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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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Case Report

Assessment of Quality and Utility of Patient-Taken Smartphone Photographs of Atopic Dermatitis: Clinical Survey Study

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Abstract

Background: Atopic dermatitis (AD) has a relapsing and remitting nature, and scheduled clinic visits only provide a snapshot of the skin condition at the moment.

Objective: This study aimed to investigate the quality of patient-taken smartphone photographs of AD skin lesions and characterize patients using smartphone photographs as a tool to assist the physician to show disease activity in between consultations.

Methods: Patients from 2 university outpatient clinics specialized in AD were surveyed. A questionnaire regarding digital readiness was completed, and a previously taken skin lesion photograph on the patients' own smartphone was evaluated.

Results: Between February 2024 and September 2024, a total of 100 questionnaires were completed, 60 (60%) by participants from the capital region of Denmark and 40 (40%) by participants from an urban area, including 62 (62%) men and 38 (38%) women. The mean age of the recruited patients was 33.9 (SD 19.9) years. A total of 78% (78/100) of the patients used a desktop computer, laptop, or tablet often or always, and 86% (86/100) corresponded with the health care system using technology (eg, via email to the general practitioner or contact with hospitals via apps). More than 50% (52/100, 52%) strongly agreed or agreed with the statement that they would prefer a remote online visit with, for example, upload of skin lesion photographs over a routine in-person office visit. Almost 3 out of 4 patients had a photograph of their AD skin lesion on their smartphone, most (38/71, 54%) with the sole intention of presenting it to a physician. The photographs were of good quality in 85% (60/71) of the cases, and most (61/71, 86%) of the smartphone photographs were assessed to be useful for diagnostic and clinical evaluation. Receiving topical monotherapy was significantly associated with increased risk of having taken a skin lesion smartphone photograph (P=.006).

Conclusions: Patients with AD followed up on in an outpatient clinic often took good-quality photographs of their skin lesions before consultations with the intention of presenting them to the physician.

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KEYWORDS

atopic dermatitis; photograph; telemedicine; teledermatology; outpatient clinic; personalized; follow-up

Introduction

Atopic dermatitis (AD) has a fluctuating nature, including unpredictable flares [1], which is why scheduled visits to an outpatient clinic only provide a momentary snapshot of the disease course. Patients' perception of the use of photographs of skin lesions in clinical settings to improve medical care is overall positive [2]. A qualitative study highlighted that patients often feel unheard when consulting their physicians in times of disease remission. It also demonstrated an unfulfilled desire to be able to show a flair either by writing down symptoms or photographing lesions during flairs. Patients also indicated that the ability to evaluate the skin in between consultations provides increased autonomy and ownership [3]. A study conducted in an urticaria outpatient clinic showed that patients often took photographs of their skin lesions with their own smartphones before their first consultation, providing the physician with an insight into their disease severity at times of flare [4]. It has also been confirmed that the use of smartphones to take photographs of skin lesions is growing rapidly, a trend that might reduce the need for referrals to face-to-face visits [5] and thereby mitigate the growing shortage of dermatologists [6]. Furthermore, the severity of AD can be reliably assessed using photographs taken using smartphones as there is a high agreement between assessments conducted in the clinic directly looking at the skin and assessments conducted based on photographs [7,8].

Due to the clearly visible morphology of AD and the growing use of photographs taken using smartphones for medical

documentation purposes, we aimed to investigate the quality of patient-taken photographs of AD skin lesions using smartphones. Second, we aimed to characterize the group of patients who take smartphone photographs as a tool to assist the physician's evaluation of disease activity in between consultations. This knowledge might help understand patient preferences and tailor an individualized plan for follow-up either face-to-face or remotely based on photographs, thereby reducing health care costs while increasing patient autonomy.

Methods

Overview

Patients were consecutively recruited from 2 university outpatient clinics specialized in AD; one clinic in the capital region of Copenhagen and one from the second-largest urban area in Denmark, Aarhus. From February 2024 to September 2024, patients with a consultation in one of the outpatient clinics were asked to complete a questionnaire and select a possible previously taken smartphone photograph of their own AD lesions for severity assessment and quality evaluation by the physician. For pediatric patients, the questionnaire was completed by the parents.

To measure the perception of the impact of AD on quality of life, the Skindex-Mini, a 3-item questionnaire assessing 3 domains (symptoms, emotions, and function) graded on a Likert scale from 0 to 6, was used [9]. The Skindex-Mini total score was used to stratify impact of skin conditions on patient's quality of life as follows: a score of 0 to 1 indicated no impact, a score of 2 to 5 indicated low impact, a score of 6 to 10 indicated moderate impact, a score of 11 to 14 indicated high impact, and a score of 15 to 18 indicated very high impact on quality of life. The questionnaire has also been validated in pediatric patients with AD [10]. Questions related to use of technology in general and for communication with health care professionals were also included [11].

On the basis of the selected photograph of an AD lesion taken by the patient on their smartphone, a questionnaire regarding the quality and utility of smartphone photographs of AD skin lesions was completed by the attending physician. The quality assessment was based on focus of the photograph, resolution, lighting, and blurriness [12,13]. The utility of smartphone photographs for diagnostic use was based on the overall assessment of the treating physician (ie, whether the treating physician felt confident when using the photograph to establish diagnosis and for clinical evaluation and severity assessment). The clinical signs from the Eczema Area and Severity Index (EASI) and Scoring Atopic Dermatitis (SCORAD), including erythema, edema or papulation, excoriation, lichenification, oozing or crusts, and dryness, were assessed for each photograph along with their intensity (0-3 for the EASI and 0-4 for SCORAD) [14,15].

Statistical Analysis

Chi-square and independent-sample 2-tailed *t* tests were used to characterize patients who took smartphone photographs of skin lesions, and 95% CIs were provided when applicable. The Fisher exact test was used when one or more of the cells had an expected frequency of 5 or less. Multiple logistic regression was used to identify the variables best related to the likelihood of patients having a smartphone photograph of a skin lesion, including age (<30 years vs >30 years), sex, capital or urban area residence, AD onset (<2 years of age vs >2 years of age), quality of life (Skindex-Mini total score), systemic treatment vs topical treatment, daily use of technology, digital contact with the health care system, and whether they preferred a remote visit. A *P* value of <.05 was considered statistically significant. All tests were carried out using the SPSS software (version 25.0; IBM Corp) [16].

Ethical Considerations

As this was a questionnaire study, there was no requirement of governmental approval or written informed consent according to Danish guidelines [17]. All study participants gave oral consent to be included in the study and have their data stored. All data used in this study were fully anonymized. No personally identifiable information was collected, stored, or processed, ensuring the privacy and confidentiality of all participants. Participants did not receive any financial or nonfinancial compensation for their participation in this study.

Results

Cohort Description

A total of 100 questionnaires were completed, 60 (60%) by participants from the capital region and 40 (40%) by participants from the urban area, including 62 (62%) men and 38 (38%) women. The median age of the recruited patients was 28.0 (IQR 20.25-48.75; mean age 33.9, SD 19.9) years. Most (n=53, 53%) had an AD onset before the age of 2 years, 25% (n=25) had an AD onset between the ages of 2 and 6 years, 10% (n=10) had an AD onset between the ages of 6 and 18 years, and the remaining 12% (n=12) had an AD onset after the age of 18 years. A total of 37% (n=37) of the patients were treated with topical corticosteroids in monotherapy at the time of consultation, 36% (n=36) were treated with dupilumab, 12% (n=12) were treated with methotrexate, 3% (n=3) were treated with tralokinumab, and 3% (n=3) were treated with baricitinib or abrocitinib. Most patients (n=64, 64%) estimated AD to have none or a small impact on quality of life, 19% (n=19) estimated AD to have a moderate impact, 10% (n=10) estimated AD to have a large impact, and 7% (n=7) estimated AD to have a very large impact based on the Skindex-Mini questionnaire (Table 1).

Table . Characteristics of the included patients from 2 atopic dermatitis outpatient clinics (N=100).

Characteristic	Values
Sex, n (%)	
Male	62 (62)
Female	38 (38)
Age (years), mean (SD)	33.9 (19.9)
Current treatment, n (%)	
Topical treatment[a] only	38 (38)
UVB	1 (1)
Traditional immunosuppressants[b]	16 (16)
Prednisolone	1 (1)
JAK[c] inhibitors	3 (3)
Biologics[d]	39 (39)
None	2 (2)
Skindex-Mini score (0-18), mean (SD)	
Symptoms	2.25 (1.88)
Emotions	1.51 (1.81)
Function	1.30 (1.77)
Total	5.02 (5.03)
Impact on quality of life, n (%)	
None	33 (33)
Small	31 (31)
Moderate	19 (19)
Large	10 (10)
Very large	7 (7)

[a]Topical corticosteroids and topical calcineurin inhibitors.

[b]Azathioprine, methotrexate, and mycophenolate mofetil.

[c]JAK: Janus kinase; inhibitors included abrocitinib and baricitinib.

[d]Dupilumab and tralokinumab.

Digital Readiness

In total, 78% (78/100) of the patients used a computer, laptop, or tablet often or always; 18% (18/100) used them seldom or once in a while; and 4% (4/100) never used them. A vast majority (86/100, 86%) corresponded with the health care system using technology (eg, via email to the general practitioner or contact with hospitals via apps). More than 50% (52/100, 52%) strongly agreed or agreed with the statement that they would prefer a remote online visit with, for example, upload of skin lesion photographs over a routine in-person office visit. Table 2 provides further details.

Table . Items related to attitudes toward digital solutions (N=100).

Digital readiness	Participants, n (%)
Daily use of a computer, laptop, or tablet	
Often or always	78 (78)
Seldom or once in a while	18 (18)
Never	4 (4)
Digital correspondence with the health care system	
Often or always	56 (56)
Seldom or once in a while	30 (30)
Never	14 (14)
Digital access to blood samples or medical records	
Often or always	53 (53)
Seldom or once in a while	34 (34)
Never	13 (13)
Search for information related to morbidity on the internet	
Often or always	42 (42)
Seldom or once in a while	35 (35)
Never	23 (23)
"I would like to replace a physical in-office visit with a remote visit."	
Strongly agree	19 (19)
Agree	33 (33)
Neutral	27 (27)
Disagree	12 (12)
Strongly disagree	9 (9)

Smartphone Photographs

Almost 3 out of 4 patients (71/100, 71%) had a photograph of their AD skin lesion on their smartphone. Of the remaining 29% (29/100) who did not have any photographs of their AD lesions on their smartphones, most (15/29, 52%) indicated that the reason was a well-controlled disease for a longer period without experiencing any flair or worsening of AD, only 3% (1/29) did not have a smartphone, 7% (2/29) used another smartphone to take photographs, and the remaining 38% (11/29) did not give a reason. The number of smartphone photographs of AD lesions taken in the previous year varied from 1 to 100, the mean number of photographs taken was 21.4 (SD 22.7), and the median number of photographs was 15 (IQR 5-25). Most of those who took photographs did so with the sole intention of presenting them to a physician (38/71, 54%), only 8% (6/71) took the photographs for their own use, and 38% (27/71) took the photographs both for their own use and for the physician. Most of the photographs were of upper limbs (26/71, 37%) or the head and neck (23/71, 32%). Of all evaluated photographs, 85% (60/71) were of good quality, 7% (5/71) were of acceptable quality, and 9% (6/71) were of bad quality based on lighting, resolution, clarity, and focus. In total, 89% (63/71) of the smartphone photographs had the skin lesion in focus, of which 92% (65/71) were sharp and 9% (6/71) were blurred. Most of the smartphone photographs (61/71, 86%) were assessed to be useful for diagnostic and clinical evaluation (Table 3).

Table . Smartphone photographs taken by the patients coming to consultation in outpatient clinics (n=71).

	Photographs, n (%)
Body region	
Head and neck	23 (32)
Chest and stomach	6 (8)
Back	11 (15)
Upper limb	26 (37)
Lower limb	4 (6)
Missing	1 (1)
Lesion in focus	
Agree	63 (89)
Disagree	8 (11)
Sharp photograph	
Agree	65 (92)
Disagree	6 (9)
Useful in diagnostic evaluation	
Agree	61 (86)
Disagree	10 (14)
Useful in severity assessment	
Agree	59 (83)
Disagree	12 (17)
Resolution	
Good	63 (89)
Acceptable	8 (11)
Bad	0 (0)
Lighting	
Good	61 (86)
Acceptable	4 (6)
Bad	6 (8)
Photo quality	
Good	60 (85)
Acceptable	5 (7)
Bad	6 (8)

For EASI items, induration (14/71, 20%) and lichenification (10/71, 14%) were often difficult to assess (Table 4), and for SCORAD items, lichenification (11/71, 16%) and dryness (13/71, 18%) proved the biggest challenge (Table 5).

Table . Severity assessment of atopic dermatitis lesion photographs based on Eczema Area and Severity Index (EASI) (n=71).

	EASI score, n (%)				
	None	Mild	Moderate	Severe	Difficult to assess
Erythema	1 (1)	20 (28)	24 (34)	22 (31)	4 (6)
Induration	16 (23)	13 (18)	21 (30)	7 (10)	14 (20)
Excoriation	27 (38)	16 (23)	13 (18)	9 (13)	6 (8)
Lichenification	26 (37)	20 (28)	7 (10)	8 (11)	10 (14)

Table . Severity assessment of atopic dermatitis lesion photographs based on Scoring Atopic Dermatitis (SCORAD) tool (n=71).

	SCORAD score, n (%)					
	None	Mild	Moderate	Severe	Very severe	Difficult to assess
Erythema	2 (3)	19 (27)	20 (28)	14 (20)	12 (17)	4 (6)
Edema	19 (27)	16 (23)	12 (17)	9 (13)	7 (10)	8 (11)
Oozing	41 (58)	15 (21)	6 (9)	2 (3)	1 (1)	6 (9)
Excoriation	31 (44)	12 (17)	12 (17)	8 (11)	2 (3)	6 (9)
Lichenification	28 (39)	12 (17)	7 (10)	10 (14)	3 (4)	11 (16)
Dryness	15 (21)	19 (27)	11 (16)	9 (13)	4 (6)	13 (18)

Characteristics of Patients Who Took Smartphone Photographs of Skin Lesions

We found a significant difference in mean age between patients who took photographs and those who did not of 16.3 years (95% CI 8.15-24.46; *P*<.001). The mean age of patients who took smartphone photographs was 29.2 (SD 18.9) years, and that of patients who did not take smartphone photographs was 45.5 (SD 17.8) years. Previous digital contact with the health care system was associated with an increased odds ratio (OR) of 7.19 (95% CI 1.31-39.51; *P*=.01) of taking a skin lesion smartphone photograph. Patients receiving topical monotherapy had a higher chance of taking a skin lesion photograph (OR 4.17, 95% CI 1.42-12.16; *P*=.006), and patients receiving systemic treatment had a lower risk of taking a skin lesion photograph (OR 0.20, 95% CI 0.07-0.59; *P*=.002; Table 6). In logistic regression analysis, use of topical treatment was a statistically significant predictor for the probability of taking a photograph of a skin lesion (OR 5.67, 95% CI 1.20-26.77; β=1.74; SE 0.79; *P*=.03).

Table . Comparison between patients who took at least 1 smartphone photograph of their skin lesions and those who did not.

Characteristic	Photograph (n=71), n (%)	No photograph (n=29), n (%)	OR[a] (95% CI)	*P* value
Sex			1.24 (0.50 - 3.05)	.64
Male	43 (61)	19 (66)		
Female	28 (39)	10 (34)		
Age (years)			0.18 (0.07-0.49)	<.001
<30	45 (63)	7 (24)		
>30	26 (37)	22 (76)		
Residence			2.03 (0.79-5.21)	.14
Capital region	40 (56)	21 (72)		
Urban area	31 (44)	8 (28)		
Age at disease onset (years)			1.08 (0.45-2.55)	.87
<2	38 (54)	15 (52)		
>2	33 (46)	14 (48)		
Topical treatment only			4.17 (1.42-12.16)	.006
Yes	33 (46)	5 (17)		
No	38 (54)	24 (83)		
Traditional immunosuppressants			0.88 (0.28-2.80)	.83
Yes	11 (15)	5 (17)		
No	60 (85)	24 (83)		
Systemic treatment[b]			0.20 (0.07-0.59)	.002
Yes	35 (49)	24 (83)		
No	36 (51)	5 (17)		
Biologics or JAK[c] inhibitors			0.25 (0.10-0.63)	.002
Yes	23 (32)	19 (66)		
No	48 (68)	10 (34)		
Preferred remote visit[d]			1.23 (0.42-3.66)	.71
Yes	37 (52)	15 (52)		
No	14 (20)	7 (24)		
Daily use of technology			8.07 (0.80-81.17)	.07
Yes	70 (99)	26 (90)		
No	1 (1)	3 (10)		
Digital contact with the health care system[e]			7.19 (1.31-39.51)	.01
Yes	69 (97)	24 (83)		
No	2 (3)	5 (17)		
Impact of disease on quality of life			0.64 (0.42-0.97)	.04
None	17 (24)	16 (55)		
Small	26 (37)	5 (17)		
Moderate	15 (21)	4 (14)		
Large	6 (8)	4 (14)		
Very large	7 (10)	0 (0)		

[a]OR: odds ratio.

[b]Systemic treatment included dupilumab, tralokinumab, baricitinib, abrocitinib, methotrexate, azathioprine, and mycophenolate mofetil.

[c]JAK: Janus kinase.

[d]Includes “strongly agree” or “agree” vs “strongly disagree” or “disagree.”

[e]Includes both digital correspondence with the health care system and digital access to blood samples or medical records.

Discussion

Hospital outpatients with AD had high digital readiness, with 78% (78/100) using a computer, laptop, or tablet often or always. Almost 3 out of 4 had taken a photograph of their AD skin lesion on their smartphone, mostly with the intention of presenting it to a physician. Furthermore, 85% (60/71) of the photographs were of good quality; however, induration, lichenification, and dryness were often difficult to assess. Receiving topical monotherapy was associated with a higher chance of taking a skin lesion photograph, supporting the demand for tailored monitoring depending on patients’ preferences and risk of flair. AD is very heterogeneous in terms of symptoms, skin manifestations, body area involved, extent, course, and comorbidities. Therefore, it is very unlikely that all patients with AD will respond equally well to treatments. Biomarkers will lead to better identification of patients who will benefit from immunomodulatory treatments, leading to more individualized management [18]. Traditionally, patients on immunosuppressive drugs have often planned consultations in the clinic at certain intervals. Due to better disease control with targeted therapies, these patients only need to be followed up on, for example, once every year; however, due to the expenses related to the treatments, close monitoring will be beneficial for timely drug dose tapering to reduce unnecessary health care expenditures. On the other hand, many patients with mild to moderate disease will still be on traditional immunosuppressive drugs, not meeting the criteria for expensive biological treatments. These patients will often experience flairs in between scheduled consultations. Our study showed that more than half of patients with AD followed up on in an outpatient clinic preferred a remote or online visit instead of an in-person visit at the clinic. Furthermore, there is increasing evidence that patients with skin diseases often take good-quality photographs of their skin lesions with their smartphones [4] and that photographs have high validity and reliability [7,8,19]. This is supported by our findings. Tailored monitoring considering the age, digital readiness, type of treatment, and preferences of the patients may lead to a reduction in health care costs and help pivot consultations toward focused care based on individual needs.

Smartphones are easily accessible and extensively used to take photographs. Many photographs are taken on a daily basis, and more than 90% of all photographs are taken in 2020 using smartphones [20]. Many people find it natural to take photographs for memory or documentation [20]; hence, taking photographs of skin lesions is widely practiced [4]. There is a demand for integrating smartphone photographs into clinical practice to assess disease fluctuation in between physical examinations. Educating patients in how to take a good clinical photograph of AD skin lesions may improve the quality and utility of the photographs in a clinical setting. Information regarding distance between the camera and the skin lesion (approximately 20 cm), using a uniform background, and taking the photograph in good natural lighting is especially important. Furthermore, using photographs in a clinical setting through a remote visit to replace a physical consultation requires thorough patient education in the assessment of body surface area and selection of representative lesions in each anatomical area included in the EASI or SCORAD.

Even though the task of evaluating the quality of photographs was clearly defined to create consistency in evaluations, this study was limited by a lack of multiple raters to evaluate the same photograph due to logistical challenges in a clinical survey.

In conclusion, patients with AD followed up on in an outpatient clinic often took high-quality photographs of their skin lesions before consultations with the intention of presenting them to the physicians. More evidence for tailored or personalized monitoring through remote visits using photographs of skin lesions and its effect on health care costs is warranted.

Conflicts of Interest

CV has received grants from Pfizer, LEO Pharma, Almirall, and Sanofi and has been a speaker or served on advisory boards for Pfizer, Almirall, LEO Pharma, AbbVie, Sanofi, Galderma, Pierre Fabre, AstraZeneca, and Novartis. All other authors declare no other conflicts of interest.

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Abbreviations

AD: atopic dermatitis
EASI: Eczema Area and Severity Index
OR: odds ratio
SCORAD: Scoring Atopic Dermatitis

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Association of Skin Cancer With Clinical Depression and Poor Mental Health Days: Cross-Sectional Analysis

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Abstract

Background: Mental health is becoming increasingly recognized as an important part of overall health, especially for patients with cancer. However, the relationship between nonmelanoma skin cancer and mental health has not been widely studied.

Objective: The aim of this study was to examine the association between nonmelanoma skin cancer diagnosis and 2 key mental health outcomes (ie, clinical depression and the number of poor mental health days).

Methods: This study used the 2023 Behavioral Risk Factor Surveillance System, a nationally representative survey of adults in the United States, which included 312,317 participants. Nonmelanoma skin cancer diagnosis, depression, and self-reported mental health days were analyzed. Logistic regression was used to evaluate the association between nonmelanoma skin cancer and depression, whereas Poisson regression was used to model the number of poor mental health days, adjusting for age, sex, race and ethnicity, education, BMI, income, and major comorbid conditions (other cancers, heart disease, lung disease, and kidney disease).

Results: Individuals with nonmelanoma skin cancer (5086/26,552, 19.15%) reported a lower overall rate of depression compared to those without nonmelanoma skin cancer (61,438/285,765, 21.50%; *P*<.001) but reported more poor mental health days on average (4.54, SD 8.37 d vs 3.20, SD 7.37 d; *P*<.001). After adjustment, nonmelanoma skin cancer diagnosis was not significantly associated with depression (adjusted odds ratio 1.01, 95% CI 0.98 - 1.05) and was associated with a slightly lower number of poor mental health days (adjusted rate ratio 0.94, 95% CI 0.91 - 0.97).

Conclusions: Adults with nonmelanoma skin cancer experienced a meaningful mental health burden, and unadjusted analyses suggested greater day-to-day distress than among adults without nonmelanoma skin cancer. However, these differences were reduced and no longer significant for depression after adjusting for sociodemographic factors and comorbid chronic illnesses. These findings support the need for mental health screenings and support services in dermatologic and oncologic care.

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KEYWORDS

mental health; nonmelanoma skin cancer; depression; sociodemographic variables; analysis

Introduction

Background

In recent years, public health conversations have continued to emphasize the importance of mental health. Mental health is increasingly viewed not as a stand-alone issue, but as a factor that deeply interacts with physical illness, such as cancer [1].

While nonmelanoma skin cancer has obvious physical consequences, it poses serious complications regarding mental health. This aspect has not received sufficient attention in the health care field [2]. Dermatologists and oncologists are facing a dramatic rise in cases of nonmelanoma skin cancer, with melanoma rates doubling over the past two decades [3]. Nonmelanoma skin cancer is one of the most diagnosed malignancies in the world today, with rates for both melanoma and nonmelanoma types on the rise [3]. The relationship between mental state and nonmelanoma skin cancer is a complex feat. While the stress of diagnosis and treatment can create or worsen mental health conditions [4,5], existing mental health conditions can also increase the chances of developing nonmelanoma skin cancer through behavioral, immunological, and systemic mechanisms [6]. Recent evidence shows that approximately 30% of patients with melanoma experience anxiety, and nearly 20% experience depression. The highest risk has been observed among women and young adults [7]. Other studies have confirmed similar trends, showing that psychological distress and the fear of recurrence remain substantial even in patients with early-stage melanoma.

Research conducted recently has started to uncover the complex relationships between mental health and nonmelanoma skin cancer. A 2016 cross-sectional study using Behavioral Risk Factor Surveillance System data found that individuals who had frequent poor mental health days had a significantly higher chance of being diagnosed with the disease of nonmelanoma skin cancer [8].

These data were confirmed even after using the multivariate logistic regression analyses. These analyses suggest a possible link between poor mental health and keratinocyte carcinoma. This could be possible through factors such as dysregulated immune responses [9]. Other studies have shown similar results, mostly highlighting a high dose of psychological distress among patients with cancer [5,8]. Additionally, approximately one-third of patients with melanoma skin cancer require professional mental health care but are not receiving that treatment [1,2].

Further literature reviews on neuroendocrine-immune interactions support the biological plausibility of this connection. Chronic mental distress is a well-known contributor to the disruption of skin immunity, wound healing, and active inflammatory mediators, which can all contribute to the progression of cancer [6]. Additionally, factors including hostility and depression have been connected to melanoma and its treatment outcomes [4]. There is an extremely minimal amount of information regarding the demographic or socioeconomic factors that shape the outcomes of mental health across nonmelanoma skin cancer subtypes [3,10].

This study aimed to address these gaps in knowledge by analyzing the association between mental health disorders and the rate of nonmelanoma skin cancer diagnosis by using the information provided by the Behavioral Risk Factor Surveillance System (BRFSS). Focusing on nonmelanoma skin cancers, assessing the link between nonmelanoma skin cancer and mental health status by sociodemographic factors, such as age, sex, race, income, BMI, and education, will provide critical insights into how mental health influences the risk and experience of nonmelanoma skin cancer.

Literature Review

Recent studies document consistent associations between multiple indicators of psychological distress and nonmelanoma skin cancer. A proportional meta-analysis of patients with melanoma reported prevalence estimates of 30% for anxiety and 20% for depression, with higher odds observed among women, younger adults, and individuals with lower education levels [7]. Similar findings have been reported in earlier clinical and observational studies, showing elevated levels of psychological symptoms across different stages of melanoma, including treatment and posttreatment phases [5,11].

Beyond symptom prevalence, multiple studies have examined behavioral and biological pathways linking mental health to nonmelanoma skin cancer. Young adults with mental health problems demonstrate higher rates of cancer-related risk behaviors, such as smoking, alcohol use, sleep disturbances, and inactivity, which may contribute to disease development or worse outcomes [10]. Experimental research has also shown that chronic psychological stress alters neuroendocrine and immune signaling, increasing inflammatory activity and harming skin repair processes [6]. Additional studies have reported relationships between melanoma severity and personality traits, such as hostility and depressive tendencies.

More recent research has shifted attention to survivorship and early-stage disease. Patients diagnosed with melanoma have reported reduced emotional well-being. They have also stated persistent uncertainty despite a favorable clinical prognosis. This suggests that psychological effects extend further than cancer itself. Moreover, fear of recurrence has been identified as a primary contributor to ongoing mental distress following the completion of treatment [12]. These findings indicate that mental health challenges in nonmelanoma skin cancer populations can include forms of distress that may not be clinically diagnosed.

Population-based research has identified variation in mental health outcomes among patients with nonmelanoma skin cancer across demographic and socioeconomic subgroups. Studies have shown that mental health service use remains limited, with unmet psychological needs concentrated among older adults and lower-income populations [1,2]. Global assessments have revealed a lower quality of life in regions with lower access to supportive care resources [3].

Globally, the burden of skin disease is high in many regions, especially Asia, and is linked to socioeconomic status and inflammatory conditions [3]. Tools such as the Skin Cancer Index have been developed to measure the quality of life in patients with nonmelanoma skin cancer [13].

Methods

Participants

This study used data from the BRFSS, a nationally representative survey conducted by the Centers for Disease Control and Prevention [9]. The data used were from the year 2023. The BRFSS surveys US adults aged 18 years or older, collecting data on health conditions, behaviors, and preventive health practices [9]. This dataset included responses to questions related to nonmelanoma skin cancer, mental health, and sociodemographic characteristics. Participants with missing, refused, or “don’t know” responses were excluded from the analyses to ensure the high quality and reliability of the study.

Exposure

The independent variable was a self-reported diagnosis of nonmelanoma skin cancer. These individuals did not have to have a current diagnosis; the diagnosis could be from any time in the past. Respondents were asked whether a health professional had ever told them they had skin cancer, including melanoma and nonmelanoma types. Individuals who answered “yes” were categorized as having a nonmelanoma skin cancer diagnosis. Those who answered “no” were the comparison group. Those with missing or ambiguous responses were excluded from the analysis to maintain the integrity of the data.

Outcomes

The 2 primary mental health–related outcomes that were examined were depression and the number of poor mental health

days an individual had. Depression was defined as being diagnosed with a depressive disorder by a health care professional [9,10]. Poor mental health days were based on the number of days during the past 30 days that an individual reported that their mental health was "not good," including stress, depression, and other emotional issues [1,3]. Respondents with invalid responses were excluded from the analysis.

Covariates

The sociodemographic variables that were included in the analysis were age (18 - 64 and ≥65 years), sex (male or female), race or ethnicity (White only, Black only, Asian only, American Indian or Alaskan Native only, Native Hawaiian or other Pacific Islander only, multiracial, and other), education (did not graduate high school, graduated high school, attended college or technical school, and graduated from college or technical school), and BMI (underweight, normal weight, overweight, and obese). Additional health-related covariates included self-reported diagnoses of other (non–skin) cancer, heart disease, chronic lung disease, and kidney disease. These covariates were specifically selected based on the evidence linking them to mental health and cancer-related outcomes [3,10].

Statistical Analysis

Descriptive statistics were first used to summarize the distribution of depression status and the number of poor mental health days by nonmelanoma skin cancer diagnosis and sociodemographic variables, including age, sex, race and ethnicity, education level, and BMI. All statistical models were run on the entire BRFSS sample, and individuals without a history of nonmelanoma skin cancer served as the reference group. This allowed a direct comparison between those with and those without nonmelanoma skin cancer. Categorical variables were summarized using frequencies and percentages, while continuous variables were described using means and SDs. Group differences in categorical variables were assessed using Pearson χ^2 tests, and differences in continuous outcomes were interpreted using independent samples *t* tests. These tests described unadjusted differences between adults with and without a history of nonmelanoma skin cancer.

To examine the association between nonmelanoma skin cancer diagnosis and depression, a multivariable logistic regression model was used [9]. Depression was treated as a yes or no outcome, and a nonmelanoma skin cancer diagnosis (yes or no) was the main comparison of interest. All statistical models were run on the full BRFSS sample, and individuals without a history of nonmelanoma skin cancer served as the reference group in all analyses. This approach allowed direct comparison of depression prevalence and poor mental health days between respondents with and without nonmelanoma skin cancer, instead of limited analyses to only the skin cancer subgroup. Additionally, adjusted odds ratios (aORs) and corresponding 95% CIs were reported.

For the continuous outcome of mental health days, a multivariable Poisson regression model with standard errors to account for potential overdispersion was used. The results were expressed as adjusted rate ratios (aRRs) with 95% CIs, which allowed for the calculation of the relative increase or decrease in the expected number of poor mental health days among individuals with nonmelanoma skin cancer compared to those without, after accounting for sociodemographic factors. Both regression models adjusted for age, sex, race and ethnicity, education level, BMI, household income, and comorbid conditions (other cancer, heart disease, lung disease, and kidney disease). These sociodemographic and health-related variables are independently associated with both mental health outcomes and cancer risk in prior studies. Logistic regression was used for the binary depression outcome, whereas a multivariable Poisson regression model was used for the count-based outcome of poor mental health days. Poisson regression was selected because the outcome represents a count of days within a fixed 30-day period and was not normally distributed, making linear regression inappropriate. Standard errors were adjusted to account for overdispersion. The distribution of days with poor mental health was examined. It was discovered that, although the data showed variability, it did not exhibit sufficient overdispersion to warrant switching to an alternative model. Therefore, the Poisson model was the best option.

All statistical tests were 2 sided. Analyses were conducted using JASP, ensuring appropriate complex survey weighting to reflect the nationally representative design of the BRFSS dataset [9].

Ethical Considerations

This study involved secondary analysis of publicly available, deidentified data from the BRFSS, administered by the US Centers for Disease Control and Prevention. As the dataset contains no identifiable private information, this study did not constitute human subjects research and was therefore exempt from institutional review board review in accordance with US federal regulations. The BRFSS protocol is reviewed and approved annually by the US Centers for Disease Control and Prevention Institutional Review Board, and informed consent is obtained from all participants at the time of data collection.

Results

Overview

Among 433,323 participants in the 2023 BRFSS questionnaire, 312,317 (72.07%) had complete demographic and disease information and were included in the analysis (Table 1). Among the analytical cohort, 154,230 (49.38%) were men, and 158,087 (50.62%) were women. Additionally, 253,634 (81.21%) identified as White participants only. The remaining racial and ethnic distribution included 26,936 (8.62%) Asian only, 6551 (2.10%) Black only, 8865 (2.84%) American Indian or Alaska Native only, 2041 (0.65%) Native Hawaiian or Pacific Islander, 5742 (1.84%) multiracial, and 8548 (2.74%) identifying as other race and ethnicity.

Table . Characteristics of the study cohort [8].

Characteristics	Values
Skin cancer diagnosis, n (%)	
No	285,765 (91.50)
Yes	26,552 (8.50)
Depression, n (%)	
No	245,793 (78.70)
Yes	66,524 (21.30)
Mental health days, mean (SD)	4.42 (8.29)
Race and ethnicity, n (%)	
White only	253,634 (81.21)
Asian only	26,936 (8.62)
Black only	6551 (2.10)
American Indian or Alaskan Native only	8865 (2.84)
Native Hawaiian or other Pacific Islander only	2041 (0.65)
Multiracial	5742 (1.84)
Other race only	8548 (2.74)
Sex, n (%)	
Male	154,230 (49.38)
Female	158,087 (50.62)
Age (y), n (%)	
18-64	198,394 (63.52)
≥65	113,923 (36.48)
BMI, n (%)	
Underweight	4802 (1.54)
Normal weight	89,431 (28.63)
Overweight	111,680 (35.76)
Obese	106,404 (34.07)
Education, n (%)	
Did not graduate high school	14,184 (4.54)
Graduated high school	73,285 (23.46)
Attended college or technical school	83,761 (26.82)
Graduated from college or technical	141,087 (45.17)
Other cancer, n (%)	
No	275,645 (88.26)
Yes	36,672 (11.74)
Heart disease, n (%)	
No	277,856 (88.97)
Yes	34,461 (11.03)
Lung disease, n (%)	
No	251,263 (80.45)
Yes	61,054 (19.55)
Kidney disease, n (%)	
No	297,584 (95.28)

Characteristics	Values
Yes	14,733 (4.72)

Most of the 312,317 respondents were aged between 18 and 64 years (n=198,394, 63.52%), with 113,923 (36.48%) aged 65 years or older. BMI classifications showed that 4802 (1.54%) were underweight, 89,431 (28.63%) had a normal BMI, 111,680 (35.76%) were overweight, and 106,404 (34.07%) were obese. Educational attainment also varied, with 14,184 (4.54%) not graduating from high school, 73,285 (23.46%) graduating from high school, 83,761 (26.82%) attending some college or technical school, and 141,087 (45.17%) graduating from a college or technical program.

Most respondents did not report a nonmelanoma skin cancer diagnosis, with 285,765 (91.50%) of 312,317 indicating no history of nonmelanoma skin cancer and 26,552 (8.50%) reporting a diagnosis. Additionally, 245,793 (78.70%) participants did not report depression, whereas 66,524 (21.30%) reported having been diagnosed with depression by a health care professional. The high average number of mental health days was consistent with high fluctuations in mental health experiences across many individuals.

Comorbid health conditions were also reported. A total of 36,672 (11.74%) participants reported another form of cancer, 34,461 (11.03%) reported heart disease, 61,054 (19.55%) reported lung disease, and 14,733 (4.72%) reported kidney disease.

The average number of poor mental health days in the past 30 days was 4.42 (SD 8.29). This was consistent with substantial variation in mental health experiences across the population.

Depression

Of the entire sample, 88,524 (21.31%) of 312,317 participants reported experiencing depression. Of those without a nonmelanoma skin cancer diagnosis, 61,428 (21.50%) of 285,765 reported depression. However, of those with a nonmelanoma skin cancer diagnosis, 5086 (19.15%) of 26,552 individuals reported depression. After the analysis was adjusted for the included covariates, nonmelanoma skin cancer diagnosis was not significantly associated with depression (aOR 1.01, 95% CI 0.98 - 1.05; P<.001; Table 2).

Table . Association between nonmelanoma skin cancer and depression [8].

Characteristics	Depression			
	No, n (%)	Yes, n (%)	*P* value	aOR[a] (95% CI)
Nonmelanoma skin cancer diagnosis			<.001	
No	224,327 (78.5)	61,438 (21.4)	<.001	Ref[b]
Yes	21,466 (80.8)	5086 (19.1)	<.001	1.01 (0.98 - 1.05)
Race and ethnicity			<.001	
White only	1,97,650 (77.9)	55,984 (22)	<.001	Ref
Asian only	22,476 (83.4)	4460 (16.5)	<.001	0.50 (0.48 - 0.52)
Black only	5135 (78.3)	1416 (21.6)	<.001	0.70 (0.66 - 0.75)
American Indian or Alaskan Native only	7863 (88.6%)	1002 (11.3%)	<.001	0.47 (0.440.50)
Native Hawaiian or other Pacific Islander only	1721 (84.3)	320 (15.6)	<.001	0.51 (0.45 - 0.58)
Multiracial	4778 (83.2)	964 (16.7)	<.001	0.60 (0.56 - 0.64)
Other race only	6170 (72.1)	2378 (27.8)	<.001	1.08 (1.04 - 1.15)
Sex			<.001	
Male	130,827 (84.8)	23,403 (15.1)	<.001	Ref
Female	114,966 (72.7)	43,121 (27.2)	<.001	1.98 (1.94 - 2.02)
Age (years)			<.001	
18-64	150,115 (75.6)	48,279 (24.3)	<.001	Ref
≥65	95,678 (83.9)	18,245 (16)	<.001	0.44 (0.440.45)
BMI			<.001	
Underweight	3581 (74.5)	1221 (25.4)	<.001	Ref
Normal weight	72,440 (81)	16,991 (18.9)	<.001	0.83 (0.77 - 0.89)
Overweight	91,376 (81.8)	20,304 (18.1)	<.001	0.87 (0.81 - 0.94)
Obese	78,396 (73.6)	28,008 (26.3)	<.001	1.18 (1.10 - 1.27)
Education			<.001	
Did not graduate high school	10,816 (76.2)	3368 (23.7)	<.001	Ref
Graduated high school	58,033 (79.1)	15,252 (20.8)	.27	0.98 (0.94 - 1.02)
Attended college or technical school	63,782 (76.1)	19,979 (23.8)	<.001	1.02 (0.98 - 1.07)
Graduated from college or technical	113,162 (80.2)	27,925 (19.7)	<.001	0.91 (0.87 - 0.95)
Other cancer			<.001	1.12 (1.08 - 1.15)
No	217,198 (78.7)	58,447 (21.2)	<.001	Ref
Yes	28,595 (77.9)	8077 (22)	<.001	1.12 (1.08 - 1.15)
Heart disease			<.001	
No	220,365 (79.3)	57,491 (20.6)	<.001	Ref
Yes	25,428 (73.7)	9033 (26.2)	<.001	1.41 (1.37 - 1.45)
Lung disease			<.001	
No	206,137 (82)	45,126 (17.9)	<.001	Ref
Yes	39,656 (64.9)	21,398 (35)	<.001	2.10 (2.05 - 2.14)
Kidney disease			<.001	

Characteristics	Depression			
	No, n (%)	Yes, n (%)	*P* value	aOR[a] (95% CI)
No	235,503 (79.1)	62,081 (20.8)	<.001	Ref
Yes	10,290 (69.8)	4443 (30.1)	<.001	1.47 (1.41 - 1.53)

[a]aOR: adjusted odds ratio.

[b]Ref: reference.

When analyzing all racial and ethnic groups, there were many considerable differences in the prevalence of depression. White respondents were used as the reference group. Using the reference group, Asian (aOR 0.50, 95% CI 0.48 - 0.52), Black (aOR 0.70, 95% CI 0.66 - 0.75), American Indian or Alaska Native (aOR 0.47, 95% CI 0.44 - 0.50), Native Hawaiian or other Pacific Islander (aOR 0.51, 95% CI 0.45 - 0.58), and multiracial respondents (aOR 0.60, 95% CI 0.56 - 0.64) all had lower adjusted odds of depression. Participants in the "other" category had slightly higher odds of depression compared to White respondents (aOR 1.08, 95% CI 1.04 - 1.15).

Women (43,121/158,087, 27.28%) reported significantly higher rates of depression compared to men (23,403/154,230, 15.19%). After adjustment, women had almost double the odds of depression when compared to men (aOR 1.98, 95% CI 1.94 - 2.02). Participants (18,245/113,923, 16.0%) aged 65 years or older had significantly lower rates of depression compared to adults (48,279/198,394, 24.3%) aged 18 to 64 years. BMI also played a substantial role. With underweight individuals as the reference group, obese individuals experienced higher odds of depression (aOR 1.18, 95% CI 1.10 - 1.27), while those who were underweight or of normal weight had lower odds compared to those who were considered overweight or obese.

After adjusting for covariates, high school graduates had similar odds of depression to the reference group (aOR 0.98, 95% CI 0.94 - 1.02). Participants who had reached the college level of education had slightly different odds (aOR 1.02, 95% CI 0.98 - 1.07), and college graduates had lower odds (aOR 0.91, 95% CI 0.87 - 0.95).

Poor Mental Health Days

Respondents with a history of nonmelanoma skin cancer reported a higher average number of poor mental health days (mean 4.54, SD 8.37) compared to those without a nonmelanoma skin cancer diagnosis (mean 3.20, SD 7.37). However, after adjustment, individuals with nonmelanoma skin cancer experienced a slight decrease in poor mental health days compared to those without (aRR 0.94, 95% CI 0.91 - 0.97; Table 3).

Table . Association between nonmelanoma skin cancer and poor mental health days [8].

Characteristics	Mental health days		
	Mean (SD)	*P* value	aRR[a] (95% CI)
Skin cancer diagnosis		<.001	
No	3.19 (7.36)	<.001	Ref[b]
Yes	4.54 (8.36)	<.001	0.94 (0.91 - 0.97)
Race and ethnicity		<.001	
White only	4.30 (8.17)	<.001	Ref
Asian only	4.80 (8.65)	<.001	0.93 (0.90 - 0.95)
Black only	5.86 (9.52)	<.001	1.07 (1.01 - 1.13)
American Indian or Alaskan Native only	3.36 (6.85)	<.001	0.82 (0.78 - 0.86)
Native Hawaiian or other Pacific Islander only	5.42 (9.34)	<.001	1.11 (1.00 - 1.24)
Multiracial	4.65 (8.70)	<.001	0.93 (0.88 - 1.00)
Other race only	6.45 (9.74)	<.001	1.25 (1.19 - 1.32)
Sex		<.001	
Male	3.64 (7.71)	<.001	Ref
Female	5.18 (8.74)	<.001	1.36 (1.34 - 1.39)
Age (y)		<.001	
18-64	5.43 (8.85)	<.001	Ref
≥65	2.66 (6.85)	<.001	0.40 (0.40 - 0.41)
BMI		<.001	
Underweight	6.37 (9.81)	<.001	Ref
Normal weight	4.18 (7.95)	<.001	0.76 (0.71 - 0.82)
Overweight	3.78 (7.70)	<.001	0.71 (0.67 - 0.76)
Obese	5.20 (8.98)	<.001	0.83 (0.78 - 0.89)
Education		<.001	
Did not graduate high school	6.13 (10.21)	<.001	Ref
Graduated high school	5.01 (9.06)	<.001	1.01 (1.01 - 1.01)
Attended college or technical school	5.01 (8.84)	<.001	1.03 (1.03 - 1.03)
Graduated from college or technical	3.59 (7.15)	<.001	0.88 (0.88 - 0.88)
Other cancer diagnosis		<.001	
No	4.47 (8.28)	<.001	Ref
Yes	4.09 (8.35)	<.001	1.12 (1.08 - 1.14)
Heart disease		<.001	
No	4.31 (8.11)	<.001	Ref
Yes	5.30 (9.55)	<.001	1.33 (1.30 - 1.37)
Lung disease		<.001	
No	3.87 (7.73)	<.001	Ref
Yes	6.67 (9.95)	<.001	1.50 (1.47 - 1.53)
Kidney disease		<.001	
No	4.36 (8.21)	<.001	Ref

Characteristics	Mental health days		
	Mean (SD)	*P* value	aRR[a] (95% CI)
Yes	5.60 (9.63)	<.001	1.28 (1.23 - 1.33)

[a]aOR: adjusted odds ratio.

[b]Ref: reference.

Significant differences in mental health days were observed by race and ethnicity. Black individuals reported the highest average (5.85 d). This group had significantly increased rates of mental health issues compared to White individuals (aRR 1.07, 95% CI 1.01 - 1.13). In contrast, American Indian or Alaska Native participants (aRR 0.82, 95% CI 0.78 - 0.86), multiracial individuals (aRR 0.93, 95% CI 0.88 - 1.00), and Asian respondents (aRR 0.93, 95% CI 0.90 - 0.95) reported fewer mental health days compared to the White reference group.

Women had significantly more poor mental health days (mean 5.18, SD 8.75) compared to men (mean 3.65, SD 7.72). After adjustment, women had substantially higher rates of mental health distress (aRR 1.36, 95% CI 1.34 - 1.39). Respondents aged 65 years and older reported fewer mental health days than those in lower age groups (aRR 0.40, 95% CI 0.40 - 0.41).

BMI was strongly associated with mental health outcomes. Underweight individuals experienced the highest number of poor mental health days (mean 6.40, SD 9.85) and served as the reference group. Compared to them, respondents of normal weight (aRR 0.76, 95% CI 0.71 - 0.82), overweight individuals (aRR 0.71, 95% CI 0.67 - 0.76), and those with obesity (aRR 0.83, 95% CI 0.78 - 0.89) all had significantly lower rates of poor mental health days.

Individuals who did not graduate high school reported the highest average number of poor mental health days (6.13 d), while college graduates reported the fewest number (3.60 d). After adjustment, graduating from college or technical school was associated with significantly fewer mental health days (aRR 0.88, 95% CI 0.88 - 0.88) compared to individuals with less education.

Several comorbid health conditions were also associated with increased mental distress. Individuals with another cancer diagnosis had more poor mental health days (mean 5.01, SD 7.56) and higher adjusted rates compared to those without other cancers (aRR 1.12, 95% CI 1.08 - 1.14). Lung disease was associated with the strongest increase in mental health burden (mean 6.77, SD 7.81; aRR 1.50, 95% CI 1.47 - 1.53). Respondents with kidney disease (aRR 1.28, 95% CI 1.23 - 1.33) and heart disease (aRR 1.33, 95% CI 1.30 - 1.37) also reported significantly higher adjusted rates of poor mental health days compared to their respective reference groups.

Discussion

Principal Findings

In this nationally representative sample, study findings reveal a subtle relationship between nonmelanoma skin cancer and mental health: while individuals with a history of nonmelanoma skin cancer were slightly less likely to report a formal diagnosis of depression in unadjusted comparisons, nonmelanoma skin cancer was not significantly associated with depression after adjusting for demographics, other cancers, and chronic diseases. However, individuals with nonmelanoma skin cancer reported a higher number of poor mental health days before adjustment but slightly fewer poor mental health days after adjustment. These findings suggest that the differences in mental health burden are largely explained by sociodemographic and comorbid factors instead of the nonmelanoma skin cancer itself.

Prior research has suggested that the association between nonmelanoma skin cancer and mental health may operate in both biological and psychological directions. Chronic psychological stress has been shown to alter neuroendocrine-immune pathways, increasing inflammatory activity, impairing wound repair, and weakening immune surveillance, which may elevate susceptibility to certain nonmelanoma skin cancers [6]. However, a nonmelanoma skin cancer diagnosis may contribute to psychological distress through concerns about recurrence, uncertainty during long-term surveillance, scarring, and changes in visible appearance. These have all been documented as drivers of anxiety and depressive symptoms in melanoma and nonmelanoma patient populations [12,13].

A cancer diagnosis itself is often associated with increased stress. Prior research has shown that uncertainty about outcomes and concerns about physical appearance can elevate psychological stress, particularly in patients with visible scars [5,11]. Although stress was not directly measured in this study, the higher number of poor mental health days reported by individuals with nonmelanoma skin cancer may reflect this psychological impact. These findings support the notion that cancer-related stress can appear in daily tasks, even when it does not meet clinical criteria for depression [2,5].

Interestingly, in adjusted models, individuals with a history of nonmelanoma skin cancer reported fewer poor mental health days compared with those without nonmelanoma skin cancer, while no association was observed with depression. Several potential mechanisms may help explain this counterintuitive pattern. Nonmelanoma skin cancer is typically detected early, treated effectively, and associated with excellent long-term outcomes, which may mitigate sustained psychological distress. Successful removal of visible lesions can also create a sense of resolution or restored control, potentially improving daily emotional well-being. In addition, patients with nonmelanoma skin cancer may often engage in regular dermatologic care, providing frequent health care touchpoints that may reduce uncertainty, reinforce preventive health behaviors, and reflect a population with generally higher health literacy or

wellness-oriented behaviors, factors that are linked to more favorable mental health profiles.

The sociodemographic differences observed in this study are consistent with broader public health literature, showing that mental health outcomes are shaped by structural, cultural, and economic factors. Higher rates of poor mental health days among women and younger adults may reflect increased stress, body image concerns, or work-related pressures. Racial variation may be influenced by differences in health care access. Educational and income-related disparities may also reflect gaps in early detection resources. These findings underscore the importance of tailoring mental health support within dermatologic and oncologic care to the needs of various groups rather than applying a uniform approach.

The nature of being diagnosed with nonmelanoma skin cancer itself may contribute significantly to this distress. Patients often experience fear of imperfections due to visible scarring from surgery, concerns about cancer recurrence, or anxiety over potential mortality, especially with melanoma [5,11]. The continuation of dermatological watch and uncertainty with treatments can further elevate emotional strain for individuals. This specifically takes place when the cancer affects visible areas, such as the face or neck [2]. These stressors may not meet the clinical definition of depression but can still influence day-to-day mental well-being [5].

These results align with previous studies that highlight psychological distress among patients with nonmelanoma skin cancer. However, some research has found higher rates of depression, suggesting variability based on sample demographics or methods of measurement [5,11]. This study adds to the conversation by emphasizing subjective mental distress, which may not always manifest as a clinical diagnosis, while also showing that much of the observed association may be explained by comorbid illness and sociodemographic factors.

We also observed key sociodemographic differences. Women, younger adults, individuals with higher BMI, and those with lower levels of education reported a higher number of poor mental health days and higher levels of depression. These outcomes are consistent with a large amount of public health literature and suggest that mental health improvements should be tailored to the vulnerabilities of different subgroups [3,10].

Following these results, a consistent routine of mental health screenings for those diagnosed with nonmelanoma skin cancer is recommended to help relieve mental distress. This may include screening tools such as the Patient Health Questionnaire-9 during dermatology or oncology visits. This incorporates automatic referral pathways to licensed mental health providers with outstanding scores. Integrated care models may also involve co-located behavioral health specialists (eg, psychologists, social workers, or psychiatric nurse practitioners) within dermatology or oncology clinics. Incorporating this may help address psychological needs associated with the diagnosis and its follow-up care. Moreover, support groups, cognitive behavioral therapy, or survivorship counseling should be offered as part of a thorough treatment plan, helping patients manage stressors, such as body image changes, fear, and long-term mental challenges [1,2].

This study has several limitations. As the BRFSS dataset is cross-sectional, the direction of the relationship between nonmelanoma skin cancer and mental health outcomes cannot be established. It is not possible to determine whether poor mental health causes the development of nonmelanoma skin cancer or arises because of diagnosis, treatment, and other factors of nonmelanoma skin cancer. Poor mental health days rely on self-report and capture broad, nonspecific distress, which may not align with clinical diagnoses. Reverse causality is possible if individuals with mental health issues are more likely to seek evaluation for skin changes, leading to higher rates of nonmelanoma skin cancer detection. Additionally, several confounding variables, such as family history of cancer, medication use, and factors such as sun exposure or smoking, were not used in the dataset and may partially explain the observed associations. Although this analysis adjusted for several major chronic illnesses (other cancers, lung disease, heart disease, and kidney disease), many clinically important conditions remain unmeasured. For instance, a participant may have both nonmelanoma skin cancer and a more psychologically burdensome condition, such as lung cancer or severe cardiac disease, which could influence their mental health outcomes. The inability to differentiate whether mental health symptoms stem from nonmelanoma skin cancer itself or from co-occurring illnesses limits the precision of our findings. Additionally, our analyses do not capture illness perceptions, cosmetic concerns, or treatment experiences that may influence psychological outcomes. Future work using datasets with richer clinical detail or linked cancer registry data may help more accurately isolate the independent effect of skin cancer on mental health. These findings should be interpreted as a correlation, and future research is needed to clarify the direction of this relationship. Finally, the BRFSS survey may not capture more nuanced mental health challenges such as anxiety or posttraumatic stress disorder, limiting the depth of insight into the psychological experiences of patients with nonmelanoma skin cancer [5,9]. All variables were self-reported, which may introduce misclassification of both exposures and outcomes.

It is also crucial to recognize that depression is frequently underdiagnosed in community populations, particularly among older adults, men, and individuals with limited access to health care. The BRFSS depression variable relies on self-reported clinical diagnosis, which does not capture unreported cases. More sensitive mental health assessments, such as the Patient Health Questionnaire-9 or validated cancer-specific screening tools, may better capture psychological distress in future studies.

Conclusions

This study highlights a major association between mental health challenges, particularly

depression and poor mental health days, and the presence of nonmelanoma skin cancer among US adults using nationally representative data from the 2023 BRFSS [9]. Adults with a history of skin cancer reported higher unadjusted levels of day-to-day mental distress than those without skin cancer, but analyses adjusted for covariates showed no significant association with depression and a slight decrease in poor mental health days. Moreover, sociodemographic factors play a

substantial role in shaping mental health, with certain groups showing greater vulnerability [3,10].

These results emphasize the importance of integrated care models that address both physical and mental health outcomes in patients with nonmelanoma skin cancer [1,2]. Public health initiatives should prioritize mental health screening and support within dermatologic and oncologic care, especially for disproportionately affected populations. The favorable mental health profile observed among individuals with nonmelanoma skin cancer may also highlight opportunities to leverage routine dermatologic care as a platform for promoting mental well-being and early identification of psychosocial needs. Future research should investigate longitudinal patterns, causal mechanisms, and the effectiveness of mental health interventions in improving quality of life and potentially clinical outcomes among patients with nonmelanoma skin cancer, and whether resilience, health care engagement, or other unmeasured attributes mediate these associations, and whether similar patterns emerge across diverse populations and cancer types [5,11].

Ultimately, recognizing and addressing the mental health burden associated with nonmelanoma skin cancer can lead to more holistic, equitable, and patient-centered care strategies.

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Data Availability

The datasets generated or analyzed during this study are available in the Behavioral Risk Factor Surveillance System repository [8].

Conflicts of Interest

None declared.

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Abbreviations

aOR: adjusted odds ratio
aRR: adjusted rate ratio
BRFSS: Behavioral Risk Factor Surveillance System

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Patient Satisfaction, Side Effects, and Other Reactions Reported by Adult Men Prescribed Compounded Topical Finasteride via a National Telehealth Platform: Retrospective Analysis of Real-World Data

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Abstract

Background: Topical minoxidil and oral finasteride are approved by the US Food and Drug Administration (FDA) for the treatment of male androgenetic alopecia (AGA). However, concerns about adverse events related to the use of oral finasteride have led to some apprehension about the treatment. Topical finasteride, though not FDA-approved, has demonstrated efficacy and safety in a limited number of clinical trials and may be a promising alternative, such that compounding pharmacies and telehealth companies in the United States now offer access to topical finasteride for patients with AGA.

Objective: This real-world, retrospective study is, to our knowledge, the largest study to date aimed to evaluate patient satisfaction and tolerability associated with the novel combinations of topical finasteride and topical minoxidil for the treatment of male AGA.

Methods: We conducted a retrospective analysis of patient data collected during routine clinical follow-up via Hims & Hers, a direct-to-consumer health and wellness platform, between April 1, 2021 and April 30, 2025 to assess the frequency of side effects and other possible medication reactions associated with the use of compounded topical finasteride and minoxidil. Data were gathered from two sources: (1) a follow-up check-in sent to patients approximately 130 days following the initiation of treatment; (2) unprompted communications sent via in-app or web-based messaging from patients to their care team. Data about patient satisfaction with treatment, the frequency of any side effect, frequency of specific side effects, need for a higher level of care, and treatment discontinuation due to a side effect were extracted from the data sources.

Results: A total of 638,629 male patients with AGA received a prescription for a compounded topical finasteride and minoxidil product between April 1, 2021 and April 30, 2025. Of 151,352 (23.7%) patients who completed a follow-up check-in, 121,615 (80.4%) reported being satisfied with treatment and 4034 (2.7%) reported experiencing a side effect. Of all the 638,629 patients, 230 (0.04%) sent their care team a message (outside of check-ins) indicating a side effect or other possible medication reactions. No patient reported seeking a higher level of care or discontinued treatment due to such an occurrence.

Conclusions: Patients prescribed novel formulations of compounded topical finasteride and minoxidil for the treatment of AGA via a national telehealth platform reported satisfaction with the treatment and tolerated it well. The limitations of the study include the use of retrospective data and the lack of a control group, both of which preclude causal inference. Future research should include randomized controlled trials to assess the efficacy, safety, and tolerability of topical finasteride.

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KEYWORDS

androgenetic alopecia; topical finasteride; topical minoxidil; patient satisfaction; side effects; telehealth

Introduction

Androgenetic alopecia (AGA), commonly referred to as "male pattern baldness," is the most common form of hair loss in men. It affects approximately 50% of men worldwide [1] and an estimated 50 million in the United States alone [2]. Although AGA is considered a physically benign medical condition, it is associated with notable psychological consequences including

low self-esteem, body dissatisfaction, social anxiety, and reduced quality of life [3].

Topical minoxidil and oral finasteride are two treatments currently approved by the US Food and Drug Administration (FDA) for the treatment of AGA. Topical minoxidil is available in both 2% and 5% formulations; the 5% formulation has been shown to be significantly superior in increasing hair regrowth, with an earlier response to treatment and good tolerance [4]. Oral finasteride has been shown, in clinical trials, to be well tolerated and effective in stabilizing hair loss and promoting hair growth [5]; however, reports of certain treatment-related adverse events such as sexual side effects and depression have led to some apprehension about the treatment, which may be negatively affecting the number of individuals who could benefit from it [6]. Notably, recent studies have questioned the purported causal relationship between oral finasteride and psychiatric symptoms [7,8].

Topical finasteride may be a promising alternative to oral finasteride. Though limited in number, studies that have examined the use of topical finasteride in the treatment of AGA have found it to be an effective and safe treatment option [9]. Two randomized controlled trials (RCTs) found topical finasteride to significantly decrease the rate of hair loss and significantly improve hair count compared to the placebo, with no differences in the incidence of adverse events or treatment discontinuation between the two groups [10,11]. Plasma concentrations of finasteride were 100-fold lower with the topical application of 0.25% finasteride spray versus 1 mg oral finasteride [11]. Furthermore, a systematic review of available RCTs, prospective studies, and retrospective medical record reviews found topical finasteride, either alone or in combination with other agents including topical minoxidil, to be non-inferior to oral finasteride and well-tolerated by patients—with the authors calling for larger cohort studies to examine the potential adverse event profile of the drug [9].

Unlike oral finasteride, topical finasteride is not currently FDA-approved for the treatment of AGA. It is, however, available as a compounded medication for those who do not want to take an oral medication or might be concerned about the reported side effects associated with oral finasteride. Several compounding pharmacies and telehealth companies in the United States now offer access to topical finasteride for patients with AGA. This real-world retrospective study is, to our knowledge, the largest study to date on patient satisfaction and tolerability associated with novel combinations of topical finasteride and topical minoxidil for the treatment of male AGA. We review anonymized patient data collected during the course of routine clinical care via a direct-to-consumer telemedicine platform to understand the patient-reported satisfaction and frequency of side effects and other possible medication reactions associated with compounded topical finasteride use (compounded topical finasteride is not FDA-approved or evaluated for safety, efficacy, or quality by the FDA).

Methods

Study Overview

Hims & Hers is a direct-to-consumer health and wellness platform that aims to increase access to treatment for adults aged 18 years and older with traditionally stigmatized conditions, including hair loss. Prospective patients seeking hair loss treatment come to the platform and complete a comprehensive clinical intake. Once the intake process is complete, a licensed medical provider thoroughly reviews the information gathered during the intake process, including medical history and treatment preferences, and has the opportunity to follow-up with the patient with any questions or remaining information deemed necessary to provide care. The provider then makes an independent clinical determination as to whether treatment is appropriate, and, if appropriate, shares a diagnosis and treatment plan. All licensed medical providers furnishing care through the platform are employed or contracted by You Health, a professional corporation owned and managed by licensed health care providers, which is the provider network associated with the platform. Patients sign up for a subscription to receive their medication dispensed by a licensed pharmacy at regular intervals. With this subscription, patients have ongoing, unlimited access to their care team via messaging and are sent follow-up check-ins to assess their treatment experience.

As of June 2025, three compounded topical finasteride and minoxidil products were available via the Hims & Hers platform to treat adult men with AGA: a spray consisting of 0.3% topical finasteride and 6% minoxidil, to be sprayed four times on the individual's affected scalp area once per day; a spray consisting of 0.3% topical finasteride, 7% minoxidil, 2.2% ketoconazole, and 0.2% biotin, to be sprayed four times on the individual's affected scalp area once per day; and a serum consisting of 0.3% topical finasteride and 6% minoxidil, 1 mL of which to be massaged into the individual's affected scalp area once per day. All patients prescribed a compounded topical finasteride and minoxidil product were made aware that the product was not FDA-approved and were provided with instructions for use as well as education regarding what to expect with the treatment, common side effects, and other precautions. Patients also had access to educational treatment information via the Hims & Hers app and could contact their care team at any time with questions or concerns. In April 2025, the FDA issued an alert to health care providers, compounders, and consumers regarding potential risks associated with the use of compounded topical finasteride. This information was also shared with patients to ensure transparent communication regarding the products available through the platform.

To assess the frequency of side effects and other possible medication reactions associated with the use of compounded topical finasteride and minoxidil available via the Hims & Hers platform, we conducted a retrospective analysis of patient data collected during the course of routine clinical follow-up via the platform between April 1, 2021 and April 30, 2025. As this was an analysis of data gathered from individuals actively engaged in treatment, there was no control group.

Data Collection

The analysis included two sets of data. The first set of data consisted of responses to a follow-up check-in assessment sent to patients approximately 130 days following treatment initiation. The check-in queried patients about their treatment satisfaction and experience with side effects. To assess treatment satisfaction, patients were asked to indicate "yes" or "no" to the following prompt: "I'm happy with the way my treatment is working." To assess experience with side effects, patients were asked to respond "yes" or "no" to the following question: "Are you bothered by any side effects or other negative reactions from your treatment?" No other questions pertaining to side effects were included in the check-in.

The second set of data consisted of unprompted communications sent via in-app or web-based messaging from patients to their care team. Patients can send these unprompted messages at any time for review by the care team. These communications undergo continuous quality assurance by a clinical quality team that monitors patient messages in real-time for mention of side effects or other possible medication reactions and follows-up as appropriate. Their work includes validating the data to ensure that such events are appropriately recorded—for example, that the side effects and reactions reported are reported by patients in relation to one of the topical finasteride and minoxidil products highlighted in this analysis. Utilizing both sets of data ensured that all occurrences, both solicited and spontaneously reported by patients, were included in the analysis.

Statistical Analysis

Descriptive statistics using Google Colab (Mountain View, CA) were used to quantify the percentage of patients who reported satisfaction with treatment in their follow-up check-in, the percentage of patients who reported having been bothered by side effects or other negative reactions in their follow-up check-in, the percentage of patients who indicated experiencing a side effect or other possible medication reaction in messages to their care team, the percentage of patients who sought a higher level of care due to such a reaction, and the percentage of patients who discontinued treatment due to such a reaction. For results regarding the percentages of patients who reported treatment satisfaction and side effects in their follow-up check-in, the number of patients who completed a check-in is used as the sample size. For results regarding the percentage of patients who reported a side effect to their care team, the total number of patients prescribed a compounded topical finasteride product is used a the sample size. This is due to the fact that all patients had the ability to message their care team; thus, all patients can be included in the denominator.

Ethical Considerations

This study was approved by the WCG Institutional Review Board (Protocol 001, Review 20244102). All study procedures were conducted in accordance with the principles of the Declaration of Helsinki. The study protocol included a Waiver of Informed Consent, as all data analyzed were collected during the course of routine care and de-identified prior to analysis. Patients were not compensated for their participation in this study.

Results

Baseline Demographics

A total of 638,629 male patients with AGA received a prescription for a compounded topical finasteride and minoxidil product between April 1, 2021 and April 30, 2025. A total of 151,352 completed the follow-up check-in querying patients about their treatment satisfaction and experience with side effects.

The mean (SD) age of all patients who received a prescription for a compounded topical finasteride product (n=638,629) was 39.6 (11.9) years, while the mean (SD) age of those who completed the follow-up check-in (n=151,352) was 41.2 (11.8) years.

Treatment Satisfaction and Side Effects as Reported During Follow-Up Check-In

Overall, 121,615 (80.4%, n=151,352, 95% CI [80.2%, 80.6%]) patients who completed the follow-up check-in reported being satisfied with their treatment. A total of 4034 (2.7%, n=151,352, 95% CI [2.6%, 2.8%]) reported experiencing side effects.

Of the 151,352 patients who completed the follow-up check-in, 138,645 had been prescribed the 0.3% topical finasteride and 6% minoxidil spray; 10,774 had been prescribed the 0.3% topical finasteride, 7% minoxidil, 2.2% ketoconazole, and 0.2% biotin spray; and 1933 had been prescribed the 0.3% topical finasteride and 6% minoxidil serum. Table 1 outlines treatment satisfaction and the frequency of side effects reported by patients receiving each treatment.

Table . Treatment satisfaction and frequency of side effects reported by patients during follow-up check-ins.

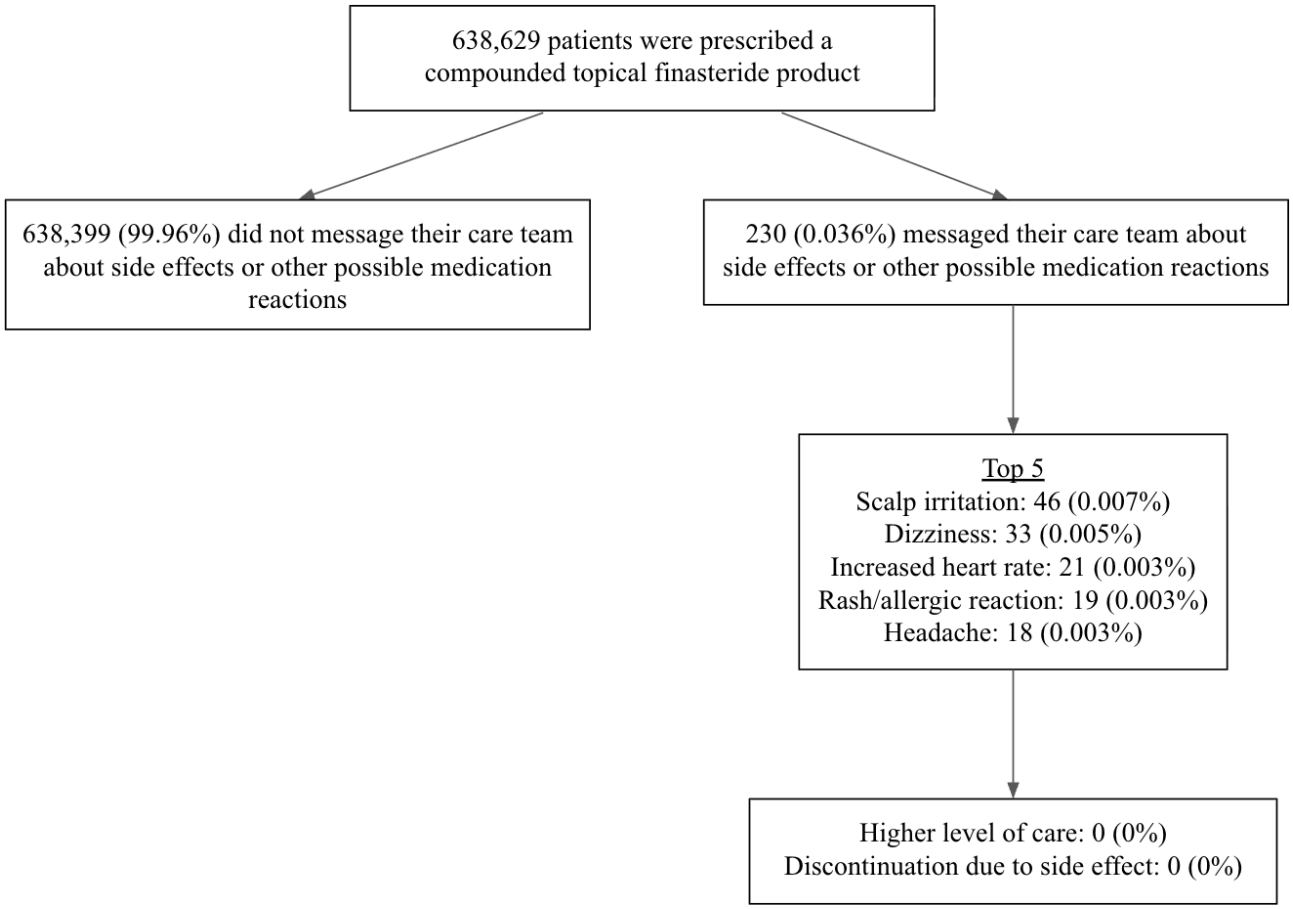
	All topical finasteride treatments (n=151,352)	Topical finasteride (0.3%) and minoxidil (6%) spray (n=138,645)	Topical finasteride (0.3%), minoxidil (7%), ketoconazole (2.2%), and biotin (0.2%) spray (n=10,774)	Topical finasteride (0.3%) and minoxidil (6%) serum (n=1933)
Treatment satisfaction, n (%)	121,615 (80.4)	111,165 (80.2)	8900 (82.6)	1550 (80.2)
Experienced side effects, n (%)	4034 (2.7)	3716 (2.7)	251 (2.3)	67 (3.5)

Side Effects and Other Possible Medication Reactions Reported in Patients' Communications to Their Care Team

Of the 638,629 patients prescribed a compounded topical finasteride and minoxidil product, 230 (0.04%, n=638,629, 95% CI [0.035%, 0.045%]) sent their care team messages concerning side effects or other possible medication reactions. The most commonly reported occurrences were scalp irritation (46/638,629, 0.007%, 95% CI [0.0064%, 0.0076%]), dizziness (33/638,629, 0.005%, 95% CI [0.0045%, 0.0055%]), increased heart rate (21/638,629, 0.003%, 95% CI [0.0026%, 0.0035%]), rash or some allergic reaction (19/638,629, 0.003%, 95% CI [0.0026%, 0.0035%]), and headache (18/638,629, 0.003%, 95% CI [0.0026%, 0.0035%]). Sexual side effects, specifically decreased libido and erectile dysfunction, were reported by 12/638,629 patients (0.002%, 95% CI [0.0017%, 0.0023%]). Depression was reported by 13/638,629 patients (0.002%, 95% CI [0.0017%, 0.0023%]). Anxiety was reported by 10/638,629 patients (0.002%, 95% CI [0.0017%, 0.0023%]). Cognitive concerns were reported by 10/638,629 patients (0.002%, 95% CI [0.0017%, 0.0023%]).

No patients reported seeking a higher level of care (eg, emergency room or urgent care visit) related to a side effect or other possible medication reaction. No patients reported discontinuing treatment due to such an occurrence. During the study period, 1 spouse reported the death of a partner. Upon follow-up, no cause was identified and no causality was established. Figure 1 provides a summary of the side effects and other possible medication reactions reported by patients via messaging.

Figure 1. Schematic of side effects and other possible medication reactions reported by patients in messages to their care team.



Discussion

In this largest study of patient satisfaction and tolerability associated with the use of novel compounded formulations of topical finasteride and minoxidil, we found that 80% of those who completed a follow-up check-in reported satisfaction with treatment and less than 3% reported experiencing side effects. An additional 0.04% of patients sent their care team messages concerning side effects or other medication reactions. The most common reactions appeared to fall into one of two categories: (1) scalp irritation and rash, likely associated with the route of administration; (2) dizziness, increased heart rate, and headache, likely attributable to minoxidil acting as a vasodilator. Of note, sexual side effects, depression, anxiety, and cognitive concerns previously associated with oral finasteride were reported by just 0.002% of patients. There were no reports of "post-finasteride syndrome" [12].

Early clinical trials of 1 mg oral finasteride for the treatment of male AGA found that 3.8% of participants experienced adverse events possibly, probably, or definitely related to treatment, specifically decreased libido, erectile dysfunction, and ejaculation disorder, and 1.4% discontinued treatment due to such adverse events [13]. Trials of 2% topical minoxidil for the treatment of male AGA found that the most common adverse events were minor respiratory events such as colds and

respiratory infections (3.37% of participants), followed by dermatological reactions such as itching (1.94%) [14]. Trials of 5% topical minoxidil for the treatment of male AGA found that headache was the most frequently reported adverse drug reaction (1.7%), followed by dermatological reactions such as pruritus (1.1%) and rash (1.1%) [14].

A comparison of our findings to the findings of these historic studies reinforces the favorable tolerability profile of topical medications. Altogether, these results demonstrate that the novel compounded formulations of topical finasteride and minoxidil available to male patients with AGA via the Hims & Hers platform are associated with high satisfaction among patients and few reported side effects.

To date, few clinical trials have examined the use of topical finasteride in the treatment of male AGA [10,11,15]. A Phase III RCT by the Topical Finasteride Study Group in Europe found that 41.4% of participants reported treatment-emergent adverse events and 9.9% experienced treatment-related adverse events [10]. Another Phase III RCT in China found that 68.4% of participants reported treatment-emergent adverse events and 8.3% experienced treatment-related adverse events [11]. In both studies, the frequency of adverse events among participants using topical finasteride was similar to those using placebo. A retrospective study of 238 patients who received topical finasteride via a German direct-to-consumer teledermatology platform and completed a 6-week follow-up questionnaire found that 11.8% of patients reported adverse events after initiating the use of topical finasteride [15].

However, the aforementioned studies are methodologically limited by their relatively small sample sizes. This study, which included over 600,000 patients who were prescribed compounded topical finasteride in a real-world context, offers a much more robust and meaningful assessment of patient-reported satisfaction and tolerability associated with treatment.

There are limitations of this analysis. First, this was a retrospective analysis of data collected during the course of routine care and not an RCT, and therefore, we cannot confirm any causal relationships between patients' use of compounded topical finasteride and minoxidil and the reported outcomes. Second, we partly relied on data from an optional follow-up check-in questionnaire sent to patients approximately 130 days after treatment initiation. The rate of check-in completion was relatively low, with 23.7% of patients completing the check-in. This may indicate some selection bias, such that patients who were more engaged in or satisfied with their treatment may have been more likely to respond to the check-in and less likely to report side effects. Patients who reported side effects or other reactions to outside health care providers may not have been captured. Third, our reliance on retrospective data meant that we were unable to systematically examine other data of interest, such as the severity of and types of intervention sought for side effects and other medication reactions reported by patients.

However, our analysis also had several strengths. First, our sample size was impressive, with 638,629 patients prescribed a compounded topical finasteride product, all of whom had the ability to communicate with their care team at any time during the course of treatment, and 151,352 of whom completed the follow-up check-in that specifically queried patients about their experience with treatment and side effects. Second, our analysis utilized real-world data. The use of real-world data enables clinicians and researchers to better understand how patients experience treatment in their daily lives, thus increasing the generalizability of results. Third, in addition to relying on the optional follow-up check-in questionnaire to collect data on patient-reported side effects, we were also able to utilize unsolicited patient communications concerning side effects and other possible medication reactions. Having these additional data increased the likelihood that we were able to capture all occurrences reported by patients.

In conclusion, our analysis found that patients prescribed novel formulations of compounded topical finasteride and minoxidil for the treatment of AGA via a national telehealth platform tolerated the treatment well. The majority reported satisfaction with the treatment, and there were few reports of side effects. Future research should include RCTs to assess the efficacy, safety, and tolerability of topical finasteride. Together, this work may help provide more treatment options for those with AGA.

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Data Availability

The datasets generated or analyzed during this study are not publicly available due to commercial restrictions; however, they may be available from the corresponding author upon reasonable request.

Conflicts of Interest

JY, SM ME, and PC are full-time employees of Hims & Hers Health, Inc. JK and AM serve as advisors to Hims & Hers Health, Inc. Hims & Hers Health, Inc. had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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ABBREVIATIONS

AGA: androgenetic alopecia
FDA: Food and Drug Administration
RCT: randomized controlled trial

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Identifying Over- and Underfunded Diseases by Comparing National Institutes of Health Funding for Skin Disease Research With US Skin Disease Burden According to 2021 Global Burden of Disease Data: Cross-Sectional Analysis

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Abstract

Background: Understanding the burden of various skin diseases can help guide funding allocation for skin disease research. A 2015 cross-sectional study found a partial correlation between US skin disease burden according to the 2010 Global Burden of Disease (GBD) study and National Institutes of Health (NIH) funding in 2012-2013.

Objective: This study aims to identify trends, correlations, and disparities in US skin disease burden and NIH research funding allocation using the latest data from the GBD 2021 and NIH funding data from the fiscal years 2021-2022.

Methods: A cross-sectional analysis was conducted to compare the disability-adjusted life years for 15 skin conditions from the GBD 2021 with NIH funding for these conditions in 2021-2022. Data were sourced from the GBD Results tool and the NIH RePORTER database.

Results: NIH funding for skin disease research and US skin disease burden according to the GBD 2021 were partially correlated, with several outliers. Malignant skin melanoma and pruritus were relatively overfunded, while psoriasis and urticaria were relatively underfunded.

Conclusions: Disease burden is just one of the many important factors that must be considered when allocating resources, including funding to encourage research efforts to improve patient outcomes and positively impact public health.

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KEYWORDS

epidemiology; burden of disease; disability-adjusted life years; research funding; melanoma; psoriasis; dermatitis

Introduction

The Global Burden of Disease (GBD) study aims to quantify worldwide health losses due to a wide variety of illnesses and injuries [1]. Disease burden is one of many important factors guiding decisions on policy development, disease prevention initiatives, and research funding allocation [1,2]. The GBD study quantifies disease burden using disability-adjusted life years (DALYs), a measure that accounts for both mortality due to disease (years of life lost) and years lived with decreased health and quality of life (years lived with disability; YLDs) [1]. GBD also accounts for the severity of disability (defined by any short-term or long-term loss of health) attributed to the variety of illnesses and injuries included in the study by factoring disability weights into the calculation of YLDs [1,3].

Skin conditions are ubiquitous worldwide and affect millions each year. As a result, dermatology continues to be a consistently innovative field that makes large strides in patient care thanks to a heavy research focus. Public funding is a major contributor to research and innovation in this field. In 2015, Hagstrom and colleagues [4] conducted a cross-sectional study that found a partial correlation between US skin disease burden according to the GBD 2010 and National Institutes of Health (NIH) funding in the fiscal years 2012 - 2013, identifying over- and underfunded diseases. Following this study, there have been major changes to the funding of dermatology research, with a 14.7% inflation-adjusted increase in research funding from 2015 to 2019 and fluctuations in funding after the COVID-19 pandemic [5,6]. This study reinvestigates the relationship between US skin disease burden using the latest GBD 2021 data and NIH funding data for 2021 - 2022.

Methods

Overview

A cross-sectional analysis was conducted to compare DALYs for the 15 skin conditions included in the GBD 2021 with NIH funding for these conditions in 2021 - 2022. Data were sourced from the GBD Results tool [1] and the NIH RePORTER database [7]. The search parameters used in GBD Results to obtain DALY metrics for all 15 aforementioned skin disease categories in the US were as follows: measure="DALYs," metric="number," location="United States of America," age="all ages," sex="both," and year="2021." DALY metrics were specifically gathered for the United States to facilitate a direct comparison between the US-specific burden of skin diseases measured by DALYs and funding allocated by the NIH in the United States for skin disease research.

To compile a comprehensive list of NIH-funded grants awarded for skin disease research during fiscal years 2021-2022, a total of 15 queries were entered into the NIH RePORTER database, with each query corresponding to one of the GBD skin disease categories. The following parameters were used to conduct all 15 of these search queries: fiscal year="2021 and 2022," text search logic="advanced," and limit project search="project title, project terms, and project abstracts." In the Text Search box, all *International Classification of Diseases, 10th Revision* codes categorized by the GBD 2021 under one specific skin disease category were strung with "AND," "OR," or "NOT" as determined necessary to capture all relevant NIH-funded grants.

All titles and abstracts of the grants obtained from NIH RePORTER were manually screened by two independent reviewers to determine inclusion versus exclusion (they were included if the grant studied any 1 of the 15 skin disease categories described by the GBD 2021). Following independent review, inclusion and exclusion decisions were cross-examined to identify conflicting decisions. A third reviewer served as a tie-breaker to resolve any discrepancies as needed.

Statistical analysis was performed assuming that the proportion of DALYs attributed to a disease should be the same as the proportion of NIH skin disease funding it receives (ie, if a specific disease is responsible for 25% of all US skin disease DALYs, that disease should receive 25% of all NIH skin disease funding). A one-to-one trendline was used to visualize this relationship and identify outliers representing relatively over- and underfunded skin diseases. An "observed-to-expected" ratio was calculated by dividing the true amount of funding a disease received by the amount of funding a disease could be expected to receive assuming a one-to-one relationship between DALYs and funding.

Ethical Considerations

This study was exempt from review by the institutional review board, and no patient or participant consent was required or obtained, as this study did not constitute human subjects research and used publicly available data.

Results

Our analysis revealed a positive correlation between the percentage of total US skin disease DALYs in 2021 and the percentage of total NIH skin disease funding in 2021 - 2022. The correlation coefficient between these two data points was 0.3167 (95% CI 0.053626-0.579774). There were several key outliers when comparing DALYs to funding, indicating that certain skin diseases were relatively over- or underfunded in comparison to their proportion of total disease burden. Pruritus and malignant melanoma received 445% and 392% of the proportion of funding expected by their proportion of DALYs (Table 1). Other relatively overfunded diseases include leprosy, decubitus ulcers, bacterial skin diseases, and nonmelanoma skin cancer (Figure 1, Table 1).

Figure 1. Scatterplot comparing proportion of National Institutes of Health (NIH) skin disease funding received in 2021 - 2022 with the proportion of total US skin disease disability-adjusted life years (DALYs) according to the 2021 Global Burden of Disease study.

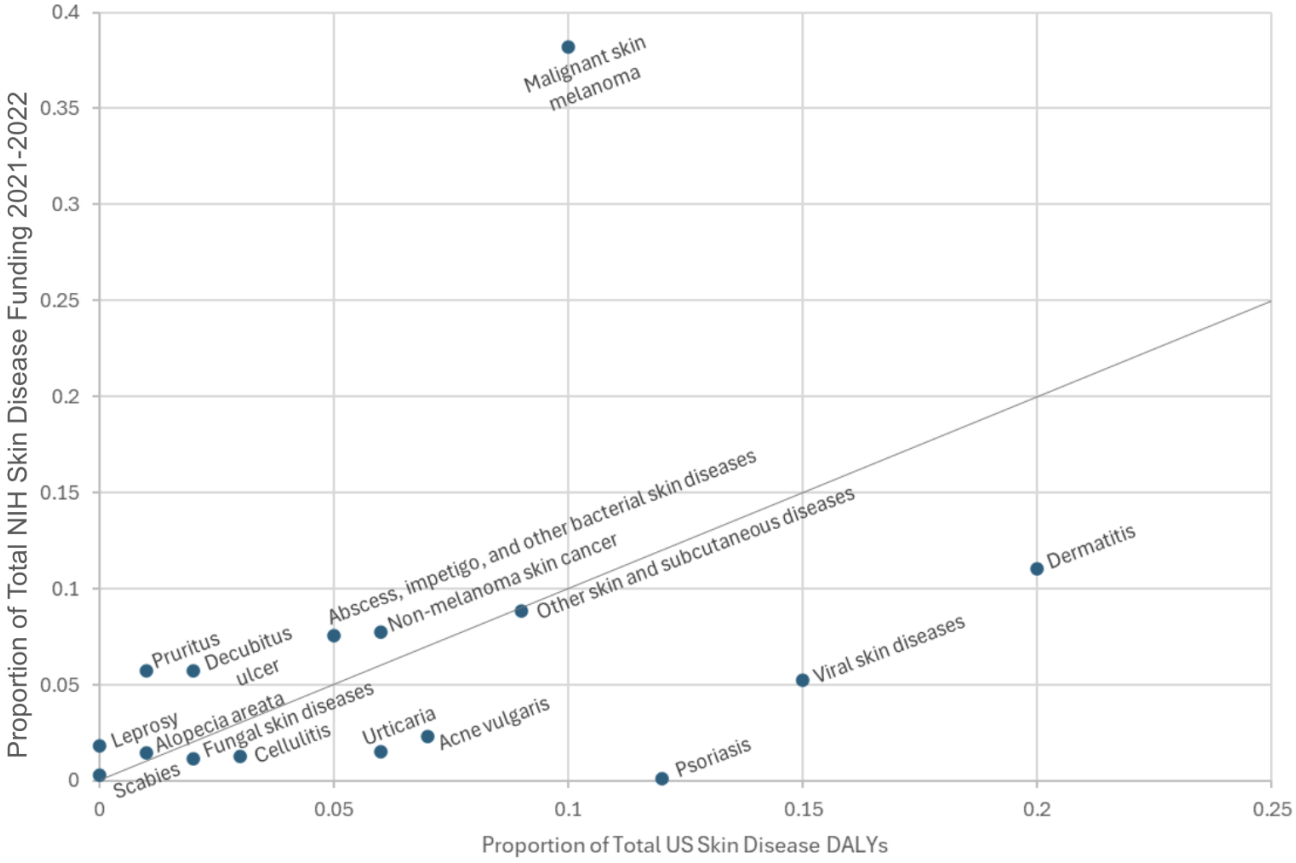

Table . Comparison of disability-adjusted life year (DALY) rank from Global Burden of Disease GBD 2010 and 2021 study data, comparison of National Institutes of Health (NIH) funding in fiscal years 2012 - 2013 (data from Hagstrom et al [4]) and 2021-2022 (data from the current analysis), and the percentage of total US skin DALYs (in 2021) and NIH skin disease funding (in 2021 - 22).

Category	US DALY rank in 2021	Proportion of total US skin disease DALYs in 2021, %	US DALY rank in 2010[a]	NIH funding rank in 2021 - 2022	Proportion of total NIH skin disease funding in 2021 - 2022, %	NIH funding rank in 2012 - 2013[a]	Observed-to-expected ratio for funding[b]
Pruritus	13	1.29	5	6	5.74	6	4.45
Malignant skin melanoma	4	9.75	3	1	38.19	1	3.92
Decubitus ulcer	11	1.87	8	7	5.74	11	3.07
Abscess, impetigo, and other bacterial skin diseases	8	4.90	13	5	7.56	9	1.54
Nonmelanoma skin cancer	6	6.10	2	4	7.73	2	1.27
Alopecia areata	12	1.36	11	12	1.48	13	1.09
Other skin and subcutaneous diseases	—[c]	9.30	—	3	8.87	3	0.95
Scabies	14	0.38	14	15	0.30	16	0.8
Dermatitis	1	19.98	1	2	11.03	5	0.55
Fungal skin diseases	10	2.17	9	14	1.14	10	0.53
Cellulitis	9	3.42	12	13	1.26	12	0.37
Viral skin diseases	2	14.61	6	8	5.22	4	0.36
Acne vulgaris	5	6.99	4	9	2.29	14	0.33
Urticaria	7	5.80	7	11	1.51	15	0.26
Psoriasis	3	12.10	10	16	0.09	7	0.0082
Leprosy[d]	15	0	15	10	1.84	8	—[d]

[a]Data obtained from Hagstrom et al [4].

[b]Percentage of funding vs percentage of DALYs.

[c]Not applicable.

[d]Ratio of funding proportion to DALY proportion could not be calculated for leprosy, as the proportion of DALYs for leprosy was 0.

Conversely, psoriasis, fungal skin diseases, cellulitis, urticaria, acne vulgaris, viral skin diseases, and dermatitis were underfunded. Notably, psoriasis received only 0.82% of the funding expected by its disease burden (Table 1). Funding for scabies, alopecia areata, and the "other skin/subcutaneous diseases" category appeared well matched to their disease burden, receiving between 80% to 110% of the funding predicted by their respective DALYs (Figure 1, Table 1).

Discussion

Principal Findings

This study reinvestigated the relationship between US skin disease burden and NIH skin disease research funding using the latest GBD 2021 data and NIH funding data from fiscal years 2021 - 2022. Compared to Hagstrom et al's [4] 2015 study, many of the same trends in relative over- and underfunding of skin diseases were observed. For example, malignant melanoma remains the most significantly overfunded skin disease relative to its disease burden (Table 1) [4]. Nonmelanoma skin cancer and leprosy also remain overfunded, while dermatitis, acne vulgaris, urticaria, fungal skin diseases, and cellulitis remain underfunded (Table 1) [4]. Interestingly, pruritus and decubitus ulcers, previously underfunded in 2015, now appear to be relatively overfunded (Table 1) [4]. Funding for psoriasis was well matched to its disease burden in 2015, but in our updated analysis, psoriasis is the most underfunded skin disease category. Similarly, viral skin diseases were well funded in 2015 and now appear underfunded (Table 1) [4].

It is important to consider disease burden when allocating research funding to ensure adequate resources are being directed toward diseases with the most significant impact. Dedicating more resources toward high-burden diseases can improve individual health and quality of life by driving the development

of innovative treatments and can also provide long-term economic benefits by reducing health care costs and increasing overall workforce productivity.

In addition to disease burden, many other factors also significantly impact resource prioritization and funding allocation. For example, more research funding is likely to be allocated to diseases with strong public awareness and advocacy campaigns, such as malignant skin melanoma. Funding is also likely influenced by disease curability and the potential for therapeutic innovation. The NIH may also prioritize funding for diseases with lower incidence or prevalence but higher mortality (ie, metastatic melanoma, metastatic nonmelanoma skin cancer) rather than diseases with lower mortality but higher incidence or prevalence (ie, dermatitis and acne vulgaris).

Limitations

It is important to keep in mind that using data strictly from the GBD study and the NIH does not fully capture all of the nuances of US skin disease burden and research funding. An important limitation of this analysis, similar to Hagstrom et al's [4] prior study, is the exclusion of industry research funding by pharmaceutical companies and other nongovernmental entities from NIH funding data [4,7]. The NIH is the largest source of public funding for biomedical research; however, a significant portion of research funding also comes from nonprofits, philanthropic organizations, and private industry [8]. Therefore, while a disease may appear underfunded relative to its disease burden using GBD and NIH data alone, additional research funding from nongovernmental agencies may be filling this perceived gap in resource allocation. For instance, although our analysis showed that psoriasis received significantly less funding from the NIH relative to its disease burden, substantial funding from pharmaceutical companies has driven the development of innovative new drugs (ie, IL-23 and IL-17 inhibitors) that have transformed the treatment of psoriasis in recent years [9]. Similarly, previous reviews have cited US $22,291,506 in nonprofit funding for dermatology research in 2019 alone and US $9.3 billion dollars of private equity investment in dermatology health care and research between 2011 and 2021 [10,11].

Conclusions

Given the wide variety of factors that must be considered in order to optimally allocate research funding, several guidelines may help ensure that funding is prioritized for research efforts that will guide clinical practice, improve patient outcomes, and positively impact public health. In addition to prioritizing high-burden diseases, prioritizing funding for translational research can help expedite the incorporation of knowledge gained from basic science research into clinical practice and patient care. Periodically evaluating the real-world impact of funded research using metrics including patient outcomes and cost-efficacy can also help ensure that funding is being distributed to research that is meaningfully impacting clinical practice. Increased funding for conditions that are impacting our patients will allow innovative solutions that improve patient quality of life. With these guidelines in mind, disease burden can easily be incorporated as one of the many important factors that should be used to inform research funding allocation, clinical practice guidelines, and health policy.

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Conflicts of Interest

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Abbreviations

DALY: disability-adjusted life year
GBD: Global Burden of Disease
NIH: National Institutes of Health
YLD: year lived with disability

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Leveraging AI Large Language Models for Writing Clinical Trial Proposals in Dermatology: Instrument Validation Study

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Abstract

Background: Large language models (LLMs) are becoming increasingly popular in clinical trial design but have been underused in research proposal development.

Objective: This study compared the performance of commonly used open access LLMs versus human proposal composition and review.

Methods: A total of 10 LLMs were prompted to write a research proposal. Six physicians and each of the LLMs assessed 11 blinded proposals for capabilities and limitations in accuracy and comprehensiveness.

Results: ChatGPT-o1 and Llama 3.1 were rated the most and least accurate, respectively, by human scorers. LLM scorers rated ChatGPT-o1 and DeepSeek R1 as the most accurate. ChatGPT-o1 and Llama 3.1 were rated as the most and least comprehensive, respectively, by human and LLM scorers. LLMs performed poorly on scoring proposals and, on average, rated proposals 1.9 points higher than humans for both accuracy and comprehensiveness.

Conclusions: Paid versions of ChatGPT remain the highest-quality and most versatile option of the available LLMs. These tools cannot replace expert input but serve as powerful assistants, streamlining the development process and enhancing productivity.

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KEYWORDS

artificial intelligence; AI; large language model; research proposal; clinical research; clinical trials; deep learning; machine learning; research design

Introduction

Advancements in artificial intelligence (AI) have led to the development of large language models (LLMs) using algorithms that learn from data and recognize patterns to make decisions based on all available data within a training set [1]. However, AI is limited by the data it is trained on and an inability to account for the nuanced contexts of individual research studies [2]. Researchers are increasingly using LLMs in clinical trial design to improve patient selection, cohort composition, and recruitment [3]. In contrast, the use of LLMs in research proposal development is largely unexplored, and thus, they are perhaps underused. This study aimed to address this gap by comparing the performance of LLMs versus the current gold standard of human proposal composition and review. Our goals were 3-fold: to rate LLMs in composing clinical trial proposals, assess LLMs in scoring clinical trial proposals, and evaluate the ease of using LLMs (including usability and efficiency).

Methods

Overview

Commonly used open access AI platforms (DeepSeek R1, ChatGPT-o3-mini [OpenAI], ChatGPT-o1 [OpenAI], ChatGPT-4o [OpenAI], Claude Sonnet [Anthropic], Claude Opus [Anthropic], OpenEvidence, Grok 2 [xAI], Gemini Advanced [Google], and Llama 3.1 [Meta AI]) were evaluated for use in research proposal drafting. We requested each of the models to do the following:

> *Write a research proposal for a study looking at the use of narrowband-ultraviolet B phototherapy for psoriasis treatment for psoriasis patients of varying skin pigmentation with 3 aims: 1. To understand the factors that affect the response of NB-UVB in psoriasis patients of varying skin pigmentation. 2. Evaluate adverse effects of NB-UVB and their impact on psoriasis patients of varying skin pigmentation. 3. Compare the acute immunologic response to NB-UVB*

in psoriasis patients of varying skin pigmentation using bulk and single-cell RNA sequencing. Include the following sections: 1 page 'Specific Aims' with details on each of the 3 aims, 1/2 page background and significance of the topic, 1 page of 'preliminary data/studies' relevant to the study, 1 page 'experimental design' (include summary of study, inclusion and exclusion criteria, study visits and procedures with an associated table describing specifics of study visits), 1/2 page of 'statistical methods, power calculations and bioinformatic analyses' specific for each aim, 1/4 page of 'potential problems and alternative strategies.' Please have approximately 30 references from reputable sources. Make the proposal a total of 7 pages long in paragraph form, in formal scientific language and at a graduate level.

To assess the outputs, each of the 11 blinded proposals (n=10, 90.9% LLM generated and n=1, 9.1% human written) was systematically reviewed and scored by 6 independent physician evaluators, all with strong research backgrounds. Each evaluator used a standardized Likert scale ranging from 1 to 5 (1="strongly disagree"; 5="strongly agree") to rate each proposal for capabilities and limitations in the LLMs' accuracy and comprehensiveness (Table 1).

Table . Criteria for assessing the accuracy, usability, comprehensiveness, and efficiency of large language models (LLMs).

Domain	Assessment criteria	Scoring methodology
Accuracy	Raters systematically fact-checked all proposal content. Only proposals with fully correct and verified factual information (including cited data, statistics, and conclusions) were rated highly. All references were checked for verifiability, relevance, and reputable source quality.	Rated independently by each evaluator on a Likert scale from 1 to 5 (1="strongly disagree: not accurate"; 5="strongly agree: fully accurate"). Scores were aggregated by calculating the mean of all raters' scores for each proposal.
Comprehensiveness	Assessed by evaluating inclusion and completeness of required proposal sections: specific aims, background and significance, preliminary data and studies, experimental design with inclusion and exclusion criteria and study visits and procedures, statistical methods, power calculations and bioinformatic analyses, and potential problems and alternative strategies. Proposals were further checked to meet format requirements: approximately 7 pages in length and 30 reputable references.	Rated independently on a Likert scale from 1 to 5. The mean score was calculated for all evaluators per proposal.
Usability	Assessed qualitatively based on researchers' (MH and DC) experience using each LLM. Criteria included intuitiveness of the interface, clarity of documentation, and ease of generating proposals without technical guidance.	Rated by 2 nontechnical investigators on a Likert scale from 1 to 5; scores were descriptively summarized.
Efficiency	The time from user input to final output was measured in minutes. Minimal delays and rapid response were rated favorably.	The time (minutes and seconds) for the LLM to complete the query was recorded.

For each domain assessed by human reviewers, individual scores were first tabulated. Scores from the 6 evaluators for each proposal were then aggregated by calculating the mean domain score, yielding an overall mean score per domain for each proposal. These aggregated scores provided a quantitative measure of each proposal's performance relative to evaluator consensus. No additional weighting was applied; each evaluator's score carried equal weight in the final aggregation.

In addition to scientific content review, LLM usability and efficiency, including description of pros and cons, were evaluated by 2 investigators. These qualitative evaluations were collected separately and did not contribute to the aggregated proposal scores.

Ethical Considerations

The authors have adhered to local, national, regional, and international law and regulations regarding protection of personal information, privacy, and human rights. This study did not involve human participants, identifiable private information, or interactions requiring human subjects protections. Accordingly, formal human ethics review approval was not required, and informed consent was not necessary. All data used in this study were deidentified prior to analysis to ensure participant confidentiality. No compensation was provided for participation in this study. These determinations are in accordance with University of Michigan policies and federal regulations (45 CFR 46) governing human research [4]. The research was conducted in compliance with the University of Michigan's guidelines on research ethics.

Results

LLMs Composing Proposals

The human-written proposal obtained a score of 5 for accuracy and comprehensiveness across all human scorers and remained the gold standard (Table 2). Human scorers rated ChatGPT-o1 as the most accurate and Llama 3.1 as the least accurate. When

assessed in scoring LLM-derived clinical trial proposals, LLM scorers rated ChatGPT-o1 and DeepSeek R1 as the most accurate (Multimedia Appendix 1). ChatGPT-o1 and Llama 3.1 were found to be the most and least comprehensive, respectively, by both human and LLM scorers.

Table . Full scores by evaluation criterion for each proposal and model.

Proposal and model	Accuracy (1-5), mean (SD)	Comprehensiveness (1-5), mean (SD)	Usability (1-5), mean (SD)	Efficiency
ChatGPT-4o	2.2 (1.2)	1.8 (1.4)	5.0 (0.0)	1 min, 37 s
Claude Opus	3.3 (1.4)	2.7 (0.6)	5.0 (0.0)	1 min, 30 s
ChatGPT-o1	3.5 (1.6)	4.3 (0.5)	3.5 (0.7)	1 min
ChatGPT-o3-mini	2.8 (1.7)	4.0 (0.6)	4.0 (0.0)	30 s
Claude Sonnet	2.0 (1.3)	1.8 (0.8)	4.0 (0.0)	28 s
DeepSeek R1	3.2 (1.5)	3.3 (1.4)	4.0 (0.0)	1 min, 23 s
OpenEvidence	2.3 (1.5)	1.3 (0.5)	3.5 (0.7)	45 s
Grok 2	3.2 (1.5)	3.0 (0.6)	4.0 (0.0)	1 min, 15 s
Gemini Advanced	2.5 (1.0)	1.5 (0.5)	4.5 (0.7)	37 s
Llama 3.1	1.7 (1.0)	1.5 (0.8)	4.5 (0.7)	20 s
Human proposal	5.0 (0.0)	5.0 (0.0)	N/A[a]	N/A (>10 working d)

[a]N/A: not applicable.

Mean and SD scores per criterion are reported for each proposal and model as assessed by 6 independent physician raters (except for usability, which was rated by 2 nontechnical investigators). Efficiency is reported as actual proposal generation time.

All raw scores are available in Multimedia Appendix 1.

LLMs Scoring Proposals

Overall, LLMs performed poorly on scoring proposals and, on average, rated proposals 1.9 points higher than humans for both accuracy (range 1.3-2.8) and comprehensiveness (range 0.7-3). The Claude Sonnet proposal showed the largest discrepancy between human and LLM scoring, with an average difference of 2.8 (SD 3.4) points for accuracy and 3 (SD 4.2) points for comprehensiveness. Interestingly, the ChatGPT-o1 and DeepSeek proposals both received top scores of 5 for both accuracy and comprehensiveness from all LLMs versus human averages of 4.3 (SD 2.2) and 3.3 (SD 1.9), respectively. The absence of variance at the top of the range (and wide variance in the middle of the range) suggests that the discriminatory power of the LLMs plateaued at the top LLM quality.

Ease of Using LLMs

All open access LLMs were highly efficient and ran in a matter of seconds to minutes (minimum of 20 seconds for Llama 3.1 and maximum of 1 minute and 37 seconds for ChatGPT-4o). When assessed for ease of use, ChatGPT-4o and Claude Opus offered the most intuitive interfaces and were highly usable for researchers (DC and MH) without computer science backgrounds.

Discussion

Principal Findings

LLMs offer powerful tools to assist humans in clinical trial proposal creation. LLMs take only minutes to generate proposals, whereas prior investigations into time commitment for generation of proposals by humans have reported estimates of 116 principal investigator hours, 55 coinvestigator hours, and 38 working days [5,6]. Therefore, judicious use of LLMs in proposal development allows researchers to save significant time in organizing sections, formatting, and ensuring coherence.

To provide guidance for readers, we performed a direct comparison of the tested LLMs, highlighting meaningful differences in performance, usability, and application. Table 3 summarizes these findings, with clear delineation of unique strengths and limitations for each model.

Table . Pros and cons of open access large language models (LLMs).

LLM (AI platform)	Pros	Cons
Overall	• Generally reliable, very user-friendly, and highly comprehensive and efficient	• Occasional factual inaccuracies and hallucinations (eg, fabricated references) • Lack of access to the most recent studies due to their training data cutoffs[a]
ChatGPT	• Most advanced and versatile option of the available LLMs • GPT-4o is the lowest-latency[b] and cheapest model	• Offers more advanced, paid "reasoning" models (GPT-o1 and GPT-o3), but they are computationally expensive and slower
Claude	• Designed with emphasis on alignment with human values • Tends to be more cautious about controversial or sensitive topics	• Models less tailored to clinical contexts compared to ChatGPT
DeepSeek	• Fully open source, promoting transparency and community contributions • Does not have associated license fees	• Struggles with fine-tuning on dialogue • Large models (eg, DeepSeek-Coder-33B) require large amounts of GPU[c] memory
Gemini	• Gemini 1.5 Pro boasts the largest context window[d] as a part of Google's ecosystem • Gemini 1.5 Flash is one of the fastest models	• Struggles to produce quality responses without significant prompt engineering • Concerns about data privacy and use with integration into various Google services
Grok 2	• Integration into X's (formerly known as Twitter) ecosystem allows Grok to stay up-to-date with current events and trends • Offers conversational capabilities tailored for social interaction	• Remains suboptimal compared to Claude 3.5 or GPT-4o • As a result of being directly linked to X, a platform with frequent user-generated content, Grok struggles to moderate sensitive or controversial interactions
Llama 3.1	• Llama 3.2 is one of the fastest models (along with Gemini 1.5) • Optimized for efficiency with lower computational requirements compared to other models	• Technical expertise required for it to run properly • Less user-friendly for researchers without technical support
OpenEvidence	• Offers access to the most recently curated medical research • Most robust and relevant citations	• Weaker reasoning capabilities than those of leading frontier models

[a]LLM training data cutoffs: October 2023 for ChatGPT, April 2024 for Claude Sonnet and July 2024 for Claude Haiku, December 2023 for Llama 3.1, May 2024 for Gemini, and unknown for OpenEvidence and Grok.

[b]Time to first token of tokens received, in seconds, after the application programming interface request is sent.

[c]GPU: graphics processing unit.

[d]Maximum number of combined input and output tokens.

ChatGPT-o1 and ChatGPT-o3-mini demonstrated the highest overall accuracy and comprehensiveness, delivering well-structured proposals with robust citations and high scientific rigor. Llama 3.1 and Gemini Advanced were notably efficient, reliably delivering full proposals with rapid turnaround times, but occasionally produced less nuanced sections in preliminary data or limited discussion. Regarding ease of use, ChatGPT-4o and Claude Opus feature intuitive interfaces and require minimal learning curves, making them ideal for researchers new to AI-powered tools. In contrast, Llama 3.1 and OpenEvidence ranked the lowest in usability as their technical requirements and specialized interfaces can be challenging for new users.

All open access LLMs can aid in initial outlining and creation of research proposals. They can assist in initial brainstorming of a clear researchable question and generating hypotheses based on existing literature. LLMs are useful in literature review and can summarize existing studies related to the proposal topic and identify gaps in current knowledge. Furthermore, all open access LLMs can propose data collection methods, define eligibility criteria based on study objectives, recommend appropriate statistical tests based on study design, and help draft proposal sections. They also allow for iterative refinements, enabling tailored outputs to meet specific requirements or needs. While human verification is always required, LLMs can greatly improve time spent on initial proposal drafting and aid in

mundane tasks associated with proposal writing, including proofreading and revisions, writing administrative sections, and optimizing citations.

Limitations to Consider

All LLMs operate similarly to traditional autocomplete and work by using available contextual clues and a statistical model to predict the most likely next "token" or word. Due to the training data cutoffs of AI models, researchers must manually incorporate the latest literature findings. AI researchers are working on incorporating more access to real-time data, for example, generative pretrained transformer actions [6], but these solutions come with their own trade-offs. Another limitation is that users must verify citations as the model may "hallucinate" or fabricate realistic-sounding but false information. Finally, although AI models such as DALL-E (or others) can create images, they are less effective at producing accurate, clinical-grade figures.

Additionally, current LLMs were largely unable to score proposals and should not replace human review for quality control. The high scores from the LLM raters indicate that the LLMs were unable to detect entire missed protocol sections. Other than Gemini Advanced (who self-scored its written proposal with 3 for accuracy and comprehensiveness), Claude Sonnet, and Llama 3.1, all the LLMs self-scored their own proposals with 5 for both accuracy and comprehensiveness, suggesting overlapping "blind spots" in LLM proposal generation and evaluation.

One limitation of this study is that the order in which the proposals were sent for respondents to review was not randomized. Additionally, the "gold standard" (human proposal) was last, and question order likely played a role, with kinder grading of the LLM-derived proposals before reviewing the human-written proposal. Had the human proposal been first, this would have highlighted missing components of LLM-derived proposals and likely led to harsher human grading of the latter.

Another important limitation is the rapid and frequent versioning of LLM platforms, which poses challenges for scientific reproducibility. As models are updated, their performance and outputs can meaningfully change over time, making it difficult to reproduce results or maintain consistency in studies that rely on AI-generated content. Researchers should document model versions and use dates to mitigate this issue and ensure transparency.

Conclusions

The future of AI in clinical research is expected to be transformative and far-reaching. As AI algorithms continue to evolve, they are likely to become more accurate, comprehensive, efficient, and interpretable, enabling researchers to leverage AI-driven insights for personalized medicine, disease prevention, and improved patient outcomes. In the coming years, AI is anticipated to play a crucial role in optimizing clinical trial design and accelerating drug discovery [7]. The integration of AI with other emerging technologies, such as blockchain and the Internet of Medical Things, could further revolutionize clinical research by improving data security, privacy, and real-time patient monitoring [8]. As these advancements continue to unfold, AI has the potential to democratize access to novel therapies, reduce health care costs, and, ultimately, usher in an era of precision medicine [9].

LLMs offer a transformative approach to drafting research proposals [10]. Paid versions of ChatGPT (ChatGPT-o3-mini and ChatGPT-o1) currently remain the highest-quality (as determined by the Artificial Analysis Quality Index) and most versatile option of the available LLMs, balancing usability, speed, accuracy, and customization [11]. While these tools cannot entirely replace expert input, they serve as powerful assistants, streamlining the development process and enhancing productivity. For optimal results, researchers should combine AI-generated content with their expertise, ensuring precision and adherence to the latest research standards.

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Data Availability

The data used in this study can be made available upon request to the corresponding author.

Authors' Contributions

Study conception and design were completed by MH and TT. Material preparation and data collection were performed by MH, DC, KY, TD, JSD, AY, JC, AB, and MN. Data analysis was performed by MH. The first draft of the manuscript was written by MH and DC, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Human and large language model (LLM) scoring of LLM performance on accuracy and comprehensiveness.
[DOCX File, 21 KB - derma_v9i1e76674_app1.docx]

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Abbreviations

AI: artificial intelligence
LLM: large language model

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Patient Perceptions of Climate Change Impacts on Atopic Dermatitis: Cross-Sectional Survey Study

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Abstract

This cross-sectional survey study (63.5% response rate) characterized how patients with atopic dermatitis (AD) perceive and experience the effects of climate change on their AD. Most participants reported that environmental factors such as heat and air pollution worsened their AD and expressed a desire for climate-health education, yet few had discussed these concerns with their dermatologist. These findings reveal a gap in patient-centered dermatologic care and support the development of tools to integrate environmental health into atopic dermatitis management.

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KEYWORDS

atopic dermatitis; eczema; climate change dermatology; climate change; environmental health; climate health impacts; patient experience; survey study; health communication; patient education

Introduction

Climate change is recognized as the foremost global health threat of the 21st century [1]. Environmental shifts (rising temperatures, air pollution, and extreme weather) can impair the skin barrier, alter the microbiome, and induce inflammation, increasing the prevalence and severity of atopic dermatitis (AD) among other skin conditions [2,3]. Among dermatologists, 79.6% agree it affects their patients [4]. Yet, few routinely discuss this with patients, and limited research explores how patients perceive and experience these impacts. To address these gaps, this cross-sectional study surveyed patients with AD to assess how they perceive climate change's impact on their condition and whether these concerns are addressed in dermatologic care.

Methods

Survey Instrument Development

The survey was informed by climate-health literature, dermatologic environmental impacts, and health communication frameworks (eg, message framing, perceived susceptibility, and severity from the Health Belief Model) [5]. Five UCSF (University of California, San Francisco) dermatologists reviewed the instrument for clinical relevance and clarity. Ten adult AD patients piloted it, and feedback informed wording and usability.

Study Population & Recruitment

Eligible participants were English-speaking adults with AD seen at UCSF dermatology clinics between August 2023 and August 2024. A total of 2164 patients were identified by the electronic health record (EHR) query. To reduce selection bias, patients were contacted via EHR messaging or mailed letters to account for differences in digital health access; 326 patients expressed interest and became the study population. These patients were sent the study description and a secure Qualtrics link to the online survey.

Statistical Analysis

Descriptive statistics using Microsoft Excel were used to summarize participant demographics and survey responses. Frequencies were calculated for categorical variables. No inferential or hypothesis testing was conducted, as the study aimed to characterize trends and patient-reported experiences rather than test associations or determine causality.

Ethical Considerations

This study received exempt certification from the UCSF medical ethical review committee (IRB 21 - 33538). All participants provided consent to participate in the study, and their responses were deidentified.

Results

Of 326 individuals, 207 completed the survey (63.5% response rate). A majority of individuals (n=166/207, 80.2%, 95% CI

74.8% - 85.6%) reported that environmental-climate factors impact their AD, particularly extreme heat (n=157, 75.8%, 95% CI 70.0% - 81.7%) and poor air quality (n=81, 39.1%, 95% CI 32.5% - 45.8%). Commonly reported effects included increased medication use (n=168, 81.2%, 95% CI 75.8% - 86.5%), more symptomatic flares (n=167, 80.7%, 95% CI 75.3% - 86.1%), more skin affected (n=139, 67.1%; 95% CI 60.8% - 73.5%), and changes to daily behaviors (n=130, 62.8%; 95% CI 56.2% - 69.4%). Most participants (n=179, 86.5%; 95% CI 81.8% - 91.1%) expressed interest in understanding how environmental-climate factors affect their AD, yet only 76 participants (36.7%; 95% CI 30.1% - 43.3%) said their dermatologist addressed these concerns. The most valued strategies for addressing climate-health impacts included more information (n=164, 79.2%; 95% CI 73.7% - 84.8%), dedicated time during visits to plan for exposures (n=105, 50.7%; 95% CI 43.9% - 57.5%), and more in-person visits (n=101, 48.8%; 95% CI 42.0% - 55.6%). Table 1 shows participant characteristics, and Table 2 shows survey response data.

Table . Participant demographics and background information.

Demographics	Participants (N=207)
Age in years (mean, SD)	46.4 (18.6)
Sex, n (%)	
Male	75 (36.2)
Female	129 (62.3)
Nonbinary	3 (1.4)
Race/Ethnicity, n (%)	
American Indian or Alaskan Native	2 (1.0)
Asian or Asian American	82 (39.6)
Black or African American	12 (5.8)
Hispanic or Latino	12 (5.8)
Native Hawaiian or Pacific Islander	1 (0.5)
White	107 (51.7)
Other	5 (2.4)
Years living with atopic dermatitis (mean, SD)	21.6 (18.3)
Treatments used for atopic dermatitis, n (%)	
Topical steroid	193 (93.7)
Topical medication other than a steroid	145 (70.4)
Topical over the counter product (does not require a prescription)	139 (67.4)
Pill medication (eg, methotrexate, cellcept, tofacitinib, upadacitinib)	47 (22.8)
Injection medication (eg, dupilumab, tralokinumab)	94 (45.6)
Phototherapy	41 (19.9)

Table . Responses to survey questions using the 5-point Likert scale, where 1 indicates “Strongly disagree,” 2 “Somewhat disagree,” 3 “Neutral,” 4 “Somewhat agree,” and 5 “Strongly agree.” A reported mean greater than 3 indicates agreement and less than 3 indicates disagreement.

Statement, agreement ranked using the 5-point Likert scale	Score, mean (SD)
Climate and environmental factors have impacted your experience with eczema	4.2 (1.0)
The following factor has impacted your experience with eczema:	
Extreme Heat	4.2 (1.1)
Wildfires	3.3 (1.1)
Poor Air Quality	3.4 (1.1)
Drought	3.2 (1.1)
Extreme Rainfall	3.0 (1.3)
Sea Level Rise	2.4 (1.0)
Flooding	2.6 (1.1)
Climate and environmental factors’ impact on your eczema include:	
More symptomatic with exacerbations or flares	4.2 (1.0)
More skin affected	3.9 (1.2)
Need for extra appointments with healthcare team	3.1 (1.2)
Sending additional messages to dermatologist or calling their office	3.0 (1.2)
Using medication more often	4.1 (1.0)
Change to your medication	3.2 (1.3)
Change to lifestyle or daily behaviors	3.8 (1.1)
You want to know how the climate and environment impact your eczema	4.2 (1.0)
Your dermatologist has talked about how the climate and environment affect your eczema	2.9 (1.3)
This strategy would be helpful in managing changes to your eczema from the climate and environment:	
More visits in person	3.4 (1.1)
More telehealth visits	3.2 (1.1)
Time during visits to make plans for climate or environmental problems	3.5 (1.1)
More information on the topic	4.1 (0.9)
Support groups	2.9 (1.1)

Discussion

Principal Findings

While this study does not evaluate clinical causality, it provides novel insight into how patients perceive and experience the effects of environmental-climate factors on their AD. Most participants perceived climate-related changes in their AD and desired clinical guidance, yet few reported receiving it. These findings suggest that dermatologists should initiate brief conversations about common triggers, particularly heat and air pollution, and provide anticipatory guidance and resources. This insight underscores previously reported low self-efficacy among dermatologists in discussing climate change with patients [4]. Understanding these patient insights is vital to providing patient-centered care and forming effective partnerships with patients about their skin health. These efforts align with the American Academy of Dermatology’s commitment to “educate our patients about the effects of climate change on the health of their skin.” [6]

Limitations and Future Direction

Limitations include a single-center design limiting generalizability, reliance on self-reported data with potential recall bias, and possible self-selection bias, as patients more affected by climate change may have been more likely to participate. Future research should validate these findings in broader populations, explore climate-health experiences in other skin conditions, and develop educational and clinical strategies to help navigate these climate-health conversations with patients. Even in short visits, dermatologists can explore patient experiences with climate change using supportive prompts (eg, “Would it be helpful to discuss how environmental factors might relate to your flares?”) to validate patient concerns and provide opportunities for personalized climate-health conversations to be continued in subsequent visits.

Conclusions

This study highlights a disconnect between how patients with AD experience climate-related triggers and how often these

concerns are addressed in clinical care. Findings underscore the need for tools and strategies to support climate-health conversations in dermatology. Integrating environmental health into AD management can enhance patient-centered care, improve outcomes, and reinforce dermatology's role at the intersection of clinical care, public health, and patient advocacy.

Data Availability

The datasets generated or analyzed during this study are available from the corresponding author on reasonable request.

Conflicts of Interest

None declared.

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Abbreviations

AD: atopic dermatitis
EHR: electronic health record
UCSF: University of California, San Francisco

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Differences in Electronic Consultation Conversion Rates Between Advanced Practice Providers and Board-Certified Dermatologists

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Abstract

In this analysis of dermatology e-consults at a large academic health system, advanced practice providers had nearly threefold higher conversion rates to in-person visits compared to board-certified dermatologists, with potential implications for access and resource utilization.

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KEYWORDS

e-consult; telehealth; dermatology; advanced practice provider; teledermatology

Introduction

Electronic consultations (e-consults) have become an increasingly valuable tool in improving access to specialty care, reducing unnecessary in-person referrals, and supporting timely management of patients by primary care providers [1,2]. By allowing clinicians to consult with specialists asynchronously through the electronic health record, e-consults can help streamline workflows, decrease wait times, and conserve specialist resources [2,3]. Dermatology services receive a high number of e-consult requests, likely due to the visual diagnostic nature of the specialty [3,4]. As the use of e-consults expands across health care systems, understanding how different provider types use this tool, particularly in high-demand specialties such as dermatology, is critical to optimizing efficiency and effectiveness. Furthermore, identifying whether variations in conversion patterns reflect provider-level practice differences or system-level routing processes is essential for ensuring that e-consults function as intended.

Methods

We conducted a retrospective analysis to evaluate whether e-consult conversion rates differed by provider type, specifically comparing advanced practice providers (APPs), including nurse practitioners and physician assistants, to board-certified dermatologists. e-consult data specific to dermatology were extracted from the University of Colorado Hospital electronic health record system for the period of January 2020 to April 2025. An e-consult was considered “converted” if it resulted in a subsequent in-person specialist visit or full referral, rather than being resolved entirely through asynchronous communication.

In this system, e-consults are routed to APPs versus dermatologists primarily based on provider availability rather than consult content or patient acuity. As a result, patients evaluated by APPs and physicians likely represent comparable clinical populations, reducing the likelihood that differences in conversion rates were driven by systematic triage of more complex cases to one provider group.

Results

A total of 2572 dermatology e-consults were submitted during the study period. Of these, 1205 were addressed by APPs, with 321 (26.6%) resulting in conversion to an in-person visit (Table 1). In contrast, only 125 of the 1367 e-consults addressed by physicians (9.1%) were converted (Table 2). e-consults managed by APPs were nearly three times more likely to lead to an in-person referral compared to those managed by physicians.

Table . Total number and percentage of e-consults converted from advanced practice professionals.

e-consult converted	N (%)
No	884 (73.4)
Yes	321 (26.6)
Total	1205 (100.0)

Table . Total number and percentage of e-consults converted from dermatologists.

e-consult converted	N (%)
No	1242 (90.9)
Yes	125 (9.1)
Total	1367 (100.0)

Discussion

This analysis reveals a notable difference in e-consult conversion rates between APPs and physicians. This disparity suggests potential differences in how each provider group approaches triage and decision-making in specialty care. If APP-handled e-consults were converted at the same rate as physician-handled e-consults, over 200 additional dermatology clinic appointments during the study period may have been available for patients with higher-acuity needs. Despite this variation in appointment conversion, it is important to note that the majority of e-consults from both groups were resolved without the need for in-person follow-up. This reinforces the broader value of e-consults in improving efficiency and reducing unnecessary specialist visits and aligns with current literature [2,3].

The higher conversion rate observed among APPs may reflect a range of underlying factors. One possibility is that APPs may be more likely to convert e-consults conservatively due to comparatively less specialty-specific training or comfort managing complex cases. Importantly, in our system, APPs and dermatologists receive e-consults based largely on provider availability rather than clinical complexity. This reduces the likelihood that differences in patient or case characteristics explain the observed variation. Existing literature on provider-level differences in e-consult use and impact have shown mixed results. For example, one study comparing e-consults submitted by nurse practitioners and family physicians found that nurse practitioners were more likely to report that the consultation led to new clinical guidance and less likely to say it avoided an in-person referral [5]. In contrast, a systematic review of referral practices found no significant difference in overall referral rates between nurse practitioners and family physicians [6]. However, these studies largely examine differences among referring providers rather than responding providers. Because our study investigates variation among the providers performing the e-consults themselves, it represents a novel contribution to the literature. To our knowledge, no published studies have specifically examined provider-level variation in dermatology e-consult outcomes from the specialist side, underscoring the importance of our findings.

While our findings shed light on differences in provider behavior, they also raise questions about the clinical appropriateness of these conversions. Without detailed outcome data, it remains unclear whether the higher conversion rate among APPs were clinically necessary or reflective of a lower threshold for referral. Future research should explore the clinical drivers and downstream outcomes of converted e-consults, considering patient complexity, consult content, and specialty-specific considerations.

In addition to clinical impact, the higher conversion rate among APPs may have broader implications for system efficiency and resource use. Given the higher conversion rate, APP-managed e-consults may increase health care utilization, with potential cost implications for patients and health systems. Assuming a standard new patient visit billed at a level 3 or level 4 (estimated reimbursement US $120–$180 per visit), the additional ~200 appointments potentially consumed due to higher APP conversion rates translates to an estimated US $24,000–$36,000 in additional health care costs during the study period. Future work could further investigate whether these conversions lead to improved outcomes or represent avoidable costs.

This study contributes to the growing body of literature on e-consult optimization and provider practice variation. As health systems increasingly adopt team-based models of care and integrate APPs more fully into specialty workflows, ensuring consistent and effective use of e-consults across provider types will be essential. Implementing structured guidance, standardized triage protocols, and targeted training modules, particularly for APPs, may help promote more consistent decision-making and appropriate referral thresholds. Additionally, health systems may consider establishing limitations or clinical guidelines regarding the types of dermatologic conditions appropriate for independent APP e-consult management to ensure high-quality care, reduce unnecessary referrals, and minimize avoidable health care costs. By equipping all members of the care team with the tools and guidance needed to manage e-consults effectively, we can improve access, preserve specialist capacity, and enhance the overall efficiency of care delivery.

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Data Availability

All data generated or analyzed during this study are included in this published article.

Authors' Contributions

Conceptualization: DH, SN
Data curation: SN
Formal analysis: DH, SN
Investigation: DH
Methodology: DH, SN
Supervision: SN
Validation: DH, SN
Writing – original draft: DH, SN
Writing – review & editing: DH, SN

Conflicts of Interest

None declared.

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Abbreviations

APP: advanced practice provider
E-consults: electronic consultations

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Chronic Facial Abscess Mimicking Cervicofacial Actinomyces From Dermal Filler Migration: Case Report

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Abstract

Dermal fillers are commonly used for facial augmentation, but delayed complications such as granulomatous inflammation and filler migration can mimic chronic bacterial infections, such as cervicofacial actinomycosis, and lead to diagnostic misdirection. We present the case of a woman aged 56 years with a chronic, draining abscess on the right cheek that persisted for 3 years and was initially suspected to represent cervicofacial actinomycosis. Tissue cultures were negative, and histopathologic analysis following excisional biopsy revealed polymethyl methacrylate microspheres and hyaluronic acid surrounded by granulomatous inflammation and reactive lymphoid aggregates, consistent with a foreign body reaction to dermal filler. The patient experienced complete resolution after surgical excision. This case underscores the diagnostic challenges posed by delayed filler complications and highlights the importance of considering prior cosmetic procedures in patients with chronic facial abscesses.

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KEYWORDS

dermal filler; foreign body reaction; facial abscess; granulomatous inflammation; filler complications; cosmetic dermatology

Introduction

The use of dermal fillers for facial augmentation has increased significantly, with both temporary (hyaluronic acid) and semipermanent or permanent fillers (polymethyl methacrylate [PMMA], calcium hydroxylapatite, silicone) [1]. While most complications occur immediately or within weeks, delayed reactions, including granuloma formation and filler migration, can present months to years after injection [2].

Foreign body granulomas are a known complication of PMMA-based fillers (Bellafill/Artefill; Suneva Medical Inc) and result from a chronic inflammatory response to nondegradable microspheres [3]. These reactions may be triggered by delayed hypersensitivity, biofilm formation, or immune dysregulation and can resemble infectious or inflammatory processes. They can also closely mimic chronic infectious processes such as cervicofacial actinomycosis, characterized by draining sinuses and subcutaneous abscesses, often prompting an extensive infectious workup before the true etiology is recognized [4]. Diagnosis relies on histopathologic evaluation, which typically reveals multinucleated giant cells, lymphoid aggregates, and fibrosis surrounding filler particles [3,4].

This case highlights the importance of early recognition of iatrogenic causes in the differential diagnosis of chronic facial abscesses and underscores the long-term risks associated with semipermanent fillers, particularly PMMA-based products. Given the varied histopathologic presentations of different filler materials, distinguishing PMMA from other injectables is crucial for accurate diagnosis and management.

Ethical Considerations

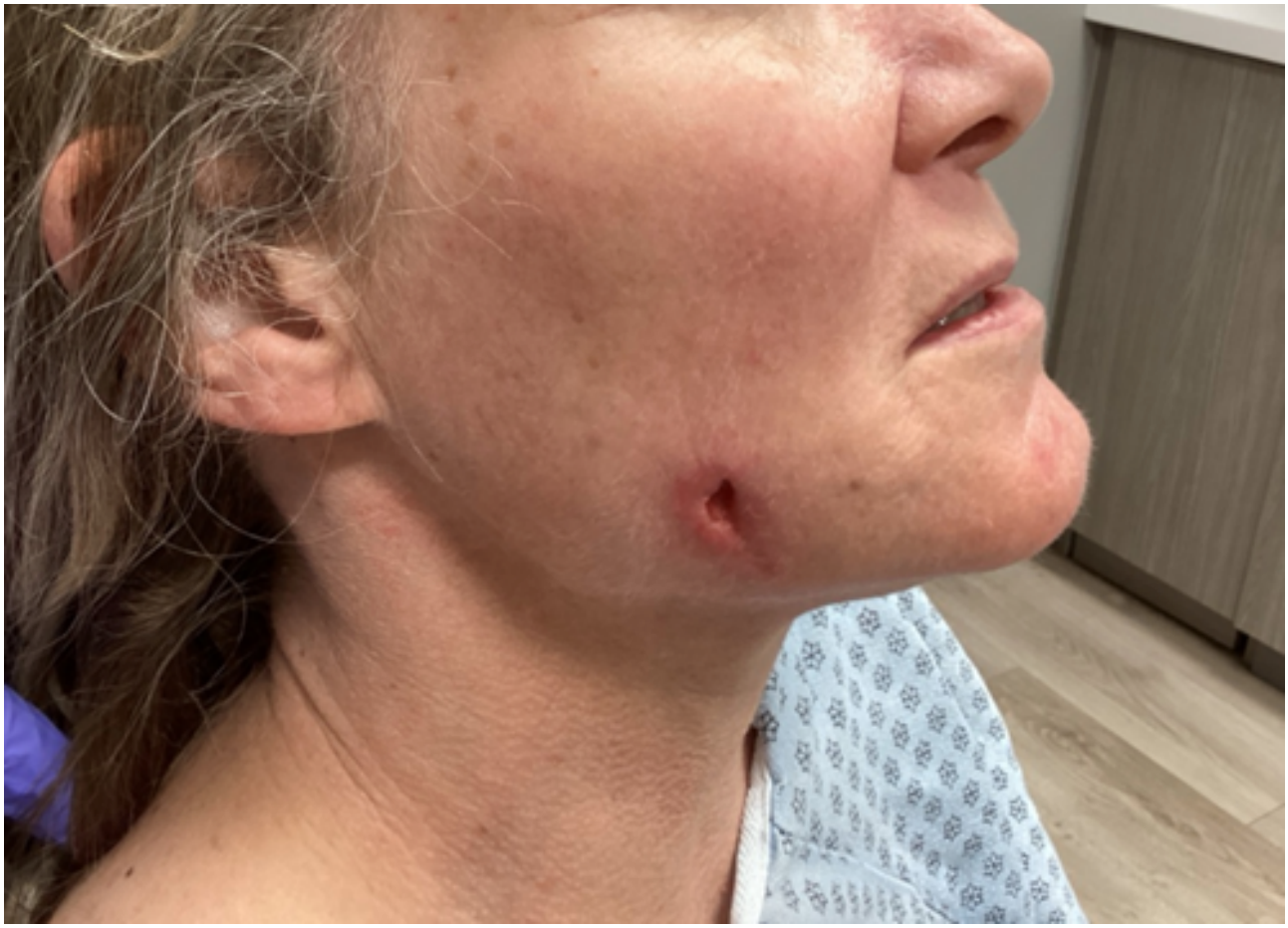
The authors obtained written consent from the patient for their photographs and medical information to be published in print and online, with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors.

Case Report

A woman aged 56 years presented with a chronic, nonhealing, draining abscess localized to the right cheek. Characterized by intermittent drainage, localized tenderness, and surrounding erythema, the nodule persisted for approximately 3 years, during which time the patient sought care from specialists on at least one occasion. The patient denied systemic symptoms such as fever, chills, dental caries, oral drainage, pain with salivation, or malaise. Past medical history was noncontributory, and the patient had no known history of immunosuppression, diabetes, or recurrent skin infections.

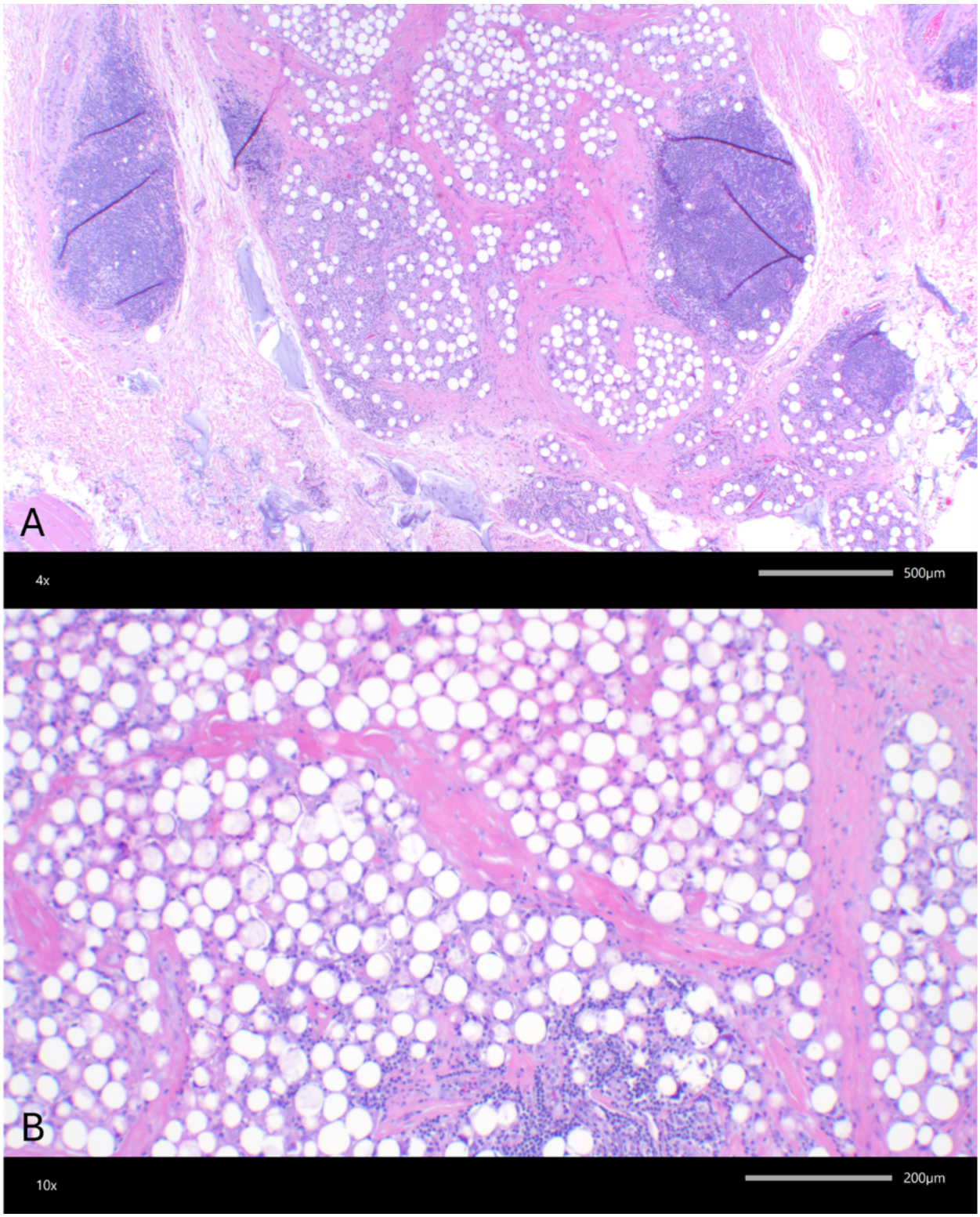
On physical examination, the deep nodule was ulcerated, with erythematous borders localized to the right inferior central malar cheek. The ulcer base exhibited crusting and purulent material, with 3 cm of surrounding induration (Figure 1). No regional lymphadenopathy was present.

Figure 1. Nonhealing ulcer with surrounding erythema and induration on the right cheek.



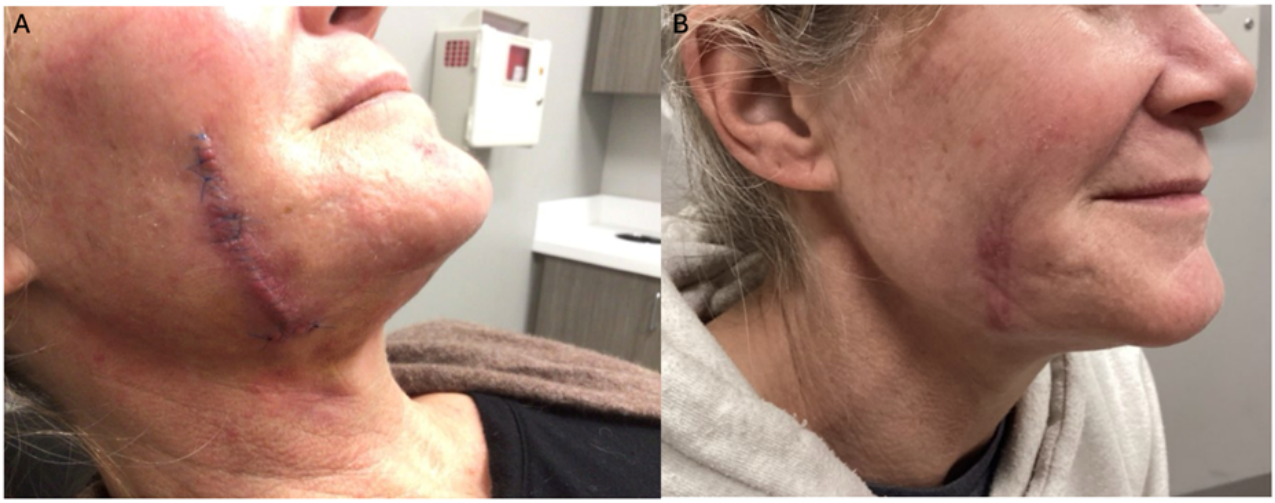
Given the persistent nature of the abscess, a tissue culture was obtained via punch biopsy, which was negative for bacterial, fungal, and atypical mycobacterial growth. Due to the size and depth of the lesion, an excisional biopsy was performed to identify potential inflammatory or neoplastic pathology. Histopathologic analysis (Figure 2) revealed foreign body granulomas with abundant reactive lymphoid tissue, along with an accumulation of PMMA microspheres and hyaluronic acid, consistent with semipermanent dermal fillers. Surrounding granulomatous inflammation was also noted. Special stains, including Grocott methenamine silver, Fite, and Gram stains, were negative for fungi, mycobacteria, and bacteria, ruling out infectious etiologies.

Figure 2. Histologic features consistent with a foreign body reaction to polymethylmethacrylate (PMMA) filler. (A) Incisional biopsy with numerous rounded vacuolated spaces, 30 - 50 µm in size, consistent with PMMA spherules and surrounding granulomatous inflammation and reactive lymphoid aggregates. Adjacent homogeneous basophilic material consistent with hyaluronic acid is also present (hematoxylin and eosin stain; 4x). (B) Higher magnification of PMMA spherules (hematoxylin and eosin stain; 10×).



The patient was seen for suture removal at 1 week (Figure 3) with an uneventful postoperative course. At 4 weeks postoperatively, the surgical site was well healed, with no signs of infection or recurrence (Figure 3). Although initially unable to recall prior dermal filler use, review of the pathology report prompted the patient to remember having received Bellafill (Suneva Medical Inc) approximately 6 years prior and Restylane (Galderma Laboratories) approximately 10 years earlier, both for treatment of acne scarring on the cheeks.

Figure 3. (A) Postoperative appearance at 1 week showing early healing. (B) Postoperative appearance at 4 weeks with complete resolution and no recurrence.



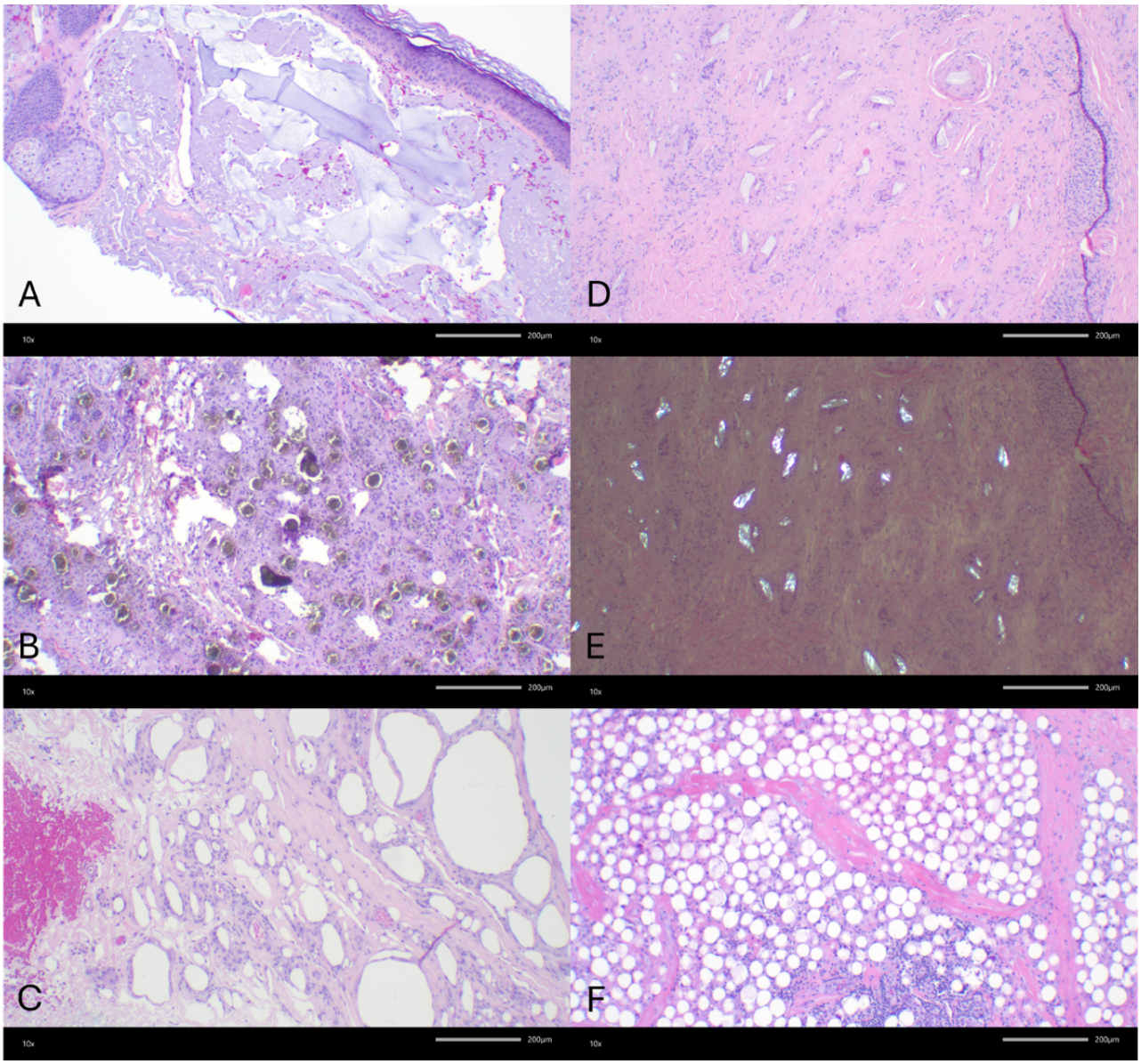
Discussion

While dermal fillers are widely used for aesthetic enhancement, their delayed complications remain an evolving area of clinical concern. Although most adverse reactions occur shortly after injection, late-onset complications can develop months to years later, often leading to diagnostic uncertainty [5]. Unlike temporary hyaluronic acid–based fillers, PMMA and other nondegradable materials persist within tissues long-term, increasing the risk of prolonged inflammatory responses [6]. The delayed presentation of PMMA-related granulomas frequently results in misdiagnosis as infection or inflammatory dermatoses, delaying appropriate intervention [7].

While complications such as filler migration and granulomatous reactions are well documented, the development of a chronic filler reaction mimicking a cervicofacial actinomycetoma is rare. Actinomycetomas are chronic, subcutaneous infections caused by filamentous bacteria, characterized by abscesses, draining sinuses, and granule production [8]. The striking clinical resemblance between the foreign body granuloma in this case and a deep-seated actinomycotic infection underscores the diagnostic challenges posed by delayed filler reactions. This case highlights the need for broad infectious and histopathologic workups in atypical, chronic soft tissue infections to prevent unnecessary antibiotic treatment and delayed surgical intervention.

Histopathologic evaluation is essential for diagnosing PMMA-related granulomas, which are characterized by multinucleated giant cells, chronic lymphohistiocytic infiltrates, and fibrosis surrounding filler particles [9]. In this case, a negative infectious workup and biopsy findings of PMMA microspheres with reactive lymphoid tissue confirmed the diagnosis and guided treatment. Management remains challenging, as PMMA-based fillers lack a reversal agent comparable to that of hyaluronic acid fillers [10]. While intralesional corticosteroid injections may offer partial improvement, surgical excision is often required for definitive diagnosis and treatment, as in this case [4]. Given the histologic variability among filler types, distinguishing PMMA granulomas from reactions to calcium hydroxylapatite, poly-L-lactic acid, and silicone is critical for guiding optimal management strategies (Figure 4).

Figure 4. Histologic features consistent with foreign body reactions to soft tissue augmentation materials. (A) Pools of wispy homogeneous basophilic material consistent with hyaluronic acid (hematoxylin and eosin; 10×). (B) Gray-green granular nonrefractile microspheres consistent with calcium hydroxylapatite with surrounding granulomatous inflammation (hematoxylin and eosin; 10×). (C) Variably sized empty lipidlike vacuoles within histiocytes consistent with silicone granuloma (hematoxylin and eosin; 10×). (D) Oval, rhomboidal, and rice-shaped clear refractile and polarizable structures consistent with poly-L-lactic acid (PLLA) particles within histiocytes (hematoxylin and eosin; 10×). (E) Polarization of PLLA fragments (hematoxylin and eosin; 10×). (F) Fairly uniform 30 - 50-µm rounded vacuolated spaces consistent with polymethylmethacrylate spherules (hematoxylin and eosin; 10×).



While PMMA fillers are used less frequently than hyaluronic acid–based products, their potential for chronic inflammatory complications requires heightened clinical awareness and a detailed risk-benefit discussion prior to injection. Semipermanent fillers pose unique challenges due to their prolonged tissue retention and risk of delayed reactions. Clinicians should maintain a high index of suspicion for foreign body granulomas and probe for a history of prior filler use in cases of chronic, nonhealing facial abscesses, particularly when standard antimicrobial therapy fails or imaging reveals localized nodularity. Following excision, patients should be informed of and monitored for delayed recurrence as well as contralateral lesions, as these may occur months to years later. This case highlights the value of histopathologic microbiologic evaluation in diagnosing facial abscesses, the limitations of nonsurgical management for PMMA-induced granulomas, and the need for increased awareness of iatrogenic factors in chronic soft tissue reactions.

Conflicts of Interest

None declared.

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Abbreviations

PMMA: polymethyl methacrylate

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