHS: National Health Service
Ophelia: Optimizing Health Literacy and Access
OTS: organ transplant recipient skin cancer surveillance
READHY: Multidimensional Readiness and Enablement Index for Health Technology

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Original Paper

The Reporting and Methodological Quality of Systematic Reviews Underpinning Clinical Practice Guidelines Focused on the Management of Cutaneous Melanoma: Cross-Sectional Analysis

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Abstract

Background: Clinical practice guidelines (CPGs) inform evidence-based decision-making in the clinical setting; however, systematic reviews (SRs) that inform these CPGs may vary in terms of reporting and methodological quality, which affects confidence in summary effect estimates.

Objective: Our objective was to appraise the methodological and reporting quality of the SRs used in CPGs for cutaneous melanoma and evaluate differences in these outcomes between Cochrane and non-Cochrane reviews.

Methods: We conducted a cross-sectional analysis by searching PubMed for cutaneous melanoma guidelines published between January 1, 2015, and May 21, 2021. Next, we extracted SRs composing these guidelines and appraised their reporting and methodological rigor using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (A Measurement Tool to Assess Systematic Reviews) checklists. Lastly, we compared these outcomes between Cochrane and non-Cochrane SRs. All screening and data extraction occurred in a masked, duplicate fashion.

Results: Of the SRs appraised, the mean completion rate was 66.5% (SD 12.29%) for the PRISMA checklist and 44.5% (SD 21.05%) for AMSTAR. The majority of SRs (19/50, 53%) were of critically low methodological quality, with no SRs being appraised as high quality. There was a statistically significant association (*P*<.001) between AMSTAR and PRISMA checklists. Cochrane SRs had higher PRISMA mean completion rates and higher methodological quality than non-Cochrane SRs.

Conclusions: SRs supporting CPGs focused on the management of cutaneous melanoma vary in reporting and methodological quality, with the majority of SRs being of low quality. Increasing adherence to PRISMA and AMSTAR checklists will likely increase the quality of SRs, thereby increasing the level of evidence supporting cutaneous melanoma CPGs.

(JMIR Dermatol 2023;6:e43821) doi:10.2196/43821

KEYWORDS

clinical practice guidelines; clinical; cutaneous melanoma; decision making; evidence; management; melanoma; practice guideline; review; systematic review

Introduction

Clinical practice guidelines (CPGs) are high-quality, evidence-based statements that have been used by health care professionals to bridge the gap between policies, best practices, local contexts, and patient preferences [1]. Through recommendations, CPGs are beneficial to medical practices by decreasing variances and mistakes in clinical practice, reducing health care costs, and improving health outcomes [1,2]. With CPGs offering various benefits to both the clinician and the patient, it is no surprise that CPGs are heavily relied upon in clinical settings and widely supported by practicing health care professionals [3,4]. Despite their widespread use and potential benefits, concerns about the quality of CPGs exist.

Research evaluating the methodological quality and reporting clarity of systematic reviews (SRs) referenced in CPGs found variability in SR quality across various fields [5-8]. For example, CPGs focused on pediatric obesity based their recommendations primarily on low-quality SRs according to both the PRISMA (Preferred Reporting Instrument for Systematic Reviews and Meta-Analyses) and AMSTAR (A Measurement Tool to Assess Systematic Reviews) appraisal instruments [7]. PRISMA is an appraisal tool that evaluates the completeness of the reporting of SRs, while AMSTAR evaluates the methodological quality of SRs [5-8].

In dermatology, quality surveys of guidelines assessed by the Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II) tool have been performed in various dermatologic conditions, including guidelines focused on the management of melanoma [9-11]. Although widely used, the AGREE II instrument was not designed to provide a comprehensive evaluation of the methodological rigor of the studies forming the guidelines and recommendations [12]. In 2020, a study found that the recommendations made by the American Academy of Dermatology (AAD) CPGs for the management of melanoma—one of the most recently published guidelines by the AAD—were supported by primarily moderate to low levels of evidence [13]. Interestingly, the lack of strong support exists despite a significant increase in published SRs and randomized controlled trials in dermatology, indicating a need for higher-quality studies [13-16]. Thus, to further improve clinical practice in dermatology, the evidence underpinning CPG recommendations needs to be rigorously developed and assessed [12,15].

With regard to limitations, the primary aim of this study was to determine the reporting and methodological quality of SRs and meta-analyses cited in CPGs for the management of cutaneous melanoma by using AMSTAR and PRISMA appraisal instruments. Our secondary aim was to evaluate the number of Cochrane SRs cited in the CPGs and explore the differences between AMSTAR and PRISMA appraisals among Cochrane SRs and non-Cochrane SRs.

Methods

Ethical Considerations

This study contained no human subject data and was thus exempt from institutional review board oversight.

Transparency, Reproducibility, and Reporting

To ensure the reproducibility of this study, all data sets and analyses were publicly available on the Open Science Framework (OSF) [17]. Additionally, to further enhance reproducibility, all analyses were independently reevaluated in a masked fashion by a third-party statistician. Lastly, all search strategies, inclusion and exclusion criteria, and data extraction methods were pilot-tested a priori and adhered to this protocol.

Outcomes

The primary objective of this study was to determine the reporting and methodological quality of SRs and meta-analyses cited in CPGs for the management of cutaneous melanoma. The methodological quality of each SR was evaluated using AMSTAR and PRISMA appraisal tools. Next, this study evaluated the number of Cochrane SRs cited in the CPG and explored the differences between AMSTAR and PRISMA appraisals among Cochrane SRs and non-Cochrane SRs.

Identification of Clinical Practice Guidelines

To identify CPGs focused on cutaneous melanoma, a PubMed search was conducted by the author (TT). A customized search query (Multimedia Appendix 1) [1-16,18-21] was made with the aid of resources from the Canadian Agencies for Drugs and Technologies in Health [17] and the American Society of Clinical Oncology [22] and was used to identify relevant CPGs in PubMed.

After performing our search, all returned CPGs were uploaded to Rayyan QCRI (Qatar Computing Research Institute), a screening platform, to undergo inclusion criteria screening. Our definition that was used to identify CPGs was adopted from the Institute of Medicine [19]. For a CPG to be included, the following must be met: (1) the focus of the CPG was on the management of cutaneous melanoma; (2) the CPG was published between January 1, 2015, and May 21, 2021; and (3) the CPG was retrievable in English. The screening of all CPGs was performed in a masked duplicate fashion by investigators (BS and MK).

Identification of Systematic Reviews and Meta-Analyses

Following the screening, our 2 investigators extracted all SRs and meta-analyses from each of the included CPGs in the same masked, duplicative fashion. An SR was included if the following three criteria were met: (1) the SR met the definition of an SR as defined by the PRISMA-P (Preferred Reporting Instrument for Systematic Review and Meta-Analysis Protocols) [20]; (2) the SR was available in English; and (3) it was cited in at least 1 of the included CPGs. According to PRISMA-P, "the key characteristics of an SR are (1) a clearly stated set of objectives with an explicit, reproducible methodology; (2) a systematic search that attempts to identify all studies that would meet the eligibility criteria; (3) an assessment of the validity of the findings of the included studies (eg, assessment of risk of bias and confidence in cumulative estimates); and (4) a systematic presentation and synthesis of the characteristics and findings of the included studies" [20]. Of the SRs identified during extraction, a total of 2 were not included due to not meeting the criteria for an SR as stated above.

Training and Data Extraction

Before data extraction, investigators underwent several days of training by another investigator (TT). During this training period, investigators received training on AMSTAR and PRISMA appraisal instruments by scoring a sample of SRs according to the instrument's instructions [21,23]. Next, both investigators discussed the results of the appraisal instruments, and additional training was provided if necessary. In addition to the AMSTAR and PRISMA appraisals, the following study characteristics were extracted from each SR: the year of publication, the population of participants, the interventions used, the number of primary studies comprising the SR, the sample size across all primary studies, and the design of each primary study. Again, all data extractions were conducted in a masked, duplicate fashion. Following data extraction, investigators were unmasked, and disagreements between data sets were resolved through group discussion. If an agreement cannot be reached, a third-party investigator (RO) is available for adjudication.

PRISMA Checklist

PRISMA, a 27-item checklist created to increase the quality of reporting in SRs, was developed by an expert panel and scored in accordance with previous studies [5-8]. Each SR received scores based on whether full criteria were met ("yes"=1 point), whether partially met ("partial yes"=0.5 point), or whether no criteria were met ("no"=0 point) for each of the 27 items. Scores were then calculated as a proportion of the criteria met.

AMSTAR Checklist

AMSTAR was a 16-item appraisal tool for SRs that contained either randomized or nonrandomized studies concerning health care [23], and assessment scoring was based on previous literature [5-8]. Each of the 16 items will receive a score based on the criteria met. For example, a "yes" was given if the SR met all criteria for that item, a "partial yes" if some but not all criteria were met, and a "no" if criteria were unmet. Each item was assigned a point value according to the PRISMA section. A total of 3 AMSTAR items (11, 12, and 15) are specific to SRs containing meta-analyses and are signified by an "N/A" if the SR contains no meta-analysis. Therefore, all SRs that did not include a meta-analysis were scored against 13 AMSTAR items instead of 16. Each SR receives a final critical appraisal rating of "high," "moderate," "low," or "critically low" according to the AMSTAR calculator [23]. Because the AMSTAR instrument was designed for SRs that investigated a specific intervention, we were unable to appraise these SRs using the AMSTAR instrument [23].

Secondary Analysis

A secondary analysis was performed by manually searching the Cochrane database for SRs, cross-referencing, and comparing the Cochrane SRs with SRs included in cutaneous melanoma CPGs.

Statistical Analysis

Descriptive statistics were calculated for both PRISMA and AMSTAR completion overall and by item. We used multiple regression to determine relationships between PRISMA completion, AMSTAR appraisal, and extracted study characteristics. Lastly, to evaluate PRISMA and AMSTAR scores between Cochrane SRs and non-Cochrane SRs, a Mann-Whitney *U* test was used. Stata 16.1 (StataCorp) was used for all statistical analyses.

Results

General Characteristics

Our search query returned 4987 possible CPGs, of which 14 CPGs for the treatment of cutaneous melanoma were included (Figure 1). Among the 14 CPGs, 50 SRs were identified in the reference sections, and 28 of these SRs directly underpinned a guideline recommendation (Table 1). The included SRs were published between 2001 and 2018, with 70% (35/50) being published after the 2010 update of the PRISMA reporting criteria (Table 2). Of the 50 SRs, 15 (30%) were focused on diagnostic or imaging techniques, 13 (26%) covered nonsurgical interventions, 5 (10%) covered surgical interventions, and 3 (6%) were focused on both surgical and nonsurgical interventions. A total of 14 (28%) SRs did not involve an intervention. Conflict of interest statements were lacking in 10 (20%) of the 50 SRs, while 16 (32%) did not include a funding statement.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of selection process for included clinical practice guidelines (CPGs).

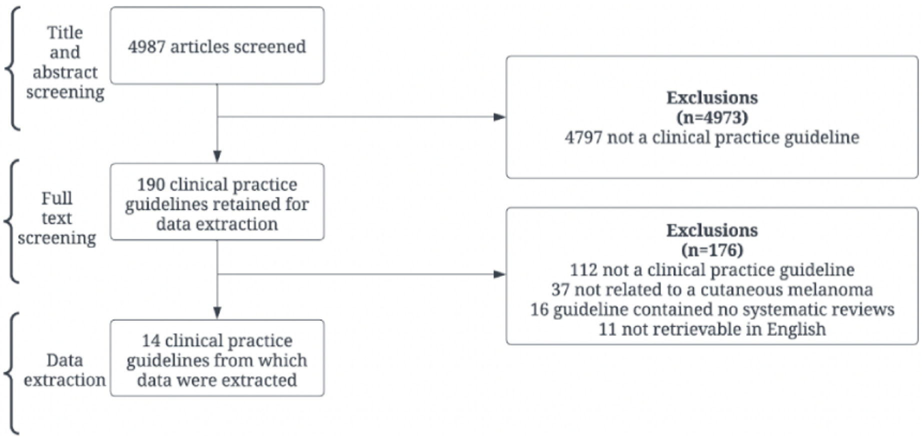

Table 1. Characteristics of the included clinical practice guidelines (CPGs).

CPG	Characteristics of the CPG				
	Year of publication	SRs[a] per guideline, n	SRs supporting a guideline recommendation, n	Average PRISMA[b] completion (%)	Average AMSTAR[c] completion (%)
Cutaneous melanoma: ESMO[d] Clinical Practice Guidelines for diagnosis, treatment, and follow-up [24]	2019	3	1	70	36
The updated Swiss guidelines 2016 for the treatment and follow-up of cutaneous melanoma [25]	2016	4	3	54	30
Brazilian guidelines for diagnosis, treatment, and follow-up of primary cutaneous melanoma-part II [26]	2016	6	3	56	32
Chinese Guidelines on the Diagnosis and Treatment of Melanoma (2015 Edition) [27]	2015	7	3	63	40
Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline-Update 2016 [28]	2016	4	0	64	42
Screening for Skin Cancer: US Preventive Services Task Force Recommendation Statement [29]	2016	3	0	67	25
Updated evidence-based clinical practice guidelines for the diagnosis and management of melanoma: definitive excision margins for primary cutaneous melanoma [30]	2018	4	2	72	51
Guidelines of care for the management of primary cutaneous melanoma [31]	2018	21	14	68	44
Cutaneous Melanoma, Version 2.2019, NCCN[e] Clinical Practice Guidelines in Oncology [32]	2019	3	0	64	28
Update on Current Treatment Recommendations for Primary Cutaneous Melanoma [33]	2019	4	3	81	62
Primary excision margins, sentinel lymph node biopsy, and completion lymph node dissection in cutaneous melanoma: a clinical practice guideline [34]	2019	1	1	77	62
Evidence-Based Clinical Practice Guidelines for the Management of Patients with Lentigo Maligna [35]	2020	3	3	70	54
SEOM[f] clinical guideline for the management of cutaneous melanoma (2020) [36]	2021	4	2	70	59
NCCN Guidelines Insights: Melanoma: Cutaneous, Version 2.2021 [37]	2021	3	3	83	66

[a]SR: systematic review.

[b]PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

[c]AMSTAR: A Measurement Tool to Assess Systematic Reviews.

[d]ESMO: European Society of Medical Oncology.

[e]NCCN: National Comprehensive Cancer Network.

[f]SEOM: Spanish Society of Medical Oncology.

Table 2. Multiple regression analysis showing the percentage of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) completeness for systematic reviews by study characteristics.

Covariables	SRs[a] (n=50), n (%)	Unadjusted model coefficient (SE)	*F* test (*df*)	2-tailed *t* test	*P* value	Adjusted model coefficients[b], (SE)	Adjusted standardized coefficients	*F* test (*df*)	2-tailed *t* test	*P* value
Year of publication[c]			3.54 (1, 48)					F (12, 23)	—	—
Before 2010	15 (30)	1 (reference)		—[d]	—	1 (reference)	1 (reference)		—	—
After 2010	35 (70)	6.96 (3.7)		1.88	.07	1.18 (4.09)	0.04		0.29	.78
Intervention type			1.70 (4, 45)					—		
Diagnostic or imaging technique	15 (30)	1 (reference)		—	—	1 (reference)	1 (reference)		—	—
Nonsurgical	13 (26)	–9.37 (4.53)		–2.07	.04	–0.07 (4.42)	0.00		–0.02	.99
No intervention[b]	14 (28)	–6.24 (4.44)		–1.40	.17	7.42 (7.54)	0.14		0.98	.34
Surgical	5 (10)	2.54 (6.17)		0.41	.68	4.09 (5.01)	0.12		0.82	.42
Surgical and nonsurgical	3 (6)	–9.35 (7.56)		–1.24	.22	–8.87 (6.99)	–0.20		–1.27	.22
Conflict of interest			3.59 (1, 48)					—		
Statement not reported	10 (20)	1 (reference)		—	—	1 (reference)	1 (reference)		—	—
Statement reported	40 (80)	8.03 (4.24)		1.90	.06	0.21 (4.6)	0.01		0.05	.97
Design of included studies			0.48 (1, 48)					—		
Non-RCTs[e]	36 (72)	1 (reference)		—	—	1 (reference)	1 (reference)		—	—
RCTs	14 (28)	2.69 (3.89)		0.69	.49	1.39 (3.62)	0.05		0.38	.70
AMSTAR[f] rating[b] (n=36)			25.06 (2, 33)					—		
Critically low	19 (53)	1 (reference)		—	—	1 (reference)	1 (reference)		—	—
Low	7 (19)	14.43 (3.56)		4.05	<.001	18.07 (4.71)	0.58		3.84	<.001
Moderate	10 (28)	21.3 (3.15)		6.76	<.001	22.01 (4.56)	0.81		4.83	< .001
High	0 (0)	—		—	—	—	—			—
Funding			0.03 (3, 46)					—		
No funding received	12 (24)	1 (reference)		—	—	1 (reference)	1 (reference)		—	—
No funding statement	16 (32)	–1.04 (4.84)		–0.21	.83	–3.91 (4.67)	–0.14		–0.84	.41
Industry	2 (4)	–2.07 (9.68)		–0.21	.83	–4.67 (11.53)	–0.06		–0.41	.69
Public or private	20 (40)	–0.14 (4.63)		–0.03	.98	–0.75 (3.57)	–0.03		–0.21	.84

[a]SR: systematic review.

[b]A total of 14 articles did not cover interventions; thus, these 14 studies were not able to be assessed by AMSTAR and were excluded from the adjusted analysis.

[c]2010 was chosen because PRISMA was first published in 2009.

[d]Not available.

[e]RCT: randomized controlled trial.

[f]AMSTAR: A Measurement Tool to Assess Systematic Reviews.

PRISMA Completion

The mean PRISMA completion percentage of SRs was 66.5% (SD 12.3%), ranging from 37% to 89% (Multimedia Appendix 2) [38-86]. Percent completion of SRs per CPG ranged from 54% to 83% complete (Table 1). Multimedia Appendix 3 demonstrates the mean scores for all 27 items included on the PRISMA checklist. A Mann-Whitney *U* test showed that SRs published after 2010 (mean 68.5%, SD 11.7%) were not significantly better than those published before 2010 (mean 61.6%, SD 12.7%; z=–1.88; P=.06).

AMSTAR Appraisal

Of the 50 SRs included, 14 did not cover interventions and, therefore, were unsuitable to be appraised using AMSTAR. Of the 36 remaining SRs, the mean percent completion was 44.6% (SD 21.1%), which ranged from 25% to 65.6% across CPGs (Table 1). Table S3 in Multimedia Appendix 4 demonstrates the mean scores for all items in SRs from the AMSTAR checklist. The methodological quality of these 36 SRs, according to the AMSTAR appraisal, was the following: 19 (53%) were appraised as "critically low" quality; 7 (19%) as "low" quality; 10 (28%) were "moderate" quality; and no SR received a rating of "high" quality (Multimedia Appendix 2).

Multiple Regression

We constructed a multiple regression model to assess the relationship between PRISMA completion and the inclusion of a conflicts of interest statement, SR funding, year of publication (pre- or post-2010), intervention type, and AMSTAR rating. This model was statistically significant ($F_{12,23}$=4.58; P<.001) and accounted for 55.1% of the variance of PRISMA completion. The model showed a statistically significant association between PRISMA completion and AMSTAR appraisals (P<.001), with "low" and "moderate" quality studies being more complete than "critically low" (Table 2).

Secondary Analysis

Of the total 50 SRs, 4 (8%) were Cochrane reviews. SRs by the Cochrane group had a mean PRISMA completion of 84.7% (SD 2.1%) compared to 64.9% (SD 11.5%) among non-Cochrane studies (Multimedia Appendix 3)—a statistically significant difference (Mann-Whitney *U* test z=–3.10; P=.002). Cochrane SRs also had a higher mean AMSTAR completion (mean 86.8%, SD 4.9%) compared to non-Cochrane SRs (mean 40.0%, SD 15.1%; Multimedia Appendix 4). The Mann-Whitney *U* test also showed this difference to be statistically significant (z=–3.23; P=.001).

Discussion

General Findings

Our findings show that the SRs used in CPGs focused on cutaneous melanoma management vary in methodological and reporting quality, with the majority of guideline recommendations supported by poor-quality SRs. Our findings are consistent with similar studies in the fields of psychiatry, addiction medicine, cardiology, and obesity medicine [5-8]. For example, in 2017, Scott et al [6] found that the quality of SRs used in CPGs for ST-elevated myocardial infarctions was variable and reported a mean PRISMA score similar to ours. No other study in dermatology has explored the quality of SRs underpinning CPGs. However, studies have explored the methodological quality of dermatology-related SRs outside of CPGs [10,87]. In the following paragraphs, we discuss our primary findings, provide recommendations aimed at improving SRs underpinning CPGs, and review the strengths and limitations of this investigation.

The most concerning findings of this investigation were the overall poor methodological and reporting quality of SRs directly supporting a guideline recommendation, which were not shown to have improved after the publication of the revised PRISMA guidance. In fact, the vast majority of SRs that underpin a recommendation had mean PRISMA scores under 70% and were rated as having critically low methodological quality according to the AMSTAR instrument. An example of a recommendation supported by low-quality evidence can be found in the Spanish Society of Medical Oncology's (SEOM) clinical guideline for the management of cutaneous melanoma. This guideline provides a recommendation covering positron emission tomography–computerized tomography scans based solely on a SR of low methodological quality and a mean PRISMA score of less than 70%. While the purpose of this study is not to explore the consequences of recommendations supported by poor-quality SRs, it becomes apparent how low-quality evidence supporting recommendations could impact patient care, especially in the management of diseases as dangerous as malignant melanoma.

All of the Cochrane SRs in our sample received the highest methodological quality and reporting in our sample. This finding is no surprise, as Cochrane SRs are known for their methodological rigor in producing higher-quality, less biased research results [88,89]. Interestingly, and despite the wealth of research supporting the use of Cochrane SRs, only 4 Cochrane SRs were referenced in the 14 CPGs. Additionally, only 1 of these Cochrane SRs was used to support a guideline recommendation directly. As of June 2021, there are 16 available Cochrane SRs related to the management of cutaneous melanoma, of which 4 were used in the 14 CPGs [90].

An investigation that evaluated the strength of recommendations constituting the AAD CPGs found that the majority of recommendations in this guideline were supported by weak to moderate levels of evidence [13]. Interestingly, in this same study, the authors found that the guideline with the fewest recommendations supported by strong evidence was the melanoma guideline [13]. Despite the amount of weak evidence supporting these guidelines, the problem appears to be the amount of high-quality evidence (such as SRs) in the field of dermatology. For example, a study published in 2021 found that 90% of published dermatology SRs are rated as critically low quality according to the AMSTAR instrument [87]. Similarly, Lin et al [91] found that 60% of SRs focused on atopic dermatitis received an AMSTAR methodological appraisal as either "critically low" or "low," with only 8.8% of SRs being of "high" quality. Lastly, a study of 136 dermatology-related SRs found that the most underreported PRISMA items were protocol registration and risk of bias [10]—consistent with our findings.

Recommendations

In an effort to improve CPGs focused on the management of cutaneous melanoma, we first recommend the use of more Cochrane SRs, as they are of the highest quality compared to non-Cochrane reviews. Next, we advocate that publishing journals update their author guidelines to require PRISMA and AMSTAR completion checklists to be submitted with manuscripts. A previous study found that mandatory PRISMA adherence was associated with improved SR reporting and methodological quality [87,92], which is similar to that found in our investigation. Furthermore, editors and peer reviewers should be provided with these checklists to ensure complete reporting and to provide revisions for improvement. Next, we advocate that journals require authors to register their protocol a priori, as registered reviews are associated with being of higher quality [93]. Finally, we advocate that evidence-based training be provided to physicians and physicians in training that focuses on these quality assessment tools. Providing this education will likely improve the knowledge and skills needed to critically appraise scientific papers included in CPGs [94].

Strengths and Limitations

To promote the transparency and reproducibility of this study, we published our protocol on OSF a priori. Additionally, we followed the recommendations outlined in the Cochrane Handbook for Systematic Reviews of Interventions, with both investigators performing all screening and data extraction in a masked, duplicate fashion [95]. However, this study is not without limitations. Unavoidably, the PRISMA and AMSTAR checklists contain some inherent subjectivity. To mitigate subjectivity, investigators were trained before title and abstract screening on the PRISMA and AMSTAR checklists. Additionally, investigators resolved any discrepancies before final data analysis, consulting a third-party arbitrator as necessary. Another limitation of this study is only using PubMed, as it is possible some CPGs focused on the management of cutaneous melanoma could have been missed. A key limitation of this study is that the evaluation of SRs' methodical quality does not take into account the specific needs of a CPG or whether or not the SR is relevant to the CPG. Lastly, our appraisal of SRs used the AMSTAR checklist published in 2017. Therefore, all SRs published before 2017 were only able to use the original AMSTAR checklist before publication.

Conclusions

Our investigation found that CPGs focused on the management of cutaneous melanoma are supported by SRs that frequently underreport PRISMA items and are of critically low to low methodological quality. Additionally, we found that Cochrane SRs are of higher quality compared to non-Cochrane SRs. Future research should focus on methods to increase PRISMA and AMSTAR adherence, as doing so results in higher-quality SRs.

Conflicts of Interest

MV reports receipt of funding from the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, the US Office of Research Integrity, the Oklahoma Center for Advancement of Science and Technology, and internal grants from the Oklahoma State University Center for Health Sciences—all outside of the present work. MH reports funding from the National Institutes of Justice for unrelated work.

Multimedia Appendix 1
Study protocol.
[DOCX File , 22 KB - derma_v6i1e43821_app1.docx]

Multimedia Appendix 2
Quality of systematic reviews included in clinical practice guidelines (CPGs).
[DOCX File , 28 KB - derma_v6i1e43821_app2.docx]

Multimedia Appendix 3
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) completeness summary for the systematic reviews comprising the 14 guidelines for the management of cutaneous melanoma.
[DOCX File , 35 KB - derma_v6i1e43821_app3.docx]

Multimedia Appendix 4
Summary of AMSTAR-2 (A Measurement Tool to Assess Systematic Reviews) completeness scores across the 5 included guidelines.
[DOCX File , 31 KB - derma_v6i1e43821_app4.docx]

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Abbreviations

AAD: American Academy of Dermatology
AGREE II: Appraisal of Guidelines for Research and Evaluation Instrument
AMSTAR: A Measurement Tool to Assess Systematic Reviews
CPG: clinical practice guideline
OSF: Open Science Framework
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRISMA-P: Preferred Reporting Instrument for Systematic Review and Meta-Analysis Protocols
QCRI: Qatar Computing Research Institute
SEOM: Spanish Society of Medical Oncology
SR: systematic review

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Original Paper

Skin-Lightening Product Use Among South Asian Americans: Cross-Sectional Survey Study

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Abstract

Background: Despite their potential for adverse health effects, skin-lightening products remain popular among South Asian Americans.

Objective: This study investigates attitudes toward skin tone and the prevalence and adverse effects of skin-lightening product use among South Asian Americans.

Methods: We conducted a cross-sectional study, recruiting and surveying 175 women or nonbinary individuals meeting the following inclusion criteria: (1) lived in the United States, (2) identified as South Asian, and (3) were raised by parents born in South Asian countries.

Results: Of the 175 participants, 55 (31%) respondents used a skin-lightening product before. Parental pressure to use skin-lightening products and decreased time spent in the United States were significantly associated with skin-lightening product use (odds ratio [OR] 8.51, 95% CI 3.33-21.78, P<.001, and OR 0.70, 95% CI 0.52-0.96, P=.03, respectively). Although only 6 of the 55 (11%) users reported being aware of the potential side effects of skin-lightening products, 33 (60%) reported adverse effects, with acne, skin sensitivity, and dry skin being the most common. Users and nonusers equally endorsed statements associating lighter skin with increased attractiveness (P=.31), marriageability (P=.94), social status (P=.98), self-esteem (P=.73), and respect received from others (P=.74).

Conclusions: The use of skin-lightening products among South Asian Americans is common and linked to social and psychological factors. Parental pressure and cultural beauty standards may play a significant role in perpetuating this practice. This study highlights the need for educational campaigns about the potential health risks associated with skin-lightening and increased efforts to challenge harmful beauty standards.

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KEYWORDS

colorism; skin-lightening products; skin bleaching; South Asian Americans; South Asian immigrants

Introduction

Fair skin is highly desired throughout South Asia, which encompasses Afghanistan, Bangladesh, Bhutan, India, Nepal, Pakistan, Sri Lanka, and the Maldives [1,2]. In India, skin-lightening products comprise 60% of the dermatological market [2]. Historical and cultural reasons exist for the popularity of these products throughout the region. During colonial times, British officers gave preferential treatment to light-skinned, high-caste South Asians, creating an association between light skin and economic prosperity [3]. To this day, India's influential Bollywood film industry primarily features light-skinned actors who also star in advertisements for skin-lightening products [4].

South Asians continue to use skin-lightening products despite their well-documented adverse side effects [5]. One cross-sectional survey study conducted in a general medical outpatient clinic in Chhattisgarh, India, found that of 148 respondents, 30 (20%) had side effects from skin-lightening product use, most commonly acne (14%) and pruritus (5.6%) [6]. Another cross-sectional survey conducted in Kerala, India, found that of 306 skin-lightening product users, 185 (60%) had adverse effects, with 58 (19%) reporting burning sensations at sites of application and 29 (9.4%) experiencing increased dryness [7]. The most common active ingredients in skin-lightening products include hydroquinone, mercury, and corticosteroids [8]. These ingredients have been linked to systemic complications like adrenal insufficiency and membranous nephropathy and cutaneous complications like leukomelanoderma, exogenous ochronosis, squamous cell carcinoma, and dermatitis [4,9-11]. Despite regulations limiting the use of harmful ingredients in skin-lightening products, products often exceed legal limits or refuse to disclose them [4,12].

Immigrant communities originating from countries where skin bleaching is common often import the practice [13]. However, to our knowledge, there are no published studies investigating how South Asian Americans use skin-lightening products or how their parents influenced their perceptions of skin tone and skin-lightening products. This study aims to determine general attitudes toward skin tone and the prevalence of, motivations for, and adverse effects of skin-lightening product use among South Asians who lived in the United States.

Methods

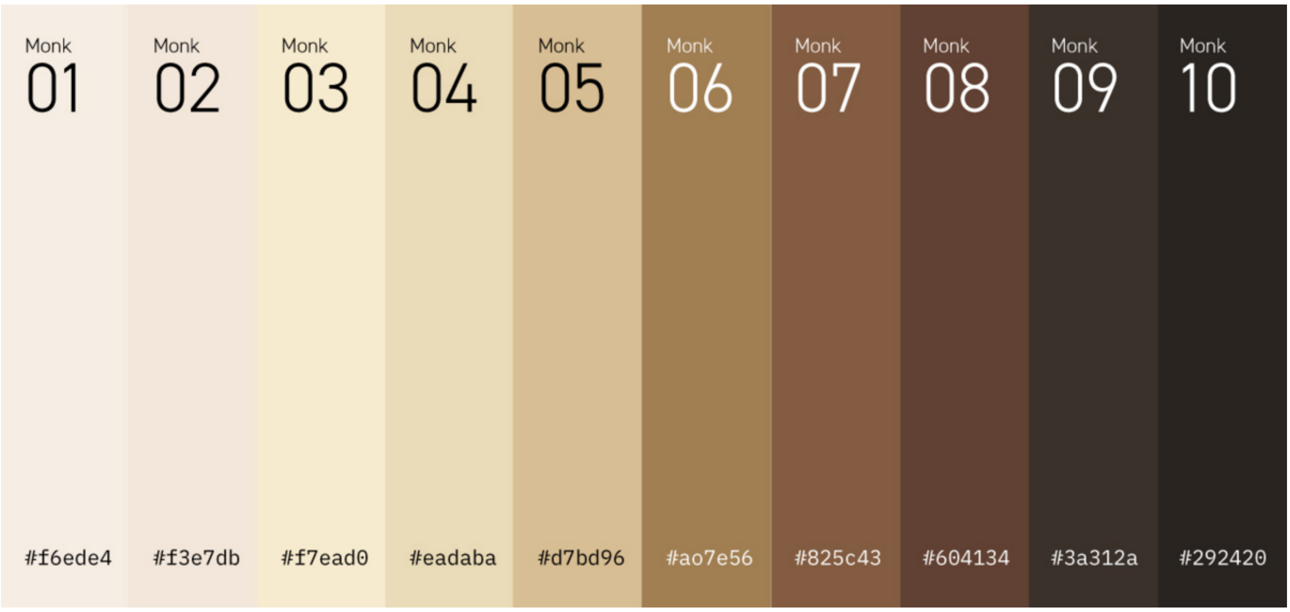
Study Design

A cross-sectional study questionnaire was administered through Qualtrics, a web-based survey tool, with the following inclusion criteria: (1) lived in the United States, (2) identified as South Asian, and (3) were raised by parents born in South Asian countries [14]. The survey link was posted in a Facebook group titled "The Little Brown Diary," a web-based community for South Asian women and gender minorities, and all members who met the inclusion criteria were asked to participate [15].

Survey Overview

Survey participants provided demographic data and indicated which skin tone in Figure 1 best matched their own. They were asked if they ever felt parental pressure to use skin-lightening products from their primary and secondary parent or if they ever felt unattractive due to their skin tone. "Primary parent" was defined in the survey as the parent who had the most influence on their upbringing. Participants also indicated if they lived in the United States for (1) less than 1 year, (2) 1-5 years, (3) 6-10 years, (4) 11-15 years, (5) 16-20 years, (6) 21-25 years, or (7) more than 25 years. A Likert scale was used to determine motivating factors associated with skin-lightening product use and asked participants to rate from strongly disagree (score 1) to strongly agree (score 6) the extent to which they felt skin tone impacted attractiveness, marriageability, social status, self-esteem, or respect received from others. The questionnaire was developed in accordance with information obtained from a literature review, and the content and validity of the questions were reviewed by a dermatologist at the University of Pennsylvania. Participants who reported past or current use of skin-lightening products provided information about the frequency of product application, location of application, and adverse effects experienced.

Figure 1. Monk's 10-shade skin color scale.



Statistical Analysis

Statistical analysis of the survey responses was conducted with SPSS Statistics (version 29; IBM Corp). Descriptive statistics were used to summarize respondents' reasons for using skin-lightening products. A 2-tailed independent samples *t* test was used to evaluate differences in motivating beliefs about skin-lightening product use between users and nonusers. A binary logistic regression model was used to assess factors associated with skin-lightening product use, using *P*=.05 as the cutoff for significance. Participants who did not answer all survey questions were excluded from the final model (n=10).

Ethical Considerations

This study was reviewed by the University of Pennsylvania's institutional review board and deemed exempt from requiring ethical approval.

Results

Study Population

Data from 175 completed surveys were analyzed. A total of 171 participants (98%) identified as women, and 4 (2.3%) identified as nonbinary. As shown in Table 1, a total of 96 (55%) respondents were between the ages of 20 and 30 years, and 53 (30%) were above the age of 30 years. A total of 110 (63%) respondents reported their highest level of education as a master's degree and 62 (35%) reported a bachelor's degree. The 175 respondents reported living across the United States. The most common states included New Jersey, California, and Texas, with 27 (15%), 25 (14%), and 14 (8%) respondents living there, respectively. The most common birth countries for respondents' primary parents were India, Pakistan, and Bangladesh, with 151 (86%), 10 (5.7%), and 9 (5.1%) primary parents born there, respectively.

Table 1. Correlation between sociodemographic characteristics and use of skin-lightening products.

Variables	Users (n=55)	Nonusers (n=120)	Total (N=175)	OR[a] (95% CI)	*P* value
Age (years), n (%)					
18-20	8 (15)	18 (15)	26 (14.9)	Reference category	.16
20-30	26 (47)	70 (58.3)	96 (54.9)	0.43 (0.13-1.48)	.18
>30	21 (38)	32 (26.7)	53 (30.3)	1.03 (0.27-3.85)	.97
Parents' combined salary (US $), n (%)					
Not answered	2 (4)	7 (5.8)	9 (5.1)	Reference category	.70
<100,000	27 (49)	46 (38.3)	73 (41.7)	1.87 (0.26-13.37)	.53
100,000-250,000	21 (38)	53 (44.2)	74 (42.3)	2.66 (0.36-19.73)	.34
>250,000	5 (9)	14 (11.7)	19 (10.9)	1.46 (0.13-16.16)	.76
Education, n (%)					
Bachelor's degree	21 (38)	41 (34.2)	62 (35.4)	Reference category	.10
Master's degree	32 (58)	78 (65)	110 (62.9)	0.58 (0.23-1.44)	.24
Some college credit but no degree	2 (4)	1 (0.8)	3 (1.7)	9.69 (0.61-154.33)	.11
Duration lived in the United States, mean (SD)	6 (2)	6.3 (1.1)	6.1 (1.3)	0.70 (0.52-0.96)	.03
Felt unattractive, n (%)	33 (60)	60 (50)	93 (53.1)	0.69 (0.26-1.83)	.46
Pressure from primary parent, n (%)	34 (62)	18 (15)	52 (29.7)	8.51 (3.33-21.78)	<.001
Pressure from secondary parent, n (%)	9 (16)	2 (1.7)	11 (6.3)	4.02 (0.58-27.84)	.16
Skin tone, mean (SD)	5 (1)	4.8 (1.2)	4.9 (1.2)	0.84 (0.47-1.49)	.55
Primary parent's skin tone, mean (SD)	4 (1)	4.5 (1.4)	4.3 (1.4)	0.85 (0.59-1.24)	.40
Secondary parent's skin tone, mean (SD)	5 (1)	5.1 (1.4)	5.2 (1.4)	1.08 (0.74-1.57)	.68

[a]OR: odds ratio.

Skin-Lightening Product Use and Adverse Effects

Of the 175 participants, 55 (31%) reported current or past use of a skin-lightening product. 43 (78%) of the 55 users' primary parents were born in India, 4 (7.2%) were born in Pakistan, and 4 (7.2%) were born in Bangladesh. Of the 55 users, 37 (67%) began using a skin-lightening product between the ages of 10 and 20 years, and 54 (98%) reported no longer using the product. The frequency of use varied, with 16 (29%) respondents using it daily and 9 (16%) only using it for special occasions. A total of 51 of 55 (93%) users reported applying the product to their faces, 12 (22%) on their arms, and 7 (13%) on their bodies. Although 33 (60%) participants experienced adverse effects, only 6 (11%) were aware of the potential adverse effects before they started using the product. The most reported adverse effects were dry skin, skin sensitivity, and acne, with 19 (35%), 15 (27%), and 9 (16%) participants experiencing them, respectively.

Factors Motivating the Use of Skin-Lightening Products

As shown in Table 2, of the 55 respondents who reported current or past use of a skin-lightening product, 33 (60%) reported feeling unattractive at some point due to their skin tone. A total of 34 (62%) respondents reported feeling pressure from their primary parent to use the product, while 9 (16%) reported feeling such pressure from their secondary parent. Of the 55 skin-lightening product users, 51 (93%) identified their primary parent as their biological mother and their secondary parent as their biological father.

Table 2. Description of the use of skin-lightening products among respondents (N=175).

Variables	Frequency, n (%)
Still using product	1 (1.8)
Primary parent pressure	34 (61.8)
Secondary parent pressure	9 (16.4)
Ever felt unattractive due to skin tone	33 (60)
Awareness of side effects	6 (10.9)
Adverse effects from use	33 (60)
Side effects	
Acne	9 (16.4)
Skin sensitivity	15 (27.3)
Dry skin	19 (34.5)
Hyperpigmentation	3 (5.5)
Hypopigmentation	3 (5.5)
Areas applied	
Face	51 (92.7)
Arms	12 (21.8)
Body	7 (12.7)
Hands	4 (7.3)
Legs	5 (9.1)
Feet	3 (5.5)
Genitals	1 (1.8)
Age when users started using product (years)	
<10	8 (14.5)
10-20	37 (67.3)
> 20	4 (7.3)
Frequency of use	
Twice daily	4 (7.3)
Once daily	16 (29.1)
Every other day	3 (5.5)
Once weekly	8 (14.5)
Once a month	6 (10.9)
Once yearly	1 (1.8)
Only for occasions	9 (16.4)
Once or twice ever	4 (7.3)
Skin tone	
Light (A-C in Figure 1)	5 (9.1)
Medium (D-G in Figure 1)	49 (89.1)
Dark (H-J in Figure 1)	1 (1.8)

As seen in Table 1, significant associations were found between some sociodemographic characteristics and the use of skin-lightening products. Specifically, the duration the respondent lived in the United States and the pressure they felt from their primary parent to use a skin-lightening product were associated with skin-lightening use (*P*=.03 and *P*<.001, respectively). Respondents were about 9 times more likely to use a skin-lightening product if they felt pressured by their primary parent to do so (odds ratio [OR] 8.51, 95% CI 3.33-21.78). They were less likely to use a skin-lightening product the longer they lived in the United States (OR 0.70, 95% CI 0.52-0.96). Other sociodemographic factors such as age, parents' combined salary, and education were not associated with skin-lightening product use. Notably, respondents' skin tones were not associated with use. Additionally, as seen in Table 3, there was no significant difference between product users' and nonusers' understanding of how lighter skin influences attractiveness, marriageability, social status, self-esteem, or respect received from others.

Table 3. Reasons for skin-lightening.

Variables	Users (n=51), mean (SD)	Nonusers (n=114), mean (SD)	*F* test (*df*)	*P* value
Increase attractiveness	2.9 (1.4)	2.9 (1.2)	1.025 (163)	.31
Increase marriageability	3 (1.6)	2.8 (1.5)	0.006 (162)	.94
Increase social status	3.3 (1.4)	3 (1.4)	0 (163)	.98
Increase self-esteem	3.3 (1.4)	3.3 (1.3)	0.119 (162)	.73
Increase respect from others	3.4 (1.4)	3.3 (1.4)	0.109 (163)	.74

Discussion

Principal Results

This study aimed to estimate the prevalence of skin-lightening product use among self-identifying South Asians who lived in the United States. About 31% of the South Asian Americans surveyed reported current or past use of a skin-lightening product. This rate is greater than the previously reported skin-lightening product usage rate of 21% among the general United States population [17]. However, use of skin-lightening products appears more prevalent in North India (60%) than among South Asian Americans in the United States [5,6]. Pressure from a primary parent and decreased duration of residency in the United States were found to significantly predict the use of skin-lightening products. The findings of this study are unique in that they offer insight into how immigrant communities, specifically the South Asian community in the United States, import cultural practices.

A total of 33 of 55 (60%) users of skin-lightening products reported experiencing adverse effects. Surprisingly, only 6 (11%) users were aware of potential adverse effects, like acne, skin sensitivity, and dry skin, before applying the product. Earlier investigations conducted among South African and Southeast Asian university students demonstrated that 89% and 79% of participants, respectively, were aware of the potential side effects associated with using skin-lightening products. However, none of the participants in the South African study and only 30% of the Southeast Asian study could name the products' active ingredients [18,19].

Interestingly, we did not find that education level or family income predicted skin-lightening product use. Despite the expectation that respondents with higher education levels would be more aware of the risks associated with bleaching products, the results showed no correlation between educational background and use. Like previous studies of populations in the United States and Saudi Arabia, this finding indicates that skin-lightening products are used by consumers of all educational backgrounds [5,20]. Additionally, skin tone did not predict skin-lightening product use. This finding is consistent with previous studies of adult women in Saudi Arabia and South Africa and suggests that skin tone also does not play a significant role in determining the use of skin-lightening products among South Asian Americans [18,20].

Like other studies, we found that skin-lightening product application often begins during users' late teenage or early adult years, which may explain the lack of awareness of potential side effects [21]. A total of 37 of the 55 (67%) users began skin-lightening product application between the ages of 10 and 20 years, supporting the suggestion that early initiation of skin bleaching stems from identity development during adolescence [22]. Encouragingly, this study also found that 54 of the 55 (98%) respondents who once used a skin-lightening product no longer use it, which may suggest that cultural, antiracist movements promoting acceptance of dark skin positively influenced South Asian users of skin-lightening products. Other potential reasons for the high discontinuation rate include dissatisfaction with the product, side effects, unavailability, or a lack of affordability. The specific motivations for ending the use of skin-lightening products should be further investigated.

We did not find a significant difference between skin-lightening product users' and nonusers' understanding of how lighter skin impacts attractiveness, marriageability, social status, self-esteem, or respect received from others. Instead, we found a significant association between skin-lightening product use and parental pressure. Notably, respondents received pressure to use skin-lightening products more often from their mothers than their fathers. Since our respondents were mostly women, this proves previous studies' findings that mothers are a key influence on their daughters' body image [23]. Previous studies highlighted that familial socialization through parents' direct comments or indirect modeling relating to body image and attractiveness has a significant impact on children's self-esteem and their beliefs about attractiveness and body image [24,25]. Respondents should be conscious of how they speak about skin tone in front of their children to minimize the possibility of pressuring them to lighten their skin and perpetuating a cycle of poor self-esteem.

Finally, our research indicated a negative correlation between the duration of respondents' residency in the United States and their use of skin-lightening products. While South Asian immigrants may have initially continued skin-lightening after moving to the United States, an extended period of living in the country appears to deter product use. Although no specific studies directly investigated this phenomenon, potential reasons for the decline in skin-lightening after moving to the United States include increased exposure to diverse ethnic and cultural backgrounds, decreased pressure to conform to South Asian beauty ideals, and limited availability of products.

Limitations

There are several limitations to the methodology and findings of this study. First, the relatively small sample population was limited to self-identifying South Asian women and nonbinary Facebook group members who lived in the United States, which does not represent the entire South Asian American population. The relatively homogenous sample regarding gender, age, income, and education level could further limit conclusions. The survey relied on self-reported data, which may have introduced bias or misreporting. Moreover, the survey did not include questions about the specific skin-lightening products used by participants, which could have provided valuable insights into the prevalence and health risks associated with the use of these products. The survey also did not inquire about the number of products users applied or when or why they stopped using them. Given the high discontinuation rate, this would have added more depth to the research.

Conclusions

In conclusion, skin-lightening remains a prevalent practice among South Asians who lived in the United States. This study sheds light on the attitudes and experiences of South Asian Americans and reveals that parental pressure encourages skin-lightening product use, but spending more time in the United States discourages it. Thus, parental pressure and South Asian cultural beauty standards may play a significant role in perpetuating this practice. This study highlights the need for educational campaigns about the potential health risks associated with skin-lightening agent use and increased efforts to challenge harmful beauty standards. Most skin-lightening product users were unaware of the products' potential side effects, and dermatologists and regulatory bodies should work to illuminate these considerations and educate consumers. Further research is needed to better understand why most participants ceased use and to develop effective ways to discourage skin-lightening.

Acknowledgments

MB and TAO participated in the research design. MB and AM participated in performing the research, analyzing the data, and writing the paper.

Conflicts of Interest

TAO is part of the medical reviewer board of Remedy Health.

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Original Paper

Investigating the Role of Upward Comparisons and Self-compassion on Stigma in People With Acne: Cross-sectional Study

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Abstract

Background: The use of image-laden social media is hypothesized as being implicated in psychological distress in individuals with conditions affecting their appearance. However, relatively little is known about the mechanisms involved in this relationship.

Objective: This cross-sectional study examined the relationship between photo-orientated social media use and feelings of stigmatization in adults with acne, and tested whether upward skin comparisons mediate and self-compassion moderates this relationship.

Methods: Adults (N=650) with acne symptoms completed web-based measures of social media use (daily Facebook or Instagram use, Facebook function use), self-compassion, skin appearance comparisons, and internalized stigmatization.

Results: Moderated-mediation and mediation analyses indicated that there was a significant indirect effect of Facebook photo use on stigmatization, mediated by upward appearance comparisons (estimation of indirect effect 11.03, SE 5.11, 95% CI 1.19-21.12). There was no significant relationship between Instagram use and feelings of stigmatization (estimation of indirect effect 0.0002, SE 0.005, 95% CI −0.011 to 0.009), yet upward appearance comparisons predicted feelings of stigmatization (B=0.99, P<.001). Self-compassion did not moderate the indirect or direct relationships between photo-orientated social media use and stigma. However, self-compassion was negatively correlated with upward appearance comparisons and feelings of stigmatization in both Facebook and Instagram users.

Conclusions: The way that individuals engage with social media, and in particular make appearance comparisons, should be considered when working with individuals with skin-related distress. Interventions aimed at boosting self-compassion and reducing appearance comparisons may provide avenues for protecting against feelings of stigma.

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KEYWORDS

acne; stigma; appearance comparisons; self-compassion; social media; psychological distress; stigmatization; acne symptoms; symptoms; Facebook; Instagram; skin; engagement; appearance; distress

Introduction

Individuals living with visible skin conditions, including acne vulgaris (acne), can experience stigmatization from others (enacted stigma) and internalize feelings of stigmatization (felt stigma) [1-9]. Individual accounts of stigma [2,4,5] are corroborated by experimental research that indicates an implicit preference for clear skin and negative assumptions about individuals with acne [6-8]. Stigma has important implications for psychosocial well-being; surveys of individuals with acne report that felt stigma explains the largest variance (25%-36%), beyond other predictors (eg, perceived severity and gender), across quality-of-life domains: self-perception, social, and emotional [1,9]. Similar findings have been reported in populations with other skin conditions [10,11].

The psychological burden of acne has been well documented [12]. Of the various domains of impact, the impact of acne on self-perception has been the most widely reported. So, acne leads to appearance-related distress [13], body image disturbance [14], and feeling unattractive or ugly [15]. In order to reduce the psychological burden associated with acne, it is essential to understand the psychological mechanisms involved in acne stigmatization. Understanding these mechanisms using psychological theory has the potential to provide theoretical "proof of concept" for suitable targets for psychological therapy. Although dermatological (severity and duration) [1,16,17] and demographic (employment status, age, relationship status, and gender) [1,16-20] variables have limited predictive power, wider sociocultural factors are likely to play a more significant role. Sociocultural factors, including contemporary media, are theorized to influence societal norms and appearance ideals, contributing to the stigmatization of individuals who are unable to meet these ideals [21-23]. Correspondingly, within a qualitative study, participants with acne, eczema, and psoriasis described a pervasive media ideal of perfect skin [24]. Failure to meet this ideal was related to greater depression and stigmatization in female, but not male participants [24]. However, there was no distinction between media platforms or investigation of the specific psychological mechanisms that might be involved.

Web-based activity now plays a major role in our lives. As of 2021, a total of 88% of all UK adults possessed a social media account [25]. Facebook remains the most popular site (66% of adult social media users report using Facebook) [25]. Instagram, an image-based platform allowing users to digitally manipulate and share images, is growing in popularity (48% of adult social media users) [25]. Acne frequently affects adolescents [26], a group who are particularly engaged with social media [27].

A number of studies have established a relationship between Facebook use and psychosocial outcomes [28], with the role of individual difference variables in social media use and behavior showing greater promise in explaining the impact of such media, over and above simple usage [29-31]. For example, higher photo-function use, over and above total Facebook usage, has been reported to predict greater weight dissatisfaction, thin-ideal internalization, appearance comparison, and self-objectification [30]. Similar findings are emerging for Instagram use, with undergraduate students experimentally exposed to idealized Instagram images of celebrities and peers, as opposed to Instagram travel pictures, reporting increased body dissatisfaction and negative mood, mediated by appearance comparisons [32].

Early theories of social comparison posited that humans have an innate drive to compare themselves with others as part of maintaining group relationships [33]. As such, a perceived sense of difference may act as a threat, which may drive unhelpful comparisons. Social comparison theory has been expanded to include appearance-based comparisons, and downward and upward comparisons, where individuals compare themselves with others they perceive as superior (upward) or inferior (downward) [34]. Social and upward appearance comparisons have been established as predictors of body dissatisfaction [35], body-shaming [36], and mediators between media exposure to idealized images and body dissatisfaction [30,31,37-39]. Social comparisons are reported to be an important mechanism in the way individuals with a stigmatized identity evaluate themselves [40] and have been theorized as a core process implicated in skin-shaming [41]. Further, Kellett and Gibert [41] have anecdotally found that patients they treat who are distressed in relation to the appearance of their skin condition are often engaging in making such comparisons. However, the relationship between skin-specific appearance comparisons, social media use, and felt stigmatization has thus far not been investigated, nor has the related role of protective factors like self-compassion.

Self-compassion is theorized to involve 3 main components that influence how we treat ourselves and react to difficulties: self-kindness, mindfulness, and common humanity [42]. Self-compassion may act as a protective factor against psychosocial distress in stigmatized populations [43,44], and intervention-based studies using compassion-based training have shown promise in reducing feelings of shame in participants with acne [45].

As a consequence of the lack of research on social media and acne stigmatization, we conducted a web-based survey to investigate the relationship between photo-related social media use and felt stigma in people with acne. We hypothesized that relative photo-based social media use (Facebook photo activity and total time on Instagram), not total time on Facebook, would be related to felt stigmatization: (1) individuals who spend proportionally more of their time using photo- or appearance-orientated social media will have higher levels of felt stigmatization, (2) this relationship will be mediated by upward skin appearance comparisons, and (3) these relationships will be moderated by self-compassion.

Methods

Ethical Approval

Ethical approval for this cross-sectional study was granted by the University of Sheffield ethics committee (reference 011937).

Sample and Recruitment

Participants with acne symptoms were recruited between February and March 2017 from a convenience community sample and offered entry into a prize draw. The study was advertised across multiple social media platforms, UK skin charities, web-based recruitment platforms, university volunteer lists, and an undergraduate credit system. To be included in the study, participants were required to meet the following inclusion criteria: (1) 16 years or older, (2) current symptoms of acne, (3) living in the United Kingdom or have UK citizenship, and (4) know sufficient English to complete the survey.

A power analysis for multiple regression with 10 predictors indicated that at least 253 participants would be needed to achieve 80% power with a significance level of .05 to detect a small effect size, *r*=0.25.

Procedure

Participants completed counterbalanced self-report measures of demographics, acne history, Facebook use, Facebook function use, Instagram use, skin-related upward or downward comparisons, self-compassion, and acne stigma via a web-based survey using Qualtrics.

Measures

Demographics and Acne History

Participants provided information about their gender, age, ethnicity, educational level and relationship status, and their acne history, including perceived severity, location of symptoms (categorized as visible and nonvisible), and whether they had received a formal diagnosis or acne treatment from a health professional. Perceived severity was measured using a question based on the fifth question of the Cardiff Acne Disability Index [46], which includes a question about the degree to which acne is a problem for the participant.

Facebook Use

Participants were asked whether they had used Facebook within the past month. If participants answered "yes," they were asked to estimate the amount of time they spent on Facebook in the past week. Daily Facebook use was calculated using the following formula: Average daily Facebook use = (Number of days Facebook used × Time spent on Facebook on these days) / 7.

Relative Facebook Photo Activity

The Facebook Questionnaire functions [30] assessed relative levels of photo activity compared with nonphoto activities on Facebook. The scale consists of 24 items (α=.86), scored on a 6-point Likert scale. The appearance- or photo-activity subscale is formed of 8 items (α=.76) related to appearance-specific photo activity. Proportionate Facebook photo activity was calculated by dividing the total for the photo-activity subscale by the total for all items. Scores range from 0 to 1; scores closer to 1 indicate a higher proportion of time spent using photo-related functions on Facebook.

Instagram Use

Instagram is an image-based platform. Instagram photo activity was measured using the average time spent on Instagram per day. Participants were asked whether they had used Instagram in the past month. If participants answered "yes," they were asked to estimate the amount of time they spend on Instagram. Daily Instagram use was calculated using the following formula: Average daily Instagram use = (Number of days Instagram used × Time spent on Instagram on these days) / 7.

Skin-Based Comparisons

The Upward and Downward Appearance Comparison Scales (UPACS, DACS) [34] measure both upward and downward appearance-based comparisons in relation to shape and size. The UPACS and DACS were adapted to measure skin comparisons, and one social media question was added each to the UPACS ("On social media I tend to compare how my skin looks to photographs of people with clearer skin than me") and the DACS ("On social media I tend to compare how my skin looks to photographs of people with worse skin than me"). Both items correlated highly with the other items in the scales and did not reduce reliability. The adapted UPACS and DACS each contained 9 items (UPACS: α=.93; DACS: α=.94), scored on a 5-point Likert scale. Higher scores indicated higher levels of upward appearance comparisons and higher levels of downward appearance comparisons.

Self-compassion

Self-compassion was measured using the Self-Compassion Scale Short Form [47]. The scale comprises 3 domains: self-kindness versus self-judgment, common humanity versus isolation, and mindfulness versus overidentification. The items (α=.86) are scored on a 5-point Likert scale. Higher scores indicate greater self-compassion.

Skin-Related Stigma

Stigma was measured using the total score on the Feelings of Stigmatization Questionnaire [13], originally developed to assess felt stigmatization in patients with psoriasis. The scale has been adapted and previously used in the context of acne [1]. Amendments to the scale for this study involved replacing the term "psoriasis" with "acne" and replacing the term "patient" with "person" as the survey uses a community sample. One question unrelated to acne ("I do not mind when a family member gives me a vacuum cleaner to clean up the scales that fall from my psoriatic skin") was deleted. The adapted measure contained 32 questions (α=.92), scored on a 6-point Likert scale. Higher scores indicate greater felt stigmatization.

Analytic Strategy

Data were analyzed using SPSS version 23 (IBM Corp).

Descriptive statistics were calculated using percentages for categorical variables and means and SDs for continuous variables. Demographic and acne history variables were assessed for covariance with felt stigma using *t* tests, ANOVAs, and bivariate correlations as appropriate. Relationships between the predictor variables, the mediator variables, and the outcome variables were initially tested using bivariate correlations. Nonparametric tests were used when analyzing average Facebook and Instagram use, as normality tests indicated that they were nonnormally distributed. Significant covariates were entered into subsequent analyses.

Hypothesized relationships between photo-related social media activity, upward appearance comparisons, self-compassion, and stigmatization were tested using (1) moderated-mediation (Figures 1 and 2) and (2) mediation-only analysis (Figures 3 and 4), using ordinary least-squares path analysis. Analyses were conducted using the PROCESS macro version 3.442 with 10,000 bootstrap samples.

Figure 1. Moderated-mediation model for Facebook photo use on acne stigma via upward appearance comparison, with self-compassion as the moderator for each path (N=591). The numbers presented in the figure represent unstandardized β values, as recommended by Hayes [48]. The numbers on the arrows intercepting paths a, b, and c represent the unstandardized β values for the interaction effects. (A) *P*=.03, (B) *P*<.001, (C) *P*=.20, (D) *P*=.25, (E) *P*=.42. For clarity, covariates are not included in the figure. The covariates that were controlled for on each pathway were gender, severity, acne diagnosis, and downward skin comparison.

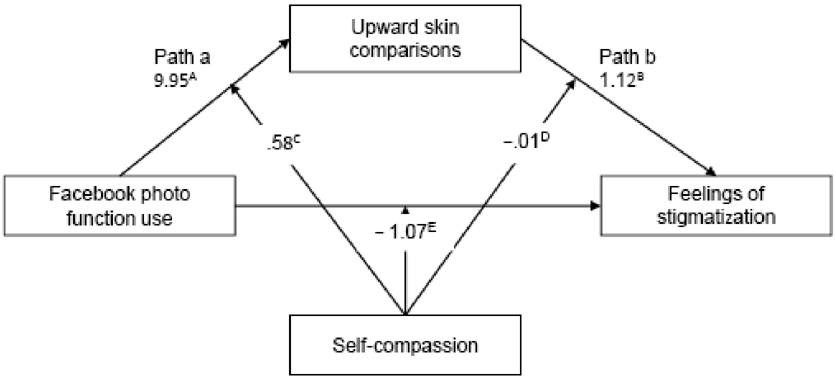


Figure 2. Moderated-mediation model for average Instagram use on acne stigma via upward appearance comparison, with self-compassion as the moderator for each path (N=429). The numbers presented in the figure represent unstandardized β values, as recommended by Hayes [48]. The numbers on the arrows intercepting paths a, b, and c represent the unstandardized β values for the interaction effects. (A) *P*=.98, (B) *P*<.001, (C) *P*=.98, (D) *P*=.25, (E) *P*=.83. For clarity, covariates are not included in the figure. The covariates that were controlled for on each pathway were gender, severity, acne diagnosis, and downward skin comparison.

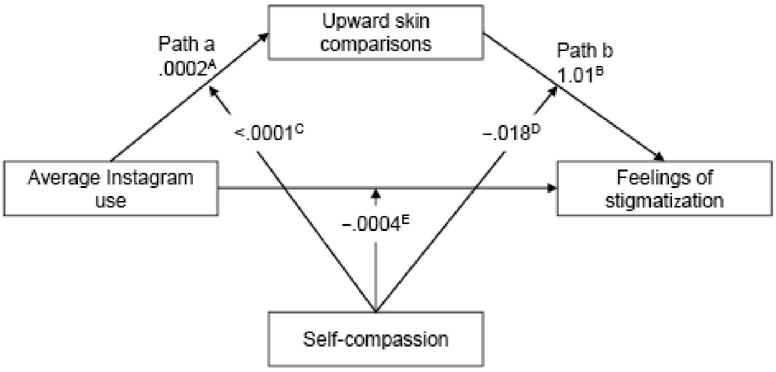


Figure 3. Mediation model for Facebook photo use on acne stigma via upward appearance comparison (N=591). The numbers presented in the figure represent unstandardized β values, as recommended by Hayes [48]. (A) *P*=.03, (B) *P*<.001, (C) *P*=.29, (D) 95% CI –11.86 to 39.93. For clarity, covariates are not included in the figure. The covariates that were controlled for on each pathway were gender, severity, acne diagnosis, downward skin comparison, and self-compassion.

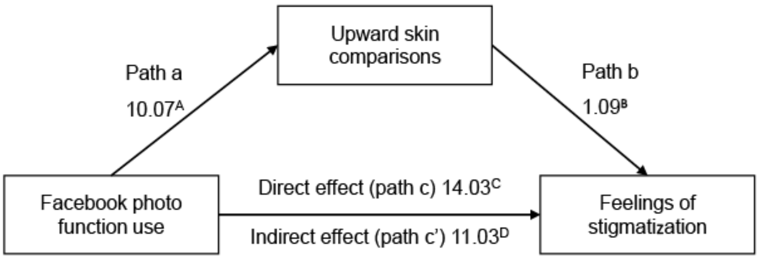
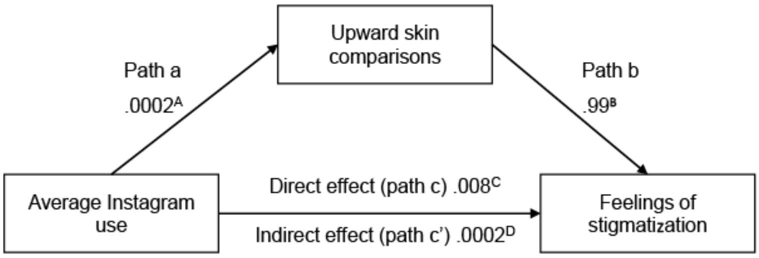


Figure 4. Mediation model for average Instagram use on acne stigma via upward appearance comparison (n=429). The numbers presented in the figure represent unstandardized β values, as recommended by Hayes [48]. (A) *P*=.98, (B) *P*<.001, (C) *P*=.53, (D) 95% CI –0.011 to 0.009. For clarity, covariates are not included in the figure. The covariates that were controlled for on each pathway were gender, severity, acne diagnosis, downward skin comparison, and self-compassion.



Results

Demographics

Of 818 participants who started the survey, 652 participants completed the survey. Two participants were excluded because of unfeasible social media use (≥24 hours per day), so overall, 650 participants (aged 16-56 years; 82.9% female) were included in the analyses (69.7% completion rate). Information on participant demographics and acne history is presented in Tables 1 and 2.

In all, 591 participants reported using Facebook, whereas 428 reported using Instagram. The 2 groups were similar in age (Facebook: mean 24.2, SD 6.4 years; Instagram: mean 23.2, SD 5.7 years). Also, there was no association between the 2 platforms (Facebook and Instagram) in terms of the frequency of participants being a student or not a student (χ^2_1=0.21, *P*=.65), or White or not White (χ^2_1=0.82, *P*=.37). However, there were a greater proportion of females in the Instagram group (female vs male + other, χ^2_1=5.11, *P*=.04) and a higher proportion of people 25 years or older (considered to have adult acne [49]) in the Facebook group (χ^2_1=5.01, *P*=.03).

Participants with a formal acne diagnosis reported higher stigma (mean 76.43, SD 25.22) compared with participants reporting acne symptoms but without a formal diagnosis (mean 67.91, SD 25.73; t_{648}=3.88; *P*<.001; Cohen *d*=0.33). Furthermore, Spearman correlations showed a small correlation between self-rated severity and stigmatization (ρ_{648}=0.33, *P*<.001). However, there was no relationship between the duration of acne symptoms and stigmatization (ρ_{648}=0.06, *P*=.11).

Free-text responses to the question "Please list any other diagnosed physical or mental health conditions" were coded into yes (1) or no (0) responses on three variables: (1) skin condition, (2) long-term health condition (excluding skin conditions), and (3) mental health conditions. There was no significant effect of other skin conditions on stigmatization (t_{632}=−0.03, *P*=.98, *d*=0.003). However, respondents disclosing a comorbid long-term health condition also reported significantly greater acne stigma (mean 78.57, SD 24.04) than participants without a long-term health condition (mean 73.03, SD 25.79; t_{632}=2.15; *P*=.03; *d*=0.22). Furthermore, participants disclosing at least 1 diagnosed mental health condition reported significantly higher levels of stigmatization (mean 84.67, SD 25.29) than participants without (mean 71.37, SD 24.92; t_{632}=5.4; *P*<.001; *d*=0.53).

Female participants reported higher stigmatization levels (mean 76.17, SD 24.74) compared with male participants (mean 63.34, SD 27.35; t_{647}=0.49; *P*<.001; *d*=0.49). No other demographic variables were related to stigma, and those that were (gender, acne diagnosis, acne severity, and long-term health condition) were controlled for in moderated-mediation and mediation analyses. Mental health diagnoses were not included as a covariate as higher levels of mental health problems have previously been identified as a consequence of internalized stigmatization in individuals with skin diseases [10,50].

Table 1. Participant demographics (N=650).

Demographics and participant characteristics	Participants
Age (years), mean (SD; range)	24.47 (6.64; 16-56)
≥25, n (%)	225 (34.6)
Gender, n (%)	
Female	539 (82.9)
Male	110 (16.9)
Other	1 (0.2)
Ethnicity, n (%)	
White or Caucasian	510 (78.5)
Asian	92 (14.4)
Mixed	26 (4.0)
Black	10 (1.5)
Arab	5 (0.8)
Latin American	4 (0.8)
"Prefer not to answer"	3 (0.5)
Employment, n (%)	
Student	409 (62.9)
Employed	209 (32.2)
Both employed and student	5 (0.8)
Unemployed or unable to work	12 (1.8)
Homemakers or carers	11 (1.7)
"Prefer not to answer"	4 (0.6)
Education level, n (%)	
Undergraduate	246 (37.8)
A level or equivalent	206 (31.7)
Postgraduate	145 (22.3)
GCSE[a] or equivalent	21 (3.2)
Vocational	22 (3.4)
Other, unsure, or "prefer not to answer"	10 (1.5)
Marital status, n (%)	
Single	285 (43.8)
In a relationship	196 (30.2)
Cohabiting with partner	84 (12.9)
Married or civil partnership	79 (12.2)
"Other" or "prefer not to answer"	6 (0.9)

[a]GCSE: General Certificate of Secondary Education.

Table 2. Participant acne and health history (N=650).

Acne history and participant characteristics	Participants
Acne duration (months), mean (SD; range)	115 (82.38; 1-480)
Acne diagnosis, n (%)	
Yes	463 (71.2)
No or unsure	187 (28.8)
Current treatment, n (%)	
GP[a]	189 (29.1)
Dermatologist	57 (8.8)
Gynecologist	4 (0.6)
Other health professional	3 (0.5)
None	395 (60.7)
Prefer not to answer	2 (0.3)
Location[b], n (%)	
Visible	638 (98.2)
Nonvisible	12 (1.8)
Subjective severity, mean (SD)[c]	2.31 (0.58)
Other diagnoses, n (%)	
Yes	277 (42.6)
No	357 (54.9)
"Prefer not to answer"	16 (2.5)
Other skin condition(s)	71 (10.9)
Long-term health condition(s)	121 (18.6)
Mental health condition(s)	129 (19.8)

[a]GP: general practitioner.

[b]Characterized as visible if the location of acne included their face, scalp, neck, hands, or arm.

[c]Range 1 (not a problem) to 4 (the worst it could be).

Relationships Between Social Media Use, Appearance Comparisons, Self-Compassion, and Stigma

Table 3 provides bivariate correlations for each outcome variable, time spent on Facebook and Instagram, and relative Facebook photo function use.

As predicted, within Facebook users, photo-related Facebook activity positively correlated with upward appearance comparison and stigmatization, whereas average daily Facebook use was not correlated with Facebook photo activity nor stigmatization. Among Instagram users, average time on Instagram correlated positively with upward appearance comparisons but not stigmatization. Furthermore, among all respondents, there was a large positive correlation between upward comparisons and stigmatization (r_{648}=0.53, P<.001). Self-compassion was negatively correlated with upward comparisons (r_{648}=−0.41, P<.001), stigmatization (r_{648}=−0.46, P<.001), and Facebook photo activity (r_{590}=−0.11, P=.009), but not average Facebook use (ρ_{590}=−0.048, P=.24) nor Instagram use (ρ_{427}=0.093, P=.06).

Downward comparisons had a small significant correlation with Instagram use, upward comparisons, compassion, and stigma, and were therefore included as a covariate within the models below.

Table 3. Bivariate correlations between each of the predictor and outcome variables (N=650).

	1, ρ	2, *r*	3, ρ	4, *r*	5, *r*	6, *r*	7, *r*
1. FB use[a]							
Coefficient	—[b]						
P value	—						
2. FB photo[a]							
Coefficient	−0.003	—					
P value	.94	—					
3. Instagram use[c]							
Coefficient	0.32[d]	0.16[d]	—				
P value	<.001	.001	—				
4. UPACS[e]							
Coefficient	0.054	0.17	0.12	—			
P value	.19	<.001	.01	—			
5. DACS[f]							
Coefficient	0.062	0.051	0.12	0.38	—		
P value	.13	.22	.01	<.001	—		
6. Compassion							
Coefficient	−0.048	−0.11	−0.093	−0.41	−0.18	—	
P value	.24	.009	.06	<.001	<.001	—	
7. Stigma							
Coefficient	0.06	0.14	0.068	0.53	0.295	−0.46	—
P value	.230	.001	.162	<.001	<.001	<.001	—
Values	Median 30 (IQR 7.5-52.5; range 0-700)	Mean 0.39 (SD 0.069; range 0.00-0.79)	Median 30 (IQR 5.0-55.0; range 0-600)	Mean 33.49 (SD 8.38; range 9-45)	Mean 24.61 (SD 9.01; range 9-45)	Mean 32.55 (SD 7.64; range 12-57)	Mean 73.98 (SD 25.64; range 7-145)

[a]Excluding participants who reported not using Facebook (n=592). FB use: average Facebook use per day; FB photo: Facebook Questionnaire functions.

[b]Not available.

[c]Excluding participants who reported not using Instagram (n=429). Instagram use: average Instagram use per day.

[d]Excluding participants who did not use both Facebook and Instagram (n=403)

[e]UPACS: Upward Appearance Comparison Scale.

[f]DACS: Downward Appearance Comparison Scale.

Mediation and Moderated-Mediation Analyses

Moderated-mediation analyses were conducted to assess the conditional direct and indirect effects of photo-related social media activity on stigmatization at values of self-compassion 1 SD below the mean, the mean, and 1 SD above the mean.

The results of the moderated-mediation analysis (Figure 1, Table 4) did not support a model of moderated mediation for Facebook photo activity and acne stigma. Interactions of self-compassion on path a (*B*=0.58, *P*=.20), path b (*B*=−0.01, *P*=.25), or path c (*B*=−1.07, *P*=.42) were nonsignificant. Likewise, the results of the moderated-mediation analysis (Figure 2, Table 5) did not support a model of moderated mediation for Instagram use and acne stigma. Interactions of self-compassion on path a (*B*<0.001, *P*=.98), path b (*B*=−0.018, *P*=.25), or path c (*B*=0.0004, *P*=.83) were nonsignificant.

Subsequently, simpler mediation models were explored. Conditional direct and indirect effects of photo-related social media activity on stigmatization were assessed with self-compassion as a covariate. Mediation analysis (Figure 3; Table 6) indicated that there was a significant indirect effect of Facebook photo use on stigmatization via upward appearance comparison (estimation of indirect effect 11.03, SE 5.11, 95% CI 1.19-21.12). There was no significant direct (estimation of direct effect 14.03, SE 13.19, 95% CI −11.86 to 39.93) or total effect (estimation of total effect 25.06, SE 15.14, 95% CI −4.68 to 54.80) of Facebook photo activity on stigmatization. Furthermore, self-compassion predicted lower levels of upward appearance comparison (*B*=−0.34, *P*<.001) and stigmatization (*B*=−0.85, *P*<.001).

Conversely, mediation analysis (Figure 4; Table 7) indicated that there was no significant direct (estimation of direct effect

0.008, SE 0.013, 95% CI −0.017 to 0.033), total (estimation of total effect 0.008, SE 0.013, 95% CI −0.018 to 0.034), or indirect (estimation of indirect effect 0.0002, SE 0.005, 95% CI −0.011 to 0.009) effect of Instagram use on stigmatization via upward appearance comparison. However, upward appearance comparisons continued to predict stigmatization in Instagram users (*B*=0.99, *P*<.001). Self-compassion also continued to predict lower levels of upward appearance comparison (*B*=−0.33, *P*<.001) and stigmatization (*B*=−1.04, *P*<.001).

Table 4. The conditional direct and indirect effects of Facebook photo function use on stigmatization at values of self-compassion 1 SD below the mean, the mean, and 1 SD above the mean (N=591).

Value of self-compassion	Direct effect		Indirect effect	
	B (SE)	95% CI	*B* (SE)	95% CI
−7.61	22.83 (18.17)	−12.84 to 58.51	6.62 (6.92)	−8.21 to19.52
0.0000	14.66 (13.60)	−12.05 to 41.37	11.11 (5.15)	1.02 to 21.25
7.61	6.49 (15.79)	−24.52 to 37.49	14.83 (6.21)	2.85 to 27.39

Table 5. The conditional direct and indirect effects of Instagram use on stigmatization at values of self-compassion 1 SD below the mean, the mean, and 1 SD above the mean (N=429).

Value of self-compassion	Direct effect		Indirect effect	
	B (SE)	95% CI	*B* (SE)	95% CI
−7.35	0.005 (0.022)	−0.038 to 0.048	0.0004 (0.008)	−0.018 to 0.015
0.0000	0.008 (0.01)	−0.019 to 0.035	0.0005 (0.0056)	−0.011 to 0.01
7.35	0.011 (0.016)	−0.021 to 0.043	0.0006 (0.0083)	−0.021 to 0.12

Table 6. Summary of the mediation analysis for Facebook photo activity (N=591).

Variable	*B* (SE)	*P* value	95% CI
Path a: Outcome: UPACS[a] (R^2=0.33, *P*<.001)			
Constant	27.07 (2.85)	<.001	21.47 to 32.67
Facebook photo activity	10.07 (4.6)	.03	1.02 to 19.11
DACS[b]	0.28 (0.035)	<.001	0.21 to 0.35
Severity	1.36 (0.52)	.009	0.34 to 2.39
Gender	3.47 (0.91)	<.001	1.68 to 5.26
Self-compassion	−0.34 (0.042)	<.001	−0.42 to −0.26
Diagnosis	1.42 (0.65)	.03	0.014 to 2.7
Long-term health condition	−0.73 (0.79)	.36	−2.28 to 0.82
Path b: Outcome: stigma (R^2=0.42, *P*<.001)			
Constant	29.37 (8.59)	<.001	12.49 to 46.25
UPACS	1.09 (0.12)	<.001	0.87 to 1.32
Facebook photo use	14.03 (13.19)	.28	−11.86 to 39.93
DACS	0.25 (0.1)	.02	0.046 to 0.45
Severity	9.56 (1.54)	<.001	6.53 to 12.59
Gender	−1.45 (2.21)	.51	−5.8 to 2.9
Self-compassion	−0.85 (0.12)	<.001	−1.08 to −0.61
Diagnosis	2.5 (1.85)	.17	−1.11 to 6.15
Long-term health condition	3.68 (2.18)	.09	−0.6 to 7.96

[a]UPACS: Upward Appearance Comparison Scale.

[b]DACS: Downward Appearance Comparison Scale.

Table 7. Summary of the mediation analysis for Instagram use (N=429).

Variable	*B* (SE)	*P* value	95% CI
Path a: Outcome: UPACS[a] (R^2=0.30, P<.001)			
Constant	31.27 (2.98)	<.001	25.5 to 37.04
Instagram use	0.0002 (0.005)	.98	−0.01 to 0.01
DACS[b]	0.25 (0.044)	<.001	0.16 to 0.33
Severity	2.01 (0.59)	<.001	0.84 to 3.17
Gender	3.02 (1.17)	.10	0.73 to 5.3
Self-compassion	−0.33 (0.048)	<.001	−0.43 to –0.24
Diagnosis	0.8 (0.75)	.28	−0.73 to 2.27
Long-term health condition	−0.88 (0.82)	.29	−2.5 to 0.74
Path b: Outcome: stigma (R^2=0.39, P<.001)			
Constant	49.21 (10.13)	<.001	29.29 to 69.14
UPACS	0.99 (0.15)	<.001	0.7 to 1.29
Instagram use	0.008 (0.01)	.53	−0.02 to 0.33
DACS	0.1 (0.12)	.39	−0.13 to 0.33
Severity	8.83 (1.75)	<.001	5.38 to 12.27
Gender	−1.42 (3.17)	.65	−7.65 to 4.81
Self-compassion	−1.04 (0.16)	<.001	−1.35 to −0.74
Diagnosis	4.4 (2.14)	.04	0.2 to 8.6
Long-term health condition	0.66 (2.58)	.80	−4.4 to 5.72

[a]UPACS: Upward Appearance Comparison Scale.

[b]DACS: Downward Appearance Comparison Scale.

Discussion

This study sought to investigate the relationship between photo-related social media use and feelings of stigmatization in adults with acne. Consistent with the hypothesis, a higher proportion of time engaged in Facebook photo activity, not overall time on Facebook, was correlated with greater feelings of stigmatization in participants with acne, and this relationship was mediated by upward appearance comparison. However, this was the case for Facebook users only, as no such relationship was identified for participants using Instagram; yet among these users, upward appearance comparisons predicted felt stigmatization. Interestingly, although greater self-compassion was related to lower stigmatization, it did not moderate the relationship between social media photo use and acne-related stigma in either Facebook or Instagram users.

It is unclear why there was an indirect relationship between relative Facebook photo activity and stigma but not between Instagram use and stigma. This may reflect the choice of measures, as the measure of Instagram usage did not differentiate between types of usage [32]. Future research should therefore distinguish between types of Instagram use.

Existing research on stigmatization in individuals with skin conditions has primarily focused on stigmatization as a predictor of depression and impaired quality of life, and demographic and condition variables as predictions of stigma. Such research has consistently identified perceived stigmatization as a predictor of reduced quality of life and psychological morbidity. In line with previous research, this study identified associations with stigmatization and gender, perceived severity, and possessing a diagnosis of acne [10,17,20]. However, skin-related comparisons and self-compassion were more consistently associated with felt stigmatization. These findings suggest that the way individuals interact with social media is more important than how long they use it for understanding the associations between social media and well-being. This is important as such meta-cognitive processes are amenable to modification within psychological therapy.

This study has a number of limitations. Clearly, the cross-sectional design prevents comment on causation, and experimental research could usefully investigate the relationship between social comparisons and social media use. Participants for this study were recruited via a web-based platform from a community sample; therefore, information on objective diagnoses and severity was not obtainable, and this prevented the investigation of treatment factors and clinical severity. It is possible that some participants did not have acne and may have had other undiagnosed skin conditions. Also, there were a greater proportion of females in the Instagram group and a higher proportion of people 25 years or older (considered to have adult acne [49]) in the Facebook group, which may have affected the results. However, the majority of individuals with acne tend to self-manage [51], and consequently, the use of a community sample has a number of merits in reaching a wider range of people living with the condition. A final important limitation is that social media use was self-reported, which may have affected the reliability of the data obtained. This could be addressed in future experimental studies.

Nevertheless, the finding that appearance comparisons were associated with stigmatization in both Facebook and Instagram users and mediated the relationship between relative Facebook photo activity and stigmatization provides further support for the important role of skin-specific appearance comparisons in the psychosocial well-being of individuals living with acne, as reported in qualitative research [5,52]. Therefore, the role of upward appearance comparisons on feelings of stigmatization should be considered when working with individuals with acne-related distress. Future research could explore whether this relationship is present in populations with other skin conditions and further explore the relationship with other measures of psychological distress, such as shame, depression, and social anxiety. Given that self-compassion was consistently related to lower levels of stigmatization, interventions based on increasing self-compassion provide an additional avenue for exploring ways of reducing feelings of stigmatization in individuals with acne.

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Conflicts of Interest

None declared.

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Abbreviations

DACS: Downward Appearance Comparison Scale
UPACS: Upward Appearance Comparison Scale

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Original Paper

Impact of, Factors for the Success of, and Concerns Regarding Transplant Patients' Skin Cancer Campaigns: Observational Study

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Abstract

Background: Due to rising health care costs, patients have sought alternative ways of addressing medical expenses. In particular, transplant patients have complex and expensive medical needs—including skin cancer surveillance—that may not be fully covered by insurance. One such method of financing medical costs is by crowdsourcing through web-based platforms, most notably GoFundMe.

Objective: Previous work identified factors associated with GoFundMe campaigns' fundraising success for dermatologic diseases. We sought to characterize these factors in transplant recipients' campaigns for funds raised for covering skin cancer–related costs. These factors include demographics, campaign traits, and subjective themes.

Methods: From January to April 2022, we analyzed GoFundMe campaigns using the following search terms chosen on the basis of author consensus: "transplant skin cancer," "transplant basal cell," "transplant squamous," "transplant melanoma," and "dermatologist transplant." Demographic data were coded from campaign text or subjectively coded based on author consensus. Campaigns were read completely by 2 independent coders and associated with up to 3 different themes. Linear regression was performed to examine the qualities associated with success, which was defined as funds raised when controlling for campaign goals. Logistic regression was used to examine qualities associated with extremely successful campaigns, defined as those raising funds over 1.5 times the IQR.

Results: Across 82 campaigns, we identified several factors that were associated with fundraiser success. Patients who experienced complications during infectious disease treatment, those who received a pancreas transplant, or those who died from their disease raised significantly more money. Patients older than 61 years raised significantly less money. Extremely successful campaigns (>US $20,177) were associated with campaigners who emphasized a disability from their disease, those who were reluctant to ask for help, or those who died due to their disease.

Conclusions: Demographic and thematic factors are associated with transplant patients' skin cancer–related fundraising success, favoring those who are younger, in more extreme situations, and appear reluctant to ask for help; these findings are consistent with those of previous studies. Additionally, transplant patients have complex and expensive dermatologic needs that may not be fully covered by insurance, as reflected in their GoFundMe campaigns. The most commonly mentioned reasons for fundraising included living expenses or loss of income, inadequate or no insurance, and end-of-life costs. Our findings may inform transplant patients how to maximize the success of their campaigns and highlight gaps in health care coverage for skin cancer–related costs. Limitations include the possibility for misclassification due to the data abstraction process and limiting data collection to fundraisers available on GoFundMe while excluding those on other websites. Further research should investigate the ethical implications of crowdfunding, financial needs of this patient population, and potential ways to improve access to routine skin cancer surveillance among patients receiving transplants.

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KEYWORDS

GoFundMe; transplant; skin cancer; nonmelanoma skin cancer; crowdfunding; fundraising; crowdsourcing; insurance; demographic; squamous cell carcinoma; basal cell carcinoma; multivariate linear regression; binary logistic regression

Introduction

GoFundMe is a web-based crowdfunding platform used to raise money for individual campaigns. Though not originally designed to raise medical funds, as of 2021, one-third of all funds raised on GoFundMe (US $650 million) are designated for covering medical costs [1]. These fundraisers aim to raise money to cover both the medical and nonmedical costs of disease, such as income support. Campaigns seek support for a wide range of medical conditions, including those for patients with a history of organ or bone marrow transplantation seeking funds for needs related to their long-term care.

Transplant patients often require costly and time-intensive multidisciplinary care. While taking immunosuppressive medication, transplant patients are encouraged to establish care with a dermatologist for regular skin cancer screenings as they are 20-100 times more likely to develop skin cancers [2]. Squamous and basal cell carcinoma comprise 90% of skin cancers among transplant recipients, with risk increasing over the duration of immunosuppressive therapy: a 65-250-fold increase in risk in squamous cell carcinoma and a 10-fold increase in risk in basal cell carcinoma [3].

Patients post organ transplantation represent a unique population with needs for regular screening, preventative therapies, and, if needed, skin cancer treatment. Our group has previously characterized the broad range of dermatologic GoFundMe campaigns and analyzed factors associated with fundraising success [4]. Given established skin cancer risks post transplantation secondary to immunosuppression [3], in this study, we aimed to characterize and analyze these factors in transplant recipients' campaigns for skin cancer–related fundraising.

Methods

This study was deemed exempt by the University of Virginia's institutional review board. From January to April 2022, we analyzed all available GoFundMe campaigns, created between 2013 and 2021, using the following search terms chosen through author consensus: "transplant skin cancer," "transplant basal cell," "transplant squamous," "transplant melanoma," and "dermatologist transplant." Exclusion criteria included campaigns active for less than a day or if organ transplantation occurred after the diagnosis of skin cancer. Demographic data were coded from the campaign's text or subjectively coded based on author consensus. Qualitative themes were coded until thematic saturation was reached, using an inductive qualitative method [5]. Campaigns were read completely by 2 independent coders and associated with up to 3 different themes.

The cleaned data were exported to R (version 4.0.2; The R Foundation). The frequencies of the themes were calculated based on the percentage of times the theme was mentioned. Two separate models were used due to concerns regarding collinearity. Multivariate linear regression was performed to investigate the amount of funds raised against demographic and thematic variables. The IQR method for identifying outliers was applied to the amount of funds raised and the goal of the campaign. Based on this outlier detection method, campaigns that raised more than US $20,177 were excluded from this regression analysis. Binary logistic regression was performed to compare demographic variables and themes among fundraisers that raised above US $20,177 to those that raised below this amount in order to investigate qualities associated with extreme success in fundraising. Extreme success was defined as an amount over 1.5 times the IQR (>US $20,177). The significance threshold was set at $P<.05$.

Results

As shown in Table 1, the majority of campaign recipients were male (n=59, 72%), older than 61 years (n=43, 52.4%), and White (n=79, 96.3%). Only a minority of campaigns were created by the recipients themselves (n=10, 12.2%), with most campaigns created by a family member (n=35, 42.7%) or friend (n=32, 39.0%). Though most campaigners did not specify the type of skin cancer, among those who did, the majority were related to melanoma (n=19, 45.2%) and squamous cell carcinoma (n=17, 40.5%). The following transplant subtypes were seen most often: kidney (n=35, 42.7%), bone marrow (n=16, 19.5%), lung (n=16, 19.5%), heart (n=10, 12.2%), liver (n=8, 9.8%), and pancreas (n=6, 7.3%). The campaigns raised an average of US $7656 and had an average goal of US $16,072 (Table 2). Few campaigns met their goal (n=22, 26.8%). The most commonly mentioned themes included the cost of daily living or inability to work, inadequate or no insurance, and end-of-life costs (Table 1).

With respect to demographic characteristics, campaigns for patients older than 61 years earned an average of US $6983 less than those for patients aged 21-40 years (P=.009). Those who mentioned that their treatment was complicated by an infection (US $7512, P=.008) or those who ultimately died from their disease (US $7946, P<.001) raised significantly more funds. Lastly, those who had a pancreas transplant raised more funds than those who did not (US $6878, P=.04; Table 3). With respect to extreme positive outliers (raising >US $20,177), those who mentioned that the campaign recipient was disabled by their disease (odds ratio [OR] 1.139, 95% CI 1.006-1.312), who were those reluctant to ask for help (OR 0.184, 95% CI 1.012-1.427), or those who died from their condition (OR 0.167, 95% CI 1.045-1.336) were associated with extreme success (Table 3).

Table 1. Demographics and themes of transplant patients' skin cancer GoFundMe campaigns (N=82).

Characteristics and themes	Values, n (%)
Gender	
Female	23 (28)
Male	59 (72)
Age[a] (years)	
11-20	2 (2.4)
21-40	14 (17.1)
41-60	23 (28)
≥61	43 (52.4)
Race[b]	
White	79 (96.3)
Hispanic	2 (2.4)
African American	1 (1.2)
Type of skin cancer	
Unspecified	40 (48.8)
Melanoma	19 (23.2)
Squamous cell carcinoma	17 (20.7)
Basal cell carcinoma	6 (7.3)
Relationship to the creator of the campaign	
Self	10 (12.2)
Partner	5 (6.1)
Family member	35 (42.7)
Friend	32 (39)
Number of skin cancers	
1	44 (53.7)
≥2	38 (46.3)
Had a liver transplant	
No	74 (90.2)
Yes	8 (9.8)
Had a kidney transplant	
No	47 (57.3)
Yes	35 (42.7)
Had a lung transplant	
No	66 (80.5)
Yes	16 (19.5)
Had a heart transplant	
No	72 (87.8)
Yes	10 (12.2)
Had a bone marrow transplant	
No	66 (80.5)
Yes	16 (19.5)
Had a pancreas transplant	

Characteristics and themes	Values, n (%)
No	76 (92.7)
Yes	6 (7.3)
Used Immunosuppressives	
Not Mentioned	31 (37.8)
Yes	51 (62.2)
Died from cancer	
No	61 (74.4)
Yes	21 (25.6)
Seen by a dermatologist	
No	75 (91.4)
Yes	7 (8.5)
Top 5 most common themes for fundraising[c]	
Cost of living	46 (25)
Inadequate insurance	34 (18.5)
End-of-life costs	24 (13)
Travel costs	22 (12)
Inability to work	16 (8.7)

[a]Age could only be evaluated as a categorical variable as many fundraisers referenced the decade of life but not specific ages.

[b]Race was either explicitly mentioned in the campaign or subjectively assigned based on author consensus.

[c]Themes (n=184) were coded through an inductive qualitative method until thematic saturation was reached, meaning that themes were continuously added as they appeared in the data until no novel themes emerged. Each campaign was read completely by 2 independent coders and was associated with any discernible themes.

Table 2. Fundraising metrics of transplant patients' skin cancer GoFundMe campaigns.

	Values	
	Mean (SD)	Median
Amount raised (US $)	7655.89 (9002.40)	3902.50
Goal of the fundraiser (US $)	16,071.94 (19,871.52)	10,000
Number of donors	73.55 (76.23)	43
Number of updates	3.54 (6.61)	2

Table 3. Stepwise linear (I)[a] and logistic (II)[b] regression analyses of demographic and thematic variables against the amount raised[c].

	β (SE)	Odds ratio (95% CI)	*P* value
Stepwise linear (I) regression; dependent variable: amount raised			
Age group (years; reference: 21-40 years)			
11-20	–5074 (6226)	N/A[d]	.42
41-60	–4171 (2440)	N/A	.09
≥61	–6983 (2609)[e]	N/A	.009
Gender (reference: female)			
Male	1017 (1931)	N/A	.60
Fundraiser themes			
Multiple comorbidities	–3142 (2340)	N/A	.18
Infection complicating treatment	7512 (2788)[e]	N/A	.009
Psychosocial	–5959 (3089)	N/A	.06
Miscellaneous[f]			
≥2 cancers	2612 (1763)	N/A	.14
Seen by a dermatologist	4634 (3085)	N/A	.14
Kidney transplant	–3396 (1805)	N/A	.06
Pancreas transplant	6878 (3357)[g]	N/A	.04
Immunosuppressives used	–3075 (1758)	N/A	.09
Insurance	6135 (4222)	N/A	.15
Died from cancer	7946 (1954)[h]	N/A	<.001
Logistic (II) regressions with outliers with themes as variables			
Goal	0.000005949 (0.000001445)[h]	1.000 (1.000-1.000)	<.001
Age group (years; reference: 21-40 years)			
11-20	0.02029 (0.1831)	1.021 (0.713-1.461)	.91
41-60	–0.04783 (0.07381)	0.953 (0.825-1.102)	.52
≥61	–0.07517 (0.08198)	0.928 (0.790-1.089)	.36
Gender (reference: female)			
Male	0.08243 (0.06081)	1.086 (0.964-1.223)	.18
Fundraiser themes			
Disability due to disease	0.1391 (0.06768)[g]	1.149 (1.006-1.312)	.04
Reluctance to ask for help	0.1838 (0.08760)[g]	1.202 (1.012-1.427)	.04
Miscellaneous			
Time of fundraiser	–0.00003655 (0.00003554)	1.000 (1.000-1.000)	.31
Died from cancer	0.1667 (0.06279)[e]	1.181 (1.045-1.336)	.01

[a]Regression I is a linear regression that depicts demographic and thematic variables against the dependent variable: the total amount raised.

[b]Regression II is a binary logistic regression investigating demographic and thematic variables more likely to be seen in extremely successful campaigns compared to the majority of campaigns.

[c]Campaigns were defined as extremely successful if they raised more than 1.5 times the IQR (ie, greater than US $20,177).

[d]N/A: not applicable.

[e]*P*<.01.

[f]Adjusted R^2=0.3457

[g]*P*<.05.

[h]P<001.

Discussion

Principal Findings

Transplant patients have complex and expensive dermatologic needs that may not be fully covered by insurance, as reflected in their GoFundMe campaigns [3,6]. In our qualitative study, the most commonly mentioned reasons for fundraising included living expenses or loss of income, inadequate or no insurance, and end-of-life costs. Our findings corroborate known gaps in transplant care, namely the difficulty for patients to afford basic necessities due to a loss of income or inadequate coverage, challenges in accessing care, and long-term care and rehabilitation needs [6]. Additionally, we found that most skin cancer–afflicted transplant campaigners seeking help were White men older than 61 years, and that specific demographic and campaign characteristics were associated with fundraiser success.

As of 2022, most transplant recipients were male (62%), White (52%), and older than 50 years (62%) [7]. While it is expected that White transplant patients become afflicted with skin cancers at higher rates than patients of color, the percentage of non-White campaigners in this study was very low (3/82, 3.7%) [3]. Additionally, 46.3% of campaigners in this study had more than 1 skin cancer and a majority of fundraisers (n=75, 91.4%) did not mention dermatologist visits prior to the development of skin cancers. It is possible that transplant patients without routine dermatologic surveillance are more likely to experience extreme presentations of skin cancer, thus requiring crowdfunding. While the lack of mention in the campaign does not preclude the possibility of prior dermatology visits, it may suggest a lower likelihood of well-established or sustained care. Additionally, in our study, several patients died (11/82, 13%) from skin cancer, transplant complications, or other diseases, exemplifying the need for improved transplant skin cancer–related follow-up and coverage. Overall, our data support the development of more robust skin cancer education for this patient population.

When analyzing factors associated with success, our findings are consistent with those of previous studies that reported that successful campaigns often feature extreme stories, emphasizing an inability to work or hesitancy to ask for help [2,8]. As mentioned above, those aged ≤60 years also found significantly greater success, which is congruent with our group's findings in a prior study [4] where the most successful fundraisers included patients aged 20-40 years. We hypothesize that fundraiser crowd appeal may in part depend on an ability to demonstrate supposed deservingness and garner sympathy from potential contributors. As mentioned above, a number of themes were associated with fundraiser success. Inability to work, disability from disease, and infectious complications suggest a debilitating and urgent condition, and reluctance to ask for help may portray a picture of resilience following the exhaustion of other means of fundraising, both of which may garner sympathy from potential donors. This finding on crowdsourcing for skin cancer following transplantation parallels the results from crowdsourcing for all cancers, where campaigns for high-mortality cancers that used emotional words to prompt empathy had raised more funds [9]. In another of our group's previous studies, where we analyzed factors associated with fundraiser success in GoFundMe campaigns raising money for plastic surgery conditions, we found that themes including inadequate insurance, travel costs, life-saving treatment, and end-of-life expenses were associated with a higher amount of funds raised (E Mark et al, unpublished data, May 2022). Similarly, these themes may suggest resilience (traveling far to receive care) and urgency (inadequate insurance or life-saving treatment). Interestingly, end-of-life expenses in our prior study and death from disease in this study were associated with greater success, suggesting that reverence for life may garner sympathy from potential donors. In summary, themes suggesting resilience, severity or urgency, and mortality are associated with greater success. As campaigns increase, competition may favor those who can create compelling narratives, adding to the disparities that health care providers must discern.

Limitations

Limitations include the possibility for misclassification due to the data abstraction process, limiting analysis to fundraisers on GoFundMe while excluding those on other websites, and inability to distinguish between anonymous donations and those from friends or family members. Campaign textual features, such as clarity, grammar, and complexity, were difficult to quantify in this study but may affect fundraiser success. Additionally, due to the limited information available on GoFundMe, factors such as education attainment, income, social support, cultural background, and differences in health systems that could impact fundraiser success could not be analyzed. Another limitation is the lack of generalizability of our findings. The results of this study are largely based on campaigns for White men older than 61 years and may not fully represent the outcomes of individuals with different cultural or socioeconomic backgrounds. Further, while this study included global campaigns, the results were heavily skewed to reflect crowdsourcing in the US health care system, which does not provide universal care like other high-income countries. Differences in health care coverage would likely impact the need for individual fundraising, thereby making these results less generalizable across health care systems.

Conclusions

In summary, demographic and thematic factors are associated with the success of transplant patients' skin cancer–related fundraising campaigns, favoring those who are younger, in more extreme situations, and appear reluctant to ask for help. Further research should investigate the ethical implications of crowdfunding, the financial needs of this patient population, and potential ways to improve access to routine skin cancer surveillance among patients receiving transplants.

Conflicts of Interest

None declared.

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Abbreviations

OR: odds ratio

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Research Letter

A Deep Dive Into Instagram's Top Skinfluencers

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Abstract

We characterized skinfluencers from various training backgrounds and compared their posts on Instagram featuring skin care products.

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KEYWORDS

Instagram; skinfluencer; skinfluencers; skin care; social media; general dermatology; training; dermatology; social media; influencer; influencers; skin

Introduction

Skinfluencers are online personalities who share information on skin care routines and products on social media. Launched in 2010, Instagram is a free photo- and video-sharing app [1]. With over 800 million users, Instagram has become a vital business platform for budding skinfluencers—those who share information on cutaneous health [1]. However, medical credentials are not required to share skin care advice online. This poses at minimum a source of confusion and is a risk to patients when inaccurate or low-quality information is shared, which has occurred among hairfluencers [2]. Therefore, the goal of our study was to characterize skinfluencers from various training backgrounds and to compare their Instagram posts featuring skin care products.

Methods

We identified skinfluencers from 4 different training backgrounds using the following Google search terms: "skinfluencers" and "physicians," "physician assistants," "nurse practitioners," or "aestheticians." The top 5 skinfluencers with the most Instagram followers from each of the 4 training backgrounds were included in the analysis. We tracked their posts on Instagram for 1 month (March to April 2021) using Microsoft Excel (Microsoft Corp) and collected the following parameters: demographics, follower count, verification status (a badge of authenticity and notability given to select users), and number of posts (total count, posts on skin care products, sponsored and self-promotional posts).

Results

A total of 20 skinfluencers were identified: 18 (90%) were female and 2 (10%) were male. All skinfluencers were from the United States, with 7 states and 11 cities represented. Physicians had the highest average follower count (n=1.1 million), followed by estheticians (n=523,000). Physician (n=4) and esthetician (n=4) accounts were most frequently verified. Estheticians published the most posts and stories (mean/skinfluencer=490.8), compared to nurse practitioners (mean/skinfluencer=292.6), physicians (mean/skinfluencer=284.6), and physician assistants (mean/skinfluencer=283.2) (Multimedia Appendix 1). Estheticians published the most posts and stories related to skin care products (mean/skinfluencer=70), followed by physicians (mean/skinfluencer=64.4) (Multimedia Appendix 2). Eight skinfluencers published posts on products from their own brands, though physicians had the most self-promotional posts (mean/skinfluencer=10.4). Estheticians had the highest average number of sponsored posts (mean/skinfluencer=1.8), followed by physician assistants (mean/skinfluencer=1.4).

Discussion

While physicians have a prominent following on Instagram and publish frequently, the greatest volume of skin-related content in this study was shared by those with the least amount of formal medical training. Although estheticians can provide valuable skin care services to patients, their training programs may be limited to only 6 months in duration. This is considerably less than the 8 or more years required for a dermatologist to practice in the United States. Yet, board-certified dermatologists comprise only a small portion (4%) of accounts that share popular dermatologic content on Instagram [3]. This poses a unique opportunity for dermatologists to engage with patients worldwide, as social media has the power to increase access to health information and can lead to behavioral change [4]. Instagram may be a particularly amenable platform for dermatologists, given the visual nature of both the specialty and the platform. However, social media involvement does not come without its pitfalls, especially with regard to self-promotion and sponsorship, which may be unethical [5]. As a result, organizations such as the American Medical Association and the Federation of State Medical Boards have issued guidelines for medical professionals on the proper use of social media [4]. Ultimately, whether dermatologists choose to engage with social media or to remain in the clinical sphere only, it is crucial that they are aware of the influence of social media on patients and of its limitations.

Conflicts of Interest

SAH is a paid lecturer for SmartPractice. The other authors declare no conflicts of interest.

Multimedia Appendix 1
Number of posts versus training background.
[PNG File , 90 KB - derma_v6i1e49653_app1.png]

Multimedia Appendix 2
Number of posts about skin care versus training background.
[PNG File , 79 KB - derma_v6i1e49653_app2.png]

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Original Paper

Saliency-Enhanced Content-Based Image Retrieval for Diagnosis Support in Dermatology Consultation: Reader Study

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Abstract

Background: Previous research studies have demonstrated that medical content image retrieval can play an important role by assisting dermatologists in skin lesion diagnosis. However, current state-of-the-art approaches have not been adopted in routine consultation, partly due to the lack of interpretability limiting trust by clinical users.

Objective: This study developed a new image retrieval architecture for polarized or dermoscopic imaging guided by interpretable saliency maps. This approach provides better feature extraction, leading to better quantitative retrieval performance as well as providing interpretability for an eventual real-world implementation.

Methods: Content-based image retrieval (CBIR) algorithms rely on the comparison of image features embedded by convolutional neural network (CNN) against a labeled data set. Saliency maps are computer vision–interpretable methods that highlight the most relevant regions for the prediction made by a neural network. By introducing a fine-tuning stage that includes saliency maps to guide feature extraction, the accuracy of image retrieval is optimized. We refer to this approach as saliency-enhanced CBIR (SE-CBIR). A reader study was designed at the University Hospital Zurich Dermatology Clinic to evaluate SE-CBIR's retrieval accuracy as well as the impact of the participant's confidence on the diagnosis.

Results: SE-CBIR improved the retrieval accuracy by 7% (77% vs 84%) when doing single-lesion retrieval against traditional CBIR. The reader study showed an overall increase in classification accuracy of 22% (62% vs 84%) when the participant is provided with SE-CBIR retrieved images. In addition, the overall confidence in the lesion's diagnosis increased by 24%. Finally, the use of SE-CBIR as a support tool helped the participants reduce the number of nonmelanoma lesions previously diagnosed as melanoma (overdiagnosis) by 53%.

Conclusions: SE-CBIR presents better retrieval accuracy compared to traditional CBIR CNN-based approaches. Furthermore, we have shown how these support tools can help dermatologists and residents improve diagnosis accuracy and confidence.

Additionally, by introducing interpretable methods, we should expect increased acceptance and use of these tools in routine consultation.

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KEYWORDS

dermatology; deep learning; melanoma; saliency maps; image retrieval; dermoscopy; skin cancer; diagnosis; algorithms; convolutional neural network; dermoscopic images

Introduction

Background

Melanoma is one of the top-5 most common cancers in Switzerland with a standardized incidence ratio per 100,000 inhabitants of 29.8 for men and 24.7 for women [1]. Longitudinal data acquired since 1989 show a linear 100% increase of the standardized incidence ratio for men [1] in the last 30 years. Unfortunately, this is a worldwide trend. According to Arnold et al [2], melanoma incidence and deaths are expected to increase 50% and 68%, respectively, by 2024. However, it is known that if diagnosed on time, skin cancer can be cured with a simple surgical procedure, dramatically increasing the survival rate. The rapid increase in cases every year has not been followed by an increase in the available number of dermatologists. This causes the system to operate inefficiently with increasing waiting times to get access to specialist consultation. To cope with such a situation, a study [3] proposed to provide specific training in skin cancer diagnosis to general practitioners to improve their competence in such cases. The outcome of that study showed a positive impact during a limited period after the initial training, but eventually, the accuracy dropped again after one year. Thus, it is necessary to explore long-term solutions that can support dermatologists to face this pandemic in a reliable way.

The use of deep learning has raised substantial interest in dermatology. Seminal studies such as Esteva et al [4] showed how deep learning algorithms can outperform board-certified dermatologists in certain dermoscopic image triage tasks. More recent studies broadened the scope by developing algorithms for automatic screening and ugly-duckling characterization in wide surface images [5]. Despite such encouraging applications and results, the transition from academic research studies to real-world application is only slowly being addressed. Different surveys showed a favorable position from dermatologists [6] as well as patients [7] with respect to the introduction of artificial intelligence (AI) in routine consultations. However, interpretability [8] and the need of a specialist to supervise the outcome are issues that concern clinical users and patients. When exploring the option of implementing such support tools in real-world consultation, there are 2 main aspects to monitor: on the one hand, diagnosis accuracy and, in the other, diagnosis confidence, since both play a key role. For example, the overdiagnosis of benign lesions as malignant lesions and diagnoses with low confidence cause unnecessary surgeries. A frequent scenario in clinical practice is the surgical removal of atypical-looking benign lesions. Even in the hands of experts, there are 5 benign lesions removed for every 1 melanoma [9], and in the hands of nonexperts, this increases exponentially. Another important fact that needs to be carefully considered is the bias that can be introduced in the user's decision-making. However, one of the main limitations in the adoption of these tools for nonexpert users comes from the interpretability of such tools, which does not transmit confidence in the predictions even if the demonstrated accuracy is high.

Use of Image Retrieval in Dermatology

Content-based image retrieval (CBIR) is a powerful tool in medical practice that proposes similar cases to the ones under study, thus mimicking an automatized bibliography search. Dermatology is not an exception, since large data sets of images are traditionally available. Early applications of CBIR in skin lesion categorization relied on the comparison retrieved from text and annotations [10] and progressed to consider colors and shapes [11,12]. However, with the introduction of convolutional neural networks (CNNs), CBIR is now using them as the backbone for feature extraction [13-17]. A pilot study [16] concluded that CBIR was perceived as easy to use and engaging; however, trust still has to be gained for routine use. Furthermore, in another high-impact study [17] where the impact of using CBIR as a support tool was evaluated, one of the conclusions was that users tend to prefer other AI approaches such per-class probability in the long term. The authors suggested exploring other CBIR architectures that might overcome this issue. One possible reason is the lack of interpretability of the retrieval process. To overcome this limitation, recent studies [18-20] evaluated the option of introducing interpretability methods such as saliency maps to guide the CNN feature extraction. These newly proposed architectures were tested using radiography data sets, which present substantial differences with dermoscopic imaging. For this reason, in this study, we proposed an updated version of the algorithm by Silva et al [18] for the specific needs of skin lesion diagnosis, which we refer to as saliency-enhanced CBIR (SE-CBIR).

The benefits of SE-CBIR in routine dermatologic consultations are as follows:

- Improved interpretability: Saliency maps provide a visual representation of the regions of interest considered by the neural network during feature extraction.
- Improved retrieval performance: By guiding feature extraction toward the regions of interests, we reduce the noise and nonrelevant information in the retrieval process.
- More efficient real-world implementation: By improving interpretability, trust by nonexperts should increase, supporting the wider adoption and implementation of such tools.

Methods

Data Set Description

For the training, validation, and testing of our algorithm, the HAM10000 data set [21,22] was used. It consists of a total of 10,015 labeled dermoscopic images belonging to 7 different categories of pigmented lesions. The ground truth was determined in more than 50% of images by histopathology, and the other half were either confirmed by follow-up examinations, expert consensus, or in vivo confocal microscopy [22]. Follow-up images of lesions were removed during the retrieval process to maximize the diversity. The HAM10000 data set designations for the 7 different classes were kept. The description for each category is as follows: actinic keratosis, squamous cell carcinoma, and Bowen disease (*akiec*); basal cell carcinoma (*bcc*); benign keratosis (*bkl*; solar lentigo, seborrheic keratosis, and lichen planus-like keratosis); dermatofibroma (*df*); melanoma (*mel*); melanocytic nevi (*nv*); and vascular lesions (*vasc*; angiomas, angiokeratomas, pyogenic granulomas, and hemorrhage). The data set is highly unbalanced, with 67% of the total number of lesions corresponding to melanocytic nevi and 11% to melanoma. To counteract such imbalance, a multiclass focal loss function was used during training.

Ethical Considerations

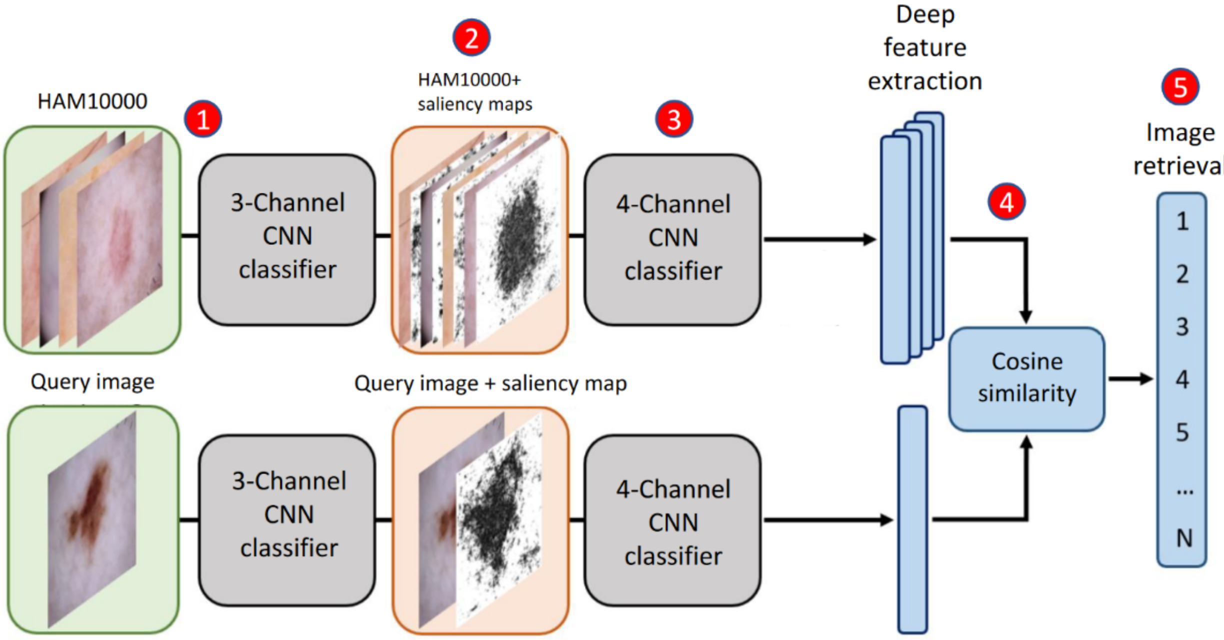
In this study, we used a public data set, namely HAM10000 [21,22]. This data set is routinely used by research studies and is available under a Creative Commons Attribution-NonCommercial 4.0 International Public License. Therefore, the use of this data set is not subject to ethics board approval.

Architecture Description

CBIR algorithms are designed to retrieve images from a data set that are related to the image under study. Their performance is boosted by introducing CNNs for feature extraction and representation. We chose EfficientNetB4 [23] as the backbone for our classifier. The choice was driven by the fact that ensemble models combining different versions of EfficientNet were used by the top teams in International Skin Imaging Collaboration (ISIC) competitions [24]. We profited from transfer learning by initializing the weights using “ImageNet” default values. The EfficientNetB4 top layer was removed and replaced by average pooling, batch normalization, and 2 combinations of a dropout and a dense layer. The output layer features a softmax activation function. We extracted the deep features just after the last convolutional layer and before the classification layers.

The traditional CBIR approach, as depicted in Figure 1, includes 3 steps: step 1, a CNN classifier using the HAM10000 data set is trained; step 4, extracted features from the query image are compared to those of each image in the retrieval set; and step 5, images are ranked according to similarity.

Figure 1. Saliency-enhanced content-based image retrieval (SE-CBIR) scheme. A 7-class classifier is trained in the first stage, from which saliency maps for each image can be extracted. The original classifier is modified by adding an additional channel to input combinations of skin lesion images and their saliency maps for fine-tuning. Finally, the retrieved images are ranked according to the cosine similarity of their deep features. Traditional content-based image retrieval (CBIR) includes only steps 1, 4 and 5, whereas SE-CBIR includes steps 1 to 5. CNN: convolutional neural network.



In clinical imaging, the relevant information is usually spatially constrained, so new approaches such as that in Silva et al [18] propose to add a fine-tuning stage, guiding the training using saliency maps to enhance the retrieval performance. With the emerging field of explainable AI, a variety of saliency methods have been developed, such as vanilla gradient [25], SmoothGrad [26], and integrated gradients [27]. Saliency methods aim to create a map highlighting the pixels that are relevant for the network’s classification of a particular input image. We chose vanilla gradient for various reasons: it is model agnostic, simple to integrate, interpretable, and consistent. In Silva et al [18], the superiority of latent representations derived from saliency maps over those directly generated from the input x-ray images was demonstrated, where latent representations of saliency maps were used for medical image retrieval purposes and in sample selection for active learning.

Due to the substantial differences between the x-ray images and our dermoscopic data set, we designed a second fine-tune stage that input the original image (3 RGB channels) plus the saliency map computed in the first step. This was done to avoid excessive loss of information included in the original colored dermoscopic images in contrast with the approach in Silva et al [18]. As shown in Figure 1, the traditional CBIR approach is comprised of 3 steps: the training of a skin lesion classifier (step 1), followed by deep feature extraction for every single image (step 4), and finally image retrieval according to similarity score (step 5), whereas SE-CBIR comprises 5 steps, adding the computation of saliency maps (step 2) and the training of a 4-channel classifier (step 3) [28]. It is worth it noting that in step 3, the input and first convolutional layer are expanded to a 4-channel input to input the saliency maps together with the original image.

Data Augmentation

Standard data augmentation techniques from the *albumentations* libraries [29] were applied during training to avoid overfitting. These transformations include geometric augmentations and noise, distortion, brightness and contrast, and color modifications. The data augmentation is applied on the fly during each epoch. All images were resized and randomly cropped to the expected EfficientNetB4 input resolution (380 × 380). Additionally, coarse dropout to enhance regularization was applied. During the training of SE-CBIR (fine-tuning stage), no data augmentation, other than random flips and rotations, was performed.

Training

For training, validation, and test purposes, the data set was randomly stratified in an 80:10:10 split, ensuring the same class distribution in all subsets. During training, an adaptative learning rate (α) approach was chosen to allow different α values for the pretrained EfficientnetB4 layers and the added layers, aiming to adapt the parameters of the pretrained layers just slightly or not at all compared to the new layers. A learning rate schedule was set up, with an initial ramp-up during the first epochs that aims to keep the learned features. After the ramp-up, the learning rate decays exponentially. Exponential decay is a widely used learning rate scheduling method to improve convergence. The adaptability of this approach reduces the time required to train neural networks and makes a neural model scalable, as they can adapt to structure and input data at any point in time while being trained.

For step 1, the learning rate was set to a low value ($\alpha=5 \times 10^{-5}$) to profit from prelearned features, whereas for the additional layers, the α was set to .01. This approach focuses the training on the classification layers. In this second step, we added an additional channel to the original input size, creating 4D images including the 3 RGB channels plus the 1D saliency maps. An adaptive learning rate approach similar to traditional CBIR was applied. However, the adapted layers were found to perform better at being trained with a 100-times larger ($\alpha=1 \times 10^{-3}$) learning rate than that in the first step. The learning rate was kept low at $\alpha=1 \times 10^{-5}$ for the pretrained layers to profit again from transfer learning, and the same number of epochs and loss function were used.

The multicategorical focal loss function [30] was chosen for training. This function adds a term to the cross-entropy loss, improving performance in imbalanced data sets such as HAM10000. This is achieved through down weighting, which reduces the influence of easy examples on the loss function, resulting in more attention to hard ones. With a softmax activation function in the last layer, the focal loss ${}_{focal}$ for each sample can be derived by:

The parameters α_i and γ define the weights on this additional term, whereas y^*_i represents the softmax prediction value of an input.

Image Retrieval and Ranking Metrics

In CBIR and image classification-based models, high-level image visuals are represented in the form of feature vectors that consists of numerical values. Image retrieval is based on the comparison of features extracted from the images. These vector features are then compared among the different image features to search and rank the "closest" ones. We chose cosine similarity to compare the features' latent representation due to its adequacy of handling high-dimensional vectors (1792 × 1 in our case). The mathematical representation is as follows:

where *A* and *B* are the feature vectors of the query image and each of the images in the labeled data set. The lower the value of S_c, the closer both images are in terms of features extracted.

To evaluate the retrieval performance and compare the traditional CBIR algorithm against SE-CBIR, we used the retrieval precision for *k* retrieved images (*P@k*) or cut-off value metric:

Similarly, for multiclass retrieval, we defined the average precision for *k* retrieved images (*AP@k*):

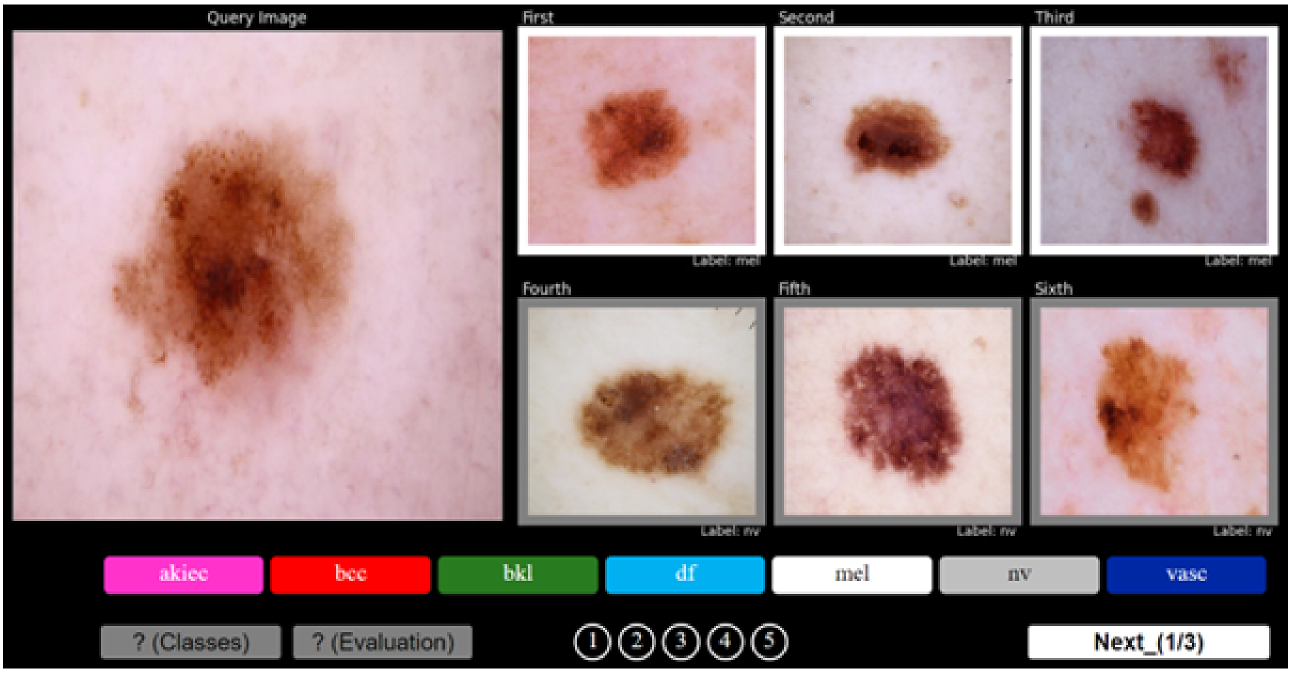
with *M* being the total number of classes.

Rater Recruitment and Reader Study Design

To evaluate the impact of this type of decision support, a reader study was designed within the University Hospital Zurich Dermatology Clinic. A total of 9 participants were recruited based on their willingness and availability to participate: 1 expert on pigmented skin lesions with more than 25 years of experience and 8 residents from the clinic with 1 to 5 years of experience. However, all of them had reasonable experience with melanoma diagnosis using dermoscopic imaging.

To evaluate the impact of the diagnosis support tool, the reader study was divided into 2 tasks. In task 1, volunteers were asked to provide a diagnosis on 100 randomly chosen dermoscopic images extracted from our HAM10000 test set. In parallel, they were also asked to provide their level of confidence in their diagnosis on a 5-point Likert scale [31]. After a break period of 1 day, the participants underwent task 2. They were asked to rediagnose the same set of images while being supported with the 6 “closest” images proposed by the retrieval algorithm that are characterized by their associated ground-truth label, as shown in Figure 2. Note that the saliency maps were not presented to the participants along with the retrievals; however, in a real-world implementation, they would be available. To minimize bias, the single images were rotated by 180° with respect to the original orientation. Additionally, each participant was presented with a different, randomly selected set of images for the evaluation. As in task 1, the volunteers were asked to provide a diagnosis and their confidence level. To facilitate participation, a web survey was created ad hoc for the evaluation process, allowing the users to examine the lesions on high-quality screens and providing flexibility on when and where to perform the evaluation.

Figure 2. Web interface developed for clinical evaluation. This screenshot corresponds with task 2, where the participants were presented with the query lesion and the 6 closest retrieved ones with their labels (colored edges). The user is asked to specify the confidence for each lesion diagnosis on a scale of 1 to 5. akiec: actinic keratosis, squamous cell carcinoma, and Bowen disease; bcc: basal cell carcinoma; bkl: benign keratosis; df: dermatofibroma; mel: melanoma; nv: melanocytic nevi; vasc: vascular lesions.



Results

Saliency Maps

An example of a saliency map calculated using the vanilla gradients is shown in Figure 3 (center). Additionally, an overlay of the original image and the saliency map is shown (right) for illustration purposes. To minimize the loss of information during the fine-tuning training step, the original image (3 RBG channels) and the corresponding saliency map (1 channel) are fed as a 4-channel input to the CNN.

Figure 3. Dermsocopic image (left), extracted saliency map (center), and the overlay of both (right).

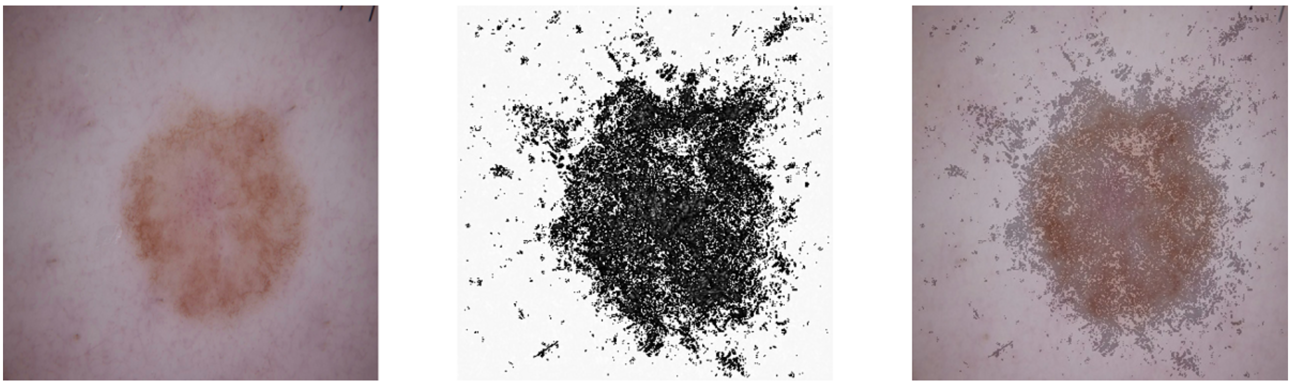


Image Retrieval Results

Retrieval precision comparing the traditional CBIR algorithm versus SE-CBIR is summarized in Table 1. The saliency-enhanced approach improves both the per-class prediction (*P@k*) and the average (*AP@k*) for all values *k* of retrieved images. The improvement in *AP@k* increases with *k*, from 7% (*k*=1) to a maximum of 18% (*k*=9). For a single class, the largest difference was found for class *df* where the prediction accuracy was almost doubled. The only class that did not experience a significant improvement was *akiec*. Both classes *df* and *akiec* were underrepresented with only 1% and 2% of the total retrieval data set. In the case of class *df*, SE-CBIR identified additional features leading to a significant improvement, whereas for class *akiec*, it could be that the limited samples available for class *akiec* presented similar appearances as solar lentigo or seborrheic keratosis and larger statistics are needed. For all other classes, *P@k* was >0.8 for *k*=1.

Table 1. Retrieval precision per class for different number of retrieved images comparing the original 3-channel classifier versus the saliency-enhanced one. Precision retrieval was evaluated for k=1, 3, 6, and 9 retrieved images. For each value of k, the average precision was also calculated.

Method and retrieval image (*k*)	Per-class *P@k*[a]							*AP@k* [b]
	akiec[c]	bcc[d]	bkl[e]	df[f]	mel[g]	nv[h]	vasc[i]	
SE-CBIR[j]								
1	0.59	0.82	0.82	1.00	0.81	0.95	0.93	0.84
3	0.57	0.82	0.78	0.97	0.72	0.95	0.88	0.81
6	0.56	0.83	0.75	0.98	0.69	0.95	0.89	0.81
9	0.56	0.83	0.75	0.96	0.69	0.95	0.90	0.81
CBIR[k]								
1	0.69	0.75	0.80	0.55	0.67	0.95	1.00	0.77
3	0.59	0.67	0.63	0.64	0.54	0.92	0.83	0.69
6	0.52	0.66	0.57	0.58	0.49	0.92	0.79	0.65
9	0.46	0.65	0.55	0.60	0.47	0.92	0.75	0.63

[a]P@k: retrieval precision for *k* retrieved images.

[b]AP@k: average precision for *k* retrieved images.

[c]akiec: actinic keratosis, squamous cell carcinoma, and Bowen disease.

[d]bcc: basal cell carcinoma.

[e]bkl: benign keratosis.

[f]df: dermatofibroma.

[g]mel: melanoma.

[h]nv: melanocytic nevi.

[i]vasc: vascular lesions.

[j]SE-CBIR: saliency-enhanced content-based image retrieval.

[k]CBIR: content-based image retrieval.

Reader Study Outcome

The outcome of the clinical evaluation by the 9 volunteers is summarized in Table 2. Diagnosis accuracy for the SE-CBIR algorithm was computed by majority voting among the *k*=6 retrieved images, which reached 89% on average for all evaluations. In task 1, participants recorded the lowest accuracy at 38%, with an average of 62.2%. The performance was not uniform with σ=12.7 points. As expected, the board-certified dermatologists performed at the same level as the algorithm. In task 2, a significant improvement in diagnosis accuracy was observed for all participants. The average accuracy increased by 22.7 points to 84.9%, which also helped to reduce diagnosis spread, bringing it down to σ=7.1 points. Since each participant was presented with a different image data set, to evaluate the consistency of their selection, the Cohen κ coefficient for each participant for tasks 1 and 2 was calculated, as well as the average among them. The results showed that agreement between raters improved with the support of AI, going from fair agreement (*k_average*=0.35) in task 1 to substantial agreement (*k_average*=0.66) in task 2. In addition, the 2 best-performing participants in task 1 were able to outperform the SE-CBIR majority-voting prediction when provided with retrieved images. It is worth noting that the HAM10000 data set is composed of hand-picked lesions whose diagnosis can be challenging without access to the patient's context. Regarding the average diagnosis confidence, an improvement from 3.11 to 3.86 was found (+24%). With the support of the retrieved cases, the confidence in the correct diagnosis increased from 3.35 to 4.03. Indeed, most (6/9, 67%) of the participants expressed a confidence level above 4, both in absolute confidence and confidence for correct diagnoses, whereas in task 1, only 1 participant showed that level of confidence. On the other hand, the confidence in incorrectly predicted lesions increased much less (2.72 to 2.90).

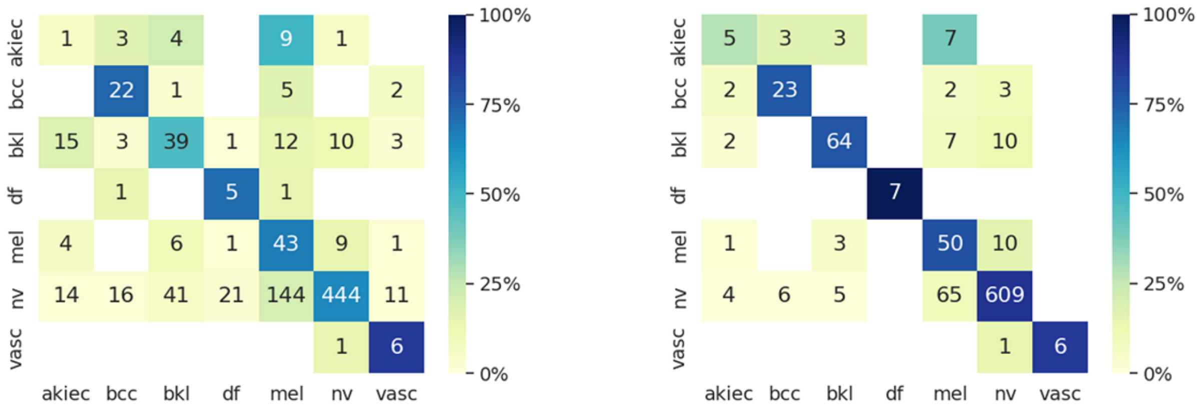
Table 2 shows the performance of the retrieval algorithm with an average accuracy of 89.2%. This result is substantially higher than the largest reader study using the ISIC18 data set published by Tschandl et al [17]; however, it used a different test set for the evaluation.

A closer look at the predictions per class is shown in Figure 4 with the help of confusion matrices. Each row represents the total number of instances of a given class, whereas each column represents the total number of instances predicted for each class. Figure 4 (right) shows a substantial improvement of per-class accuracy with the help of SE-CBIR–retrieved images.

Table 2. Qualitative evaluation results for all participants. Diagnosis accuracy and confidence level on a 5-point Likert scale. Saliency-enhanced content-based image retrieval (SE-CBIR) accuracy was computed by majority voting among 6 retrieved images. The absolute confidence is reported for both tasks, with separate values for correct and incorrect diagnoses.

Participant	SE-CBIR, accuracy (%)	Task 1				Task 2			
		Accuracy (%)	Absolute confidence	Confidence for correct diagnosis	Confidence for incorrect diagnosis	Accuracy (%)	Absolute confidence	Confidence for correct diagnosis	Confidence for incorrect diagnosis
Dermatologist	89	85	3.38	3.48	2.8	92	4.09	4.17	3.13
Resident 1	90	44	2.92	3.45	2.5	84	4	4.12	3.38
Resident 2	89	60	2.43	2.92	1.7	74	2.85	3.31	1.54
Resident 3	92	80	2.51	2.6	2.15	96	3.45	3.51	2
Resident 4	89	62	2.7	2.97	2.26	88	4.41	4.56	3.33
Resident 5	86	66	4.05	4.32	3.53	83	4.46	4.62	3.65
Resident 6	92	65	3.84	3.93	3.66	79	4.06	4.19	3.57
Resident 7	93	60	3.14	3.4	2.75	89	4	4.12	3
Resident 8	88	38	3.04	3.03	3.05	79	3.38	3.56	2.71
Total, mean (SD)	89.2 (2.3)	62.2 (12.7)	3.11 (0.6)	3.35 (0.5)	2.72 (0.6)	84.9 (7.1)	3.86 (0.51)	4.03 (0.5)	2.9 (0.7)

Figure 4. Aggregated confusion matrix for all participants for task 1 (left) and task 2 (right). Overall diagnosis accuracy was improved when using saliency-enhanced content-based image retrieval (SE-CBIR) as a support tool. The melanoma overdiagnosis was reduced by 53% in task 2, mainly driven by changes from initial melanoma diagnosis to nevi. akiec: actinic keratosis, squamous cell carcinoma, and Bowen disease; bcc: basal cell carcinoma; bkl: benign keratosis; df; dermatofibroma; mel: melanoma; nv: melanocytic nevi; vasc: vascular lesions.



Class *nv* represented almost 80% of the test data set, and the SE-CBIR results show that almost 25% of the diagnoses were reconsidered into the correct class. Similarly, for class *bkl*, incorrect diagnoses were corrected in task 2 improving the accuracy by 17%. For class *mel*, the accuracy improved to 79% for correct melanoma cases. In total, just 20 correct decisions of task 1 were changed to an incorrect diagnosis in task 2, whereas 224 misclassified lesions from task 1 were correctly classified in task 2. This is an important indication that the algorithm does not lead to overconfident misclassifications but rather improves the number of correct diagnoses and their confidence—although we should note that 12 of the incorrectly overturned diagnoses agreed with the algorithm's majority voting. Those cases probably would require additional patient-context information for a better evaluation. From a skin management point of view, melanoma overdiagnosis is a conservative approach where a negative biopsy might be justified. Regarding melanoma (*mel*) diagnosis, in task 1, a total of 21 cases were underdiagnosed (33% of the 64 total *mel* cases), whereas in task 2, this value decreased to 14 (22%) out of 64 cases. Regarding overdiagnosis in task 1, a total of 171 nonmelanoma cases (where 144 were *nv* cases) were misclassified into *mel*, whereas in task 2, this value decreased to 81 cases (with 65 *nv* cases).

Discussion

This study presents a novel algorithm for skin lesion diagnosis support based on the use of saliency maps for feature extraction guidance in contrast to state-of-the-art image retrieval (CBIR). We refer to this architecture as SE-CBIR due to the addition of a second fine-tuning stage, combining saliency maps and dermoscopic imaging.

It was shown that SE-CBIR improved retrieval precision in dermoscopic data sets compared to traditional CBIR by 7%. Clinical relevance was assessed by a reader study where the participants improved their overall diagnosis accuracy by +22%, as well their confidence level by +24%. Considering only melanomas, the study demonstrated that SE-CBIR helped to decrease overdiagnosis by 53%.

However, the study has limitations, such as the use of a single data set and the fragility of saliency maps. It is well-known that different methods for saliency map calculation might lead to different results. Another potential limitation identified in the evaluation process is the fact that the participants did not have access to the patient's context, which penalizes the diagnosis accuracy in certain difficult cases. Future work should include increasing the number of participants, including different target groups such as general practitioners, nurses, or technicians, to evaluate the impact and usefulness of such tools in different scenarios, as well as addressing the imbalance of the classes such as *akiec*, where the current data set does not seem to be representative and is difficult to generalize. In this case, data augmentation techniques will not solve the issue and additional images of such a class should be sought and included.

In conclusion, we have demonstrated the superior quantitative performance of SE-CBIR in comparison to the state-of-the-art CBIR by introducing saliency maps for feature extraction. By introducing interpretable methods, we also expect to improve acceptance by users since they have access to human-understandable information to better comprehend the algorithm's decision process.

Acknowledgments

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Data Availability

The origin of the image data set is reported in the data set publication of HAM10000 [22].

The code used in the study is available upon request to the corresponding author for academic purposes.

Authors' Contributions

M Gassner, JBG, ST-L, RPB, AA, NA, M Guckenberger, and MR contributed to the conception and design of the study. M Gassner developed the web-based tool for the reader study. M Gassner and JBG performed the analysis with the supervision of ST-L, RPB, and AA. RPB, FB, FF, SH, CP, PS, DS, RS, and FV participated in the reader study. M Gassner and JBG wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version. Funding acquisition and project administration was carried out by M Guckenberger, NA, RPB, and ST-L.

Conflicts of Interest

None declared.

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Abbreviations

AI: artificial intelligence
AP@k: average precision for k retrieved images
CBIR: content-based image retrieval
CNN: convolutional neural network
ISIC: International Skin Imaging Collaboration
P@k: retrieval precision for k retrieved images
SE-CBIR: saliency-enhanced content-based image retrieval

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Original Paper

Improving Skin Cancer Diagnostics Through a Mobile App With a Large Interactive Image Repository: Randomized Controlled Trial

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Abstract

Background: Skin cancer diagnostics is challenging, and mastery requires extended periods of dedicated practice.

Objective: The aim of the study was to determine if self-paced pattern recognition training in skin cancer diagnostics with clinical and dermoscopic images of skin lesions using a large-scale interactive image repository (LIIR) with patient cases improves primary care physicians' (PCPs') diagnostic skills and confidence.

Methods: A total of 115 PCPs were randomized (allocation ratio 3:1) to receive or not receive self-paced pattern recognition training in skin cancer diagnostics using an LIIR with patient cases through a quiz-based smartphone app during an 8-day period. The participants' ability to diagnose skin cancer was evaluated using a 12-item multiple-choice questionnaire prior to and 8 days after the educational intervention period. Their thoughts on the use of dermoscopy were assessed using a study-specific questionnaire. A learning curve was calculated through the analysis of data from the mobile app.

Results: On average, participants in the intervention group spent 2 hours 26 minutes quizzing digital patient cases and 41 minutes reading the educational material. They had an average preintervention multiple choice questionnaire score of 52.0% of correct answers, which increased to 66.4% on the postintervention test; a statistically significant improvement of 14.3 percentage points (P<.001; 95% CI 9.8-18.9) with intention-to-treat analysis. Analysis of participants who received the intervention as per protocol (500 patient cases in 8 days) showed an average increase of 16.7 percentage points (P<.001; 95% CI 11.3-22.0) from 53.9% to 70.5%. Their overall ability to correctly recognize malignant lesions in the LIIR patient cases improved over the intervention period by 6.6 percentage points from 67.1% (95% CI 65.2-69.3) to 73.7% (95% CI 72.5-75.0) and their ability to set the correct diagnosis improved by 10.5 percentage points from 42.5% (95% CI 40.2%-44.8%) to 53.0% (95% CI 51.3-54.9). The diagnostic confidence of participants in the intervention group increased on a scale from 1 to 4 by 32.9% from 1.6 to 2.1 (P<.001). Participants in the control group did not increase their postintervention score or their diagnostic confidence during the same period.

Conclusions: Self-paced pattern recognition training in skin cancer diagnostics through the use of a digital LIIR with patient cases delivered by a quiz-based mobile app improves the diagnostic accuracy of PCPs.

Trial Registration: ClinicalTrials.gov NCT05661370; https://classic.clinicaltrials.gov/ct2/show/NCT05661370

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KEYWORDS

dermoscopy; nevi; skin neoplasms; benign skin tumors; melanoma; skin cancer; medical education; eLearning; digital learning; diagnostic test; mHealth; mobile app; recognition training; skin lesions

Introduction

Skin cancer diagnostics and skin tumor triage are challenging, and mastery often requires many years of clinical practice. A previous study by our research group has shown that it takes 6-10 years to become proficient [1], while others have not found any correlation between primary care physicians' (PCPs) ability to diagnose and manage patients with skin cancer and years of clinical experience [2], rendering "bedside" education insufficient at best. Several strategies to help PCPs with this challenging task have been developed, including mnemonic techniques, checklists [3-10], and diagnostic Artificial Intelligence [11,12], neither of which can stand alone [13,14]. If properly trained, inspection of skin lesions using dermoscopy is associated with a higher detection rate of melanoma [15-17], a reduction in needed referrals and excisions [18-20], better management of pigmented skin lesions [21,22], and this provides an increase in melanoma sensitivity without a decrease in specificity [23] that is cost-effective [24]. Furthermore, comparing lesions over time using digital dermoscopy offers earlier detection [25]. Yet despite the strong evidence many PCPs still do not use dermoscopy [22,26], few have received training in dermoscopy [22], and those that use a dermoscope often do so without training [27], which has been suggested to decrease diagnostic ability [28]. Training in dermoscopy was the focus of a recent Cochrane review which highlights the need for research to identify the optimal approach [15]. Courses teaching dermoscopy with physical attendance improve PCPs' skills in skin cancer diagnostics in the short term but require refresher training to maintain the acquired skills [29]. Many different types of web-based or electronic learning have been used to improve the diagnostic abilities of PCPs [30]. A trial by our research group has recently shown that medical students with no clinical experience, by spending approximately 3.5 hours with a newly developed educational mobile app that presents the user with a digital large-scale interactive image repository (LIIR) containing patient cases and educational material, improved their diagnostic accuracy significantly from 31% to 52% [31]. This has never been tested among PCPs. With this study, we aimed to examine if self-paced training in skin cancer diagnostics using a LIIR with patient cases improves PCPs' diagnostic skills. In addition, we will investigate their ability to set the correct diagnosis (diagnostic accuracy) and to correctly classify digital patient cases as benign or malignant, their change in diagnostic confidence, and measure their time spent on the intervention.

Methods

Study Design and Setting

This randomized controlled trial used block randomization in blocks of 4, using a web-based randomizer [32] to generate a random number sequence of numbers 1 through 4. Participants were allocated continuously and sequentially as they signed up to either "Intervention" or "Control" with a 3:1 ratio, as we anticipated a large effect size of our primary outcome and desired further power for the analysis of data from the intervention group. Study recruitment was open for 30 days from mid-November to mid-December 2021.

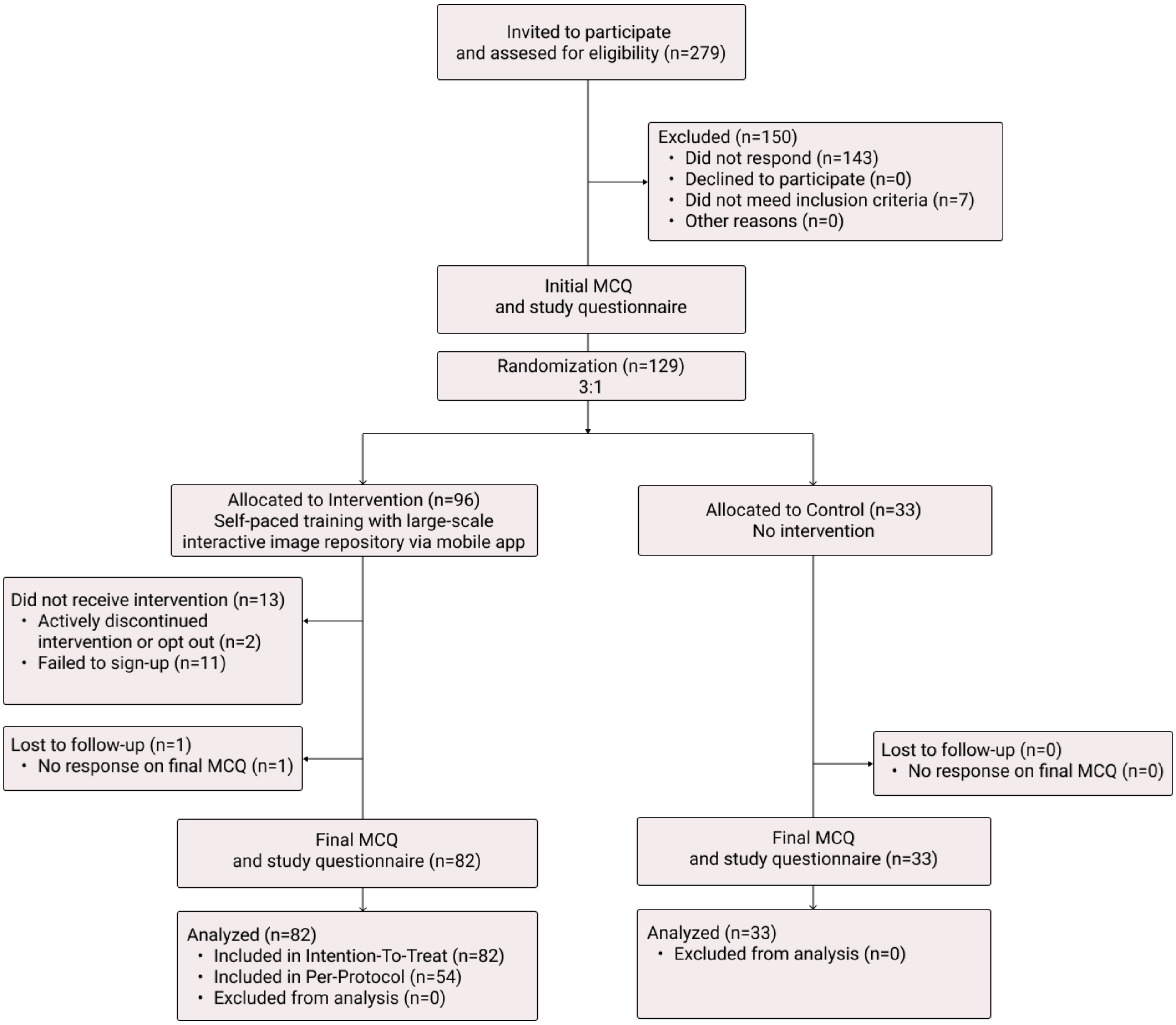
Participant Recruitment and Intervention

Eligible PCPs (doctors currently working in the primary care sector) were recruited at a conference in November 2021 (Lægedage) in Denmark by the speakers at 3 skin cancer and melanoma sessions. Interested physicians scanned a QR code and signed up to receive information material and an invitation to participate in the study by email, including a link to a web-based survey (Google Forms, Google Ireland Limited, 2022) which contained a consent form. The survey also included questions about their experience with and use of dermoscopy, including their confidence in their diagnostic abilities on a scale from 1 (low) to 4 (high), and ended with a skin cancer multiple choice questionnaire (MCQ) including 12 patient cases from a list of 25 skin lesion cases with previously established validity evidence [1]. The maximum number of points acquired on the test is 12, indicating high diagnostic accuracy.

Participants in the intervention group were invited to one of several web-based initiation meetings where they were instructed on how to download, install, sign up, and access the LIIR through a quiz-based smartphone app for practicing skin cancer diagnostics. Participants could also download and install the app independently using a pdf-guide. After installation, the participants in the intervention group were given 8 days of access from the day of their sign-up in the app, in which they were asked to diagnose 500 digital patient cases. They were sent email reminders on days 4, 7, and 8. After the 8 days, they were told to abstain from using the app for 8 days (washout period) before answering a final skin cancer MCQ with 12 new cases.

Participants in the control group continued their clinical practice as usual. They were not given access to the LIIR nor received any intervention before they completed the final skin cancer MCQ 16 days after their initial MCQ. See the study diagram in Figure 1.

Figure 1. Consort Diagram. Of the 96 participants allocated to receive the intervention, 13 did not receive it at all and did not finish the final MCQ, one did not finish the final MCQ, and 28 only received the intervention partially, resulting in 82 participants included in the intention-to-treat analysis and 54 in the per-protocol analysis. MCQ: multiple choice questionnaire.



Outcomes

The trial's primary outcome was the participants' score on a skin cancer MCQ before and after the intervention, with both per-protocol and intention-to-treat analysis.

Secondary outcomes included the progression of the participants' ability to correctly diagnose and classify digital patient cases in the LIIR across the intervention period, descriptive analysis of which diagnoses were most commonly misclassified and misdiagnosed, change in the participants' diagnostic confidence, and the average time spent training.

Blinding

Participants were unaware of their allocation until they had answered the initial questionnaire and MCQ. No measurements were taken to blind the principal investigator when receiving questionnaire responses and MCQ test results or when performing the statistical analysis comparing the 2 groups.

Large-Scale Interactive Image Repository

For the educational intervention in this study, we used the educational mobile app Dermloop Learn (Melatech ApS) [33] and its LIIR that has 3 main functionalities: Quizzes with anonymized digital patient cases, written learning modules, and user tracking.

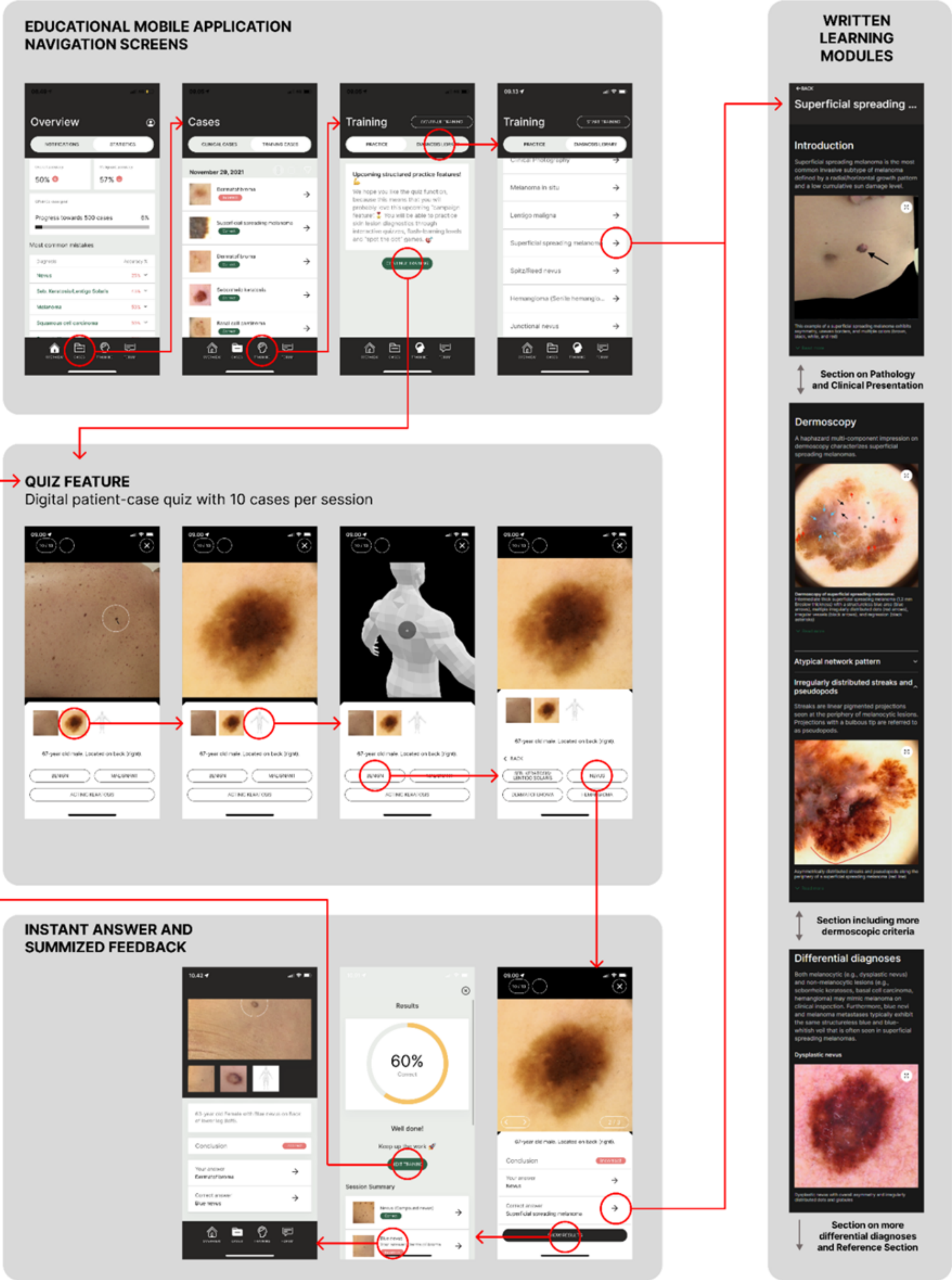
The app used a library of 2376 digital patient cases with a diagnosis (either confirmed by histopathology or clinical consensus of 2 or more clinicians) belonging to 1 of 7 diagnosis groups (nevus, seborrheic keratosis (SK) or solar lentigo, dermatofibroma, hemangioma, melanoma, basal cell carcinoma or squamous cell carcinoma) where any subtype was considered correctly diagnosed if the participant answered the diagnosis-group correctly (eg, "Melanoma" was correct for both superficial spreading melanoma and lentigo maligna). Each digital patient case included the age and gender of the patient, a clinical and a dermoscopic image of the lesion, and its location on a 3D avatar; all of which are referred to as a "case." See Figure 2 for an overview and example.

The participants trained in pattern recognition (quizzing) with sessions containing 10 cases selected from the library. One case was presented at a time with a clinical image, dermoscopic image, and the lesion's location. The participant selected benign (and picked the suspected diagnosis from among nevus, SK or solar lentigo, dermatofibroma, or hemangioma) or malignant (and picked the suspected diagnosis from among melanoma, basal cell carcinoma, or squamous cell carcinoma). Immediately after answering a case, the user got feedback on whether the answer was correct or not, what the correct answer was, and an option of being taken to a written learning module on the correct and incorrect answer, respectively. The smartphone app has written learning modules on 36 diagnoses and subdiagnoses corresponding to the diagnoses of the cases contained in the LIIR. Each written learning module has an introductory section followed by sections on histopathology, clinical presentation, dermoscopic features, and differential diagnoses to the diagnosis, all including illustrations or examples from the LIIR.

As the user answered cases, the app compiled a list of the diagnoses for which the individual user had the most difficulty giving correct answers. The list was shown on the front page of the app (Overview page in Figure 2), nudging the user towards reading the corresponding written learning modules. The app also tracked how many cases each user had diagnosed, their answer to each case, how long they spent with each case, what written modules they opened, and how long they spent reading each time they opened a written module.

The Dermloop Lean app underwent no changes, updates, or bug fixes and there was no downtime during the trial period.

Figure 2. The quiz-based smartphone app uses a digital large-scale interactive image repository, Dermloop Learn, in the version used in the study. The red circles indicate where a user would “press” to progress from one screen to another, and the red arrows indicate which screen is shown next. On the “Overview” screen, the user can navigate to “Cases” or “Training” to either see a list of previously encountered cases or start or continue a training session or access the “Diagnosis Library,” which contains a list of the 36 written learning modules on the included diagnoses and subdiagnoses. When using the “Quiz Feature,” the user starts a session with 10 patient cases. For each case, a clinical and dermoscopic image and the location of the lesion on a 3D avatar are shown. When the user presses benign or malignant, an array of new buttons representing the included benign or malignant differential diagnoses appear. When the user presses a diagnosis, they receive immediate feedback and buttons to the written learning modules on both the chosen and correct diagnosis. Once all 10 cases in a session are diagnosed a short report including the user’s diagnostic accuracy for the session and a list of the cases is presented. From here, the user can reexamine their answered cases or start a new session.



Statistical Analysis

Sample size and power calculations were done by assuming a 50% diagnostic accuracy at baseline. Based on the preliminary results of a previous study using the same intervention on medical students [31], we anticipated a 20% (SD 15%) effect of the educational intervention, which should let us show a difference between the groups by including 96 participants with a 3:1 allocation ratio with a statistical significance level of .05 and 80% power.

Based on the methods of the similar and recent study by our research group [31] using Generalized Estimating Equations, learning curves of the participants' probability to diagnose cases correctly were expressed as linear splines with a single knot at 100 cases using a logistic regression model with random intercept with correct diagnosis or not as an outcome. A similar model was made with the correct classification of each case as malignant or benign as the outcome. The participants' time spent reading and quizzing was summed separately for each 100-case period.

MCQ scores for both groups before and after the study period were compared using 2 tailed Welch 2 Sample *t* test.

In this study, the intention-to-treat analysis included those individuals who participated and also answered the final questionnaire. The per-protocol analysis included those individuals who completed the stipulated 500 cases.

Statistical analyses were performed in R [34] (version 4.2.0; R Foundation for Statistical Computing) using GEE R Pack [35,36] for the primary analysis and learning curves and Excel (Microsoft Corp) [37] for descriptive statistics of study questionnaire responses.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. All participating doctors were given oral and written information about the study. All participants were informed that filling out the survey was seen as consent to participate. There was no financial compensation for the participants in the study. The study intervention is an educational intervention for medical doctors with no patient participation which does not require ethics board review [38].

Results

Participant Demographics and Study Flow

A total of 279 people applied for more information about the study, 135 accepted the invitation and finished the initial questionnaire, of which 7 were excluded as they were not doctors from the primary care sector. Initially, 96 were randomized to the intervention and 33 to the control group. From the intervention group, 84 subsequently set up a user profile granting them access to the smartphone app and its LIIR, of which 82 answered the final MCQ and were included in the intention-to-treat analysis (see CONSORT [Consolidated Standards of Reporting Trials] diagram in Figure 1). Demographics on all participants and their experience with dermoscopy can be found in Tables 1 and 2. The intervention group completed 467 cases on average (median 505, range 0-1679), and 54 participants completed 500 cases (as per protocol) or more and were included in the Per-Protocol analysis. All 33 participants from the control group finished the final MCQ. The time from the initial to the final MCQ was 21 and 19 days for the intervention and control groups, respectively.

Table 1. Participant demographics.

Participant demographics	Intervention (n=82)	Control (n=33)	*P* value[a]
Age (years), mean (range)	40.7 (27-73)	41.4 (26-63)	.69
Gender, n (%)			
Male	36 (44)	17 (52)	.59
Female	46 (56)	16 (48)	.59
Clinical position, n (%)			
Intern (KBU)[b]	9 (11)	4 (12)	>.99
Resident (Intro)[c]	1 (1)	5 (15)	.01
Specialist Registrar[d]	29 (35)	4 (12)	.02
Consultant	43 (52)	20 (61)	.56

[a]*P* value derived from a chi-square or Fisher exact test.

[b]Klinisk Basisuddannelse," the first year after graduating.

[c]Introduction employment position, the second year after graduating.

[d]Typically the third-seventh year after graduating.

Table 2. Participants' responses on the questionnaire regarding experience with skin cancer diagnostics including use of and thoughts about dermoscopy.

Questionnaire on skin cancer diagnostics and use of dermoscopy	Intervention (n=82)	Control (n=33)	*P* value[a]
Years of experience with skin diagnostics, mean (range)	5.7 (0-30)	6.6 (0-20)	.48
Experience with dermoscopy, n (%)			
0-3 months	26 (32)	11 (33)	>.99
4-11 months	17 (21)	8 (24)	.87
1-2 years	21 (26)	5 (15)	.33
3-5 years	15 (18)	7 (21)	.92
6-10 years	3 (4)	2 (6)	.62
Training in skin cancer diagnostics or use of dermoscopy, n (%)			
None	15 (18)	6 (18)	>.99
Peer-To-Peer training	40 (49)	16 (48)	>.99
Self-initiated learning	51 (62)	22 (67)	.81
Web-based course in dermoscopy	2 (2)	3 (9)	.14
Physically attended a course in tumors of the skin	33 (40)	12 (36)	.86
Physically attended a course in dermoscopy	9 (11)	4 (12)	>.99
Patients per week seen on suspicion of skin cancer, n (%)			
0-2	50 (61)	16 (48)	.31
3-4	26 (32)	13 (39)	.57
5-6	4 (5)	4 (12)	.22
>6	0 (0)	0 (0)	>.99
Patients referred to a dermatologist or plastic surgeon each week on suspicion of skin cancer, n (%)			
0-2	78 (95)	32 (97)	>.99
3-4	4 (5)	1 (3)	>.99
5-6	0 (0)	0 (0)	>.99
>6	0 (0)	0 (0)	>.99
Access to some form of teledermatology, n (%)			
No	25 (30)	14 (42)	.31
Yes, for a select number of dermatological issues	13 (16)	4 (12)	.77
Yes, for nonpigmented skin lesions	20 (24)	6 (18)	.64
Yes, for all skin conditions	23 (28)	8 (24)	.85
Preferred technique or algorithm when inspecting potential malignant melanoma lesions, n (%)			
ABCDE[b]	71 (87)	25 (76)	.26
Ugly Duckling[c]	44 (54)	19 (58)	.86
Dermoscopic pattern recognition[d]	19 (23)	11 (33)	.37
No preferred technique	5 (6)	2 (6)	>.99
Preferred type of inspection when evaluating pigmented skin lesions, n (%)			
Dermoscopic inspection	60 (73)	26 (79)	.70
Naked eye inspection	40 (27)	74 (21)	.70
Preferred type of inspection when evaluating nonpigmented skin lesions, n (%)			
Dermoscopic inspection	48 (59)	22 (67)	.55
Naked eye inspection	52 (41)	78 (33)	.55
Access to dermoscope, n (%)			

Questionnaire on skin cancer diagnostics and use of dermoscopy	Intervention (n=82)	Control (n=33)	*P* value[a]
No	9 (11)	6 (18)	.36
Shared dermoscope in the clinic	42 (51)	12 (36)	.22
A colleague has one that I with difficulty can burrow	1 (1)	0 (0)	>.99
A colleague has one that can burrow easily	13 (16)	5 (15)	>.99
In my consultation room	17 (21)	10 (30)	.39
Diagnostic confidence on a scale from 1 (low) to 4 (high)	(1.6)	(1.6)	.81
Main advantage of using dermoscope, n (%)			
Fewer referrals to the dermatologist	17 (21)	6 (18)	.96
Earlier recognition of skin and mole cancer	43 (52)	18 (55)	>.99
Use of the dermoscope puts me at ease	13 (16)	4 (12)	.77
Use of the dermoscope puts the patient at ease	4 (5)	1 (3)	>.99
No advantages	1 (1)	1 (3)	.49
Main disadvantage of using dermoscope, n (%)			
Using a dermoscope requires experience	53 (65)	15 (45)	.09
The dermoscope is expensive	3 (4)	6 (18)	.02
The dermoscope is technically challenging to use	6 (7)	1 (3)	.67
Using the dermoscope is time-consuming	0 (0)	1 (3)	.29
No disadvantages	15 (18)	8 (24)	.64

[a]*P* value derived from a chi-square or Fisher exact test.

[b]"ABCDE" is the acronym for Asymmetry, Boarder, Color, Diameter, and Evolution or Elevation, a commonly used acronym in diagnosing melanoma without the use of a dermoscope.

[c]"Ugly Duckling" is a technique widely used to evaluate if a lesion is suspicious from a patient's other nevi.

[d]"Dermoscopic Pattern Recognition" refers to any technique used by the respondent to recognize dermoscopic features (patterns) indicating malignancy.

Intervention Effect

The average MCQ score of the PCPs in the intervention group (intention-to-treat analysis) improved from 52.0% (6.2 correct answers out of 12) to 66.4% (8.0 correct answers out of 12); an improvement of 14.3 percentage points (95% CI 9.8-18.9; *P*<.001). Those participants who diagnosed 500 patient cases or more (per-protocol analysis) on average improved from 53.9% (6.5 correct answers out of 12) to 70.5% (8.5 correct answers); an improvement of 16.6 percentage points (95% CI 11.3-22.0; *P*<.001). The MCQ score of the control group did not improve during the study period (*P*=.94). See Figure 3 for a box-and-whiskers plot of each group's initial and final MCQ percentages.

A post hoc analysis of the participant's initial MCQ score and their years of experience diagnosing skin lesions found no correlation, as shown in Figure 4.

Analysis revealed a statistically significant difference in MCQ scores between participants who diagnosed less than the protocolled 500 cases and participants who diagnosed 500 or more (1.5 points, *P*<.001; 95% CI 0.7-2.3), and post hoc analysis found similar results between participants who diagnosed less or more than 200 cases (1.5 points, *P*=.004; 95% CI 0.5-2.4), respectively, as depicted in Figure 5. There was no statistically significant difference between the MCQ scores of those participants that diagnosed between 449-549 cases and those that did 550 or more (*P*=.12).

The participants in the intervention group performed a total of 39,022 diagnostic evaluations during the study period. When comparing the participants' answers on the first (case 0-50) and last (case 451-500) 50 cases, we found that their probability of correctly classifying a case as benign or malignant increased by 6.6 percentage points from 67.1% (95% CI 65.0%-69.3%) to 73.7% (95% CI 72.5%-75.0%). Their probability of setting the correct diagnosis (nevus, melanoma, dermatofibroma, etc) increased by 10.5 percentage points from 42.5% (95% CI 40.2%-44.8%) to 53.0% (95% CI 51.3%-54.9%). Learning curves were most steep during the first 100 cases, as shown in Figure 6.

A descriptive analysis of the 39,022 diagnostic evaluations made by the participants during the entire training period showed that 72.6% of the malignant cases were correctly classified as malignant. Lesions were misclassified as malignant or benign 26.9% and 27.4% of the time, respectively. The most often misclassified benign lesions were seborrheic keratoses, compound nevi, and junctional nevi, which were classified as malignant in 31.9%, 28.9%, and 27.8% of the assessments, respectively. Lentigo maligna, nodular melanoma, and melanoma in situ were misclassified as benign in 48.7%, 42.2%, and 42.1% of the assessments, respectively. Participants guessed a different diagnosis than the correct diagnosis most commonly when assessing dermal nevi (misdiagnosed in 66.1% of cases), nodular melanoma (misdiagnosed in 63.4% of cases), and lentigo maligna (misdiagnosed in 61% of cases). See Table 3 for further details on the distribution of the participants' answers on these and all other diagnoses.

Figure 3. Box-and-whisker plot showing median scores (thick black horizontal lines), 95% CI (boxes), range (vertical whiskers), and outliers (circle) for the participants' MCQ scores before and after the intervention. Asterix indicates a statistically significant difference on 2-tailed Welch t test. MCQ: multiple choice questionnaire.

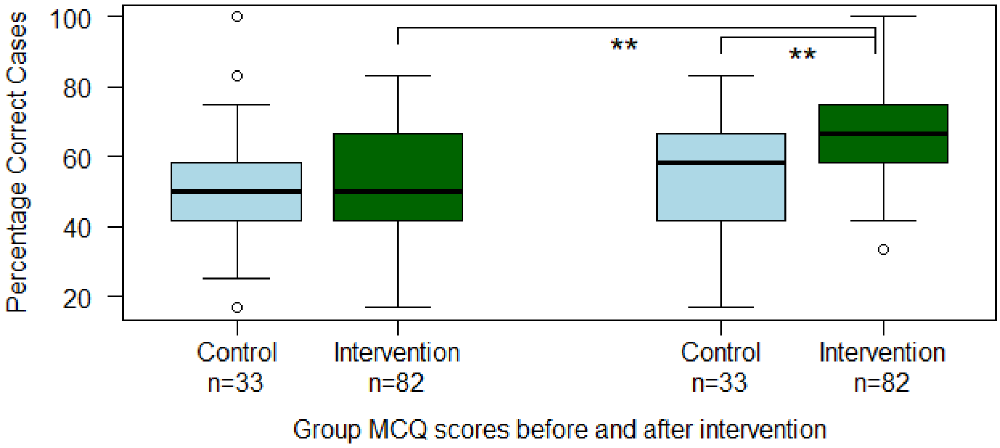


Figure 4. Scatter plot of all participants' scores on initial MCQ and their years of experience diagnosing skin and mole cancer. The trend line reveals no correlation between the 2. MCQ: multiple choice questionnaire.

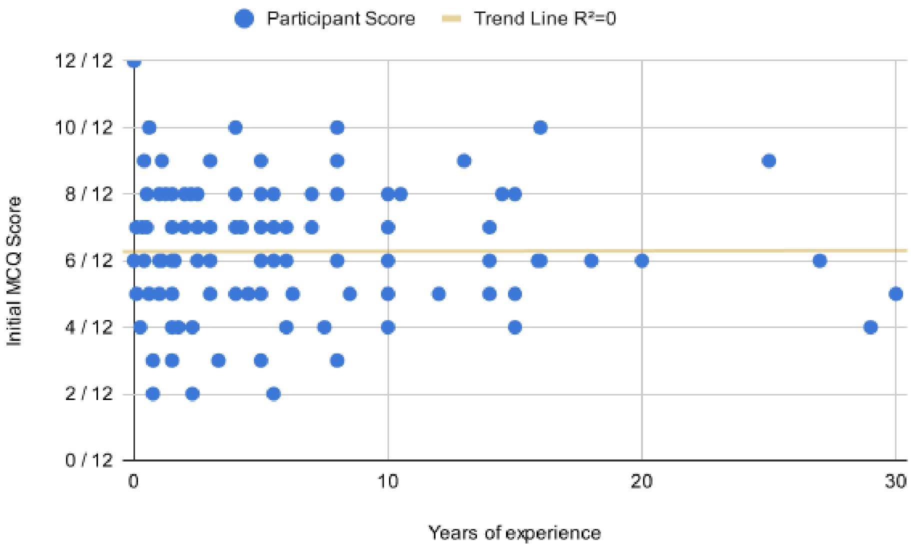


Figure 5. Box-and-whisker plot of participants' MCQ scores separated by their number of diagnosed patient cases. The figure shows median scores (thick black horizontal lines), 95% CI (boxes), range (vertical whiskers), and outliers (circle) for the participants' scores on their final MCQ test. Asterix indicates a statistically significant difference on 2 tailed Welch t test. MCQ: multiple choice questionnaire.

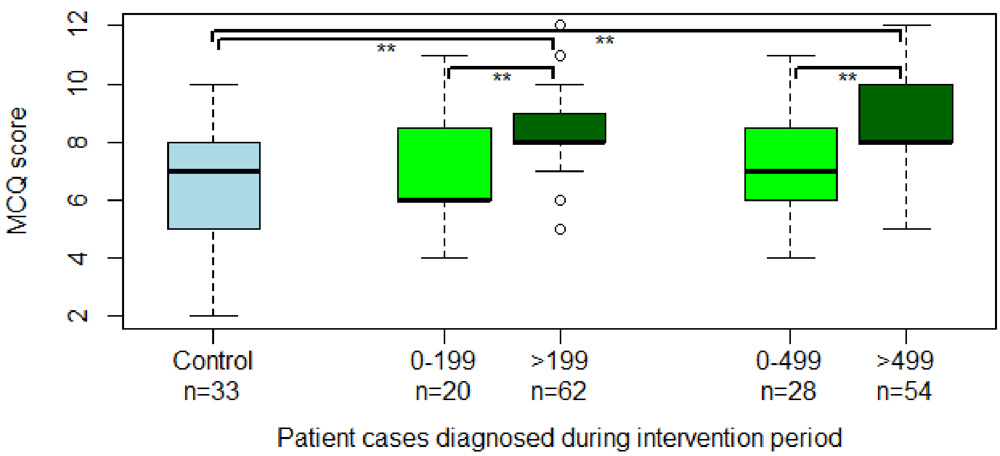


Figure 6. Learning curves for participants in the intervention group. The figure depicts the users' progressive means (solid black lines) and 95% CI (teal and light red areas). The solid red and solid dark blue lines, respectively, depict time spent quizzing patient cases and time spent reading written learning modules separated into 100-case segments with 95% CI shown using whiskers.

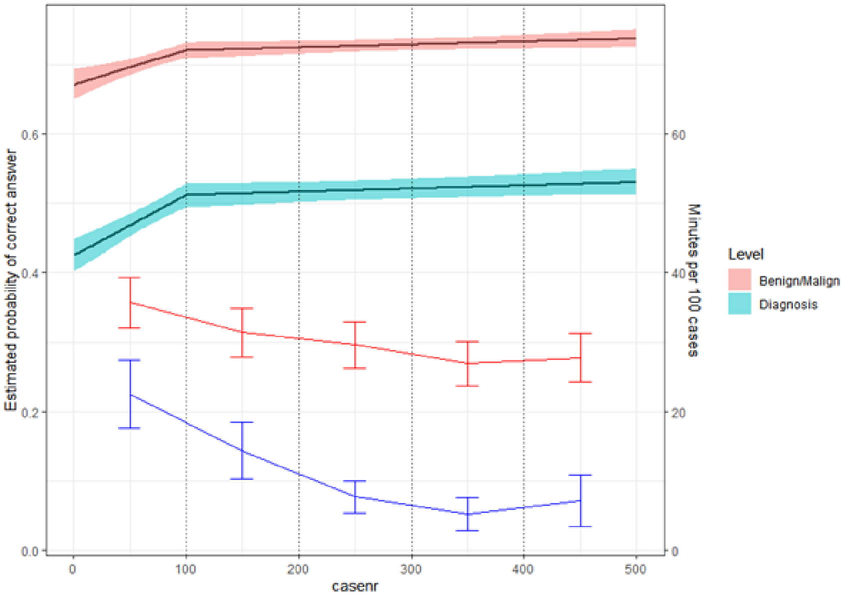


Table 3. The participants' 39,022 case answers were distributed across the true diagnoses with percentage, number of encounters, and totals for each row. Explanatory example: Of the 6194 times a seborrheic keratosis was seen, they were answered correctly as a seborrheic keratosis 50% of the time (3087 instances), and correctly classified as benign 68% of the time (4218 instances) and misclassified as malignant 32% of the time (1976 instances).

True diagnosis	Distribution of participants' answers									
	Benign, n (%)					Malignant, n (%)				Grand total, n (%)
	Dermatofibroma	Hemangioma	Nevus	SK[a] or Lentigo solaris	Benign total	BCC[b]	Melanoma	SCC[c]	Malignant total	
Benign										
Dermatofibroma	*1998 (51)* [d]	102 (3)	480 (12)	400 (10)	2980 (76)	332 (8)	438 (11)	176 (4)	946 (24)	3926 (100)
Hemangioma	234 (6)	*2539 (66)*	224 (6)	64 (2)	3061 (79)	280 (7)	280 (7)	239 (6)	799 (21)	3860 (100)
Blue nevus	45 (7)	53 (8)	*350 (52)*	48 (7)	496 (74)	24 (4)	150 (22)	2 (0)	176 (26)	672 (100)
Compound nevus	300 (6)	55 (1)	*2593 (49)*	846 (16)	3794 (71)	125 (2)	1384 (26)	34 (1)	1543 (29)	5337 (100)
Dermal nevus	58 (12)	41 (8)	*167 (34)*	130 (26)	396 (80)	44 (9)	39 (8)	14 (3)	97 (20)	493 (100)
Junctional nevus	30 (3)	5 (0)	*661 (57)*	141 (12)	837 (72)	9 (1)	309 (27)	4 (0)	322 (28)	1159 (100)
Spitz nevus	35 (19)	12 (6)	*84 (45)*	6 (3)	137 (74)	4 (2)	45 (24)	0 (0)	49 (26)	186 (100)
Lentigo solaris	79 (5)	0 (0)	279 (18)	*836 (53)*	1194 (75)	80 (5)	279 (18)	36 (2)	395 (25)	1589 (100)
SK	337 (5)	207 (3)	587 (9)	*3087 (50)*	4218 (68)	536 (9)	949 (15)	491 (8)	1976 (32)	6194 (100)
Benign total	3116 (13)	3014 (13)	5425 (23)	5558 (24)	*17,113 (73)*	1434 (6)	3873 (17)	996 (4)	6303 (27)	23,416 (100)
Malignant										
BCC	332 (8)	178 (4)	122 (3)	453 (11)	1085 (27)	*1597 (40)*	440 (11)	877 (22)	2914 (73)	3999 (100)
Lentigo maligna	3 (1)	2 (1)	21 (8)	104 (39)	130 (49)	26 (10)	*103 (39)*	8 (3)	137 (51)	267 (100)
LMM[e]	2 (2)	0 (0)	15 (11)	30 (23)	47 (36)	8 (6)	*74 (56)*	3 (2)	85 (64)	132 (100)
Melanoma in situ	47 (2)	4 (0)	494 (26)	267 (14)	812 (42)	57 (3)	*1040 (54)*	22 (1)	1119 (58)	1931 (100)
Nod. melanoma	1 (0)	63 (21)	52 (17)	13 (4)	129 (42)	34 (11)	*112 (37)*	31 (10)	177 (58)	306 (100)
SSM[f]	187 (4)	100 (2)	601 (12)	623 (12)	1511 (30)	284 (6)	*3132 (62)*	144 (3)	3560 (70)	5071 (100)
SCC	248 (6)	100 (3)	20 (1)	198 (5)	566 (15)	1069 (27)	110 (3)	*2155 (55)*	3334 (85)	3900 (100)
Malignant total	820 (5)	447 (3)	1325 (8)	1688 (11)	4280 (27)	3075 (20)	5011 (32)	3240 (21)	*11,326 (73)*	15,606 (100)
Grand total	3936 (10)	3461 (9)	6750 (17)	7246 (19)	21,393 (55)	4509 (12)	8884 (23)	4236 (11)	17,629 (45)	39,022 (100)

[a]SK: seborrheic keratosis.

[b]BCC: basal cell carcinoma.

[c]SCC: squamous cell carcinoma.

[d]Italicized figures represent true positives.

[e]LMM: lentigo maligna melanoma.
[f]SSM: superficial spreading melanoma.

Time Spent Quizzing and Reading

During the 8-day intervention period, participants from the intervention group, on average, spent 2 hours 26 minutes (ranging from 0 minutes to 8 hours 35 minutes) practicing pattern recognition (quizzing) and 41 minutes (ranging from 0 minutes to 3 hours 23 minutes) reading the written educational modules included in the app. The majority of the participants' reading activity was done at the beginning of the period and fell drastically after the first 100 cases (solid blue line in Figure 4). The average time spent diagnosing each case decreased from 36 to 28 seconds (solid red line in Figure 4).

Diagnostic Confidence

The participants in both groups initially had identical relatively low confidence in their diagnostic ability to diagnose skin lesions using a dermoscope of 1.6 on a scale from 1 (low) to 4 (high), which increased significantly for participants in the intervention group by 32.9% to 2.1% (P<.001) after the intervention, but not for the control group (P=.23).

Discussion

Principal Findings

Participants who used the LIIR increased their ability to set the correct diagnosis by 10.5 percentage points and their ability to correctly classify lesions as benign or malignant by 6.6 percentage points. The steepest part of the learning curve was seen during exposure to the first 100 patient cases. This is consistent with previous studies [31,39,40]. Our findings align with previous research, indicating no direct relationship between years of experience and diagnostic competence in assessing skin lesions [2].

This study of 115 PCPs is one of the largest randomized controlled trials testing an educational intervention on PCPs' ability to diagnose skin cancer [30] and the most extensive study using self-paced learning with a LIIR as the main component in the educational intervention. The participants were given no compensation for their time spent, which was done primarily in their spare time. Despite the trial period extending across the busy time before and during Christmas and New Year, the study had a high level of adherence. Of the 96 participants randomized to the intervention, 82 (85%) received it. A total of 12 participants did not manage to download and install the mobile app, which was yet to be released to the general public at the time. Despite this, 54 (62%) received the educational intervention as per protocol, and there were no dropouts from the control group. This level of adherence is similar to or higher than that of previous studies with a comparable intervention [30,41-43]. Post hoc calculations revealed a 98.1% statistical power for the intention-to-treat and 99.8% for the per-protocol analysis.

Limitations

Limitations of this study include the recruitment method of inviting doctors at continuing education sessions about skin cancer. These doctors were perhaps more interested in or concerned about skin cancer diagnostics than the general population of PCPs. Evidence of this was that our participants had a relatively high initial diagnostic accuracy, most (84%) reported having access to a dermoscope in their clinic, and the percentage of participants who had received training (not including peer-to-peer and self-initiated training) in dermoscopy was also relatively high (46%). The effect of the educational intervention would possibly be more distinct in the general PCP population, where a lack of specific training in skin cancer diagnostics is more common [22]. Our study did not test long-term retention, and it is likely that the acquired skills will fade without continued use of the educational material [29]. Another limitation was that the 2376 patient cases presented in the LIIR were extracted from a department of dermatology and therefore likely to be more difficult than what is generally seen by the PCP. Therefore, the diagnostic accuracy found in this study might not reflect the PCPs' diagnostic accuracy on the patients they meet in their clinic. Another discrepancy between diagnosing cases using the LIIR and the clinical examinations of a patient's skin is that when encountering an irregular nevus in the clinic, examination of the patient's other nevi may reveal that the nevus resembles the patient's other nevi and therefore not an "ugly duckling," but rather "regularly irregular," reducing the suspicion of melanoma. Yet, with these cases being evaluated 39,022 times, it does reveal the most common diagnostic pitfalls in the population and where to intensify future educational interventions: SK, early melanomas, and nodular melanoma.

It was our initial hypothesis that PCPs, who possess the ability to apply the educational material in a clinical context, would exhibit a steeper learning curve with a higher end point from using this educational tool compared to medical students [31]. Contrary to our hypothesis, we did not observe a difference in the learning curve between primary care providers and medical students. One potential reason for this could be that primary care providers have a greater awareness of the consequences of their diagnostic decisions, which may have limited their assessment of the patient cases. They may have reacted as in the clinical setting and rather chosen a more serious diagnosis than miss a potentially malignant lesion.

As PCPs are the first to triage patients with skin cancer, improving the diagnostic accuracy of PCPs is necessary as the incidence of skin cancer has been rising [44,45] and is expected to keep rising [46-48]. The underlying causes for this growing disease burden are likely multifactorial, including biological and demographic factors such as increased ultraviolet exposure and a rapidly aging population. Skin cancer screening and general awareness increase the number of patients referred and biopsied [49], straining an already hard-pressed health care system. Adding to that, it has been stipulated that revised histopathologic criteria and historic underdiagnosis [50] but also current overdiagnosis [49,51,52] may contribute significantly to the growing incidence of skin cancer. It has previously been shown that increased awareness of skin cancer of PCPs does not increase the number of patients biopsied or referred to the dermatologist, etc [53], but rather that education and use of a dermoscope reduce the number needed to biopsy to detect melanoma in the primary health care setting [54]. Our results show a marked increase in the participants' diagnostic confidence, which often does not correlate with diagnostic competence. Yet, with PCPs feeling more confident in their abilities, they could engage in doing more digital sequential follow-up, which has higher diagnostic accuracy than single-appointment evaluations [25]. This could potentially reduce the number of referrals and biopsies even further, leading to fewer excisions and, thereby, fewer overdiagnosed "melanomas" [55,56].

With the results of this study, we can address one of the leading causes of reluctance toward using dermoscopy in general practice: The time needed for training [57]. As digital education is easily accessible, can be acquired flexibly and on-demand, and does not require the participant to travel to and from the educational institute, it might be a more efficient way of increasing the diagnostic accuracy of multiple participants over a short period at a low cost. Our results show that the time needed to improve diagnostic skills using dermoscopy might not be more than a few hours at one's own pace.

The perspectives of these results are potentially quite important; however, this trial did not test whether the observed improvements in diagnostic accuracy transfer to the participants' clinical diagnostic accuracy and, in turn, if it changed their clinical patient management. This transfer of knowledge and its effect on clinical patient management should be the focus of future research.

Conclusions

Using self-paced training in skin cancer diagnostics using a digital LIIR with patient cases delivered by a quiz-based mobile app improves PCPs' diagnostic skills and confidence. The time spent by each participant does not need to be very long, nor must it be done in 1 sitting. Significant improvements can be seen from an average of 3.5 hours over the course of 8 days.

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Conflicts of Interest

NKT is the Chief Executive Officer of the software company Melatech ApS, which has developed the mobile app Dermloop Learn. The remainder of the authors have no conflicts of interest.

Multimedia Appendix 1
CONSORT-EHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 1420 KB - derma_v6i1e48357_app1.pdf]

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Abbreviations

LIIR: large-scale interactive image repository
MCQ: multiple choice questionnaire
PCP: primary care physician
SK: seborrheic keratosis

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Review

Use of Social Media for Patient Education in Dermatology: Narrative Review

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Abstract

Background: Social media has rapidly become one of the main avenues for news and communication among those with access to technology. Nearly 60% or 4.7 billion people worldwide use social media. Different social media networks provide users with a barrage of posts, opinions, and transformations. With this noticeable uptick in physician and patient education usage of social media, exploration of the impacts of social media on patient education in dermatology is crucial.

Objective: The goal of this narrative review was to evaluate existing peer-reviewed literature examining the use of social media for patient education in dermatology and to establish trends and implications. Additional attention was given to different social media sites, and potential differences in modalities of posts such as short-form videos on TikTok and Instagram Reels, long-form videos on YouTube, and infographics on Twitter, Instagram, and Facebook.

Methods: PubMed, Access DermatologyDxRx, and Scopus searches of peer-reviewed publications were performed to discover articles with social media and patient education keywords in combination with other health care–relevant or dermatology-relevant keywords. Subsequently, the screening of these studies was performed by the author who has experience with education and research experience in health care, dermatology, social media, and telehealth. Ultimately, the selected articles were summarized through qualitative analysis of key points and presented for further discussion.

Results: Through this narrative review, the researcher was able to identify several publications focusing on dermatology and social media. Some common subject areas included the use of social media for the promotion of private dermatology practices, residency programs, and research journals. So long as providers, such as dermatologists, take ethical considerations into account, these platforms can provide patients with curated educational content. In addition, several publications emphasized the use of social media as a form of patient education on dermatologic conditions but also as a source of misinformation.

Conclusions: This narrative review illuminated the use of social media as a form of patient education for dermatology, with its applications addressed across many demographics and situations. As social media platforms continue to update their algorithms, content filters, and posts, social media may become a reputable form of patient education in dermatology. Future studies and innovations should continue to explore innovations in this space, the efficacy of different modalities of posts, and longitudinal differences in patient outcomes and health literacy.

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KEYWORDS

dermatology; health literacy; innovation; patient education; social media

Introduction

The popularity of social media platforms has increased over the past decade with nearly 60% or 4.7 billion people worldwide using social media [1]. These platforms allow users to engage with people beyond their in-person social sphere, and many users use social media for anything from catching up on news to learning about a topic. Different social media platforms allow for different user experiences to cater to their different wants and needs. Considering the COVID-19 pandemic, even more time has been spent on social media and on the internet. The average daily time (in minutes spent on social media worldwide) has increased to 63.3% from 2012 to 2022 [2]. Over time, social media usage has become a mainstay in the daily routine of billions.

Among social media's many uses, a few are of crucial and rising importance: a source of misinformation, a source of patient education, and a promotion for private practices and academic research. Of all dermatology content created on social media platforms, content creators consisted of nonphysicians (52%), physicians (32%) of which 84% were dermatologists, and private companies (16%) [3]. This suggests that much of the content currently circulating is not created by dermatologists. Many platforms recognize that content requires additional moderation to combat the spread of misinformation. For example, Facebook and Instagram have recently instituted third-party fact-checking software, and TikTok has a duet feature that allows physicians to dispel misinformation directly [4]. Health misinformation can lead to a plethora of issues. Some examples include undergoing risky procedures or taking remedies without a clear idea of the potential benefits and side effects. Some patients are now using social media to discover and determine which dermatology practices to frequent. Indeed, in a recent survey, 66% of participants indicated that they went to a dermatologist that they knew about and 21% of participants indicated that they knew about their dermatologist solely from social media content alone [5]. It is likely that as the number of dermatologists using social media for their practices increases, this number may increase as well.

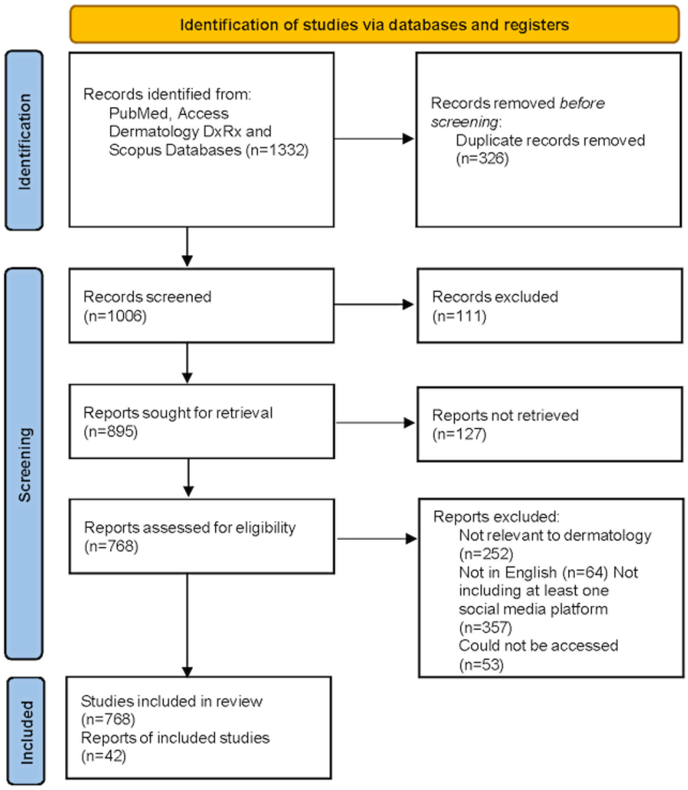
As social media platforms continue to expand and develop new features, understanding how to tackle misinformation and use social media for patient education in dermatology are crucial areas for consideration. Given social media's increasing popularity as a source of information and their established utility as a means of enhancing human communication, research must consider their growing influence on patients and the spread of current innovations. Effective social media practices are crucial to building a community of users that trust the information that they are being presented with. As such, physicians should be aware of and develop effective social media practices to cater to younger populations without sacrificing patient privacy or professionalism. Integrating social media as a component of private practices, programs and academic research journals can help combat misinformation, promote health literacy, and allow patients to make more informed decisions about their care [6]. Furthermore, if used properly, social media can also help to increase diversity and inclusivity by increasing the opportunity for more open discussions among trainees, physicians, and patients, with different skin conditions across a variety of demographics [7].

Methods

A PubMed, Access DermatologyDxRx, and Scopus survey of peer-reviewed publications was conducted from July 2022 to January 2023 to discover relevant articles related to social media and social media usage in the contexts of dermatology and academia. The publications selected were published between May 2014 and January 2023. PubMed, Access DermatologyDxRx, and Scopus databases were used for this narrative review although many duplicate sources were found. It is important to note that many of the articles had a specific focus on 1 or 2 social media sites; however, some articles drew broader comparisons across all social media platforms. For clarity, we broadly discuss social media platforms and emphasize specific examples in the literature as needed. For the purpose of this study, social media, social media apps, and social networks are terms that are used interchangeably. In the initial screening, literature searches were conducted using combinations of keywords, such as "dermatology," "dermatologists," "dermatology journals," "dermatology education," "social media," "social network," "misinformation," and "patient education." A data analysis plan and inclusion and exclusion criteria were established before screening to minimize potential biases. A total of 1006 records were screened, of which, 895 were sought for retrieval and 768 were assessed for eligibility. Figure 1 shows the process using a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram. These sources were individually examined by the researcher for relevance and recency. Sources were included if their claims were corroborated in other peer-reviewed literature. Triangulation of sources was used to ensure that the data were valid and reliable. Each individually examined publication required a detailed review for inclusion to ensure relevance and ensure that the publication was focused on social media platforms and not just used in the discussion section. Study selection and subject area determinations were confirmed in consultation with a dermatology researcher with editorial experience in health care and social media. Disagreements were resolved in discussion with a third-party researcher in the department. Any duplicate results and non-English publications were excluded except for 1 article that had been translated into English from Spanish and another article that had been translated into English from German.

A narrative review format was selected as opposed to another type of systematic review because of its broader scope and ability to focus on observed trends. Narrative reviews typically do not require the presentation of reporting methodology, search terms, databases used, and inclusion and exclusion criteria; however, many of these are included in this study to ensure as much detail and transparency as possible [8]. The PRISMA guidelines checklist was adhered to complete this manuscript. For instance, these guidelines informed eligibility criteria for the studies, search strategy, certainty and bias assessments, implications for practice, and limitations [8]. The aim of this study was to formulate a narrative review of recent and relevant literature, so a qualitative analysis focused on examining the use of social media in dermatology with an emphasis on different social media platforms and different uses of social media. After the literature was evaluated, findings were synthesized, trends were established, and future implications were established. A small group of articles, grouped by subject areas established from observed trends, were selected for in-depth discussion.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram for the identification of studies [8].



Results

Overview

This narrative review draws from 42 recently published articles on patient education, social media usage, health misinformation, and dermatology. Many of these studies were published from research teams in the United States. However, a few of the studies were published in other countries, including Canada, Saudi Arabia, Turkey, Spain, Croatia, Germany, India, China, France, and Australia. These were analyzed after screening relevant literature, and many of the articles were published within the past 3 years. Of the current literature, there were several main subject areas including health misinformation, patient education, professionalism, and other potential uses of social media in dermatology. A narrative review of our findings has been outlined in the following sections, which have been organized based on these main subject areas. A summary of the studies used and examined, including country, year of publication, and platform, is summarized in Tables 1-4.

Table 1. Summary of articles in narrative review: health misinformation.

Authors	Country	Year of publication	Platform	Summary/key findings
Salah et al [9]	Saudi Arabia	2022	YouTube	Study shows a low overall accuracy and quality of YouTube videos on vitiligo.
Yeung et al [10]	Canada	2022	TikTok	Study shows approximately half of the analyzed TikTok videos about ADHD[a] were misleading.
Szeto et al [4]	United States	2021	All	Study shows the potential for the propagation of inaccurate or even dangerous information is high.
Park et al [11]	United States	2018	Instagram	Study shows 45% of consumers report that social media health information influences their decision to seek care.
Yousaf et al [12]	United States	2020	Instagram, Reddit, YouTube	Study shows only 31% of participants consulting social media made changes fully aligned with AAD[b] clinical guidelines.
Reddy [13]	United States	2021	Reddit	Study shows advice on the Reddit subreddit lacks evidence and pseudoscientific recommendations are often accepted as factual.
Zamil et al [14]	United States	2022	Instagram	Study shows that there is a prevalence of dermatologic supplements on social media with inaccurate health claims.

[a]ADHD: attention-deficit/hyperactivity disorder.

[b]AAD: American Academy of Dermatology.

Table 2. Summary of articles in narrative review: patient education.

Authors	Country	Year of publication	Platform	Summary/key findings
De Angelis et al [15]	Canada	2018	Discussion forums	Study shows health professionals find discussion forums and collaborative projects to be useful social media platforms to facilitate chronic disease self-management with patients.
Guzman et al [16]	United States	2020	YouTube	Study shows social media's merits to help facilitate chronic disease management for patients.
Cooper et al [17]	United States	2022	All	Study shows social media's use as a form of education for common dermatologic conditions.
Kaundinya et al [18]	United States	2020	All	Study shows that existing web-based resources for cirrhosis are too long and complex.
Karimkhani et al [19]	United States	2014	Instagram	Study shows how Instagram is used for engaging and informing patients.
Mansour et al [3]	United States	2022	TikTok	Study shows the effectiveness of TikTok patient education content for Keratosis Pilaris.
Nguyen et al [20]	United States	2021	TikTok	Study shows the content and creators making dermatology videos on TikTok.
Whitsitt et al [21]	United States	2015	Pinterest	Study shows informative pins were the most common (49%) followed by advocacy (37%) and home remedies (14%).
Daneshjou et al [22]	United States	2021	Twitter	Study shows how academic Twitter is used to spread health care information and promote research collaboration.
Chirumamilla and Gulati [23]	United States	2021	All	Study shows scientific communication on social media as a form of patient education benefits health literacy.
Boyers et al [24]	United States	2014	YouTube	Study shows of the total videos, 35% were uploaded by or featured an MD/DO/PhD in dermatology or other specialty/field, 2% FNP/PA, 1% RN, and 62% other.
Morrison et al [25]	United States	2019	Facebook	Study shows social media is an opportunity for targeted public health interventions for skin cancer.
Patel et al [26]	United States	2017	Snapchat	Study shows limited use of Snapchat by Dermatologists and professional entities.
Liakos et al [27]	United States	2021	Instagram	Study shows that social media, in particular Instagram, can be a successful platform to enhance the exposure of peer-reviewed medical information.
Correnti et al [28]	United States	2014	Tumblr	Study shows Tumblr remains a social media domain that lacks a strong presence from dermatology journals and organizations, remaining an untapped resource for information dissemination and interaction with the public.
Güder and Güder [29]	Turkey	2022	Instagram	Study shows hashtags used by physicians in their social media posts should be chosen from the words used in the folk language.
Taberner [30]	Spain	2015	All	Study shows that different social media sites may play different roles in patient education for dermatology.

Table 3. Summary of articles in narrative review: professionalism.

Authors	Country	Year of publication	Platform	Summary/key findings
Vukušić Rukavina et al [31]	Croatia	2021	All	Study shows existing recommendations for including e-professionalism in the educational curriculum for health care professionals.
Ahmed and Lipoff [6]	Germany	2022	All	Study shows benefits, risks, and role of dermatologists in social media content creation.
Janagond and Inamadar [32]	India	2021	WhatsApp	Study shows considerations for clinical photography utilizing WhatsApp.
Militello et al [33]	United States	2021	All	Study shows many dermatologists are currently influencers, but this requires formal training and the need to monitor online presence to prevent legal consequences.
Ko et al [7]	United States	2017	All	Study shows potential considerations for trainees and physician dermatological education.
Zhu et al [34]	China	2019	TikTok	Study shows the use of social media as a form of health communication for provincial health committees.

Table 4. Summary of articles in narrative review: other uses.

Authors	Country	Year of publication	Platform	Summary/key findings
Voillot et al [35]	France	2022	All	Study shows the benefit of social media support groups for patients with Atopic Dermatitis.
Hill et al [36]	United States	2018	Google+	Study shows the differential usage of Google+ for private practices in dermatology and dermatology journals.
Hopkins et al [37]	United States	2020	All	Study shows the influence of social media on cosmetic procedure popularity as measured by Google Trends.
Tan et al [38]	United States	2020	WeChat	Study shows the importance of cultural considerations in patient health-seeking behavior on social media.
Albeshri et al [5]	Saudi Arabia	2020	All	Study shows the role of social media in dermatologist selection by patients.
Patel et al [39]	United States	2018	All	Study shows among the professional dermatology organizations, 114 (47.1%) were on Facebook, 69 (28.5%) on Twitter, and 50 (20.7%) on LinkedIn. In comparison, 68 (87.2%) patient-centered organizations were on Facebook, 56 (71.8%) on Twitter, and 56 (71.8%) on LinkedIn.
Vasconcelos Silva et al [40]	Australia	2020	Twitter	Study shows sharing by celebrities or non-health–related organizations and individuals with a high following can all contribute to greater spread of skin cancer and sun-related messages.
St Claire et al [41]	United States	2019	All	Study shows of the 126 dermatology residency programs, 29 (23%) were active on Facebook, 14 (11%) on Twitter, and 9 (7%) on Instagram.
Petukhova et al [42]	United States	2020	Facebook	Study shows themes in a keratinocyte carcinoma support group including personal experience and provided psychosocial support (50%), there were a significant number of posts offering medical advice (35%), with most of such replies being unsupported by evidence-based medicine (87%)
Sharifzadeh and Smith [43]	United States	2022	Facebook, Twitter, and Instagram	Study shows that increased social media use resulted in a greater number of reviews, but not necessarily higher ratings.
Muralidhara and Paul [44]	United States	2018	Instagram	Study shows the most prevalent health information on social media is related to diet and exercise.
Gorman et al [45]	United States	2023	All	Studies have shown that skin cancer education should be expanded to include the skin of color patients and that social media is used by many individuals who otherwise do not have access to this information at frequent doctor appointments.
Zamil et al [14]	United States	2022	Instagram	Study shows that there is a prevalence of dermatologic supplements on social media with inaccurate health claims.

Health Misinformation

Generally, it is known that health misinformation can spread quickly due to technology, such as social media platforms. On forums such as Reddit, which allow users to anonymously share information, a large portion of advice surrounding skincare lacks evidence, and pseudoscientific recommendations are also often accepted as factual [13]. This highlights one key issue with social media communities—the predisposition of these communities to becoming echo chambers that uphold pseudoscientific or otherwise not scientifically proven advice. To determine whether claims were valid, articles typically compared claims with American Academy of Dermatology (AAD) clinical guidelines for the condition and measured DISCERN scores. The latter, DISCERN, is a questionnaire that provides users with a valid and reliable way of assessing the quality of written information on treatment choices for a health issue [46]. Overall, health information on skincare for a variety of conditions appeared to contain misinformation across social media platforms.

However, misinformation may also be able to be combated through social media. A promising finding was that a recent study found that 68% of respondents who used social media for acne treatment advice were more likely to consult a medical professional [12]. This may result in more individuals seeking professional insight from dermatology professionals that may help counter misinformation encountered on social media. DISCERN scores indicate that there is a statistically significant difference in the quality of content between health care and non–health care sources (*P*=.009) [9]. Outside of dermatology content on social media, similar findings appear for other health information. Indeed, user-generated content on attention-deficit/hyperactivity disorder on TikTok has low actionability, with non–health care providers uploading the majority of misleading videos and health care providers uploading higher quality and more useful videos [10]. This may suggest that having more health care sources producing content can help increase the availability of quality health information on social media. On platforms like Instagram, self-identified dermatologists were responsible for only 16% of top dermatology posts, and only 5% of the top posts were made by the American Board of Dermatology–certified dermatologists [11]. This indicates that there are not only more posts made by nondermatologists on dermatology across social media but that more dermatologists using social media may provide higher-quality health information. Many of the articles agree that dermatologists should increase their presence on social media apps to counteract misleading information with evidence-based knowledge [4].

Patient Education

A key component of this narrative review focuses on social media as a potential tool for patient education and distributing patient education materials. To determine the effectiveness of patient education materials, some studies used the Patient Education Materials Assessment Tool (Audiovisual Materials) to assess readability [18]. Considering that the average readability level in the United States is at a sixth-grade level or lower, many health materials may be perceived by individuals as difficult to understand [18]. It has been well established that young, White, and educated patients tend to have higher health literacy, whereas those from lower socioeconomic backgrounds, rural areas, and minority groups tend to have lower health literacy. Social media may provide an opportunity to close this health literacy gap by providing less complex patient education materials in a variety of formats, including video and infographics. Although social media is often associated with younger people, older demographics have also been increasingly using social media to increase their health literacy [23]. Patients are not only able to use social media to learn more about conditions but also use social media to lobby for decreases in disparities of care [23].

A main hurdle to understanding various health conditions has to do with the complex and often technical verbiage. A key part of the scientific process depends upon communication and dissemination of research findings, also referred to as scientific communication [22]. Many words typically used in academia and by physicians are often technical and, therefore, inaccessible. Simple changes such as using hashtags that use folk or colloquial language in lieu of complex terminology may help to improve accessibility [29]. Twitter, specifically a subset of users referred to as “academic Twitter,” provides a novel avenue for scientific communication. By using Twitter, the academic community can quickly disseminate information, and due to character limits on posts, much of this information is condensed and simplified [22]. A post, referred to on Twitter as a tweet, can consist of a single-sentence summary of a paper, an image of a key figure, the account names of the journal and scientists involved, and relevant keywords in hashtag format [22]. The use of social media to post articles demonstrated a significant (*P*<.0001) positive effect on both views (mean difference 175.5, SE 16.4) and downloads (mean difference 31.5, SE 4.0) when compared to matched articles not published on social media [27]. Social media may therefore be able to expand the reach of research articles and academic journals that are otherwise typically only accessed by individuals within the field.

Social media advertising, such as through Facebook Ads, is a feasible approach to reaching individuals within a target population with public health interventions [25]. Indeed, Facebook Ads allow users to specify a target demographic including their age, location, and other pieces of information. Compared to traditional outlets, health behavior changes, such as avoiding tanning beds to prevent skin cancer, can be quickly brought to the attention of relevant users [25]. Across the major social media sites such as Instagram, Pinterest, YouTube, Snapchat, and Tumblr, as recently as 2015 many journals and private practices did not have accounts [19,21,24,26,28]. This means the use of targeted social media advertising and, more broadly, the usage of social media by the dermatology community is a very recent phenomenon. TikTok, the largest growing social media network since 2019, has rapidly become one of the most used social media platforms for accessing health posts [20]. TikTok is also perhaps one of the most user-catered social media networks in use today. A key feature of TikTok is the For You Page that provides each user with tailored video content based on their interests, likes, and dislikes. As patients increasingly turn to social media for health information, dermatology-related TikTok videos have gained appeal as they provide education by laypeople for laypeople [20]. Yet, unlike other sites, board-certified dermatologists accounted for 15.1% of total posts but authored a significant percentage of posts with the hashtag "dermatology" (45%) [20]. This may suggest a higher presence of dermatologists on TikTok. Regardless, it will be important for dermatologists to continue to adapt to digital media to find new and efficient ways to communicate with patients and the broader scientific community [30].

Professionalism

There exist several benefits and dangers of social media not only on patient education but also professionalism on the part of dermatologists and trainees. Some dangers of social media on professionalism are as follows: (1) less accountability, (2) breaching confidentiality, (3) blurred professional boundaries, (4) depiction of unprofessional behavior, and (5) legal issues [31]. These dangers may also exist when some health professionals use social media platforms to facilitate disease self-management, although this is still a relatively rare phenomenon due to the amount of time required by the physician [15]. However, a notable benefit to social media usage is that each platform has unique qualities and features that people can use to educate and learn [17]. Currently, the top 5 platforms are Twitter, Instagram, TikTok, YouTube, and Facebook [17]. So long as providers, such as dermatologists, take ethical considerations into account these platforms can provide patients with educational content catered to their learning style and preferred modality [17]. Dermatologists must also balance creating educational content and maintaining ethical standards while also remaining transparent about commercial interests such as brand sponsorships [16,33].

Other Potential Uses of Social Media in Dermatology

It is important to consider how social media provides users with support and knowledge which can help them better advocate for themselves in health care settings. Support groups on social media can be a form of psychosocial support since these groups allow individuals to share their personal experiences and openly discuss their concerns [42]. Private groups, such as those on Facebook for patients with skin cancer, can allow for a close-knit community experience on a large social networking site [42]. Because patients are able to candidly discuss treatments, their perceptions, and commentary on their quality of life, social media can be a crucial tool in the development of new approaches that consider patient concerns [35]. Beyond psychosocial support, patients can use these forums to broaden their understanding of their condition and treatment options, which can empower them to have more productive discussions with their health care provider and to ultimately make more informed health decisions.

Another potential use of social media in dermatology is the promotion and marketing of academic journals and trainee programs. However, social media has been underutilized in this space. Google+ is another example of a social media site and its uniqueness lies in its search engine optimization services. Although some private practices are on Google+, the majority of dermatology journals have yet to use Google+ to expand their audiences [36]. As of 2018, there were 22 (17.7%) dermatology journals active on Facebook and 21 (16.9%) on Twitter [39]. Among the professional dermatology organizations, 114 (47.1%) were on Facebook, 69 (28.5%) on Twitter, and 50 (20.7%) on LinkedIn [39]. This suggests that dermatology journals have been slower at using social media and establishing a social media presence compared to professional organizations and private practices. Residency programs for dermatology have had similarly slow social media uptake. As of 2019, of the 126 dermatology residency programs, 29 (23%) were active on Facebook, 14 (11%) on Twitter, and 9 (7%) on Instagram [41]. Other groups, such as Provincial Health Committees in China, have started to expand their TikTok presence to engage with local residents and communicate public health information [34].

Yet another use of social media in dermatology is to promote private practices and individual providers. However, it is crucial to reiterate that dermatologists must do so while maintaining ethical standards, remaining transparent about commercial interests such as brand sponsorships, and maintaining patient consent for sharing images [16,32,33]. Not all social media sites are created equal. Interestingly, the terms *dermatologist*, *Botox*, *Juvederm*, *Radiesse*, *CoolSculpting*, and *Kybella* were associated with both Instagram and Facebook users, but *blepharoplasty* and *rhinoplasty* were only associated with Instagram users ($P<.01$) [37]. Although many individuals state that they trust Dermatologists, celebrities with a high number of followers also achieve a substantial amount of likes and influence on skin cancer–related communication on sites like Twitter [40]. Besides sharing educational content, dermatologists should also remain up-to-date on understanding social media trends and advising patients to exercise caution in regard to invasive, potentially dangerous cosmetic procedures without doing their own research [38,44]. With these considerations in mind, many Dermatologists are using social media to promote themselves and their private practices. Many patients learn about their dermatologist from social media and dermatologists who maintain a social media presence typically have higher web-based reviews [5,43]. All this is to say, there are benefits for dermatologists to stay up-to-date on social media.

Discussion

Principal Results

It can be suggested that social media has been leveraged as the latest form of patient education in dermatology. Using social media can help to bridge patient-provider relationships, provide social support, enhance patient understanding of treatment options, spread current research information previously only shared in academic spheres, and cater content based on user preferences. This is a novel approach to scientific communication, health literacy, and patient education and will help to bridge disparities that lead to subpar health care in dermatology. Although social media's ability to provide catered user-centered content has yielded favorable results, challenges persist regarding efficient and appropriate use of social media as a form of patient education. Therefore, dermatologists and trainees must consider pitfalls to social media as a form of patient education, such as less accountability, blurred professional boundaries, and challenges in maintaining transparency about commercial interests [16,31]. Despite this, dermatologists that use social media have reaped immediate benefits, including a broader client base and higher web-based reviews for their private practices [5,43]. For patients, social media is not only useful as an overt form of patient education but also a means to find community, support and ultimately have the tools to make informed health care decisions [42]. Some limitations of this narrative review include the exclusion of publications that are not indexed in PubMed. Future reviews should build upon this initial survey to assess a broader scope of literature and potentially establish other potential uses of social media in dermatology.

It is important to consider that innovations in technology will continue to increase the number of people turning to social media and telemedicine for health information, but that tailored content can also have legal implications. To develop patient education content on social media, it is important to consider the different demographics that access various social media sites as demonstrated [1]. For instance, 37% of social media news consumers are Republican or lean Republican [1]. Education level varies across platforms. Facebook, Instagram, and TikTok had 28%, 30%, and 15% of users with a college degree or higher, respectively [1]. Using this information can help with content development that is catered to the users' demographic information. There is a great realm of potential for providers and patients to become more informed on treatment options and common concerns to improve bidirectional communication in health care settings [42]. Although catered, easily accessible content is part of the appeal of social media as an avenue for patient education, its use may also trigger legal implications because of not only blurred professional boundaries, but rising concerns over data privacy and social media [31,47].

Although tailored content is a promising avenue for public health interventions and preventative health care in dermatology, targeted messaging can be applied to affect patient behavior, bypassing existing regulations on disclosure and informed consent and thus raising legal implications [14,45,47]. This shows the need for subsequent research on these implications and potential solutions to deliver patient education content without bypassing existing regulations and ethical guidelines.

Implications

Perhaps most promising is the potential of the dermatology community to directly combat health misinformation through social media. The use of social media to post research has demonstrated a significant (P<.0001) positive effect on both views (mean difference 175.5, SE 16.4) and downloads (mean difference 31.5, SE 4.0) when compared to matched articles not published on social media [27]. This suggests social media play an important role in the spread of the most recent innovations. As peer-reviewed research becomes more available and accessible, patients and social media users will be able to make more informed health care decisions. Some social media platforms are already seeing increases in content created by board-certified dermatologists such as on TikTok where board-certified dermatologists accounted for 15.1% of total posts but authored a significant percentage of posts with the hashtag "dermatology" (45%) [20]. Unique features of different social media sites can allow for additional moderation and curb the spread of medical misinformation. TikTok's Duet feature allows physicians and scientists to directly refute medical misinformation, Facebook has instituted a Coordinated Harm Policy (and related policies) that removes misinformation content, and Twitter now contains a disclaimer that urges users to read articles before sharing content.

Limitations

There are a few limitations of this current narrative review. There is not yet an established set of guidelines for validating health information on social media which are applicable to all the different platforms. Therefore, this review is unable to establish a generalizable set of best practices for tackling this concern. The narrative review methodology was used, which provided advantages such as a more inclusive picture of available research and the ability to provide rationales for future research. However, the weaknesses of the narrative review methodology include selection bias. To limit, though not entirely eliminate bias, the author established explicit criteria for article selection and used multiple databases. This review did not have other full-time contributors although other experts were consulted during the initial stages to reduce the risk of bias. Another limitation is that this narrative review does not include differences in behavior across intersectional demographic groups. Some of the selected papers may have their own biases as some may be written by groups or individuals who currently use social media for patient education or health information. Many of the studies in this review are from the United States and most studies in this review are from predominantly White, educated, industrialized, rich, and democratic societies (WEIRD societies). However, social media is used globally, and several studies analyzed global trends and data from social media regardless of the country of origin of the researchers.

Conclusions

Social media has rapidly become a staple in the daily lives of billions. Social media has become a modality for patient education, misinformation, and marketing in dermatology. Although there are many unique features across all platforms that allow for the rapid and simplified dissemination of research and relevant health information, misinformation spreads equally as well. Integration of social media into dermatology practice has risen in prevalence in the past few years, but there continue to be avenues to expand the social media presence of academic Dermatology and private practices alike. Examining successful social media strategies while ensuring ethical standards of dermatology is upheld and will be crucial to the continued growth of social media as a form of dermatologic patient education. This narrative review aims to highlight current uses of social media, pitfalls, and benefits of social media use for patient education and emerging applications for social media usage in dermatology. Further research should aim to analyze the efficacy of different strategies to mitigate health misinformation on social media. Future studies and innovations should also continue to explore innovations in this space, efficacy of different modalities of posts, and longitudinal differences in patient outcomes and health literacy. It is especially important for future studies to explore whether existing social media patient education materials provide culturally competent and diverse representations.

Conflicts of Interest

None declared.

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Abbreviations

AAD: Academy of Dermatology
ADHD: attention-deficit/hyperactivity disorder
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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Review

Consensus Guidelines for Teledermatology: Scoping Review

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Abstract

Background: Consensus guidelines and recommendations play an important role in fostering quality, safety, and best practices, as they represent an expert interpretation of the biomedical literature and its application to practice. However, it is unclear whether the recent collective experience of implementing telemedicine and the concurrent growth in the evidence base for teledermatology have resulted in more robust guidance.

Objective: The objective of this review was to describe the extent and nature of currently available guidance, defined as consensus guidelines and recommendations available for telemedicine in dermatology, with guidance defined as consensus or evidence-based guidelines, protocols, or recommendations.

Methods: We conducted a single-reviewer scoping review of the literature to assess the extent and nature of available guidance, consensus guidelines, or recommendations related to teledermatology. We limited the review to published material in English since 2013, reflecting approximately the past 10 years. We conducted the review in November and December of the year 2022.

Results: We identified 839 potentially eligible publications, with 9 additional records identified through organizational websites. A total of 15 publications met the inclusion and exclusion criteria. The guidelines focused on varied topics and populations about dermatology and skin diseases. However, the most frequent focus was general dermatology (8/15, 53%). Approximately half of the telemedicine guidance described in the publications was specific to dermatology practice in the context of the COVID-19 pandemic. The publications were largely published in or after the year 2020 (13/15, 87%). Geographical origin spanned several different nations, including Australia, the United States, European countries, and India.

Conclusions: We found an increase in COVID-19–specific teledermatology guidance during 2020, in addition to general teledermatology guidance during the period of the study. Primary sources of general teledermatology guidance reported in the biomedical literature are the University of Queensland's Centre for Online Health and Australasian College of Dermatologists E-Health Committee, and the American Telemedicine Association. There is strong evidence of international engagement and interest. Despite the recent increase in research reports related to telemedicine, there is a relative lack of new guidance based on COVID-19 lessons and innovations. There is a need to review recent evidence and update existing recommendations. Additionally, there is a need for guidance that addresses emerging technologies.

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KEYWORDS

COVID-19; dermatology; teledermatology; telehealth; telemedicine; consensus guidelines; guidelines; recommendations

Introduction

The use of telemedicine in dermatology practice dates to the mid-1990s when early innovators recognized it as a promising means of delivering dermatology specialty care to remote and underserved populations [1]. However, "teledermatology" lacked widespread adoption before the COVID-19 pandemic due to policies restricting practice and negatively affecting teledermatology services reimbursement. In 2020, the public health measures and policy changes triggered by the COVID-19 pandemic led to considerable growth in the adoption of telemedicine. The regulatory changes related to telemedicine that occurred in the United States during 2020 are summarized elsewhere [2] and include important changes in Centers for Medicare & Medicaid Services policies related to interstate licensure, reimbursement, and Health Insurance Portability and Accountability Act of 1996 encryption requirements. Empowered by these regulatory changes, individuals and groups quickly adopted telemedicine to deliver patient care, employing the best available methods and models or none, out of sheer necessity.

A bolus of telemedicine-focused reports in the biomedical literature accompanied widespread and dramatic increases in the adoption of telemedicine during 2020. In the biomedical literature database PubMed [3], the number of records containing the keyword "telemedicine" in 2020 and 2021 is approximately double the number in 2019, with over 8000 records per year. The array of digital health technologies available to support telemedicine delivery has also continued to mature, with the widespread availability of biosensors and communication platforms (eg, SMS text messaging platforms, chatbots, and mobile apps) and smartphone imaging, alongside transformative advancements in artificial intelligence. Many recent reports describe applications of these rapidly developing technologies in dermatology [4-9]. Attention is turning to quality, safety, and best practices in a sustained health care delivery model that incorporates telemedicine in a rapidly evolving landscape of digital health technologies.

Consensus guidelines and recommendations play an important role in fostering quality, safety, and best practices, as they represent an expert interpretation of the biomedical literature and its application to practice. However, it is unclear whether the recent collective experience of implementing telemedicine and the concurrent growth in the evidence base for teledermatology have resulted in more robust guidance. The objective of this review was to describe the extent and nature of currently available guidance, defined as consensus guidelines and recommendations, available for the practice of telemedicine in dermatology, with guidance defined as consensus- or evidence-based guidelines, protocols, or recommendations.

Methods

Overview

We conducted a single-reviewer scoping review of the literature to assess the extent and nature of available guidance, consensus guidelines, or recommendations related to the use of telemedicine in dermatology practice. Here, we define telemedicine according to the Health Resources and Services Administration of the US Department of Health and Human Services [10] definition as "the use of electronic information and telecommunications technologies to support and promote long-distance clinical health care, patient and professional health-related education, public health, and health administration." According to the US Department of Health and Human Services, these technologies include "videoconferencing, the internet, store-and-forward (SAF) imaging, streaming media, and terrestrial and wireless communications" [10]. Before initiating the review, we searched 6 sources for existing protocols or reviews on this subject and found none. Sources searched on November 21, 2022, included PROSPERO [11], Epistemonikos [12], Cochrane Library [13], and CINAHL Complete (EBSCOhost) [14]. One closely related review is that recently published by Dovigi et al [15], which focuses on quality assessment.

We conducted the review according to guidance from the latest *JBI Manual for Evidence Synthesis* [16]. Specifically, we followed the process of a scoping review with Arksey's five stages: (1) identifying the research question; (2) identifying relevant studies; (3) study selection; (4) charting the data; and (5) collating, summarizing, and reporting the results [17]. However, we streamlined and expedited the review process by using a single reviewer to screen and code publications. We used EndNote (Clarivate Analytics) to manage and deduplicate citations. We used Covidence (Veritas Health Innovation) to further deduplicate, screen, and select studies and to perform data extraction.

Literature Search

We searched multiple web-based databases: Cochrane Library, Scopus, PubMed, Epistemonikos, Cochrane Library, and CINAHL Complete (EBSCOhost). We used keywords and controlled subject headings unique to each database and detailed in Multimedia Appendix 1, designed to identify terms that included telehealth, telemedicine, teledermatology, dermatology, guidelines, and recommendations. We excluded the ECRI Guidelines Trust, as it was publicly unavailable during the review. We also examined materials found on the following federal and organizational websites: the American Telemedicine Association, the American Academy of Dermatology, the American Dermatological Association, and the US Agency for Healthcare Research and Quality. We summarize the search strategy and results in Multimedia Appendix 1. We limited the review to published material in the English language, published since 2013, reflecting approximately the past 10 years. We conducted the review in November and December 2022.

Article Selection (Eligibility Criteria)

The eligibility criteria for article selection are listed in Textbox 1.

Textbox 1. Eligibility criteria for article selection.

Inclusion criteria:

• We included reports of consensus-based practice guidelines or aggregated sets of recommendations related to dermatology using telehealth or telemedicine, published since January 1, 2013, and originating from any country.

• We include reports that present guidelines published separately in a more comprehensive format, consistent with this commonly encountered reporting pattern for guidelines and recommendations.

Exclusion criteria:

• We excluded reports without a primary focus on dermatology or dermatological conditions and guidelines that lack specific telehealth or telemedicine practice recommendations.

• We also excluded guidance not based on a consensus process or study. Additionally, we excluded material not available in the English language.

Assessment, Extraction, and Analysis

We did not conduct a formal quality assessment of underlying studies because consensus guidelines constitute an evaluation and recommended application of evidence by experts. Our goal was to map available consensus guidance rapidly. A single reviewer extracted variables (Table 1) describing the characteristics of the publications using Covidence. We conducted an initial manual data review to identify and resolve any needs for categorization or standardization of nomenclature. We conducted frequency analysis to describe the type and distribution of variables as presented in Table 1 and provide a summary list of articles, guidelines, and their characteristics (Table 2).

Table 1. Descriptive summary of publications.

Authors	Years	Guideline described	Brief description of the publication
Abbott and Soyer [18]	2020	A CLOSE-UP guide to capturing clinical images	Supplement to the Australian teledermatology guidelines; presents an acronym that guides capture of clinical images.
Abbott et al [19]	2020	Practice guidelines for teledermatology in Australia	Presents a review of the literature on which the guidelines were based.
Abbott et al [20]	2020	Practice guidelines for teledermatology in Australia	Guidelines for teledermatology for the Australian context, developed by The University of Queensland's Centre for Online Health in collaboration with The Australasian College of Dermatologists E-Health Committee.
Arruda et al [21]	2020	Recommendations for Dermatology Office Reopening in the Era of COVID-19	"A group of international experts was assembled to formulate guidance and best-practices for resuming dermatology practices in a COVID-19 era" [21].
Belinchón et al [22]	2020	Managing psoriasis consultations during the COVID-19 pandemic: recommendations from the Psoriasis Group of the Spanish Academy of Dermatology and Venereology	Statement of recommendations to guide dermatologists "who treat psoriasis, especially in cases where patients are receiving treatment or are about to initiate treatment with selective immunomodulators or immunosuppressants" [22].
Brochez et al [23]	2020	Recommendations for skin cancer consultation and surgery during COVID-19 pandemic	"Recommendations developed by the Belgian Association of Dermato-Oncology for prioritization of patients in the field of dermato-oncology during COVID-19 pandemic." [23]
Chatterjee and Das [24]	2021	Management of vitiligo amidst the COVID-19 pandemic: a survey and resulting consensus	Survey of experts re: appropriate management of vitiligo during the COVID-19 pandemic.
Deda et al [25]	2022	Dermoscopy practice guidelines for use in telemedicine	Summary of American Telemedicine Association teledermoscopy guidelines.
de Vere Hunt et al [26]	2021	Telehealth for older adults with skin disease: a qualitative exploration of dermatologists' experiences and recommendations for improving care	Recommendations for use of telehealth with older adults based on qualitative interviews with a sample of dermatologists.
Finnane et al [27]	2017	ISIC recommendations for imaging standardization	Article "translates" ISIC recommendations for imaging standardization into clinical application [27].
Frieden et al [28]	2020	Management of infantile hemangiomas during the COVID pandemic	"The Hemangioma Investigator Group has created consensus recommendations for management of IH [infantile hemangioma] through telemedicine" [28].
McKoy et al [29]	2016	American Telemedicine Association Teledermatology Practice Guidelines	Practice guidelines for teledermatology.
Micali et al [30]	2020	The Italian dermatologic community facing COVID-19 pandemic: recommendation from the Italian Society of Dermatology and Venereology	Emergency plan for dermatology practice during the COVID-19 pandemic.
Stoff et al [31]	2020	Guiding principles for prioritization of limited in-person dermatology appointments during the COVID-19 pandemic	Guiding principles for allocating in-person dermatology appointments during COVID-19.
Zic et al [32]	2020	United States cutaneous lymphoma consortium recommendations for treatment of cutaneous lymphomas during the COVID-19 pandemic	US consortium recommends strategies for treating cutaneous lymphomas during the COVID-19 pandemic.

Table 2. Characteristics of included reports.

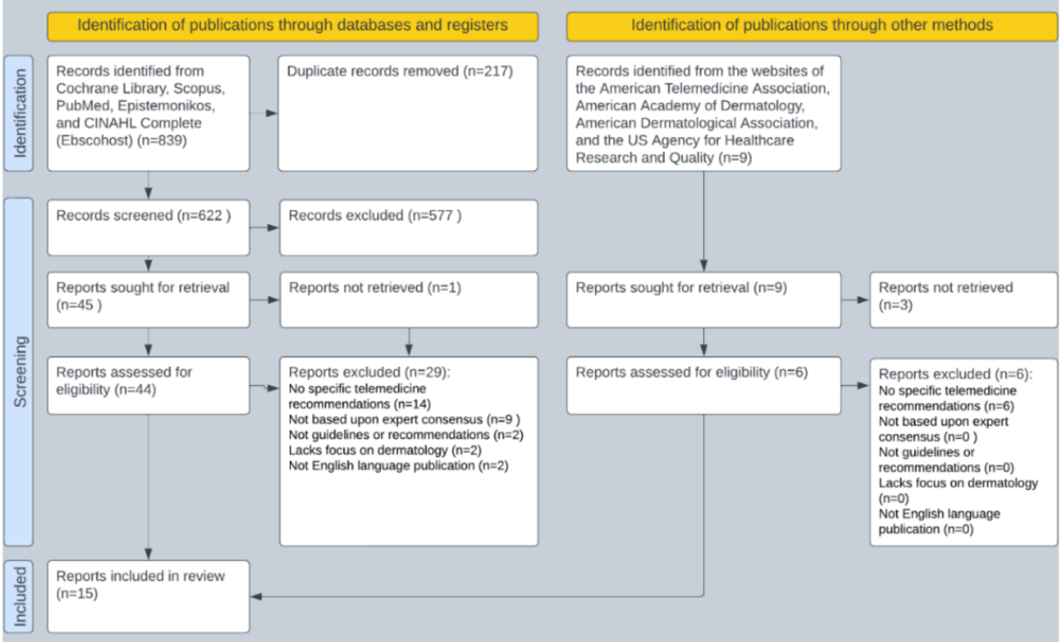
Variables	Frequency		Reports, %
	Absolute	Relative	
Year published			
2016	1	0.07	7
2017	1	0.07	7
2020	10	0.67	67
2021	2	0.13	13
2022	1	0.07	7
Total	15	1	100
Country of origin			
Australia	4	0.27	27
Belgium	1	0.07	7
India	1	0.07	7
International (multiple)	2	0.13	13
Italy	1	0.07	7
Spain	1	0.07	7
United States	5	0.33	33
Total	15	1	100
COVID-19–specific guidance?			
Yes	7	0.47	47
No	8	0.53	53
Total	15	1	100
Focus			
Dermato-oncology	2	0.13	13
General	8	0.53	53
Infantile hemangioma	1	0.07	7
Older adults	1	0.07	7
Psoriasis	1	0.07	7
Vitiligo	1	0.07	7
Total	15	1	100
Consensus group			
Professional society	11	0.73	73
Author-assembled panel	4	0.27	27
Total	15	1	100
Nature of guidance			
Guideline	7	0.47	47
Recommendation	8	0.53	53
Total	15	1	100

Results

Screening and Selection

We summarize the search, screening, and selection process results in Figure 1. The biomedical literature search process identified 839 potentially eligible publications, with an additional 9 records identified through organizational websites. After deduplicating search results, we manually screened the titles and abstracts of 622 records for inclusion, followed by 54 full-text reviews (both biomedical literature and publications retrieved from organizational websites), to verify possibly eligible reports. After we completed screening and full-text review, 15 publications met the inclusion and exclusion criteria (Table 1). We provide a list of all the reports included in Table 1.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram of the review process.



Publication Characteristics

We present publication characteristics (Tables 1 and 2 and Figure 2). The included items were primarily published in or after the year 2020 (13/15, 87%). The origin of reports spans several different nations, including Australia, the United States, European countries, and India (Figure 2). Approximately half of the guidance consisted of guidelines (7/15, 47%), with the remaining guidance presenting more general recommendations (8/15, 53%). Also, about half of the telemedicine guidance described in the publications was specific to dermatology practice in the context of the COVID-19 pandemic (7/15, 47%).

In most cases, the source of the guidance was a professional organization or society (11/15, 73%) rather than an independently assembled sample or panel. The guidelines focused on varied topics and populations (Tables 1 and 2) related to dermatology and skin diseases. However, the most frequent focus was general dermatology (8/15, 53%). We briefly describe each report and the guidelines described in each publication (Table 1). Given multiple guidelines addressing common imaging aspects, we present a summary comparison of recommendations in Table 3.

Figure 2. Frequency and percentage of report origin.

Table 3. Imaging-focused recommendations.

	Abbott and Soyer [18]	Abbott et al [20]	Deda et al[a] [25]	Finnane et al [27]	McKoy et al [33]
Preparation	• Obtain consent	• Obtain consent • Remove jewelry and clothing	• Apply liquid or gel to the skin	• Remove jewelry	• Avoid jewelry and clothing • Use chaperone or legal guardian if appropriate • Clean skin with alcohol pad
Lighting	• Maximize natural light • Use overhead light with flash	• Use flash	—[b]	• Natural light is best • Broad spectrum lighting • Avoid flash • Position light oblique to skin surface	• Minimal background lighting • Diffuse, indirect • Additional fluorescent or full-spectrum lighting may be needed • Use flash in case of shadow
Positioning, framing, and orientation	• Position patient to optimize image accuracy • Center lesion in frame • Overview, midrange, and close-up images	• Camera position perpendicular to skin surface • Identification markers adjacent to lesion • Center lesion in frame • Overview, midrange, and close-up images • Begin and end with a photograph of identifying information	• Consistent orientation across images • Inclusion of anatomical sites in regional images • Place camera perpendicular to skin surface	• Center lesion in frame • Close-up images should include lesion plus equal area of surrounding skin • Multiple close-up images if needed for large lesions • Consistent orientation across images • Cephalic orientation preferred	• Overview, midrange, and close-up images • Camera perpendicular to skin • Center lesion in frame • Use identification markers
Measurement	—	• Dermoscopic images should include sizing	• Inclusion of diameter scale	• Include digital or physical ruler. • Place ruler with same orientation as camera	• Use measurement tools as appropriate; include a ruler in dermoscopy images
Background	• Neutral blue or gray	• Solid, neutral	—	• Solid • Color dependent upon skin color; black for lighter skin; sky blue for darker skin	• Solid, neutral, and nonreflective
Resolution	—	• Minimum resolution, consistent settings	• Sufficient resolution for regional and close-up images with file size of at least 200 KB • Digital scales (integrated with device) preferred to physical scales • Place scale with same orientation as the dermatoscope	—	• Minimum resolution of 1024 × 768 pixels
Focus or field	—	—	• Deep depth of field • Manually or automatically focus image	—	• Use macro mode • Use autofocus

	Abbott and Soyer [18]	Abbott et al [20]	Deda et al[a] [25]	Finnane et al [27]	McKoy et al [33]
Color	—	—	• Image color resolution of 24 bits	• Periodically calibrate equipment to prevent changes	• Calibrate color and white balance
Process	• Carefully evaluate image quality with attention to focus, overexposure, representative color • Recapture images if necessary	• Review images for quality before sending them to a dermatologist • Review of images by a dermatologist on appropriate or newer display using review software	—	—	—
Image management	• Delete from photography device after uploading to patient's file • Include narrative of clinical context with photos	• Secure image storage as part of medical record	• Image transmission, processing, and storage according to DICOM (Digital Imaging and Communications in Medicine) standard	• Images should be stored • May require manual link to patient record • Storage according to DICOM	• Images become part of the medical record
Dermoscopy considerations	—	• Consider whether both polarized and nonpolarized dermoscopy images are appropriate	• Polarized vs nonpolarized lighting at discretion of clinician, but generally at least one polarized image • Nonpolarized light under specific circumstances	• Use of polarized vs nonpolarized at discretion of clinician, dependent upon lesion • Generally, at least one polarized image • Polarized light for blood vessels, red areas, shiny white lines or clods or rosettes • Nonpolarized light for structures such as milia cysts	—
Videography	—	—	—	—	• Freeze-frame capture is useful • Gradual movement of a video camera for overview, mid-range, and close-up images

[a]The recommendations by Deda and colleagues [25] pertain entirely to dermoscopy; the recommendations by McKoy and colleagues [29] encompass both synchronous and asynchronous imaging.

[b]Not available.

Discussion

Principal Results

We conducted a single-reviewer scoping review to assess available guidance for the practice of teledermatology. We identified 15 reports describing 13 unique guidelines or sets of recommendations. We conducted our analysis based on publications, as in some cases, the publications described different aspects of guidelines that were not otherwise available. Professional societies or organizations created most guidance, and the guidance addressed the management of multiple specific skin diseases, in addition to general dermatology.

We found that most publications were published during or after 2020, the onset of the COVID-19 pandemic. Approximately half of the publications contained guidance specific to the circumstances of the COVID-19 pandemic, which included shortages of personal protective equipment, quarantine, and public health measures that had lockdowns [34]. For example, the report by Belinchón et al [22] provides recommendations for managing psoriasis in the context of COVID-19 amidst health considerations and Italy's public health measures. Specifically, they recommended that a consistent clinician supervise care delivery across in-person and telemedicine encounters and alternating in-person and telemedicine visits. The Belgian Association of Dermato-Oncology similarly reported guidance on prioritizing patients for skin cancer consultation and surgery, with direction to simply consider teleconsultation when feasible [23].

The remaining part of the reports pertained to the use of telemedicine in dermatology, independent of pandemic circumstances. The two primary sources of general teledermatology guidance discovered in this review were as follows: (1) the University of Queensland's Centre for Online Health and the Australasian College of Dermatologists E-Health Committee (UQ-ACD) [18-20], and (2) the American Telemedicine Association (ATA) [25,29]. Most of the UQ-ACD and ATA guidance was issued before the COVID-19 pandemic. The UQ-ACD guidelines address general dermatology practice in Australia and encompass technology, environment, quality and safety, patient selection, informed consent, and the acquisition and storage of clinical images [20]. There is also companion clinical guidance for capturing clinical images [18]. Although access to the ATA guidelines is limited to those holding organizational memberships, the guidelines are partially described in publicly available reports. ATA guidance consists of practice guidelines for general teledermatology as well as teledermoscopy. The general teledermatology guidelines were originally issued in 2007 and revised in 2016, with teledermoscopy guidelines issued most recently in 2021-2022 (report published in 2022). They are topically comprehensive, encompassing environmental, clinical, and administrative considerations, with specific guidance for imaging [25,29].

Most guidance originated in Australia or the United States. However, our review evidences global engagement in creating guidance for teledermatology, as shown in Figure 2. There is international interest in guidance for teledermatology, despite international variation in payment, infrastructure, health system characteristics, and health priorities. However, only 2 reports described international guidance, one focusing on imaging standards [27] and the other focusing on reopening clinics during the COVID-19 pandemic [21].

Given the high recall search strategy, the items excluded during the screening process typically mentioned the keywords but were unrelated to guidelines or recommendations. Others represented literature reviews or systematic reviews of scientific evidence. We excluded 8 reports at the full-text review stage because they were not consensus-based; these were primarily letters to the editor by individuals or small teams; 2 reports were educational or tutorial. For example, Mondal and Mondal [35] presented a tutorial on electronic signatures and document storage for teledermatology practitioners.

COVID-19–Specific Recommendations

As previously indicated, approximately half of the reports focused on guidance for dermatology practice during the COVID-19 pandemic. These reports focus on emergency plans for providing dermatology care, including triaging patients for in-person and telemedicine visits and highlighting the relevant considerations for integrating telemedicine into practice. For example, the Psoriasis Group of the Spanish Academy of Dermatology and Venereology published recommendations to guide dermatologists who treat psoriasis [22]. Those recommendations indicate that telemedicine visits between a patient and provider may be acceptable. Arruda et al [21] presented international recommendations for reopening dermatology offices, with summary guidance for the successful integration of telemedicine into practice, including SAF consultation, new consultations, and attention to local government regulations. Brochez et al [23] made pragmatic recommendations about triaging the care of dermato-oncology patients and deciding when care can and cannot be postponed. They organized encounter or presentation types into 3 categories: urgent, semiurgent, and low-priority. Chatterjee and Das [24] surveyed expert dermatologists to determine when patients with vitiligo can be appropriately managed via telemedicine.

Imaging

Imaging is critical for teledermatology practice. The multiple reports and the guidelines they describe address imaging considerations [18,20]. The CLOSE-UP guideline is a particularly useful tool for clinicians photographing lesions to obtain teledermatology consultation using a SAF model [18]. CLOSE-UP addresses the need for informed consent with any image capture and storage. It also guides clinicians in the photography process to use natural light or, overhead lighting with flash against a gray or neutral blue background. This guideline also describes a method of taking a series of photographs, including a wider frame overview image, a mid-range image, and one or more close-up images, all with a consistent orientation. The purpose of a sequence of images is to enable assessment of how lesions are distributed and their location on the body, in addition to the more closely photographed lesions themselves. The CLOSE-UP guidelines encourage the evaluation and recapture of images as necessary, uploading them to a patient's file, then deleting them from the photography device. It also highlights the importance of providing the teledermatologist with relevant clinical context, in addition to images, including findings that are not evident in the images.

Finnane et al [27] call for standardization of image capture in dermatology and present a series of recommendations developed by the International Skin Imaging Collaboration (ISIC), broadly consistent with CLOSE-UP, but also addressing dermoscopy. Among multiple lighting considerations, they recommend avoiding the use of flash in clinical photography, noting its effects on image contrast, the inclusion of reflections in images, and effects on skin tone. They also address considerations that the teledermatologist should apply in using polarized and nonpolarized lighting in dermoscopy. The ISIC recommendations, like CLOSE-UP, specify an optimal background color. However, ISIC recommends using different background colors for different skin tones, with black for lighter skin and blue for darker skin. ISIC recommends using digital scales, integrated into photographic devices or software, rather than adhesive scales, because applying the adhesive causes some variability and obscures skin and appropriate placement of a ruler can be challenging. ISIC notes the importance of high-resolution images and provides a detailed guide for selecting a resolution. They also provide guidance on color calibration, noting that photography devices must be regularly calibrated. The ISIC guidance on image storage notes that both clinical information and images need to be stored as part of the medical record, and points to the existing and widely adopted DICOM (Digital Imaging Communication in Medicine) standard for doing so.

The ATA guidelines described by Deda et al [25] provide specific guidance for dermoscopy in telemedicine. The scope of the guidelines is consistent with the imaging considerations noted in CLOSE-UP and the ISIC recommendations, but specific to dermoscopy. These guidelines provide indicators of appropriate resolution and lighting, as well as focus or depth of field, field of view, color, and image quality with an easy-to-consume quality checklist and a step-by-step process diagram for photography in the context of SAF consultation. These guidelines also favor using digital scales versus physical scales, high-resolution images, and multiple images with varied field of view but a consistent orientation.

When is Teledermatology Appropriate?

Multiple reports emphasize the importance of provider expertise, and caution that telemedicine should only be carried out by appropriately credentialed specialists. Further, these reports emphasize the importance of the clinician's judgment in assessing whether teledermatology is appropriate for a given patient. There is less agreement on the specific circumstances and models that should be used. Guidance was frequently focused on particular clinical conditions within general dermatology. However, multiple reports note the various factors to be considered, including whether the patient is new or established, the nature of their presentation, and the role of teledermatology in a more extensive care delivery process with sequenced encounters that can include both in-person and teledermatology visits. Factors that influence the appropriateness of teledermatology include the need for a head-to-toe physical examination, whether the patient is new or under ongoing treatment, and the availability of appropriate tools and environment (eg, dermoscopy, established systems and processes for managing images, teleconsent process, etc). There is an acknowledgment that certain types of encounters, such as initial consultation for cosmetic procedures, can easily be appropriate for teledermatology. One of the major use cases for teledermatology is consultation with referring providers, which is carried out using an established process with more controlled and standardized image capture, and clinical assessment information is captured during an in-person visit with the referring provider, a very different scenario from direct-to-patient assessment. There is a need to ensure that patient expectations regarding their ability to obtain care via telemedicine versus in-person visits are realistic and that they understand that clinical circumstances may warrant a different care modality.

Recent Evidence

From 2020 to the present, thousands of publications in the biomedical literature focused on aspects of telemedicine and telehealth. Many of these studies were an outgrowth of widespread adoption during the COVID-19 pandemic and the opportunity to study numerous aspects of telemedicine and teledermatology. Among these studies were trials of teledermatology interventions, for example, a trial of teledermatology with psoriasis patients, and pilot studies of teledermatology consultation in novel settings, such as the emergency department and inpatient environments [36-39]. There has been substantial growth in the literature describing the acceptability of teledermatology from the patient and provider perspective across many settings and cultures [40-45]. Technical innovations are also evolving; guidelines and recommendations could address new dermoscopy devices, artificial intelligence, and ultrasonography [46,47]. The pandemic yielded new insights into the process and workflow considerations of implementing teledermatology [48,49]. In effect, there is a substantial amount of recent literature that requires expert review and consideration in updates to existing guidelines. This recent evidence could enable more explicit guidelines for determining the appropriateness of teledermatology.

Limitations

The primary limitation of this review is that we were unable to discover consensus guidance that exists but has not been reported in the biomedical literature. We surmise that panels of experts have generated guidance for internal use by large health care organizations, but the guidance was not shared externally or reported in the biomedical literature or were not revealed using the search strategy that we employed. Additionally, we could not access some guidance because access was restricted to members. This finding highlights the need for open access to consensus guidance and the importance of communicating about guidance in the biomedical literature so that clinicians from resource-constrained settings can benefit from it. We acknowledge that teledermatology is not frequently used in low- to middle-income countries, and so these geographical areas may be underrepresented in the review.

As a single-reviewer scoping review, this review lacked the benefit of a second reviewer in making determinations during the screening and selection process. However, we chose this approach to expedite the process and ensure timely publication, which is often challenging for structured reviews [50]. Moreover, we adhered to the recommended process and reporting standards for this type of review.

Conclusions

This single-reviewer scoping review described the extent and nature of currently available teledermatology guidance. We observed a large number of COVID-19–specific guidelines or recommendations during 2020 and fewer reports of general teledermatology guidance. The primary sources of general teledermatology guidance are the UQ-ACD and ATA, and there is strong evidence of international engagement and interest. Given a substantial recent increase in reports of research related to telemedicine, there is relatively little new guidance based on COVID-19 lessons and innovations. There is a need to review recent evidence and update existing recommendations. Additionally, there is a need for guidance that addresses emerging technologies. Open access and public availability are crucial to meet the global demand for quality and safety of teledermatology.

Authors' Contributions

MRC, TO, JI, and BEB conceived and designed the review. MRC carried out the review and served as primary author of the manuscript. JFB, HW, HS, and BMW contributed telemedicine specialty expertise to the background and discussion sections.

Conflicts of Interest

BMW is the founder, CEO, and shareholder of Doxy.me Inc, a commercial telemedicine company. All other authors are employees of the same company. The authors declare no other conflicts of interest.

Multimedia Appendix 1
Search strategy.
[DOCX File , 9 KB - derma_v6i1e46121_app1.docx]

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Abbreviations

ATA: American Telemedicine Association
ISIC: International Skin Imaging Collaboration
SAF: store-and-forward
UQ-ACD: University of Queensland's Centre for Online Health and Australasian College of Dermatologists E-Health Committee

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Review

Store-and-Forward Teledermatology for Assessing Skin Cancer in 2023: Literature Review

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Abstract

Background: The role of teledermatology for skin lesion assessment has been a recent development, particularly, since the COVID-19 pandemic has impacted the ability to assess patients in person. The growing number of studies relating to this area reflects the evolving interest.

Objective: This literature review aims to analyze the available research on store-and-forward teledermatology for skin lesion assessment.

Methods: MEDLINE was searched for papers from January 2010 to November 2021. Papers were searched for assessment of time management, effectiveness, and image quality.

Results: The reported effectiveness of store-and-forward teledermatology for skin lesion assessment produces heterogeneous results likely due to significant procedure variations. Most studies show high accuracy and diagnostic concordance of teledermatology compared to in-person dermatologist assessment and histopathology. This is improved through the use of teledermoscopy. Most literature shows that teledermatology reduces time to advice and definitive treatment compared to outpatient clinic assessment.

Conclusions: Overall, teledermatology offers a comparable standard of effectiveness to in-person assessment. It can save significant time in expediting advice and management. Image quality and inclusion of dermoscopy have a considerable bearing on the overall effectiveness.

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KEYWORDS

telemedicine; skin neoplasm; skin cancer; store-and-forward; melanoma; squamous cell carcinoma; basal cell carcinoma; cancer; dermoscopy; mobile phone

Introduction

Background

The number of studies relating to teledermatology continues to rise exponentially. The reasons for this are multitude, including the COVID-19 pandemic limiting in-person consults, advances in technology meaning better availability of telemedicine and, in particular, teledermoscopy, as well as more familiarity and interest from health care professionals in using teledermatology. There are various methods of teledermatology. The main distinguishing factor is whether a pathway uses video consultations or store-and-forward, also known as advice and guidance. The former uses real-time technology to provide assessment, while the latter involves taking images for later review. Teledermatology can also be distinguished by the specialties involved, whether this is the more common general practitioner (GP) to a dermatologist, dermatologist to dermatologist, GP to GP, or patient to GP.

There are many variables to consider when assessing store-and-forward teledermatology due to the variation in the way it is implemented and assessed. This review aims to collate information from the breadth of available data.

Objective

This literature review discusses time to advice, effectiveness, and image quality for store-and-forward teledermatology for skin lesion assessment.

Methods

MEDLINE was searched using the keywords “telemedicine” or “teledermatology” and “skin neoplasms” or “skin cancer” for papers from January 2010 to November 2021. The period was chosen due to the inclusion of several review papers that summarize prominent earlier work as well as significant advances in technology over the last 10 years. A single database search was chosen to maximize efficiency, reliability, and reproducibility. A narrative review method was selected to allow flexibility in discussing the heterogeneous results for each outcome of interest. Papers about store-and-forward teledermatology for skin lesion assessment reporting effects on time, effectiveness, and image quality were included. All study designs were included, including reviews, interventional studies, and observational studies.

Results

In total, 45 papers meeting the inclusion criteria were identified after removing duplicate reports, of which, 4 were review papers, 10 were interventional studies (including 2 randomized controlled trials), and 31 were observational studies.

Time to Advice and Management

In total, 11 papers reporting time outcomes were identified with measures including time to advice, time to biopsy, and time to definitive surgery. The results are outlined in Table 1.

Table 1. Studies reporting time to advice and management.

Type	Setting	Sample	Outcome	Reference
Observational	Single-center study in the United States	212 patients (146 teledermatology consults and 66 in-person consults)	Decreased time to treatment by 2 weeks. Increased the percentage of lesions treated within 60 days.	Lee et al [1]
Observational	Single-center study in Australia	Aggregated probabilities analysis	Mean time to clinical resolution was 9 (range 1-50) days with teledermoscopy referral compared with 35 (range 0-138 days) days for conventional referrals.	Snoswell et al [2]
Observational	Single-center study in New Zealand	613 lesions in 310 patients	Median time between referral and attendance at the virtual clinic was 9 days compared to 26.5 days for conventional referrals.	Congalton et al [3]
Observational	Single-center study in the United States	293 patients	Mean time to biopsy of skin cancer was 9.7 (median 9.0) days for teledermatology referrals compared to 13.8 days for conventional referrals (median 12.0 days).	Kahn et al [4]
Observational	Single-center study in the United States	79 referrals	Median time to evaluation was 0.5 (IQR 0.172-0.94) days for teledermatology referrals compared to 70.0 (IQR 33.25-83.0) days for conventional referrals.	Carter et al [5]
Observational	Single-center study in the United States	2385 referrals (1258 conventional referrals and 1127 teledermatology referrals)	Implementation of teledermatology allowed median wait times to reduce from 77 to 28 days.	Naka et al [6]
Observational	Single-center study in Spain	43,677 patients	Average time to skin lesion advice of 72 hours for teledermatology referrals.	Moreno-Ramírez and Ferrándiz [7]
Observational	Single-center study in France	1079 referrals (1043 conventional referrals and 36 teledermatology referrals)	Teledermatology referrals resulted in a mean of 7.8 more days waiting for surgery compared to conventional referrals.	Duong et al [8]
Observational	Single-center study in the United States	1021 referrals (434 teledermatology referrals compared to 587 conventional referrals)	No significant difference found in time from initial consult to biopsy of suspicious lesions (47.3 vs 45.5 days; *P*=.8) or in time from biopsy to definitive treatment of malignant tumors (65.4 vs 67.5 days; *P*=.8) for teledermatology referrals compared to conventional referrals.	Creighton-Smith et al [9]
Observational	Single-center study in the United Kingdom	4589 teledermatology referrals	Teledermatology allowed a reduction of 86.3% (range 78%-93%) of the number of patients requiring in-person assessment.	Lowe et al [10]
Systematic review	N/A[a]	21 studies	Three studies reported reduced waiting times with teledermatology referrals.	Finnane et al [11]

[a]N/A: not applicable.

Effectiveness

In total, 34 papers assessing the effectiveness of teledermatology assessment were identified. These included accuracy and its derivations, concordance, positive and negative predictive values, and impact on subsequent in-person assessment. The results are outlined in Table 2.

Table 2. Studies reporting the effectiveness of teledermatology.

Type	Setting	Sample	Outcome	Reference
Systematic review	N/A[a]	22 studies	Overall sensitivity 94.9% (95% CI 90-97.4) and specificity 84.3%.	Chuchu et al [12]
Observational	Single-center study in Austria	955 lesions	Diagnostic accuracy was 94% with sensitivity of 100% and specificity of 95.8%.	Massone et al [13]
Observational	Single-center study in Serbia	120 patients and 121 pigmented lesions	Diagnostic accuracy between teledermoscopy and histopathology was 90.91%.	Bandic et al [14]
Observational	Single-center study in Ukraine	314 lesions	Accuracy of 90.3%-100.0% for teledermatology assessment compared to in-person and 85.1%-8.9% compared to histopathological diagnoses.	Kravets et al [15]
Observational	Single-center study in the United States	7960 patients	45 (74%) of melanomas were correctly diagnosed, and 57 (93%) were correctly managed, resulting in similar diagnostic and management accuracy of teledermatology compared to in-person assessment.	Wang et al [16]
Observational	Single-center study in Brazil	39 patients	Comparable sensitivities of teledermatology in comparison to in-person assessment (80.8% for teledermatology compared to 80.8% for in-person).	Silveira et al [17]
Observational	Single-center study in Denmark	519 patients	No significant difference in sensitivity between teledermatology and conventional referrals. Specificity was lower in teledermatology referrals.	Vestergaard et al [18]
Observational	Single-center study in Spain	636 patients and 1000 keratotic lesions	The sensitivity, specificity, and positive and negative predictive values for actinic keratosis diagnosis by teledermatology were high (range 82.2-95.0).	Sola-Ortigosa et al [19]
Observational	Single-center study in Austria	113 lesions	High concordance, sensitivity, and specificity for all diagnostic categories.	Kroemer et al [20]
Interventional	Single-center study in New Zealand	200 patients and 491 lesions	Sensitivity of teledermoscopy assessment was close to 100%, and specificity was 90%.	Tan et al [21]
Observational	Single-center study in the United States	321 lesions	The sensitivity for keratinocytic skin cancer diagnosed by teledermatology was 92%, and specificity 49%, resulting in positive and negative predictive values of 61% and 88%.	Cotes et al [22]
Observational	Single-center study in the Netherlands	108 teledermatoscopy referrals	Agreement between teledermatologist and in-person assessment was κ=0.61 (substantial agreement) for diagnosis and κ=0.23 (fair) for management.	van der Heijden et al [23]
Systematic review	N/A	21 studies	Diagnostic accuracy for teledermatology assessment slightly inferior to in-person assessment at 51%-85% (κ=0.41-0.63) compared to 67%-85% (κ=0.90).	Finnane et al [11]
Observational	Single-center study in New Zealand	3470 referrals	Teledermatology assessment of pigmented lesions yielded a positive predictive value of 38.1% and number needed to excise of 2.6.	Sunderland et al [24]
Observational	Single-center study in the United States	8706 patients	69 lesions diagnosed as melanoma resulting in a positive predictive value of 13.7%.	Gemelas et al [25]
Observational	Single-center study in the United States	3021 lesions and 2152 patients	Agreement was fair to substantial for primary diagnosis (45.7%-80.1%; κ=0.32-0.62), substantial to almost perfect for aggregated diagnoses (primary plus differential; 78.6%-93.9%; κ=0.77-0.90), and fair for management (66.7%-86.1%; κ=0.28-0.41).	Warshaw et al [26]
Observational	Single-center study in the United States	1021 referrals (434 teledermatology referrals compared to 587 conventional referrals)	Perfect diagnostic concordance was 36% (18/50) for teledermatology consults compared to 43.1% (69/160) for in-person assessment (*P*=.4). Partial concordance (benign vs malignant) was higher for teledermatology consults (26/50, 52%) compared to in-person (58/160, 36.3%; *P*<.05).	Creighton-Smith et al [9]
Interventional	Single-center study in Sweden	172 lesions	No difference in agreement between teledermatology diagnoses between 2 image sets.	Dahlén Gyllencreutz et al [27]

Type	Setting	Sample	Outcome	Reference
Observational	Single-center study in the United States	79 referrals	Diagnostic concordance between teledermatologists was at least partially concordant in 79 (100%) patients. For those subsequently seen in-person at least partial concordance with teledermatologist was observed in 16/29 (89.7%).	Carter et al [5]
Interventional	Single-center study in Germany	26 patients	The concordance between teledermatologist and in-person assessment was 92.3% for diagnosis and 76.9% for management.	Zink et al [28]
Interventional	Single-center study in Austria	23 lesions	Agreement as calculated by prevalence and bias-adjusted κ showed almost perfect agreement (0.9-0.982).	Arzberger et al [29]
Interventional	Single-center study in the United States	137 lesions and 86 patients	Diagnostic concordance was 82% between the in-person dermatologist and the teledermatologist (95% CI 0.73-0.89), with a κ coefficient of 0.62 (good agreement).	Lamel et al [30]
Interventional	Single-center study in Italy	10 lesions	Teledermatology consults resulted in lower diagnostic concordance compared to in-person assessment and did not improve with the addition of teledermoscopy.	de Giorgi et al [31]
Observational	Single-center study in New Zealand	2108 lesions	1303 (83%) of 1571 lesions with histology available were found to be benign, and 260 (17%) lesions were diagnosed as melanoma, resulting in a melanoma-specific benign:malignant ratio of 5.0:1.	Greenwald et al [32]
Observational	Single-center study in the United States	59,279 patients	One teledermatology pathway resulted in 39% fewer in-person assessments (relative risk 0.61, 95% CI 0.57-0.65).	Marwaha et al [33]
Observational	Single-center study in the United Kingdom	40,201 teledermatology consultations, 77% lesions	Teledermatology allowed 50% of referrals to be discharged to general practice, and 33% to proceed straight to biopsy.	Mehrtens et al [34]
Observational	Single-center study in the United Kingdom	76 patients	Benign diagnoses were made in 52 (68%) patients avoiding subsequent in-person assessment.	Cheung et al [35]
Randomized controlled trial	Single-center study in Switzerland	981 lesions from 39 general practitioners	3 (1.5%) lesions triaged as requiring no further investigation were found to be malignant.	Tandjung et al [36]
Narrative review	N/A	5 papers included in the skin cancer surveillance discussion	Most guidelines suggest in-person review for suspected malignant lesions. Improved accuracy noted with teledermoscopy.	Beer et al [37]
Systematic review	N/A	6 studies	All studies concluded that "high-quality" and dermoscopy images improve diagnostic accuracy. None considered it an adequate replacement for in-person assessment.	Woodley [38]
Observational	Two-center study in Spain	395 consultations	Increased interobserver concordance found with the use of teledermoscopy, resulting in an increased coefficient of agreement from 0.486 to 0.641.	Gómez Arias et al [39]
Interventional	Single-center study in Turkey	150 patients	Diagnostic reliability (κ) for teledermatology without dermatoscopy was 0.75 and 0.77 for 2 different dermatologists, which increased with the addition of dermoscopy to 0.86 and 0.88 (P<.05).	Şenel et al [40]
Observational	Single-center study in Sweden	686 patients and 883 pigmented lesions	The sensitivity for the diagnosis of melanoma by means of teledermatology monitoring was 88.9%, and specificity 93.9%.	Berglund et al [41]
Observational	Single-center study in Sweden	157 referrals (80 teledermoscopy referrals and 77 conventional referrals)	The interobserver concordance was moderate with both teledermatology and conventional paper referrals.	Dahlén Gyllencreutz et al [42]
Randomized controlled trial	Single-center study in Australia	234 participants	Mobile teledermoscopy did not increase sensitivity for skin cancer detection in self-examination.	Janda et al [43]

[a]N/A: not applicable.

Image Quality

In total, 8 papers about image quality in store-and-forward teledermatology were identified. The results are outlined in Table 3.

Table 3. Studies reporting image quality of teledermatology.

Type	Setting	Sample	Outcome	Reference
Observational	Single-center study in Austria	955 lesions	851 out of 962 (88%) dermoscopic lesions and 95 out of 123 (77%) clinical images noted to be of excellent quality.	Massone et al [13]
Observational	Single-center study in Denmark	519 patients	Substantial agreement noted between 2 dermatologists reviewing 600 images (AC2=0.68).	Vestergaard et al [18]
Observational	Single-center study in Austria	113 lesions	7% of images deemed inadequate for diagnosis.	Kroemer et al [20]
Observational	Single-center study in the Netherlands	108 teledermatoscopy referrals	The image quality was reported as bad in 36% of cases, reasonable in 28%, and good in 36%. Accuracy was improved in cases with good-quality images.	van der Heijden et al [23]
Randomized controlled trial	Single-center study in Switzerland	981 lesions from 39 general practitioners	2 (0.2%) images were deemed inadequate for inclusion.	Tandjung et al [36]
Observational	Single-center study in Brazil	333 lesions	12 cases (8.05%) were deemed inadequate. The introduction of a structured protocol increased the odds of acceptable imaging 38.77 times.	Piccoli et al [44]
Interventional	Single-center study in Sweden	172 lesions	Images were of intermediate to high quality in 95.5%-97.7% of primary care images and 96.5%-98.8% of dermatology images.	Dahlén Gyllencreutz et al [27]
Interventional	Single-center study in Australia	10 participants and 66 images	88% of images were deemed to be of good quality.	Janda et al [45]

Discussion

Principal Findings

The majority of studies assessing store-and-forward teledermatology are observational studies. Of the small number of interventional studies identified, only 2 were randomized controlled trials. The area with the most evidence available is for effectiveness, with 34 out of 45 studies reporting various outcomes of efficacy. Overall, the majority of studies in this literature review report that store-and-forward teledermatology services allow reduced time to advice, comparable effectiveness to in-person assessment, and at least adequate image quality for most skin lesions.

Time to Advice and Management

One of the main advantages of teledermatology in skin lesion analysis is the potential for expedited treatment through the reduction of time between referrals and management. There have been several studies assessing this question. They predominantly show improvement with reduction ranging between 4 and 70 days for outcomes such as biopsy, definitive treatment, or clinic appointment [1-6]. Moreno-Ramírez and Ferrándiz [7] report reviewed 43,677 patients over 10 years with an average time to advice of 72 hours. Only 2 studies showed no difference in time to biopsy or definitive treatment [8,9]. A study by Duong et al [8] was underpowered with only 36 patients in the teledermatology pathway and compared in-person consults from 3 to 5 years earlier when there was potentially lower service demand. Very little detail on the teledermatology process used by Creighton-Smith et al [9] is provided. Perhaps, the lack of time reduction is a product of their teledermatology pathway design in this single-center study.

A retrospective review of 4589 referrals by Lowe et al [10] showed that using community imaging for skin lesion referrals enabled 86.3% of referrals to be managed without subsequent in-person assessment. A systematic review of 21 studies by Finnane et al [11] concluded that teledermatology could allow reduced wait times and earlier skin lesion management based on variable reduction in waiting time in 3 studies. Overall, there is a significant time-saving benefit when using teledermatology to review skin lesions.

Effectiveness

The effectiveness of teledermatology is difficult to evaluate. One of the most prominent reasons is the heterogeneity in teledermatology services, making direct comparisons difficult. There is variable use of teledermoscopy and the provider experience in teledermoscopy. The study designs are often small, single-center studies, and the nature of teledermatology means that significant selection bias is often at play. The existing interventional studies often limit generalizability to clinical use by recruiting from settings other than primary care and have no way of allowing blinding. Another issue is the gold standard in diagnosis. Ideally, this would be a histological diagnosis; however, this is usually only available in a small proportion of the most suspicious lesions. In the absence of histology, often the reference standard defaults to in-person dermatologist assessment, which biases the diagnostic effectiveness away from teledermatology assessment. Despite this, a Cochrane review by Chuchu et al [12] focusing on diagnostic accuracy in teledermatology for skin lesion assessment concluded that teledermatology was accurate enough to diagnose most malignant lesions. This was a review of 22 studies published up to August 2016. Their estimate of the overall sensitivity was 94.9% (95% CI 90.1-97.4), and specificity 84.3% (95% CI 48.5-96.8) [12]. Even with their concerns regarding the quality of the studies, they recommended that teledermatology be used to triage patients requiring in-person assessment.

Overall diagnostic accuracy of teledermatology in assessing skin lesions is high. Multiple studies have shown it to be similar to in-person reviews, with figures ranging from 79.5% to 100% [13-17]. Often, this consists of high sensitivity and relatively lower specificity [18-21]. One study, focusing on 321 nonpigmented lesions for consideration of Mohs micrographic surgery, found that despite the high sensitivity of 92%, the specificity was only 49% [22]. van der Heijden et al [23] reported a lower accuracy, with only moderate teledermatology and histology agreement on 108 lesions, likely due to a high proportion of poor-quality images. The trend of high accuracy is consistent with a systematic review published by Finnane et al [11], which included studies from 2009 to 2015. This showed high diagnostic accuracy with the use of teledermatology. It was slightly inferior to in-person assessment at 51%-85% compared to 67%-85% [11]. The generally higher values of accuracy and sensitivity seen in studies from more recent years may reflect improvements in technology and greater experience with teledermatology diagnosis. Two studies looked specifically at positive predictive value when diagnosing melanoma [24,25]. They obtained values of 38.1% and 13.7%. The difference may reflect variability in dermatologist assessment with 9 readers, and significant variability within these noted in the latter study.

Similar to accuracy, there is a high degree of variation in diagnostic concordance reported in skin lesion teledermatology research. Overall, most studies indicate a high diagnostic concordance level compared to in-person dermatologist reviews and histopathology. A well-designed, repeated measures study by Warshaw et al [26] compared dermatologist and teledermatologist diagnoses of 3021 skin lesions from primary care. They report fair to substantial agreement for primary diagnosis of 45.7%-80.1% (κ=0.32-0.62) and substantial to perfect agreement for aggregated diagnoses (a primary diagnosis and up to 2 differential diagnoses) of 78.6%-93.9% (κ=0.77-0.9) [26]. Creighton-Smith et al [9] showed improved rates of partial concordance, and no difference in perfect concordance for teledermatology diagnoses compared to in-person dermatology diagnoses at 52% versus 36.3% ($P<.05$) and 36% versus 43.1% ($P=.4$), respectively. Dahlén Gyllencreutz et al [27] reported high interobserver agreement in skin lesion diagnosis between 2 dermatologists reviewing 172 images from primary care (81.4% and 83.7%). Zink et al [28], Arzberger et al [29], Lamel et al [30], Carter et al [5], and Kroemer et al [20] reported high diagnostic concordance for teledermatology compared to in-person or histology. In contrast, a small study of 10 lesions showed higher concordance for in-person review than teledermatology (κ=0.6 vs 0.52) [31]. Greenwald et al [32] conducted a real-world study assessing the histological diagnosis of pigmented lesions excised on the advice of a store-and-forward teledermatology service. In total, 260 of 1572 lesions (17%) were found to be melanoma, leading to a benign:malignant ratio of 4.9:1 [32]. This reduced with increased dermatologist diagnostic confidence to 2.8:1 for "excise, possible melanoma" and 1:1 for "excise, likely melanoma" when compared to the default "excise to remove doubt."

A benefit of teledermatology is the reduction in patients requiring in-person assessment. A retrospective review of 59,279 primary care referrals found a 39% decrease in face-to-face appointments using the teledermatology pathway [33]. Mehrtens et al [34] found that teledermatology allowed 50% of referrals to be discharged to GPs and 33% to proceed straight to biopsy, saving an estimated 16,282 in-person appointments. Several other studies also noted substantial reductions in face-to-face appointments after implementing teledermatology services [13,35,36].

One of the most important distinctions when reviewing skin lesion assessment by teledermatology is the use of teledermoscopy. This is particularly important when pigmented lesions are assessed. Most research suggests adding dermoscopy images for teledermatology is more effective than clinical images alone. Reviews by Beer et al [37] and Woodley [38] concluded that teledermoscopy increases lesion diagnosis accuracy. Gómez Arias et al [39] compared diagnostic concordance with and without teledermoscopy in 395 cases and showed increased concordance when dermoscopy was included. Şenel et al [40] reported improved accuracy in diagnosing 150 patients with nonpigmented lesions with dermoscopy compared to without (0.86 and 0.88 vs 0.75 and 0.77; $P<.05$ for 2 different dermatologists). Several studies have reported the high effectiveness of teledermatology when using dermoscopic images [24,41,42].

In contrast, Janda et al [43] and de Giorgi et al [31] found no increase when dermoscopy images were added to teledermatology assessments. In the former, images were acquired directly from 234 participants through skin self-examination. Images were likely to be particularly poor if participants were unaware of the need to optimize the skin surface before obtaining dermoscopy imaging. The latter was a small trial of 10 lesions, and as the authors note, there were many difficult lesions.

The availability of clinical history is another factor that may impact teledermatology diagnosis. Surprisingly, it is difficult to find details on this area within studies, making the effect of this difficult to determine.

Image Quality

Image quality is an essential aspect of skin lesion teledermatology. Many studies have reported the proportion of images adequate for diagnosis. These range from 0.2% to 36% [13,18,20,23,36,45]. Dahlén Gyllencreutz et al [27] compared image quality from primary care practices using iPhone 4 cameras with dermoscopy attachments to those taken by dermatologists with Canon EOS D550 cameras. In total, 172 cases were reviewed by 2 dermatologists not familiar with the cases. Despite the differences in camera resolution and operator experience with dermoscopy, there was no statistical difference in the quality of images obtained. The evaluators rated 1.7% and 4.7% of primary care images as poor compared to 1.2% and 3.5% of dermatology images ($P=.25$ and $P=.28$) [27]. They postulate that the difference between evaluators reflects the subjective nature of image quality assessment. Vestergaard et al [18] also had individual dermatologists review the quality of 600 images from primary care. Unlike Dahlén Gyllencreutz et al [27], Vestergard et al [18] found substantial agreement in image quality, with approximately 10% reported as poor quality by each reviewer.

Image quality in teledermatology depends on several factors, such as the equipment used, the inclusion of dermoscopy, and the experience of the person taking images. Studies have shown images obtained by dermatologists or dermatology nurses to be of higher quality than those from primary care [23]. Images obtained by patients generally have the lowest image quality [45]. This is likely due to the increased difficulty taking the images, less experience in focusing lesions, and in the case of dermoscopy, unfamiliarity with the need to prepare the skin, such as removing make-up or applying a fluid to the lesion. Given advances in imaging quality, notably improved smartphone camera resolution, more recent research is likely to report higher image quality regardless of the operator.

Conclusions

Overall, teledermatology offers a comparable standard of effectiveness to in-person assessment. It can save significant time in expediting advice and management. Image quality and inclusion of dermoscopy have a considerable bearing on the overall effectiveness. There is a need for large interventional studies, particularly those with high proportions of histology available to enable definitive conclusions regarding teledermatology outcomes. There is a gap in the literature for studies comparing different teledermatology methods.

Authors' Contributions

AO and LKJ conceptualized and validated the study and managed the resources. They were the project administrators. LKJ managed the methodology, software, formal analysis, and data curation and prepared the original draft. AO supervised the study and reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

AO is a named author in 4 papers referenced in this review. AO receives a fee for service from MoleMap New Zealand, a teledermatology company.

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Abbreviations

GP: general practitioner

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Review

Isotretinoin Use in Transmasculine Patients and Its Implication on Chest Masculinization Surgery: Scoping Review of the Literature

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Abstract

Background: Acne often worsens in transmasculine patients who are on prolonged testosterone therapy. Isotretinoin is an oral retinoid used in the treatment of severe or refractory cases of acne, but it has the potential to cause delayed wound healing. Transmasculine patients may potentially be prescribed treatment for acne with isotretinoin while also planning to undergo chest masculinization surgery.

Objective: This scoping review aims to determine whether isotretinoin has a negative impact on postoperative healing in transmasculine patients undergoing chest masculinization surgery.

Methods: A scoping review was performed using the PubMed and Ovid databases. A total of 16 publications were selected for inclusion.

Results: Acne tends to peak in transmasculine patients 6 months after initiation of testosterone treatment. Severe cases can be treated with isotretinoin; however, acne may recur once treatment is discontinued, given ongoing hormone therapy. There is little to no evidence in the medical literature regarding perioperative use of isotretinoin specifically among transmasculine patients undergoing chest masculinization surgery. In general, however, recent studies have found no evidence of increased hypertrophic scars or keloids in patients taking isotretinoin.

Conclusions: Further studies are required to strengthen the current evidence that suggests that isotretinoin does not need to be discontinued before or after incisional or excisional surgeries, including chest masculinization surgery in transmasculine patients.

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KEYWORDS

acne; isotretinoin; transsexual; scoping; post operative; surgical; pharmacology; pharmaceutic; retinoid; testosterone therapy; sex reassignment; gender affirmation surgery; masculinization surgery; gender reassignment; derm; dermatology; dermis; oily skin; hormone therapy; perioperative; operation; scar; keloid; surgery; surgeries; trans; transmen; transgender; transex; top surgery; chest masculinization; accutane; roaccutane

Introduction

Acne is an inflammatory condition of the skin commonly treated by dermatologists. While the pathogenesis of acne is multifactorial, recent research has emphasized the importance of hormones in the function of the pilosebaceous unit [1]. In sebaceous glands, testosterone is converted to dihydrotestosterone and binds to cytoplasmic androgen receptors, promoting epidermal growth and sebocyte proliferation. This increased sebum production plays a principal role in the development of acne. This is of particular relevance to female-to-male transgender patients (herein referred to as "transmasculine patients") who are often prescribed masculinizing doses of exogenous testosterone as part of gender-affirming hormone therapy. Isotretinoin may be prescribed for more severe or refractory cases of acne, but it has the potential to delay wound healing due to its effect on the stem cells responsible for repopulating the epidermis. Studies in animal models have demonstrated isotretinoin's effect on the pilosebaceous unit, whereby the sebaceous glands were greatly reduced in volume [2]. Given that transmasculine patients may pursue bilateral mastectomy and chest masculinization surgery (often referred to as "top surgery") as a means of gender affirmation, it is vital for dermatologists to be aware of how isotretinoin use may impact chest masculinization surgery in this population. A scoping review [3] of relevant literature available via a web-based database search was performed in order to assist clinicians in making informed, evidence-based decisions with their patients and to identify any existing knowledge gaps regarding isotretinoin treatment and chest masculinization surgery.

Methods

A search of the available biomedical literature was performed using the PubMed database on September 1, 2022. An initial query using the search string, "(transmen OR "trans men" OR trans-men OR transgender* OR transex* OR transmasc*) AND ("top surgery" OR "Chest masculinization") AND (isotretinoin OR accutane OR roaccutane)," yielded zero results. A more focused search used the string, "(transmen OR "trans men" OR trans-men OR transgender* OR transex* OR transmasc*) AND (isotretinoin OR accutane OR roaccutane)," yielded 19 results, all of which were published between 2015 and 2022. Another search using the string, "(surg*) AND (heal* OR scar*) AND (isotretinoin OR accutane OR roaccutane)," limited to publications within 10 years, yielded 109 results, for a combined total of 128 articles selected for title and abstract screening. This was performed by 2 independent reviewers (DS and TS), with 40 articles selected for subsequent full-text review. After full-text review, a total of 11 studies were selected for inclusion. Surveying the references of these 11 articles revealed an additional 5 relevant studies, which were also chosen for inclusion.

An additional search was later conducted using the Ovid database on June 18, 2023. The search terms "(transmen OR "trans men" OR trans-men OR transgender* OR transex* OR transmasc*) AND ("top surgery" OR "Chest masculinization") AND (isotretinoin OR accutane OR roaccutane)" yielded zero results. A search using the key terms "(transmen OR "trans men" OR trans-men OR transgender* OR transex* OR transmasc*) AND (isotretinoin OR accutane OR roaccutane)" yielded 17 results, though no articles were new in respect to the previously conducted PubMed search. The key terms "(surg*) AND (heal* OR scar*) AND (isotretinoin OR accutane OR roaccutane)," limited to publications within 10 years, yielded 33 results, all of which were similarly included in the previous PubMed search.

Results

Acne and Isotretinoin Use in Transmasculine Patients

Masculinizing hormone therapy used in transmasculine patients has the potential to worsen acne, mediated largely by testosterone's effect on the pilosebaceous unit [4]. In a prospective study of 20 transmasculine patients undergoing exogenous testosterone therapy, rates of facial acne increased from 35% to 82.4% following 6 months of treatment, whereas rates of chest and back acne increased from 15% to 88.2% within the same time frame [4]. Another prospective cohort study of 193 transmasculine patients demonstrated that self-reported scores of acne severity peaked 6 months after initiating testosterone therapy, and were still significantly higher than those at baseline after 12 months of therapy [5]. A retrospective review of medical records of 55 transmasculine patients also demonstrated a significant association between acne and a serum testosterone level greater than 630 ng/dL [6].

No evidence-based guidelines currently exist for treating acne in the context of testosterone therapy [7]. Though acne caused by exogenous testosterone is often mild to moderate in severity [8], more persistent or extensive cases may necessitate treatment with isotretinoin. While isotretinoin can be an appropriate treatment for acne in the setting of prolonged testosterone therapy, there are many special considerations when prescribing isotretinoin for transmasculine patients [9]. Given the teratogenicity of isotretinoin, clinicians should be prepared to engage their patients in thorough but sensitive conversations regarding their risk of pregnancy. Additionally, though the relationship between isotretinoin use and idiosyncratic depression is largely controversial, it should be noted that depressive symptoms, suicidal ideation, and self-harm are more common in transgender individuals. These comorbidities are posited to be largely the result of social stresses including bullying, harassment, social stigma, and decreased support from family members [10]. It also unclear whether long-term remission can be achieved with one "cycle" of isotretinoin in the context of ongoing testosterone therapy. No large-scale randomized studies have examined isotretinoin use in this specific population, but several case studies have demonstrated the efficacy of isotretinoin therapy in the treatment of testosterone-dependent acne; these results are presented in Table 1 [11,12].

All 4 patients presented in these case studies had a positive response to isotretinoin therapy. Patients 1 and 2 achieved resolution of their acne, but ultimately presented with recurrence necessitating ongoing isotretinoin therapy. Patient 3 achieved remission and decided to discontinue treatment at 4 months. Patient 4 demonstrated partial clearance of his acne, but associated therapy with a depressive episode and discontinued at 3.5 months of treatment.

Table 1. Case series of transgender males treated with isotretinoin [11,12].

Patient number	Patient age (years)	Testosterone dose	Length of testosterone treatment before starting isotretinoin	Isotretinoin dose
1	20-29[a]	Testosterone undecanoate, 1000 mg every 3 months	6 months	30 mg/day for 9 months, discontinue for 3 months, ongoing at 20 mg/day
2	20-29[a]	Testosterone undecanoate, 1000 mg every 3 months	6 months	20 mg/d for 8 months, discontinue for 6 months, ongoing at 20 mg 3 times per week
3	17	Testosterone (formulation unspecified), 250 mg every 21 days	6 months	20 mg/day for 3.5 months
4	17	Testosterone (formulation unspecified), 250 mg every 21 days	5 months	20 mg/day for 4 months

[a]The patient in the original case report was referred to as being "in his 20s."

Isotretinoin and Surgical Healing

It has traditionally been taught that surgical procedures should not be performed while a patient is taking oral isotretinoin, given concerns that retinoids may alter connective tissue healing or lead to keloids or hypertrophic scarring. These recommendations are based largely on 3 case series published in the 1980s, which reported the formation of keloids in 9 patients on isotretinoin therapy, who subsequently underwent dermabrasion or argon laser phototherapy [13,14]. However, recent literature on the subject contradicts these earlier reports, as noted by the American Society for Dermatologic Surgery (ASDS).

The ASDS guidelines (published in 2017) for following comprehensive literature review and task force consensus state, "The data for incisional and excisional cutaneous surgery on isotretinoin is insufficient to make any recommendations. In particular cases, incisional or excisional surgery may be medically necessary in patients receiving isotretinoin" [15]. Quality of Evidence was assigned a "D" score by task force members, using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system, and representing "very low" confidence in their final recommendation [15]. Another systematic review with consensus recommendations, also published in 2017, determined that there is "insufficient evidence to delay cutaneous surgery for patients currently taking or having recently completed isotretinoin therapy" [16].

More recently, a randomized controlled trial of 303 patients, published in 2020, examined the effects of perioperative isotretinoin therapy on rhinoplasty outcomes [17]. This study suggests that isotretinoin caused no significant disturbances in postoperative healing, with no hypertrophic scarring or cartilaginous deformities. A case study published in 2022 demonstrated normal scar tissue healing in 2 cisgender females who underwent bilateral reduction mammoplasty while on isotretinoin therapy [18]. Neither patient had a family history of keloids or hypertrophic scarring. Our review did not reveal any studies that specifically examined postoperative healing in transmasculine patients on isotretinoin therapy undergoing chest masculinization surgery.

Discussion

Acne is common in transmasculine patients undergoing masculinizing hormone therapy, and some individuals with testosterone-induced acne may benefit from isotretinoin therapy. In a survey of transgender individuals, those who self-identified as men were more likely to prioritize treatment of the chest over that of their face or genitals [19]. In a cross-sectional analysis of 90 transgender men, exogenous testosterone demonstrated a significant effect on the presence of chest acne, which was present in 52% of transmasculine patients on testosterone therapy, compared to 9% of those who were not on testosterone therapy. Given that exogenous testosterone therapy has a prominent effect on the chest [20], it is vital for clinicians to recognize the impact that acne treatment has on patients' body image–related quality of life.

When initiating isotretinoin therapy in transgender male patients, it should be standard practice for dermatologists to discuss plans for any upcoming surgery, including chest masculinization surgery, with their patients. While current literature does not suggest any effect of isotretinoin on postsurgical wound healing, risks and benefits of perioperative treatment should be discussed with patients, and a treatment plan should be formulated on the basis of their individual goals of care and severity of acne. Given the lack of specific evidence in this patient population, surgery would ideally be performed before initiation of isotretinoin therapy in order to minimize any interactions. However, in cases of severe acne with a risk of scarring, it is not recommended to delay treatment with isotretinoin or to discontinue isotretinoin before chest masculinization surgery.

Further research is needed on this particular subject matter and patient population in order to better to characterize the exact relationship between isotretinoin use and chest masculinization surgery, so that dermatologists may better coordinate care for their transgender patients.

Conflicts of Interest

RPD is the Editor-in-Chief of *JMIR Dermatology*, joint coordinating editor for Cochrane Skin, a dermatology section editor for UpToDate, and a coordinating editor representative and cochair on the Cochrane Council. TES is an editorial board member–at-large for *JMIR Dermatology* and a member of the Cochrane Collaboration. DS is a social media editor for *JMIR Dermatology*.

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Abbreviations

ASDS: American Society for Dermatologic Surgery
GRADE: Grading of Recommendations, Assessment, Development, and Evaluation

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Review

Public Health Risks, Dermatological Manifestations, and Environmental Justice Associated With Vinyl Chloride Exposure: Narrative Review

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Abstract

Background: Environmental vinyl chloride (VC) exposure may result in serious acute and chronic dermatological conditions. Because existing literature largely focuses on exposures in occupational settings, a gap persists in our understanding of the medical consequences of large-scale chemical spills.

Objective: This study aims to examine the potential dermatological manifestations of VC exposure in the context of industrial spills and other environmental disasters and to highlight the public health and justice implications of such releases.

Methods: In this narrative review, relevant evidence-based, peer-reviewed scientific sources, gray literature, and media reports were identified via searches of search PubMed and Google using predetermined keyword search terms related to VC, VC spills and releases, train derailment, cutaneous disease, public health, and vulnerable and marginalized populations.

Results: Contact dermatitis and frostbite may arise acutely, highlighting the importance of swift decontamination. Long-term manifestations from chronic VC exposure due to persistence in environmental reservoirs include Raynaud disease, sclerodermatous skin changes, acro-osteolysis, and cutaneous malignancies. The clinical severity of cutaneous manifestations is influenced by individual susceptibility as well as duration, intensity, and route of exposure. Additionally, chemical releases of VC more frequently impact Communities of Color and those of lower socioeconomic status, resulting in greater rates of exposure-related disease.

Conclusions: With environmental release events of hazardous chemicals becoming increasingly common and because the skin has increased contact with environmental toxins relative to other organs, an urgent need exists for a greater understanding of the overall short- and long-term health impacts of large-scale, toxic exposures, underscoring the need for ongoing clinical vigilance. Dermatologists and public health officials should also aim to better understand the ways in which the disproportionate impacts of hazardous chemical exposures on lower-income and minority populations may exacerbate existing health disparities. Herein, we describe the health implications of toxic releases with particular consideration paid to marginalized and vulnerable populations. In addition to legal and regulatory frameworks, we advocate for improved public health measures, to not only mitigate the risk of environmental catastrophes in the future, but also ensure timely and effective responses to them.

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KEYWORDS

vinyl chloride; cutaneous manifestations; dermatology; industrial accident; climate advocacy; public health; environmental toxins; environmental health; acute; chronic; utilization; malignancy; community; socioeconomic; hazardous chemicals; toxicology

Introduction

In a now well-publicized event, a Norfolk Southern Railway train hauling 149 cars, 20 of which were tanker cars containing hazardous industrial chemicals, derailed in East Palestine, Ohio, in the evening hours of February 3, 2023 [1] (Figure 1). As highly toxic vinyl chloride (VC) was released into the air, soil, and water surrounding the crash site, evacuation orders, region-wide contamination fears, and a federal investigation ensued. The National Transportation Safety Board's (NTSB) preliminary report identified an overheated wheel bearing as responsible for the derailment, which was deemed entirely preventable [1]. Norfolk Southern set a critical threshold for its hot bearing detectors at 93.33 °C above ambient temperature, so despite escalating readings, a critical warning was not transmitted until the faulty bearing's temperature was 122.78 °C above ambient temperature [1]. Fires resulting from the accident burned for 2 days before containment. However, because of the continued temperature rise within VC-containing tankers, the concern for an ongoing VC polymerization reaction with an impending explosion was heightened. Consequently, a controlled venting and burning of VC from 5 tankers was undertaken on February 6, requiring the expansion of the evacuation zone to 2 miles [1]. Although the exact amount of VC spilled remains under investigation, the NTSB estimates 115,580 gallons were released [1].

Figure 1. Aerial photograph of the train derailment site. Photo credit: National Transportation Safety Board [1].

VC is a manmade organochloride used in the production of plastics composed of polyvinyl chloride (PVC). Occupational, environmental, and accidental exposure to VC is associated with a range of health effects spanning multiple organ systems [2]. Although the emphasis of this review is on the dermatologic manifestations of VC exposure, the interconnectedness of these effects with toxicity to other organ systems must be acknowledged. The liver is identified as a major target organ; however, acute exposure–related illness along with chronic carcinogenic, immunologic, and neurologic effects are also widely characterized [2]. Acute exposure via inhalation causes respiratory irritation, headache, nausea, vomiting, dizziness, fatigue, weakness, and confusion. In high concentrations, exposure leads to nervous system depression, arrhythmias, coma, and death [2]. Importantly, prolonged exposure is linked to numerous cancers, namely hepatic angiosarcoma, hepatocellular carcinoma, and malignancies of the brain, lungs, skin, and hematopoietic system. Other chronic health effects include peripheral neuropathy, nephrotoxicity, immune disorders, steatohepatitis and cirrhosis, and acro-osteolysis (AOL) [2].

VC is transported as a liquefied gas under vapor pressure. Given its flammability, exposure to intense heat may result in container explosion, greatly magnifying dispersal during transportation and industrial accidents. Historically, VC exposure occurred among factory workers in direct contact with the chemical during PVC manufacturing. However, community exposures secondary to intentional industrial releases and accidental spills have occurred for decades and are well-reported [3] (Table 1). Despite these reports, VC exposure remains an underrecognized public health threat. Herein, this review emphasizes valuable insights into the serious health risks of VC exposure, with particular attention to cutaneous manifestations, and the broader impact of environmental toxin releases, particularly for vulnerable populations.

Table 1. VC[a] chemical spills, industrial accidents, and environmental contamination in the United States.

Year	Location	Source	Type of release	Amount or scope of VC released
1964	Hebronville, Massachusetts	Thompson Chemical Company	Industrial facility fire and explosion	70 tons released [4].
1950s-1985	US Marine Corps Base Camp Lejeune, North Carolina	Multiple sources	Leaking underground storage tanks, industrial site spills, and contamination from waste disposal sites	Unknown amount released. One million military and civilian staff and their families were potentially exposed [5].
1983	Delaware City, Delaware	Stauffer Chemical Company and Formosa Chemical Corp	The plant was deemed a Superfund site due to contamination from earthen lagoons and pits used for the disposal of PVC[b] waste and sludge	EPA[c] testing demonstrated VC contamination of groundwater at 220 µg/L (limit 5 µg/L), which is used locally for drinking water and agricultural purposes. Soil contamination was also identified [6,7].
2004	Illiopolis, Illinois	Formosa Chemical Corp	Industrial plastics manufacturing facility fire and explosion	150,000 gallons were present on site; an estimated 6000 gallons were released [8].
2005	Point Comfort, Texas	Formosa Chemical Corp	Industrial plastics manufacturing facility fire and explosion	Unknown amount released [6].
2005	Delaware City, Delaware	Formosa Chemical Corp	Industrial plastics manufacturing facility release due to equipment design flaw	2500 pounds released [6].
2012	Paulsboro, New Jersey	Conrail Company	Train derailment–related spill	24,000 gallons released [3,9].
2013	Westlake, Louisiana	Axiall Chemical	Industrial facility fire	Unknown amount released [10].
2017	Houston, Texas	Multiple chemical plants	Flooding and damage to industrial facilities during Category 4 Hurricane Harvey	Unknown amount released [11].
2020	Westlake, Louisiana	Multiple manufacturing plants and industrial facilities including Westlake Chemical	Damage to industrial facilities during Category 4 Hurricane Laura	Unknown amount released. Possible VC release reported to US Coast Guard's National Response Center. Westlake Chemical incurs facility damage and power outages and declares force majeure [12,13].
2022	Flint, Michigan	Lockhart Chemical	Manufacturing facility spill	Unknown amount released [14].
2023	East Palestine, Ohio	Norfolk Southern Railway	Train derailment–related spill	Unknown amount was released but estimated to be as much as 1.1 million pounds [15].

[a]VC: vinyl chloride.

[b]PVC: polyvinyl chloride.

[c]EPA: Environmental Protection Agency.

Methods

To characterize the cutaneous effects associated with VC exposure, especially those resulting from industrial releases and accidental spills, a narrative review was conducted using a comprehensive approach to identify relevant evidence-based, peer-reviewed scientific sources, gray literature, and media reports. Searches were performed in reputable databases such as PubMed and Google, using predetermined keyword search terms related to VC, spills and releases, train derailment, cutaneous disease, public health, and vulnerable and marginalized populations. We recognize this nonsystematic approach has inherent limitations of content selection, such as the potential for subjectivity and bias [16], but given the paucity of recent scientific studies in the medical literature on this topic and the critical importance of considering investigations by and proceedings of federal agencies, commissioned governmental assessments, litigation documents, investigative journalistic reporting, and media accounts to the exploration of this issue, a narrative approach was pursued in order to more broadly capture the public health and equity implications of VC-related exposures.

Results

Production and Environmental Contamination in the United States

Production of VC began in the 1930s. Currently, 99% of VC is used to manufacture PVC, of which 7.2 million metric tons were produced in 2019 in the United States [2,17]. The largest concentration of facilities that currently produce, process, or use VC are located in Texas (12 sites), Louisiana (8 sites), and Kentucky and Ohio (3 sites each) [2]. These facilities house massive amounts of VC, with some authorized to store 500 million pounds [2]. Among US states, Louisiana ranks as a top producer of toxic wastes per capita, a fact which community activists have long decried as the source of disproportionate health impacts observed in residents living near the state's many chemical plants [6]. Not surprisingly, the heavily industrialized corridor between New Orleans and Baton Rouge is known as "cancer alley" because of the region's markedly higher rates of malignancy [18].

Under the Toxics Release Inventory (TRI) Program, the Environmental Protection Agency (EPA) tracks toxic chemicals that pose a threat to human health and the environment, including VC [2,19]. Manufacturing facilities are encouraged to first pursue source reduction of toxic waste; however, for generated waste, preferred management methods include recycling, treatment, and neutralization, and as a last resort, disposal or release into the environment. In 2021, approximately 428,500 pounds of VC were released into the environment based on mandatory reporting to the EPA under the provision of the TRI program [19].

While VC should volatilize to the atmosphere, its water solubility may allow leaching through soil and into groundwater prior to evaporation [2]. As a result, chemical releases and leaks can lead to extensive soil and groundwater contamination and are known to persist for years, as evidenced by enduring levels exceeding regulatory limits in groundwater wells. VC may also enter household air via volatilization from contaminated water that is heated and used for bathing, cooking, or laundry [20]. Consequently, populations residing in heavily industrialized areas surrounding plastic manufacturing plants may experience ongoing exposure to this carcinogen.

A particularly noteworthy example is the Axiall Chemical Plant in Westlake, Louisiana, which reportedly stores 100 million pounds of VC and has a long history of industrial accidents, fires, and major environmental violations [21]. EPA surveys identified contamination by hazardous substances, including VC, in sediments, surface waters, and the biota of the nearby Calcasieu Estuary. This prompted a federal lawsuit in 2021 against Axiall and 8 other petrochemical manufacturers under the Comprehensive Environmental Response, Compensation, and Liability Act "seeking reimbursement of response costs incurred or to be incurred for response actions taken at or in connection with the release or threatened release of hazardous substances at the Calcasieu Estuary" [22].

Beyond EPA-tracked and regulated toxic releases, uncontrolled or illegally released hazardous substances as a result of acute chemical incidents also pose a significant public health threat. According to the last report by the National Toxic Substance Incidents Program, 14,175 acute chemical incidents, including VC releases, were documented in the United States in 2013 with 64% associated with fixed facility releases and 36% attributed to transportation-related releases [23]. Volatilization and chemical spills account for the 2 most common release types, with volatilization contributing to 54.4% of injuries and 27% of fatalities. Chemicals that readily volatilize, such as VC, have the potential to quickly expose large numbers of people before evacuation or shelter-in-place orders are issued, explaining why a VC release from a train derailment caused a mass injury event that year [23]. Alarmingly, 1044 train derailments occurred in the United States in 2022 [24]. The sheer number of acute chemical incidents reported annually and the magnitude of the recent VC release in Ohio clearly highlight that future response plans must reduce public exposure following chemical incidents.

The Dermatological Effects of VC Exposure

The full magnitude of health impacts resulting from the recent VC spill in Ohio may not be realized for years to come. However, acute health concerns have already emerged. For example, many residents have anecdotally noted skin "rashes" in the aftermath of the spill [25]. Acute dermatological manifestations were similarly reported in 5.1% of patients presenting to emergency rooms in 2012 following VC release from a New Jersey train derailment [26]. Cutaneous toxicities resulting from chemical spills may be significant because, relative to other organs, the skin has the greatest surface area in contact with a given environmental exposure, underscoring the vital need for dermatologists and other health professionals to recognize the potential acute and delayed cutaneous manifestations of VC exposure following industrial accidents and chemical spills.

Most existing reports focus on chronic occupational exposure and predate 1995. Accordingly, the medical literature appears to have an incomplete understanding of the impacts of acute and persistent environmental VC exposure following toxic environmental release events. As such, health care providers may struggle to identify and treat the immediate and long-term effects of VC exposures, suggesting that further studies are needed to fully elucidate the health risks posed by VC in these situations. Despite existing limitations, evidence suggests that VC exposure causes short- and long-term skin-related manifestations, which we describe in detail herein [27,28].

Cutaneous exposure to VC may cause contact dermatitis, while rapid evaporative cooling of liquid VC on the skin may result in frostbite with erythema, blistering, and desquamation [2]. Individuals whose clothing or skin is contaminated with pressurized liquid VC can secondarily contaminate others via direct contact or through airborne release of the chemical [29].

VC exposure may lead to the development of vinyl chloride disease, which is characterized by the triad of Raynaud symptoms, sclerodermatous skin changes, and lytic bone lesions known as AOL [27]. Variable phenotypic presentations are observed after VC exposure with 10% displaying cutaneous sclerodermoid changes, 6% demonstrating Raynaud phenomenon, and 3% developing AOL [30].

The scleroderma-like changes observed in VC exposure are characterized by unique clinical features that help in distinguishing this entity from primary systemic sclerosis (SS). Namely, the cutaneous lesions in VC-associated disease primarily affect the dorsal hands and forearms and present as papules, nodules, and plaques with associated pruritus and hyperhidrosis. Additionally, coarsening of the skin on the forehead and cheeks may occur, whereas microstomia, matted telangiectasias, and calcinosis—classic features of limited cutaneous SS—are generally absent. Clubbing and fingertip shortening accompanied by lytic lesions in the distal phalanges, the key features of AOL, typify VC-associated scleroderma rather than the more common distal tufting observed in SS [3,30]. VC-induced scleroderma is typically seronegative for antinuclear, anticentromere, and anti-Scl-70 antibodies [2,30]. Histology of VC-associated sclerodermatous lesions has both shared and distinct features when compared to SS. In both conditions, hyperkeratosis, epidermal atrophy, and thickening of dermal collagen bundles with disorganization and fragmentation of elastic fiber are observed. Interestingly, these histological changes are also seen in clinically uninvolved skin in one-quarter of individuals exposed to VC, suggesting genetic factors likely play a role in the phenotypic presentation of VC disease among those exposed [30]. Notably, adnexal structures, specifically eccrine glands, are often atrophic in classic SS but preserved in VC disease [30].

Raynaud syndrome, a dominant sign resulting from VC exposure, may be severe and accompanied by trophic changes and digital ulceration. Progressive bone resorption and deformity of the distal phalanges in AOL may damage underlying vasculature, causing secondary skin and nail changes, including clubbing and nail dystrophy [2]. In one report, one-third of workers in contact with VC developed Raynaud syndrome, with symptoms persisting for ≥15 years after exposure [31]. In classic Raynaud, chronic abnormal vasospastic responses produce microangiopathic changes over time; however, the pathomechanisms underlying VC-induced Raynaud disease remain incompletely understood. Hand angiographic findings in patients with VC-associated Raynaud disease universally identified arterial abnormalities including vascular occlusion, stenosis, thread-like narrowing, and development of collateral circulation [32]. Although microvascular alteration is a contributing factor, it does not explain the entire picture. For example, relative to controls in one study, the VC-exposed cohort exhibited persistent nail fold capillary changes and carried a significantly higher prevalence of Raynaud symptoms, yet those symptoms were not statistically related to the degree of capillaroscopic modification [31]. Functional proof tests provide further insight into potential mechanisms driving chronic cutaneous symptoms of VC exposure. Abnormal plethysmography, vibration perception, and cooling tests in exposed individuals suggest that VC-induced cutaneous vascular and peripheral neuropathic damage play a role [28].

Additionally, evidence suggests that VC exposures alter immunologic function and may lead to the observed autoimmune presentations observed clinically. Prior studies in VC-exposed workers and animal models dating back decades demonstrate a range of responses, including B-cell proliferation, hypergammaglobulinemia, oxidative stress, elevated complement levels, and production of proinflammatory cytokines (tumor necrosis factor-α and interleukin-1β, -6, and -8) [2]. Interestingly, similar cytokine profiles are observed after activation of cutaneous xenobiotic receptors and transcription factors, such as the aryl hydrocarbon and pregnane-X receptors, in response to binding by environmental pollutants including particulate matter, polycyclic aromatic hydrocarbons, and benzene [33]. Unfortunately, little research has focused on elucidating the molecular pathways responsible for cutaneous toxicities to VC, highlighting the large gaps in our understanding of the pathogenesis.

However, studies suggest that VC-induced Raynaud disease may, in part, be triggered by immune complex deposition. A study examining 22 patients with a history of VC exposure, who subsequently developed Raynaud disease, detected cryoglobulins in 81% of sera samples with cryoglobulinemia occurring, in part, due to hyperactivation of humoral responses following the exposure [34]. Disturbances in humoral immunity are likely to also play a role in the systemic effects of VC, including hepatotoxicity and neurologic disease [2]. Genetic factors, such as human leukocyte antigen (HLA)-B8 and HLA-DR3, correlated with severe scleroderma-like disease following VC exposure, whereas the HLA-DR5 haplotype may also increase the susceptibility risk of Raynaud disease [2]. Moreover, polymorphisms in the M-1 and T-1 genes encoding glutathione-S-transferases, which are involved in VC-metabolism, are linked to the development of Raynaud [2].

Tissue fibrosis within the liver, skin, lungs, and kidneys is a well-reported consequence of VC toxicity, but the pathomechanisms responsible for inducing cutaneous fibrosis remain poorly understood. Studies of VC-associated hepatic, renal, and pulmonary fibrosis demonstrate upregulation of plasminogen activator inhibitor-1, transforming growth factor-β, platelet-derived growth factor, vascular endothelial growth factor, and connective tissue growth factor [35-37]. Since these growth factors are implicated in the pathogenesis of SS, we purport this serves as a likely corollary for cutaneous fibrosis observed after VC exposure [38]. However, further research is needed to fully elucidate the immunological, vascular, and neuropathic factors in VC-mediated dermatological disease.

The carcinogenicity of VC was established in the 1960s [39]. Evidence suggests a possible association of VC with cutaneous malignant melanoma and squamous cell carcinoma. Immune dysregulation and genetic-environmental interactions mediated by CYP2E1 metabolism lead to reactive intermediates that induce tumor suppressor gene mutations in *ras* and *p53*, which are implicated in cutaneous carcinogenesis [40-42]. Genetic polymorphisms in CYP2E1 and glutathione-S-transferases increase VC-induced mutations, allowing for the potential identification of high-risk individuals [42]. Moreover, geographic mapping of industrial releases and accidents may help to identify high-risk populations who should receive serial monitoring for cutaneous malignancy [18].

Additionally, cutaneous stigmata of chronic hepatic injury, including spider angiomas, palmar erythema, xanthelasma, jaundice, and pigmentary changes may occur, as well as thrombocytopenic purpura as a consequence of portal hypertension-induced splenomegaly and platelet sequestration [28]. One report described VC-associated purpura in the setting of lymphohistiocytic infiltrate within dermal arterioles on histopathology, circulating immune complexes, and anti–smooth muscle autoantibodies on laboratory work-up, suggesting immunological dysfunction was playing an etiological role [43].

When assessing dermatological effects, the volume of VC released into the environment along with the duration, intensity, and route of exposure (eg, direct skin contact, inhalation, and ingestion) must be considered. Variability in individual susceptibility to VC toxicity based on overall medical status and underlying genetic predisposition should dually be considered. For example, those with preexisting atopy, autoimmunity, vascular injury, or polymorphisms that increase VC-induced carcinogenic mutations may be at increased risk of cutaneous disease [42]. Finally, it is important to account for the possibility that VC may synergistically interact with other toxins released during spills and industrial accidents as this could lead to novel health effects.

Treatment and Prevention of VC-Induced Disease

To minimize the risk of long-term health issues, prompt medical evaluation is crucial in cases of VC exposure. Dermatologists, public health experts, and frontline health workers play a critical role in identifying and treating exposure-related skin conditions as well as detecting individuals at risk of internal sequelae. Following acute exposure, the priority is decontamination by removing saturated clothing and cleansing exposed skin and hair with soap and water to halt further exposure. Notably, children are more susceptible to skin absorption than adults due to a higher surface area to body weight ratio [29]. Frostbite injury is treated by rewarming affected areas in a hot-water bath (38.89-42.22 °C), and chemical burns are treated as thermal burns [29]. With no established treatments for VC-associated cutaneous manifestations, the efficacy of standard therapeutic agents—such as calcium channel blockers, α-1-adrenergic receptor antagonists, angiotensin receptor blockers, topical nitrates, fluoxetine, phosphodiesterase inhibitors, endothelin-1 receptor antagonists, or antiplatelet agents for Raynaud symptoms and methotrexate, mycophenolate mofetil, cyclophosphamide, D-penicillamine, intravenous immunoglobulin, hematopoietic stem cell transplantation, tocilizumab and rituximab for VC-induced SS—remains uncertain [44,45]. Thus, further investigation into effective and safe therapeutic approaches in VC-associated autoimmune diseases is warranted.

Because VC persists in environmental reservoirs for years, clinicians should remain alert to long-term manifestations arising from chronic exposure. The Occupational Health and Safety Administration [46] recommends annual medical surveillance for any exposure over the minimal risk level of 0.5 ppm. However, no standardized guidelines currently exist for surveillance and long-term management of chronic dermatological conditions. Moreover, VC exposure may affect other organ systems with dermatological conditions often arising as a cutaneous manifestation of systemic disease. Therefore, we also advocate for longitudinal screening for dermatological manifestations as a component of required medical surveillance and as a compensated benefit to victims of industrial accidents or chemical spills. However, we recognize that currently available data is insufficient to mandate longitudinal dermatology screening, underscoring a key evidence gap. Consequently, emergency room physicians, frontline and public health professionals, and primary care physicians play a crucial role in screening individuals with VC exposure for health impacts both acutely and longitudinally, underscoring the need to recognize the associated cutaneous manifestations of VC exposure and generate referrals to dermatologists for appropriate evaluation and treatment.

With limited treatment options for VC-related exposure, prevention is paramount. Public health officials play an integral role in preventing and mitigating chemical exposure–related health conditions through regulatory oversight and health policy implementation. While the precise cause of the Ohio derailment remains under investigation, decades of divestment in government spending for maintenance of infrastructure, including transportation networks, coupled with industry participation in the EPA's peer review process for scientific assessments in which disease thresholds and exposure limits to toxic substances are established, widespread environmental deregulation, and successful lobbying against broad definitions for high-hazard flammable trains and implementation of electronically controlled pneumatic brakes on trains transporting hazardous materials contribute collectively to the likelihood of future disasters [39,47,48]. Moreover, the increasing frequency and intensity of extreme weather events due to climate change amplifies the risk of secondary disasters due to toxic environmental releases resulting from damage to industrial facilities, such as those documented following Hurricanes Katrina, Harvey, and Laura [49,50]. This further emphasizes the need to ensure the integrity of industrial infrastructure, climate resiliency, disaster management and response, improved railroad safety, safety inspections for transportation of hazardous materials, enforcment of safety regulations, mandatory release notifications, ongoing monitoring of chemical spills and releases, and development of public health campaigns to promote education on chemical exposures.

Environmental Justice and Public Health Implications

With respect to health equity, dermatologists, public health professionals, and primary care providers should recognize that hazardous chemical exposures exacerbate existing health disparities among marginalized populations. In the United States, most railroads traverse neighborhoods of lower socioeconomic status and racially divide cities, while fenceline communities in industrial zones are predominantly Black [6,51]. In East Palestine, Ohio, the median household income was US $49,407 in 2020, versus US $64,994 nationally [52]. Beyond overwhelming concerns for health impacts, the average cost to evacuate after a disaster is US $5000 per family [53]. Consequently, the financial ramifications on this community are significant as the derailment forced residents from their homes, shuttered businesses, contributed to lost wages, sickened livestock, and portends looming medical bills [54]. Disproportionate exposures to toxic pollution are well-documented. Nationally, hazardous waste sites and industrial facilities are more often sited in proximity to Black communities and those of lower socioeconomic status, a historic legacy of discriminatory practices such as redlining [6,55]. However, such practices persist. Due to existing disparities in the granting of permits by state regulators in Louisiana, where a large number of PVC plants operate, industrial emissions are 7- to 21-fold higher in Communities of Color. Not surprisingly, these same communities have higher rates of cancer and respiratory disease and overall greater health impacts from pollution [6]. The dermatologic manifestations of environmental pollution are well described in the medical literature. Therefore, it is imperative to recognize that existing disparities in skin health, including higher incidence of cutaneous disease and limited access to health care, among lower-income and minority populations are further amplified by the unequal impact of hazardous exposures in these groups [56].

Discussion

The 2023 Ohio train derailment has renewed the spotlight on the health consequences arising from chemical exposures following environmental releases. Because most existing literature on VC is decades old and focuses primarily on occupational exposure, accurately assessing potential risks to public health associated with chemical spills, including identification and treatment of exposure-related dermatological conditions, is challenging for health professionals. Despite these limitations, evidence suggests acute dermatological manifestations may include contact dermatitis and frostbite. Notable subacute-to-chronic manifestations include Raynaud disease, acral sclerodermatous changes, AOL, skin cancer, and cutaneous stigmata of liver disease. In addition to individual susceptibility, factors that may influence severity include duration, intensity, and route of exposure.

We advocate for the consideration of viable alternatives to plastic products requiring the use of VC in their production. Examples of such alternatives include glass, ceramics, and linoleum. European nations have implemented restrictions and outright bans on VC use, signaling growing recognition of the importance of risk reduction associated with this hazardous chemical [57]. Furthermore, greater awareness of the dermatological effects of environmental chemical exposures is needed, with special consideration for marginalized and vulnerable populations, underscoring the urgency for improved public health measures, legal and regulatory frameworks, and policies to ensure timely and effective responses to and prevention of chemical spills and other environmental disasters.

Conflicts of Interest

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Abbreviations

AOL: acro-osteolysis
EPA: Environmental Protection Agency
HLA: human leukocyte antigen
NTSB: National Transportation Safety Board
PVC: polyvinyl chloride
SS: systemic sclerosis
TRI: Toxics Release Inventory
VC: vinyl chloride

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Review

Diagnosing the Dermatologic Blues: Systematic Review of the Rare Conundrum, Psychogenic Purpura

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Abstract

Background: Psychogenic purpura is an idiopathic psychodermatologic condition of recurrent, painful purpura precipitated by psychological stress, predominantly affecting young females. Little consensus exists on the diagnostic guidelines for this rare condition, often resulting in costly, unnecessary, and stressful investigations as well as prolonged hospital admissions.

Objective: With this first up-to-date systematic review of 134 cases of psychogenic purpura in over a decade, we aim to thoroughly investigate the diagnostic strategy and treatment regimens used in the last decade. With a sooner diagnosis, patient stress and nosocomial ecchymoses can be minimized, and treatment can be expedited.

Methods: We conducted a literature review of 4 databases (PubMed, Ovid Embase, Ovid MEDLINE, and Web of Science) on October 5, 2022 that yielded 46 full-text articles, which were reviewed and extracted by 2 independent reviewers.

Results: We analyzed a total of 134 cases, consisting largely of females (125/134, 93.3%) with purpura on the upper (103/134, 76.9%) or lower limbs (112/134, 83.6%). Apart from a paresthesia prodrome, patients commonly experienced headaches, malaise, and arthralgia or myalgia. Approximately 70% (95/134) of patients reported a physiological or psychological stressor or psychiatric diagnosis before the development of the purpura. Laboratory testing almost always revealed unremarkable results. The intradermal washed autoerythrocyte sensitization test was positive in 98% (42/43) of cases. Histopathology biopsy findings commonly revealed dermal erythrodiapedesis or hemorrhage (n=34) and perivascular inflammatory infiltrates (n=17). Approximately 42% (56/134) of patients received a novel psychiatric diagnosis, with depression being the most common (40/72, 56%). In both patients with and those without a novel psychiatric diagnosis, observation, counseling, treatment with antidepressants (ie, selective serotonin reuptake inhibitors), and psychotherapy (ie, cognitive behavioral therapy) prevailed in the resolution of the purpura.

Conclusions: Due to the unclear etiology and infrequent presentation of this condition, it remains a diagnosis of exclusion based on clinical suspicion evaluating the presence of stressors or psychiatric comorbidities and exclusion of systemic conditions. Clinical confirmation can be sought through a positive autoerythrocyte sedimentation test, characteristic histopathology findings, and remission of purpura after psychiatric treatment.

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KEYWORDS

autoerythrocyte sensitization syndrome; dermatology; edema; female; gardner-diamond syndrome; painful purpura; psychocutaneous disorder; psychodermatology; psychogenic purpura; psychological stress; psychological stress; skin lesions; somatization; stress; stress-induced ecchymoses

Introduction

Psychogenic purpura (PP), also known as Gardner-Diamond syndrome or autoerythrocyte sensitization syndrome, is an idiopathic psychodermatologic condition in which patients exhibit recurrent, spontaneous, and painful purpura, often preceded by psychological distress or psychiatric comorbidity. The first case of autosensitization to a patient's own blood was described by Gardner and Diamond [1], though PP-like dermatological manifestations of psychological factors have been described earlier by Schindler [2], where hypnosis of patients resulted in skin hemorrhages, and Jacobi [3], where patients with psychiatric comorbidities demonstrated purpura. Although the exact pathophysiology is unknown, it is hypothesized to be caused by psychological stress, estrogen, autoimmunity [4], low serotonin [5], and even religious "Holy Stigmata" [6]. It predominantly affects the young female demographic for reasons that remain unknown. Most challengingly, the clinical picture occurs in the absence of any pathognomonic homeostatic imbalances, with completely unremarkable hematologic, vascular, and immunologic results in most cases [7]. Histological results are generally characteristic of dermal hemorrhage but nonspecific. As a result, it has thus far been called a diagnosis of exclusion based on the clinical picture.

The aim of our systematic review of 134 cases is to describe the clinical presentation and most up-to-date diagnostic strategy of PP and provide a brief overview of treatment options available. To this end, we hope for improved patient experience and outcomes by reducing the duration of hospital admissions, unnecessary testing, and multiple physician and department transfers.

Methods

This systematic review was completed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The PubMed, Ovid Embase, Ovid MEDLINE, and Web of Science databases were searched on October 5, 2022, for all relevant articles with the search terms "psychogenic purpura," "Gardner Diamond Syndrome," or "autoerythrocyte sensitization." Using our searches, we hoped to address the following research questions: how do patients with PP present and how is it diagnosed? What level of evidence exists for the diagnosis and management of this disorder?

Articles that were not published in English were excluded. Research articles published before May 2013 were excluded on the basis of keeping our study relevant to current research published within the last 10 years. This is to prevent outdated medical and psychiatric knowledge from distorting pertinent data; importantly, the aim was to exclude out-of-date psychiatric perceptions and diagnoses from before the current version of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) was published on May 18, 2013. Due to the rarity of PP in the clinic, case reports were included and comprised a majority of the papers included in our review. Conference abstracts, posters, review articles, opinion articles that did not contain case reports or sufficient case information, and nonoriginal research were excluded.

Research articles pertaining to the diagnosis and clinical picture of PP were included. Initially, our search of the 4 databases revealed 727 articles; once duplicates were removed, 340 articles remained to be screened. All of the searched articles were reviewed by 2 independent reviewers (AZS and PKG). The Covidence systematic review software was used for article screening and data collection [8].

Title and abstract screening were performed using the inclusion and exclusion criteria given in Textbox 1.

Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

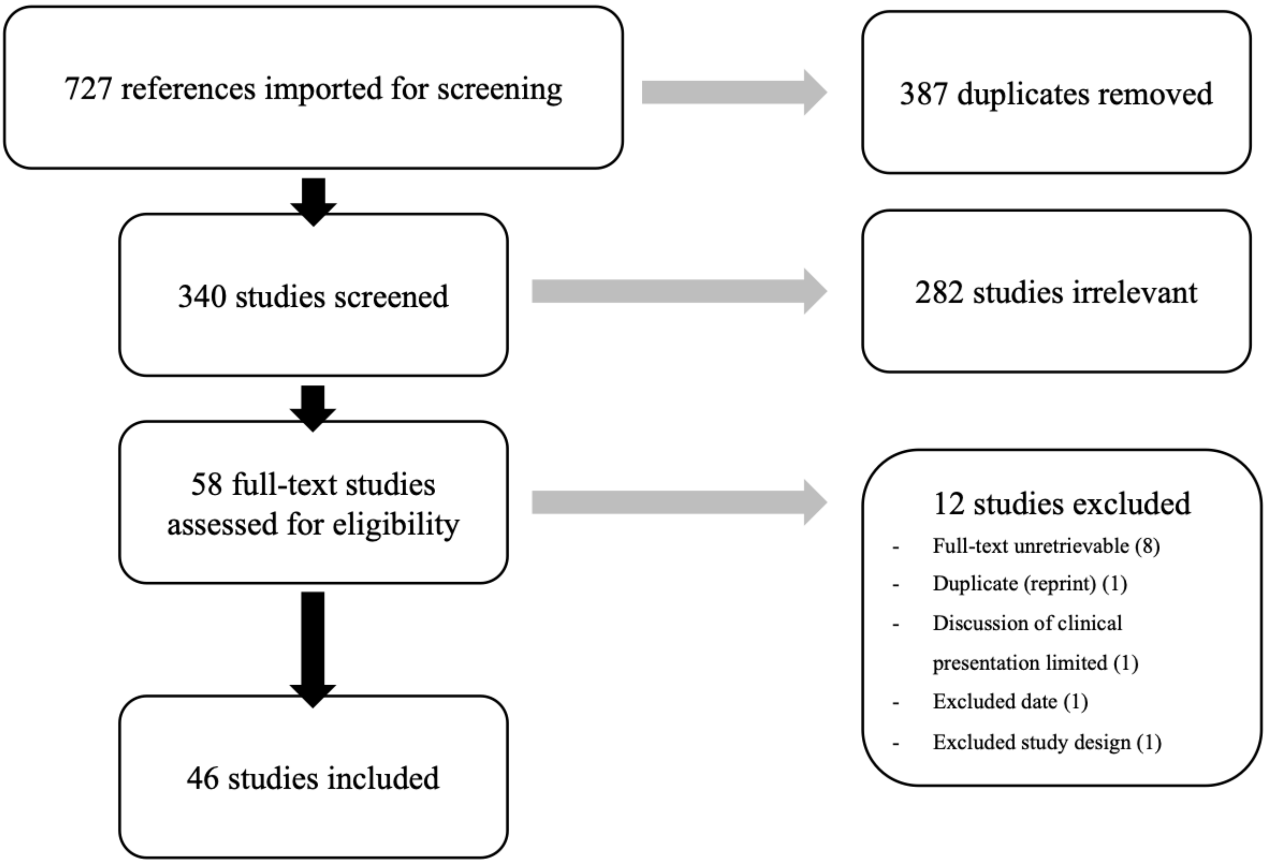
- English
- Full text available
- Published within the last 10 years since the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) publication (from May 18, 2013, to October 5, 2022)
- Original research article (ie, case reports, case-control, or cohort study)
- Study related to diagnosis and clinical presentation of psychogenic purpura

Exclusion criteria

- Review papers, opinion articles, and letters to the editor without a case report
- Full text unretrievable
- Research articles unrelated to the diagnosis and clinical presentation of psychogenic purpura
- Article not in English
- Article older than May 2013

After title and abstract screening, 282 studies were excluded. A total of 58 full texts were accessed and screened for eligibility. Subsequently, 12 full texts failed to meet the criteria and were excluded. In the end, 46 full texts remained and underwent review and data extraction (Figure 1).

Figure 1. Title, abstract, and full-text screening flow chart.



Articles that passed full-text review were extracted for relevant data, as outlined below. Extracted data were exported into an Excel (version 16.59; Microsoft Corp) file. The data extracted from the papers are given in Textbox 2.

Textbox 2. Data extracted.

Demographic data

- Type of study (case study, case-control, or randomized)
- Age of patients
- Sex of patients

Clinical presentation data

- Chief complaint
- Attending department (dermatology, psychiatry, family medicine, hematology, or internal medicine)
- Ruled out medication etiology
- Other etiologies ruled out (ie, factitious purpura or dermatitis artefacta, nonaccidental trauma, vasculitis, or panniculitis)
- Average size and number of purpura
- Pain with palpation of purpura
- Location of purpura
- Associated symptoms
- Past medical history
- Past social history (ie, low socioeconomic status and psychological or physiological stressor before the onset of purpura)
- Past family medical history (including of psychogenic purpura)

Investigation data

- Laboratory tests (ie, hemoglobin, erythrocyte sedimentation rate, platelet counts, prothrombin time and international normalized ratio, activated partial thromboplastin time, bleeding time, fibrinogen, antinuclear antibody, Coombs, cryoglobulin, anticardiolipin antibody, anti–double-stranded DNA, lupus anticoagulant, thrombocyte, and other abnormalities on peripheral blood smear)
- Histological findings from biopsy (ie, extravasation of erythrocytes in the dermis, perivascular infiltration of inflammatory cells, and dermal and subcutaneous hemorrhage)
- Autoerythrocyte sedimentation test

Diagnosis and treatment data

- New psychiatric diagnoses
- Treatment
- Remission status of purpura
- Other notes and important facts about the study

Results

Study and Patient Demographics

A total of 46 studies were included in our review [4,5,9-52], including 45 case studies and 1 retrospective study (Table S1 in Multimedia Appendix 1). A total of 134 cases were described in the case reports and retrospective study, of which 125 (95.4%) patients were female. The ages of the patients ranged from 8 years to 70 years. Among female cases where age was reported, 96% (49/51) of them were younger than 50 years.

Patient Presentation

Patients commonly presented to dermatology or psychiatry, followed by hematology, rheumatology, pathology, pediatrics, internal medicine, or emergency medicine, with a history of purpura, often with pain upon palpation (112/134, 83.6%). The average duration of purpura was 16 months, ranging from 3 days to 6 years, and it was mostly found on the lower limbs (112/134, 83.6%) and the upper limbs (103/134, 76.9%; Table 1). Apart from a paresthesia prodrome, which was reported in 61% (70/114) of cases where symptoms were described, the symptoms accompanying the purpura were largely heterogeneous (Table 2). Other common symptoms included headache (31/114, 27%), malaise (30/114, 26%), arthralgia or myalgia (30/114, 26%), fever (17/114, 15%), and abdominal pain (15/114, 13%).

Table 1. Location of purpura in patients with psychogenic purpura (N=134).

Location of purpura	Patients, n (%)
Shoulders, arms, or hands	103 (76.9)
Legs or feet	112 (83.6)
Head or neck	41 (30.6)
Anterior trunk (abdomen or chest)	40 (29.9)
Posterior trunk (shoulders, dorsum, or buttocks)	32 (23.9)
Oropharyngeal	3 (2.2)
Unspecified	2 (1.5)

Table 2. Accompanying symptoms in patients with psychogenic purpura (N=114).

Accompanying symptoms	Patients, n (%)
Paresthesia (burning, tingling, or numbness)	70 (61.4)
Headache	31 (27.2)
Malaise	30 (26.3)
Arthralgia or myalgia	30 (26.3)
Fever	17 (14.9)
Abdominal pain	15 (13.2)
Fatigue or weakness	6 (5.3)
Epistaxis	4 (3.5)
Nausea	3 (2.6)
Vomiting	2 (1.8)
Pruritus	2 (1.8)
Hematuria	2 (1.8)
Hemoptysis	1 (0.9)
Hematemesis	1 (0.9)
Hematochezia	1 (0.9)
Bullae	1 (0.9)
Bleeding gums	1 (0.9)
Hemolacria	1 (0.9)
Urticaria	0 (0)
Other (“palpitations,” “dizziness,” “sore throat,” “edema,” “erythema,” “vasomotor changes like diaphoresis and hyperalgesia,” “aphthous stomatitis,” “miosis,” “conjunctival injection,” “lacrimation,” “night sweats,” “diarrhea,” “dysphagia,” “odynophagia,” “dyspnea,” “eye pain,” “loss of appetite,” “sleeping problems,” and “prodrome of bursting pain followed by swelling”)	10 (8.8)

Of 134 cases, just 1 case reported a family history of PP [5], and 2 cases reported low socioeconomic status [27,42]. Approximately 70% (95/134) of patients reported a physiological or psychiatric stressor before the development of the purpura. More specifically, 65.6% (88/134) of cases reported a psychological or physiological stressor before the onset of purpura (Textbox 3), and 27% (36/134) of cases had a previous psychiatric diagnosis.

Textbox 3. Types of stressors reported among 81 patients with psychogenic purpura.

General stress and anxiety

Home-related

- Marital conflict or divorce
- Poor interpersonal relationships
- Parental divorce
- Stress related to the family member's comorbidities

Loss or bereavement

- Child leaving for army
- Death of loved one
- Failed financial venture
- Living apart from spouse
- Relationship breakup
- Reduced interest in family members

Maladaptive coping mechanisms

- Binge drinking
- Self-harm

Medical-related

- Infection
- Hospitalization
- Hemodialysis
- Previous procedure or recovery
- Psychiatric comorbidity
- Surgery

School-related

- Academic decline
- Bullying
- Emotional distress
- Examinations—pressure of performance
- Learning delay
- Low self-esteem
- Performance anxiety

Trauma

- Abuse
- Natural disaster
- Sexual abuse

Investigations and Diagnosis

On history, potential differential diagnoses (Textbox 4) were ruled out based on past medical and psychiatric history (Table S2 in Multimedia Appendix 1), and psychiatric and physiological stressors were investigated (Textbox 3), followed by laboratory investigations. Laboratory investigations, consisting of a combination of hemoglobin, erythrocyte sedimentation rate, platelet count, prothrombin time and international normalized ratio, partial thromboplastin time, bleeding time, fibrinogen, antinuclear antigen, Coombs test, cryoglobulin, anticardiolipin, anti–double-stranded DNA, and lupus anticoagulant, were negative in nearly all cases

(84.4%-91.8%). Notable positives are listed in Supplemental Table S3 in Multimedia Appendix 1.

Textbox 4. List of alternative etiologies ruled out before the diagnosis with psychogenic purpura. Adapted from previous reviews [7,53].

Medication-induced

- Antipsychotic medications
- Aspirin
- Nonsteroid anti-inflammatory drugs
- Recreational drug intake or abuse

Vasculopathy

- Deep vein thrombosis
- Cutaneous vasculitis (eg, nodular vasculitis, Henoch-Schonlein purpura, progressive pigmented purpura, cryoglobulinemia, angiitis, polyarteritis nodosa, superficial thrombophlebitis, capillaritis, such as disseminated pruriginous angiodermatitis)
- Panniculitis (eg, Pfeifer–Weber–Christian disease)

Coagulopathy

- Disseminated intravascular coagulation
- Idiopathic thrombocytopenic purpura
- Factor XIII deficiency
- Von Willebrand disease

Connective tissue disorders (eg, Ehlers-Danlos syndrome)

Autoimmune conditions (eg, systemic lupus erythematosus)

Inflammatory dermatosis (eg, stasis dermatitis)

Other dermatological abnormalities with wood's lamp test (eg, porphyria and ringworm)

Hematological malignancy (eg, cutaneous T-cell lymphoma)

Other systemic illnesses (eg, malignancy)

Infectious process (eg, atypical bacteria, tuberculosis, or deep mycoses)

Trauma

Foreign body

Psychocutaneous conditions (eg, factitious purpura or dermatitis artefacta)

Additional tests commonly completed include the autoerythrocyte sedimentation test and biopsy results. The autoerythrocyte sensitization test involves intradermally injecting autologous washed erythrocytes into the patient. A positive result is marked by the development of lesions after 24 hours alongside an absence of lesions in a negative control. The autoerythrocyte sensitization test is controversial due to its suspected low sensitivity and unknown specificity; nonetheless, it remains a popular diagnostic tool in the literature. In our cohort, 43 cases reported the use of the autoerythrocyte sensitization test to corroborate the diagnosis of PP, of which 42 had a positive result. These data suggest that the autoerythrocyte sensitization test equates to a sensitivity of 98% (Textbox S1 in Multimedia Appendix 1).

Histological findings from a biopsy of lesions demonstrated extravasation of erythrocytes in the dermis or dermal and subcutaneous hemorrhage (n=34). Next, perivascular infiltration of inflammatory cells was a frequent finding (n=17). Uncommon yet notable findings include 3 cases that reported hemosiderin pigment deposition in macrophages or dermis, 2 cases with fibrinoid deposition, and 2 cases with panniculitis. Other less common case-specific findings are summarized in Table S4 in Multimedia Appendix 1.

Treatment

After diagnosis with PP, prompt treatment is crucial to address not only the etiology of the purpura but also the baseline psychological status of the patient. Some patients (56/134, 41.8%) received a novel psychiatric diagnosis in addition to PP (Figure 2). Depressive disorder was the most typical novel codiagnosis (40/72, 56%), followed by personality disorder (18/72, 25%), and anxiety disorder (9/72, 14%). The most common treatment administered to patients was observation, counseling, and support (50/127, 39%), followed by the commencement of antidepressant therapy (35/127, 27%), most commonly selective serotonin reuptake inhibitors (SSRIs; 23/127, 18%). Psychotherapy was frequently prescribed (25/127, 20%), followed by antihistamines (18/127, 14%), anti-inflammatory and immunosuppressant medications (16/127, 13%), and benzodiazepines (13/127, 10%). Historically, many other treatments have been used, including topical treatments and vitamins; these are summarized in Table S5 in Multimedia Appendix 1. Treatment practices have changed over time, with a greater emphasis on addressing psychological factors at present, likely due to the concomitant psychiatric comorbidities in patients with PP (Table 3). Before 2000, anti-inflammatory and immunosuppressant medications, such as nonsteroidal anti-inflammatory drugs, steroids, and hydroxychloroquine, were prescribed more often [18].

Figure 2. Proposed diagnostic algorithm for psychogenic purpura (PP). CBT: cognitive behavioral therapy; SSRI: selective serotonin reuptake inhibitor.

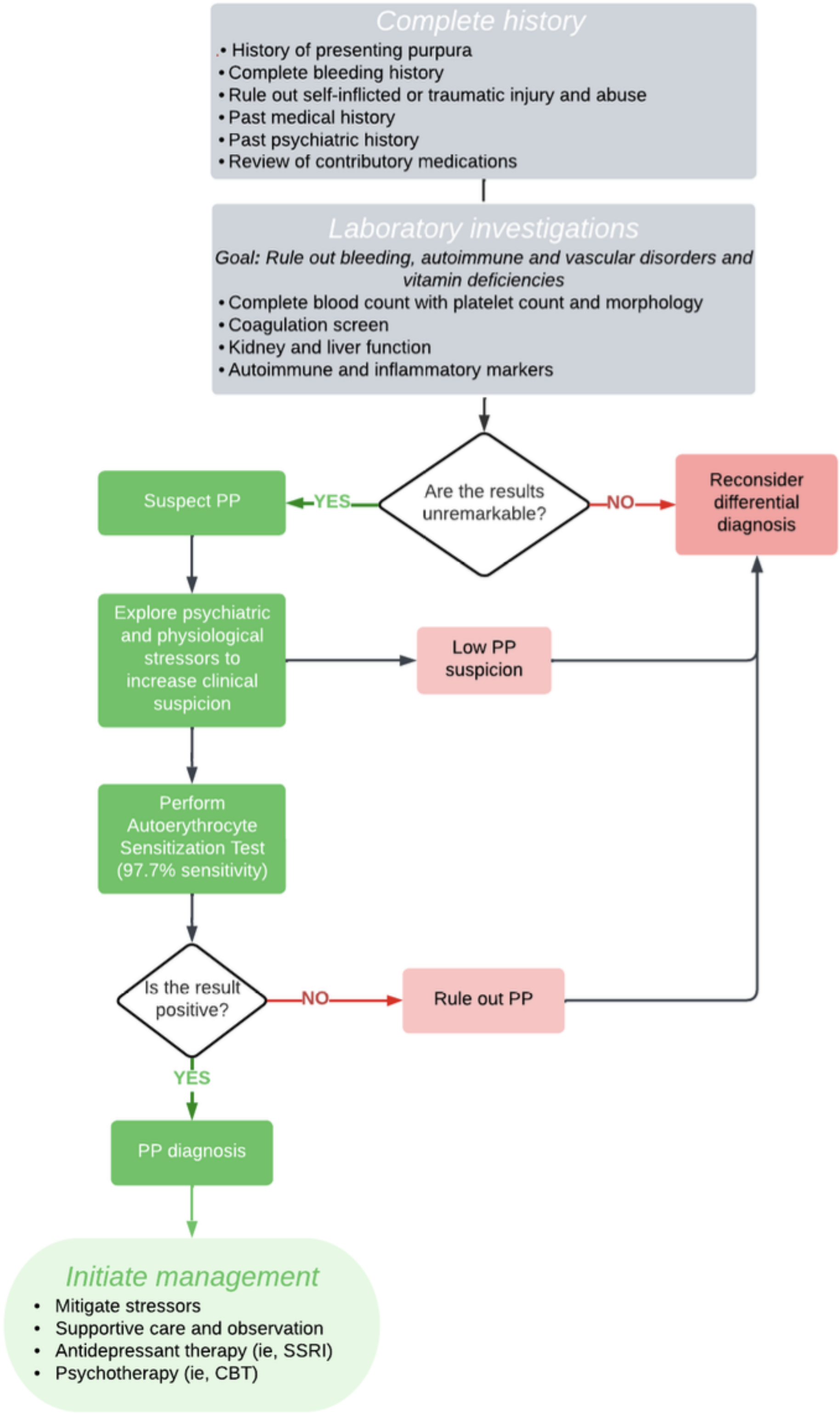


Table 3. Breakdown of novel comorbid Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) psychiatric diagnoses given to patients with psychogenic purpura. Note that some of these disorders overlap in the same patient and the total number of diagnoses exceed the total number of patients diagnosed with a psychiatric condition.

Psychiatric disorders	Patients (n=72), n (%)
Depressive disorder (ie, MDD[a], other specified depressive disorder with anxious distress)	40 (56)
Personality disorder	18 (25)
Anxiety disorder (ie, generalized anxiety disorder, panic disorder panic disorder, or illness anxiety disorder)	9 (14)
Obsessive-compulsive disorder	1 (1)
Somatic symptom disorder	1 (1)
Conversion disorder	1 (1)
Trauma and stressor disorder (ie, adjustment disorder)	1 (1)
Unspecified mental disorder	1 (1)

[a]MDD: major depressive disorder.

Nearly all cases that were addressed with an effective treatment and had sufficient follow-up had initial remission of symptoms, with 74% of patients (n=52) having complete remission and 26% (n=18) having a relapse among cases with sufficient follow-up. Notably, of the 4 patients who did have a recurrence of PP and for which their treatment regimen was recorded, all refused or did not receive any psychotherapy (1 received oxygen inhalation and verapamil for pain [29], 1 received therapeutic plasma exchange [36], and 2 others received only SSRIs and benzodiazepines [47]). Incidentally, 1 patient completely refused all treatments and still experienced remission. Similarly, 63% of patients did not receive psychotherapy or counseling and still had full remission (n=30), while 38% of patients who had no therapy did have a relapse of PP (n=18). Interestingly, only 8% of patients (n=3) who received ≥1 form of psychiatric treatment (medication or therapy) had a relapse; in other words, 92% of patients (n=34) who received ≥1 form of psychiatric treatment (medication or therapy) had PP remission. Other comorbidities must also be adequately addressed as they come up; for example, 1 patient developed compartment syndrome that eventually required a fasciotomy [21].

Discussion

Our study specifically focuses on the diagnosis and management of 134 cases published in the past decade, shining a fresh light on current practices. Similar to previous findings, we found PP presented predominantly in female patients younger than 50 years, accompanied by a prodrome of pain, burning, and paraesthesias, followed by rubor discoloration progressing into larger and darker ecchymotic lesions over the next 24-48 hours on the trunk, upper, or lower extremities [7,53,54]. While many patients presented with solely ecchymotic lesions, others presented with a plethora of other symptoms, such as headache, arthralgias, myalgia, fever, and abdominal pain [7]. Some patients had rarer prodromes, such as rapid progression of purpura on the anterior neck and oropharynx accompanied by dysphagia, odynophagia, and dyspnea [44], and another case with oral bleeding, epistaxis, and hematemesis recurring every 5-6 days [31]. However, none of the cases in our review reported internal organ bleeding, uterine hemorrhage, or renal hemorrhage despite reports of these in cases before May 2012 [54]. This study is the first up-to-date comprehensive review of PP in over a decade and one of the few to focus on the clinical presentation and diagnosis of this rare disorder. The past main reviews focused on treatment options [7] or were written before the DSM-5 was published [53].

Laboratory values are grossly normal in patients with PP, ruling out alternative etiologies [7]. Biopsy, when completed, commonly shows extravasation of erythrocytes in the dermis, perivascular infiltration of inflammatory cells, and dermal and subcutaneous hemorrhage [7], though it is not required for diagnosis [53]. The most common test for PP, sometimes referred to as the "gold standard," is the washed autoerythrocyte sensitization test. In the cases included in our study, 98% (42/43) of cases tested had a positive result, compared with 85.7% (24/28) of cases tested in a previous review [7], demonstrating a relatively high test sensitivity. While PP can be diagnosed clinically in most cases, this test can be used in instances of clinical uncertainty. Our results suggest that the autoerythrocyte sensitization test has a high sensitivity of 98% for PP. With this new finding, we propose the following diagnostic algorithm for PP (Figure 2). Clinical judgment should be exercised. Due to the test's historically postulated low sensitivity in the literature, a negative test may not always rule out PP if the clinical picture and investigations both support the diagnosis.

A large proportion of patients have a psychological stressor before the onset of the purpura (Textbox 3), and many have a concomitant psychiatric disorder, most commonly depression [7,53] (Table 3), necessitating psychiatric assessment [55]. In a previous review, 93% of cases had either a stressor or psychiatric comorbidity, relative to 70% (95/134) in our study. After diagnosis, patients are successfully treated with supportive counseling, psychotherapy, or antidepressants (ie, SSRIs) tailored to address the underlying psychiatric comorbidities and stressors [53,54]. Purpuric lesions tend to resolve alongside a psychiatric response to therapy or mitigation of stressors [7]. Additional therapies, such as antihistamines, steroids, and other topical agents, may also be prescribed based on symptoms [53]. Although PP follows a chronic disease course with relapses after trauma or stress, many patients achieve remission with favorable prognosis [53,54]. Mental illness can have a significant psychogenic impact on dermatology, as seen in the strong correlation between anxiety and mood disorders with acne, eczema, psoriasis, psychogenic pruritus, and psychogenic excoriation [56]. Dermatologic conditions and their aftermath, including scars, can in turn affect and exacerbate self-esteem, body image, and psychological distress [57,58]. A study reported suicidal ideation in 67.6% of patients with psoriasis and 68% of patients with atopic dermatitis [59]. This can create a vicious cycle, which is very clearly evident in the case of PP.

The appearance of purpura and subsequent social stigma can trigger psychological distress, worsening physical symptoms. The distress can become economically taxing, with time taken away from school or work and frequent health care–seeking behaviors. Extended time in hospital until diagnosis can exacerbate illness anxiety and precipitate additional nosocomial purpura. Prompt intervention and reassurance can stop this chain of events. In patients with PP overly distraught with their purpura, somatic symptom disorder or illness anxiety disorder may be additionally considered on the differential [60]. Comparably, due to symptomology overlap, PP could be characterized as a variant of the DSM-5's conversion disorder. Care providers should recognize the dynamic relationship between mental health and dermatology and collaborate with mental health professionals. Each person's experience with PP is unique; some individuals may have better coping mechanisms and support systems that help mitigate the challenges of living with this condition, while others may need increased support and resources.

Our data are limited by the 45 case reports and single retrospective study included. Case studies are heterogeneous, limited in statistical inference strength, and inconsistent. For example, not all papers tested for autoerythrocyte sensitization, limiting our ability to conduct a meta-analysis. Furthermore, our data may exclude clinical presentations that were misdiagnosed, unreported, undiagnosed due to a mild course, or experienced by individuals with health inequities lacking access to care. In addition, due to the limited number of cases in the literature and the criterion of excluding outdated papers from before May 2013, external validity may be attenuated. For this reason, our high sensitivity calculation of the autoerythrocyte sensitization test does not serve as enough evidence to recommend screening all patients with purpura but rather should enlighten physicians that the test may have an important role in the differential diagnosis toolkit.

Our study also has various strengths, notably its comprehensiveness in including both case reports and a retrospective study, as well as dissemination by 2 independent reviewers from 4 different databases, reducing selection bias and increasing reliability, reproducibility, and validity.

The pathophysiology of PP remains to be fully established; however, there are numerous theories implicating immune processes, the kallikrein-kinin system, and vascular properties. Female predominance of PP suggests involvement of estrogen and an autoimmune component [4], which is supported by the successful treatment of 1 case with plasmapheresis [61]; however, a case in our study treated by plasmapheresis did not have remission of purpura [36]. Incubation of erythrocytes from healthy individuals in the plasma of patients with PP containing immunoglobulin E to cardiolipin and phosphatidylserine, the phosphoglyceride of erythrocyte membranes, results in greater than 50% erythrocyte phosphatidylserine to be redistributed on the outer surface of the cell membrane [62]. This builds on the original theory that PP results from autosensitization to phosphatidylserine [1,63]. Abnormal tonus regulation of venous capillaries by the kallikrein-kinin system may also be involved, as well as extravasation of erythrocytes with sensitizing antibodies, defective synthesis of fibrin in the endothelium, and structures in the capillary wall [64]. Capillaritis, characterized by an inflammatory infiltrate of lymphocytes, just like some patients with PP, involves vascular fragility in the pathogenesis. This vascular fragility may occur in PP, whereby lymphocytes may interact with the vascular endothelium to affect permeability [65]. The role of low serotonin in the disease process has been speculated as SSRIs are effective in remitting purpura and preventing disease relapse. Serotonin, which is low in mood and anxiety disorders, is stored in platelets and plays a vital role in hemostatic aggregation and coagulation pathways, as well as reflexive vasoconstriction. Hemorrhage risk increases with peripheral serotonin depletion [66], possibly contributing to purpura. Many hypotheses exist on the pathophysiology of PP, but the evidence is lacking. Pertinent future research should investigate platelet or serum serotonin levels, autoimmunity, and vascular elements in patients with PP to further our understanding behind the disease process.

Ultimately, the diagnosis of PP is based on a thorough clinical history and physical examination, along with normal laboratory investigations. Diagnostic certainty is aided by the resolution or regression of purpura following the commencement of psychiatric therapy. A positive autoerythrocyte sensitization test and histological findings further support the diagnosis in times of clinical uncertainty. Increasing understanding and developing an evidence-based approach to managing this psychodermatologic condition can improve patient outcomes through earlier and appropriate psychiatric treatment interventions. A staggering number of cases demonstrate the repercussions of unfocused, prolonged differential investigations delaying diagnosis, leading to worsened purpura, physical symptoms, and psychological stress. Thus, physicians must remember to factor in a patient's mental health when treating skin conditions and recognize dermatological manifestations of psychological status. Patients can receive more effective and comprehensive care by addressing both the physical and psychological aspects of skin conditions.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Supplemental material.
[DOCX File , 105 KB - derma_v6i1e48153_app1.docx]

Multimedia Appendix 2
PRISMA checklist.
[PDF File (Adobe PDF File), 1362 KB - derma_v6i1e48153_app2.pdf]

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Abbreviations

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
PP: psychogenic purpura
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SSRI: selective serotonin reuptake inhibitor

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Review

Congenital Telangiectatic Erythema: Scoping Review

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Abstract

Background: Congenital telangiectatic erythema (CTE), also known as Bloom syndrome, is a rare autosomal recessive disorder characterized by below-average height, a narrow face, a red skin rash occurring on sun-exposed areas of the body, and an increased risk of cancer. CTE is one of many genodermatoses and photodermatoses associated with defects in DNA repair. CTE is caused by a mutation occurring in the *BLM* gene, which causes abnormal breaks in chromosomes.

Objective: We aimed to analyze the existing literature on CTE to provide additional insight into its heredity, the spectrum of clinical presentations, and the management of this disorder. In addition, the gaps in current research and the use of artificial intelligence to streamline clinical diagnosis and the management of CTE are outlined.

Methods: A literature search was conducted on PubMed, DOAJ, and Scopus using search terms such as “congenital telangiectatic erythema,” “bloom syndrome,” and “bloom-torre-machacek.” Due to limited current literature, studies published from January 2000 to January 2023 were considered for this review. A total of 49 sources from the literature were analyzed.

Results: Through this scoping review, the researchers were able to identify several publications focusing on Bloom syndrome. Some common subject areas included the heredity of CTE, clinical presentations of CTE, and management of CTE. In addition, the literature on rare diseases shows the potential advancements in understanding and treatment with artificial intelligence. Future studies should address the causes of heterogeneity in presentation and examine potential therapeutic candidates for CTE and similarly presenting syndromes.

Conclusions: This review illuminated current advances in potential molecular targets or causative pathways in the development of CTE as well as clinical features including erythema, increased cancer risk, and growth abnormalities. Future studies should continue to explore innovations in this space, especially in regard to the use of artificial intelligence, including machine learning and deep learning, for the diagnosis and clinical management of rare diseases such as CTE.

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KEYWORDS

rare diseases; rare disease; artificial intelligence; AI; dermatology; dermatologist; DNA repair; teledermatology; systematic review; erythema; deoxyribonucleic acid; bloom syndrome; postnatal growth deficiency; immune abnormality; cancer; oncology; DNA mutation; heredity

Introduction

Congenital telangiectatic erythema (CTE), also known as Bloom syndrome (BS), is a rare autosomal recessive disorder characterized by impaired DNA repair and increased susceptibility to cancer. As the name suggests, it is a condition characterized by visible, small, and linear broken blood vessels. In addition to this, photosensitivity is a very common feature in individuals with CTE. CTE was first described by David Bloom in 1954 upon observing several pediatric patients with similar physical features and cancer susceptibilities. In the 1960s, CTE was identified as a genetic disorder caused by loss-of-function mutations in the *BLM* gene and subsequent impairments in genomic repair mechanisms. Since then, research has largely been focused on understanding the biomolecular basis of symptom development and improving diagnostic methods for this disorder. Given the potential for cancer development, early detection is of crucial importance. Recently, artificial intelligence (AI) and machine learning advancements have resulted in more efficient identification of patterns of disease occurrence, management considerations, and the potential of aiding in finding novel therapeutics for screening [1]. These advancements may also eventually contribute to a greater understanding of CTE.

CTE is typically inherited in an autosomal recessive pattern where both parents are heterozygous carriers of the mutated *BLM* gene [2]. Existing knowledge on CTE suggests that mutations in RecQ helicases such as *BLM* result in accelerated aging symptoms and cancer incidence [2]. CTE has been most commonly observed in populations of Ashkenazi Jewish descent [3]. It has also been observed in consanguineous families. There are several dermatologic syndromes with similar presentations such as Rothmund-Thomson Syndrome, Erythropoietic Protoporphyria, and Cockayne Syndrome [3]. Rothmund-Thomson Syndrome in particular is also due to a mutation in a RecQ helicase [2]. Future studies, aimed at improving clinical management of CTE, will likely address how to differentiate between these similarly presenting syndromes.

CTE is characterized by a wide range of symptoms affecting multiple physiological systems. Common physical manifestations include short stature, delayed growth and puberty, a skin rash that occurs with sun exposure, in addition to a butterfly-shaped facial rash across the nose and cheeks. Common immunological manifestations include an increased susceptibility to infections and a higher risk of developing various cancers. The development of the erythematous skin rash upon sun exposure has been associated with a higher risk of developing squamous cell carcinomas [4]. CTE has also been associated with reduced fertility in women and infertility in men. While there are no known genetic differences in the *BLM* gene that lead to the development of heterogeneous symptoms, several cases of external genetic or environmental factors have been explored [5]. Our current understanding of the progression of CTE and its different presentations is limited given the rarity of the condition. A majority of current literature has elucidated key clinical features due to the willingness of current patients to participate in case studies and other forms of research.

Methods

Search Strategy

A literature search was conducted on PubMed, DOAJ, and Scopus using search terms such as "congenital telangiectatic erythema," "bloom syndrome," and "bloom-torre-machacek." Due to limited current literature, studies published from January 2000 to January 2023 were considered for this review.

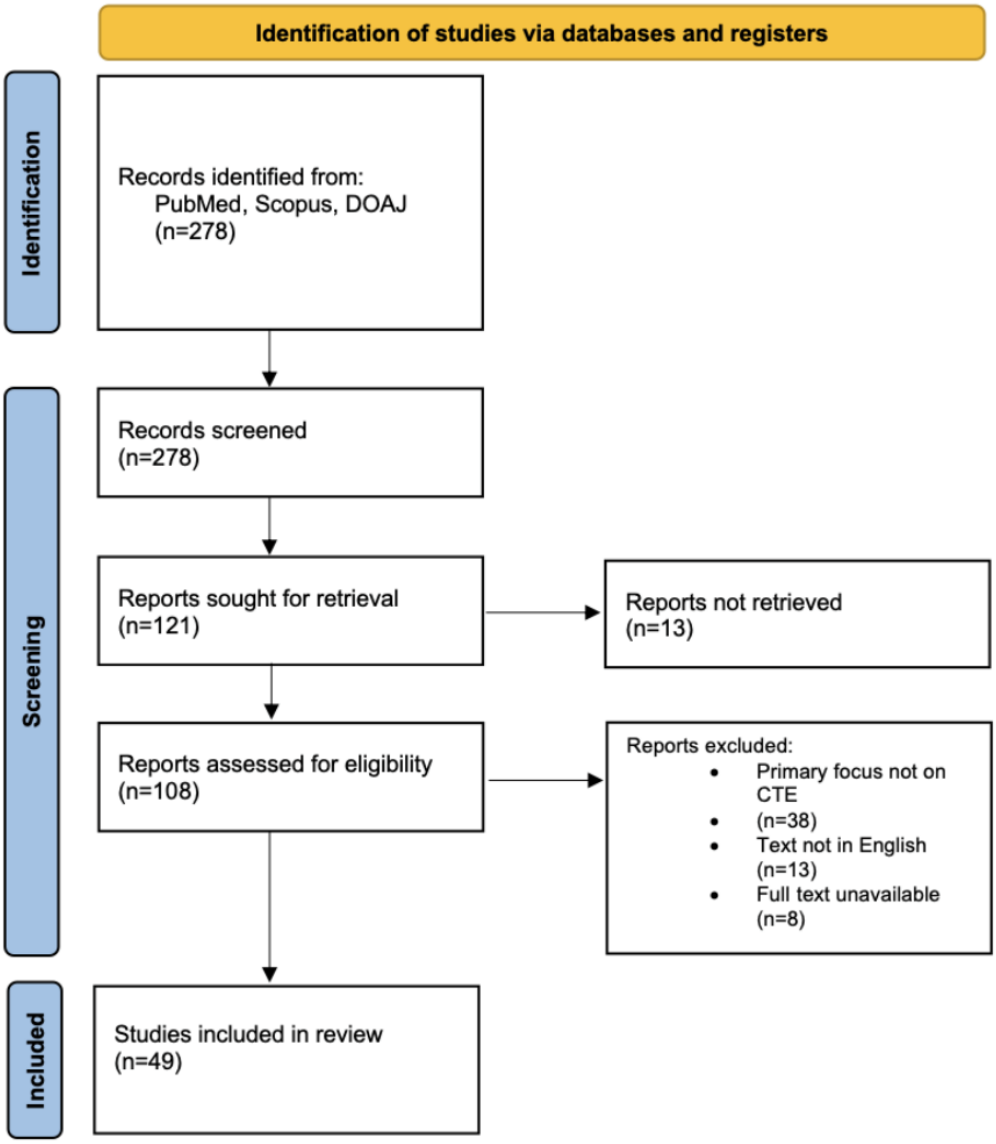
Study Selection Process

The references of included articles were subsequently screened for potential addition. After we determined which papers were relevant according to title and abstract screening, full-text articles were obtained. These full-text articles were then screened and checked for inclusion and exclusion criteria. The data analysis plan and inclusion and exclusion criteria were established before screening to minimize potential biases. Two authors (MSW and JK) independently screened titles, abstracts, and full-text articles for potential inclusion in this review. Any discrepancies or disagreements were resolved and decided by the additional author (MZ). Ultimately, 278 records were screened, 121 were sought for retrieval, and 47 were assessed for eligibility.

Inclusion and Exclusion Criteria

All studies included in this review were published in English. Clinical trials were excluded from this review. Our criteria for inclusion were (1) relevance to CTE, (2) publication in English, and (3) full-text availability. Studies were further evaluated regarding demographic features, different clinical presentations, and management of CTE. The literature search yielded 278 studies, of which 47 initial studies met the inclusion criteria for further analysis. Any duplicates were removed, and papers that were not in English were also excluded from this review. After looking through the references of included studies, 2 additional sources were added for inclusion in the review and thus 49 studies were analyzed (Figure 1).

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram for the identification of studies [7].



Results

Overview

This systematic review draws from 49 recently published articles on CTE heredity, CTE clinical presentation, management of CTE, and recent advancements. These studies were published in various countries including Australia, Canada, the United States, the United Kingdom, Saudi Arabia, Poland, Morocco, Japan, and China. These were analyzed after screening relevant literature. Due to the limited availability of research on rare diseases such as CTE, many of these articles have been published within the past 2 decades. The current literature focused on several main subject areas such as heredity, clinical manifestations, and management of CTE. A systematic review of our findings has been outlined in the following sections, which have been organized based on these themes. A summary of the studies used and examined, including country, year of publication, and key takeaways, are shown in Tables 1-3.

Table 1. Summary table for included studies focused on heredity.

Authors (years)	Characteristics	Summary
Ababou (2021) [7]	Patient data obtained from Bloom Syndrome Registry 1954-2018	Other than Ashkenazi Jewish descent, populations with high consanguinity rates have a higher prevalence of BS[a].
Arora et al (2014) [3]	Patient data obtained from Bloom Syndrome Registry 1954-2009	BS shares similar clinical features to Rothmund-Thomson Syndrome, Erythropoietic Protoporphyria, and Cockayne Syndrome.
Bythell-Douglas and Deans (2021) [8]	Patient data obtained from cell cultures and from animal models	When the BS Complex is not present, the synapse is more likely to occur with the wrong sequence, which will lead to translocation and rearrangement.
Cunniff et al (2017) [9]	Patient data obtained from Bloom Syndrome Registry 1954-2017	The absence of functional BLM protein causes chromosome instability and excessive homologous recombination.
Enomoto (2001) [10]	RecQ family helicase biochemical assays	BLM is necessary for DNA replication—reserved in ND10s and is involved in a DNA surveillance mechanism operating during the S Phase.
Kaur et al (2021) [11]	Study data from yeast, Drosophila, mouse, and human	*BLM* has tumor-suppressing and pro-oncogenic characteristics, the paper focuses on the conditions under which the gene shows each of these characteristics.
Maciejczyk et al (2017) [12]	Study data from yeast, Drosophila, mouse, and human	The role of cellular redox alternations in the BS phenotype points to elevated superoxide dismutase activity and more production of reactive oxygen species in BS.
Mo et al (2018) [2]	RecQ family helicase biochemical assays	Mutations in RecQ helicases (including *BLM* that causes the BS) result in autosomal recessive syndromes characterized by accelerated aging symptoms and cancer incidence.
Monnat (2010) [13]	RecQ family helicase biochemical assays	Human RecQ helicases in cellular DNA metabolism need further research by studying conditions such as BS and how the acquired loss of RecQ function may provide new opportunities to improve cancer therapy.
Nakayama (2002) [14]	RecQ family helicase biochemical assays	*BLM* is identified as a caretaker-type tumor suppressor protein and a gatekeeper class of tumor suppressor proteins.
Vallance and Ford (2003) [15]	Data collected from genetic testing of carriers	A common mutation has been identified that involves the deletion of six bases and insertion of seven bases (2281 delATCTGAinsTAGATTC, abbreviated *blmAsh*) and leads to early termination of the BLM gene product.

[a]BS: Bloom syndrome.

Table 2. Summary table for included studies focused on clinical manifestations.

Authors (year)	Clinical manifestations
Bouman et al (2018) [16]	BS[a] with a lack of sun-sensitive facial erythema
Giordano et al (2016) [17]	BS with erythema, telangiectasia, proportionate dwarfism, and increased risk of internal cancers. Cellular or genetic defects: quadriradial chromosomes; cells sensitive to ionizing radiation and alkylating agents
Capell et al (2009) [18]	BS with increased risk of cancer, ultraviolet hypersensitivity, hyper- and hypopigmented skin changes, decreased subcutaneous fat, immune deficiency, anemia, increased susceptibility to type II diabetes mellitus, severe growth retardation, and death by the age of 30 years usually due to cancer
Diaz et al (2006) [19]	BS with altered carbohydrate metabolism (however, small cohort, n=11)
Klein and Günther (2021) [20]	BS with photosensitivity and symptoms of immunodeficiency such as more frequent respiratory and gastrointestinal infections
Maciaszek et al (2020) [21]	BS with Wilm tumor—the most common childhood kidney cancer
Martin et al (2010) [22]	BS with growth abnormalities, hematopoietic defects, mutagen sensitivity, and cancer predisposition
Schierbeck et al (2019) [4]	BS with severe photosensitivity, poikiloderma, and erythematous telangiectasia, skin cancer, other malignancies of the upper and lower gastrointestinal and urinary tract
Prime et al (2001) [23]	BS with leukemia or lymphomas or solid tumors
Prokofyeva et al (2013) [24]	BS with epithelial carcinomas like breast cancer (not just lymphomas and leukemia)
Taylor et al (2019) [25]	BS with congenital abnormalities, pancytopenia, and cancer proneness

[a]BS: Bloom syndrome.

Table 3. Summary table for included studies focused on management.

Authors (year)	Clinical management suggestions
Balajee (2021) [26]	Using RecQL4 as a novel cancer therapeutic target
Ben Dhia et al (2023) [27]	Using dose reduction, regardless of chemotherapy type
Campbell et al (2018) [28]	Using dose reduction regardless of chemotherapy type
Frances and Cordelier (2020) [29]	Using cytidine deaminase as a novel cancer therapeutic target
Jastaniah (2017) [30]	Using rituximab-based chemotherapy protocol
Karalis et al (2011) [31]	Using greater awareness and patient education
Mojumdar (2020) [32]	Using RecQ as a novel cancer therapeutic target
Shen et al (2012) [33]	Using first-apparent cutaneous changes in the face
Walsh et al (2017) [34]	Using effective cancer screening

Heredity of CTE

CTE is a rare genetic disorder usually found in an autosomal recessive pattern. Patients with CTE develop higher risk factors such as extremely high cancer rates up to “150 to 300 times” [8]. This is mostly due to the development of carcinogenesis in CTE-affected cells that may have laid the preset conditions for the development of multiple types of cancers. CTE is caused by a mutation in the *BLM* gene, which is responsible for the DNA repair enzyme RecQL3 helicase [3]. The mutation causes this essential repair enzyme to falter in its ability to repair and dispose of abnormal cells. The CTE complex consists of several protein components that function independently but in the grand scheme of DNA repair, and are crucial for rapid homologous recombination as well as the exchange of sister chromatids that carry the design information for CTE [10]. This uncontrollable flaw in the design information replication is what leads to genomic issues and the rise of abnormal conditions and cells.

The development of the erythematous skin rash, a characteristic feature of CTE, upon sun exposure has also been associated with a higher risk of developing squamous cell carcinomas [4].

It has been observed that these proteins that are essential for DNA replication interact with RecQ homologs that function in a pathway that instigate the transition from DNA replication checkpoint to homologous recombination [11]. This leads to genomic instability that leads to the development of cancers such as lymphoma and leukemia which are prevalent in patients with CTE. With the formation of these many cancers, it has been noted that there is an increase in copy number, transcript, and protein levels which along with the fact there is a lack of wild-type *BLM* has increased the sensitivity of chemotherapeutic agents and has been labeled as pro-oncogenic. Therefore, there is a possible indication that BLM may act as a tumor suppressor [14]. This is also possible because within the *BLM* gene, resides the RecQ homologs, in particular, the RecQL4 helicase acts as a tumor suppressor. The RecQ homologs also act in the unwinding of intermediates of recombination, which prevents the unwanted execution and its defamation leading to the rise of unwanted genomic anomalies [35]. Various sources agree that there is a relationship between CTE and the rise of oncogenic conditions within these patients. Namely, this finding has been corroborated through the Bloom Syndrome Registry. This is an ongoing digital registry that serves as a surveillance mechanism to observe the effects of CTE over time [9]. Individuals with CTE are at a greater risk of complications such as various cancers, chronic obstructive lung disease, and diabetes [9]. Due to these complications, individuals with CTE stand to benefit greatly from improvements in screening and early detection.

Current literature suggests that CTE is more prevalent in certain ethnic groups than the others. Patients with CTE are mostly of Ashkenazi Jewish descent. Patients with CTE display certain physical phenotypes such as narrow facial features, elongated limbs, and several dermatologic complications including photosensitivity, poikiloderma, and telangiectatic erythema [3]. About 1 in 100 people with Ashkenazi Jewish heritage have the common founder mutation *blmAsh*, and there are also recurrent founder mutations among other ethnicities. Multiexonic deletions, nonsense mutations, frameshift mutations, and missense mutations have all been reported [13]. These essential processes occur because helicases use the energy of adenosine triphosphate hydrolysis to separate double-stranded nucleic acids [12]. Other phenotypes present in CTE are endogenous reactive oxygen species overproduction and impairment of mitochondrial homeostasis. Excess activity of antioxidant enzymes and an insufficient amount of low molecular weight antioxidants indicate new pharmacological strategies for patients having CTE [12].

Clinical Presentations of CTE

CTE presents itself in a variety of symptoms and signs, some of which lead to further complications, and the studies that focused on clinical presentation displayed many similar trends and ideas with respect to how the syndrome manifests itself in the body. Most of the time, though not always, BS presents with sun-sensitive conditions, such as resulting facial erythema [16]. One case study showed some degree of phenotypic variation in facial erythema clinical presentations in CTE [16]. It is important for studies to establish the different possible clinical presentations of CTE in order to prevent delays in screening and early detection. However, photosensitivity and specifically facial erythema does remain one of the most common presenting signs [17]. This dermatologic feature is still one of the main components of initial diagnosis and screening for CTE. Altered carbohydrate metabolism is also very common in CTE and is often present from childhood [19]. BS dwarfism is not believed to be related to growth hormone deficiency or malabsorption, so the basis for growth restriction in CTE is unknown. It is believed that some of the variabilities in clinical manifestations are due to different pathomechanisms. A recent paper has suggested that the different pathomechanisms may be dependent on the number of micronuclei and the activity of BLM1 helicase and that interferon induction is possibly promoted or inhibited [20]. Other studies have suggested that because CTE is a constitutional chromosomal instability, it can result in a variety of syndromes including growth abnormalities, hematopoietic defects, and cancer predisposition [22].

BS also brings upon a predisposition for internal cancers, especially Wilm tumor, a common childhood kidney cancer [21]. Multiple articles present that factors such as chromosomal instability and mutations in the tumor suppressor genes in BS can cause a predisposition to lymphomas, leukemia, breast cancer, skin cancer, and oral cancer. An early paper demonstrated that patients with CTE were predisposed to either leukemia or lymphoma [23]. A more recent meta-analysis revealed that the BLM defect common in CTE not only increases the risk of leukemia or lymphomas but also epithelial carcinomas like breast cancer [24]. Most of the risk comes from when the signaling pathways of the ReqQ helicases are disrupted, which makes it similar to Werner and Rothmund-Thomson syndromes. Still, CTE brings on various results besides cancer, including immune deficiency, growth abnormalities, and susceptibility to diabetes mellitus.

Management of CTE

The management of CTE and CTE-related cancers is presented with a unique set of challenges that is inherent to the impaired DNA repair mechanisms and subsequent DNA instability. Three studies describe the DNA-damaging effects of chemotherapy and radiation, and the associated risk of developing secondary cancers or myelodysplasia [27,28,36]. In such cases, chemotherapy dosage and duration reduction are recommended for individuals with CTE [27,36]. A study also suggests the benefit of broad-spectrum sunscreen with an SPF of at least 30 and the use of gamma-globulin infusions for reducing the frequency and severity of CTE-related infections [36].

With limited available treatments, several novel therapies are underway for more effective management and potential treatment. Two studies investigating novel therapies for CTE-related cancers suggest the use of RecQ helicases as a potential therapeutic target [26,32]. The catalytically active domains of RecQ helicases are described as a potential direct and tumor-specific target for small molecule inhibitors to be administered in conjunction with chemotherapy [32]. A case study in Saudi Arabia describes a successful treatment of CTE-related lymphoma in an 11-year-old patient with rituximab-based chemotherapy [30]. This demonstrates a safe treatment alternative for mature B-cell lymphoma in patients with CTE [30]. Another study describes potential therapeutic strategies through the modulation of cytidine deaminase (CDA) activity [29]. CTE is typically characterized by CDA deficiency, which has been observed to induce replicative stress [29]. The study presents CDA manipulation as a promising strategy for cancer therapy; however, greater research is warranted to better understand the role of CDA in oncogenesis [29].

Several studies emphasize the need for greater awareness and screening strategies for effective diagnosis [31,33,34,37]. A study discusses the use of candidate gene sequencing as a helpful tool for achieving a genetic diagnosis in children with distinct phenotypes [37]. However, the study also discusses the need for greater emphasis on the causative genetic mutations in phenotype-based diagnoses [37]. Another study summarizes the dermatological manifestations of inherited cancer and indicates cutaneous changes in the face as one of the most common early indicators of genetic syndromes with malignancies [31]. Furthermore, this study emphasizes the need for greater discussion and awareness among clinical practitioners, particularly dermatologists, for the effective diagnosis and treatment of those affected by CTE [31].

Discussion

Principal Results

CTE, also known as BS, is a rare genetic disorder that affects several physiological systems. CTE arises from mutations in the BLM gene which encodes the DNA repair enzyme RecQL3 helicase [3]. RecQL3 is a multidomain enzyme that constitutes the Bloom Syndrome Complex (BSC) and is able to repair double-stranded breaks in DNA [6,38]. BSC plays an integral role in the homologous recombination of DNA during DNA repair. Without a properly functioning BSC, chromosomal synapsis is more likely to occur with incorrect sequences, resulting in elevated levels of recombination-mediated insertions, deletions, and chromosome rearrangements. More than 60 different CTE-associated mutations have been identified within the BLM gene, including nonsense, missense, and exon-skipping mutations [6]. All forms of nonsense mutations have been associated with the absence of a C-terminal nuclear localization sequence, a C-terminal ssDNA annealing domain, and a portion of the helicase and RNaseDC domain, leading to improper localization of the enzyme [6]. A frameshift mutation that involves the deletion of 6 bases and the insertion of 7 bases (2281 delATCTGAinsTAGATTC, abbreviated *blmAsh*) has been associated with early termination of the *BLM* gene product and accounted for 97% of CTE alleles in patients of Ashkenazi Jewish descent [15]. Notably, CTE has an estimated incidence of 1 in 48,000 in the general population, while an estimated incidence of 1 in 120 has been identified in patients of Ashkenazi Jewish descent [39]. However, CTE has also been observed in consanguineous families [7]. The *BLM* gene is inherited in an autosomal recessive pattern, which means that an individual must inherit 2 copies of the mutated gene, 1 from each parent, in order to develop the condition [3].

CTE presents a range of clinical manifestations and impacts multiple systems in the body. As previously discussed, the absence of BSC has several detrimental effects on homologous repair such as reduced accuracy of gene regulation, decreased resection, and increased nuclease-mediated crossovers [38]. Such decreases in regulation fidelity during meiosis lead to reduced fertility in women and infertility in men [40]. In immune cells, the increased levels of incomplete recombination are known to stimulate the release of immunostimulatory DNA, inducing autoimmunity [41]. Associated symptoms include increased susceptibility to infections and sustained inflammation. In epithelial cells, genomic rearrangements from BSC infidelity have been associated with cancer initiation and progression [18]. In addition, the alterations in cellular redox regulatory mechanisms have been associated with elevated levels of superoxide dismutase activity and increased generation of reactive oxygen species in patients with CTE [12]. Given the breadth of physiological systems affected by the dysfunctional enzyme, CTE is characterized by a wide range of symptoms including growth deficiency, sun sensitivity, and predisposition to diabetes and cancer [25]. The severity and variability of CTE symptoms can vary widely among affected individuals, even among those with the same underlying genetic mutation. Some individuals may experience a milder form of the condition with only a few clinical manifestations, while others may have more severe and life-threatening complications. For instance, variations in immunological abnormalities have suggested a potential role in the frequency of infections in the affected individual [36]. Much research remains to elucidate the specific factors involved in the variation of clinical manifestations. CTE shares several clinical similarities with other chromosomal instability disorders such as Fanconi anemia and ataxia-telangiectasia [25]. These disorders are characterized by defective DNA repair and increased chromosomal instability, leading to similar clinical features, such as increased susceptibility to cancer and other complications [25]. Nonetheless, each disorder has distinct clinical and genetic features that differentiate them from one another.

Implications

AI, including machine learning and deep learning types, are interesting areas of future study. There is limited current literature due to its recent advancements and it will likely be some time before it is applied specifically to CTE. Other rare diseases have already benefited from the use of machine learning to establish more efficient identification of patterns of disease occurrence, management considerations, and the potential of aiding in finding novel therapeutics for screening [1]. However, it is important to note that these advances are not a silver bullet solution and still require additional research inputs in order to provide accurate outputs.

AI and machine learning are harnessed by today's modern health care systems to improve medical image processing, disease prediction and prevention, and hospital operations [42]. AI can also have use cases in all stages of drug development including discovery, preclinical stage, and clinical stage. For instance, it can contribute to initial validation, progression modeling, and diagnostic imaging. Through incorporating these approaches, better precision and effectiveness can be possible. AI and machine learning systems can allow health care providers and researchers to further optimize and accelerate the timeline for the diagnosis, treatment, and management of diseases [43]. For example, a recent study showed a use case that analyzed brain function and structural imaging data to determine whether a person with Huntington disease will receive a clinical diagnosis within 5 years (pre-Huntington disease) [44]. Especially in the case of rare diseases such as CTE, technological advances currently under development may be able to address many current challenges.

Limitations

Our study has several limitations. First, we focused predominantly on existing peer-reviewed literature and were thus limited to drawing conclusions from case studies and existing information. Given the rarity of this condition, there were a limited number of publications that met our inclusion criteria despite broadening the time range. Since our review only included peer-reviewed scientific literature, however, some studies could be missed from nonmedical journal sources. Second, we did not assess in depth the intersection of any potential comorbidities that patients with CTE may commonly have. There were limited findings on patient attitudes toward different clinical management strategies for CTE or their experiences with disease progression. Another limitation is that this review does not include differences across intersectional demographic groups. Specifically, there is limited literature examining clinical presentation in skin of color dermatologic patients.

Conclusions

BS, also known as CTE, is a rare autosomal recessive disease and as a result, there is a limited, but growing, body of scientific literature over the past 2 decades. Between 2000 and 2023, we identified 49 studies with a specific focus on heredity, clinical manifestations, and management of CTE. The incidence of CTE is unknown; however, the Bloom Syndrome Registry and initiatives within several rare disease organizations hope to help provide a clearer picture of key molecular markers and expand genetic testing access. Furthermore, using AI and machine learning platforms can help further elucidate potential therapeutic candidates and disease screening and progression. Diagnosis of CTE currently involves the identification of characteristic clinical features and molecular testing to identify changes to the *BLM* gene [45]. BS's clinical features include telangiectatic erythema and growth abnormalities. Key changes to the *BLM* gene, based on current literature, include an inverse relationship with chromosomal instability. Chemotherapy dosages for individuals with CTE should be reduced due to an increased likelihood of developing severe infections.

Overall, we were able to show what advancements have been made in understanding the heredity, clinical manifestations, and management of CTE. We have concluded that future studies should focus on answering several gaps identified in this review including which sequences in the *BLM* gene should be looked at as a marker for CTE in genetic testing. Additionally, future studies should continue to develop best practices for physicians consulting patients who have CTE. We conclude that CTE can also be challenging to diagnose due to a lack of access to genetic testing, low awareness of this rare condition, and other biological variations. Patients with CTE may also require alterations to typical chemotherapy or targeted immunotherapies in the treatment of cancer. Therefore, this topic is currently of great relevance for both oncologists and dermatologists. Continued efforts to widen information on CTE will support the development of a more comprehensive understanding of the clinical manifestations, heredity, and clinical management of CTE. Additional research will help to improve subsequent usage of AI to streamline candidate therapeutic selection, genetic testing, and clinical management of CTE.

Authors' Contributions

MSW was responsible for the initial conceptualization of this review. MSW and JK devised the methods. MSW, JK, and MZ contributed to data extraction and the writing of this manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.
[PDF File (Adobe PDF File), 646 KB - derma_v6i1e48413_app1.pdf]

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Abbreviations

AI: artificial intelligence
BS: Bloom syndrome
BSC: Bloom Syndrome Complex
CDA: cytidine deaminase
CTE: congenital telangiectatic erythema

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Review

Rosacea and Its Association With Malignancy: Systematic Review

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Abstract

Background: Rosacea is a chronic inflammatory skin condition that predominantly manifests as facial flushing, irritation, and acne. Rosacea and cancer are thought to be linked by the commonality of inflammatory and immune response dysfunction. Studies that have looked into this possible association have reported mixed results.

Objective: Given the conflicting literature on this topic, our study sought to evaluate the overall association between rosacea and several cancers commonly investigated in the literature.

Methods: A systematic review was conducted using the Cochrane, PubMed, Embase, and Ovid databases. Studies were screened independently for inclusion of rosacea and glioma and breast, thyroid, hepatic, or skin cancers. Using information from the articles, rosacea and each cancer were categorized as having a positive, negative, or unclear association.

Results: Our systematic review included 39 full-text studies that investigated the association between rosacea and various malignancies. Among the malignancies of concern, 41% (16/39) of the studies reported an association with basal cell carcinoma, with 2 cohorts revealing an adjusted risk ratio (RR) of 1.50 (95% CI 1.35-1.67) and 0.72 (95% CI 0.56-0.93). In total, 33% (13/39) of the studies reported an association with squamous cell carcinoma, with 2 cohorts revealing an adjusted RR of 1.4 (95% CI 1.02-1.93) and 1.30 (95% CI 0.90-1.88). A total of 8% (3/39) of the studies reported an association between breast cancer and melanoma, with breast cancer cohorts revealing an adjusted RR of 8.453 (95% CI 1.638-43.606), 1.03 (95% CI 0.89-1.20), and 1.36 (95% CI 1.18-1.58) and melanoma cohorts revealing an adjusted RR of 1.10 (95% CI 0.95-1.27), 0.63 (95% CI 0.47-0.85), and 0.96 (95% CI 0.57-1.62). A total of 5% (2/39) of the studies reported an association among nonmelanoma skin cancers, hepatic cancer, and thyroid carcinomas, with nonmelanoma skin cancer cohorts revealing an adjusted RR of 1.36 (95% CI 1.26-1.47) and 2.66 (95% CI 1.53-4.61), hepatic cancer cohorts revealing an adjusted RR of 1.42 (95% CI 1.06-1.90) and 1.32 (95% CI 0.89-1.95), and thyroid carcinoma cohorts revealing an adjusted RR of 1.06 (95% CI 0.68-1.65) and 1.59 (95% CI 1.07-2.36). Only 1 cohort reported an association with glioma, revealing an adjusted RR of 1.36 (95% CI 1.18-1.58). According to our review, patients with rosacea were statistically more likely to have nonmelanoma skin cancers, breast cancer, and glioma. Rosacea was not found to be substantially associated with melanoma. The associations between rosacea and hepatic and thyroid cancers were unclear because of conflicting results.

Conclusions: The current literature shows that rosacea is significantly associated with increased odds of nonmelanoma skin cancers, glioma, and breast cancer. Rosacea does not appear to be associated with melanoma. Further studies should be conducted to clarify the association between thyroid and hepatic cancers and rosacea.

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KEYWORDS

rosacea; malignancies; skin cancer; glioma; breast cancer; hepatic cancer; thyroid cancer; systematic review

Introduction

Background

Rosacea is a chronic inflammatory skin condition that predominantly manifests as persistent facial flushing, irritation, and acneiform papules or pustules. Although the etiology of rosacea remains unclear, a variety of factors both genetic and environmental seem to play a role in its pathogenesis. It has been hypothesized that elements of immune system dysregulation, deregulation of neurovascular signaling, and overgrowth of cutaneous pathogens are involved [1]. These abnormal inflammatory processes impair the skin's ability to act as a protective barrier for the body [2]. A genetic component has been suggested as well given that rosacea tends to appear more frequently in patients of Northern European and Celtic ancestry [1]. As the pathogenesis of rosacea is known to involve an abnormal inflammatory response, studies have been conducted to investigate its co-occurrence with other systemic diseases. Recent studies have suggested that rosacea is associated with a heightened risk of various chronic systemic diseases, including hypertension, autoimmune disease, cardiovascular disease, gastrointestinal disorders, and dyslipidemia [3], as well as multiple psychiatric comorbidities (major depressive disorder, persistent mood disorders, adjustment disorder, and generalized anxiety disorder) [4]. The complex relationship between inflammation and mental health is yet to be clearly understood, but there is evidence that chronic low-grade inflammation can contribute to mental illnesses such as depression [5]. Therefore, the inflammatory qualities of a chronic disease such as rosacea can potentially have far-reaching effects on patients' mental and physical health.

In addition to the aforementioned illnesses, there have also been many studies that have examined the association between rosacea and various cancers. The current understanding of the pathophysiology of this relationship is limited. However, it is hypothesized that patients with rosacea may have an increased risk of skin cancer because of inflammatory changes in the skin barrier, including reduced epidermal levels of photoreceptive transurocanic acid [6].

Objectives

Studies that have investigated the relationship between rosacea and cancer have reported inconsistent results. A recent study in Denmark [3,6] found that patients with rosacea had an increased risk of developing glioma, nonmelanoma skin cancer (NMSC), breast cancer, and hepatic cancer, whereas another study in the United States noted that females who had a history of rosacea had a subsequently increased risk of thyroid and basal cell carcinoma (BCC) [7]. Dupont [8], in contrast, found no substantial association between rosacea and skin cancers. Given the ambiguity of these findings, we conducted a systematic review of the current published work to evaluate the relationship between rosacea and various commonly studied cancers in the literature, including BCC; squamous cell carcinoma (SCC); Merkel cell carcinoma; melanoma; glioma; and hepatic, breast, and thyroid carcinomas.

Methods

Eligibility and Criteria

In accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, we conducted a review of observational studies on the association between rosacea and various cancers. Case reports, case series, case-control studies, cross-sectional studies, and cohort studies were included.

Literature Search and Study Selection

The Cochrane, PubMed, Embase, and Ovid databases were searched for relevant studies from inception to March 3, 2021. The search was then updated on June 9, 2023. The search terms are provided in detail in Multimedia Appendix 1.

Studies were included or excluded from a meta-analysis based on the criteria outlined in Textbox 1.

All studies were screened by 2 independent reviewers (LT and JX), and eligibility for inclusion was determined by screening the titles and reviewing the full texts. Any conflicts of eligibility were resolved by a third-party reviewer (WG). Using information obtained from the articles, rosacea and each cancer were categorized as likely or unlikely associated, whereas cancers with conflicting results were categorized as having an unclear association.

Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

1. Studies that investigated patients with a diagnosis of basal cell carcinoma; nonmelanoma skin cancer; squamous cell carcinoma; Merkel cell carcinoma; melanoma; glioma; or hepatic, breast, or thyroid carcinoma and a diagnosis of rosacea
2. Patients diagnosed with erythematotelangiectatic rosacea, papulopustular (or acne) rosacea, rhinophyma, or ocular rosacea
3. Papers studying populations in different countries
4. Case reports; series; and case-control, cohort, or cross-sectional studies
5. Patients of all ages, sexes, and nationalities

Exclusion criteria

1. Papers for which full text was not available
2. N<1 patients
3. Papers not written in English
4. Studies conducted on nonhuman subjects
5. Studies including concurrent acne and rosacea
6. Studies including diagnoses of perioral dermatitis

Data Extraction and Risk-of-Bias Assessment

Data extracted from the included studies comprised author, publication year, title, study location, study type, total number of patients, number of patients with rosacea vs control patients without rosacea, general mean age, mean age of patients presenting with rosacea, general percentage of female patients, percentage of female patients presenting with rosacea, number of patients who presented with a history of smoking, drinking, confounding diseases, type of rosacea, inclusion and exclusion criteria used for the study, method of diagnosis of rosacea, mean duration of rosacea, socioeconomic status association with prevalent rosacea, number of patients with cancer in general, number of patients with cancer and rosacea, *P* value, odds ratio (OR; 95% CI), hazard ratio (HR), incidence rate ratio, risk ratio (RR), and any adjustments made to the statistical values. To assess the risk of bias of the included studies, the Newcastle-Ottawa Quality Assessment Scale was used.

Results

Search Results

Among the 3004 articles originally identified, 2786 (92.74%) remained after deduplication and were screened. After initial screening, of the 2786 remaining articles, 104 (3.73%) full-text articles were assessed for eligibility, of which 39 (37.5%) were eligible for our systematic review (Table 1). A total of 62.5% (65/104) of the full texts were excluded for reasons such as being in a non-English language, being the wrong publication type (including conference abstracts), having the wrong study design (including research papers), or looking at the wrong outcomes (Figure 1). Owing to a lack of available studies, we were not able to conduct a meta-analysis.

Table 1. Characteristics of the studies.

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
BCC[a]	Li et al [7], 2015	Personal history of rosacea and risk of incident cancer among women in the United States (prospective-retrospective mixed cohort study)	75,088 (United States)	Rosacea: 37.6 (4.1); control: 36.2 (4.7)	100%	Pathologically confirmed invasive cases via medical record and self-report	NHS II[b] records excluding records for which there was missing date of birth, record of all cancers at baseline, and all responses from racial and ethnic minority people	Outcome: BCC was found to be significantly higher among patients with rosacea as compared with controls; adjusted RR[c]=1.50 (95% CI 1.35-1.67) and *P*<.05; adjusted for age, BMI, alcohol consumption, physical activity, physical examination, multivitamin use, smoking status, oral contraceptive use, menopausal status, postmenopausal hormone use, and use of medications (including tetracycline, isotretinoin, and antibiotics)
BCC	Lin et al [9], 2023	Single-institution retrospective study evaluating personal history of rosacea and risk of BCC of the face (retrospective, population-based cohort study)	4537 (United States)	Nonrosacea: 72.4 (12.8); rosacea: 72.2 (12.3)	Nonrosacea: 1048 (45%); rosacea: 59 (47.6%)	Confirmed via the ICD-10[d] code, whereas 267 had a history of provider- or patient-reported rosacea according to available medical records	N/A[e]	Outcome: BCC occurring on the face or head and history of rosacea were significantly lower than in patients without history of rosacea; aOR[f] 0.72 (95% CI 0.56-0.93); facial BCC: *P*<.001; nonfacial BCC: *P*<.58; adjusted for multivariate logistic regression analysis adjusted for age, sex, smoking history, and skin of color

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
SCC[g]	Lin et al [10], 2022	Prospective study evaluating the personal history of rosacea and risk of cutaneous SCC among women in the United States (retrospective, population-based cohort study)	90,238 (United States)	Nonrosacea: 36.1 (4.7); rosacea: 37.6 (4.1)	N/A	Study participants completed biennial questionnaires that gathered medical history, including clinician-diagnosed cSCC[h] and rosacea. During the follow-up, 577 cSCC cases were documented and confirmed via pathology reports.	N/A	Outcome: rosacea had an overall significant association with cSCC, especially when developed on the head and neck. Rosacea had no significant association with non–head and neck SCC; adjusted RR=1.4 (95% CI 1.02-1.93); Cox proportional hazard model and multivariate model with adjustments for age and other cancer risk factors
SCC	Li et al [7], 2015	Personal history of rosacea and risk of incident cancer among women in the United States (prospective-retrospective mixed cohort study)	75,088 (United States)	Rosacea: 37.6 (4.1); control: 36.2 (4.7)	100%	Pathologically confirmed invasive cases via medical record and self-report	NHS II records excluding records for which there was missing date of birth, record of all cancers at baseline, and all responses from racial and ethnic minority people	Outcome: there were no statistically significant associations found between rosacea and SCC; adjusted HR[i]=1.30 (95% CI 0.90-1.88); adjusted for age, BMI, alcohol consumption, physical activity, physical examination, multivitamin use, smoking status, oral contraceptive use, menopausal status, postmenopausal hormone use, and use of medications (including tetracycline, isotretinoin, and antibiotics)
NMSC[j]	Egeberg et al [6], 2017	Rosacea and risk of cancer in Denmark (retrospective, population-based cohort study)	4,361,688 (Denmark)	Rosacea: 53.7 (16.5); control: 48.6 (18.0)	Rosacea: 68%; control: 50.6%	ICD-10 code C73 in DNPR[k] medical record	All Danish adults (aged 18 years) alive and residing in Denmark on January 1, 2008. Patients were followed up from study start until December 31, 2012; death; migration; or the occurrence of an end point, whichever came first.	Outcome: patients diagnosed with rosacea were statistically more likely to develop NMSC compared with patients in the reference population; adjusted HR=1.36 (95% CI 1.26-1.47) and *P*<.001; adjusted for age, sex, SES[l], and health care consumption

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
NMSC	Cho et al [11], 2022	Risk of Skin Cancer and Actinic Keratosis in Patients with Rosacea: A Nationwide Population-based Cohort Study (retrospective, population-based cohort study)	11,420 (South Korea)	61.2% (n=6698) were in the age range of 40 to 59 years.	64.7% (n=7092)	NHISS[m] in South Korea was used to compile claims from January 2010 to December 2019 with ≥1 relevant ICD-10 codes (actinic keratosis: L570; KC[n]: C44 and D04; melanoma: C43 and D03; gastric cancer: C16; colorectal cancer: C18, C19, and C20; and liver cancer: C22)	Patients with preexisting principal diagnoses of the target disease before the index date were excluded. To establish a well-matched control group, they used specific criteria, including sex, age, income, and residence, at a 1:2 ratio. Any study patients lacking suitable matched controls and control patients with previous target disease diagnoses were subsequently excluded from the analysis. The index date for patients with rosacea was set as the date of their initial diagnosis, with control patient index dates adjusted accordingly. The observation period extended until December 31, 2019, and individuals who passed away without experiencing the target disease diagnosis were censored.	Outcome: rosacea had a significant association with the development of NMSC; adjusted HR=2.66 (95% CI 1.53-4.61); multivariable stratified Cox proportional hazard model
Breast cancer	Egeberg et al [6], 2017	Rosacea and Risk of Cancer in Denmark (retrospective, population-based cohort study)	4,361,688 (Denmark)	Rosacea: 53.7 (16.5); control: 48.6 (18.0)	Rosacea: 68%; control: 50.6%	ICD-10 code C73 in DNPR medical record	All Danish adults (aged 18 years) alive and residing in Denmark on January 1, 2008. Patients were followed up from study start until December 31, 2012; death; migration; or the occurrence of an end point, whichever came first.	Outcome: patients with rosacea were more likely to develop breast cancer compared with patients without a history of rosacea; aOR 8.453 (95% CI 1.638-43.606) and *P*=.01; adjusted for multivariate model

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
Breast cancer	Li et al [12], 2020	Epidemiological features of rosacea in Changsha, China: A population - based, cross - sectional study (population-based cross-sectional case-control study)	794 analyzed and 10,095 enrolled (China)	Overall: 35.5 (19.1); female patients with rosacea: 37.4 (10.1); male patients with rosacea: 42.8 (15.2); patients with rosacea overall: 38.4 (11.3)	Rosacea: 82.61%; control: 70.65%	Previous diagnosis at clinics or superior-level hospitals	5 randomly selected neighborhoods that were then classified into socioeconomic strata (rich, moderate, and poor), with one community from each stratum selected. All Han Chinese citizens from these 15 communities with 4025 families and 12,775 individuals were included. Of these, 628 families chose not to attend the interview and were excluded from the study. The final sample size was 10,095.	Outcome: no significant increase in the occurrence of breast cancer in patients with rosacea; adjusted RR=1.03 (95% CI 0.89-1.20); adjusted for age, BMI, alcohol consumption, physical activity, physical examination, multivitamin use, smoking status, oral contraceptive use, menopausal status, post-menopausal hormone use, history of severe teenage acne, and use of medications (including tetracycline, isotretinoin, and antibiotics). Additionally adjusted for personal history of benign breast disease, family history of breast cancer, age at first birth and parity, age at menarche, height, and BMI at the age of 18 years.
Breast cancer	Li et al [7], 2015	Personal history of rosacea and risk of incident cancer among women in the United States (prospective-retrospective mixed cohort study)	75,088 (United States)	Rosacea: 37.6 (4.1); control: 36.2 (4.7)	100%	Pathologically confirmed invasive cases via medical record and self-report	NHS II records excluding records for which there was missing date of birth, record of all cancers at baseline, and all responses from racial and ethnic minority people	Outcome: female patients with a diagnosis of rosacea were more likely to have had breast cancer; however, male patients with rosacea had no significant increase in breast cancer incidence; IRR[o] (person-years): overall=1.36 (95% CI 1.18-1.58); females=1.27 (95% CI 1.05-1.54); males=1.47 (95% CI 1.17-1.84); overall: *P*<.001; females: *P*=.02; males: *P*<.001; IRR adjusted for age, sex, and SES

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
Glioma	Egeberg et al [3], 2016	Association of Rosacea With Risk for Glioma in a Danish Nationwide Cohort Study (nationwide cohort study)	5,416,138 (Denmark)	Rosacea: 42.2 (16.5); control: 40.8 (19.7)	Rosacea: 67.3%; control: 50.4%; females: 45,994 (67.3%) with rosacea and 2,732,029 (50.4%) controls; males: 22,378 (32.7%) with rosacea and 2,684,509 (49.6%) controls	Hospital diagnosis of glioma (ICD-8[p] code 191 and ICD-10 codes C71, D33, and D43) recorded in the DNPR	Inclusion: Danish citizens aged ≥18 years on January 1, 1997, or the subsequent day they reached 18 years. Individuals were followed up until December 31, 2011; migration; a diagnosis of glioma; or death owing to any cause, whichever came first. Exclusion criteria: patients with rosacea or glioma at baseline	Outcome: although the correlation was weak, the study found a significantly increased risk of glioma in patients with rosacea; rosacea-associated increased risk of glioma was greater in males than in females; IRR (person-years): overall=1.36 (95% CI 1.18-1.58); females=1.27 (95% CI 1.05-1.54); men=1.47 (95% CI 1.17-1.84); overall: *P*<.001; females: *P*=.02; males: *P*<.001; IRR adjusted for age, sex, and SES
Hepatic cancer	Egeberg et al [6], 2017	Rosacea and Risk of Cancer in Denmark (retrospective, population-based cohort study)	4,361,688 (Denmark)	Rosacea: 53.7 (16.5); control: 48.6 (18.0)	Rosacea: 68%; control: 50.6%	ICD-10 code C73 in DNPR medical record	All Danish adults (aged 18 years) alive and residing in Denmark on January 1, 2008. Patients were followed up from study start until December 31, 2012; death; migration; or the occurrence of an end point, whichever came first.	Outcome: patients with rosacea had an increased risk of developing hepatic cancer; adjusted HR=1.42 (95% CI 1.06-1.90) and *P*=.02; adjusted for age, sex, SES, and health care consumption

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
Hepatic cancer	Cho et al [11], 2022	Risk of Skin Cancer and Actinic Keratosis in Patients with Rosacea: A Nationwide Population-based Cohort Study (retrospective, population-based cohort study)	11,420 (South Korea)	61.2% (n=6698) were in the age range of 40 to 59 years.	64.7% (n=7092)	NHISS in South Korea was used to compile claims from January 2010 to December 2019 with ≥1 relevant ICD-10 codes (actinic keratosis: L570; KC: C44 and D04; melanoma: C43 and D03; gastric cancer: C16; colorectal cancer: C18, C19, and C20; and liver cancer: C22)	Patients with preexisting principal diagnoses of the target disease before the index date were excluded. To establish a well-matched control group, they used specific criteria, including sex, age, income, and residence, at a 1:2 ratio. Any study patients lacking suitable matched controls and control patients with previous target disease diagnoses were subsequently excluded from the analysis. The index date for patients with rosacea was set as the date of their initial diagnosis, with control patient index dates adjusted accordingly. The observation period extended until December 31, 2019, and individuals who passed away without experiencing the target disease diagnosis were censored.	Outcome: rosacea had no significant association with the development of hepatic cancer; adjusted HR=1.32 (95% CI 0.89-1.95); multivariable stratified Cox proportional hazard model
Thyroid cancer	Egeberg et al [6], 2017	Rosacea and Risk of Cancer in Denmark (retrospective, population-based cohort study)	4,361,688 (Denmark)	Rosacea: 53.7 (16.5); control: 48.6 (18.0)	Rosacea: 68%; control: 50.6%	ICD-10 code C73 in DNPR medical record	All Danish adults (aged 18 years) alive and residing in Denmark on January 1, 2008. Patients were followed up from study start until December 31, 2012; death; migration; or the occurrence of an end point, whichever came first.	Outcome: no significant increase in the development of thyroid cancer in patients with rosacea; adjusted HR=1.06 (95% CI 0.68-1.65) and *P*=.80; adjusted for age, sex, SES, and health care consumption

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
Thyroid cancer	Li et al [7], 2015	Personal history of rosacea and risk of incident cancer among women in the United States (prospective-retrospective mixed cohort study)	75,088 (United States)	Rosacea: 37.6 (4.1); control: 36.2 (4.7)	100%	Pathologically confirmed invasive cases via medical record and self-report	NHS II records excluding records for which there was missing date of birth, record of all cancers at baseline, and all responses from racial and ethnic minority people	Outcome: found an increase in the development of thyroid cancer in patients with rosacea; adjusted RR=1.59 (95% CI 1.07-2.36) and *P*<.05; adjusted for age, BMI, alcohol consumption, physical activity, physical examination, multivitamin use, smoking status, oral contraceptive use, menopausal status, postmenopausal hormone use, and use of medications (including tetracycline, isotretinoin, and antibiotics)
Melanoma	Egeberg et al [6], 2017	Rosacea and Risk of Cancer in Denmark (retrospective, population-based cohort study)	4,361,688 (Denmark)	Rosacea: 53.7 (16.5); control: 48.6 (18.0)	Rosacea: 68%; control: 50.6%	ICD-10 code C73 in DNPR medical record	All Danish adults (aged 18 years) alive and residing in Denmark on January 1, 2008. Patients were followed from study start until December 31, 2012; death; migration; or the occurrence of an end point, whichever came first.	Outcome: no increased occurrence of melanoma in patients with rosacea; adjusted HR=1.10 (95% CI 0.95-1.27) and *P*=.19; adjusted for age, sex, SES, and health care consumption
Melanoma	Erickson et al [13], 2019	Sex differences for incident cancer in patients with rosacea: Real-world evidence from a large Midwestern US patient population (retrospective, population-based cohort study)	186,829 (United States)	N/A	Overall: 76% diagnosed with cancer of some type (not necessarily melanoma)	N/A	A medical record data repository (>6 million patients) was searched (using ICD-9[q] and ICD-10 codes) for data from patients of dermatology with a rosacea diagnosis vs patients without rosacea as a control population (≥1-year follow-up; January 2001-November 2018) and who had a subsequent diagnosis of any cancer	Outcome: cutaneous melanoma was inversely associated with rosacea in female patients (aOR 0.63, 95% CI 0.47-0.85; *P*=.003; IRR=10.41 per 10,000 females/y) but not in male patients; adjusted for age and race

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
Melanoma	Li et al [7], 2015	Personal history of rosacea and risk of incident cancer among women in the United States (prospective-retrospective mixed cohort study)	75,088 (United States)	Rosacea: 37.6 (4.1); control: 36.2 (4.7)	100%	Pathologically confirmed invasive cases via medical record and self-report	NHS II records excluding records for which there was missing date of birth, record of all cancers at baseline, and all responses from racial and ethnic minority people	Outcome: no significant increase in the development of malignant melanoma in patients with rosacea; adjusted RR=0.96 (95% CI 0.57-1.62); adjusted for age, BMI, alcohol consumption, physical activity, physical examination, multivitamin use, smoking status, oral contraceptive use, menopausal status, post-menopausal hormone use, and use of medications (including tetracycline, isotretinoin, and antibiotics)

Cancer type	Study	Title (study type)	Total number of patients	Age (years), mean (SD)	Female patients	Method of cancer diagnosis	Inclusion and exclusion criteria	Statistical results
Melanoma	Cho et al [11], 2022	Risk of Skin Cancer and Actinic Keratosis in Patients with Rosacea: A Nationwide Population-based Cohort Study (retrospective, population-based cohort study)	11,420 (South Korea)	61.2% (n=6698) were in the age range of 40 to 59 years.	64.7% (n=7092)	NHISS in South Korea was used to compile claims from January 2010 to December 2019 with ≥1 relevant ICD-10 codes (actinic keratosis: L570; KC: C44 and D04; melanoma: C43 and D03; gastric cancer: C16; colorectal cancer: C18, C19, and C20; and liver cancer: C22)	Patients with preexisting principal diagnoses of the target disease before the index date were excluded. To establish a well-matched control group, they used specific criteria, including sex, age, income, and residence, at a 1:2 ratio. Any study patients lacking suitable matched controls and control patients with previous target disease diagnoses were subsequently excluded from the analysis. The index date for patients with rosacea was set as the date of their initial diagnosis, with control patient index dates adjusted accordingly. The observation period extended until December 31, 2019, and individuals who passed away without experiencing the target disease diagnosis were censored.	Outcome: rosacea had no significant association with the development of melanoma; adjusted HR=1.69 (95% CI 0.25-11.37); multivariable stratified Cox proportional hazard model

[a]BCC: basal cell carcinoma.

[b]NHS II: Nurses' Health Study II.

[c]RR: risk ratio.

[d]ICD-10: International Classification of Diseases, 10th Revision.

[e]N/A: not applicable.

[f]aOR: adjusted odds ratio.

[g]SCC: squamous cell carcinoma.

[h]cSCC: cutaneous squamous cell carcinoma.

[i]HR: hazard ratio.

[j]NMSC: nonmelanoma skin cancer.

[k]DNPR: Danish National Patient Register.

[l]SES: socioeconomic status.

[m]NHISS: National Health Insurance Sharing Service.

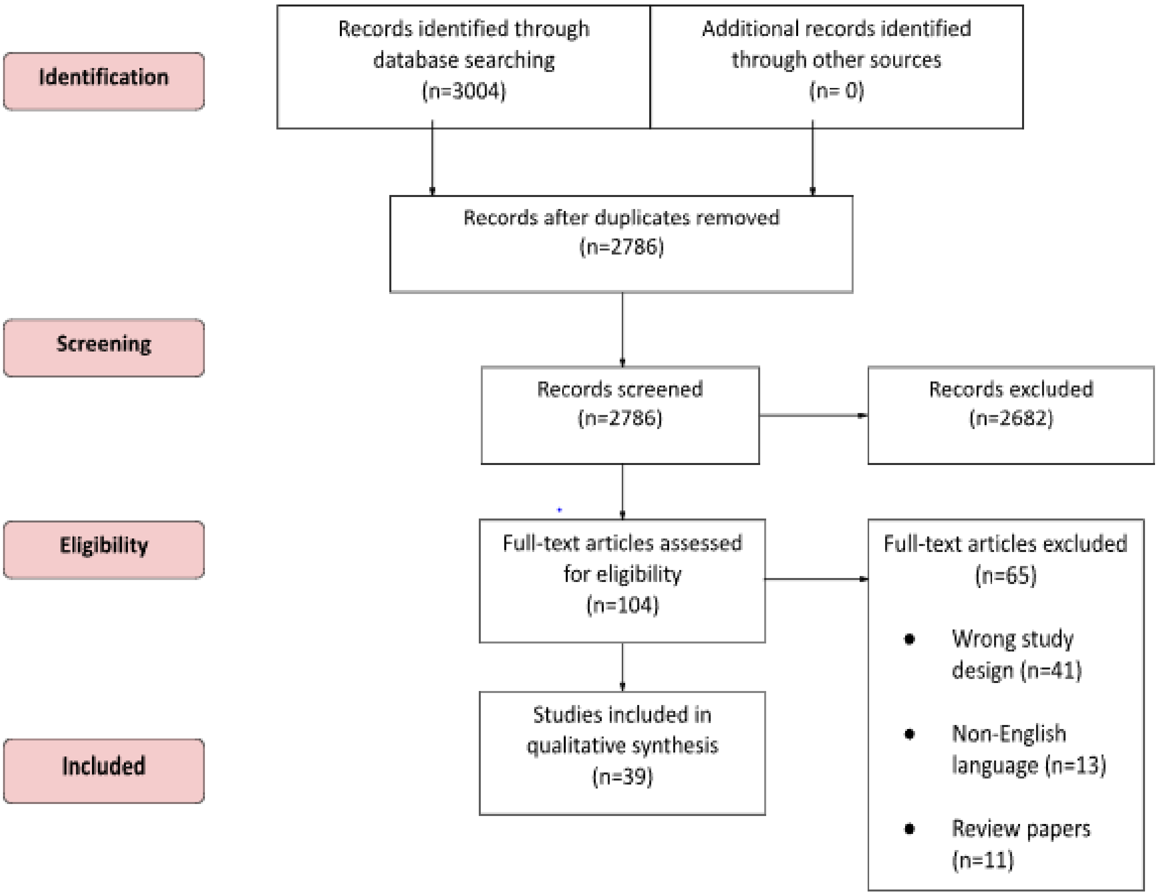
[n]KC: keratinocyte carcinoma.

[o]IRR: incidence rate ratio.

[p]ICD-8: International Classification of Diseases, Eighth Revision.

[q]ICD-9: International Classification of Diseases, Ninth Revision.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram for the review on rosacea and its association with various cancers.

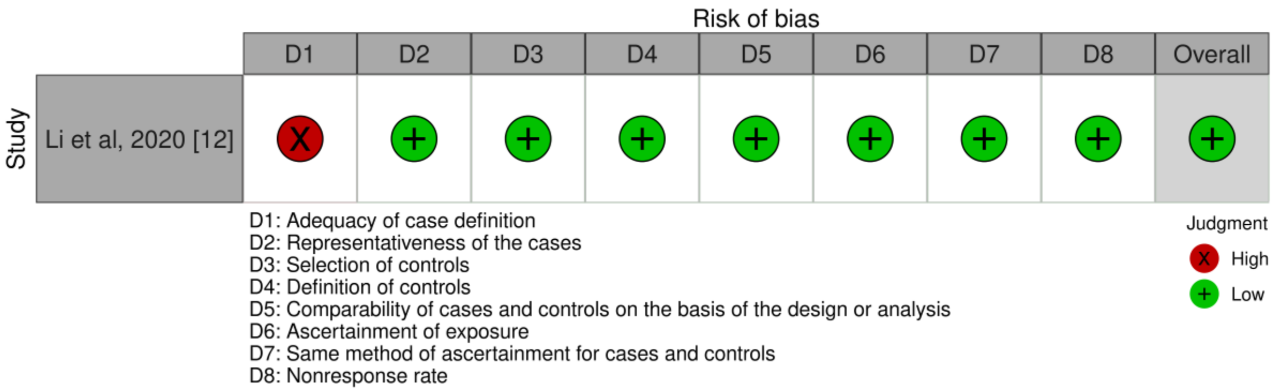


Risk of Bias of the Included Studies

The risk of bias of the studies included for the statistical analysis is summarized in Figures 2 [3,6,7,9-11,13] and 3 [12]. The Newcastle-Ottawa Quality Assessment Scale was used to assess the bias found in a total of 21% (8/39) of the studies included for analysis. Of these 8 studies, 7 (88%) were rated as having a low risk of bias based on a Newcastle-Ottawa Quality Assessment Scale for cohort studies score of ≥5 (Figure 2). There was 1 study for which we had to use the Newcastle-Ottawa Quality Assessment Scale for case-control studies and that was also determined to have a low risk of bias with a score of ≥5 (Figure 3).

Figure 2. Detailed Newcastle-Ottawa Quality Assessment Scale of each included cohort study [3,6,7,9,10,11,13,14].

Figure 3. Detailed Newcastle-Ottawa Quality Assessment Scale of each included case-control study [12,14].



Rosacea and BCC

Our search returned 41% (16/39) of papers examining the relationship between rosacea and BCC. Of these 16 papers, 2 (12%) were cohort studies, the first investigating the impact of a personal history of rosacea on the risk of developing BCC in females in the United States and the second investigating the impact of a personal history of rosacea on the risk of developing facial BCC in females in the Providence, Rhode Island, region [7]. In the first study, 424 patients with rosacea and 4552 age- and sex-matched controls without rosacea were followed up for reports of the development of cancer. The mean age of the study sample was 37.6 (SD 4.1) years for patients with rosacea and 36.2 (4.7) years for the control group. The prevalence of BCC was found to be significantly higher among patients with rosacea compared with controls [7].

In the second study, of the 4537 patients diagnosed with BCC from October 2016 to November 2020 in the Rhode Island region, 2453 had BCC on the face, and of them, 267 had a history of rosacea. A multivariate model with adjustments for age, sex, smoking history, skin color, and other cancer risk factors was developed. Results for chi-square and *R* statistic analysis indicated that facial BCC in patients with a history of rosacea was significantly lower than in patients without rosacea (3.80 vs 5.07 per 100 patients; $P<.001$). When comparing BCC of the body, no significant difference was found between patients with a history of rosacea and patients without rosacea (3.95 vs 4.22 per 100 patients; $P<.58$) [9].

The other 88% (14/16) of papers on rosacea and BCC comprised case series or case reports. Notably, all reported cases detailed male patients with rhinophymatous rosacea who were later diagnosed with BCC in the area of the nodular lesion (Table 2). Lazzeri et al [15] presented a case series and literature review in which they found a total of 46 patients (including 3 new cases of their own) with rhinophyma that went on to develop cutaneous cancer. Of these patients, 28 were diagnosed with BCC, 11 were diagnosed with SCC, 4 were diagnosed with SCC and BCC, and 1 was found to have angiosarcoma. Common presenting symptoms in these patients included sudden progressive enlargement of long-standing rhinophyma in both BCC and SCC cases and additional symptoms of ulceration, malodorous drainage, and serous discharge in SCC cases [15]. Interestingly, BCC was less likely than SCC to present with sudden ulceration, bleeding, or serous discharge, although such symptoms have certainly been observed [16-20].

Table 2. Characteristics of case series and reports that investigated basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) in patients with rosacea.

Study, year	Cancer type	Cases, n	Type of preexisting rosacea	Geographic location
Acker and Helwig [21], 1967	BCC	5	Rhinophyma	Washington, DC
Baruchin et al [22], 1998	BCC	4	Rhinophyma	Israel
Keefe et al [17], 1988	BCC	1	Rhinophyma	Scotland
Kwah and Lawrence [18], 2011	BCC	1	Rhinophyma	North Carolina
Lazzeri et al [15], 2012	BCC	2	Rhinophyma	Pisa, Italy
Leyngold et al [23], 2008	BCC	1	Rhinophyma	Nevada, United States
McKenna and McKenna [19], 2006	BCC	1	Rhinophyma	Northern Ireland, United Kingdom
Nambi et al [20], 2008	BCC	1	Rhinophyma	Saudi Arabia
Plenk [24], 1995	BCC	2	Rhinophyma	Utah, United States
Rees [25], 1955	BCC	2	Rhinophyma	New York, United States
Silvis and Zachary [26], 1990	BCC	1	Rhinophyma	Minneapolis, United States
Zabbia et al [27], 2014	BCC	6	Rhinophyma	Palmero, Italy
Kornblut and Evers [28], 1973	SCC	1	Rhinophyma	Maryland, United States
Broadbent and Cort [29], 1977	SCC	2	Rhinophyma	England
Barankin [16], 2005	BCC	1	Rhinophyma	Canada
Jain et al [30], 1973	SCC	1	Rhinophyma	Udaipur, India
Kesty and Baldwin [31], 2017	SCC	1	Rhinophyma	Florida, United States
Lazzeri et al [15], 2012	SCC	1	Rhinophyma	Pisa, Italy
Lutz and Otley [32], 2001	SCC	1	Rhinophyma	Florida, United States
Rizzi et al [33], 2016	SCC	1	Rosacea	Milan, Italy
Ross and Davies [34], 1991	SCC	1	Rhinophyma	London, United Kingdom
Tamir et al [35], 1999	SCC and BCC	1	Rhinophyma	Washington, United States
Theotoka et al [36], 2020	SCC	2	Ocular rosacea	Miami, United States
Chlebicka et al [37], 2021	BCC	2	Rhinophyma	Wrocław, Poland

Rosacea and SCC

Our search returned 33% (13/39) of studies examining the relationship between rosacea and SCC. Of these, one was a cohort study investigating the impact of a personal history of rosacea on the risk of developing SCC in females in the United States. In this study, 577 cases of SCC were isolated from a population of 90,238 females. A Cox proportional hazard model and multivariate model with adjustments for age and other cancer risk factors were developed. The results indicated that rosacea was significantly associated with overall cutaneous SCC (RR 1.40, 95% CI 1.02-1.93). In this study, the location of SCC was also divided into 2 groups—head and neck and non–head and neck—which were also compared with the history of rosacea. The results indicated that rosacea was significantly associated with head and neck SCC (RR 1.71, 95% CI 1.09-2.69). Findings indicated no significant statistical associations between rosacea and non–head and neck SCC (RR 1.21, 95% CI 0.78-1.90) [10].

The second study investigated various cancer risks among females in the United States with a history of rosacea. Among a total of 75,088 females, 6015 patients were diagnosed with rosacea from 1991 to 2011, with 452 SCC diagnoses documented. A Cox proportional hazard model and multivariate model with adjustments for age, BMI, alcohol consumption, smoking history, and other cancer risk factors were developed. The results indicated that there were no statistically significant associations between rosacea and SCC (HR 1.30, 95% CI 0.90-1.88) [7].

The other 85% (11/13) of the studies were case series and reports that examined the association between rosacea and SCC. Again, all studies identified SCC development in patients with long-standing rhinophyma (Table 2). Notably, Kesty and Baldwin [31] reported the case of a patient aged 67 years with no previous history of cancer who presented with an enlarging left nasal mass of 4 months. An initial punch biopsy diagnosed rhinophyma, and the patient was sent home. The patient presented back to the hospital several weeks later with new reports of ulceration, drainage, and rapid growth of the mass and had another biopsy indicating invasive SCC. Although a total rhinectomy could be performed, the patient was ultimately found to have metastases to the lungs and submandibular area [31]. Although such cases are rare and no overall association can be made, these reports may serve as a warning to physicians to remain vigilant for the possibility of carcinoma in patients with rhinophyma, particularly those with rapidly growing and ulcerating masses.

Rosacea and NMSC

Our search returned 5% (2/39) of studies that did not differentiate between NMSCs. In the first case, Egeberg et al [6] conducted a cohort study analyzing data from the nationwide Danish registry. The study included 49,475 patients with rosacea with an average age of 53.7 (SD 16.5) years and a reference population of 4,312,213 patients without rosacea with an average age of 48.6 (SD 18.0) years. Their findings noted that patients diagnosed with rosacea were statistically more likely to develop NMSC compared with patients in the reference population (HR 1.36, 95% CI 1.26-1.47) [6]. In the second case, Cho et al [11] conducted a nationwide population-based retrospective cohort study in South Korea. The study included 11,420 patients compared using a multivariable stratified Cox proportional hazard model. Their findings noted that patients with rosacea had a significant association with the development of NMSC compared with the reference population (HR 2.66, 95% CI 1.53-4.61) [11].

Rosacea and Breast Cancer

A total of 8% (3/39) of the studies analyzed the association between rosacea and breast cancer. Of these 3 studies, 2 (67%) were cohort studies. Egeberg et al [6] conducted a cohort study that analyzed data from the nationwide Danish registry and found that patients with rosacea were more likely to develop breast cancer compared with patients without a history of rosacea (HR 1.25, 95% CI 1.15-1.36). However, Li et al [7] found no significant increase in the occurrence of breast cancer in patients with rosacea (RR 1.03, 95% CI 0.89-1.20).

Li et al [12] also conducted a case-control study to determine the present epidemiological status of rosacea in China. From a total of 10,095 patients enrolled in the study, 351 were observed to have rosacea, 290 of whom were female and 61 of whom were male. The overall average age of patients with rosacea was 38.4 (SD 11.3) years, whereas the average age of the control population was 35.5 (SD 19.1) years. A previous diagnosis of melasma, hypertension, coronary heart disease, hyperthyroidism, diabetes, chronic gastritis, peptic ulcer, gastrointestinal cancer, breast cancer, and gynecological cancer was then identified in patients in both the control and rosacea populations. It was found that female patients with a diagnosis of rosacea were more likely to have had breast cancer (OR 8.453, 95% CI 1.638-43.606), among other diseases such as melasma, hypertension, and hyperthyroidism. Regarding male patients with rosacea, there was no significant increase in breast cancer incidence. A meta-analysis of observational studies on the association between rosacea and breast cancer was ultimately not conducted because of heterogeneity between the studies; however, it would seem that most of the current data available point to a positive correlation [12].

Owing to the directionality of the studied relationship, we were unable to include in the meta-analysis a case-control study by Long et al [38] that looked at rosacea incidence in various cancers in China. However, they found that patients with breast cancer had a significantly higher incidence of rosacea compared with individuals without rosacea (OR 5, 95% CI 4.02-6.2) [38]. Although this is the only study that was found of the inverse relationship, the potential for a bidirectional association lends further credence to the hypothesis that these 2 conditions are related.

Rosacea and Melanoma

A total of 8% (3/39) of the studies analyzed the association between rosacea and malignant melanoma. Egeberg et al [6] found no increased occurrence of melanoma in patients with rosacea (HR 1.10, 95% CI 0.95-1.27). Similarly, Li et al [7] also found no significant increase in the development of malignant melanoma in patients with rosacea (RR 0.96, 95% CI 0.57-1.62). Finally, the findings of Cho et al [11] noted that patients with rosacea had no association with the development of melanoma compared with the reference population (HR 1.69, 95% CI 0.25-11.37).

Although excluded from the meta-analysis because of not being in full text, an abstract by Erickson et al [13] investigated sex-specific differences in patients with rosacea and their likelihood of developing certain cancers. The study included 11,466 patients with rosacea, 8676 of whom were female, and 175,363 patients who did not have rosacea, 929 of whom were female. Interestingly, this abstract found that rosacea was inversely associated with the development of melanoma in female patients (RR 0.63, 95% CI 0.47-0.85). No significant relationship was found in male patients with rosacea [13]. Overall, despite the small number of studies available, there was no evidence of an association between the 2 conditions.

Rosacea and Hepatic Cancer

A total of 5% (2/39) of studies were found that examined the association between rosacea and hepatic cancer. Egeberg et al [6] noted that patients with rosacea have an increased risk of developing hepatic cancer (HR 1.42, 95% CI 1.06-1.90). The findings of Cho et al [11] noted that patients with rosacea had no association with the development of hepatic cancer compared with the reference population (HR 1.32, 95% CI 0.89-1.95).

Rosacea and Glioma

In total, 3% (1/39) of studies were found that examined the association between rosacea and glioma. Egeberg et al [3] conducted a cohort study on Danish citizens aged >18 years on January 1, 1997, and followed them through to December 31, 2011. Patients with rosacea or glioma at baseline were excluded to allow for the study of the temporal relationship between the conditions. The reference population for the study was 5,416,138 individuals with a mean age of 40.8 (SD 19.7) years, and the rosacea diagnosis group contained 68,372 patients with a mean age of 42.2 (SD 16.5) years. The reference population consisted of 2,684,509 male patients and 2,732,029 female patients. Although the correlation was weak, the study found a significantly increased risk of glioma in patients with rosacea (incidence rate ratio 1.36, 95% CI 1.18-1.58). Interestingly, it was found that the rosacea-associated increased risk of glioma was greater in males than in females [3].

In addition, the excluded case-control study by Long et al [38] found that patients with glioma were more likely to have had rosacea (OR 2.16, 95% CI 1.12-4.17), pointing to a potential bidirectional relationship between the 2 conditions.

Rosacea and Thyroid Cancer

A total of 5% (2/39) of the studies analyzed the association between rosacea and thyroid cancer, reporting conflicting results. Egeberg et al [6] found no significant increase in the development of thyroid cancer in patients with rosacea (HR 1.06, 95% CI 0.68-1.65), whereas Li et al [7] found an increase in the development of thyroid cancer in patients with rosacea (RR 1.59, 95% CI 1.07-2.36).

Discussion

Summary of Principal Findings

Our review found that, based on the available literature, there is a positive association between rosacea and glioma, NMSC, and breast cancer. Rosacea was not found in any study to be significantly associated with melanoma. Regarding BCC, SCC, and thyroid and hepatic cancers, a clear conclusion could not be drawn because of conflicting results across 2 studies.

Our review found conflicting evidence regarding the association between BCC and rosacea. Although Li et al [7] found a positive association between BCC and rosacea in a cohort study of female patients, Lin et al [10] found no association between BCC of the body and rosacea in female patients and an inverse association between BCC of the face and rosacea in female patients. More studies will be needed to determine whether an association truly exists. Interestingly, across our reviewed cohort studies, no positive associations were found between rosacea and facial BCC or facial SCC. This may be due to patients with rosacea adopting better sun-protective measures such as sunscreen and broad hats to avoid flaring their rosacea, simultaneously reducing their risk of facial NMSC. It should be noted that there are currently no comparative studies analyzing the association between BCC and rosacea in male patients. Our review also found 14 case reports and case series discussing the presence of BCC in male patients with rhinophyma. It is uncertain whether the increased prevalence of BCC in this population is due to the male sex, the increased severity of rosacea in patients with rhinophyma, or both. Although rosacea is more commonly seen in females, rhinophyma, a subtype of rosacea, is found to be more common in White males aged >50 years. Although the reason for this is unknown, it is important to note that, according to the current literature, males with rhinophyma are 3% to 10% more likely to develop some form of skin cancer at the site of the nodular lesion [39]. Characteristics to be watchful for in patients with long-standing rhinophyma include sudden changes in ulceration of the lesion and rapid growth associated with malodorous drainage [15].

Our review found a positive association between rosacea and NMSC. It should be noted that actinic keratosis was also found to be associated with rosacea in one cohort study [11]. UV exposure is thought to be a common pathogenic factor in the development of skin cancer, actinic keratosis, and rosacea. It is thought that patients with rosacea have an altered skin barrier and are more likely to have had higher UV exposure at early ages, which may predispose them to skin cancers such as SCC and BCC [3,7]. UV radiation is a known risk factor for skin cancers and also plays an important chronic role in rosacea development through the generation of reactive oxygen species and cathelicidin expression, in addition to being a known acute trigger for rosacea outbreaks [40]. It should be noted that, although NMSC had a positive association with rosacea, SCC showed conflicting results. Although Lin et al [10] found an overall positive association between SCC and rosacea, Li et al [7] found no such association. The conflicting findings between studies on NMSC versus BCC and SCC when it comes to rosacea may be because all current comparative studies regarding BCC, SCC, and rosacea have exclusively used female patients. In comparison, Cho et al [11] found an increased risk of NMSC in patients with rosacea in a cohort that included male patients with SCC and BCC. It is possible that there are gender-specific differences when it comes to rosacea and NMSC, perhaps because of different sun-avoidant practices when having rosacea. In addition, although many studies on rosacea, NMSC, BCC, and SCC controlled for age, smoking status, BMI, and alcohol intake among other potential confounders, race and socioeconomic status were brought up as additional possible confounders that were not adjusted for. More studies are needed to analyze the impact of sex, racial, and socioeconomic differences when it comes to rosacea and NMSCs.

It should be noted that, regarding melanoma, all comparative studies (3/3, 100%) analyzed in our review found no association between melanoma and rosacea. Wu et al [41] proposed that the risk of SCC and BCC is positively associated with cumulative UV exposure, whereas melanoma tends to be more associated with intermittent UV exposure. Therefore, it is possible that cumulative UV radiation may be an important confounding factor in the development of both skin cancers and rosacea, accounting for the seemingly positive association that we observed between rosacea and NMSC or SCC but not melanoma.

Other than one study indicating no association, the relationship between rosacea and breast cancer seemed to be positive. Given the prevalence of both rosacea and breast cancer in females, there may be a component of hormonal changes and estrogen mediating some common inflammatory and immune-related causes [38]. However, there was conflicting evidence regarding the association between hepatic cancer and rosacea. Egeberg et al [6] found a positive association between hepatic cancer and rosacea; however, this result was potentially confounded by the fact that the rosacea group also reported greater alcohol consumption than the controls. Regarding glioma, underlying the increased odds of glioma development in patients with rosacea may be common inflammatory pathways dependent on matrix metalloproteinases and the activation of interleukin-17. In particular, matrix metalloproteinase-9 plays an important role in both rosacea pathogenesis and regulation of cell invasion in malignant glioma [3]. One study found increased expression of matrix metalloproteinase-9 in tumor tissue specimens from 76% of patients with glioblastoma, the most common and aggressive malignant form of glioma [42]. Interleukin-17 upregulation is also recognized as a hallmark of rosacea and may play a role in immune suppression in glioma [43,44].

Studies examining the association between rosacea and thyroid cancer reported conflicting results. Accumulating evidence demonstrates that chronic inflammation plays a pivotal role in the pathogenesis of thyroid cancer [45,46]. Therefore, inflammation may be a potential link between rosacea and thyroid cancer. However, more studies need to be conducted to clarify this relationship.

Limitations

Our study was not able to conduct a meta-analysis because of the statistical heterogeneity between the studies. A meta-analysis would have further clarified the association between rosacea and the various cancers. In addition, there were a small number of studies on most of the cancers included in our review. Other limitations include a lack of studies examining the association between rosacea and cancer in skins of color. Most of the research described in this review was conducted on White, middle-aged, and female populations; further studies are needed regarding rosacea and cancer incidence in skins of color and male populations. In addition, the field of literature regarding BCC and rhinophyma or ocular rosacea is shallow and only comprises case reports/case series. These case series or case reports were included; however, they have an inherent bias because of the absence of a comparative group.

Conclusions

Our review of the current literature found that rosacea is significantly associated with NMSC, glioma, and breast cancer. An association between rosacea and thyroid cancer as well as between rosacea and hepatic cancer was also reported, but more studies are needed because of the limited amount of data. Rosacea does not appear to be associated with melanoma. Further studies should be conducted to determine whether there is an association between thyroid cancer and rosacea.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategies.
[DOCX File , 18 KB - derma_v6i1e47821_app1.docx]

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Abbreviations

BCC: basal cell carcinoma
HR: hazard ratio
NMSC: nonmelanoma skin cancer
OR: odds ratio
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RR: risk ratio
SCC: squamous cell carcinoma

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Review

Clinical Efficacy of Nutritional Supplements in Atopic Dermatitis: Systematic Review

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Abstract

Background: Atopic dermatitis (AD), also known as eczema, is a chronic inflammatory skin condition that presents with symptoms of intense pruritus, dryness, and erythema. Dissatisfaction with first-line therapies for AD, the desire to avoid steroids, and the extreme cost of effective biologics have created a demand for alternative treatment options such as oral vitamins and nutritional supplements.

Objective: The purpose of this review was to assess the effectiveness of oral nutritional supplements, pre- and probiotics, and vitamin deficiencies and supplements on AD symptomology and clinical course.

Methods: We searched Scopus, PubMed, and MEDLINE (Ovid interface) for English-language articles published between 1993 and 2023. The final search was conducted on June 22, 2023. The search terms comprised the following: "(Atopic Dermatitis or Atopic Eczema) AND (supplement OR vitamin OR mineral OR micronutrients OR Fish Oil OR Omega Fatty Acid OR Probiotics OR Prebiotics OR apple cider vinegar OR collagen OR herbal OR fiber)."

Results: A total of 18 studies—3 (17%) evaluating vitamins, 4 (22%) evaluating herbal medicine compounds, 2 (11%) evaluating single-ingredient nutritional supplements, and 9 (50%) evaluating pre- and probiotics—involving 881 patients were included in this review.

Conclusions: Overall, there is weak evidence to support any one nutritional supplement intervention for the alleviation of AD symptoms. Multiple trials (4/18, 22%) showed promise for supplements such as Zemaphyte, kefir, and freeze-dried whey with *Cuscuta campestris* Yuncker extract. The most evidence was found on the effectiveness of probiotics on the clinical course of AD. *Lactiplantibacillus plantarum*, *Ligilactobacillus salivarius*, and *Lactobacillus acidophilus* specifically showed evidence of efficacy and safety across multiple studies (6/18, 33%). However, larger, more extensive randomized controlled trials are needed to determine the true effectiveness of these supplements on the broader population.

Trial Registration: PROSPERO CRD42023470596; https://tinyurl.com/4a9477u7

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KEYWORDS

atopic dermatitis; eczema; nutrition; dietary supplement; oral supplement; vitamin; probiotic; dermatology; over the counter

Introduction

Background

Atopic dermatitis (AD), also known as eczema, is a chronic inflammatory skin condition that presents with symptoms of intense pruritus, dryness, and erythema. In the acute phase, inflammatory changes are dominated by edema, vesicles, and weeping skin lesions, which lead to chronic cutaneous manifestations, including thickening of the skin and fibrosis [1]. AD has 2 classifications: intrinsic (endogenous) and extrinsic (exogenous). Extrinsic AD accounts for approximately 80% of patients and is characterized by early onset and elevated levels of total serum immunoglobulin E (IgE). Sensitization to IgE is fundamental to the pathogenesis of extrinsic AD [2]. Conversely, intrinsic AD is associated with normal total serum IgE levels and the absence of IgE-mediated sensitization [2].

The pathogenesis of AD has been well studied—the acute phase is characterized by a T helper cell type 2 (Th-2) dominant response triggered by the cytokines interleukin (IL)-4, IL-5, and IL-13. This cascade results in increased IgE synthesis, mast cell activation, and eosinophil stimulation [2]. In addition, keratinocytes in the epidermis of patients with AD produce thymic stromal lymphopoietin, a cytokine that promotes the activation of dendritic cells that subsequently produce more cytokines, resulting in amplification of the Th-2 allergenic response [2].

Filaggrin, a structural protein, plays a vital role in protecting the skin barrier. Mutations or deficiencies in filaggrin can lead to the loss of transepidermal water and cause detrimental changes in the pH of the skin. These changes make the skin barrier increasingly vulnerable to environmental allergens and have been shown to be major predisposing factors for AD [3].

Given this, treatment for AD includes the restoration of the factors necessary to maintain the epidermal barrier function. Dissatisfaction with first-line therapies for AD, the desire to avoid steroids, and the extreme cost of effective biologics create a demand for alternative treatment options such as oral vitamins and nutritional supplements. Oral supplements are a growing industry garnering the attention of patients and medical professionals alike. The market for oral supplements is flooded with a wide range of products offering broad availability and convenience supported by a spectrum of customer testimonials. Currently, these supplements are regulated as food rather than drugs under the governance of the Food and Drug Administration.

Objectives

The "food" classification allows these products to become available to customers without proof of meeting the efficacy and safety standards required of pharmaceuticals to enter the market. To ensure that physicians are providing evidence-based advice regarding adjunctive over-the-counter treatment options and that they are able to educate patients when inevitable questions arise regarding supplementation, it is paramount that they understand the utility, safety, and knowledge gaps associated with common dietary supplements. The purpose of this review was to assess the effectiveness of oral nutritional supplements, pre- and probiotics, and vitamin deficiencies and supplements on AD symptomology and clinical course.

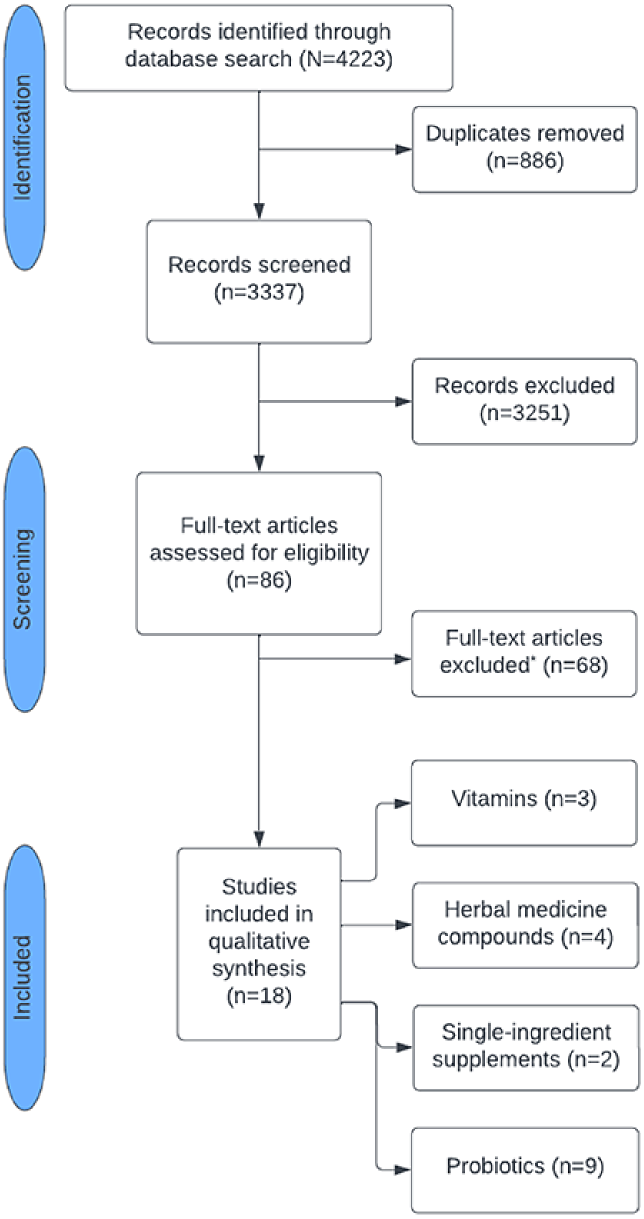
Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was used to conduct this study. Case-control studies, cross-sectional studies, cohort studies, and randomized controlled trials (RCTs) with ≥5 participants conducted on individuals aged >12 years were included. We excluded case reports, case series, review papers, and studies with participants aged <13 years. Eligible interventions included any study evaluating oral vitamins, minerals, or nutritional supplements in relation to AD and any vitamin, mineral, or nutritional supplement intervention for AD. Eligible methodologies to measure changes in AD severity included the Scoring Atopic Dermatitis (SCORAD) index, Eczema Area and Severity Index (EASI), Rajka-Langeland scores, Investigator Global Assessment (IGA) score, Three-Item Severity (TIS) score, Dermatology Life Quality Index (DLQI), subjective AD severity, and AD severity evaluated by a physician.

We searched Scopus, PubMed, and MEDLINE (Ovid interface) for English-language articles published between 1993 and 2023. The final search was conducted on June 22, 2023. The search terms comprised the following: "(Atopic Dermatitis or Atopic Eczema) AND (supplement OR vitamin OR mineral OR micronutrients OR Fish Oil OR Omega Fatty Acid OR Probiotics OR Prebiotics OR apple cider vinegar OR collagen OR herbal OR fiber)."

Literature search results were exported to CADIMA (Julius Kühn-Institut) to remove duplicates and review articles. A total of 3337 unique studies were screened and assessed for eligibility by 2 reviewers working independently. Disagreements were resolved through a third reviewer's decision. After applying the inclusion and exclusion criteria, 18 studies (n=3, 17% evaluating vitamins; n=4, 22% evaluating herbal medicine compounds; n=2, 11% evaluating single-ingredient nutritional supplements; and n=9, 50% evaluating pre- and probiotics) involving 881 patients were selected for inclusion (Figure 1).

Figure 1. Study selection. *All full-text articles were excluded due to lack of inclusion criteria eligibility.



Results

Overview

Table 1 summarizes the included studies' findings and evidence levels according to the ratings of the Oxford Centre for Evidence-Based Medicine [4]. The levels of evidence are defined as level 1 (randomized trials or systematic reviews of randomized trials, cross-sectional studies, inception cohort studies, or nested case-control studies), level 2 (a systematic review of surveys, randomized trials, individual cross-sectional studies with consistent reference standards and blinding, inception cohort studies, or [exceptional] observational studies with dramatic effect), level 3 (cohort studies, local nonrandom sample, nonconsecutive studies, or studies without a consistently applied reference standard), level 4 (case series, case-control studies, or historically controlled studies), and level 5 (mechanism-based reasoning). Level 1 represents evidence generally considered to be stronger, and level 5 represents evidence generally considered to be weaker. The Cochrane Collaboration tool for assessing the risk of bias was used to evaluate each study [5].

Table 1. Included studies (N=18).

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Vitamins/minerals							
Hata et al [6]	Randomized double-blind placebo-controlled trial	Moderate to severe AD[a] determined via a Rajka-Langeland score of 4-9; mild psoriasis determined using the Psoriasis Area and Severity Index; nonatopic participants	76	Participants were randomized to receive either 4000 IU[b] of vitamin D3 or a placebo daily for 21 days; AD assessed using the EASI[c] and Rajka-Langeland score	No correlation between baseline 25(OH)D[d] levels and baseline Rajka-Langeland scores (r=0.04; P=.85); no change in mean EASI score was observed following supplementation; adverse events: none	Confounding variables and small sample size	1
Javanbakht et al [7]	Randomized double-blind placebo-controlled trial	Patients with AD aged 13-45 years diagnosed based on the Hanifin and Rajka criteria	52	Participants were randomly divided into 4 groups receiving the following daily for 60 days: vitamin D3 and E placebos (group P), 1600 IU of vitamin D3 plus a vitamin E placebo (group D), 600 IU of all-racemic α-tocopherol plus a vitamin D3 placebo (group E), and 1600 IU of vitamin D3 plus 600 IU of all-racemic α-tocopherol (group DE); AD assessed using the SCORAD[e] and topical steroid use (recorded in times per day)	Compared with baseline SCORAD score (P=.004): group D—reduction of 34.8%, group E—reduction of 35.7%, group DE—reduction of 64.3%, and group P—reduction of 28.9%; compared with baseline objective symptoms (P=.002): group D—improvement of 38.2%, group E—improvement of 30.1%, group DE—improvement of 64.3%, and group P—improvement of 31.04%; the change in intensity was 25.2%, 36.8%, 23%, and 62% for groups P, D, E, and DE, respectively (P=.001)	Confounding variables (topical steroid use per day was recorded, but the potency of the steroid was not) and small sample size	1
Amestejani et al [8]	Randomized double-blind placebo-controlled trial	Patients with AD aged ≥14 years diagnosed at an outpatient dermatology clinic	60	Participants were randomly divided into 2 groups (1600 IU of vitamin D and a placebo) and treated once daily for 60 days; AD assessed using the SCORAD and TIS[f] administered by the same physician before and after the trial	SCORAD score significantly improved in the vitamin D group for the following metrics: mean patients SCORAD, patients with mild, moderate, and severe AD (P<.05); TIS value significantly improved in the vitamin D group for the following metrics: mild, severe, and total patients TIS value (P<.05); no improvement in SCORAD or TIS scores in the placebo group (P<.05)	Small sample size, confounding variables, and study design (lack of longitudinal design)	1
Herbal medicine compounds							

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Latchman et al [9]	Open case-control trial	Adult patients with moderate to severe recalcitrant AD; controls: age and sex matched with no history of atopy	48	Treatment with Zemaphyte, a standardized formulation of plant materials containing *Ledebouriella seseloides*, *Potentilla chinensis*, *Clematidisarmandii*, *Rehmanniaglutinosa*, *Paeonia lactiflora*, *Lophatherum gracile*, *Dictamnus dasycarpus*, *Tribulus terrestris*, *Glycyrrhizauralensis*, and *Schizonepeta tenuifolia* for 8 weeks; AD assessed using erythema and surface damage scores	Significant improvement in erythema and surface damage scores from baseline in the treatment group (*P*<.001)	Confounding variables and small sample size	4
Sheehan et al [10]	Double-blind placebo-controlled crossover trial follow-up	Patients with recalcitrant AD aged 16-65 years diagnosed via recognized clinical criteria who had previously completed a placebo-controlled trial of Zemaphyte	28	Participants were divided based on their choice into either group 1 (continue with 200 mL of Zemaphyte [daily for 3 months then reduce the frequency of treatments to alternate daily if the clinical assessment of disease activity improved by 70% from the baseline assessment and to every third day if there was a >90% improvement] for 1 year) or group 2 (discontinue Zemaphyte); AD assessed using erythema and surface damage (papulation, vesiculation, scaling, excoriation, and lichenification) with a standardized scoring system	The geometric mean scores for erythema and surface damage of patients were as follows: group 1—149 (95% CI 133-177) and 151 (95% CI 133-177), respectively, for month 0; 6.83 (95% CI 2.15-21.7) and 6.09 (95% CI 2.07-18.1), respectively, for month 2; and 11 (95% CI 5.77-21.1) and 8.92 (95% CI 4.67-17.0), respectively, for month 12; group 2—163 (95% CI 147-181) and 146 (95% CI 123-172), respectively, for month 0; 5.37 (95% CI 1.35-17.3) and 5.4 (95% CI 1.47-19.9), respectively, for month 2; and 53 (95% CI 21.3-132) and 55.3 (95% CI 22.7-135), respectively, for month 12; significant difference in erythema (*P*=.006) and surface damage (*P*=.002) after 12 months between groups 1 and 2; adverse events: transient nausea and abdominal distension, mild laxative effect in more than one-third of patients in group 1, no anomalous hematological or biochemical values (full blood count, serum bilirubin, aspartate aminotransferase, alkaline phosphatase, albumin, urea and electrolytes, creatinine, calcium and phosphate, glucose, and creatinine phosphokinase)	Small sample size, confounding variables, and open nature of the study introducing bias	2

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Alves et al [11]	Controlled crossover intervention study	Adults aged 19-56 years with AD; controls: healthy adults	52	Daily consumption of 100 mL of kefir for 8 weeks; AD assessed using the SCORAD	Significant decrease in SCORAD scores in the intervention group at 8 weeks compared with the control group (*P*<.001); significant decrease in SCORAD scores in the intervention group at 8 weeks compared with week 0 (*P*<.05); adverse effects: none	Absence of a double-blind placebo-controlled design, small sample size, and uncontrolled confounders	2
Mehrbani et al [12]	Randomized double-blind placebo-controlled clinical trial	Adults aged >18 years diagnosed with moderate to severe AD using the Hanifin and Rajka criteria	52	Participants were randomized to receive 30 g of freeze-dried whey powder with 2 g of spray-dried water extract of *Cuscuta campestris* Yuncker (field dodder) or a placebo daily for 15 days, with follow-up at 15 days after treatment ended; AD assessed using self-reported pruritus and sleep disturbances; safety profile: anorexia (54.1%) and GI[g] upset (16.6%) and no abnormalities in liver and kidney function tests, blood cell count, blood pressure, or body weight	15 days: significant improvement in pruritus in the treated group compared with the placebo group (*P*<.001); 15 days: no significant improvement in sleep disturbance in the treated group compared with the placebo group (*P*=.09); 30 days: significant improvement in pruritus in the treated group compared with the placebo group (*P*<.001); 30 days: significant improvement in sleep disturbance in the treated group compared with the placebo group (*P*=.005)	Short study period, small sample size, and confounding factors	1
Single-ingredient supplements							
Kawamura et al [13]	Double-blind placebo-controlled clinical trial	Adults with mild to moderate AD diagnosed according to the criteria of the Japanese Dermatological Association	112	200 mg of GLA[h] (18:3n-6)-enriched oil extracted from the *Mucor circinelloides* fungus for 4 weeks with 4 weeks of follow-up; AD evaluated using VAS[i], range and frequency of pruritus, and observations of skin manifestations graded by a physician (erythema, papules, crusting, nodules, lichenification, area of eruption, or the sum of these items)	Compared with baseline: VAS score significantly improved at week 8 in the intervention group (*P*<.05); compared with baseline: pruritus intensity and frequency of nocturnal itching significantly improved at weeks 4 and 8 in the intervention group (*P*<.05); no significant changes in VAS score, pruritus intensity, or frequency of nocturnal itching were observed in the control group; no significant differences were found between the groups in the judgment of skin manifestations as graded by a physician; no significant differences in topical treatment were observed in either group during the 8 weeks; adverse events: none	Confounding factors and inclusion of only mild to moderate AD	1

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Callaway et al [14]	Randomized controlled single-blind crossover study	Patients aged 25-60 years with AD and a BMI of <30	20	30 mL of cold-pressed hempseed oil daily for 4 weeks followed by a 4-week wash-out period and 4 weeks of olive oil (or vice versa); AD evaluated using patient ratings of atopic symptoms and medication use	Compared with baseline: subjective decreases in skin dryness (*P*=.03) and pruritus (*P*=.02) were statistically significant in the intervention group; compared with baseline: use of medication for AD significantly decreased in the intervention group (*P*=.02); no significant improvement in any metric was observed in the control group; no significant difference was found between the intervention and control groups in any metric; adverse events: none	Small sample size and short study period	1
Probiotic							
Moroi et al [15]	Prospective randomized double-blind placebo-controlled parallel-group comparative study	Adults aged 20-65 years with mild to moderate AD diagnosed according to the criteria of the Japanese Dermatological Association	34	100 mg (2×10^{11} bacteria) of heat-killed *Lacticaseibacillusparacasei* K71 daily for 12 weeks; AD assessed using skin severity scores, VAS and QOL[j] impairment scores (Skindex-16 questionnaire), and topical medication use	Skin severity scores (no significant difference between the groups) decreased significantly from baseline by 18.6% (*P*<.05) at week 8 and 27.1% (*P*<.01) at week 12 in the intervention group, and there was no significant decrease in the placebo group; VAS score (no significant difference between the groups) decreased significantly from baseline by 23% (*P*=.03) at week 4 with no significant improvement at weeks 8 (*P*=.06) or 12 (*P*=.35) in the intervention group, and there was no significant decrease in the placebo group; QOL impairment scores (no significant difference between the groups) decreased significantly from baseline by 28% (*P*<.05) at week 4, by 36.1% at week 8 (*P*<.01), and by 29.3% at week 12 (*P*<.05) in the intervention group and decreased significantly from baseline by 28.3% (*P*<.01) at week 4, by 42.5% at week 8 (*P*<.01), and by 41.9% at week 12 (*P*<.01) in the placebo group; no significant difference between the intervention and control groups in topical medication use; adverse events related to the intervention: none	Small sample size and confounding factors	1

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Prakoeswa et al [16]	Randomized double-blind placebo-controlled trial	Adults aged >14 years with mild to moderate AD according to the Hanifin and Rajka criteria and serum IgE[k] levels of >100 IU/mL	30	2240 g (20^{10} CFU[l]) daily of a probiotic microencapsulation of *Lactiplantibacillus plantarum* IS-10506 for 8 weeks; AD assessed using the SCORAD	SCORAD significantly improved in the intervention group compared with the control group after 8 weeks (*P*=.002)	Small sample size, confounding factors, and short observation period	1
Fang et al [17]	Placebo-controlled trial	Adult patients with AD evaluated by a dermatologist	109	Patients were randomly divided into 4 groups receiving a placebo, 10^9 CFU of *Bifidobacterium bifidum* F35 CCFM16, oligosaccharide, or 10^9 of *L plantarum* CCFM8610 for 8 weeks; AD assessed using the SCORAD and DLQI[m]	After 8 weeks of intervention, patients in the CCFM8610 group had a significantly improved SCORAD score compared with their baseline values (*P*<.05); no significant improvement was noted in the placebo, oligosaccharide, and CCFM16 groups; adverse events: none	Confounding factors	2
Drago et al [18]	Randomized double-blind placebo-controlled trial	Adults aged 18-46 years with moderate to severe AD	38	Twice-daily 1 × 10^9 CFU/g of *Ligilactobacillus salivarius* LS01-DSM 22775 for 16 weeks; AD assessed using the SCORAD and DLQI	SCORAD: significant reduction in the probiotic-treated group (T0: 27.57, SD 3.4 vs T16: 13.14, SD 0.27; *P*<.001) and no significant improvement in the placebo group; DLQI: significant improvement after 8 weeks of intervention (T8), which was maintained 4 weeks after the end of treatment (T20; T0: 8.28, SD 1.79 vs T8: 4.57, SD 1.11 and *P*=.02; T0: 8.28, SD 1.79 vs T16: 4.42, SD 0.27 and *P*=.04; T0: 8.28, SD 1.79 vs T20: 3.71, SD 0.27 and *P*=.02); no significant improvement in the placebo group; adverse events: none	Small sample size and confounding factors	1
Drago et al [19]	Prospective controlled pilot trial	Adult patients with AD aged 25-63 years with predominant rough and fissured skin as well as pruritus for at least 2 months and diagnosed using the Hanifin and Rajka criteria	25	Once-daily freeze-dried mixture of 5 × 10^9 CFU per sachet of *L salivarius* LS01, *Streptococcus thermophilus* ST10 at 2 × 10^9 CFU per sachet, and tara gum (125 mg) for 4 weeks; AD assessed using the SCORAD	SCORAD score significantly improved in the active group from baseline after 4 weeks (*P*<.001); no significant improvement in SCORAD score in the placebo group after 4 weeks; after 1 month of treatment, the SCORAD index in the intervention group was significantly lower than in the placebo group (*P*=.02); adverse events: none	Small sample size, lack of follow-up data after probiotic discontinuation, and confounding factors	2

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Litus et al [20]	Open controlled randomized trial	Adults with AD diagnosed using the European Academy of Dermatology and Venereology recommendations	37	Treatment with fluticasone propionate 0.005% ointment twice daily, emollient twice daily, and a probiotic capsule containing *Lactobacillus acidophilus* and *Bifidobacterium animalis lactis* 2 times daily; participants in this study were divided into groups based on total IgE levels, with the exogenous or IgE-dependent AD group comprising participants with a total IgE level of >100 IU/mL and the endogenous or IgE-independent AD group comprising participants with a total IgE level of <100 IU/mL; patients were then further stratified according to genotypes of the CD14 receptor gene, CC and TT; each subset of participants received either fluticasone propionate 0.005% ointment twice daily and emollient twice daily or fluticasone propionate 0.005% ointment twice daily, emollient twice daily, and a probiotic capsule containing *L acidophilus* and *B animalis lactis* 2 times daily; AD assessed using the SCORAD and DLQI		Small sample size and confounding factors	1

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
					SCORAD in the exogenous AD group: intervention group had a significant improvement from baseline at week 4 (*P*=.001) for the CC genotype and a significant improvement from baseline at week 4 (*P*=.02) for the TT genotype, and there were no significant differences in the control group; SCORAD in the endogenous AD group: intervention group had a significant improvement from baseline at 4 weeks (*P*=.006) for the CC genotype, the control group had a significant improvement from baseline at 4 weeks (*P*=.04) for the CC genotype, and the intervention group had a significant improvement from baseline at 4 weeks (*P*=.01) for the TT genotype; SCORAD score was significantly lower (*P*=.02) in patients with the CC genotype who received standard treatment with probiotics compared with other groups; no other SCORAD intergroup comparisons were significant; DLQI in the exogenous AD group: intervention group had a significant improvement from baseline at week 4 (*P*=.001) for the CC genotype, the control group had a significant improvement from baseline at 4 weeks (*P*=.04) for the CC genotype, and the intervention group had a significant improvement from baseline at week 4 (*P*=.02) for the TT genotype; DLQI in the endogenous AD group: intervention group had a significant improvement from baseline at 4 weeks (*P*=.03) for the CC genotype, the control group had a significant improvement from baseline at 4 weeks (*P*=.03) for the CC genotype, and the intervention group had a significant improvement from baseline at 4 weeks (*P*=.03) for the TT genotype; DLQI was significantly lower (*P*=.01) in patients with the CC genotype who received standard treatment with probiotics compared with other groups; no other		

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
					DLQI intergroup comparisons were significant		
Yamamoto et al [21]	Placebo-controlled double-blind parallel-group comparison study	Patients aged >16 years with mild to moderate AD defined according to the Japanese Dermatological Association criteria	57	20.7 mg once daily of heat-killed *L acidophilus* L-92 for 24 weeks; AD assessed using the IGA[n], EASI, and SCORAD	IGA: significant improvement at 16 (*P*=.03), 20 (*P*=.03), and 24 weeks (*P*<.001) when compared with the placebo; EASI: significant improvement at 8 (*P*=.05) and 24 weeks (*P*=.01) when compared with the placebo; SCORAD: significant improvement at 8 (*P*=.02), 12 (*P*=.01), 16 (*P*=.02), 20 (*P*=.01), and 24 weeks (*P*<.001) when compared with the placebo; adverse events: none	Small sample size and confounding factors	1
Wang et al [22]	Cohort pilot study	Adults aged 18-73 years with mild to severe chronic AD (>3 years)	41	Once-daily probiotic mixture of 2×10^{10} CFU per capsule of *Lacticaseibacillus rhamnosus* GG, *L acidophilus* GKA7, *Lactococcus lactis* GKL2, *Lacticaseibacillus casei* GKC1, *L paracasei* GKS6, *B bifidum* GKB2, and *B animalis lactis* GKK2; 10 mg per capsule of postbiotic heat-killed *Lplantarum*; and 22 mg per capsule of triple prebiotics containing inulin for 2 months; AD assessed using the EASI	EASI was significantly reduced (*P*<.001) after 8 weeks of intervention regardless of baseline disease severity, although the minimal clinically important difference was not reached; more patients with mild AD significantly improved (82.4%) after the intervention compared with patients with severe AD (41.7%; *P*<.001)	Lack of a control or a placebo group, small sample size, and confounding factors (inclusion of numerous probiotic strains)	3

Study	Study design	Participants	Sample size	Intervention	Findings	Limitations	Evidence level [4]
Matsumoto et al [23]	Double-blind placebo-controlled crossover study	Adult patients aged >15 years with moderate AD diagnosed by a clinician	10	100 g of yogurt fermented with 5.2×10^7 CFU/g of *B animalislactis* LKM512 and 4.7×10^8 CFU/g of *Lactobacillus delbrueckiibulgaricus* LKM175 and *S thermophilus* LKM1742 daily; participants received yogurt or placebo for 4 weeks followed by a 4-week wash-out period and 4 weeks of yogurt or placebo; AD assessed using a questionnaire evaluating subjective symptoms	Intervention: 40% of participants experienced improvement in pruritus, and 37.5% of participants experienced improvement in burning; placebo: 10% of participants experienced improvement in pruritus, and 25% of participants experienced improvement in burning	Small sample size and lack of clarity as to whether the results were significant	1

[a]AD: atopic dermatitis.

[b]IU: international unit.

[c]EASI: Eczema Area and Severity Index.

[d]25(OH)D: 25-hydroxyvitamin D.

[e]SCORAD: Scoring Atopic Dermatitis.

[f]TIS: Three-Item Severity.

[g]GI: gastrointestinal.

[h]GLA: gamma-linolenic acid.

[i]VAS: visual analog scale.

[j]QOL: quality of life.

[k]IgE: immunoglobulin E.

[l]CFU: colony-forming unit.

[n]IGA: Investigator Global Assessment.

Vitamins

A total of 17% (3/18) of the studies evaluated either the relationship between levels of serum 25-hydroxyvitamin D (25(OH)D) and AD severity or vitamin D3 and vitamin E as an intervention for AD. Hata et al [6] (N=76) conducted a randomized, placebo-controlled, double-blind trial that examined whether 25(OH)D levels correlated with AD severity; in addition, this study evaluated the effect of 4000 international units (IU) of oral vitamin D3 for 21 days on patients with moderate to severe AD. At the onset of the trial, 25(OH)D levels were found to be similar between patients with AD and control patients, and no correlation was found between baseline 25(OH)D levels and baseline AD severity evaluated using Rajka-Langeland scores [6]. Participants were randomized to receive either a placebo or 4000 IU of vitamin D3, and no difference was found in the mean EASI score between the groups after supplementation [6].

Javanbakht et al [7] (N=52) conducted a separate randomized, placebo-controlled, double-blind trial evaluating the effect of 1600 IU of vitamin D3 for 60 days as an intervention for AD. This study found a significant reduction in baseline SCORAD scores after 60 days in the vitamin D3 group (34.8%; P=.004); however, the difference between the placebo and vitamin D3 groups was not significant [7]. The change in objective symptoms and intensity in the intervention group was found to be 38.2% and 36.8%, respectively, compared with a more modest improvement of only 31.04% and 25.2% in the placebo group (P=.001 and P=.002, respectively) [7]. No association was found between serum 25(OH)D levels and SCORAD score [7].

Another randomized, double-blind, placebo-controlled trial by Amestejani et al [8] (N=60) also evaluated the effects of 1600 IU of oral vitamin D3 daily for 60 days on patients with AD. This study found significant improvements in SCORAD and TIS values in patients with mild and severe AD after 60 days of the intervention. In addition, an improvement in mean SCORAD and total TIS values was found in the intervention group after 60 days compared with baseline (P<.05) [8]. No significant improvement in either metric was found in the placebo group [8].

Javanbakht et al [7] (N=52) conducted a randomized, double-blind, placebo-controlled trial evaluating the effect of 600 IU of all-racemic α-tocopherol (Vitamin E) daily for 60 days on AD severity. Patients receiving vitamin E showed a significant reduction in SCORAD scores compared with baseline (35.7%; P<.001) and a more drastic reduction compared with the placebo group (28.9%). However, objective symptoms and intensity did not significantly improve when compared with the placebo group [7].

This study also evaluated the effects of a combined regimen of 600 IU of vitamin E and 1600 IU of vitamin D3 daily for 60 days [7]. This group showed a significant and marked improvement in SCORAD scores (64.3%; *P*<.005) compared with baseline, with the vitamin D and E groups showing reductions in severity to lesser degrees (34.8% and 35.7%, respectively) [7]. This study did find that topical steroid use as a class decreased in the vitamin D group (66.8%), the vitamin E group (70.2%), and the combined vitamin D and E group (88.7%), with use decreasing in the placebo group by only 37.5% (*P*=.05) [7].

Overall, there is minimal evidence supporting the efficacy of vitamin D or E for the treatment of AD. Any significant difference elicited in these studies was only found in relation to baseline severity, with no study showing a significant intergroup difference between the intervention and placebo groups. Larger trials with higher power are required to determine the true efficacy of combined vitamin D and E supplementation.

Herbal Medicine Compounds

A total of 22% (4/18) of the studies evaluated the effects of herbal medicine compounds on AD symptoms. Mehrbani et al [12] (N=52) conducted a randomized, double-blind, placebo-controlled clinical trial evaluating the efficacy of 30 g of freeze-dried whey powder with 2 g of freeze-dried *Cuscuta campestris* Yuncker (field dodder) extract daily on patients with moderate to severe AD for 15 days. This study found significant improvements in subjective symptoms, specifically pruritus and sleep disturbance, in the treatment group when compared with the control group at 30 days (*P*<.001 in both cases) [12].

The side effects noted by participants in the treatment group included anorexia (54.1%) and mild gastrointestinal discomfort (16.6%) [12]. No other side effects were reported, and no dropouts resulted from these symptoms [12].

A placebo-controlled crossover trial by Alves et al [11] (N=52) evaluated the effect of daily consumption of 100 mL of kefir for 8 weeks in patients with AD. Importantly, these researchers conducted a survey evaluating the eating habits of the study participants and found no significant difference in macronutrients or dietary habits between participants who drank the kefir and their controls, indicating similar baseline dietary characteristics between the control and treatment groups [11]. This study found that, after 8 weeks, the treatment group had a significant decrease in SCORAD scores compared with the control group (*P*<.001) [11]. In addition, paired individual comparisons exhibited significantly lower SCORAD indexes compared with baseline (*P*<.001) [11].

A double-blind, placebo-controlled crossover trial follow-up (the initial study did not fit within our date parameters) by Sheehan et al [10,24] (N=28) evaluated the efficacy of a standardized formulation of plant materials known as Zemaphyte (*Ledebouriella seseloides*, *Potentilla chinensis*, *Clematidis armandii*, *Rehmannia glutinosa*, *Paeonia lactiflora*, *Lophatherum gracile*, *Dictamnus dasycarpus*, *Tribulus terrestris*, *Glycyrrhiza glabra*, and *Schizonepeta tenuifolia*) on patients with recalcitrant AD. Participants were administered 200 mL of Zemaphyte solution once daily for 3 months and then once daily, once every other day, or once every third day depending on disease severity for the next 9 months [24]. This study found significant improvement in erythema and surface damage (*P*=.006 and *P*=.002, respectively) at 12 months in the treatment group when compared with the control group [24]. Of note, the original 2-month study found no significant difference in AD symptom improvement between the treatment and control groups [10]. No abnormalities in biochemical profiles were elicited throughout the 12-month period, but side effects noted by participants in the treatment group included transient nausea and abdominal distension [24].

An open case-control study by Latchman et al [9] (N=48) also evaluated the effects of 8 weeks of Zemaphyte on patients with moderate to severe recalcitrant AD. This study found significant improvement in erythema and surface damage in patients after 8 weeks of the intervention (*P*<.001) [9].

Overall, these studies support the short-term safety and efficacy of supplements such as Zemaphyte and kefir for alleviating subjective AD symptoms, with significant intergroup differences elicited in validated AD metrics. Larger studies are needed to confirm these findings and the impressive results obtained by these small, controlled trials.

Single-Ingredient Supplements

A total of 11% (2/18) of the trials assessed single-ingredient nutritional supplements as an intervention for AD. A double-blind controlled trial conducted by Kawamura et al [13] (N=120) studied the effects of 200 mg of gamma-linolenic acid (GLA; 18:3n-6) supplementation on patients with mild to moderate AD daily for 4 weeks. This study found significant improvement in pruritus and visual analog scale (VAS) scores after 8 weeks compared with baseline in the treatment group; however, no significant differences were found between the treatment and control groups regarding VAS, subjective pruritus intensity, or frequency of itching after 4 weeks [13]. There was also no difference noted in physician-evaluated skin manifestations (erythema, papules, crusting, nodules, lichenification, area of eruption, or the sum of these items) [13]. No adverse effects were experienced by either group [13]. The use of steroids before and after treatment was recorded, and no changes were found in the frequency of use between the intervention and control groups [13].

Callaway et al [14] (N=20) conducted a randomized controlled, single-blind crossover trial evaluating the effects of 30 mL of hempseed oil compared with 30 mL of olive oil for 20 weeks on patients with AD [14]. This study found a decrease in the use of topical medications and an improvement in skin dryness and pruritus in the intervention group compared with baseline measurements (*P*=.02, *P*=.03, and *P*=.02, respectively); however, the difference between the intervention and control groups was not significant [14]. No significant side effects were experienced by any study participant [14].

These studies do little to provide evidence of the efficacy of GLA or hempseed supplementation on AD because of the lack of significant intergroup improvement. There is minimal evidence supporting their use for alleviating AD symptoms in adults.

Probiotics

In total, 50% (9/18) of the studies that met the inclusion criteria evaluated the effects of probiotics on AD symptoms and clinical course. Moroi et al [15] (N=34) conducted a prospective, double-blind RCT investigating the effect of a daily dose of 100 mg (2×10^{11} colony-forming unit [CFU]/g) of heat-killed *Lacticaseibacillus paracasei* K71 daily for 12 weeks. Subjective skin severity scores significantly decreased from baseline in the intervention group at 8 and 12 weeks (*P*<.05 and *P*<.01, respectively), with no significant improvement noted in the placebo group [15]. However, there was no significant difference found between the intervention and placebo groups at the end of the 12 weeks for changes in skin severity score, itch score, or quality of life improvement [15]. This study also found no significant difference in the use of topical medications between the intervention and control groups over the 12-week period [15]. No severe adverse events related to the study diet were experienced [15].

Prakoeswa et al [16] (N=30) conducted a randomized double-blind controlled trial comparing 2240 g (2×10^{10} CFU/g) of *Lactiplantibacillus plantarum* IS-10506 with a placebo daily for 8 weeks. This study found that, after 8 weeks, the intervention group had a significantly lower SCORAD index compared with the control group (*P*=.002) [16].

Fang et al [17] (N=109) also conducted a placebo-controlled trial exploring the efficacy of 1×10^9 CFU of *L plantarum* CCFM8610 or *Bifidobacteriumbifidum* F35 CCFM16 lyophilized powder daily for 8 weeks on patients with AD. This study found that, after 8 weeks, patients taking *L plantarum* had significantly improved SCORAD scores when compared with baseline (*P*<.05) [17]. No improvement in SCORAD scores was found in any other group [17]. No significant difference was found between the groups, and no significant improvement was found in DLQI scores for any group [17]. No adverse events were experienced by any patient in any group.

Another randomized, double-blind, placebo-controlled trial by Drago et al [18] (N=38) looked at the effects of 1×10^9 CFU/g of *Ligilactobacillus salivarius* LS01 on adults with moderate to severe AD daily for 16 weeks. At the end of the treatment period, this study found a significant reduction in SCORAD scores in the probiotic group only (*P*<.001) [18]. It also found significant improvement in the DLQI scores after 8 and 16 weeks of treatment, which persisted for at least 4 weeks after the cessation of treatment (*P*=.002, *P*=.004, and *P*=.002, respectively) [18]. No significant improvement in either metric at any period was found in the placebo group, and no significant adverse events were reported by either group during the 16 weeks [18].

Drago et al [19] (N=25) conducted an additional prospective, controlled pilot trial evaluating the efficacy of a freeze-dried mixture of 5×10^9 CFU per sachet of *L salivarius* LS0, *Streptococcus thermophilus* ST10 at 2×10^9 CFU per sachet, and 125 mg of tara gum on patients with AD for 1 month. At the end of 30 days, patients in the intervention group showed significantly improved SCORAD scores when compared with baseline (*P*<.001) [19]. In addition, at the end of the month, the SCORAD index in the intervention group was significantly lower than in the placebo group (*P*=.02) [19]. No significant adverse events were experienced by any of the participants during this study [19].

Litus et al [20] (N=37) conducted an open, controlled, randomized parallel trial evaluating the efficacy of adding a twice-daily probiotic (*Lactobacillus acidophilus and Bifidobacterium animalislactis)* to standard treatment for AD (fluticasone propionate 0.005% ointment and emollients) for 4 weeks. Participants in this study were divided into groups based on total IgE levels, with exogenous or IgE-dependent AD classified as patients with a total IgE level of >100 IU/mL and endogenous or IgE-independent AD classified as patients with a total IgE level of <100 IU/mL [20]. Patients were further stratified according to genotypes of the CD14 receptor gene (CC and TT) [20].

This study found a significant improvement in SCORAD scores after 28 days in the exogenous AD group for both the CC and TT genotypes in patients who received probiotics in addition to topical therapy (*P*=.001 and *P*=.02, respectively) [20]. No significant difference was found in the topical treatment–only group. In patients with endogenous AD, the study found a significant improvement in SCORAD scores in all groups (those treated with additional probiotics and those not); however, the improvement in SCORAD scores was significantly higher at 28 days in both participants with endogenous and exogenous AD who received probiotics and topical therapy than in the group that received topical therapy alone (*P*=.02 and *P*=.02, respectively) [20].

This study also evaluated the change in DLQI scores and found a significant improvement in both patients with exogenous AD with the CC and TT genotypes who took probiotics in addition to topical treatment for 4 weeks and those who only used topical therapy; however, the study did find a significant difference between these 2 groups (*P*=.01) [20]. It also found a significant improvement in DLQI scores in all groups with endogenous AD (both genotypes and interventions), but no significant difference was found among any of these groups [20].

Another placebo-controlled, double-blinded, parallel-group comparison study by Yamamoto et al [21] (N=57) evaluated the effects of 20.7 mg of heat-killed and dried *L acidophilus* L-92 on AD daily for 24 weeks. No adverse effects were experienced by either the placebo or the intervention group [21]. The IGA, EASI, and SCORAD scores of the intervention group were significantly lower at weeks 8 and 24 than those of the placebo group [21]. More specifically, significant differences between the intervention and placebo groups were found at 8, 16, and 24 weeks for SCORAD scores (*P*=.02, *P*=.01, and *P*<.001, respectively); at 8 and 16 weeks for EASI scores (*P*=.05 and *P*=.09, respectively); and at 16 and 24 weeks for IGA scores (*P*=.03 and *P*<.001, respectively) [21]. The SCORAD was the first measure to improve, suggesting that subjective symptoms related to itching and lack of sleep decreased first with probiotic use.

Wang et al [22] (N=41) conducted a cohort pilot study to evaluate the effect of a probiotic mixture of 2 × 10^{10} CFU per capsule of *Lacticaseibacillus rhamnosus* GG, *L acidophilus* GKA7, *Lactococcus lactis* GKL2, *Lacticaseibacillus casei* GKC1, *L paracasei* GKS6, *B bifidum* GKB2, and *B animalis lactis* GKK2; 10 mg per capsule of postbiotic heat-killed *L plantarum*; and 22 mg per capsule of triple prebiotics with inulin on mild to severe AD for 2 months. This study found a significant improvement in the EASI scores of patients with AD after 8 weeks when compared with baseline, which did not meet the minimal clinically important difference (*P*<.001) [22]. Wang et al [22] did find that more patients with mild AD improved compared with those with severe AD (*P*<.001), possibly because of the relatively easier restoration of dysbiosis in patients with mild AD when compared with the more severely imbalanced gut flora in those with severe AD.

An additional double-blind, placebo-controlled crossover study by Matsumoto et al [23] (N=10) investigated the effect of 100 g of probiotic yogurt containing *B animalislactis* LKM512 (5.2 × 10^7 CFU/g), *Lactobacillus delbrueckiibulgaricus* LKM1759 (4.7 × 10^8 CFU/g), and *S thermophilus* LKM1742 (4.7 × 10^8 CFU/g). This study found improvement in “itch” and “burning” in 40% and 37.5% of patients in the intervention group compared with 10% and 25% in the placebo group, respectively [23].

Overall, there is weak evidence supporting the use of certain strains of probiotics for improving AD symptoms with a minimal side effect profile. *Lactobacillus acidophilus*, *L salivarius*, and *L plantarum* all significantly improved AD symptoms using validated metrics when compared with a placebo. More research is needed to determine adequate dosing, time course, and effective additives such as inulin to maximize these supplements’ benefits.

Discussion

Vitamins

Vitamin D is a fat-soluble vitamin obtained from diet or sun exposure and plays a crucial role in the development of bones, the regulation of calcium, and the immune response against infections [25]. Subclinical vitamin D deficiency is common, affecting >1 billion people worldwide [25]. Vitamin D plays a role in the production of cathelicidin, an antimicrobial peptide that modulates the innate immune system [26]. Cathelicidins assist in protecting the skin against infections, which are a common cause of resistance to topical steroid therapy in AD [7]. The vitamin D receptor is also present in many cell types, including keratinocytes, natural killer cells, and dendritic cells [27]. In addition, UV phototherapy is an effective treatment for severe AD, with evidence supporting phototherapy playing a role in immune suppression and the production of vitamin D [7].

A total of 11% (2/18) of the studies evaluated the association between baseline vitamin D levels and AD severity, though neither study found a correlation between the 2 [6,7]. Of the 18 studies, 3 (17%) RCTs evaluated the efficacy of daily vitamin D on AD symptoms, with the shorter trial finding no change in mean EASI scores with vitamin D supplementation [6]. The other 67% (2/3) of the trials extended the treatment period to 60 days, and both found significant improvements in SCORAD and TIS scores compared with baseline; however, these improvements were not significantly different from those in the placebo group, weakening the evidence for vitamin D as an effective intervention for AD.

The limitations of these studies include the unmeasured differing use and potency of topical steroids and AD therapy between patients. In addition, the small sample sizes make it difficult to derive adequate power to show a significant difference between the treatment and placebo groups. Longitudinal studies with variable doses of vitamin D are necessary to provide evidence of its efficacy and significant intergroup differences.

Vitamin E is a fat-soluble vitamin and an essential nutrient that acts as the primary physiological barrier antioxidant in human skin, with some studies finding an association between dietary antioxidants and atopic disease [28,29]. Higher concentrations of vitamin E intake have also been found to be associated with decreased serum IgE levels and allergen sensitization [30].

Of the 18 studies, only 1 (6%) RCT evaluated vitamin E supplementation in addition to a combined regimen of vitamin D and E (1600 IU and 600 IU, respectively) [7]. Similar to the vitamin D trials, this study found significant improvements in baseline SCORAD scores compared with the placebo group; however, these improvements were not significantly different [7]. Of note, the combined vitamin D and E group did have markedly improved SCORAD scores and objective symptoms at the end of the 60-day trial period when compared with the other intervention and placebo groups, suggesting that dual supplementation could play a role in ameliorating AD severity to a greater degree [7]. This study also found a significant decrease in topical steroid use across the participant groups, with the greatest decrease in use again occurring in the combined vitamin D and E group [7]. The singular nature of this study provides a basis for more research on vitamin supplementation for the adjunctive treatment of AD and suggests that combined supplementation could have a beneficial effect.

Herbal Supplements

Whey is a protein derived from milk and has been suggested to possess antioxidant properties owing to its intracellular conversion of cysteine into glutathione, an intracellular antioxidant [31]. *Cuscuta campestris* Yuncker (field dodder) is a parasitic plant commonly used in traditional medicine for the treatment of epilepsy, psychosis, paralysis, and skin diseases [12]. The *Cuscuta* seed is rich in flavonoids, specifically quercetin, kaempferol, and rutin, which are therapeutic compounds shown to have immunomodulatory and anti-inflammatory effects [32]. Quercetin, in particular, reduces inflammation by inhibiting Th cytokine production and inhibiting mast cell secretion [33,34].

Of the 18 studies, 1 (6%) RCT evaluated the effects of freeze-dried whey powder and extract of *C campestris* Yuncker on AD for 15 days, finding significant improvement in pruritus and sleep disturbances in the intervention group when compared with the control group [12]. This significant improvement also persisted for 15 days after treatment was stopped [12]. The limitations of this study include the small sample size, the presence of numerous confounding factors, and the subjective nature of symptom reporting in contrast to the use of a validated scale. However, these promising results suggest the need for additional longitudinal and larger trials using validated metrics for measuring AD severity to truly determine the efficacy and safety of this supplemental therapy.

Kefir is a fermented food reported to have beneficial effects on the intestinal microbiota and improve the health of the digestive system owing to its probiotic properties [35]. There is evidence suggesting that intestinal dysbiosis can contribute to epithelial permeability because of the release of proinflammatory cytokines and immune dysregulation [36,37]. Kefir consists of a mixture of lactic acid bacteria and yeast that produce numerous bioactive compounds shown to have various beneficial effects, including anti-inflammatory and antimicrobial activity [38-40].

A single crossover study looked at the effects of daily kefir consumption on patients with AD, finding a significant improvement in SCORAD scores compared with both baseline and the control group [11]. These findings are weakened by the lack of a double-blind, placebo-controlled design, with the crossover nature of the study introducing limitations because of the long-term changes in gut microbiota that can occur and persist for longer than the study wash-out period [11]. However, the positive results of this small trial and the lack of side effects over 8 weeks provide an impetus for larger RCTs to evaluate the effectiveness of this intervention.

Of the 18 studies, 2 (11%) separate studies that met the inclusion criteria evaluated the efficacy of Zemaphyte, a standardized formulation of plant materials consisting of *L seseloides, P chinensis, C armandii, R glutinosa, P lactiflora, L gracile, D dasycarpus, T terrestris, G glabra*, and *S tenuifolia* [9,24]. This compound provokes immunologic changes and has been shown to decrease both serum-complexed IgE and serum IL-2 receptors [9]. Decreased complexed IgE prevents the binding of IgE to mast cells, B cells, eosinophils, and monocytes, reducing inflammatory molecules that can exacerbate skin damage [9]. IL-2 receptors are expressed by activated T cells, and their quantity in serum reflects surface expression; thus, this parameter is useful for monitoring T cell activation [9]. Serum-soluble IL-2 receptor levels have been shown to correlate with AD disease activity and improve with treatment using topical steroids [41].

Both studies found significant improvements in erythema and surface damage in the treatment group when compared with baseline [9,24]. The trial with a longer duration (1 year) also found a significant difference in both of these metrics in the intervention group when compared with the placebo group [24]. The results of these studies provide promising evidence regarding the efficacy of Zemaphyte in the treatment of adult AD, with larger RCTs needed to truly assess the effectiveness and safety of this supplement. The limitations of both studies include their open nature, which introduces bias as participants drop out; the small sample sizes; and the presence of a multitude of confounding factors.

Single-Ingredient Supplements

GLA has been shown to be beneficial in improving transepidermal water loss and reversing epidermal hyperproliferation [42,43]. GLA is metabolized from linolenic acid (LA), and both GLA and LA are polyunsaturated essential omega-6 fatty acids with anti-inflammatory and anticarcinogenic effects [44]. GLA specifically reduces inflammatory cytokines such as IL-1β, IL-6, and tumor necrosis factor (TNF)-α [44].

Of the 18 studies, 1 (6%) RCT evaluated the efficacy of GLA on AD severity and found significant improvement in symptoms from baseline in the intervention group, with no significant change in the control group [13]. However, the difference between these 2 groups was not significant, thus restricting the conclusions that can be drawn from this study [13]. Further limitations include the small sample size and the inclusion of patients with only mild to moderate AD, which may make it more difficult to ascertain meaningful symptom improvement in those with less severe symptoms. In addition, the lack of change in the use of topical corticosteroids between the groups also suggests the limited efficacy of GLA as a therapy [13].

Hempseed oil also has high concentrations of the essential fatty acids LA and α-LA in addition to the biologically active metabolites GLA and stearidonic acid [14]. These polyunsaturated fatty acids are present at an omega-6 to omega-3 ratio of 2.1:1, which may have various beneficial effects on human health, including reducing inflammation and reducing the risk of colorectal cancer [45]. It is hypothesized that an imbalance between omega-3 and omega-6 fatty acids contributes to the atopic and inflammatory responses observed in AD [46].

A single crossover study evaluated the effects of daily hempseed oil compared with olive oil on subjective AD symptoms, finding significant improvement in skin dryness and pruritus after 4 weeks of the intervention [14]. However, there was no significant difference between the olive oil and hempseed oil groups [14]. This study was limited by its small sample size, short study period, and lack of controls. The low power of the study and lack of significant intergroup findings make it difficult to accurately assess the efficacy of hempseed oil on AD, and larger, more rigorous studies are needed to assess polyunsaturated fatty acids' true effect on AD.

Probiotics

Probiotics are live microorganisms thought to restore the normal balance of the intestinal gut flora. Probiotics consist of many different bacterial species and strains, most commonly belonging to the *Lactococcus, Saccaromyces*, and *Bifidobacterium* genera [47]. Studies conducted on mice and skin models have shown that probiotics attenuate immune dysregulation through the inhibition of inflammatory cytokines and improved skin hydration [47]. Patients with AD also have abnormal intestinal microflora when compared with healthy patients, with lower concentrations of *Bifidobacterium* and higher concentrations of *Staphylococcus* [48]. Probiotics are thought to be beneficial for patients with AD because of their ability to restore the normal gut microbiome, but whether the atypical flora is the cause or a result of AD remains a controversial topic.

Lacticaseibacillus paracasei K71 decreases IgE synthesis both in vitro and in vivo [15]. A single RCT evaluated the effects of this strain on patients with AD for 12 weeks, finding improved skin severity, VAS, and quality of life impairment scores in the intervention group when compared with baseline but with no significant difference in improvement when compared with the placebo group. The limitations of this study include the small sample size and lack of controls.

Dysregulation of the immune system because of an imbalance of Th-1, Th-2, Th-17, and Foxp3 Treg cells is a key component of the pathological process of AD [16]. There is evidence supporting an increased production of IL-10 and a reduction in IgE, TNF-α, IL-5, and IL-17 in those taking probiotics [49,50]. *Lactiplantibacillus plantarum* IS-10506 improves Th-1 and Th-2 cytokine profiles by stimulating the intestinal microbiota through modulation of toll-like receptors, suggesting the possibility of alleviating AD symptoms [16].

Of the 18 studies, 2 (11%) separate RCTs evaluated the effectiveness of daily *L plantarum* on SCORAD scores for 8 weeks. Both showed that SCORAD scores significantly improved in the treatment group from baseline [16,17]; however, only 1 study found a significant difference in SCORAD scores in the intervention group when compared with the control group [16]. Important limitations include a multitude of confounding factors in both studies in addition to the small sample size and short observation period. However, the results provide promising evidence supporting the short-term efficacy of this intervention. The lack of a significant intergroup difference in both studies weakens the findings but could be the result of an underpowered study size and supports more extensive research into this specific strain.

Of the 18 studies, 2 (11%) separate studies evaluated the efficacy of another *Lactobacillus* strain, *L salivarius*. This strain decreases allergen-induced respiratory hyperresponsiveness and increases interferon-γ levels [51]. One trial evaluated the effectiveness of this strain alone, whereas the other used a dual combination of probiotic strains that included *S thermophilus* [18,19]. Both studies found significant improvement in SCORAD scores from baseline; the latter study also found significant differences in the intervention group compared with the control group [18,19]. The latter study also used a higher dose of *L salivarius* with the additional probiotic strain in combination with tara gum [19]. This combination has been shown to form a gel complex that adheres to the gastric mucosa and enhances intestinal barrier function [19]. A month after the intervention was stopped, the treatment group continued to show significant improvement in SCORAD scores when compared with the controls [19]. These promising results provide an impetus for further study of *L salivarius* and its use with *S thermophilus* and tara gum. However, the limitations of these studies include the lack of data on concurrent topical therapy or other treatments. In addition, the small sample sizes and lack of follow-up data 4 weeks after discontinuation make it difficult to gauge long-term efficacy.

An additional *Lactobacillus* strain, *L acidophilus*, was also tested for efficacy in patients with AD in 11% (2/18) of the studies: one evaluating the strain alone and one adding *B animalis lactis* [20,21]. Patients in the pure *L acidophilus* trial showed significant improvements in IGA, EASI, and SCORAD scores after 24 weeks compared with the placebo group [21]. Participants in the dual probiotic intervention trial were divided into groups based on total IgE levels (exogenous: total IgE level of >100 IU/mL; endogenous: total IgE level of <100 IU/mL) [20]. Patients were then further stratified according to the genotypes of the CD14 receptor gene, CC and TT [20]. The CD14 receptor gene locus on chromosome 5q31.1 contains the genes responsible for the synthesis of IgE [20].

This study found the most significant improvements in SCORAD and DLQI scores compared with the placebo group and the other intervention groups in participants with the exogenous form of AD and the CC genotype [20]. However, improvements in SCORAD and DLQI scores were noted from baseline in the endogenous and TT genotype groups as well, though these did not have significant intergroup differences [20].

A possible explanation for the differences between the endogenous and exogenous groups and patients with the TT and CC genotypes is an increased type-II immune response in patients with exogenous AD and the CC genotype [52]. Genetic polymorphisms and the immune system response to micro-organisms may contribute to the skin inflammation observed in AD, and part of this response is thought to stem from the activation of the CD14/ and TLR4 receptor complex by endotoxins of Gram-negative bacteria [20]. Various polymorphisms, including CC and TT (homozygous cytosine and thymine, respectively), affect the development of atopic disease, with studies showing that the number of positive skin tests, the risk of atopy, and the level of total IgE are increased in individuals with the CC genotype compared with those with the TT genotype [52-54]. Probiotics reduce total IgE, reduce inflammation, and stimulate regulatory T cells, thus inhibiting Th-2 cells and reducing TNF-α levels, mast cell degranulation, and eosinophil proliferation [55]. This is accomplished by probiotic lactic acid bacteria that enhance the Th-1 response and stimulate anti-inflammatory cytokines such as IL-10 and Transforming growth factor beta- [21].

Bifidobacterium is an additional genus of probiotics purported to have various beneficial effects on human health, including influencing the immune system by modulating the adaptive and innate immune responses, limiting pathogen colonization and invasion, and improving gut homeostasis [56]. One placebo-controlled trial looked directly at *Bbifidum*'s effect on SCORAD scores, and there was no improvement with this intervention compared with the baseline or control group [17].

Another 11% (2/18) of trial studies examined the effectiveness of a combination of probiotic strains, including both *Lactobacillus* and *Bifidobacterium* [22,23]. Decreased levels of numerous intestinal bacteria, including *Bifidobacterium*, *Akkermansia*, and *Faecalibacterium*, may be related to early-onset AD [57]. Thus, these studies hoped that repopulating multiple strains, such as *Lactobacillus*, which can directly colonize microflora, and *Bifidobacterium*, which is a normally abundant genus in the human gut, would ameliorate AD symptoms [58]. These growth-promoting effects have the potential to exert anti-inflammatory action owing to the production of short-chain fatty acids such as propionate, acetate, and butyrate by numerous bacterial species [23]. The study evaluating the effects of combination probiotics with the addition of prebiotics found a significant change in EASI scores from baseline, and the trial evaluating combination probiotics alone found improvement in subjective symptoms to a greater degree in the intervention group, but this difference was not significant [22,23].

These trials do little to advance knowledge of these specific interventions because of their extremely small sample sizes and the inclusion of numerous probiotic strains and prebiotics, which confound the effective component of treatment. More research is needed into these combination therapies to determine their overall efficacy and effectiveness compared with single-strain probiotic supplements.

Conclusions

Oral supplements continue to surge in popularity, with patients often turning to these over-the-counter options as medical alternatives for treating and alleviating AD symptoms. These supplements are not regulated by the Food and Drug Administration and, thus, do not have to meet the same safety or efficacy criteria that drugs do before entering the market. Therefore, to provide patients with accurate and up-to-date information, it is fundamental that medical professionals are aware of the current clinical data available regarding oral supplements.

Overall, there is weak evidence supporting any one nutritional supplement intervention for the alleviation of AD symptoms. Multiple trials (4/18, 22%) showed promise for supplements such as Zemaphyte, kefir, and freeze-dried whey with *C campestris* Yuncker extract; however, the small sample sizes and lack of controls in many of these trials make larger, higher-powered RCTs a necessity for determining the true value of these interventions. The most evidence was found on the efficacy of probiotics on the clinical course of AD; numerous studies (9/18, 50%) evaluated a multitude of bacterial probiotic strains, with many showing significant promise in improving AD symptoms. *Lactiplantibacillus plantarum*, *L salivarius*, and *L acidophilus* specifically showed evidence of efficacy and safety across multiple studies (6/18, 33%), but there is weak evidence supporting their use as an adjunctive treatment for AD. There is a need for larger, more extensive RCTs to determine the true effectiveness of these supplements on the broader population.

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Data Availability

This protocol was registered and can be accessed at PROSPERO with the registration number CRD42023470596. The data used for the analysis can be obtained from IW by request.

Conflicts of Interest

RPD is an editor for Cochrane Skin, editor-in-chief of JMIR Dermatology, a dermatology section editor for UpToDate, and a social media editor for the Journal of the American Academy of Dermatology. He is a coordinating editor representative on the Cochrane Council. TES served as an editorial board member-at-large for JMIR Dermatology until July 2023. The author did not participate in the editorial oversight or review process for this paper.

Multimedia Appendix 1
PRISMA Checklist.
[PDF File (Adobe PDF File), 67 KB - derma_v6i1e40857_app1.pdf]

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Abbreviations

25(OH)D: 25-hydroxyvitamin D
AD: atopic dermatitis
CFU: colony-forming unit
DLQI: Dermatology Life Quality Index
EASI: Eczema Area and Severity Index
GLA: gamma-linolenic acid
IGA: Investigator Global Assessment
IgE: immunoglobulin E
IL: interleukin
IU: international unit
LA: linolenic acid
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT: randomized controlled trial
SCORAD: Scoring Atopic Dermatitis
Th: T helper cell
TIS: Three-Item Severity
TNF: tumor necrosis factor
VAS: visual analog scale

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Review

Integrative Approaches to Sleep Management in Skin Disease: Systematic Review

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Abstract

Background: Dermatological conditions, especially when severe, can lead to sleep disturbances that affect a patient's quality of life. However, limited research exists on the efficacy of treatments for improving sleep parameters in skin conditions.

Objective: The objective was to perform a systematic review of the literature on dermatological conditions and the treatments available for improving sleep parameters.

Methods: A literature review was performed using the PubMed, Ovid MEDLINE, Embase, Cochrane, and ClinicalTrials.gov databases from 1945 to 2021. After filtering based on our exclusion criteria, studies were graded using the SORT (Strength of Recommendation Taxonomy) algorithm, and only those receiving a grade of "2" or better were included.

Results: In total, 25 treatment studies (n=11,025) assessing sleep parameters related to dermatological conditions were found. Dupilumab appeared to be the best-supported and most effective treatment for improving sleep in atopic dermatitis (AD) but had frequent adverse effects. Topical treatments for AD were mostly ineffective, but procedural treatments showed some promise. Treatments for other conditions appeared efficacious.

Conclusions: The evaluation of sleep parameter changes in dermatological treatments is predominantly restricted to AD. Systemic interventions such as dupilumab and procedural interventions were the most efficacious. Sleep changes in other dermatoses were limited by a paucity of available studies. The inclusion of a sleep assessment component to a broader range of dermatological treatment studies is warranted.

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KEYWORDS

sleep; dermatology; atopic dermatitis; chronic idiopathic urticaria; quality of life; literature review; parameter; teledermatology; dermatologist; skin; epidermis; review; polysomnography; polysomnographic; sleep medicine

Introduction

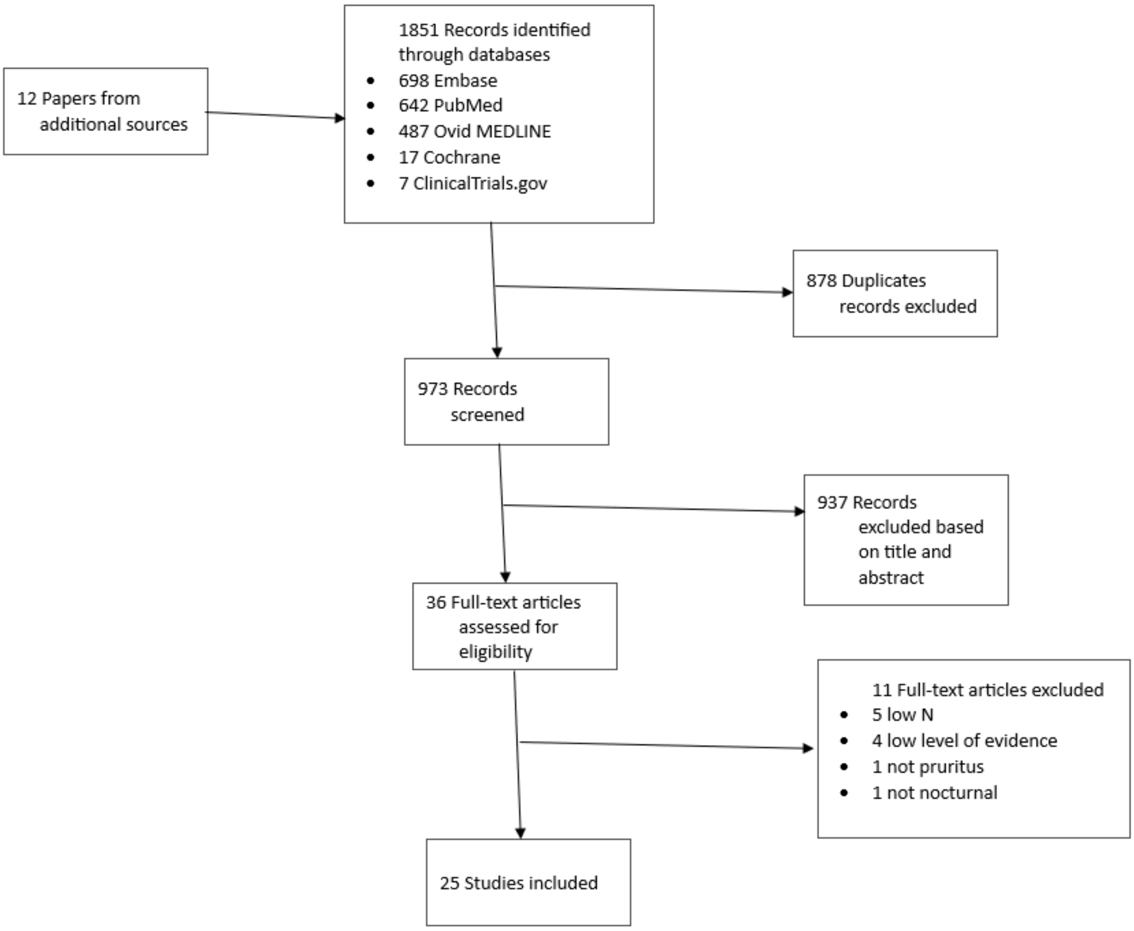
The importance of sleep and the consequences of sleep deprivation on the patient's quality of life have been thoroughly defined, with decreased health-related quality of life survey measures and daytime impairment [1,2]. Dermatological conditions can affect patients' lives in numerous ways, with sleep disturbance as one of the most debilitating effects. Sleep may cause aberrations of skin functions, specifically with thermoregulation and fluid balance maintenance. Disruptions in these regulatory mechanisms may contribute to nocturnal pruritus [3,4].

The impact of these conditions on sleep, whether in terms of quality or duration, however, remains understudied. The efficacy of different dermatological treatments for improving sleep parameters is not always clear to clinicians. In this review, we performed a literature search regarding the effects of different treatments on sleep disturbances across dermatological conditions. After filtering studies according to our exclusion criteria, those relating to atopic dermatitis, pruritus and xerosis, prurigo nodularis, and chronic idiopathic urticaria were found.

Methods

We conducted a literature search using the keywords “sleep disturbance,” “dermatology,” and “management” from the PubMed, Ovid MEDLINE, Embase, Cochrane, and ClinicalTrials.gov databases. We included studies from 1945 to September 2021 in our initial review, yielding 1863 results. After discarding duplicates, 973 unique studies were analyzed by 2 independent reviewers (VG and IM) for relevant information pertaining to treatments for sleep management in dermatological conditions, yielding 25 studies for further analysis (Figure 1 and Multimedia Appendix 1 [5]).

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart.



All disputes were settled by a third independent reviewer (VK). Inclusion criteria included peer-reviewed original articles involving various treatment modalities for sleep management in the form of randomized controlled trials (RCTs) and cohort studies. Only studies that focused solely on dermatological conditions were included. The SORT (Strength of Recommendation Taxonomy) algorithm was used to quantify the level of evidence [6]. Studies that received a level of evidence score worse than a “2” were excluded.

Results

Characteristics of Included Studies

The 26 studies included in this review encompass a total of 11,022 patients. Of these, 21 studies were included for AD, encompassing 4111 patients (n=164, ~4% pediatric patients). A total of 2 studies were included for pruritus and xerosis, including 5965 patients. Only 1 study was included for prurigo nodularis, psoriasis vulgaris, and chronic idiopathic pruritus, analyzing 27 patients, 394 patients, and 525 patients, respectively. Collectively, the studies spanned a period from 1979 to 2021.

Treatment for Atopic Dermatitis

Overview

A wide array of studies has evaluated the efficacy of treatments for AD and concomitant sleep disturbances. These can broadly be arranged into 3 groups, according to whether the treatment modality was systemic, topical, or procedural. Each of the study details, with respective treatment adverse effects, is further delineated in Tables 1 and 2. Sources of funding for each study are provided in Table 3.

Table 1. Treatments for sleep management in skin disease.

Study	Disease	Intervention	Level of evidence	Study design	Sample size, N	Dosage	Sleep scale	Outcomes
Fargnoli et al [7] (2019)	AD[a]	Dupilumab	2	Retrospective cohort	109	• Single subcutaneous injection of 600 mg, then 300 mg Q2W[b]	• Sleep-NRS[c]	• Reduction from 6.9 (SD 2.5) to 3.3 (SD 2.4) at 4 wk and to 1.9 (SD 2.2) at 16 wk (*P*<.001 for both)
Cork et al [8] (2019)	AD	Dupilumab	1	Pooled data from RCTs[d]	1379	• Subcutaneous injection of 300 mg QW[e] • Subcutaneous injections of 300 mg Q2W	• SCORAD[f] • POEM[g]	• Reduction by 3.4 (QW) and 3.3 (Q2W) vs 0.82 (placebo) (*P*<.001) • More patients in the text group reported the absence of sleep disturbance: 51.2% (n=234, Q2W), 43.5% (n=199, QW), 17.6%, (placebo, n=81; *P*<.001)
Tsianakas et al [9] (2017)	AD	Dupilumab	1	RCT	64	• 300 mg QW subcutaneous dupilumab or placebo for 12 wk	• SCORAD VAS[h] scores for pruritus and sleep loss	• Decrease in mean % change from baseline when compared to placebo of −65.6 (17.78, 95% CI 101.27-30.01; *P*<.001)
Tofte et al [10] (2018)	AD	Dupilumab	1	Pooled data from RCTs	233	• 300 mg QW and 300 mg Q2W vs placebo	• SCORAD VAS for sleep loss	• Decrease in SCORAD VAS sleep loss score at wk 12: QW: 75.4% (5.13, n=118) vs 19.7%, (6.17, n=115) for placebo (*P*=.0001); Q2W: 51.9% (10.79, n=64) vs 3.8%, (11.55, n=61) for placebo (*P*=.001)
Paller [11] (ongoing clinical trial)	AD	Dupilumab	2	Open label	40 (pediatric)	• Weight-based dosage for 12 wk	• PROMIS[i] • Wake after sleep onset	• None posted
Chang et al [12] (2016)	AD	Melatonin	1	RCT	73 (pediatric)	• 3 mg QD[j] for 4 wk	• SCORAD • Actigraphy • Subjective description	• Reduction by 9.1 (95% CI –13.7 to –4.6; *P*<.001) • Reduction of the sleep-onset latency by 21.4 min compared with placebo[k] (95% CI –38.6 to –4.2; *P*=.02) • No significant difference in subjective measures
Harper et al [13] (2000)	AD	Cyclosporine	2	Prospective, parallel, open label	40 (pediatric)	• Maximum 5 mg/kg QD	• SASSAD[l] score and area of involvement (rule of 9s)	• Significant improvement was seen in all treatment groups. (no *P* values given)

Study	Disease	Intervention	Level of evidence	Study design	Sample size, N	Dosage	Sleep scale	Outcomes
Silverberg et al [14] (2021)	AD	Abrocitinib	1	Pooled data from RCTs	942	• Oral 200 mg, 100-mg monotherapy, or placebo QD for 12 wk	• NTIS[m]	• ≥4-point improvement in NTIS; 57% (n=207), 42.7% (n=158), and 12.7% (n=27); no *P* values given • Difference in proportion of patients who achieved NTIS response at wk 12 vs placebo • 200 mg: 44.6% (n=162; *P*<.001) • 100 mg: 29.8% (n=110; *P*<.001)
Lio et al [15] (2021)	AD	Baricitinib	1	Prospective analysis from RCT data	440	• 1 mg or 2 mg QD for 16 wk	• ADSS[n]	• For patients with BSA[o] involvement of 10%-50%, a decrease of at least 1.5 points in number of nighttime awakenings caused by itch was observed for 2 mg (*P*=.001) but not 1 mg (*P*=.15) vs placebo • For patients with baseline ADSS Item 2 score ≥1.5, a decrease of at least 1.5 points in number of nighttime awakenings caused by itch was observed for 1 mg (*P*=.04) and 2 mg (*P*<.001) vs placebo
Kawana et al [16] (2010)	AD	Tandospirone citrate	1	RCT	37	• 30 mg QD for 4 wk	• SCORAD index and VAS for insomnia	• There was a significant decrease in the SCORAD Index after 4 wk for the TC[p] group (before treatment 49.6, after treatment 36.4, change –13.2; *P*<.001), but not in the untreated group (before treatment 44.5, after treatment 37.9, change –6.7 • No significant difference in SCORAD or VAS insomnia scores between groups
Munday et al [17] (2002)	AD	Chlorpheniramine	1	RCT	151	• 2.5 mL (1-5 y) or 5 mL (6-12 y) QDpm[q]	• The severity of daytime drowsiness, number of episodes of sleeplessness due to scratching	• No significant difference when compared to placebo
Ebata et al [18] (1997)	AD	Nitrazepam	2	RCT crossover	10	• 5 mg QD for 2 nights, then 5 mg BID[r] for 1 night, followed by a 4-d washout period	• TST[s] divided by total recording time (TST%)	• Decrease in frequency of scratching bouts but increase in mean duration. Thus, no significant difference in TST%
	AD		2	RCT	12			

Study	Disease	Intervention	Level of evidence	Study design	Sample size, N	Dosage	Sleep scale	Outcomes
Savin et al [19] (1979)		Trimeprazine and trimipramine				• 20 mg trimeprazine tartrate, 50 mg trimipramine maleate, or placebo, taken 1 h before sleeping for 3 nights	• EEG[t] recordings: 20-s periods in terms of wakefulness and the usual stages of sleep (1, 2, and 3 or 4)	• No significant differences were found among the 3 treatments for total time asleep, time spent before falling asleep, or in total wakefulness after first falling asleep. There was a tendency toward longer sleep duration and shorter sleep latency with both drugs
Parikh-Das et al [20] (2017)	AD	Colloidal oatmeal cream	1	RCT	23 (pediatric)	• Applied topically for 14 d "per the label instructions"	• Clinical and instrumental assessments of sleep parameters	• Improvement in sleep parameters, specifically the duration of continuous sleep and number of wakings at night (no *P* values given)
Ständer et al [21] (2016)	AD	Sertaconazole 2% cream	1	RCT	70	• 2% cream BID for 4 wk, followed by a 2-wk washout period	• SCORAD	• No significant difference was observed between experimental and test groups (*P* values not given)
Kubota et al [22] (2009)	AD	Corticosteroids and tacrolimus (both topical)	2	Open label, uncontrolled	28 (pediatric)	• Phase 1: 0.03% tacrolimus ointment QDam[u] and weak or strong potency corticosteroid ointment QDpm for 2 wk • Phase 2: 0.03% tacrolimus ointment BID on weekdays with concurrent corticosteroids on weekends for 2 wk • Phase 3: 0.03% tacrolimus ointment BID for 2 wk • Phase 4: emollient QD with 0.03% tacrolimus as necessary for 6 weeks	• 4-point sleep disturbance scale	• Decrease from baseline of 1 to 0.03 and 0.04 at 6 and 12 wk, respectively (*P*<.001)
Doss et al [23] (2009)	AD	Tacrolimus 0.03% ointment	1	RCT	240	• Tacrolimus 0.03% ointment BID until clearance, maximum 3 wk, then if lesions still present, QD for another 3 wk	• Sleep quality (1-100 mm VAS)	• Quality of sleep improved in both tacrolimus and flutacisone treatment groups, with no significant between-group difference (n=236, –91.5% vs n=237, –92.6%)
Leo et al [24] (2004)	AD	Pimecrolimus cream 1%	2	RCT	19	• Pimecrolimus cream 1% and control cream applied BID for 2 wk	• Actigraph motion logger was used to assess periods of sleep and wakefulness	• Sleep parameters generated from the actigraphy were not significantly different between the 2 groups
	AD		2		42		• AIS[v]	

Study	Disease	Intervention	Level of evidence	Study design	Sample size, N	Dosage	Sleep scale	Outcomes
Jaworek et al [25] (2020)		UV-B/cyclosporine		Open label, uncontrolled		• UV-B: 0.22-0.26 J/cm2 to start, increased until erythema appeared. 3×/wk over 12 wk • Cyclosporine: 3.5 mg/kg/d given over 2 doses, then increased after 2 wk. Treatment over 12 wk		• UV-B: reduction from 13.5 (SD 2.4) to 4 (SD 1.1) (*P*<.001) • Cyclosporine: reduction from 13.9 (SD 1.8) to 5.9 (SD 0.9; (*P*<.001)
Pustišek et al [26] (2016)	AD	Short-term structured educational program	1	RCT	134	• Structured education about AD via a 2-h lecture by a physician specialist and written material	• SCORAD and PO[w] SCORAD index, changes in symptom scores for pruritus and sleep disturbance	• Treatment group had significantly lower SCORAD (*P*<.001), PO SCORAD (*P*<.001) index, and sleep disturbance (*P*=.001) at the second visit (2 mo)
Bae et al [27] (2012)	AD	PMR[x]	2	RCT	25	• PMR therapy BID for 4 wk	• VAS was used for the subjective assessment of LOS[y]	• Degree loss of sleep was significantly decreased in the PMR group (*P*=.007)
Deleuran et al [28] (2020)	Pruritus and xerosis	ADE-G1[z] emollient	2	Open label	5910	• BID for 7 d	• SCORAD	• Reduction from 3.3 (SD 2.9) to 1.3 (SD 1.8) after 7 d (*P*<.001)
Rossi et al [29] (2016)	Pruritus and xerosis	Polidocanol (2%) and prucidine-4 (0.5%) lotion	2	Open label	55	• At least BID for 28 d	• Insomnia score (0-10)	• Reduction from 2.2 to 0 after 28 d (*P*<.001)
Chiricozzi et al [30] (2020)	Prurigo nodularis	Dupilumab	2	Retrospective cohort	27	• Single subcutaneous injection of 600 mg, then 300 mg Q2W	• Sleep-NRS	• Reduction from 8.2 to 1.7 after 16 wk (*P*<.001)
Kontochristopoulos et al [31] (2016)	Psoriasis vulgaris	Calcipotriol-betamethasone dipropionate gel	2	Prospective open-label study	394	• Calcipotriol-betamethasone dipropionate gel QD	• Subjective Surveys about sleep (1-10 rating)	• Significantly lower mean scores for pruritus and sleep disorders (*P*<.001)
Zuberbier et al [32] (2009)	Chronic idiopathic pruritus	Bilastine or levocetirizine	1	RCT	525	• Bilastine: 20 mg QD for 28 d • Levocetirizine: 5 mg QD for 28 d	• 5-point sleep disturbance scale	• A greater percentage of patients at 14 and 28 d treated with bilastine (n=89, 54.6% and n=106, 62.7%) and levocetirizine (n=103, 66.9%, and n=115, 72.3%) reported no sleep disturbance compared to placebo (n=55, 33.4% and n=76, 42.7%; *P*<.001)

[a]AD: atopic dermatitis.

[b]Q2W: once every 2 weeks.

[c]NRS: numerical rating scale.

[d]RCT: randomized controlled trial.
[e]QW: once weekly.
[f]SCORAD: Scoring Atopic Dermatitis.
[g]POEM: Patient-Oriented Eczema Measure.
[h]VAS: visual analog scale.
[i]PROMIS: Patient Reported Outcome Measurement Information System.
[j]QD: once a day.
[k]Using a linear mixed-effects model after controlling for age and sex.
[l]SASSAD: 6 area, six sign atopic dermatitis.
[m]NTIS: Night Time Itch Scale.
[n]ADSS: Atopic Dermatitis Sleep Scale.
[o]BSA: body surface area.
[p]TC: tandospirone citrate.
[q]QDpm: once a day in the evening.
[r]BID: twice a day.
[s]TST: total scratching time.
[t]EEG: electroencephalogram.
[u]QDam: once a day in the morning.
[v]AIS: Athens Insomnia Scale.
[w]PO: patient oriented.
[x]PMR: progressive muscle relaxation.
[y]LOS: loss of sleep.
[z]ADE-G1: *Aquaphilus dolomiae* extract.

Table 2. Adverse effects of treatment.

Disease and therapy	Recommended dosage or treatment schedule	Adverse effects	References
AD[a]			
Dupilumab	• 300 mg subcutaneous injection Q2W[b] for 12 wk	Exacerbation of AD symptoms, nasopharyngitis, headache, conjunctivitis, and fatigue	[7-11]
Melatonin	• 3 mg QD[c] for 4 wk	None	[12]
Cyclosporine	• Maximum 5 mg/kg QD	Rhinitis, infected eczema, bronchospasm, upper respiratory tract infection, and headache	[13]
Tandospirone citrate	• 30 mg QD for 4 wk	Not mentioned	[16]
Abrocitinib	• 200 mg or 100 mg QD for 12 wk	Not mentioned	[14]
Baricitinib	• 1 mg or 2 mg QD for 16 wk	Not mentioned	[15]
Chlorpheniramine	• 2.5 mL or 5.0 mL QDpm[d] depending on age	Mentioned but not described	[17]
Nitrazepam	• 5 mg QD for 2 nights, then 5 mg BID[e] for 1 night, followed by a 4-d washout period	Not mentioned	[18]
Trimeprazine	• 20 mg taken 1 h before sleeping for 3 nights	Not mentioned	[19]
Trimipramine	• 50 mg taken 1 h before sleeping for 3 nights	Not mentioned	[19]
Sertaconazole 2% cream	• 2% cream BID for 4 wk, followed by a 2-wk washout period	Exacerbation of AD	[33]
Tacrolimus 0.03% or corticosteroids	• 0.03% tacrolimus ointment QDam[f] and topical corticosteroid QDpm for 2 wk • Then, 0.03% tacrolimus ointment BID, with addition of topical corticosteroid BID on weekends, for 2 wk • Then, topical emollient QD and 0.03% tacrolimus PRN[g]	Folliculitis	[21]
Tacrolimus 0.03%	• 0.03% cream BID until clearance for a maximum of 3 wk • Then, if lesions are still present, apply QD for another 3 wk	Burning sensation, pruritus, bronchitis, rhinitis	[22]
Pimecrolimus 1%	• 1% cream BID for 2 wk	Not mentioned	[24]
Colloidal oatmeal cream	• Apply topically for 2 wk	Not mentioned	[20]
UV-B	• 0.22-0.26 J/cm2 to start, increased until erythema appeared, 3× per wk for 12 wk	None	[25]
PMR[h] therapy	• PMR therapy BID for 4 wk	Not mentioned	[27]
Structured education program	• Single 2-h lecture and written materials	Not mentioned	[26]
Pruritus and xerosis			
ADE-GI[i] emollient	• BID for 7 d	Skin irritation, itch, and burning sensation	[28]
Polidocanol (2%) and prucidine-4 (0.5%) lotion	• At least BID for 28 d	Not mentioned	[29]
Chronic idiopathic urticarial			
Bilastine	• 20 mg QD for 28 d	Headache and somnolence	[32]

Disease and therapy	Recommended dosage or treatment schedule	Adverse effects	References
Levocetirizine	• 5 mg QD for 28 d	Headache and somnolence	[32]
Prurigo nodularis			
Dupilumab	• Single subcutaneous injection of 600 mg, then 300 mg Q2W	Conjunctivitis	[30]

[a]AD: atopic dermatitis.
[b]Q2W: once every 2 weeks.
[c]QD: once a day.
[d]QDpm: once a day in the evening.
[e]BID: twice a day.
[f]QDam: once a day in the morning.
[g]PRN: as needed.
[h]PMR: progressive muscle relaxation.
[i]ADE-GI: *Aquaphilus dolomiae* extract.

Table 3. Funding sources.

Study	Disease	Funding sources
Fargnoli et al [7] (2019)	AD[a]	None
Cork et al [8] (2019)	AD	Sanofi/Regeneron
Tsianakas et al [9] (2017)	AD	Sanofi/Regeneron
Tofte et al [10] (2018)	AD	Sanofi/Regeneron
Paller [11] (ongoing clinical trial)	AD	Not mentioned
Chang et al [12] (2016)	AD	National Taiwan University Hospital and the Yonghe Cardinal Tien Hospital
Harper et al [13] (2000)	AD	Novartis Pharmaceuticals
Silverberg et al [14] (2021)	AD	Pfizer
Lio et al [15] (2021)	AD	Eli Lilly and Company
Kawana et al [16] (2010)	AD	Not mentioned
Munday et al [17] (2002)	AD	Not mentioned
Ebata et al [18] (1997)	AD	Not mentioned
Savin et al [19] (1979)	AD	May and Baker Ltd
Parikh-Das et al [20] (2017)	AD	Johnson & Johnson
Ständer et al [21] (2016)	AD	Not mentioned
Kubota et al [22] (2009)	AD	None
Doss et al [23] (2009)	AD	Astellas Pharma Europe Limited
Leo et al [24] (2004)	AD	Not mentioned
Jaworek et al [25] (2020)	AD	Not mentioned
Pustišek et al [26] (2016)	AD	None
Bae et al [27] (2012)	AD	Korea Health 21 R&D Project
Deleuran et al [28] (2020)	Pruritus and xerosis	Pierre Fabre Dermo-Cosmetique
Rossi et al [29] (2016)	Pruritus and xerosis	Not mentioned
Chiricozzi et al [30] (2020)	Prurigo nodularis	None
Kontochristopoulos et al [31] (2016)	Psoriasis vulgaris	Leo Greece
Zuberbier et al [32] (2009)	Chronic idiopathic pruritus	Not mentioned

[a]AD: atopic dermatitis.

Systemic

Dupilumab, a monoclonal antibody that exerts its effect by blocking interleukin (IL)-4 and IL-13 signaling, is a frequently studied treatment of AD. Using pooled data from 2 RCTs comprising a total of 1379 patients, 1 study using dupilumab found improvements in 2 sleep measures, Scoring Atopic Dermatitis (SCORAD) and Patient-Oriented Eczema Measure (POEM), in 2 treatment groups compared with a control. SCORAD and POEM are clinical tools used to define the eczema severity and monitor its progression [34]. The 2 cohorts either received a once weekly or once every 2 weeks injection of 300 mg dupilumab. Mean decreases in SCORAD were 3.4 (SE 0.14) and 3.3 (SE 0.14) for the weekly and biweekly treatments, respectively. Both significantly outperformed the placebo group (*P*<.001). In the POEM measure, more patients reported an absence of sleep disturbance in the weekly (n=199, 43.5%) and biweekly (n=234, 51.2%) groups compared with the placebo group (n=81, 17.6%; *P*<.001) [8].

Another study found significant improvement in visual analog scale (VAS) sleep loss scores for patients with AD undergoing dupilumab treatment. In the 2 pooled RCTs, 300 mg injections were given subcutaneously either weekly or every other week. At week 12, the mean decrease in VAS sleep loss scores for weekly injections was 75% (SD 5.13%) and for biweekly was 52% (SD 10.79%) when compared to the 19.7% (SD 6.17%) and 3.8% (SD 11.55%) reductions for each respective placebo group (*P*=.001) [10]. Similarly, another study that investigated 300 mg dupilumab implemented SCORAD VAS scores to assess sleep loss. A mean percentage decrease of 66% (SD 17.78%) was observed in the dupilumab group when compared to the placebo group [9]. In a retrospective cohort study, 109 patients received an initial injection of 600 mg dupilumab followed by another 300 mg every other week. A reduction in the Sleep numerical rating scale was seen in the treatment group at 4 weeks (7 to 3) and at 16 weeks (3 to 2; *P*<.001) [7].

A single ongoing, phase 4 clinical trial using dupilumab for patients with pediatric AD was also found. An estimated 40 participants will be recruited, and a once-weekly subcutaneous injection, based on body weight, will be administered for a total of 12 weeks. Primary sleep outcome measurements include the PROMIS (Patient Reported Outcome Measurement Information System) parent-proxy score, the PROMIS patient score, and a polysomnography-based wake after sleep onset [11].

Melatonin supplementation, given its suppressive effects of autotaxin, has also been attempted as a treatment for sleep disturbance in children with AD [35]. In a double-blinded RCT of 73 children and adolescents, 3 mg of melatonin daily was compared to a placebo. Sleep measures included SCORAD, actigraphy, and subjective assessment. Compared with placebo, melatonin reduced the SCORAD measure by 9.1 (*P*<.001) and reduced sleep-onset latency by 21.4 minutes (*P*=.02) [12].

Cyclosporine therapy, given it reduces epidural nerve density, is another potential treatment option for childhood AD [36]. One prospective randomized, parallel study compared short course versus continuous treatment schedules. A total of 40 pediatric patients either underwent multiple 12-week courses or a continued 1-year course of 5 mg/kg/day cyclosporine. Improvement in sleep disturbance was observed in all treatment groups, although no values or *P* values were given. A tolerability of 80% was observed at week 12 and at the end of the study [13].

Tandospirone citrate, a 5-HT1A receptor agonist, has been used to reduce stress-related symptoms of AD. One RCT of 37 patients assessed the efficacy of tandospirone citrate at a dosage of 10 mg 3 times daily for 4 weeks. Both SCORAD and an insomnia VAS were used to measure changes in sleep. A significant decrease was observed in SCORAD for the treatment group after 4 weeks (*P*<.001), which was not observed with the control group. However, no significant difference was observed between the groups in either SCORAD or the insomnia VAS [16].

Abrocitinib, a JAK1 inhibitor, was assessed in 1 study using pooled data from 3 RCTs, with a total of 942 patients [37]. Patients received 200 mg, 100 mg, or placebo once daily for 12 weeks, with sleep outcomes measured using the Night Time Itch Scale (NTIS). The percentage of patients reporting a change in NTIS score of >4 was 57% (n=207), 42.7% (n=158), and 12.7% (n=27) for 200 mg, 100 mg, and placebo, respectively. Moreover, the percentage of patients who reported a response in NTIS score after 12 weeks, when compared to placebo, was 44.6% for 200 mg (n=162; *P*<.001) and 29.8% for 100 mg (n=110; *P*<.001) [14].

Baricitinib, another JAK inhibitor, was studied in post hoc analysis of data from a phase 3, multicenter, double-blinded RCT of 440 patients, which compared once-daily dosages of 1 mg and 2 mg baricitinib to placebo after 16 weeks. In patients with a baseline body surface area involvement of 10% to 50%, a decrease of at least 1.5 points in the number of nighttime awakenings caused by itch was observed for 2 mg (*P*=.001) but not 1 mg (*P*=.15) groups versus placebo. For patients with a baseline Atopic Dermatitis Sleep Scale score ≥1.5, a decrease of at least 1.5 points in the number of nighttime awakenings caused by itch was observed for both 1 mg (*P*=.04) and 2 mg (*P*<.001) versus placebo. Adverse effects were not mentioned [15].

Chlorpheniramine, an antihistamine, was assessed in 1 RCT of 151 patients with AD, with no significant difference being observed in AD symptoms when compared to placebo. Dosages included 2.5 mL versus 5 mL, given once at night. There was also no difference in the severity of daytime drowsiness and the number of episodes of sleeplessness [17].

Ebata et al [18] investigated nitrazepam, a benzodiazepine believed to reduce itch by sedation, and found no significant effects on nocturnal scratching behavior. Ten patients either took 5 mg nitrazepam once nightly for 2 consecutive days or 10 mg for 1 night, followed by a 4-day washout period. A decrease in frequency in nocturnal scratching bouts was observed at the 10 mg dosage; however, this coincided with an increase in mean scratching duration. Hence, no significant difference was observed in TST% when compared to placebo [18].

Trimeprazine, an antihistamine and sedative, and trimipramine, a tricyclic antidepressant, were tested against a placebo in 1 double-blinded randomized trial of 12 patients with severe AD. Patients underwent a 3-day treatment course of either 20 mg trimeprazine tartrate, 50 mg trimipramine maleate, or placebo once at night. Electroencephalogram recordings were used to measure wakefulness and stages of sleep. No significant differences were found in total time asleep, sleep latency, or wakefulness once asleep [19].

Topical

Sertaconazole, an antifungal that inhibits ergosterol synthesis, was studied in 1 double-blind RCT with 70 subjects [33]. Topical 2% sertaconazole cream was applied twice daily for 4 weeks. The SCORAD measure was used to assess changes in sleep. No significant differences were observed between sertaconazole and the vehicle control [21].

Given AD has been hypothesized to arise from immune dysregulation, studies have also examined tacrolimus, a calcineurin inhibitor that inhibits T-cell proliferation [38]. In 1 study, 28 patients were treated with sequential application of topical tacrolimus and corticosteroids in a 4-phase treatment process. In phase 1, patients applied 0.03% tacrolimus ointment every morning and a corticosteroid ointment every night for 2 weeks. In phase 2, the same concentration of tacrolimus ointment was applied twice daily for 2 weeks, with the addition of the corticosteroid ointment on weekends. Phase 3 eliminated the corticosteroid treatment while continuing tacrolimus twice daily for 2 weeks. The fourth and final phase involved the application of an emollient once daily, with tacrolimus application as needed for a total of 6 weeks. A 4-point sleep disturbance scale was used to assess changes in sleep disturbance. A decrease was observed from a baseline of 1.0 to 0.03 and 0.04 at 6 and 12 weeks, respectively (P<.001) [22].

Topical tacrolimus has also been compared to topical fluticasone, a corticosteroid agent and T-cell proliferation inhibitor [39]. Tacrolimus or fluticasone was applied twice daily until the clearance of lesions. If lesions persisted by week 3, the application was continued once daily for an additional 3 weeks. Sleep quality, measured with VAS, improved in both groups but with no significant difference [23].

Another immunomodulatory agent, which inhibits calcineurin, pimecrolimus, has also been tested for AD treatment [40]. In 1 RCT of 19 pediatric patients experiencing AD, pimecrolimus cream was not shown to be effective in improving sleep parameters, specifically sleep duration and wakefulness. Moreover, no difference was observed in sleep parameters between the treatment and control groups [24].

Colloidal oatmeal, an anti-inflammatory and antihistaminergic agent via avenanthramide, is another potential treatment option for AD [41]. In 1 study, 23 infants and toddlers with AD received colloidal oatmeal lotion for 14 days. Sleep quality was assessed “clinically and instrumentally,” with improvement noted in continuous sleep duration and number of wakings. The degree and timing of these improvements were not specified [20].

Procedural

UV phototherapy is a common treatment for dermatoses by stimulating prostaglandins and cytokine synthesis [42]. One study compared the efficacy of UV-B and cyclosporine on sleep disturbance secondary to AD, by implementing the Athens Insomnia Scale. UV-B dosage began at 0.22-0.26 J/cm^2 and was increased every second session until erythema appeared. Doses were given 3 times a week, with a maximum dose of 0.56 J/cm^2. The baseline cyclosporine dosage was 3.5 mg/kg/d, divided in 2 doses, and increased after 2 weeks, with a maximum dose of 5 mg/kg/d. Patients either received UV-B or cyclosporine for a period of 12 weeks. Itch reduction was achieved in both treatment groups, with more significant itch reduction in the UV-B cohort (P<.001). Moreover, UV-B treatment resulted in a reduction from 13.5 to 4 in mean Athens Insomnia Scale scores (P<.001). Cyclosporine, likewise, led to a mean reduction of 13.9 (SD 1.8) to 5.9 (SD 0.9; P<.001) [25].

Progressive muscle relaxation (PMR) therapy is a form of psychological therapy primarily used for stress management [43]. In 1 RCT, 25 patients were randomly assigned to either receive 1 month of PMR therapy in addition to conventional treatment or only undergo 1 month of conventional treatment. A significant decrease in sleep loss horizontal VAS scores was observed in the PMR group but not the control group (P=.007) [27].

Structured parental intervention, which consisted of a 2-hour physician lecture, was evaluated for improving sleep in 1 study of 134 children with AD. Sleep parameters were measured using SCORAD, patient-oriented (PO) SCORAD index, and sleeplessness and evaluated at the second visit (2 mo after initial evaluation). By the second visit, the mean SCORAD scores for the intervention group were 23.08 (SD 15.188) versus 36.44 (SD 16.760) for the control group (P=.001), and PO SCORAD index scores were 24.92 (SD 16.572) and 38.31 (SD 16.253), respectively (P=.001). Likewise, sleep disturbance means were 2.94 (SD 2.981) for the intervention group and 4.69 (SD 2.943) for the control group (P=.001) [26].

Treatment for Pruritus and Xerosis

Aquaphilus dolomiae extract, a biomanufactured derivative from *Aquaphilus dolomiae*, has been shown in vitro to counteract the mitogenic effects on CD-4$^+$ T-cells, which may result in immunosuppressive effects [44-46]. One open-label study of 5910 patients evaluated the effects of an emollient containing *Aquaphilus dolomiae* extract on pruritus and xerosis severity and sleep disturbance. The application was done twice daily for 7 days. A VAS derived from the SCORAD index was used to measure changes in sleep, with 0 representing “no sleep disturbance” and 10 representing “very severe sleep disturbance.” After the treatment period, a decrease from 3.3 to 1.3 in sleep score was observed (P<.001) [28].

Polidocanol is a local anesthetic agent shown to have an antipruritic effect on nonhistamine-induced itch [47]. Prucidine-4 is an antipruritic formulation reported to act as a TRPV1 antagonist [48]. One open-label study with 55 patients with xerosis compared compounded polidocanol (2%) to prucidine-4 (0.5%) lotion. Both were applied at least twice daily for 28 days, and each led to a decrease in insomnia scores from 2 to 0 after 28 days (*P*<.001) [29].

Treatment for Chronic Idiopathic Urticaria

Bilastine and levocetirizine, both H_1-receptor antagonists, were compared in 1 RCT on sleep parameters of 525 patients diagnosed with chronic idiopathic urticaria. Patients either received 20 mg bilastine or 5 mg levocetirizine once daily for 28 days. Assessment of sleep was measured using a 5-point sleep disturbance scale. Overall, by 14 and 28 days, a greater percentage of patients treated with bilastine (n=89, 54.6%; n=106, 62.7%) and levocetirizine (n=103, 66.9%; n=115, 72.3%) reported having no sleep disturbance, respectively, when compared to placebo (n=55, 33.4%; n=76, 42.7%; *P*<.001) [32].

Treatment for Prurigo Nodularis

One retrospective study of dupilumab was performed with 27 patients with prurigo nodularis. An initial loading dose of 600 mg was given via subcutaneous injection, followed by 300 mg injections every other week. Mean sleeplessness numerical rating scale scores decreased from a baseline of 8.2 (SD 2.0) to 1.7 (SD not given), after 16 weeks of treatment (*P*<.001) [30].

Treatment for Psoriasis Vulgaris

One open-label study evaluated the effect of calcipotriol-betamethasone dipropionate gel in 394 Greek patients with psoriasis vulgaris. The gel was applied once daily for 4 weeks, with various quality-of-life assessments performed before and after the treatment period. Sleep disturbance was measured using a subjective survey, ranging from 1 (no itching) to 10 (worst state). By the end of the treatment period, a significant decrease in mean score from baseline was observed (*P*<.001) [31].

Discussion

Summary

In this review, a variety of studies assessed treatment efficacy in influencing sleep parameters for dermatological conditions, predominantly AD. Given the inclusion of sleeplessness in SCORAD, a robust clinical tool to assess atopic dermatitis, this result is not surprising. Therefore, the inclusion of a sleep measure into clinical tools assessing other kinds of dermatological conditions may be beneficial.

In terms of atopic dermatitis, 3 broad classes of treatment were found: systemic, topical, and procedural. Among systemic treatments, dupilumab was the most studied. It was shown to be efficacious in improving sleep parameters. All published dupilumab studies for AD found significant improvements in sleep disturbance, sleep quality, and sleep loss. This may be secondary to the notable effect of dupilumab to rapidly reduce pruritis in patients with AD [49]. The adverse effects (AEs) of dupilumab, however, should be taken into consideration (Table 2). While usually mild, AEs were frequently observed in dupilumab treatment studies. Other systemic treatments including melatonin, abrocitinib, and cyclosporine showed promising results in improving sleep parameters, but further studies will be needed to establish their efficacy. While not always discussed in these studies, the potential AEs of these other treatments also warrant further consideration. For example, abrocitinib and baricitinib have been associated with increased risk for infections and malignancy [50,51]. Clinicians should keep such AEs in mind, particularly the immunosuppressive effects of abroctinib, barictinib, and to a lesser extent dupilumab, when attempting a new treatment plan.

The current gap in research on nonimmunosuppressive treatment options for sleep disturbances also deserves mention. Of note, there was a lack of studies for many medications commonly prescribed by dermatologists to assist with sleep, such as sedating antihistamines, tricyclic antidepressants, mirtazapine, gabapentin, and naltrexone. Further research into the sleep-related effects of these drugs is warranted.

Contrary to systemic treatments, topical treatments for AD were mostly ineffective in influencing sleep. One study using a steroid-tacrolimus combination treatment did find a significant improvement in a 4-point sleep disturbance measure in pediatric patients. However, given a relatively small sample size and lack of blinding, more evidence is needed to verify this effect. Similarly, procedural treatments for AD such as UV-B, PMR, and structured educational programs appeared highly efficacious in improving sleep, but replication is needed before definite conclusions can be drawn. The relative absence of AEs in these interventions, however, makes them promising directions for future research.

For dermatoses other than AD, only a limited number of treatment studies were found that included any kind of sleep measure. For the studies that were found, however, significant benefits to sleep measures were observed. Given the importance of sleep for patients' quality of life, broader inclusion of sleep measures in treatment studies, whether as part of a standardized clinical assessment tool or as a standalone assessment, merits further consideration.

Several limitations of this review exist. First, there was a lack of homogeneity in the studies found, which precluded the performing of a meta-analysis. The time range of our studies also only encompasses studies up to 2021, meaning newer research may not have been included. Additionally, the nature of funding for some of the treatment studies could have introduced a source of bias, especially for recently introduced medications such as dupilumab (Table 3). Lastly, while the methodology of this review fulfilled most requirements of AMSTAR 2 (A Measurement Tool to Assess systematic Reviews), it did not include a risk of bias assessment [52].

Conclusions

Assessment of sleep changes remains an understudied aspect of dermatological treatment studies. A majority of the studies that did measure changes in sleep were related to AD; however, studies related to pruritus and xerosis, prurigo nodularis, psoriasis vulgaris, and chronic idiopathic pruritus were also found. Dupilumab was most effective at improving sleep measures for AD, but its side effect profile must be taken into consideration. For other dermatoses, given the small number of studies found, further research is needed to establish their efficacy. A broader inclusion of sleep change measures in dermatological treatment studies is warranted.

Conflicts of Interest

TES served as an editorial board member-at-large for JMIR Dermatology. They did not participate in the editorial oversight or review process for this paper. PL reports research grants/funding from AbbVie, AOBiome, National Eczema Association; is on the speaker's bureau for AbbVie, Arcutis, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oreal, MyOR Diagnostics, ParentMD, Pfizer, Pierre-Fabre Dermatologie, Regeneron/Sanofi Genzyme, Verrica; reports consulting/advisory boards for Alphyn, AbbVie, Almirall, Amyris, Arcutis, ASLAN, Boston Skin Science, Bristol-Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosci, Dermavant, Eli Lilly, Galderma, Janssen, Johnson & Johnson, Kimberly-Clark, LEO Pharma, Lipidor, L'Oreal, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Skinfix, Theraplex, UCB, Unilever, Verrica Yobee Care; stock options with Codex, Concerto Biosciences and Yobee Care. In addition, PL has a patent pending for a Theraplex product with royalties paid and is a Board member and Scientific Advisory Committee Member of the National Eczema Association.

Multimedia Appendix 1
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.
[DOCX File , 32 KB - derma_v6i1e48713_app1.docx]

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Abbreviations

AD: atopic dermatitis
AE: adverse effect
AMSTAR: A Measurement Tool to Assess systematic Reviews
IL: interleukin
NTIS: Night Time Itch Scale
PMR: progressive muscle relaxation
PO: patient-oriented
POEM: Patient-Oriented Eczema Measure

PROMIS: Patient Reported Outcome Measurement Information System
RCT: randomized controlled trial
SCORAD: Scoring Atopic Dermatitis
SORT: Strength of Recommendation Taxonomy
VAS: visual analog scale

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Research Letter

From the Cochrane Library: Foam Surfaces for Preventing Pressure Ulcers

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KEYWORDS

pressure ulcer; decubitus ulcer; foam surface; prevention; systematic review; wound; dermatology; ulcer; skin; pressure sore; bedsore; bed sore

As an essential component of the total body skin exam, dermatologists should recognize early signs of pressure ulcer development [1] and provide evidence-based preventive measures for patients who are at high risk. Pressure (decubitus) ulcers are common injuries to the skin and underlying soft tissue, resulting from prolonged pressure or shear force. Severe pressure ulcers may deepen, causing localized damage to muscles, tendons, and bones. Patients with limited mobility, systemic comorbidities, or decreased skin integrity [2] are most susceptible. Commonly affected areas include the lower back, sacrum, hips, and heels. A 2021 Cochrane review [3] offers a comprehensive review of the evidence regarding foam as a support surface.

The review [3] included all publications prior to the literature search (November 2019). Included were 29 studies encompassing over 9500 people considered at risk for, or who currently have, pressure ulcers that compared foam mattresses with surfaces like gel, air cells, or water bags. Participants were mainly from acute care settings; the median study sample size was 101 participants, with an age range of 47.0-85.3 years. Support surfaces were categorized into either reactive or alternating pressure types. The primary outcome was pressure ulcer incidence, and secondary outcomes (patient comfort, adverse events, health-related quality of life, and cost-effectiveness) were also evaluated. The relative risk (RR) of pressure ulcer development with foam surfaces compared to alternating pressure air surfaces was 1.59 (95% CI 0.86-2.95); despite failing to reach statistical significance, the authors reported this finding as low-certainty evidence that foam surfaces may increase the risk of pressure ulcer development compared to alternating pressure air surfaces. Many surface comparisons demonstrated very low–certainty evidence [3].

In evaluating time-to-pressure ulcer development, one study suggested that viscoelastic foam surfaces with densities of 40-60 kg/m^3 may decrease new pressure ulcer development over 11.5 days compared to lower-density foam surfaces of 33 kg/m^3. Another study assessed solid versus convoluted foam surfaces and found that the latter may decrease the risk of pressure ulcer development over 1 month. Despite these conclusions, both studies had low-certainty evidence. Furthermore, the authors reported low confidence in the effect estimate of secondary outcome measures overall. One such measure was cost-effectiveness, for which one study provided moderate-certainty evidence suggesting that alternating pressure air surfaces may be superior to foam surfaces in preventing pressure ulcers when such factors are considered [3].

This review is among four that examine specific surface types for pressure ulcer prevention. Further research is needed given the low strength of evidence regarding various surface types in preventing decubitus ulcers. Factors to consider in future studies are an emphasis on time-to-event outcomes, adverse effects, and the cost-effectiveness of various surface types. Notably, more than half (58.6%) of the studies analyzed were considered to have a high risk of bias, mostly concerning the nonblinding of participants, personnel, and outcome assessments; therefore, careful attention to reducing the risk of bias should also be an element of future studies. Trials should be designed to minimize the risk of detection bias, for example, by using digital photography and by blinding adjudicators of the photographs to group allocation.

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Conflicts of Interest

RPD is a joint coordinating editor for *Cochrane Skin*, editor in chief of the *JMIR Dermatology*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology* (*JAAD*), and a podcast editor for the *Journal of Investigative Dermatology* (*JID*). He is a coordinating editor representative on *CochraneCouncil*. TS serves as an editorial board member-at-large for *JMIR Dermatology*. RD receives editorial stipends (*JAAD*, *JID*), royalties (*UpToDate*), and expense reimbursement from *Cochrane Skin*. TS receives fellowship funding from Pfizer (grant 25B1519; principal investigator: Stanca Birlea) and the National Institutes of Health (grant 2T32AR00741136A1; principal investigator: Dennis Roop).

Editorial Notice

This article is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2021, Issue 5, DOI: 10.1002/14651858.CD013621.pub2 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review. The views expressed in this paper are those of the author(s) and in no way represent the Cochrane Library or Wiley.

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Research Letter

From the Cochrane Library: Optical Coherence Tomography for Diagnosing Skin Cancer in Adults

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KEYWORDS

systematic review; optical coherence tomography; tomography; diagnostic imaging; optical imaging; laser; skin lesions; diagnostic techniques; melanoma; basal cell carcinoma; cancer; skin cancer; clinical; cell; diagnose

Since the development of optical coherence tomography (OCT), technological improvements have made this diagnostic imaging tool adaptable to clinical settings [1]. OCT provides an alternative modality for assessing skin abnormalities. The standard procedure for the evaluation of suspicious skin lesions involves visual inspection, often with dermoscopy, which may be followed by a biopsy for histological confirmation of diagnosis. OCT magnifies the skin for a more detailed examination compared to standard techniques. Using near-infrared light, tissue can be viewed on a microscale in real time [1]. Although the use of OCT is more prevalent, its effectiveness in diagnosing skin cancer and its overall accuracy are insufficiently characterized [2].

A 2018 Cochrane review, "Optical Coherence Tomography for Diagnosing Skin Cancer in Adults," provides an in-depth review of the accuracy of OCT for detecting skin abnormalities. Data from five test accuracy studies were obtained, permitting comparison of the index test to a reference standard. The diagnostic accuracy of OCT was assessed for melanoma (n=2) and keratinocyte carcinomas (n=3). There were insufficient data to determine the diagnostic accuracy of OCT for melanoma or cutaneous squamous cell carcinoma. In a sample of 346 lesions (n=2 studies), the sensitivity and specificity of OCT for detecting basal cell carcinoma (BCC) was potentially superior versus visual assessment and dermoscopic exam—however, given a limited sample size and the high prior probability of BCC, results must be interpreted cautiously. Applied to a hypothetical population (n=1000 people), OCT had better outcomes than visual and dermoscopic exams, correctly identifying 53 more BCC lesions while reducing the incidence of false positives and unnecessary excisions by 87 [2].

The high sensitivity and specificity of OCT for BCC diagnosis are noted in subsequent reviews and expert consensus [3,4]. An increasing emphasis on aesthetically mindful outcomes highlights the importance of noninvasive modalities like OCT, with minimally invasive treatment options such as Mohs surgery increasing over 300% in a 15-year span [5]. For BCC, the use of OCT could potentially reduce the need for biopsy and histological confirmation by as much as 33% [3]. Despite its promise for BCC diagnosis, OCT accuracy may not be generalized to all suspect lesions. In cases of nonmelanoma lesions where the differential excludes BCC, OCT may result in overdiagnosis and, in some reports, a high incidence of false negatives [4]. Applying OCT to other skin lesions may, therefore, result in negative consequences (eg, misdiagnosis, repeat testing); with insufficient data regarding its accuracy [2], this raises the question of whether the benefit of noninvasive testing outweighs the risks.

The insufficient number of studies available for inclusion, study heterogeneity, and restricted study populations limit the conclusions that may be drawn regarding the diagnostic utility of OCT [2]. Included studies exhibited poor reporting, prohibiting a risk of bias assessment; additionally, study results may not be applicable to standard clinical practice [2]. Future studies should be of high methodological quality, clarify recruitment methods, and incorporate a blinded reference standard for results comparison [2]. Considering rapid technological advancements in OCT [1], well-conducted studies may enable its broader application to clinical practice in the near future.

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Conflicts of Interest

RPD is the editor in chief of JMIR Dermatology, a joint coordinating editor of Cochrane Skin, a dermatology section editor for UpToDate, and a social media editor for the Journal of the American Academy of Dermatology. He is a coordinating editor representative on Cochrane Council. TS is an editorial board member-at-large for JMIR Dermatology. RPD receives editorial stipends (JMIR Dermatology, Journal of Investigative Dermatology), royalties (UpToDate), and expense reimbursement (Cochrane Skin). TS receives fellowship funding from Pfizer (grant 25B1519; principal investigator: Stanca Birlea) and the National Institutes of Health (grant 2T32AR00741136A1; principal investigator Dennis Roop).

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Abbreviations

BCC: basal cell carcinoma
OCT: optical coherence tomography

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Research Letter

From the Cochrane Library: Interventions for Ulceration and Other Skin Changes Caused by Nerve Damage in Leprosy

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KEYWORDS
leprosy; ulcers; zinc tape; nerve damage; ulceration; skin; dermatology; systematic review

Introduction

Leprosy (Hansen disease) is a chronic and infectious bacterial disease that was responsible for 127,558 new cases worldwide in 2020 [1]. The disease is most prevalent in developing countries, particularly in India, Indonesia, Brazil, Nigeria, and Bangladesh [2]. The pathogenic bacteria responsible for the disease, *Mycobacterium leprae*, infects peripheral nerves, causing nerve damage and sensory loss in up to 30% of patients [2]. This sensory loss can lead to debilitating neuropathic ulcers that can be found on any part of the body, although they are most commonly found on the hands and feet. There are a variety of treatment interventions available [3]. Given the persistence of leprosy as a global disease, physicians must be aware of the most effective treatments for ulcers to prevent further growth and additional infections. A 2019 Cochrane review by Reinar et al [4], “Interventions for ulceration and other skin changes caused by nerve damage in leprosy,” provides a comprehensive review of evidence regarding the effectiveness of various treatments for leprosy-caused skin damage.

Methods

The review [4] extracted data across 14 studies and 854 patients to evaluate different therapeutic interventions and the associated healing time for leprosy-related ulcers. Of these studies, 13 assessed treatment options for existing ulcers and 2 evaluated the prevention of new ulcers. The studies investigating treatment for existing ulcers assessed interventions including laser therapy, light-emitting diode (LED), zinc tape, intralesional pentoxifylline, pulsed magnetic fields, wax therapy, ketanserin, human amniotic membrane gel, phenytoin, plaster shoes, and protective footwear. The interventions were compared in terms of mean reduction in the ulcer area and the number of ulcers healed over time, with healing time ranging from 2 weeks to 4 months.

Results

Of the 14 studies evaluated, 3 analyzed the effectiveness of zinc tape compared to other interventions and found that zinc tape resulted in a shorter healing time. However, Reinar et al [4] cautioned that the studies may be affected by bias and wide CIs. Two additional studies compared phenytoin to saline dressing and found that phenytoin resulted in a more significant mean percentage reduction in ulcer area and volume after 4 weeks. Another study examined preventative care by comparing canvas shoes with polyvinyl chloride boots and found there was no significant difference between the two interventions, as none of the 72 participants developed new ulcers over a 1-year period.

The authors note that it is challenging to draw firm conclusions from the results of these studies because most of the studies included had a high and unclear risk of bias. These biases included, but are not limited to, selection, performance, detection, and attrition bias. To improve the quality of future research, larger sample sizes and increased patient follow-up are needed.

Since the publication of this review, there have been several studies exploring further treatments that should be taken into consideration. For example, one study compared the use of topical epigallocatechin gallate (EGCG) 1% to topical antibiotic gauze and found EGCG 1% to be a more effective treatment [5]. Another study looked at the efficacy of a topical insulin solution (10 units) compared to topical normal saline and found the topical insulin to be more effective [6].

Discussion

The *Journal of the American Academy of Dermatology* does not provide specific recommendations for treating leprosy-related ulcers, emphasizing the importance of early detection and treatment of the disease with oral medications [7]. Preventative measures for ulcers, such as protective footwear, and interventions, including zinc and phenytoin, should be further investigated in areas with high disease prevalence to determine the most effective treatments for patients with advanced stages of the disease [3].

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Conflicts of Interest

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Editorial Notice

The views expressed in this paper are those of the author(s) and in no way represent the Cochrane Library or Wiley.
This article is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2019, Issue 7, DOI: 10.1002/14651858.CD012235.pub2 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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Abbreviations

EGCG: epigallocatechin gallate
LED: light-emitting diode

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Original Paper

Experiences Regarding Use and Implementation of Artificial Intelligence–Supported Follow-Up of Atypical Moles at a Dermatological Outpatient Clinic: Qualitative Study

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Abstract

Background: Artificial intelligence (AI) is increasingly used in numerous medical fields. In dermatology, AI can be used in the form of computer-assisted diagnosis (CAD) systems when assessing and diagnosing skin lesions suspicious of melanoma, a potentially lethal skin cancer with rising incidence all over the world. In particular, CAD may be a valuable tool in the follow-up of patients with high risk of developing melanoma, such as patients with multiple atypical moles. One such CAD system, ATBM Master (FotoFinder), can execute total body dermoscopy (TBD). This process comprises automatically photographing a patient´s entire body and then neatly displaying moles on a computer screen, grouped according to their clinical relevance. Proprietary FotoFinder algorithms underlie this organized presentation of moles. In addition, ATBM Master's optional convoluted neural network (CNN)-based Moleanalyzer Pro software can be used to further assess moles and estimate their probability of malignancy.

Objective: Few qualitative studies have been conducted on the implementation of AI-supported procedures in dermatology. Therefore, the purpose of this study was to investigate how health care providers experience the use and implementation of a CAD system like ATBM Master, in particular its TBD module. In this way, the study aimed to elucidate potential barriers to the application of such new technology.

Methods: We conducted a thematic analysis based on 2 focus group interviews with 14 doctors and nurses regularly working in an outpatient pigmented lesions clinic.

Results: Surprisingly, the study revealed that only 3 participants had actual experience using the TBD module. Even so, all participants were able to provide many notions and anticipations about its use, resulting in 3 major themes emerging from the interviews. First, several organizational matters were revealed to be a barrier to consistent use of the ATBM Master's TBD module, namely lack of guidance, time pressure, and insufficient training. Second, the study found that the perceived benefits of TBD were the ability to objectively detect and monitor subtle lesion changes and unbiasedness of the procedure. Imprecise identification of moles, inability to photograph certain areas, and substandard technical aspects were the perceived weaknesses. Lastly, the study found that clinicians were open to use AI-powered technology and that the TBD module was considered a supplementary tool to aid the medical staff, rather than a replacement of the clinician.

Conclusions: Demonstrated by how few of the participants had actual experience with the TBD module, this study showed that implementation of new technology does not occur automatically. It highlights the importance of having a strategy for implementation to ensure the optimized application of CAD tools. The study identified areas that could be improved when implementing AI-powered technology, as well as providing insight on how medical staff anticipated and experienced the use of a CAD device in dermatology.

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KEYWORDS

artificial intelligence; AI; computer-assisted diagnosis; CAD; dermatology; diagnostic tool; FotoFinder; implementation; interview; melanoma; Moleanalyzer Pro; total body dermoscopy; TBD

Introduction

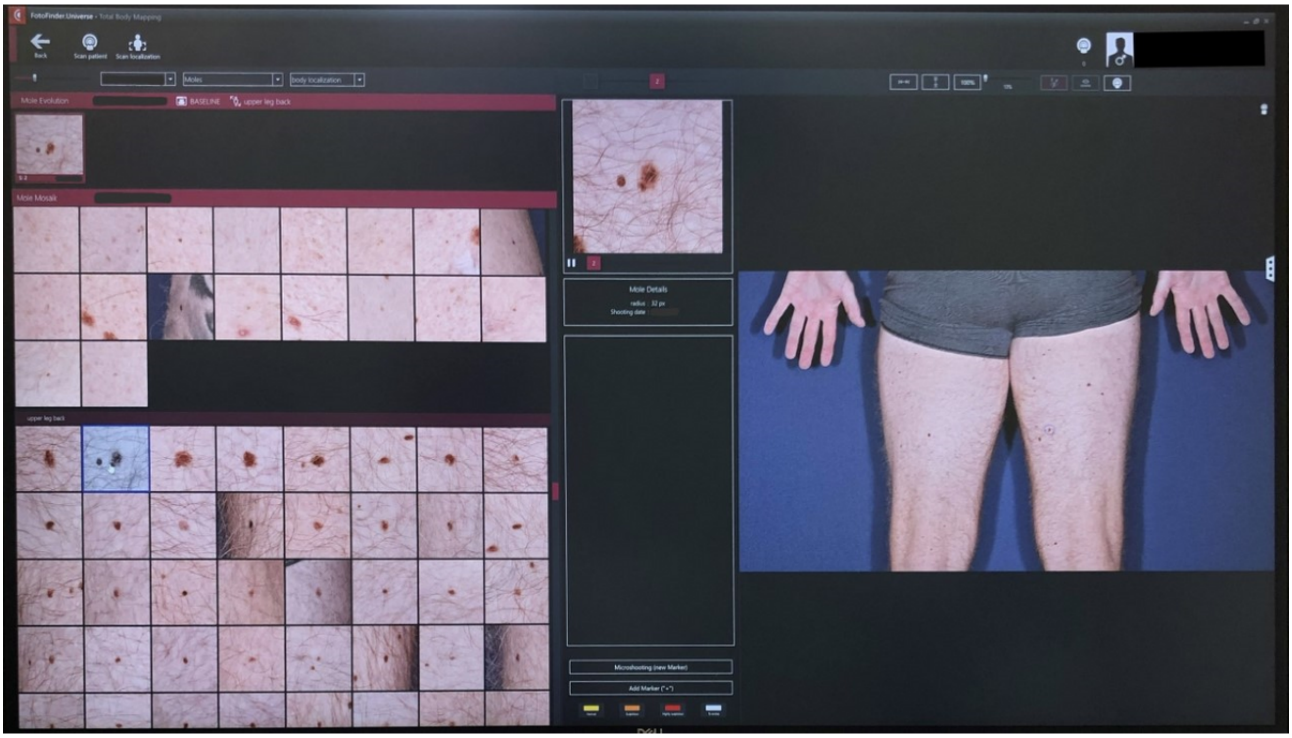
Background

Artificial intelligence (AI) can be defined as the use of technology and computer algorithms to perform assignments that normally require human intelligence [1,2]. AI is increasingly applied in numerous medical fields [3]. In dermatology, AI can be used when assessing and diagnosing suspicious skin lesions [4]. Such AI-powered methods are known as computer-assisted diagnosis (CAD) systems, and they are capable of analyzing images of the skin and subsequently recognizing malignant lesions [5]. FotoFinder (FF) is a multifunctional imaging platform that implements this CAD technology [6]. FF comprises various units adaptable for disorders related to skin, hair, and nails [7]. One such unit is the ATBM Master (Figure 1), which is optimized to detect and document changes in moles and other skin lesions [8]. This mobile system consists of an upright pole mounted with a screen, a moveable camera, a video dermoscope, and a Q-processor to power it all [9]. Together, these components can execute total body dermoscopy (TBD) [6]. TBD is an automatic way of performing the 2-step method of digital follow-up (DFU) [6]. DFU is a common approach when assessing for skin malignancy and involves taking photos of a patient´s entire body, known as total body photography (TBP), and subsequently digital dermoscopy [10].

Thus, ATBM Master´s TBD module can automatically take photos of a patient from head to toe [9] to obtain a baseline image in which changes in skin lesions can be recognized at successive checkups [10]. Next, after minimum 2 TBP sessions, this CAD system can organize moles according to their clinical relevance and display them on the screen in a so-called mosaic view [9] (Figure 2). In the mosaic view, moles can be neatly arranged into 3 groups, namely new, changed, and unchanged moles [6].

Figure 1. ATBM Master automatically takes photos of a patient's entire body. The images can be used for future reference, to more easily detect changes in the skin (image shown with patient's consent).

Figure 2. Mosaic View (left), close-up image (center) and overview (right).



The incidence of skin cancer, both melanoma and other types, is increasing all over the world [11]. Early diagnosis is crucial to improve prognosis [10] and enhance survival of melanoma patients [5]. As over two-thirds of melanomas [12], a potentially lethal skin cancer [5], arise de novo, and about one-third of melanomas develop from preexisting moles [12], TBD can aid in the early identification of harmful changes and malignancy [6]. In particular, TBD may be a valuable tool for the clinician in the follow-up of patients with high risk of developing melanoma, such as patients with multiple atypical moles [13].

The technology behind this includes both the ATBM Master's individual components and the underlying AI-powered CAD techniques [9]. The camera takes high-resolution, raw-processed polarized photos with a xenon flash [9] and makes use of intricate image modifications [6]. Because of this, the camera system is able to reveal dermoscopic structures when the moles are displayed on the screen [6]. Proprietary FF algorithms are used to identify lesions from the TBP and organize them in the mosaic view [9].

Moreover, ATBM Master's optional Moleanalyzer Pro software can be used to further assess the moles [9]. This software can give valuable information on lesion parameters such as colors, symmetry, networks, and size [14]. Then, based on these structural attributes, Moleanalyzer Pro can generate a so-called AI score [15] estimating the probability of malignancy of the lesion [16]. Moleanalyzer Pro uses deep learning algorithms [15], more specifically convolutional neural networks (CNN) [17]. This architecture has proven to be suitable for computer-based classification of images, as its multiple neural layers serve as filters detecting the presence or absence of certain features, which in turn determines whether an image should be binary classified into, for instance, benign or malignant [3].

The CNN architecture used in Moleanalyzer Pro is based on a modified version of Google's Inception v4 [17]. The system comprises 27 layers and was trained and tested through dermoscopic pictures collected from both the International Skin Imaging Collaboration's (ISIC) dermoscopic archive and several collaborating dermatologists [17]. The broad source of images used for training ensured that the possibility of overfitting was reduced [17]. To validate the CNN's generalizability, 2 open, external image databases were additionally assessed, namely the Memorial Sloan Kettering data set and ISIC-2018 challenge data set [17]. The performance of this CNN in classifying skin lesions has been compared with that of dermatologists, showing that the two are able to perform on par [17].

Thus, the expanding application of CAD techniques in the medical field [3] could be valuable when responding to medical issues such as skin cancer [18]. However, because the development of many of these systems often focuses on technicalities, rather than practical application in clinical settings, the implementation of such systems may face various obstacles and consequently suboptimal use [19].

Objectives

To our knowledge, few qualitative studies have been conducted on the topic of implementation of CAD procedures in dermatology. Therefore, the purpose of this study was to investigate how doctors and nurses experience the use of devices having CAD systems, like FF's ATBM Master unit, in particular the TBD module. In this way, the study seeks to elucidate any barriers to the implementation and application of AI-driven equipment. By discovering these barriers, actions can be taken to ensure a better environment for implementation of additional technologies in the future.

Methods

Study Design

The material for the study was obtained through 2 semistructured focus group interviews held at the Department of Dermatology and Allergy Center at Odense University Hospital (OUH). In contrast to traditional interviews, focus group interviews typically consist of 4-8 participants, an interviewer, and an observer [20]. As the goal of this type of interview is to create an interaction and discussion between the participants, in order to explore various perspectives on a certain topic [20], this approach seemed suitable for our purpose.

When preparing the questions for the focus group interviews, the Consolidated Framework for Implementation Research (CFIR) was used. CFIR is a framework designed to orderly assess various aspects of implementation in health care and other disciplines, including any potential barriers [21]. CFIR offers a practical interview guide tool with proposals of relevant questions [22]. Although CFIR encompasses 5 domains [23], this study only focused on three domains: (1) intervention characteristics (FF's TBD module), (2) inner settings (Department of Dermatology at OUH), and (3) involved individuals (nurses and doctors working with ATBM Master at OUH). Questions about outer settings and processes were left out, mainly due to time constraints for conducting the study. The questions were freely translated from English to Danish.

The device used was the FotoFinder ATBM Master, with Universe software.

The Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist guided the reporting of this study [24].

Participants

A total of 18 participants, 10 doctors (either dermatologists or dermatology registrars) and 8 nurses, were invited to the focus group interviews by email. Of these, 2 nurses and 2 doctors were unable to attend. Thus, 14 clinicians participated in the interviews. Their working experience in the dermatological field ranged from 6 months to 17 years. The invited participants were chosen because they all regularly worked in the pigmented lesions clinic (PLC), where the ATBM Master unit was commonly used. Thus, all the 14 participants had considerable experience using some functions of the ATBM Master. The TBD module was introduced to the staff at the PLC in June 2021, with subsequent teaching sessions. The participants' demographics are displayed in Table 1.

Table 1. Participants' demographics.

Category	Participants, n (%)
Profession	
Doctor	8 (57)
Nurse	6 (43)
Dermatological work experience (years)	
0-5	5 (36)
5-10	5 (36)
10-15	2 (14)
>15	2 (14)
Gender	
Male	3 (21)
Female	11 (79)
Experience using FotoFinder's ATBM Master	
Yes	14 (100)
No	0 (0)
Experience using total body dermoscopy	
Yes	3 (21)
No	11 (79)

Data Collection

The focus group interviews were conducted by one of the authors, ERH, and took place in an undisturbed conference room. One more author, BT, was also present and functioned as an external observer taking notes and asking additional questions to clarify issues, if necessary. The 2 interviews took place in October 2021. They lasted approximately 1 hour each, and both were audio recorded and transcribed verbatim.

Data Analysis

The analysis and interpretation of the interviews were based on the thematic analysis of Braun and Clarke [25]. This framework involves a stepwise process with a thorough acquaintance of the qualitative data, followed by coding, in order to identify patterns within the set of data [25]. Through this approach, vast amounts of data are consolidated into focused topics, available for analysis and interpretation.

Thus, the interviews were transcribed and repeatedly reviewed to increase the accuracy of the transcription. The transcript was read several times in order to further familiarize with the data. Afterward, it was manually coded by one of the authors (ERH). The themes chosen for subsequent analysis were data driven and thus extracted from the data after coding. The findings were discussed among the entire research team. Finally, the particularities of each theme were analyzed when producing the report. The participants were not invited to provide feedback on the findings, mainly because they were all engaged in full-time work in the Department of Dermatology. Any additional involvement in the study would entail them using their spare time, which the authors did not want to advocate.

Ethics Approval

Before conducting the interviews, the participants were given both written and oral information about the study. All participants signed consent forms. There was no financial compensation for the participation in the interviews.

The study was registered and approved by the Danish Data Protection Agency (21/63319).

Results

Overview

The primary aim of this study was to investigate the experiences regarding use and implementation of CAD-based tools such as FF's ATBM Master unit, in particular the TBD module. However, our research revealed that the participants had less experience with TBD than initially expected. All of them had used parts of the ATBM Master unit, such as its video dermoscope, but during the study it was revealed that only 3 participants had experience using the specific TBD module. In spite of this, all participants were able to provide many reflections and anticipations during the interviews, and 3 major themes and 11 minor themes concerning this topic emerged from the focus group interviews (Textbox 1).

Textbox 1. Overview of the results in this study: major themes and subthemes.

1. Organizational matters

- Lack of guidelines
- Time pressure
- Insufficient training

2a. Advantages

- Better monitoring
- Unbiased method
- Faster overview

2b. Disadvantages

- Low specificity
- Hidden angles
- Poor technicalities

3. Perspective and expectations

- Considered a supplement
- Open attitudes

Organizational Matters

The first major theme that was identified within the data was organizational matters concerning the application of the TBD component.

Lack of Guidance

The TBD module had been available in the department since January 2021, but only 3 of the participants had used this function. A lack of guidelines was revealed as the main reason for this. One doctor stated:

> *I haven't used it yet because I don't really know which patients it is intended for.*

The participants wanted written instructions with clear definitions and detailed guidance on which patients should be offered TBD, how often these patients should be followed in the clinic, and how to practically perform the TBD function. Most doctors had an idea about which patients they thought were suitable for TBD, namely patients with atypical moles and atypical mole syndrome. However, there were some disagreements about the definitions for these patient groups. As one nurse said:

> *You have one opinion, but then other doctors have other opinions...*

She continued:

> *The definitions of the various conditions are not clear to all of us, causing us to do things differently.*

Due to the variations in definitions and lack of guidance, the participants were seeking somebody to take charge and create universal definitions and guidelines for all of them to follow, to accommodate their uncertainty about TBD's use. In particular, the "primus motor for such new technologies" was one of the department's supervising consultants, and the participants awaited this doctor to make the final decision about which patients the TBD module was intended for.

Time Pressure

Time was found to be another reason for why the participants were not using the TBD component. A total of 15 minutes were allotted for each consultation. This was perceived as insufficient time to perform TBD, in addition to the standard consultation. One doctor said:

> *Time is a major limitation to the introduction of new technologies. So, it is necessary to add some time to the consultations, but this has to be organized by the management.*

A total of 30 minutes was said to be the minimum time needed to use TBD. However, the participants noted that because they had limited experience using the TBD module fully, this time slot was an estimation.

Insufficient Training

Training was yet another organizational matter discovered as being suboptimally addressed. A total of 3 teaching sessions had been arranged in the department since the introduction of TBD. However, due to holidays, meetings, or other reasons, not all participants had taken part in these sessions. When asked about their training preferences, both peer-to-peer training and creating a group of so-called "super users" was requested. Further, the participants wanted to train using the TBD component under small-scale conditions. One nurse explained:

> *It would be nice to try on some uncomplicated patients, to learn the strengths and weaknesses and get a sense of how the machine works.*

A doctor shared this opinion but added:

> *I need to know which buttons to push and how to save the picture. That is, the technicalities of the machine.*

A few of the participants claimed to have enough knowledge to use TBD straight away.

Advantages and Disadvantages

The advantages and disadvantages experienced and anticipated by the participants when using FF's ATBM Master and its TBD component were discovered as the second major theme.

Advantages

Among the benefits was the ability to compare moles over time. Moles appearing clinically benign upon examination could be revealed as clearly altered when compared with an earlier photo. Changes such as increased size, color deviations, and other irregularities, which otherwise might not have been discovered, could consequently be found. This was especially true in patients with atypical moles, where all moles tend to look irregular. It was perceived as a huge benefit that malignant melanomas could be more easily found in this patient group. One doctor stated:

> *The fact that the machine can say: this mole used to look like this, but now it looks like that, so it has changed, makes TBD obvious to use.*

The unbiasedness of the TBD procedure was another acknowledged benefit. As long as the ATBM Master unit was handled correctly, it should take the same photos regardless of who operated it. Since a variety of doctors worked in the PLC, this feature was anticipated to be helpful in handling the large turnover of doctors.

Lastly, the participants reported that they faster got an overview of the skin, and a pattern among the moles, when the nevi were displayed on a screen. This however, was said to be an advantage of ATBM Master´s screening mode, and not specifically the TBD function.

Disadvantages

Among the perceived weaknesses of the TBD component was its low specificity, exemplified by this comment:

> *It shows an eyebrow or changed lighting as being a new or changed nevus.*

This made it challenging to fully trust TBD's results and made its use very time consuming since the doctors had to sort out structures erroneously marked as new or changed moles. However, the participants claimed that because the TBD module uses AI, it needed to be fed with numerous photos of moles in order to learn to recognize moles and patterns of moles and consequently become better at identifying the malignant nevi.

Other mentioned weaknesses were so-called hidden angles, such as the scalp, behind ears, and genitalia, which the ATBM Master unit was not able to photograph.

The participants also had concerns about the FF device's user-friendliness and technicalities. When someone used TBD for the first time, one nurse shared the following:

> *I frequently have to help and assist, until they become familiarized with the machine. Then, the need for help fades out.*

Another nurse described how the ATBM Master had missed to photograph part of a patient´s back, causing the nurse not being able to locate a mole of interest. The reason for this was believed to be that wrong height was registered on the patient, causing the TBD to incorrectly adjust the images. This led to frustration as the pictures that had been taken could not be used. A similar example was mentioned about a patient having gained 20-30 kg since the first photographing session, leaving the machine unable to adjust the latter images correctly.

Perspective and Expectations

The third major theme emerging from the interviews was perspective, referring to the mindset and approach the participants had toward ATBM Master and other new technologies, and expectations, referring to the outlook they had for future use of the TBD module.

Supplement

The participants considered the TBD module to be a supplement and broadly agreed that it could not replace the doctor. They believed a manual clinical assessment always should take place, and that the doctors should examine with a dermoscope, even if they used TBD. One doctor said:

> *If I were to use TBD, I would do the exact same thing as I do today. That is, first thoroughly examine the entire skin with a dermoscope and then compare with an overview photo. Afterwards I would look to see what additional information TBD could possibly give me.*

Attitudes

The Department of Dermatology's attitude regarding new technologies was considered open-minded, as it was positive to modern devices and showed a willingness to use resources on purchasing new equipment. For example, the department had 4 ATBM Master machines, compared to other similar hospitals, which only had 2. Some participants, however, described the department as being "too open." They believed new machines were hastily bought without first ensuring that somebody could operate them, and without first making sure funds were simultaneously put aside for training and implementation. One participant commented:

> *I feel there is lots of equipment here which is not really used, because time is not set aside for training. When buying a machine, one should also plan for how to implement it.*

The individual doctors and nurses also expressed an eagerness toward trying and using the new devices. The COVID-19 pandemic was mentioned as a reason for this openness, and it was said that:

> *After corona, both health care workers and patients have become more open to digitalizations and technologies.*

When asked about how the participants experienced the patients' attitudes toward being photographed and analyzed by an AI-powered device, it was said that patients were pleased with FF's ATBM Master, and they considered it an additional safety measure.

Regarding the outlook of the TBD module, the clinicians wanted it to sort out irrelevant spots such as shadows and wrinkles. One participant specified what they wanted:

> *I want it to display, with 100% certainty, lesions with malignant potential and malignant lesions. That would be the ultimate goal when it comes to AI.*

Discussion

Principal Findings

This study discovered 3 major themes and 11 minor themes regarding the experiences and the implementation of CAD systems such as ATBM Master, with a focus on the TBD module. The first major theme was organizational matters, with lack of guidance, time pressure, and insufficient training being the subthemes. The second major theme was advantages and disadvantages of TBD use, such as improved lesion monitoring and imprecise identification of moles respectively, among others. The third major theme was perspective and expectations, encompassing viewing the TBD module as a supplement and having an open attitude toward implementing new technologies.

Barriers to Implementation of the TBD Module

Unstructured and inadequate organizational planning has been found to be a hindering factor in the process of AI implementation in health care [26]. For example, the absence of guidelines regarding AI application can cause inconsistent and suboptimal use [26]. This finding aligns well with our study, which discovered that the lack of guidelines concerning use of the TBD module was a major reason for its inconsistent application. This result suggests that the participants were dutiful and wanted to practice their work in a way that was recommended by the department. Moreover, one might speculate that the participants found assurance in knowing they performed their work in the same way as their colleagues.

The absence of designated medical staff in charge of the ATBM Master's TBD component was identified as another barrier for its implementation. This finding could indicate that the participants felt insecure and sought stability in the fast-paced setting of CAD technology. The presence of a person with executive responsibility for the TBD module could be an assurance for the medical staff, who would have a specific individual to consult on questions about TBD. The term *champion* has been used to describe the existence of such a responsible person taking the lead [26]. For example, in their study about the implementation of AI, Strohm et al [26] described a champion as a person with great interest in the applications of AI and with remarkably good knowledge about its technical aspects. Strohm et al [26] concluded that a champion was a crucial facilitating factor in the initiation and implementation of AI in the organization. A study by Miech et al [27] corroborated this view and identified the existence of champions to be among the elements associated with successful implementation in health care.

This study found that the 15 minutes allotted per consultation were perceived as insufficient time to perform TBD, and that this was an important reason why the clinicians did not use it. To use the TBD module, the participants wanted the consultations to last a minimum of 30 minutes. This finding could imply a worry among the doctors about not being able to perform their work in a satisfactory manner within the given time frame. Time pressure is a common phenomenon among doctors, and executing additional tasks such as TBD, could be perceived as too demanding and subsequently lead to work-related stress [28]. Several studies have found that obtaining full-body photos can be a time-consuming process, as the procedure requires the patient to pose in several positions, and numerous photos are taken [29,30]. A study by Haenssle et al [31] found consultations with patients having over 100 atypical moles, to last up to 60 minutes. This illustrates how some consultations can be very time demanding.

Experiences and Thoughts Regarding Use of the TBD Module

This study found that the participants considered the TBD module to be a supplementary tool, rather than a replacement for the doctor. In line with this finding, this study also revealed that a major anticipated advantage of TBD was its ability to aid the doctor, especially in the detection and monitoring of subtle changes that could be challenging to find, such as in patients with atypical moles. These results suggest that the doctors trusted their own knowledge, more than they trusted ATBM Master's TBD module and its technology. At the same time, the participants were open to incorporating this AI-supported CAD device into their clinical work. This could mean they recognized the possibility of the new technology giving them improved diagnostic confidence. A similar result was found by Shen et al [32] in a study concerning dermatologists' attitude toward AI, which described how AI was considered an assisting tool in the dermatologist's everyday diagnostic activities. The term augmented intelligence has been used by several to describe this auxiliary role of AI [33,34]. Thus, augmented intelligence illustrates the potent relationship between doctors and technology [34], and some claim this collaboration has a synergic effect [2] resulting in higher diagnostic accuracy [35].

Despite the promising potential of AI-powered CAD systems, this study found that some aspects of the TBD module were currently substandard. A perceived weakness was revealed to be its inability to photograph areas such as the scalp and behind the ears. A similar finding was found in a study by Mar and Soyer [36] about AI for melanoma diagnosis. Their study pointed out that a thorough examination of the skin, including the aforementioned areas, is an important part of a skin cancer consultation [36]. The same study also mentioned how dermatology is a visual, but also a tactile speciality, as some melanomas are best detected upon palpation [36].

Another major weakness was that TBD identified items such as an eyebrow to be a mole. This made it hard for the participants to fully trust ATBM Master's results and could possibly make them hesitant to use the TBD module. However, AI technology and CAD systems are constantly advancing [18]. In their study, Esteva et al [37] found similar performance levels between dermatologists and certain types of AI when comparing their ability to classify skin lesions, and in this way illustrating how AI has exciting potential for the future.

Limitations, Strengths, and Future Research

This study has limitations. First, because it was set in Denmark, the results might not be applicable to settings elsewhere. Second, only 3 of the participants had actual experience with the inquired TBD module. Many of the statements were therefore based on the participant's anticipations. Third, questions about outer settings and processes were left out, leaving these aspects of implementation unexplored. The strength of this study is that it reflected an authentic setting. Just as the focus group interviews that served as the foundation for this study, the dynamic situations encountered in everyday clinical practice are influenced by the various health professions and individuals that take part.

Future research should continue to explore how to implement and make use of CAD systems in ways which could improve patient care. It is important that these new devices are perceived as helpful by clinicians, not a time-consuming burden.

Conclusions

The use of AI is rapidly expanding in numerous medical fields, including dermatology [3]. However, this study has shown that implementation of new technology does not occur automatically, demonstrated by how only 3 of the participants had used the inquired TBD module.We conclude, that to ensure optimized application of methods using AI, such as CAD systems, a strategy for their implementation should exist. Qualitative studies like ours can provide valuable insight on implementation of AI-supported devices. In this way, better implementation strategies can be created, to make the most of the flourishing potential of AI.

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Authors' Contributions

All authors participated in the concept and design of this study. ERH and BT are responsible for acquisition of data. ERH undertook coding of data. ERH, TV, and BT were involved in analysis and interpretation of data. ERH drafted the manuscript. ERH, TV, and BT engaged in critical revision of the manuscript for important intellectual content. TV took the images.

Conflicts of Interest

None declared.

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Abbreviations

AI: artificial intelligence
CAD: computer-assisted diagnosis
CFIR: Consolidated Framework for Implementation Research
CNN: convolutional neural network
DFU: digital follow-up
FF: FotoFinder
ISIC: International Skin Imaging Collaboration
OUH: Odense University Hospital
PLC: pigmented lesion clinic
TBD: total body dermoscopy
TBP: total body photography

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Research Letter

Skin of Color Dermatology Representation in American College of Mohs Surgery Educational Cases on Instagram: Content Analysis

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skin of color; inequality; color; skin; social media; content analysis; dermatology; cancer; diversity; equity; inclusion; representation, Mohs surgery; skin tone; dermatologic surgery; Instagram; education; medical education

Social media is a prominent avenue for health care information delivery. The American College of Mohs Surgery (ACMS) in particular is an established professional organization for dermatologic surgeons, and its most popular social media platform is @mohs.college on Instagram (2000+ followers). As a respected resource for Mohs surgery, the ACMS and @mohs.college provides education for patients, students, and dermatologic surgeons.

While social media can be highly educational, skin cancers in skin of color (SoC) patients are often underdiagnosed or diagnosed at later stages with worse outcomes [1], likely due in part to inadequate training and exposure to the visual appearance of conditions on different skin tones. Thus, we assessed SoC representation in the popular weekly “Flap Friday” content on the @mohs.college page, featuring pre- and postprocedure Mohs cases (Figure 1). Two independent raters categorized and tabulated patients’ constitutive skin tones (light, fair, medium, or dark) following previously published methods [2], with discrepancies resolved by independent tiebreakers and consensus meetings. While Fitzpatrick phototypes are commonly used, the scale is intended to define sun sensitivity and reactivity rather than pigmentary phenotypic appearance. White skin phenotypes may be predictive of Fitzpatrick classification, while nonwhite phenotypes may not [2]. Therefore, this 4-tone scale was used to categorize photos, especially since the patient’s sun reactivity may not be known.

Out of 114 weeks (July 2020 to September 2022), 93 “Flap Friday” cases were analyzed. Overall, 83.9% (78/93) were considered to be of light skin tones, and 16.1% (15/93) were considered fair. Interrater agreement was 77.4%, and reliability was substantial with a Cohen κ of 0.643. None of the cases depicted medium or dark skin tones, although the proportions of fair (darker) skin tones were observed to increase every year from 14.3% (3/21) in 2020 to 25.9% (7/27) in 2022 (Figure 2).

These results corroborate current trends [3] where only up to 15% to 18% of resources included SoC patients. A recent analysis of 2451 cases in *JAAD Case Reports* revealed that for cases published in 2015, pictured skin tones were perceived as 73% light, 15% medium, and 12% dark; promisingly, percentages of SoC increased slightly in later years [4]. Furthermore, from 1995 to 2010, it was seen that African American patients received Mohs surgery in 44.2% of skin cancer visits, compared to 9.6% for Caucasians [5]. Given this high Mohs utilization and SoC skin cancer underdiagnosis, academic resources, including social media from prominent national organizations such as the ACMS, should be encouraged to increase SoC exposure and alleviate SoC representation gaps to improve care for the United States's increasingly diverse population. Parity in social media representation may boost patient outcomes, by spreading awareness of the appearance of skin conditions on darker skin tones and encouraging patients to promptly seek care. The current state of SoC representation reflects health disparities, and we hope to encourage diversity not only in the literature but across social media platforms.

Figure 1. Example of a highly viewed American College of Mohs Surgery "Flap Friday" case on Instagram (@mohs.college), posted on April 29, 2022, showcasing Mohs patient photos and the clinical approach (accessed September 20, 2022).

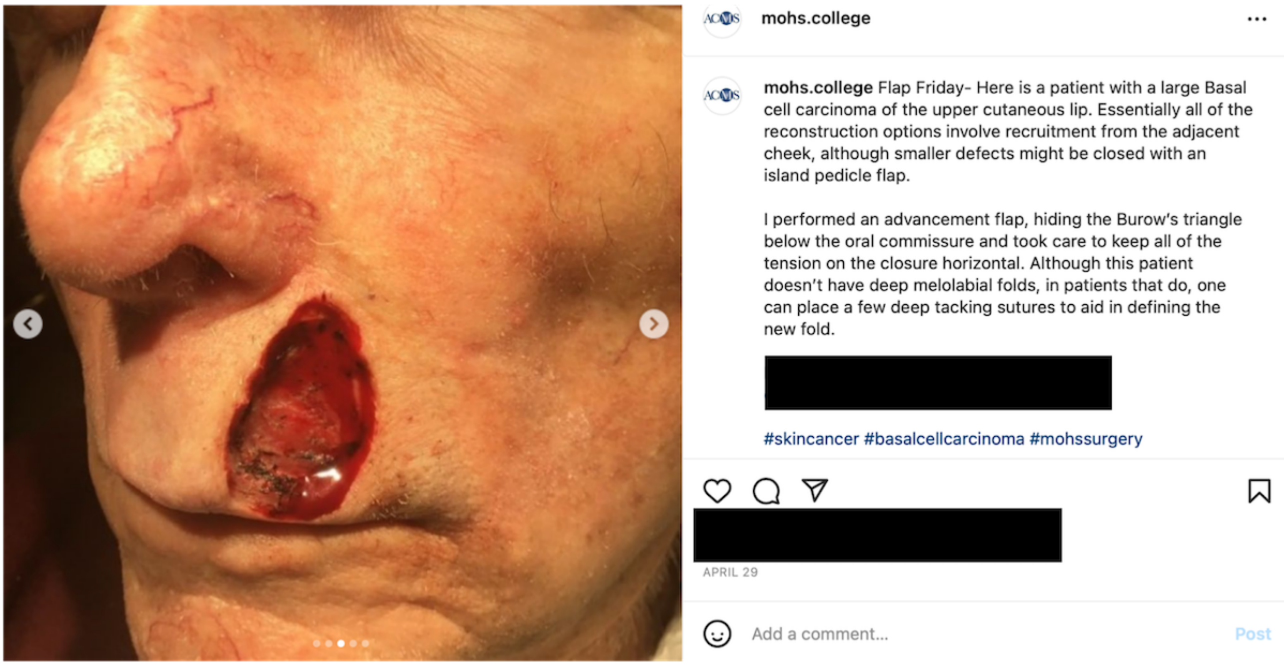
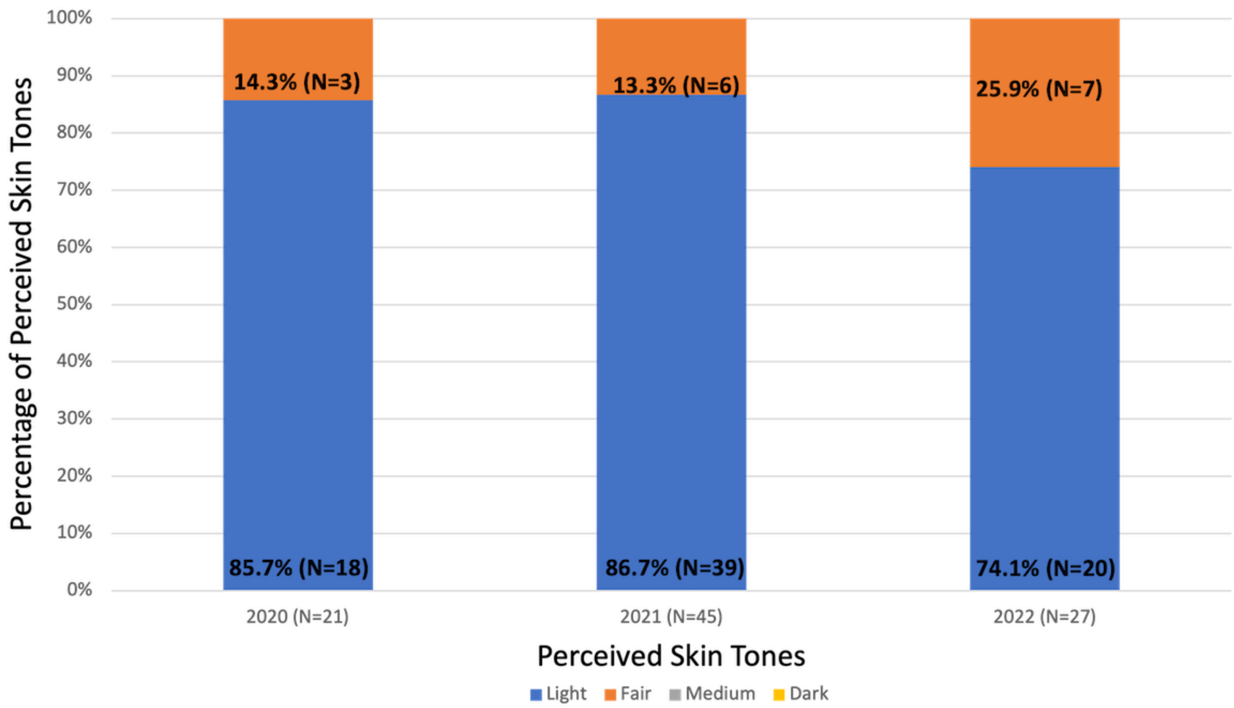


Figure 2. Percentages of perceived light, fair, medium, and dark skin tones depicted by weekly American College of Mohs Surgery "Flap Friday" cases on Instagram (@mohs.college) from 2020 to 2022.



Disclaimer

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Abbreviations

ACMS: American College of Mohs Surgery
SoC: skin of color

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Research Letter

Telangiectasia-Related Social Media Posts: Cross-sectional Analysis of TikTok and Instagram

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KEYWORDS

social media; telangiectasias; varicose veins; health information; misinformation; dermatology; health education; dermatologic information; health content; accuracy; educational content

Introduction

While social media is increasingly used by dermatologists to educate the public [1], any social media user can freely create and disseminate content. As a result, the public may interact with errant recommendations or dermatologic misinformation [1]. Myths surrounding telangiectasias, a condition affecting up to 79% of men and 88% of women, encapsulate this problem [2]. We analyzed published content and its authors on TikTok and Instagram to appraise telangiectasia-related content.

Methods

TikTok and Instagram were selected for their size and dearth of published literature, compared to the known presence of misinformation on platforms like Twitter and Facebook [1]. On TikTok and Instagram, #spiderveins was searched. The top 13 hashtags were collected from captions of posts including #spiderveins. The 10 most popular posts were analyzed for each hashtag. Non-English posts were excluded. Posts without medical explanations or marketing intent were excluded. The remaining posts were classified as educational, promotional, or advertisement, as in prior research studies [3]. Educational posts explained dermatologic conditions or procedures, promotional posts endorsed a practice or provider without offers for purchase, and advertisements offered services or products for purchase. Creator classification, post type, and post engagement were also collected.

Results

Nondermatologists made up the majority (50/74, 68%) of telangiectasia-related content on TikTok (Table 1). Of 123 posts, 80.4% (n=99) of posts were educational, 11.4% (n=14) were advertisements, and 5.7% (n=7) were promotional; 57.7% (n=71) of posts were published by medical providers or practices, 16.3% (n=20) by influencers, and 26% (n=32) by businesses. On Instagram, #varicoseveins and #spiderveinremoval were the most popular hashtags for terminology and treatment, respectively (Table 2). From 117 posts, educational (n=59, 50.4%) content was once again the most common, followed by inspirational (n=27, 23.1%) and promotional (n=31, 26.5%). Influencers were responsible for 16.2% (n=19) of posts, medical providers for 59% (n=69), and businesses for 24.8% (n=29).

Table 1. Varicose veins and telangiectasia search terms, average user engagement, post content, type, and creator on TikTok.

Hashtag	Average likes	Average comments	Average shares	Content: advertisement, n (%)	Content: educational, n (%)	Content: promotional, n (%)	Post type: video, n (%)	Post source: influencer, n (%)	Post source: medical provider, n (%)	Post source: business, n (%)
#spiderveins	4152	143.7	639.8	1 (10)	8 (80)	1 (10)	10 (100)	3 (30)	4 (40)	3 (30)
#varicoseveins	32,493.80	214.9	11,171.80	0 (0)	9 (90)	1 (10)	10 (100)	3 (30)	7 (70)	0 (0)
#varicose	2551.10	56.5	379.6	0 (0)	9 (90)	1 (10)	10 (100)	4 (40)	6 (60)	0 (0)
#legveins	2050	40.8	111.1	5 (50)	4 (40)	1 (10)	10 (100)	0 (0)	6 (60)	4 (40)
#varicosevein	1244.10	42.9	523.1	0 (0)	10 (100)	0 (0)	10 (100)	2 (20)	8 (80)	0 (0)
#spidervein	89.5	6.4	2.8	0 (0)	10 (100)	0 (0)	10 (100)	3 (30)	4 (40)	3 (30)
#telangiectasia	41.7	0.333	1	0 (0)	10 (100)	0 (0)	10 (100)	0 (0)	10 (100)	0 (0)
#sclerotherapy	399,510.10	440.1	13,684.30	0 (0)	10 (100)	0 (0)	10 (100)	2 (20)	8 (80)	0 (0)
#varicosetreatment	1493.80	27.6	291.3	0 (0)	10 (100)	0 (0)	10 (100)	1 (10)	8 (80)	1 (10)
#veintreatment	1136.70	18.3	38	3 (30)	5 (50)	2 (20)	10 (100)	0 (0)	5 (50)	5 (50)
#spiderveinremoval	308.5	11.9	15.7	2 (20)	8 (80)	0 (0)	10 (100)	1 (10)	4 (40)	5 (50)
#laserveinremoval	399.5	7.4	13.1	5 (50)	5 (50)	0 (0)	10 (100)	0 (0)	2 (20)	8 (80)
#spiderveintreatment	284.8	6.5	5.9	1 (10)	8 (80)	1 (10)	10 (100)	1 (10)	5 (50)	4 (40)

Table 2. Varicose veins and telangiectasia search terms, average user engagement, post content, type, and creator on Instagram.

Hashtag	Average likes	Average comments	Post type: photo	Content: inspirational	Content: educational	Content: promotional	Post type: video	Post source: influencer	Post source: medical provider	Post source: business
#spiderveins	221.125	31.111	8 (89)	6 (67)	2 (22)	1 (11)	1 (11)	7 (78)	1 (11)	1 (11)
#varicoseveins	617.75	25.778	8 (89)	4 (44)	4 (44)	1 (11)	1 (11)	5 (56)	3 (33)	1 (11)
#varicose	534.25	55	9 (100)	2 (22)	5 (56)	2 (22)	0 (0)	2 (22)	7 (78)	0 (0)
#legveins	268.333	7.556	6 (67)	3 (33)	4 (44)	2 (22)	3 (33)	1 (11)	6 (67)	2 (22)
#varicosevein	184.667	12.667	2 (22)	0 (0)	5 (56)	4 (44)	7 (78)	0 (0)	7 (78)	2 (22)
#spidervein	250	34.889	8 (89)	0 (0)	8 (89)	1 (11)	1 (11)	0 (0)	8 (89)	1 (11)
#telangiectasia	406.833	16.556	6 (67)	2 (22)	6 (67)	1 (11)	3 (33)	0 (0)	4 (44)	5 (56)
#sclerotherapy	198	24.111	3 (33)	3 (33)	5 (56)	1 (11)	6 (67)	0 (0)	8 (89)	1 (11)
#varicosetreatment	89.714	5.333	7 (78)	3 (33)	5 (56)	1 (11)	2 (22)	3 (33)	5 (56)	1 (11)
#veintreatment	193.571	16.556	7 (78)	1 (11)	4 (44)	4 (44)	2 (22)	0 (0)	6 (67)	3 (33)
#spiderveinremoval	565	22.222	5 (56)	1 (11)	4 (44)	4 (44)	4 (44)	1 (11)	6 (67)	2 (22)
#laserveinremoval	146.8	108.889	5 (56)	0 (0)	4 (44)	5 (56)	4 (44)	0 (0)	3 (33)	6 (67)
#spiderveintreatment	93	14.333	2 (22)	4 (44)	4 (44)	1 (11)	7 (78)	1 (11)	5 (56)	3 (33)

Discussion

Many patients use social media platforms for dermatologic information [4]. Our findings demonstrate the potential for the dissemination of misinformation from nonmedical users, with 35.7% (39/108) and 46.6% (61/132) of content from disease nomenclature and treatment generated by influencers and businesses, respectively. Prior research has demonstrated that information not produced by board-certified dermatologists has a higher propensity to be inaccurate [5]. There are existing features within social media platforms, like the duet feature on TikTok, where two videos are played simultaneously, that medical providers can use to their advantage to combat misinformation [3]. This study serves as a reminder that dermatologists should warn patients about inaccurate dermatologic information potentially found on social media apps and can do so in simple targeted messages. The limitations of our study include the evaluation of only two social media platforms, with a predominantly English userbase.

This study provides a sample of content creators in telangiectatic-related content. This study reinforces the importance of social media presence of board-certified dermatologists to comment on and combat inaccuracies by creating educational content and reacting to erroneous information. Further research is necessary to evaluate the scope of misinformation and its deleterious effects.

Conflicts of Interest

CLP is a section editor for the Current Dermatology Reports.

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Research Letter

The Research Scholarly Output of Africa in Dermatology From 2012 to 2021: Focus on the Top 10 Dermatology Journals

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Africa's contributions to dermatology research have been underreported in the literature, prompting our investigation of the number and quality of scholarly output across the continent's 49 countries. Using Scopus/SciVal, we analyzed publications from 2012 to 2021 and found only 4579 articles with 36,691 citations, indicating limited productivity. A total of 1804 (39.6%) papers, with 23,414 citations, were published with international collaboration.

To evaluate productivity by country, we used four indicators: number of publications, citations, citations per publication, and field-weighted citations impact. Egypt published the most documents (n=1688), followed by South Africa (n=685), Tunisia (n=388), Ethiopia (n=351), Morocco (n=290), Nigeria (n=249), and Kenya (n=206). The countries with the highest citations were Egypt (n=13,667), South Africa (n=8558), Morocco (n=2413), Kenya (n=2197), and Ethiopia (n=2176). Table 1 presents data for all 49 countries.

Journal ranking and metrics can indicate research quality, and Scopus categorizes journals into seven groups or quartiles. Of the 4579 African publications, 4267 are in one of the seven quartiles (Q1-Q7). Only 24 (0.56%) and 195 (4.01%) were published in the top 1% (Q1) and top 5% (Q2) of Scopus sources, respectively. The highest number of documents were in Q5 and Q6.

We also analyzed African contributions to the top 10 dermatology journals globally (Table 2). From 2012 to 2021, these journals collectively published 108,577 articles, but only 1060 (0.98%) came from Africa, with only 576 published without collaboration with high-income countries. The lack of investment, resources, and infrastructure in Africa likely contributes to low productivity, as well as the challenges faced by researchers in pursuing scientific careers in Africa [1].

Research is crucial for development and productivity growth, but Africa lags behind in investment. In 2011, while worldwide expenditure on research was 1.77% of the total global gross domestic product, Kenya spent only 0.1% and South Africa spent 0.76% of their gross domestic product on research [2,3]. This decline in research quality is attributed to insufficient spending. Only 2% of the 3000 publications from low-income countries are listed in MEDLINE, and only 10% of medical research is conducted in low-income nations. Even in the case of Ebola research, most of it was done in the United States [4].

African scholars must remain dedicated to addressing their continent's problems and should consider stepping outside their comfort zones to pursue knowledge, develop long-term partnerships with high-income countries, and use applied research to bring new information to the continent [2,3]. Ongoing discussions among stakeholders, including local governments and research institutions, are essential for putting local research into practice. Regular engagement with regional and international researchers and policy makers is necessary to understand global concerns and priorities. To support these efforts, financial aid, research budgets, collaboration, and exchange programs are urgently needed.

Table 1. The scholarly output for all 49 countries.

Country/region	Scholarly output, n	Citations, n	Citations per publication	Field-weighted citation impact
Egypt	1688	13,667	8.1	0.96
South Africa	685	8558	12.5	1.21
Tunisia	388	2118	5.5	0.68
Ethiopia	351	2176	6.2	0.51
Morocco	290	2413	8.3	0.69
Nigeria	249	1788	7.2	0.6
Kenya	206	2197	10.7	0.87
Uganda	152	1672	11	0.85
Tanzania	124	1213	9.8	0.74
Malawi	65	571	8.8	0.75
Cameroon	60	462	7.7	0.54
Ghana	54	346	6.4	0.56
Botswana	53	277	5.2	0.46
Côte d'Ivoire	53	253	4.8	0.5
Zimbabwe	50	638	12.8	0.93
Burkina Faso	42	202	4.8	0.54
Senegal	41	316	7.7	0.79
Togo	36	141	3.9	0.43
Zambia	32	302	9.4	0.65
Benin	31	169	5.5	0.52
Rwanda	30	305	10.2	0.84
Sudan	30	351	11.7	1.1
Algeria	26	223	8.6	1.21
Libyan Arab Jamahiriya	21	791	37.7	1.88
Mali	19	117	6.2	0.57
Mozambique	17	149	8.8	0.89
Madagascar	12	43	3.6	0.3
Congo	10	51	5.1	0.39
Guinea	10	69	6.9	0.68
Democratic Republic Congo	9	38	4.2	0.61
Gabon	8	83	10.4	0.77
Mauritius	8	51	6.4	1.11
Reunion	8	50	6.3	1.03
Lesotho	7	23	3.3	0.32
Namibia	7	81	11.6	0.61
Liberia	6	7	1.2	0.09
Angola	5	13	2.6	0.54
Somalia	4	9	2.3	0.4
Central African Republic	3	41	13.7	1.16
Niger	3	13	4.3	0.42
Guinea-Bissau	3	37	12.3	1.12
Sierra Leone	3	15	5	0.45

Country/region	Scholarly output, n	Citations, n	Citations per publication	Field-weighted citation impact
Swaziland	3	23	7.7	0.71
Burundi	2	10	5	0.33
Gambia	2	27	13.5	1.19
Mauritania	2	14	7	0.99
Chad	1	3	3	0.44
Comoros	1	8	8	0.54
South Sudan	1	10	10	0.93

Table 2. The list of the top 10 journals with the total number of publications, number of countries involved, number of African countries, African total publications with collaboration, African total publications without collaboration, the top six African countries, and their contribution to each journal.

Title	Publications, n	Countries, n	African countries, n	Total African publications with collaboration, n	Total African publications without collaboration, n	Egypt, n	South Africa, n	Tunisia, n	Malta, n	Nigeria, n	Morocco, n
Journal of the American Academy of Dermatology	26,474	116	29	154	68	60	33	9	5	7	6
JAMA Dermatology	3638	83	17	18	2	1	3	2	1	3	0
American Journal of Clinical Dermatology	1452	62	6	14	8	5	4	2	1	1	0
Journal of the European Academy of Dermatology and Venereology	11,571	134	38	237	127	86	16	45	36	8	10
Experimental Dermatology	4480	74	8	36	10	18	8	5	0	0	1
Journal of Dermatological Science	3721	73	7	23	9	11	6	0	0	1	2
Clinics in Dermatology	3534	80	18	54	24	13	13	4	4	0	0
Journal of Investigative Dermatology	21,065	95	14	57	6	11	16	10	0	0	5
British Journal of Dermatology	29,828	123	35	439	306	66	229	20	19	22	0
Dermatologic Clinics	2814	61	8	28	16	4	17	0	1	0	0

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Conflicts of Interest

None declared.

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Research Letter

Retractions in Dermatology Literature Between 1982 and 2022: Cross-sectional Study

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publication; retraction; bibliometrics; dermatology

The recent growth in the number of dermatology publications, as well as the increasing rate of retractions in other fields of medicine, has raised questions about how the field of dermatology compares in terms of this metric [1,2]. In this study, we evaluated retracted publications in the field of dermatology and explored the trends of retraction over the past four decades.

All retracted dermatology-related articles from 1982 to 2022 were identified on the Retraction Watch Database. The Retraction Watch Database, compiled and maintained by the Retraction Watch team, is the largest searchable database of retracted scientific articles publicly available to researchers [3]. Information regarding article type, country of authors, reasons for retraction, publication year, and the number of months between publication and retraction for each paper were collected, and linear regression was performed to assess trends of retractions over time.

Between 1982 and 2022, there were a total of 178 retracted articles in the field of dermatology. The most common article types were “Research Article” (n=91), “Review Article” (n=31), “Clinical Study” (n=25), and “Case Report” (n=21). The majority of these papers originated from China (n=33), the United States (n=32), the United Kingdom (n=20), India (n=19), and South Korea (n=16). The most frequent reasons given for retraction included “Errors in Analyses, Data, Image, Materials, Methods, Text, Results, or Conclusions” (n=46) and “Duplication of Article, Data, Image, or Text” (n=45). Eight articles were retracted due to falsification or fabrication of data and results. Linear regression determined a moderate negative correlation between the year of publication and the number of months between publication and retraction, with $P<.001$ and multiple $R^2=0.48$ (Figure 1).

Consistent with the findings in other fields [2,4], these results reveal that the absolute number of retracted dermatology publications has markedly increased over the past two decades (Figure 2). The exact reason for this phenomenon is unclear, whether it is due to an increase in the number of dermatology publications, an increase in the rate of duplications submitted by authors, or a greater vigilance by journals to identify reasons for potential retraction. However, it appears that more recent dermatology publications have been undergoing the process of retraction significantly quicker than older papers. The negative association observed between the year of publication and the time between publication and retraction indicates that the latter rationale may contribute the most to this occurrence.

While there is no evidence to suggest that the increase in the number of retractions in dermatology has been accompanied by an increase in the output of low-quality research, the mantra of “publish-or-perish” is frequently discussed among academics concerning the field of medicine in general [5]. Despite the pressure to publish from their institution, their colleagues, or their own self-interest, authors must continue to accurately analyze data and adhere to ethical research guidelines, as it appears that most retractions occur due to errors rather than falsifications and fabrications. Similarly, journal staff members should continue to diligently monitor the articles for potential issues that may warrant retraction. Limitations to this study include the reliance on the Retraction Watch Database to identify retracted publications in the field of dermatology, which may have resulted in unidentified articles relevant to this analysis.

Our study naturally does not account for manuscripts that were rejected during the peer-review process due to errors, duplications, and falsifications; however, observing the trend in retractions of published papers in the dermatology literature benefits researchers and journal editors alike.

Figure 1. Scatter plot depicting the moderate negative association between the year of publication and retraction time in months. P<.001 and multiple R^2=0.48.

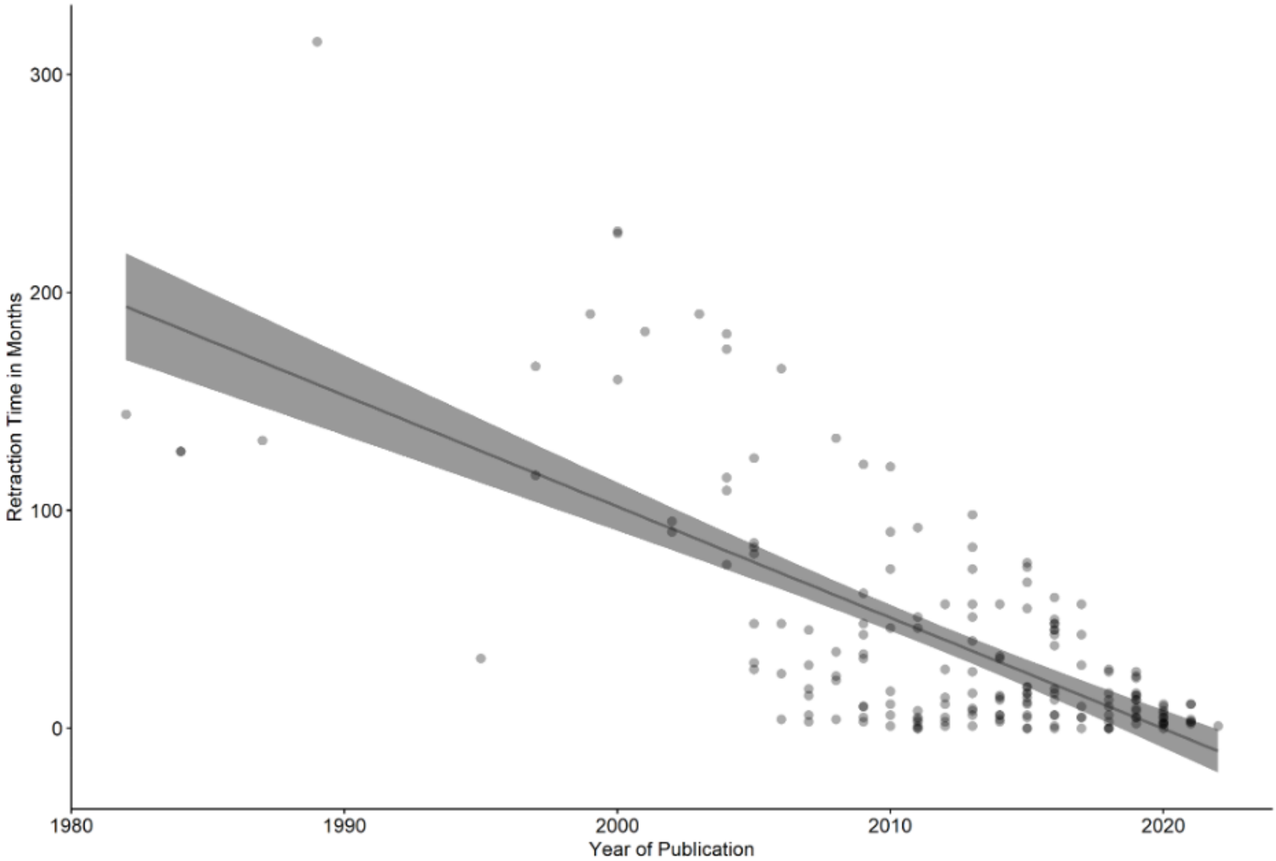

Figure 2. Line chart depicting the increase in the number of retracted articles in the dermatology literature over the past two decades.

Conflicts of Interest

AH is a reviewer for JMIR Dermatology and provides scientific and technical direction for Corza Medical.

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Research Letter

Patient Engagement With the Myderma Platform for Psoriasis During the COVID-19 Pandemic

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KEYWORDS

psoriasis; social media; online health-related information; COVID-19; disease awareness; disease awareness website; digital campaigns; patient activation; patient engagement; COVID-19 pandemic

Social media's impact on health care ranges from enabling the discovery of new medical knowledge and information to providing cost-effective ways to improve physician-patient communication [1]. This paper assessed social media's usefulness in the psoriasis setting by analyzing the Myderma website, with a focus on the impact of the COVID-19 pandemic on users' reachability and engagement.

LEO Pharmaceutical Hellas developed the Myderma website [2] (launched on September 1, 2016) to play an active role in supporting patients with psoriasis and their symptoms. The website provides access to a wide variety of topics, including disease-related information, available treatment options, and useful tips on psoriasis and improving quality of life. Myderma is also available through Facebook (launched on July 5, 2016) and YouTube (launched on May 31, 2016). This health care social media platform provides an interactive way to communicate, as users can participate in questionnaires and short polls about psoriasis and the ways it is affecting their lives. Patients with psoriasis are often stigmatized due to the high visibility of the disease; therefore, searching for information over the internet and taking advantage of the anonymity provided might be beneficial [3,4]. Through Myderma, patients could also look for a nearby dermatologist, simply by clicking on the "Find Dermatologist" icon, which leads to the Hellenic Society of Dermatology and Venereology, with call-to-action requests.

Participants in our analysis included visitors to the Myderma website as well as its Facebook, Instagram (launched in October 2019), and YouTube pages. Two periods were defined: before the COVID-19 pandemic, from January to December 2019, and during the COVID-19 pandemic, from January 2020 to June 2021. There were no major differences in the company's advertising expenditure during the two periods.

During the COVID-19 pandemic, a significant increase was observed in the number of visitors to the website, from 35,067 users prior to the pandemic to 82,479 users during the pandemic. The increase was consistent across all age groups (Tables 1 and 2).

Despite significant progress over the last decades, psoriasis is still associated with increased stigmatization, accompanied by significant psychosocial burden, especially for women [4]. This was reflected by the increased prevalence of female users of the website and Facebook.

The COVID-19 pandemic led to increased psychosocial burden, changes in treatment, and disrupted access to dermatologists [5]. During COVID-19, lockdown measures were implemented for approximately 7 months in Greece [6]. Polls and questionnaires conducted on the website or via Facebook and Instagram during the pandemic confirmed that most participants reported no access to a treating physician for over a year. Surprisingly, despite the disrupted relationship with their physicians and associated undertreatment, there was no increase in visits related to psoriasis treatment or COVID-19 vaccines.

Overall, our findings reveal that health care social media capabilities play an important role in patient engagement in challenging disease state settings, including in the psoriasis setting. Most importantly, health care–related social media platforms perform well during periods when the regular patient-physician relationship has been disrupted, such as during the COVID-19 pandemic.

Table 1. Distribution of participants who visited the Myderma website and social media pages by age group and gender.

Characteristic	Website, n (%)	Facebook, n (%)	YouTube (%)[a]
Age group (years)			
<18	—[b]	—	2.31
18-24	14,831 (8.22)	1770 (4.00)	20.03
25-34	40,037 (21.83)	6551 (15.80)	19.38
35-44	40,141 (21.97)	8880 (21.30)	19.37
45-54	37,959 (20.85)	10,718 (26.00)	18.15
55-64	29,788 (16.28)	8604 (20.80)	13.17
≥65	19,873 (10.84)	4902 (12.10)	7.59
Gender			
Male	63,237 (35.27)	8666 (19.60)	49.23
Female	117,128 (64.73)	32,798 (80.40)	50.77

[a]Counts were not provided by YouTube.

[b]Not applicable.

Table 2. Distribution of participants who accessed the website by age group.

Age group (years)	Jan 1, 2019, to Dec 31, 2019 (n=35,067), n (%)	Jan 1, 2020, to Jun 30, 2021 (n=82,479), n (%)	Jan 1, 2019, to Jun 30, 2021 (n=117,546), n (%)
18-24	1560 (4.45)	7500 (9.09)	9060 (7.71)
25-34	8880 (25.32)	13,974 (16.94)	22,854 (19.44)
35-44	7424 (21.17)	18,297 (22.18)	25,721 (21.88)
45-54	5939 (16.94)	21,161 (25.66)	27,100 (23.05)
55-64	6260 (17.85)	13,487 (16.35)	19,747 (16.80)
≥65	5004 (14.37)	8060 (9.77)	13,064 (11.11)

Conflicts of Interest

ET reports research support, consultantship, and lecturer fees for AbbVie, LEO Pharmaceutical Hellas, Janssen, Sanofi, Genesis Pharma, UCB, Mylan, and Novartis, unrelated to the submitted work. The remaining authors have no conflicts of interest to declare.

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Research Letter

Cross-sectional Analysis of Dermatologists and Sponsored Content on TikTok

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social media; TikTok; sponsorship; stewardship; ethics; dermatology; dermatologist; content analysis

The prevalence and nature of sponsored posts on Instagram by dermatologists have been well characterized within the literature [1]. Dermatologists use social media to provide education and recommend products; however, well-intended products and misinformation may be convoluted by financial or personal interests, potentially risking patient welfare. With the growing use of social media, we aimed to characterize the prevalence of sponsored posts by dermatologists on TikTok (ByteDance Ltd), a popular and rapidly growing video-sharing platform [2,3].

The following keywords were used to search for dermatologists' profiles on TikTok: *dermatology*, *dermatologist*, *board-certified dermatologist*, and *doctor*. Exclusion criteria included profiles that were private or those without first or last name, degree, and specialty. Of the profiles included, the following data were collected for each profile: username, gender, training level (attending, resident, fellow), follower count (as a proxy for engagement), total number of posts, number of self-reported sponsored posts, number of dermatology-relevant sponsored posts, and category of sponsored posts (Table 1).

A total of 94 profiles were included; 67 (71.3%) belonged to female users and 27 (28.7%) belonged to male users. Attendings and residents/fellows accounted for 89.4% (n=84) and 10.6% (n=10), respectively. Of the 94 profiles, 38 (40.4%) had sponsored content, of which 32 (84.2%) were attending and 6 (15.8%) were trainee profiles. Among the 38 sponsored dermatologists, 34 (89.5%) had dermatology-relevant content. Residents/fellows had a greater median number of followers compared to attendings (28,650 vs 20,950). Sponsored dermatologists had a greater median number of followers than nonsponsored dermatologists (66,100 vs 1639) (Table 1). Sponsored dermatologists had significantly more followers even after subdividing by training level ($P<.001$ for attendings and $P=.02$ for residents/fellows). Table 2 displays the Spearman ρ and the corresponding P values for the number of followers, sponsored posts, and number of dermatologist sponsors.

Our study identified that less than half of the surveyed dermatologists on TikTok had sponsored posts. Dermatologists that had sponsored content had a higher number of followers, with a correlation between increased number of sponsored posts and number of followers. This highlights that product advertisement reaches larger audiences than medical education. Companies often seek highly followed "influencers" to maximize brand marketing [1,4].

Dermatologists with large followings and sponsored content have stewardship to educate their viewers and not only advertise. Dermatologists on TikTok can educate a wide audience about skin, nail, and hair health, and should do so mindfully. If patient welfare is prioritized above personal interests from sponsorship, dermatologists can have a profoundly positive impact on their TikTok audience. To prevent such biases, sponsored dermatologists must remain transparent on social media and disclose conflicts of interest clearly.

Social media is an integral part of society and influences the health care provider–patient dynamic, the dissemination of medical knowledge, and the delivery of care [5]. Dermatologists have leveraged TikTok to connect and educate the public and promote brands and best practices. The wide reach of social media augments the negative impact of promoting non–evidence-based products, sharing inaccurate information, and making wrongful claims. Dermatologists must be aware that the ethical standards that apply to patient care also apply to social media so that patient well-being is prioritized.

Table 1. Demographic characteristics.

Characteristic	Value[a]
Sex, n (%)	
Female	67 (71.3)
Male	27 (28.7)
Training, n (%)	
Attendings	84 (89.4)
Residents/fellows	10 (10.6)
Sponsored dermatologists, n (%)	38 (40.4)
Attendings	32 (84.2)
Residents/fellows	6 (15.8)
Dermatology sponsors, n (%)	34 (89.5)
Nondermatology sponsors, n (%)	4 (10.5)
Number of followers of attendings, median (IQR)	20,950 (703.8-148,600)
Number of followers of residents/fellows, median (IQR)	28,650 (1934.5-1,025,300)
Number of followers of sponsored attendings, median (IQR)	61,400 (18,150-409,425)
Number of followers of sponsored residents/fellows, median (IQR)	514,100 (35,847-4,550,000)
Number of followers of sponsored dermatologists, median (IQR)	66,100 (19,250-470,025)
Number of followers of nonsponsored dermatologists, median (IQR)	1639 (105.5-34,025)
Number of sponsored posts among dermatologists with sponsors, median (IQR)	8 (1.8-29.5)
Number of nonsponsored posts, median (IQR)	110 (41-232.3)
Number of posts with dermatology sponsors, median (IQR)	8 (1-28.8)
Number of posts with nondermatology sponsors, median (IQR)	0 (0-0)[b]
Sponsored post details[c]	
Posts on skincare and hair, n	877[d]
Posts on cosmetics, n	6[d]
Posts on clothing/accessories, n	4[d]
Posts on prescription medications/procedures, n	1[d]
Miscellaneous posts, n	31[d]

[a]Decimal places were rounded to the tenth decimal point when available.

[b]The median and IQR values were 0 with a maximum of 8. The mean was 0.6.

[c]Sponsored posts were subdivided into the following categories: skincare and hair, cosmetics, clothing/accessories, prescription medications/procedures, and miscellaneous.

[d]Values reported as total post count in each category.

Table 2. Demographic characteristics based on sponsorship status.

Characteristic	*P* value[a]	Correlation coefficient (Spearman ρ[b])
Number of sponsored posts between male and female dermatologists	.07[c]	—[d]
Number of sponsored posts between attendings and residents/fellows	.84[e]	—
Number of followers between sponsored and unsponsored group	*<.001*[f]	—
Number of followers between attending sponsored and unsponsored group	*<.001*[g]	—
Number of followers between resident/fellow sponsored and unsponsored group	*.02*[h]	—
Number of followers and number of sponsored posts among dermatologists with sponsored posts	*<.001*	0.6216
Number of followers and number of dermatologist sponsors among all dermatologists with sponsored posts	*.001*	0.5136

[a]Italics denotes a significant difference.

[b]The Spearman correlation coefficient was used given the nonparametric nature of the data.

[c]Median (IQR): females, 4 (1-19); males, 24 (3-55).

[d]Not applicable.

[e]Median (IQR): attendings, 8 (2-39.5); residents, 13 (1-31.8).

[f]Median (IQR) for follower count in the sponsored group was 66,100 (19,250-470,025) while that of the nonsponsored group was 1639 (105.5-34,025).

[g]Median (IQR) for follower count in the attending sponsored group was 61,400 (18,150-409,425) while that of the attending nonsponsored group was 1443.5 (85.5-37,975).

[h]Median (IQR) for follower count in the resident/fellow sponsored group was 514,100 (35,847-4,550,000) while that of the resident/fellow nonsponsored group was 1853 (532.8-8679).

Conflicts of Interest

CLP is a section editor for *Current Dermatology Reports*. RPD is a joint coordinating editor for *Cochrane Skin*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology*, editor-in-chief of the *JMIR Dermatology*, and co-chair of Cochrane Council. RPD is the Editor-in-Chief of *JMIR Dermatology* and receives editorial stipends. RPD also receives royalties from *UpToDate* and expense reimbursement from Cochrane Council.

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Research Letter

From the Cochrane Library: Interventions for Cutaneous Molluscum Contagiosum

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KEYWORDS

Cochrane; systematic review; randomized controlled trial; RCT; molluscum contagiosum; dermatology; intervention; skin; dermis; derma; epidermis; dermatologist; poxvirus; skin infection; molluscum; cutaneous; skin lesion

Molluscum contagiosum (MC) is a cutaneous and mucosal condition that primarily affects children and immunocompromised adults. It presents with skin-colored, dome-shaped papules on the skin and may be associated with pain, pruritus, erythema, and, rarely, bacterial superinfection. Although spontaneous resolution generally occurs, treatment may be indicated for cosmetic purposes or to prevent spread.

A 2017 Cochrane systematic review [1] evaluated 22 randomized controlled trials (N=1650 participants, aged 0-36 years) and sought to provide an evidence base supporting specific treatments. Inclusion criteria required participants to have a clinical diagnosis of MC, excluding those with immune deficiency or sexually transmitted MC, as well as assessment of physical ablative methods (curettage, cryotherapy), topical agents (potassium hydroxide, iodine, trichloroacetic acid, salicylic acid, 10% phenol/70% alcohol, tretinoin, oils, cantharidin, podophyllotoxin, imiquimod), and systemic therapy (cimetidine, 35 mg/kg per day; calcarea carbonica, daily for 15 days).

The primary outcome was short‐term clinical cure, defined as the complete disappearance of lesions up to 3 months after the initiation of treatment, as assessed by a physician. The secondary outcomes were clinical cure up to and beyond 6 months, time to cure, recurrences (after 3, 6, and 12 months), adverse effects (pain, blistering, sensitization, scarring, erosion, and pigmentary changes), spread, and disease‐related quality of life.

The treatment comparisons performed in the included studies are summarized in Table 1. Data from this review strongly support awaiting spontaneous resolution of molluscum lesions and demonstrated that 5% imiquimod was no more effective in terms of clinical cure than the placebo (with an identical vehicle). Furthermore, the use of 5% imiquimod was reported to be more harmful regarding application site reactions and no more effective than its vehicle over a 3-month period.

Newer studies have proposed novel treatment options. Notably, a 2020 case study and literature review [2] described the effectiveness of photodynamic therapy (2 sessions, 2 weeks apart using 630-nm red light lasting 9 minutes) in association with incubation with 5’-Aminolevulinic acid in completely resolving giant MC (larger than 1 cm in diameter). An alternate review by Wells et al [3] discussed intralesional immunotherapies in the treatment of MC and highlighted case reports exhibiting resolution rates between 36% and 100% with minimal adverse reactions (erythema, mild edema) with Candida antigen, MMR (measles, mumps, and rubella) vaccine, vitamin D3, and OK- 432 (a penicillin- and heat-treated lyophilized powder of the *Streptococcus pyogenes* A3 substrain). A retrospective cohort study by Chauhan et al [4] assessed 22 patients between the ages of 6 to 50 years treated with 1 to 3 doses of 0.5 ml of intralesional MMR. They found that 18 (81.8%) patients had complete clearance of lesions and 4 (18.18%) patients had a partial response of more than 50% clearance. This benefit was observed in both injected and distant lesions in both studies.

Limitations of these studies include their observational design and lack of a control group. Furthermore, these studies did not equally delineate the time frame in which the participants experienced the lesions, nor whether the participants' results were affected by other dermatologic diagnoses. There is a need for larger, placebo-controlled, and prospective studies using both intralesional immunotherapy and phototherapy to confirm their efficacy.

Table 1. Treatment comparison with respective results and statistics.

Comparison	Measurement	Result	Statistics
5% imiquimod vs cryospray	Physician assessment	Cryotherapy was superior	1 study, N[a]=74; RR[b] 0.60, 95% CI 0.46-0.78
5% imiquimod vs 10% potassium hydroxide	Physician assessment	Potassium hydroxide was superior	2 studies, N=67; RR 0.65, 95% CI 0.46-0.93
5% imiquimod vs placebo	Physician assessment	Neither intervention was superior	4 studies, N=850; RR 1.33, 95% CI 0.92-1.93
Topical 10% Australian lemon myrtle oil vs olive oil	Physician assessment	10% Australian lemon myrtle oil was superior	1 study, N=31; RR 17.88, 95% CI 1.13-283
10% benzoyl peroxide cream vs 0.05% tretinoin	Physician assessment	10% benzoyl peroxide cream was superior	1 study, N=30; RR 2.20, 95% CI 1.01-4.79
5% sodium nitrite coapplied with 5% salicylic acid vs 5% salicylic acid alone	Physician assessment	5% sodium nitrite coapplied with 5% salicylic acid was superior	1 study, N=30; RR 3.50, 95% CI 1.23-9.92
Iodine plus tea tree oil vs tea tree oil	Physician assessment	Iodine plus tea tree oil was superior	1 study, N=37; RR 0.20, 95% CI 0.07-0.57
Iodine plus tea tree oil vs iodine alone	Physician assessment	Iodine plus tea tree oil was superior	1 study, N=37; RR 0.07, 95% CI 0.01-0.50
Homeopathic calcarea carbonica vs placebo	Physician assessment	Neither intervention was superior	1 study, N=20; RR 5.57, 95% CI 0.93-33.5
2.5% potassium hydroxide solution vs 5% potassium hydroxide solution	Physician assessment	Neither intervention was superior	1 study, N=25; RR 0.35, 95% CI 0.12-1.01
10% povidone-iodine solution plus 50% salicylic acid plaster vs salicylic acid plaster alone	Physician assessment	Neither intervention was superior	1 study, N=30; RR 1.43, 95% CI 0.95-2.16

[a]N: number of participants.

[b]RR: risk ratio.

Conflicts of Interest

RD is a joint coordinating editor for Cochrane Skin, a dermatology section editor for UpToDate, a social media editor for the *Journal of the American Academy of Dermatology*, a podcast editor for the *Journal of Investigative Dermatology*, editor-in-chief of *JMIR Dermatology*, and a coordinating editor representative on Cochrane Council. TS is an editorial board member at large for *JMIR Dermatology*.

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Abbreviations

MC: molluscum contagiosum
MMR: measles, mumps, and rubella

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Research Letter

Teledermatology Within Correctional Settings in the United States: A Narrative Review of the Literature

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legal; patients who are incarcerated; vulnerable populations; teledermatology; volunteerism; correctional; teleconsultation; telemedicine; eHealth; skin disorders

Teledermatology is an emerging modality of care delivery. To broadly understand the role of teledermatology in the US correctional system, we conducted a narrative review using PubMed, Scopus, Embase, and gray literature. We identified 5 studies (Figure 1) analyzing over 1261 teledermatology encounters within correctional settings in the United States (summary characteristics are in Table 1; the search strategy used is in Multimedia Appendix 1).

The first published study on the use of teledermatology for incarcerated populations was in 1996 from East Carolina University in Greenville, North Carolina [1]. Since then, several single-center observational and cohort studies have reported the implementation of teledermatology across several localities, including Utah and Connecticut [2-4]. All studies have indicated the partnership between the dermatology providers and the state prison system. The Federal Bureau of Prisons (BOP) also established a teledermatology program in 2012 covering over 50 institutions. The collaboration between dermatologists and a government agency is critical and unique for teledermatology in correctional settings [5].

Teledermatology has proven to improve access to care and efficiently diagnose a broad spectrum of skin disorders, particularly inflammatory conditions, and skin infections. Common diagnoses reported included cutaneous infection [4], acne (9%-14.9%) [2-4], eczema (9.3%-18%) [2-4], psoriasis (28.1%) [3-4], and prurigo nodularis or lichen simplex chronicus (10%) [2]. One study showed that 86.3% of cases could be managed via teledermatology alone, with 86% of patients prescribed new topical therapeutics and 57.9% receiving systemic therapies, including biologics [4]. Medical management via teledermatology was confirmed to be successful and continued to serve patients well according to medical records [4]. When compared with face-to-face visit cohorts, teledermatology cohorts involved more medication recommendations (84.8% vs 48.4%; $P<.001$) and fewer procedures and referrals ($P<.001$), likely resulting from appropriate triage by a prison primary care physician [3].

Different teledermatology modalities have been adopted. Live videoconference is the most commonly implemented modality via various videoconference platforms, including Picture Tel, Skype, Zoom, etc. Store-and-forward has also been used alone or in combination with live video teledermatology (Table 1). Due to a lack of private internet access for inmates, all teledermatology encounters were conducted via institution health care staff, the provider-to-provider module. Teledermatology and face-to-face encounters can be transitioned both ways. Patients who need procedures or biopsies for diagnosis often require face-to-face visits but may transfer back to teledermatology for continuous care after surgery or a definite diagnosis [3,4].

In addition to improved access, teledermatology in one program decreased wait time with an average turnover time of 1-2 weeks compared with 4-12 weeks for an in-person consultation [5]. The economic benefits are significant. According to the BOP report, there is an average of US $895 in savings per teledermatology consult from administration costs, particularly regarding securing transportation [5].

Overall, patients who are incarcerated are an underserved population with limited access to specialty care. Teledermatology has increased access and shown capability in addressing wide-spectrum conditions with economic benefits. Future teledermatology initiatives in correctional settings may prioritize high-quality photographs with video, integrate teledermoscopy to aid in diagnosing, emphasize the continuity of care, and expand to more sites.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses): teledermatology in correctional settings.

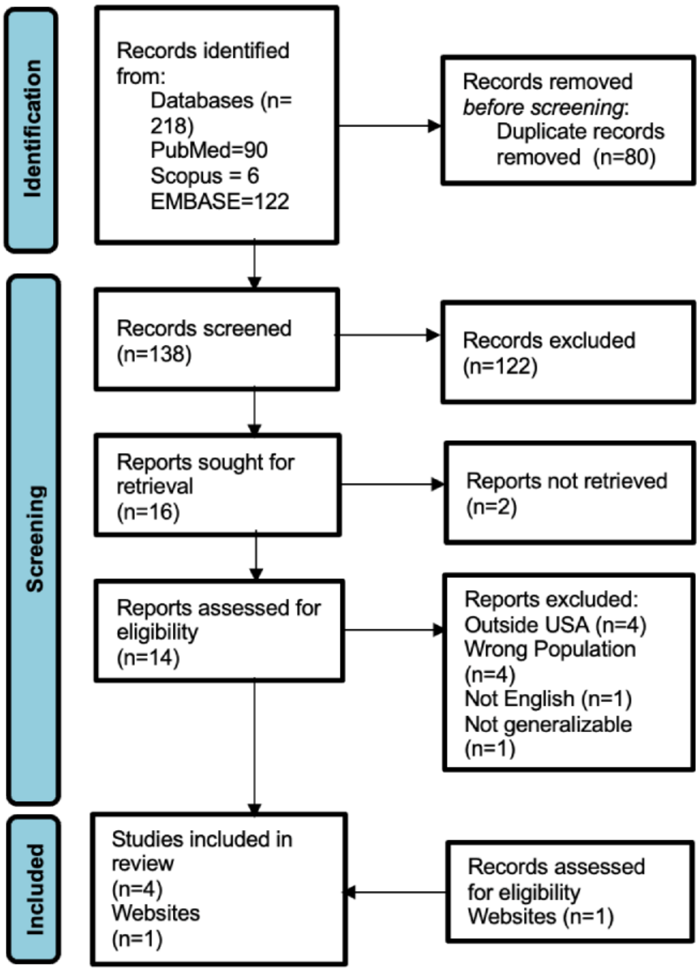

Table 1. Studies reporting on the use of teledermatology in correctional settings.

Study	Population/sample	Type of consultation	Results	Conclusion
Norton et al [1], 1997	189 teleconsultations	Live video (REACH-TV)	• Most common diagnosis included: eczema, appendageal disorders, papulosquamous disorders • Cost saving of US $1000 per visit • 355 specific treatment recommendations • 66 diagnostic recommendations	Remote visits yielded monetary and time savings compared to resources needed for face-to-face visits
Phillips et al [2], 1996	138 teleconsultations	Live video (Picture Tel 4000)	• 159 diagnoses and 252 treatments • Eczema and acne common diagnosis • 72% African American/average age 32 years	Provider confidence in diagnostic capabilities and ability to successfully manage patient care
Clark et al [3], 2021	779 encounters from 359 patients (335 teleconsultations, 444 face-to-face)	Live video vs face-to-face	• Psoriasis (28.1%), acne (14.9%), unspecified rash (9.3%) • Teledermatology less likely led to secondary diagnosis (52% vs 26.3%; *P*<.001) • Teledermatology more likely to prescribe medication (84.8% vs 48.4%; *P*<.001) but less likely to get referred for procedures (*P*<.001) • The average teledermatology follow-up period was 2.3 months vs 4.8 months for face-to-face visits (*P*<.001)	Cost-effective for managing common skin conditions. Success with managing severe psoriasis and acne even when using systemic treatments and lab monitoring.
Stoj and Lu [4], 2021	98 teleconsultations	Live video (Skype) and store-and-forward	• Teledermatology diagnoses: 78.1% (57/73) new diagnoses, and 17 consistent with established diagnoses • 86.3% (63/73) diagnoses involved only telemedicine after initial diagnosis • Face-to-face was required for 21.9% (16/73) and 13/16 being subsequently managed with telemedicine	Effective for diagnosing and managing acute and chronic dermatological conditions including those that require systemic treatment
Federal Bureau of Prisons (website) [5], 2014	Per 2014, 50+ institutions across the Bureau of Prisons, 501 consults in 2013	Store-and-forward	• US $448,395 annual savings • Teledermatology consultation wait time 1-2 weeks in correctional setting vs 30-90 days in correctional setting • Identifying optimal medications via efficacy and costs considerations • Average saving of US $895 per visit	Significant savings, reduction in wait times, continuity of care, and expanded reach to geographically inaccessible or rural areas

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategy.
[DOCX File , 17 KB - derma_v6i1e47115_app1.docx]

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Abbreviations

BOP: Bureau of Prisons

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Research Letter

Skin of Color Representation Trends in JAAD Case Reports 2015-2021: Content Analysis

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KEYWORDS

skin of color; case report; diversity; diverse; equity; inclusion; representation; skin tone; image classification; case photo; case image; racism; skin color; race; racial; skin

Underrepresentation of skin of color (SoC) in academic resources may curtail diagnostic training and exacerbate health disparities given an increasingly diverse US population [1]. Case reports are important starting points and foundational for high-quality studies in the research pyramid evidence hierarchy [2], thus inclusivity and diverse representation should be encouraged. We therefore sought to examine SoC representation and race/ethnicity reporting in all case photos published by *JAAD Case Reports* since its inception in 2015 through 2021.

Skin tones represented by each available case photo were assessed by two independent blinded reviewers with dermatology experience and recorded as either light (corresponding to Fitzpatrick I-II), medium (III-IV), or dark (V-VI) [3], with a third independent reviewer resolving any discrepancies prior to analysis. Case author–reported race/ethnicity was tabulated as White, Black, Hispanic, Asian, or other and was compared to the case image if one was presented.

A total of 2451 cases were reviewed. In 2015, images were perceived as 73% light, 15% medium, and 12% dark skin toned (Figure 1). Percentages of light skin tones decreased to 59% from 2015 to 2021 (chi-square P=.008), corresponding with increasing percentages of dark- and medium-toned images. Total cases that reported any race/ethnicity decreased from 40% in 2015 to 24% in 2021 (P<.001), and of those fractions, the proportion of White race reported largely remained equal (~50%) to that of Black, Hispanic, Asian, and other combined. Patients with light skin tones were more commonly reported by case authors as White, and patients with dark skin tones were more frequently reported as Black. However, ~65% of cases that did not include a corresponding image were reported as White (Figure 2).

While *JAAD Case Reports* continues to publish light skin tones more frequently, trends toward increasing SoC representation are promising. Interestingly, the frequent omission of photos among White case report participants could suggest that authors and editors perceive image necessity differently for White patients compared to patients of other races. Without further explanation of image omission, this presents a challenge for the field in preventing unconscious bias and the erroneous concept of race as a biological construct [4]. Indeed, a previous 2018-2020 analysis of 52 dermatology journals revealed that only 16.3% of publications on average were focused on diversity or SoC, perhaps related to ongoing disparities in access to dermatologic care among SoC populations [5]. Given that case reports are foundational for further research and the urgent need to address underrepresentation and health disparities, we hope to motivate further discussion and urge journals to consider establishing consistent reporting criteria when publishing case reports, whether that requires including or omitting images or race/ethnicity descriptors, for example. In parallel, greater attention should be afforded to the nuances of how bias could potentially be introduced via reporting decisions. Nevertheless, including more examples of conditions appearing on different skin tones can bolster the relevance of case reports in improving clinical care for diverse populations.

Figure 1. Percentages of perceived skin tones in JAAD Case Report images by publication year, 2015-2021.

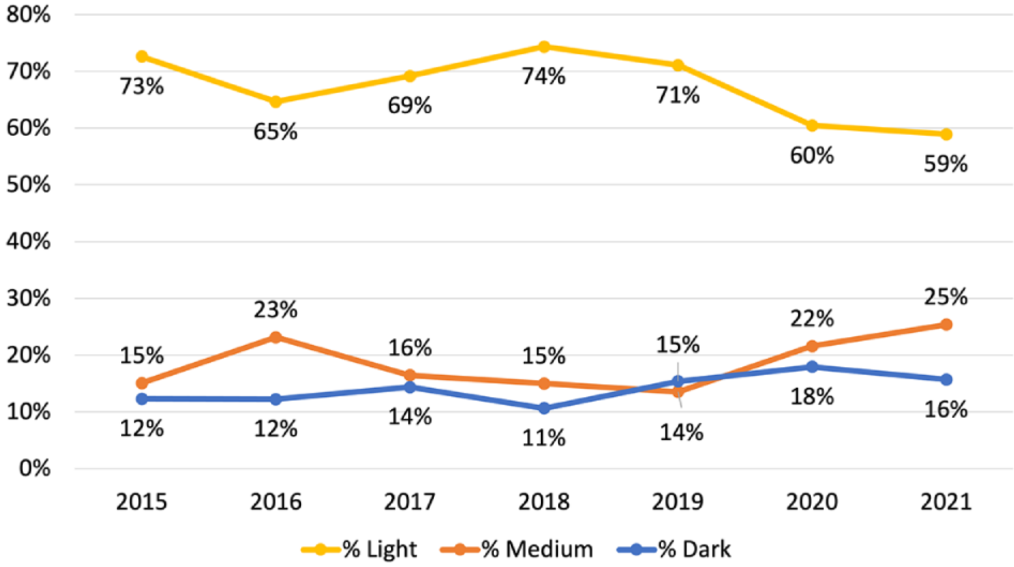
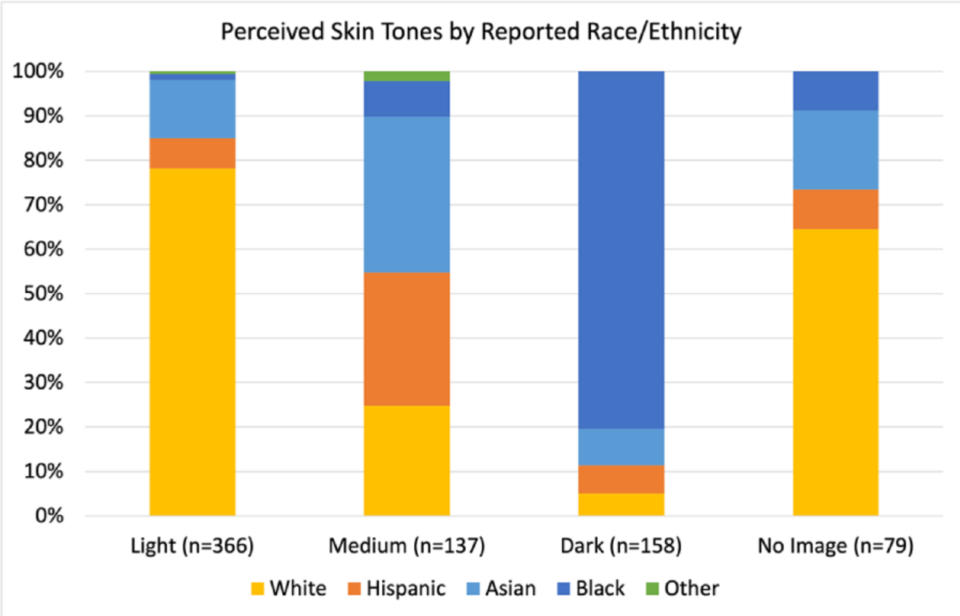


Figure 2. Perceived skin tones for JAAD Case Report images from 2015 to 2021 with reported race/ethnicity.



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Conflicts of Interest

RPD is a joint coordinating editor for *Cochrane Skin*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology*, a podcast editor for the *Journal of Investigative Dermatology*, editor in chief of *JMIR Dermatology*, and a coordinating editor representative on the Cochrane Council. RPD receives editorial stipends (*JAMA Dermatology*, *Journal of Investigative Dermatology*), royalties (*UpToDate*), and expense reimbursement from *Cochrane Skin*.

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Abbreviations

SoC: skin of color

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Research Letter

Gender and Ethnic Disparities in Teledermatology Clinical Trial Participants: Cross-Sectional Analysis of ClinicalTrials.gov-Registered Trials

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KEYWORDS

teledermatology; tele; gender disparities; clinical trial; ClinicalTrials.gov; gender; disparity; disparities; ethnic; dermatology; research subject; participant; skin; derma; derm; dermatologist; dermatology; epidermis

Teledermatology enables the remote viewing of diagnostic images and clinical histories, with the ability to diagnose and offer treatment recommendations [1]. An increase in telemedicine, in the form of teledermatology, for the management of dermatologic diagnoses was observed in early 2020 [2]. This increase in teledermatology coincided with the need for patients to access providers remotely during the COVID-19 pandemic. Despite this increase in teledermatology, the composition of the trial participants underlying the evidence has not been assessed. Given disparities in representation, measured through the ratio of participation in clinical trials to prevalence, across sex, race, and ethnicity, in clinical trials for interventions such as dermatological drugs [3], it is important to assess whether these disparities exist within teledermatology trials.

This analysis evaluates available trial participant data from the ClinicalTrials.gov trial registry of the US National Library of Medicine. We included all studies related to the use of teledermatology. Relevant participant data were extracted for analysis from their respective ClinicalTrials.gov registration when available. These variables included trial status, funding source, and trial participant demographic information.

Our search yielded 35 clinical trials, of which 25 (71%) were completed and 3 (9%) had available results. Of the 35 clinical trials, 7 (20%) are currently recruiting, 2 (6%) have unknown status, and 1 (3%) was withdrawn, with a total mean start year of 2016.62 (SD 4.21). About 77% (27/35) were funded by non–National Institutes of Health, non–US federal funding (ie, industry). In terms of study type, 8 (23%) studies were observational and 27 (77%) were interventional.

Among the completed trials with results [4-6], 1153 participants were analyzed. Women and Hispanic or Latino participants comprised a minority of participants (Table 1): 227 (19.7%) and 114 (9.9%), respectively. The pooled mean age of the participants was 59.12 (14.31) years. While all 3 trials reported gender and ethnicity (Hispanic or Latino status), only 1 reported on the racial composition of the participants. The racial composition among the 296 participants analyzed was as follows: 187 (63.2%) were White, 70 (23.6%) belonged to more than one race, 19 (6.4%) were Asian, 8 (2.7%) were Black or African American, 5 (1.7%) were American Indian or Alaska Native, and 5 (1.7%) were Native Hawaiian or other Pacific Islander. In 2 (0.7%) cases, race was unknown or not reported.

We found 3 completed clinical trials related to teledermatology with results on the registry [4-6]. Pooled counts and proportions indicate an underrepresentation of women and Hispanic or Latino participants. The pooled participant age was akin to that of an older adult (59.12 years). Only one of these studies reported race. Despite contributing to 19% of the US population in 2021 [7], Hispanic individuals comprised only 9.9% of the participants in these trials and are thus underrepresented as a proportion of the population. A study of teledermatology use in the United States reported an elevated proportion of teledermatology use compared to in-person use among female, younger, non-White, and out-of-state patients [8]. In this cohort, female patients comprised 65,023 (65.9%), non-White patients comprised 8920 (15%), and patients aged less than 40 years comprised 62,695 (83.2%) of those using teledermatology. The findings related to teledermatology use differ from the trial enrollment data for the trials we analyzed in this study.

Teledermatology is postulated to improve health equity by eliminating barriers to care. To this end, a retrospective study found a significant reduction in no-show rates among teledermatology visits compared to clinic visits among females, racial/ethnic minority patients, and Medicare/Medicaid beneficiaries [9]. These findings suggest that access to care, measured through no-show rates, may be improved through teledermatology.

None of the 3 studies with results report income or Medicaid beneficiary status. A study of direct-to-patient teledermatology in a low-income, older adult population found that among those older than 65 years, nearly 32.7% of encounters involved use of video and/or photo sharing compared to 60.6% among those aged <65 years [10]. The pursuit of health equity through use of teledermatology should address the intersecting dimensions of digital literacy with demographic and socioeconomic status contexts. Given the potential for teledermatology to improve health equity, it is important for these groups to be enrolled in clinical trials assessing teledermatology.

Our findings indicate that disparities exist in the gender and ethnic composition of trial participants for teledermatology along with a lack of adequate reporting of trial participants by race.

Table 1. Characteristics of completed teledermatology studies with results on ClinicalTrials.gov.

Trial characteristic	Total	Identifier		
		NCT00488293	NCT02358135	NCT03241589
Gender (female), n (%)	227 (19.7)	9 (2.3)	147 (49.7)	71 (15.2)
Ethnicity (Hispanic or Latino), n (%)	114 (9.9)	2 (0.5)	100 (33.8)	12 (2.6)
Age (years), mean (SD)	59.12 (14.31)	62.3 (14.4)	49.0 (14.0)	62.89 (14.43)
Reports racial composition?	N/A[a]	No	Yes	No
Study type	N/A	Interventional	Interventional	Observational

[a]N/A: not applicable.

Conflicts of Interest

None declared.

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Research Letter

Where Are We With Teledermatology? Two Years in the Wake of COVID-19

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teledermatology; telehealth; teleconsultation; COVID-19; dermatology; trends; sustainability; uptake; telemedicine; global trend; low quality of care; technological barrier; virtual care

Introduction

Much attention was brought to teledermatology during the COVID-19 pandemic, but how has this trend held up? Two years on, we review the trends of teledermatology in our institute and globally, and discuss the role of teledermatology moving forward.

Methods

Outpatient live video teleconsults planned and conducted in the National University Hospital between January 2020 to December 2022 were retrospectively extracted. Planned teleconsults were defined as those scheduled by doctors for a future date (typically between 1 week to 1 year). Teleconsults conducted refer to those that had actualized. These numbers were presented as percentages of total outpatient consultations (teleconsults and physical). In our setting, teleconsults are typically planned for patients on chronic follow-up who do not require in-clinic procedures, regardless of diagnosis and disease severity. All new referrals and first visits were seen in person. Reasons for patients declining a planned teleconsult were collected and tabulated.

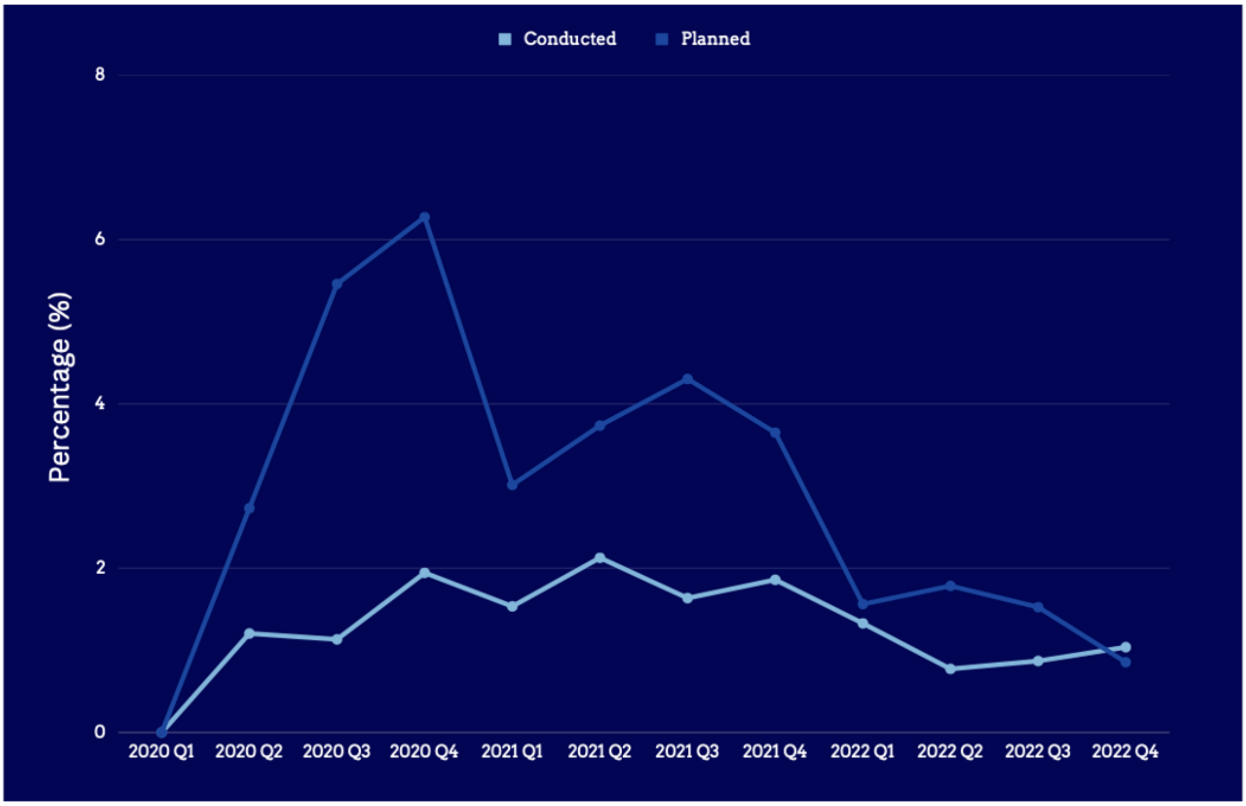
Results

After the initial uptake of teledermatology in Q2 2020 secondary to the COVID-19 pandemic, the percentage of teleconsults conducted remained largely stable between 1% and 2%. In contrast, the percentage of teleconsults planned showed fluctuations, increasing from 0% in Q1 2020 to 6.3% in Q4 2020, decreasing to 3% in Q1 2021 before increasing again to 4.3% in Q3 2021.

Subsequently, the percentage of teleconsults planned decreased again to 0.9% in Q4 2022 (Figure 1). These increases in teleconsults planned over the 2 years corresponded with institutional efforts to promote teledermatology through visual (clinic posters) and verbal prompts (weekly department meetings). Clinic service assistants were also trained to schedule and manage video teleconsults including setting up, alerting patients, and managing waiting rooms to facilitate the transition between physical and virtual consultations and to improve patient experience.

Reasons cited by patients for declining a proposed teleconsult included having to pay the same price as physical consults (n=80) and a perceived lower quality of care (n=79), which they worry could lead to misdiagnosis or inadequate management of flares. Technological barriers (n=49) such as difficulty in setting up videoconferencing applications are another commonly cited reason.

Figure 1. Percentage of conducted and planned teleconsults of total outpatient consultations. In Q2 2020, a lockdown in Singapore (termed "Circuit Breaker") limited movement outside the house to essential activities, and nonurgent outpatient services were advised to be postponed or switched to teleconsult. In the following quarters of Q3 and Q4 2020, outpatient services were prioritized based on necessity and capacity. From 2021 Q1 onward, a "Safe Nation" approach allowed for the full resumption of outpatient services, businesses, and reopening of borders. *Total refers to the combined number of teleconsults and physical consultations.



	2020				2021				2022			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Teleconsults conducted (n)	0	29	39	70	82	111	87	110	91	52	65	51
Teleconsults planned† (n)	0	66	188	226	161	195	229	216	107	120	114	42
Total* (n)	3201	2409	3445	3604	5346	5223	5324	5921	6855	6732	7477	4916

Discussion

The stable percentage of teleconsults conducted despite institutional and physician efforts to promote teleconsultations is interesting. It may reflect a small but stable population of patients keen to do teleconsultation, with the remaining that are harder to convince for reasons such as perceived lower quality, lack of financial incentives, and technological barriers.

Our findings indicate a lower uptake of teledermatology compared to global reports [1], where for example, 50% of patients with acne and 72% of patients with atopic dermatitis preferred teledermatology [2]. Besides the reasons shared by patients for declining proposed teleconsults, additional contextual factors may be involved. In our setting, patients still had the option of physical consultation or to postpone nonurgent consultations even during lockdown periods. Physical accessibility is also seldom an issue in the city-state of Singapore; thus, the time and cost savings from transportation for medical care are marginal. Furthermore, consulting a dermatologist physically is financially accessible to most Singaporeans, and teledermatology is therefore not used as a means to access care (as opposed to some underserved areas in the United States where teledermatology through a store-and-forward system may be the only affordable avenue for patients to access dermatological consult) [3,4].

Then, is there a role of teledermatology in areas like Singapore? We believe there is. First, we should recognize the potential need to pivot rapidly from physical to virtual consultation due to pandemics, natural disasters, armed conflicts, or other mass casualty events. Second, the inclusion of teledermatology during peacetime provides an additional service option that increases patient satisfaction especially if it is seamless, secure, and easy to use [5]. It also offers a glimpse into the possible futures of health care delivery such as in the metaverse.

The pandemic has shown that teledermatology can be an effective and feasible model of care; however, the suitability of teledermatology may be individual specific. The willingness to teleconsult is influenced by patient factors such as the patient’s disease perception and the purpose of the consult [6,7]. For example, teledermatology was more acceptable to patients with stable and mild diseases [1,7]. Other patient factors include younger age, higher perceived accuracy of teledermatology, and increased willingness to show sensitive body areas, which is correlated with increased security of teleconsult platforms [5,7,8]. Teledermatology may also help primary care physicians triage patients, expedite and facilitate timely referrals, and has also been shown to reduce face-to-face specialist appointments leading to cost-effective dermatological care [5,9,10].

Conflicts of Interest

None declared.

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Research Letter

Analysis of Dermatology Content by Top Influencers on Twitter and Their Academic Impact: Cross-Sectional Study

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KEYWORDS
dermatology; social media; Twitter; influencers; publication citations; h-index; board certified; board certification; education

Introduction

Social media platforms such as Twitter allow dermatologists to collaborate, share information with the public, expand their practices, and communicate directly with patients [1]. Concerningly, popular dermatology social media content is often generated by prolific content creators known as "influencers," not board-certified dermatologists or individuals with evidence-based training [2]. We, therefore, conducted an analysis of top dermatology accounts on Twitter, the content posted by these accounts, and their users' academic productivity and impact.

Methods

The content aggregator Cronycle [3], which has been used in multiple peer-reviewed studies of social media in health care, was used to identify the top 100 Twitter accounts in May 2021 for the topic "dermatology." Two independent researchers with experience in dermatology and social media extracted the accounts' self-reported names, credentials, and geographic locations. Content from the 3 most recent Twitter posts for each account was categorized as "educational" if relaying dermatology or health care information, "professional" if associated with promoting conferences or professional events, "advertising" if related to specific products or services, or "personal" for all other posts. A consensus meeting resolved any discrepancies. Foreign language content was translated using Google Translate (Google LLC) if an English translation was not directly available from Twitter. Account users' names were checked for American Board of Medical Specialties certifications through the Certification Matters search tool [4]. Academic citation metrics as of August 2021 (including the h-index [5] and the number of total publications and citations over an individual's career) according to the Web of Science and Google Scholar databases were also recorded.

Results

Of the top 100 accounts, 92 appeared to represent individuals and 8 were organizations (Table 1). Most were US board-certified physicians (n=52), and of these, 45 (87%) were dermatologists. However, credential verification was difficult for physicians certified or practicing outside the United States.

Table 1. Dermatology-related top influencers on Twitter in May 2021, number of followers, and board certification status or location outside of the United States.

Influencer rank	Twitter account	Name	Twitter followers, n	US board certified or non-US location
1	jamaderm	JAMA Dermatology	19,800	N/A[a] (organization)
2	poschchristian	Christian Posch M.D. Ph.D.	16,900	Germany
3	ducrest	Dominique du Crest	8200	France
4	drdorisday	Dr Doris Day	9500	Yes; dermatology
5	dermatologistmd	Susan J. Huang MD	8600	Yes; dermatology
6	jmgardnermd	Jerad Gardner, MD	28,100	Yes; pathology, dermatopathology
7	drrodrohrich	Rod Rohrich, M.D.	133,900	Yes; plastic surgery
8	cdndermatology	Canadian Dermatology	5200	N/A (organization)
9	globaldermie	Josette McMichael MD FAAD	4500	Yes; dermatology
10	sergiovanog	Dr. Sergio Vañó	34,200	Spain
11	dermdoc	Jeff Benabio, MD MBA	22,000	Yes; dermatology
12	harveylui	Harvey Lui	2100	Yes; dermatology
13	socinvestderm	SID	2900	N/A (organization)
14	drstefaniew	Dr Stefanie Williams	12,200	United Kingdom
15	dranjalimahto	Dr Anjali Mahto	6300	United Kingdom
16	adeadamson	Ade Adamson, MD MPP	6100	Yes; dermatology
17	aedv_es	Academia Española de Dermatología y Venereología	9900	N/A (organization)
18	seemalrdesaimd	Seemal R. Desai, MD, FAAD	1900	Yes; dermatology
19	dermdrhale	Dr. Elizabeth Hale	3900	Yes; dermatology
20	carriekovarik	Carrie Kovarik, MD, FAAD	1500	Yes; dermatology, dermatopathology
21	roxanadaneshjou	Roxana Daneshjou MD/PhD	13,400	Yes; dermatology
22	juleslipoff	Jules Lipoff, MD	2900	Yes; dermatology
23	misharosenbach	Misha Rosenbach, MD	3300	Yes; dermatology
24	skinpathology	Paul Drury	6200	Australia
25	lupodermatology	Dr. Mary Lupo	3200	Yes; dermatology
26	drsteventchen	Steven Chen 陳持威	9300	Yes; dermatology, internal medicine
27	sgottesmanmd	Silvija Gottesman MD	6800	Yes; dermatology, dermatopathology
28	desaze	David Saceda Corralo	4300	Spain
29	drlopezbran	Eduardo López Bran	7600	Spain
30	antoniotejera	Antonio Tejera Vaquerizo	2500	Spain
31	dedeemurrell	Dedee Murrell	1400	Yes; dermatology
32	harkerdavid	David Harker, MD, FAAD	13,700	Yes; dermatology
33	dermatologaroo	Elia Roo	3000	Spain
34	drjohnbarbieri	John Barbieri, MD, MBA	2700	Yes; dermatology
35	drjoelgelfand	Joel M Gelfand MD MSCE FAAD	1800	Yes; dermatology
36	dravasays	Dr. Ava Shamban	10,000	Yes; dermatology
37	julianconejomir	Julián Conejo-Mir	8600	Spain
38	rosataberner	Rosa Taberner	17,000	Spain
39	dra_njimenez	Natalia Jiménez-Dermatóloga	4900	Spain
40	marcelasaebl	Marcela Saeb Lima	11,000	Mexico

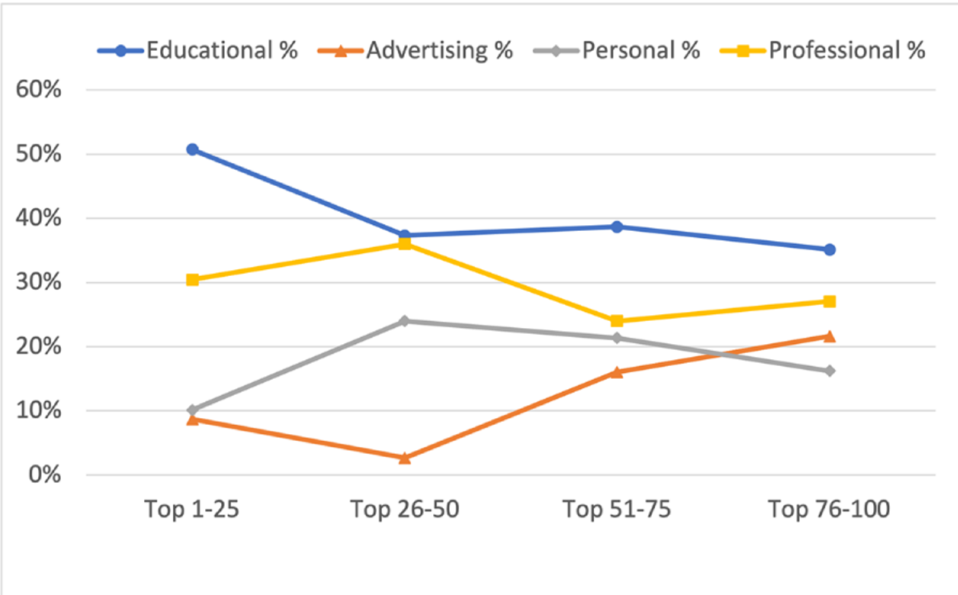
Influencer rank	Twitter account	Name	Twitter followers, n	US board certified or non-US location
41	elena_heras	Maria Elena de las Heras Alonso	2100	Spain
42	drboixeda	Pablo boixeda	2600	Spain
43	ealtmanmd	Emily M. Altman, MD	1600	Yes; dermatology, dermatopathology
44	doctormartorell	Dr.Antonio Martorell	2400	Spain
45	danielbutlermd	Daniel Butler MD	1500	Yes; dermatology
46	amostaghimi	Arash Mostaghimi	2100	Yes; dermatology, clinical informatics
47	hpsoyer	H. Peter Soyer	1900	Australia
48	lauzurica_derma	Eduardo Lauzurica	2700	Spain
49	dranthonyrossi	Dr. Anthony Rossi MD	1100	Yes; dermatology, micrographic dermatologic surgery
50	dermalegre	Adrián Alegre	2700	Spain
51	pielsana_aedv	Fundación Piel Sana de la AEDV	4800	N/A (organization)
52	drdidacbarco	Dr. Dídac Barco	3100	Spain
53	drramongrimalt	Dr. Ramon Grimalt	7500	Spain
54	drestherfreeman	Esther Freeman MD PhD	2100	Yes; dermatology
55	askdermmd	A. Shadi Kourosh, MD, MPH	11,500	Yes; dermatology
56	harrisvitiligo	John E. Harris, MD, PhD	3200	Yes; dermatology
57	drrobertanolik	Dr. Robert Anolik	2700	Yes; dermatology
58	msldermatopato	Marcel Saeb Lima	2800	Mexico
59	mightydermpath	Sara Shalin	3800	Yes; pathology, dermatopathology
60	dermatosilva	DOMINGUEZ SILVA	2600	Spain
61	drahermosag	Ángela Hermosa	3200	Spain
62	lpdermatologos	Lidia Perez dermatologos	1200	Spain
63	dermoguillenvlc	Carlos Guillen	1600	Spain
64	allisonlarsonmd	Allison Larson, MD	2100	Yes; dermatology, dermatopathology
65	melanoma_mama	Donna Regen	2500	No; melanoma awareness activist
66	hlgreenberg	H.L. Greenberg, M.D.	1700	Yes; dermatology
67	mrodriguesmd	Michelle Rodrigues	1300	Australia
68	katiefarquhar	Dr Katie Farquhar	1400	United Kingdom
69	dolevderm	Jacqueline Dolev MD	1500	Yes; dermatology
70	franvilmar	Francisco Vílchez	1700	Spain
71	larocheposayusa	La Roche-Posay USA	8000	N/A (organization)
72	leohealthyskin	LEO Pharma	16,100	N/A (organization)
73	cbaileymd	Cynthia Bailey	4300	Yes; dermatology
74	drmichellelevy	Michelle Levy, MD, Dermatologist	1200	Yes; dermatology
75	drwhitneybowe	Dr. Whitney Bowe	4600	Yes; dermatology
76	aaron_drucker	Aaron Drucker	933	Yes; dermatology
77	condetaboada	Alberto Conde	1400	Spain
78	your_skin_dr	Dr Anton Alexandroff	4800	United Kingdom
79	beerdermatology	Beer Dermatology	2500	Yes; dermatology, dermatopathology
80	drgrantstevens	Grant Stevens, MD	5600	Yes; plastic surgery
81	springerderma	Springer Dermatology	1800	N/A (organization)
82	laumiguelg	Laura M.G.	1500	Spain

Influencer rank	Twitter account	Name	Twitter followers, n	US board certified or non-US location
83	dermaforyou	Dra Carmen Galera	1500	Spain
84	ecoalfageme	Dr.Fernando Alfageme	1400	Spain
85	germainderm	Germain Dermatology	2500	Yes; dermatology
86	leoshmu	Leo Shmuylovich, MD PhD	1100	Yes; dermatology, pediatric dermatology
87	ilanarosman	Ilana Rosman, MD	3000	Yes; dermatology, dermatopathology
88	drkatiebeleznay	Dr. Katie Beleznay	1800	Yes; dermatology
89	doctoraston	Dr. Sherrell Aston	5100	Yes; surgery, plastic surgery
90	theskinmd	Jessica Krant MD	1700	Yes; dermatology
91	hellmanderm	Dr Judith Hellman	2100	Yes; dermatology
92	alvaro_gonza	Álvaro González-Cantero	1100	Spain
93	paolijohn	John Paoli	917	Sweden
94	elenacondemon	Elena Conde Montero	2300	Spain
95	mydermpath	Raj Singh MD	5100	Yes; pathology, dermatopathology
96	drbilumartin	Donna Bilu Martin, MD	2100	Yes; dermatology
97	dr_weiss	Robert A. Weiss	1100	Yes; dermatology
98	drdayan	Dr. Steven Dayan	2700	Yes; otolaryngology
99	_dermatologist	Dr Edward Seaton	3000	United Kingdom
100	drlisakates	Lisa Kates, M.D.	2000	Yes; dermatology

[a]N/A: not applicable.

Academic citation metrics according to the h-index (mean 14, SD 13; median 12, range 0-71) and total publications (mean 89, SD 148; median 43, range 2-950) were highly variable for 81 individuals with citation profiles. Educational posts were the most common (118/293, 40%), followed by professional content (86/293, 29%), personal posts (53/293, 18%), and lastly, advertising (36/293, 12%). Top quartile accounts by Cronycle rank posted far more educational content (>50%) than other categories of posts (Figure 1), and the educational category occurred most frequently in each quartile. Advertising was the least common content category, in contrast to other platforms such as Instagram, where the most common content was related to advertising [6] and posted predominantly by nondermatologist influencers [7].

Figure 1. Percentages of educational, advertising, personal, and professional posts by dermatology-related top influencers on Twitter in May 2021.



Discussion

We offer a cross-sectional snapshot of associations between content, popularity, and academics, prompting many avenues for further work and repeat assessment. For example, it remains to be seen whether social media branding affects academic influence, or vice versa. Twitter excels at encouraging user interactions through "mentions" and "follows," with the "hashtag" function allowing easy searching and content propagation. However, without further protections, Twitter could also risk spreading harmful misinformation as an educationally oriented platform. While Twitter verification policies are currently in flux, account registration does not require identity verification, though this could be explored in the future to highlight board-certified physician accounts, especially for international dermatologists where external credential verification resources are limited.

Conflicts of Interest

RPD is a joint coordinating editor for Cochrane Skin, a dermatology section editor for UpToDate, a social media editor for the *Journal of the American Academy of Dermatology* (JAAD), a podcast editor for the *Journal of Investigative Dermatology* (JID), editor-in-chief of the *JMIR Dermatology*, and a coordinating editor representative on Cochrane Council. RPD receives editorial stipends (JAAD, JID), royalties (UpToDate), and expense reimbursement from Cochrane Skin. TES is editorial board member-at-large for *JMIR Dermatology* and receives fellowship funding from Pfizer.

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Research Letter

Distinguishing Gender Identity From Biological Sex in Dermatologic Health Care: Methods, Harms, and Paths Forward

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Abstract

Accurate assessment of gender identity and biological sex in dermatology research is crucial since their conflation or poor demarcation undermines patient respect and study accuracy. Clearer guidance is needed for health care researchers, particularly in light of the notable disparities in skin disease rates, skincare practices, literature representation, and the persistent underrepresentation of transgender and nonbinary patients.

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KEYWORDS

gender identity; biological sex; gender differences in health; dermatologic health; literature representation; sex-gender bias; gender assessments; skincare; communication strategies; health care questionnaires; healthcare questionnaires; dermatology

Introduction

Although gender identity is a social determinant of health, its assessment in health care research is inadequate. We highlight the intricacy of gender and biological sex in dermatology research, revealing the need for more robust protocols for their assessment. We begin by evaluating the current protocols used to make such assessments, demonstrating lack of consensus. Next, we evaluate the relationships between biological sex and gender identity and how these impact skin health. We then examine the inadequate representation of gender minorities—including those who identify as transgender or gender nonbinary—in academic literature and how this disparity compromises the applicability of evidence-based medicine to all. Finally, we consider the importance of physician communication about gender identity.

Methods

The articles analyzed in this study emphasize the importance of transparency when delineating differences between biological sex and gender identity. In addition, researchers should be coached on techniques to extinguish investigators' biases. The models and tools for discerning gender identity and biological sex are shown in Textbox 1.

Note that the results obtained from the above methods were analyzed in conjunction with other questionnaires to assess correlations between the factors affecting overall population health [1,2,4]. Gender identity assessment tools must be regularly updated to accurately reflect the specific generational, cultural, and institutional contexts of the time.

Textbox 1. Tools for discerning gender identity and biological sex.

Questionnaires

- Stanford Gender-Related Variables for Health Research (GVHR) [1]
- Bem Sex-Role Inventory (BSRI) [1,2]
- BSRI: short form [1,2]
- GENESIS-PRAXY (Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond-Premature Acute Coronary Syndrome) [1]

Guidelines and recommendations

- Sex and Gender Equity in Research (SAGER) guidelines [3]
- Sex-gender variable: methodological recommendations for increasing scientific value of clinical studies [4]

Results

Gender Differences in Dermatologic Health

Cisgender (gender identity corresponds to sex assigned at birth) males and females exhibit different rates of various skin diseases [5]. Increased awareness of gender differences is central to constructing mechanisms for prevention, diagnosis, and therapy [5]. Those assigned male at birth tend to have higher sebum content, thicker skin, and deeper facial wrinkles than those assigned female [6]. However, research regarding gender and dermatologic care is limited. Most articles discuss gender in terms of cisgendered participants. This research is likely based on the conflation of biological sex and gender identity in electronic health records [7]. Systemic change within electronic health records is a critical step for gathering gender-precise data.

Gender-affirming therapies may induce drastic skin changes. Hormone therapies increase the risk of acne vulgaris, androgenetic alopecia, excessive sebum production, melasma, and hirsutism [8]. Dermatologists must be conscious of gender-affirming treatments in order to help minimize associated risks.

Gender Minorities in Literature Representation

Researchers believe numerous factors contribute to skin differences between gender identities [8]. Transmale and transfemale populations (gender identity does not correspond with sex assigned at birth) face underdiagnosed conditions resulting from underresearched gender-affirming therapies [8]. This representation disparity is a growing area of investigation for its contribution to gender inequality.

Gender minority populations also face health care barriers from noninclusive treatment eligibility models. For instance, despite the increased prevalence of acne vulgaris in transgender populations, iPledge medication guidelines for isotretinoin use sex assigned at birth and require contraception to remain eligible [8].

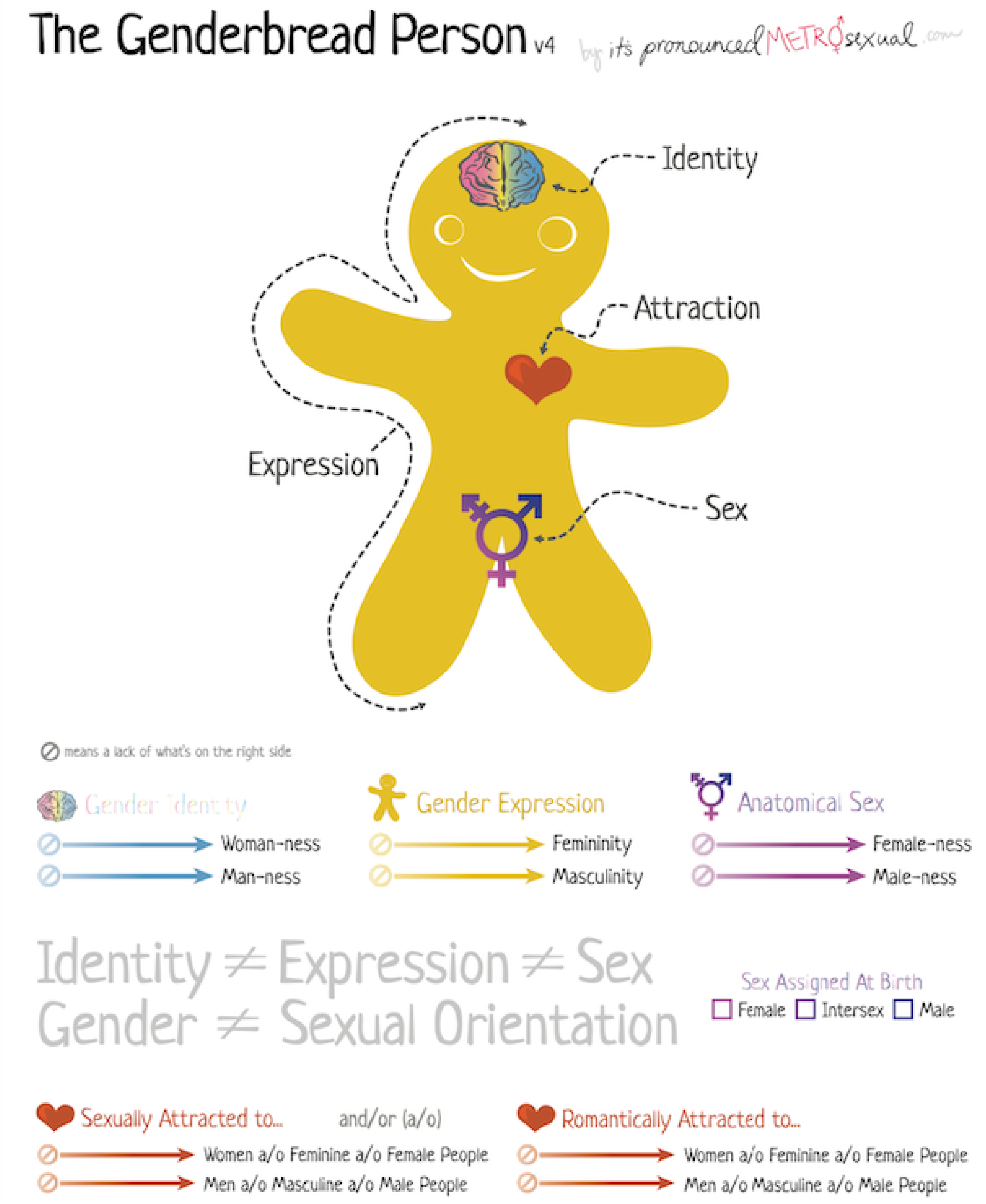
Although increasing female participation in clinical trials is widely supported, data on gender minority participation is nonexistent. Additionally, the risks of some conditions fluctuate depending on the stage of gender-affirming therapies. Although existing data sets may not use inclusive models of gender identity assessment, there is value in their implementation given the prospect of large-scale observational studies and meta-analyses in which these variables could be better assessed. As gender minority populations grow, these inclusive models will help physicians support all patients while ensuring that salient trends and health impacts are captured by research analyses.

Physician Communication

About 28% of transgender individuals delay seeking preventative care because of mistreatment by health care workers; thus, inclusive language is important to build trust in these communities [9]. Medical professionals should receive training in gender-inclusive terminology to foster a welcoming environment where patients feel comfortable sharing information relevant to their health [7]. Physicians should avoid assumptions and ask patients about their preferred terminology [7]. Figure 1 displays a “Genderbread Person” and provides guidance on the terminology used in this paper.

Misgendering patients can have profound effects on patients’ health and safety and can damage the patient-provider relationship [11]. As ideas about gender identity evolve, mistakes will inevitably happen; when mistakes occur, sincere and brief apologies should be made, with an assurance that they will not recur [11].

Figure 1. A “Genderbread Person” outlining differences in gender identity, expression, and sex [10].



Discussion

Robust methodologies exist to eliminate subjectivity and maximize data accuracy and utility. Current approaches to distinguishing gender identity and biological sex are inadequate and threaten the applicability of research findings to many patients. Conflating sex and gender neglects the unique dermatologic health impacts of these attributes and contributes to the underrepresentation of gender minority populations in medical literature. While more research is needed to address these issues, communication training for physicians and other health care providers could be improved. The language used must respect patients’ identities while maintaining objectivity in clinical research.

Conflicts of Interest

RD is an editorial board member of Cochrane Skin and the *Journal of the American Academy of Dermatology*, a dermatology section editor for UpToDate, and editor-in-chief of *JMIR Dermatology*. He is a coordinating editor representative on Cochrane

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Research Letter

Characteristics of Dermatology Residency Program Morbidity and Mortality Conferences: A Survey of Program Directors

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KEYWORDS

morbidity and mortality conference; MMC; dermatology residency; Accreditation Council of Graduate Medical Education; ACGME; medical education; graduate medical education; quality improvement; health quality; quality assurance

Introduction

Quality improvement (QI) education is important for physician training and is a common program requirement set by the Accreditation Council of Graduate Medical Education (ACGME). Some programs use morbidity and mortality conferences (MMCs) as a traditional forum to address medical errors and adverse events. However, little is known about MMCs in dermatology. Understanding how programs approach the ACGME QI requirement can provide insight into the role that QI education plays in dermatology training. Thus, this study aimed to assess how dermatology residency programs meet the ACGME QI requirement, with a focus on the characteristics of MMCs.

Methods

An anonymous, voluntary, open survey was developed with Qualtrics [1], pilot-tested among the authors for validity, and sent to residency program directors through the Association of Professors of Dermatology's listserve [2] from December 2021 to February 2022. Survey questions can be found in Multimedia Appendix 1.

Ethical Considerations

The Office of Human Research Ethics at the University of North Carolina at Chapel Hill determined that this survey was not considered human subjects research (IRB# 21-2630).

Results

Of 138 dermatology residency programs, 53 (38%) responded to the survey. All respondents completed the survey in its entirety. Most respondents (39/53, 74%, 95% CI 62%-86%) reported that residents participate in a regularly scheduled MMC. The ACGME's QI requirement for most programs with no MMCs was met through resident QI projects (11/14, 79%, 95% CI 47%-96%). A few used other quality assurance meetings or periodic reminders and real-time feedback. MMCs were important for QI education for 12 (86%, 95% CI 69%-100%) of the 14 respondents from programs with no MMCs versus all 39 (100%, 95 % CI 99%-100%) respondents from programs with MMCs. The primary goals for MMCs were similar and included promoting a culture of safety (24/52, 46%, 95% CI 33%-59%) or improving patient care (23/52, 44%, 95% CI 32%-58%).

MMCs were held 1 to 3 (15/39, 38%, 95% CI 25%-55%) or 4 to 6 (19/39, 49%, 95% CI 35%-68%) times per year and were not open to other staff (Table 1). Programs (27/39, 69%, 95% CI 56%-86%) most commonly had resident presenters. Prominent themes discussed are unanticipated morbidity and physician-related errors (37/39, 92%, 95% CI 89%-100%) or system-related errors (37/39, 92%, 95% CI 78%-98%). Some programs (31/39, 79%, 95% CI 66%-91%) chose topics based on their teaching value. The most discussed issues included errors or delays in diagnosis (35/39, 90%, 95% CI 81%-100% and 34/39, 87%, 95% CI 74%-96%, respectively). Other error types were widely distributed (Table 1). Regardless of the meeting characteristic or format, 36 (92%, 95% CI 78%-96%) of 39 respondents reported tangible changes in their department/division because of their MMC.

Table 1. Morbidity and mortality conference (MMC) characteristics across dermatology residency programs in the United States.

Characteristic	Responses, n (%; n=39)	95% CI (%)
MMCs offered per year (n)		
1-3	15 (38)	25-55
4-6	19 (49)	35-68
≥7	5 (13)	6-27
Nursing or other ancillary staff participation		
Yes	9 (23)	12-40
No	30 (77)	N/A[a]
Presenter		
Resident	27 (69)	56-86
Other	12 (31)	N/A
Case type (multiple answers allowed)		
Unanticipated morbidity	37 (95)	89-100
Physician-related error	37 (95)	89-100
System-related error	36 (92)	78-98
Teaching value	31 (79)	66-91
Unanticipated mortality	26 (66)	50-80
Patient-related error	20 (51)	32-65
Error type (multiple answers allowed)		
Error in diagnosis	35 (90)	81-100
Delay in diagnosis	34 (87)	74-96
Lost/mishandled specimen	30 (77)	61-88
Inadequate monitoring	29 (74)	61-88
Failure to act on results	29 (74)	61-88
Transfer or handoff error	28 (72)	58-86
Patient barriers to care	28 (72)	58-86
Tangible changes within department due to MMC?		
Yes	36 (92)	78-96
No	3 (8)	N/A

[a]N/A: not applicable.

Discussion

This is the first study to assess MMC objectives and characteristics in US dermatology training programs and to report how programs with no MMCs fulfill the ACGME's QI requirement. Differences in the importance of MMCs in QI education and their primary objectives could explain why some programs choose alternative methods to fulfill the ACGME's QI requirements. While nearly all respondents with an MMC believed MMCs were important for QI education, some respondents with no MMCs disagreed. Similarly, more respondents in programs with MMCs (19/38, 50%, 95% CI 34%-65%) believed that the primary goal was to promote a culture of safety, while those with no MMCs (5/14, 36%, 95% CI 16%-61%) reported that the primary goal was likely to improve patient care (7/14, 50%, 95% CI 26%-73%).

Acknowledging mistakes and learning from them can make one feel vulnerable. Improper handling of MMCs can come across as accusatory and undermine their teaching value [3]. In fact, blaming increases the likelihood of medical errors [4], and openly admitting mistakes can cause emotional distress [3,5]. Other specialties select MMC cases based on teaching value rather than adverse events [6]. Although adverse events may have teaching value, some argue MMCs may not be as effective because it is hard to talk about medical mistakes rather than focusing on discussing interesting and unusual cases [3,7]. Discussing cases based on educational interest or teaching value may be easier, but they may not align with the scope of an MMC. In dermatology, cases were primarily selected because of unanticipated morbidity and physician- or system-related errors rather than for their teaching value. Topics like unanticipated mortality or patient-related errors may be less discussed because they may be less frequent or are underreported. Intimidating physicians may discourage dermatology residents from reporting adverse events [8]. An MMC model to promote error disclosure in dermatology has been proposed [9]. Despite differences in objectives and formats, however, 92% (36/39) of respondents reported tangible changes to their departments/divisions due to MMCs, emphasizing their importance in QI education. In conclusion, this is the first study to provide insight into the role and objectives of MMCs within dermatology.

Acknowledgments

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Authors' Contributions

All authors contributed to all aspects of the study conception and design. CVA-S, DSM, and EVB participated in the data collection and execution. All authors contributed to the data analysis, interpretation, and writing of this manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Survey sent to dermatology program directors asking about morbidity and mortality conferences at their program.
[DOCX File , 20 KB - derma_v6i1e45194_app1.docx]

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Abbreviations

ACGME: Accreditation Council of Graduate Medical Education
MMC: morbidity and mortality conference
QI: quality improvement

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Research Letter

Short-Form Medical Media: A Multi-Platform Analysis of Acne Treatment Information in TikTok Videos, Instagram Reels, and YouTube Shorts

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general dermatology; medical dermatology; acne; acne treatment; social media; TikTok; Instagram Reels; YouTube Shorts; YouTube; Instagram; video; dermatology; skin; patient education; health information; online information; dermatologist

Introduction

Social media has emerged as a medium for dermatologists to disseminate educational content [1-3]. Adolescents extensively use social media as a resource [1], with 75% of adolescent patients with acne reporting they consult social media for treatment information [4]. However, many dermatologic posts are low in educational quality, especially those made by non–board-certified dermatologists [2]. TikTok has emerged as a wide-reaching, short-form video platform used by millions of adolescents and adults worldwide [1,3]. The short-form video structure has since been emulated in Instagram Reels (IGR) and YouTube Shorts (YTS). However, little is known about how the quality of acne treatment content varies across these platforms and how they compare to each other.

Methods

To assess the content and educational quality of videos on acne treatment across TikTok, IGR, and YTS, we acquired the top 300 videos per platform from TikTok (search: "acne treatment"), IGR (search: "#acnetreatment"), and YTS (search: "#shorts + acne treatment") on March 9, 2023. Videos were excluded if they were irrelevant to acne treatment, noneducational, duplicate content, not in English, or made unavailable, as well as if they had hidden metrics or the treatment was unspecified. Video metrics and video engagement rate (VER) ([likes + comments per post]/[followers] × 100] were determined [3]. Video creators were stratified by creator type through review of their profile (dermatologist/dermatology practice, nondermatologist physician/medical clinic, layperson, influencer, or other). "Influencer" was defined as a layperson with at least 40,000 followers [3]. "Other" was categorized as having a specific profession or niche related to skin health (eg, skincare company, aesthetician). Two independent reviewers rated videos using the DISCERN Instrument, which allows health care providers to evaluate the quality of consumer health information, and the Global Quality Scale (GQS), which scores each video based on clinical usefulness [5]. Any discrepancies were handled by consensus. Following video exclusion, a multiple regression analysis was performed to evaluate the association between the platform (ie, TikTok, IGR, and YTS) and creator type with DISCERN and GQS scores, controlling for upload date.

Results

Of the videos analyzed, 32.8% (82/250) were created by dermatologists/dermatology practices, 5.60% (14/250) were by nondermatologist physicians/medical clinics, 27.2% (68/250) were by laypersons, 20.8% (52/250) were by influencers, and 13.6% (34/250) were by others. The average number of views per video was 1,639,969 on TikTok, 689,897 on YTS, and 27,192 on IGR. DISCERN and GQS scores were significantly higher for dermatologists than any other creator type across all platforms (Table 1). Posts from laypersons had a significantly higher VER compared to posts from dermatologists (Table 1). The most common therapies discussed were benzoyl peroxide, salicylic acid, adapalene, and preventative measures. IGR had a higher rate of discussion of complementary and alternative therapies compared to other platforms (Table 2).

Table 2 presents the number of treatment recommendations among those videos. Topical prescription medications included retinoids, antibiotics, antiandrogens, and steroids. Oral hormonal therapy included birth control pills and spironolactone. Procedural treatments included lasers or lights, chemical peels, extraction, and corticosteroid injections. Complementary and alternative therapies included treatments and suggestions that did not fall into any other category and were nonpreventative measures. Preventative measures included optimizing diet, avoiding pore-clogging makeup, managing stress, exercising, and avoiding picking at pimples.

Table 1. Analysis of the DISCERN score, the Global Quality Scale (GQS) score, and the video engagement rate (VER).

	DISCERN			GQS			VER		
	Score, mean	Coefficient (95% CI)	*P* value[a]	Score, mean	Coefficient (95% CI)	*P* value	Rate (%), mean	Coefficient (95% CI)	*P* value
Platform									
Instagram Reels (n=64)	36.9	Ref[b]		2.70	Ref		4.3	Ref	
TikTok (n=112)	40.8	1.99 (–0.19 to 4.17)	.07	2.94	–0.03 (–0.26 to 0.21)	.83	689.4	1025.87 (479 to 1572.75)	*<.001*
YouTube Shorts (n=74)	42.4	1.49 (–1.27 to 4.25)	.29	3.26	0 (–0.3 to 0.3)	.98	62.4	492.64 (–199.73 to 1185)	.16
Creator type									
Dermatologist/dermatology clinic (n=82)	46.1	Ref		3.88	Ref		80.7	Ref	
Nondermatologist physician/medical clinic (n=14)	41.6	–4.41 (–8.09 to –0.73)	*.02*	3.00	–0.88 (–1.28 to –0.49)	*<.001*	86.8	149.1 (–774.82 to 1073.01)	.75
Layperson (n=68)	36.3	–9 (–11.19 to –6.81)	*<.001*	2.41	–1.46 (–1.7 to –1.22)	*<.001*	973	1069.21 (519.91 to 1618.51)	*<.001*
Influencer (n=52)	37.5	–8.25 (–10.53 to –5.96)	*<.001*	2.60	–1.27 (–1.52 to –1.02)	*<.001*	70.3	–47.59 (–621.53 to 526.35)	.87
Other (n=34)	38.1	–7.67 (–10.28 to –5.06)	*<.001*	2.50	–1.37 (–1.65 to –1.08)	*<.001*	131	11.22 (–644.61 to 667.06)	.97

[a]Italicized values are significant.

[b]Ref: reference.

Table 2. Acne treatments specified across platforms TikTok, Instagram Reels, and YouTube Shorts and creator types.

	TikTok		Instagram Reels		YouTube Shorts	
	Dermatologist/dermatology practice (n=36)	Nondermatologist (n=76)	Dermatologist/dermatology practice (n=10)	Nondermatologist (n=54)	Dermatologist/dermatology practice (n=36)	Nondermatologist (n=38)
Treatments mentioned, N	97	176	16	84	109	67
Benzoyl peroxide, n (%)	18 (19)	22 (13)	2 (13)	3 (4)	20 (18)	8 (12)
Salicylic acid, n (%)	15 (15)	26 (15)	1 (6)	24 (29)	17 (16)	12 (18)
Other topical OTC[a] treatments, n (%)	21 (22)	53 (30)	4 (25)	41 (49)	19 (17)	24 (36)
Adapalene (OTC), n (%)	17 (18)	8 (5)	2 (13)	0 (0)	14 (13)	1 (1)
Topical prescription medications, n (%)	6 (6)	24 (14)	2 (13)	1 (1)	12 (11)	3 (4)
Oral antibiotics, n (%)	1 (1)	2 (1)	0 (0)	0 (0)	3 (3)	3 (4)
Oral hormonal therapy, n (%)	3 (3)	6 (3)	1 (6)	0 (0)	5 (5)	1 (1)
Isotretinoin, n (%)	7 (7)	5 (3)	0 (0)	0 (0)	6 (6)	1 (1)
Procedural treatments, n (%)	1 (1)	7 (4)	0 (0)	5 (6)	5 (5)	6 (9)
Complementary and alternative therapies, n (%)	0 (0)	8 (5)	3 (19)	6 (7)	0 (0)	2 (3)
Preventative measures, n (%)	8 (8)	15 (9)	1 (6)	4 (5)	8 (7)	6 (9)

[a]OTC: over the counter.

Discussion

Our study demonstrates that short-form social media platforms predominantly feature dermatology content created by nondermatologists; however, content produced by board-certified dermatologists was of significantly higher quality as evaluated by the DISCERN and GQS scores. Given the popularity of social media among adolescents with acne [1,4], there is an opportunity for more dermatologists to create content in these spaces where patients seek information. Although the rigorous outcome assessment with DISCERN and GQS scores is a strength of this study, given the rapidly evolving nature of social media, it will be important to reassess these findings over time.

Overall, content on these platforms heavily skewed toward over-the-counter (OTC) treatments, which may reflect the types of treatments that those with acne seek out on social media. However, for many with acne, OTC treatments will be insufficient and prescription therapy will be required. Consequently, dermatologists may find an opportunity on social media to better educate the community regarding prescription acne treatments and to correct misconceptions regarding how to approach OTC management of acne.

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Authors' Contributions

CJT created the study. CJT and DG scored the videos in the study. JT acquired all study videos and video metrics. JSB performed the statistical analysis and supervised the study design and implementation. JBL assisted in data interpretation and table design. CJT, DG, JBL, and JSB drafted the manuscript.

Conflicts of Interest

JSB has received consulting fees from Dexcel Pharma for work unrelated to the current submission. JBL is an editorial board member of *JMIR Dermatology*. The authors have no other conflicts to declare.

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Abbreviations

GQS: Global Quality Scale
IGR: Instagram Reels
OTC: over the counter
VER: video engagement rate
YTS: YouTube Shorts

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Short Paper

Altmetric Analysis of Dermatology Manuscript Dissemination During the COVID-19 Era: Cross-Sectional Study

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Abstract

Background: Alternative bibliometrics or altmetrics, is a measure of an academic article's impact on social media outlets, which is quantified by the Altmetric Attention score (AAS). Given a lack of data for altmetric trends during the COVID-19 pandemic, we conducted a comprehensive, multivariable analysis of top dermatology manuscripts published during this time period.

Objective: We aim to assess (1) the relationship between traditional bibiliometrics and Altmetrics and (2) factors associated with high AAS.

Methods: All abstracted articles published in the top-5 (ranked by SCImago Journal Rankings) peer-reviewed dermatology journals published in 2021 were included in our study. We collected AAS as the dependent variable and categorical predictor variables included journal title, whether a conflict of interest existed, open access status, whether the article was related to COVID-19 or skin-of-color research, and the type of research (eg, clinical, basic science, review, etc). Numerical predictor variables consisted of the impact factor of journal, total citations, and number of authors. Multivariable linear or logistic regression models were used.

Results: The relationship between AAS and citation number was significant by multivariable analysis during the COVID-19 pandemic (P<.001). Numerous factors, including studies related to COVID-19, whether the article was open access, title of the journal, and journal impact factor were also independently related to higher AAS (P<.002).

Conclusions: Our results validate the use of altmetrics as a complement to traditional bibliometrics, especially in times of widespread scientific interest. Despite existing in a complex realm of bibliometrics, there are also discernable patterns associated with higher AAS. This is especially relevant in the era of growing technologic importance and utility to assess the impact of scientific works within the general public.

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KEYWORDS

altmetric; media dissemination; citation number; bibliometric; attention score; social media

Introduction

With rapid web-based communication, scientific literature is more widely disseminated now than ever [1]. Traditional metrics (eg, citation number), however, do not account for the dissemination of scientific research through general public engagement. Altmetric Attention score (AAS) is based on both the quality and quantity of mentions in media sources not considered by traditional bibliometrics and is calculated by a point system, with each attention source being assigned a specific weight (Table 1) [2-4]. While traditional bibliometrics may take time to progress, AAS tracks the immediate spread of scholarly work and assesses dissemination shortly after publication [1].

Table 1. Contributors to Altmetric Attention Score and weight of each source.

Attention source	Weight	Modifier notes
News outlet	8	News outlets ranked by tiers. More popular news outlets have greater contributions (eg, NY times>2Minute Medicine)
Blog	5	—[a]
Policy document	3	+3 per policy document mention
Patent	3	+3 per patent in "different" jurisdictions
Wikipedia	3	Mention in multiple pages does not increase the score more than single page mention
Peer review (Publons, Pubpeer)	1	—
F1000	1	—
Syllabi	1	—
Facebook	0.25	Only a curated list of public Pages count
Reddit	0.25	—
Stack Exchange	0.25	—
YouTube	0.25	—
Twitter	0.25-1.1	Score range based on following (retweets have a 0.85x modifier): • Reach: increased with account follower number • Promiscuity: decreased with frequency that account tweets about research output • Bias: decreased with frequency that account tweets about research from the same domain (promotional intent)

[a]Not available.

There have been recent concerns related to inadequacies of solely relying on traditional bibliometrics to measure impact [5]. Thus, bibliometric research has been increasingly incorporating altmetric parameters. For example, a novel artificial intelligence bibliometric search engine model emphasized considering altmetric parameters as a strength of the model [6].

Fields including radiology, pathology, or orthopedic surgery, have shown strong relationships between AAS and traditional bibliometrics [7-9], representing a case for altmetrics to complement traditional bibliometrics [8]. In dermatology, however, evidence of this relationship is scarce [10].

The COVID-19 pandemic held unique ramifications for scientific article dissemination, resembling a sudden assault on an area of previously unknown vulnerability [11]. These novel circumstances made early identification of research outcomes crucial for guiding clinical decision-making, decreasing the effectiveness of traditional bibliometrics [11].

Given the novel circumstances, we suspected that there may be unique AAS trends in dermatology publications during the COVID-19 pandemic. With the increasing usage of social media in disseminating dermatologic information [12] and a scarcity of data on AAS trends in dermatology during the pandemic, we sought to perform a comprehensive Altmetric analysis to assess the following during this time period:

1. What is the nature of the relationship between AAS and citation number?
2. What factors are associated with a higher AAS score?

Methods

All full-length, abstracted articles published in the top-5 peer-reviewed dermatology journals ranked by the SCImago Journal Rankings (SJR) from 2021 were included in our study. As a newer generation measure of journal impact, SJR has been deemed a more reliable measure of impact by accounting for factors such as dilutional citations (eg, editor self-citations) which can falsely inflate a journal's impact factor (IF) [13].

For each journal, we reviewed every abstracted manuscript from January-December issues of 2021 and AAS scores were collected using the Altmetric Bookmarklet tool (Euan Adie) [14]. Other article-specific parameters were gathered as independent variables. The categorical independent variables included journal title, whether a conflict of interest existed, open access status, whether the article was related to COVID-19 or skin-of-color research, and the type of research (eg, clinical, basic science, review, etc). Numerical independent variables consisted of IF of journal, total citations, and number of authors.

All articles were accessed in a 2-week window in June 2022 to avoid variability in AAS changes.

Univariable linear regression or Kruskal-Wallis testing was used, and significant predictors of AAS were incorporated into a multivariable linear regression or quasi-Poisson logistic regression model, respectively. Calculations were done in RStudio (version 2022.02.0; Joseph J. Allaire).

Results

We analyzed 747 articles, with an average AAS of 24.2. Articles related to COVID-19 or skin-of-color research consisted of 3.6% (27/747) and 1.1% (8/747) of the total article population, respectively. Clinical research was the most popular article type (494/747, 66.1%; Table 2). In our multivariable logistic regression model, “JAMA dermatology” predicted higher AAS and “Journal of the European Academy of Dermatology and Venereology” predicted lower AAS (*P*<.001). The presence of conflicts of interest and open access articles predicted higher AAS (*P*<.001). COVID-19 research also predicted higher AAS (*P*<.001), despite accounting for only 4% (27/747) of total publications (Table 2). In our multivariable linear regression model, both citation number and IF independently correlated with AAS, accounting for 20% of the variation in AAS (*P*<.001; Figure 1).

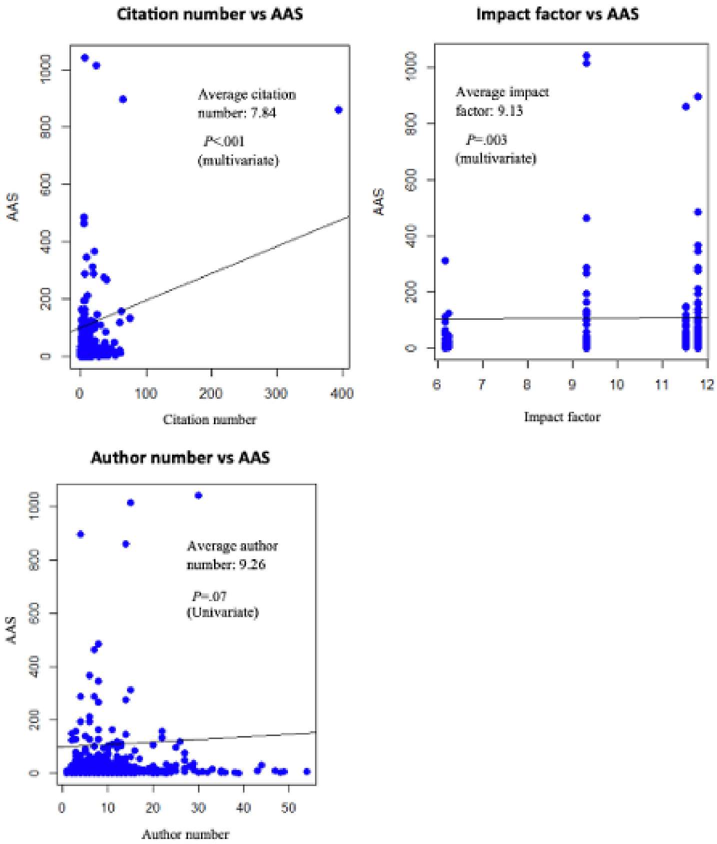
Table 2. Relationships between Altmetric Attention Score (AAS) and categorical manuscript factors.

	Count (%)	Average Altmetric Attention Score	95% CI	Univariable *P* Value	Multivariable *P* Value
Total	747 (100)	24.2	18.3-30.2	—[a]	—
Journal					
British Journal of Dermatology (BJD)	179 (24.0)	29.5	12.2-46.8	.27	—
American Journal of Clinical Dermatology (AJCD)	68 (9.1)	9.26	5.29-13.2	.32	—
JAMA Dermatology [b]	107 (14.3)	66	44.5-87.5	<.001	<.001
Journal of the American Academy of Dermatology (JAAD)[b]	195 (26.1)	19.9	10.8-28.9	<.001	.72
Journal of the European Academy of Dermatology and Venereology (JEADV)[b]	198 (26.5)	6.31	2.79-9.83	<.001	<.001
Conflicts of interest[b]					
Yes	376 (50.3)	32.7	22.7-42.8	.002	.002
No	371 (49.7)	15.6	9.4-21.8	.002	.002
Open access[b]					
Yes	285 (38.2)	39.3	25.7-52.8	.001	<.001
No	462 (61.8)	15	10.3-19.6	.001	<.001
COVID-19–related?[b]					
Yes	27 (3.6)	194	60.5-327.5	<.001	<.001
No	720 (96.4)	17.9	14.7-21.0	<.001	<.001
Skin-of-color related?[b]					
Yes	8 (1.1)	87.2	–21.12 to 195.6	.01	.41
No	739 (98.9)	23.5	17.6-29.5	.01	.41
Article type					
Systematic Review	118 (15.8)	15.4	8.70-22.2	.58	—
Narrative Review	84 (11.2)	8.46	5.1-11.9	.06	—
Case report or series	14 (1.9)	93.9	–42.4 to 230.3	.11	—
Clinical[b]	494 (66.1)	28.4	13.1-26.0	.03	.34
Basic science[b]	31 (4.1)	5.55	3.3-7.8	.05	.15
Other	6 (0.8)	8.67	–7.6 to 25.0	.39	—

[a]Not available.

[b]Indicates variables found significant by univariable Kruskal-Wallis testing that were incorporated into the multivariable logistic regression model.

Figure 1. Relationships between AAS and quantitative manuscript factors. Plots of AAS against citation number, impact factor (IF), and author number with a univariable regression line. Both citation number and IFs were significant by univariable linear regression and incorporated into the multivariable regression model. Overall multivariable regression model: AAS=IF*3.43+Citation Number*2.08–25.24; Adjusted R2=0.2; *P*<.001. AAS: Altmetric Attention Score.



Discussion

The magnitude of the relationship between AAS and citation number is not well quantified [1], but our multivariable model (AAS=IF*3.43+Citation Number*2.08–25.24, R^2=0.2, *P*<.001) quantifies the strength of this relationship.

Previous studies have analyzed the attributes of the top COVID-19 articles [15,16], but none have directly compared the AAS scores of COVID-19–related versus non–COVID-19–related articles. We found that despite consisting of only 4% (27/747) of the manuscripts published, the average AAS for COVID-19–related articles was nearly 10-fold higher than non–COVID-19–related articles, which was significant by multivariable analysis (*P*<.001). The COVID-19 pandemic represents the first international, widespread assault on human health in the modern era, resulting in a frantic race to understand and combat the novel coronavirus by scientists and laypeople alike. Thus, it is natural that the popularity of any manuscript related to COVID-19 would be reflected in both traditional and alternative bibliometrics.

Outside of studies related to COVID-19, we found that AAS was associated with citation numbers during this period. In dermatology, a previous study did not find a significant association between AAS and citation number [10], suggesting that the scientific interest sparked by the COVID-19 pandemic potentially strengthened the relationship between alternative and traditional bibliometrics. Given this close relationship, our findings support the potential for use of AAS complimentary to traditional bibliometrics especially in eras of global interest in scientific works.

Web of Science (WoS) is a database distinct from Scopus, the main database used in SJR. We used the Scopus or SJR database to determine the top-5 dermatology journals because journal rankings by discipline in WoS are not publicly published. Additionally, Scopus or SJR includes a broader spectrum of journals and provides a faster citation analysis [17]. Nonetheless, assessing the differences between altmetrics in top WoS versus Scopus or SJR rankings is an interesting direction for future research as both databases have unique attributes [17].

There are multiple reasons for the use of AAS. For researchers, altmetrics may be a clue for an urgent topic to investigate. For community members, the use of altmetrics promotes a form of patient-centered care, where the viewpoints of the general public are considered by investigators through the AAS. Greater consideration of altmetrics by current researchers in their scholarly pursuits may result in increased engagement with the future generation of researchers more likely to be on social media channels considered by the altmetric scoring system, thus inspiring young or aspiring researchers to focus on research topics particularly salient to society.

The profiles of the authors that publish in journals with higher AAS were outside the scope of our study as we focused on specific articles rather than authors. However, we found that the presence of conflicts of interest was independently related to higher AAS. We suspect that authors that publish in journals with greater AAS may have more funding or affiliations, resulting in an increased likelihood of conflicts of interest. In fact, AAS patterns seem to emerge early in training, as dermatologists from medical schools with greater research funding had significantly higher total AAS in their early research papers than those who did not (67.9 vs 22.9 P<.001) [18]. Other author-specific parameters, such as H-index may also be correlated to higher AAS publications.

Limitations of our analysis include the exclusion of nonabstracted articles, which may have different AAS patterns. It is also important to note that AAS should only complement and not replace other traditional metrics, as they are not a traditional marker of scientific importance and may further legitimize sensationalism if taken in isolation [1]. Nonetheless, we outline a model that demonstrates a significant relationship between AAS and traditional bibliometrics showing that there are several independent predictors of AAS of dermatology articles published during the COVID-19 pandemic.

The field of bibliometrics is undoubtedly complex, with multiple databases and methods to assess impact, and external forces, such as that of the COVID-19 pandemic, that can affect bibliometric patterns. Altmetrics are emerging as a unique tool in bibliometrics with utility that is especially relevant with the accessibility of technology in the modern era. There are multiple reasons to consider the public engagement of scientific manuscripts through alternative bibliometrics, including understanding of topics that are currently influential within the status quo, a focus on patient-centered care, and the potential to inspire future generations of scientists. While our work clarifies relationships between altmetrics and manuscript-specific factors such as citation number, further research is required to assess the relationship between author-specific, rather than manuscript-specific predictors of higher AAS.

Conflicts of Interest

None declared.

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Abbreviations

AAS: Altmetric Attention Score
IF: impact factor
SJR: SCImago Journal Ranking
WoS: Web of Science

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Research Letter

A Review of Software and Mobile Apps to Support the Clinical Diagnosis of Hansen Disease

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Abstract

This scoping review indicates a lack of scientific articles that specifically explore software and mobile applications designed to assist in the clinical diagnosis of leprosy, and our findings have provided insights into the available tools, their usage methods, and the benefits offered by health technologies.

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KEYWORDS

software; mobile apps; leprosy; medical informatics; Mycobacterium leprae; clinical diagnosis; Hansen disease; mHealth; mobile health; mobile app; Hansen; dermatology; scoping review; skin; diagnosis; diagnostic

Introduction

Hansen disease, or leprosy, is a chronic infectious disease caused by *Mycobacterium leprae* (*M leprae*). It mainly affects the skin's superficial nerves and peripheral nerve trunks and can also impact the eyes and internal organs. If untreated, leprosy becomes contagious and can lead to physical disabilities. Additionally, it imposes significant social, emotional, and economic burdens [1].

The diagnosis of leprosy is based on assessing clinical presentation, including signs and symptoms. Leprosy cases are classified into two types for treatment: paucibacillary and multibacillary. Paucibacillary cases have 1 to 5 skin lesions and no bacilli in a bacilloscopy, whereas multibacillary cases have more than 5 skin lesions and/or the presence of bacilli in a bacilloscopy [1,2].

The World Health Organization (WHO) encourages early leprosy detection and supports the development of mobile health (mHealth) innovations for this purpose [2]. The use of computational tools in health care is expanding, providing health care professionals with enhanced agility and precision and improving the overall patient-physician experience [3,4].

This study aimed to identify the scientific literature on software and mobile apps designed to assist in the clinical diagnosis of leprosy and describe their main characteristics.

Methods

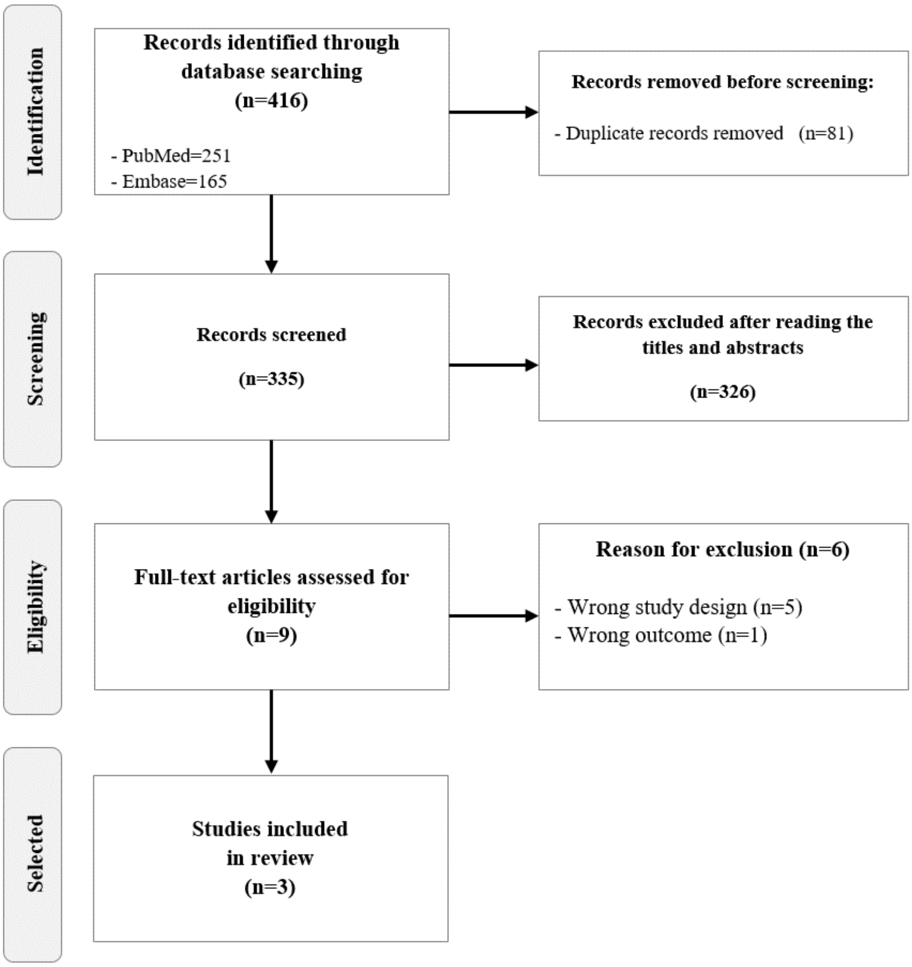
We used the methodology developed by Arksey and O'Malley [5], following the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) checklist. This included defining the eligibility criteria, devising a search strategy (Multimedia Appendix 1), selecting sources of evidence (PubMed and Embase), collecting data, and synthesizing results. All steps of the methodology were documented in a previously registered protocol [6].

Results

Selection of Studies

In step 1, a database search yielded 416 publications. After removing duplicates (n=81), step 2 involved an eligibility assessment based on title and abstract analysis. Step 3 included reading the full texts of the selected studies. Excluded articles were mainly protocols or conference abstracts. Ultimately, 3 publications were analyzed in this scoping review [7-9] (Figure 1).

Figure 1. Flowchart outlining the study selection and inclusion process.



Characteristics of the Included Studies

The studies included in this review were published between 2018 and 2021 (Table 1). Two were initiatives conducted in Brazil [8,9], and one was from the not-for-profit organization Netherlands Leprosy Relief [7]. One of the studies analyzed [8] used a computerized method to assess the Mitsuda test. This test involves assessing the skin's immune response and can aid in identifying individuals at risk of developing illness upon exposure to *M leprae*. SkinApp, as described by Mieras et al [7], was still in development and was undergoing updates based on applicability tests, despite having already undergone several development stages. De Souza et al [9] proposed a cross-platform app, comprising a vast database to assist in the screening and differentiation of leprosy types. The Brazilian database Information System for Notifiable Diseases was used to develop this app.

Table 1. Aims and outcomes of the included studies.

Reference and year of publication	Study aims	Software/app	Methodology used by the software/app	Positive aspects	Negative aspects
Mieras et al [7], 2018	• To describe the development process of a mobile phone app that supports peripheral health workers in diagnosing and treating skin diseases in resource-poor settings	• SkinApp	• Algorithm to support the process of diagnosis • Descriptions of skin diseases, supporting photos, as well as treatment and referral advice	• Training tool • Easy to use • Clear treatment advice (ie, narrative and illustrative content was considered clear) • Clinical validation of a patient with a skin disease • Available in English and Portuguese (Android, Google Play Store; iOS, Apple App Store) • Free of charge • Can be used offline	• Needs to improve intelligibility; a glossary explaining dermatological terminology could help • A reporting option was also mentioned as a possible improvement • Not all treatment options may be available • The studies that were carried out did not address the performance of SkinApp as a diagnostic tool
Alecrim et al [8], 2019	• To compare the results between the standardized reading and the total area of the Mitsuda test obtained by a computerized method that was structured by associating the digital dermatoscopy, the Dermatology Web system, and the Image Tool 3.0 software	• Dermatology Web + Image Tool 3.0	• Dermatology Web: photographic documentation of dermatological treatments and photo storage • Image Tool 3.0: view, edit, analyze, process, save, and print images	• Dermatology Web: can be used on any mobile platform or computer connected to the internet; ensured security and confidentiality of data stored in medical records • Image Tool 3.0: area calculation; image calibrated in millimeters; delineation of the contours of the reaction; results in a total area in square millimeters • Dermatology Web + Image Tool 3.0: improves reading precision; allows for the computerization of records	• Dermatology Web + Image Tool 3.0: functions are not centralized in a single software
De Souza et al [9], 2021	• To develop a cross-platform app for leprosy screening based on artificial intelligence	• App for leprosy screening	• Supervised learning (random forest)	• Improves coverage and scalability to the health service regarding the choice of an appropriate treatment for leprosy • Accessibility via mobile or desktop option • Speed, scalability, and broadcasting to fight leprosy without compromising accuracy • High accuracy (92.38%), sensitivity (93.97%), and specificity (87.09%)	• Not available without an internet connection • Quality of the data used by the app depends on many factors (quality of the items requested by the forms and their correct interpretation, correct clinical assessment of the patient, proper filling out of the forms)

Discussion

Principal Findings

This review indicates a scarcity of software and mobile apps specifically designed to assist in the clinical diagnosis of leprosy, with their development documented in scientific articles. Despite their promising attributes for clinical practice, it is advisable to test these technologies using controlled trials to determine their actual impact.

The Global Leprosy Strategy 2021-2030 [2], initiated by the WHO, emphasized the importance of developing eHealth innovations to improve the diagnosis and care of patients with leprosy. Others have also supported the potential of digital technologies in health care [3,4]. As a result, our study aligns with the WHO initiative and offers valuable insights for enhancing strategies in this domain.

In 2020, a total of 127,396 new cases of leprosy were reported worldwide. As a result, Brazil ranks second globally in terms of leprosy cases, with India having the highest number of cases [2]. These data may help explain why the majority of the software and apps described in our study was developed in Brazil.

It is important to note that not all health technology tools have their development documented in scientific studies [10], and it is possible that relevant evidence might not have been indexed in the databases we used for our search. Consequently, some initiatives [10] did not meet our inclusion criteria. Nevertheless, our study underscores the importance of documenting technological advancements in scientific studies and encourages their implementation through controlled trials.

Limitations

Our study involved searching for relevant studies using 2 databases. We did not use additional health databases or multidisciplinary databases, which may have influenced our results. Furthermore, we specifically focused on publications related to the clinical diagnosis of leprosy, excluding studies pertaining to laboratory diagnosis and disease follow-up. As a result, the scope of our findings was limited.

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Authors' Contributions

WDLC, GJA, LMACdS, LRAdS, DdCBD, FF, and AMdO contributed to the writing of this manuscript as well as data acquisition, analysis, and interpretation. AMdO and MACF contributed to the study concept and design, writing of the manuscript, and critical review of the manuscript for important intellectual content. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategy for databases.
[DOCX File , 15 KB - derma_v6i1e47142_app1.docx]

Multimedia Appendix 2
PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) checklist.
[PDF File (Adobe PDF File), 150 KB - derma_v6i1e47142_app2.pdf]

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Abbreviations

mHealth: mobile health
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews
WHO: World Health Organization

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Research Letter

A Descriptive Analysis of Dermatology Content and Creators on Social Media in the Philippines

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KEYWORDS

social media; dermatology; dermatologist; creator; content; impact; Philippines; Facebook; Instagram; Twitter; TikTok; YouTube

Introduction

The use of social media in health information dissemination is an emerging concept, and the quality and reliability of dermatology-related content pose great challenges for creators and end-users, particularly in the Philippines where 80.7% of the population are active social media users [1]. Exposure to and awareness of dermatology health information on social media largely influences the behaviors and practices of populations with access to the internet and social media [2]. Our objective was to describe the content and creators of the most popular Filipino-made dermatology-related image and video posts on Facebook, Instagram, Twitter, TikTok, and YouTube.

Methods

A web-based search and analysis based on the methods used by Nguyen et al [3] on TikTok were conducted using hashtag terms related to 10 diagnoses (#acne, #alopecia, #cyst, #rash, #eczema, #dermatitis, #tinea, #leprosy, #psoriasis, and #warts), 10 procedures (#botox, #filler, #acnescars, #tattooremoval, #hairremoval, #whitening, #laser, #facelift, #steroidinjection, and #hairtransplant), and 5 general terms (#dermatology, #dermatologist, #boardcertifieddermatologist, #skincare, and #skindisease). The top 40 posts from each of the 25 hashtag queries were sampled from the 5 social media platforms, producing a total of 5000 posts for analysis.

Results

Figure 1 shows that more health care providers were identified as creators on Instagram (n=226, 48.1%) and TikTok (n=145, 26.9%) compared to YouTube, Twitter, and Facebook. Specifically, the majority of health care provider creators were board-certified dermatologists (n=154, 64.4% on Instagram; n=99, 66.9% on TikTok; n=25, 71.4% on Twitter; n=7, 87.5% on Facebook; n=36, 100% on YouTube) (Figure 2). This is a substantially higher proportion of board-certified dermatologist creators compared to the findings in previous studies on Instagram where they only comprised 4% of creators [4] but is similar to the findings of studies on TikTok [3] and YouTube [5]. This implies that more Filipino board-certified dermatologists have Instagram and TikTok accounts, making them more visible on these platforms. Laypeople, on the other hand, were the major creators on Twitter, YouTube, and TikTok, implying that dermatology-related data from these platforms may not be reliable or evidence based [2]. Businesses and the pharmaceutical industry comprised the majority of creators on Facebook, implying it is primarily used for business promotions and transactions.

Figure 1. Distribution of content creators (N=2635).

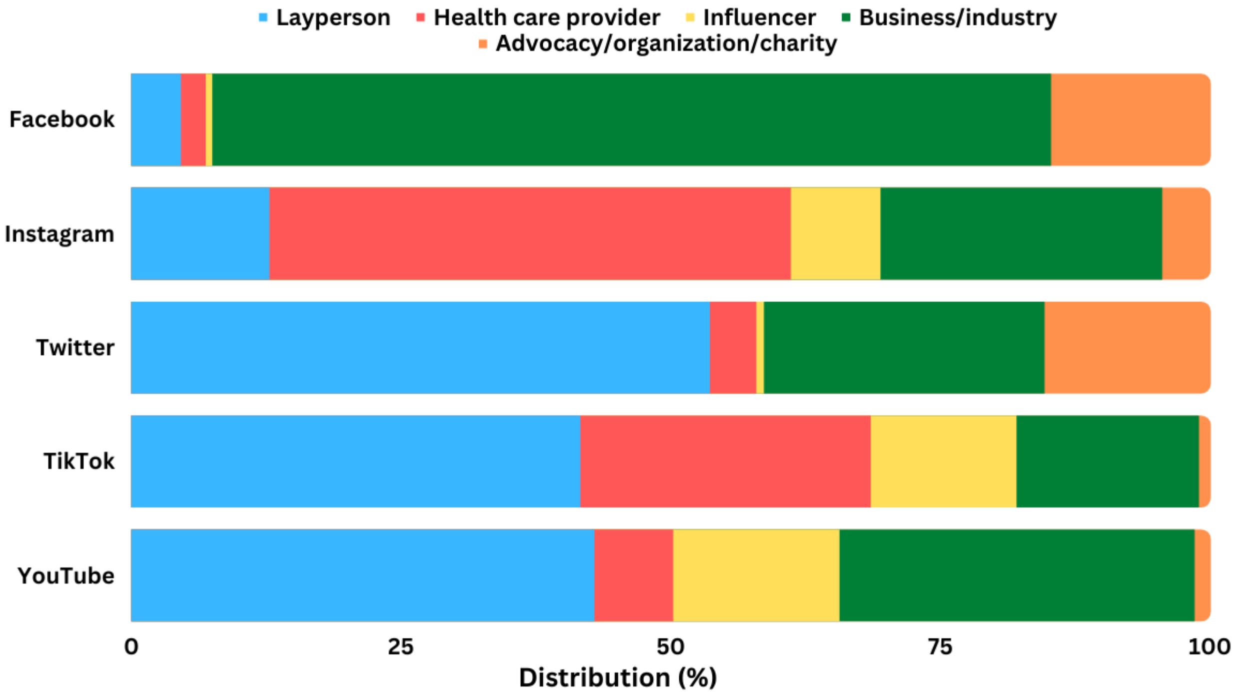
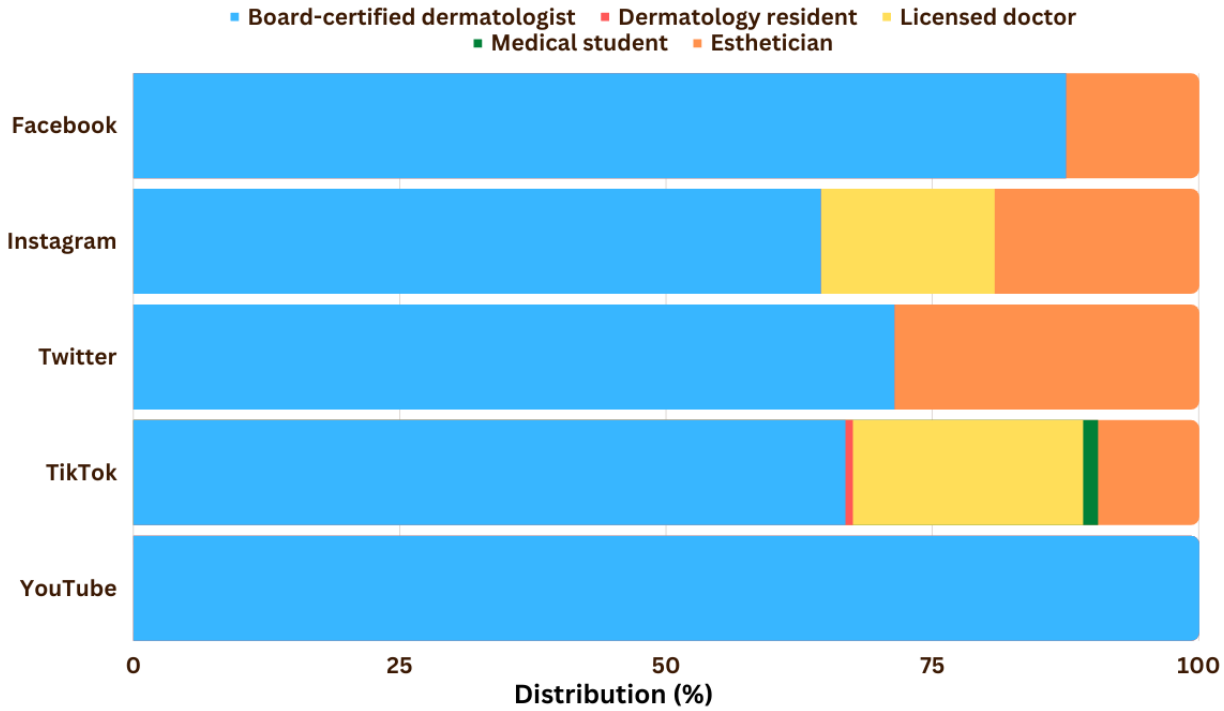


Figure 2. Distribution of health care provider creators (n=465).



Discussion

Promotional content comprised the majority of posts across all social media platforms, which contrasted a previous study on TikTok where personal posts by laypeople garnered the highest proportion of creators [3]. Most educational content comprised videos that featured dermatology topics in educational shows, news reports, tutorial videos, and documentaries on skin conditions. This is similar to a study on YouTube [5], where educational videos were found to be more popular among dermatology-related content.

The findings of this study indicate that there is heterogeneity in popular dermatology-related content, creators, and their impacts across social media platforms. Some platforms, such as Instagram, have more health care provider content creators, while others such as Twitter and Facebook, have more laypeople and business/industry creators, respectively. Although board-certified dermatologists make up the majority of health care provider content creators on all platforms, there is still a need to augment their social media presence to further facilitate the provision of evidence-based information. There is also an apparent lack of social media presence from reliable sources on YouTube, Twitter, and Facebook, which necessitates more intervention in these platforms. Promotional content was more common in the majority of search query results in all social media platforms used, followed by educational content, patient experience, and entertainment. Overall, social media truly possesses the power and convenience of access to dermatology health information, and measures to promote and maximize evidence-based content and creators must be implemented, particularly in the Philippines.

Conflicts of Interest

None declared.

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Research Letter

Evaluating the Global Digital Impact of Psoriasis Action Month and World Psoriasis Day: Serial Cross-Sectional Study

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KEYWORDS

psoriasis; psoriasis awareness; social media; digital health; Psoriasis Action Day; World Psoriasis Day; skin; dermatology; awareness; health promotion; trends; Twitter; tweets; cross-sectional

Introduction

Psoriasis is one of the most common chronic inflammatory skin disorders, affecting over 100 million people globally [1]. The chronic nature of psoriasis contributes to its overall burden, leading to a significant psychological and social impact on those who are affected [2]. Hence, with the objective of educating, dismissing stereotypes, and providing information about timely management by involving the global community, Psoriasis Action Month (previously Psoriasis Awareness Month) in August and World Psoriasis Day on October 29 are recognized worldwide. Social media platforms have developed into powerful information sources that influence opinions about medicine in a variety of ways [3]. We evaluated the digital impact of Psoriasis Action Month and World Psoriasis Day by studying trends in total tweets posted, identifying top keywords, understanding collaborations via a network analysis, and studying the global reach of these awareness initiatives to steer future policy development.

Methods

In this serial cross-sectional analysis, we used broad search queries to study the total number of tweets posted from 2014 to 2022 targeting psoriasis, Psoriasis Action Month, and World Psoriasis Day via Sprout Social. Being consistent with previous studies [4-7], a social network analysis using the ForceAtlas2 model was conducted to contextualize the tweets via Socioviz. Each entity was depicted as a node with a size set proportional to its frequency in tweets. Similar colors depicted sets of arguments that are frequently associated together. Collaboration proportion was studied using connections between users. Beyond social media, we analyzed Google Trends relative search volume data by region from 2014 to 2022 to gauge interest in Psoriasis Action Month and World Psoriasis Day without any language or geographic restrictions.

Results

A total of 3384 and 1925 tweets were identified in 2022 related to Psoriasis Action Month and World Psoriasis Day, respectively, during the specified time period, showing a change of +67.68% and –15.75%, respectively, when compared to total tweets in 2021 (Table 1). Tweets related to Psoriasis Action Month and World Psoriasis Day constituted 7.99% and 31.18%, respectively, of the total tweets posted about psoriasis during their respective time range in 2022. Yearly trends in the total tweets about Psoriasis Action Month showed a plateau over the last few years, but volumes have now increased. On the other hand, tweets on World Psoriasis Day were previously increasing annually but have now declined in a somewhat cyclical way. Interestingly, more users tweeted about World Psoriasis Day than Psoriasis Action Month between 2019 and 2021. The network analysis showed that the collaboration proportion among the top 100 influencers was 42%. The most frequently associated keywords were "fries," "eczema," "butter," "scrub," and "health." The most frequently associated hashtags were "#psoriaticarthritis," "#psoriasisawarenessmonth," "#medtwitter," "#splinterhemorrhage," and "#clubbing." Additional themes linked to other skin diseases and chronic illnesses, skincare, and management options were identified (Figure 1). The Google Trends analysis demonstrated that the majority of web searches were from the American, European, Russian, South Asian, and Australian regions with limited involvement from African and Central Asian countries.

Table 1. Tweets posted about psoriasis, Psoriasis Action Month, and World Psoriasis Day from 2014 to 2022.

Year	Total tweets about Psoriasis Action Month (August 1-31; search query 1[a])	Total tweets about psoriasis (August 1-31; search query 2[b])	Proportion[c] (%)	Total tweets about World Psoriasis Day (October 28-30; search query 3[d])	Total tweets about psoriasis during (October 28-30; search query 2)	Proportion[e] (%)
2014	995	15,709	6.33	1827	9466	19.30
2015	1420	23,884	5.95	2614	12,532	20.86
2016	1905	20,063	9.50	1739	10,840	16.04
2017	1684	16,416	10.26	1503	7263	20.69
2018	2363	23,228	10.17	2203	7159	30.77
2019	2342	61,354	3.82	2363	8466	27.91
2020	1882	32,574	5.78	2977	8435	35.29
2021	2023	23,067	8.77	2285	6333	36.08
2022	3384	42,353	7.99	1925	6174	31.18

[a]Search query 1: psoriasis awareness month OR #psoriasisawarenessmonth OR psoriasis month OR #psoriasismonth OR psoriasis action month OR #psoriasisactionmonth OR psoriasis awareness OR #psoriasisawareness.

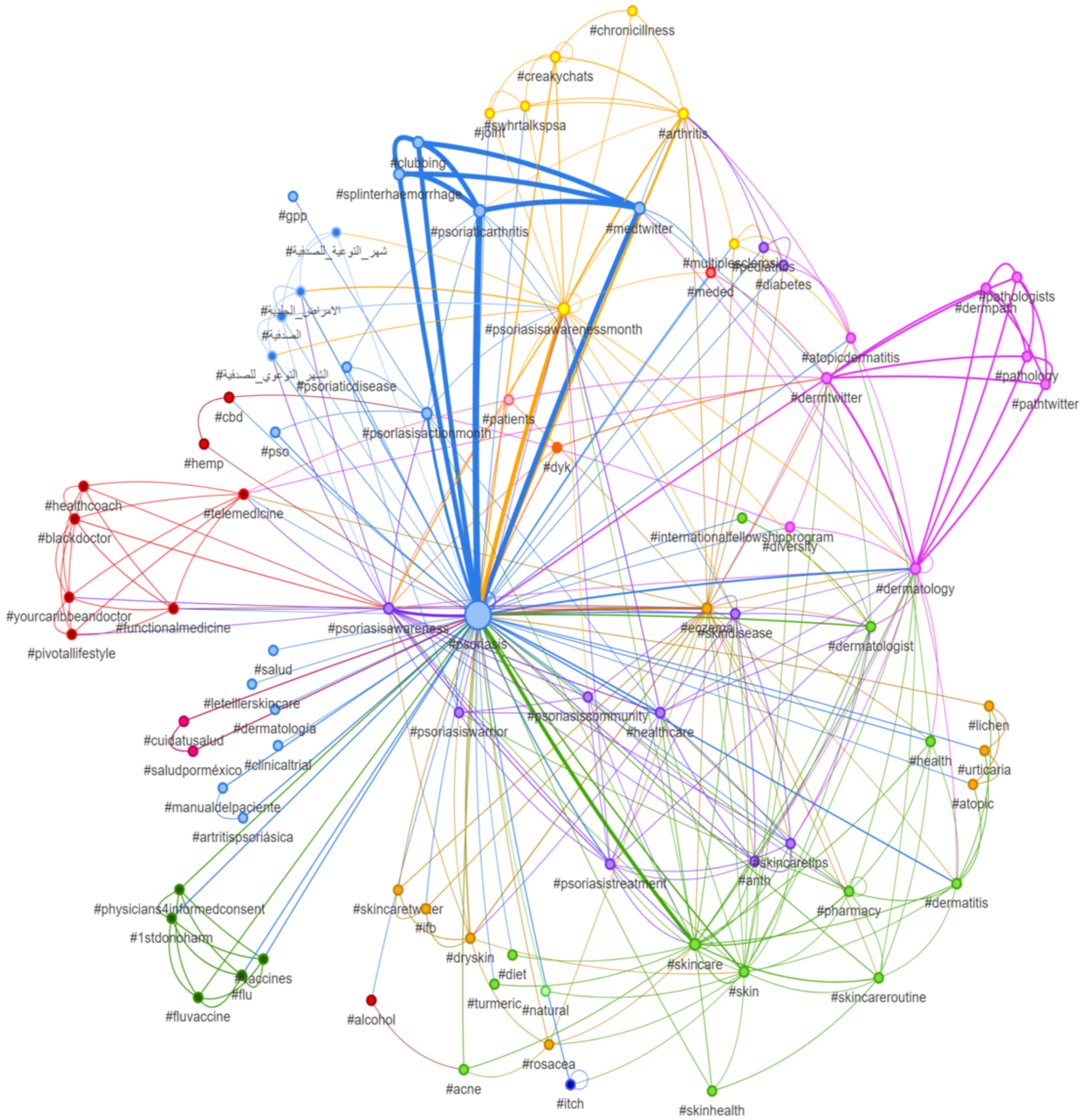
[b]Search query 2: psoriasis OR #psoriasis.

[c]Proportion was calculated as search query 1/search query 2 × 100.

[d]Search query 3: world psoriasis day OR #worldpsoriasisday OR psoriasis awareness day OR #psoriasisawarenessday OR psoriasis day OR #psoriasisday OR psoriasis awareness OR #psoriasisawareness.

[e]Proportion was calculated as search query 3/search query 2 × 100.

Figure 1. Social network analysis of tweets related to psoriasis during Psoriasis Action Month using the ForceAtlas2 model (search query: psoriasis OR #psoriasis).



Discussion

The limited presence of psoriasis-related content on digital media platforms highlights a missed opportunity to effectively engage a wider audience and disseminate accurate information about psoriasis [8]. Our ballpark estimates highlight the need to increase collaboration, targeted efforts, and partnerships among low-, middle-, and high-income countries especially in Africa, as shown in previous publications [9,10]. Because of the greater cumulative reach, one could naturally assume that an awareness month will have a greater impact than a 1-day campaign. However, the case of World Psoriasis Day recently amassing more reach than Psoriasis Action Month needs to be further studied, and constructive feedback should be implemented for other similar events. More emphasis needs to be given to prioritizing event-specific hashtags and promoting collaboration in digital toolkits to amplify messages on social media, which may also later help to assess impact and plan ahead.

The unavailability of data sets from other social media platforms, such as Facebook, Instagram, and TikTok, due to a lack of access to their application programming interface is a limitation of this study. Furthermore, Google Trends provides only relative search volume data, which are not equivalent to absolute values. It is crucial to study linked keywords and hashtags within the appropriate context as these could represent noise, off-topic posts, or misclassifications as seen in the associated hashtag “#fries.” Considering the dynamic nature of online media, statistical techniques such as controlled experiments, data normalization, and segmented analysis are needed in future large-scale studies to mitigate platform-induced biases and study user behavior shifts to collect detailed insights.

Data Availability

The data presented in this study are included in the paper. Further inquiries can be directed to the corresponding author.

Conflicts of Interest

None declared.

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Research Letter

Assessing Public Interest in Mpox via Google Trends, YouTube, and TikTok

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Abstract

Public response to the recent Mpox outbreak was analyzed using internet search trends and social media posts.

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KEYWORDS

monkeypox; Mpox; social media; internet; Google Trends; YouTube; TikTok; dermatologists; dermatology; dermatologist; awareness; interest; infectious; sexually transmitted disease; STD; sexually transmitted infection; STI; sexual transmission; sexually transmitted; outbreak; outbreaks; information seeking; information behaviour; information behavior; search; information quality; communicable

Introduction

With the advent of Mpox (formerly known as monkeypox), it is crucial for patients to better understand its symptoms and dermatological presentations. Social media platforms are accessible sources that can enhance disease awareness and knowledge of treatment options [1]. Unfortunately, video content on social media is not screened prior to dissemination, so misinformation on Mpox has increased tremendously. Content created by physicians is needed to increase awareness of the disease and its treatment options. We sought to evaluate the quality of social media posts related to Mpox on TikTok and YouTube.

Methods

We used Google Trends to search for the term "monkeypox" to assess recent changes in searches between May and July 2022. YouTube and TikTok searches were performed with the term "monkeypox." Results were evaluated for the presence or absence of a physician, and videos were assessed using DISCERN criteria. The Student *t* test was used to compare mean DISCERN scores between physician and nonphysician creators. DISCERN is a tool that is useful for evaluating consumer health information [2]. Previous studies have shown it is also useful in determining the quality of social media posts on health-related topics [3]. Only the first 50 videos on YouTube and TikTok were analyzed in order to replicate the general audience viewing experience. Videos not in English, videos without words, and duplicate videos were excluded.

Results

We found that Google searches for the term "monkeypox" correlated with the prevalence of cases by state using Google Trends and data from the Centers for Disease Control and Prevention (Pearson r=0.74, P<.001) (Multimedia Appendix 1). Of the 50 TikTok videos analyzed (Table 1), 32 (64%) videos featured nonphysicians and 18 (36%) featured physicians. Videos featuring nonphysicians had an average DISCERN score of 1.82 (SD 0.44) whereas physician-created videos had an average score of 2.56 (SD 0.57) (P<.001).

Table 1. Overview of Mpox content on TikTok.

	Videos, n	Number of views, mean (SD)	Number of likes, mean (SD)	Number of comments, mean (SD)	DISCERN score, mean (SD)
Content creator					
Physician	18	432,800 (503,684)	32,529 (53,659)	1038.83 (1518)	2.56 (0.57)
Nonphysician	32	1,578,069 (2,209,723)	169,024 (307,217)	2286 (3260)	1.82 (0.44)
Video type					
Educational	24	599,654 (1,091,832)	41,193 (74,693)	935.33 (4176)	2.41 (0.55)
News	16	1,995,819 (2,751,170)	258,969 (409,353)	3352 (4176)	1.82 (0.29)
Personal testimony	10	1,196,380 (1,111,310)	86,214 (93,152)	1576.80 (1656)	1.77 (0.72)

Our analysis revealed that physician-created YouTube videos had a mean DISCERN score of 3.31 (SD 1.15), while nonphysician videos had a mean score of 1.99 (SD 0.36) (Table 2). However, the difference between the DISCERN scores was not statistically significant (P=.35). Of the 50 YouTube videos evaluated, 37 videos featured nonphysicians describing the outbreak in the United States, while only 2 videos were created solely by physicians, which likely caused limitations in the DISCERN analysis. A total of 11 videos were excluded from the analysis: 2 were duplicate videos, 1 was a YouTube "short," and 8 videos were created by news sources that featured physician speakers.

Table 2. Overview of Mpox content on YouTube.

Content Creator	Videos, n	Number of views, mean (SD)	Number of likes, mean (SD)	Number of comments, mean (SD)	DISCERN score, mean (SD)
Physician[a]	2	250,803 (138,908)	7100 (3652)	980 (550)	3.31 (1.15)
Nonphysician[b]	37	27,066 (83,888)	361 (1144)	304.73 (507)	1.99 (0.36)

[a]The video type was "educational" for both videos.

[b]The video type was "news" for all videos.

Discussion

Principal Findings

Based on the Google Trends analysis, there was an increase in public interest for Mpox, which occurred during the disease outbreak. This shows an increase in community response to the Mpox outbreak by searching for additional information via Google.

Analysis of videos on YouTube and TikTok identified a need for physician-created content to provide quality educational information on Mpox. With increased social media usage by physicians, these platforms can be used as an educational tool while also decreasing the spread of both infection and misinformation.

Physician-created TikTok videos had a significantly higher DISCERN score, indicating a higher quality of consumer health information. Physicians scored particularly well on the questions "is it balanced and unbiased?" and "does it describe how each treatment works?". The majority of YouTube videos found were created by news sources, and the difference in DISCERN averages between nonphysician and physician data was not significant. A limitation of this study is the inclusion of only a small number of physician-created videos in the analysis.

Conclusion

To summarize, Google Trends remains a useful tool for analyzing the public response to local disease outbreaks [4]. This could hold future potential in monitoring the spread of disease even before statistical data indicate a local outbreak. Additional research is needed to investigate whether a temporal relationship between Google searches and local disease outbreaks exists.

In general, the quality of videos on both TikTok and YouTube can be improved if content creators discuss the risks and benefits of treatments, provide references for the information shared in their videos, and collaborate with physicians.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Cases reported by the Centers for Disease Control and Prevention from May 1, 2022, to July 26, 2022 (left) and "monkeypox" searches by state from the same period (right).

[PNG File , 57 KB - derma_v6i1e48827_app1.png]

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Research Letter

A Survey of Patient Demographics in Inflammatory Skin Disease Case Reports

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Abstract

Case reports serve many functions in the medical literature. We explore patient demographics in case reports for common inflammatory skin diseases.

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KEYWORDS

inflammatory skin diseases; acne; alopecia areata; atopic dermatitis; psoriasis; rosacea; demographic; survey; case reports; case report; skin; inflammatory; inflammation; dermatitis; dermatology; demographics

Introduction

What functions do case reports serve in the medical literature and practice? Their functions are numerous, including the dissemination of unique clinical observations, novel treatment approaches, and hypothesis generation [1]. While individual case reports have inherent limitations such as publication bias and limited scope, previous work has shown situations in which meta-analyses of case reports and formal clinical studies agree [2]. By aggregating large numbers of published case reports, the impact of clinical and treatment outliers (ie, "black swan" events [3]) reported in the dermatology literature can potentially be dampened. However, little work has been carried out to assess which diseases and demographics have a greater number of published case reports associated with them. In this paper, we use a novel data set to explore the potential biases in case report publications in inflammatory skin conditions by disease for demographic factors.

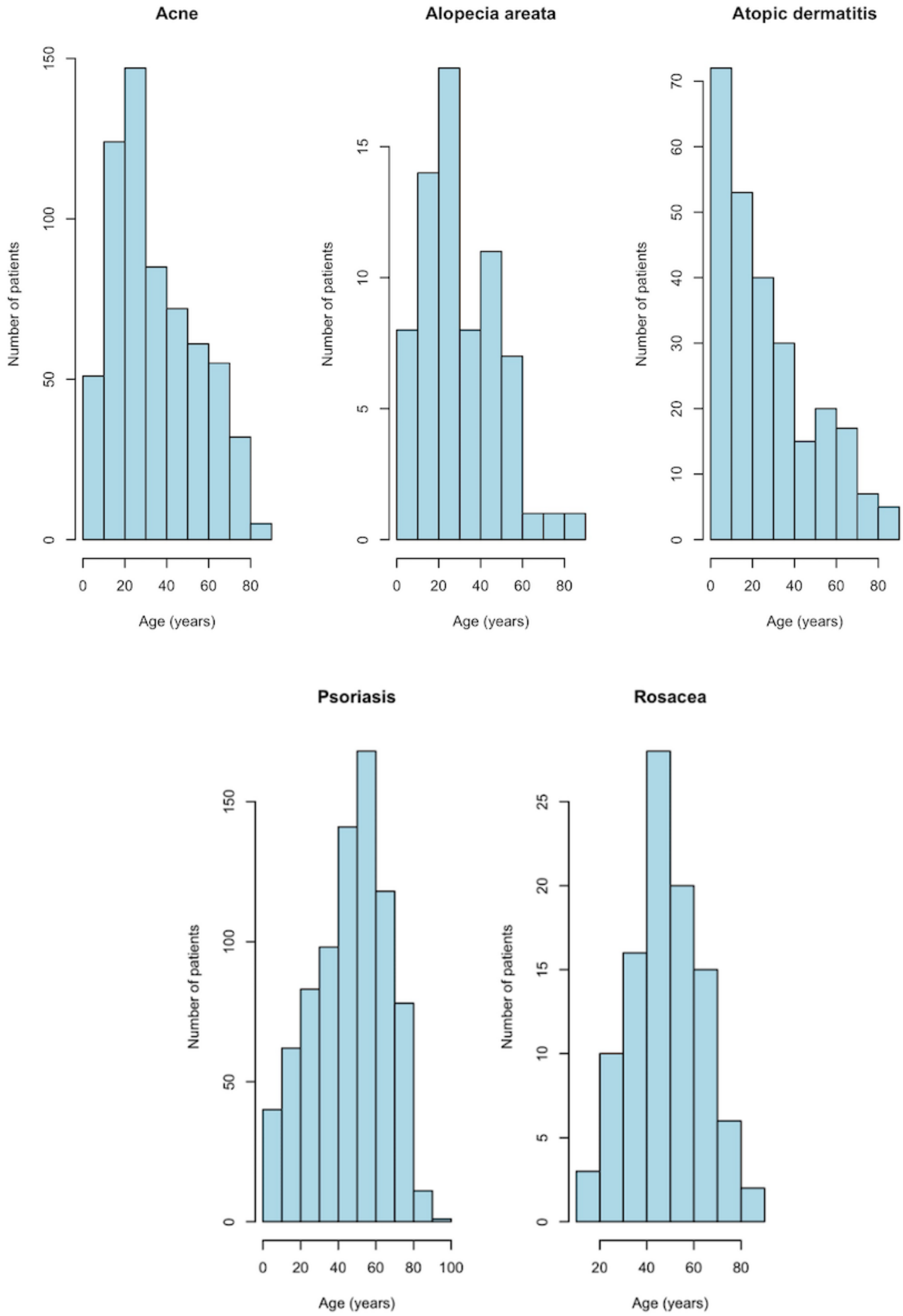
Methods

In this study, we evaluated the frequency of case reports of 5 common inflammatory skin diseases using PubMed Central Patients (PMC-Patients), a collection of 167,000 patient summaries extracted from case reports [4]. Reports on patients with diseases of interest were collected using string match for the disease, and demographic information of the patients in the identified case reports was extracted from PMC-Patients. All analyses and figures were generated using R (version 4.2.2; R Core Team). This study did not require institutional review board approval.

Results

Case reports were found for patients with acne (n=632), alopecia areata (AA; n=69), atopic dermatitis (AD; n=259), psoriasis (n=800), and rosacea (n=100). We found that AD had the smallest percentage of female patients (n=107, 41.3%), and rosacea had the largest (n=58, 58%). Female patients accounted for 53.5% (n=338), 49.3% (n=34), and 43.5% (n=348) of case reports on acne, AA, and psoriasis, respectively. The mean age was 34.6 (SD 20.1) years for patients with acne, 30.9 (SD 18.1) years for patients with AA, 27 (SD 22.2) years for patients with AD, 46.4 (SD 19.8) years for patients with psoriasis, and 48.4 (SD 15) years for patients with rosacea. Plotting histograms of patient ages indicated that rosacea cases had a normal distribution, AD and acne had a right-sided skew, psoriasis had a left-sided skew, and AA was bimodal (Figure 1).

Figure 1. Histograms of patient age by inflammatory skin disease type in case report literature.



Discussion

This study summarizes the frequency of case reports of inflammatory skin diseases and describes their demographic distributions. Although some findings are in line with published studies, such as the decreasing prevalence of AD with age, or the congruent age distribution of AD and AA, which can co-occur in a large proportion of patients, other aspects were less representative, with the cases focusing more on male patients despite a generally female predominance in AD [5]. Additionally, there were over 11 times more cases reported about psoriasis than AA, despite prevalence estimates that are closer in magnitude. To the best of our knowledge, there is no clear reason why there would be such stark variations in gender demographics or disease representation. These results suggest that case reports may not be entirely reflective of the demographic makeup of different diseases. Study limitations include the use of automated review technologies that may lead to some missed case reports and that race and ethnicity were not available data points. Further research is needed to better understand how demographic representation is produced in inflammatory skin disease case reports.

Conflicts of Interest

BU is an employee of Mount Sinai and has received research funds (grants paid to the institution) from Incyte, Rapt Therapeutics, and Pfizer. He is also a consultant for Arcutis Biotherapeutics, Castle Biosciences, Fresenius Kabi, Pfizer, and Sanofi.

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Abbreviations

AA: alopecia areata
AD: atopic dermatitis
PMC-Patients: PubMed Central Patients

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Research Letter

Outreach Through Facebook: Do Patients With Atopic Dermatitis Provide Clinically Relevant Information When Recruited for Surveys on Social Media?

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KEYWORDS
social media; atopic dermatitis; digital survey; recruit; patient perspectives; patient-reported outcomes; real-world data

Introduction

Atopic dermatitis (AD) is a common chronic skin disease with a prevalence of up to 20% in children and up to 10% in adults [1]. There has been an increasing focus on the impact on the quality of life of the patients, family members, and caregivers [2], yet performing surveys to elucidate this is often laborious, time-consuming, and expensive. Social media has been used as a new platform for gaining insights into diseases through surveys, but for AD this has not been adequately tested. We have investigated the results obtained from a web-based survey recruiting respondents from a Facebook group hosted by the Danish Atopic Eczema Patients' Organization (DAEPO) concerning whether it was representative of the population and if it returned relevant information on their disease.

Methods

The survey consisted of 35 close-ended questions with checkboxes and was designed together with DAEPO. The inclusion criteria (self-reported) were being 18 years or older, previously or currently using a topical corticosteroid, and having been diagnosed with AD. No incentives were offered to participants. Data were collected anonymously between November 11 and December 22, 2021. Data collection and storage were compliant with European Union regulations on General Data Protection Regulation (GDPR). For the analysis, respondents were stratified into three groups according to severity as defined by the Patient Oriented Eczema Measure (POEM) instrument.

Results

In total, 140 participants of 182 respondents met the inclusion criteria (recruitment rate 76.9%). Table 1 presents demographics, symptoms, and comorbidities. Table 2 shows health care use and disease management. Representativeness of survey responders (age, gender, and educational level) was investigated using chi-square test for goodness of fit, which confirmed the overrepresentation of younger female respondents with a higher educational level compared to the general Danish population. The limited participation of older adults has likewise been observed in previous studies using social media platforms [3]. Our data also indicated that the severity of AD correlated inversely with educational level in line with previous registry-based results, showing severe AD decreases the chance of completing higher education [4].

Table 1. Demographics and symptoms of respondents with atopic dermatitis (AD), stratified by disease severity.

	Mild (n=37)	Moderate (n=48)	Severe (n=55)	All (N=140)	*P* value (between AD severity group comparison)[a]
Age (years; N=140), n (%)[b]					
18-29	5 (14)	21 (44)	18 (33)	44 (32)	.01
30-39	9 (24)	8 (17)	17 (32)	34 (24)	.24
40-49	12 (32)	10 (21)	11 (20)	33 (24)	.33
≥50	11 (30)	9 (19)	9 (16)	29 (21)	.28
Female (n=138), n (%)[b]	30 (83)	44 (92)	51 (94)	125 (91)	.20
Educational level (n=139), n (%)[b]					.17
Basic compulsory education[c]	0 (0)	1 (2)	7 (13)	8 (6)	
Youth education[d]	13 (35)	20 (42)	24 (44)	57 (41)	
Higher education[e,f]	23 (60)	25 (52)	22 (40)	69 (50)	
Education not completed	1 (3)	0 (0)	0 (0)	1 (1)	
Other	1 (3)	2 (4)	1 (2)	4 (3)	
Age at diagnosis (years; n=139), n (%)					
0-2	14 (38)	19 (40)	31 (56)	64 (46)	.11
3-12	14 (38)	10 (21)	8 (15)	32 (23)	.04
Older than 12 years[g]					.33
13-19	3 (8)	4 (9)	6 (11)	13 (9)	
20-40	4 (11)	9 (19)	7 (13)	20 (14)	
>40	2 (5)	5 (11)	2 (4)	9 (7)	
Do not know	0 (0)	0 (0)	1 (2)	1 (1)	N/A[h]
Comorbidities (N=140), n (%)					
Asthma	18 (49)	16 (33)	24 (44)	58 (41)	.33
Allergic rhinitis	24 (65)	27 (56)	34 (62)	85 (61)	.71
Food allergies	12 (32)	15 (31)	24 (44)	51 (36)	.36
No asthma nor allergy	15 (41)	21 (44)	24 (44)	60 (43)	.67
Other types of allergies	5 (14)	9 (19)	7 (13)	21 (15)	.95
Bothersome symptoms (N=140), n (%)					
Itch	29 (78)	47 (98)	55 (100)	131 (94)	<.001
Dry skin	32 (87)	45 (94)	54 (98)	131 (94)	.08
Red rash	27 (73)	36 (75)	52 (95)	115 (82)	.008
Exudation	7 (19)	15 (31)	28 (51)	50 (36)	.005
Swelling	9 (24)	15 (31)	26 (47)	50 (36)	.06
Poor night's sleep	6 (16)	15 (31)	39 (71)	60 (43)	<.001
Skin pain	16 (43)	22 (46)	41 (75)	79 (56)	.002
Other	0 (0)	6 (13)	5 (9)	11 (8)	.10
No symptoms	2 (5)	0 (0)	0 (0)	2 (1)	.06

[a]Pearson chi-square test for AD severity group comparison. Significance level 5%.

[b]Chi-square goodness-of-fit test for responders' representativeness with the Danish general population—age: χ^2 goodness of fit=47.8, df=3, *P*<.001; gender: goodness of fit χ^2_1=87.9, *P*<.001; education: goodness of fit χ^2_1=13.8, *P*<.001).

[c]Basic compulsory education includes 9th and 10th grade.

[d]Youth education includes high school and vocational school.

[e]Higher education includes bachelor's, master's, or PhD programs.

[f]Pearson chi-square test for AD severity group comparison split between higher education or not.

[g]Pearson chi-square test performed for the AD severity group whose age at diagnosis was older than 12 years.

[h]N/A: not applicable.

Table 2. Management of disease, stratified by disease severity.

	Mild (n=37)	Moderate (n=48)	Severe (n=55)	All (N=140)	*P* value (between AD[a] severity group comparison)[b]
Time since last AD consultation by dermatologist (n=139), n (%)					.10
Within last 6 months	13 (36)	16 (33)	32 (58)	61 (44)	
Within last 6-12 months	4 (11)	7 (15)	3 (6)	14 (10)	
Within last 1-2 years	9 (25)	9 (19)	6 (11)	24 (17)	
More than 2 years ago	9 (25)	14 (29)	14 (26)	37 (27)	
Never	0 (0)	2 (4)	0 (0)	2 (1)	
Do not know	1 (3)	0 (0)	0 (0)	1 (1)	
Use of moisturizers (n=137), n (%)					.45
Daily	31 (89)	40 (83)	50 (93)	121 (88)	
At least once a week	2 (6)	3 (6)	3 (6)	8 (6)	
Less than once a week	0 (0)	1 (2)	0 (0)	1 (1)	
When needed	2 (6)	4 (8)	0 (0)	6 (4)	
Never	0 (0)	0 (0)	1 (2)	1 (1)	
Moisturizers are recommended by the treating physician (n=137), n (%)	31 (89)	42 (89)	49 (89)	122 (89)	N/A[c]
TCS[d] group, current or ever used (N=140), n (%)[e]					
Group I	17 (46)	22 (45)	22 (40)	61 (44)	.79
Group II	23 (62)	38 (79)	34 (62)	95 (68)	.12
Group III or IV	30 (81)	37 (77)	54 (98)	121 (86)	.004
Do not know which group	1 (3)	2 (4)	0 (0)	3 (2)	.33
Frequency of current TCS use (n=136), n (%)					<.001
Daily	3 (9)	8 (17)	22 (40)	33 (24)	
3-5 times a week	5 (14)	16 (35)	18 (33)	39 (29)	
1-2 times a week	9 (26)	11 (24)	6 (11)	26 (19)	
1-3 times a month	5 (14)	6 (13)	3 (6)	14 (10)	
Less than once a month	13 (37)	5 (11)	6 (11)	24 (18)	
Periods of proactive use of TCS the last year (n=134), n (%)					.05
Less than 1 month	5 (15)	11 (24)	9 (17)	25 (19)	
1-6 months	5 (15)	7 (15)	6 (11)	18 (14)	
More than 6 months	5 (15)	12 (26)	24 (44)	41 (31)	
No	19 (56)	16 (35)	15 (28)	50 (37)	
Reactive use of TCS within the last month (n=131), n (%)					<.001
1 week	8 (25)	16 (36)	9 (16)	33 (25)	
2 weeks	2 (6)	9 (21)	2 (4)	13 (10)	
3 weeks	0 (0)	4 (9)	4 (7)	8 (6)	
All last month	7 (22)	10 (23)	31 (56)	48 (37)	
I have not used reactive treatment	15 (47)	5 (11)	9 (16)	29 (22)	

[a]AD: atopic dermatitis.

[b]Pearson chi-square test for atopic dermatitis severity group comparison. Significance level 5%.

[c]N/A: not applicable.

[d]TCS: topical corticosteroid.

[e]Pearson chi-square tests for AD severity group comparison for each of the TCS groups.

The majority of respondents had their AD diagnosis in childhood. Many across the three AD severity groups had asthma and allergy comorbidities. Symptoms such as itch, red rash, exudation, poor night's sleep, and skin pain were significantly more frequent among patients with severe AD (Table 1). The frequency of dermatology visits did surprisingly not differ significantly between severity groups, whereas reactive treatment use patterns in the last month were observed significantly more in those with severe AD (Table 2). This indicates that many patients with AD are not adequately treated and should have closer contact with the health care system to receive timely and optimal treatment.

Discussion

In conclusion, we found that social media may be used for disease surveys, although with a risk of lack of representativeness of the general population (ie, favoring those who are female, younger, and well educated). With this in mind, however, outreach through social media is an easy cost-effective way of acquiring a large amount of information and may be a useful platform to obtain relevant disease information on patient-reported outcomes for patients with AD, and female patients in particular.

Conflicts of Interest

STG, AGF, and PBP are employees at Pfizer Denmark. AGF and PBP own shares in Pfizer Inc. CV has received honoraria for lectures and add boards from Sanofi Genzyme, Eli Lilly, Pfizer, LEO Pharma, Novartis, and AbbVie. He has received research grants from Sanofi Genzyme, LEO Pharma, Novartis, and Pfizer.

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Abbreviations

AD: atopic dermatitis
DAEPO: Danish Atopic Eczema Patients' Organization
GDPR: General Data Protection Regulation
POEM: Patient Oriented Eczema Measure

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Research Letter

Topical Application of Tea Tree Oil for the Treatment of Verruca Vulgaris

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KEYWORDS
aromatherapy; human papillomavirus; naturopathy; tea tree oil; warts; verruca vulgaris

Introduction

Warts (verruca vulgaris) are benign epithelial proliferations associated with human papillomavirus (HPV) infection. They are a DNA virus belonging to the Papillomaviridae family [1]. Worldwide, 10% of the population is affected, and the prevalence is high in children attending school [2]. Common warts are excessive growths with an irregular surface ranging from 1 millimeter to several centimeters and are commonly seen on the upper and lower extremities [2]. Conventional treatment for warts includes topical application of salicylic acid, podophyllotoxin, trichloroacetic acid, formaldehyde, 5-fluorouracil, and photodynamic therapy [1]. Procedures such as cryotherapy, laser ablation, electrocautery, and surgical excision are painful and have higher chances of reoccurrence [1]. In aromatherapy, tea tree oil (TTO), extracted through steam distillation of the leaves and terminal branches of the Australian plant *Melaleuca alternifolia*, is used for the management of various dermatological conditions, including HPV [3,4], by naturopathy physicians. This letter aims to present TTO as a potential remedy for HPV warts, highlighting its properties, benefits, and the need for further research to establish its effectiveness and safety.

Methods

We performed a comprehensive literature search to include original articles, case reports and case series, and abstracts that discussed the effect of TTO on HPV verruca vulgaris; in PubMed, Embase, and Google Scholar; and were published on April 9, 2022, or earlier. Reviews and articles that used TTO with other interventions were excluded. The following keywords were used: “tea tree oil” OR “aromatherapy” OR “naturopathy” AND “human papillomavirus” OR “HPV” OR “verruca vulgaris” OR “warts.”

Results

A total of 4 articles involving 5 patients with warts treated with aromatherapy were included (Table 1). Warts were predominantly found on the upper and lower extremities, except for one case where the location was periungual [5]. The efficacy was assessed by using the visual analog scale [3] and clinical photographs daily [1,3]. Additionally, a follow-up was conducted to monitor for any recurrence [1]. All the studies included in this analysis reported complete clearance of warts.

Table 1. Characteristics of the studies included in the research letter.

Study, year, and participants	Country	Age (years)	Diagnosed by	Site of warts	Intervention details	Outcome
Millar and Moore [4], 2008						
Female pediatric patient	United Kingdom	7	Dermatologist	Distal phalanges of the right middle finger	Topical application of tea tree oil once daily for 12 days	Complete clearance of warts without reoccurrence
Alsanad and Alkhamees [3], 2016	Saudi Arabia		Dermatologist			Complete clearance of warts without reoccurrence
Male child		9		Left sole	Topical application of tea tree oil twice a day for 20 days	
Male child		14		Proximal phalanges of the right little finger	Topical application of tea tree oil twice a day for 10 days	
Lim et al [5], 2020						
Female child	South Korea	12	Dermatologist	Periungual and plantar	Topical application of tea tree oil for 9 months	Complete clearance of warts without reoccurrence
Deenadayalan et al [1], 2022						
Adult female	India	22	Dermatologist	Distal phalanges of the right hand	Topical application of tea tree oil once a day for 7 days, afterward alternative day for 2 weeks	Complete clearance of warts without reoccurrence

Discussion

This research letter indicates that TTO can be beneficial in treating warts, which are caused by HPV and commonly occur in pediatric and school-aged children. The potent anti-inflammatory and antiviral properties of TTO have been widely used to treat HPV infections. In vitro studies have also used TTO to treat herpes simplex virus [4]. Terpinene-4-ol and α-terpineol in TTO are known for their antiviral property and inhibit viral replication in both enveloped and nonenveloped viruses [4]. Terpinene-4-ol can inhibit the synthesis of proinflammatory cytokines, tumor necrosis factor, interleukin-1 (IL-1), IL-8, and prostaglandin E2 while increasing anti-inflammatory cytokines (IL-10 and IL-4), thereby reducing pain [1]. In addition to pain management and warts clearance, a pleasant scent may play a role in patient satisfaction. The treatment is also less expensive and has no adverse effects. The limitation of this letter was using single case reports with a small number of patients.

TTO should be considered a safe, cost-effective, noninvasive modality in the management of HPV warts. More research is necessary to understand the clinical applications and other long-term systemic effects.

Conflicts of Interest

None declared.

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Abbreviations

HPV: human papillomavirus
IL: interleukin
TTO: tea tree oil

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Research Letter

Smartwatch Technology in Medicine: A Call for Future Dermatologic Research

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digital health; dermatology; smartwatch; ultraviolet radiation; ultraviolet; UV; skin cancer; pruritus; sunscreen; device; support; patient education; clinical management; cardiovascular; cancer prevention; prevention; cancer; technology; wearable technology

Introduction

The use of smartwatches and other wearable devices has been increasingly empowering users with the ability to monitor numerous critical aspects of their health. From monitoring heart rate and blood pressure to detecting arrhythmias, seizure activity, and falls, noninvasive smartwatch technology has proven to be an effective screening tool that can be used to inform patient care and improve outcomes [1]. Additionally, smartwatches are highly portable, relatively affordable, and adequately available to the public, making them an attractive investment for consumers.

The application of smartwatch technology to the field of dermatology has not been well described; however, smartwatch technology could greatly aid in both risk assessment and prevention of skin cancer. This paper examines smartwatch-associated research across all medical specialties and proposes future applications to dermatology, specifically for skin cancer prevention and intervention.

Methods

A review of the use of smartwatches across all medical specialties was performed. The search terms “smart watch” and “smartwatch” were searched in PubMed for English-language articles published from database inception to April 10, 2023. Multimedia Appendix 1 summarizes the inclusion and exclusion criteria. One reviewer (MAR) screened all articles for inclusion. Studies that satisfied the inclusion and exclusion criteria were included for data extraction. Two reviewers (MAR and TAB) independently performed the full-text review and data extraction, with the primary variable of interest being the medical specialty associated with each article.

Results

Of the 1333 identified articles, 346 met the study eligibility criteria. Multimedia Appendix 2 displays the frequency of each medical specialty represented. The majority of studies examined smartwatches in the context of cardiovascular research (174/346, 50.4%). Neurology was represented in 15.1% (52/346) of the studies, and the remaining 34.5% (120/346) of studies were distributed across 12 other specialties.

Only 3 studies (<1%) represented dermatologic research (Table 1). One used wrist actigraphy to measure nocturnal scratching in patients with pruritus [2]. The second, by Jang et al [3], measured sleep duration and its impact on skin characteristics in women. Finally, Dey et al [4] used smartwatches to track cumulative UV exposure in patients.

Table 1. Summary of dermatology-related smartwatch studies.

Article (author, year, journal)	Methods	Feature of watch used	Outcome studied	Key findings	Smartwatch used
Dey et al [4], 2017, *Eng Med Biol Soc*	Integration of UV sensors into 1200 smartwatches and smartphones	UV exposure	Cumulative UV tracking	Integration of UV sensors into these devices provided an accurate estimate of cumulative UV exposure	Android
Ikoma et al [2], 2019, *Acta Derm Venereol*	Creation of a smartwatch app to detect nocturnal scratching using accelerometer data	Wrist actigraphy	Nocturnal scratching in patients with pruritus	High reliability and clinical usefulness of the newly created app was demonstrated	Apple
Jang et al [3], 2020, *Skin Res Technol*	Already existing sleep-tracking capabilities in smartwatches were used and longitudinally compared to the characteristics of skin aging among participants	Sleep time monitoring	Skin characteristics in women	Negative changes were seen in the skin characteristics of patients who averaged less sleep	Xiaomi

Discussion

Principal Findings

Great disparities exist in the use of smartwatch technology across various medical specialties. We propose this is in part due to the specialty-specific capabilities found within smartwatches. For example, the majority of included studies examined applications of smartwatch technology in cardiology, likely due to the device's ability to measure pulse and respiration rate and perform electrocardiograms [1].

As smartwatches sit on the skin and are thus exposed to the same environmental factors as the wearer, they represent a valuable opportunity to better understand both the UV and non-UV environmental, occupational, and avocational exposures that may contribute to the development of skin cancer. With the incidence of both melanoma and keratinocyte carcinomas continuously increasing [5], understanding the risk factors for the development of skin cancer becomes important for determining individual patient risk, early detection, and improving clinical outcomes. Furthermore, because smartwatches provide continuous monitoring capabilities, personalized alerts could be implemented to notify users of behavioral changes they could employ to reduce the risk of developing skin cancer (ie, "Your UV exposure over the last 7 days is higher than normal. To minimize cancer risk, ensure proper UV protection."). Use of these continuous monitoring capabilities could be further applied to advance research within the field, allowing for minimally invasive yet highly accurate data collection, which can aid in the development of personalized treatment plans.

Smartwatch technology continues to be refined and improved to better meet the health care needs of consumers. This is perhaps best exemplified by the development of smartwatch-based oxygen saturation measurement capabilities during the COVID-19 pandemic. We propose that future smartwatches be equipped with the technology to measure UV-A and UV-B rays, time spent in water, and air quality, as well as prompt users to reapply sunscreen at regular intervals. The benefits of these implementations are summarized in Table 2.

The benefits of smartwatch technology in skin cancer prevention and intervention are numerous. However, it must be acknowledged that smartwatches can be costly and not accessible to everyone. As such, the quantifiable and generalizable impact of this technology may be somewhat diminished.

Table 2. Dermatological applications and benefits of smartwatches.

Intervention	Mechanism	Effect	Special populations of benefit
UV sensor and sunscreen reminder	• Provide individuals with a quantitative, cumulative estimate of UV exposure • Remind individuals at appropriate intervals to reapply sunscreen	• Encourage individuals to reapply sunscreen at regular intervals and to limit time spent outdoors during high UV-index hours	• Patients with xeroderma pigmentosum, porphyrias, photoallergy, lupus erythematosus, and other photosensitivity disorders • Individuals who are occupationally or recreationally exposed to the sun
Time spent in water monitor	• Provide individuals with quantitative estimates of total time spent in water • Remind individuals at appropriate intervals to reapply sunscreen	• Encourage reapplication of sunscreen	• Patients with conditions exacerbated by water such as aquagenic keratoderma • Swimmers, surfers, and divers
Air quality	• Alert individuals to chemical hazards, pollen levels, or other irritating substances in the atmosphere	• Promote the use of protective clothing, sunscreen with topical antioxidants, and the usage of indoor air purifiers or ventilators	• Individuals with atopic conditions

Conclusion

A significant gap in the medical literature exists surrounding the potential uses of smartwatches in the field of dermatology. Nonetheless, the application of smartwatches within dermatology represents a point of meaningful implication, especially as it relates to skin cancer prevention and intervention. As such, future research on smartwatch technology in dermatology is warranted.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Inclusion and exclusion criteria for study eligibility.

[DOCX File , 7 KB - derma_v6i1e47252_app1.docx]

Multimedia Appendix 2

Representation of smartwatch-related clinical research among all medical specialties.

[PNG File , 148 KB - derma_v6i1e47252_app2.png]

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Research Letter

The Impact of Temperature, Humidity, and Sunshine on Internet Search Volumes Related to Psoriasis

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Abstract

We examined internet searches on psoriasis in Germany and found that in weeks with high search volume, mean temperature and humidity were lower and sunshine level was higher compared to weeks with low search volume.

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KEYWORDS

psoriasis; infodemiology; internet search; internet searching; web search; information seeking; information search behavior; information search behaviour; dermatology; skin; weather; temperature; humidity; sunshine

Introduction

A connection between psoriasis severity and weather has long been suspected. Cold, dry weather has been noted anecdotally to exacerbate symptoms, whereas sunshine improves the condition [1]. Psoriasis is more prevalent in the northern hemisphere, possibly due to colder temperatures [2]. Studies examining internet search data show that searching is more common during winter than summer, suggesting a relationship with temperature [3]. A recent systematic review [4] presented inconclusive results; no seasonal changes were seen in half the studies examined and summertime improvement was found in only 30% of studies. Few studies have assessed specific weather features like temperature, humidity, and sunshine levels.

Methods

In this study, we examined internet searches related to psoriasis in Germany, looking at whether patterns in searching were weather related. The internet search volume for the search term "psoriasis" (disease) for Germany was obtained from Google Trends [5]. This website provides the relative search volume (RSV) of specific search terms, with values representing the number of searches for a term relative to the total number of searches done. The week of maximum searching is assigned an RSV of 100 against which searching done during other weeks is calibrated. Weekly data from January 2018 to 2023 was downloaded.

Weather data from the German Wetterdienst (national meteorological service) was used. Daily data for mean temperature, percentage relative humidity, and total hours of sunshine was obtained for 6 weather stations: Berlin, Cologne, Frankfurt, Hamburg, Munich, and Stuttgart. Weekly mean values for temperature and humidity as well as total weekly hours of sunshine were calculated. A value for all of Germany was calculated using data from the 6 stations.

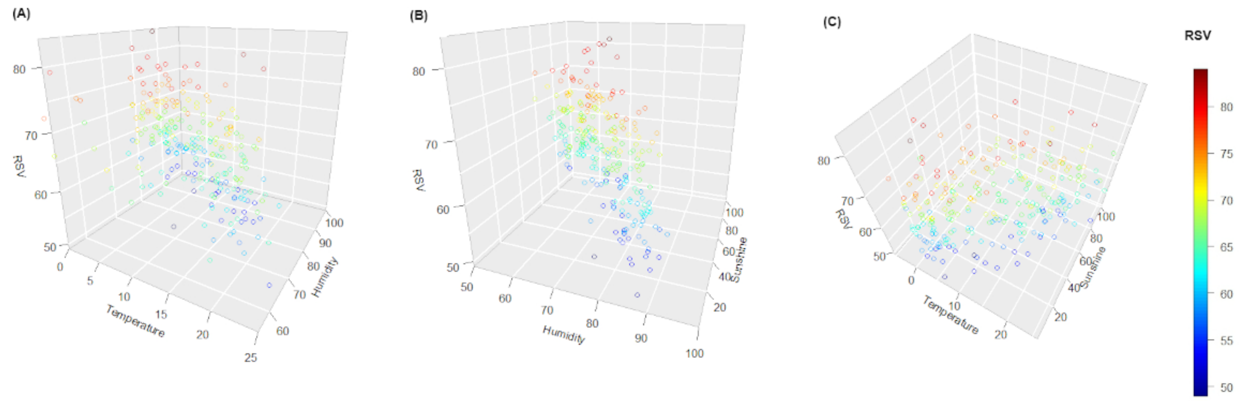
Results

The RSV ranged from 53 to 100. Although there was only a slight correlation between searching and specific weather features (temperature: ρ=–0.13, humidity: ρ=–0.23, sunshine: ρ=0.11), 3D scatter plots suggested differences between weeks of high and low searching. Low search weeks (blue in Figure 1A) occurred across greater temperature ranges than high search weeks (red in Figure 1A). Most high search weeks occurred when temperatures were low. Similarly, low search weeks occurred across a greater range of humidity levels than high search weeks, which occurred more frequently at low humidity levels (Figure 1B). Given comparable levels of sunshine, high search weeks occurred at lower temperatures than low search weeks (Figure 1C).

Notable differences were apparent when comparing mean values between the lowest (RSV≤60; n=43) and highest (RSV≥70; n=86) search weeks. The mean temperature was higher during low rather than high search weeks (low: 11.18±7.00 °C; high: 8.60±6.30 °C), as was humidity (low: 79.73±9.12%; high: 71.25±9.99%), but sunshine hours was lower (low: 27.61±21.64 hours; high: 36.48±24.46 hours). The difference for humidity was significant (2-tailed *t* test: *P*<.001).

These trends were further explored using linear regression. Since the search data were not normally distributed (Shapiro-Wilk W=0.96; *P*<.001), they were logged. Separate regressions were performed with logged values for temperature, humidity, and sunshine as dependent variables. The resulting coefficients indicated that higher temperature and humidity led to lower search volumes but more sunshine was associated with increased searching (temperature: –0.01, humidity: –0.13, *P*<.001; sunshine: 0.01, *P*=.04). Regression fitting suggests an RSV of 78 at 10 °C, declining to an RSV of 40 at 15 °C. At 65% humidity, an RSV of 93 is expected; when humidity rises to 80%, the RSV should drop to 47. With 40 hours of sunshine per week, an RSV of 68 is expected.

Figure 1. 3D scatter plots showing the association between the weekly search volume of "psoriasis" and (A) temperature (°C) and humidity (%), (B) humidity and hours of sunshine, and (C) temperature and hours of sunshine. Data are for weekly mean values from select German weather stations. RSV: relative search volume.



Discussion

This study revealed that weeks of high internet searching related to psoriasis were associated with cold, dry weather conditions. Differences were most apparent when comparing the highest and lowest search weeks. The possible association between high searching and more sunshine is of interest; this is contrary to anecdotal evidence but supports recent survey work [4], which underlines that the factors influencing psoriasis are multifactorial. More extensive research to ascertain the influence of specific weather factors is required.

Google Trends data allowed for the examination of search volume trends over long time periods and on a weekly basis. However, only national data were available, meaning regional assessment was not possible. Local differences may exist. We assumed that internet searching is constant throughout the year, but increases in winter months may occur when people spend more time on computers due to longer, darker evenings. Future studies could control for this problem by calibrating search volume with results from nonseasonal conditions. Another assumption is that internet searching reflects the severity of psoriasis. One would expect this to be the case because people are more likely to search when their symptoms worsen and discomfort is felt. It is well known that internet searching reflects the incidence of a condition [6]. The effects of weather are unlikely to be apparent in clinical settings.

Conflicts of Interest

None declared.

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Abbreviations

RSV: relative search volume

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Research Letter

A Social Media Analysis of Pemphigus

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Abstract

An analysis of the pemphigus content on Facebook, Twitter, Instagram, and YouTube social media platforms.

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KEYWORDS

pemphigus; social media; pemphigus vulgaris; Facebook; YouTube; Twitter; Instagram; dissemination; medical information; autoimmune disease; diagnosis; engagement; educational; content; awareness

Introduction

In 2021, an estimated 4.26 billion people reported using some type of social media including approximately 80% of dermatology patients [1]. Social media has advanced health research and practice, enhanced social mobilization, and facilitated health services and events [2]. Approximately 61% of US adults utilize the web for health-related information, most commonly for diseases and treatments [3].

Pemphigus represents a spectrum of autoimmune skin-blistering diseases, with a prevalence of 5.2 cases per 100,000 adults, and is associated with diagnostic delay [4,5]. Social media may be used to shorten diagnostic delays, disseminate disease information, and connect affected individuals to support groups. The purpose of this study is to characterize the most popular and recent social media footprint of pemphigus across common social media platforms.

Methods

Four social media platforms—Facebook, Instagram, YouTube, and Twitter—were evaluated using the search term "pemphigus." Data collection was conducted at singular date cutoff timepoints to collectively evaluate the most recent and popular social media content. Only English content related to human pemphigus was included. The exclusion criteria were posts that discussed nonhuman pemphigus, non-English content, and YouTube videos longer than 20 minutes. The Quality Evaluation Scoring Tool (QUEST) score is a validated metric used to analyze the quality of medical content posted on the web and was used to evaluate content on YouTube. Details regarding the data collection process are available in Multimedia Appendix 1.

Results

YouTube

Of the 10 identified eligible YouTube videos, 5 (50%) were made by physicians, 4 (40%) by various organizations, and 1 (10%) by patients (Table 1). All videos were educational, and the average length of the videos was 4 minutes and 42 seconds. The average number of views per video was 23,404, and the average number of likes and comments was 411 (SD 653) for each video. The average QUEST score for the selected videos was 14.6 (SD 4.1; Table 1).

Table 1. Analysis of top YouTube, Instagram, and Twitter content.

Author or content category	Views/posts[a], n	Post sender or type of content, n (%)	Engagement[b]	QUEST[c] score, mean (SD)
Top 10 YouTube videos		• N/A[d]		
1. Physician, educational	50,718		• 601	19 (1.4)
2. Patient/organization, personal	1726		• Not disclosed	9.5 (2.1)
3. Health care professional, educational	7222		• 150	11 (0.0)
4. Physician, educational	4367		• 37	19.5 (3.5)
5. Physician, educational	171		• 2	20 (2.8)
6. Organization, educational	115,321		• 1983	13.5 (0.7)
7. Organization, educational	3442		• 36	9.5(0.7)
8. Organization, educational	44,549		• 781	13 (0.0)
9. Physician, educational	2844		• 60	18 (0.0)
10. Organization, educational	3677		• 50	12.5 (0.7)
Top 50 Instagram post				N/A
Promotional	17	• Organization: 13 (76) • Physician/Professor: 4 (24)	• Likes, n: 240 • Likes, mean (SD): 14.1 (11.6) • Comments, n: 13	
Educational	15	• Organization: 9 (60) • Physician: 3 (20) • Patient: 3 (20)	• Likes, n: 321 • Likes, mean (SD): 21.4 (32.3) • Comments, n: 8	
Recruitment	16	• Organization: 16 (100)	• Likes, n: 151 • Likes, mean (SD): 9.44 (5.2) • Comments, n: 5	
Personal	2	• Patient: 2 (100)	• Likes, n: 33 • Likes, mean (SD): 16.5 (19.5) • Comments, n: 18	
Top 50 Twitter posts				N/A
Physician	25	• Educational: 16 (64) • Personal: 7 (28) • Promotional 2 (8)	• Total: 1608 • Int/Post[e], mean (SD): 64.3 (178.7)	
Patients/individuals	3	• Personal: 2 (67) • Educational: 1 (33)	• Total: 10 • Int/Post, mean (SD): 3.3 (0.6)	
Organization	15	• Educational: 9 (60) • Personal: 2 (13) • Promotional: 3 (20) • Recruitment: 1 (7)	• Total: 101 • Int/Post, mean (SD): 6.7 (5.8)	
Pharmaceutical company	1	• Recruitment: 1 (100)	• Total: 25 • Int/Post: 25	

Author or content category	Views/posts[a], n	Post sender or type of content, n (%)	Engagement[b]	QUEST[c] score, mean (SD)
Promoter	2	• Promotional: 2 (100)	• Total: 0 (17 video views) • Int/Post: 0	
Researcher	4	• Educational: 2 (50) • Personal: 1 (25) • Promotional: 1 (25)	• Total: 54 • Int/Post, mean (SD): 13.5 (17.3)	

[a]For YouTube, this column is a count of views for each video. For Instagram and Twitter, this column is the count of posts for each category.

[b]For YouTube, engagement is the total number of likes + comments for each video. For Instagram, engagement includes the total number of likes and comments and the average number of likes for each category of post. For Twitter, engagement includes the total number of likes + retweets + comments, as well as the average interactions per post.

[c]QUEST: Quality Evaluation Scoring Tool.

[d]N/A: not applicable.

[e]Int/Post: interactions per post.

Instagram

A total of 49 Instagram posts were excluded. Of the 50 included eligible posts, 17 (34%) were categorized as “promotional,” 15 (30%) were “educational,” 16 (32%) were “recruitment,” and 2 (4%) were “personal” (Table 1). Organizations were the most common post senders (n=38, 76%) and contributed the majority of promotional (13/17, 77%), educational (9/15, 60%), and recruitment (16/16, 100%) posts (Table 1).

Twitter

Of the 50 tweets identified, approximately 39 (78%) included images, 3 (6%) had videos, and 8 (16%) were only text. Physicians were the most common tweet senders, with 25 (50%) tweets and the highest average engagement (64.3, SD 178.7 interactions/post). The majority of posts were educational (n=29, 58%).

Facebook

The majority of the top Facebook groups were private and focused on pemphigus vulgaris support (8/10 groups) with the top 3 Facebook groups having over 1000 members each (Table 2). Of the 25 identified posts, individual posts were the most common (n=17, 68%), while posts made by patients/caregivers generated the highest average engagement (272.2, SD 264.7 interactions/post).

Table 2. Analysis of Facebook support group and post content.

	Access type	Posts, n	Members, n	Type of content, n (%)	Activity	Total engagement (likes/reactions + shares + comments) and Int/Post[a]
Top 10 Facebook support groups		N/A[b]		• N/A		• N/A
1. Pemphigus Vulgaris	Private[c]		4900		4 posts/day	
2. Pemphigus Vulgaris	Private		2300		9 posts/week	
3. Pemphigus Vulgaris Support and Awareness	Private		1400		2 posts/month	
4. Pemphigus Vulgaris	Public		112		0 posts	
5. Pemphigoid and Pemphigus Nation	Public		244		8 posts/year	
6. Living with Pemphigus Foliaceus	Private		350		2 posts/week	
7. Pemphigus Vulgaris in India	Private		300		1 post/month	
8. Pray4Elyse MCD Castleman's Disease/Paraneoplastic pemphigus	Public		90		3 post/year	
9. Pemphigus and Pemphigoid Australia/NZ	Private		90		0 posts/week	
10. Pemphigus Vulgaris Victoria	Private		4		2 posts/month	
Top 25 Facebook posts	N/A		N/A		N/A	
Physician		0		• N/A		• Total: 0 • Int/Post: 0
Patient/caregiver		5		• Personal: 4 (80) • Educational: 1 (20)		• Total: 1361 • Int/Post, mean (SD): 272.2 (264.7)
Individual		17		• Awareness: 16 (94) • Educational: 1 (6)		• Total: 432 • Int/Post, mean (SD): 25.4 (17.7)
Organization		2		• Educational 2 (100)		• Total: 359 • Int/Post, mean (SD): 179.5 (248.2)

[a]Int/Post: interactions per post.

[b]N/A: not applicable.

[c]Private groups require admin approval before content can be accessed by the user.

Discussion

Principal Findings

Social media provides an avenue for physicians, patients, and organizations to share educational, personal, and promotional content to improve rare disease awareness [6]. Approximately half of the YouTube videos were made by physicians, yet content made by organizations had the highest engagement. The average QUEST score (14.6, SD 4.1) across the analyzed YouTube videos was higher than those for other dermatologic conditions, suggesting higher quality content [7].

Instagram had the highest portion of nonhuman–related pemphigus content, highlighting a need for more reliable human-related pemphigus information. Although Twitter has the highest rate of medical misinformation, half of the top filtered posts were made by physicians, and the majority of posts were educational [8].

Social media has enhanced clinical trial recruitment, and given the rarity of pemphigus, social media can improve awareness of ongoing clinical trials [9]. However, Twitter and Instagram are the only identified platforms with recruitment posts (2/50, 4% and 16/50, 32%, respectively). Additionally, Facebook groups allow patients to connect with others to discuss disease-related concerns and resources.

Limitations and Future Directions

The limitations of this study include that our data was collected at a singular time point for each platform with largely descriptive data. Additionally, other platforms such as TikTok, Snapchat, WhatsApp, and Reddit were not analyzed. Future studies should evaluate the accuracy of medical content and implications of misinformation posted on the web.

Conclusion

Current uses of social media for pemphigus revolve around better understanding the disease, developing support groups, and improving awareness. Physicians can use these avenues to connect patients globally to discuss their experiences. Social media also offers a platform for greater clinical trial recruitment for those with rare diseases.

Conflicts of Interest

SRF has received research, speaking, or consulting support from AbbVie, Accordant, Almirall, Alvotech, Amgen, Arcutis, Arena, Argenx, Biocon, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Eurofins, Forte, Galderma, Helsinn, Janssen, Leo Pharma, Micreos, Mylan, Novartis, Ono, Ortho Dermatology, Pfizer, Regeneron, Samsung, Sanofi, Sun Pharma, UCB, Verrica, Voluntis, and vTv Therapeutics. He is the founder and part owner of Causa Research and holds stock in Sensal Health. All other authors have no conflicts of interest to declare.

Multimedia Appendix 1
Supplementary methods.
[DOCX File , 14 KB - derma_v6i1e50011_app1.docx]

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Abbreviations

QUEST: Quality Evaluation Scoring Tool

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Research Letter

Hell's Itch: A Unique Reaction to UV Exposure

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Abstract

We present a survey-based exploration of Hell's Itch, a severe dermatologic reaction often mistaken for sunburn, that reveals distinct symptoms including intense pain, unrelenting itching, paresthesia, and even suicidal ideation, differentiating it from a typical sunburn.

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KEYWORDS

Hell's Itch; social media; sunburn; sun; survey; skin; dermatology; dermatological; itch; itchiness; itchy; symptoms; experience; ultraviolet; UV; dermatologist; teledermatology; hair; nails; scratch

Introduction

Hell's Itch is an inciting dermatologic reaction that can occur after sun exposure and is often characterized by symptoms such as intense pain, itching, paresthesia, and suicidal ideation. A patient with Hell's Itch described their experience as follows: "Dozens of white-hot sewing needles being repeatedly stabbed into my upper back. The pain is unrelenting and unbearable... It drives you completely insane." Patient accounts like this distinguish Hell's Itch from a typical sunburn.

One in 3 people in the United States experience a sunburn annually [1]. Sunburn is characterized by cutaneous erythema appearing 24 to 72 hours following sun exposure. The cause of sunburn is excessive exposure to UV radiation, commonly causing acute, transient inflammation in the skin [2]. Symptoms depend on sunburn severity and may include blistering, peeling, and pruritus due to peeling [2]. Like sunburn, Hell's Itch is a manifestation of cutaneous damage after unprotected UV exposure. However, Hell's Itch exhibits key differences in presentation. Hell's Itch is reported as an acute, uncontrollable itch that causes stabbing pain when scratched [3]. In addition, Hell's Itch results from a key inciting event such as topical cream application or water exposure.

Hell's Itch is commonly misdiagnosed as sunburn. Misdiagnosis leads patients to seek medical advice from alternative sources such as social media. There are social media platforms with groups comprising up to 4000 members who share experiences and anecdotal treatment remedies.

Here, we explore the differences in symptomatology between Hell's Itch and a typical sunburn using a patient survey.

Methods

Hell's Itch is not well characterized in the scientific literature, with only 3 published case reports to date [3-5]. Without objective diagnostic criteria available to establish a diagnosis of Hell's Itch, our survey relied on subjective, self-reported data as the source to identify the distinguishing symptoms. We surveyed patients in social media groups with approximately 5500 total members to identify common symptoms, the incidence of symptoms, and symptom severity rated from 0 (none) to 10 (worst imaginable). Study inclusion criteria included adults aged ≥18 years with at least 1 episode of Hell's Itch.

Results

A total of 100 people with self-diagnosed Hell's Itch completed the survey. The defining differences between the symptoms of

Hell's Itch and sunburn identified in the survey included unrelenting pruritus, intense pain, difficulty sleeping, paresthesia, and suicidal ideation (Table 1). Hell's Itch symptoms commonly occurred after sun exposure and were often triggered by inciting events like water exposure (eg, showering, bathing, swimming, humidity, or sweating) or application of a topical cream (88/100, 88%).

Table 1. Hell's Itch survey results (N=100).

Symptom	Prevalence (%)	Average symptom severity rating[a]
Pruritis	98	9.17
Pain	90	8.42
Difficulty sleeping	87	8.62
Paresthesia or tingling	77	7.61
Suicidal ideation	44	6.93
Peeling skin	33	6.20
Numbness	13	5.13
Other	32	8.94

[a]Symptom severity was rated from 0 (none) to 10 (worst imaginable).

Discussion

The incidence rate of Hell's Itch is currently unknown as it is commonly misdiagnosed as a sunburn. Our survey characterizes the prevalence and severity of key symptoms differentiating Hell's Itch from a typical sunburn—intense pain, itching, paresthesia, and even suicidal ideation—which are distinctive symptoms absent with sunburn. However, the survey may be limited in its strength because it relied on patients self-diagnosing their condition. Future efforts should move beyond convenience samples and include studies to characterize pathophysiology, risk factors, and effective treatments.

Conflicts of Interest

None declared.

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Research Letter

Skin of Color Representation for Atopic Dermatitis on TikTok: Cross-Sectional Analysis

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KEYWORDS

dermatology; dermatologist; derm; derma; telederm; teledermatology; skin; color; atopic; dermatitis; eczema; TikTok; media; atopic dermatitis; disparity; social media; post; clinical presentation; educational information; digital platform; digital health

Introduction

Atopic dermatitis affects millions of people worldwide, with potentially substantial impacts. With the popular social media platform TikTok, dermatologists can share skin health information with a larger audience. Since launching in 2016, TikTok has had over 1 billion monthly active users and is the world's fastest-growing social media platform [1]. The quality of dermatology-related content on TikTok has been shown to be largely inaccurate, with patients, rather than board-certified dermatologists, being the most popular creators [1,2]. Additionally, the quality and inclusivity of information on these platforms may be limited, particularly for patients with skin of color (SoC) [3]. Despite increasing efforts to represent patients with Fitzgerald skin types III-VI in dermatologic literature, additional evidence is needed [4]. We aim to evaluate the quality of dermatology content and representation of patients with SoC on TikTok. We hope to identify opportunities to improve the dissemination of accurate and inclusive information.

Methods

TikTok was searched with the term #eczema on July 27, 2022, and the first 136 videos were assessed. We included nonduplicative English videos with relevant content. Of the 136 videos, 119 met the inclusion criteria and 17 did not. Videos by board-certified physicians were categorized as physician; those by individuals without recognized medical qualifications were categorized as nonphysician. Two independent researchers rated 119 videos using the DISCERN criteria, assessing the information quality and reliability [5]. DISCERN is a well-established tool with criteria designed to assess the quality of health-related information and materials, evaluating various aspects of the content, including information accuracy and source reliability. Cohen κ was calculated at 0.9375, indicating high interrater reliability and agreement in the DISCERN analysis.

A single researcher analyzed videos for SoC representation, assessing examples of patients affected by atopic dermatitis using the Fitzpatrick scale when included. Accurately assessing Fitzpatrick skin type based on videos may have limitations.

Results

Of the 119 videos, 102 were created by nonphysicians and 17 by physicians (dermatologists: n=14; nondermatologists: n=3). The average DISCERN score was 1.26 (Table 1) for nonphysician posts and 2.24 for physician posts (t_{236}=0.0006496729527; P<.001). Of the nonphysician posts, 30 contained images or videos featuring SoC. Only 1 of the physician videos and none of the dermatologist videos contained SoC. Nonphysician posts had three times more views than physician posts. There was no significant difference (P=.21) between the number of views of physician and nonphysician videos. Among physicians, dermatologists had higher average view counts compared to nondermatologists (597,357 vs 105,033).

Table 1. DISCERN scores for skin of color (SoC) inclusion in TikTok posts created by nonphysicians and physicians.

	Videos, n	Views, mean (SD)	DISCERN score, mean (SD)	Videos with SoC, n (%)
Nonphysician	102	1,711,392 (2,553,537)	1.25888 (0.2694)	30 (29.4)
Physician	17	510,476 (605,589)	2.24265 (0.4377)	1 (5.9)
Dermatologist	14	597,357 (636,551)	2.21205 (0.3891)	0 (0.0)
Nondermatologist	3	105,033 (26,626)	2.38542 (0.2818)	1 (33.3)
Total	119	1,539,832 (2,400,033)	1.39942 (0.4607)	31 (26.1)

Discussion

Dermatologists can use the visual nature of their field to engage a broad audience on social media platforms like TikTok [6]. By creating informative videos that showcase diverse clinical presentations and treatment options, dermatologists can enhance the dissemination of accurate and educational health content.

Our study underscores the need for high-quality health content and improved SoC representation in atopic dermatitis–related posts on TikTok. We observed a significant difference in the DISCERN scores between physician and nonphysician content (P<.001), suggesting that physicians can potentially elevate the quality and reliability of health information on social media platforms.

This study also highlights a gap in SoC representation in posts about atopic dermatitis. Physicians appear to lag behind nonphysicians in this regard, most likely due to the available number of physician videos compared to nonphysician videos. Individuals with SoC often manifest with clinical findings that look different than patients with a lighter skin tone. Therefore, by improving SoC representation in TikTok videos, such as including atopic dermatitis examples of patients with Fitzpatrick skin types III-VI, we can bridge this informational gap and ensure a more diverse audience receives accurate and relevant content. Inclusivity in dermatological education is not only a matter of equity but also a means to enhance the overall impact and reach of health-related messages on TikTok. To address this, health care professionals should better represent the diverse patient population they serve on social media platforms. The low viewership of physician videos on TikTok suggests that even if physicians improved SoC representation in their videos, the impact may be limited.

Another limitation was our relatively small sample size, comprising 119 videos. Although we believe our sample was representative of a general search result for atopic dermatitis, other TikTok videos meeting our inclusion criteria were possibly not captured. Furthermore, we exclusively searched TikTok, so the generalizability of our findings to other social media platforms or online resources may be limited.

Our study underscores the current underrepresentation of SoC in atopic dermatitis content on TikTok while highlighting the potential for dermatologists and health care professionals to enhance accessibility and accuracy by leveraging social media, emphasizing the importance of an expanded and reliable online presence by physicians.

Conflicts of Interest

None declared.

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Abbreviations

SoC: skin of color

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Research Letter

Mohs Surgery Price Transparency and Variability at Academic Hospitals After the Implementation of the Federal Price Transparency Final Rule

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KEYWORDS

Mohs micrographic surgery; Mohs surgery; Mohs; dermatologic surgery; price transparency; healthcare costs; health care costs; healthcare policy; health care policy; dermatology; dermatological; surgery; surgical; Medicare; insurance; coverage; cost; costs; economic; economics; fee; fees; price; prices; pricing; transparency; reporting

Introduction

In response to rising health care costs, which can lead to high out-of-pocket patient costs, the US federal government implemented the Hospital Price Transparency Final Rule in 2021 [1,2]. This legislation mandates that hospitals disclose cash and commercial insurance prices for at least 300 medical services. The goal was to foster price transparency, stimulate price competition, and ultimately lower health care costs. As use of Mohs micrographic surgery (MMS) continues to expand, understanding the cost variability of this procedure across hospitals and geographic regions is crucial. Our study aimed to elucidate the current landscape of price transparency and variability for MMS procedure costs at academic hospitals, inclusive of facility and physician fees.

Methods

Overview

To ensure the hospitals evaluated offered MMS, we limited our selection criteria to academic hospitals with MMS fellowships. Private clinics were excluded as they are not subject to the Price Transparency Rule. Using Turquoise Health, a company that compiles nationwide price information from hospitals, we evaluated hospital-reported cash and commercial insurance prices for Current Procedural Terminology (CPT) code 17311 for the calendar year 2022; additional MMS CPT codes (17312-17315) were not reported by hospitals [3]. For reference, we gathered Medicare-reported facility and physician fees, adjusted by state [4]. We calculated the percentage of hospitals reporting cash and commercial insurance prices and compared median prices by payment type.

Ethical Considerations

This study used publicly available online data sets and did not qualify as human subject research; therefore, institutional review board approval was not required at the University of Connecticut Health Center.

Results

Among 62 hospitals, 36 (58.1%) reported commercial insurance prices and 27 (43.5%) reported cash prices, with 26 (41.9%) reporting both. Hospitals in the Northeast more frequently reported cash prices as compared to other regions (73.7% vs 27.3%-35.7%, *P*=.02); regional differences in commercial insurance price reporting did not reach significance (*P*=.16). Hospitals in the Northeast reported the highest median cash prices ($1266.8 vs $514.8-$838.7, *P*=.04); regional differences in median commercial insurance prices did not reach significance (*P*=.07). Across all hospitals, cash prices were more frequently (n=16, 59.3%) higher than commercial prices (Table 1).

Table 1. Price[a] reporting and variation for Mohs micrographic surgery by payor type among academic hospitals.

Region and payor type	Hospitals reporting price, n (%)	Price (US $), median (IQR)	Payor type as lowest reported price, n (%)[b]
All regions (N=62 hospitals)			
Cash	27 (43.5)	838.7 (585.6-1711.8)	16 (59.3)
Commercial	36 (58.1)	717.4 (539.2-1330.0)	11 (40.7)
Medicare, facility fee	—[c]	457.9 (432.7-527.3)	—
Medicare, facility plus physician fees	—	806.1 (780.2-886.2)	—
Northeast (n=19 hospitals)			
Cash	14 (73.7)	1266.8 (690.4-1856.2)	11 (78.6)
Commercial	15 (78.9)	707.3 (633-1135.8)	3 (21.4)
Medicare, facility fee	—	459.6 (457.9-574.6)	—
Medicare, facility plus physician fees	—	819.2 (805.6-971.2)	—
Midwest (n=14 hospitals)			
Cash	5 (64.3)	514.8 (494.0-585.6)	3 (60)
Commercial	7 (50)	531.8 (513.0-539.9)	2 (40)
Medicare, facility fee	—	441.7 (432.7-459.7)	—
Medicare, facility plus physician fees	—	786.7 (765.4-808.1)	—
South (n=18 hospitals)			
Cash	5 (27.8)	773.0 (461.5-827.1)	1 (25)
Commercial	8 (55.6)	1254.5 (700.9-1831.7)	3 (75)
Medicare, facility fee	—	429.6 (403.9-437.2)	—
Medicare, facility plus physician fees	—	780.3 (767.2-790.7)	—
West (n=11 hospitals)			
Cash	3 (27.3)	838.7 (542.3-1214.9)	0 (0)
Commercial	6 (54.5)	1178.2 (686-1330)	3 (100)
Medicare, facility fee	—	681.6 (527.3-681.6)	—
Medicare, facility plus physician fees	—	1058.8 (886.2-1058.8)	—

[a]Hospital-reported median cash prices, commercial insurance prices, and reference Medicare facility and physician fees for Mohs micrographic surgery. Commercial insurance prices for each hospital indicate the median across all payors (eg, UnitedHealth, Anthem, Humana, etc) as reported by the hospital. While the intention of the Hospital Price Transparency Final Rule is to provide comparable holistic pricing information, certain hospitals include only hospital facility fees while others additionally include physician fees in the reported prices. For this reason, Medicare facility and physician fees are provided for contextual purposes but direct comparisons to the hospital-reported prices are not made.

[b]Analysis only conducted for hospitals with both prices listed; at 1 hospital, median cash and commercial prices were equivalent.

[c]Not applicable.

Discussion

Principal Findings

The findings indicate that fewer than half of hospitals reported both cash and commercial insurance prices for MMS, and median prices varied substantially across payor types and regions. This is consistent with findings in other surgical fields [1,5-7]. Regional variations may be partially explained by studies that have shown a hospital's compliance with the Price Transparency Rule is most strongly associated with the compliance status of its peer hospitals in the same area [8]. Interestingly, cash prices tended to be the highest, possibly because this helps hospitals offset losses incurred treating uninsured patients. Other studies have shown that compliance with the Price Transparency Rule is below 30%, yet only 2 hospitals have been fined for noncompliance [1]. The cost of compliance, requiring adequate information technology expertise and personnel, can be a barrier to hospitals with fewer financial resources [8]. Strategies to increase compliance include implementing positive incentives, proper enforcement, and increased financial penalties [9]. Many MMS procedures are performed in private clinics, which the Price Transparency Rule does not apply to. Fully enabling price shopping for MMS would require the Price Transparency Rule mandating MMS prices be reported by both hospital systems and private clinics. Additionally, pricing information would need to be easier for patients to access, comprehend, and compare.

Conclusion

Our findings indicate that significant variability and opacity exist in MMS pricing at academic hospitals. Across all of health care, pricing is not often clearly defined or publicly available. This ambiguity can be confusing for both health care providers and patients, possibly leading to wider cost variability and hindered health care access for select patients. Additional studies exploring health care costs may help shed light on the factors influencing price variability. Limitations to this study include the inability to generalize to nonacademic hospital settings such as private clinics, which perform many MMS procedures but to which the Price Transparency Rule does not apply. Additionally, benchmarking to Medicare pricing, which contains well-delineated facility and physician fees, is difficult as not all hospitals report both fee components despite the intention of the Price Transparency Rule to provide a complete picture of the total cost for a given service [2]. Nonetheless, this analysis provides an important initial characterization of the current state of MMS pricing transparency and variability at academic hospitals.

Conflicts of Interest

HF is a consultant for Cytrellis Biosystems, Inc and Soliton, Inc.

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Abbreviations

CPT: Current Procedural Terminology
MMS: Mohs micrographic surgery

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Research Letter

Evaluation of ChatGPT Dermatology Responses to Common Patient Queries

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ChatGPT; dermatology; dermatologist; artificial intelligence; AI; medical advice; GPT-4; patient queries; information resource; response evaluation; skin condition; skin; tool; AI tool

Introduction

Patients often turn to online resources for medical advice [1]. The chat-based artificial intelligence (AI) service ChatGPT has gained over 100 million users given its impressive responses to complex queries, and it is likely that patients are using it regularly [2]. For example, ChatGPT has demonstrated that it can provide largely appropriate medical advice to questions about cardiac disease [3].

Recently, ChatGPT has been upgraded to use the GPT-4 engine released in March 2023 and is more advanced than its predecessor, GPT-3.5 [4]. We aimed to assess the appropriateness of responses generated by ChatGPT using GPT-4 to common questions by dermatology patients.

Methods

To assess the appropriateness of ChatGPT's responses, 3 experienced dermatologists (JMG-K, TO, and JBL) designed questions to interrogate ChatGPT based on the prevalence of 6 common skin conditions [5] and common queries, supported by a literature review and the dermatologists' professional perspectives. The questions were categorized into 7 groups: acne, atopic dermatitis, alopecia, psoriasis, rosacea, skin cancer, and miscellaneous. ChatGPT Plus was used to access GPT-4. This structured approach aimed to include a set number of 3 questions for each of the 6 primary skin conditions plus a miscellaneous category, resulting in 31 total questions when miscellaneous questions were added.

In April 2023, we queried ChatGPT with each question 3 times, yielding 93 responses. A new chat was initiated for each question to avoid prior context bias. The same 3 dermatologists independently assessed the responses, grading them as "appropriate" or "inappropriate" based on their expertise. Responses were then evaluated as "appropriate" or "inappropriate" based on majority agreement among the 3 dermatologists. In selecting 3 reviewers and repetitions for each question, we aimed to balance the need for a diverse range of evaluations with the practical considerations of managing the data.

Results

ChatGPT generated 88% (82/93) appropriate and 12% (11/93) inappropriate responses (Table 1). Of the 31 questions, 16.1% (n=5) had an overall inappropriate response average, with at least 2 out of 3 dermatologists rating 2 out of 3 responses as inappropriate (Table 2). The appropriateness of ChatGPT's responses was assessed based on the dermatologists' perception of response accuracy and general public understanding. For instance, a question about common forms of alopecia prompted a reply that incorrectly stated alopecia areata was the most common cause; the response also did not mention traction and hair treatments as possible etiologies. All 3 dermatologists deemed this answer inappropriate due to its incompleteness and potential for misinformation.

Table 1. Proportion of appropriate and inappropriate ChatGPT responses by category.

Category	Questions, n	Total responses, n	Appropriate responses, n (%)	Inappropriate responses, n (%)
Acne	3	9	9 (100)	0 (0)
Atopic dermatitis	4	12	9 (75)	12 (25)
Alopecia	3	9	7 (77)	2 (22)
Psoriasis	4	12	10 (83)	2 (17)
Rosacea	3	9	9 (100)	0 (0)
Skin cancer	2	6	9 (100)	0 (0)
Miscellaneous	12	36	29 (80)	7 (20)
Total	31	93	82 (88)	11 (12)

Table 2. Example questions and ChatGPT responses.

Question	Response	Majority rating
What causes acne?	*Acne is a common skin condition that occurs when hair follicles become clogged with oil (sebum) and dead skin cells. Several factors contribute to the development of acne, including hormones, excess sebum production, dead skin cells, bacteria, inflammation, diet, and stress. It's important to note that acne severity and triggers can vary greatly from person to person, and a combination of factors often contributes to the development of the condition.*	Appropriate
Will my child outgrow eczema?	*I am not a doctor, but I can provide you with some general information about eczema. Many children with eczema tend to see improvement as they grow older. In some cases, children may outgrow eczema completely by their teenage years or early adulthood. However, this is not true for everyone. Some individuals may continue to experience eczema symptoms into adulthood or have recurrent flare-ups throughout their lives. It is essential to work closely with your child's pediatrician or dermatologist to manage their eczema effectively and monitor their progress over time.*	Appropriate
What are the best treatments for alopecia?	*I am not a doctor, but I can provide you with some general information on treatments for alopecia. Alopecia is a term that refers to hair loss, and it can have various causes, including genetic predisposition, autoimmune disorders, hormonal imbalances, or even stress. The most common type is alopecia areata, an autoimmune disorder that causes patchy hair loss. Some possible treatments for alopecia include topical treatments, oral medications, injections, light therapy, lifestyle changes, and alternative treatments. It's important to note that the effectiveness of these treatments can vary depending on the individual and the underlying cause of hair loss. A healthcare professional can help determine the best course of treatment based on the specific case.*	Inappropriate

Discussion

GPT-4–based ChatGPT shows potential as a public dermatology resource, producing 88% (82/93) appropriate responses. However, the responses were sometimes inaccurate, incomplete, or not evidence based, indicating the need for model improvements and emphasizing the importance of professional dermatologist consultations. For instance, ChatGPT incorrectly stated alopecia areata as the most common form of alopecia. This incorrect assertion may have been due to widely circulated information on the internet about alopecia areata compared to androgenetic alopecia despite the former being less common.

ChatGPT provided suitable answers for questions on acne, rosacea, and skin cancer but was inconsistent regarding diet, naturopathic remedies for eczema and psoriasis, antiaging treatments, skin care routines, and wound healing. These limitations may reflect ongoing debates and limited evidence in the dermatology community. This may also indicate a default bias toward producing answers rather than acknowledging no good answer exists, a flaw that could potentially perpetuate health misinformation. Indeed, ChatGPT's performance on controversial or complex topics was suboptimal, often neglecting the lack of consensus or evidence.

Interestingly, ChatGPT provided different answers to the same question with varying completeness and accuracy. For instance, when asked about natural eczema treatments, one response suggested numerous unsupported methods whereas another advised consulting a health care professional.

Our results suggest that ChatGPT's algorithmic curation does provide mostly relevant and accurate information in response to dermatologic queries. However, such tools may provide biased or inaccurate information. As such, we recommend that ChatGPT should not replace professional medical advice and should remain a supplementary informational tool for now. As AI advances, dermatologists must engage in developing clinical and patient-facing AI tools, considering public health and patient safety implications.

In the development of AI-based medical resources, it is crucial to rely on objective data, and we advocate for algorithms that are informed by rigorous, evidence-based sources such as PubMed, Web of Science, and Embase, weighted based on the standard assessments for the quality of research findings. Additionally, dermatologists should anticipate patients using ChatGPT for their skin-related questions and be familiar with the types of responses it generates.

Conflicts of Interest

JMGK is a medical advisor to Dermasensor. The authors have no further interests to declare.

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Abbreviations

AI: artificial intelligence

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Research Letter

Derm-ographics: The Australian Dermatologist and Social Media

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Abstract

Social media significantly affects how patients understand their health and choose their healthcare providers, yet Australian dermatologists have a limited online presence compared to their global peers.

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KEYWORDS

dermatology; social media; patient education; LinkedIn; Facebook; online presence; dermatologist; dermatologists; demographic; Twitter; X; YouTube; TikTok; ResearchGate; Instagram; provider; physician; technology use

Introduction

Social media has become ubiquitous in modern life. Of 4.76 billion internet users worldwide, half use social media for 2.5 hours each day [1]. The ever-expanding use of these sites poses a relatively new consideration for doctors, especially in private practice. Evidence suggests patients have begun to rely on social media when choosing a clinician [2,3]. As a relatively visual specialty, dermatology lends itself well to social media. In this paper, we aimed to characterize the extent of online uptake by contemporary Australian dermatologists and to inform clinicians of their colleagues' practices in regards to this emerging marketing and educational platform.

Methods

We searched the Australian Health Practitioner Regulation Agency (AHPRA) register of practitioners for those listed on the Australian College of Dermatology (ACD) "Find a Dermatologist" service on August 1, 2022. Of the 411 ACD-listed dermatologists, 8 were no longer AHPRA registered, 6 were practicing outside of Australia, and 6 worked exclusively in the public health system; these 20 were excluded. Duration of practice, location of practice, and sex were taken from AHPRA data (Multimedia Appendix 1). Location of practice was then assigned as either metropolitan or rural in accordance with the Australian Government's Modified Monash Model.

A Google search was done for each dermatologist identified, using their full professional name and the term "dermatologist." Professional websites were used to identify practice size. Further searches of the following social media platforms were then performed: Facebook, X (formerly Twitter), Instagram, YouTube, ResearchGate, LinkedIn, and TikTok. Only publicly accessible, professional accounts were included in our analysis.

Results

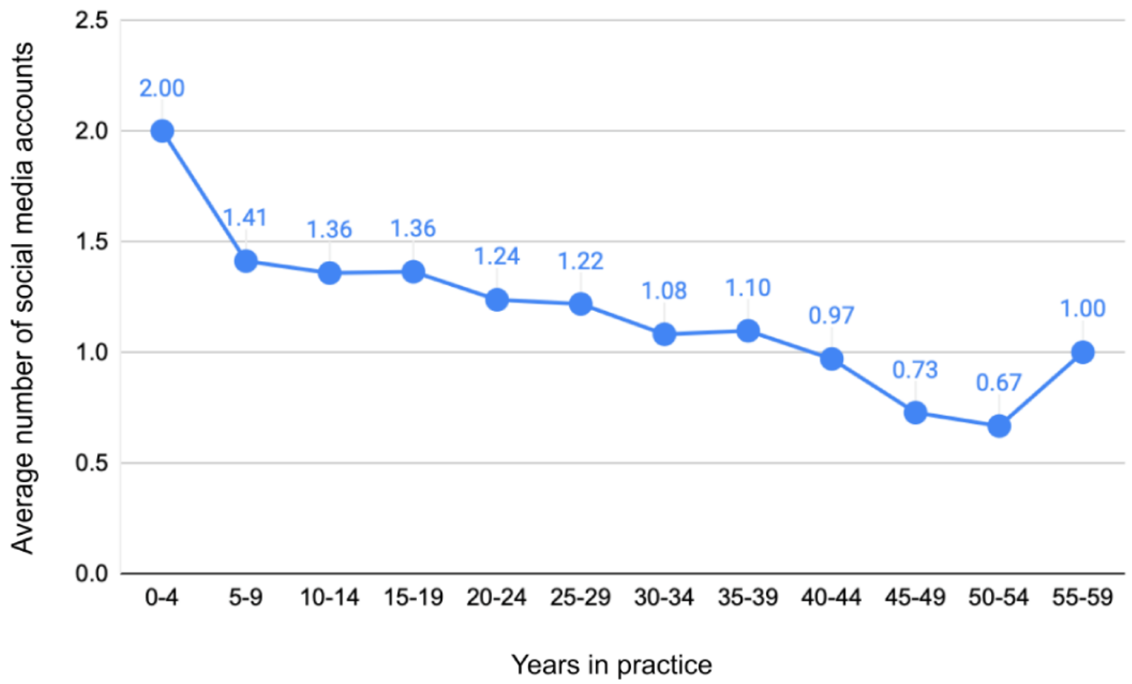
Professional social media use was not prevalent among the 391 Australia-based private dermatologists identified (Table 1). The most commonly subscribed platform for professional use was LinkedIn. Of the dermatologists analyzed, 212 (54.2%) did not have LinkedIn, 168 (43%) had an individual LinkedIn, 2 (0.5%) had a practice LinkedIn, and 9 (2.3%) had both an individual and practice LinkedIn. The next most commonly used platform was Facebook. In decreasing frequency of use followed ResearchGate, Instagram, X, YouTube, and TikTok, respectively. Only 1 (0.3%) Australian dermatologist had an individual TikTok.

Table 1. Proportion of Australian dermatologists with professional social media accounts (N=391).

	LinkedIn, n (%)	Facebook, n (%)	ResearchGate, n (%)	Instagram, n (%)	X, n (%)	YouTube, n (%)	TikTok, n (%)
No account	212 (54.2)	288 (73.7)	299 (76.5)	329 (84.1)	368 (94.1)	373 (95.4)	390 (99.7)
Individual	168 (43)	22 (5.6)	92 (23.5)	21 (5.4)	11 (2.8)	10 (2.6)	1 (0.3)
Practice	2 (0.5)	74 (18.9)	0 (0)	32 (8.2)	8 (2)	8 (2)	0 (0)
Both	9 (2.3)	7 (1.8)	0 (0)	9 (2.3)	4 (1)	0 (0)	0 (0)

There were no significant differences in the average number of accounts by location of practice (*P*=.89) or sex (*P*=.34). While the mean number of social media accounts decreased with duration of practice, this trend did not reach statistical significance (*P*=.18) (Figure 1). Group practitioners, however, were more likely than sole practitioners to hold professional social media accounts (*P*=.003); group practitioners held on average 1.34 accounts versus 0.89 for those practicing alone.

Figure 1. Average number of social media accounts by years in practice.



Discussion

Studies are mixed regarding the importance of social media to patients in selecting a dermatologist [2,3]; younger, less-educated patients, and those seeking cosmetic interventions are likely to rely more heavily on information available online [2]. Of surveyed American patients, 32% have used social media to make health care decisions [4]. The quality of such information remains a concern; as little as 5% of dermatologic content on Instagram is posted by qualified dermatologists [5,6]. Similarly, only 27% of keratosis pilaris content on TikTok is created by dermatologists [7]. There is evidence that most Saudi and American dermatologists plan to increase their social media presence [3,8]. We found that Australian dermatologists, regardless of most demographic influences, have a limited online presence, with an average 1.21 accounts per individual, and with no social media platform attracting more than half the overall group. American dermatologists rate Instagram as their most "valuable" platform, followed by Facebook [8]. We conversely found that LinkedIn was the most subscribed platform among our cohort, followed by Facebook. Given the nature of these sites, this implies a greater Australian uptake of social media for professional networking among medical colleagues, rather than for patient-oriented promotional or educational endeavors.

In summary, social media is an underused avenue among Australian dermatologists, with international data suggesting the public is increasingly informed in their medical decision-making by online content, including practitioner selection. A majority of Australian dermatologists do not use social media for professional purposes, although the most prevalent platform, LinkedIn, is used by 1 in 2 dermatologists. LinkedIn and ResearchGate are typically used by individuals, presumably for academic promotional purposes, and Facebook and Instagram by practices, presumably for client engagement. This fact may inform readers' uptake according to their intentions around the type of publicity.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Demographic details of included Australian dermatologists.
[DOCX File , 17 KB - derma_v6i1e48975_app1.docx]

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Abbreviations

ACD: Australian College of Dermatology
AHPRA: Australian Health Practitioner Regulation Agency

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Research Letter

The Accuracy and Appropriateness of ChatGPT Responses on Nonmelanoma Skin Cancer Information Using Zero-Shot Chain of Thought Prompting

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KEYWORDS

ChatGPT; artificial intelligence; large language models; nonmelanoma skin; skin cancer; cell carcinoma; chatbot; dermatology; dermatologist; epidermis; dermis; oncology; cancer

Introduction

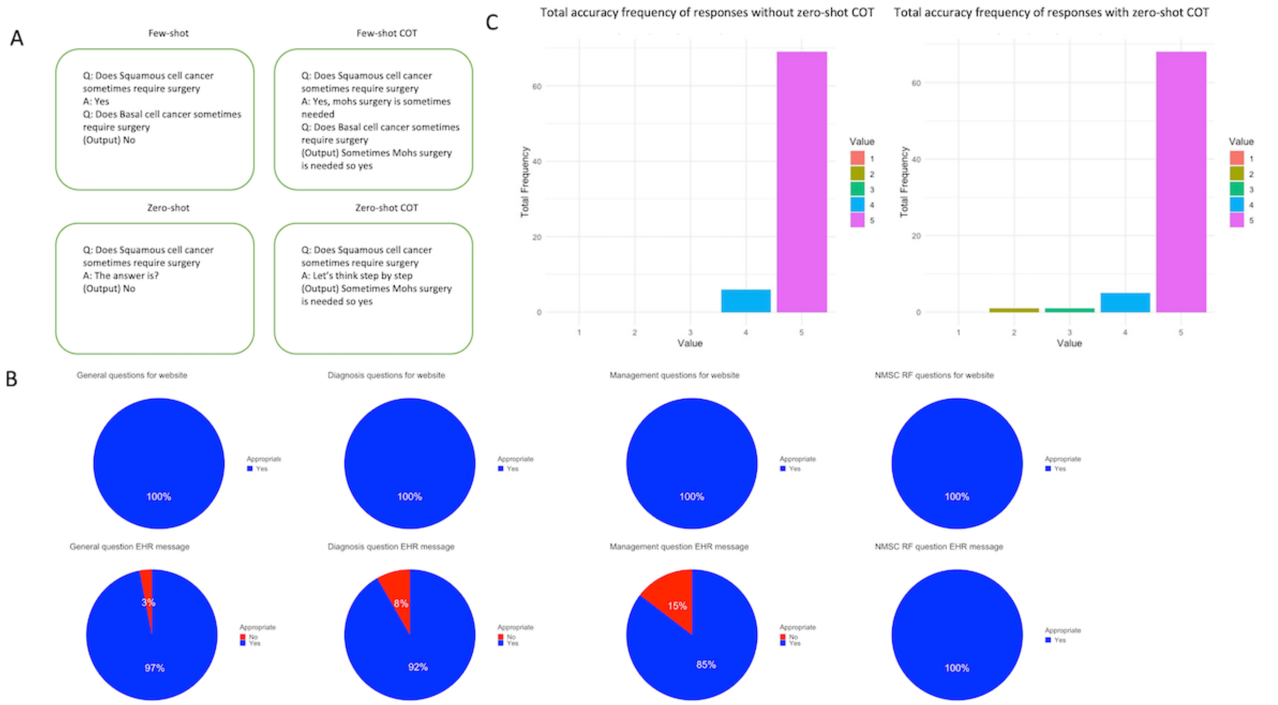
Nonmelanoma skin cancer (NMSC) represents the most prevalent form of cancer worldwide [1]. Patients with NMSC seek information from various resources. Work has already shown that language learning models (LLMs) such as ChatGPT can generate medical information in response to questions [2]; however, results vary significantly based on the prompts entered. Previous work has shown that a few-shot approach, where one provides several example prompts and outputs, has good results [3], as does the few-shot chain of thought approach, where answers include examples and the reasoning for correct answers, encouraging the model to reason through the question [4]. Zero-shot chain of thought (ZS-COT) prompting does not provide example prompts; instead, it uses phrases to encourage the LLMs to "think" through their responses, with significant improvement in accuracy in some contexts [5]. In this study, we explore ChatGPT's performance in answering questions about NMSC using both standard and ZS-COT prompting.

Methods

Overview

We generated 25 common clinical questions about NMSC in four categories: general, diagnosis, management, and risk factors. Prompts were entered into ChatGPT 4.0 on March 31, 2023, and responses were recorded for both standard and ZS-COT prompting (Figure 1A). Ending ZS-COT prompting queries with "Let's think step by step" has been shown to improve performance in previous papers [5]. Three attending dermatologists independently reviewed and graded whether the outputs would be appropriate for a patient-facing website and an electronic health record (EHR) message draft to a patient. Responses were also evaluated for accuracy on a 5-point scale, with 1 being completely inaccurate and 5 being completely accurate, and reviewers assessed which of the two prompting styles they preferred. Statistical differences between prompts were computed using the Wilcoxon test. Statistical analysis was performed in R version 4.2.2 (R Foundation for Statistical Computing).

Figure 1. (A) Example of several popular language learning model prompting techniques. (B) Percent of appropriate responses for each question category by medium. (C) Accuracy scores by prompt style. COT: chain of thought; EHR: electronic health record; NMSC: nonmelanoma skin cancer; RF: risk factor.



Ethical Considerations

This study did not require institutional review board approval.

Results

Averaging all accuracy scores from a scale (range 1-5), we found that the combined accuracy for both the original prompt and ZS-COT prompt was 4.89. The average accuracy score from all 25 questions asked for the original prompt and ZS-COT prompt was 4.92 and 4.87, respectively, representing a nonsignificant difference of 1.03%. Both models were deemed 100% appropriate for a patient-facing information portal for general, diagnosis, management, and risk factor questions. For EHR message responses, outputs were appropriate for 97% of general questions, 92% of diagnosis questions, 85% of management questions, and 100% of risk factor questions (Figure 1B). The lowest accuracy grade for the standard prompting responses and ZS-COT prompting was 4 and 2, respectively (Figure 1C). This score was given for the prompt "What causes basal cell carcinoma?" (Multimedia Appendix 1).

Discussion

This exploratory qualitative study found that LLMs can provide accurate patient information regarding NMSC appropriate for both general websites and EHR messages. We found that ZS-COT prompting does not provide more accurate dermatology information. The limitations of this study include that we only explored a subset of clinical questions patients may have about NMSC, there is no objective standard for appropriateness, and the personal biases of the dermatologists may bias response preference. As LLMs continue to grow and be adapted, clinicians must monitor their clinical utility and how different prompting methods may change the quality of results.

Conflicts of Interest

BU is an employee of Mount Sinai and has received research funds (grants paid to the institution) from Incyte, Rapt Therapeutics, and Pfizer. He is also a consultant for Arcutis Biotherapeutics, Castle Biosciences, Fresenius Kabi, Pfizer, and Sanofi. JU is an employee of Mount Sinai and is a consultant for AbbVie, Castle Biosciences, Dermavant, Janssen, Menlo Therapeutics, Mitsubishi Tanabe Pharma America, and UCB. The rest of the authors declare no relevant conflicts of interest.

Multimedia Appendix 1
Evaluated nonmelanoma skin cancer questions.
[DOCX File , 18 KB - derma_v6i1e49889_app1.docx]

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Abbreviations

EHR: electronic health record
LLM: language learning model
NMSC: nonmelanoma skin cancer
ZS-COT: zero-shot chain of thought

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Research Letter

From the Cochrane Library: Interventions for Pemphigus Vulgaris and Pemphigus Foliaceus

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KEYWORDS

pemphigus vulgaris; pemphigus foliaceus; Cochrane; rituximab; desmoglein; vesiculobullous; immunoglobulin; corticosteroids; skin; dermatology; systematic review

Introduction

Cochrane systematic reviews are rigorous in methodology and contribute to our understanding of evidence-based treatments of diseases. Among these diseases is pemphigus, a group of acquired autoimmune vesiculobullous diseases (pemphigus vulgaris [PV], pemphigus foliaceus [PF], and pemphigus paraneoplastic [PNP]), characterized by B-cell–mediated immunoglobulin G antibodies against desmogleins 1 and 3. Cutaneous bullae cause loss of barrier function and pain, dehydration, superimposed infections, and psychological distress. Due to a lack of expert consensus and the poor efficacy of previous therapies, a Cochrane systematic review of randomized controlled trials (RCTs) sought to define the best treatment for pemphigus [1]. Here, we highlight takeaways from the review [1] and discuss advances in therapy. PNP was excluded from the review due to its rarity and because its management depends on the underlying malignancy.

Methods

A total of 11 RCTs were analyzed to assess efficacy and safety among treatments for PV and PF. The primary outcomes were death and disease remission, with secondary outcomes including disease severity indexes, time to disease control, cumulative glucocorticoid dose, serologic markers, and the proportion of patients achieving disease control and relapse. The RCTs used various combinations and doses of steroid-sparing agents with or without corticosteroids. We contrasted therapies, outcomes, and comparison effect size and conducted 4 meta-analyses.

Results

A recent (2021) network meta-analysis [2] found rituximab (Table 1), a CD20 B-cell–depleting therapy, as the most effective therapy for key outcomes like disease relapse, withdrawal from adverse events, remission, and cumulative glucocorticoid dose. The right-most column of Table 1 contrasts therapies relative to rituximab among the 4 key outcomes evaluated. Although the included trials [2] risked bias due to inadequate allocation concealment and lack of participant, personnel, and outcome blinding, the results align with emerging expert consensus and other important clinical trials [3] directly comparing rituximab to other therapies like mycophenolate.

Table 1. Summary of interventions, outcomes assessed, and effect size from 2009 (left) and 2021 (right).

2009			2021	
Intervention	Effect size: RR[a] (95% Cl)	Outcomes	Effect size: pooled OR[b] (95% CI)	Rituximab vs intervention
Prednisolone (1mg/kg vs 0.5 mg/kg)				Steroid alone
1	Not estimable	Disease control	—[c]	
2	0.7 (0.43 to 1.14)	Relapse	0.38 (0.12 to 1.15)	
3	Not estimable	Withdrawal due to adverse event	0.05 (0 to 0.083)	
Pulsed oral dexamethasone vs placebo				Steroid alone
1	1.91 (0.68 to 5.33)	Relapse (after discontinuing or stopping)	—	
2	2.45 (0.31 to 19.74)	Withdrawal due to adverse event	—	
Azathioprine vs glucocorticoid (prednisolone) alone				
1	1.04 (0.8 to 1.36)	Remission	14.45 (4.71 to 43.68)	Steroid alone
2	–3.91 (–6.71 to –1.12)	Cumulative glucocorticoid dose	–11.10 (–14.08 to –9.57)	Steroid alone
3	2 (0.19 to 20.9)	Withdrawal due to adverse event	0.02 (0 to 0.56)	Azathioprine
Cyclophosphamide vs glucocorticoid (prednisone/prednisolone) alone				Azathioprine
1	0.96 (0.71 to 1.28)	Remission	10.10 (2.67 to 38.23)	
2	0 (0)	Disease control	—	
3	0.5 (0.05 to 4.67)	Relapse	0.60 (0.10 to 3.63)	
4	–3.35 (–6.14 to –0.56)	Cumulative glucocorticoid dose	–8.79 (–11.60 to –5.98)	
5	0.33 (0.01 to 7.87)	Withdrawal due to adverse events	—	
Cyclosporine vs glucocorticoid (prednisone/methylprednisolone) alone				Cyclophosphamide
1	0 (0)	Remission	9.59 (2.42 to 37.96)	
2	1.06 (0.86 to 1.32)	Disease control	—	
3	0.92 (0.23 to 3.65)	Relapse	0.42 (0.08 to 2.28)	
4	–0.05 (–0.18 to 0.081)	Cumulative glucocorticoid dose	–9.36 (–12.16 to –6.55)	
5	0 (0)	Withdrawal due to adverse event	0.10 (0 to 4.20)	
Dapsone vs placebo				Cyclophosphamide
1	1.85 (0.61 to 5.63)	Remission (<7.5 mg prednisone) at 12 months	—	
2	0.37 (0.05 to 2.95)	Withdrawal due to adverse event	—	
Mycophenolate vs glucocorticoid (prednisolone) alone				Dexamethasone-cyclophosphamide (6 and 12 months)
1	0.91 (0.67 to 1.24)	Remission	47.11 (4.99 to 445.07), 6 months	
2	–1.83 (–4.94 to 1.28)	Cumulative glucocorticoid dose	—	
3	1.0 (0.07 to 15.26)	Withdrawal due to adverse events	0.06 (0 to 7.06), 6 months	
Plasma-exchange vs control				Dexamethasone-cyclophosphamide (6 and 12 months)
1	7.43 (0.43 to 129.55)	Death	—	
2	1.12 (0.70 to 1.78)	Disease control (study definition involving relative healing time)	—	
3	44.38 (–222.43 to 311.19)	Reduction antibody titer (baseline to end protocol, mean difference)	—	
4	7.2 (0.42 to 124.08)	Withdrawal due to adverse events	—	

2009			2021	
Intervention	Effect size: RR[a] (95% CI)	Outcomes	Effect size: pooled OR[b] (95% CI)	Rituximab vs intervention
Azathioprine vs cyclophosphamide				
1	1.09 (0.82 to 1.44)	Remission	5.48 (0.71 to 42.02), 12 months	Dexamethasone-cyclophosphamide (6 and 12 months)
2	1.8 (0.89 to 3.64)	Disease control (healing of >50% of lesions and/or occurrence of <5 blisters/month)	—	Dexamethasone-cyclophosphamide (6 and 12 months)
3	1.0 (0.53 to 1.88)	Relapse	0.67 (0.04 to 11.13)	Dexamethasone-cyclophosphamide (6 and 12 months)
4	1.0 (0.53 to 1.88)	Relapse	0.063 (0.12 to 3.47)	Mycophenolate
5	–5.64 (–1.04 to –0.79)	Cumulative glucocorticoid dose	—	Mycophenolate
6	3.91 (0.45 to 33.66)	Withdrawal due to adverse events	0.05 (0 to 1.18)	Mycophenolate
Azathioprine vs mycophenolate				Mycophenolate
1	1.14 (0.85 to 1.53)	Remission	10.80 (3.07 to 38.05)	
2	0.72 (0.52 to 0.99)	Disease control	—	
3	–2.07 (–3.54 to –0.60)	Cumulative glucocorticoid dose	–11.10 (–13.70 to –8.49)	
4	3.01 (0.48 to 18.97)	Withdrawal due to adverse events	—	
Cyclophosphamide vs cyclosporine				
1	0 (0)	Remission (<10 mg prednisone equivalent) at 5 years	—	Mycophenolate
2	0 (0)	Disease control	—	Mycophenolate
3	0.4 (0.04 to 3.66)	Relapse	0.81 (0.05 to 13.72)	Cyclosporine
4	0 (0)	Withdrawal due to adverse events	0.04 (0 to 5.92)	Cyclosporine
Cyclophosphamide vs mycophenolate				Cyclosporine
1	1.05 (0.76 to 1.44)	Remission	11.96 (1.92 to 74.49)	
2	–1.52 (–2.98 to –0.056)	Cumulative glucocorticoid dose	–11.77 (–14.04 to 9.51)	
3	0.33 (0.01 to 7.87)	Withdrawal due to adverse events	—	
Topical epidermal growth factor vs placebo	2.35 (1.62 to 3.41)	Time to control (hazard ratio)	—	Cyclosporine
Traditional Chinese Medicine	0.75 (–1.12 to 2.62)	Antibody titer	—	Cyclosporine

[a]RR: relative risk.

[b]OR: odds ratio.

[c]The 2021 network review assessed withdrawal due to adverse events, remission, relapse, and cumulative glucocorticoid dose. Other measures were not available.

Induction dosing for rituximab was two 1 g intravenous infusions 2 weeks apart followed by a 6-month prednisone taper of 1 mg/kg/day. Additionally, 2 novel higher-affinity CD20-blocking agents, ofatumumab and veltuzumab, demonstrated efficacy in isolated cases of rituximab-resistant pemphigus. Ofatumumab and veltuzumab are not used for pemphigus outside of clinical trials and for compassionate use. In addition, trials are underway for other immunotherapies targeting the fragment crystallizable region, B-cell–activating factor, and Bruton tyrosine kinase [4]. The meta-analyses revealed that some interventions were superior for certain outcomes: improved disease remission with mycophenolate relative to azathioprine, a steroid-sparing effect with azathioprine and cyclophosphamide, and a decreased time to erosion control with topical epidermal growth factor (Table 2). At the time of the 2009 study, systematic analysis including rituximab and clinical trials including intravenous immunoglobulin were ongoing [5].

Table 2. Summary of conclusive secondary outcomes (2009).

Therapeutic	Secondary outcome
Mycophenolate mofetil	Improved disease control compared to azathioprine (RR[a] 0.72, 95% CI 0.52 to 0.99; NNT[b] 3.7)
Azathioprine	Decreased the cumulative glucocorticoid dose (MWD[c] –3919 mg prednisolone, 95% CI –6712 to –1126)
Cyclophosphamide	Deceased the cumulative glucocorticoid dose compared to prednisolone alone (MWD –3355 mg prednisolone, 95% CI –6144 to –566)
Topical epidermal growth factor	Decreased time to erosion healing compared to the control intervention (HR[d] 2.35, 95% CI 1.62-3.41)

[a]RR: relative risk.
[b]NNT: number needed to treat.
[c]MWD: difference in means.
[d]HR: hazard ratio.

Discussion

With an increasing understanding of the immune system, B-cell physiology, and the pathogenesis of pemphigus, therapies continue to emerge, making previous therapies obsolete. Here, we placed important Cochrane review findings in the context of recent advancements in the treatment of pemphigus. Further studies are needed to determine therapeutic regimens, safety, and efficacy of novel medical therapies for pemphigus.

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Conflicts of Interest

RPD is editor-in-chief of *JMIR Dermatology* and Cochrane Council cochair. TES serves as an editorial board member-at-large for *JMIR Dermatology*. RR is an editorial fellow for *JMIR Dermatology*. DM serves on the advisory boards or is an investigator for ArgenX, Roche, Lilly, Principiabio, Sanofi, and Janssen. DM is also the cocreator of the Pemphigus Disease Area Index and the creator of the Autoimmune Bullous Disease Quality of Life (ABQOL) and Treatment Autoimmune Bullous Disease Quality of Life (TABQOL) questionnaires.

Editorial notice: This article is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2009, Issue 1, DOI: 10.1002/14651858.CD006263.pub2 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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Abbreviations

PF: pemphigus foliaceus
PNP: pemphigus paraneoplastic
PV: pemphigus vulgaris
RCT: randomized controlled trial

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Case Report

Confluent and Reticulated Papillomatosis Resembling Pityriasis Versicolor and Acanthosis Nigricans: Case Report

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Abstract

Confluent and reticulated papillomatosis (CARP) is a rare disorder mostly seen in young adults. It is characterized by persistent dull-brown, centrally confluent, peripherally reticulate macules and papules, which coalesce to form patches and plaques on the upper trunk and neck. It is commonly confused with pityriasis versicolor and acanthosis nigricans (AN). We report the case of a 15-year-old male with multiple pigmented confluent and reticulated patches and plaques on the neck, trunk, and chin for 3 years, which was successfully treated with oral minocycline, resulting in complete resolution of lesions within 2 weeks. The morphology of CARP resembles that of various other dermatological conditions such as AN and pityriasis versicolor, and, as a result, it is frequently misdiagnosed and mistreated, leading to social embarrassment for the patient. Therefore, it is prudent for dermatologists to carry out comprehensive clinical and histopathological assessments to facilitate prompt diagnosis and management of this condition.

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KEYWORDS

CARP; confluent and reticulated papillomatosis; pityriasis versicolor; acanthosis nigricans; minocycline

Introduction

Confluent and reticulated papillomatosis (CARP), which is also known as Gougerot-Carteaud syndrome, is an uncommon disorder of defective epidermal keratinization characterized by hyperkeratotic papules that may coalesce into confluent and reticulated plaques. It predominantly affects adolescents [1]. The etiology is unclear, but an aberrant host reaction to commensal organisms such as *Malassezia furfur* or *Dietzia papillomatosis* has been proposed [2]. CARP may masquerade as acanthosis nigricans (AN) or tinea versicolor, with few cases even showing an association with the latter [3]. We came across a case of a 15-year-old adolescent male with multiple asymptomatic pigmented lesions on the neck, upper back, chest, and chin for 3 years, which was misdiagnosed as pityriasis versicolor and AN. Treatment with oral minocycline led to successful resolution of lesions within 14 days.

Case History

A 15-year-old male presented at our outpatient department with a history of multiple, flat, hyperpigmented lesions on the neck, upper back, upper chest, and chin since the past 3 years. Lesions started on the nape of the neck, following a progressive course to involve the whole neck and upper back area. The patient complained of a rapid increase in the appearance of new lesions on the upper chest, presternal area, and chin area since the past 2 months. The lesions were asymptomatic. The patient had taken multiple unknown oral and topical medications with no effect on the size and number of lesions. There was no family history of similar lesions. His BMI was within the normal range. Dermatological examination revealed multiple hyperpigmented macules with mild scaling, which were confluent in the center and reticular toward the periphery over the neck, upper back, chest, and presternal region. Lesions over the nape of the neck and chin were hyperpigmented and verrucous (Figure 1). Differential diagnoses of CARP, AN, pityriasis versicolor, and macular amyloidosis were considered. Histopathological sections showed orthokeratotic hyperkeratosis, acanthosis, and low papillomatosis with few fungal spores in the stratum corneum. Sparse perivascular lymphocytic infiltrate was seen in the papillary and superficial dermis. Based on clinical and histopathological evaluation, a diagnosis of CARP was made (Figure 2).

Oral minocycline (100 mg once daily) was initiated for the patient, and follow-up evaluation was conducted after 14 days, which revealed complete clearing of lesions from all involved sites (Figure 3).

Figure 1. Multiple hyperpigmented macules, which are confluent at the center and reticulate at the periphery, involving the (A) chest and (C) upper back. A hyperpigmented and verrucous lesion with a reticular pattern over the (B) nape of the neck and (D) chin.

Figure 2. Histopathological assessment. (A) Skin section under low power (10× magnification) showing hyperkeratosis and acanthosis nigricans with low papillomatosis. The papillary dermis shows sparse perivascular lymphocytic infiltrate. (B) Few fungal spores are seen in the stratum corneum under high power (40× magnification).

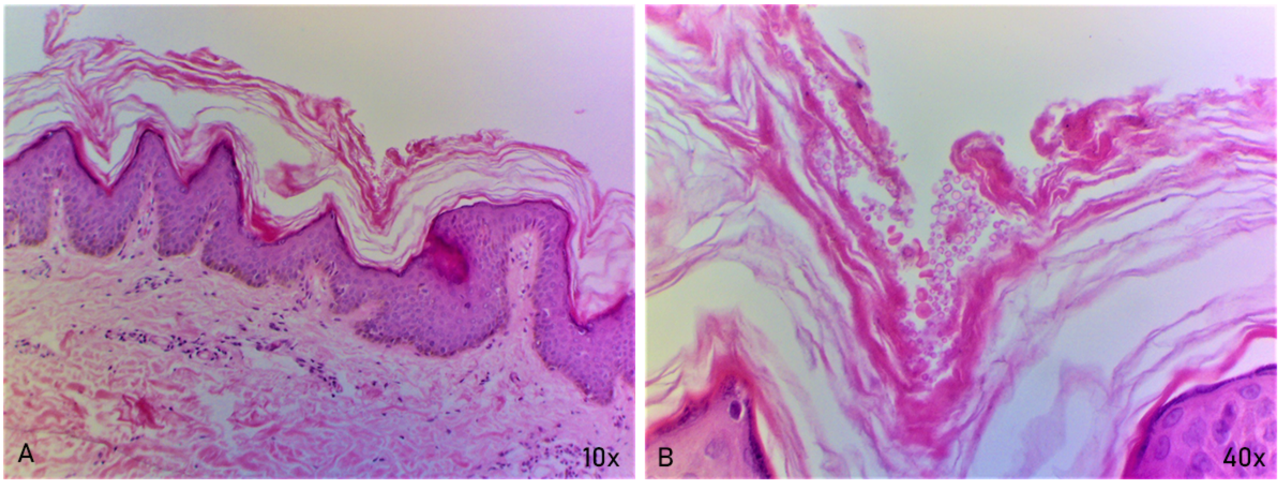

Figure 3. Complete resolution of all lesions post 14 days of treatment with oral minocycline on the (A) chest, (B) back, (C) nape of the neck, and (D) chin.

Discussion

Principal Findings

CARP of Gougerot and Carteaud is a rare dermatosis seen usually in adolescents. It clinically manifests as persistent brown, scaly macules, papules, patches, or plaques. These lesions tend to be confluent at the center and become reticulated toward the periphery and are commonly located on the neck, interscapular, and intermammary regions and the axillae [4]. The etiopathogenesis of CARP is obscure till date, but data from few studies have hypothesized defective epidermal hyperkeratinization and an inherent tendency toward a hyperproliferative response to colonization by *M furfur* [5]. Recently, the presence of *Dietzia* spp in the skin has been proposed as an etiological factor in CARP. Other possible causes of CARP include endocrine abnormalities such as insulin resistance and hypothyroidism, a reaction to UV light, a variant of cutaneous amyloidosis, and genetic predisposition [1]. The histopathological characteristics of CARP include undulating basket-weave hyperkeratosis, focal acanthosis limited to the areas of elongated rete ridges, papillomatosis, and increased basal melanin pigmentation [6]. Occasionally, a mild perivascular lymphocytic infiltrate can be seen in the papillary dermis [5]. CARP is often clinically mistaken for pityriasis versicolor and usually shows no response to therapy with antifungal agents [7]. It was previously considered a clinical form of AN, but AN differs in location (axillae and neck in AN) and has a darker appearance than CARP [3,8]. Pseudoatrophoderma colli is a rare entity and is usually considered a variant of CARP. It clinically presents as atrophic and wrinkled lesions predominantly over the trunk and neck (thus named “colli”) [3].

The diagnostic criteria for CARP, as proposed by Davis et al [7] and Srinivas [9], require the following: (1) clinical presentation of scaly brown reticulated and papillomatous macules and patches; (2) the upper trunk and neck as the site; (3) negative potassium hydroxide staining of scales for spores and hyphae; (4) no response to antifungal agents; and (5) an excellent response to minocycline.

Jo et al [10] proposed a change to the original criteria, which are as follows: (1) clinical presentation of scaly brown macules and patches, some reticulated and papillomatous; (2) the upper trunk, neck, or flexures as the site; (3) negative potassium hydroxide staining or lack of response to antifungal treatment; and (4) an excellent response to antibiotic treatment.

The main differentiating features of CARP, AN, and pseudoatrophoderma colli are summarized in Table 1 [3].

A variety of treatments for CARP are available, among which oral minocycline (50-100 mg twice daily) is the treatment of choice. Recently, azithromycin (250-500 mg thrice per week) has been used, given its better safety profile than that of minocycline. Other less effective oral treatments options for CARP include isotretinoin, acitretin, and etretinate. Various topical agents have also been used, including selenium sulfide, ketoconazole cream, tacalcitol, tazarotene, tretinoin, and calcipotriene (calcipotriol) [1].

Table 1. Differentiating features between confluent and reticulated papillomatosis (CARP), acanthosis nigricans (AN), and pseudoatrophoderma colli.

Features	CARP	AN	Pseudoatrophoderma colli
Age	Adolescents	Any age	15-36 years
Gender	Male predominance	Equal distribution	Female predominance
Site	Upper trunk, neck, or flexures	Neck and axillae	Trunk and neck
Clinical presentation	Scaly brown macules and patches with some appearing reticulated and papillomatous	Velvety brown plaques	Atrophic and wrinkled lesions predominantly located on the trunk and neck
Microscopic features	Undulating basket-weave hyperkeratosis, papillomatosis, focal acanthosis limited to the areas of rete ridge elongation, and increased basal melanin pigmentation	Higher degree of acanthosis and papillomatosis than CARP and pseudoatrophoderma colli, and increased melanogenesis	Loosely thickened stratum corneum, stratum spinosum of variable thickness, irregular acanthosis, hypogranulosis, and mild dermal lymphocytic infiltrate
Treatment	Excellent response to minocycline	Improvement of insulin resistance, topical retinoids, ammonium lactate, and calcipotriene	Good response to minocycline

Conclusions

CARP is a rare dermatosis with a chronic and recurrent course, predominantly afflicting adolescents. Its etiology is controversial, but it is widely considered a disorder of keratinization. Its morphology resembles that of various other dermatological conditions such as AN and pityriasis versicolor, and, as a result, it is frequently misdiagnosed and mistreated, leading to social embarrassment for the patient. Therefore, it is prudent for dermatologists to carry out comprehensive clinical and histopathological assessments to facilitate prompt diagnosis and management of this condition. There is no standard therapy for CARP, but various therapeutic options are available such topical and systemic retinoids, oral antibiotics, topical antifungals, urea, calcipotriol, etc. Minocycline remains the first-line treatment for this condition as patients respond well to it and have minimal side effects.

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Conflicts of Interest

None declared.

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Abbreviations

AN: acanthosis nigricans
CARP: confluent and reticulated papillomatosis

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Case Report

Stevens-Johnson Syndrome in Adult Patient Secondary to COVID-19 Infection: Case Report

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Abstract

COVID-19 is a global pandemic caused by a novel zoonotic RNA virus named SARS-CoV-2. Various cutaneous manifestations associated with COVID-19 have been described, including urticarial rash, confluent erythematous rash, papulovesicular exanthem, chilblain-like acral pattern, livedo reticularis, and purpuric vasculitis pattern. Here, we are presenting a case of a 45-year-old male with mucocutaneous features of Stevens-Johnson syndrome.

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KEYWORDS

COVID-19 dermatology; SJS/toxic epidermal necrolysis; infection-induced SJS; infection; rash; Steven-Johnson syndrome; case report; adult patient; skin; skin rash; epidermal necrolysis; male; older adult; skin reaction; allergic reaction; allergy; allergies; toxic epidermal necrolysis; vasculitis; cutaneous; cytokine storm; sequelae; COVID-19; macule; dermatology

Introduction

COVID-19 is an ongoing global pandemic caused by a novel zoonotic RNA virus named SARS-CoV-2 [1]. Though COVID-19 is known for causing respiratory symptoms, cytokine storms, and thromboembolic sequelae, it has also been reported to be associated with extremely polymorphic cutaneous manifestations [2]. A wide range of cutaneous manifestations associated with COVID-19 has been described, like urticarial rash, confluent erythematous/maculopapular/morbilliform rash, papulovesicular exanthem, chilblain-like acral pattern, livedo reticularis, purpuric vasculitic pattern, and toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome (SJS) [1,3]. SJS is a rare, severe, life-threatening, adverse drug reaction affecting <10% of the skin and mucous membrane. Some reported cases of infection-induced SJS were caused by mycoplasma pneumonia, viruses, bacterial infections such as streptococcus group A, and mycobacterium [4]. Viruses interact with the immune system and can trigger severe cutaneous adverse reactions in several ways [5]. Here, we report a biopsy-confirmed case of SJS in an adult patient secondary to COVID-19 infection with an unvaccinated status.

Case Report

A 45-year-old male presented to us with multiple fluid-filled lesions on the upper and lower extremities and raw areas in the oral cavity for 3 days. The patient complained of fever, malaise, and burning of eyes prior to the onset of lesions. The patient denied any history of taking any oral or topical over-the-counter products before the onset of lesions. However, there was an associated history of hypertension and diabetes for which he was taking regular medications for the last 4 years (with no change in medication). The general physical examination was poor. The patient was afebrile, the pulse rate was 130 beats per minute, the SpO_2 was 96%, and the respiratory rate was 20 cycles per minute. Dermatological examination revealed multiple tender erythematous to purple macules and a few flaccid blisters over the trunk, extremities, and palms and soles (Figure 1). The Pseudo Nikolsky sign was positive. Multiple superficial ulcers were observed on the tongue, lips, eyes, scrotum, and shaft of the penis including the glans penis, with matted eyelashes (Figures 2-4). The systemic examination was unremarkable.

The hematological investigations were normal (hemoglobin: 13 g/dl; white blood cell: 5100 cell/mm^3; platelets: 1 lac/mcl). Liver function tests, chest x-ray, electrocardiogram, and ultrasonography of the abdomen and pelvis were normal. The patient tested negative for HIV, hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antigen, and herpes simplex virus (HSV) IgM and IgG antibodies. However, real-time polymerase chain reaction (RT-PCR) was positive for COVID-19 infection with an elevated C-reactive protein (80.55 mg/L) and erythrocyte sedimentation rate (40 mm/hr). D dimer and lactate dehydrogenase were within normal limits. Histopathological examination of the purple macule showed spongiosis, necrosis of the epidermis, and mild superficial perivascular lymphocytic infiltrate (Figures 5-7). Based on history, clinical examination, and investigations, we confirmed our diagnosis as SJS most likely due to the COVID-19 virus. We informed the patient about his condition and general measures were taken care of: strict isolation and monitoring of temperature, pulse, respiratory rate, blood sugar levels, and urine output were carried out periodically. Fluids and parenteral nutrition were provided intravenously. Injection of 8 mg of dexamethasone thrice daily was started with rapid tapering every 3 days. The patient reported improvement in a span of 10 days.

Figure 1. Multiple superficial flaccid blister and violaceous macules on trunk.

Figure 2. Multiple superficial ulcers and swollen lips.

Figure 3. Multiple superficial ulcers involving bilateral upper and lower eyelid with matting of eyelashes.

Figure 4. Multiple erosion on glans penis.

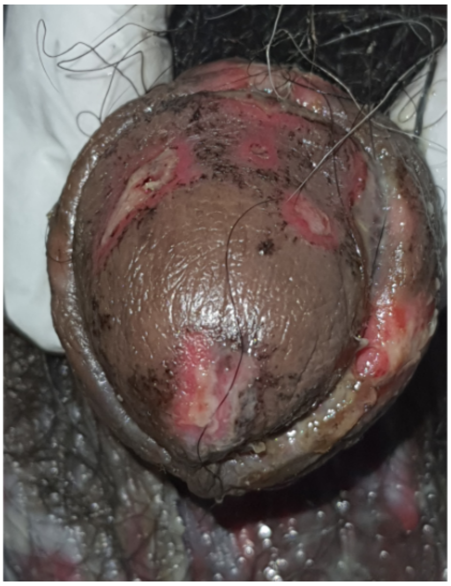


Figure 5. Subepidermal split, spongiosis, necrosis of whole epidermis, and mild superficial perivascular infiltrate (4x).

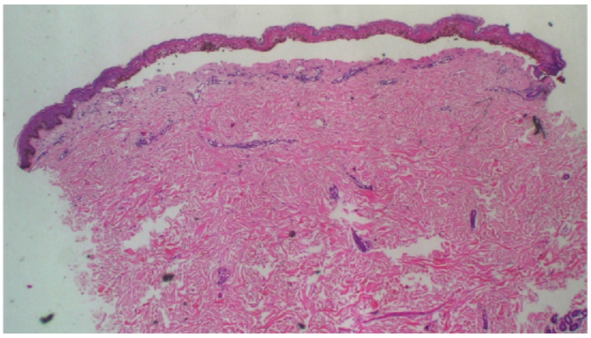


Figure 6. Sheet of epidermal necrosis (40x).

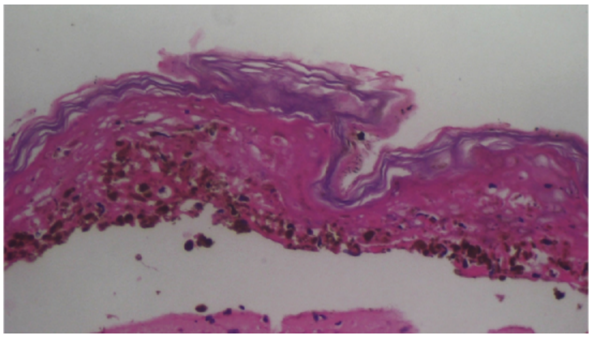
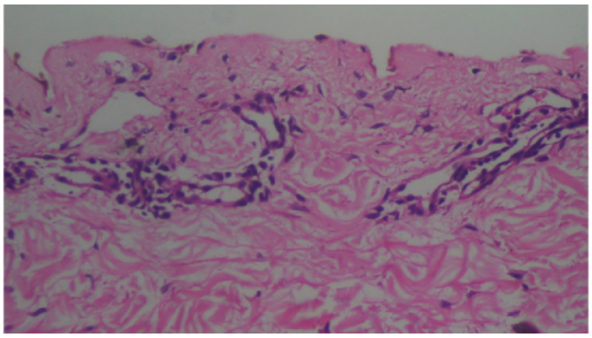


Figure 7. Sparse superficial perivascular lymphocytic infiltrate (40x).



Discussion

SJS is a serious life-threatening disease of the skin and mucous membranes [6]. Most cases of SJS/TEN are triggered by drugs, mainly sulfonamides, beta-lactam antibiotics, nonsteroidal anti-inflammatory drugs, and allopurinol. It usually occurs 4-28 days after drug exposure [2,4]. Hence, obtaining a detailed drug exposure history is important. Various microbes, especially viruses, play an active role in triggering an immune response, which leads to SJS/TEN [5]. There have been case reports of SJS/TEN associated with coxsackievirus, influenza virus, Epstein-Barr virus, human herpes virus 6 and 7, cytomegalovirus, and parvovirus infection [4].

However, the exact pathogenesis of infection-induced SJS is unknown, but the immunological response to infectious agents causing generalized apoptosis of keratinocytes by T lymphocytes and proteins like granulysin and Fas ligand has been postulated [7]. The entry of the virus activates the host immune response mechanism. Viral reactivation activates the resident memory T-cells. Resident memory T cells are important cells in infection-induced SJS/TEN, which decide viral control, viral latency, or viral lethality and tissue damage. They release various cytokines like interferon- , which causes viral clearance and keratinocyte damage [8].

SJS occurrence in patients with COVID-19 has been reported to be associated mostly with medications like paracetamol, naproxen, azithromycin, hydroxychloroquine, allopurinol, cotrimoxazole, lenalidomide, and lamotrigine [4,6,9]. To date, only 3 cases of COVID-19–induced SJS have been reported [10,11].

In this case, our patient was on antihypertensive and antidiabetic medications for 4 years with no change or addition of any other medication. Hence, the possibility of drug-induced SJS was ruled out. In contrast to drug-induced SJS, infection-induced SJS shows more mucosal involvement than cutaneous involvement. This finding is similar to our case [2,12].

As per a study done by Wetter and Camilleri [13], individual necrotic keratinocytes, dense dermal and appendageal infiltrate, red blood cell extravasation, pigment incontinence, parakeratosis, and a substantial number of eosinophils or neutrophils are important features found in drug-related SJS, which were absent in our case [13].

In this case, the patient tested negative for HIV, HBsAg, HCV antigen, and HSV IgM and IgG antibodies and mycoplasma pneumonia antigen. However, our patient’s throat swab was positive for COVID-19 infection (tested by RT-PCR).

Primary COVID-19 infection may have caused the disease through the pathophysiology mentioned above. The immune system can be activated by virus-associated antigen patterns, as well as viral genomes [2,8]. As the course of infection-induced SJS is benign, these patients do not show severe symptoms and show a good response to treatment [12]. We have treated our patient with tapering doses of injection dexamethasone and prophylactic antibiotics as per COVID-19 protocol. Our patient improved in a span of 2 weeks.

Here, we would like to conclude that primary COVID-19 infection may have caused SJS by triggering the immunological response of the host. This causes generalized apoptosis of keratinocytes by T lymphocytes. Therefore, one should suspect COVID-19 infection as a rare etiology of SJS.

Conflicts of Interest

None declared.

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Abbreviations

HBsAg: hepatitis B surface antigen
HCV: hepatitis C virus
HSV: herpes simplex virus
RT-PCR: real-time polymerase chain reaction
SJS: Stevens-Johnson syndrome
TEN: toxic epidermal necrolysis

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Original Paper

Cyclosporine in the Treatment of Drug Reaction With Eosinophilia and Systemic Symptoms Syndrome: Retrospective Cohort Study

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Abstract

Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe, life-threatening reaction to a culprit drug that frequently involves end-organ damage. Corticosteroids are the first-line treatment for DRESS syndrome; however, corticosteroids may be contraindicated in certain patient populations. There are currently only 54 cases detailing the use of cyclosporine for the treatment of DRESS syndrome reported in the literature.

Objective: The aim of this case series was to examine the treatment of DRESS syndrome with cyclosporine in a large patient cohort by aggregating time to symptom resolution, recurrence rate, and treatment dose and duration.

Methods: This study was a retrospective cohort study. Patients diagnosed with DRESS syndrome by a board-certified dermatologist and treated at the University of Colorado Hospital from 2015 to 2019 were included.

Results: Our inclusion criterion was met by 19 occurrences of DRESS syndrome. With a short course of cyclosporine, 17 of 19 patients in our cohort (89%) had resolution of symptoms (mean treatment length of 5.26 days). DRESS syndrome's relapse after treatment with cyclosporine occurred in 3 of 19 (16%) occurrences of the cohort.

Conclusions: Our study supports the use of cyclosporine in the treatment of DRESS syndrome, particularly in patients who are unable to sustain prolonged immunosuppression. Further research is necessary to compare the efficacy of cyclosporine to the current standard of care in a larger study population and investigate long-term outcomes.

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KEYWORDS

drug reaction with eosinophilia and systemic symptoms; drug-induced hypersensitivity syndrome; drug reactions; eosinophils; cyclosporine; treatment; skin; rash; dermatology; drug reaction; adverse reaction; eosinophil; eosinophilia; Systemic Symptoms; drug-induced; drugs; cohort study; case series; pharmaceutic; pharmacology; pharmacy

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome causes severe cutaneous and systemic complications with a mortality rate of ≈10% [1,2]. The current standard of care for DRESS syndrome involves the removal of the culprit drug, supportive therapy, and systemic corticosteroids. Corticosteroid therapy must be tapered for weeks to months to prevent DRESS syndrome relapse [1]. Additionally, corticosteroid therapy may be contraindicated, induce adverse events (such as hyperglycemia and hypertension), and increase the risk of viral reactivation. To the best of our knowledge, there are only 54 previously reported cases of cyclosporine use in the treatment of DRESS syndrome [2-16]. Half of these previously reported cases (27 of 54) are reported in a retrospective study comparing cyclosporine to corticosteroid use in the treatment of DRESS syndrome, which found that there was no significant difference in time to resolution of DRESS syndrome between the 2 groups. However, there were more adverse events in the corticosteroid group compared to the cyclosporine group [12]. Of the remaining, 27 cases, 23 cases have demonstrated cyclosporine to be an effective alternative therapy to corticosteroids [2-11]. Despite these promising results, the number of cases reported in the literature remains low.

Methods

Participants

This retrospective review of medical records analyzed patients with DRESS syndrome who were treated with cyclosporine at the University of Colorado Hospital (UCH) from January 2015 to August 2019. Medical record numbers for patients with a diagnosis of DRESS syndrome who had received cyclosporine were collected using Health Data Compass, yielding 26 patients with 36 cases of DRESS syndrome. Researchers subsequently examined these patient charts to determine if each case of DRESS syndrome met the following inclusion criteria: a Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) score >2 [17], age greater than 18 years, diagnosis of DRESS syndrome made by a board-certified dermatologist, and treatment with systemic cyclosporine for at least 3 days after DRESS syndrome diagnosis. The RegiSCAR score was calculated retrospectively using data from the electronic medical record, including laboratory results, imaging, physical exam findings, and clinical symptoms. This inclusion criterion was met by 17 patients with a total of 19 occurrences of DRESS syndrome. Of these 19 occurrences, 18 were treated in the inpatient setting. Recurrence of DRESS syndrome and follow-up time were determined by reviewing the University of Colorado Health System's electronic medical record from initial DRESS syndrome occurrence through March 2022.

Outcomes

The primary outcome of the study was to determine time to clinical resolution, which was defined as sustained temperature <38.5 °C with rash improvement, when treated with cyclosporine. Secondary outcomes included recurrence of DRESS syndrome, cyclosporine dose, and treatment length.

Ethical Considerations

This study was reviewed and exempted by the Colorado Multiple Institutional Review Board.

Results

Participants

The mean RegiSCAR score of the 19 DRESS syndrome cases was 3.42. The patients were mostly male (11/19, 58%) with cases of DRESS syndrome occurring at an average age of 48.1 years. The most common causative agents were phenytoin and vemurafenib. Approximately 11 of 19 (58%) of the patients were treated with prednisone prior to admission at UCH or for conditions other than DRESS syndrome. Six of the 11 patients who had prior systemic corticosteroid exposure were treated for 2-4 days at outpatient clinics or outside hospitals (patients 1, 7, 10, 12, 15, and 17). Upon presentation to UCH and dermatology consultation, corticosteroids were discontinued, and a cyclosporine course was initiated. These patients were switched to cyclosporine due to failure to improve on corticosteroids or to avoid exacerbating concurrent medical comorbidities, such as diabetes or wound infections. In 1 of the 11 cases of prior corticosteroid exposure (patient 3), the patient had been receiving a course of a high dose of prednisone (40 mg on day 1 followed by 80 mg daily) prior to dermatology consultation. Given the increased risk of DRESS syndrome rebound with abrupt discontinuation of the high-dose corticosteroid, the patient was continued on a steroid taper in conjunction with the cyclosporine treatment. In 2 of the 11 cases, patients had a DRESS syndrome recurrence while on a systemic corticosteroid taper (patients 2 and 13). In these instances, the corticosteroid taper was continued in addition to the initiation of cyclosporine due to the risk of DRESS syndrome rebound with abrupt cessation of corticosteroids. In 1 of the 11 cases (patient 6), the patient had received 5 days of systemic corticosteroid for adrenal insufficiency prior to initiation of a cyclosporine course, which was continued along with the corticosteroid course. Finally, in 1 of the 11 cases (patient 18), the patient was on their fifth month of a prednisone taper at the time of DRESS syndrome onset. Given the risk of adrenal insufficiency with abrupt discontinuation of prednisone, the patient was continued on their corticosteroid taper in addition to cyclosporine treatment for the treatment of DRESS syndrome.

In 8 of 19 DRESS syndrome occurrences, cyclosporine initiation occurred without prior corticosteroid exposure. Cyclosporine was the preferred treatment due to concern for prolonged prednisone taper, to avoid extended immunosuppression in the setting of recent or concurrent infection, to restart immunologic treatment of metastatic melanoma, for more rapid improvement of symptoms, and due to previous successful treatment of DRESS syndrome with cyclosporine.

Outcomes

Of the 19 cases in this case series, 17 patients had a resolution of DRESS syndrome (17/19, 89%) with treatment of cyclosporine. One of the patients who did not have a resolution with cyclosporine was the only patient not hospitalized and was lost to follow-up after initiation of cyclosporine (patient 10). The second patient that did not resolve with cyclosporine (patient 19) was switched to prednisone after 2 days of cyclosporine treatment and had improvement of DRESS syndrome symptoms on prednisone. Of the 17 patients who had a resolution of DRESS syndrome when treated with cyclosporine, 16 (94%) had resolved DRESS syndrome symptoms on discharge when treated with cyclosporine, with an average time to resolution of 2.83 days (Table 1). The patient with symptoms that did not resolve by discharge (patient 4) had clinical resolution prior to their follow-up appointment with an outpatient dermatologist.

Table 1. Cyclosporine dosing and outcomes in patients at the University of Colorado Hospital (UCH) diagnosed with drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome.

Patient	Age	Sex	Causative drug	RegiSCAR score[a]	Prior systemic corticosteroid exposure	Cyclosporine dose (orally taken, unless indicated)	Cyclosporine duration (days)	Days to resolution[b]
1	21	M[c]	Carbamazepine	3	Yes – 4 days	2 mg/kg BID[d]	7	1
2	49	M	Carbamazepine	3	Yes – 13 days	2.5 mg/kg BID	5	3
3	48	F[e]	Dabrafenib	2	Yes – 1 day	2 mg/kg Q12 IV	5	1
4	19	F	Phenytoin or oxcarbazepine	2	No	2.5 mg/kg BID	5	9
5	22	F	Phenytoin	3	No	2.5 mg/kg BID	7	1
6	22	M	Phenytoin	5	Yes – 5 days	2.5 mg/kg BID	3	10
7	47	M	Phenytoin	4	Yes – 4 days	2.5 mg/kg BID	5	1
8	75	M	Phenytoin	4	No	1.5 mg/kg BID	3	2
9	75	M	Phenytoin	2	No	2 mg/kg BID	7	1
10	38	F	Empagliflozin/ Metformin HCl tablets (Synjardy)	3	Yes – 3 days	2.5 mg/kg BID	7	N/A[f]
11	43	F	Vancomycin	6	No	0.667 mg/kg Q12 IV	5	3
12	56	F	Vancomycin	5	Yes – 2 days	2.5 mg/kg BID	7	1
13	65	M	Vancomycin	2	Yes – 45 days	2 mg/kg BID	5	3
14	75	M	Vancomycin	3	No	2.5 mg/kg BID	5	2
15	45	M	Vemurafenib	4	Yes – 3 days	2 mg/kg BID	5	2
16	50	M	Vemurafenib	5	No	2 mg/kg BID	5	1
17	51	M	Vemurafenib	3	Yes – 4 days	2 mg/kg BID	7	2
18	53	F	Vemurafenib	3	Yes – 5 months	2 mg/kg IV Q12; 2 mg/kg PO BID	3.5; 1.5 (respectively)	3
19	59	F	Vemurafenib	2	No	2 mg/kg BID	2	5

[a]RegiSCAR: Registry of Severe Cutaneous Adverse Reaction.

[b]"Days to resolution" refers to days after starting cyclosporine to resolution of fever and rash improvement.

[c]M: male.

[d]BID: twice per day.

[e]F: female.

[f]N/A: not applicable.

The median dose of a cyclosporine treatment course was 2 mg/kg twice per day (BID; mean 2.11) with a median treatment duration of 5 (mean 5.26) days. This dose is consistent with the common initial dosing regimen in the treatment of other skin diseases, such as psoriasis. This dosing regimen has been supported by previously published cases, which commonly used 2.5-5 mg/kg daily of oral cyclosporine [2,3,5-9,15,18]. Patient 11 was treated with a decreased dose of cyclosporine (0.667 mg/kg IV every 12 hours) due to treatment with IV as opposed to oral cyclosporine. This dose adjustment was determined with the assistance of pharmacy to account for the differences in bioavailability. Patient 19 had a shortened course of cyclosporine and was switched to prednisone due to adrenal insufficiency. Only 3 of 19 (16%) of DRESS syndrome occurrences resulted in a recurrence after being treated with cyclosporine. Treatment outcomes for patient 10 are unknown due to the loss of follow-up. Average follow-up time for this cohort was 2.3 years. Three patients were lost to follow-up after hospital discharge. Mortality due to DRESS syndrome was 0% (0/19 patients) for patients in this study.

Discussion

Principal Results

In total, 17 of 19 (89%) of our cohort were successfully treated with cyclosporine within 5.26 days of treatment initiation on average. Our study supports findings in the literature and increases the number of cases reported by approximately 26%. The only patient that did not have known DRESS syndrome resolution was lost to follow-up. The approach to treating patients with cyclosporine typically started with a 5-day treatment course with progression to a 7-day treatment course if patients had initially responded to cyclosporine but could benefit from additional immunosuppression based on end-organ damage. In contrast, treatment with prednisone typically includes a taper and may last up to 3-6 months in order to prevent recurrence [19]. Therefore, a short course of cyclosporine may be particularly useful in patients with contraindications to long-term immunosuppression or poor medical follow-up.

Furthermore, the low rate of DRESS syndrome relapse following cyclosporine treatment (16%) is promising, as DRESS syndrome frequently involves recurrence, despite discontinuation of the original causative drug. Studies have found up to a 25% recurrence rate in their cohorts treated with the standard of care. The corticosteroid taper has been implicated in some recurrences [20]. In 1 of the 3 cases of recurrence in this study, the second case of DRESS syndrome was thought to result from a different causative agent that occurred 17 months after the first occurrence of DRESS syndrome. The patient had a second recurrence of DRESS syndrome 13 months after their first recurrence, which was due to a retrial of the initial causative agent. The remaining 2 cases of recurrence occurred within the same hospitalization as the initial occurrence of DRESS syndrome. The first of these recurrences involved worsening symptoms 3 days after completion of a cyclosporine course and 1 day after discontinuing methylprednisolone. Notably, the patient had also been receiving methylprednisolone for limbic encephalitis. The second case of these recurrences within the same hospitalization was successfully treated with a longer duration of cyclosporine at a higher dose (2 mg/kg BID for 7 days instead of the initial 1.5 mg/kg for 3 days) without a known subsequent recurrence.

Limitations

The mean RegiSCAR score of 3.42 was low due to a lack of documentation required to fully calculate a RegiSCAR score. As this was a retrospective study, the RegiSCAR criteria were not used to make the diagnosis, and there are features included in the RegiSCAR criteria that were not evaluated when making the diagnosis. Thus, 12 of 19 (63%) patients had complete data for 6 of the 8 categories [17]. Most patients did not have complete laboratory and imaging data to fully assess organ involvement, particularly for the lung, pancreas, and muscle or heart. Laboratory data for other possible causes of symptoms, including antinuclear antibodies, hepatitis serologies, and evaluation of concomitant mycoplasma or chlamydia pneumonia infection, were not completely evaluated. However, a mean RegiSCAR score of 3.42 is between a "possible case" and "probable case" of DRESS syndrome. Additionally, all patients included in this study were diagnosed with DRESS syndrome by a board-certified dermatologist due to experiencing a suspected drug-related reaction, acute morbilliform rash involving at least 75% body surface area, and internal organ involvement.

This study is limited by its retrospective nature and lack of long-term patient follow-up. Median follow-up time was shorter than expected due to the loss of 3 patients to follow-up and 3 patient deaths due to their primary disease. Additionally, most patients were on a corticosteroid at the time of DRESS syndrome diagnosis. This limitation is likely a consequence of UCH being a tertiary referral center because patients may have already been trialed on a corticosteroid prior to presentation to UCH or dermatology consults and subsequent initiation of cyclosporine.

The concomitant use of corticosteroids is a common limitation to previous literature on using cyclosporine in DRESS syndrome [2,3,5,8-11,14-16]. However, the promising results of our 19 cases further support the consideration of cyclosporine in the treatment of DRESS syndrome, particularly when corticosteroids are contraindicated, or the patient may be unable to consistently take a long steroid taper. Further studies that may expand on this data include those with more consistent long-term follow-up with patients, comparison of outcomes between cyclosporine treatment regimens, and studies with larger samples of patients treated with cyclosporine.

Comparison With Prior Work

Corticosteroids, as opposed to cyclosporine, are the standard of care in the treatment of DRESS syndrome. Therefore, this literature on cyclosporine in the treatment of DRESS syndrome has been limited to primarily small case reports, 1 case-control study with 5 patients treated with cyclosporine compared to 21 patients treated with corticosteroids [4], and 1 retrospective study with 27 patients treated with cyclosporine compared to 53 patients treated with corticosteroids [12]. The previous cases are summarized in the Multimedia Appendix 1 [2-11,13-16]. Data from the retrospective study are not included in the summary, as the data were aggregated and could not be separated into individual cases. The vast majority of these previous studies have suggested that cyclosporine is effective and may lead to rapid clinical resolution of DRESS syndrome [2-12,16]. In the case-control study, the patients treated with cyclosporine were found to have a shorter time to clinical resolution than those treated with corticosteroids [4]. These results are further supported by the retrospective study, in which hospitalization length, treatment length, and time to resolution of DRESS syndrome symptoms were found to be comparable between cyclosporine and corticosteroid treatment groups, while the cyclosporine group had fewer adverse events from treatment [12]. Additionally, in 15 of the 27 cases, cyclosporine was successfully used after symptoms failed to resolve or relapsed with corticosteroid treatment [5-11]. Of the 3 cases in which cyclosporine failed, 2 cases also did not resolve with corticosteroid treatment alone [13,14]. Cyclosporine failed with successful methylprednisolone rescue in only 1 of the 27 cases reported in the literature [15]. There was 1 reported case of recurrence after resolution with the use of cyclosporine. This recurrence was treated with a prolonged taper of both cyclosporine and methylprednisolone [16].

Additionally, the average time to resolution of DRESS syndrome after initiation of cyclosporine was 2.83 days. Our findings are consistent with the case-control study, in which 5 patients treated with cyclosporine had a shorter time to resolution of symptoms compared to patients treated with glucocorticoids (3.5 days versus 5.5 days, respectively) [4]. The discrepancy in time to resolution between treatment with cyclosporine and treatment with prednisone or no treatment, suggests that cyclosporine may have improved clinical resolution compared to the current standard of care.

Conclusions

The current standard of care for DRESS syndrome includes the removal of the causative agent, supportive therapy, and a course of corticosteroids. However, DRESS syndrome continues to have a mortality rate of around 10% and a recurrence rate of 25% [1,2,20]. Cyclosporine shows promise as an effective treatment of DRESS syndrome with possible reduced rates of relapse, more rapid resolution of symptoms, and shorter treatment courses when compared to the current standard of care. Therefore, cyclosporine may be useful in patients who are unable to tolerate 4-6 weeks of immunosuppression. This study supports the use of a 5-day trial with cyclosporine (2 mg/kg BID) in the treatment of DRESS syndrome as an alternative to corticosteroids, particularly in patients who fail to respond to or are intolerant of corticosteroids. Further research is needed to compare treatment outcomes and long-term complications of cyclosporine to those of corticosteroids. Limitations to the use of cyclosporine as a first-line agent include nephrotoxicity and hepatotoxicity [21,22]. However, in the case of DRESS syndrome, medication courses are shorter than that for corticosteroids, limiting medication exposure compared to the current standard of care.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Summary of the current cases concerning cyclosporine in the treatment of DRESS.
[DOCX File , 20 KB - derma_v6i1e41391_app1.docx]

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Abbreviations

BID: twice per day
DRESS: drug reaction with eosinophilia and systemic symptoms
RegiSCAR: registry of severe cutaneous adverse reaction
UCH: University of Colorado Hospital

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Research Letter

From the Cochrane Library: Interventions for Pityriasis Rosea

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pityriasis rosea; acyclovir; antiviral; randomized controlled trial; Cochrane; evidence-based medicine; systematic review

Pityriasis rosea (PR) is a benign, self-limited skin disease characterized by the eruption of multiple erythematous plaques on the trunk and proximal extremities. The proposed etiology links the eruption to the reactivation of human herpesvirus (HHV) 6 and 7 in the skin [1]. HHV-6 viral reactivation during pregnancy has been associated with adverse birth outcomes in the first trimester of pregnancy [2]. PR may be asymptomatic or mildly pruritic and usually resolves without treatment within 12 weeks. PR and PR-like eruptions may also occur after vaccinations, other infections, and medications [3]. Patients with severe symptoms or extensive skin involvement may seek medical treatments.

A 2007 Cochrane review [4] and its updated 2019 version [5] investigated the efficacy of treatments for PR. We aim to provide a summary of the findings from the systematic review in this letter. A total of 14 randomized controlled trials (N=761) assessed two primary outcomes: good or excellent rash improvement within 2 weeks (participant-rated) and serious adverse events. Secondary outcomes included resolution of pruritus within 2 weeks (participant-rated), reduction in pruritus score within 2 weeks (participant-rated), good or excellent rash improvement within 2 weeks (investigator-rated), improvement in quality of life (participant-rated), and minor participant-reported adverse events. Interventions included macrolide antibiotics (erythromycin, azithromycin, clarithromycin), acyclovir, phototherapy, corticosteroids, antihistamines, and a traditional Chinese medicine called potenline. A meta-analysis was performed using a random-effects model for studies with similar interventions and controls. Most studies were conducted in Asia with participants ranging from the age of 2 to 60 years and the study duration lasting between 5-26 months. Three studies were funded by pharmaceutical manufacturers. There were no studies on pregnant women.

Macrolide antibiotics are not recommended for the treatment of PR. Erythromycin was shown in a single clinical trial to significantly reduce the pruritus score compared to a placebo ($P<.001$) [5]. However, there was no difference in investigator-rated rash improvement, and more adverse events were reported with erythromycin. Azithromycin showed no difference in investigator-rated rash improvement versus placebo.

Acyclovir monotherapy may be useful for the treatment of PR. Compared to a placebo, participants on acyclovir experienced greater resolution of pruritus ($P=.04$) [5]. Three trials showed a significant improvement in investigator-rated clearance with acyclovir versus a placebo ($P=.004$) [5]. Acyclovir and standard care (calamine lotion and cetirizine) reduced pruritus score ($P<.001$) and resolution of pruritus ($P=.02$) compared to standard care alone [5].

Using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework, there is moderate quality evidence to support the use of acyclovir monotherapy for the rash and pruritus of PR and low to moderate quality evidence for erythromycin to treat pruritus in PR. A range of acyclovir dosages has been used in studies with unclear evidence based on different regimens (Table 1). Antivirals for severe or recalcitrant clinical presentations of PR may be used in patients who fail standard care.

In general, the self-limited nature and overall low incidence of PR pose challenges to study designs. Additional high-quality studies are needed to determine if acyclovir or other antivirals are superior to supportive care.

Table 1. Comparison of acyclovir dose regimens.

Study	Comparison	Dose regimen	Participants, n	Outcome	RR[a] or MD[b] (95% CI)
Ehsani et al [6], 2010	Acyclovir vs erythromycin	800 mg 5×/day for 10 days	14	• Resolution of pruritus within 2 weeks (participant-rated)	• 13.22[a] (0.91-192.02)
Rassai et al [7], 2011	Acyclovir vs no treatment	400 mg 5×/day for 1 week	54	• Good or excellent rash improvement within 2 weeks (investigator-rated)	• 2.92[a] (1.51-5.66) • 1.52[a] (1.14-2.01)
Ganguly [8], 2014	Acyclovir vs vitamin C	800 mg 5×/day for 1 week	60	• Good or excellent rash improvement within 2 weeks (investigator-rated)	• 2.6[a] (1.54-4.4)
Das et al [9], 2015	Acyclovir + calamine lotion + cetirizine vs calamine lotion + cetirizine	400 mg 3×/day for 1 week	24	• Resolution of pruritus within 2 weeks (participant-rated) • Reduction in pruritus score within 2 weeks (participant-rated) • Minor participant-reported adverse events	• 4.50[a] (1.22-16.62) • 1.26[b] (0.74-1.78) • 7.00[a] (0.40-122.44) • 2.00[a] (0.21-19.23) • 5.00[a] (0.27-94.34) • 3.00[a] (0.13-67.06)
Singh et al [10], 2016	Acyclovir vs placebo	800 mg 5×/day for 1 week	27	• Resolution of pruritus within 2 weeks (participant-rated) • Good or excellent rash improvement within 2 weeks (investigator-rated) • Minor participant-reported adverse events	• 0.34[a] (0.12-0.94) • 0.19[a] (0.01-3.56) • 0.31[a] (0.01-7.02)

[a]RR: risk ratio.

[b]MD: mean difference.

Conflicts of Interest

A Méndez and CS do not have any conflicts of interest. A Murina is a speaker for Abbvie, Amgen, Bristol-Meyers-Squibb, Eli Lilly and Company, Janssen, Ortho-Dermatologics, and consultant for Bristol-Meyers-Squibb, Janssen, Novartis, Ortho-Dermatologics and UCB.

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Abbreviations

GRADE: Grading of Recommendations, Assessment, Development, and Evaluations
HHV: human herpesvirus
PR: pityriasis rosea

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Editorial

Diversity, Equity, and Inclusion of Dermatology Journals and Their Editorial Board Members

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Abstract

Dermatology as a whole suffers from minority underrepresentation. We conducted a search of the top 60 dermatology journals for mention of their approach to increasing diversity, equity, and inclusion (DEI) within their publication through editorial board members or peer-review processes. Of those 60, only 5 had DEI statements or editorial board members dedicated to increasing DEI. There are publications with checklists and frameworks for increasing DEI within the literature. We propose that more journals implement these resources within their peer-review process to increase diversity within their publication.

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KEYWORDS

diversity; equity; inclusion; dermatology

Research journals with diverse editorial board members are more likely to publish research from diverse perspectives [1]. As the dermatologic specialty suffers from minority underrepresentation [2], it is pivotal that dermatology journals strive to achieve diverse editorial boards and peer reviewers. Only one study has explored the racial and ethnic demographics of two high-impact dermatology journals, *JAMA Dermatology* and the *Journal of the American Academy of Dermatology* (*JAAD*), finding that their racial demographics mirror that of dermatology, although unrepresentative of the United States population [3]. To the authors' knowledge, no other studies have explored the diversity of other dermatology journal editorial board members. Improving the diversity, equity, and inclusion (DEI) of academic dermatology requires acknowledgment, leadership roles, and future directions to broaden representation, reduce bias, and improve health disparities. Thus, our goals were to identify DEI efforts of top dermatology journals; to recommend resources for dermatology journal DEI improvement; and to propose *JMIR Dermatology*'s efforts to improve DEI in our peer-review process.

We identified the 60 highest-impact dermatology journals on Scimago by their h-index score. Each journal's website was examined for statements on DEI, editorial board members dedicated to DEI, or other information regarding DEI in their peer-review process. Two independent reviewers performed website searches and documented the results separately to improve accuracy. If the journal was a subsidiary of an academic society, we did not include diversity statements made by the society unless it was explicitly stated on the journal's website.

Of the 60 dermatology journals reviewed, only 5 (8%) referenced DEI either as a policy on its impact on publication processes or identified individuals or groups dedicated to increasing the diversity of published research. For example, *JAMA Dermatology* has an associate editor for diversity, a mission statement, and mentorship initiatives aimed at advancing DEI within publications. Further, *JAAD* and the *British Journal of Dermatology* have editorial groups dedicated to DEI. *Pediatric Dermatology* has a DEI statement. Finally, *Actas Dermo-Sifiliograficas* has listed the gender diversity of editors. No other journals met our inclusion criteria. The JAMA Network and American Society of Nephrology created editorial policies and a DEI checklist, respectively, to provide a framework and criteria to ensure DEI is an integral part of the editorial and peer-review processes [4-6]. The recommendations by these journals can be used as a resource for dermatology journals, editors, and peer reviewers desiring to increase DEI in their publications.

JMIR Dermatology is dedicated to improving the DEI within our publications and our peer-review process. We plan to appoint a DEI editor to our editorial board who will lead a diverse editorial review committee. The DEI committee will provide manuscript feedback, recommendations, and guidance to encourage diverse author representation and ensure the use of inclusive language. We urge dermatology journals to join in this step toward improving racial and ethnic DEI in journal review boards.

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Conflicts of Interest

RR is an editorial board fellow/member for *JMIR Dermatology* and a Dermatology Clinical Trial fellow. RD is the Editor-in-Chief of JMIR Dermatology.

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Abbreviations

DEI: diversity, equity, and inclusion
JAAD: Journal of the American Academy of Dermatology

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Editorial

Dermatology Journals' Editorial Boards Require Improved Gender Equity: JMIR Dermatology's Future Directions

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Abstract

Gender disparities exist across all facets of academic medicine including within the editorial boards of dermatology journals. Only 22% of these editorial boards comprised women, even though 51% of full-time, faculty dermatologists are female. When inviting academic dermatologists to our editorial board at *JMIR Dermatology*, we invited 50% women to represent the gender distribution of academic dermatologists; however, we have not sufficiently reached gender equity among accepted editorial board members. We will continue to strive toward the goal of gender equity on our editorial board and invite other dermatology journals to do the same.

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KEYWORDS

gender equity; dermatology; editorial board members; diversity; gender; inclusion; equity; academia; equality

Although roughly equivalent rates of women and men have applied, been accepted to, and graduated from medical school since the early 2000s, gender disparities persist in academic medicine. In dermatology specifically, the percentage of female medical school graduates and residents did not reach 50% until the 1990s [1,2]. The gender discrepancy is seen in many facets of academia including lower rates of publishing, first-author publications, receiving National Institutes of Health grants, serving as journal editors, and being included on journal editorial boards [3-7].

Women constitute a minority in dermatology journal editorial boards. One review study of all dermatology journals found that only 22% of editorial board members were women [8]. Another recent analysis exploring gender parity of the top 20 dermatology journals' editorial boards found that women comprised a median of 33.4% (IQR 27.2%-46.9%) of their editorial boards [9]. Only in 4 of the 20 top journals did women comprise a >50% average of the editorial board [9], even though a 2018 report by the Association of American Medical Colleges found that 51% of full-time, faculty dermatologists are women [10]. Among the top 20 journals, 75% had a male editor-in-chief [9] and 81% of all dermatology journals had a male editor-in-chief [8].

At *JMIR Dermatology*, our goal was to represent the gender distribution of academic dermatologists by inviting 50% women to join our editorial board. After recruitment and acceptance, we found that the gender distribution of our editorial board closely resembles that of the top 20 dermatology journals, with only 8 (32%) out of 25 board members being women. Although our goal was to create an equitable editorial board, *JMIR Dermatology* has fallen short of our 50% target. Based on our in-house review, it will be necessary to invite more than 50% female dermatologists to achieve our gender equity goal.

Although gender equity in academia is a widely discussed topic, gender disparities persist across all facets of academic medicine. The specialty of dermatology is no exception. Improving equity in certain parts of academia could start with improving the equitable distribution of editorial board membership; yet, a majority of the top dermatology journals today have failed to reach these goals. We at *JMIR Dermatology* will continue to work toward gender equity on our editorial board. Further steps for our journal may include inviting inequitable proportions of female dermatologists until we reach our goal or investigating the reasons behind why there was lower acceptance among applications from women. We hope our generation and future generations of dermatologists will continue to work toward the goal of gender equity in academia.

Conflicts of Interest

RD is the Editor-in-Chief of *JMIR Dermatology*.

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In Memoriam

In Memoriam: William Weston

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KEYWORDS

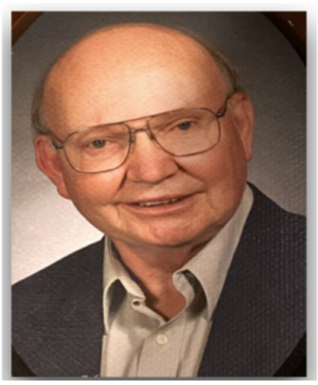
pediatric dermatology; neonatal lupus

Dr William "Bill" Weston, born on August 13, 1938, in Grand Rapids, MN, passed away on November 13, 2022, at the age of 84 years in Denver, CO. His family relocated to Richmond, WA, when he was a young child. He graduated from Whitman College in Walla Walla, WA, in 1960 with a bachelor's degree in chemistry. He received a Bachelor of Medical Sciences degree from the University of South Dakota, where he studied from 1961 to 1963 and met the love of his life, his wife Janet Atkinson Weston, MD, who also trained in pediatrics.

He pursued medicine at the University of Colorado, where he received his medical degree in 1965, completed an internship, and started a residency in pediatrics under the mentorship of C Henry Kempe, MD. He completed his pediatric residency at the University of California San Francisco. After serving in the US Army, he returned to Colorado to complete another residency in dermatology (1970-72) and a fellowship in immunodermatology (1972-73).

Dr Weston served as the chair of the Department of Dermatology at the University of Colorado School of Medicine for over 25 years from 1976 to 2001 and as the section head of Pediatric Dermatology for 33 years from 1972 to 2005. He was also on staff at the Fitzsimons Army Medical Center (1972-96), the Denver Veterans Administration Medical Center (1976-2006), and the Denver Health Medical Center (1976-2007).

Figure 1. This is an undated photo of Dr William Weston.



Dr Weston's impact on the field of pediatric dermatology was remarkable. He authored a leading textbook in the field [1] and trained more than 30 practicing pediatric dermatologists globally. He was a founding father of the field and among the first to describe the signs of neonatal lupus [2].

Throughout his career, Dr Weston received numerous accolades, including the University of Colorado School of Medicine–Florence Rena Sabin Award in 2000, the American Academy of Pediatrics–Alvin H Jacobs Award in 2003, and the University of Colorado Medal in 2022. He published over 350 articles during his career.

Dr Weston was an accomplished clinician, educator, scholar, leader, mentor, and friend. His research mentorship was instrumental in launching the careers of many academic dermatologists, and his knowledge was encyclopedic. Dr Weston had a genuine love of children and a unique way of describing them. He was also an avid baseball fan and traveled to every Major League Baseball field in the country with his son to watch a game on each team's home field.

Dr Weston was an unassuming man who approached each patient with humility and compassion. His legacy as a humble and generous leader and role model will always guide the relationships of his trainees and colleagues. We are grateful to have received so many gifts from Dr Weston, and we owe our success to his early involvement in our careers.

We celebrate Dr Weston's life with deep gratitude. Thank you, Dr Weston, for investing in us and in every other trainee who had the privilege of learning from you. Thank you for sharing your talents, time, and energy with the world so freely. Your memory will always be cherished, and your impact will be felt for generations to come.

Conflicts of Interest

RPD is an editor for Cochrane Skin, a dermatology section editor for UpToDate, a social media editor for the *Journal of the American Academy of Dermatology*, editor-in-chief of *JMIR Dermatology*, and cochair of Cochrane Council. RPD receives editorial stipends (*JMIR Dermatology*), royalties (UpToDate), and expense reimbursement from Cochrane.

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Viewpoint

The Importance of Basal Cell Carcinoma Risk Stratification and Potential Future Pathways

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Abstract

Background: Basal cell carcinoma (BCC) is the most common human cancer. Although there are surgical and topical treatments available, surgery remains the mainstay of treatment, leading to higher costs. What is needed is an accurate risk assessment of BCC so that treatments can be planned in a patient-centered manner.

Objective: In this study, we will review the literature about guidelines for the management of BCC and analyze the potential indicators of high-risk BCC. Using this risk assessment approach, we will propose pathways that will be able to optimize treatments more efficiently.

Methods: This paper presents a perspective from a skin cancer expert and clinic involved in the treatment of both simple and complex cases of BCC. It addresses the key challenges associated with accurate risk stratification prior to any treatment or procedure. Different immunohistochemical and angiogenic markers for high-risk BCC were reviewed in this study.

Results: The expression of interleukin-6, vascular endothelial growth factor, and mast cells within BCC correlates with its aggressiveness. Other immunohistochemical markers, such as Cyclin D1 and Bcl-2, also play a significant role—Cyclin D1 is higher in the aggressive BCC, while Bcl-2 is lower in the aggressive BCC, compared to the nonaggressive variants.

Conclusions: Based on our research, we will conclude that using immunohistochemical and angiogenic markers for risk assessment and stratification of BCC can help optimize treatment, ensuring that surgical procedures are used only when necessary.

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KEYWORDS

skin cancer; BCC; basal cell carcinoma; dermatology; histology; cancer; tumour markers; angiogenic agents; angiogenic; carcinoma; skin; risk assessment; management; surgery; angiogenic marker; markers; immunohistochemistry

Introduction

Basal Cell Carcinoma

Basal cell carcinoma (BCC) is the most common cancer in humans, with the estimated incidence having risen by 20% and 80% over the past 30 years. As a result, it is expected that 1 in 5 Americans may develop BCC in their lifetime [1]. Mutagenesis of p53 appears preferentially in the aggressive variants of BCC, and BCC in sun-exposed and sun-protected sites seem to have different biology and morphology [2].

Excisional surgery is the mainstay of treatment, but the biology of BCC always entails a recurrence rate, with reports suggesting a recurrence rate of 2%-8% at 5 years following standard surgery [3] and 3%-4% following Mohs micrographic surgery [4]. This may be because the biological transformation of BCC tends to occur at the base and edges of the lesion [5]. Given this recurrence rate, it is even more important to differentiate between high- and low-risk BCC (aggressive and indolent variants) so surgical and nonsurgical options can be used appropriately.

High- and Low-Risk BCC

Superficial and nodular BCCs are considered indolent, whereas infiltrative BCC, metatypical BCC, and morpheaform or sclerosing BCC are considered aggressive [6]. Some clinical presentations and histopathology insights are illustrated in Figures 1 and 2. It is well known that micronodular BCC has a higher recurrence rate because tumor extensions are more difficult to assess both clinically and histologically [7]. There are also clinical and pathological parameters used to assess the risk of BCC (Figure 3 [8]) [9].

Figure 1. Basal cell carcinoma (clinical appearance); low risk nodular BCC and high risk infiltrating BCC.

Figure 2. Basal cell carcinoma (histology); low risk nodular BCC and high risk infiltrating BCC.

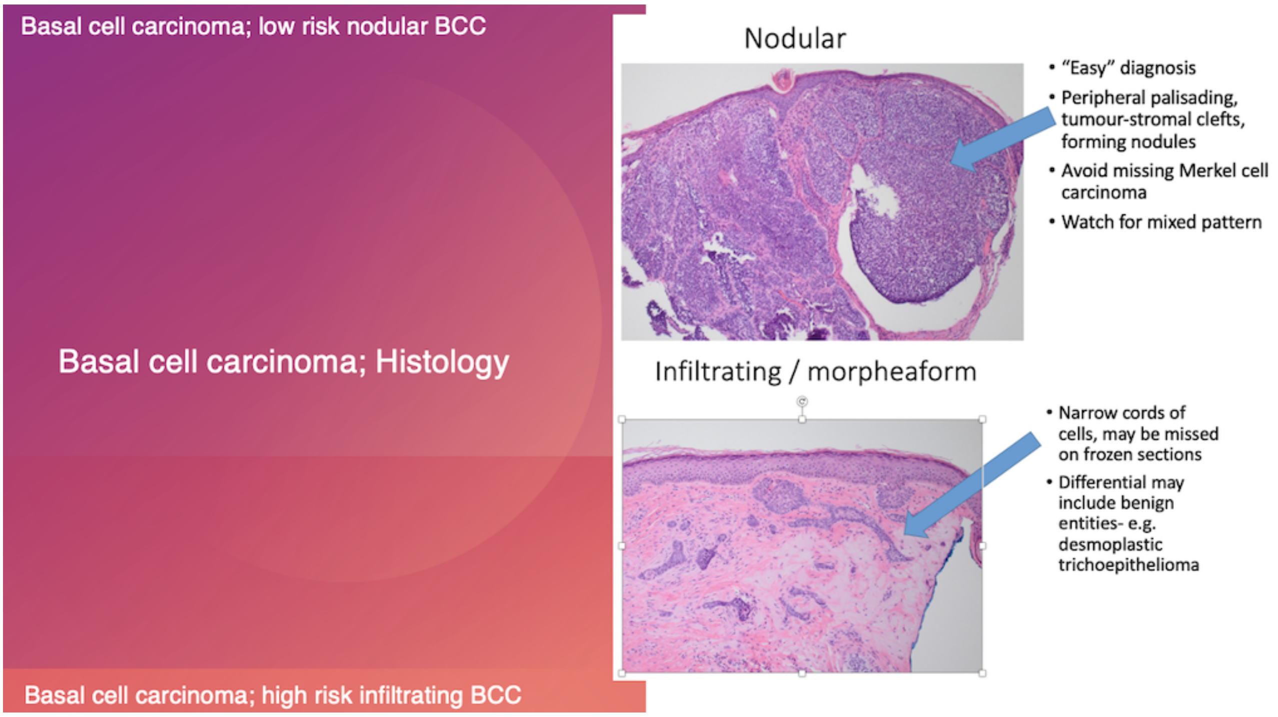

Figure 3. Clinical and pathological parameters to determine basal cell carcinoma (BBC) risk (adapted from Badash et al [9]).

	PARAMETERS	LOW RISK	HIGH RISK
Clinical	Location/size	Area L < 20 mm	Area L ≥ 20 mm
		Area M < 10 mm	Area M ≥ 10 mm
			Area H
	Borders	Well defined	Poorly defined
	Primary vs recurrent	Primary	Recurrent
	Immunosuppression	No	Yes
	Site of prior radiation therapy	No	Yes
Pathologic	Growth pattern	Nodular, superficial	Aggressive
	Perineural involvement	No	Yes

Treatment of BCC

The aims of surgical treatment for BCC are fourfold: to remove both the clinically visible tumor and its microscopic extensions into the surrounding normal-appearing skin, to prevent recurrence in the future, to avoid any functional impairment from the surgery, and to provide the best possible cosmetic outcomes for the patient. Surgical approaches to BCC, including recommended margins for high- and low-risk BCC, vary across different geographical locations, and they are summarized in Table 1.

One of the major issues related to the management of BCC has been the cost of treatment, which has raised concerns among health authorities. In Australia, the total cost of keratinocyte skin cancers (BCC and squamous cell carcinoma) in 2021 was US $426.2 million, and in New Zealand, it was US $129.4 million [10]. Even more than a decade ago, the costs of nonmelanoma treatment for skin cancer in the United States were substantial. In a study conducted between 2007 and 2011 [11], 4.9 million US adults were treated for skin cancer per annum, with an annual treatment cost of US $8.1 billion. Authorities have also shown concerns about doctors' overtreatment. The US Department of Justice and the Centers for Medicare and Medicaid Services have investigated dermatologists for alleged Medicare fraud related to overuse of Mohs surgery [12]. Therefore, it is crucial for clinicians to be able to identify high-risk and low-risk BCC before any expensive surgery is planned.

Up to a third of BCC cases are classified as superficial BCC (sBCC) [13]. Topical treatments effective for sBCC include imiquimod, 5-fluorouracil, and photodynamic therapy, with imiquimod considered the most effective [14]. However, the difficulty in differentiating subtypes clinically makes the accurate risk stratification of BCC even more important.

Table 1. Recommended margins for high- and low-risk basal cell carcinoma (BCC) in different countries.

Organization	Low-risk BCC margins	High-risk BCC margins	Deep margin
National Cancer Care Network, United States	Surgical excision 4 mm	Mohs or surgical excision ≥4 mm	Not specified
European Dermatology Forum	Surgical excision 3-4 mm	Mohs or surgical excision 5-10 mm	Level of fascia, perichondrium, or periosteum; less deep for superficial lesions
British Association of Dermatology	Surgical excision 4-5 mm	Mohs or surgical excision ≥5 mm; morphoeic BCC >13-15 mm	Subcutaneous fat (through)
Cancer Council Australia	Surgical excision or Mohs 2-3 mm	Surgical excision or Mohs 3-5 mm	Subcutaneous fat (include)
Sweden National Guidelines	Surgical excision ≥3-4 mm	Surgical excision ≥5 mm	Not specified

Methods

This paper presents a perspective from a skin cancer expert and a well-established clinic specializing in the treatment of both simple and complex cases of BCC. It addresses the key challenges associated with accurate risk stratification prior to any treatment or procedure. Different immunohistochemical and angiogenic markers for high-risk BCC were also reviewed.

What biomarkers can we use to identify high-risk BCC prior to excisional surgery? Dermatoscopy has improved BCC diagnosis, but the sensitivity and specificity of high-risk BCC signs are not sufficient for accurate diagnosis. For example, the superficial subtype of BCC can be identified in about 80% of cases [15], but this level of accuracy does not apply to specific subtypes of high-risk BCC. A literature review was conducted to identify potential histological markers, and below, the immunohistochemical and angiogenic agent expressions that show promise as BCC risk evaluators are discussed.

Results

The immunohistochemical and angiogenic markers for BCC risk evaluation are as follows:

Vascular Endothelial Growth Factor

Vascular endothelial growth factor (VEGF) is implicated in the development of nonmelanoma skin cancers, such as BCC, because keratinocytes respond directly to VEGF, which in turn affects skin carcinogenesis by altering the proliferation and survival of these cells [16]. Studies on the vascular and angiogenic patterns of BCC reveal that the lowest VEGF expression is found in sBCC, while infiltrative and metatypical subtypes exhibit the highest values [17].

Interleukin-6

It has been known that interleukin-6 (IL-6) concentrations are significantly higher in BCC tumor microenvironments compared to other skin cancers, such as squamous cell cancers [18]. Mawardi et al [19] examined both VEGF-A and IL-6 and discovered a strong correlation with high-risk BCC. They found that a strong VEGF-A expression was significantly more frequent in high-risk aggressive BCC compared to nonaggressive BCC, and IL-6 levels were also indicative of risk (Table 2).

Table 2. Vascular endothelial growth factor A (VEGF-A) and interleukin-6 (IL-6) expressions in basal cell carcinoma (BCC) punch biopsy samples from head and neck [19].

Agent expression	Aggressive BCC	Nonaggressive BCC	*P* value
VEGF-A	16	3	<.003
IL-6	13	2	<.001

Mast Cells

The study by Mawardi et al [19] found that the highest number of mast cells were in the micronodular BCC subtype—a subtype prone to recurrence—and there was a significant difference in mast cell numbers between high-risk aggressive BCC and nonaggressive BCC. Although some authors have suggested that mast cells may not be strictly classifiable as friends or foes in a tumor setting, dermal mast cells may promote skin carcinogenesis by creating an immunosuppressive microenvironment [20]. Recently, for the first time, mast cell activation was observed noninvasively through staining-free visualization of dermal mast cells using two-photon fluorescence lifetime imaging [21]. If such imaging becomes clinically available, it can enhance our ability to stratify BCC risk more accurately before surgery, even without needing a biopsy.

Cyclin D1 and Bcl-2

Studies have shown statistically significant differences between nonaggressive (ie, nodular) and aggressive (ie, micronodular and infiltrative) types using both these markers. Cyclin D1 levels were higher in the aggressive group (*P*=.04), while Bcl-2 levels were lower in the aggressive group compared to the nonaggressive group (*P*=.01) [22].

Discussion

Because BCC is the most common tumor in humans and the global incidence of these tumors is increasing, it is important to stratify the risk. This helps reduce health care costs and spares patients from unnecessary invasive surgical procedures. In this context, identifying immunohistochemical and angiogenic markers, such as VEGF-A, IL-6, Cyclin D1, Bcl-2, and mast cells from punch or shave biopsy samples, can assist in determining the need for surgery or when topical therapies may be more suitable. Noninvasive two-photon tomography, in combination with fluorescence lifetime imaging, has been used to visualize human skin mast cells in vivo using a staining-free method, which also holds promise for future applications.

Visualizing immunohistochemical and angiogenic agents in vivo, with or without staining techniques, hints at a future where BCC risk can be assessed accurately prior to surgery, ultimately leading to more patient-centered treatments.

Conflicts of Interest

None declared.

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Abbreviations

BCC: basal cell carcinoma
IL-6: interleukin-6
sBCC: superficial basal cell carcinoma
VEGF: vascular endothelial growth factor

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Original Paper

Efficacy and Safety of Makabuhay (Tinospora rumphii) 25% Cream Versus Hydrocortisone 1% Cream in the Management of Mosquito Bite Reactions: Randomized Double-Blind Controlled Trial

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Abstract

Background: Most insect bite reactions resolve spontaneously, but the inflammation and pruritus induced have been shown to decrease the quality of life. Previous studies have shown the potential anti-inflammatory properties of *Tinospora rumphii*.

Objective: The aim of the study is to assess the efficacy and safety of *T rumphii* 25% cream versus hydrocortisone 1% cream in the management of local cutaneous reactions caused by mosquito bites.

Methods: This study was a parallel-group, double-blind, randomized, placebo-controlled trial with a 1-week duration in a span of 3 months (June 2019 to August 2019). Participants were exposed to sterile noninfectious mosquitoes (*Aedes aegypti*) for 5-10 minutes to elicit cutaneous lesions. *Tinospora* 25% cream or hydrocortisone 1% cream was applied twice daily throughout the 7-day study period. Of the 70 participants screened for this study, which was approved by an institutional review board (IRB 2019-07) at the Dermatology Outpatient Department of the Research Institute for Tropical Medicine, Alabang, Muntinlupa, Philippines, 58 participants in total met the inclusion criteria and were randomized to treatment (*Tinospora*: n=29) and active control (hydrocortisone: n=29) groups.

Results: In total, 58 participants were randomized to receive *Tinospora* cream (n=29) or hydrocortisone cream (n=29). All participants completed the follow-up. There was a significant decrease in lesion size in both groups from the first 15 minutes to day 7 (P<.001). Comparing the lesion size in both groups, there was a statistically significant decrease in lesion size in the first hour (P=.003) and after 24 hours (P=.03). On day 1, 10% (n=29) of participants in the hydrocortisone group and 7% (n=29) in the *Tinospora* group experienced complete resolution. On day 3, all participants experienced complete resolution. No adverse effects were documented.

Conclusions: *Tinospora* 25% cream is safe, effective, and comparable to hydrocortisone 1% cream as an anti-inflammatory agent for mosquito bite reactions based on the decrease in lesion size, the proportion of participants with complete resolution of wheals, and improvement in pruritus intensity score using a visual analog scale. Long-term safety studies are recommended.

Trial Registration: Philippine Health Research Registry PHRR230716-005932; https://www.herdin.ph/index.php/registry?view=research&layout=details&cid=5932

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KEYWORDS

tinospora; hydrocortisone; mosquito bite reaction; randomized controlled trial

Introduction

Although mosquitoes are well-known vectors of infectious diseases such as malaria, encephalitis, West Nile infection, and the yellow, dengue, and Zika fevers [1], these insects more frequently cause innocuous reactions on the skin when they feed on their hosts [2]. These cutaneous reactions to mosquito bites are caused by an immunologic response to proteins in mosquito saliva, and many who are bitten develop an immune response to these proteins [3]. Pruritus is a sensation limited only to the skin, which causes the desire to scratch. Certain stimuli like insect bites may cause intense allergic reactions and the production of immediate inflammatory responses in humans. Mosquito saliva induces activation of mast cells causing them to degranulate and secrete mediators, such as histamine, neutral proteases, and proteoglycans, and some cytokines, such as tumor necrosis factor-α. Allergic reactions in response to mosquito bites might be urticarial, tuberculin, or eczematoid [4]. Activation of these mediators causes vasodilation and enhancement of vascular permeability and stimulatory sensory nerves and can manifest clinically as wheals, edema, and pruritus [5]. The immunological responses to mosquito saliva in humans can range from the more common immediate and delayed local cutaneous reactions to the rarer, more severe, generalized reactions such as urticaria or angioedema of the skin and mucous membranes [6,7]. Immediate cutaneous reactions to mosquito bites often present as wheals with surrounding erythema that peak at 20 minutes, while delayed cutaneous reactions manifest as pruritic, indurated papules that peak at 24 to 36 hours and resolve over the next 7 to 10 days [8]. Lymphocytes, immunoglobulin E (IgE), and immunoglobulin G contribute to the pathophysiology of local cutaneous reactions. Both serum mosquito salivary gland–specific IgE and immunoglobulin G levels correlate significantly with the size of the wheals seen in immediate local reaction to mosquito bites, while an increase in the number of lymphocytes correlates with delayed cutaneous reactions [3]. While most insect bite reactions resolve spontaneously within 7-10 days, the inflammation and pruritus caused by these bites are often bothersome and have even been shown to decrease the quality of life. A quality-of-life study performed by Halasa et al [9] explored the impact of mosquitoes in the community. Quality of life was measured using the EuroQOL EQ-5D descriptive system that explored the 5 dimensions mobility, self-care, usual activities, pain or discomfort, and anxiety or depression for each dimension that has 3 levels: no problems, some problems, and extreme problems. Of the 121 residents, the majority (54.6%) of the respondents considered mosquitoes to be a problem. In total, 59.5% of the residents said the presence of mosquitoes prevented them from enjoying their outdoor activities. Based on this study, mosquito bites during summer may be comparable to living with up to 2 risk factors for diabetes (ie, abdominal obesity, BMI of 28 or more, reported cholesterol problems, diagnosis of hypertension, or history of cardiovascular disease) or women experiencing menstrual disorders [9,10]. The incessant scratching of these pruritic lesions may also lead to secondary infections and lichenification that require further treatment [11]; hence, there is merit in stopping the itch-scratch cycle early in the history of the insect bite. There is no gold standard in the management of mosquito bite reactions. Topical corticosteroids, topical antipruritic agents (eg, calamine), and oral antihistamines are often prescribed for immediate and delayed mosquito bite reactions, but there is a lack of clinical evidence for the efficacy of these treatments and, in general, recommendations for these are based on expert opinion or clinical experience, and rarely, randomized controlled clinical trials [12]. Inflammation is defined as the local response of living mammalian tissues to injury due to any agent. It is a body defense reaction in order to eliminate or limit the spread of injurious agents. Depending upon the defense capacity of the host and duration of response, it is classified as acute or chronic. Among them, the main features of acute inflammation are the accumulation of fluid and plasma, intravascular activation of platelets, and recruitment of neutrophils as initial inflammatory cells. Histamine, 5-hydroxytryptamine, and bradykinin are the first detectable mediators in the early phase of carrageenan-induced inflammation, whereas prostaglandins are detectable in the late phase of inflammation [13].

Tinospora rumphii, synonymous with *Tinospora cordifolia* and *Tinospora crispa* and locally known as Makabuhay, is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae, distributed in Southeast Asia [14]. In vitro and in vivo studies have demonstrated immunomodulatory [15], antiangiogenic [16], anti-inflammatory [17], and antipruritic [18] properties of *Tinospora* species. These properties have been postulated to be due to the alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, and polysaccharides present in the *Tcordifolia* plant [19]. There are several studies on inflammation responding to *Tinospora* species. An in vitro study by Zalawadia et al [18] showed that *T cordifolia* showed an inhibitory effect on histamine-induced paw edema in mice. The mice were injected with 30 µg of histamine diphosphate to induce the paw edema and were subsequently given the test drugs (*Tinospora* extracts at increasing concentrations ranging from 125 to 1000 mg/kg) per orem. The negative control group was given saline, while the positive control group was given cetirizine, an antihistamine medication. *Tinospora cordifolia* treatment showed a significant reduction in paw volume as compared to the negative control group. Furthermore, as compared to the positive control group, *Tinospora* also demonstrated H1 antihistamine activity as well as mast cell stabilization properties. The authors of the study suggested that the antioxidant potential of *T cordifolia* may have reduced the reactive oxygen species present in the activation of the mast cells and subsequently prevented histamine release [19]. A literature search on clinical studies on the topical preparation of *Tinospora* yielded results for its antiscabies, antibiotic, and antiangiogenic properties [20]. Only an unpublished in vivo study by Delos Santos et al [20] showed that *T cordifolia* is stable in lotion form and is an effective anti-inflammatory and wound healing agent. Rat paw edema was induced using 0.1% mL of 1% formalin and was administered to the right hind paw of each rat subject. The application of 10% and 25% *T cordifolia* lotion and diclofenac gel (positive control) twice a day for 7 days showed a significant decrease in edema compared to the application of plain lotion base [20].

Local studies have demonstrated the safety of using *Tinospora* in both animals and humans. A study by Lagda and Galang [21] on patch testing of *T rumphii* cream on rabbits showed no irritation after 72 hours and the succeeding 7 days after the initial application. The cream can be used safely in concentrations of 25%, 50%, 75%, and 90% [21]. Galang et al [22] performed patch testing of the *T rumphii* cream on human participants, and their results also showed no irritation after 72 hours and the succeeding 2 weeks after the initial application and can be safely used in concentrations of 25%, 50%, and 90%.

To date, there are no published clinical trials investigating the use of *Tinospora species* on cutaneous reactions due to mosquito bites. Steroids have been previously used for mosquito bite reactions. Its misuse may be associated with adverse effects such as pigmentary changes, striae, skin atrophy, glaucoma (if used around the eyes), acneiform eruptions, and bruising, among others. The anti-inflammatory potential of *T rumphii* may provide a safe and natural alternative therapy for mosquito bite reactions. The general objective of our study is to compare the efficacy and safety of *T rumphii* 25% cream versus hydrocortisone 1% cream in the management of local cutaneous reactions caused by mosquito bites. Specifically, we will explore the proportion of participants experiencing complete resolution of wheals after 1 hour and on days 1, 3, and 7 of the study period; the lesion size after 1 hour and on days 1, 3, and 7 of the study period; the pruritus intensity scores using a visual analog scale (VAS) after 1 hour and on days 1, 3, and 7 of the study period; and the proportion of participants experiencing adverse effects.

Methods

Study Design or Study Area or Setting

This was a parallel-group, double-blind, randomized, placebo-controlled trial with a 1-week duration. This study was conducted at the Dermatology Outpatient Department and the Entomology Laboratory of the Research Institute for Tropical Medicine, Alabang, Muntinlupa, Philippines. The study was conducted over a span of 3 months from June 2019 to August 2019.

Sample Size

The sample size was calculated using the formula for a difference in proportions, using a power of 80% and a 5% level of significance. The proportion of success for the *T cordifolia* group and the hydrocortisone group was assumed to be 75% and 45%, respectively, based on the results of a previous study [23,24]. Calculations indicated that a total of 38 participants were needed (19 participants in each study arm). We recruited 58 participants to allow for a 20% dropout rate.

α=level of significance=0.05, $1-\beta$=power=0.80, $f(\alpha-\beta)$=7.85

π_1=the anticipated proportion in those in the control group=45%

π_2=the anticipated proportion in those in the treatment group=75%

Recruitment and Selection of Participants

Purposive sampling was used in this study. Participants were recruited through the following methods: (1) direct recruitment (talking with potential participants about the study and using considerable care that the person does not feel pressured to participate); (2) posting institutional review board (IRB)–approved advertisements on bulletin boards at the lobby, dermatology department, training center, and triage area; and (3) through referrals (physicians and colleagues).

Study Population

The inclusion criteria are the following: healthy men or women aged between 18 and 60 years, participants willing to sign an informed consent form after having read and understood its content upon the investigator's explanation, participants willing to comply with the study protocol requirements, and participants willing to have photos taken for documentation purposes.

Exclusion criteria are the following: participants with a history of severe reactions to mosquito bites (swelling and induration several centimeters in diameter, extensive periorbital swelling, lip swelling, and extensive limb swelling), pregnant or lactating women, participants with severe physical or mental illness, participants with active skin lesions or other dermatological disorders (ie, psoriasis, atopic dermatitis, and other eczemas), and participants with prior or current use of any oral antihistamines or corticosteroids in the past 2 weeks.

Enrollment and Informed Consent

Those who fulfilled the inclusion criteria were recruited. Participants were brought to a private room, where the study protocol was explained. Written informed consent was secured by the investigators and participants. The participants were requested to return on a separate day for the study.

Method of Randomization and Allocation Concealment

The study statistician generated a list of random numbers (simple randomization 1:1) using the computer-generated list of random numbers. A third party not directly involved in the study was assigned to the treatment arms as either 1 (hydrocortisone) or 2 (*Tinospora* species). Sealed opaque envelopes were used to allocate participants to either treatment (1 or 2). The envelope contained either 1 or 2, and assigned coinvestigators dispensed the jars accordingly. Only the pharmacist knew which code (1 or 2) corresponds to *Tinospora* cream or hydrocortisone cream. A diary card was given to participants and evaluated by investigators to ensure the compliance of participants. At the end of the study period, all case report forms (CRFs) were collected.

Preparation of the Plant Material

The fresh mature stems of *T rumphii* were collected from the Sierra Madre mountain range at Infanta, Quezon Province, Philippines. These were authenticated by a botanist at the Bureau of Plant Industry (Multimedia Appendix 1 [25]). The samples were brought to the Department of Science and Technology—Industrial Technology Development Institute (DOST-ITDI) for preparation of the extracts. The organic constituents from the air-dried and chopped *T rumphii* stems were obtained by soaking the stems in 95% ethanol for 48 hours. The soaked solution was passed through Whatman No. 1 filter paper, and the filtrate was concentrated in a vacuum rotary evaporator at 60 °C in order to reduce the volume. The crude extracts yielded were submitted to DOST-ITDI for phytochemical analysis. A licensed pharmacist formulated the *Tinospora* 25% cream. Cultures of the cream were performed to ensure the absence of contaminants. The test product used for the active control group was hydrocortisone 1% cream (Marife C Biscocho Pharmacy). Both creams were unscented and similar in consistency. These were placed in identical white jars. The jars were coded (1 or 2) by the pharmacist. The investigators were unaware of the contents of each container applied to the participants.

Study Intervention

A screened aluminum cage measuring 60×60×60 cm with a 15×15 cm diameter square opening fitted with cloth sleeves was used in this study (Figure 1). All the mosquitoes used were sterile and sucrose-starved for 48 hours prior to the test to ensure biting. These vectors have been grown in the laboratory under a controlled setup, are "clean" mosquitoes, and will not be able to transmit dengue or dengue hemorrhagic fever or other vector-borne diseases. Adequate safety precautions were ensured in order to prevent the introduction of "unclean" mosquitoes to the controlled setup. These measures are the use of a well-established entomology laboratory, aluminum cages with small holes that were kept closed, and a controlled opening of the aluminum cage for the arms of the participants.

The participants were instructed to wash their forearms with plain water and dry them with a clean towel prior to exposure to mosquitoes. The participants were asked to wear rubber gloves with an 8×3.5 cm opening on the volar aspect (Figure 2). This was done to limit the biting area.

Bite exposure with *Aedes aegypti* mosquitoes was performed between noon and 3 PM. A batch of 20 female laboratory-reared *A aegypti* mosquitoes were introduced in the cage every exposure period. Only 1 arm was exposed per participant. The range of exposure was 5-10 minutes, but once 5 mosquito bites were observed, the investigators asked the participant to remove the arm from the cage even before 5 minutes (Figure 3). The mosquitoes that have landed or fed were removed using a suction tube and were placed in a holding chamber and subsequently disposed.

During the whole test period, the participants were instructed not to rub or scratch their arms with mosquito bites. Any adverse cutaneous reaction such as burning and popular or vesicular or bullous eruptions was recorded. Each participant was given 1 jar of *Tinospora* 25% cream or hydrocortisone 1% cream (Figure 4). The first application of the cream was 15 minutes after the mosquito bites. The participants were advised to apply the cream twice a day thereafter on the lesions. To ensure compliance, they were provided a diary to record their application and were required to bring the test product container on every visit. The diary also contained an adverse reaction section to record any reactions. They were advised not to apply any other medication or emollient or take any oral antihistamines or corticosteroids during the study period. The same mild soap (Dove; Unilever) was given to all participants. Photos were taken after the exposure to the mosquitoes in the cage at 15 minutes (when there are mosquito bites), after 1 hour, and on days 1, 3, and 7 of the study period.

Figure 1. Cage containing female laboratory-reared *Aedes aegypti* mosquitoes.

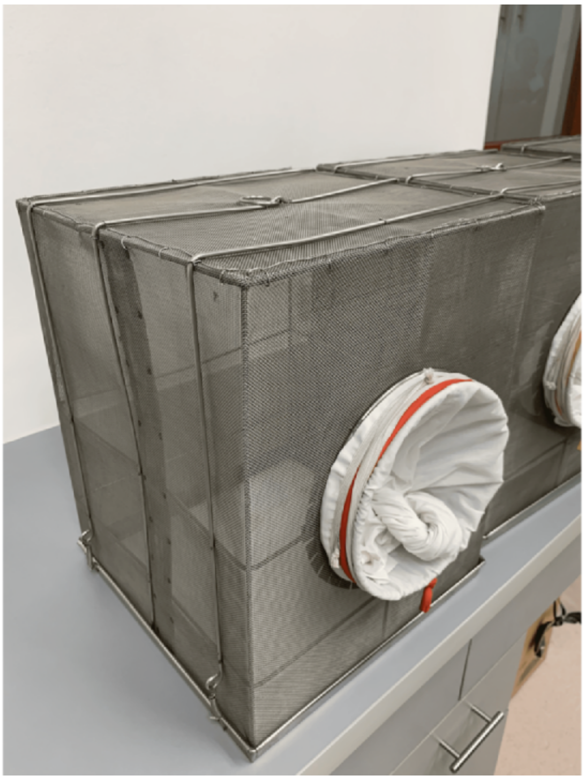


Figure 2. Rubber gloves with an 8 × 3.5 cm opening on the volar aspect.

Figure 3. Mosquitoes feeding on the exposed volar aspect of the arm of participants.

Figure 4. Jars containing either (1) hydrocortisone 1% cream and (2) *Tinospora* 25% cream.

Outcome Measures and Tools for Outcome Measurement

Primary Outcome Measure

Investigators assessed if there was no change, with worsening, with improvement, and complete resolution (0=no change, 1=with worsening, 2=with improvement, and 3=complete resolution). There must be no visible lesions seen on the volar aspect to be considered to have a complete resolution of lesions.

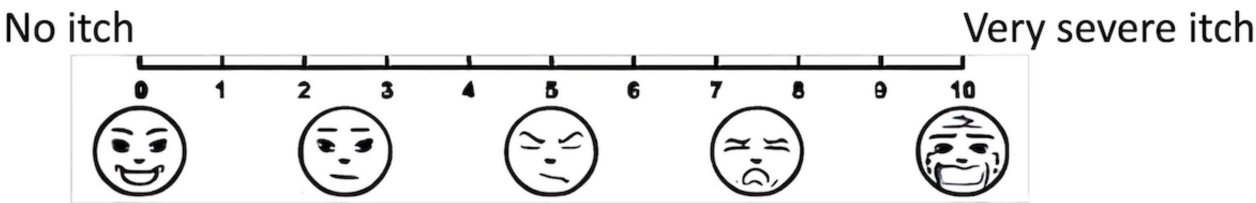
Secondary Outcome Measures

The lesion diameter was measured by the investigators using a single 150-mm stainless steel ruler (Robbins Instrument).

Pruritus Score

The VAS was used to evaluate the itching parameter. A VAS is an instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. Operationally, a VAS is usually a horizontal line, 10 mm in length, anchored by word descriptors at each end or with vertical lines and descriptors. The patient marks a line at the point that represents their perception of their current state. The VAS score is determined by measuring in millimeters from the left-hand end of the line to the point that the patient marks (Figure 5).

Figure 5. A 10 mm visual analog scale.



Adverse Effect

Following the 4-point scale by the Standards of International Drug and Test Products, adverse cutaneous reactions were reported as shown in Table 1.

Table 1. Scoring of the adverse events using the 4-point scale (Standards of International Drug and Test Products).

Scale	Grade	Presentation
0	None	No adverse reactions
1	Mild	Erythema, itching, dryness, scaling, or stinging
2	Moderate	Burning, tenderness, or pain or the above mild
3	Severe	Vesicles, erosion, excoriation, or crusting or above mild or moderate

Data Collection

All CRFs were filled up completely by the primary investigators. These were kept inside the cabinet at the research unit of the department. All forms were kept by the investigators and filed according to participant number. The initial wheal size 15 minutes after the mosquito bite was recorded. Participant assessment of change in lesion size, VAS, and pruritus score were recorded after 1 hour and on days 1, 3, and 7 of the study period. Adverse events (if any) were likewise recorded. Participants were required to bring their diary and product container to monitor compliance.

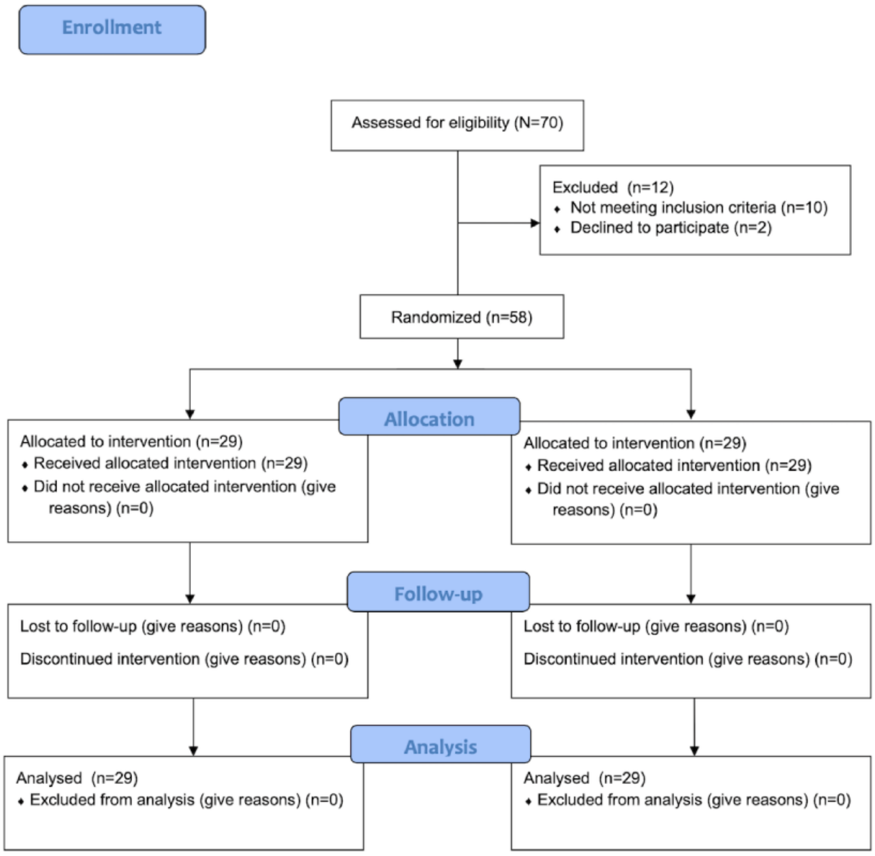
Stopping Guidelines

This study was stopped in participants who experienced adverse reactions (severe pruritus, erythema, burning sensation, and vesicular or bullous eruption) to the creams or worsening of the mosquito bites (redness, warmth, swelling or induration that ranged from 2 to more than 10 cm in diameter, periorbital edema, extensive periorbital swelling, lip swelling, and extensive limb swelling). Participants were monitored based on World Health Organization guidelines for monitoring and reporting of adverse effects. Once a severe reaction occurred, the results were recorded, and participants were given the necessary medications. Unblinding was not necessary as the treatment would not have been different. Participants who did not comply with the protocol of applying test creams twice per day and those who applied other products or medications other than those stated in the protocol were considered to be withdrawn from the study. Dropouts referred to participants who were unable to return for assessment of lesions, and their outcomes were unknown by the end of the study period. The experiment was conducted in a controlled environment, with physicians trained in basic and advanced life support on standby. Although exceedingly rare, if participants experienced signs and symptoms of anaphylaxis, first aid was administered. Medications for anaphylaxis and other foreseeable adverse events, such as epinephrine, diphenhydramine, and intravenous and oral steroids, among others, were made accessible and available. Participants were brought to the nearby emergency room, which was within the vicinity of the outpatient clinic. Medical expenses for adverse events related to the study were shouldered by the study investigators. Participants could be withdrawn from the study due to (1) adverse events, (2) failure of therapy, (3) poor compliance, (4) lost to follow-up, and (5) voluntarily.

Data Processing and Analysis

To ensure blinding of the outcome assessor, a research assistant was hired for the collation of data. A standardized CRF approved by the IRB was used. CRFs were checked for completeness and errors by the primary investigators. Data were encoded by the research assistant in Microsoft Excel 2017 (Microsoft Corp). Collated data were given to the statistician for data analysis. All statistical analyses were performed using the R statistical package (version 3.2.0; R Foundation for Statistical Computing). Data on age were summarized using means and SDs. Frequencies and proportions were shown to describe sex and complete resolution of lesions. The size of lesions and pruritus scores were summarized using median and IQR. The *t* test for independent means was used to determine significant differences between the 2 groups in terms of age. It was a 2-tailed test. A chi-square test was conducted to determine if there were significant differences between the proportion of participants with complete resolution of mosquito bites (primary outcome measure) and the proportion of patients experiencing adverse effects. This test was also used to compare the age distribution of the 2 groups. The median of all lesion sizes and the median visual analog scores between hydrocortisone and *Tinospora* were compared using the Wilcoxon rank sum test. Friedman test was used to compare the change in lesion sizes and visual analog scores across a time period between hydrocortisone and *Tinospora*. No intention-to-treat analysis was done since there were no dropouts. Test results with $P<.05$ were considered to be statistically significant. The flow of participants through each stage of the trial is further seen in Figure 6 [26].

Figure 6. CONSORT 2010 flow diagram. Flow of participants through each stage of the trial (adapted from Schultz et al [26], with permission from Kenneth Schultz). CONSORT: Consolidated Standards of Reporting Trials.



Ethics Approval

This study was approved by the IRB of the Research Institute for Tropical Medicine (IRB 2019-07), registered at the Philippine Health Research Registry (PHRR230716-005932), and conducted in accordance with the tenets of the Declaration of Helsinki 2013 and National Ethical Guidelines for Health Research 2017.

Results

Phytochemical Analysis

In total, 500 mL of *Tinospora* extracts were sent to DOST-ITDI for qualitative phytochemical analysis. The results of the analysis are shown in Table 2. Sterols and triterpenes were strongly positive in the specimen submitted. Alkaloids, saponins, and tannins, as well as traces of glycosides, were found in the stem extracts of *Tinospora* that were used in our study.

Table 2. Qualitative analysis of phytochemicals present in the stem extract of Tinospora rumphii.

Sample code—sample—sample description/identification and test parameter[a]	Result[b]	Method used, Evans [27]
ICS-2019-0466—extract—brownish turbid extract in a glass jar, marked as Makabuhay extract, approximately 500 mL		
Sterols	+++	Liebermann-Burchard test
Triterpenes	+++	Liebermann-Burchard test
Flavonoids	–	Magnesium turning test
Alkaloids	++	Mayer test
Saponins	++	Froth test
Glycosides	+	Fehling test
Tannins	++	Ferric chloride test

[a]Units are inapplicable considering that the tests conducted are qualitative.

[b]Legend: (+) traces, (++) moderate, (+++) abundant, and (–) absence of constituent.

Study Population

Of the 70 participants screened, 58 met the inclusion criteria and were randomized to treatment (*Tinospora*, n=29) and active control (hydrocortisone, n=29) groups (Figure 1). All patients completed the follow-up period. There were no dropouts and withdrawals in the study. Baseline characteristics of the study population are summarized in Table 3. The mean age of participants given hydrocortisone was 37 (SD 7) years, while participants given *Tinospora* were younger with a mean age of 31 (SD 5) years.

Table 3. Demographic profile of patients with mosquito bite treated with hydrocortisone and Tinospora rumphii.

Demographic profile	Hydrocortisone (n=29)	*Tinospora* (n=29)	*P* value
Male sex, n (%)	11 (38)	12 (41)	.79[a]
Female sex, n (%)	18 (62)	17 (59)	—[b]
Age (years), mean (SD)	37 (7)	31 (5)	.01[c]

[a]Significance set at *P*<.05 using the chi-square test.

[b]Not available.

[c]Significance set at *P*<.05 using the *t* test for independent means.

Primary Outcome Measure

All participants treated with *T rumphii* 25% cream and hydrocortisone 1% cream showed improvement in lesion size after 1 hour. After 1 day, 10% (n=3) of participants given hydrocortisone had complete resolution compared to 7% (n=2) of those given *Tinospora* (*P*=.33), but this was not statistically significant. On the third day, 100% (n=29) of participants from both treatment groups had complete resolution of mosquito bites (Table 4).

Table 4. Proportion of participants with complete resolution of mosquito bites after treatment with hydrocortisone and Tinospora rumphii.

Time period	Hydrocortisone (n=29), n (%)	*Tinospora* (n=29), n (%)	*P* value[a]
After 1 hour			N/A[b]
No change	0 (0)	0 (0)	
Worsened	0 (0)	0 (0)	
Improved	29 (100)	29 (100)	
Total clearing	0 (0)	0 (0)	
After 1 day			.33
No change	0 (0)	2 (6.9)	
Worsened	0 (0)	0 (0)	
Improved	26 (90)	25 (86)	
Total clearing	3 (10)	2 (7)	
After 3 days			N/A
No change	0 (0)	0 (0)	
Worsened	0 (0)	0 (0)	
Improved	0 (0)	0 (0)	
Total clearing	29 (100)	29 (100)	

[a]Significance set at *P*<.05 using the chi-square test.

[b]N/A: not applicable.

Secondary Outcome Measures

The 29 participants who received hydrocortisone had a total of 126 lesions ranging from 1.0 to 16.0 mm, while 29 participants who received *Tinospora* had a total of 123 lesions ranging from 1.00 to 18.00 mm (Figures 7 and 8). Participants in both groups demonstrated a significant decrease in median lesion size from baseline to the seventh day (hydrocortisone: *P*<.001 and *Tinospora*: *P*<.001; Figure 9). Comparing the lesion sizes between the 2 groups, there were significant differences noted in the first hour (*P*=.003) and after 24 hours (*P*=.03). There were no significant differences between the 2 groups after 15 minutes and on the third and seventh day post treatment (Table 5).

Figure 7. Representative photos showing the effect on lesion sizes treated with *Tinospora* 25% cream.

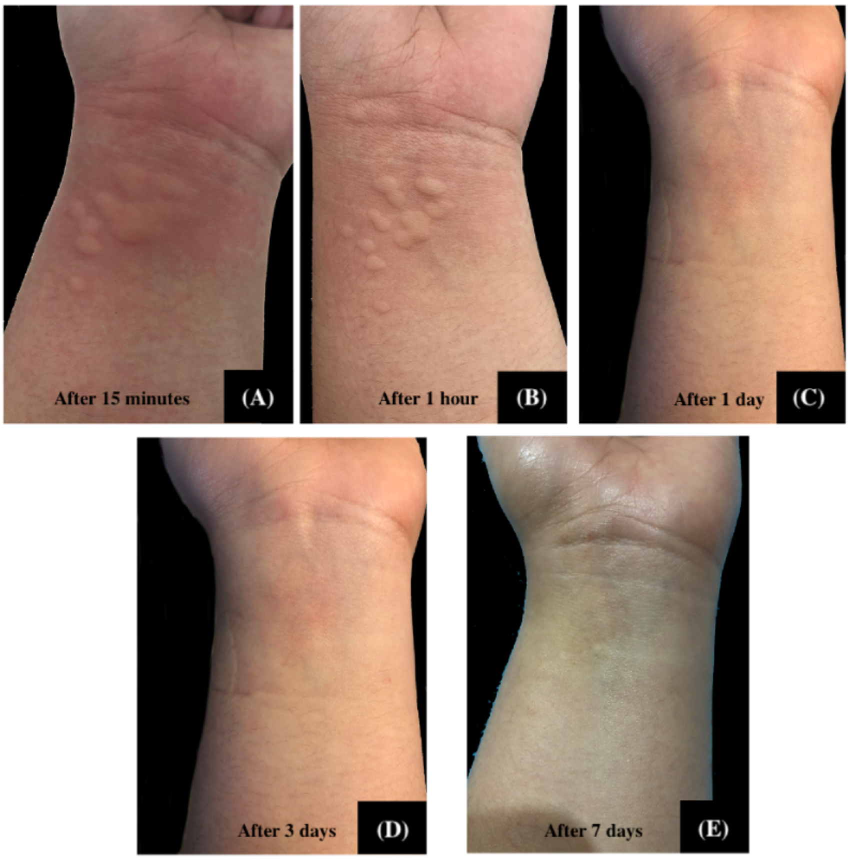


Figure 8. Representative photos showing the effect on lesion sizes treated hydrocortisone 1% cream.

Figure 9. Graph showing the comparison of change in the median of all lesion size in mosquito bites treated with hydrocortisone 1% cream and *Tinospora* 25% cream during the 7-day study period.

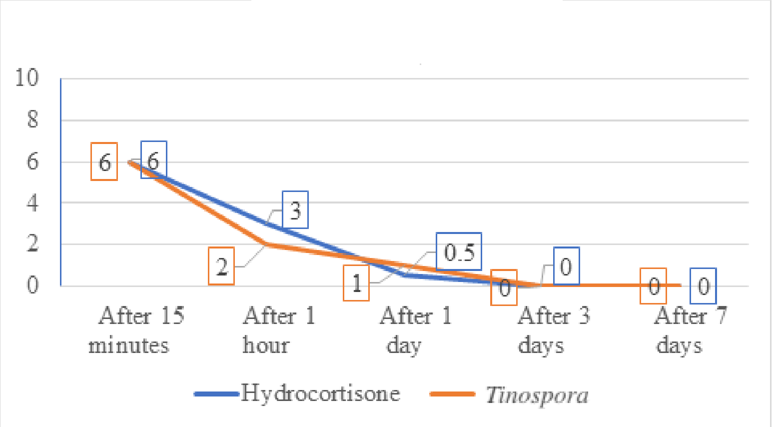


Table 5. Median of all lesion sizes of participants with mosquito bites treated with hydrocortisone and *Tinospora rumphii*..

	Hydrocortisone (mm), median (range)	*Tinospora* (mm), median (range)	*P* value[a]
Time period			
After 15 minutes	7 (2-10)	7 (0-10)	.91
After 1 hour	1 (0-3)	0 (0-2)	.001
After 1 day	0 (0-3)	0 (0-0)	.005
After 3 days	0 (0-0)	0 (0-0)	N/A[b]
After 7 days	0 (0-0)	0 (0-0)	N/A
P value[c]	.001	.001	N/A

[a]Significance set at *P*<.05 using the Wilcoxon rank sum test.

[b]N/A: not applicable.

[c]Significance set at *P*<.05 using the Friedman test.

Visual Analog Score

Visual analog scores for both groups significantly decreased over time (hydrocortisone: *P*<.001 and *Tinospora*: *P*<.001; Figure 10). Baseline visual analog score for participants given hydrocortisone (median 7, range 2-10 mm) and *Tinospora* cream (median 7, range 0-10 mm) was not statistically different (*P*=.91). On days 3 and 7, there was absence of pruritus for both treatment groups. There was no statistically significant difference in the medians of visual analog scores for both treatment arms after 15 minutes. After 1 day and 3 days, a significant difference was observed (Table 6).

There were no reported adverse reactions using the 4-point scale for the 2 test products throughout the entire study period.

Figure 10. Comparison of changes in the median visual analog scores in mosquito bites treated with hydrocortisone 1% cream and *Tinospora* 25% cream during the 7-day study period.

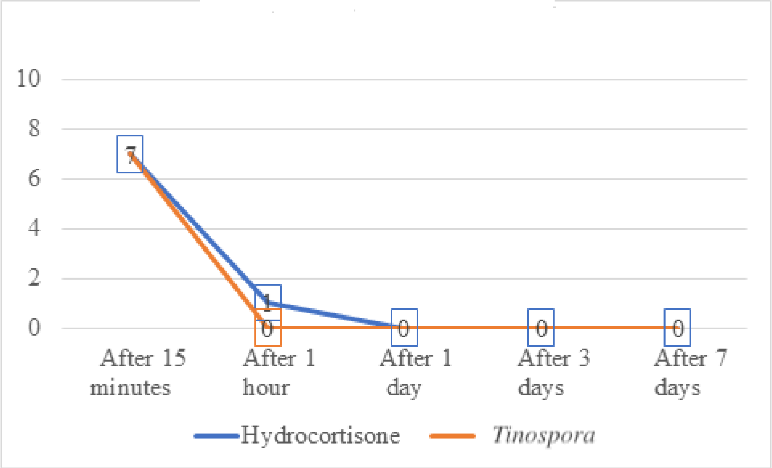


Table 6. Median visual analog score of participants with mosquito bites treated with hydrocortisone and Tinospora rumphii.

	Hydrocortisone (mm), median (range)	*Tinospora* (mm), median (range)	*P* value[a]
Time period			
After 15 minutes	7 (2-10)	7 (0-10)	.91
After 1 hour	1 (0-3)	0 (0-2)	.001
After 1 day	0 (0-3)	0 (0-0)	.005
After 3 days	0 (0-0)	0 (0-0)	N/A[b]
After 7 days	0 (0-0)	0 (0-0)	N/A
P value[c]	.001	.001	N/A

[a]Significance set at $P<.05$ using the Wilcoxon rank sum test.
[b]N/A: not applicable.
[c]Significance set at $P<.05$ using the Friedman test.

Discussion

Principal Findings

Tinospora 25% cream is safe, effective, and comparable to hydrocortisone 1% cream as an anti-inflammatory and antipruritic agent in the management of mosquito bite reactions based on a decrease in lesion size, the proportion of participants with complete resolution of wheals, and improvement in pruritus intensity score using VAS. The CONSORT (Consolidated Standards of Reporting Trials) checklist can be found in Multimedia Appendix 2.

Our results showed a significant decrease in lesion size over time in both treatment groups. Between the 2 groups, there was a statistically significant difference after the first hour and after 24 hours. The timing of application of the topical agents may be significant due to the natural inflammatory course of the host to the mosquito bites. The reactions to mosquito bites can occur immediately after 1 to 2 hours and may be delayed as the lesions gradually enlarge over 24-48 hours after the bite [3]. Immediate reactions are mediated by IgE antibodies that bind to receptors with high affinity on mast cells causing mast cell degranulation along with other polymorphonuclear cells. Late-phase allergic reactions are mediated by lymphocytes and other polymorphonuclear cells such as eosinophils and neutrophils. In a study by Badar et al [28], decreased histamine-induced bronchospasm and a reduced number of disrupted mast cells were observed in animal studies. In an in vitro study by Chi et al [29], ethanol extracts of *Tinospora* revealed inhibitory activities on cyclooxygenase-1, cyclooxygenase-2, 5-lipoxygenase, and Pa2 with the IC_{50} values of 63.5, 81.2, 92.1, and 30.5 µg/mL, respectively. Decrease in the levels of inducible nitric oxide synthase, cyclooxygenase-2, and intracellular adhesion molecule-1 is responsible for the reduction in the release of proinflammatory mediators such as tumor necrosis factor-α, interleukin-4, nitric oxide, and IgE [29].

The efficacy of *Tinospora* species in the management of mosquito bite reactions can be explained by the presence of anti-inflammatory components such as sterols, triterpenes, flavonoids, alkaloids, saponins, glycosides, and tannins. Phytochemical analysis performed by DOST-ITDI on the *Tinospora* extract used in this study demonstrated the presence of the aforementioned active components. The most common phytosterols present in numerous amounts in the extracts of *Tinospora* were β-sitosterol. These sterols seem to target specific T-helper lymphocytes and result in improved T-lymphocyte and natural killer cell activity.

Aside from the decrease in lesion size, there was also complete resolution of lesions in both groups by day 3. Using the Friedman and Wilcoxon rank sum tests, there was no statistically significant difference in the change in mean lesion size for both treatment arms across all observation periods. Furthermore, a decreasing trend in the visual analog scores of the participants was observed. These suggest that the *Tinospora* cream has comparable efficacy to hydrocortisone cream.

There were no reported adverse reactions using the 4-point scale for the 2 test products. However, caution should always be observed in the use of standard of care such as corticosteroids because of their known side effects. These include local reactions such as epidermal atrophy, changes in pigmentation, contact dermatitis, and acneiform eruptions, among others. Furthermore, tachyphylaxis and rebound effects are also major concerns. Previous studies have demonstrated the safety of *Tinospora* cream. There were no cutaneous reactions observed in patch testing done on the participants in the study of Galang et al [22]. No adverse events were noted up to concentrations of 90% [22].

It is important to note that although the baseline characteristics are comparable, participants in the *Tinospora* group are younger compared to the hydrocortisone cream (P=.007). An epidemiological study by Kar et al [30] was similar to our study in that there was no age preponderance in the mosquito bites.

Limitations

Among well-studied variables that attract mosquitoes are sex, carbon dioxide, body odor, secretions, and blood type. A study by Kulthanan et al [31] concluded that females were frequently bitten by mosquitoes due to their use of floral fragrances from perfumes. On the other hand, Rebollar-Tellez [32] reported that men were readily bitten due to having larger bodies that generate larger relative heat or carbon dioxide output. A study by Raji et al [33] showed that the loss of ionotropic receptor 8a (Ir8a) in *Aedes* species reduced the mosquitos' attraction to humans and their odor. Shirai et al [34] demonstrated in their study that blood group O participants attracted more *Aedes* species as compared to groups with other blood types (B, AB, and A). Participants with blood type O possess components used by mosquitoes for the production of eggs. Some of these variables could have played a role, but these are beyond the scope of this study. This study did not take into account the attraction of mosquitoes to inherent human characteristics such as the color of skin and blood type.

Recommendations

Future studies on *Tinospora* cream may include a concentration-response study in order to determine the ideal, safe, and effective doses of the compound. A quantitative phytochemical analysis along with an exploration of other vehicles (gel, lotion, cream, and ointment) to deliver the maximal dose is also recommended. A long-term safety study may also be performed. Furthermore, studies on children and patients with other inflammatory conditions such as psoriasis, atopic dermatitis, and other eczemas may be explored.

Acknowledgments

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Authors' Contributions

JGG conceptualized the study and conducted the data curation. JGG and JKGG-D wrote the original paper. JD and MTG reviewed and edited the paper.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Plant authentication by the Republic of the Philippines Department of Agriculture Bureau of Plant Industry Manila.
[PDF File (Adobe PDF File), 2844 KB - derma_v6i1e50380_app1.pdf]

Multimedia Appendix 2
CONSORT-EHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 289 KB - derma_v6i1e50380_app2.pdf]

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Abbreviations

CRF: case report form
DOST-ITDI: Department of Science and Technology—Industrial Technology Development Institute
IgE: immunoglobulin E
IRB: institutional review board
VAS: visual analog scale

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Research Letter

Assessing the Accuracy and Comprehensiveness of ChatGPT in Offering Clinical Guidance for Atopic Dermatitis and Acne Vulgaris

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KEYWORDS

ChatGPT; artificial intelligence; dermatology; clinical guidance; counseling; atopic dermatitis; acne vulgaris; skin; acne; dermatitis; NLP; natural language processing; dermatologic; dermatological; recommendation; recommendations; guidance; advise; counsel; response; responses; chatbot; chatbots; conversational agent; conversational agents; answer; answers; computer generated; automated

Introduction

When facing barriers to timely and accessible in-person dermatologic care, patients may look for guidance on skin health from alternative sources like artificial intelligence platforms. ChatGPT, a language processing tool trained on web-based articles, books, and websites, has the potential to enhance information accessibility [1,2]. However, literature assessing its dermatologic utility is scant [3]. This study characterizes the accuracy and comprehensiveness of ChatGPT in responding to common patient questions for acne vulgaris and atopic dermatitis (AD).

Methods

Overview

For each condition (acne vulgaris and AD), 32 potential patient questions were created based on American Academy of Dermatology (AAD) guidelines and web-based resource centers [4,5]. To the extent possible, questions were generated using explicit wording from the guideline "clinical questions" and resource center bullet points, and were approved by consensus from board-certified dermatologists. The questions aimed to address various disease aspects and incorporate lay terminology (eg, "blackheads"; Textbox 1 and Multimedia Appendix 1). Each question was presented to ChatGPT-3.5, and the responses were independently graded for quality by board-certified dermatologists.

Textbox 1. Sample of ChatGPT input questions for atopic dermatitis and acne vulgaris. For the comprehensive list of questions, please see the corresponding Appendix.

Natural history

- Atopic dermatitis
  - What causes eczema?
  - At what age does childhood atopic dermatitis usually start?
  - What can trigger flares of atopic dermatitis?
- Acne vulgaris
  - What causes acne?
  - What is the role of diet in acne vulgaris?
  - Why do adults get acne?

Symptoms and differential diagnosis

- Atopic dermatitis
  - What other conditions are associated with atopic dermatitis?
  - Can acne cause scars?
  - What are the signs and symptoms of atopic dermatitis in children?
- Acne vulgaris
  - How is acne different from rosacea?
  - What signs suggest acne is related to polycystic ovarian syndrome?
  - How is acne different from hidradenitis suppurativa?

Treatment and management

- Atopic dermatitis
  - What is the efficacy of topical corticosteroids for the treatment of atopic dermatitis?
  - What is the efficacy of phototherapy for the treatment of atopic dermatitis?
  - What environmental modifications around the house can be implemented to improve atopic dermatitis?
- Acne vulgaris
  - What is the efficacy of benzoyl peroxide in the treatment of acne vulgaris?
  - What are the potential side effects of isotretinoin in the treatment of acne vulgaris?
  - What topical agents can be combined in the treatment of acne vulgaris?

Ethical Considerations

This study used publicly available web-based data sets; institutional review board approval was not required at the University of Connecticut Health Center.

Results

Across both diseases, 78% (50/64) of ChatGPT responses were correct but inadequate (score ≤2), with 45% (29/64) of answers being fully comprehensive (score 1). No responses were completely inaccurate (score 4). For AD and acne specifically, 88% (28/32) and 66% (21 of 32) of responses were correct but inadequate (score ≤2), and 53% (17/32) and 34% (11/32) were fully comprehensive (score 1), respectively. This *broadly* indicates acceptable performance of ChatGPT across both conditions. However, whereas ≥75% of responses for AD *within each category* (including natural history, symptoms and differential diagnosis, and treatment and management) were correct (score ≤2), the accuracy of responses for acne treatment/management (score ≤2) specifically was relatively low (9/16, 56%), suggesting a deficit in ChatGPT in advising treatment recommendations for this condition (Table 1). The interrater reliability, as measured by the weighted Cohen κ coefficient, was 0.44, indicating moderate agreement among the board-certified dermatologists in our study.

Table 1. Evaluation of ChatGPT output responses for atopic dermatitis and acne vulgaris.[a]

	Atopic dermatitis (n=8), n (%)	Acne vulgaris (n=8), n (%)	Both conditions (n=16), n (%)
Natural history			
1. Comprehensive	4 (50)	5 (63)	9 (56)
2. Correct but inadequate	3 (38)	1 (13)	4 (25)
3. Mixed with correct and incorrect/outdated data	1 (13)	2 (25)	3 (19)
4. Completely incorrect	0 (0)	0 (0)	0 (0)
Symptoms and differential			
1. Comprehensive	5 (63)	2 (25)	8 (44)
2. Correct but inadequate	3 (38)	4 (50)	7 (44)
3. Mixed with correct and incorrect/outdated data	0 (0)	2 (25)	2 (13)
4. Completely incorrect	0 (0)	0 (0)	0 (0)
Treatment and management[b]			
1. Comprehensive	8 (50)	4 (25)	12 (38)
2. Correct but inadequate	5 (31)	5 (31)	10 (31)
3. Mixed with correct and incorrect/outdated data	3 (19)	7 (44)	10 (31)
4. Completely incorrect	0 (0)	0 (0)	0 (0)

[a]The table demonstrates scores for ChatGPT responses for atopic dermatitis and acne vulgaris. Each question was presented to ChatGPT-3.5 (queries entered on February 27, 2023, using the February 9, 2023, release version), and response quality was graded independently by two board-certified dermatologists (authors GW and NL) using a scale previously referenced in the literature: (1) comprehensive, (2) correct but inadequate, (3) mixed with correct and incorrect/outdated data, (4) completely incorrect [1]. If reviewers agreed, their score was used. Discrepancies in scoring of ≥1 point (29/64, 45% of responses) were evaluated independently by a third board-certified academic dermatologist (author BS) with over 25 years of clinical experience, and the majority score was used; if there was no majority, the third reviewer score was prioritized. See Multimedia Appendix 2 for a sample of ChatGPT output responses, associated scores, and commentary on response accuracy and comprehensiveness.

[b]For the treatment and management category, 16 responses were evaluated for atopic dermatitis and acne vulgaris each, for a total of 32 responses.

Discussion

In the realm of dermatological care, platforms like ChatGPT can serve as supplementary educational tools, enhancing information accessibility for patients with conditions such as acne vulgaris or AD. However, the reviewers found that the accuracy and comprehensiveness were lower for questions on acne treatment as compared to AD, occasionally omitting information on treatment effectiveness, lacking guidance on treatment expectations, and failing to provide age-appropriate and patient-specific recommendations. For example, while ChatGPT accurately described the mechanism of tetracyclines in treating acne vulgaris, it did not identify patients with moderate inflammatory acne who are typically candidates for this medication. Similarly, it failed to recognize more recent randomized controlled trials supporting the use of spironolactone in female patients with hormonal acne and stated that it is not a first-line treatment. Acne treatment is nuanced and expanding, and includes a plethora of topical and oral treatments that depend on a patient's age, gender, severity, skin tone, and preferences, likely minimizing ChatGPT's ability to provide accurate and patient-specific guidance. While responses were often conversational in tone, they sometimes incorporated advanced terminology that may be confusing for patients (eg, antiandrogen or meta-analysis; Multimedia Appendix 2).

These findings underscore the ethical dilemma surrounding ChatGPT and other artificial intelligence platforms—specifically, whether the benefit of more accessible dermatologic information outweighs the risk of harm from potentially confusing or incomplete information [3]. The findings encourage dermatologists to assess patients' baseline understanding and inquire about the educational resources used. In addition to targeted counseling, providing patients with educational handouts or links to AAD patient resource centers may be prudent to ensure access to comprehensive, patient-targeted, up-to-date information.

This assessment has limitations. There is inherent variability in ChatGPT's responses; however, through our extensive interactions with the software, we did not find meaningful differences in the answers' content when we presented the same question several times. Additionally, our findings' reliability and applicability are contingent upon the type of generative AI models used and the specific phrasing of questions. These findings also do not apply to queries on all skin conditions. Moreover, this research used the popular ChatGPT-3.5 model; subsequent models with more advanced training may yield varying outcomes.

Nonetheless, these findings provide an initial characterization of the accuracy and comprehensiveness of ChatGPT in two common skin conditions. Additional studies are required to further understand the clinical benefits and risks of artificial intelligence in patient-initiated dermatologic education. Our findings are time sensitive. As AI models like ChatGPT evolve and guidelines update, the performance and relevance of our results with ChatGPT-3.5 may change. Continuous reassessments are crucial for maintaining accuracy and relevance.

Conflicts of Interest

HF is a consultant for Cytrellis Biosystems, Inc and Soliton, Inc. The other authors declare no conflicts of interest.

Multimedia Appendix 1
ChatGPT input questions and associated scores for atopic dermatitis and acne vulgaris.
[DOCX File , 40 KB - derma_v6i1e50409_app1.docx]

Multimedia Appendix 2
Sample ChatGPT output responses for atopic dermatitis and acne vulgaris and associated physician scores and author commentary.
[DOCX File , 20 KB - derma_v6i1e50409_app2.docx]

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Abbreviations

AAD: American Academy of Dermatology
AD: atopic dermatitis

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Viewpoint

Cutaneous Manifestations of Anabolic-Androgenic Steroid Use in Bodybuilders and the Dermatologist's Role in Patient Care

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Abstract

Young adults have been increasingly facing pressure to achieve an appealing athletic physique, often influenced by social media influencers on platforms like Instagram. This viewpoint highlights the association between image-centric social media, dissatisfied body image, the use of anabolic-androgenic steroids (AAS) to achieve desired results, and the overlooked dermatological side effects of AAS, including acne and acne fulminans. We underscore the importance of recognizing acne fulminans as an indicator of possible AAS abuse and encourage dermatologists to actively identify and address AAS use to improve their patients' well-being.

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KEYWORDS

anabolic steroids; androgenic steroids; anabolic-androgenic steroids; acne; acne fulminans; isotretinoin; bodybuilding; bodybuilder; social media; skin; dermatology; dermatologist; athlete; sport; steroid; cutaneous

Physicians should be aware of the increased pressure on young adults to achieve an appealing athletic physique promoted by many influencers on social media platforms such as Instagram. While many claim to have achieved these physiques naturally, some admit to the use of anabolic-androgenic steroids (AAS). Young adults pursuing bodybuilding often use social media as a means of obtaining information for training, nutrition, and supplements [1]. Frequent exposure to these social media images and videos may influence individuals into using AAS to achieve similar results. Image-centric social media is associated with a dissatisfied body image due to physique comparisons to an idealized body, which is also positively associated with AAS use [1]. In the United States, AAS usage is increasing dramatically, reaching up to 80% of amateur bodybuilders and 38% to 58% of weightlifters [2].

While the dangers of AAS are widely known, often overlooked are dermatological side effects including acne, alopecia, striae distensae, hirsutism, and furuncles at injection sites [3]. Acne is a common side effect, reported by 43% of AAS users [3]. AAS are synthetic exogenous testosterone derivatives that result in the enlargement of sebaceous glands, where increased sebum production promotes a suitable environment for the proliferation of *Cutibacterium acnes* [3,4]. Androgen receptors have been found in sebocytes and follicular keratinocytes [3]. The specific AAS mechanism of action depends on the structural variations of each derivative affecting androgen receptor affinity. AAS can increase androgens to supraphysiologic levels, in turn causing increased receptor binding as well as sebum production and *C. acnes* activity, thus risking development of acne vulgaris and acne fulminans (AF) [3].

While rare, AF can be painful and hemorrhagic and is considered the most severe form of acne [2]. The acute development of tender, ulcerative AF nodules on the face, chest, shoulders, and back has been documented by various Instagram AAS users. Systemic symptoms including fever, fatigue, lymphadenopathy, and musculoskeletal pain are possible, as well as an elevated erythrocyte sedimentation rate and leukocytosis [5]. Those who develop AF should be instructed to stop AAS immediately. The treatment of choice for AF is systemic steroids (prednisone 0.5-1 mg/kg/day) and oral isotretinoin (0.1 mg/kg/day). Care should be taken when adding isotretinoin, as it can be a precipitant of AF in the context of AAS use [5]. Initially, steroids should be used alone for 2 to 4 weeks, before adding isotretinoin for 4 weeks. After treatment, the provider should assess the need for continued therapy, steroid tapering, or the addition of other medications.

In a sport where the goal is to build the best physique possible, the effects of AF can be physically and emotionally devastating. The use of AAS and the development of AF, although benign, can lead to permanent scarring, negative self-scrutiny, anxiety, and depression [1]. We hope this viewpoint can highlight this issue while encouraging dermatologists and other care providers to play an active role in recognizing AAS use in patients. Since 50% of AAS users develop acne, AF should be an indicator of possible drug abuse. By recognizing and screening for AAS abuse, dermatologists can help curtail steroid addiction and improve health outcomes for these patients [3].

Conflicts of Interest

RPD is a joint coordinating editor for Cochrane Skin, a dermatology section editor for UpToDate, a social media editor for the *Journal of the American Academy of Dermatology*, editor-in-chief of *JMIR Dermatology*, and cochair of Cochrane Council. RPD receives editorial stipends (*JMIR Dermatology*), royalties (UpToDate), and expense reimbursement from Cochrane.

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Abbreviations

AAS: anabolic-androgenic steroids
AF: acne fulminans

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Original Paper

The Impact of WhatsApp as a Health Education Tool in Albinism: Interventional Study

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Abstract

Background: Oculocutaneous albinism is a congenital disorder that causes hypopigmentation of the skin, hair, and eyes due to a lack of melanin. People with albinism are at increased risk of developing skin complications, such as solar keratosis and skin cancers, leading to higher morbidity. As education is crucial in managing albinism, leveraging information technology, such as WhatsApp, can provide an effective intervention for digital health education.

Objective: This study aims to assess the impact of WhatsApp as a tool for providing health education among people with albinism.

Methods: The design of the study was interventional. The intervention consisted of weekly health education sessions conducted in a WhatsApp group for the duration of 4 weeks. The topics discussed were knowledge of albinism, sun protection practices, the use of sunscreen, and myths about albinism. They were all covered in 4 WhatsApp sessions held in 4 separate days. A web-based questionnaire was filled out before and after the intervention by the participants. Mann-Whitney *U* test was used to compare the pre- and postknowledge scores. Spearman correlation was used to correlate data.

Results: The mean age of the study participants was 28.28 (SD 11.57) years. The number of participants was 140 in the preintervention period and 66 in the postintervention period. A statistically significant increase in overall knowledge (P=.01), knowledge of sunscreen (P=.01), and knowledge of sun protection (P<.01) was observed following the intervention. Before the intervention, a positive correlation was observed between age (r=0.17; P=.03) and education level (r=0.19; P=.02) with participants' overall knowledge. However, after the intervention, there was no significant correlation between knowledge and age or education level. A percentage increase of 5.23% was observed in the overall knowledge scores following the intervention.

Conclusions: WhatsApp is an effective tool for educating people with albinism and can act as an alternative to the conventional methods of health education. It shows promising outcomes irrespective of the health literacy level of people with albinism. This educational intervention can positively impact behavior change and translate to consistent sun protection practices. The limitations of this study include the possibility of social desirability bias and data security.

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KEYWORDS

WhatsApp; oculocutaneous albinism; health education; smartphone; mobile phone; teledermatology; photodermatoses; digital health intervention; photoprotection; West Africa; social media; albinism; albino; skin; dermatology; melanin; patient education; sun; sunscreen; discussion group; digital health education

Introduction

Oculocutaneous albinism is an inherited disorder of hypopigmentation in which there is little or no production of melanin. People with albinism usually have light-colored skin, white hair, and red eyes. Melanin plays a major role in photoprotection and its lack in people with albinism increases the risk of photodermatoses. These may range from benign conditions like freckles or solar lentigos to more severe skin issues, such as nonmelanoma skin cancers—basal cell cancers and squamous cell cancers. Notably, the prevalence of nonmelanoma skin cancers is 20.9% in Nigeria [1], 11.8% in Togo [2], and 26% in Brazil [3]. These sun-related skin conditions increase morbidity and affect the quality of life of people with albinism.

Preventing these photodermatoses includes promoting sun protection practices and educating people with albinism, which is crucial for this purpose. Studies conducted in Africa have documented that health education programs can improve compliance with sun protection practices among individuals with albinism [4,5].

In recent times, IT has revolutionized the dissemination of information, and the use of social media is a prime example. Social media refers to internet-based platforms or application software that enables individuals to communicate, gather, and exchange information, ideas, and images in real time with other users [6]. These platforms, such as WhatsApp, Facebook, Twitter, YouTube, and Instagram, may serve as delivery vehicles for digital health interventions. Social media provides opportunities for public health promotion, patient education, and professional interactions [7]. In addition, it can increase patient engagement and empowerment resulting in better outcomes [8]. On social media, patients with similar conditions and experiences can connect, share knowledge, and support one another [9].

Among the apps employed in digital health education interventions, WhatsApp holds a unique position. It is a messenger app that enables users to make voice calls and send instant messages, photos, videos, and voice messages over the internet [10]. In contrast to the original text messaging function on mobile phones, WhatsApp allows users to send and receive messages at no cost per message [11]. It supports the formation of group chats and permits numerous users to participate, observe, and respond to conversations [10]. It is the third most popular social networking platform in the world, after Facebook and YouTube (which comes second) [12,13]. In Nigeria, WhatsApp is the most preferred social media platform among active users aged 16 to 64 years [14].

Although several studies have used WhatsApp as a health education intervention, there is limited literature available on its application in dermatology in West Africa, specifically for people with albinism [15-17]. The aim of this study was to assess the effectiveness of WhatsApp in health education for this population.

Methods

Ethical Considerations

Ethical clearance was obtained from the ethical review board of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria (NAUTH/CS/66/VOL.16/VER.3/86/2023/039). All study participants gave informed consent. Data anonymity and confidentiality were guaranteed.

Participants

The study was designed as an educational interventional study. A WhatsApp group was created for the purpose of this study, and it was named People With Albinism Health Education Group. Participants were recruited from various WhatsApp groups for people with albinism in Nigeria, and this was done by sending a group invite link via the group admins to these groups. Participant Disclosure Form (Multimedia Appendix 1) was posted in the People With Albinism Health Education Group. This group had 4 admins who were well-trained dermatologists. Their function was to moderate the conversations in the group and answer questions. A convenience sampling method was used. The inclusion criteria were the following: people with albinism aged 18 years and older or caregivers of children with albinism younger than 18 years of age, who had access to smartphones or tablets and could use WhatsApp.

Intervention

The WhatsApp messenger app was used as the intervention tool. The participants used their smartphones or tablets. The intervention included weekly sessions of health education delivered through text, images, videos, and voice messages, lasting for a month (January 9 to January 30, 2023). The topics covered in the sessions were the following: (1) understanding albinism, (2) skin problems associated with albinism, (3) sun avoidance and sun protection practices in albinism, as well as (4) myths about albinism and debunking them. In each session, a group admin educated the group for 1 hour (Multimedia Appendix 2). After each session, there was time for questions and comments.

A web-based questionnaire was created using Google Forms, and the link for the form was posted in the People With Albinism Health Education Group. The participants filled out the forms before and after the intervention. The questionnaire consisted of sections consisting of questions on social demographics and 4 domains (ie, questions on understanding albinism, sun protection, the use of sunscreens, and myths about albinism).

The reliability of the questionnaire was analyzed using the Cronbach alpha test and achieved a score of .72. This indicates that the questionnaire demonstrates a reasonable level of internal consistency. The questionnaire was reported in accordance with the Checklist for Reporting Results of Internet E-Surveys (CHERRIES).

Data Analysis

Data from the web-based questionnaires was downloaded as a CSV file, and data cleaning was done using Microsoft Office Excel (version 2021). Duplicated and incomplete data were removed. Further analysis of data was done using SPSS (version 25; IBM Corp). All continuous variables were tested for normality using the Shapiro-Wilk test and found to be nonnormally distributed; thus, median and IQR values were used as measures of central tendency. Age was further classified into 4 groups based on their quartile distribution. All noncontinuous variables were summarized using frequencies and percentages.

To create a measure of respondents' knowledge, their responses were graded as follows: strongly disagree=0, disagree=1, neutral=2, agree=3, and strongly agree=4. Responses to questions that included negative or false statements were reverse-scored. The sum of scores for each person was obtained in each domain, namely knowledge of albinism, knowledge of sun protection, knowledge of sunscreens, and knowledge of myths. The percentage score for each person was determined by dividing their sum score by the maximum achievable score in the domain and multiplying by 100. The percentage knowledge scores thus generated were treated as continuous variables.

To compare initial and final responses to individual questions, the Fisher exact test was performed on the frequency of each question. Mann-Whitney *U* test was used to compare the percentage knowledge scores before and after the intervention. Furthermore, Spearman correlation was used to correlate percentage knowledge scores before the start of WhatsApp sessions with age and the highest level of education. We also used Spearman correlation to assess the relationship between percentage knowledge scores after sessions and variables such as the number of sessions attended, age, and the highest level of education. Alpha level was set at $P<.05$.

Results

A total of 246 people were recruited in the group. The number of respondents to the web-based survey was 140 before the intervention and 66 after the intervention. Figure 1 shows the flow diagram of the sample selection. Table 1 shows the baseline demographics of the study participants. The median age of the participants was 28 (IQR 22.75-33.25) years. Comparing responses before and after the intervention showed a better understanding of certain knowledge—albinism is inherited, the substance produced in the skin that protects us from the sun is melanin, wide-brimmed hats are better than face caps, and the color of the fabrics is important in sun protection (Multimedia Appendix 3).

Figure 1. Flowchart of sample selection.

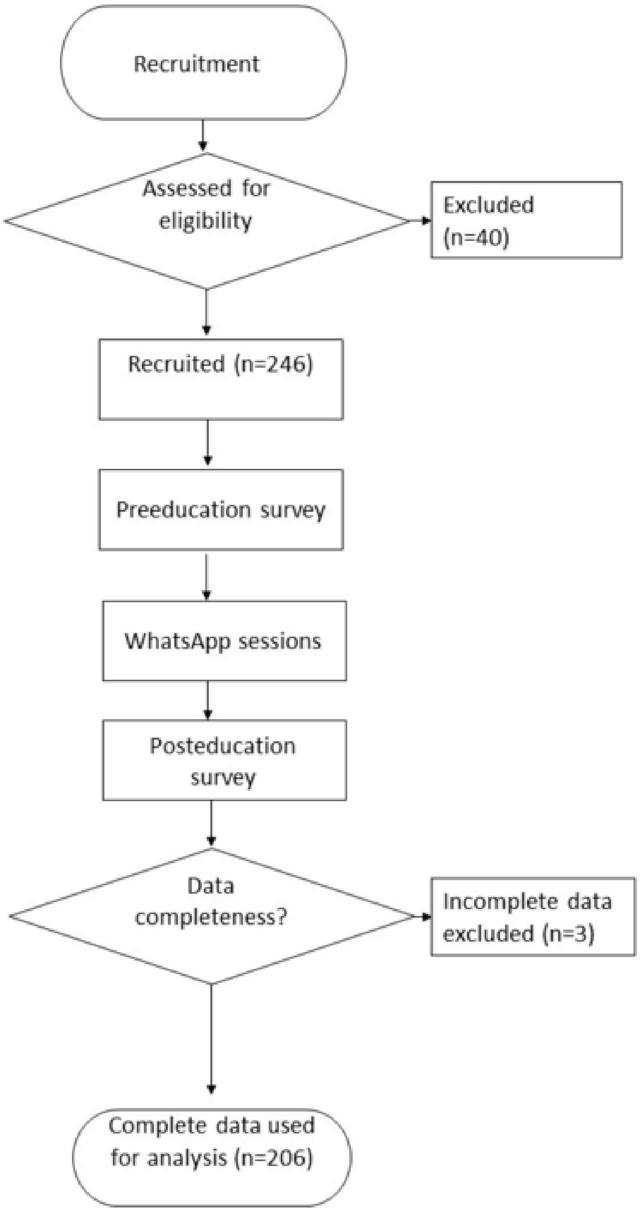

Table 1. Sociodemographic distribution of participants (N=206).

Characteristics	Frequency, n (%)
Gender	
Male	78 (37.9)
Female	128 (62.1)
Are you a person with albinism?	
Yes	177 (85.9)
No	29 (14.1)
Ethnic group	
Igbo	91 (44.2)
Hausa	16 (7.8)
Yoruba	67 (32.5)
Others	32 (15.5)
Age range (years)	
First quartile (≤23)	61 (29.6)
Second quartile (24-28)	46 (22.3)
Third quartile (29-35)	48 (23.3)
Fourth quartile (>35)	51 (24.8)
Marital status	
Single	136 (66)
Married	68 (33)
Widowed	2 (1)
Education	
None	1 (0.5)
Primary	8 (3.9)
Secondary	44 (21.4)
Tertiary	153 (74.3)
Occupation	
Unemployed or students	104 (50.5)
Petty trader, laborer, or messenger	23 (11.2)
Junior civil servant or senior school teacher	26 (12.6)
Junior school teacher or artisan	14 (6.8)
Professional, senior civil servant, or contractor	39 (18.9)
Have you seen a dermatologist?	
Yes	77 (37.4)
No	129 (62.6)
Time of filling this questionnaire	
Before intervention	140 (68)
After intervention	66 (32)

Table 2 displays the comparison of the median overall knowledge scores of the study participants before and after the intervention. There was a statistically significant improvement in the overall knowledge scores of the participants after the intervention, particularly in sun protection and sunscreen knowledge. In addition, we found a 5.3% rise in the overall knowledge scores following the intervention. The correlation between age, level of education, number of sessions attended, and knowledge levels was analyzed and presented in Multimedia Appendix 4. There was a positive correlation between age and preintervention overall knowledge scores. Similarly, a positive correlation was seen between the level of education and preintervention overall knowledge scores.

Table 2. Comparison of overall knowledge scores before and after sessions. Median and IQR values are presented in percentages.

Characteristics	Preintervention, median (IQR)	Postintervention, median (IQR)	Percentage increase	*U* value	*P* value
Overall score	78.4 (68.6-84.3)	82.5 (69.4-82.4)	5.23	3587	.01
Knowledge of albinism	77.1 (69.4-85.4)	80.2 (68.7-88.0)	4.02	4091.5	.19
Knowledge of sun protection	77.3 (68.1-86.3)	84.1 (72.7-89.2)	8.80	3507	.01
Knowledge of sunscreens	66.7 (55.0-77.7)	72.2 (61.1-83.3)	8.25	3480	<.001
Myths about albinism	91.7 (75.0-95.8)	91.7 (75.0-100)	0.00	4328	.46

Conversely, after the intervention, the correlation of knowledge score with age or level of education was weak and not statistically significant. Moreover, the overall knowledge scores and various knowledge domains correlated significantly with the number of sessions attended. Table 3 shows the normality of all continuous variables using the Shapiro-Wilk test.

Table 3. Test for normality of variables.

Variables	Tests of normality (Shapiro-Wilk)	
	Statistic	*P* value
Age	0.980	<.01
Overall score	0.962	<.01
Knowledge of albinism	0.953	<.01
Knowledge of sun protection	0.956	<.01
Knowledge of sunscreens	0.969	<.01
Myths about albinism	0.885	<.01

Discussion

Principal Findings

The main finding of this study was a notable improvement in the overall knowledge of participants following the intervention. This study assessed the effectiveness of WhatsApp as a channel for providing health education to people with albinism. It is one of the most popular social media apps in Nigeria and can be used to share information, thereby strengthening the link between health care and IT.

The median age of the participants was 28 years. This is consistent with the age group that uses WhatsApp the most in Nigeria [14]. A notable finding was that 129 (62.6%) of the 206 participants never visited a dermatologist for skin checks. Possible explanations for this may be the paucity of dermatologists in Nigeria and the lack of awareness of the importance of skin checks in albinism. In our intervention, we emphasized the importance of skin checks and encouraged participants to visit dermatologists regularly for such checks.

Significant improvement was seen in the overall knowledge score after the intervention, specifically in the domains of sun protection and sunscreen use. This may be a result of using a combination of texts, images, videos, and audio messages during the intervention. The possibility of using multimedia through WhatsApp distinguishes this app from other digital health interventions that rely solely on text messaging. Mayer [18] stated that well-developed multimedia content can improve learning compared to using a single modality in the educational process [18]. Another reason for the remarkable improvement in overall knowledge after the intervention is the possibility of interaction between the group admins and the participants. This is also enhanced by the fact that WhatsApp group notifications can be received immediately after they are sent. The use of social media platforms, such as WhatsApp, has created room for connecting, sharing, and feedback, thereby enabling better communication [19]. Learning activities carried out through WhatsApp can be effective and impactful, and when used creatively, can serve as an alternative to the face-to-face approach [20].

Comparing the outcomes of this study is difficult due to the paucity of research that used WhatsApp as an intervention tool for health education among individuals with albinism. Pereira et al [15] conducted a pre-post intervention aimed at enhancing breast cancer knowledge among 35 women using WhatsApp, and they reported a statistically significant difference in the postintervention knowledge level. Likewise, Nayak et al [16] and Sartori et al [17] conducted interventional research using WhatsApp to improve knowledge of oral cancer and medication adherence among patients with hypertension and diabetes, respectively. These studies included control groups that received the traditional education method, yet they observed significant differences in the WhatsApp intervention group. Conversely, Al-ak'hali et al [21] indicated that WhatsApp is equally effective as traditional means and reported that WhatsApp had no added benefit compared to traditional education. This could be because, in their study design, all participants in the intervention and control groups had a baseline visit, when they were all educated in the clinic.

Age and educational level of people with albinism correlated positively with the overall knowledge level in the preintervention stage. After the intervention, there was no correlation observed, as the intervention benefitted people with albinism of all age groups and different educational statuses. This implies that the majority of the participants were brought to the same knowledge level irrespective of their age or educational status. This study also demonstrated that the number of sessions attended affected the knowledge levels, highlighting the importance of early involvement of the participants in such interventions to achieve maximum impact. Overall. These findings showed that WhatsApp is a valuable tool in digital health interventions that can be explored in the field of dermatology.

The increased knowledge among participants following our intervention may lead to behavior-based sun protection practices. This adjustment in behavior can be reinforced by periodic conversations and reminders regarding albinism and photoprotection in the WhatsApp group. Recent reviews of social media interventions for health behavior change have shown that social media can have a substantial effect on health behavior [22].

With regard to myths of albinism, we noted that there was no statistical significance in knowledge levels before and after the intervention. A possible explanation for this is that most of the participants had a good understanding of the myths about albinism before the intervention. This can be attributed to the educational status of the participants. The highest educational level of most of the participants was tertiary education, indicating that they were sufficiently informed to distinguish between myths and facts about albinism. This is supported by the finding that knowledge of myths was significantly correlated with the educational status of respondents.

Further work will be required to explore the long-term impact of WhatsApp-based health education on sun protection practices among people with albinism and to investigate the scalability and cost-effectiveness of such interventions in larger populations.

Limitations

As an interventional study, there is a possibility of social desirability bias [17]. This can be seen in health interventions for individuals with chronic diseases [23]. Participants would be likely to portray themselves or certain behaviors in a favorable light.

Data security is another limitation of WhatsApp. Although WhatsApp offers end-to-end encryption of messages that ensure the security of information, there is still the chance of data security breaches.

Additionally, the smaller number of postintervention participants compared to the number of participants before the intervention probably affected the overall power of the study.

Recommendations

Further studies could be conducted on the long-term effectiveness of WhatsApp in attitudes and behavior changes related to photoprotection in people with albinism. Additionally, research with a control group of people with albinism undergoing traditional methods of communication could allow for a comparison between WhatsApp and traditional means of health education. Further research on expanding the use of mobile apps in dermatology would improve health care services, especially in Nigeria.

Conclusions

WhatsApp has been useful in the health education of people with albinism, providing them with knowledge on albinism, sun protection practices, and myths about albinism. Interactive messaging and the use of multimedia were important in the success of this intervention program. Therefore, WhatsApp has proven to be a promising tool in teledermatology in Nigeria. There is a paucity of studies evaluating the effectiveness of using WhatsApp in the health education of people with albinism. However, we consider this study to be the first of its kind in demonstrating it as a suitable approach.

Acknowledgments

CCA conceived the study and contributed to the data collection, data analysis and interpretation, as well as drafting and editing the manuscript. OIE, CIO, and NAE designed the study, participated fully in the weekly health intervention, and revised the draft substantially. OKN made a substantial contribution to the conception and design of the study. DEM participated in the data analysis and interpretation as well as editing of the manuscript. All authors have read and agreed to the final manuscript and have equally contributed to its content.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Participant disclosure form.
[DOCX File , 29 KB - derma_v6i1e49950_app1.docx]

Multimedia Appendix 2

Screenshots of the intervention.
[PDF File (Adobe PDF File), 18724 KB - derma_v6i1e49950_app2.pdf]

Multimedia Appendix 3
Comparison of responses to questions before and after WhatsApp sessions.
[DOCX File , 39 KB - derma_v6i1e49950_app3.docx]

Multimedia Appendix 4
Correlation of age, highest level of education, and the number of sessions attended with knowledge levels.
[DOCX File , 26 KB - derma_v6i1e49950_app4.docx]

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Abbreviations

CHERRIES: Checklist for Reporting Results of Internet E-Surveys

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