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# JMIR Dermatology

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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

Volume 7 (2024) ISSN 2562-0959 Editor in Chief: Robert Dellavalle, MD, PhD, MSPH

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Original Paper

# A Content Analysis of Indoor Tanning Twitter Chatter During COVID-19 Shutdowns: Cross-Sectional Qualitative Study

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## Abstract

**Background:** Indoor tanning is a preventable risk factor for skin cancer. Statewide shutdowns during the COVID-19 pandemic resulted in temporary closures of tanning businesses. Little is known about how tanners reacted to losing access to tanning businesses.

**Objective:** This study aimed to analyze Twitter (subsequently rebranded as X) chatter about indoor tanning during the statewide pandemic shutdowns.

**Methods:** We collected tweets from March 15 to April 30, 2020, and performed a directed content analysis of a random sample of 20% (1165/5811) of tweets from each week. The 2 coders independently rated themes ( $\kappa=0.67-1.0$ ; 94%-100% agreement).

**Results:** About half (589/1165, 50.6%) of tweets were by people unlikely to indoor tan, and most of these mocked tanners or the act of tanning (562/589, 94.9%). A total of 34% (402/1165) of tweets were posted by users likely to indoor tan, and most of these (260/402, 64.7%) mentioned missing tanning beds, often citing appearance- or mood-related reasons or withdrawal. Some tweets by tanners expressed a desire to purchase or use home tanning beds (90/402, 22%), while only 3.9% (16/402) mentioned tanning alternatives (eg, self-tanner). Very few tweets (29/1165, 2.5%) were public health messages about the dangers of indoor tanning.

**Conclusions:** Findings revealed that during statewide shutdowns, half of the tweets about indoor tanning were mocking tanning bed users and the tanned look, while about one-third were indoor tanners reacting to their inability to access tanning beds. Future work is needed to understand emerging trends in tanning post pandemic.

(*JMIR Dermatol* 2024;7:e54052) doi:[10.2196/54052](https://doi.org/10.2196/54052)

## KEYWORDS

attitude; attitudes; content analysis; dermatology; opinion; opinion; perception; perceptions; perspective; perspectives; sentiment; skin; social media; social media; sun; tan; tanner; tanners; tanning; tweet; tweets; Twitter

## Introduction

In the United States, 1 in 5 people will develop skin cancer in their lifetime [1]. Melanoma, the deadliest type of skin cancer, is the most common cancer among young adults aged 25-29 years [2]. Excessive exposure to UV radiation from either the sun or artificial sources (eg, tanning beds) is a major risk factor

for skin cancer [3]. On March 11, 2020, the World Health Organization declared COVID-19 a pandemic, and states across the United States enforced stay-at-home orders, forcing businesses to close their doors. The shutdowns in the United States served as a natural experiment of the impact of tanning businesses closing on indoor tanners, as demand for tanning services tends to peak between January and June, coinciding

with the COVID-19 2020 shutdowns [4]. Twitter (subsequently rebranded as X) data may be useful for understanding indoor tanning attitudes, given that young adults who are indoor tanning are almost twice as likely to use Twitter regularly than those who do not [5]. Another study assessed the frequency of mentions of indoor tanning on Twitter and found that in a 2-week period, 120,354 unique users made 154,486 tweets that mentioned the words indoor tanning, tanning bed, tanning booth, tanning salon, sun bed, or sun lamp, and these tweets reached 113,888,616 users [6].

Other studies have delved into the content of tweets about indoor tanning. For example, 1 study examined tweets that contained the phrases “tanning bed” or “tanning salon” and found that most tweets (71.2%) were posted by tanners and either expressed positive sentiment about indoor tanning, negative tanning bed experiences, or tanning-related injuries [7]. Another study of tweets containing keywords for tanning bed use and burning revealed that in 2013, over 15,000 had these keywords, and 64% described a tanning bed–induced burn [8]. Together, these studies reveal that Twitter may provide insights into tanners’ attitudes and behaviors.

This study aimed to examine Twitter chatter about indoor tanning during the COVID-19 shutdowns (March 15 to April 30, 2020). Stay-at-home orders became colloquially known by several terms, such as “shutdowns” and “lockdowns,” but all terms refer to the orders issued by local and state officials that limited business activities to those deemed essential (eg, grocery stores, pharmacies, and hospitals) and limited residents’ “nonessential” travel outside of the home [9]. The majority of stay-at-home orders (eg, shutdowns) began in March 2020, and by March 31, 2020, a total of 42 states and US territories had issued stay-at-home orders, affecting 73% of all US counties [10,11]. Location data from mobile devices suggest that compliance with restrictions was high, with 97.6% of counties with mandatory stay-at-home orders reporting a decrease in

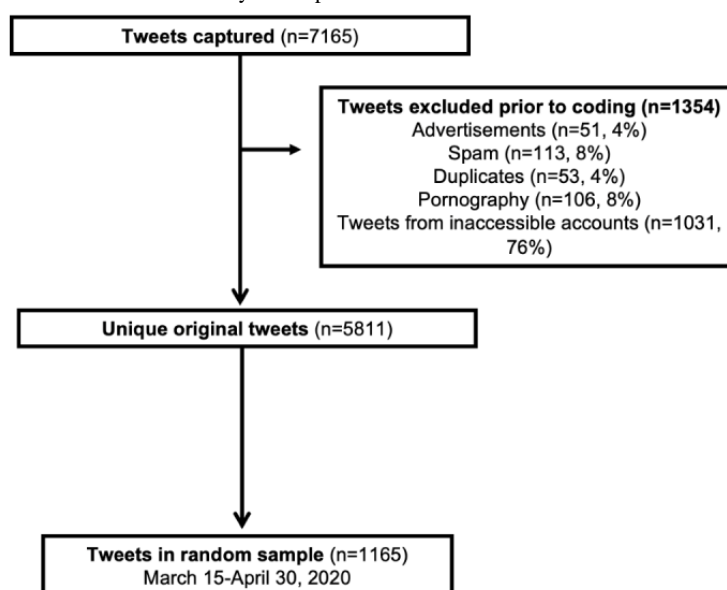
median population movement immediately after the start dates of the stay-at-home orders [10]. We were interested in whether tanners found alternative means of accessing tanning beds if they discussed interest in UV tanning alternatives (eg, sunless tanners), and their reactions to having no access to commercial tanning beds. Given the proliferation of misinformation about the impact of UV radiation on COVID-19 that appeared to have begun after former US President Donald Trump proposed the idea that UV light could be used inside the body to remedy COVID-19 [12], we also examined the presence of misinformation in tweets about tanning beds [13,14].

## Methods

### Overview

This was a cross-sectional qualitative study of public tweets about indoor tanning during the COVID-19–related shutdowns. We searched Twitter for 2 common lay terms, “tanning bed” and “tanning salon,” that refer to “indoor tanning,” a public health term that refers to tanning using artificial UV light–producing devices [7,15]. Using the R package (R Foundation for Statistical Computing) *rtweet*, we captured tweets that occurred between March 15, 2020, one of the first days of the COVID-19 statewide business shutdowns, and April 30, 2020 [16,17]. We excluded retweets because our interest was in the original thoughts of users, but we included “quote tweets,” which contain the tweeter’s own sentiments. We removed tweets that were advertisements, pornography, or from accounts that became private or were suspended between the data capture and the qualitative coding process in April 2021 (Figure 1). Of the 5811 tweets captured, we randomly sampled 20% (n=1165) of eligible tweets captured per week during the sampling window to capture conversation from the entire sampling window, consistent with other studies of tweets [18]. Table 1 contains paraphrased tweets to protect the privacy of the users.

**Figure 1.** Tweet sampling and the construction of the analytic sample.



**Table 1.** Topics of tweets (n=1165) about indoor tanning on Twitter during statewide shutdowns (March 15 to April 30, 2020), by user type. Tweets could be coded in more than 1 tweet category.

Tweet category by user type	Tweets, n (%)	Illustrative examples <sup>a</sup>
<b>People who likely do not tan indoors (n=589 tweets)</b>		
Mocking tanners, tan people, or the act of tanning	562 (95.4)	Some people are about to meet their real girlfriends for the first time with the tanning bed closed hahaha.
Mocking tweets mentioning Donald Trump	448 (76.1)	Trump went in the tanning bed too long. Looks like a burnt Cheeto.
Health warnings	30 (5.1)	Sorry if you're a person that uses the tanning bed, you are ruining your skin's health and look! Proud to be pale and skin cancer free. I used to tan in a tanning bed, but you get older and your wrinkles hide small objects.
<b>People likely to tan indoors (n=402 tweets)</b>		
<b>Missing tanning</b>	260 (64.7)	I need the tanning bed to reopen, being pale makes me depressed. Having serious tanning bed withdrawals, this is killing me!
Appearance-related missing tanning	77 (30)	I need the tanning bed to open back up. I look so pale I can't stand it.
Mood-related missing tanning	13 (5)	I need the tanning bed to reopen, that's my stress reliever!
Withdrawal from indoor tanning	12 (4.6)	Anyone else going through tanning bed separation anxiety? This hurts
Expressing a desire to buy a home tanning bed, bought a tanning bed, or looking to use someone else's home tanning bed	90 (22.4)	I will buy a tanning bed if this quarantine continues. PSA who's got a tanning bed for me to use?! I'm desperate.
Positive sentiment about tanning	69 (17.2)	So happy I have a tanning bed during this, I need to be tan.
Use of alternative behaviors	15 (3.9)	Give me some recs for self-tanners since my tanning salon is closed! Ordered some self-tanner because this no tanning bed thing is killing me.
Arguments against messages that tanning is unhealthy or presents indoor tanning misinformation	24 (6)	Let's reopen the tanning salon, I think we can all agree that UV light will help kill the virus.
Other	27 (6.9)	Burnt my face in the tanning bed and now I don't look good.
<b>Tanning salon employees (n=4 tweets)</b>		
Tanning salon employee chatter	4 (100)	Will these mandatory closing impact the tanning salon I work at?
<b>People whose tweets do not indicate whether they indoor tan (n=170 tweets)</b>		
Unrelated to indoor tanning, tweets by people who do not indoor tan, or unclear whether the speaker is a tanner	168 (98.8)	That tanning bed scene in the final destination movie is creepy.
Argues against messages that tanning is unhealthy or presents indoor tanning misinformation	2 (1.2)	I'm gonna open a coronavirus clinic, ordered a tanning bed and some Lysol. I'll save everyone!

<sup>a</sup>While all tweets included in the analysis were posted publicly, to protect the privacy of individuals who posted these tweets, we paraphrased the words of tweets in a way that prevents the content of the tweet from being searchable without changing its meaning.

## Statistical Analysis

We conducted a directed content analysis of tweets using a codebook from our 2016 Twitter study about indoor tanning [7,19]. We modified the codebook after examining a subsample of 100 tweets. The original codebook had 9 codes: a desire to use a tanning bed, sleeping in a tanning bed, tanning-related injury, a complaint about or negative experiences tanning, tanning salon employee chatter, mocking tanners or tanning, health warnings about indoor tanning, pushback against "tanning is unhealthy" messaging or antitanning legislature, and references to indoor tanning in the context of an unrelated topic (eg, movie quote). We expanded the codebook to include 3 additional codes for tweets in which the user expressed that

they missed being able to go indoor tanning, expressed a desire to buy a home tanning bed, crowdsourced followers to use a home tanning bed, and mentioned the use of UV tanning alternatives (eg, self-tanners). We eliminated 3 codes (ie, sleeping in a tanning bed, tanning-related injury, a complaint about, or negative experiences) because they were not represented within the current data set. We also coded tweets as posted by people who were likely to indoor tan (based on their admission of tanning or having tanned in their tweets), tanning salon employees (based on the content of their tweets), people who are not likely to indoor tan (based on their mocking indoor tanning or discussing the risks of indoor tanning), and people whose tweets do not indicate if they indoor tan or not. If a tweet seemed to be posted by a tanning salon employee but

referred to their individual tanning behavior, we coded the tweet as being posted by someone likely to indoor tan. After finalizing the codebook, 2 coders independently coded all 1165 tweets (100% double-coded). Discrepantly coded tweets were discussed to reach a consensus.

We calculated interrater reliability and Cohen  $\kappa$  for each coding category. Interrater agreement of tweet categories ranged from 94% to 100%, and Cohen  $\kappa$  statistics ranged from 0.6654 to 1.0. Interrater agreement among coders was 94% ( $\kappa=0.9106$ ). We summarized the proportion of tweets posted by those likely to indoor tan, tanning salon employees, those unlikely to indoor tan, and those whose tweets do not indicate whether they indoor tan. We then reported the frequency of tweet categories by user types. Analyses were conducted using SAS 9.4 (SAS Institute, Inc).

## Ethical Considerations

This study does not meet the definition of human participants research and thus did not require Institutional Review Board approval. However, to protect the privacy of users who may not expect public tweets to be used in research, we paraphrased tweets to render the tweet's content unsearchable while preserving the meaning. We confirmed that the paraphrased content did not produce the original tweet through searches.

## Results

### Overview

In our final sample of 1165 tweets, 1144 (98%) were posted by unique Twitter accounts. A total of 93% (1084/1165) of tweets in our analytic sample were from the search term "tanning bed," while only 7% (81/1165) were from the search term "tanning salon."

Half of the tweets (589/1165, 50.6%) came from users unlikely to indoor tan, while 34.5% (402/1165) were posted by users who seemed likely to indoor tan (Table 1). Very few tweets (4/1165, 0.4%) appeared to be posted by tanning salon employees, and in the remaining 14.5% (170/1165) of tweets, the content did not clearly indicate whether the user was an indoor tanner.

### Tweets From People Unlikely to Indoor Tan

The majority (562/589, 95%) were classified as mocking tanners, tan people, or the act of tanning. Among these, the majority (446/589, 75.7%) mocked former US President Donald Trump's skin tone, and 20.6% (116/589) mocked the appearance of tanners and the use of tanning beds in general. The remaining 5% (30/589) of tweets from users unlikely to be indoor tanners contained health warnings about indoor tanning.

### Tweets From People Likely to Indoor Tan

Nearly two-thirds (260/402, 64.7%) were coded as "missing tanning," meaning the user expressed they missed tanning, their frustration that they could not go tanning, or their eagerness to get back to tanning (Table 1). Within this category, 60% (156/260) of tweets did not mention a specific reason they missed tanning, but 30% (77/260) indicated they missed indoor tanning for appearance-related reasons, 5% (13/260) indicated

they missed indoor tanning for mood-related reasons, and 5% (12/260) indicated withdrawal symptoms from being restricted from indoor tanning. The second most common theme among tweets from likely tanners was general positive attitudes about indoor tanning (69/402, 17.2%), followed by the desire to buy a home tanning bed or use someone else's (90/402, 22.3%), misinformation about tanning (24/402, 6%), and finally, use of alternative tanning methods such as self-tanner and bronzer makeup (16/402, 3.9%; Table 1).

### Other Tweets

The content of the remaining tweets (170/174, 98.8%) made it unclear whether the user was an indoor tanner. The vast majority (165/170, 95.9%) mentioned tanning beds in the context of an unrelated topic (eg, movie scene). Tweets posted by tanning salon employees ( $n=4$ ) were rare and included observations of occurrences in the workplace.

## Discussion

### Overview

About half of the tweets (589/1165, 50.6%) using the keywords "tanning bed" or "tanning salon" during the COVID-19 pandemic shutdowns in March and April 2020 were not by people who likely use tanning beds. Most of these tweets were mocking people who tan, tanning beds, or the tanned look. The next largest set of tweets (402/1165, 34.5%) seemed to be by people who use tanning beds, as evidenced by their content, which focused on lamenting the inability to tan during the shutdown, expressing the desire for a home tanning bed, expressing positive sentiment about tanning beds, discussing alternative ways to get a tan in the absence of tanning beds, or promoting misinformation.

The finding that only about one-third of tweets (402/1165, 34.5%) appeared to be from indoor tanners is in contrast to a similar investigation by Waring et al [7], where twice the proportion of tweets (699/978, 71.2%) using the same search terms in March 2016 appeared to be from indoor tanners [7]. This finding could be due to declining rates of tanning bed use in recent years [20] or that COVID-19 shutdowns curtailed indoor tanning, which may have decreased chatter about it [20]. Another possibility could be that the proportion of tanning-related tweets that were negative chatter about former US President Donald Trump's skin color increased from 2016 to 2020 [21-25]. Waring et al [7] found only 10.7% of tweets in 2016 were mocking tanners and the tanned look, compared to 48% (562/1165) of tweets from 2020 in this study. Among tweets that mocked tanners, the vast majority (448/562, 79.7%) mocked former US President Donald Trump, accounting for 38% (446/1165) of all tweets. Criticism of a tan-appearing public figure may shift social norms about indoor tanning for the better or worse, depending on how people feel about that public figure. Perceived social norms strongly predict indoor tanning [26] and increased negative sentiment toward indoor tanning and a tan appearance may shift appearance-related social norms. Future research should explore how negative sentiment on social media about tanned celebrities influences indoor tanning behavior and attitudes.



While most posted tweets lamented the inability to tan, interestingly, very few (16/402, 3.9%) mentioned using tanning alternatives (eg, sunless tanners). Some tanners may have been more interested in gaining access to UV tanning than non-UV tanning, even though the latter was far more accessible. However, those who switched to non-UV tanning may have been less inclined to discuss this on Twitter, perhaps simply because non-UV tanning was more accessible or perhaps to the extent they felt the stigma around admitting to getting a “fake tan” [27,28]. The COVID-19–related shutdowns may have been a missed opportunity to promote sunless tanning products. Because orange-appearing skin was also the focus of tweets mocking Donald Trump (eg, “Trump been in the tanning bed too long? He looks like a Cheeto”), these tweets may have also negatively impacted social norms around sunless tanning products. Many tanners fear sunless tanning products will create an orange appearance because early products had this effect [27,28]. Future research should examine how social norms around tanning beds and sunless tanning are influenced by social media conversations.

The most common type of tweet among tanners expressed that they missed tanning and 39% (260/402) of these mentioned reasons they missed tanning. Appearance-related reasons were by far the most common (77/260, 30%). The increase in the use of videoconferencing software during the COVID-19 pandemic has been shown to have exacerbated appearance-related concerns, leading to an increase in cosmetic surgery consults [29,30]. Because physical appearance is well established to be among the most common reasons people use tanning beds [31,32], future studies should examine how the widespread use of videoconferencing has impacted tanning behavior.

Additional reasons people cited for missing indoor tanning included the positive impact they perceive tanning has on their mood or their discomfort with the negative effect they experience when they are unable to use tanning beds. Research has shown that 8% to 20% of tanners meet criteria for “tanning addiction,” indicators of which may include the experience of mood enhancement from tanning and withdrawal symptoms (eg, irritability) when they cannot tan [33–36]. Future research should explore how the shutdowns may have impacted tanning behavior among people qualifying as “tanning addicted.” The forced period of “cold turkey” could possibly have led some tanners to reduce or quit their tanning habit altogether. Alternatively, when tanning salons reopened, a disinhibition effect may have occurred, such that tanners increased their tanning beyond prepandemic levels after being involuntarily restricted.

Some tweets from tanners (90/402, 22%) expressed their interest in gaining access to a home tanning bed. Future studies should examine whether the small segment of indoor tanners (<10%) who use home beds grew following the pandemic shutdowns [37,38]. The impact of restricted or discouraged access to tanning beds has implications for legislative and public health efforts. For example, Australia banned commercial tanning services in 2016. Governments initiated buyback programs to discourage home tanning bed use in the states of Victoria and

New South Wales [39,40]. Afterward, Australian consumer interest in tanning beds declined to less than one-fourth of preban seasonal peaks, but interest in sunless tanning was high [41]. While home tanning beds are still legally marketed in Australia, spray tanning remains more popular [41,42]. Therefore, buyback programs or legislation restricting the sale of home tanning beds may be necessary accompaniments to legislation restricting tanning businesses in the United States.

Unfortunately, we observed very few public health messages regarding the dangers of indoor tanning. Only 2.5% (29/1165) of tweets were of this type, which is even less than the 4.3% that was observed in the previous investigation of tanning bed chatter on Twitter [7]. To be sure, public health efforts were heavily focused on COVID-19 at this time. However, given the misinformation about UV and COVID-19 prevention [14], this would have been an important opportunity to underscore the dangers of indoor tanning. Interestingly, only 5 (0.4%) out of 1165 tweets contained misinformation. Misinformation themes included that UV radiation from tanning beds could kill COVID-19, that UV radiation from the sunbathing could kill COVID-19, and that indoor tanning is healthy to use as therapy. However, because tweets in our study must have contained the words tanning bed or tanning salon, they may not have captured the full range of misinformation circulating about UV and COVID-19.

This study has limitations. Our data capture was limited to 2 common lay terms typically used in the United States to refer to indoor tanning. We may not have captured tweets containing other terms that refer to indoor tanning or tweets about using non-UV tanning alternatives. Additionally, states started reopening at different times during the end of the sampling window, which may have impacted the types of tweets in our sample [43]. Further, we may have captured tweets that were posted by users outside of the United States. Few Twitter users activate their location data [44], so it is difficult to determine where all the tweets originated. As we only coded 1165 tweets from the nearly 5000 unique tweets captured during the sampling window, we may have missed interesting yet rare topics of conversation. Additionally, tanners who were most upset by the shutdowns may have been more likely to tweet about them. Among the 23% of adults in the United States that use Twitter, only 18% reside in rural areas [45,46], so our data may not have captured the full range of sentiment about indoor tanning in rural areas of the United States.

## Conclusion

Many indoor tanners appeared to miss indoor tanning during the pandemic shutdown, particularly due to appearance concerns, and some were seeking alternative ways to access tanning beds. We also discovered that, compared to a similar investigation 5 years ago, a much larger percentage of tweets about indoor tanning were very critical of indoor tanning [7]. The use of tanning beds or the appearance of having used them appears to be the target of insults that are often politically motivated on social media. Future research is needed to examine how the pandemic and the surrounding political climate affected tanning behavior and attitudes.

## Acknowledgments

This project was supported by the National Institutes of Health (grant K24HL124366; Principal Investigator: SP).

## Data Availability

The data sets generated and analyzed during this study are available from the corresponding author on reasonable request.

## Authors' Contributions

LG conceptualized the idea, collected and analyzed data, interpreted results, and drafted the manuscript. MEW assisted with conceptualizing idea, supervised analyses, interpreted results, and edited the manuscript. AJB assisted with conceptualizing idea, interpreted results, and edited the manuscript. SB analyzed data, interpreted results, and edited the manuscript. LP interpreted the results and edited the manuscript. SP conceptualized idea, supervised data collection, interpreted results, and edited the manuscript.

## Conflicts of Interest

None declared.

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*Edited by R Dellavalle, D Devaraj; submitted 27.10.23; peer-reviewed by C Heckman, J Makin; comments to author 14.12.23; revised version received 11.01.24; accepted 12.01.24; published 04.03.24.*

*Please cite as:*

Groshon L, Waring ME, Blashill AJ, Dean K, Bankwalla S, Palmer L, Pagoto S

*A Content Analysis of Indoor Tanning Twitter Chatter During COVID-19 Shutdowns: Cross-Sectional Qualitative Study*  
*JMIR Dermatol* 2024;7:e54052

URL: <https://derma.jmir.org/2024/1/e54052>

doi: [10.2196/54052](https://doi.org/10.2196/54052)

PMID: [38437006](https://pubmed.ncbi.nlm.nih.gov/38437006/)

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Original Paper

# Oral Cannabidiol for Seborrheic Dermatitis in Patients With Parkinson Disease: Randomized Clinical Trial

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## Abstract

**Background:** Seborrheic dermatitis (SD) affects 18.6%-59% of persons with Parkinson disease (PD), and recent studies provide evidence that oral cannabidiol (CBD) therapy could reduce sebum production in addition to improving motor and psychiatric symptoms in PD. Therefore, oral CBD could be useful for improving symptoms of both commonly co-occurring conditions.

**Objective:** This study investigates whether oral CBD therapy is associated with a decrease in SD severity in PD.

**Methods:** Facial photographs were collected as a component of a randomized (1:1 CBD vs placebo), parallel, double-blind, placebo-controlled trial assessing the efficacy of a short-term 2.5 mg per kg per day oral sesame solution CBD-rich cannabis extract (formulated to 100 mg/mL CBD and 3.3 mg/mL THC) for reducing motor symptoms in PD. Participants took 1.25 mg per kg per day each morning for 4 ± 1 days and then twice daily for 10 ± 4 days. Reviewers analyzed the photographs independently and provided a severity ranking based on the Seborrheic Dermatitis Area and Severity Index (SEDASI) scale. Baseline demographic and disease characteristics, as well as posttreatment SEDASI averages and the presence of SD, were analyzed with 2-tailed *t* tests and Pearson  $\chi^2$  tests. SEDASI was analyzed with longitudinal regression, and SD was analyzed with generalized estimating equations.

**Results:** A total of 27 participants received a placebo and 26 received CBD for 16 days. SD severity was low in both groups at baseline, and there was no treatment effect. The risk ratio for patients receiving CBD, post versus pre, was 0.69 (95% CI 0.41-1.18; *P*=.15), compared to 1.20 (95% CI 0.88-1.65; *P*=.26) for the patients receiving the placebo. The within-group pre-post change was not statistically significant for either group, but they differed from each other (*P*=.07) because there was an estimated improvement for the CBD group and an estimated worsening for the placebo group.

**Conclusions:** This study does not provide solid evidence that oral CBD therapy reduces the presence of SD among patients with PD. While this study was sufficiently powered to detect the primary outcome (efficacy of CBD on PD motor symptoms), it was underpowered for the secondary outcomes of detecting changes in the presence and severity of SD. Multiple mechanisms exist through which CBD can exert beneficial effects on SD pathogenesis. Larger studies, including participants with increased disease severity and longer treatment periods, may better elucidate treatment effects and are needed to determine CBD's true efficacy for affecting SD severity.

**Trial Registration:** ClinicalTrials.gov NCT03582137; <https://clinicaltrials.gov/ct2/show/NCT03582137>

**KEYWORDS**

cannabidiol; cannabis; CBD treatment; CBD; image; photograph; photographs; imaging; sebum; clinical trials; seborrheic dermatitis; Parkinson disease; clinical trial; RCT; randomized; controlled trial; drug response; SEDASI; drug; Parkinson; dermatitis; skin; dermatology; seborrheic dermatitis; treatment; outcome; cannabis; chi-square

## Introduction

Seborrheic dermatitis (SD) is related to increased sebum production and an inflammatory response to cutaneous *Malassezia*, and it affects 18.6%-59% of persons with Parkinson disease (PD) [1,2]. The mechanism connecting these two pathologies is not entirely clear; however, increasing evidence suggests a direct role of *Malassezia* in the pathogenesis of PD [2]. Other proposed mechanisms include gene polymorphisms leucine-rich repeat kinase 2 (LRRK2), glucocerebrosidase (GBA), and phosphatase and tensin homolog-induced kinase 1 (PINK1); these have been shown to play a role in lipid regulation and increase the risk for PD in affected individuals [2]. Traditional first-line SD treatment relies on topical antifungals or anti-inflammatories, with systemic therapies reserved for recalcitrant or severe cases, which become more common in patients with immune dysfunction [2]. These systemic therapies, such as oral terbinafine and itraconazole, have numerous side effects, including hepatotoxicity and interactions with concomitant medications [3].

Delta-9-tetrahydrocannabinol (THC) induces a “high,” psychosis, cognitive dysfunction, and anxiety, while cannabidiol (CBD) has been reported to reduce sebum production and improve motor and psychiatric symptoms in PD [2-9]. CBD is likely safer than THC; however, some individuals with PD report the use of both and claim greater benefits from THC [4,10]. After oral consumption, THC travels to the liver, where the majority is eliminated or metabolized into other molecules by cytochrome P450 2C (CYP2C) and CYP3A [11]. The bioavailability of ingested THC is between 4% and 12% [11]. The pharmacokinetics of CBD are complex, and the bioavailability of oral CBD is estimated to be only 6% [11]. In general, the most abundant metabolites of CBD are hydroxylated 7-COOH (7-carboxy) derivatives that are excreted either intact or as glucuronide conjugates [12].

The use of CBD on human sebocytes has been shown to reduce sebaceous gland proliferation and induce anti-inflammatory changes [13]. However, few studies exist evaluating oral CBD's effect on SD severity. CBD may be beneficial in both PD and SD, and research is needed to define what cannabinoids and doses are useful in both conditions. Based on current literature, an oral formulation with the following combination was pursued: greater CBD than delta-9-THC, with between 150 and 1000 mg CBD, and <10 mg THC daily [4-9,14,15]. This study investigates whether oral CBD therapy is associated with a decrease in SD severity in PD.

## Methods

### Overview

Facial photographs were collected as a component of a randomized, parallel, double-blind, placebo-controlled trial assessing the efficacy of a short-term 2.5 mg per kg per day of oral sesame solution CBD-rich cannabis extract for reducing motor symptoms in PD. The study drug, supplied by the National Institute of Drug Abuse as a frozen extract, was formulated to a 100 mg per mL CBD and 3.3 mg per mL THC sesame oil solution by a PharmD team. The placebo was compounded with *United States Pharmacopeia (USP)*-grade sesame oil, food coloring, and strawberry extract. ElSohly Laboratories, Inc performed stability, potency, and microbial analyses.

Participants took 1.25 mg per kg per day each morning (approximately 1 mL) for  $4 \pm 1$  days and then twice daily for  $10 \pm 4$  days. To test short-term use, the duration of time on the study drug was at least the minimum time needed for CBD to be at a steady state concentration. The half-life of oral CBD and oral THC is approximately 2 days and 4 hours, respectively [16]. To facilitate the interpretation of effects, cannabinoid plasma levels were documented at the final dose visit.

Eligibility criteria were defined by adults 40-85 years of age with idiopathic PD participating in the above trial and who had concurrent SD. Data were collected from the University of Colorado Hospital from September 2018 to January 2022. The sample size was determined by the number of patients in the trial meeting eligibility criteria. Eligible candidates were randomized 1:1 to the study drug or placebo by a computer-generated randomization schedule, stratified by age (45-60 vs 61-85 years) and modified Hoehn and Yahr scale score (1-2.5 vs 3-5) into blocks of four, with 2 participants per block being assigned to each treatment group [17].

The statistician (author SHS) and the PharmD team were the only unblinded study staff. The statistician generated the random allocation sequence. The statistician notified the lead PharmD (author JB) via encrypted email of the allocation assignment. The appropriate study drug was prepared by the PharmD team within days of the baseline visit. Blinded study staff enrolled participants and provided them with the study drug.

Despite best efforts, the placebo was slightly different in appearance and odor, so procedures were developed to optimize the preservation of the blinding. The design of the study was changed from crossover to parallel; the study drug for each participant was prepared in a brown opaque bottle that was placed into a “masking envelope,” a thick brown postage envelope with plastic bubble wrap lining to obscure odor, and the study drug was administered in a closed, vented room that removes the odor of cannabis within 4 minutes. Blinded study

staff did not enter for at least 10 minutes. Further, the study drug was transported by the participants to their homes and the clinic in the masking envelope.

Deidentified photographs pre- and posttreatment were provided to two board-certified dermatologists to assess along with reference images external to the study. Reviewers analyzed the photographs independently, providing a severity ranking based on the Seborrheic Dermatitis Area and Severity Index (SEDASI) scale, a quantitative grading instrument [18]. Severity scores were averaged between reviewers for the final SEDASI score, and reviewers determined whether each participant's SD had improved, worsened, or was unchanged. The possible range of scoring is 0 to 60, with 60 being the most severe.

Baseline demographic and disease characteristics were compared between treatment groups with 2-tailed *t* tests and Pearson  $\chi^2$  or Fisher exact association tests. The presence of SD was analyzed longitudinally with generalized estimating equations relative risk models. Covariates of gender, age, and log-scaled PD disease duration were considered as time-interacting covariates. The final CBD blood level was also considered as an adjusting covariate for the posttreatment time point in the CBD group. SEDASI was analyzed with longitudinal regression. The change in SEDASI averages was analyzed with change scores, paired *t* tests for within-group changes, and a 2-sample *t* test on the change scores for the difference between groups. The CONSORT (Consolidated Standards of Reporting Trials) reporting guidelines were used and followed in the reporting of this trial [19].

### Ethical Considerations

The Colorado Multiple Institutional Review Board granted ethical approval (17-2318). All participants provided written

informed consent. An independent data and safety monitoring board provided oversight.

## Results

A total of 27 participants received a placebo and 26 received CBD for 16 days; cannabinoid plasma levels are shown in [Table 1](#). Baseline participant characteristics were similar between groups for most variables, although the study drug group trended toward longer disease duration ( $P=.07$ ) and higher total Movement Disorders Society Modified Unified Parkinson's Disease Rating Scale (MDS-UPDRS) score ( $P=.08$ ), but this was not significant. There were no effects on orthostatic blood pressure, heart rate, or temperature, comparing before the first study medication dose to the final dose and comparing before a dose to 1-3 hours afterward. There were also no notable changes in blood laboratory studies, including liver tests. The study drug was tolerated with no unexpected and serious adverse effects and no significant dermatological adverse events. SD severity was low in both groups at baseline, and there was no treatment effect, as shown in [Table 2](#). Generalized estimating equation regression analysis, where final blood level of CBD was included as an explanatory variable and for which there were 26 patients receiving CBD and 27 patients receiving placebo with data, revealed that CBD treatment trended toward reducing the presence of SD compared with the placebo ( $P=.07$  at the mean CBD final blood level of 49.29 ng/mL) because there was an estimated improvement for the CBD group and an estimated worsening for the placebo group, but this finding did not reach statistical significance. The estimated prevalence post-pre ratio of SD in the CBD group was 0.69 (95% CI 0.41-1.18;  $P=.15$ ), compared to 1.20 (95% CI 0.88-1.65;  $P=.26$ ) in the placebo group.

**Table 1.** Demographic characteristics and presence of seborrheic dermatitis for patients with Parkinson disease in oral cannabidiol (CBD) and placebo treatment groups.

Characteristic	CBD (n=26)	Placebo (n=27)	<i>P</i> value <sup>a</sup>
Age (years), mean (SE; SD)	70.6 (1.2; 6.3)	68.7 (1.4; 7.5)	.34
<b>Gender, n (%)</b>			.33
Female	10 (38)	7 (26)	
Male	16 (62)	20 (74)	
<b>Race</b>			>.99
Asian	0 (0)	1 (4)	
White	26 (100)	26 (96)	
<b>Ethnicity</b>			>.99
Hispanic or Latino	1 (4)	0 (0)	
Not Hispanic or Latino	25 (96)	28 (96)	
Not reported	0 (0)	1 (4)	
<b>Employment</b>			>.99
Disabled, permanently or temporarily	1 (4)	1 (4)	
Retired	20 (77)	21 (78)	
Working now	4 (15)	4 (15)	
Partly retired	1 (4)	0 (0)	
Retired, still involved in business	0 (0)	1 (4)	
<b>Marital status</b>			>.99
Divorced	4 (15)	4 (15)	
Living with partner	0 (0)	1 (4)	
Married	21 (81)	21 (78)	
Widowed	1 (4)	1 (4)	
Duration of PD <sup>b</sup> (years), mean (SE; SD)	6.6 (1.3; 6.8)	4.6 (0.8; 4.0)	.19
<b>Dosing<sup>c</sup>, mean (SD; SE)</b>			N/A <sup>d</sup>
Final CBD dose (mg/day)	187.50 (56.68; 11.12)	N/A	
Final THC <sup>e</sup> dose (mg/day)	6.28 (1.90; 0.37)	N/A	
CBD level at final dose visit (ng/mL)	49.29 (32.85; 6.44)	0.00 (0.00; 0.00)	
THC level at final dose visit (ng/mL)	0.85 (0.91; 0.18)	0.00 (0.00; 0.00)	
Time on study drug (days), mean (SD; SE)	15.5 (1.8; 0.3)	16.2 (1.6; 0.3)	.15

<sup>a</sup>Two-tailed *t* tests and Pearson  $\chi^2$  or Fisher exact association tests.<sup>b</sup>PD: Parkinson disease.<sup>c</sup>Blood levels reflect 26 participants in the CBD group and 17 in the placebo group. Blood levels were not obtained for 3 participants in the CBD group and 2 in the placebo group.<sup>d</sup>N/A: not applicable.<sup>e</sup>THC: tetrahydrocannabinol.

**Table 2.** Results for patients with Parkinson disease in oral cannabidiol (CBD) and placebo treatment groups.

	Pretreatment	Posttreatment	P value
<b>Presence of seborrheic dermatitis <sup>a</sup>, n (%; 95% CI)</b>			
CBD	12 (46.2; 30.5-69.9)	9 (34.6; 20.4-58.7)	.26
Placebo	15 (55.6; 39.7-77.9)	18 (66.7; 51.1-87.0)	.26
Treatment effect	N/A <sup>b</sup>	N/A	.12
<b>SEDASI <sup>c</sup> average <sup>d</sup>, mean (95% CI; SD)</b>			
CBD	3.63 (1.41-5.86; 5.50)	3.79 (1.38-6.20; 5.96)	.81
Placebo	5.39 (2.75-8.03; 6.68)	4.65 (2.76-6.54; 4.77)	.35
Treatment effect	N/A	N/A	.38

<sup>a</sup>Presence of seborrheic dermatitis indicates patients exhibiting any signs of seborrheic dermatitis after assessing the final SEDASI score. Numbers calculated for generalized estimating equation model with log link (ie, relative risk model with repeated measures).

<sup>b</sup>N/A: not applicable.

<sup>c</sup>SEDASI: Seborrheic Dermatitis Area and Severity Index.

<sup>d</sup>SEDASI average is calculated by averaging the two scores assigned by independent reviewers to each patient.

Discussion

Principal Findings

This study does not provide solid evidence that oral CBD therapy reduces the presence of SD among patients with PD. While this study was sufficiently powered to detect the primary outcome (efficacy of CBD on PD motor symptoms), it was underpowered for these secondary outcomes of detecting changes in the presence and severity of SD. CBD has shown significant promise in improving SD in a topical form; however, no current literature exists to evaluate its effect when taken orally [20].

The pathophysiology of SD is still not entirely understood, but the colonization of *Malassezia* is strongly associated with the condition [1]. *Malassezia* is found on sebum-rich skin, and its metabolites have been shown to induce inflammation and stimulate keratinocyte differentiation, resulting in dysfunction in the stratum corneum, a disruption of the epidermal barrier, and perpetuation of an inflammatory response, leading to a cycle of more skin barrier disruption and the clinical manifestations of SD [21-23].

CBD possesses the ability to inhibit the lipogenic action of arachidonic acid, linoleic acid, and testosterone in human sebocytes; in addition, it has been shown to suppress sebocyte proliferation via ion channel activation [13,24]. CBD also possesses anti-inflammatory properties through the inhibition

of nuclear factor kappa B (NF-κB) and signaling and upregulation of tribbles pseudokinase 3 (TRIB3) [13]. These mechanisms help explain its success in improving SD symptoms with topical therapy and provide a strong impetus for further study with oral CBD and SD.

Limitations

Limitations include study drug availability constraints, limiting the time participants were on the study drug. A 16-day treatment period may not have been long enough to achieve maximal clinical benefit. Additionally, although the prevalence of SD for study participants was similar to existing estimates, low levels of disease severity in the cohort, both pre- and posttreatment, posed a challenge for assigning scores and may have impacted the reviewers' ability to detect change. Possible confounders include participants' concurrent topical medication use, which also hinders the interpretation of the findings.

Conclusion

Larger studies, including participants with increased disease severity and with longer treatment periods, may better elucidate treatment effects and are needed to determine CBD's true efficacy for SD severity. Oral CBD has shown promise in improving Parkinsonian symptoms; therefore, if future studies can elicit improvement in SD as well, it could act as a useful adjunct for patients struggling with PD to improve both neurologic and common cutaneous symptoms.

Acknowledgments

The study is funded by the Colorado Department of Public Health and Environment medical marijuana research grant program (contract #17-90046, RFA-1353). The study is partially supported by a National Institutes of Health (NIH) and National Center for Advancing Translational Sciences Colorado Clinical and Translational Science Awards grant (UL1 TR001082-05). Contents are the authors' sole responsibility and do not necessarily represent official NIH views.

The authors would like to acknowledge Elizabeth Wallace for her role as a tiebreaker in the evaluation of participant photos.



## Conflicts of Interest

RPD is the editor in chief of JMIR Dermatology. RPD receives editorial stipends (JMIR Dermatology), royalties (UpToDate), and expense reimbursement from Cochrane. TES and MA received fellowship funding from Pfizer. TES receives fellowship funding from the NIH (grant 5T32AR007411-37; principal investigator: Dennis Roop).

## Multimedia Appendix 1

CONSORT (Consolidated Standards for Reporting Trials) checklist.

[[PDF File \(Adobe PDF File\), 104 KB - derma\\_v7i1e49965\\_app1.pdf](#)]

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## Abbreviations

**7-COOH:** 7-carboxy

**CBD:** cannabidiol

**CONSORT:** Consolidated Standards of Reporting Trials

**CYP2C:** cytochrome P450 2C

**GBA:** glucocerebrosidase

**LRRK2:** leucine-rich repeat kinase 2

**MDS-UPDRS:** Movement Disorders Society Modified Unified Parkinson's Disease Rating Scale

**NF-κB:** nuclear factor kappa B

**PD:** Parkinson disease

**PINK1:** phosphatase and tensin homolog-induced kinase 1

**SD:** seborrheic dermatitis

**SEDASI:** Seborrheic Dermatitis Area and Severity Index

**THC:** tetrahydrocannabinol

**TRIB3:** tribbles pseudokinase 3

**USP:** United States Pharmacopeia

*Edited by R Alhusayen; submitted 15.06.23; peer-reviewed by V Long, M Gasmi ; comments to author 04.12.23; revised version received 23.01.24; accepted 28.01.24; published 11.03.24.*

*Please cite as:*

Weber I, Zagana-Prizio C, Sivesind TE, Adelman M, Szeto MD, Liu Y, Sillau SH, Bainbridge J, Klawitter J, Sempio C, Dunnick CA, Leehey MA, Dellavalle RP

*Oral Cannabidiol for Seborrheic Dermatitis in Patients With Parkinson Disease: Randomized Clinical Trial*

*JMIR Dermatol* 2024;7:e49965

URL: <https://derma.jmir.org/2024/1/e49965>

doi: [10.2196/49965](https://doi.org/10.2196/49965)

PMID: [38466972](https://pubmed.ncbi.nlm.nih.gov/38466972/)

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Original Paper

# Barriers and Facilitators to Teledermatology and Tele-Eye Care in Department of Veterans Affairs Provider Settings: Qualitative Content Analysis

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## Abstract

**Background:** Veterans Affairs health care systems have been early adopters of asynchronous telemedicine to provide access to timely and high-quality specialty care services in primary care settings for veterans living in rural areas. Scant research has examined how to expand primary care team members' engagement in telespecialty care.

**Objective:** This qualitative study aimed to explore implementation process barriers and facilitators to using asynchronous telespecialty care (teledermatology and tele-eye care services).

**Methods:** In total, 30 participants including primary care providers, nurses, telehealth clinical technicians, medical and program support assistants, and administrators from 2 community-based outpatient clinics were interviewed. Semistructured interviews were conducted using an interview guide, digitally recorded, and transcribed. Interview transcripts were analyzed using a qualitative content analysis summative approach. Two coders reviewed transcripts independently. Discrepancies were resolved by consensus discussion.

**Results:** In total, 3 themes were identified from participants' experiences: positive perception of telespecialty care, concerns and challenges of implementation, and suggestions for service refinement. Participants voiced that the telemedicine visits saved commute and waiting times and provided veterans in rural areas more access to timely medical care. The mentioned concerns were technical challenges and equipment failure, staffing shortages to cover both in-person and telehealth visit needs, overbooked schedules leading to delayed referrals, the need for a more standardized operation protocol, and more hands-on training with formative feedback among supporting staff. Participants also faced challenges with appointment cancellations and struggled to find ways to efficiently manage both telehealth and in-person visits to streamline patient flow. Nonetheless, most participants feel motivated and confident in implementing telespecialty care going forward.

**Conclusions:** This study provided important insights into the positive perceptions and ongoing challenges in telespecialty care implementation. Feedback from primary care teams is needed to improve telespecialty care service delivery for rural veterans.

(JMIR Dermatol 2024;7:e50352) doi:[10.2196/50352](https://doi.org/10.2196/50352)



## KEYWORDS

telemedicine; dermatology; eye; implementation science; stakeholder participation; veterans' health

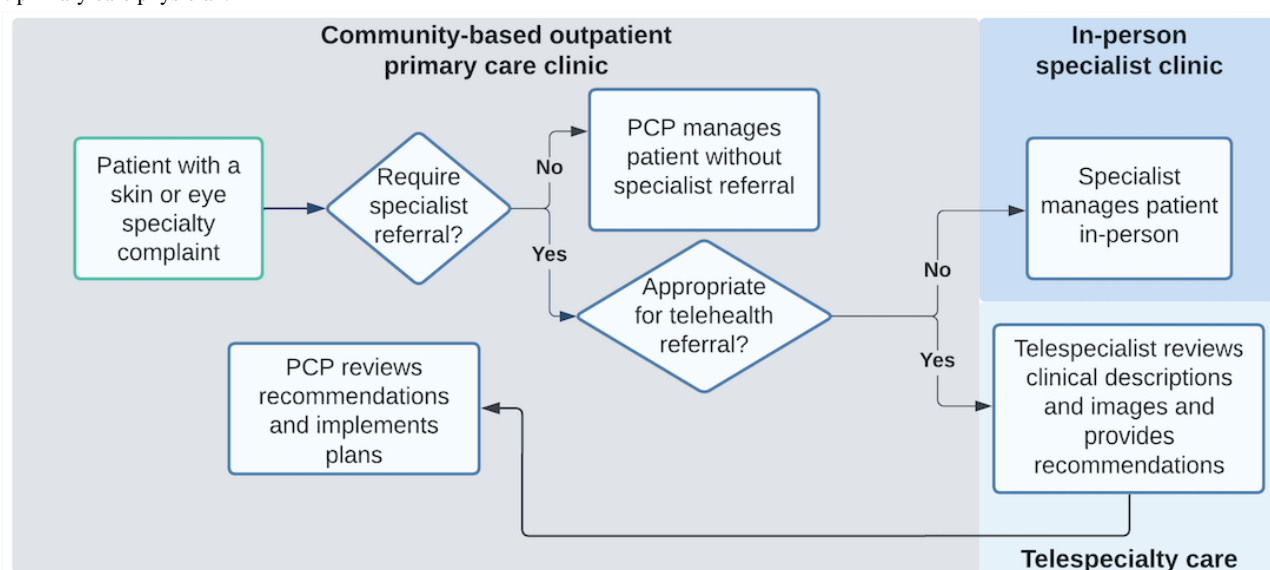
## Introduction

The use of telemedicine has been steadily increasing and has expanded rapidly during the COVID-19 pandemic [1]. Veterans' health care systems have been early adopters of asynchronous telemedicine, also known as the store-and-forward mode of consultation and sometimes referred to as "eConsult" or "eTriage." In this approach, a brief clinical history and images are collected during an in-person primary care visit at a community-based outpatient clinic. These records are subsequently transmitted to telespecialists at a distant site for evaluation, and the results are communicated to the patient by the referring primary care provider (Figure 1). Patients with

additional needs are identified through this process for expedited treatment. In this manner, veterans are provided timely access to high-quality specialty care services in primary care settings, especially in rural areas [2].

With an emphasis on visual diagnosis, asynchronous telemedicine is well-suited for Teledermatology and Technology-Based Eye Care Services [3]. However, concerns have been raised to adopt telemedicine for specialty care on a larger scale, as certain sites may be disadvantaged with the lack of clinical resources and administrative experience in implementing complex programs. The goal of this qualitative study is to better understand implementation process facilitators and barriers to telemedicine use for specialty care.

**Figure 1.** Asynchronous telehealth referral flowchart. In-patient primary care evaluation determines patient management by the PCP or referral to a specialist. If a specialist is needed, the PCP decides between in-person specialist clinic or telespecialty care. For telespecialty care, clinical data and images are sent to the telespecialist for analysis. The results are then communicated by the PCP to the patient, speeding up further treatment processes. PCP: primary care physician.



## Methods

## Study Design

Between October 2, 2020, and January 31, 2021, we conducted in-depth interviews with primary care providers, nurses, telehealth clinical technicians, medical and program support assistants, and administrators from 2 community-based outpatient clinics and distant reading sites. Semistructured interviews (interview guide detailed in Textbox 1) aimed to explore perspectives, identify telespecialty care facilitators and

barriers, and derive solutions from community-based outpatient clinics [4]. A trained interviewer (TS) conducted 30 individual telephone interviews lasting 30-60 minutes, with digital audio recording and participant consent. Interviews were transcribed professionally and deidentified. Qualitative content analysis followed a summative approach [5] with latent content analysis for underlying meanings and patterns. Coders (CP and JD) independently reviewed transcripts, resolving discrepancies by consensus. Diagramming mapped conceptual relationships across stakeholder perceptions to identify facilitators, barriers, and solutions.

**Textbox 1.** Qualitative interview questions.

- Q1. What percentage of your time is dedicated to TECS (Technology-Based Eye Care Services) or TD (Teledermatology), as compared to face-to-face care?
- Q2. How do you feel about TECS or TD at our location?
- Q3. How motivated or committed do you feel your site is in implementing TECS or TD?
- Q4. How ready do you feel your site is, to implement TECS or TD?
- Q5. What has been your experience in working with the regional telehealth service reading hub, in which veterans' images taken at your CBOC (community-based outpatient clinic) or site are interpreted by a clinician outside of your site?
- Q6. What worked well in facilitating implementation of TECS or TD at your site?
- Q7. What types of data or reports were helpful in facilitating implementation of TECS or TD at your site?
- Q8. What issues or barriers have you experienced in implementing TECS or TD at your site?
- Q9. What have been some unintended consequences following implementation of TECS or TD at your site?
- Q10. How were challenges in implementation of TECS or TD managed at your site?
- Q11. What changes do you recommend in sustaining TECS or TD at your site?
- Q12. What recommendations would you offer to other CBOC sites providing, or considering providing, TECS or TD?
- Q13. Please share any additional thoughts or information that you would like us to know.

**Ethical Considerations**

This study received approval from the Emory University Institutional Review Board (STUDY00000383) on June 3, 2020, and from the Atlanta Veterans Affairs (VA) Medical Center Research and Development Committee. The results are reported in accordance with COREQ (Consolidated Criteria for Reporting Qualitative Research) guidelines [6]. All participants provided verbal informed consent prior to the study conduct, and participant data were deidentified. No compensation was provided to the participants.

**Results****Overview**

Of the 30 participants, a total of 27 (90%) had experienced the hybrid format of telespecialty encounters, where patients visited the community-based outpatient clinic site for image acquisition during the study period, and 3 (10%) had in-person visits only. Interviews identified two primary facilitators to telespecialty care: (1) positive perception of telespecialty care and (2) optimized implementation processes (task lists, deadlines, and bringing together multiple capable diverse stakeholders in regular meetings).

**Positive Perception of Telespecialty Care****Overview**

Stakeholders from various roles provided insights indicating positive telespecialty care experiences reported by veterans (domain I). Telemedicine saved commute and waiting times, enhancing access for rural veterans (domain II). The telespecialty care programs are regarded to provide good quality of care (domain III). Telespecialty care increased resources for routine care, saved appointments at the main facility, and allowed VA health care to receive more workload credit (domain IV).

**Domain I: Patient Satisfaction**

Patient satisfaction is the first domain emerging from interviews. Interviewees speculated about the reasons, but all stated that patients were satisfied with the services they received. One participant explained:

*I don't know if it's because we're more accessible right now, that may be the reason. But they all seem to be very satisfied with their care and feel like they've got a very good exam.*

Another participant explained that:

*[The patients] love this. Having the specialty Technology-based Eye Care Services and then being able to come to a clinic in their community to pick up their glasses, all their services they need for their eyes are done in one stop shop.*

The interviews highlighted the patient satisfaction benefits of the Teledermatology and Technology-Based Eye Care Services programs.

**Domain II: Access****Overview**

Access was a frequently discussed domain in the interviews. Participants believed telespecialty care services increased veterans' health care access, especially benefiting those in rural areas. Factors contributing to this enhanced access included travel (distance and time), timely care, and integration with primary care.

**Travel**

Telespecialty care programs at local community-based outpatient clinics offer improved health care access compared to traveling to a main VA facility with on-site specialty care. With more community-based outpatient clinic locations than main VA facilities, traveling distance and time for veterans are reduced. One participant highlighted the challenges and difficulties veterans faced when seeking specialty care.

*Technology-based Eye Care Services is very helpful when it's out in rural areas ... Dermatology as well. You know, I think a lot of times people go under the assumption that everybody is close by, that there's a VA everywhere and that if there's a VA in your community and your community is small enough for you to get to that VA within 30-45 minutes or maybe an hour. I think that having forward thinking or being very realistic would help because some people travel, you know, three or four hours, to get to their clinic.*

Telespecialty care services provided at community-based outpatient clinic locations enable veterans to receive crucial care without burdensome travel.

### Timely Care

The main VA medical centers provide various services from annual checkups to major surgeries. However, these centers frequently have long waitlists due to the limited providers and availabilities. Telespecialty care services at community-based outpatient clinics help reduce wait times and enable timely care. One interviewee stated that:

*... the speed that we're able to provide the care is better. So instead of waiting for the patient to have an appointment in a face-to-face grid with limited access, we're using these technologies at all of our sites and the time that passes between the patient needing the care, the provider consulting for the care, and then receiving it, it decreases a great deal.*

Further, wait times for community-based outpatient clinic appointments tend to be shorter than the main VA medical centers. One interviewee revealed:

*... mostly about the technicians that they see, the fact that they were able to quickly get in and out. It wasn't a long wait time for them. Usually with eye exams, they have to wait maybe between two and four hours when they go to the main hospital, so that's a big plus.*

### Convenient Access Integration Into Primary Care or In-House Service

Another benefit that telespecialty care provides at community-based outpatient clinic locations is the ease of referrals from primary care providers. Community-based outpatient clinics provide the most common outpatient services (eg, primary care) and typically lack in-house specialty care providers. When patients require ophthalmology or dermatology referrals, they typically need to make an appointment at the main VA medical center community clinics. With telespecialty care programs at a community-based outpatient clinic, patients can often undergo specialty care imaging acquisition during the same visit as their primary care appointment.

One interviewee stated:

*... from the Derm aspect. If it was something that, say, the primary physician sees while they're there physically in the clinic or face-to-face, they can immediately put in a Teledermatology consult while the patient is at the clinic and the patient doesn't have to come back for a second trip to the clinic.*

This remote access reduces the burden on the patients for having to return to the clinic for follow-up care. One of the primary care physicians provided:

*Many of our veterans did not want to travel the sometimes 40 to sometimes 1 ½ hour commute between traffic and the time of day. And so to be able to have a dermatology and ophthalmology consultation at the local site, was very convenient for the veteran population that we served.*

The integration with primary care clinics at community-based outpatient clinics adds even more convenience to patients, and they can get "one-stop shop" health care.

### Domain III: Quality of Care

Teledermatology and Technology-Based Eye Care Services provide telespecialty services with improved access while maintaining quality of care comparable to in-person care, meeting their goal of providing veterans with high-quality specialty care in a timely manner.

One interviewee pointed out:

*... as far as [s/he] know[s] about it, it provides the same quality of care as a face-to-face visit would.*

Other interviewers echoed this and stated:

*I feel the quality of care is excellent.*

One of the participants posits:

*It would be nearly impossible for me to replicate the quality of care that I get from the Technology-based Eye Care Services.*

### Domain IV: Workload Credit

The last domain relates to how the telespecialty care programs benefit the VA. Teledermatology and Technology-Based Eye Care Services effectively triage patients into those who can be managed remotely, thereby freeing up appointments for patients needing face-to-face care. One interviewee explained that:

*They were able to stream-line the process so that only those who have cancerous appearing lesions could be brought to the medical center and so therefore you were able to get to the greatest number of veterans that truly needed that service.*

## Optimized Implementation Process

### Overview

Communication process emerged as a central theme for successful telespecialty care program implementation. The implementation team's engagement approach, communication, and availability at regular and frequent huddles to work through issues were viewed as important. The implementation team lead functioned as an ally and integrated as part of the site team. Clinical staff found communication between the site and the implementation team to be important. One interviewee stated:

*Two-way communication on a day to day, week to week, month to month basis was very helpful.*

Regularly scheduled meetings are a crucial aspect of implementing a successful program launch. By providing structure and opportunities to discuss progress and overcome barriers, these meetings are essential for tracking progress and achieving objectives. Key stakeholders from local VA departments participate in these meetings, ensuring that all necessary perspectives are considered. According to one interviewee, the involvement of stakeholders from different departments facilitates efficient communication and problem-solving:

*It is good because it's several different people from different locations that are tackling it. I feel like everybody that connects are different people, so if one person doesn't know exactly who to speak to, someone else may know, and so we can get it done pretty quickly.*

Regular engagement with stakeholders from various departments helps to streamline operations and minimize delays while also promoting collaboration and a shared sense of purpose. This can lead to increased efficiency as well as a greater focus on shared goals and objectives.

### Concerns and Challenges of Implementation

Participants voiced concerns about technical challenges, staffing shortages to cover both in-person and telehealth visit needs, overbooked schedules leading to delayed referrals, the need for a more standardized operation protocol, and more hands-on training with formative feedback among supporting staff. Participants also faced challenges with appointment no-shows and last-minute cancellations and struggled to find ways to efficiently manage both telehealth and in-person visits to streamline patient flow.

#### Domain I: Staffing

Staffing presented a barrier when sites were limited in size and limited trained telehealth clinical technicians or their turnover, as these 2 participants portrayed:

*My facility is a small community-based outpatient clinic and we have four nurses and four nurses are required to triage patients and we're going to have to have one of those nurses dedicated to doing the tele-imaging, then that's going to be a barrier for that clinic.*

*I feel like we need to have more imagers trained. So basically, if someone calls in sick, Tele dermatology just shuts down. We have to have a backup plan.*

#### Domain II: Scheduling

Participants described difficulty with scheduling due to telespecialty care appointment cancellations:

*Because a clinic has been canceled so many times due to equipment failure and patients being rescheduled, it kind of clogged up the availability, you know, it ran availability out more than 30 days, so a patient is not able to get to a clinic that's close by them at times so there was an issue, or there is an*

*issue with that. That's an ongoing issue with Technology-based Eye Care Services.*

Among the unintended consequences of the implementation of Tele dermatology and Technology-Based Eye Care Services was the additional time required for scheduling, as extra visits were added for referrals from primary care.

*It did impact face-to-face care from a primary care perspective because we were the face for Tele dermatology and Technology-based Eye Care Services ... the prerequisite is that the primary care physicians were the ones who were submitting the consults. So, it required us to at least see that's going on. And so, it was an additional visit with us that we had to fit in outside of maybe a normally scheduled primary care visit.*

At the heart of scheduling, a technician advised that referrals of complex patients with multiple morbidities can be a barrier:

*Not everybody is a candidate for the program; If they have multiple diseases, if they have certain levels of complications, they're not suited for the Technology-based Eye Care Services program, and they shouldn't be scheduled because then they wait to see you and then they've got to wait to see somebody else because you couldn't do what they needed to have done. So, there are several little things that can really wreak havoc on a day and on a schedule.*

#### Domain III: Equipment

Equipment failure was seen as increasing wait times, causing appointment cancellations and rescheduling. One huge barrier was streamlining the reporting process for equipment failure, involving cameras, computers, dermatoscopy, and nonmydriatic fundus photography equipment. With equipment failure or technician absence, veteran care was canceled, and no accurate estimation could be given to schedule the next available appointment, as illustrated by this participant:

*And equipment failure leads to wait time, longer wait times, and patients having to be cancelled and rescheduled, and a lot of times these patients are coming from, you know, 30, 40, 50, 70 miles away. So when you have to push back their appointment time or cancel it altogether, it gets very frustrating for the veterans and for the technicians.*

#### Domain IV: Protocol

Participants also observed a need for specific personnel delegation and a standard operating protocol in place for troubleshooting.

*There is a need. It's a great program, but that way, no matter what role you're in, and if you get looped in, you know, if you don't have the key people in place, you might just have something to go by, just like a checklist, would be my only recommendation as far as that goes.*



Domain V: Training

Training was identified as an ongoing need that affects service provision. Training needs to concentrate on orienting staff at all levels, including those not directly performing Teledermatology and Technology-Based Eye Care Services on the scope of telespecialty care practices. The awareness of the programs will enable them to make the best use of the services, as this technician describes:

*... because the Technology-based Eye Care Services program is a new way of providing eye care, and the other departments not really being familiar with what we do, there was a period of months where it took, I*

*felt like longer, than expected to help the staff understand what we provided.*

Discussion

Principal Findings

This study identified facilitators and potential challenges to telespecialty care implementation through summative content analysis, highlighting the complexity of telespecialty care as an intervention to bridge the access issue for veterans. In line with these findings, recommendations provided in [Textbox 2](#) further complement this study, offering actionable steps for improving the implementation of telespecialty care.

Textbox 2. Telespecialty care implementation recommendations.

<p><b>Staffing</b></p> <ul style="list-style-type: none"><li>• Ensure telespecialty care technicians are not simultaneously assigned regular clinical duties.</li><li>• Train additional telehealth technicians and standardize backup plans for staff absences.</li></ul> <p><b>Scheduling</b></p> <ul style="list-style-type: none"><li>• Implement real-time scheduling to optimize time use with appointment cancellations.</li><li>• Streamline referral process from primary care providers to reduce redundant appointments.</li><li>• Review patient suitability for telespecialty care.</li></ul> <p><b>Equipment</b></p> <ul style="list-style-type: none"><li>• Standardize plan for maintaining software access, reporting and troubleshooting equipment failure, and purchasing new equipment.</li><li>• Identify backup plans for care continuation during equipment or software downtime.</li></ul> <p><b>Protocol</b></p> <ul style="list-style-type: none"><li>• Standardize personnel delegation in telespecialty care.</li></ul> <p><b>Training</b></p> <ul style="list-style-type: none"><li>• Train all staff regularly on the scope and practices of telespecialty care.</li><li>• Promote awareness of telespecialty care across departments.</li></ul> <p><b>Others</b></p> <ul style="list-style-type: none"><li>• Implement a feedback system using patient and staff surveys to identify areas for improvement.</li><li>• Develop and iterate for regular communication and feedback mechanisms within the program.</li></ul>
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Comparison to Prior Work

Our findings are consistent with previous research, providing further support for the numerous advantages of telespecialty care for patients. In line with existing literature [7-11], this study highlights that telespecialty care offers several facilitators, including improved efficiency, convenience, and reduced travel and wait times. Telespecialty care enhances access to health care, especially for underserved areas, enabling access to specialized services [12-16] and addressing emergent conditions that patients may not have initially recognized [17]. Specifically, using store-and-forward teledermatology offers comparable effectiveness to in-person assessment, significantly reduces travel time, and expedites management [18].

Organizational barriers stemming from staffing shortages and lack of designated personnel hindered telespecialty care

implementation. This barrier was exacerbated by the clinic's unmodified workflow, forcing nurses with in-person duties to take on extra work for telespecialty appointments. Consistent with our findings, a study examining the perspectives of primary care physicians on telespecialty care referral reported that teledermatology can disrupt the existing in-person workflow [13]. In situations where staffing shortages occurred, informal temporary workaround strategies were frequently used to handle exceptions to normal workflow [19]. However, reliance on workaround strategies added to the already heavy workload of staff members, as they attempted to manage the demands of telespecialty care within their existing schedules. While workarounds are commonly used in medical settings, it is important to recognize that they have the potential to increase the occurrence of medical errors [20] and place additional strain on clinics with limited resources [21].

This study highlights the criticality of establishing standardized protocols and providing ongoing training for the successful telespecialty care implementation. Stakeholders emphasized the need for protocols to guide troubleshooting and equipment failure and ensure consistent practices. These findings align with existing research, which consistently identifies limited technological knowledge, skills, and a lack of education and training as significant barriers to the implementation and acceptance of telemedicine interventions [22,23]. Furthermore, effective planning for equipment maintenance is paramount to ensure the efficient and effective provision of telespecialty care [24]. Previous research investigating the challenges of maintaining eye care equipment revealed that equipment breakdowns led to frustrating delays in conducting proper examinations and increased the risk of disease progression, resulting in poorer treatment outcomes [25]. Therefore, implementing regular maintenance protocols and establishing contingency plans are critical for minimizing disruptions and optimizing the delivery of telespecialty care.

This study reveals an increase in administrative workload for primary care providers and their support staff due to the surge in specialty care referrals. This underscores the complexities and unintended consequences of telespecialty care implementation, particularly the challenge of managing this heightened workload within limited time constraints [26]. The amplified workload pressures from specialty care referrals have compelled health care professionals to dedicate more time to collecting comprehensive patient histories for teleconsultation referrals. This additional time investment is crucial for maintaining the quality of telehealth consultations and preventing potential errors [27]. Our findings align with broader

literature concerns about the workload burden imposed by administrative tasks in telehealth, emphasizing potential consequences, such as system failures, resulting from increased workload [27].

### Strengths and Limitations

This study has several limitations. First, the use of convenience sampling and unequal sample sizes across stakeholder groups may have introduced selection bias into this study. Additionally, participant perspectives were obtained solely from Teledermatology and Technology-Based Eye Care Services providers at the 2 referring sites within the VA Southeastern Network, which may not be representative of other health care settings, potentially limiting the generalizability of the findings. Future patient interviews may provide additional perspectives on telespecialty care to supplement our providers' perspectives.

### Future Directions

Implementation of telespecialty care should apply implementation science framework to align technology, people, organizations, and context and to add value to patient care and health care systems [28]. Adapting a learning system approach that continually improves telespecialty care implementation is needed to account for health care system complexity and different user needs and to avoid unintended consequences and challenging workflow issues [28-32]. This study provided insights into the intricacies of telespecialty care implementation, shedding light on both facilitators and barriers encountered in the delivery of these services. Addressing these challenges and opportunities has the potential to increase access to care, enhance the quality of care provided, and promote the sustainability of telespecialty care innovations.

### Acknowledgments

This study is supported by the Rapid Pilot Projects Program from the Veterans Affairs (VA) Health Services Research & Development and Charleston VA Health Equity and Rural Outreach Innovation Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veteran Affairs. HY is supported by VA Health Services Research & Development (grant I01-HX003473).

### Authors' Contributions

All authors made substantial contributions to the conception and design, acquisition of data, analysis, and interpretation of data; were involved in drafting the paper and revising it critically for important intellectual content; and gave final approval of the version to be published. All authors agree to be accountable for all aspects of the work.

### Conflicts of Interest

None declared.

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## Abbreviations

**COREQ:** Consolidated Criteria for Reporting Qualitative Research

**VA:** Veterans Affairs

*Edited by R Dellavalle; submitted 30.06.23; peer-reviewed by A Oakley, D Gunasekeran; comments to author 06.09.23; revised version received 04.11.23; accepted 08.01.24; published 07.02.24.*

*Please cite as:*

*Li Y, Pope C, Damonte J, Spates T, Maa A, Chen S, Yeung H*

*Barriers and Facilitators to Teledermatology and Tele-Eye Care in Department of Veterans Affairs Provider Settings: Qualitative Content Analysis*

*JMIR Dermatol* 2024;7:e50352

URL: <https://derma.jmir.org/2024/1/e50352>

doi: [10.2196/50352](https://doi.org/10.2196/50352)

PMID: [38324360](https://pubmed.ncbi.nlm.nih.gov/38324360/)

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## Research Letter

# The Value of Teledermatology Advice for Skin Toxicity in Oncology: Experience From a Pilot Study

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(*JMIR Dermatol* 2024;7:e40053) doi:[10.2196/40053](https://doi.org/10.2196/40053)

**KEYWORDS**

e-health; teledermatology; oncology; epidermal growth factor receptor; EGFR-inhibitors; skin toxicity; cancer; dermatology; therapy; pilot study

## Introduction

Epidermal growth factor receptor (EGFR) inhibitors are increasingly used in oncologic treatments. Skin toxicity is a possible side effect and can seriously impair quality of life (QoL) and result in treatment tapering or discontinuation [1-4]. Despite several preventive and treatment guidelines, oncologists encounter difficulties in managing skin toxicities [5,6]. In Belgium, this struggle is compounded by some hospitals having no or only part-time in-house dermatologists. We initiated a teledermatology pilot project in 3 Belgian hospitals with no or limited access to dermatological advice and evaluated its value in anti-EGFR-induced skin toxicity for both patients and oncologists.

## Methods

**Overview**

Patients receiving anti-EGFR treatment and developing skin toxicity were eligible. Clinical imaging data were exchanged through an existing secured platform (Mediris). Three oncologists from 3 different Belgian nonuniversity hospitals participated. Clinical information and images were uploaded to the platform and sent to the teledermatologists. Three dermatologists from Ghent University Hospital were involved as teledermatologists and formulated their advice within 48

hours. Questionnaires on expectations and satisfaction with the teledermatology platform were completed by both patients and oncologists at the start and end of the study.

**Ethical Considerations**

Ethical approval was obtained from Ghent University Hospital (EC2018/0984) and participating hospitals, and participants provided written informed consent.

## Results

The study started in January 2019 and was prematurely terminated in mid-March 2020 because of the COVID-19 pandemic. In total, 35 store-and-forward consultations were performed for 6 patients. The most frequent reasons for advice involved xerosis or eczema (n=27, 77%) and papulopustular rash (n=18, 51%). All patients had grade 2 toxicity according to the CTCAE (Common Terminology Criteria for Adverse Events; version 5.0).

Three out of 6 patients completed the questionnaires; they were overall positive about the project and felt that teledermatology was reliable, valuable, and efficient. Although all the participating oncologists reported difficulties in accessing dermatological advice, they used the teledermatology platform less than anticipated. They all reported uploading of images and patient information to be difficult and time-consuming.

Nevertheless, the oncologists noted that teledermatology was as valuable (1/3) or more valuable (2/3) than expected.

In 37% (13/35) of all teleconsultations, teledermatologists reported that more information was needed to provide tailored advice. In 29% (10/35) of consultations, teledermatologists indicated that a live consultation would have been relevant, either to collect additional information for decision-making or to explain and motivate the patient about a specific treatment.

Discussion

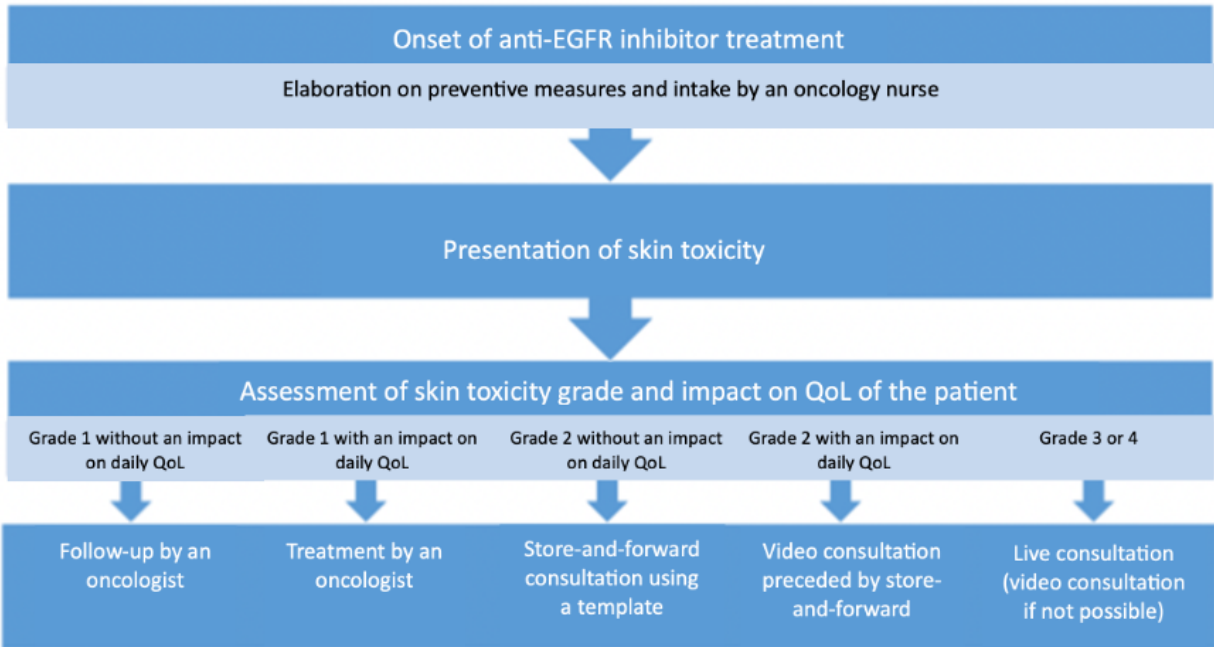
Although skin toxicity during anti-EGFR treatment might be considered a minor, non-life-threatening side effect, it is known to markedly impact patients' QoL. This may lead to dose tapering or early treatment discontinuation, thereby potentially interfering with its anticancer effects [1-4]. Skin toxicity is reported as being more discouraging than complete hair loss and as discouraging as nausea [6]. Oncologists intend to initiate skin-focused treatment in cases of skin toxicity of grades 2 and 3 and only refer 8% of their patients for specialized dermatological advice [4]. This small multicenter pilot study aimed to investigate the value of teledermatology to facilitate dissemination of dermatological advice to patients treated with EGFR inhibitors.

From January 2019 until mid-March 2020, overall 35 teleconsultations were provided to 6 patients. Images and clinical

information were uploaded to a secured eHealth platform and evaluated by a teledermatologist within 48 hours. Unfortunately, the enrollment was lower than anticipated, most probably because the teledermatology platform was perceived as non-user-friendly. The teledermatologists reported clinical information to be missing in about one-third of the teleconsultations. They indicated the lack of direct communication to promote diagnostic accuracy and therapeutic adherence. A suggested workflow is depicted in Figure 1. Store-and-forward teledermatology has been shown to be able to improve the efficiency of and access to care [7]. The COVID-19 lockdown has demonstrated that teledermatology can help in minimizing unnecessary in-person visits. Many skin conditions may be adequately managed remotely, while others may be selected for an additional step (triaging). This could imply a physical or video consultation to advise patients in other hospitals or at home.

Although several guidelines on skin toxicity management are available, skin toxicity and its impact on QoL seem not always properly recognized. Teledermatology may offer benefits including reduced waiting times, travel costs and sanitary costs, and equalization of access to specialist advice. In this pilot study, both oncologists and patients acknowledged the added value of teledermatological advice on skin toxicity during anti-EGFR therapy. However, several shortcomings of a store-and-forward consultation are revealed. More specifically, the importance of a practical teleplatform should be emphasized.

Figure 1. Proposition of the ideal workflow for the management of anti-EGFR-related skin toxicity. EGFR: epidermal growth factor receptor; QoL: quality of life.



Acknowledgments

We would like to thank Drs Koen Thorrez, Peter Van Lint, and Joanna Van Erps for their efforts and critical insights in this project. This study was supported as a value-based health care project by Amgen.

## Conflicts of Interest

None declared.

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## Abbreviations

**CTCAE:** Common Terminology Criteria for Adverse Events

**EGFR:** epidermal growth factor receptor

**QoL:** quality of life

*Edited by R Dellavalle; submitted 03.06.22; peer-reviewed by V Long, H Wu; comments to author 09.11.22; revised version received 20.02.23; accepted 07.02.24; published 29.02.24.*

### Please cite as:

Mylle S, Papeleu J, Hoorens I, Verhaeghe E, Brochez L

*The Value of Tele dermatology Advice for Skin Toxicity in Oncology: Experience From a Pilot Study*

*JMIR Dermatol* 2024;7:e40053

URL: <https://derma.jmir.org/2024/1/e40053>

doi: [10.2196/40053](https://doi.org/10.2196/40053)

PMID: [38422495](https://pubmed.ncbi.nlm.nih.gov/38422495/)

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## Original Paper

## Public Interest in Acetyl Hexapeptide-8: Longitudinal Analysis

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**Abstract**

**Background:** Acetyl hexapeptide-8, also known as Argireline, is a topical, short-acting, synthetic peptide that has recently gained popularity for its antiwrinkle effects. This agent has emerged as a more accessible alternative to botulinum neurotoxin.

**Objective:** This study evaluates the public interest in acetyl hexapeptide-8 in the United States from 2013 to 2023, as described by search volume on Google, the most-used search engine.

**Methods:** We analyzed the longitudinal relative monthly search volume from January 1, 2013, to January 1, 2023, for acetyl hexapeptide-related terms. We compared the internet search trends for “Botox” during this period to “Argireline.”

**Results:** The terms “Argireline” and “Botox in a Bottle” both had substantial increases in search volume in 2022. Although its search volume is drastically increasing, “Argireline” was less searched than “Botox,” which had a stable, up-trending search volume over the past decade.

**Conclusions:** The increasing interest in acetyl hexapeptide-8 may be due to its cost-effectiveness and use as a botulinum neurotoxin alternative. Affordability, over-the-counter availability, and ease of self-application of the agent suggest its potential to enhance accessibility to cosmetic dermatologic care.

(*JMIR Dermatol* 2024;7:e54217) doi:[10.2196/54217](https://doi.org/10.2196/54217)

**KEYWORDS**

acetyl-hexapeptide-8; anti-aging; anti-wrinkle; Argireline; BoNT; botox; botulinum neurotoxin; cosmetic dermatology; cosmetic; dermatologist; dermatology; injectable neurotoxin; neurotoxin; skin specialist; topical agent; topical

**Introduction**

Botulinum neurotoxins (BoNTs) have long been considered the most effective cosmetic intervention to reduce wrinkles and fine lines [1]. However, many individuals face barriers such as cost and transportation when seeking BoNT treatment.

Acetyl hexapeptide-8, which acts similarly to BoNTs, has gained traction due to its low cost, topical application method, and increased safety of use [2]. The peptide may be referred to as acetyl hexapeptide-3 or acetyl hexapeptide-8 amide, and it is more commonly identified by its trade name, Argireline, produced by the Lubrizol Corporation. The topical peptide is a synthetic compound mimicking the N-terminus of synaptosomal-associated protein of 25 kDa (SNAP-25) [3]. This structure allows for inhibition of the soluble N-ethylmaleimide-sensitive factor activating protein receptor (SNARE) ternary complex assembly and consequently inhibits

Ca<sup>2+</sup>-dependent exocytosis of acetylcholine into the neuromuscular junction [2,3]. This mechanism is similar to that of BoNT type A, yielding comparable outcomes that are shorter-acting with milder neurotoxicity [2,3]. As of 2020, acetyl hexapeptide-8 was reported as an ingredient in 452 cosmetic products [4]. Though there are limited data on the price ranges of these products, a recently popularized brand of 10% Argireline water-based serum costs US \$9.40 for an approximately 4-month supply. Prices may vary, but acetyl hexapeptide-8 products appear to cost less than cosmetic BoNT injections, which range from US \$300 to US \$600 per treatment [5]. This affordability expands access to antiwrinkle care across a broader socioeconomic demographic. Additionally, the product is considered safe for topical use with minimal risk of complications or adverse effects [4,6,7].

A large-scale study published in 2013 revealed the efficacy of acetyl hexapeptide-8 in reducing periorbital wrinkles [8].

However, Argireline became popular on TikTok, a social media platform where users share short clips, in 2022 [9,10]. The term “Botox in a Bottle” was coined to describe the product on TikTok, where users praised the compound for its antiaging properties by reducing wrinkles and fine lines [11]. Acetyl hexapeptide-8 is marketed as a low-cost alternative to BoNT treatments for those hesitant or unable to afford injection therapies [11].

With casual reporting of increased acetyl hexapeptide-8 popularity [11], it is imperative to quantitatively analyze trends in public interest in the agent. Such analysis serves as a reflection of trends in consumer interest and use [12]. With Google being the most widely used search engine globally and in the United States [13], it serves as a primary platform for individuals interested in acetyl hexapeptide-8 products to seek further information. This study is the first to comprehensively examine public interest in acetyl hexapeptide-8 on the internet, offering a realistic view of its trends in the United States and the necessity for further medical research on the product.

## Methods

The relative monthly volume of acetyl hexapeptide-related Google searches was determined using the Google Trends database [14]. Google Trends is a tool that provides insight into longitudinal search volume data on Google and has been used in recent literature to study human behaviors and interests without consumer barriers such as cost and transportation [14-16].

In this analysis, search volume data were collected between January 1, 2013, and January 1, 2023. The following search terms were examined: “Argireline,” “Botox in a Bottle,” “Acetyl hexapeptide-3,” and “Acetyl hexapeptide-8.” These terms were selected to encompass the scientific nomenclature, trade name,

and colloquial phrases relating to acetyl hexapeptide-8. Additionally, the term “Botox” was included to provide a basis for comparison between traditional BoNT injections and the newer topical alternative, Argireline.

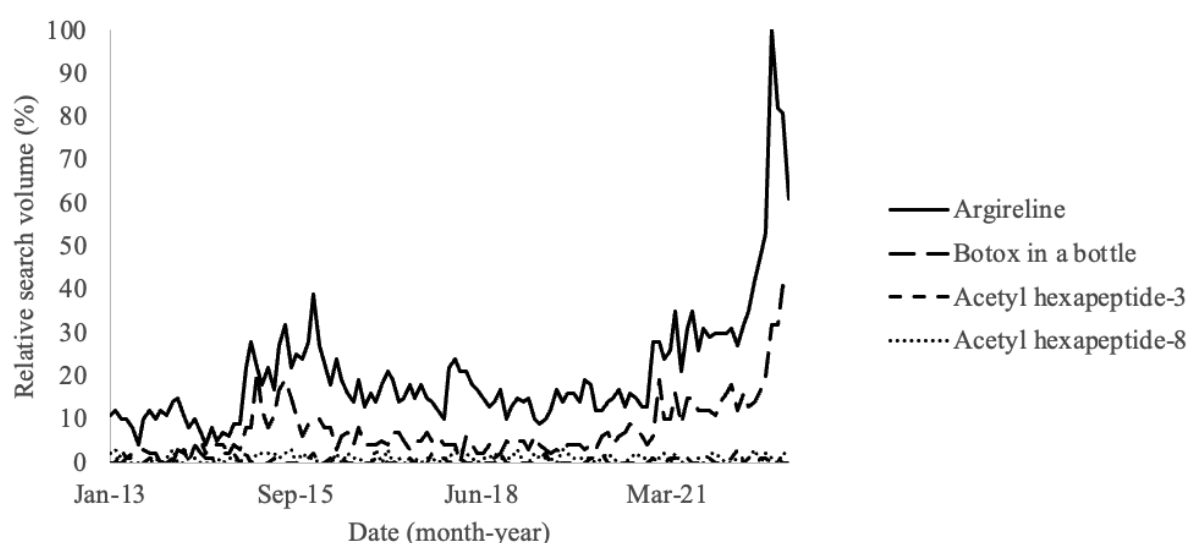
Monthly search volumes for each of these terms were obtained from Google Trends as normalized values on a relative search index. The index scale used for analysis ranged from 0, representing minimal search volume, to 100, indicating maximal search volume.

## Results

Search terms “Argireline” and “Botox in a Bottle” followed similar trends in web-based popularity, while “Acetyl hexapeptide-8” and “Acetyl hexapeptide-3” did not (Figure 1). There appeared to be relatively sparse online interest in acetyl hexapeptide-related search terms before February 2015. Following this spike, public interest, as described by search volume, stabilized before rising in May 2021, with a peak in October 2022. Google users primarily searched for acetyl hexapeptide-8 by its trade name, “Argireline,” followed by the colloquial name, “Botox in a Bottle.” The terms “Acetyl hexapeptide-3” and “Acetyl hexapeptide-8” had the lowest search volumes with relatively stable searches over the past decade.

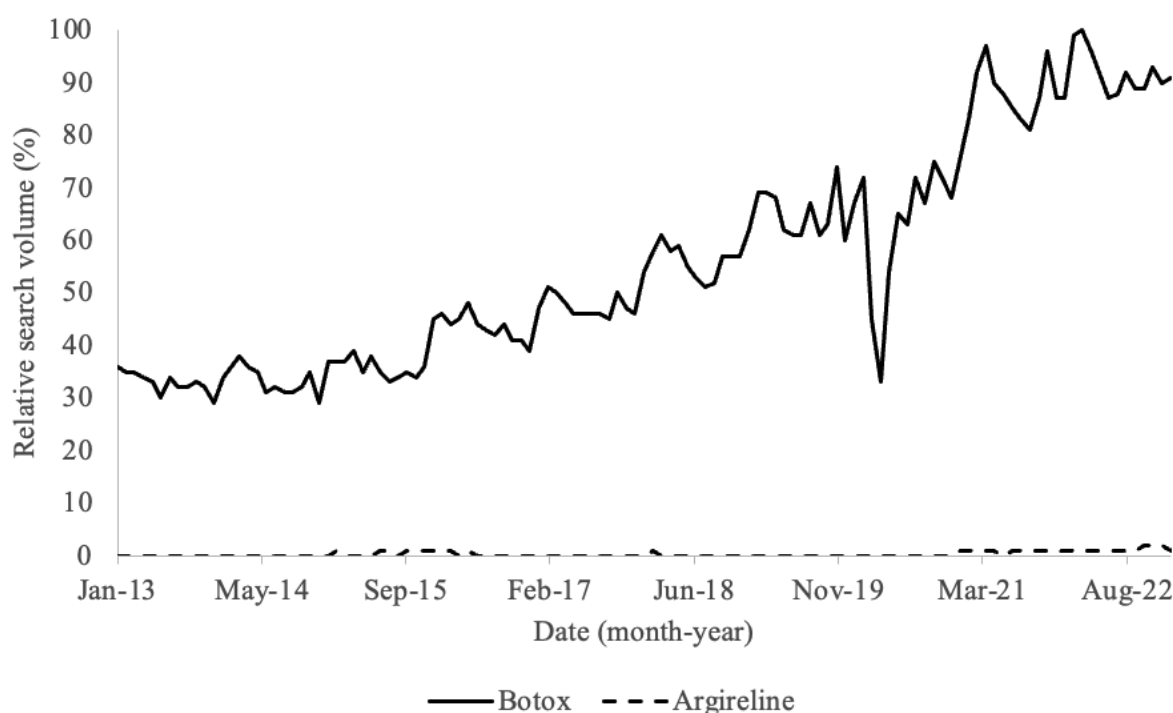
Acetyl hexapeptide-8 is frequently compared to BoNTs due to their similar mechanism of action and overlapping use as antiwrinkle agents. However, despite its recent uptrend in Google searches (Figure 1), “Argireline” is searched less than the term “Botox,” which has steadily up-trended over the past decade (Figure 2). Botox appears to have relatively substantial and consistent internet popularity compared to the newly popularized Argireline peptide.

**Figure 1.** Relative search volume of acetyl hexapeptide-related terms on Google from January 1, 2013, to January 1, 2023.





**Figure 2.** Comparison of relative Google search volume for search terms “Argireline” and “Botox” from January 1, 2013, to January 1, 2023.



## Discussion

### Overview

This study is the first to describe the longitudinal internet popularity of the topical antiwrinkle agent acetyl hexapeptide-8 over the past decade. Viewers likely searched the internet to purchase or research Argireline peptide following exposure through social media or other sources. Though important studies demonstrating the antiwrinkle effects of acetyl hexapeptide-8 were published in 2013, the search volume of the product's trade name, Argireline, increased exponentially in the year 2022 (Figure 1) [7]. This was likely due to the popularization of the serum through social media platforms such as TikTok. The longitudinal increase in Argireline and related terms' search volumes confirms a growing public interest in the agent, likely as an alternative to traditional BoNTs. Despite its marketing as a cost-effective, less-invasive, and shorter-acting alternative to BoNTs [1,11], Google Trends data analysis revealed that the internet popularity of “Botox” increased within the last decade as well. Botox was searched for far more frequently than the newly popularized Argireline. This may be due to the perceived reliability of BoNTs, as they have been approved by the Food and Drug Administration for cosmetic use since 2002 [17,18].

The relatively low search volume for the terms “Acetyl hexapeptide-3” and “Acetyl hexapeptide-8” may stem from the knowledge barrier of scientific jargon and specialized terminology [19,20]. Products containing acetyl hexapeptide-8 appear to use the agent's scientific nomenclature or its trade name in ingredient lists, with no consensus on the use of a single term. Internet users may be familiar with terms or phrases commonly used in English, such as “Botox in a Bottle” or “Argireline,” and rely on them to better comprehend the effects of the product [19,20]. Importantly, the conflicting public search

trends between lay and scientific jargon may indicate a need for further scientific research on the agent and clarification to consumers regarding their acetyl hexapeptide-8 product options.

The less-invasive nature of acetyl hexapeptide-8, the ability to self-apply cost-effectively, and the minimal side effects are potential reasons for its increasing popularity over the past decade. Due to its lesser neurotoxicity and shorter-acting effects, acetyl hexapeptide-8 does not carry the risks of ptosis, eyebrow asymmetry, and other complications seen in facial BoNT injections [4,6,21]. The ability to self-apply acetyl hexapeptide-8 products brings down the cost of their usage, as sterile equipment and a medical professional are not required for their application. Argireline peptide solutions typically cost less than US \$100 when purchased over the counter, whereas BoNT injections require a medical professional for administration, costing an average of US \$300-US \$600 [5,22]. The relatively low price point and over-the-counter status of acetyl hexapeptide-8 products allow them to improve accessibility to cosmetic dermatologic care. Self-application also improves accessibility to antiwrinkle care, as transportation to a site and appointment time are no longer barriers to treatment.

There are various strengths to this project. The anonymity of Google Trends big data limits interviewer and chronology bias. Observing internet search volume gauges consumer interest and exposure without the financial barrier of product purchase. As of 2022, Google is the most-used search engine, occupying 86.99% of the United States search engine market [13]. Therefore, Google search volumes provide the most complete understanding of public interest and internet exposure to acetyl hexapeptide-8. A limitation of Google Trends' big data is the lack of community and individual-level data, hindering assessment groups with differing representation. It also allows

for potential bias from differences in the interests of Google users compared to those who use other search engines.

Understanding consumers' skincare preferences can guide future research regarding trending products' efficacy, safety, and innovation. Future directions for acetyl hexapeptide-8 research include its potential use as a therapeutic agent alongside the current cosmetic indications. Assessing Argireline use in various socioeconomic groups, age groups, and geographic locations may provide greater insight into its role as an accessible option for dermatologic health maintenance.

## Conclusion

This study was the first to analyze public interest in acetyl hexapeptide-8, as described by the relative search volume of acetyl hexapeptide-related terms on Google over the past decade. Though the agent's antiwrinkle effects were published in 2013, results indicate a recent surge in internet popularity in 2022. Acetyl hexapeptide-8 can improve access to antiwrinkle care due to its low price point, over-the-counter status, and ability to be self-applied. The authors recommend additional research assessing the safety profiles of acetyl hexapeptide-8 products as well as their use and interest among various demographics.

## Conflicts of Interest

None declared.

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## Abbreviations

**BoNT:** botulinum neurotoxin

**SNAP-25:** synaptosomal-associated proteins of 25 kDa

**SNARE:** soluble N-ethylmaleimide-sensitive factor activating protein receptor

*Edited by R Dellavalle, S Zhao; submitted 01.11.23; peer-reviewed by A Kluczyk, A Cao; comments to author 25.12.23; revised version received 30.12.23; accepted 28.01.24; published 20.02.24.*

*Please cite as:*

Olsson SE, Sreepad B, Lee T, Fasih M, Fijany A

Public Interest in Acetyl Hexapeptide-8: Longitudinal Analysis

JMIR Dermatol 2024;7:e54217

URL: <https://derma.jmir.org/2024/1/e54217>

doi: [10.2196/54217](https://doi.org/10.2196/54217)

PMID: [38376906](https://pubmed.ncbi.nlm.nih.gov/38376906/)

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Research Letter

# Diversity Among American Dermatological Association Members by Sex and Geographic Region

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(*JMIR Dermatol* 2024;7:e47802) doi:[10.2196/47802](https://doi.org/10.2196/47802)

**KEYWORDS**

American Dermatological Association; disparity; representation; dermatology; urban; rural; dermatological society; diversity; inclusion; equity; sex; membership; acquisition; demographic

## Introduction

Professional societies create networking, mentorship, and research collaboration opportunities, but disparities in gender, sex, geographic, ethnic, and racial composition within societies disadvantage professional development among underrepresented individuals. Our group evaluated the American Dermatological Association (ADA) since election occurs through a nomination by existing members; we hypothesize this process creates gaps in representation. Given the professional implications for underrepresented individuals, this review aims to quantify the disparities in sex and geographic location of ADA members. Ethnicity/race was not analyzed because the information was not publicly available.

## Methods

**Overview**

In February 2023, the ADA directory identified 767 members. Two independent reviewers recorded member names,

self-identified sex, city, and state listed on their national practitioner identifier, and those who were deceased; a third reviewer resolved data conflicts. Sex was identified on national practitioner identifier databases. Data were omitted for retired, deceased, or unidentified members. The statistical analysis was performed using R software (R Foundation for Statistical Computing), and the package “usmap” was used to create the figure. The directory was updated to include the 2023 inductees.

**Ethical Considerations**

Data was publicly available and deidentified, and did not require institutional review board review.

## Results

Of the 688 ADA members, 227 (33%) were female and 461 (67%) were male. A total of 581 (84.4%) members practiced in the United States, while 107 (15.6%) members practiced internationally; 26 (24.3%) of the 107 international members were female, and 81 (75.7%) international members were male. Among the 41 represented states, 2 had a similar number of

male and female members (Figure 1). The top 5 states represented 247 (42.5%) members: California had 79 (13.6%) members, followed by 60 (10.3%) members in New York, 38 (6.5%) members in Massachusetts, 37 (6.3%) members in Pennsylvania, and 33 (5.6%) members in Florida (Table 1).

Figure 1. Representation of the American Dermatological Association members by sex and geographic region.

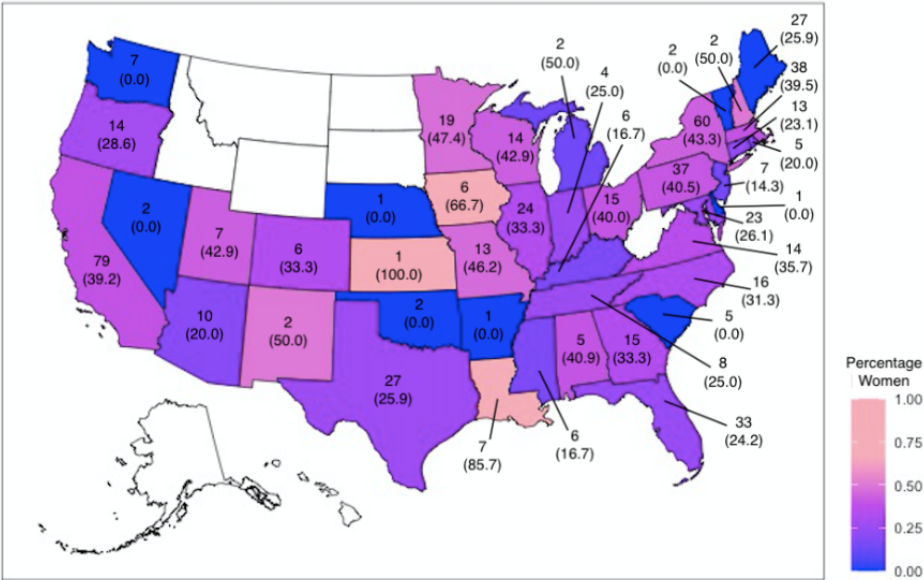


Table 1. Breakdown of American Dermatological Association membership by US region and top 10 states in female membership.

US regions	Members, n (%)	Female members, n (%)	Members per 1,000,000 people, n	Female members per 1,000,000 people, n
Northeast	166 (28.6)	62 (37.3)	2.90	1.08
South	176 (30.3)	53 (30.1)	1.38	0.42
Midwest	112 (19.3)	43 (38.4)	1.63	0.62
West	127 (21.9)	43 (33.9)	1.61	0.55
Total	581 (100.0)	201 (34.6)	1.75	0.61

Discussion

Our study demonstrates that ADA membership does not represent the female dermatology workforce relative to geographic location and academic practice setting. Per Centers for Medicare & Medicaid Services data from 2020 and dividing US regions per the US Census Bureau criteria, female dermatologists ranged from 1430 of 1508 (48.7%) to 1148 of 1043 (52.4%) of the workforce in all regions of the United States [1]. In academic dermatology, the female workforce increased from 18 of 167 (10.8%) in 1970 to 749 of 1464 (51.2%) in 2018 [2]. Furthermore, as of 2020, 1125 (47.6%) of 2363 dermatologists who graduated medical school 28-36 years ago after graduating medical school are female [1], suggesting a diversified candidate pool for late-career recognitions like ADA membership.

Societies should aim to represent the dermatology workforce, which by extension should aim to represent the diverse composition of the United States. Data demonstrates direct benefits to patients stemming from a diverse workforce. For instance, an analysis of practice characteristics using the Black Dermatologist Directory identified 221 individuals (80% female). It was found that Black dermatologists served a higher

proportion of non-Hispanic Black patients relative to other dermatologists (21.0 vs 2.7;  $P<.001$ ) [3]. This data suggests a racial concordance preference, which can impact patient outcomes. For instance, data shows an 11% decrease in primary medication nonadherence among racial concordant Black dermatologists–Black patient dyads, independent of insurance status [4]. Research on ethnic/racial concordance can differ between ethnic/racial groups; however, cultural sensitivity is cited as a component of positive interactions [5]. Thus, honoring underrepresented individuals and diversifying professional societies can encourage cultural sensitivity among dermatologists through interactions with each other.

For dermatology-specific professional societies, data quantifying the impact of increased female representation is limited. However, interviews [6] of a women-focused professional organization report improved academic advancement, leadership experiences, awards, promotions, mentorship, and peer support, and reduced professional isolation. Other themes were the development of initiatives addressing systemic gender inequities/challenges like navigating bias, promoting pay equity, and family-friendly workplace policies. Given these benefits, there is a clear need for improved female representation in professional societies.

Specifically for the ADA, per the bylaws [7], candidates undergo membership proposition, review, and evaluation by a membership committee before proceeding to a ballot election. ADA leadership can promote diversity in different steps. For example, societies like the American Academy of Dermatology and The Skin of Color Society have mentorship programs dedicated to increasing diversity. A similar program may help identify competitive individuals for ADA membership to help improve their recognition among ADA members. In addition, including a race/sex-conscious nomination round can help

diversify the pool of candidate reviews. Limitations of this study include the moment-in-time design and the exclusion of the race/ethnicity of members; the data needed to address these points could show important trends that demonstrate increased diversity. Future research can focus on evaluating the epidemiological characteristics of membership within other dermatologic societies, how these societies have changed over time, and identifying outcome measures to quantify the impact that diverse professional societies have on professional development.

## Conflicts of Interest

RPD is an editor for Cochrane Skin, the editor in chief of JMIR Dermatology, the coordinating editor representative on the Cochrane Council, and a Cochrane Council cochair. RR is an editorial fellow for JMIR Dermatology. RPD receives editorial stipends (JMIR Dermatology), royalties (UpToDate), and expense reimbursement (Cochrane). RR receives fellowship funding from the National Institutes of Health (5T32AR007411-37; principal investigator: Dennis Roop).

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## Abbreviations

**ADA:** American Dermatological Association

*Edited by J Lipoff; submitted 01.04.23; peer-reviewed by S Feldman, H Zhang, X Zhang; comments to author 23.05.23; revised version received 06.07.23; accepted 24.10.23; published 10.01.24.*

### *Please cite as:*

Rodriguez R, Anderson L, Woolhiser E, Balmorez T, Cook B, Hauptman M, Kirk J, Keime N, Dellavalle RP  
Diversity Among American Dermatological Association Members by Sex and Geographic Region  
*JMIR Dermatol* 2024;7:e47802  
URL: <https://derma.jmir.org/2024/1/e47802>  
doi: [10.2196/47802](https://doi.org/10.2196/47802)  
PMID: [38198199](https://pubmed.ncbi.nlm.nih.gov/38198199/)

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Editorial

# Themes and Topics on Diversity, Equity, and Inclusion in JMIR Dermatology Publications

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## Abstract

Publications dealing with topics considered to be pertinent to diversity, equity, and inclusion are increasing. Due to the increasing trend, dermatology journals have started to implement ways to evaluate and understand these publications. Here, we discuss a keyword approach to identify and then categorize these publications. Keywords identified 43 manuscripts. Two reviewers screened the articles' titles and abstracts, and recommended a full manuscript review for 24 publications. Through the scope of definitions from the National Institutes of Health, an editorial board member performed a full-text review and assigned a primary theme to the publications. Themes included equity (n=20) and diversity/inclusion (n=4). Topics were racial/ethnic differences in care delivery or society (n=17), incomplete understanding of gender and sex (n=3), gender identity (n=2), socioeconomic class and its impact on health (n=1), care for rural underserved communities (n=1), and religion (n=1). The results of this review demonstrate a predominance of equity-related publications, particularly emphasizing racial/ethnic differences in health care delivery, in the publications identified in *JMIR Dermatology*. Future research can focus on creating a review aid to assist editorial board members when providing feedback to manuscripts, refining the keywords, and using thematic analysis methodology to evaluate large sets of publications.

(*JMIR Dermatol* 2024;7:e48762) doi:[10.2196/48762](https://doi.org/10.2196/48762)

**KEYWORDS**

diversity; equity; inclusion; editor; DEI; committee; disparity; underrepresented; dermatology; skin of color; SOC

## Introduction

Disparities in racial/ethnic diversity within dermatology prevail. Despite the disparity, dermatology journals published more articles on topics related to diversity, equity, and inclusion (DEI) from 2008 to 2019 compared to other specialties [1]. In the absence of a formal DEI review process, publications risk propagating an incomplete understanding of social determinants of health and their interplay with race/ethnicity, gender identity, sex assignment at birth, and religion [2].

To the authors' knowledge, evidence-based approaches to reviewing manuscripts dealing with DEI topics and the impact of DEI committees or a DEI editorial board member are limited. *The Journal of Vascular Surgery* noted a similar pattern [3], appointed a DEI editor, and subsequently observed an increase in publications on DEI topics. *JAMA Dermatology* published an article [4] describing a DEI framework in editorial reviews, publication diversity, the need for publishing measures/metrics, and future steps required for implementation. The *Journal of the American Academy of Dermatology (JAAD)* has also instituted extra review layers for manuscripts exploring sexuality, gender identity, race/ethnicity, religion, or other



potentially emotive topics [5]. *JMIR Dermatology* acknowledges the need for understanding these topics. Thus, the purpose of this paper is to improve the understanding of DEI manuscripts and identify themes and topics within publications.

Methods

Overview

Previous research defined DEI publications using target keywords [6]. Our diverse team assigned DEI keywords

(Textbox 1) and used JMIR Publication’s editorial management system (Open Journal Systems [OJS]) to find and identify 43 potential DEI manuscripts. Two independent reviewers read the abstracts to determine if a dedicated DEI editor would be recommended and the reason for their assessment. Conflicts prompted a third full-text review. A total of 24 manuscripts received a DEI review recommendation. A *JMIR Dermatology* editorial board member then performed a full-text review and categorized each manuscript’s primary theme and topic. The primary theme was selected within the scope of definitions from the National Institutes of Health (NIH) [7] (Textbox 1).

Textbox 1. Key terms and words used to identify and define publications dealing with diversity, equity, and inclusion.

<b>Keywords</b>
Disparities, diversity, equity, inclusion, disparity, underserved, rural, Black, Hispanic, Latinx, Latino, LGBTQ, skin of color, Asian, Pacific Islander, Native American, American Indian, Alaska Native, White, gender, sex, underrepresented in medicine, minority, URM
<b>Diversity</b>
The practice of including many communities, identities, races, ethnicities, backgrounds, abilities, cultures, and beliefs of people, including underserved communities.
<b>Equity</b>
The consistent and systematic fair, just, and impartial treatment of all individuals, including individuals who belong to underserved communities that have been denied such treatment.
<b>Inclusion</b>
The recognition, appreciation, and use of the talents and skills of individuals of all backgrounds.

Ethical Considerations

Data was publicly available and deidentified, and did not require institutional review board review.

Results

In the 24 reviewed manuscripts, primary publication themes dealt with equity (n=20), followed by diversity and inclusion (n=4). The topics included racial/ethnic differences in care or society (n=17), incomplete understanding of gender and sex (n=3), gender identity (n=2), socioeconomic class and its impact on health (n=1), care for rural underserved communities (n=1), and religion (n=1).

Conclusion

DEI publications are more common relative to previous decades. Dermatology journals are incorporating measures to provide

evidence-based methods to improve our understanding of DEI publications. Here, we described a way to evaluate DEI publications within *JMIR Dermatology* and their common themes/topics. Limitations of our study include the sample size. The themes of DEI can also overlap among publications. Standard definitions of DEI assisted the primary theme assignment. Based on the definitions adapted from the NIH, diversity is characterized by including individuals. Inclusion is distinguished by recognizing and appreciating them. Equity was the most prevalent theme and highlights the fair, just, and equal treatment of individuals in the scope of bias. While our authors are diverse, our perspectives are limited and may not be inclusive of all themes or topics within DEI literature. Future research can focus on creating a DEI review aid for editorial boards, broadening and refining the keywords, and using thematic analysis methodology to identify themes/topics among larger sets of publications.

Acknowledgments

RR receives fellowship funding from the National Institutes of Health (2T32AR007411-31A1; principal investigator: Dennis Roop).

Conflicts of Interest

RR is an editorial diversity, equity, and inclusion board member/fellow for *JMIR Dermatology* and a Dermatology Clinical Trial fellow. RPD is the editor-in-chief of *JMIR Dermatology*. The other authors have no conflicts of interest to declare.

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## Abbreviations

**DEI:** diversity, equity, and inclusion

**JAAD:** *Journal of the American Academy of Dermatology*

**NIH:** National Institutes of Health

**OJS:** Open Journal Systems

*Edited by R Alhusayen; submitted 06.05.23; peer-reviewed by S Feldman, D Verran; comments to author 23.05.23; revised version received 21.09.23; accepted 27.12.23; published 02.02.24.*

*Please cite as:*

Rodriguez R, Osman KM, Anderson L, Pascual M, Dellavalle RP

*Themes and Topics on Diversity, Equity, and Inclusion in JMIR Dermatology Publications*

*JMIR Dermatol* 2024;7:e48762

URL: <https://derma.jmir.org/2024/1/e48762>

doi: [10.2196/48762](https://doi.org/10.2196/48762)

PMID: [38306177](https://pubmed.ncbi.nlm.nih.gov/38306177/)

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Research Letter

# Visibility of Board-Certified Dermatologists on TikTok

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## Abstract

Tik Tok is an emerging social media platform that provides a novel opportunity for health practitioners such as dermatologists to disseminate accurate health information.

(*JMIR Dermatol* 2024;7:e46085) doi:[10.2196/46085](https://doi.org/10.2196/46085)

**KEYWORDS**

board; certification; board certification; health; media; public; social; TikTok; social media; health information; misinformation; diagnosis; users; medical training; training; media content; skin; derma; dermatologist; dermatology; epidermis; dermatitis; cellulitis; skin doctor; skin; hair; nail

## Introduction

TikTok is a video-sharing social media platform with over 1.1 billion active users since its launch in 2016 [1]. Social media platforms such as TikTok are used by medical and nonmedical professionals to share health information. However, health misinformation spreads more quickly than evidence-based information, posing a public health issue [2]. Our study aimed to categorize popular dermatology-related posts and analyze the visibility of board-certified dermatologists (BCD) on TikTok.

## Methods

The methods were designed based on a previous study that examined dermatology content on Instagram by Park et al [3]. First, a list of top dermatologic diagnoses and procedures was compiled based on the National Ambulatory Medical Care Survey and the American Society of Dermatologic Survey of Dermatologic Procedures [4,5]. Then, all of the terms were

queried as hashtags in TikTok's search feature on January 2, 2021.

The 20 dermatologic conditions and procedures with the highest total views were identified. Profession-specific hashtags (#dermatology, #boardcertifieddermatologist, #dermatologist, and #derm) were also queried. The term with the highest total views was chosen among synonymous terms.

The first 10 posts under each of the 44 hashtags were then viewed. Top posts were selected through TikTok's private algorithm, which uses total views, followers, and other metrics. Users' self-reported occupations were identified, and board certifications were confirmed through the Certification Matters website [6]. Posts were categorized into 4 categories: educational, self-promotional, non-paid product placements, and advertisements. Educational content was identified as any post that aimed to provide informative material regarding a dermatologic condition and/or procedure. Self-promotional content was defined as posts intended to advance the user's professional pursuits. Non-dermatology-related posts were excluded.

Results

Of the 18.68 billion total views of the hashtags investigated, 12.9 billion (69.1%) were related to skin conditions, 4.26 billion (22.8%) were related to dermatologic procedures, and 1.52 billion (8.17%) were profession-specific.

Out of 231 unique user profiles that accounted for the 360 top dermatology-related posts, 70 (30.3%) were patients, 66 (28.57%) were medical professionals, and 11 (4.76%) were estheticians (Table 1).

BCD and dermatology residents made up 15 (6.49%) and 7 (3.03%) of the top dermatology-related content creators,

respectively. In the queried hashtags, verified BCD and dermatology residents created 13.89% (50/360) and 8.89% (32/360) of the top posts, respectively.

Of the identified top posts, 46.67% (168/360) were educational, 27.50% (99/360) were self-promotional, 13.89% (50/360) were non-paid product placements, and 0.83% (3/360) were advertisements.

A total of 29.76% (50/168) and 70.24% (118/168) of educational posts were created by nonmedical and medical professionals, respectively; specifically, BCD created 20.83% (35/168) and dermatology residents created 18.45% (31/168). BCD were responsible for only 30% of the profession-specific hashtag-identified posts (Table 2).

Table 1. Medical professionals versus nonmedical professionals who created top dermatology-related TikTok videos (total unique creators: N=231).

Category	Self-identified, n (%)	Residency or board-certified status confirmed, n (%) of total unique creators
<b>Medical professionals</b>		
Dermatologists	15 (6.49)	13 (5.63)
Dermatology residents	7 (3.03)	7 (3.03)
Physicians in other specialties	21 (9.09)	16 (6.93)
Nurse practitioners	6 (2.6)	4 (1.73)
Physician's assistants or associates	2 (0.87)	2 (0.87)
Registered nurses	4 (1.73)	2 (0.87)
Unspecified	11 (4.76)	0 (0)
All medical professionals	66 (28.57)	44 (19.05)
<b>Nonmedical professionals</b>		
Patients	70 (30.3)	N/A <sup>a</sup>
Estheticians	11 (4.76)	N/A
Verified account (brand or influencer)	12 (5.19)	N/A
Other	72 (31.17)	N/A
All nonmedical professionals	165 (71.43)	N/A

<sup>a</sup>N/A: not applicable.

Table 2. Users responsible for the top 10 videos under each profession-specific hashtag.

Users	Hashtag, n				Total, n (%)
	#dermatology	#derm	#dermatologist	#boardcertifieddermatologist	
Board-certified dermatologist	2	1	1	8	12 (30)
Dermatology resident	4	0	8	1	13 (32.5)
Internal medicine physician	0	7	0	0	7 (17.5)
Registered nurse	1	0	0	1	2 (5)
Esthetician	0	1	0	0	1 (2.5)
Other	3	1	1	0	5 (12.5)

Discussion

Our results suggest that most of the popular dermatology-related content on TikTok is created by individuals without verifiable medical training. This highlights a space for BCD to showcase

their profession and prevent the spread of health misinformation. As the use of social media platforms like TikTok continues to grow, BCD have an opportunity to increase their presence as a credible source for the public to acquire dermatologic knowledge.

The use of hashtags explicitly related to dermatology by users who are not BCD or dermatology residents may mislead TikTok users. Transparency regarding professional health care credentials on TikTok may improve credibility. There is currently no way to verify professional credentials on TikTok;

a feature to distinguish medical professionals from nonmedical professionals can add to the visibility of BCD and help users make informed decisions regarding their source of health information online.

## Conflicts of Interest

RKS is a scientific advisor for LearnHealth, Arbonne, and Codex Labs Corp and a consultant for Burt's Bees, Novozymes, Nutrafol, Incyte, Fotona, Biogena, Image Skincare, Bristol Myers Squibb, Novartis, Pfizer, AbbVie, LEO Pharma, UCB, Sun, Sanofi, and Regeneron Pharmaceuticals.

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## Abbreviations

**BCD:** board-certified dermatologists

*Edited by R Dellavalle; submitted 30.01.23; peer-reviewed by J Ornelas, T Harpel; comments to author 29.04.23; revised version received 13.09.23; accepted 01.10.23; published 05.01.24.*

### Please cite as:

Subramanyam C, Becker A, Rizzo J, Afzal N, Nong Y, Sivamani R  
Visibility of Board-Certified Dermatologists on TikTok  
*JMIR Dermatol* 2024;7:e46085  
URL: <https://derma.jmir.org/2024/1/e46085>  
doi:[10.2196/46085](https://doi.org/10.2196/46085)  
PMID:[38180786](https://pubmed.ncbi.nlm.nih.gov/38180786/)

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Viewpoint

# Social Media Use in Dermatology in Turkey: Challenges and Tips for Patient Health

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## Abstract

Social media has established its place in our daily lives, especially with the advent of the COVID-19 pandemic. It has become the leading source of information for dermatological literacy on various topics, ranging from skin diseases to everyday skincare and cosmetic purposes in the present digital era. Accumulated evidence indicates that accurate medical content constitutes only a tiny fraction of the exponentially growing dermatological information on digital platforms, highlighting an unmet patient need for access to evidence-based information on social media. However, there have been no recent local publications from Turkey analyzing and assessing the key elements in raising dermatological literacy and awareness in digital communication for patients. To the best of our knowledge, this study is the first collaborative work between health care professionals and a social media specialist in the medical literature. Furthermore, it represents the first author-initiated implementation science attempt focusing on the use of social media in addressing dermatological problems, with the primary end point of increasing health literacy and patient benefits. The multidisciplinary expert panel was formed by 4 dermatologists with academic credentials and significant influence in public health and among patients on digital platforms. A social media specialist, who serves as a guest lecturer on “How social media works” at Istanbul Technical University, Turkey, was invited to the panel as an expert on digital communication. The panel members had a kickoff meeting to establish the context for the discussion points. The context of the advisory board meeting was outlined under 5 headlines. Two weeks later, the panel members presented their social media account statistics, defined the main characteristics of dermatology patients on social media, and discussed their experiences with patients on digital platforms. These discussions were organized under the predefined headlines and in line with the current literature. We aimed to collect expert opinions on identifying the main characteristics of individuals interested in dermatological topics and to provide recommendations to help dermatologists increase evidence-based dermatological content on social media. Additionally, experts discussed paradigms for dermatological outreach and the role of dermatologists in reducing misleading information on digital platforms in Turkey. The main concluding remark of this study is that dermatologists should enhance their social media presence to increase evidence-based knowledge by applying the principles of patient-physician communication on digital platforms while maintaining a professional stance. To achieve this goal, dermatologists should share targeted scientific content after increasing their knowledge about the operational rules of digital channels. This includes correctly identifying the needs of those seeking information on social media and preparing a sustainable social media communication plan. This viewpoint reflects Turkish dermatologists’ experiences with individuals searching for dermatological information on local digital platforms; therefore, the applicability of recommendations may be limited and should be carefully considered.

**KEYWORDS**

social media; dermatology; internet; health promotion; patient education; Instagram; YouTube; online social networking; social networking; Turkey; patient health; skin; skin disease; skincare; cosmetics; digital communication; misinformation

**Introduction**

Skin problems affect one-third of the general population worldwide, decreasing patients' quality of life and adversely impacting their social lives [1]. Empowered by the widespread use of the internet, advances in mobile technology, digitalization of health care, and fundamental changes in interpersonal communication, patients with skin problems currently prefer to obtain prompt responses to health-related queries from digital platforms [2-5]. Therefore, seeking health information on the internet has become the predominant trend for patients in the digital age due to convenience, easy accessibility, anonymity, cost-effectiveness, and promotion of health equity [3,6]. Furthermore, patients seek convenient access to health tips at any time [1,7,8].

As one of the most prevalent health care resources, social media provides informative, "trendy," and entertaining content independent of time and geographical distance [8-10]. Remarkably, social media networks, such as Facebook, Twitter, Instagram, YouTube, and TikTok, became more prevalent across all medical subspecialties during the COVID-19 pandemic [11]. Based on internet search data, the most frequently asked dermatological topics on social media networks include skincare, anti-aging, hair products, and acne vulgaris (AV) in Turkey and globally [7,12].

Relying on the information on social media and the limited social media presence of medical experts, patients are likely to make medical decisions based on posts created by individuals without medical or dermatological certifications [13]. These engaging posts may enhance the distribution of misleading information on social media, leading to harmful patient outcomes [9,14,15]. A digital survey study on hashtags from 9 dermatology-related Instagram posts with the highest number of followers reports that only 4%-5% of the hashtags were created by dermatologists registered with the American Board of Medical Specialties [14,16]. On the other hand, 93% of posts created by board-certified dermatologists were reported to have educational content for patients [16]. Recent reviews and studies have reported that most dermatology-related posts are prepared by individuals lacking formal training. Using engaging multimedia tools, these account owners substantially dominate most dermatological information on social networks [1,5,9,11,17-19]. According to a phone interview conducted in the United States, 1 in 3 US citizens use social media to search for information about health issues, and 46% of them are identified as "online diagnosticians" [13]. Strikingly, 38% of these online diagnosticians claimed they could handle their problems at home. The survey revealed that 82% of internet users aged 18-29 years sought health information on Google, Bing, Yahoo, or other search engines [13]. Another study revealed that 40% of internet users stopped taking their prescribed medications due to information on social media [20]. The national statistics

showed that social media ranked first (80.9%) among reasons to use the internet in Turkey, while searching for health-related information ranked third (66.3%) [20]. In a nationwide study on social media use for AV, 70% of participants stated that dermatologists or dermatology associations should create posts about AV, and 51% agreed that only dermatologists should convey medical information on AV [7].

As an indispensable source for public health matters, social media may be an effective platform for dermatological outreach, facilitating access to evidence-based information and public education on dermatological issues in Turkey. To this end, it is necessary to identify the leading factors for dermatologists to maximize patient benefit through social media. However, there is a gap in local literature to guide dermatologists in establishing an effective social media presence. The expert panel aimed to collect expert opinions on identifying the main characteristics of individuals seeking health information related to dermatology and ways to increase patients' knowledge and understanding of skin problems by creating evidence-based medical content on social media. Additionally, the panel aimed to address paradigms for dermatological outreach and define dermatologists' roles in reducing misleading information on digital platforms.

**Methods**

The goal was to form a multidisciplinary panel consisting of dermatologists and a social media specialist. A social media agency screened all popular social networks in Turkey, including Instagram, Twitter, and YouTube. The agency ranked the account owners who regularly posted dermatological content and had the highest number of followers in the past 6 months. Dermatologists without recorded professional credentials on social media accounts and those with a self-promotion or intervention promotion rate  $\geq 20\%$  per month were excluded from the candidate list.

The panel member candidates were selected according to the following criteria:

- Having professional credentials recorded on social media accounts
- Maintaining an active clinical practice
- Holding an academic title
- Having a high number of scientific publications
- Having a high number of followers on social media within the past 6 months
- Posting educational content regularly for the public (at least 3-4 posts per month)
- Achieving high engagement rates within the past 6 months.

Dermatologists who fulfilled these criteria were invited to participate in Pfizer's project entitled "How to Use Social Media in Dermatology in Turkey." A total of 4 dermatologists (2 from Istanbul, 1 from Ankara, and 1 from Denizli) accepted the

invitation. To form a multidisciplinary expert panel, we sought a social media specialist who had relevant experience in creating communication strategies and managing crises on digital platforms and was experienced in conducting large-scale medical projects (not necessarily in dermatology) related to or on social media. After the final review of candidates, the social media specialist, who also held an academic position as a guest lecturer on “How social media works” at Istanbul Technical University, was invited to the expert panel.

Before the kickoff meeting, held on April 11, 2023, panel members were requested to review personal social media account statistics for characteristics of digital patients or health information seekers, identify the top 5 inquiry topics from the past 6 months, and read the national survey study about expectations of patients with AV from social media [7]. At the kickoff meeting, panel members agreed on 5 headings to be reviewed in the advisory board meeting (held on April 26, 2023). These headings were as follows: (1) general characteristics of Turkish health information seekers and preferred digital platforms in Turkey, (2) commonly inquired topics (eg, cosmetic vs medical dermatology and skincare vs treatment or interventional procedures), (3) algorithmic or digital communication parameters that may improve the dissemination of scientific knowledge on social media, (4) key elements of content creation for digital platforms or social media, (4) future perspectives of experts regarding social media impacts in dermatology.

In the advisory board meeting, personal account statistics, experiences related to requests from information seekers, and problems caused by non-board-certified content creators (including physicians from other subspecialties) were discussed. The social media expert explained the cornerstones of digital communication and how to evaluate engagement quality on social media. In addition, dermatologists shared their experiences in effectively addressing the unmet needs of patients and disseminating clinically relevant information to health information seekers in dermatology across different digital media platforms on social media. Finally, the key recommendations resulting from these discussions were summarized and stated in this viewpoint.

### **Characteristics, Behavioral Patterns, and the Unmet Needs of Turkish Dermatology Patients on Social Media**

According to insights from participating dermatologists, approximately 60%-85% of dermatology patients were women aged 25-44 years with advanced digital skills who lived in megacities and used social media to obtain information on dermatological issues and choose a physician. Younger patients were more interested in cosmetic dermatology topics, whereas middle-aged patients often inquired about medical dermatology topics. In line with the digital data of 2023, the experts declared that they received nearly 90% of dermatology-related queries from Instagram [21].

In the present era, media and omnichannel communication have reshaped societal perceptions and self-perceptions of beauty standards [22,23]. As a result, young women consider self-image

to be at the forefront of social acceptance. Under the pressing desire “to be within the societal beauty standards,” young adults are open to various cosmetic procedures and collect information mainly through digital platforms. Therefore, medical interactions on social media are slightly inclined toward cosmetic dermatology.

The leading causes of social media use among Turkish patients include seeking a diagnosis and learning about treatment options or procedures. Generally, a Google search is the first step in seeking dermatological information on the internet. However, most social media users are unfamiliar with the personalization algorithms of these platforms, which operate backstage to select and bring forth specific content according to previous search activities, labeling it as “recommended” or “suggested.” Moreover, depending on the topic, social media users often encounter massive amounts of information and have trouble determining whether the information is evidence based and relevant to their skin problems. With limited medical literacy in dermatology and digital competence, patients often perceive content shared on social media accounts with a “high number of followers” as “reliable.” However, most patients seeking information on the internet do not confirm whether the information is supported by scholarly sources or endorsed by dermatologists. Furthermore, it should be emphasized that individuals without professional training in dermatology cannot correctly categorize, evaluate, and discern accurate information by surfing websites, watching videos, and reading posts.

In cosmetic issues, especially, the procedure outcomes are presented with “before” and “after” photos, the majority of which are digitally edited. The medical content is prepared in a promising and appealing tone to draw the attention of nonmedical audiences. Therefore, dermatology patients should be vigilant and skeptical about medical content on social media lacking citations and making exaggerated promises about health outcomes. Inevitably, the absence of quality control and low levels of skepticism among social media users may lead them to websites broadcasting nonfactual information; this could delay access to effective treatment or result in patients experiencing complicated outcomes. Unlike in real life, patients have easy access to many websites via the internet, receive many recommendations, and use various skin products without consulting a dermatologist. Patients usually consult a dermatologist only when skin problems are not resolved with suggestions found on social media. Experts underlined the challenge of managing complex skin problems in daily clinical practice. Relying on overly promising posts and receiving dermatological treatment at later stages of the disease, patients have difficulty complying with more extended and comprehensive treatment plans. Additionally, it has been observed that the effectiveness of therapy is decreased in some cases due to delayed intervention.

According to recent national data, Turkey has a relatively young (median age 31.6 years), highly urbanized (77.2%) population, with equal gender distribution (women comprise 49.9% of the population) and an overall adult (age >15 years) literacy rate of 96.7% [21].

Some essential digital headlines of the Turkish population are as follows [21]:

- Internet access is available to 83.4% of the population.
- In total, 73.1% of the population are active social media users.
- Cell phone connection is available to 95.4% of the population.
- Approximately 85% of web traffic is from mobile phones.
- The population aged 16-64 years spends an average of 3 hours daily on social media networks.

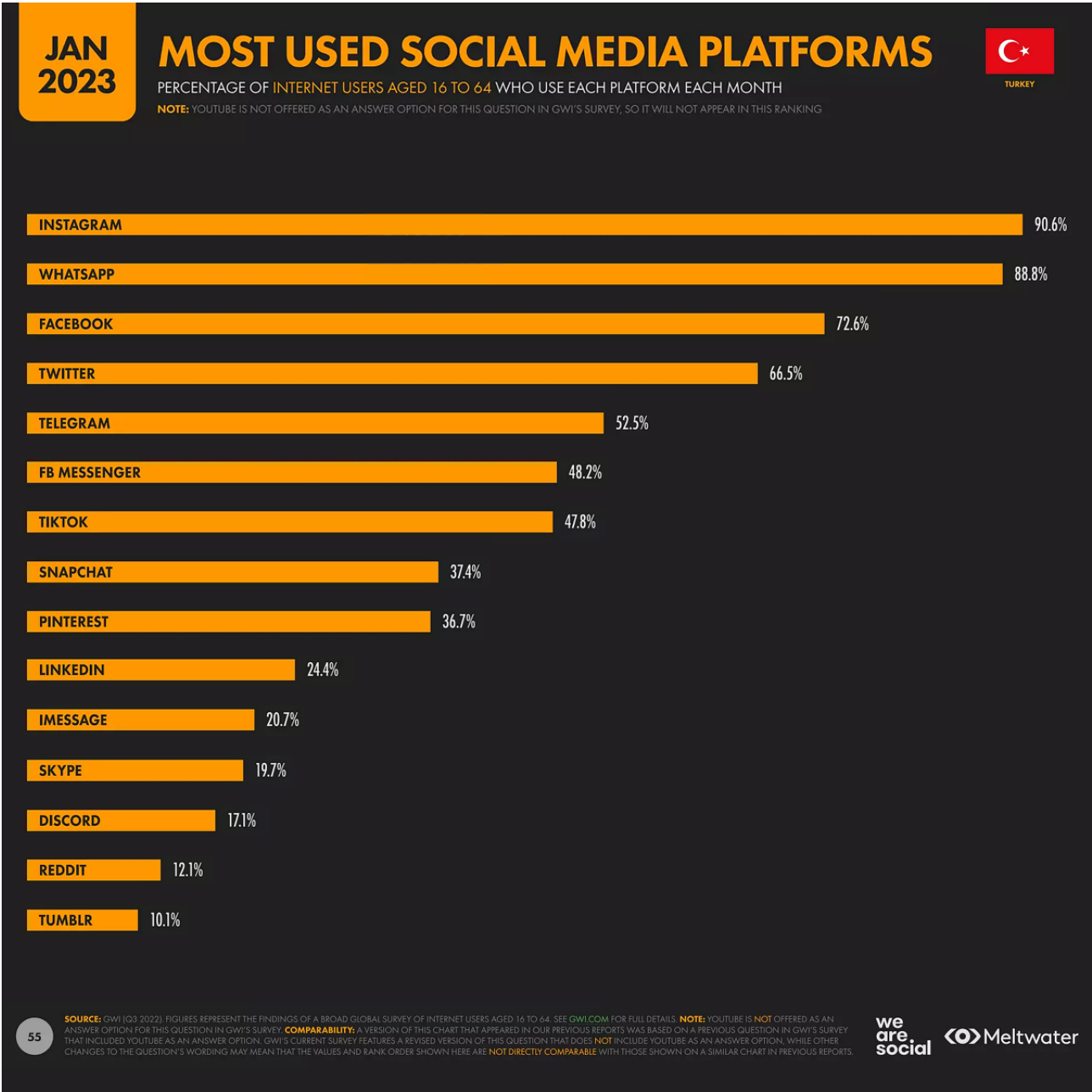
Since dermatology patients on social media are a subset of internet users in Turkey, it is imperative to delineate the essential

patient characteristics. Instagram, WhatsApp, Twitter, TikTok, and Facebook are the most frequently used platforms, and with 90.6% of users, Instagram is the most popular social network in Turkey (Figure 1) [21].

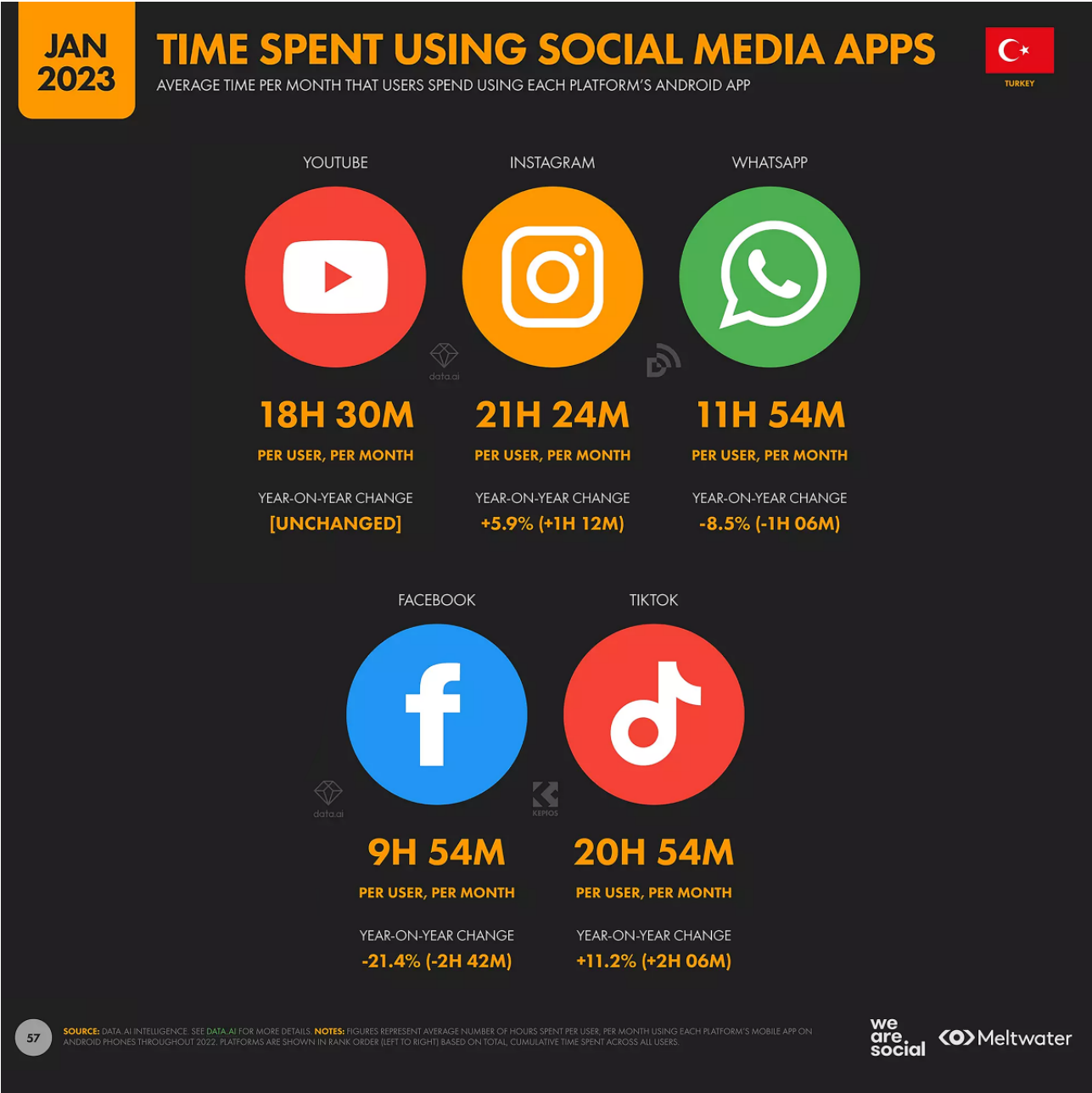
The average time spent on Instagram per capita in Turkey was 20.2 hours per month in 2022, but it increased to 21 hours and 24 minutes in 2023 (Figure 2) [21].

Of the population aged 16-64 years, 39.5% use the internet for “researching health issues and healthcare products” as one of the main reasons, and 17.7% follow beauty experts [21]. Figure 3 illustrates the reasons for internet use among the population aged 16-64 years in Turkey.

**Figure 1.** The most used social media platforms among the population aged 16-64 years in Turkey (reproduced from We Are Social & Meltwater et al [24], which is published under Fair Dealings as defined by Singapore Law according to copyright holder DataReportal [25]).

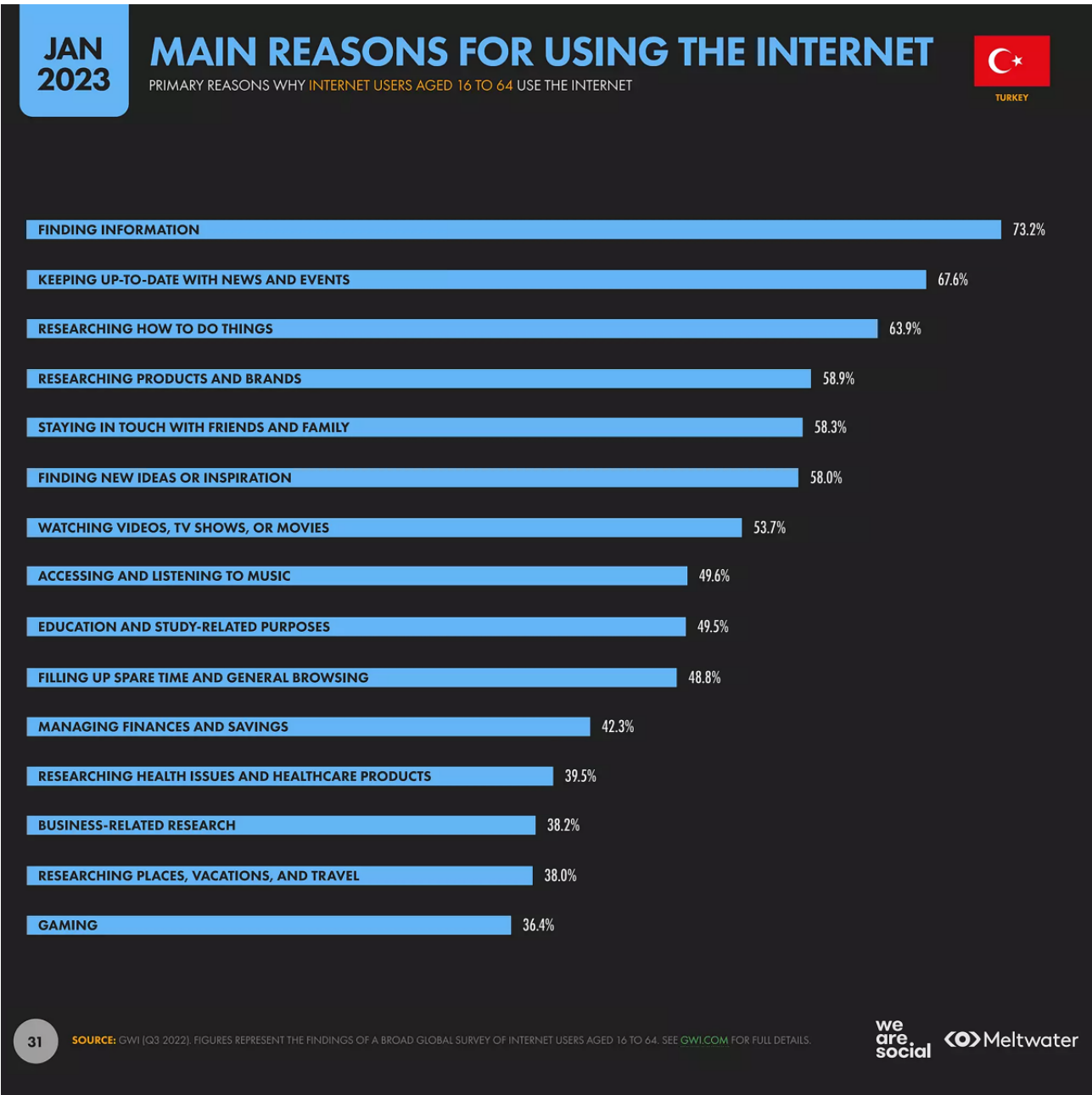


**Figure 2.** The average time spent per month on social media in Turkey (reproduced from We Are Social & Meltwater et al [24], which is published under Fair Dealings as defined by Singapore Law according to copyright holder DataReportal [25]).





**Figure 3.** Reasons for internet use among the population aged 16-64 years in Turkey (reproduced from We Are Social & Meltwater et al [24], which is published under Fair Dealings as defined by Singapore Law according to copyright holder DataReportal [25]).



In a recent survey study on patients with seborrheic dermatitis, 81% of patients declared that they trusted the dermatologist’s decision on the treatment. However, 78.8% (104/132) also consulted social media for additional remedies for their diseases [26]. Among those who consulted social media, 54.8% started to use over-the-counter products, 35.6% implemented diet and lifestyle changes, and 7.7% started supplement use recommended on social media. The rest of the cohort (1.9%) started to use self-made products. Similar to our findings, 85.6% of those who consulted social media were female patients, and 78.8% were between the ages of 18 and 30 years. Instagram (63.6%) and YouTube (53%) were the most commonly used digital platforms for seeking health information [26].

**Non–Board-Certified Profiles Should Not Orchestrate Dermatological Outreach**

Dermatological diseases are common, immediately noticeable, and generally nonfatal, yet they have similar symptoms. Although the skin is the largest organ in the human body, public awareness about skin health has increased only recently. It is a typical underestimation that most skin problems can be overcome without consulting a physician. Therefore, patients consult a dermatologist after unsuccessful self-treatment attempts, when the symptoms get worse and more problematic. Increasing patients’ health literacy is the cornerstone to improving patient understanding of cutaneous problems. In this respect, social media presents an excellent opportunity to disseminate scientific facts, as it readily engages large audiences without restrictions related to time and location.

Many studies have revealed that most individually prepared medical content is not based on scientific evidence or is occasionally entirely false [9,27]. For example, a recent cross-sectional analysis of a trendy topic, keratosis pilaris, on TikTok revealed that 52% of the content creators are nonphysicians, 16% are private companies, and 32% are physicians [28]. Interestingly, 16% of content-creating physicians were in medical branches other than dermatology (84% were dermatologists). In addition, a study characterizing the credentials of dermatology influencers on Instagram reported that board-certified dermatologists constitute only 4% of the Instagram accounts with popular dermatology content [29]. Furthermore, 71% of all influencers and 27% of health care influencers did not mention credentials on their accounts [29]. Finally, recent studies about effective communication on social media underlined that patients preferred dermatological content created by certified dermatologists and wished such content was more broadly available [7,9,19].

Dermatologists who want to participate in social media platforms should realize that in addition to patient education and heightened awareness, social media enables them to provide services they cannot offer in overcrowded outpatient settings. For example, sharing evidence-based information about routine skincare or aging will help patients on the internet differentiate scientific quality from temptation-provoking rhetoric in the content source. Furthermore, physicians can perform patient follow-ups more effectively, that is, they can communicate medication side effects and remind patients of medication use instructions. These efforts will soon lead to more medically literate patients in both the digital and real worlds.

Content creation, user engagement, and maintenance of digital patient communication require a time commitment, a budget to allocate a professional team, and follow-up on current advancements. Combating misleading dermatological information on social media is not a mission that the participation of a few dedicated dermatologists can accomplish. Instead, it demands the involvement of specialty associations, academic institutions, and reputable scientific journals to act in unison for the common objective. High-impact journals and leading institutions in dermatology have recently recognized the power of social networking worldwide, and therefore, activated social media accounts on different platforms [5,9,15,18,30,31]. There is an emerging need for Turkish patients to access verified information presented in lay summaries from scholarly sources. However, unfortunately, the social media presence of relevant institutions is far behind what is desired in Turkey.

The level of social media presence varies mainly according to age and the perception of dermatologists toward social media. Being exceptionally acquainted with digitalization early in life,

younger dermatologists are more competent with the algorithms of digital platforms and eager to build a successful career, including maintaining a strong social media presence. On the other hand, being active on social networks may be controversial for more experienced dermatologists and academicians. There may be various underlying reasons, such as timidity in communication in the digital world, incompetence with digitalization, and discomfort with or prejudice against social networks due to everyday use. Furthermore, the social media presence of dermatologists may depend on the institution in which they work. In Turkey, private hospitals use social media extensively to broadcast information about diseases, procedures performed, and technical expertise.

### What Matters in Social Media Presence? Roles of Dermatologists

Dermatologists have a leading role in high-quality health information available on the internet. It should be remembered that whether in the digital or real world, a physician is a respected, trusted source of medical information for patients and a role model for the next generation of physicians as well as colleagues. Considering social platforms as meeting points for academia and the general population, dermatologists need to fulfill their scientific roles in disseminating reliable information. In contrast to this, most social media account owners who have a substantial impact on patients are not health care professionals. Some patients have noted that they follow popular profiles for “fun” but do not rely on them to solve critical health issues. Moreover, a survey about patients’ self-reported trust in physicians based on their behaviors on digital platforms has shown that social media users prefer professionalism in essential matters such as health [32]. Therefore, it should be noted that it is difficult to earn trust and to reestablish it when it is lost. A physician-patient relationship built on medical facts will result in guidance and permanent engagement with most patients and health information seekers on social networks, eventually counteracting misleading content by disseminating accurate information. Therefore, dermatologists should preserve their professional stances on social media despite the complexities of digital platforms.

Since dermatology is one of the hot topics on social networks, most content creators in this field need help in their leadership role in the cosmetics market, which can readily promote unrealistic promises and propagate harmful trends. As a result, globally and locally, academic institutions, medical associations, and legal authorities have recently passed professionalism policies to regulate digital medical communication and preserve patient privacy and confidentiality (Textbox 1) [33-36]. It should be noted that policies and codes of ethics for social media use should be applied to every account owner who broadcasts health-related content.

**Textbox 1.** The American Medical Association's recommendations for social media use.

**Physicians should consider the following:**

- Be cognizant of patient confidentiality and refrain from posting any identifiable patient information online.
- Use privacy settings to safeguard personal information on social networking sites.
- Maintain appropriate boundaries of the patient-physician relationship following professional ethics guidance.
- Consider separating professional and personal content online.
- Recognize that content shared online may have negative impacts on their reputation.

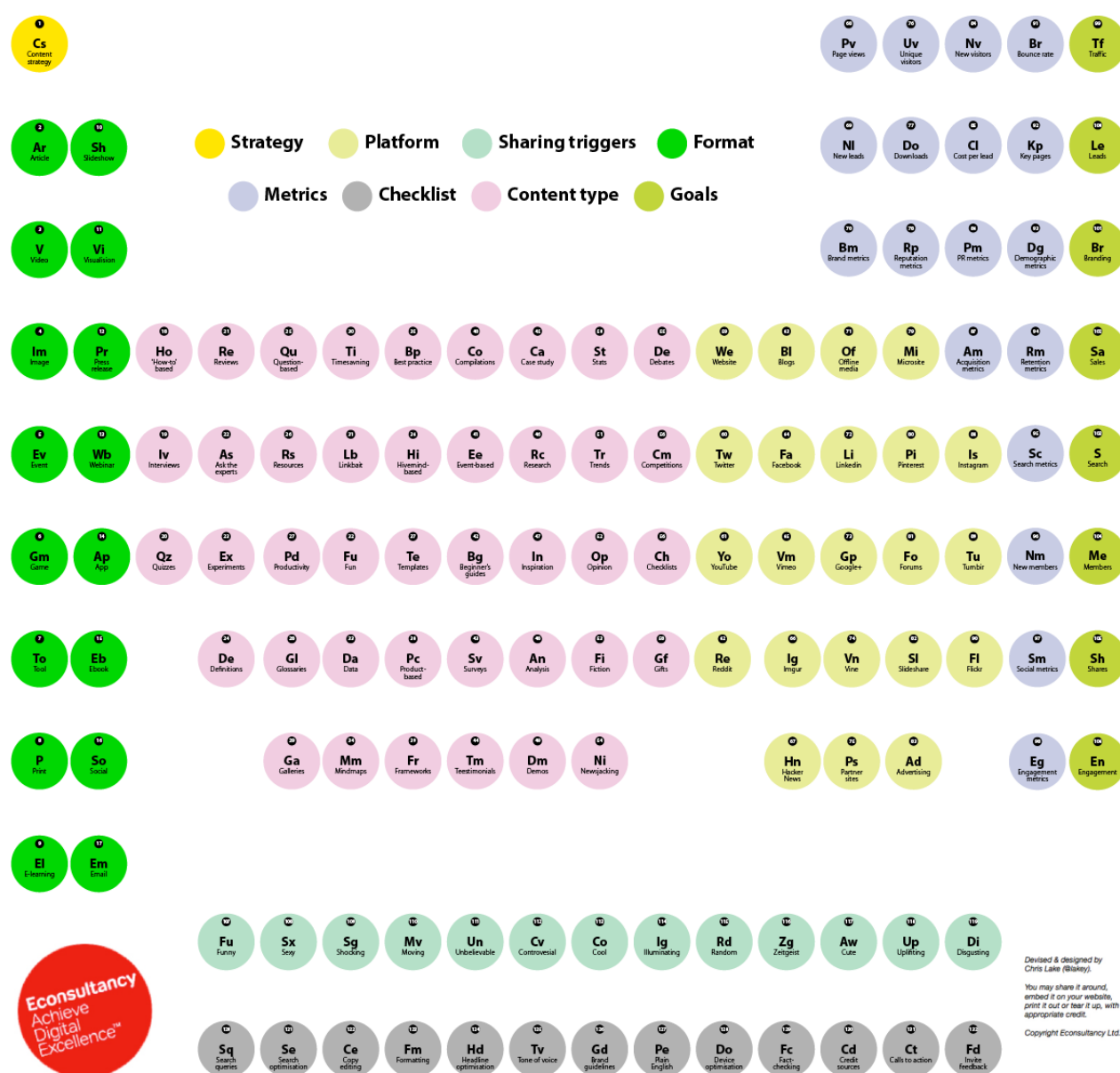
### **Essentialities in Social Media Contact and Content Creation**

The underlying essential elements of effective communication on social media include a well-structured strategy, content creation, and engagement metrics. When creating content, the device(s) on which the content will be shared should also be considered; for instance, if most website traffic comes from smartphones, posts should be mobile-friendly.

Searching for accurate information is the primary driver of social media use for most dermatology patients. Therefore,

broadcasting on social media is crucial to increasing factual dermatological knowledge on digital networks [37,38]. The panelists believe that dermatologists with predefined strategies before broadcasting on social media will have successful engagement rates. The strategy should be individualized for the target population with the help of search engine optimization workups. Some steps, outlined in the following sections, should be carefully defined before posting content on digital platforms, including the platform selection, format, and multimedia tools to use. The panelists believe that the most straightforward, yet practical steps of content creation and sharing are summarized in [Figure 4](#) [37].

Figure 4. Key elements of content creation.



Broadcasting informative content involves the selection of the social media platform and content topics as well as the frequency of broadcasting. For a dermatologist, content creation is a time-consuming process, as it requires literature review, rewriting for the target audience, preparation of visuals, and editing according to the format of the digital platform.

Most new social media account owners prefer to stay socially active by copying content they like from other accounts. However, such an approach can facilitate the dissemination of misinformation from the original site, causing the account holder to lose patients' trust and increasing the cited site's rankings by transmitting linked tools. In fact, patients understand and prefer authentically created content in lay language. With transparency, professionalism, and clear boundaries, dermatologists should refrain from overpromising results to attract attention; instead, they should be open to receiving negative reviews and accept them as part of digital communication.

Not all followers who use social media are patients or advice seekers. One out of 10 followers is reported to write intentionally provocative and offensive messages on social media and is labeled as a troll [39]. Keeping up with the rules of physician-patient communication upheld in face-to-face settings on digital platforms may be a practical way to sustain professionalism on these platforms [39].

### Content Creation

Content creation involves selecting the topic and the platforms (Figure 4) [37]. Digital tools provide keywords (hashtags) with high search volumes on the internet. Therefore, informative content that guides patients should be included in them so that the content can be more readily shown to other relevant searchers. They can be provided by periodically used search engine optimization workups.

Cross-posting is an effective measure to reach a broader audience on social media. Sharing the same content on different platforms with specific interfaces enables influencing more patients, staying up-to-date, and saving time. It is observed that Turkish patients on social media prefer short videos and a combination of videos and images, namely carousel posts, on dermatological topics. Shooting less-than-1-minute videos is generally recommended to maintain the audience's attention. For written content, catchy titles, including relevant keywords (hashtags), attract patients' attention. Informative content should be in lay language with simplified explanations of medical terms to support patient engagement. The posting frequency depends on how much time the dermatologist can spend on the networks.

### ***Increasing Patient Engagement***

Social media metrics serve as data points to evaluate the quality of digital communication. Engagement metrics guide content creators in identifying posts that resonate better with followers by providing data on session durations, page views, conversion rates, and followers' feedback. These metrics can reveal areas for improvement in previous posts, including deficiencies in content writing or images, to enhance future ones. With the help of engagement metrics, patient behavior on digital platforms can be better determined to build effective communication.

### ***What Lies in the Future***

Experts note that emerging technologies and tools, especially artificial intelligence and applications for better photography in teledermatology, have significantly increased diagnostic accuracy. Considering the present technological advances, one may expect the computer systems to perform tasks that require human intelligence, such as skin lesion classification, improving the diagnosis and management of psoriasis, assessing ulcer specifications, and early evaluation of skin cancer via artificial intelligence-based machine learning and convolutional neural networks [40,41]. For example, the recently launched ChatGPT has already become very popular in writing patient care discharge summaries and promoting healthy lifestyle practices. During the pandemic, teledermatology increased worldwide to ensure patients and health care providers had access to dermatologists [42-44]. Moreover, teledermatology enabled patients from remote areas to obtain access while reducing wait times for dermatology referrals [45-47]. Recent advances have improved the quality of smartphone photos, and dermoscopy through smartphone microscope apps using convolutional neural networks is increasingly applied in teledermatology consultations [48].

It should be foreseen that advances in the field of technology will continue at a rapid pace. Nevertheless, increasing digital possibilities will allow people with dermatological problems to access medical information from more channels. Therefore, policies and codes of ethics for health care topics should be implemented in all aspects of the digital world as soon as possible. Dermatologists, academic institutions, and specialty

associations should take their place in disseminating dermatological knowledge on social media networks.

### **Conclusions**

The experiences of Turkish dermatologists with a strong social media presence and inquiries from patients on informative digital channels indicate that medical advice-seeking individuals need help accessing scientific information. Therefore, dermatologists who master this field should become critical players in the dissemination of accurate knowledge and in raising public awareness in digital settings. Recently accumulated local data on the impact of social media on dermatology-related professions have pointed out that patients or health information seekers are misguided by unconfirmed and unmonitored digital content. Given that the digital world will soon be much more indispensable in dermatology and patient-physician relationships, combating misleading information created by nonqualified account owners should be a shared responsibility of dermatologists, academic institutions, and board associations. The authors of this paper state that increasing the digital operational competence of dermatologists, while complying with the ethical rules of the medical profession, is the cornerstone for disseminating evidence-based information and patient awareness in the field of dermatology on digital platforms. For the highest benefits of health information seekers, social media presence rates of institutions and dermatologists should be increased collaboratively.

### **Key Recommendations**

Some key recommendations drawn from this study are as follows:

- Dermatologists should be authentically present on social media within their medical profession.
- The communication on social media should be aimed at establishing a reputable, enlightening, and reliable patient-physician relationship on digital channels.
- Patient communication should be direct, natural, sincere, and convincing, rather than artificial.
- Patients' confidential information must not be shared in any way, and patient privacy must be meticulously protected.
- Raising patient awareness and combating misleading information should be the primary goal of the digital presence of dermatologists.
- Content should be original and created with proven data. Content should be brief for easy understanding.
- Posts should support patient feedback, and the access rate should be measured with metrics.
- Content interaction should be periodically evaluated.
- Cross-posting in different social media channels provides uninterrupted patient communication.
- Academic institutions and associations need to be more involved in digital platforms.

### **Acknowledgments**

This study was sponsored by Pfizer.



Editorial and medical writing support was provided by Evin Isgor, MD, at Genetik Istanbul and was funded by Pfizer.

ASK was affiliated with the Department of Dermatology, Medical School of Istanbul Arel University, Istanbul-Turkey at the time of trial and is currently affiliated with the Private Clinic.

## Conflicts of Interest

SS and SC are employees of Pfizer. Other authors declare no conflicts of interest related to this work.

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## Abbreviations

**AV:** acne vulgaris

*Edited by R Dellavalle, E Parker; submitted 02.08.23; peer-reviewed by A Anastasiou, J Avis, M Gasmi ; comments to author 30.11.23; revised version received 25.01.24; accepted 28.01.24; published 28.03.24.*

*Please cite as:*

Karadag AS, Kandi B, Sanlı B, Ulusal H, Basusta H, Sener S, Calıka S

Social Media Use in Dermatology in Turkey: Challenges and Tips for Patient Health

JMIR Dermatol 2024;7:e51267

URL: <https://derma.jmir.org/2024/1/e51267>

doi: [10.2196/51267](https://doi.org/10.2196/51267)

PMID: [38546714](https://pubmed.ncbi.nlm.nih.gov/38546714/)

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Review

# The New Media Landscape and Its Effects on Skin Cancer Diagnostics, Prognostics, and Prevention: Scoping Review

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## Abstract

**Background:** The wide availability of web-based sources, including social media (SM), has supported rapid, widespread dissemination of health information. This dissemination can be an asset during public health emergencies; however, it can also present challenges when the information is inaccurate or ill-informed. Of interest, many SM sources discuss cancer, specifically cutaneous melanoma and keratinocyte cancers (basal cell and squamous cell carcinoma).

**Objective:** Through a comprehensive and scoping review of the literature, this study aims to gain an actionable perspective of the state of SM information regarding skin cancer diagnostics, prognostics, and prevention.

**Methods:** We performed a scoping literature review to establish the relationship between SM and skin cancer. A literature search was conducted across MEDLINE, Embase, Cochrane Library, Web of Science, and Scopus from January 2000 to June 2023. The included studies discussed SM and its relationship to and effect on skin cancer.

**Results:** Through the search, 1009 abstracts were initially identified, 188 received full-text review, and 112 met inclusion criteria. The included studies were divided into 7 groupings based on a publication's primary objective: misinformation (n=40, 36%), prevention campaign (n=19, 17%), engagement (n=16, 14%), research (n=12, 11%), education (n=11, 10%), demographics (n=10, 9%), and patient support (n=4, 3%), which were the most common identified themes.

**Conclusions:** Through this review, we gained a better understanding of the SM environment addressing skin cancer information, and we gained insight into the best practices by which SM could be used to positively influence the health care information ecosystem.

(*JMIR Dermatol* 2024;7:e53373) doi:[10.2196/53373](https://doi.org/10.2196/53373)

## KEYWORDS

social media; communication; skin cancer; melanoma; misinformation; scoping review

## Introduction

As of April 2023, 4.8 billion people, or 59.9% of the world's population, were identified as social media (SM) users [1]. In the age of omnipresent internet exposure, more people than ever receive and seek medical information from SM. More than 80% of US state health departments have an SM account, and SM

has become a safe space for patients with cancer to discuss diagnoses and seek education [2]. Over 80% of patients with cancer reported using SM to connect with peers, and over 77% of patients with cancer cited the internet as the most important source of medical information [3]. When compared to legacy public health forums, SM and the new media landscape carry both promise and risk. While accurate information can be rapidly

distributed, so can misinformation, and this spread happens at a pace and scale that is inconceivable to prior communication environments [4].

Our scoping review focuses specifically on SM information and skin cancer, including melanoma and keratinocyte cancer (basal cell and squamous cell carcinoma). While keratinocyte cancers are more common, melanoma carries a higher risk of mortality [5] and is projected to be the second most common cancer in the United States by 2040 [6]. Melanoma offers opportunities for primary, secondary, and tertiary prevention. Campaigns for ultraviolet exposure reduction, skin cancer risk factors education, and guideline-concordant care awareness are all uniquely positioned for SM-based efforts. In this review, we explore how SM interfaces with skin cancer information and dissect the current research landscape as it pertains to this topic.

Methods

Overview

Scoping reviews are exploratory studies that aim to examine the extent of research performed on a given topic [7]. While similar to systematic reviews, scoping reviews differ in that they are broad and do not synthesize data via a meta-analysis.

Textbox 1. Inclusion and exclusion criteria.

<p><b>Inclusion criteria</b></p> <ul style="list-style-type: none"><li>• Melanoma</li><li>• Keratinocyte cancer (Basal cell carcinoma, Squamous cell carcinoma)</li><li>• X (Twitter)</li><li>• Facebook</li><li>• Instagram</li><li>• TikTok</li><li>• YouTube</li><li>• Pinterest</li><li>• Other forms of new media</li><li>• Tanning ideation</li><li>• Skin cancer prevention</li></ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"><li>• Conference abstracts</li><li>• No full-text availability</li><li>• No translation to English language</li><li>• Unfinished study</li><li>• Artificial intelligence technology rather than social media</li><li>• Teledermatology rather than social media</li><li>• Not dermatologic information</li><li>• No skin cancer information</li><li>• No social media information</li></ul>
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Scoping reviews are useful because they provide an organized description of the available literature, particularly with topics that have been heavily studied from various perspectives [8].

Search Strategy

A medical research librarian (DPF) developed a systematic search for relevant papers in MEDLINE, Embase, Cochrane Library, Web of Science, and Scopus covering January 1, 2000, to June 9, 2023. Publications were not limited by geography. The search was limited to texts that had full-text availability in the English language and discussion of the new communication environments and skin cancer. The search used controlled vocabulary and language terms selected to include SM and skin cancer. Search sensitivity was tested by the ability of preliminary search strategies to include known, relevant citations. The full search strategy can be found in [Multimedia Appendix 1](#).

Eligibility Criteria

The inclusion and exclusion criteria are listed in [Textbox 1](#). Studies that were eligible for inclusion investigated the connection between skin cancer and SM. The search was conducted between January 1, 2000, and June 9, 2023, to limit the number of papers and to only include records that were relevant to this era of new communication, after the SM boom.



## Data Extraction

Two authors (PLH and AJ) independently screened the titles and abstracts of each citation produced by the search strategy using the inclusion and exclusion criteria to decide which papers would progress to full-text review. Each record was reviewed twice, and, if a conflict was found, the lead investigator (KCN) would make the final decision. The full texts of all potentially eligible records were then analyzed independently by the investigators. Disagreements were resolved by reexamination and discussion. A flowchart was developed using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guidelines to demonstrate the study selection process ([Multimedia Appendix 2](#)) [9]. Author, publication year, study type, geographic location, platform investigated, principal findings, and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) score were extracted from each included publication. A copy of the STROBE score criteria can be found in [Multimedia Appendix 3](#) [10]. The STROBE scoring system was used to ensure this review included high-quality studies.

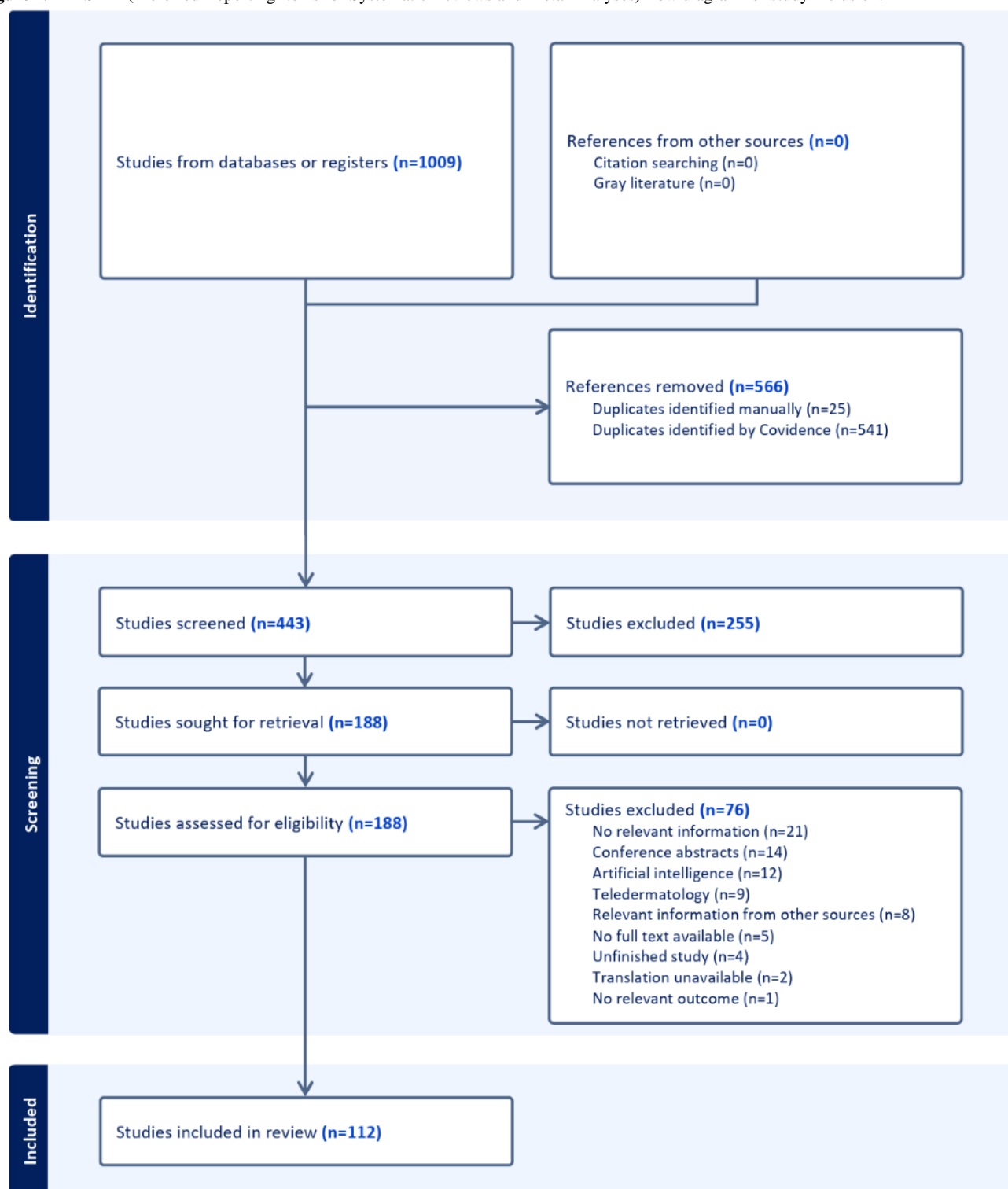
The included publications were divided into 7 categories based on the primary evaluated aspect of the study: engagement, campaigns, demographics, research, education, patient support, and misinformation. To be included in the engagement category, a publication must discuss an attribute of interaction, participation, connection, and involvement designed to illicit a result [11]. Engagement can be understood as the likes, comments, and shares posts acquire. Campaigns include publications that describe a new media intervention designed to promote primary or secondary skin cancer prevention and its effect on the population. A publication was included in the demographics category if it discussed demographic differences

in skin cancer SM advertising. The research category encompasses papers that demonstrate how SM aids in skin cancer research recruitment. A publication in the education category must discuss a way new media communication can be used for physician-to-physician or physician-to-patient skin cancer education. The patient support category includes records that demonstrate how the new communication environment lends itself to supporting patients with skin cancer. Scientific misinformation is defined as misleading information relative to the best available scientific evidence [12]. Therefore, to be included in the misinformation section, a publication must discuss false information dissemination or poor information quality regarding skin cancer across SM platforms.

## Results

### Overview

We identified 1009 records through the initial search, with the removal of 556 duplicate records via Covidence (Veritas Health Innovation; [Figure 1](#)). Two investigators (PLH and AJ) independently screened the remaining studies' titles and abstracts, with 188 records receiving full-text review. After full-text review, 76 were excluded through dual reviewer evaluation. Records with contradictory decisions were sent to a third-party reviewer (KCN), who provided the deciding vote. The included studies were divided into 7 groupings based on the publication's primary objective: misinformation (n=40, 36%), prevention campaign (n=19, 17%), engagement (n=16, 14%), research (n=12, 11%), education (n=11, 10%), demographics (n=10, 9%), and patient support (n=4, 3%), which were the most common identified themes. The data were extracted from each record into a characteristics table ([Multimedia Appendix 4](#) [5,13-123]).

**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram for study inclusion.

## Engagement

X (previously known as Twitter) has enormous potential for public health engagement; of the 112 included papers, 16 were included in the category of engagement [13]. X is more public than Instagram or Facebook and is used more often than other SM platforms to promote scientific papers and increase interactions with scientific literature [14]. On X, the top hashtag for skin cancer is #melanoma, and the key drivers of discussion are patient-focused entities [15]. Posts using shock or humor

generate the most likes or comments, and informative posts are most likely to be shared [16]. Engagement with posts about skin cancer correlates not with skin cancer incidence in a given geography, but instead with SM literacy of the exposed users [17]. To optimize the impact of X as a tool for skin cancer engagement, more information is needed to increase message dissemination and uniformity [18].

TikTok is a rapidly growing new media platform with over 755 million users in 2022 [124]. The most popular skin cancer content on TikTok includes videos with on-screen text and

health care attire, such as a white coat or scrubs [19]. Skin cancer is among the top 8 dermatological TikTok topics, with patient testimonies being the most common format, followed by educational videos and clinical demonstrations [20].

Most Instagram content addressing skin cancer originates from influencers and celebrities, not dermatologists [21]. Instagram offers a venue for patients to share their skin cancer journey (often with the #skincancerawareness hashtag [22]) and increase users' exposure to skin cancer information. Instagram posts referencing negative emotions (fear and anger), physical consequences, technical treatment information, or real skin cancer images increase audience interactivity, while positive posts have no effect on engagement [23].

This trend continues with Facebook, where the most-used technique to increase audience engagement is inducing fear [24]. Like X, Facebook posts with a humorous element increase viewer satisfaction and attention [25]. One advertising study compared Facebook user engagement of a parody video, a celebrity video, or a fact-based video regarding skin cancer and found engagement to be the highest for the parody video [25]. Facebook also allows individuals to post their personal skin cancer narratives. For example, Tawny Willoughby went viral due to a graphic selfie of her significant facial inflammation during treatment with topical 5% 5-fluorouracil: the post received over 50,000 views and was correlated to a 162% increase in internet search queries about skin cancer [26].

Increased user interactivity correlates with enhanced engagement with the information. This trend is consistent across platforms but is specifically noticed in support groups and on websites. Support groups are particularly effective if they are larger and have active, web-based comment sections [27], whereas the interactivity of skin cancer websites promotes an individual's intention to use sun protection [28].

## Prevention Campaigns

The category of prevention campaigns encompassed 19 of 112 included papers. The YouTube video "Dear 16-year-old Me" is a prime example of a successful SM prevention campaign. This video uses mixed emotion methods to address the importance of sun protection, which amplifies the impact of the message by evoking compassion to increase positive social behaviors [29,30]. After viewing the video, surveys demonstrated increased viewer intent to pursue a professional skin examination [31]. The video made a compounding impact when presented alongside lighthearted face-aging software [32].

Other YouTube skin cancer awareness campaigns include the "It's a beautiful day ... for Cancer" and "Don't be a Lobster." The "It's a beautiful day ... for Cancer" video was an ironic music video that spurred conversation of sun protection behaviors: it received 250,000 views, and 44% of viewers reported changed opinions on sun protection [31]. The "Don't be a Lobster" campaign consisted of an anonymous YouTube video highlighting the replacement of the red dragon of the Welsh flag with a red lobster. This anonymity and clever placement of the red lobster image quickly gained media attention and started the viral campaign. The campaign's effectiveness was quantified by Google Trends, showing a 10%

increase in skin cancer and a 300% increase in "sun cream" searches [33].

X's #dontfryday made a significant impact globally, with over 12 million impressions. The most influential posts were sent out by celebrities. One study found that while noncelebrity individuals contributed the most content for the campaign, celebrities made a monumental impact, with only 18 contributors generating 8,735,549 impressions [34,35].

As seen with #dontfryday, celebrity influence plays a huge role in enhancing the success of a prevention campaign. Actor Hugh Jackman has posted his skin cancer experience on SM. Each time he posts, the search "skin cancer" spikes on Google [36,37]. Like Jackman, Dayanara Torres, a former Miss Universe, used her platform to discuss her diagnosis of melanoma. One dermatology clinic in New Jersey noted that after Torres' announcement, many Hispanic patients came to their clinic specifically with skin cancer screening concerns rather than their usual motivating factors [38]. Now, Torres partners with the Melanoma Research Foundation as a spokesperson for the #GetNaked awareness campaign, promoting monthly self-screenings and yearly dermatologist skin examinations [125]. In Portugal, athletes distributed skin cancer screening messages, and by the end of the study, more individuals were screened than in the previous years [39].

SM can perpetuate the tanned ideology, but with targeted interventions, this risk can be mitigated. Appearance-focused interventions, or interventions that use aging, wrinkles, and sunspots in their educational material, successfully reduced Instagram users' positive associations with SM images featuring people with tanned skin [40]. Increasing SM literacy can also decrease the internalization of the tanned ideology. SM literacy is the ability of a user to evaluate and critically analyze posts, which aims to promote greater skepticism of appearance-related media [41,42]. The self-persuasion theory is another method that can predict healthy behaviors and enhance skin protection intentions: individuals who share skin protection information predictably use those same practices [43-45].

A Danish antisunbed campaign focused on decreasing tanning bed use among adolescents, generating intense public debate, and increasing legislative support [46]. With the new legislation, a parent must sign off on indoor tanning if a child is younger than 18 years. Targeting educational messages to mothers is a promising approach, as mothers who are more educated about the dangers of indoor tanning and equipped to discuss those dangers are less likely to allow their children to use tanning beds [47].

## Demographics

In total, 10 of the 112 papers were categorized in the demographics group. The new communication environment offers an opportunity for skin cancer prevention but primarily targets younger demographics: the success of SM skin cancer prevention campaigns decreases as participant age increases [48-50]. However, many young adults consider SM prevention messages to be uninfluential, because they are lost in the influx of other information [51,52].

One underrepresented demographic is individuals with darker-pigmented skin, as many skin cancer educational and prevention messages do not engage these populations. For example, 97% of skin cancer pins on Pinterest were of white skin individuals [53]. Similarly, a review demonstrated that 100% of skin cancers depicted on SM advertisements had a background of Fitzpatrick type I or II skin [54]. SM representation is critical, as a study that interviewed 27 African American individuals found SM to be a primary means by which people with darker pigmentation are exposed to public health messages related to skin cancer [55]. Participants also stated it would be important for skin cancer awareness messages on SM to feature Black communities to feel that the information is relevant to them [55].

Sexual orientation and gender identification also have a role in engagement and prevention advertising [56]. Indoor tanning motivations in sexual minority men have not been investigated; thus, targeted prevention campaigns are lacking. Compounding, sexual minority men are specifically targeted by tanning salons through SM marketing, further encouraging deleterious tanning behaviors in this population [57].

### Research Recruitment

In total, 12 of the included 112 papers were designated as research recruitment, collecting a total of 2912 patient responses [5,58-63]. By distributing surveys through SM platforms, scientists can recruit patients with rare skin cancers (such as dermatofibroma sarcoma protuberans [58]) and distribute research recruitment efforts globally. Additionally, SM can be used in studies to assess patients' health-related quality of life. This concept was validated in one such study, which showed the alignment of current electronic health record data to SM data mining of symptoms that are common for patients receiving skin cancer treatment [64,65]. SM can also support data crowdsourcing to help physicians understand the patient experience and identify high-risk individuals for prevention [66,67]. New communication technology offers a unique opportunity for physicians to directly communicate with and understand their patients on a deeper level [68].

### Education

Education through new media resources allows dermatologists to have a more substantial global reach in skin cancer prevention, which is what was primarily discussed in the 11 papers included within this category. In the past, studies have shown that the presence of dermatology-related content from reputable journals on SM is limited [69-72]. It is effective to use social networking sites to provide an avenue for health care providers to communicate, share knowledge, and discuss care [73]. For example, Doximity is a platform for health professionals to freely discuss topics such as skin cancer. Dermatologists can use Doximity to share skin cancer awareness messages, prevention strategies, or scientific papers with the broader physician community. Anyone can then share information from Doximity to SM sites to reach the wider patient population [74].

Similarly, physicians share posts during the American Society of Clinical Oncology meeting. From 2011 to 2012, "melanoma"

was a trending term at the American Society of Clinical Oncology conference, and attending physicians dispersed the latest scientific research over X [75]. Physicians can also connect with patients and teach proper skin self-examination through SM [76]. One study noted that 79% of patients had increased confidence in performing skin self-examination after watching eHealth YouTube videos, which proved superior to classic methods such as informational brochures [77].

Education strategies using beauty technicians can also serve as an intervention tactic for skin cancer. For example, the Pele Alerta Project built a website to assist beauty professionals in the early detection of skin cancers [78]; in addition, tattoo artists were targeted to provide skin protection information in their aftercare instructions [79]. Each educational opportunity gives patients a greater chance of catching their skin cancer early.

### Patient Support

In total, 4 of the 112 included papers discussed social media and its use in patient support. Patients often use SM to share their firsthand experiences, such as skin cancer excision procedures, to help provide realistic expectations for other patients [80]. They also use SM to discuss the effects of skin cancer on their quality of life. Mental health struggles and uncertainty were the 2 most common themes for forums for patients with skin cancer [81], and emotional burden, treatment, and diagnosis were common conversation topics throughout these support groups [82]. Over 52% of melanoma Facebook groups are used to support patients [83].

### Misinformation

Finally, the majority of included records discussed misinformation, with 40 of 112 papers belonging to this category. Participants in one study viewed a misinformation video and afterward had less intention to wear sunscreen, demonstrating the detrimental effect of misinformation. Comments posted correcting the misinformation in the video showed no significant increase in attitudes regarding sunscreen use [84].

Many misinformation studies verify a positive correlation between SM use and indoor tanning behaviors [85-87]. Not only does SM propagate skin tone dissatisfaction, but it also has provided a place of advertisement for tanning salons. Indoor tanning businesses propagate misleading information to increase their customer base, such as "indoor tanning is a safe way to get vitamin D" [88,89]. Companies have used "#paleshaming" to bring adolescents to their salons by damaging their self-esteem and motivating their engagement in tanning behaviors [90]. Not only do tanning salons use SM for business promotion, but also tanning, in general, is glorified across new media [91]. A review of tanning hashtags was conducted for TikTok, Pinterest, YouTube, and X, where 90%, 85%, 68%, and 68.9% of tanning content was positive, respectively [92-95]. Further research showed that, over a 2-week period, only 2.56% of 154,496 tanning posts on X mentioned skin cancer as a risk [96]. In summary, SM propagates indoor tanning behaviors by adding to skin tone dissatisfaction, advertising for tanning salons, and broadcasting a positive attitude toward tanning and sunburn.



YouTube attracts over 866 million users monthly [97]. Multiple studies identified that the current YouTube video landscape is of low quality, reliability, understandability, and actionability [98-107]. A table with the extrapolated results from each quality analysis study can be found in [Multimedia Appendix 5](#) [98-107]. While there has been a positive progression in educational content on YouTube from 2014 to 2018 [108,109], misinformation and low-quality information still plague the viewing streams. For instance, YouTube creators grossly overestimate the relationship between COVID-19 and vitamin D, encouraging tanning behaviors during the pandemic [110]. Similarly, multiple studies found blatant misinformation from many YouTube videos regarding alternative therapies, especially concerning “black salve” as a “100% cure for skin cancer” [111,112]. The largest issue is there is no correlation between the quality of content and the amount of engagement that content receives [113]. Even if dermatologists developed high-quality educational videos, users may still engage with lower-quality, inaccurate videos, as YouTube offers no verification or credentialing functionality.

Like YouTube, many reviewers found a trend of misinformation, high variability, and low readability on websites. The readability scores of sampled skin cancer websites averaged at the high school level, whereas the recommended readability score for medical information is at the seventh-grade level [114,115].

Misinformation is found across all SM platforms. A review of skin cancer records across Facebook, X, and Pinterest found that 44.7% of records were imprecise and 20% were confusing [116]. The #Stop5G campaign that went viral on X and Facebook broadcasted inaccurate health information, stating that 5G phones were causing skin cancer [117]. Longitudinal melanonychia also went viral on TikTok in 2022. Of the 100 videos examined, only 30% of TikTok postings regarding longitudinal melanonychia encouraged patients to see their physician, and the information was of poor quality as seen by the DISCERN score average of 1.58/5 [118]. Pinterest portrays a low general risk of skin cancer to its users, recommends alternative medicines twice as often as traditional biomedical treatments, and spreads false sunscreen information [119]. Antisunscreen campaigns have become more popular, specifically targeting parents and encouraging homemade sunscreen that is ineffective in protecting the skin [120,121]. Even skin cancer screening examinations, a well-established early detection intervention, are impacted by misinformation: 25% of screening posts on Pinterest were negative, expressing doubts regarding the merit of skin examinations [122]. Facebook support groups may also be poor sources of cancer care

information: in one examination of Facebook skin cancer support group comments, 35% of posts had comments that offered medical advice, of which 87% did not align with guideline-concordant care [123].

## Discussion

### Principal Findings

This review has addressed SM’s positive and negative effects on skin cancer. SM drives most persons’ day-to-day communication and can be a powerful tool for health care leaders to communicate important cancer control information. However, communication via SM also introduces the risk of disseminating misinformation. A critical knowledge gap regarding methods to reduce health misinformation within SM has developed. Studies indicate how increasing interactivity and emotions can increase engagement and success of cancer prevention campaigns. Platforms have the potential to disseminate and gather information quickly and to target patients of many demographics. This review identifies the best practices of SM regarding skin cancer and the drawbacks of the ever-changing information environment to help public health figures use SM in the most productive ways and curb the harmful effects of digital media.

### Best Practices

[Table 1](#) is a culmination of the most effective and engaging ways for health officials to use SM to discuss skin cancer. New communication strategies have so much potential and, if used properly, could increase awareness of skin cancer. Many of the studies included in this review attempted to understand the most engaging ways for physicians and researchers to use SM for public health purposes. The most effective strategies use interactivity, emotion, and promotion from a public influencer. Through the education of patients, providers, and other technicians, the opportunity for skin cancer to be caught early and in turn treated easily will increase. Physicians can also use SM to educate themselves on the popular complaints of skin cancer treatments and to understand their patients’ questions and concerns. SM opens a new line of communication that will revolutionize the patient-physician relationship. The affordable nature of the platforms along with the ease of information spread would allow physicians or researchers to easily educate individuals on the best ways to protect themselves from skin cancer and to protect patients from other misinformation across new communication platforms. If public health officials apply these best practices on SM, they can encourage skin health and publicize prevention methods.



**Table 1.** Best practices demonstrating the best ways to increase audience engagement and the educational benefits of social media.

Objective	Best practices
Increase engagement	<ul style="list-style-type: none"><li>• Interactivity<ul style="list-style-type: none"><li>• Cognitive dissonance</li><li>• Self-persuasion theory</li></ul></li><li>• Emotional communication<ul style="list-style-type: none"><li>• Fear</li><li>• Compassion</li><li>• Humor</li><li>• Shock</li></ul></li><li>• Influential backing<ul style="list-style-type: none"><li>• Celebrities</li><li>• Physician credibility (white coat)</li><li>• Legislation blocking indoor tanning</li></ul></li></ul>
Provide beneficial educational content	<ul style="list-style-type: none"><li>• Dermatologists to patients<ul style="list-style-type: none"><li>• Self-skin examinations</li><li>• Prevention information and practices</li><li>• High-risk behaviors</li></ul></li><li>• Dermatologists to primary care physicians<ul style="list-style-type: none"><li>• Share the most up-to-date literature</li><li>• Share best practices for prevention education</li></ul></li><li>• Dermatologist to another technician<ul style="list-style-type: none"><li>• Hairdressers</li><li>• Nail technicians</li><li>• Tattoo artists</li></ul></li><li>• Patient to dermatologist<ul style="list-style-type: none"><li>• Understand the effects of treatments and diseases from the patient’s perspective</li></ul></li></ul>

**Drawbacks**  
Limited statistical data regarding user demographics on SM make developing targeted interventions and drawing clear conclusions from SM data mining incomprehensible [126,127].

SM research demographics do not accurately represent the entire patient population with skin cancer. This disables researchers in applying SM trends to the general population with skin cancer, specifically regarding gender or higher education distribution (Table 2) [66].

**Table 2.** A collection of the studies that used SM to recruit participants, broken down by demographics.

	Platform	Responses, n	Female participants, n (%)	Male participants, n (%)	Age (years), mean (SD)	Higher education, n (%)
Strome et al [61]	Unspecified	977	507 (51.9)	470 (48.1)	19.3 (2.4)	__ <sup>a</sup>
Al-Atif [5]	WhatsApp	529	466 (88)	63 (12)	36 (10)	449 (87)
Guo et al [59]	WeChat	135	70 (51.9)	65 (48.1)	55.8 (14.2)	—
Telvizian et al [62]	Facebook and X (Twitter)	407	330 (81)	77 (19)	36.2(13.2)	—
David et al [58]	Facebook support groups	214	169 (78.9)	45 (21.1)	40.7 (12.1)	—
Makady et al [60]	Facebook and X (Twitter)	89	62 (69.66)	27 (30.33)	35-64	57 (64)
Wohlk et al [63]	Facebook	561	561 (100)	0 (0)	30	235 (41.8)

<sup>a</sup>Not available.

The educational value of prevention campaigns remains in question. When health care leaders or influencers abuse campaign power, it can reduce the public health campaign’s credibility and effectiveness. While some campaigns have proven effective, there are significant demographic discrepancies in which they reach. These campaigns display a bias toward

White individuals, and they cannot significantly reach older individuals or young adults due to ineffective communication methods or minimally engaging content. Campaigns require modification with SM changes to remain relevant and reach all demographics.

The current landscape of skin cancer SM content is poor, and dermatologists' presence is lacking across platforms. After observing the quality of health care content available to patients, SM cannot be considered a reliable source and should remain unsanctioned by physicians.

Medical misinformation research has demonstrated that the presence of misinformation has increased with new technology. Medical misinformation was extensively studied following the COVID-19 pandemic, and it was found that patients' trust in misinformation increased as their opinion on public health and medical institutions became more negative [128]. This mistrust may come from the growing influence of misinformation, which may lead patients to resist corrections coming from accredited sources [129]. The challenges seen through this scoping review have mirrored other research findings, showing that web-based platforms pose a challenge due to the ease of distribution of medical misinformation. Furthermore, SM provides a platform for users to share information without consequence or peer review and under the protection of freedom of speech. One pilot study discovered that practitioners encountered misinformation regularly across all specialties. Specifically, they found that 92% of the surveyed dermatologists had encountered medical misinformation presented by their patients [130].

While it is accepted that misinformation is generating obstacles for practitioners, the solution is still heavily debated. To combat misinformation, practitioners must have knowledge of what is being spread to provide their patients with high-quality, evidence-based resources. Through our scoping review of the current SM research environment, we may provide clinicians with an actionable understanding of the current state of SM information. In conjunction, SM platforms and new media technology can adapt content algorithms to modify patterns of misinformation exposure. These platforms could additionally develop technologies that allow users to flag problematic content for other SM users [128].

### Future Research and Interventions

Future research is needed to understand the quality of skin cancer content and develop, implement, and evaluate new prevention campaigns on SM platforms, such as TikTok. The current lack of research on TikTok is alarming, considering the frequency of its use among younger patients. SM requires effective and efficient physician engagement methods to reduce misinformation and promote accurate skin cancer content. Increasing dermatologist engagement could ensure high-quality information and establish credible sources for users. As seen through the studies discussing research recruitment, SM data mining offers enormous opportunities to understand the skin cancer landscape on SM. Future studies using data mining related to skin cancer are needed to understand the scope of skin cancer information across new media.

This review identified specific populations who could benefit from SM interventions, specifically, low SM literate individuals and populations commonly disregarded by prevention campaigns. Increasing SM literacy is one of the most influential methods to ensure users properly digest information and are protected from misinformation. In the past, campaigns and advertisements regarding sun protection have underemphasized people of darker complexion. SM provides an easy, affordable campaign platform to target all audiences. The Dayanara effect [38] and Admassu's use of Grindr to target sexual minority men [56] demonstrate the credibility of targeting specific audiences through SM. Both campaigns amplified cognizance of skin cancer in communities demographically underrepresented by prevention campaigns. It is essential to diversify our intervention strategies to educate all people who could be diagnosed with skin cancer.

### Limitations

As with all literature reviews, ours is reliant on the quality of the previously published data. Other limitations include word choice and database selection, which inadvertently exclude relevant publications. A language bias may be present, as we excluded all papers for which an English full text could not be identified. Interpretation of data, either our own or that of the original author, potentially risks data misinterpretation. The amount of quantitative data available on this topic was limited, and each study's variables differed. In addition, much of the research currently involving SM's effects on skin cancer is contradictory. Some studies conclude that SM has immense potential for prevention, while others argue that it is a source of misinformation. This contradiction was often due to study design or sampling bias by the original authors.

### Conclusions

New communication technology represents both an opportunity to improve public health practices and an obstacle for practitioners to overcome. The full potential of SM has yet to be reached, and health care leaders can make these platforms educational and productive regarding skin cancer prevention. Every day users are at risk for exposure to misinformation, which can decrease their trust in evidence-based medicine and increase their intentions to engage in harmful skin behaviors. This review uncovered the importance of collaboration between health care and SM industries to develop techniques to decrease the spread of misinformation. As SM becomes ubiquitous in society, developing quality strategies that break through and reach target populations becomes essential. Establishing a symbiotic relationship between public health officials and SM communication enables new communication technologies to be used as an accurate source of skin cancer information and could prevent harmful behaviors.

### Acknowledgments

The research described was supported in part by a cancer prevention educational award for PLH supported by the National Cancer Institute (R25 CA056452, Shine Chang, PhD, Principal Investigator).

## Authors' Contributions

PLH wrote the paper, performed data extraction, developed all figures and tables, and conducted analysis for the development of discussion and conclusions. AJ did data extraction and collection. MT edited the paper and assisted in review. HS edited the paper. DPF performed the literature search. KCN served as principal investigator, project oversight, data collection, writing, and editing the paper.

## Conflicts of Interest

None declared.

### Multimedia Appendix 1

Search strategy.

[PDF File (Adobe PDF File), 84 KB - [derma\\_v7i1e53373\\_app1.pdf](#)]

### Multimedia Appendix 2

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.

[DOCX File, 28 KB - [derma\\_v7i1e53373\\_app2.docx](#)]

### Multimedia Appendix 3

STROBE score worksheet used for scoring included papers (scores can be found in Multimedia Appendix 3) [10].

[PDF File (Adobe PDF File), 15 KB - [derma\\_v7i1e53373\\_app3.pdf](#)]

### Multimedia Appendix 4

Table of characteristics of all included records.

[PDF File (Adobe PDF File), 167 KB - [derma\\_v7i1e53373\\_app4.pdf](#)]

### Multimedia Appendix 5

Ten different studies evaluating YouTube videos for quality (DISCERN, Journal of the American Medical Association, and General Quality Score), understandability (Patient Education Management Assessment Tool-Understandability), and actionability (Patient Education Management Assessment Tool-Actionability) of videos on skin cancer topics.

[PDF File (Adobe PDF File), 102 KB - [derma\\_v7i1e53373\\_app5.pdf](#)]

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## Abbreviations

**PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses

**SM:** social media

**STROBE:** Strengthening the Reporting of Observational Studies in Epidemiology

*Edited by R Dellavalle; submitted 09.10.23; peer-reviewed by B Southwell, W Guo; comments to author 11.12.23; revised version received 01.02.24; accepted 06.02.24; published 08.04.24.*

*Please cite as:*

*Haff PL, Jacobson A, Taylor MM, Schandua HP, Farris DP, Doan HQ, Nelson KC*

*The New Media Landscape and Its Effects on Skin Cancer Diagnostics, Prognostics, and Prevention: Scoping Review*

*JMIR Dermatol* 2024;7:e53373

URL: <https://derma.jmir.org/2024/1/e53373>

doi: [10.2196/53373](https://doi.org/10.2196/53373)

PMID: [38587890](https://pubmed.ncbi.nlm.nih.gov/38587890/)

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## Research Letter

# Online Patient Attitudes Toward Cutaneous Immune-Related Adverse Events Attributed to Nivolumab and Pembrolizumab: Sentiment Analysis

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(*JMIR Dermatol* 2024;7:e53792) doi:[10.2196/53792](https://doi.org/10.2196/53792)

**KEYWORDS**

immune checkpoint inhibitor; immunotherapy; pembrolizumab; nivolumab; cutaneous immune-related adverse event; medical dermatology; oncology; sentiment analysis

## Introduction

Online forums provide patients with platforms to connect, share experiences, and learn about conditions and treatments [1]. Drugs.com, one publicly available website, hosts patient reviews on medication-related adverse events. Since 2011, immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy. Increasing use of ICIs has led to more patients experiencing ICI-induced cutaneous immune-related adverse events (cirAEs), occurring in 30%-60% of patients [2]. However, many nondermatologist physicians feel unequipped to manage cirAEs, making dermatologists with expertise in skin-related conditions crucial in detection, diagnosis, and management [3]. Furthermore, despite cirAEs being linked to improved survival and treatment response, they are frequently distressing to patients. Patient reviews of ICIs could offer insights into attitudes and expectations about cirAEs during cancer treatment, aiding physician-patient education. Previous literature highlights the potential for natural language processing to provide valuable insights [4,5]. Our study aims to characterize public online oncology patients' attitudes toward dermatologic symptoms (DSs) during ICI treatment and explore whether patients mentioning DSs also report improved cancer outcomes.

## Methods

**Overview**

Data on ICIs nivolumab and pembrolizumab were collected from Drugs.com using Python ([Multimedia Appendix 1](#)). Reviews were screened for DSs using the following terms: skin, dermatitis, rash, blisters, dry, itch, and peeling. Sentiment scores were derived using cardiffnlp/twitter-roberta-base-sentiment-latest, a Robustly Optimized Bidirectional Encoder Representations From Transformers (RoBERTa)-based artificial intelligence technique that captures contextual semantics [6,7]. Two-tailed Mann-Whitney *U* tests compared median ratings and sentiment scores in DS-containing reviews versus those without. Positive cancer outcomes were determined by manual review, including the words remission, gone, resolution, shrunk/shrink, smaller, reduction, disappeared, cancer-free, and saved. Significance was evaluated using a Fisher test. After examining the distribution ([Table 1](#)), patient reviews were divided into three score ranges (1-3, 4-7, and 8-10 out of 10) by dividing the maximum rating of 10 into thirds and rounding to the nearest nonoverlapping whole number. A row-wise Fisher test was used to compare DS-containing versus non-DS-containing reviews across the three score groups, with a Benjamini-Hochberg procedure to adjust *P* values.



**Table 1.** Distribution of patient ratings of nivolumab and pembrolizumab.

	Scores 1-3, n	Scores 4-7, n	Scores 8-10, n	Total reviews, n
Nivolumab	52	6	43	101
Pembrolizumab	121	14	56	191
All	173	20	99	292

Ethical Considerations

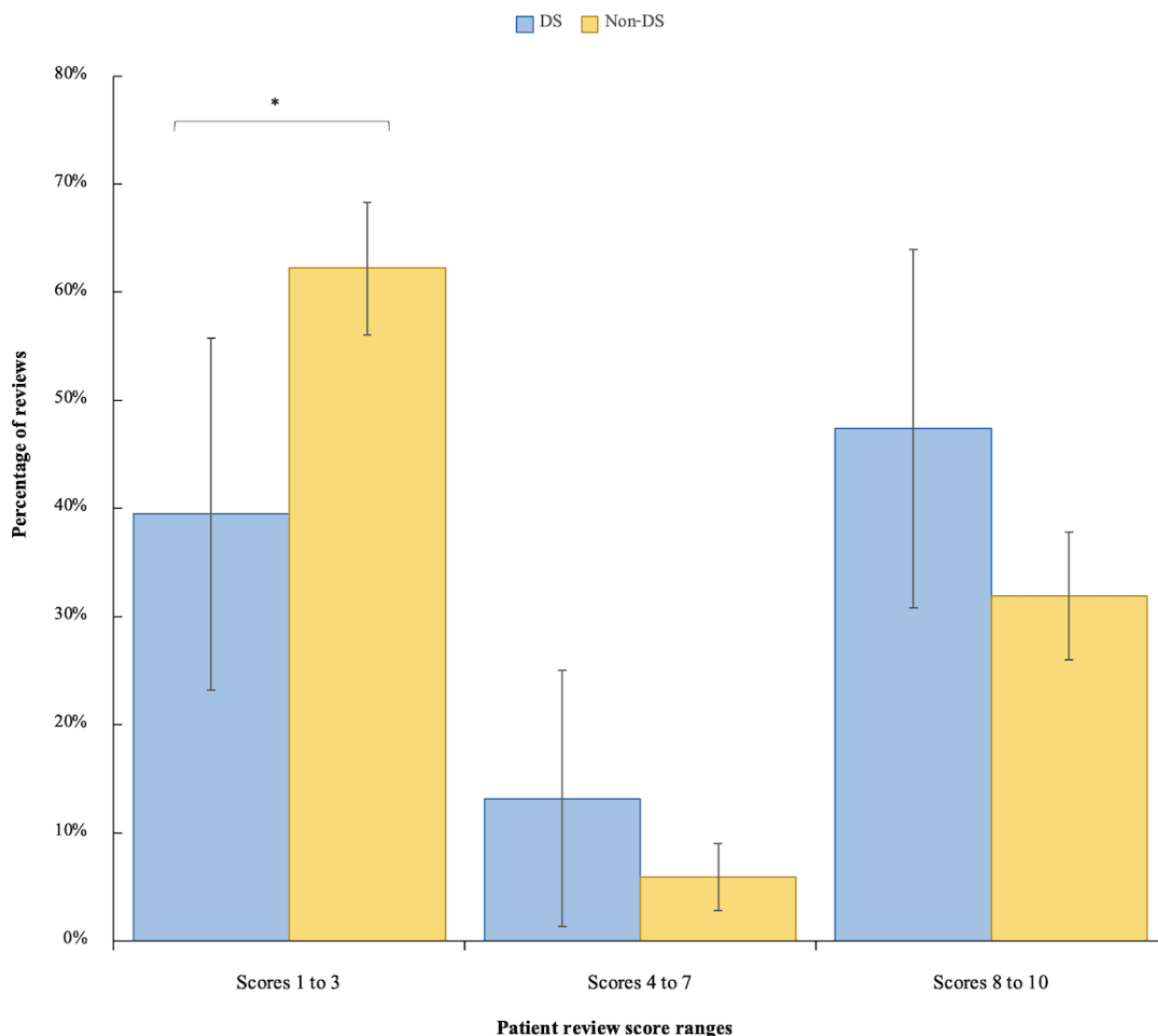
Given the publicly available nature of the data, no institutional review board approval was warranted for this study. We prioritized patient privacy and minimized potential harms by anonymizing data, analyzing all reviews, transparently documenting our methods, and comparing findings to existing literature.

Results

Of 292 reviews, 38 mentioned DSs (21 for nivolumab and 17 for pembrolizumab), while 254 did not. The distribution of ratings was heavily skewed toward extremes, but a handful of reviews were moderately rated. The top two ICI indications were non–small cell lung cancer (117/292, 60.9%) and melanoma (52/292, 17.8%). Mean patient ratings were

significantly higher for nivolumab than pembrolizumab (mean 4.97, SD 4.08 vs mean 3.85, SD 3.79 out of 10;  $P=.02$ ). DS-containing reviews had significantly higher patient ratings (median 6.5, IQR 1-10 vs median 1.0, IQR 1-9 out of 10;  $P=.007$ ). A trend toward higher sentiment scores was exhibited in DS-containing reviews, though it did not reach statistical significance ( $P=.07$ ). Overall, 16 of 38 (42%) DS-containing reviews compared to 40 of 254 (15.8%) non–DS-containing reviews self-reported positive cancer outcomes, including remission or tumor size reduction ( $P<.001$ ). A significantly lower proportion of DS-containing compared to non–DS-containing reviews had ratings of 1 to 3 out of 10 (15/38, 39% vs 158/254, 62.2%;  $P=.04$ ). Higher proportions of DS-containing reviews were in the score ranges of 4-7 and 8-10, but these did not reach statistical significance ( $P=.16$  and  $P=.10$ , respectively; [Figure 1](#)).

**Figure 1.** Percentages of patient reviews mentioning DSs versus not mentioning DSs in each score range. All scores are out of 10 and were extracted from patient ratings of nivolumab or pembrolizumab on Drugs.com. The error bars represent 95% CIs, calculated by the Clopper-Pearson method. DS: dermatologic symptom. \*Significant by row-wise Fisher test, defined as  $P < .05$ .



## Discussion

In summary, DS-containing reviews correlated with higher patient ratings and more self-reported positive cancer outcomes. Nivolumab was rated higher than pembrolizumab. The FDA reports the prevalence of pembrolizumab- and nivolumab-associated DS as 13.57% and 12.61%, respectively, aligning with the 13% (38/292) of DS-mentioning reviews in our study [8]. While not compared directly, pembrolizumab and nivolumab have both been associated with improved patient-reported quality of life [9,10]. CirAE development was associated with more self-reported positive cancer outcomes, reinforcing the presence of DS as a promising indicator of treatment efficacy [2]. Higher patient ratings were likely influenced by improvements in cancer. Thus, patient counseling by dermatologists regarding the prognostic value of cirAEs may improve patient satisfaction.

Online patient reviews have limitations. They skew toward younger English-speaking individuals with higher digital literacy and extremely positive or negative experiences. Patient reviews include subjective accounts of cancer diagnoses and improvement, lacking medical history and social context, may be emotionally biased or inaccurate and represent only a snapshot in time. Sentiment analysis tools may also carry biases; for example, our study's chosen model was trained on social media data, not health care data [7]. However, we believe this model is applicable due to the online and short-form nature of the reviews. Analyzing patient reviews offers direct feedback to clinicians and informs unmet patient needs. Future research could involve prospective data collection to quantify patients' subjective experiences alongside objective clinical cirAE grading to better guide the treatment of oncodermatologic conditions.

## Acknowledgments

The authors have not received grant support or research funding from any funding agency in the public, commercial, or not-for-profit sectors for this project. There are no proprietary interests in the materials described in this letter.

## Data Availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

Supplemental methods.

[DOCX File, 12 KB - [derma\\_v7i1e53792\\_appl.docx](#)]

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## Abbreviations

**cirAE:** cutaneous immune-related adverse event

**DS:** dermatologic symptom

**ICI:** immune checkpoint inhibitor

**RoBERTa:** Robustly Optimized Bidirectional Encoder Representations From Transformers

*Edited by W Guo; submitted 18.10.23; peer-reviewed by M Gasmi, V Long, M Elbattah; comments to author 07.03.24; revised version received 14.04.24; accepted 21.04.24; published 02.05.24.*

*Please cite as:*

*Powers CM, Yang AK, Verma H, Orloff J, Piontkowski AJ, Gulati N*

*Online Patient Attitudes Toward Cutaneous Immune-Related Adverse Events Attributed to Nivolumab and Pembrolizumab: Sentiment Analysis*

*JMIR Dermatol 2024;7:e53792*

*URL: <https://derma.jmir.org/2024/1/e53792>*

*doi: [10.2196/53792](https://doi.org/10.2196/53792)*

*PMID: [38696235](https://pubmed.ncbi.nlm.nih.gov/38696235/)*

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Review

# Hyaluronidase for Dermal Filler Complications: Review of Applications and Dosage Recommendations

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## Abstract

**Background:** Hyaluronidase (Hyal) can reverse complications of hyaluronic acid (HA) fillers, which has contributed substantially to the popularity of such procedures. Still, there are differing opinions regarding Hyal treatment, including dosage recommendations in filler complication management.

**Objective:** We aimed to address unanswered questions regarding Hyal treatment for HA filler complications, including timing and dosage, skin pretesting, properties of various Hyals and interactions with HA gels, and pitfalls of the treatment.

**Methods:** PubMed and Google Scholar databases were searched from inception for articles on Hyal therapy for filler complications. Articles were evaluated regarding their contribution to the field. The extensive literature review includes international leaders' suggestions and expert panels' recommendations.

**Results:** There are limited controlled data but increasing clinical experience with Hyal treatment. The currently used Hyals provide good results and have an acceptable safety profile. Nonemergent complications such as the Tyndall effect, noninflamed nodules, and allergic or hypersensitivity reactions should be treated with low or moderate Hyal doses. Hyal should be considered with prior or simultaneous oral antibiotic treatment in managing inflammatory nodules. Hyal may be tried for granulomas that have not responded to intralesional steroids. Emergent complications such as vascular occlusion and blindness require immediate, high-dose Hyal treatment. Regarding blindness, the injection technique, retrobulbar versus supraorbital, remains controversial. Ultrasound guidance can increase the efficacy of the above interventions.

**Conclusions:** Hyal is essential in aesthetic practice because it can safely treat most HA filler complications. Immediate Hyal treatment is required for emergent complications. Aesthetic practitioners should be versed in using Hyal and effective dosage protocols.

(*JMIR Dermatol* 2024;7:e50403) doi:[10.2196/50403](https://doi.org/10.2196/50403)

## KEYWORDS

hyaluronidase; hyaluronic acid; filler; complications; nodule; vascular occlusion; therapy; treatment; application; dosage; management; skin; data; inflammatory nodule; inflammatory; injection

## Introduction

Fillers are classified into three major classes based on their longevity in the tissues, which in turn depends on their structure and composition: (1) temporary, lasting less than 18 months;

(2) semipermanent, lasting greater than 18 months; and (3) permanent, lasting longer than 24 months. It is generally believed that permanent fillers are nonbiodegradable and nonreversible, and therefore, complications with the inflammatory process are more likely to occur with permanent



fillers. Dermal fillers have gained popularity over the past 2 decades despite the large spectrum of complications associated with their use, including nodule formation, misplacement, migration, infection, and vascular occlusion [1-3]. Hyaluronic acid (HA) fillers are temporary or semipermanent and remain the most used filler type [4]. Fillers that cannot be dissolved by hyaluronidase (Hyal), such as poly-L-lactic acid, calcium hydroxylapatite, and polymethylmethacrylate, are not discussed here. The ease and efficacy of Hyal in reversing HA gels' (HAG's) complications have contributed to such fillers' popularity [5]. Performing Hyal injections under high-frequency ultrasound (HFUS) guidance, a recent advance in soft tissue augmentation, allows for higher accuracy and efficacy of the treatment, thereby maximizing the benefits [6].

Still, there has been a small number of well-designed randomized controlled trials (RCTs) on Hyal injections in aesthetics. Borzabadi-Farahani et al [7-11] found only 5 RCTs evaluating the effectiveness of Hyal in removing uncomplicated HA nodules. Dosing recommendations are often based on the suggestions of leading authorities and assessment by expert panels. The objective of this review is to discuss the aesthetic applications of Hyal injections and provide an updated assessment of dosing recommendations, including dosage (international units [iu]), treatment sessions, and incremental dose adjustments (titration). We discuss gaps and present our experience with Hyal treatments.

## Methods

We have completed a narrative review, as a systematic review is not feasible due to the high heterogeneity of articles on this broad topic. We searched PubMed and Google Scholar databases from inception for articles on Hyal therapy for filler complications. Complication is an adverse effect emphasizing direct causality between the filler procedure and the adverse outcome or event [1]. Key terms in the search included "complication OR adverse event," "safety," "prevention," "management OR treatment OR intervention," "hyaluronidase," and "filler." We performed separate searches for important complications using the terms "reaction," "granuloma," "nodule," "infection OR biofilm," "vascular occlusion OR vascular compromise," and "skin necrosis." A separate search for using ultrasound (key term "ultrasound") in filler procedures was performed. We searched the reference lists of relevant articles. We included expert opinions, panel recommendations, and professional body guidance.

## Results and Discussion

### Principal Findings

We review the findings of publications relevant to Hyal action [12-23], products available [14,18,19,21-23], reconstitution and

storage [1,18,20,21,24,25], dosage considerations [5,9-11,16,18,21,26-30], skin pretesting [18,21,24,31-33], use in the management of filler complications [1,2,5-8,16,18,21,24,34-75], and the pitfalls of Hyal treatment [1,13,19,24,37,76-79].

### Action of Hyal

Hyal is an endoglycosidase that can depolymerize HA leading to its degradation into monosaccharides by hydrolyzing the disaccharides at hexosaminidic  $\beta$ -1 through  $\beta$ -4 linkages [12]; however, it also breaks down to some extent other polysaccharides in the connective tissue [13,14]. In humans, 6 Hyals have been identified (HYAL-1, -2, -3, -4, HYALP1, and PH-20) [15]. Hyal has an immediate effect and a half-life of 2 minutes with the duration of action being 24 to 48 hours [16,17]. However, it is effective for a longer time period which may be related to the fact that a low number of iu is required to have a clinically significant effect; thus, even when the Hyal has mostly degraded, its action continues [18]. Commendably, Hyal breaks cross-links in the HA filler, which behaves like native HA in the skin, which has a half-life of 24 to 48 hours [15]. Hyal dissolves native HA, but the body restores native HA in 15-20 hours [19]; therefore, there are no detrimental long-term effects of Hyal on skin quality.

Hyal is a tissue permeability modifier and is indicated as an adjuvant in subcutaneous fluid administration for achieving hydration, increasing the dispersion and absorption of other injected drugs such as anesthetics and in subcutaneous urography for improving resorption of radiopaque agents [20]. Hyal is used off-label in aesthetics.

### Available Hyals

Hyals are derived from mammals (obtained from the testes), hookworms or leeches, and microbes [19]. Animal origin Hyals have been used clinically for almost 80 years [21]. Hyals that are currently available are of either animal origin or human recombinant (Table 1). Food and Drug Administration -approved Hyals include bovine (Amphadase), ovine (Vitrase) products, and recombinant human (Hylenex) products. Still, in many countries, only 1 Hyal type is available—Hylase "Desau" in Germany and "Hyalase" in the United Kingdom require reconstitution (product should be used within 6 hours) [14,22]. Recombinant human Hyal has a purity 100 times higher than some of the bovine preparations [23]. The recombinant type is thought to have a lower incidence of allergic reactions than animal-derived products that are more immunogenic, but long-term data are lacking [18,21].

**Table 1.** Some of the commercially available Hyal products<sup>a</sup>.

Trade name, country of origin	Source	Product details	Reconstitution required	Storage
Amphadase, United States <sup>b</sup>	Bovine	150 iu/mL in 2 mL vial; contains thimerosal	No	2 °C-8 °C
Hydase, United States <sup>b</sup>	Bovine	150 iu/mL in 2 mL vial	No	2 °C-8 °C
Hylenex, United States <sup>b</sup>	Human recombinant	150 iu/mL in 2 mL vial; contains human albumin	No	2 °C-8 °C
Vitrase, United States <sup>b</sup>	Ovine	200 iu/mL in 2 mL vial; contains lactose	No	2 °C-8 °C
Hylase “Desau,” Germany	Bovine	150, 300, 1500 iu/mL in vial	Yes	25 °C±2 °C; 60% relative humidity
Hyalase, United Kingdom	Not specified	1500 iu/mL in vial	Yes	≤25 °C

<sup>a</sup>Pregnancy category C.

<sup>b</sup>Food and Drug Administration–approved.

**Reconstitution and Storage**

Hyal is reconstituted in bacteriostatic normal saline, which is less painful upon injection than water and has additional anesthetic properties [18]. Bacteriostatic normal saline contains benzyl alcohol to prevent bacterial contamination. An aseptic technique should be used during the reconstitution process. One should gently swirl or mix the vial to dissolve the Hyal powder in the saline and avoid vigorous shaking to prevent foaming. The volume of the diluent depends on the indication and surface area to be treated, and a range of 1 to 10 mL has been evidenced in clinical practice [1]. Increased volumes of diluent or subsequent dilutions of a fraction of the reconstituted Hyal are needed if a small number of Hyal units are injected. These authors reconstitute 1500 iu Hyal (Hyalase) in 1 mL bacteriostatic saline and subsequently dilute fractions of the reconstituted Hyal product to achieve the desired number of units per 0.1 mL.

There is a theoretical concept that using a lower dilution (higher Hyal concentration) might provide a more focused effect, especially when targeting specific areas like nodules.

While a lower dilution may theoretically lead to more localized effects, it is crucial to balance this with the risk of excessive filler degradation by Hyal which can result in a complete loss of the aesthetic benefit of the filler procedure.

Some authors suggested diluting Hyal in lidocaine to decrease pain in cases of vascular occlusion [24]. However, this has not gained wide support as the enzymatic action of Hyal can be affected by pH and the pH of low lidocaine concentrations is not ideal for Hyal [18]. Additionally, there is a risk of widespread, increased systemic absorption of the anesthetic and potential complications. No evidence supports using lidocaine, with or without epinephrine, solvent to reduce bruising. In a report, a patient presented with soft blue nodules post-HA filler in bilateral infraorbital areas. The lesions were treated with 75 iu Hyal (reconstituted in 1 mL 1% lidocaine with epinephrine); lidocaine with epinephrine was selected to reduce bruising but was ineffective [25].

The Hyal products approved by the Food and Drug Administration (Table 1) should be stored at cool temperatures (2 °C-8 °C) to maintain the quality of the product over a long period of time [18,21]. The Hyal vial should be stored unopened in a refrigerator [20]. If Hyal is stored at room temperature (25 °C), the stability is only guaranteed for 12 months [18]. The provider should follow the product guidelines for storage. The product should be injected immediately after preparation.

**Hyal Dosage**

**Considerations**

The Hyal dosage required depends on the indication (emergent vs nonemergent complication), location, volume, physical properties of the HAG to be dissolved, and patient factors [9,26]. The use of Hyal often involves a titration approach, where the practitioner assesses the response after each injection. Incremental adjustments of Hyal dosage are recommended—smaller doses and a gradual approach allow for fine-tuning, minimizing the risk of excessive filler degradation.

Vascular complications require larger doses than nonemergent (overcorrection, misplacement, and inflammatory reaction). Thinner skin (eg, lower lids and infraorbital areas) should be treated with lower Hyal doses. Larger filler volumes, larger particle size, higher concentrations of the filler, higher amount of cross-linking, and higher amount of G-prime contribute to increased durability of the filler requiring higher Hyal dosage for dissolution [9,26]. Also, monophasic (without distinct particles) HA formulations are more resistant to degradation than biphasic (particles suspended in gel) [26].

**Physical Properties of HAGs**

HA fillers have different physical properties that influence their degradation by Hyal in a time- and dose-dependent manner [21]. In an in vivo study using recombinant Hyal, Juve´derm Voluma required higher doses of Hyal than Restylane-L and Juve´derm Ultra for dissolution [11]. Therefore, Juve´derm Voluma may require repeat doses of Hyal for complete reversal.

A study by Rao et al [27] demonstrated Restylane (Galderma Laboratories) dissipated most and Belotero (Merz

Pharmaceuticals) was most resistant to degradation. The authors showed that responses were similar for Vitrase and Hylenex, suggesting that these products can be used interchangeably. However, a subsequent study showed that Belotero was the fastest to degrade and Juvederm Voluma (Allergan) and Restylane Lyft were the slowest, with the authors concluding that a high concentration of HA, larger particle size, and increased cross-linking increase filler durability [9]. Jones et al [28] showed that Restylane and Prevelle (Mentor Corp) displayed greater sensitivity to ovine Hyal than Juvederm Ultra and contributed to the degradation resistance of Juvederm Ultra to higher HA content and level of cross-linking.

### Drug Interactions

Drug interactions of Hyal should be considered. Salicylates, anti-inflammatories, cortisone, herbal meds, heparin, vitamin C, estrogens, and antihistamines make tissues resistant to Hyal [5,18]. One should consider a higher Hyal dosage or repeated injections in such cases. Therefore, having a thorough drug history before injecting Hyal is extremely important.

### Dosage Recommendations for Nonemergent Complications

Regarding dosing, there are no accepted standardized guidelines. However, the rule of thumb for treating uncomplicated nodules is 5 iu Hyal for 0.1 mL HAG 20 mg/mL [16]. In the study by Zhang-Nunes et al [11] a cross-linked filler (Juvederm Voluma, 20 mg/mL) required higher Hyal doses for dissolution, that is, more than 20 iu Hyal per 0.2 mL filler. In another study, in vivo degradation of cross-linked, highly cohesive HA fillers required 30 iu Hyal [29]. Woodward et al [30] recommended 30 iu to dissolve 0.1 mL. However, a study showed no statistical difference between using 20 or 40 iu Hyal in degrading 0.2 mL of various fillers (4-6 mg HA) [9]. Alam et al [10] showed that, although small Hyal doses (1.5-9 IU) can remove HA fillers, slightly higher doses often result in more rapid resolution.

Hyal dose for reversing overcorrection depends on the location and quantity of filler—in such cases, one may inject 15-30 iu in nasal or perioral areas, 3-4.5 in the periorbital area, 10-15 in the infraorbital area, and 1.5 in the lower [5]. However, even lower Hyal doses may be effective in reversing excessive augmentations. More resistant HAGs require higher Hyal doses of repetitive injections [21].

### Skin Pretesting

As detailed in the section “Pitfalls” below, allergic reactions to Hyal are uncommon in aesthetics; they have been mainly reported in cases of peribulbar injection in the ophthalmology practice [31,32]. Therefore, no pretest is warranted in emergencies, such as vascular occlusions, as the risks of delaying the therapeutic intervention outweigh the potential benefit from pretesting [18,21]. However, bedside availability of epinephrine is required. Skin pretesting is considered optional when treating nonemergency complications of HAGs, such as overcorrection, superficial implantation, or inflammatory reactions. No pretesting is required for recombinant Hyal but may be considered for ovine, bovine, or compounded Hyals.

The testing consists of intradermal injection of 0.02-0.05 mL Hyal (to achieve a bleb of 5 mm) followed by observation for local wheal and flare within 5 minutes [21,24]. It is positive if such a reaction persists for 20-30 minutes. There is a lack of consistency regarding the optimal Hyal dose or concentration for pretesting. Doses 5-16 iu have been chosen [21,24], with the proponents of the higher doses indicating that lower doses may be unreliable since the drug causes an irritant reaction that could be misinterpreted as an allergy.

Before injecting Hyal, one should check for possible or conformed allergy to bee and wasp stings; such allergies pose a significant risk of cross-reactivity [24,33]. There are no standard precautions for using Hyal in patients allergic to bee and wasp stings [21]. In nonemergent filler complications, when a history of a large, localized reaction or anaphylaxis to bee or wasp stings exists, an intradermal test by an allergist is recommended. In emergent complications requiring Hyal in such a patient, the risks and benefits of not performing a skin pretest should be weighed [21].

### Managing Filler Complications

#### Overview

This section reviews the elective use of Hyal for complications such as the Tyndall effect, noninflamed nodules resulting from overcorrection or misplacement of HA filler, inflammatory nodules, and allergic or immunogenic reactions to HA filler (Table 2). It also details the emergency use of Hyal in managing vascular occlusion to prevent tissue necrosis and blindness from periocular emboli. We discuss Hyal dosing for such complications and present our experience with Hyal treatments.

**Table 2.** Hyaluronidase dosage and considerations for treating complications of facial filler injections.

Aesthetic indication	Hyal dosage <sup>a</sup>	Hyal dosage (authors' experience)	Considerations <sup>b</sup>
Tyndall effect	10-75 iu <sup>c</sup> [2,34]	≤150 iu	<ul style="list-style-type: none"><li>• Nature of HA<sup>d</sup> filler (eg, cross-linked)</li><li>• Patient's wish to maintain cosmetic benefit of filler injection</li></ul>
Noninflammatory nodules (overfilling or misplacement)	5-150 iu [21,25]	≤300 iu or more, depending on severity and filler type and volume	<ul style="list-style-type: none"><li>• Nature and location of filler</li><li>• Volume of filler to be degraded</li></ul>
Asymmetry or contour irregularities	As above	≤225 iu	<ul style="list-style-type: none"><li>• As above</li></ul>
Inflammatory nodules	500 iu every 48 hours to be administered after OAB <sup>e</sup> have been tried for ≥2 weeks [39]; 30-300 iu combined with OAB [40]	Variable; often in conjunction with other treatments	<ul style="list-style-type: none"><li>• Results of skin biopsy</li><li>• Results of microbiology testing (if nodule fluctuant or abscess)</li><li>• Nature of HA filler (eg, cross-linked)</li></ul>
Vascular occlusion	450-1500 iu total (high-dose protocol) [60] in up to 4 Hyal cycles; 35-50 iu under HFUS <sup>f</sup> guidance (low dose protocol) [6]	300-1000 iu or more, depending on size of ischemic area	<ul style="list-style-type: none"><li>• Nature of HA filler (eg, cross-linked)</li><li>• Size of ischemic area</li><li>• Embolus size</li><li>• Timing of intervention</li><li>• Patient factors (eg, scar in the area)</li><li>• HFUS imaging availability</li></ul>

<sup>a</sup>Multiple Hyal sessions are often required, and the provider may use incremental dose adjustments depending on the response.

<sup>b</sup>Considerations are crucial to decision-making and building an individualized approach to Hyal therapy.

<sup>c</sup>iu: international unit.

<sup>d</sup>HA: hyaluronic acid.

<sup>e</sup>OAB: oral antibiotics.

<sup>f</sup>HFUS: high-frequency ultrasound.

**Tyndall Effect**

When particulate HA fillers are inappropriately injected too superficially, a bluish discoloration (Tyndall effect) can result and may persist for a long time [1]. Treatment with 30-75 iu Hyal can be effective [34]—a smaller number (10-20 iu) may be used if a small amount of HA needs to be degraded [2]. This will often lead to complete resolution of the complication within 24 hours, although occasionally, a second Hyal treatment may be required [24]. The focus of the provider is on degrading the superficially placed filler. Also, Hyal dosage depends on whether the patient requests the filler to be completely removed or just eliminate the Tyndal effect [35]. The practitioner should follow up with the patient in 3-4 days to check whether additional Hyal is needed. Hyal may be used at any time and has been effective 63 months after the initial injection of HA [36].

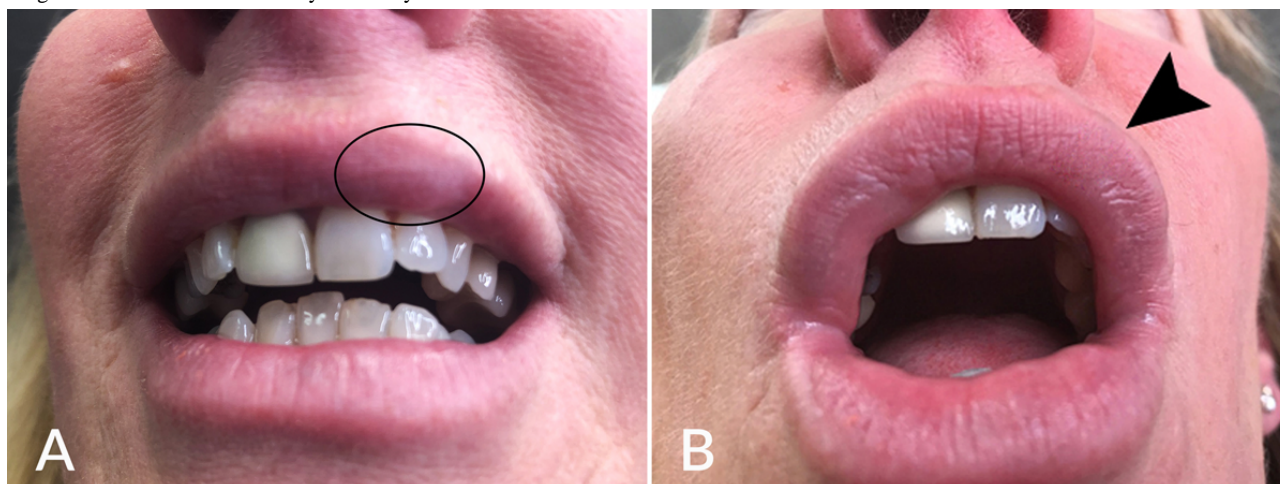
**Noninflamed Nodules**

Noninflamed nodules are typically firm, feel rubbery, and tend to be painless. They are not usually associated with redness or significant discoloration. Their incidence is unknown.

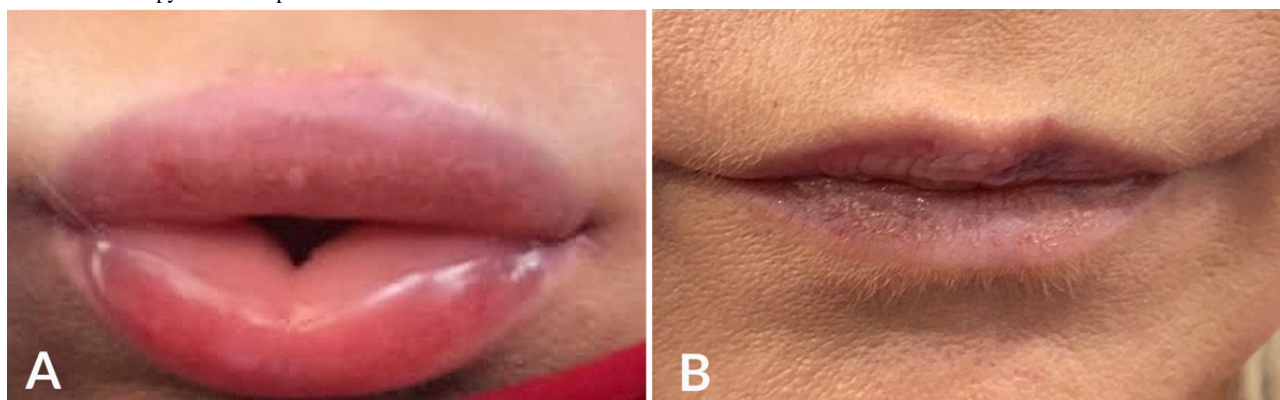
Noninflamed nodules result from overcorrection, filler misplacement, or migration (Figures 1 and 2). HFUS imaging is a first-line tool to identify the filler, assess its size, and exclude a soft tissue neoplasm (peer-reviewed by Kroumpouzou et al [1]). It may also help identify severe distant filler migration. Treatment of noninflamed nodules is warranted if painful, aesthetically bothersome, or associated with prolonged edema (ie, malar edema for >4 weeks). Hyal is delivered to the skin and subcutaneous tissue by directly infiltrating the visible or palpable HA depot [21]. Massage is recommended to mix the enzyme with HA and promote filler degradation. One may treat with a low dose, that is, 5-15 iu Hyal, and reassess in 1 week. However, higher doses (up to 150 iu) have been reported as effective [21,25]. As mentioned above, the volume and properties of the filler to be dissolved should be considered when deciding the dose to inject. A prospective trial included 8 participants who received 3 injections with 0.2 mL HA, and after 3-5 days each site was injected with 10, 20, or 30 iu Hyal. There were no differences among Hyal doses [8]. However, the study is limited by the small size and not including higher Hyal doses (ie, >50 iu).



**Figure 1.** (A) Noninflamed nodule (encircled) developed after HA filler misplacement on the upper lip vermilion. (B) Lesion resolved (arrow) after injecting 15 iu recombinant human Hyal. HA: hyaluronic acid.



**Figure 2.** (A) Upper lip overfilling and edema that developed after HA filler overcorrection on the upper vermilion. (B) Complication resolved after injecting 150 iu recombinant human Hyal. As an allergic reaction was considered, intramuscular epinephrine (1:1000 solution) and 100 mg intravenous hydrocortisone therapy were also provided.



The location of the filler should be considered as areas with thin skin, such as the eyelids, require low Hyal dosage (1.5-3 iu). Injecting a low dose helps prevent the loss of the HAG treatment effect. A retouch of another 1.5-3 iu 2-3 days later can be considered. Precautions to prevent ecchymosis should be taken when injecting the eyelids and infraorbital areas, especially as Hyal has been reported to spread the ecchymosis in these areas [37]. One should use a thin needle (30 G or thinner) and a single needle insertion point that helps minimize tissue trauma from the injection.

### Undesired Aesthetic Outcomes

To prevent suboptimal aesthetic outcomes, the injector should consider patient characteristics, choose an appropriate filler for the area to be injected, avoid overfilling, and inject with a knowledge of anatomy. Overfilling can result in nodule formation and filler migration. Still, asymmetries, nodules, and other contour irregularities can occur even when patients are injected by experienced providers. Hyal is an appropriate therapy for such complications caused by HA fillers. The dosage approach is like that detailed for noninflamed nodules above. One should consider the amount of filler that needs to be degraded and titrate the Hyal dosage according to the response. These authors have used 150-300 iu Hyal for such complications (Table 2).

### Inflammatory Nodules

Inflammatory nodules are often red and may feel warm to the touch. They can be associated with tenderness or pain. Inflammation may result from an immune response to the filler material, infection, or other complications [1]. Delayed-onset nodules (DONs) are usually inflammatory (ie, immune response to filler material), granulomatous (on histology), or related to infection or biofilm [1]. DON formation has a 0.5% incidence, a median time of onset of 4 months, and a median time to resolution of 6 weeks [38]. A subsequent retrospective study reported an incidence of 1% [39]. A skin biopsy and microbiologic testing should rule out granuloma formation and infection. A culture test of a draining or fluctuant lesion can aid in antibiotic selection. If an infection is suspected, oral antibiotic therapy should be administered, and the nodule should undergo incision and drainage if fluctuant. The American Society of Dermatologic Surgery recommended that noninflamed DONs without suspicion of infection might be treated initially with oral steroids for 1 to 2 weeks, rather than Hyal, should the retention of the aesthetic filler effect be desired [40]. The addition of antibiotics (doxycycline or minocycline) can be considered for anti-inflammatory and antimicrobial properties.

Regarding inflamed DONs, an expert panel recommended that high Hyal doses (ie, 500 iu every 48 hours until resolution) be



administered after oral antibiotics have been tried for at least 2 weeks [41]. The panelists indicated that Hyal may break down the bacterial biofilm, thus facilitating the spread of infection; therefore, it should not be used as first-line therapy for inflammatory DONs. Another expert panel favored administering Hyal injection (30-300 iu) as first-line therapy with oral antibiotics [42]. Participating experts recommend a watchful approach of 48 hours to 2 weeks after starting antibiotic therapy, unless a more resistant HA (ie, Vycross) has been injected, in which case Hyal must be given as early as possible. Vycross technology has a 1% to 4% DON risk [40]. Highly cross-linked fillers may require higher doses and more sessions of Hyal for effective degradation due to their resilient nature. Early intervention with Hyal is preferred to prevent the development of more persistent complications. The above dose recommendations were made while also acknowledging that the Hyal dose depends on the size of the nodule, location (eg, tear troughs require a lower dose than midface), and filler properties [41,42]. The clinical practice supports injecting Hyal into the center of the nodule with a low gauge (18 or 21 G) needle to disrupt an encapsulated (filler) organization by allowing more penetrations [42]. Subsequent dissolution via Hyal with increasing dosages should be repeated after 2-3 weeks; however, Hyal injections should be limited to 2-3 cycles if there has been no response [42].

HFUS-guided injection can increase the likelihood of response of a nodule or granuloma to Hyal [16]. The inflamed nodule or granuloma has a “capsule” (ie, prominent chronic inflammatory and granulomatous reaction at the periphery); in such case, ultrasound can show in real time that the needle or cannula injecting the medication has penetrated the “capsule” before Hyal is injected [1].

Granuloma is a rare complication (0.01%-1%) of fillers and appears after a latent period, which can be several months to years postinjection [43,44]. Granulomas caused by HAs appear as cystic granulomas [45]. Encapsulation occurs at advanced stages, and histology shows palisaded granulomatous tissue mainly composed of giant cells and macrophages. Biofilm formation has been a suggested trigger [46]. Granulomas can be treated with Hyal dosed up to 150 iu [47]. Multiple Hyal sessions are often required. Granulomas with conspicuous fibrosis and abundant giant cells may not respond to Hyal. Still, most authors suggest using as first-line therapy high-concentration intralesional steroids, such as 20-40 mg/mL of triamcinolone or a combination of intralesional triamcinolone 10 mg/mL, 5-fluorouracil 50 mg/mL, and lidocaine [48]. Intralesional steroids interfere with the activities of fibroblasts, macrophages, giant cells, and collagen synthesis [45]. Intralesional steroids should be considered when inflammation is a significant component of the granulomatous reaction and 5-fluorouracil when there is excessive tissue growth associated

with the granuloma. Treatment should be repeated every 3 to 4 weeks until resolution [48]. Surgical excision should be the last resort.

### Allergic and Hypersensitivity Reactions

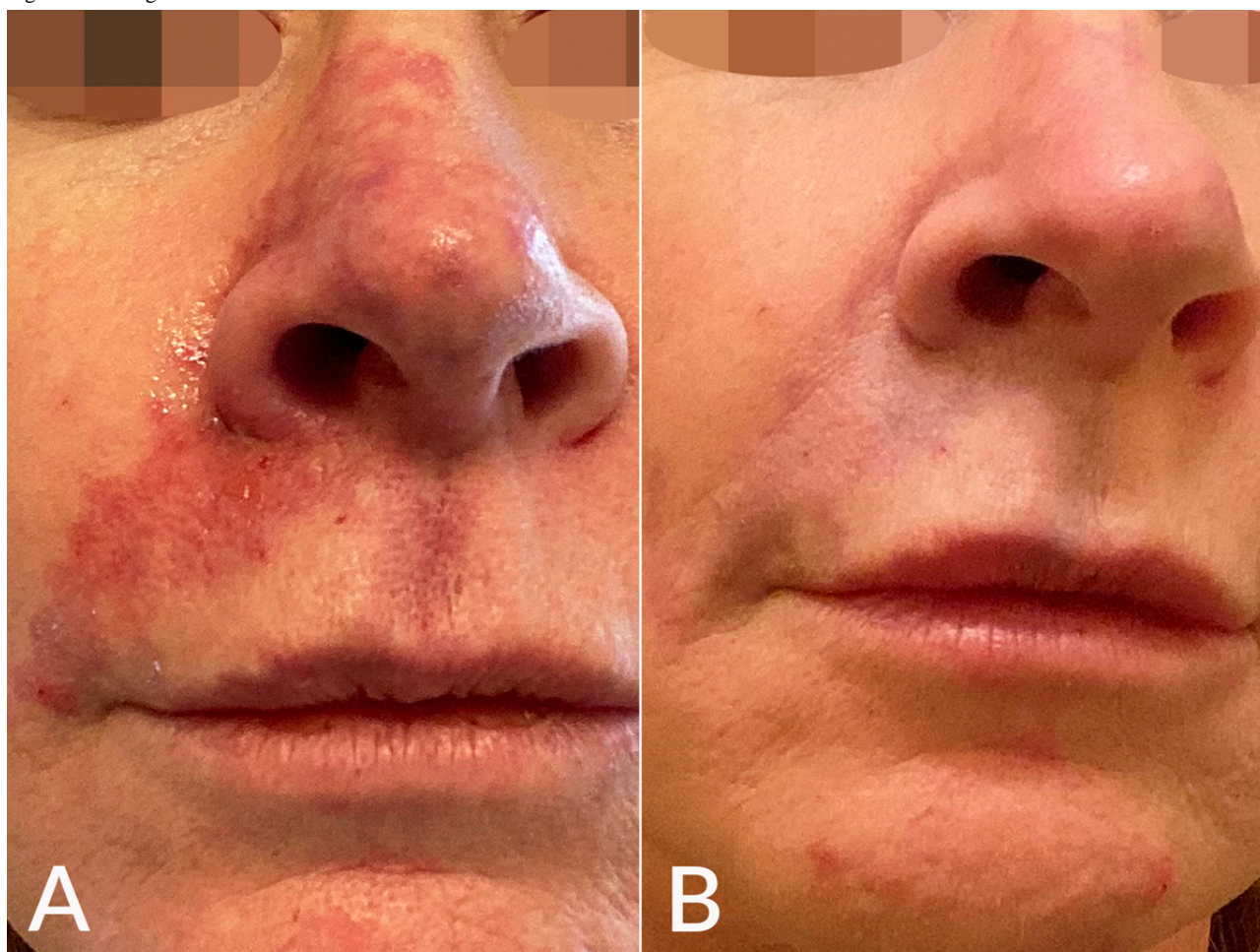
Most reactions to HA fillers are localized and manifest with edema, induration, and erythema at the injection site, pruritus, pain or tenderness, and eruption as early as a few days and as late as years after injection [49,50]. There have been no reports of type II or III reactions. Type I hypersensitivity reactions, such as localized angioedema, are uncommon as are type IV (delayed) reactions that are noted in less than 1% of cases [51]. Type IV reactions can manifest with painful erythematous nodules [50]. A delayed onset facial edema may be caused by type IV reaction and can develop several days to weeks after filler injection [52].

Type I reactions typically respond to oral antihistamines with or without intralesional or oral steroids [1,48,50]. Epinephrine should be administered in systemic reactions such as anaphylaxis or other severe cases. Providers should have an emergency kit containing epinephrine pens, oral steroids, and antihistamines in the treatment room [1]. Type IV reactions may not respond to antihistamines. Degradation of the filler depot with Hyal can be considered when an allergic or hypersensitivity reaction does not improve with a course of antihistamines or systemic corticosteroids. If the reaction is considered moderate or severe, oral corticosteroids should be taken before Hyal use to manage or prevent the potential initial worsening of symptoms due to increased antigens as the HA is broken down [52]. Hyal can be an alternative treatment for delayed facial edema as it does not carry the risks associated with prolonged systemic steroid treatment [52]; however, multiple treatment sessions are typically required, and Hyal can lead to at least partial loss of the filler treatment effect that may not be acceptable by the patient. COVID-19 vaccines have been reported to cause delayed reactions to HA fillers [53]. Two cases of COVID-19 vaccine-triggered delayed inflammatory reaction to HA filler were treated with Hyal [54,55].

### Vascular Compromise and Skin Necrosis

The incidence of impending necrosis following dermal filler treatment was estimated at 0.001% (1 in 100,000 cases) in 2013 [56] and increased to 0.009% in 2020 [57]. Vascular occlusion associated with filler injection may be due to intravascular embolism, extravascular compression, and vascular spasm [1]. Pain is the earliest symptom, and coolness, blanching (immediate; may be transient), and livedo pattern are the earliest signs (Figure 3) [57]. A delayed capillary refill (normal, 1-2 seconds) is noted within minutes. A blue-gray appearance follows within tens of minutes to hours due to deoxygenated blood in the tissue. Skin breakdown is noted within days, and the following repair phase lasts days to weeks [57,58].

**Figure 3.** (A) Vascular compromise after embolization of the angular artery with HA injected in the nasolabial fold manifested with a livedoid pattern over the right nasolabial fold, lateral upper cutaneous lip, and nose. (B) Resolution of the complication is shown 2 days after treatment with 700 iu Hyal and vigorous massage.



Vascular compromise requires immediate treatment. However, there is no consensus regarding the Hyal protocol in this complication [7]. Hyal should be administered as soon as possible, optimally within 4 hours [5]. The number of Hyal sessions depends on the severity of the complication and how quickly the intervention occurs. An animal study showed a significant reduction of the ischemic areas within 4 hours of Hyal treatment but no improvement after 24 hours [59]. In a series of patients with impending nasal skin necrosis related to the nose and nasolabial fold augmentation with HA fillers, full resolution of the complication occurred when Hyal treatment was administered within 2 days [60]. In a systematic review, Hyal failed to eliminate the large area of necrosis but played a moderate role in earlier recovery in limited necrosis [61].

A high-dose (total of 450-1500 iu in up to 4 Hyal cycles) pulsed Hyal protocol should be adopted [18,21,62]. Delorenzi suggested a simplified determination of Hyal dosage in the high-dose protocol considering the size of the ischemic area [62]. For a “single area” (eg, one-half of the upper lip) low-volume vascular event (by definition, <0.1 mL of filler embolus) Hyal dose should be about 450 iu; if a second area is affected, such as the nose, then the dose would be 900 iu. Hyal should be infiltrated diffusely into the ischemic tissues, including the vessel’s course. Perivascular Hyal will permeate vascular walls. Delorenzi showed *ex vivo* that cross-linked HA contained within the intact

artery is susceptible to hydrolysis by Hyal found outside the vessel in its immediate surroundings [63]. Hyal injections should be followed by warm compresses and vigorous massage of the areas to improve drug diffusion and enhance blood flow. Then one should observe and reassess skin color and capillary refill after 60 minutes [62]; however, other authors recommend assessment every 15-20 minutes [24]. If vascular compromise persists, repeat Hyal treatment for up to 4 cycles should be administered [18,62]. Daily follow-up should occur, and more Hyal treatment performed until there is a satisfactory resolution. If treatment is completed within 72 hours of the onset of ischemia, success is possible [62].

An important study by Schelke et al [6] showed that when Hyal is injected under HFUS guidance, lower dosages (35-50 iu) than those in current “high dose” protocols (>500 iu) can be used. This is due to the higher accuracy of Hyal injections performed under HFUS guidance. Also, the study showed that a single Hyal injection yields a full resolution of the vascular complication compared to hourly injections over several hours in the current, high-dose protocol.

The patient should be kept under observation in the clinic for any adverse reactions—when anaphylaxis to Hyal occurs, it is usually within minutes, but there have been cases of delayed onset [18]. All patients should be warned about allergic or



anaphylactic response symptoms and instructed to seek medical attention promptly.

### Vision Loss

This is a rare but severe complication. A literature review by Belezny et al [64] identified 146 cases in 2019. In recently reported cases, the nasal region (56.3%) was at the highest risk, and HA filler was the most common (81.3%) cause of this complication. Blindness due to periocular embolism of HA is instant and associated with excruciating ocular pain. The mechanism of action of blindness after filler injection is thought to involve intra-arterial injection of filler followed by subsequent retrograde embolization into the ophthalmic artery system [64]. The retinal circulation needs to be restored within 60 to 90 minutes if the retina is to survive. Blindness is an emergency; the patient should be transferred immediately to the nearest hospital ophthalmology department [65].

Currently, there is no evidence-based, accepted standard of care for treating visual compromise caused by filler [64]. Treatments that have been used vary widely and successful attempts are rare. If an HA filler was used, Hyal should be injected into the skin at the injection site and along the path of anastomosing arteries. Retrobulbar Hyal (RBH) injection (150-200 iu in 2-4 mL of diluent) into the inferolateral orbit should be considered by practitioners who have appropriate experience and competence while waiting for an ambulance [66]. A total of 3 cases experienced partial or complete vision recovery after treatment with RBH, although only 1 case directly attributed success to the RBH [64]. In that case, full vision restoration was achieved with Hyal (450 iu as retrobulbar injections and 300 iu to surround the supraorbital and infraorbital foramina) in a patient who received HA fillers in the midface [67]. RBH did not improve vision in other reports [68,69]. Zhu et al [68] failed to show any improvement in visual loss following 1500 to 3000 iu RBH in 4 patients. The authors indicated that Hyal is ineffective at recanalizing the retinal artery occlusion or improving the visual outcome after 4 hours of the onset of blindness.

However, other authors have challenged the RBH approach because Hyal did not demonstrate the ability to cross the dural sheath of the optic nerve and reach an occlusion of the central retinal artery [70,71]. In a cadaver model, Hyal could not cross the optic nerve's dura into the space where it could bathe the central retinal artery [70]. Most importantly, hardly 5 mm of the ophthalmic artery is exposed in the orbit that is not covered with dura. An alternative approach was suggested, injecting into the supraorbital or supratrochlear artery. In the supraorbital method, Hyal is injected into the supraorbital artery in the supraorbital foramen [72]. The supraorbital approach is less invasive than the retrobulbar and can be effective in cases where the blood vessel blockage is closer to the skin's surface. This technique has resulted in 2 cases of immediate vision recovery [72,73]. This approach requires no special skills compared to retrobulbar injections which are technically difficult procedures even for a competent ophthalmological surgeon. Still, other authors have challenged the feasibility and practicality of the supraorbital approach as the supraorbital and supratrochlear

arteries are difficult to cannulate [64,74]. However, ultrasound guidance may facilitate this approach [75].

### Limitations

Pitfalls include the loss of HAG treatment effect and adverse effects of Hyal such as allergic reactions. High Hyal doses can result in complete loss of the HAG effect. In a retrospective review of 20 patients with lower eyelid edema post-HA filler injection, Hyal 20-75 iu (injected 0.2-0.5 mL) per region was administered. All patients responded to treatment without recurrence. However, in 2 cases, all injected HA was degraded, resulting in a loss of treatment effect [76]. To prevent loss of the HAG effect, most authors recommend multiple treatment sessions with smaller Hyal doses in nonemergent filler complications, such as noninflammatory nodules, with reassessment after each session. The patient should be consulted regarding at least partial filler effect loss when Hyal is injected.

Adverse effects of Hyal injections are mainly local and include pruritus, burning sensation, swelling, erythema, ecchymosis limited to the injection site, spread of infection, and allergic reactions [1,24,77]. A total of 3 cases of ecchymosis away from the Hyal injection site in the infraorbital area were reported by this author who suggested that Hyal may facilitate the spread of ecchymosis on thin skin [37].

The overall allergy rates are low, reported 0.03%-0.13% with peribulbar injections [24]. immunoglobulin E-mediated type I hypersensitivity with the Hyal doses administered in aesthetic medicine is rare (incidence about 0.1%), but it is quoted high (33%) with large intravenous doses (>200,000 iu) [13,24]. Delayed hypersensitivity (type IV reaction) to Hyal has been rarely reported in aesthetic practice [77-79]. A case report described delayed hypersensitivity after Hyal treatment of granulomatous HA reaction [78]. In case of severe allergy caused by exogenous Hyal, autologous serum may be considered in nonacute cases requiring accelerated removal of HA filler [19].

This narrative literature review is limited by the sole inclusion of studies published in English available in PubMed and Google Scholar, which may have excluded studies unavailable in English or indexed in other databases. There is a limited number of controlled studies. Many studies included small sample sizes and reported descriptive outcomes. There is controversy regarding the most effective Hyal protocol for managing HA filler-associated vision loss.

### Conclusions

Properly used Hyal can resolve nonemergent HA filler complications. The physical properties of the HA filler influence its degradation by Hyal and higher Hyal doses are required for HAGs resistant to degradation. Emergent complications such as vascular occlusion with impending skin necrosis should be treated promptly with high Hyal doses flushed into ischemic tissues. Hyal treatment of vision loss has met limited success, and the injection technique, retrobulbar versus supraorbital, remains controversial. More sufficiently powered controlled studies are needed. Hyal treatment has an acceptable safety profile, with allergic or hypersensitivity reactions uncommon in aesthetic practice.

## Declaration of Patient Consent

The patient has given informed consent for the patient's images and other clinical information to be published in a medical journal. The patient understands that the patient's name and initials will not be published and due efforts will be made to conceal their identity, but complete anonymity cannot be guaranteed.

## Conflicts of Interest

None declared.

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## Abbreviations

**DON:** delayed onset nodule  
**HA:** hyaluronic acid  
**HAG:** hyaluronic acid gel  
**HFUS:** high-frequency ultrasound  
**Hyal:** hyaluronidase  
**iu:** international units  
**RBH:** retrobulbar Hyal  
**RCT:** randomized controlled trial

*Edited by R Dellavalle; submitted 30.06.23; peer-reviewed by RG Geronemus, J Stroh, A AL-Asadi; comments to author 13.09.23; revised version received 17.10.23; accepted 11.12.23; published 17.01.24.*

*Please cite as:*

Kroumpouzou G, Treacy P

Hyaluronidase for Dermal Filler Complications: Review of Applications and Dosage Recommendations

*JMIR Dermatol* 2024;7:e50403

URL: <https://derma.jmir.org/2024/1/e50403>

doi: [10.2196/50403](https://doi.org/10.2196/50403)

PMID: [38231537](https://pubmed.ncbi.nlm.nih.gov/38231537/)

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Review

# Worldwide Distribution and Extracutaneous Manifestations of Henoch-Schönlein Purpura in Adults: Narrative Review

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## Abstract

**Background:** Henoch-Schönlein purpura (HSP), a leukocytoclastic small vessel vasculitis, exhibits both cutaneous and systemic manifestations. While predominantly observed in childhood, it may manifest in adults with more pronounced systemic involvement. Furthermore, HSP is a global phenomenon showcasing epidemiological and systemic variances.

**Objective:** This study aims to scrutinize extracutaneous manifestations in adults with HSP, discerning distinctions according to geographical regions on a worldwide scale.

**Methods:** A comprehensive search encompassing PubMed, Embase, Cochrane Library, and Web of Science was executed, covering papers published from January 1, 1970, to December 1, 2019. Keywords used included “Henoch-Schönlein purpura,” “henoch schonlein purpura+adult,” “IgA vasculitis+adult,” “HSP+adult,” and “IgAV.” A total of 995 publications were identified, from which 42 studies encompassing 4064 patients were selected, with a predominant focus on cases reported in Asia, Europe, and the Americas.

**Results:** Among adults afflicted with HSP, European patients exhibited a higher propensity for male predominance ( $P<.001$ ), gastrointestinal involvement ( $P<.001$ ), and musculoskeletal complications ( $P<.001$ ). Conversely, patients from the Americas were least likely to experience genitourinary involvement ( $P<.001$ ).

**Conclusions:** HSP demonstrates a variance in distribution and extracutaneous manifestations within distinct geographical boundaries. In the adult population, European patients exhibited a higher prevalence of male gender and gastrointestinal and musculoskeletal involvement. Asian patients were more predisposed to genitourinary involvement when compared to their American counterparts. The establishment of prospective studies using standardized reporting measures is imperative to validate the relationships unveiled in this investigation.

(JMIR Dermatol 2024;7:e49746) doi:[10.2196/49746](https://doi.org/10.2196/49746)

**KEYWORDS**

extracutaneous manifestations; HSP; Henoch-Schönlein purpura; immunoglobulin A vasculitis; IgAV; IgA vasculitis; narrative review

## Introduction

Henoch-Schönlein purpura (HSP), also known as immunoglobulin A vasculitis (IgAV), stands as the most

prevalent form of vasculitis in childhood [1]. This condition exhibits a considerable disparity in incidence between children and adults, with palpable purpura constituting a hallmark feature in both populations [1-7]. Approximately 90% (135/150) of

HSP cases manifest within the first decade of life. Notably, the United States reports an annual incidence in children ranging from 6.1 to 20.4 cases per 100,000. In the United Kingdom and France, children aged 17 years or younger demonstrate an annual incidence of approximately 20 to 70 cases per 100,000. It is noteworthy that Asian studies have documented an even higher incidence, reaching 56 cases per 100,000 [2,3,7-14].

In contrast, the annual incidence of HSP in adults exhibits a lower prevalence, estimated to range from 1.4 to 5.1 cases per 100,000, with a heightened frequency observed during the fifth and sixth decades of life [8-11]. In both pediatric and adult populations, HSP has been reported to display a male predilection, barring exceptions identified in 2 Korean studies [11-13].

Despite individual investigations focusing on the correlation between cutaneous manifestations and systemic involvement, no prior studies have undertaken a comprehensive assessment of the global geographical disparities concerning extracutaneous manifestations in adult patients. Our primary aim, therefore, is to meticulously scrutinize the existence and distribution of extracutaneous manifestations in adult patients with HSP, stratified by geographic regions across the world.

Methods

Search Parameters

To comprehensively assess extracutaneous manifestations in adults with HSP, an exhaustive review of the literature was conducted. This review encompassed the databases PubMed, Embase, Cochrane Library, and Web of Science, scrutinizing papers published from January 1, 1970, through December 1, 2019. A search was facilitated using the following keywords: “Henoch-Schönlein purpura” OR “henoch schonlein purpura+adult,” “IgA vasculitis+adult,” “HSP+adult,” and “IgAV.” A total of 995 publications were initially identified.

Inclusion Criteria

Stringent inclusion criteria were applied, focusing exclusively on papers presenting original data that contained pertinent information regarding gastrointestinal (GI), genitourinary (GU), and musculoskeletal (MSK) involvement. Specifically, GI involvement was delineated as the onset of abdominal pain, melena, or hematochezia; MSK involvement was defined by the emergence of new arthritis or arthralgia; and GU involvement was ascribed to the appearance of new proteinuria, hematuria, acute kidney injury, or the exacerbation of chronic kidney disease. Individual case reports and publications limited solely to pediatric patients were excluded from the analysis.

Screening Process

This meticulous screening process resulted in the inclusion of 42 eligible studies that adhered to the predefined criteria. The majority of the reported cases were drawn from 3 predominant regions, namely, Asia, Europe, and the Americas. Subsequently, patients were categorized according to their respective geographical regions, and a comparative analysis was performed to discern the number of cases and the mean involvement of the GI, GU, and MSK systems within each region. Statistical analyses, including omnibus tests and post hoc pairwise comparisons, were executed using MedCalc (version 19.1; MedCalc Software Ltd).

Results

Age and Gender by Geography

A total of 42 studies incorporating data from 4064 adult patients were included in this comprehensive analysis. These studies were divided into 23 European studies, 17 Asian studies, and 4 papers published in North and South America. Notably, the age of onset in Asian patients was significantly earlier, with an average of 29.8 (SD 7.02) years, compared to their European counterparts (mean 49.3, SD 9.14 years;  $P<.001$ ) and individuals in the Americas (mean 48.6, SD 4.17 years;  $P<.001$ ). In terms of gender distribution, a marked discrepancy emerged, with male patients exhibiting a higher prevalence in Europe ( $n=997$ , 62.2%), while both genders demonstrated a relatively equitable distribution in Asia and North and South America ( $n=135$ , 47.7% vs  $n=1120$ , 51.4%;  $P=.12$ ).

Extracutaneous Manifestations by Geography

Furthermore, the clinical presentation of HSP exhibited noteworthy regional variations. Europeans displayed a higher propensity for GI involvement, affecting 58.2% ( $n=932$ ) of patients, a percentage significantly greater than the 31.4% ( $n=89$ ) observed in the Americas ( $P<.001$ ) and the 44.7% ( $n=974$ ) in Asian populations ( $P<.001$ ). Additionally, MSK involvement was notably prevalent among Europeans, with 57.9% ( $n=928$ ) of individuals manifesting such symptoms. This proportion exceeded the figures observed in the Americas ( $n=135$ , 47.7%;  $P<.001$ ) and Asia ( $n=1034$ , 47.4%;  $P<.001$ ). Interestingly, among adults in Asia with HSP, GU involvement was the most frequent, impacting 72.3% ( $n=1575$ ) of patients, although this did not display a statistically significant difference from the 67.2% ( $n=1077$ ) observed in European populations ( $P=.08$ ). Conversely, individuals in North and South America exhibited the lowest likelihood of GU involvement at 47% ( $n=133$ ;  $P<.001$ ). A comprehensive summary of demographics and the extent of extracutaneous organ involvement can be found in Table 1.

Table 1. Age, gender, and extracutaneous involvement of Henoch-Schönlein purpura separated by geographic region (N=4064).

Region	Total patients, n (%)	Age (years), mean (SD)	Male patients, n (%)	Female patients, n (%)	Gastrointestinal involvement, n (%)	Musculoskeletal involvement, n (%)	Genitourinary involvement, n (%)
Europe	1602 (39.4)	49.3 (9.14)	997 (62.2)	605 (37.8)	932 (58.2)	928 (57.9)	1077 (67.2)
Americas	283 (6.9)	48.6 (4.17)	135 (47.7)	148 (52.3)	89 (31.4)	135 (47.7)	133 (47)
Asia	2179 (53.6)	29.8 (7.02)	1120 (51.4)	1059 (48.6)	974 (44.7)	1032 (47.4)	1575 (72.3)



## Discussion

### Pathophysiology

The etiology of HSP remains elusive; however, this systemic vasculitis is widely regarded as an immune-mediated disorder, characterized by the deposition of immunoglobulin A (IgA) complexes, which underlie the pathological alterations observed in the skin, kidneys, GI tract, and joints [15,16]. Various triggers have been postulated for the onset of HSP, encompassing recent upper respiratory infections, medications, and malignancies [13,17]. Notably, HSP appears to exhibit a seasonal predilection with a peak incidence during the winter months, while occurrences during the summer months are relatively rare [8,17].

### Clinical Manifestations

HSP in the adult population is frequently associated with heightened disease severity and less favorable outcomes, particularly when it involves the integumentary system, renal function, and systemic vasculitic manifestations, in stark contrast to its typically benign and self-limiting course in children [11,16,18-20]. On rare occasions, HSP may extend its impact to include the pulmonary, cardiac, or nervous systems. The hallmark clinical features of HSP encompass the characteristic purpuric rash, joint pain, abdominal discomfort, edema, and hematuria [4,21,22].

Cutaneous manifestations of HSP commence as erythematous macules or urticarial papules, evolving into nonblanching palpable purpura, which symmetrically affect extensor surfaces, notably the buttocks and lower extremities. In some cases, involvement may extend to the trunk, face, and upper extremities [2]. Hemorrhagic bullae and vesicles appear to be more prevalent in older individuals [1,22].

There exists a divergence of evidence regarding the correlation between the severity of skin lesions and the extent of renal involvement and overall disease trajectory. Some investigations suggest that renal involvement is more frequent in individuals displaying skin direct immunofluorescence (DIF), indicative of immunoglobulin M (IgM) deposition and necrotic bullous skin lesions [1,23]. Conversely, other studies have failed to establish cutaneous IgM as a reliable indicator of renal or systemic disease in adult patients with HSP [24]. It is noteworthy that younger males presenting with generalized purpura and concurrent bowel involvement tend to experience less favorable outcomes, thus implying that the extent of skin involvement may serve as a predictive factor for the disease course and potentially guide therapeutic decisions [25].

Joint pain stands as a prevalent clinical manifestation of HSP, with its occurrence noted in over 60% of adult cases, with a higher likelihood observed in those 60 years and younger of age [26,27]. Joint disease may manifest in the form of arthritis or arthralgias, typically exhibiting a symmetric distribution, and most frequently impacting the knee and ankle joints [27]. Importantly, joint involvement typically resolves without enduring sequelae [28].

GI involvement, in conjunction with renal complications, constitutes a significant source of morbidity in adult patients with HSP [26]. Roughly two-thirds of HSP presentations include

GI manifestations, most commonly manifesting as abdominal pain. Predominant abdominal symptoms encompass vomiting, diarrhea, periumbilical pain, and hematochezia. Notably, intussusception occurs in approximately 5% of patients, representing a significant GI complication. Other less frequent complications encompass bowel ischemia or infarction, necrosis, perforation, stricture formation, and GI hemorrhage [2,21,22,29].

Renal involvement is a common occurrence in HSP, yet its severity displays considerable variability. Indications of renal compromise manifest as hematuria and soft tissue edema due to proteinuria. Hematuria associated with HSP is typically macroscopic and may coincide with relapses of purpura or occur long after the resolution of extrarenal manifestations. The extent of proteinuria and the development of nephrotic syndrome exhibit a variable course, potentially leading to deterioration in glomerular filtration rate, azotemia, or end-stage renal failure. Predictors of renal involvement encompass recent infectious history, pyrexia, extension of purpura to the trunk, and biological markers of inflammation [22,23,30-32].

Notable predictors of adverse outcomes comprise renal insufficiency, hypertension, and the parameter of “young age” in adult patients [33-35]. Age at the onset of HSP has been postulated as a pivotal factor influencing disease severity and prognosis. Studies conducted by Hung et al [36] identified patients aged 20 years and older, male gender, bloody stools, and a rash persisting beyond 1 month as adverse prognostic factors for HSP. Schaier et al [37] reported that older patients with HSP presenting with renal involvement exhibited poorer outcomes than those aged 60 years and younger.

HSP nephritis stands as the most serious complication of HSP, with an incidence ranging from 20% to 80%. An adverse prognosis is particularly pronounced in patients presenting with nephrotic syndrome, renal failure, and, notably, hypertension at the time of diagnosis [38]. The presence of HSP nephritis aligns with the severity of renal histopathological changes [30-32,34].

### Diagnosis

The diagnosis of HSP fundamentally relies upon clinical manifestations. In adults, biopsy is more frequently used to confirm the diagnosis, while pediatric patients typically necessitate biopsy only in cases of atypical presentations. While no specific diagnostic tests for HSP exist, a normal platelet count and coagulation studies play a crucial role in excluding other diseases that may be present with palpable purpura [8,17].

The diagnostic criteria for HSP, developed by European League Against Rheumatism/Paediatric Rheumatology International Trials Organisation/Paediatric Rheumatology European Society, exhibit a sensitivity of 100% and a specificity of 87%. The diagnostic criterion mandates the presence of purpura or petechiae, characterized by a lower limb predominance, along with a minimum of one of four of the following criteria [39]: (1) acute onset of diffuse abdominal pain, (2) histopathological evidence demonstrating leukocytoclastic vasculitis or proliferative glomerulonephritis with predominant IgA deposits, (3) acute onset of arthritis or arthralgia, and (4) renal involvement, as indicated by proteinuria or hematuria.



For diagnosing the cutaneous vasculitis associated with HSP, the gold standard is a skin biopsy illustrating leukocytoclastic vasculitis in postcapillary venules, with the presence of IgA deposition, with or without eosinophils [22,40]. Notably, individuals aged 40 years and older, lacking eosinophils on skin biopsy, are reported to exhibit nearly a 3-fold heightened risk of developing renal involvement compared to those with eosinophils observed on skin biopsy [22,40].

HSP lacks specific biomarkers for diagnosis; nevertheless, certain markers hold effectiveness in monitoring disease activity and prognosis. DIF may reveal perivascular IgA and C3 deposition; however, individuals who otherwise meet clinical HSP criteria may not display IgA deposition on DIF [22]. In cases where diagnostic uncertainty exists or severe renal involvement is evident, a renal biopsy may be deemed necessary. Renal biopsies may illustrate mesangial hypercellularity (grades I through VI) and crescents on light microscopy. Characteristic of HSP nephritis is the presence of granular mesangial IgA and C3 deposition on light microscopy (with IgM and immunoglobulin G to a lesser extent) [13,22]. It is noteworthy that, on renal biopsy, the pathognomonic granular IgA and C3 deposition in the mesangium is indistinguishable from IgA nephropathy [22]. Moreover, the extent of interstitial fibrosis, the percentage of sclerotic glomeruli, and the presence of glomeruli displaying fibrinoid necrosis on renal biopsy have been associated with an unfavorable renal prognosis [27].

## Treatment

The management of adult IgAV has garnered limited investigation and remains a subject of controversy [26,41]. Notably, adults often necessitate more aggressive therapeutic approaches compared to pediatric patients. The mainstay of treatment involves supportive care and corticosteroids, complemented by varying use of immunosuppressive agents and plasma exchange [42].

Corticosteroids contribute to the swift resolution of renal manifestations and serve as a valuable tool in the management of joint and abdominal pain along with the duration of skin lesions. However, their efficacy in preventing palpable purpura or complications such as glomerulonephritis, bowel infarction, or intussusception remains unproven [11,26,41-43].

Immunosuppressive agents, including cyclophosphamide, cyclosporine, and rituximab, have been subjects of study in the context of HSP treatment. In instances marked by severe organ involvement and life-threatening complications, corticosteroids and immunosuppressive drugs are often initiated. Nevertheless,

the augmentation of immunosuppressant agents to corticosteroid regimens does not appear to confer additional benefits when juxtaposed with the use of corticosteroids in isolation. Pillebout et al [27], for instance, conducted a comparative analysis between corticosteroids alone and corticosteroids combined with cyclophosphamide in patients with biopsy-confirmed IgAV and discerned no discrepancy at 12 months with regard to remission rates, renal outcomes, and adverse events. However, it is noteworthy that overall survival was more favorable in the corticosteroids plus cyclophosphamide group [26,27,41]. In a study by Maritati et al [44], rituximab, a B-cell depleting antibody, exhibited safety and efficacy in the treatment of adult-onset IgAV, with 20 of 22 patients achieving remission, although 7 of those 20 experienced disease relapse [44].

An illustrative case series by Augusto et al [45] highlighted the potential benefits of combining corticosteroids and plasma exchange in the treatment of severe HSP in adults. This approach yielded swift improvements in the patient Birmingham Vasculitis Activity Score, estimated glomerular filtration rate, and proteinuria, culminating in positive long-term outcomes at 6 and 12 months [45]. Nevertheless, renal involvement can precipitate end-stage renal failure, and it may manifest rapidly, necessitating the imperative need for dialysis or renal transplant, notwithstanding the concerns surrounding disease relapse [41]. Encouragingly, in 1 case series, none of the 12 transplant recipients lost their grafts due to relapse [41]. However, it should be acknowledged that renal transplant recipients have been subject to relapses, with 1 instance suggesting a potential role for plasmapheresis in addressing disease recurrence [46].

## Limitations

The primary limitation of this review is related to the simplicity of our search strategy. The volume of publications indexed in PubMed, Embase, Cochrane Library, and Web of Science in combination with the stringent screening process used limited our review to the 42 papers included in the results.

## Conclusions

Our comprehensive review underscores the noteworthy observation that adults afflicted with HSP frequently manifest pronounced extracutaneous involvement, with a proclivity toward progressive renal disease. Furthermore, it highlights the prospect of regional disparities in the risk of developing extracutaneous manifestations associated with HSP. To corroborate the relationships elucidated in this investigation, there is a compelling need for prospective studies that use standardized reporting measures.

## Conflicts of Interest

None declared.

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## Abbreviations

**DIF:** direct immunofluorescence  
**GI:** gastrointestinal  
**GU:** genitourinary  
**HSP:** Henoch-Schönlein purpura  
**IgA:** immunoglobulin A  
**IgAV:** Immunoglobulin A vasculitis  
**IgM:** immunoglobulin M  
**MSK:** musculoskeletal

*Edited by R Dellavalle; submitted 08.06.23; peer-reviewed by C Price, O Kasapcopur; comments to author 21.09.23; revised version received 21.10.23; accepted 27.12.23; published 25.01.24.*

### *Please cite as:*

Harris BW, Maxfield L, Hunter A, Alhajj M, Ban B, Pulsipher KJ

Worldwide Distribution and Extracutaneous Manifestations of Henoch-Schönlein Purpura in Adults: Narrative Review

*JMIR Dermatol* 2024;7:e49746

URL: <https://derma.jmir.org/2024/1/e49746>

doi: [10.2196/49746](https://doi.org/10.2196/49746)

PMID: [38271008](https://pubmed.ncbi.nlm.nih.gov/38271008/)

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Review

# The Potential of Exercise on Lifestyle and Skin Function: Narrative Review

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## Abstract

**Background:** The skin is an important organ of the human body and has moisturizing and barrier functions. Factors such as sunlight and lifestyle significantly affect these skin functions, with sunlight being extremely damaging. The effects of lifestyle habits such as smoking, diet, and sleep have been studied extensively. It has been found that smoking increases the risk of wrinkles, while excessive fat and sugar intake leads to skin aging. Lack of sleep and stress are also dangerous for the skin's barrier function. In recent years, the impact of exercise habits on skin function has been a focus of study. Regular exercise is associated with increased blood flow to the skin, elevated skin temperature, and improved skin moisture. Furthermore, it has been shown to improve skin structure and rejuvenate its appearance, possibly through promoting mitochondrial biosynthesis and affecting hormone secretion. Further research is needed to understand the effects of different amounts and content of exercise on the skin.

**Objective:** This study aims to briefly summarize the relationship between lifestyle and skin function and the mechanisms that have been elucidated so far and introduce the expected effects of exercise on skin function.

**Methods:** We conducted a review of the literature using PubMed and Google Scholar repositories for relevant literature published between 2000 and 2022 with the following keywords: exercise, skin, and life habits.

**Results:** Exercise augments the total spectrum power density of cutaneous blood perfusion by a factor of approximately 8, and vasodilation demonstrates an enhancement of approximately 1.5-fold. Regular exercise can also mitigate age-related skin changes by promoting mitochondrial biosynthesis. However, not all exercise impacts are positive; for instance, swimming in chlorinated pools may harm the skin barrier function. Hence, the exercise environment should be considered for its potential effects on the skin.

**Conclusions:** This review demonstrates that exercise can potentially enhance skin function retention.

(*JMIR Dermatol* 2024;7:e51962) doi:[10.2196/51962](https://doi.org/10.2196/51962)

## KEYWORDS

skin function; lifestyle; exercise; reviews; knowledge synthesis; Review methods; review methodology; literature review; literature reviews; narrative review; narrative reviews; skin; dermatology; exercise; physical activity; fitness; lifestyles; smoking; diet; sleep; sugar intake; life habits; skin barrier

## Introduction

The skin is the largest human organ that acts as a barrier between the body and the environment. Its role is to protect the body

from the invasion of pathogens and to shield it from chemical and physical stimuli originating from the external environment; furthermore, it also prevents dehydration by mitigating water loss from the body [1,2]. The stratum corneum primarily serves



as this barrier [1]. Skin functionality declines with age, a process evidenced not only in appearance, such as fine wrinkles, but also in quantitative indicators such as reduced skin elasticity and a decrease in the water content of stratum corneum [3-5].

A complex variety of factors, beyond age-related changes, influence the functional decline of the skin. Typical examples of influencing factors include lifestyle habits such as sun exposure, smoking, and diet [3,6,7]. Various studies have been conducted on the relationship between lifestyle habits and skin function. Specific lifestyle habits that are associated with skin function include daily moisturizing [8], bathing habits [8], stress [9,10], and sleep quality [11]. Improvement of these lifestyle habits is expected to prevent the functional decline of the skin.

In addition to the lifestyle habits mentioned above, exercise is gaining attention as a way to prevent skin dysfunction and improve aesthetics [12]. It is widely known that regular exercise not only aids in the prevention of various diseases but also plays a significant role in maintaining mental health [13-15]. However, the impact of exercise on skin function remains largely unexplored. In this review, we will briefly summarize the relationship between lifestyle and skin function and the mechanisms that have been elucidated so far. Additionally, we will introduce the expected effects of exercise on skin functionality.

## Methods

A review of the literature was conducted using PubMed and Google Scholar repositories for relevant literature published between 2000 and 2022 using the following keywords: exercise, skin, and life habits. The search was expanded to discover relevant literature on specific lifestyle habits. To discover relevant literature showing the effects of specific lifestyle habits on skin function, searches were conducted using the following keywords: smoking, dietary habits, ultraviolet light, hormones, and stress.

However, articles on the relationship between skin diseases such as atopic dermatitis and lifestyle habits were excluded.

## Results

### Skin Function

Preserving moisture and acting as a barrier are important functions of the skin [2]. These functions are mainly performed by the stratum corneum, which consists of keratinocytes stacked in a brick-like structure (brick and mortar model), with the cells being akin to bricks and intercellular lipids acting as the mortar, filling the spaces between the cells. These cells are further interconnected by desmosomes [2]. The natural moisturizing factors in the keratinocytes and intercellular lipids maintain skin hydration [16]. In addition, the dermis layer beneath the stratum corneum contains elastic fibers, such as collagen and elastin, which make the skin elastic and provide a barrier against physical stimuli [6]. When the skin's moisturizing and barrier functions are compromised, it can lead to issues such as skin dryness and infections, which are caused by microorganisms entering the body's defenses [17]. Hormones such as estrogen and growth hormones play an important role in maintaining

these skin functions, including supporting skin elasticity and moisture retention. As we age, the secretion of these hormones declines, leading to a decrease in skin elasticity and hydration [18,19].

### Internal Factors Related to Skin Function

#### *Aging*

Age-related declines in skin functions, such as loss of elasticity, are explained by a decrease in collagen synthesis due to fewer fibroblasts in the dermis, a decrease in the number of sebaceous and sweat glands, and diminished blood flow to the skin [6,20,21]. These factors cause skin changes characteristic of older adults, such as coarse and dry skin, spots and dullness, wrinkles, and sagging. Various hypotheses have been made about the causes of age-related changes. Leading hypotheses include the generation of reactive oxygen species (ROS) or free radicals by normal endogenous metabolic processes, telomere shortening, and the accumulation of advanced glycation end products [22-25]. These age-related changes vary greatly in their intensity, depending on the individual's race, personal characteristics, and different sites within the same person's body [4,26]. The reasons for this variation are thought to be related to differences in the number of cells in the stratum corneum, the amount of melanin, and the amount of light exposure [26,27].

#### *Hormone Balance (Estrogen and Growth Hormone)*

Various hormones are associated with skin function. Of these, estrogen and growth hormones have been the focus of many studies as they are associated with age-related declines in skin functionality [17,28,29]. Changes in the secretion of these hormones occur with aging. The effects of decreased estrogen secretion on the skin are more pronounced in postmenopausal women because women secrete less estrogen after menopause [30]. Two important roles of estrogen for the skin are collagen production and wound healing [28,31]. Research has demonstrated that the decrease in estrogen levels associated with menopause results in reduced collagen levels in the skin. Conversely, estrogen replacement therapy in postmenopausal women has been shown to increase these collagen levels [32,33]. Collagen plays a crucial role in skin elasticity and skin thickness; consequently, a decrease in collagen content leads to skin wrinkling and thinning [28,31]. Although the direct relationship between skin elasticity and skin hydration is not clear, skin elasticity and skin hydration act as similar indicators of skin function, as skin elasticity and skin hydration decrease with reduced skin function [6]. The role of estrogen in wound healing is to suppress the inflammatory response and promote epithelialization in the wound [34]. The wound healing process encompasses several stages, starting with hemostasis and coagulation, followed by the inflammatory phase, and then the proliferative phase. An excessive inflammatory response can delay the inflammatory phase. Estrogen has been shown to regulate and suppress the inflammatory response in wounds [34,35]. In addition, since collagen production is active during the proliferative phase, estrogen administration has been shown to increase the amount of collagen in the wound and promote wound healing [34].

The secretion of growth hormone is involved in the synthesis of collagen [36]. It has been shown that excessive secretion of growth hormone causes thickening of the skin, while a deficiency in growth hormone causes skin thinning and a loss of elasticity [37,38]. In addition, growth hormone is involved in the development of sweat glands. An excess or deficiency in this hormone has been shown to cause excessive sweating or decreased sweating, respectively [19].

## External Factors Related to Skin Function

### Sunlight

The most significant external factor affecting skin aging is ultraviolet radiation (UVR) from sunlight. Since most of the sun's UVR (290-400 nm) is blocked by the Earth's atmosphere, UVR reaching the Earth's surface consists of >95% ultraviolet A (320-400 nm) and approximately 5% ultraviolet B (290-320 nm) [39,40]. UV energy is absorbed by skin cells and generates ROS that cause oxidative stress and damage various molecules, including DNA, in cells and tissues [39]. Additionally, UV light damages the collagen in the skin [41]. As a result, skin with prolonged and repeated exposure to sunlight becomes yellowish in tone, more stained, has an increase in fine and deep wrinkles, and loses its luster, becoming rough and dry [6].

### Lifestyle Habits

#### Diet

Dietary habits refer to preferences for food and beverages, and various studies have revealed the effects of diet on the skin, albeit in rats.

One specific diet known to affect the skin is a high-fat diet. Dietary fat intake is closely related to the lipid composition of body adipose tissue and skin [42]. A high-fat diet can potentially induce oxidative stress and inflammatory responses in the skin, delay skin healing by decreasing protein synthesis, and cause morphological changes in the skin [43]. A close association has also been established between the consumption of sugars and fried foods and the acceleration of skin aging. The metabolism of sugars and proteins generates advanced glycation end products, and their accumulation accelerates skin aging [44]. Therefore, limiting the intake of sugars and proteins can be expected to delay skin aging [44].

Alcohol consumption may also expedite skin aging. Ethanol and acetone, byproducts of alcohol metabolism, may promote the proliferation of keratinocytes in the skin, thereby increasing its permeability and impairing its barrier function [45]. Additionally, the degree of facial aging increases in correlation with alcohol intake and time [46].

#### Smoking

Smoking is the most common lifestyle habit that adversely affects skin function. Studies examining the effect of past smoking history on current skin condition have shown that each pack-year increases the risk of wrinkle development by more than 5-fold. Additionally, smoking has also been shown to alter skin thickness and promote skin pigmentation [47-49]. Smoking constricts skin blood vessels and deteriorates skin blood flow, thereby reducing the oxygen supply to skin tissues. This

promotes a decline in skin function, including a decrease in skin elasticity and skin hydration [50,51].

### Stress and Sleep

The impact of stress and sleep quality on skin function has been evaluated using skin hydration and transepidermal water loss (TEWL) [9,11]. Stress can undermine the integrity of the stratum corneum by decreasing the production and secretion of lamellar body and keratinocyte proliferation, leading to a weakened skin barrier function and structural damage to the skin [52]. Stressed individuals have also been found to have delayed recovery from changes in TEWL due to stratum corneum removal by tape stripping [9]. The effects of sleep on the skin have been shown to occur in individuals with poor sleep quality and sleep deprivation. These individuals typically exhibit higher TEWL, reduced skin barrier function, and cosmetic changes [11,53,54]. These studies were cross-sectional or included results reported immediately after stressful exposure, and the effects of long-term stressful exposure on the skin are not clear.

### The Relationship Between Exercise and Skin

Exercise has been shown to increase cutaneous blood flow, with acute maximal exercise increasing the cutaneous blood perfusion total spectrum power density approximately 8-fold [55,56]. This is a physiological function of skin vasodilation, which is accompanied by an increase in skin temperature, to dissipate the heat generated by exercise [57]. The dilation of skin vessels is attenuated by nonexercise habits and aging, and it is affected by the moisture levels in the skin. Interestingly, there are no sex differences in the pattern of skin temperature changes [55,57-59]. However, regular exercise in older and postmenopausal women has been shown to improve cutaneous vasodilation by approximately 1.5-fold [60,61]. This is thought to be due to the increased responsiveness to nitric oxide in the dilation of cutaneous blood vessels [60]. In other words, having an exercise routine not only increases cutaneous blood flow during exercise but also improves cutaneous vasodilatory function. Since skin hydration occurs through a moisture gradient between the deeper layers and the surface of the skin, maintaining adequate skin blood flow is an important factor in preserving skin hydration [16]. Although there is no direct evidence that exercise promotes skin hydration, various cross-sectional studies have shown that the skin of regularly exercising adults and hospitalized older people is more hydrated than the skin of those who do not [62,63]. Additionally, exercise can reduce hot flashes in postmenopausal women [64]. Hot flashes are thought to be caused by a dysfunction in the body's thermoregulatory control system [65], as well as vascular dysfunction [66]. Exercise has the potential to improve these functions.

Exercise can also improve age-related changes in sedentary older adults' skin structure [67]. One possible cause of systemic dysfunction due to aging, including skin, is increased ROS production due to age-related mitochondrial dysfunction [68]. Exercise has received significant attention because it can prevent mitochondrial dysfunction and promote mitochondrial biosynthesis, thereby helping to prevent systemic functional decline [67,69]. It has been shown that exercise stimulates the secretion of interleukin-15, which activates mitochondrial

biosynthesis in muscles. This mechanism is expected to prevent age-related changes in middle-aged women's skin [69]. In fact, in mice that exercised, there was an improvement in skin structure due to an increase in the amount of collagen in the dermis layer. Moreover, it has been shown that when older adults exercise twice a week for 12 weeks, the stratum corneum of the skin, which has thickened with age, becomes thinner [67]. In middle-aged women, daily facial exercises for 8 weeks have caused cosmetic changes in facial appearance [70], and changes in skin structure can lead to cosmetic changes as well. Exercise also affects hormone secretion, including stimulating the secretion of growth hormone and estrogen [71-73]. As mentioned in the *Hormone Balance* section, growth hormone and estrogen are involved in the production of cutaneous collagen [28,36]. In the skin, collagen is involved in skin

elasticity and skin thickness [28,31], and a decrease in collagen content leads to skin wrinkling and thinning. Therefore, it can be inferred that it may also affect skin elasticity and other factors. Future research is expected in these areas.

However, exercise does not always have a positive effect on the skin. An example of this is the risk of skin eczema due to the composition of swimming pools [74,75]. Although this is not a direct effect of swimming exercise, it has been suggested that the chlorine used in pool disinfection may damage the skin barrier function [76]. Therefore, it is necessary to consider the possibility that the environment in which exercise is performed may adversely affect the skin.

Finally, Table 1 shows which exercises improve skin function.

Table 1. Exercise needed to improve skin function.

Improved skin function	Exercise details
Skin blood flow	Acute maximal exercise [55,56] Aerobic Training [56]
Vasodilator function in cutaneous microvessels	Aerobic Training [60,61]
Moisturizing function	Daily activity level [62,63]
Postmenopausal hot flushes	Moderate-intensity exercise training [64]
Structural of skin	Endurance exercise [67]
Facial appearance	Facial exercise [69]

Discussion

Skin aging is a complex and lengthy biological process influenced by genetic and environmental factors. Although there are various therapeutic approaches to combat skin aging, such as hyaluronic acid injections and hormone replacement therapy, each method has its drawbacks. With people's increasing demands for effective, safe, and sustainable treatment methods, the prevention and mitigation of skin aging through lifestyle management has become a trend.

It is undeniable that the skin is affected by lifestyle habits, and a consensus exists around lifestyle habits that negatively affect skin function. However, numerous questions remain unanswered regarding the effects of dietary and stress-coping interventions on skin function. This is likely due to ethical issues and the lack

of guaranteed uniformity in clinical experimental conditions, which can lead to ambiguous results.

Exercise interventions have a relatively small potential for ethical problems and can have uniform experimental conditions. This review demonstrates that exercise can potentially enhance skin function retention. Although the design of the studies that were conducted varied, it was clear that exercise increases skin blood flow, increases keratin water content, and changes skin structure. The effects of exercise on the skin have previously been shown piecemeal, but this review has allowed us to synthesize the findings. These findings suggest the effectiveness of habitual exercise in improving skin function. Future studies should investigate the effects of exercise on the skin under different experimental conditions, such as varied exercise content and duration, as well as the physiological mechanisms involved.

Acknowledgments

This study was funded by a research grant from the Institute of Health Science, Shijonawate University.

Conflicts of Interest

None declared.

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## Abbreviations

**ROS:** reactive oxygen species

**TEWL:** transepidermal water loss

**UVR:** ultraviolet radiation

*Edited by R Dellavalle; submitted 18.08.23; peer-reviewed by M Gasmi, A Batrakoulis; comments to author 27.12.23; revised version received 24.01.24; accepted 06.02.24; published 14.03.24.*

*Please cite as:*

Oizumi R, Sugimoto Y, Aibara H

*The Potential of Exercise on Lifestyle and Skin Function: Narrative Review*

*JMIR Dermatol* 2024;7:e51962

URL: <https://derma.jmir.org/2024/1/e51962>

doi: [10.2196/51962](https://doi.org/10.2196/51962)

PMID: [38483460](https://pubmed.ncbi.nlm.nih.gov/38483460/)

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Research Letter

# From the Cochrane Library: Leukotriene Receptor Antagonists for Eczema

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(*JMIR Dermatol* 2024;7:e50434) doi:[10.2196/50434](https://doi.org/10.2196/50434)

**KEYWORDS**

eczema; atopic dermatitis; leukotriene receptor antagonists; systematic reviews; dermatitis; inflammatory; skin disease; skin; clinical; medications; management; receptor; antagonist

## Introduction

Atopic dermatitis (AD), a chronic inflammatory skin disease, is estimated to affect up to 10% of adults and 20% of children worldwide [1]. Clinical manifestations include pruritus, skin lesions, and dry scaly skin [2,3]. First-line treatment includes topical steroids and emollients, with systemic steroids or immune modulators for moderate-to-severe AD. Despite the standard practice of using topical corticosteroids in AD treatment, long-term use poses the risk of local adverse effects of skin thinning, striae, and purpura, or systemic effects such as growth suppression and suppression of the hypothalamic-pituitary axis [4]. Other medications, such as leukotriene receptor antagonists (LTRAs), are being researched as an alternative treatment option [5]. A 2018 Cochrane review, “Leukotriene receptor antagonists for eczema” [6], examined clinical trials to determine if there is sufficient evidence to recommend LTRAs for use in patients with AD but concluded that there was limited, low-quality evidence of its efficacy and safety.

## Methods

This Cochrane review extracted data across 5 studies and 202 participants to evaluate the evidence of LTRA effectiveness in AD. Of these studies, 3 assessed the efficacy of LTRAs compared to a placebo and 2 assessed the effectiveness of LTRAs versus conventional treatment (combined antihistamines and topical steroids). All assessed the effectiveness of the LTRA montelukast, met inclusion criteria of being a randomized controlled trial (RCT) and assessing patients with moderate-to-severe eczema, and tested interventions for the acute or chronic phase of AD. Interventions assessed independent administration of montelukast (oral or intravenous) or montelukast in combination with other topical and systemic treatments (corticosteroids, topical calcineurin inhibitors, immunomodulators, or placebo).

## Results

Only 1 RCT resulted in greater improvement with LTRA intervention compared to conventional treatment but was of low quality. None of the studies addressed long-term control (primary outcome) or higher quality of life and lower emollient requirement (secondary outcomes) at all (Table 1). The quality

of supporting evidence was assessed by GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) based on 5 domains: limitations and risk of bias, inconsistency, direct relation of evidence, imprecision, and publication bias. While valuing the certainty of evidence, it is essential to be aware that judgments may vary between individuals with this method. The authors note it is challenging to draw firm conclusions from the results of these studies because the studies had an unclear or high risk of bias, including but not limited to selection and detection. Limitations of the studies included the

absence of testing other LTRAs besides montelukast, inclusion of only adult participants and participants with moderate-to-severe eczema, and a small sample size. Detection biases were present in 2 studies due to the lack of blinding of the outcome assessment; performance bias was of concern in 1 study due to the lack of blinding of participants and personnel in an open RCT. Potential confounders (eg, diet, detergent, household chemicals, climate, location, allergens) were not assessed, which could contribute to an underestimate or overestimate of the true association between LTRAs and AD.

**Table 1.** Summary of randomized controlled trials assessed in the Cochrane review, “Leukotriene receptor antagonists for eczema” [6].

	Study (year)				
	Capella et al (2001)	Friedmann et al (2007)	Nettis et al (2002)	Rahman et al (2006)	Veien et al (2005)
Study title	A randomized trial of leukotriene receptor antagonist montelukast in moderate - to-severe atopic dermatitis of adults	A double - blind, placebo - controlled trial of montelukast in adult atopic eczema	Efficacy and tolerability of montelukast as a therapeutic agent for severe atopic dermatitis in adults	Effectiveness of montelukast in the treatment of atopic dermatitis	Montelukast treatment of moderate to severe atopic dermatitis in adults: a randomized, double - blind, placebo - controlled trial
Participants, N	32	58	20	31	53
Type of trial	Single blind	Double blind	Double blind	Open label	Double blind
Length of study	6 weeks	8 weeks	6 weeks	4 weeks	4 weeks
Intervention vs comparator	Oral montelukast + oral placebo + topical placebo gel vs (conventional) oral cetirizine + oral clarithromycin + topical steroid creams	Montelukast vs placebo	Montelukast vs placebo	Montelukast vs (conventional) antihistamine + 1% topical hydrocortisone	Montelukast vs placebo
Montelukast dose	10 mg for adults, 5 mg for children	10 mg for adults, 5 mg for children	10 mg for adults, 5 mg for children	10 mg for adults, 5 mg for children	10 mg for adults, 5 mg for children
Scale	SCORAD <sup>a</sup>	SASSAD <sup>b</sup>	SCORAD	SCORAD	Modified EASI <sup>c</sup>
Study conclusions	Significant improvement in SCORAD scores of both montelukast and placebo groups but no significant difference	No significant difference between montelukast and placebo for pruritus improvement	20% significant reduction in SCORAD with montelukast. Montelukast was superior	Significant improvement in SCORAD with montelukast compared to conventional treatment. Montelukast was superior	No significant difference between the EASI scores of montelukast and placebo groups
Reason for lack of evidence	Low quality of evidence, small sample size, high risk of bias	Low quality of evidence, small sample size	Low quality of evidence, small sample size	Low quality of evidence, small sample size	Low quality of evidence, small sample size, high risk of bias
Standard mean difference (95% CI), inverse variance, random	Not provided	−0.03 (−0.54 to 0.49)	1.09 (0.13 to 2.04)	10.57 (4.58 to 16.56)	0.20 (−0.34 to 0.74)
Adverse effects	None	Dizziness reported; mild in nature except for a brief septicemic illness	None	None	None

<sup>a</sup>SCORAD: Scoring Atopic Dermatitis.

<sup>b</sup>SASSAD: Six Area, Six Sign Atopic Dermatitis.

<sup>c</sup>EASI: Eczema Area and Severity Index.

## Discussion

Experimental data on the involvement of leukotrienes in allergic inflammation suggests LTRA therapy might be promising for the treatment of AD [3]; however, the results to date are unclear and lack uniformity. The increasing incidence of AD highlights

the need for additional investigation to identify the most effective treatments, especially those that can be used as long-term maintenance therapy. While there is no compelling evidence in this review for or against LTRA use for AD treatment, a large, well-designed RCT with multiple LTRAs would help better understand LTRA's role in long-term AD management.

## Acknowledgments

We would like to thank our Cochrane colleagues for their contributions to the original systematic review of this topic.

## Conflicts of Interest

RPD is editor-in-chief of *JMIR Dermatology*, a joint coordinating editor for Cochrane Skin, a dermatology section editor for UpToDate, and a social media editor for the *Journal of the American Academy of Dermatology*. He is a coordinating editor representative on the Cochrane Council. TES is an editorial board member-at-large for *JMIR Dermatology* and is a member of the Cochrane Collaboration.

RPD receives editorial stipends (*JMIR Dermatology*, *Journal of Investigative Dermatology*), royalties (UpToDate), and expense reimbursement from Cochrane Skin. TES receives fellowship funding from Pfizer Inc.

## Editorial Notice

The views expressed in this paper are those of the author(s) and in no way represent the Cochrane Library or Wiley.

This article is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2018, Issue 10, DOI: 10.1002/14651858.CD011224.pub2 (see [www.cochranelibrary.com](http://www.cochranelibrary.com) for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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## Abbreviations

**AD:** atopic dermatitis

**GRADE:** Grading of Recommendations, Assessment, Development, and Evaluations

**LTRA:** leukotriene receptor antagonist

**RCT:** randomized controlled trial



*Edited by J Lipoff; submitted 30.06.23; peer-reviewed by K Kamel, C Barsoum; comments to author 08.09.23; revised version received 23.02.24; accepted 27.02.24; published 12.04.24.*

*Please cite as:*

*Toledo LM, Rodriguez R, Sivesind TE, Vakirlis E, Kojima R, Dellavalle RP*

*From the Cochrane Library: Leukotriene Receptor Antagonists for Eczema*

*JMIR Dermatol 2024;7:e50434*

*URL: <https://derma.jmir.org/2024/1/e50434>*

*doi: [10.2196/50434](https://doi.org/10.2196/50434)*

*PMID: [38607671](https://pubmed.ncbi.nlm.nih.gov/38607671/)*

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Research Letter

# REDCap as a Platform for Cutaneous Disease Management in Street Medicine: Descriptive Study

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(*JMIR Dermatol* 2024;7:e48940) doi:[10.2196/48940](https://doi.org/10.2196/48940)

**KEYWORDS**

REDCap; unsheltered homelessness; street medicine; informatics; cutaneous; homeless; homelessness; data capture; data collection; skin; dermatology; vulnerable; low income; low resource; database; chart; health record; health records; EHR; electronic health record

## Introduction

According to the 2022 Annual Homelessness Report to Congress, on a single night, 582,462 people experienced homelessness across the United States, and 233,832 (over 40%) of those experienced unsheltered homelessness [1]. A 2020 systematic integrative review of health and social care in people experiencing homelessness showed that this population experienced inequities in access to basic human needs, health care, and social support [2], which are compounded by poor interpersonal dimensions such as a lack of provider support and stigmatization. Altogether, people experiencing homelessness are at risk for morbidity and premature death [3,4]. People experiencing homelessness require programs that bypass social barriers to health care. The street medicine approach uses teams of health care providers and volunteers to meet patients where they are currently living on the streets of major cities, bypassing barriers such as lack of transportation, ability to pay, and lack of primary care by bringing a mobile clinic with medications, supplies, and providers directly to people experiencing homelessness [5].

Because student-led street medicine is often volunteer based and not directly affiliated with hospital systems, many lack robust electronic medical record (EMR) systems [6]. Correspondingly, the lack of efficient medical care documentation is an obstacle to providing longitudinal care to

patients experiencing homelessness. REDCap is a Health Insurance Portability and Accountability Act-compliant free web application used to create databases for clinical research and projects [7,8]. However, per our evaluation of the medical literature, there are no reports of medical record keeping or using REDCap among street medicine organizations.

This retrospective descriptive study describes the use of a custom REDCap-based EMR for the management of cutaneous diseases in a Miami-based street medicine organization, Miami Street Medicine (MSM).

## Methods

**Ethical Considerations**

The University of Miami Institutional Review Board (IRB) approved reviewing records of cutaneous disease among people experiencing homelessness (IRB ID: 20230666).

**Overview**

A custom REDCap-based EMR was developed in November 2020 for MSM. The MSM custom REDCap includes forms for medical notes, vitals, labs, and more. The EMR was further customized to the unique needs and circumstances of people experiencing homelessness.

Specific drop-down lists about cutaneous pathology were created. The drop-down menus allow for selecting a location

on the body, wound characterization, whether the wound was infected, if debridement was done, and supplies used.

Between July 2021 and January 2022, patients were seen curbside in Miami once per week. Patients were assigned medical record numbers and had medical histories taken, vitals examined, and medications distributed as needed or called into a pharmacy by an attending physician. Records about skin and nail complaints were reviewed by board-certified dermatologists who made diagnoses of cutaneous conditions, recommended medical plans, and called in prescriptions. Diagnoses were not based on standard codes, but rather on clinical expertise, as all services were free and not reported to health insurance agencies.

Skin and nail pathologies were categorized by diagnosis as chronic infections, acute infections, inflammatory, wounds, miscellaneous, nail disorders, and undetermined.

## Results

Among 140 patients experiencing homelessness seen from July 2021 to January 2022, 112 skin and nail diagnoses were recorded. The sample included a diverse cohort that was 50.2% (n=56) Black and 45.8% (n=51) White, with the remainder being Asian or Native American patients. Hispanic patients of any race made up 34.8% (n=39) of the sample. A total of 68.1% (n=77) of patients identified as male and 31.9% (n=35) as female. The highest morbidity lesions resulting in disability or infection were chronic wounds and ulcers requiring multiple care instances.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Distribution of skin diagnosis by type.

[PNG File, 42 KB - [derma\\_v7ile48940\\_app1.png](#)]

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The most common dermatologic diagnosis outside of the miscellaneous category was acute infections, with the most common type of medication dispensed being for wound care (Multimedia Appendix 1).

## Discussion

The use of a free customizable REDCap EMR system was instrumental in recording the high burden of cutaneous diseases and connecting patients with specialists and follow-up care. Charitable health care organizations can use REDCap as it provides cost-effective, modifiable, and accessible management of patient data. One of the benefits of using REDCap as an EMR for special populations is its customizability and ease of data analysis.

Limitations of using the REDCap EMR include data entry errors by volunteer scribes and the great effort required to build and maintain this system. As a transient population, we noted 71.6% (80/112) patient attrition from care. This could be improved by communication via phone or email. Further, many topical medications offered to patients were distributed without documentation; only medications specifically ordered for patients were included in this synthesis.

A REDCap-based EMR is a valuable tool for established street medicine teams and may improve the delivery of care to people experiencing homelessness.

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## Abbreviations

**EMR:** electronic medical record

**MSM:** Miami Street Medicine

*Edited by R Dellavalle; submitted 18.05.23; peer-reviewed by K Fultz Hollis, CMJ Wong; comments to author 27.06.23; revised version received 21.09.23; accepted 29.11.23; published 09.01.24.*

*Please cite as:*

*Eachus E, Schwartz K, Rasul T, Bergholz D, Keri J, Henderson A*

*REDCap as a Platform for Cutaneous Disease Management in Street Medicine: Descriptive Study*

*JMIR Dermatol* 2024;7:e48940

URL: <https://derma.jmir.org/2024/1/e48940>

doi: [10.2196/48940](#)

PMID: [38194246](#)

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## Research Letter

# From the Cochrane Library: Systemic Interventions for Steven-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and SJS/TEN Overlap Syndrome

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(*JMIR Dermatol* 2024;7:e46580) doi:[10.2196/46580](https://doi.org/10.2196/46580)

**KEYWORDS**

Steven-Johnson syndrome; toxic epidermal necrolysis; necrolysis; fatal; life-threatening; treatment; dermatology; skin; dermatological; SJS; TEN; corticosteroids; intravenous immunoglobulin; IVIG; etanercept; prednisolone; systematic; corticosteroid; corticoid; steroid; steroids

## Introduction

Steven-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and SJS/TEN overlap syndrome are a spectrum of potentially life-threatening, rare, and severe cutaneous adverse reactions that are triggered by medication use typically within weeks of medication initiation. The pathogenesis of SJS/TEN is theorized to be a T lymphocyte-mediated immune response to an antigen of the offending medication causing epidermal necrosis [1]. There is limited evidence to support the use of therapies, such as glucocorticoids, intravenous immunoglobulins (IVIGs), cyclosporine, and etanercept, for the treatment of SJS and TEN [1]. We aim to summarize the key findings of a Cochrane review on the effects of systemic therapies for SJS/TEN.

## Methods

To evaluate systemic therapies for SJS/TEN, a systematic review of randomized controlled trials (RCTs) and prospective observational comparative studies (up to March 2021) of patients

of all ages with SJS/TEN was conducted [1]. The primary end points were disease-specific mortality (DSM) and adverse events leading to the discontinuation of systemic treatment therapy. Secondary end points included time to complete re-epithelialization, intensive care unit length of stay, total hospital length of stay, illness sequelae, and adverse events.

## Results

In total, 9 studies with a total of 308 patients from across 7 countries were included in the analysis, of which 3 were RCTs and 6 were prospective observational studies; 2 studies were included in a meta-analysis. The risk of bias for the three RCTs was respectively rated as high, moderate, and low; all the prospective comparative studies were rated as having a high risk of bias. The interventions that were assessed included systemic corticosteroids, tumor necrosis factor- $\alpha$  inhibitors, and others (Table 1).

The overall level of certainty for the parameters of interest was low, so most findings were “uncertain.” It was uncertain if corticosteroids had a higher risk of DSM versus no



corticosteroids (relative risk [RR] 2.55, 95% CI 0.72-9.03). It was also uncertain if there was a difference between IVIGs and no IVIGs in terms of DSM (RR 0.33, 95% CI 0.04-2.91), time to re-epithelialization (mean difference -2.93, 95% CI -4.4 to -1.46 d), or length of hospital stay (mean difference -2.00, 95% CI -5.81 to 1.81 d). Etanercept did not significantly reduce DSM compared to corticosteroids (RR 0.51, 95% CI 0.16-1.63;

$P=.72$ ), and serious adverse events, such as sepsis and respiratory failure, occurred in treatment with both groups. It was also uncertain if there was any difference between the cyclosporine and IVIG groups in terms of the risk of DSM (RR 0.13, 95% CI 0.02-0.98). A summary of other comparator studies is included in [Table 2](#).

**Table 1.** Key characteristics of included trials.

Study (author, year)	Study design	Sample size, n	Intervention	Outcome measured
Azfar et al [2], 2010	Prospective observational study	40	Corticosteroids (dose unknown) vs supportive care	Disease-specific mortality
González-Herrada et al [3], 2017	Prospective controlled study	22	Cyclosporine (PO <sup>a</sup> 3 mg/kg/d or IV <sup>b</sup> 1 mg/kg/d until re-epithelialization, then taper off 10 mg/d every 48 h) vs IVIG <sup>c</sup> (0.75 g/kg/d for 4 d; lower dose for renal insufficiency), systemic corticosteroids (37.5- to 100-mg prednisone equivalents for 4 d), or supportive care	All-cause mortality, expected death rate based on SCORTEN <sup>d</sup> , time to stabilization of BSA <sup>e</sup> involvement, time to re-epithelialization start, and time to complete re-epithelialization
Han et al [4], 2017	Prospective comparator study	28	Plasmapheresis (1-time dose of 1000 mL of Ringer-Locke and 2-3 L of plasma at 1 L/h) vs IVIG or corticosteroids (unknown dose)	Hospital length of stay
Jagadeesan et al [5], 2013	Prospective comparator study	36	IVIG (0.2- to 0.5-g/kg cumulative dose over 3 d) and IV dexamethasone (0.1-0.3 mg/kg/d; tapered within 1-2 wk) vs IV dexamethasone (0.1-0.3 mg/kg/d; rapidly tapered within 1-3 wk)	Disease-specific mortality, AEs <sup>f</sup> leading to discontinuation, other AEs, mean days to full skin healing, mean length of hospital stay, and illness sequelae
Kakourou et al [6], 1997	Prospective comparative study	16	Corticosteroids (methylprednisolone bolus 4 mg/kg/d for 2 d after fever subsided) vs supportive care only	Mortality
Paquet et al [7], 2014	Open-label randomized controlled trial	10	IV NAC <sup>g</sup> in 5% glucose over 20-h period (150 mg/kg in 250 mL over first h; then 150 mg/kg in 500 mL for 4 h; and, lastly, 150 mg/kg in 1000 mL over 15 h) and IV infliximab (5 mg/kg over 2 h) vs NAC-only regimen (same as former)	Disease-specific mortality
Saraogi et al [8], 2016	Prospective observational study	43	IV corticosteroids, IVIG, and combination of corticosteroids and IVIG vs supportive care	Arrest of disease progression, time to re-epithelialization, and mortality
Wang et al [9], 2018	Open-label randomized controlled clinical trial	91	Subcutaneous etanercept 25 mg (50 mg if >65 kg) twice weekly until skin lesions healed (n=48) vs IV prednisolone 1-1.5 mg/kg/d until skin lesions healed (n=43)	Disease-specific mortality and other AEs
Wolkenstein et al [10], 1998	Double-blind randomized controlled trial	22	Thalidomide 200 mg BID <sup>h</sup> PO × 5 d vs placebo at same dosing regimen	Disease-specific mortality

<sup>a</sup>PO: per os.  
<sup>b</sup>IV: intravenous.  
<sup>c</sup>IVIG: intravenous immunoglobulin.  
<sup>d</sup>SCORTEN: Score for Toxic Epidermal Necrolysis.  
<sup>e</sup>BSA: body surface area.  
<sup>f</sup>AE: adverse event.  
<sup>g</sup>NAC: N - acetylcysteine.  
<sup>h</sup>BID: twice per day.

**Table 2.** Summary of key study findings.

Comparison	Number of patients (number of studies)	Anticipated absolute effects (95% CI)	Relative effect (95% CI)	Certainty of evidence (GRADE <sup>a</sup> )
Corticosteroids vs supportive care	56 (2 OS <sup>b</sup> ) [2,6]	DSM <sup>c</sup> : 91 per 1000 (supportive care) vs 232 per 1000 (corticosteroid); TTCR <sup>d</sup> : NR <sup>e</sup> ; ICU-LOS <sup>f</sup> : NR; TH-LOS <sup>g</sup> : NR; AE/DC <sup>h</sup> : NR	DSM: 2.55 (0.72 to 9.03); TTCR: NR; ICU-LOS: NR; TH-LOS: NR; AE/DC: NR	Very low
IVIG <sup>i</sup> and supportive care vs supportive care	36 (1 OS) [5]	DSM: 55 (6 to 386) per 1000 (IVIG) vs 167 per 1000 (supportive care); TTCR: mean 10.93 d, mean difference 2.93 d lower (4.4 d lower to 1.46 d lower); ICU-LOS: NR; TH-LOS: mean 15.33 d, mean difference 2.00 d lower (5.81 d lower to 1.81 d higher); AE/DC: NR	DSM: 0.33 (0.04 to 2.91); TTCR: NR; ICU-LOS: NR; TH-LOS: NR; AE/DC: NR	Very low
Etanercept vs supportive care	No studies fit criteria	N/A <sup>j</sup>	N/A	N/A
Cyclosporine vs supportive care	No studies fit criteria	N/A	N/A	N/A
IVIG vs corticosteroids	No studies fit criteria	N/A	N/A	N/A
Etanercept vs corticosteroids	91 (1 RCT <sup>k</sup> ) [9]	DSM: 163 per 1000 (corticosteroids) vs 83 (26 to 265) per 1000 (etanercept); TTCR: NR; ICU-LOS: NR; TH-LOS: NR; AE/DC: NR	DSM: 0.51 (0.16 to 1.63); TTCR: NR; ICU-LOS: NR; TH-LOS: NR; AE/DC: NR	Low
Cyclosporine vs corticosteroids	No studies fit criteria	N/A	N/A	N/A
Etanercept vs IVIG	No studies fit criteria	N/A	N/A	N/A
Cyclosporine vs other treatments (IVIG: n=4; corticosteroids: n=1; no specified treatment: n=1)	22 (1 OS) [3]	DSM: 500 per 1000 (other treatments) vs 65 (10 to 468) per 1000 (cyclosporine); TTCR: NR; ICU-LOS: NR; TH-LOS: NR; AE/DC: NR	DSM: 0.13 (0.02 to 0.98); TTCR: NR; ICU-LOS: NR; TH-LOS: NR; AE/DC: NR	Very low
Etanercept vs cyclosporine	No studies fit criteria	N/A	N/A	N/A
N-acetylcysteine and infliximab vs infliximab alone	10 (1 OS) [7]	NR	DSM: 2.00 (0.26 to 15.62)	NR
Thalidomide vs placebo	22 (1 RCT) [10]	NR	DSM: 2.78 (1.04 to 7.40)	NR
Plasmapheresis vs other treatments	28 (1 OS) [4]	NR	TH-LOS: mean difference -7.37 (-16.09 to 1.35) d	NR

<sup>a</sup>GRADE: Grading of Recommendations, Assessment, Development, and Evaluation.

<sup>b</sup>OS: observational study.

<sup>c</sup>DSM: disease-specific mortality of Steven-Johnson syndrome and toxic epidermal necrolysis.

<sup>d</sup>TTCR: time to complete re-epithelialization.

<sup>e</sup>NR: not reported.

<sup>f</sup>ICU-LOS: intensive care unit length of stay.

<sup>g</sup>TH-LOS: total hospital length of stay.

<sup>h</sup>AE/DC: adverse effects leading to discontinuation of Steven-Johnson syndrome/toxic epidermal necrolysis therapy.

<sup>i</sup>IVIG: intravenous immunoglobulin.

<sup>j</sup>N/A: not applicable.

<sup>k</sup>RCT: randomized controlled trial.

**Discussion**

The authors of the original review concluded that “etanercept (25 mg [50 mg if weight > 65 kg]) twice weekly ‘until skin

lesions healed’) may reduce DSM compared to corticosteroids (intravenous prednisolone 1 to 1.5 mg/kg/day ‘until skin lesions healed’) (RR 0.51, 95% CI 0.16 to 1.63; 1 study; 91 participants; low - certainty evidence); however, the CIs were consistent with possible benefit and possible harm” [1]. Overall, data from

the included studies were limited, with few direct clinical comparator studies for the different therapeutic agents assessed. Future multicenter large-scale studies are needed to better outline SJS/TEN medication therapy and evaluate agents of choice in disease management.

## Conflicts of Interest

BR is a speaker for Incyte and Amgen. AAJ has received the Cochrane Scholarship for the original Cochrane review from the American Academy of Dermatology. All other authors have no conflicts of interest to declare.

## Editorial Notice

This article is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2022, Issue 3, DOI: 10.1002/14651858.CD013130.pub2 (see [www.cochranelibrary.com](http://www.cochranelibrary.com) for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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## Abbreviations

**DSM:** disease-specific mortality  
**IVIG:** intravenous immunoglobulin  
**RCT:** randomized controlled trial  
**RR:** relative risk  
**SJS:** Steven-Johnson syndrome  
**TEN:** toxic epidermal necrolysis

*Edited by R Dellavalle; submitted 16.02.23; peer-reviewed by E Brenaut, D Zheng; comments to author 12.07.23; revised version received 20.09.23; accepted 27.12.23; published 30.01.24.*

*Please cite as:*

*Pathak GN, Truong TM, Singal A, Taranto V, Rao BK, Jacobsen AA*

*From the Cochrane Library: Systemic Interventions for Steven-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and SJS/TEN Overlap Syndrome*

*JMIR Dermatol 2024;7:e46580*

*URL: <https://derma.jmir.org/2024/1/e46580>*

*doi: [10.2196/46580](https://doi.org/10.2196/46580)*

*PMID: [38289652](https://pubmed.ncbi.nlm.nih.gov/38289652/)*

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Research Letter

# Direct-to-Patient Mobile Teledermoscopy: Prospective Observational Study

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## Abstract

Direct-to-patient mobile teledermoscopy is a feasible and useful adjunct to smartphone imaging for monitoring patient-identified lesions of concern, achieving comparable diagnostic and management accuracy as in-office dermatology.

(*JMIR Dermatol* 2024;7:e52400) doi:[10.2196/52400](https://doi.org/10.2196/52400)

**KEYWORDS**

mobile teledermoscopy; teledermatology; direct-to-patient; full body skin exam; diagnostic concordance; mobile health; mHealth; dermoscopy; dermatology; dermatological; imaging; image; images; smartphone; lesion; lesions; skin; diagnostic; diagnosis; diagnoses; telehealth; telemedicine; eHealth

## Introduction

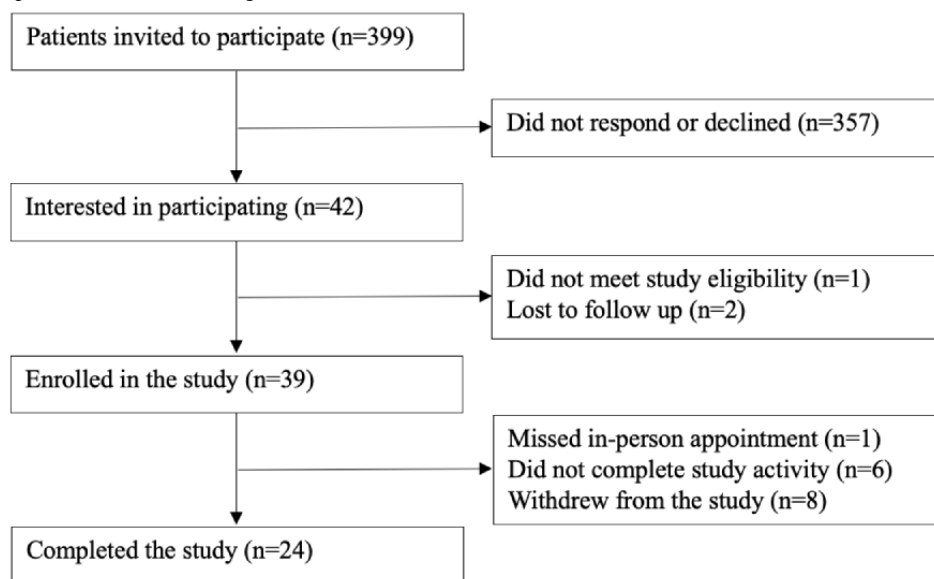
Teledermoscopy is promising for improving the diagnostic accuracy of store-and-forward consultations [1]. However, few studies have explored using direct-to-patient mobile teledermoscopy to bypass in-person imaging [2-4]. Within the Veterans Health Administration system, teledermatology involves in-person visits with trained imaging technicians. Dermoscopy is not universally used. This prospective observational study evaluates a direct-to-patient mobile teledermoscopy program at the San Francisco Veterans Affairs Medical Center (SFVAMC) on its effectiveness in diagnosing and managing patient-identified lesions of concern.

## Methods

**Recruitment and Implementation**

Adults scheduled for full-body skin exams between May and August 2022 were recruited (Figure 1) and given a Sklip mobile dermatoscope, valued at US \$99.99. They were instructed to image 1-3 lesions of concern using both smartphones and dermatoscopes. A teledermatologist reviewed all images for diagnosis, management, quality, and clinical utility. Clinical utility was defined as images that increased the teledermatologist's confidence in diagnosis and management. A dermatologist different from the teledermatologist evaluated the same lesions in-office.



**Figure 1.** Study participant recruitment flow diagram.

### Statistical Analysis

The degree of agreement was assessed using the percentage of agreement and Cohen  $\kappa$  (95% CI). Cohen  $\kappa$  values were interpreted using the scale developed by Landis and Koch [5]. Excel (Microsoft Corporation) was used for data collection and analysis.

### Ethical Considerations

This study was approved by the institutional review board (IRB) of the UCSF Human Research Protection Program and SFVAMC Research and Development Committee, IRB study number 21-33538. Participants provided informed consent with the option to opt out of the study. Participants were not compensated, and their data was anonymized and stored in a password-protected file.

### Results

This study included 24 participants (male:  $n=20$ , 83%; mean age 65.3, SD 14.9 years). The average distance between their home zip codes and SFVAMC was 54.9 (SD 77.1) miles. A total of 12 (50%) participants had a history of skin cancer: 10 with basal cell carcinoma, 5 with squamous cell carcinoma, 4 with melanoma, and 1 with melanoma in situ.

A total of 56 lesions were imaged: 9 (17%) on the head, 1 (2%) on the neck, 8 (15%) on the posterior trunk, 16 (30%) on the

anterior trunk, 15 (28%) on the arms, and 3 (9%) on the legs. The teledermatologist rated most dermoscopic images ( $n=37$ , 66%) as acceptable to good quality. There was substantial agreement between the teledermatologist and in-person dermatologist in diagnoses and management (Table 1;  $\kappa=0.65$ , SE 0.13, 95% CI 0.39-0.91 and  $\kappa=0.67$ , SE 0.11, 95% CI 0.47-0.88, respectively). Most discordant diagnoses had concordant management ( $n=3$ , 60%).

Over 85% ( $n=48$ ) of lesions were diagnosed as benign neoplasms. Two participants had additional lesions suspected of malignancy identified by in-office dermatologists, one of which was biopsy-proven basal cell carcinoma. Teledermatologists considered 59% ( $n=33$ ) of smartphone images to have clinical utility, while 66% ( $n=37$ ) of dermoscopic images provided additional utility when used alongside smartphone images.

For 65% ( $n=15$ ) of participants who responded to a questionnaire, nondermoscopy smartphone imaging was easy, whereas 52% ( $n=12$ ) reported mobile teledermoscopy as easy. Most ( $n=18$ , 78%) were willing to perform mobile teledermoscopy again. Barriers to dermoscopy use included difficulty performing with nondominant hand ( $n=1$ , 4%) and requiring assistance ( $n=5$ , 22%). All dermatoscopes were returned undamaged.

**Table 1.** Distribution of diagnoses and management by the teledermatologist and in-office dermatologists.

	Teledermatologist (n=56), n (%)	In-office dermatologist (n=56), n (%)
<b>Diagnostic category</b>		
Benign	48 (85.7)	48 (85.7)
Premalignant	1 (1.8)	3 (5.4)
Malignant	0 (0.0)	0 (0.0)
Infectious	0 (0.0)	1 (1.8)
Inflammatory	7 (12.5)	4 (7.1)
Neoplasm of uncertain behavior	0 (0.0)	0 (0.0)
<b>Management</b>		
Monitor	44 (78.6)	43 (76.8)
Cryotherapy	1 (1.8)	3 (5.4)
Biopsy or excision	4 (7.1)	2 (3.6)
Antibiotic	1 (1.8)	2 (3.6)
Steroid/anti-inflammatory	6 (10.7)	6 (10.7)

Discussion

Principal Findings

Substantial agreement was found between the teledermatologists and in-office dermatologists, consistent with previous studies [2,6]. However, the wide CIs indicate the need for further studies with larger sample sizes and implementation improvements, especially for identifying life-threatening malignancies. We recommend providing patients’ medical history to teledermatologists. In one discordant case, a history of vitiligo could have differentiated from postinflammatory hypopigmentation. A recent study developed a checklist for mobile teledermoscopy image quality [7], which could be shared with patients to improve image quality. Because the teledermatologist had a lower threshold for biopsies, a follow-up office visit should be pursued when a procedure is recommended.

Given the high proportion of benign neoplasms in our study, teledermoscopy implementation for patient-identified lesions could lead to an increased burden for telediagnosis services. To increase the malignancy detection, we recommend providing patient education on high-risk features, such as the ABCDEs

(asymmetry, border, color, diameter, and evolving) of melanoma or the 7-point checklist, before imaging [8].

Limitations

This study is limited by its single-center design, small study population, and voluntary participation. The nonresponse rate to the initial invitation was 89% (n=399), which may be due to mail delivery issues, lack of interest, or time constraints. While premalignant lesions were identified, no malignant lesions were imaged. Future studies that involve larger cohorts, different health care settings, and more teledermatologists could elicit additional information on the efficacy of direct-to-patient mobile teledermoscopy.

Conclusions

Substantial agreement was found between direct-to-patient mobile teledermoscopy and in-office evaluation in the diagnoses and management of patient-identified lesions. Most participants reported ease with mobile teledermoscopy use; however, most lesions were benign, indicating the need for patient education on high-risk features to ensure appropriate lesions are imaged. Providing direct-to-patient mobile teledermoscopy services may expand the reach of existing teledermatology practice.

Acknowledgments

We would like to thank Daniel Butler, MD; Maria Wei, MD, PhD; Yiyin Chen, MD, PhD; Ruby Ghadially, MD; and Bahram Razani, MD, PhD, who participated in the study and provided in-office dermatologic care for the study population. We would also like to thank Dennis Oh, MD, PhD, for his input and review of the publication. This study received funding through the University of California, San Francisco Inquiry Office and San Francisco Veterans Affairs Medical Center Office of Education.

Authors' Contributions

WF wrote the original draft, developed the methodology, and supported in conceptualizing the study. GM conducted the formal analysis, led the project administration, and reviewed and edited the manuscript. AT conceptualized the study, acquired the funding, supervised the study, supported in development of the methodology, supported the project administration, and reviewed and edited the manuscript.

## Conflicts of Interest

None declared.

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## Abbreviations

**ABCDE:** asymmetry, border, color, diameter, and evolving

**SFVAMC:** San Francisco Veterans Affairs Medical Center

*Edited by R Dellavalle; submitted 02.09.23; peer-reviewed by A Oakley, C Horsham; comments to author 17.09.23; revised version received 06.10.23; accepted 22.01.24; published 12.02.24.*

### Please cite as:

Fan W, Mattson G, Twigg A

*Direct-to-Patient Mobile Teledermoscopy: Prospective Observational Study*

*JMIR Dermatol* 2024;7:e52400

URL: <https://derma.jmir.org/2024/1/e52400>

doi: [10.2196/52400](https://doi.org/10.2196/52400)

PMID: [38345831](https://pubmed.ncbi.nlm.nih.gov/38345831/)

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Research Letter

# Evaluating Participation in Gender-Affirming Care: Cross-Sectional Analysis of Dermatology Program Websites in the United States

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(*JMIR Dermatol* 2024;7:e54480) doi:[10.2196/54480](https://doi.org/10.2196/54480)

**KEYWORDS**

dermatology; gender-affirming care; transgender; dermatology residency; medical education; website; digital platform; media; gender; websites; school; resident; residencies; residency; schools; universities; universities; cross-sectional

## Introduction

Transgender and gender-diverse (TGD) patients have unique dermatologic needs, including management of complications from gender-affirming hormone therapy or surgery [1]. Dermatologists play a pivotal role addressing these needs and providing services for gender-affirming care (GAC), such as laser hair removal, management of androgenetic alopecia, injectable neurotoxins, or soft tissue augmentation. To ensure culturally competent care, dermatology residency programs should provide/promote didactic and experiential training tailored to the health needs of TGD patients [2]. Additionally, prospective residents may benefit from being able to ascertain whether certain programs are involved in GAC, including education and research. We aimed to assess the current landscape of GAC participation among dermatology programs and propose strategies to enhance the visibility of such participation.

## Methods

Using Doximity 2022-2023 Residency Navigator, dermatology residency programs were identified (N=141). From April to July 2023, the websites of each department, residency program, and associated institution were examined to identify participation

in GAC. Next, web-based searches were conducted using department and residency program names plus the following terms: “LGBTQ health,” “gender affirming care,” “transgender healthcare,” or “transgender.” Search results were used to identify institutional multidisciplinary GAC programs, volunteer-based services/clinics participating in GAC, and participation in GAC not otherwise mentioned on program websites. Programs were independently reviewed and categorized by authors MC and JS. Interrater reliability was calculated using Cohen  $\kappa$ . Scores  $\geq 0.8$  were considered acceptable [3]. For discrepancies in categorization, searches were reconducted with the results discussed to reach a consensus.

## Results

Among the 141 examined websites, we found that 22 (15.6%) dermatology programs mentioned providing GAC; the type of participation was variable (Table 1). The remaining programs (n=119, 84.4%) did not mention participating in dermatologic GAC. Of this group, 62 were part of institutions with multidisciplinary GAC programs, while 57 were not. Among the 22 programs participating in GAC, geographic distribution was variable, with the greatest number in the New England region (Figure 1).

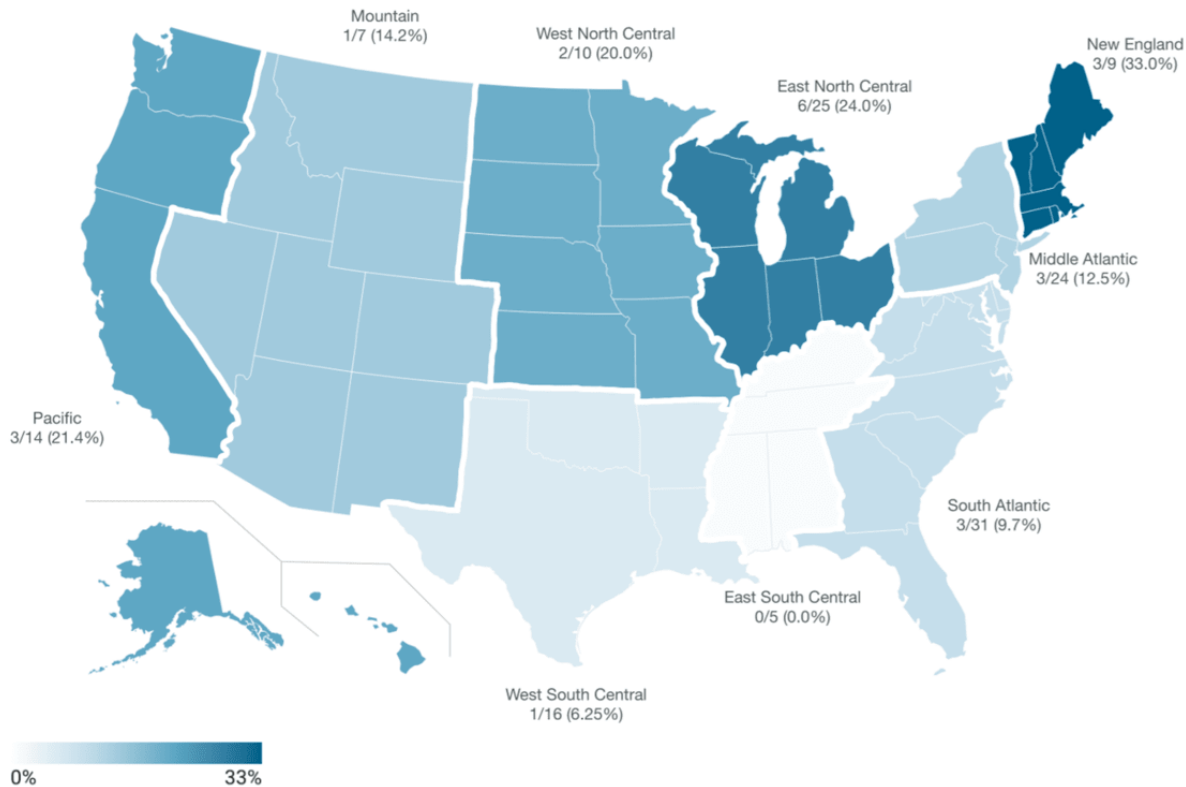
**Table 1.** US dermatology residency programs mentioning involvement in gender-affirming care (GAC).

	Programs (N=141), n (%)
<b>Mentioning participation in GAC</b>	22 (15.6)
Participation in an institutional multidisciplinary GAC clinic <sup>a</sup>	22 (100.0)
Listing a directory of SGM <sup>b</sup> health providers	19 (86.4)
Listing specific gender-affirming dermatologic procedures (eg, electrolysis or neurotoxins)	12 (54.5)
Listing GAC under a “services offered” tab	6 (27.3)
GAC program led by dermatology department	3 (13.6)
<b>Not mentioning participation in GAC</b>	119 (84.4)
Multidisciplinary GAC clinic at institution but no mention of dermatology involvement	62 (52.1)
No mention of gender-affirming care on institutional website	57 (47.9)

<sup>a</sup>Participation in a multidisciplinary clinic was defined as at least one faculty member representing the department in the clinic.

<sup>b</sup>SGM: sexual and gender minority.

**Figure 1.** Geographic distribution of dermatology programs participating in gender-affirming care. The choropleth map shows the proportion of programs involved in gender-affirming care (GAC) per geographic region, as defined by the Association of American Medical Colleges. The number of programs with GAC out of total programs in the region are displayed, along with associated percentages and color according to the scale.



Discussion

We found that a minority of dermatology programs mentioned participating in GAC, indicating that there remains a considerable gap between the desired and current state of resident education in gender minority health [4,5]. Indeed, dermatology residents receive, on average, 75 minutes of sexual and gender minority (SGM) health education yearly [5] and report low competency and confidence in caring for TGD patients [5,6]. Furthermore, dermatology program directors report barriers to implementing SGM health training, such as lack of funding, curricular time, and experienced faculty [4].

We observed that over 60 dermatology programs did not mention participating in GAC but are affiliated with institutions with multidisciplinary GAC clinics. These programs may consider collaborating with providers in those clinics to improve resident education and care of TGD patients. Highlighting such collaborations may aid recruitment of SGM-identifying residency/faculty candidates, especially those interested in teaching or studying SGM dermatology.

Furthermore, it is possible that some programs actually participate in GAC but do not “advertise” it on websites. Importantly, scrutiny or legal repercussions may affect the visibility or availability of GAC services of some programs,



particularly those affiliated with pediatric hospitals. Thus, when permissible, programs can implement simple measures to highlight their efforts. Program websites could identify departmental or institutional providers passionate about providing GAC. Programs may provide information on whether they perform minimally invasive procedures for GAC, like laser hair removal, injectable neurotoxins, or soft tissue augmentation. Likewise, displaying images of providers wearing pronoun badges or “pride pins” may foster an inclusive environment for patients and providers [7]. These measures do not require curricular time or funding and are associated with improved health outcomes [1,7].

Overall, our results expand upon those of a recent study, specifically by indicating how dermatology programs participate in GAC beyond involvement in multidisciplinary clinics [8]. Our study’s limitations include using publicly available websites, which may not fully reflect TGD health content within

curricula, collaborations with GAC experts, or dermatology research related to TGD patients. Future research can address these limitations by surveying program directors or multidisciplinary GAC clinics to ascertain the specifics of departmental involvement.

Our study provides insights into the various types of participation in GAC among dermatology residency programs, as well as existing challenges program directors face and potential clinical and nonclinical opportunities for improvement. Program websites may serve as a valuable and accessible resource to help TGD patients obtain GAC and to attract diverse residency and faculty candidates to a program. To cultivate a safe environment for patients and providers alike, program directors could consider, when possible/permissible, relatively easy yet impactful ways to use their program/departmental websites to enhance and advertise their participation in GAC.

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## Conflicts of Interest

None declared.

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- 

## Abbreviations

**GAC:** gender-affirming care

**SGM:** sexual and gender minority

**TGD:** transgender and gender-diverse

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*Edited by R Dellavalle, CC Chi; submitted 10.11.23; peer-reviewed by H Yeung, OP Hammvik; comments to author 17.12.23; revised version received 24.01.24; accepted 25.01.24; published 12.02.24.*

*Please cite as:*

Costanza M, Sobieraj J, Wang F

*Evaluating Participation in Gender-Affirming Care: Cross-Sectional Analysis of Dermatology Program Websites in the United States*  
*JMIR Dermatol* 2024;7:e54480

URL: <https://derma.jmir.org/2024/1/e54480>

doi: [10.2196/54480](https://doi.org/10.2196/54480)

PMID: [38345853](https://pubmed.ncbi.nlm.nih.gov/38345853/)

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## Research Letter

# Risk Factors Associated With Burden of Disease of Psoriasis From 1990 to 2019: Epidemiological Analysis

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(*JMIR Dermatol* 2024;7:e48749) doi:[10.2196/48749](https://doi.org/10.2196/48749)

**KEYWORDS**

psoriasis; dermatology; gross domestic product; epidemiology; sociodemographic index; Global Burden of Disease; obesity; burden; skin; epidemiological; sociodemographic; chronic; noncommunicable; autoimmune; inflammation; inflammatory

## Introduction

Psoriasis is a chronic inflammatory skin condition characterized by red, itchy, scaly patches that affects approximately 2% of the global population and has a significant effect on the patient's quality of life [1]. Exploring epidemiological trends and relevant risk factors for psoriasis is vital to effectively reduce the global burden of the disease by directing efforts toward countries with the highest prevalence. This study aims to characterize trends in global rates of psoriasis and their associations with relevant risk factors.

## Methods

We obtained global psoriasis data from the University of Washington Institute for Health Metrics and Evaluation Global Burden of Disease (GBD) Database and sorted it by age-standardized incidence, prevalence, and years lost to disability (YLD) rates per 100,000 people from 1990 to 2019 [2]. We further filtered these metrics by the four world regions (Asia, Africa, America, and Europe), sociodemographic index (SDI) quintiles, and the 204 countries/territories listed in the GBD database. Country-level indicator data was extracted from the World Health Organization Global Health Observatory database for possible associations with psoriasis [3]. Linear

regression analyses were conducted between risk factors and incidence, prevalence, and YLD rates of psoriasis.

## Ethical Considerations

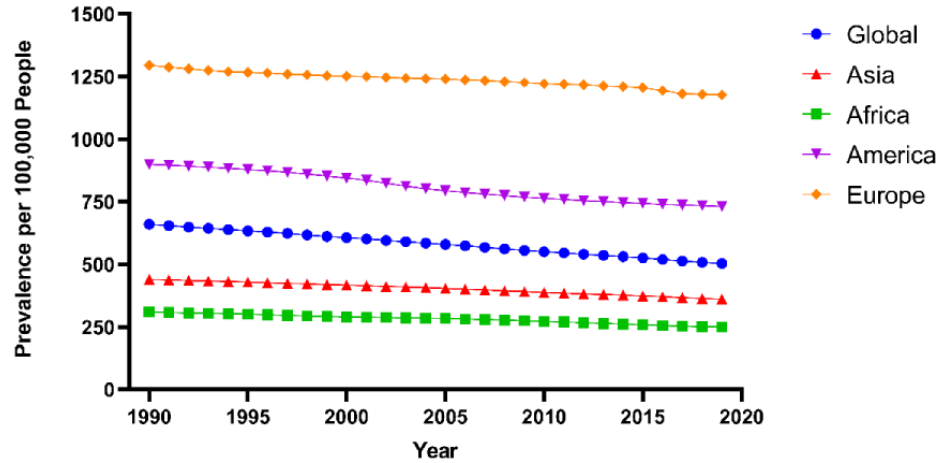
This paper was conducted using publicly available databases. Therefore, no ethics approval was required.

## Results

The global age-standardized prevalence rate of psoriasis per 100,000 people in 1990 was 660 (95% CI 637-681). It decreased to 504 (95% CI 487-519) in 2019. Across the world regions, psoriasis prevalence, incidence, and YLD were highest in Europe and lowest in Africa (Figure 1). Psoriasis prevalence rates were higher in the highest quintile of SDI (1990: 1256; 2019: 1073) than in the lowest quintile of SDI (1990: 338, 2019: 301) from 1990 to 2019. Similar trends were found for incidence and YLD rates.

Psoriasis incidence rates were positively associated with overweight prevalence ( $R^2=0.36$ ), mean cholesterol ( $R^2=0.21$ ), mental hospital admissions ( $R^2=0.25$ ), medical doctors ( $R^2=0.50$ ), and psychiatrists in the mental health sector ( $R^2=0.58$ ) while being negatively associated with air pollution mortality rates ( $R^2=0.40$ ; Table 1). Similar trends were noted for risk factor associations with psoriasis prevalence and YLD rates ( $P<.001$ ).

**Figure 1.** Global age-standardized prevalence rates of psoriasis per 100,000 people by Global Burden of Disease World Region.



**Table 1.** Linear regression analyses of risk factors associated with incidence, prevalence, and years lost to disability (YLD) rates of psoriasis.

Risk factors and Y value	Association	Countries, n	R <sup>2</sup>	P value
<b>Overweight prevalence (BMI ≥25, age-standardized estimate; %)</b>		182		
Incidence of psoriasis	Positive		0.26	<.001
Prevalence of psoriasis	Positive		0.22	<.001
YLDs of psoriasis	Positive		0.19	<.001
<b>Mean total cholesterol (age-standardized estimate)</b>		184		
Incidence of psoriasis	Positive		0.31	<.001
Prevalence of psoriasis	Positive		0.26	<.001
YLDs of psoriasis	Positive		0.23	<.001
<b>Mortality rate attributed to household and ambient air pollution per 100,000 population (age-standardized)</b>		182		
Incidence of psoriasis	Negative		0.40	<.001
Prevalence of psoriasis	Negative		0.35	<.001
YLDs of psoriasis	Negative		N/A <sup>a</sup>	<.001
<b>Mental hospital admissions per 100,000 population</b>		98		
Incidence of psoriasis	Positive		0.25	<.001
Prevalence of psoriasis	Positive		0.21	<.001
YLDs of psoriasis	Positive		0.17	<.001
<b>Medical doctors per 100,000 population</b>		184		
Incidence of psoriasis	Positive		0.50	<.001
Prevalence of psoriasis	Positive		0.44	<.001
YLDs of psoriasis	Positive		0.41	<.001
<b>Psychiatrists working in mental health sector (per 100,000 population)</b>		102		
Incidence of psoriasis	Positive		0.58	<.001
Prevalence of psoriasis	Positive		0.56	<.001
YLDs of psoriasis	Positive		0.53	<.001

<sup>a</sup>N/A: not applicable.

Discussion

There are a few reasons why global psoriasis prevalence consistently decreased since 1990. Psoriasis may go into

remission, decreasing the duration of the disease and ultimately its prevalence, especially in older individuals. Additionally, comorbidities and adverse health behaviors may lead to increased mortality rates among individuals with psoriasis,

resulting in decreased prevalence rates [4]. However, a significant global disease burden remains. Europe has the highest incidence, while Africa has the lowest. These findings were consistent with a prior study on the epidemiology of psoriasis [5]. Factors that were characteristic of wealthier countries such as high SDI, high overweight prevalence, higher mean cholesterol, and lower air pollution mortality rates were found to be associated with higher psoriasis incidence, prevalence, and YLD. Despite greater access to medical resources, high psoriasis prevalence in the highest SDI countries remains. Strong positive associations between psoriasis rates and medical doctors per 100,000 population and psychiatrists per 100,000 population further highlight this trend, underscoring the burden of psoriasis in areas more densely populated with medical professionals. Additionally, psoriasis rates are associated with mental hospital

indications, indicating possible psychiatric comorbidities among patients with psoriasis. Solutions must be tailored to more complex causes of psoriasis, such as the gut-brain-skin axis' role in skin disorders, smoking exposure, alcohol intake, specific medications, and even genetic causes [6].

Limitations of this study include underreporting in some sub-Saharan regions and potentially inaccurate modeling algorithms by the GBD website. Additionally, there may potentially be an ecological fallacy as the populations analyzed in this study may not be representative of the individual members. This study provides a unique and recent perspective on the epidemiological trends of psoriasis. To effectively reduce the burden of psoriasis in these countries, more research on the complex environmental and genetic risk factors of psoriasis should be conducted.

## Conflicts of Interest

TS serves as an editorial board member-at-large for *JMIR Dermatology*. All other authors report no conflicts of interest. TS receives fellowship funding from Pfizer (grant 25B1519; principal investigator: Stanca Birlea) and the National Institutes of Health (grant 2T32AR00741136A1; principal investigator: Dennis Roop).

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## Abbreviations

**GBD:** Global Burden of Disease

**SDI:** sociodemographic index

**YLD:** years lost to disability

*Edited by R Alhusayen; submitted 09.05.23; peer-reviewed by H Zhang, WF Khaw, H Guo, C Shah; comments to author 07.08.23; revised version received 11.01.24; accepted 28.01.24; published 15.02.24.*

*Please cite as:*

Kulkarni V, Liu D, Gamsarian V, Grewal T, Sivesind T

Risk Factors Associated With Burden of Disease of Psoriasis From 1990 to 2019: Epidemiological Analysis

*JMIR Dermatol* 2024;7:e48749

URL: <https://derma.jmir.org/2024/1/e48749>

doi: [10.2196/48749](https://doi.org/10.2196/48749)

PMID: [38358797](https://pubmed.ncbi.nlm.nih.gov/38358797/)



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## Research Letter

# From the Cochrane Library: Visual Inspection and Dermoscopy, Alone or in Combination, for Diagnosing Keratinocyte Skin Cancers in Adults

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(*JMIR Dermatol* 2024;7:e41657) doi:[10.2196/41657](https://doi.org/10.2196/41657)

**KEYWORDS**

nonmelanoma skin cancer; dermoscopy; dermatoscopy; teledermatology; dermoscopic; dermatoscope; oncology; skin; cancer; basal cell carcinoma; dermatology; cutaneous squamous cell carcinoma; diagnostic odds ratio; skin; lesion; diagnostic; diagnosis; keratinocyte carcinoma

## Introduction

Given the prevalence of keratinocyte carcinomas (KCs), it is imperative to identify accurate diagnostic tools for evaluating suspicious skin lesions [1,2]. Misdiagnosis carries significant harms, including unnecessary scarring, anxiety, and increased cost [3].

## Methods

A 2018 Cochrane review [3] assessed dermoscopy as an adjunct to visual inspection (VI) for KC diagnosis among adults with skin lesions suspicious for malignancy or at risk of KC development [3]. Diagnosis was verified by histology for all malignant lesions, while clinical follow-up or histologic diagnosis was required for at least 50% of participants with benign lesions to be included in the review [3]. When these parameters were met, cancer registry and “expert opinion” were also allowed as reference standards, although this was considered less desirable [3].

## Results

The review [3] included 24 studies conducted between 1987 and 2016, encompassing adult participants from North America, the Middle East, Europe, Oceania, and East Asia. Table 1 presents further information about the included studies. Among

the included studies, there were a total of 8805 visually inspected lesions and 6855 lesions inspected with dermoscopy and VI. Face-to-face and teledermatology settings were evaluated separately, although no clear difference was found between settings.

For in-person basal cell carcinoma (BCC) diagnosis, the diagnostic odds ratio revealed dermoscopy and VI were 8.2 (95% CI 3.5-9.3) times more effective than VI alone (likelihood-ratio test  $P < .001$ ), supporting the predicted sensitivity difference of 14% (79% vs 93%) at a fixed specificity of 80% and predicted specificity difference of 22% (77% vs 99%) at a fixed sensitivity of 80%. The predicted values for sensitivity and specificity were estimated using summary receiver operating characteristic (SROC) curves, which were constructed based on data points derived from individual studies included in the review [4]. It is crucial to note that secondary to substantial heterogeneity between studies, the reported differences in sensitivity and specificity are illustrative examples of the values that might be achieved based on the observed data and do not necessarily reflect how the tests might perform in specific settings.

Sources of heterogeneity were unclear due to poor reporting and lack of available data, although the authors suggest that observer experience, type of dermatoscope used, and the case mix of included lesions may have contributed. Risk of bias and concerns regarding applicability were generally high or unclear

across most domains assessed, particularly in participant selection, flow, and timing. Although the strength of the conclusions was limited, the addition of dermoscopy to in-person evaluations increased diagnostic accuracy on average. To estimate the impact of the predicted differences in specificity and sensitivity derived from the SROC curve for lesions inspected in person with VI alone versus VI and dermoscopy for the detection of BCC, they were applied to a hypothetical

cohort of 1000 lesions. At the median prevalence of 17%, an additional 24 BCC would be identified and 183 fewer non-BCC would be treated unnecessarily with the use of dermoscopy and VI. This information is further illustrated in Table 2. Insufficient data were available for thorough analysis of cutaneous squamous cell carcinoma detection, and it could not be determined whether evaluator expertise or use of a formal algorithm improved the accuracy of KC detection.

Table 1. Quantity of evidence for target lesions.

Setting and test (number of studies)	Total lesions, n	Total cases, n
<b>Basal cell carcinoma quantity of evidence (n=21)</b>		
<b>In person</b>		
VI <sup>a</sup>	7017	1586
VI + D <sup>b</sup>	4683	363
<b>Image based</b>		
VI	853	156
VI + D	2271	737
<b>Cutaneous squamous cell carcinoma quantity of evidence (n=4)</b>		
<b>In person</b>		
VI	2684	538
VI + D	— <sup>c</sup>	—
<b>Image based</b>		
VI	—	—
VI + D	717	119
<b>Any skin cancer quantity of evidence (n=11)</b>		
<b>In person</b>		
VI	3618	2021
VI + D	277	85
<b>Image based</b>		
VI	517	124
VI + D	1526	847

<sup>a</sup>VI: visual inspection.  
<sup>b</sup>VI + D: visual inspection and dermoscopy.  
<sup>c</sup>Not applicable.

**Table 2.** Extrapolation of estimated sensitivity and specificity differences applied to a hypothetical cohort of 1000 lesions<sup>a</sup>.

	Sensitivity <sup>a</sup>		Fixed specificity <sup>b</sup>		Fixed sensitivity <sup>b</sup>		Specificity <sup>c</sup>	
	True posi- tive, n	False nega- tive, n	False posi- tive, n	True nega- tive, n	True posi- tive, n	False nega- tive, n	False posi- tive, n	True nega- tive, n
<b>10% prevalence</b>	— <sup>d</sup>	—	180	720	80	20	—	—
VI <sup>e</sup>	79	21	—	—	—	—	207	693
VI + D <sup>f</sup>	93	7	—	—	—	—	9	891
<b>17% prevalence</b>	—	—	166	664	136	34	—	—
VI	134	36	—	—	—	—	191	639
VI + D	158	12	—	—	—	—	8	822
<b>53% prevalence</b>	—	—	94	376	424	106	—	—
VI	419	111	—	—	—	—	108	362
VI + D	493	37	—	—	—	—	5	465

<sup>a</sup>The dermoscopy test had a sensitivity of 79%, and the visual inspection and dermoscopy test had a sensitivity of 93%.  
<sup>b</sup>Both tests had a fixed specificity and fixed sensitivity of 80%.  
<sup>c</sup>The dermoscopy test had a specificity of 77%, and the visual inspection and dermoscopy test had a specificity of 99%.  
<sup>d</sup>Not applicable.  
<sup>e</sup>VI: visual inspection.  
<sup>f</sup>VI + D: visual inspection and dermoscopy.

Discussion

Recent advancements in learning algorithms using dermoscopic images, particularly deep learning techniques like convolutional neural networks (CNNs), have shown promise in improving diagnostic accuracy. In a systematic review [5] of 19 studies conducted between 2017 and 2021, CNNs demonstrated comparable or improved diagnostic accuracy compared to dermatologists. However, it is important to note that these studies primarily focused on melanoma due to its significant risk, leaving a gap in research specifically targeting KCs. Further research dedicated to KC diagnosis is crucial for a comprehensive evaluation of these conditions.

The authors of the review [3] postulated that adjunctive dermoscopy may aid specialists in identifying BCC. However, the results should be considered suggestive rather than conclusive, given the marked heterogeneity and concerns about the methodological quality of the included studies. Further investigation is required to determine any definitive benefit of dermoscopy for BCC diagnosis. Clear identification of evaluator expertise is essential to ensure meaningful results. Moreover, additional evaluation of the use of formal algorithms may benefit clinicians in varying levels of care. The ubiquity of KCs and risks of misdiagnosis underscore the need for transparent reporting of future studies to optimize diagnostic tools and improve outcomes for patients with suspicious skin lesions.

Conflicts of Interest

RPD is a joint coordinating editor for *Cochrane Skin*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology* (JAAD), and a podcast editor for the *Journal of Investigative Dermatology* (JID). He is a coordinating editor representative on the Cochrane Council. He is editor in chief of *JMIR Dermatology*. TES is an editorial board member at large for *JMIR Dermatology*. RPD receives editorial stipends (JAAD and JID), royalties (*UpToDate*), and expense reimbursement from *Cochrane Skin*.

Editorial Notice

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## Abbreviations

**BCC:** basal cell carcinoma

**CNN:** convolutional neural network

**KC:** keratinocyte carcinoma

**SROC:** summary receiver operating characteristic

**VI:** visual inspection

*Edited by CC Chi; submitted 03.08.22; peer-reviewed by H Shakshouk, C Sibbald, J Solomon, V Long; comments to author 23.02.23; revised version received 18.07.23; accepted 03.02.24; published 07.03.24.*

*Please cite as:*

*Klein CM, Sivesind TE, Dellavalle RP*

*From the Cochrane Library: Visual Inspection and Dermoscopy, Alone or in Combination, for Diagnosing Keratinocyte Skin Cancers in Adults*

*JMIR Dermatol* 2024;7:e41657

URL: <https://derma.jmir.org/2024/1/e41657>

doi: [10.2196/41657](https://doi.org/10.2196/41657)

PMID: [38451581](https://pubmed.ncbi.nlm.nih.gov/38451581/)

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Research Letter

# Does Male Skin Care Content on Instagram Neglect Skin Cancer Prevention?

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## Abstract

This research letter assesses male skin care content on social media in order to bring to light the lack of content regarding skin cancer prevention posted on Instagram for male audiences.

(*JMIR Dermatol* 2024;7:e50431) doi:[10.2196/50431](https://doi.org/10.2196/50431)

**KEYWORDS**

men; male; male skin care; male skincare; sunscreen; sun protection; photoprotection; anti-aging; skin cancer prevention; Instagram; social media; marketing; advertising; dermatology; dermatologist; skin; man; oncology; oncologist

## Introduction

Social media platforms can be efficient and engaging avenues for delivering information to target audiences [1]. A recent survey showed that 42% (n=1060) of US adults obtain health care information via social media, and 45% of respondents would take health-related actions after viewing medical content on these platforms [1]. Social media outreach regarding male skin care and sun protection may be an unrealized opportunity as an effective approach for skin cancer prevention, especially considering that men comprised most new skin cancer cases worldwide in 2020 (men: n=896,192, 59%; women: n=626,516, 41%; calculated based on data from Sung et al [2]), including cases of melanoma (men: n=173,844, 54%; women: n=150,791, 46%) and nonmelanoma (men: n=722,348, 60%; women: n=475,725, 40%) of the skin. Despite there being scientific evidence that consistent topical sunscreen use aids in the prevention of most skin cancers, the vast majority of men often neglect sunscreen compared to women, statistically [3].

Furthermore, male skin could also be more susceptible to UV damage, photoaging, and greater levels of UV exposure [4]. These patterns may be associated with a lack of tailored messaging from sources of health information [3]. Traditional advertising for male-focused skin care was mostly related to beard care, razors, and shaving products, and men historically were less likely to be receptive to targeted marketing content overall [5]. However, social media may have shifted attitudes such that influencer endorsements are now the most reliable form of outreach to both men and women [6].

## Methods

We aimed to evaluate male skin care social media on Instagram (Meta Platforms) and highlight any potential gaps in content related to sun safety and sunscreen use. Independent researchers investigated the following five relevant Instagram hashtags from January through March 2023: #maleskincare, #skincareformen, #skincaremen, #maleskincareroutine, and

#maleskincareproducts. A total of 60 top posts were collected for each hashtag, after excluding posts with no likes, accounts with <20 followers, and videos. Posting dates, account names, followers, likes, and types of products advertised were recorded. A third reviewer categorized each post (N=300) by the topic or product discussed, as follows: beard/hair care, antiaging, cleansing, skin care routine, skin care educational infographics, acne, sunscreen, moisturizers, fragrance, or scar care.

Results

Sunscreen comprised only 4.7% (14/300) of all topics or products promoted, while skin care routines were the most

common (83/300, 27.7%; Table 1). The “skin care routine” category encompassed posts that focused on product lines or groups of products that could be used in a skin care routine, rather than centering on 1 product. Posts regarding beard/hair care (43/300, 14.3%), antiaging (45/300, 15%), cleansing (35/300, 11.7%), educational infographics about general skin care (31/300, 10.3%), acne (4/300, 1.3%), moisturizers (39/300, 13%), fragrance (1/300, 0.3%), and scar care (5/300, 1.7%) were also examined.

Table 1. Numbers and percentages of male skin care Instagram posts by topic.

Topic discussed	#maleskincare posts (N=60), n	#skincareformen posts (N=60), n	#skincaremen posts (N=60), n	#maleskincareroutine posts (N=60), n	#maleskincareprod-ucts posts (N=60), n	Posts (N=300) by topic, n (%)
Beard/hair care	9	7	9	5	13	43 (14.3)
Antiaging	7	8	11	15	4	45 (15)
Cleansing	6	9	6	4	10	35 (11.7)
Skin care routine	19	13	19	18	14	83 (27.7)
Skin care educa-tional infographic	7	14	2	1	7	31 (10.3)
Acne	1	1	1	1	0	4 (1.3)
Sunscreen	2	2	5	0	5	14 (4.7)
Moisturizers	9	6	6	11	7	39 (13)
Fragrance	0	0	1	0	0	1 (0.3)
Scar care	0	0	0	5	0	5 (1.7)

Discussion

While the literature has suggested that men are motivated to use sunscreen due to prior knowledge of skin cancer risk reduction and a desire to appear younger [3], Instagram content related to sunscreen failed to address these factors. Shifting the focus of male skin care advertising may lead to greater interest in preventative measures and mitigate rising rates of skin cancer morbidity and mortality in men. Coupling sun protection and sunscreen promotion with the already substantial content on antiaging products may be promising, as sunscreen is known

to have antiaging benefits. Interestingly, compared to women, men were more likely to rely on straightforward messaging and the credibility of the social media influencer when considering a product’s advantages and drawbacks [6]. Credentialed dermatologists therefore could play an important role in social media outreach and recommendations to men about sunscreen use, in conjunction with exploiting the more subtle marketing tactics that demonstrated prior success with male consumers [5]. This study underscores an opening for social media users and influencers to bring greater attention to an underrepresented issue.

Conflicts of Interest

RPD is the editor-in-chief of *JMIR Dermatology*, an editor of *Cochrane Skin*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology (JAAD)*, and a *Cochrane Council* cochair. RPD receives editorial stipends (*JMIR Dermatology*), royalties (*UpToDate*), and expense reimbursement from *Cochrane*.

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*Edited by R Rodriguez; submitted 30.06.23; peer-reviewed by J Makin, A Black; comments to author 17.01.24; revised version received 30.01.24; accepted 18.02.24; published 13.03.24.*

*Please cite as:*

Carboni A, Martini O, Kirk J, Marroquin NA, Ricci C, Cheng M, Szeto MD, Pulsipher KJ, Dellavalle RP

*Does Male Skin Care Content on Instagram Neglect Skin Cancer Prevention?*

JMIR Dermatol 2024;7:e50431

URL: <https://derma.jmir.org/2024/1/e50431>

doi: [10.2196/50431](https://doi.org/10.2196/50431)

PMID: [38477962](https://pubmed.ncbi.nlm.nih.gov/38477962/)

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Research Letter

# Inequities in Technology Access and Digital Health Literacy Among Patients With Dermatologic Conditions: Cross-Sectional Analysis of the National Health Interview Survey

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## Abstract

Certain sociodemographic factors are associated with low technology access and digital healthy literacy.

(*JMIR Dermatol* 2024;7:e51511) doi:[10.2196/51511](https://doi.org/10.2196/51511)

**KEYWORDS**

teledermatology; telemedicine; telehealth; health care research; health care disparities; digital health literacy; technology access; access; accessibility; health literacy; digital literacy; disparities; disparity; equity; inequity; inequities; dermatology; dermatological; skin; cross-sectional; survey; surveys; national; HINTS; digital divide

## Introduction

As telemedicine expands, disparities in this care format should be identified and addressed. Technology access (TA) and digital health literacy (DHL)—defined by the ability to seek and appraise health information from electronic sources—are required for patients to utilize telemedicine successfully [1]. Dermatology is well suited for telemedicine due to the ability to conduct cutaneous exams with asynchronous photographs. The increased utilization of telemedicine makes it critical to identify vulnerable populations with dermatologic needs who may be unable to fully access this modality of care. Studies have shown that certain populations are less likely to participate in teledermatology visits; however, TA and DHL rates have not been described [2]. Using the National Health Interview Survey (NHIS), we sought to identify factors associated with low levels of TA and DHL among people with dermatologic conditions [3].

## Methods

**Ethical Considerations**

All NHIS respondents provided oral consent prior to participation, which was voluntary. The Institutional Review Board of the Boston Children's Hospital reviewed and exempted this study since it does not include human subjects research as defined in federal regulations (45 CFR 46.102; IRB-P00036281).

**Study Design**

Participants throughout the United States were randomly selected and queried by NHIS personnel regarding their skin conditions or those of their children. The demographic data obtained included sex, age, birth country, citizenship, income, language, and insurance. Low TA was defined by reports of access to 1 or none of the following: cell phones and internet. Low DHL was defined by reports of performing 1 or none of the following health-related technology usage behaviors: using a phone or computer to receive medical information, schedule

provider appointments, fill prescriptions, email providers, look up health information, or access chat groups for health information [3]. Multivariable logistic regression was used to identify factors associated with low TA and DHL. Between-group comparisons were performed via 2-tailed *t* tests for continuous variables and Wald chi-square tests for categorical variables. Sampling weights were used to account for selection variability from the complex survey design.

Results

In 2017, a total of 26,742 adults responded (response rate: 80.7%); 7.9% (n=2113) reported a skin issue for themselves or their children. Among respondents with skin issues, 23.3%

(492/2113) reported low TA, and 66.8% (1411/2113) reported low DHL. In this population, low TA was significantly associated with older age (odds ratio [OR] 1.71, 95% CI 1.54-1.91; *P*<.001), Hispanic ethnicity (OR 2.68, 95% CI 1.56-4.60; *P*<.001), living below the poverty level (OR 1.86, 95% CI 1.14-3.04; *P*=.01), public insurance (OR 2.36, 95% CI 1.46-3.82; *P*<.001), and no insurance (OR 1.99, 95% CI 1.04-3.82; *P*=.04). These factors, male sex (OR 1.70, 95% CI 1.33-2.18; *P*<.001), and Black race (OR 1.77, 95% CI 1.08-2.91; *P*=.02) were associated with low DHL (Table 1). In the total population, these demographic factors were similarly significant; however, a non-English interview language was also associated with low TA and DHL.

**Table 1.** Multivariate model of sociodemographic factors affecting low technology access and digital health literacy among patients with dermatologic issues from the 2017 National Health Interview Survey.

Characteristics	Multivariable model of low technology access		Multivariable model of low digital health literacy	
	Odds ratio (95% CI)	<i>P</i> value	Odds ratio (95% CI)	<i>P</i> value
<b>Sex</b>				
Female (reference)	N/A <sup>a</sup>	N/A	N/A	N/A
Male	1.29 (0.98-1.68)	.07	1.70 (1.33-2.18)	<.001
Age (increase by 10 years)	1.71 (1.54-1.91)	<.001	1.14 (1.06-1.22)	<.001
<b>Race and ethnicity</b>				
White non-Hispanic (reference)	N/A	N/A	N/A	N/A
Asian non-Hispanic	1.30 (0.49-3.41)	.60	0.46 (0.23-0.89)	.02
Black non-Hispanic	1.70 (0.90-3.21)	.10	1.77 (1.08-2.91)	.02
Other non-Hispanic	1.30 (0.49-3.03)	.66	0.68 (0.30-1.53)	.34
Hispanic	2.68 (1.56-4.60)	<.001	2.19 (1.30-3.68)	.003
<b>Language</b>				
Other (reference)	N/A	N/A	N/A	N/A
English only	1.29 (0.56-2.95)	.55	1.02 (0.23-4.42)	.98
<b>US citizenship</b>				
No (reference)	N/A	N/A	N/A	N/A
Yes	0.53 (0.24-1.20)	.13	0.45 (0.19-1.07)	.07
<b>Poverty threshold</b>				
Above poverty threshold (reference)	N/A	N/A	N/A	N/A
Below poverty threshold	1.86 (1.14-3.04)	.01	1.85 (1.05-3.27)	.04
<b>Saw general physician in the last year</b>				
Yes (reference)	N/A	N/A	N/A	N/A
No	0.95 (0.67-1.35)	.77	1.92 (1.42-2.59)	<.001
<b>Insurance</b>				
Private insurance (reference)	N/A	N/A	N/A	N/A
Public insurance	2.36 (1.46-3.82)	<.001	1.64 (1.07-2.53)	.03
Uninsured	1.99 (1.04-3.82)	.04	2.09 (1.09-4.02)	.03
Unknown insurance	1.10 (0.79-1.54)	.57	0.93 (0.69-1.27)	.65

<sup>a</sup>N/A: not applicable.



The proportion of patients with skin issues and low TA (492/2113, 23.3%) or low DHL (1411/2113, 66.8%) was significantly smaller when compared to patients without skin issues (low TA: 6649/24,629, 27%;  $P=.001$ ; low DHL: 19,842/26,742, 74.2%;  $P<.001$ ).

## Discussion

We identified older age, Hispanic ethnicity, poverty, and inadequate health insurance as risk factors for low TA and DHL among people reporting dermatologic issues, highlighting the importance of paying special attention to patient populations who are vulnerable to the widening gap in telemedicine access [4-6]. Male sex and Black race were associated with low DHL but not with low TA, suggesting that while these groups may have tools to access health care information, they may not know about these resources or have difficulties with utilizing them. While our study is limited by the survey's self-reported nature,

self-perceptions of TA or DHL may be more pertinent to health care technology use than objective measures.

Our results indicate that sociodemographic factors should be considered when developing telemedicine platforms for dermatologic care. Providers and office staff should ask all patients about their TA before offering telemedicine visits, and they should be aware that even patients with phones or computers may not know how to use these devices to access health care. Dermatology clinics should have trained staff to serve people who need additional assistance in accessing web-based appointments. Trust (or lack thereof) in digital health should also be considered, particularly among historically marginalized groups. On the state or national level, funding could be allocated to build community programs that promote digital health education. As telemedicine expands, it is important that practice changes do not exacerbate existing disparities for vulnerable patients.

## Conflicts of Interest

None declared.

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## Abbreviations

**DHL:** digital health literacy

**NHIS:** National Health Interview Survey

**OR:** odds ratio

**TA:** technology access

*Edited by R Dellavalle; submitted 03.08.23; peer-reviewed by J Bjerkan, V Brahmhatt; comments to author 12.10.23; revised version received 29.01.24; accepted 06.02.24; published 22.03.24.*

*Please cite as:*

Linggonegoro D, Williams K, Hlobik M, Huang J

*Inequities in Technology Access and Digital Health Literacy Among Patients With Dermatologic Conditions: Cross-Sectional Analysis of the National Health Interview Survey*

*JMIR Dermatol* 2024;7:e51511

URL: <https://derma.jmir.org/2024/1/e51511>

doi: [10.2196/51511](https://doi.org/10.2196/51511)

PMID: [38517468](https://pubmed.ncbi.nlm.nih.gov/38517468/)

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Research Letter

# A Survey of Demographics and Treatments in Melanoma Case Reports: Retrospective Bibliometric Analysis

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## Abstract

Melanoma case reports show variations in treatment by age and sex.

(*JMIR Dermatol* 2024;7:e56684) doi:[10.2196/56684](https://doi.org/10.2196/56684)

**KEYWORDS**

melanoma; surgery; chemotherapy; immunotherapy; radiation therapy; case reports

## Introduction

Case reports provide valuable insights into clinical practices. However, dermatological case reports are not perfect, with some diseases being overreported and others having sex imbalances relative to patient populations [1]. Melanoma is a skin cancer that has differences in outcomes based on patient demographics [2,3]; thus, it is important to understand the treatments reported in case reports and their demographic variations. Therefore, we assessed the demographics represented in melanoma case reports, the various treatment modalities listed, and how treatments vary by demographics.

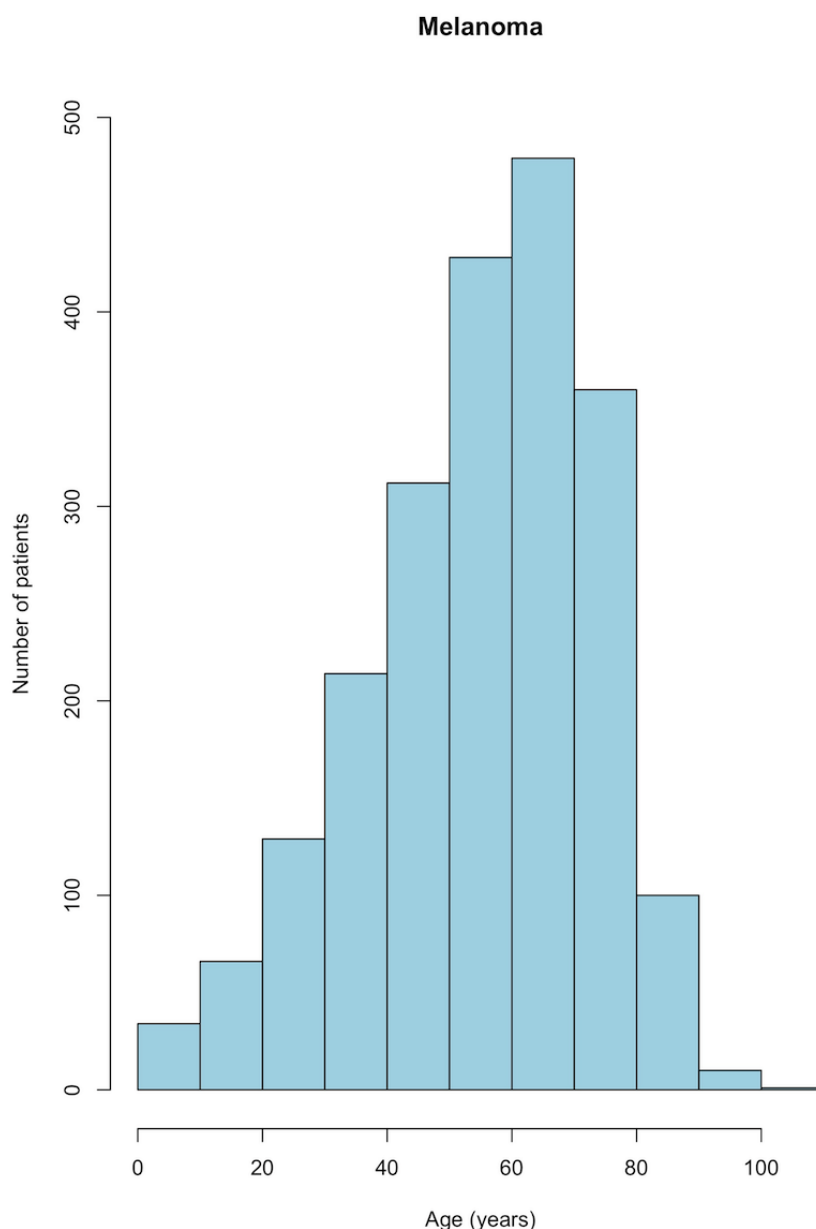
## Methods

To explore the demographics of patients in PubMed-listed case reports, we used techniques previously described [1,4]. Patients

with melanoma and their treatment regimens were determined via string match. Included patients had the text “melanoma” listed in their case report summary. Each treatment modality was included in the analysis if its name was found in the case report summary. Age and sex information was listed in the PMC-Patients database. Differences in treatment by sex and mean age were determined by calculating odds ratios (ORs). Analysis was performed using R (version 4.2.2; R Foundation for Statistical Computing).

## Results

Of the 167,034 patients listed in the PMC-Patients database, 2133 (1.3%) had case reports that mentioned “melanoma.” The mean age of patients with melanoma was 55.4 (SD 18.3) years (Figure 1), and 1173 (55%) of the 2133 patients were male.

**Figure 1.** Age histogram of patients with melanoma.

Of the 2133 patients, the most mentioned treatment modality was surgery ( $n=693$ , 32.5% patients). The least frequently mentioned modality of treatment was radiation therapy ( $n=156$ , 7.3% patients; [Table 1](#)). Of the chemotherapies mentioned, the most common was dacarbazine ( $n=102$ , 4.8% patients). Of the immunotherapies mentioned, the most common was ipilimumab ( $n=341$ , 16% patients; [Table 1](#)).

Female patients were significantly more likely to receive surgery than male patients (OR 1.27, 95% CI 1.06-1.53;  $P=.009$ ), and

male patients were significantly more likely to receive immunotherapy (OR 1.34, 95% CI 1.10-1.62;  $P=.003$ ). There were no significant differences by sex for receiving radiation therapy ( $P=.84$ ) or chemotherapy ( $P=.49$ ). Those older than the median age of 58 years were more likely to receive immunotherapy (OR 1.94, 95% CI 1.60-2.35;  $P<.001$ ). There were no significant differences by age for surgery ( $P=.11$ ), radiation therapy ( $P=.09$ ), or chemotherapy ( $P=.42$ ).

**Table 1.** Treatment modalities, chemotherapies, and immunotherapies in case reports (n=2133).

Mentions	Case report, n (%)
<b>Treatment modality</b>	
<b>Surgery</b>	
Included	693 (32.5)
Not included	1440 (67.5)
<b>Radiation therapy</b>	
Included	156 (7.3)
Not included	1977 (92.7)
<b>Chemotherapy</b>	
Included	613 (28.7)
Not included	1520 (71.3)
<b>Immunotherapy</b>	
Included	597 (28)
Not included	1536 (72)
<b>Chemotherapy</b>	
Dacarbazine	102 (4.8)
Cisplatin	88 (4.1)
Paclitaxel	62 (2.9)
Temozolomide	61 (2.9)
Carboplatin	61 (2.9)
Nab-paclitaxel	6 (0.3)
<b>Immunotherapy</b>	
Ipilimumab	341 (16)
Nivolumab	272 (12.8)
Pembrolizumab	182 (8.5)
Atezolizumab	7 (0.3)
T-VEC <sup>a</sup>	7 (0.3)
Relatlimab	1 (0.05)

<sup>a</sup>T-VEC: talimogene laherparepvec.

## Discussion

This study explores the demographics represented in melanoma case reports, their treatments, and how treatments vary by demographics. The most common treatment modality was surgery, and the least common treatment modality was radiation therapy. There were significant differences in treatment modalities between sexes, with more male patients receiving immunotherapy and more female patients receiving surgery. Finally, older patients were more likely to receive immunotherapy. Previous work has highlighted the increased stage of melanoma at diagnosis in male patients [3]. Thus, it is plausible that some variations in treatment could be secondary

to staging differences. Previous work looking at patients with metastatic melanoma from 2011 to 2015 found that older patients were less likely to receive immunotherapy, despite its greater survival benefit [5]. These differences may stem from practice changes or publication bias. If treatment variations were found to be present in clinical practice, such variations in management by sex could lead to suboptimal patient care and outcomes. Our study was limited in that the use of string-matched case report information may have missed some treatments. Additionally, the PMC-Patients database did not include information on race and ethnicity. Our study highlights the need for more research on treatment variations by demographics in melanoma cases.



## Conflicts of Interest

BU is an employee of Mount Sinai and has received research funds (grants paid to the institution) from Incyte, Rapt Therapeutics, and Pfizer. He is also a consultant for Arcutis Biotherapeutics, Bristol Myers Squibb, Castle Biosciences, Fresenius Kabi, Pfizer, Sanofi, and UCB. JU is an employee of Mount Sinai and is a consultant for AbbVie, Bristol Myers Squibb, Castle Biosciences, Dermavant, Janssen, Menlo Therapeutics, Mitsubishi Tanabe Pharma America, and UCB. RO, JN, and NG declare no relevant conflicts of interest.

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## Abbreviations

**OR:** odds ratio

*Edited by R Dellavalle; submitted 23.01.24; peer-reviewed by A Ahmadi, M Ben Amar, M Yadav; comments to author 21.03.24; revised version received 22.03.24; accepted 10.04.24; published 22.04.24.*

Please cite as:

O'Hagan R, Ngandjui J, Ungar B, Ungar J, Gulati N

A Survey of Demographics and Treatments in Melanoma Case Reports: Retrospective Bibliometric Analysis

*JMIR Dermatol* 2024;7:e56684

URL: <https://derma.jmir.org/2024/1/e56684>

doi: [10.2196/56684](https://doi.org/10.2196/56684)

PMID: [38648085](https://pubmed.ncbi.nlm.nih.gov/38648085/)

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Letter to the Editor

# Strengthening TikTok Content Analysis in Academia Using Follower Count and Engagement

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**Related Article:**

Comment on: <http://www.jmir.org/2023/1/e48635/>

(*JMIR Dermatol* 2024;7:e54439) doi:[10.2196/54439](https://doi.org/10.2196/54439)

**KEYWORDS**

social media; skin of color; skin of colour; representation; TikTok; atopic dermatitis; dermatology; dermatologist

## Letter

We read with great interest Abdelnour et al's paper titled "Skin of color representation for atopic dermatitis on TikTok: cross-sectional analysis" [1] and express our gratitude for the findings.

Using the search term #eczema in July 2022, the study evaluated the representation of patients with skin of color (SoC) and the quality of atopic dermatitis videos on TikTok. A review of 119 eligible videos revealed that physicians produced significantly higher-quality content than nonphysicians but may underrepresent SoC. Viewer count was a secondary measure, with its mean value lower for physicians compared to nonphysicians, though the difference was not significant. The authors noted that this lower viewer count may limit the impact of better SoC representation in physicians' videos. However, we believe that this conclusion cannot be made without further analysis.

Using the viewer count, one may infer that physician content is less popular. However, in instances where there is an insignificant difference in viewer count between sources, this measure alone provides limited information. On TikTok, a view is "counted" within the 3 seconds of playback, meaning a user does not have to view the entire video. Additionally, the viewer count corresponds to the number of times a video has been played rather than unique views [2]. These factors, coupled with TikTok automatically replaying its videos once they finish,

mean the viewer count does not reflect the number of individuals that have viewed a video.

Follower count and engagement (likes, saves, shares, and comments) provide additional context. These measures, alongside viewer count, enable the calculation of a video's engagement rate and reach percentage (view rate). Engagement rate estimates the percentage of viewers that engage with a video ( $\text{engagement} \times 100 / \text{viewer count}$ ) [3], whereas reach percentage estimates the percentage of a source's followers that view a video ( $\text{viewer count} \times 100 / \text{followers}$ ) [2]. Marketing companies suggest a "good" engagement rate lies between 1% to 5% [3] and define the average reach percentage as 14.49% [2]. To demonstrate the application of these formulas, we reviewed the results from Pagani et al [4] below.

This cross-sectional study screened the top 50 videos when searching "slugging" (defined as thickly coating the skin with a petrolatum-based ointment like Vaseline and can form the final step of a nighttime skincare routine [4]) on TikTok and analyzed their upload source, content, and quality. Videos were categorized by source into health care providers, influencers, and others. Assessing follower count and engagement (likes and comments) revealed that although influencers have a nonsignificantly lower median viewer count than health care providers (94,500 vs 102,150), their videos had a greater reach percentage (65.3% vs 24.9%) and engagement rate (8.1% vs 4.3%). These values suggest that influencers created more

engaging content, which may be better promoted by TikTok's algorithm and result in a higher viewer count long term.

We observe that TikTok content analysis is becoming a prevailing means of understanding public dermatology-related information, an unsurprising trend since the platform's video-based format favors dermatology's visual nature, and

believe follower count and engagement aid this analysis. Regarding the work of Abdelnour et al [1], these measures may assist in determining the impact of improved SoC representation in physician-produced atopic dermatitis videos. If these measures are low, targeted recommendations for improving engagement and reach can be suggested, such as integrating popular trends or cross-promoting content.

## Conflicts of Interest

None declared.

## Editorial Notice

The corresponding author of "Skin of Color Representation for Atopic Dermatitis on TikTok: Cross-Sectional Analysis" declined to respond to this letter.

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## Abbreviations

**SoC:** skin of color

*Edited by T Leung; submitted 05.12.23; this is a non-peer-reviewed article; accepted 11.01.24; published 30.01.24.*

*Please cite as:*

*Ramjee S, Hasan ZU*

*Strengthening TikTok Content Analysis in Academia Using Follower Count and Engagement*

*JMIR Dermatol* 2024;7:e54439

URL: <https://derma.jmir.org/2024/1/e54439>

doi: [10.2196/54439](https://doi.org/10.2196/54439)

PMID: [38289654](https://pubmed.ncbi.nlm.nih.gov/38289654/)

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Case Report

# An Unusual Case of Anderson-Fabry Disease: Case Report

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## Abstract

Angiokeratoma is a group of capillary malformations characterized by the formation of variably sized dark red hyperkeratotic papules. Initially, it was believed that angiokeratoma corporis diffusum was a telltale sign of Anderson-Fabry disease; however, current consensus states that it is also seen in various other lysosomal enzymatic deficiencies. In this report, we present the case of a 12-year-old boy who developed angiokeratoma corporis diffusum with sensorineural deafness, acroparesthesias, and renal involvement.

(*JMIR Dermatol* 2024;7:e49573) doi:[10.2196/49573](https://doi.org/10.2196/49573)

**KEYWORDS**

angiokeratoma; Fabry disease; angiokeratoma corporis diffusum; vascular; capillary; capillaries; blood vessel; lysosome; lysosomal; enzyme; enzymatic; case report; circulatory; skin; dermatology; dermatological

## Introduction

Angiokeratoma is a group of capillary malformations characterized by the formation of variably sized dark red hyperkeratotic papules. The capillaries are dilated in the papillary dermis with reactionary epidermal hyperplasia and hyperkeratosis. Clinically, various patterns of angiokeratoma have been identified, namely, solitary isolated or multiple angiokeratomas, angiokeratoma of Fordyce, angiokeratoma corporis diffusum, angiokeratoma circumscripta, and angiokeratoma of Mibelli. The generalized variant of angiokeratoma is known as angiokeratoma corporis diffusum [1,2].

Initially, it was believed that angiokeratoma corporis diffusum is a telltale sign of Anderson-Fabry disease, but current consensus states that it is also seen in various other lysosomal enzymatic deficiencies. In this case report, we present the case of a 12-year-old boy who developed angiokeratoma corporis diffusum with sensorineural deafness, acroparesthesias, and renal involvement.

## Case Report

A 12-year-old boy with average intelligence presented to us with multiple pinhead-sized dark red papular eruptions all over his body since the age of 6. The lesions first appeared on the legs and gradually increased over several years, involving bilateral limbs and trunks, with clustering over the genitalia (Figure 1A, 1B, and 1C). Upon examination, discreet and grouped nonblanchable angiomatous papules were observed, distributed symmetrically across the entire body, with relative sparing of the face, palms, soles, and mucosa. There was the presence of hyperkeratosis over some of the angiomatous papules.

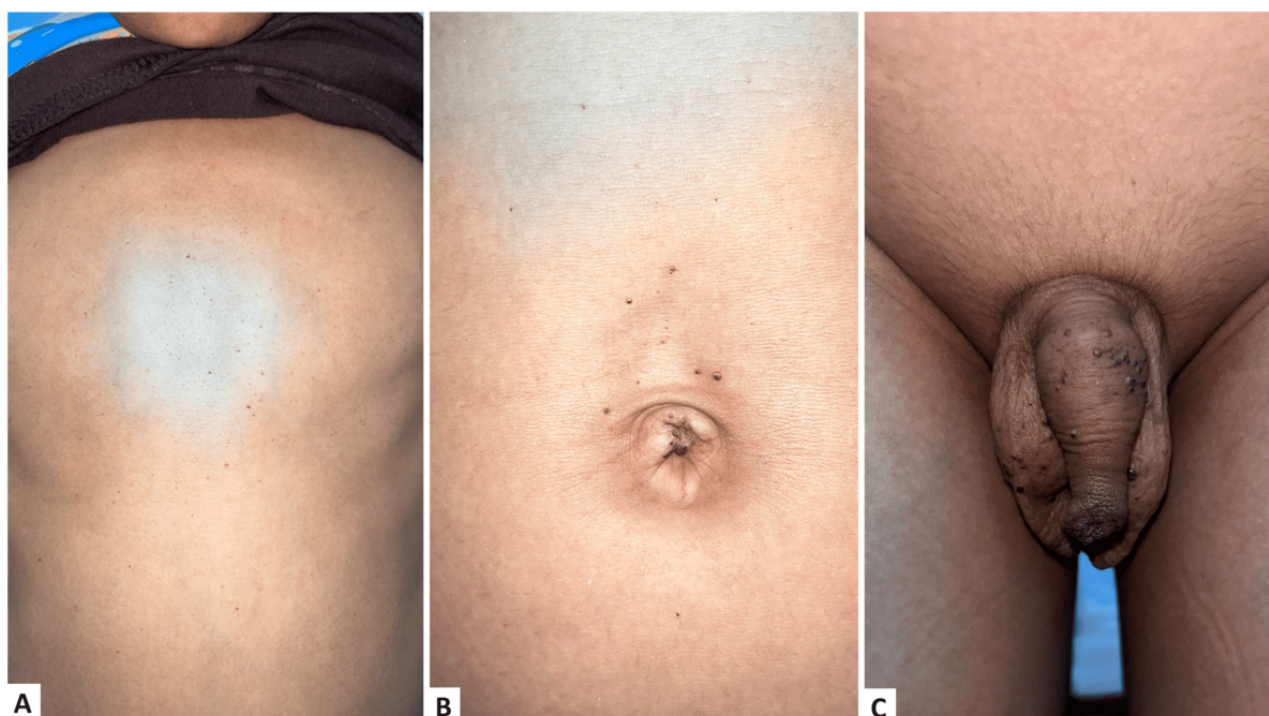
The patient confirmed that the lesions would bleed when scratched. The patient also reported experiencing generalized asthenia and a low-grade fever 4 months prior. On further inquiry, the patient revealed that he had shooting pains starting from the back and radiating to bilateral lower limbs for the past 3 months. However, until his current visit, his family had not sought any treatment for his condition.

The child had no history of seizures, visual disturbances, hearing loss, or atypical facial features. There was no history of similar skin lesions or associated features in any family members. The child also had bilateral cervical lymphadenopathy. On pure tone audiometry, there was sensorineural hearing loss in both ears. No ocular abnormalities were detected on the slit lamp and fundus examination. Lab investigations revealed microcytic hypochromic anemia, thrombocytopenia, and hypoproteinemia. On further biochemical analysis, the child's leukocyte  $\alpha$ -Galactosidase A activity was very low (0.1 nmol/h/mL). The child's galactosidase alpha gene study revealed a missense mutation in  $\alpha$ -Galactosidase A. The remaining investigations and imaging (ie, electrocardiogram, high-resolution computed tomography, ultrasonography, and chest x-ray) were unremarkable.

Due to the patient's low socioeconomic status, a genetic study could not be carried out for the rest of the family members.

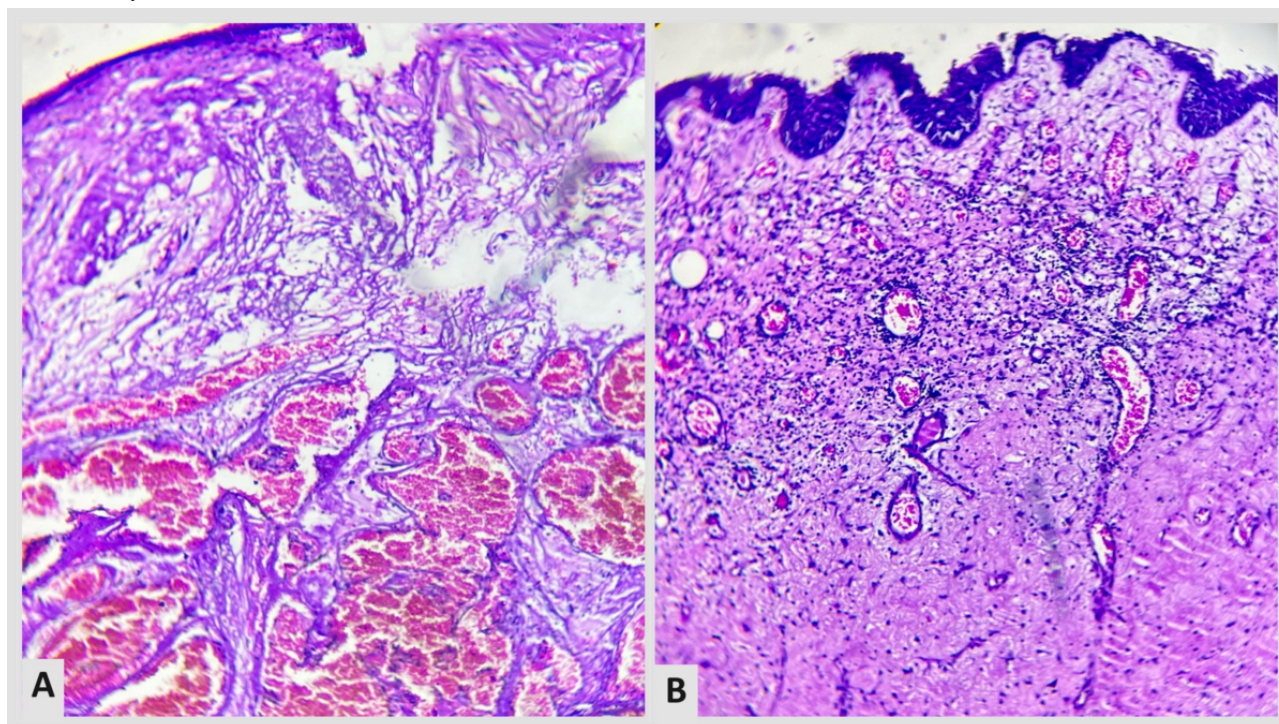
Upon histopathological evaluation, thin-walled ectatic capillaries having vacuolated endothelial cells were observed in the upper dermis. The epidermis had elongated rete ridges and hyperkeratosis (Figure 2A and 2B). Enzyme assay could not be done due to resource limitations and financial constraints. A diagnosis of angiokeratoma corporis diffusum was made. The course and prognosis of the disease were explained to the patient and his family. The large angiokeratomas were removed using radiofrequency ablation, and the patient is currently being managed with a multidisciplinary approach, including intravenous  $\alpha$ -Galactosidase A enzyme replacement therapy infusion. The case is still being followed up with a measure of improvement in his acroparesthesia following 3 months of treatment.

**Figure 1.** (A) discreet angiokeratoma over trunk; (B) clustered angiokeratoma over umbilicus; (C) clustered angiokeratoma over genitalia.





**Figure 2.** (A) hyperkeratosis with ectatic dermal blood vessels (hematoxylin and eosin; 100 times magnification under a microscope); (B) dilated capillaries lined by vacuolated endothelium.



## Discussion

Angiokeratoma corporis diffusum was described for the first time in 1898. Although Angiokeratoma corporis diffusum has often been used interchangeably with Anderson-Fabry disease, the latter may be associated with lysosomal defects, including fucosidosis, mannosidosis, sialidosis, Kanzaki disease, and monosialotetrahexosylganglioside gangliosidosis [3,4]. Anderson-Fabry disease is an X-linked disorder. In this disease, there is a deficiency in the enzyme  $\alpha$ -Galactosidase A, which is responsible for glycosphingolipid catabolism. This deficiency leads to the accumulation of glycosphingolipids, chiefly globotriaosylceramide (GL3) and a metabolite of GL3 called globotriaosylsphingosine (lyso-GL3) in various cells. This accumulation predominantly affects the kidney, heart, and nervous system, contributing to systemic involvement [5].

Fabry disease mutations are observed in around 1 in 22,000-40,000 male individuals, whereas atypical presentations are linked to approximately 1 in 1000-3000 male and 1 in 6000-40000 female individuals [6].

This condition can be categorized into 2 main types: a severe classical form, typically observed in men with no residual enzyme activity, and a milder nonclassical form. Classical Fabry disease is associated with neuropathic pain, cornea verticillate, and angiokeratoma. Over time, it can lead to issues like cardiac rhythm problems, hypertrophic cardiomyopathy, progressive renal failure, and stroke.

On the other hand, nonclassical Fabry disease, also known as late-onset or atypical Fabry disease, displays a more variable progression. Patients with this form are generally less severely affected, and their symptoms may be confined to 1 organ. Despite its X-linked inheritance pattern, women can also

experience Fabry disease symptoms, but their condition is typically less severe than that of men due to X-inactivation patterns in women [7].

Often, acroparesthesia in Anderson-Fabry disease is precipitated by emotional or physical stress, febrile illness, and prolonged temperature variation [8]. In our patient, acroparaesthesia was triggered by an episode of febrile illness.

Our patient also had hypoalbuminemia, an indicator of renal disease. Kidneys are one of the most commonly involved organs in Anderson-Fabry disease, often resulting in end-stage renal disease and a high mortality rate in untreated patients. Manifestations often mirror diabetic nephropathy's progression—initial hyperfiltration, followed by albuminuria, heavy proteinuria, and gradual kidney function decline. Tubular manifestations, though rarer, involve renal tubular acidosis, Fanconi syndrome, and impaired urine concentration. Renal involvement is attributed to GL3-induced inflammation and oxidative damage to the glomeruli and podocytes in the kidneys [9].

Fabry disease has no complete cure. To manage it, enzyme replacement ( $\alpha$ -Galactosidase A) is initiated upon diagnosis, irrespective of symptoms in affected male patients or those on renal therapy. Female carriers and male patients with low  $\alpha$ -Galactosidase A levels receive enzyme replacement only if they exhibit kidney, neurological, or heart issues. Patients with a history of long-term dialysis also receive enzyme replacement. Hypertension is managed with medications like angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Enzyme infusions (alpha or beta) are administered every 2 weeks based on body weight [6].

## Conclusions

This report highlights the high reliability of a thorough clinical evaluation for diagnosing atypical and unusual variants of

genodermatoses, including Anderson-Fabry disease. Angiokeratoma is a reliable clinical indicator when screening patients for Anderson-Fabry disease. Early identification of these lesions aids in early detection of the disease, enabling timely treatment.

## Declaration of Patient Consent

The patient's parent has given informed consent for the patient's images and other clinical information to be published in a medical journal. The patient's parent understands that the patient's name and initials will not be published and due efforts will be made to conceal his identity, but complete anonymity cannot be guaranteed.

## Data Availability

The data that support the findings of this series are available from the corresponding author upon reasonable request.

## Conflicts of Interest

None declared.

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## Abbreviations

**GL3:** globotriaosylceramide

*Edited by R Dellavalle; submitted 02.06.23; peer-reviewed by E Mengel, S Zhao; comments to author 08.08.23; revised version received 08.11.23; accepted 23.12.23; published 16.01.24.*

*Please cite as:*

Mohta A, Mohta A, Kumari P

An Unusual Case of Anderson-Fabry Disease: Case Report

JMIR Dermatol 2024;7:e49573

URL: <https://derma.jmir.org/2024/1/e49573>

doi: [10.2196/49573](https://doi.org/10.2196/49573)

PMID: [38227354](https://pubmed.ncbi.nlm.nih.gov/38227354/)

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Case Report

# Merkel Cell Carcinoma on the Face: Case Report

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## Abstract

Merkel cell carcinoma (MCC) is a rare primary neuroendocrine skin tumor that presents as a flesh-colored or bluish-red nodule on the face, neck, or head. Long-term ultraviolet radiation exposure and Merkel cell polyomavirus are associated with MCC pathogenesis. We present a case of MCC on the right cheek in a male patient aged 87 years. Our primary goal in presenting the case is to bring MCC, which is a diagnostic challenge, to the notice of dermatologists and oncologists, as early detection and prompt treatment are important. The patient had a significant past medical history, including diabetes mellitus, hypertension, dyslipidemia, stage 3 chronic kidney disease, benign prostatic hyperplasia, chronic hyponatremia, acute pancreatitis, essential thrombocytosis on hydroxyurea, and ischemic heart disease. The patient presented with a mildly swollen right upper lip showing a poorly defined, relatively homogeneous subcutaneous lesion with a history of persistence for 1.5 months. The clinical examination revealed a 5 × 3-cm nodular lesion on the right side of the cheek with swelling of the right upper lip. Immunohistochemistry markers and histopathological features confirmed the diagnosis of MCC. The patient was referred to the oncology department for further management. MCC of the skin is an aggressive lesion with a high risk of metastasis and recurrence, which is more common in immunocompromised people. Prompt management and treatment of MCC is essential because if left untreated, it can spread to other parts of the body and can also metastasize to lymph nodes and other organs. The patient is 87 years old and has a significant past medical history of diabetes mellitus, hypertension, dyslipidemia, chronic kidney disease stage 3, benign prostatic hyperplasia, chronic hyponatremia, acute pancreatitis, essential thrombocytosis on hydroxyurea, and ischemic heart disease. Currently, the patient presented with a mildly swollen right upper lip showing a poorly defined, relatively homogenous subcutaneous lesion with a history of persistence for 1.5 months. The clinical examination revealed a 5x3 cm nodular lesion on the right side of the cheek with swelling of the right upper lip. Immunohistochemistry markers results and histopathological features confirmed the diagnosis of Merkel cell carcinoma. The patient was referred to the oncology department for further management. Merkel cell carcinoma of the skin is an aggressive lesion with a high risk of metastasis and recurrence, which is more common in immunocompromised people. Prompt management and treatment of Merkel cell carcinoma is essential because if left untreated, it can spread to other parts of the body and can also metastasize to lymph nodes and other organs.

(*JMIR Dermatol* 2024;7:e56658) doi:[10.2196/56658](https://doi.org/10.2196/56658)

**KEYWORDS**

carcinoma; metastasis; lesion; biopsy; lesions; skin; Merkel; dermatology; nodules; cancer; oncology; lab; WBC: white blood cell; platelets; dermis; tumor; immunology; histology; histopathology; histopathological; immunological; immunohistochemistry

## Introduction

Merkel cell carcinoma (MCC) is a rare primary neuroendocrine skin tumor [1] that usually presents as a flesh-colored or bluish-red nodule on the face, neck, or head [2]. It primarily affects White men older than 65 years and immunocompromised people [3]. Long-term ultraviolet (UV) radiation exposure and

Merkel cell polyomavirus are associated with MCC pathogenesis. MCC patients often appear with a quickly developing, painless, hard, glossy, flesh-colored, or bluish-red intracutaneous nodule [4]. Here, we present a case of MCC in a male patient aged 87 years with a mildly swollen right upper lip showing a poorly defined, relatively homogeneous subcutaneous area with a history of persistence for 1.5 months.



Ethical Considerations

Ethical consent was obtained from the patient before reporting the case for using the patient’s images and clinical information in this paper. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity.

Case Report

The patient was aged 87 years and had a past medical history of diabetes mellitus, hypertension, dyslipidemia, stage 3 chronic kidney disease, benign prostatic hyperplasia, diabetic neuropathy, chronic hyponatremia, acute pancreatitis, essential thrombocytosis on hydroxyurea, and ischemic heart disease. He was also a hepatitis B carrier. The patient had a coronary artery bypass graft more than 30 years ago. He had a recent history of sphincterotomy and stone extraction from the common bile duct. He had spondylodegenerative changes of the cervical spine and spinal cord edema at the C3/C4 disc level. The patient presented with a mildly swollen right upper lip that had persisted for 1.5 months. Physical examination showed an erythematous

plaque on the right upper lip extending to the nasolabial fold, as shown in Figure 1. Induration and nodules were felt under the plaque. No pain or discharge were present. No enlarged lymph nodes were present. All other systems were reviewed and were negative.

The patient underwent a complete blood count, which showed that white blood cell count, platelet count, and creatinine were high; hemoglobin and hematocrit were low. A summary of the test results is provided in Table 1. Additional immunohistochemistry markers were as follows: TTF-1 (thyroid transcription factor-1) was negative and CK20 (cytokeratin 20) was positive in the tumor cells. Ki67 (Kiel 67) showed a high proliferative index. A summary of the immunohistochemistry results is provided in Table 2.

Immunohistochemistry markers confirmed the diagnosis of MCC and ruled out a metastatic deposit of small cell carcinoma of the lung. Histopathological features were also in favor of MCC. They are represented in Figure 2.

The patient was referred to the oncology department for further management.

Figure 1. Erythematous plaque on the right upper lip extending to the nasolabial fold. No lesions were seen on the oral mucosal surface.



Table 1. The results of recent laboratory tests.

Name	Results	Normal range
White blood cells, n×10 <sup>3</sup> /uL	16.4	3.6-11.0
Hemoglobin, g/dL	8.1	13.0-17.0
Hematocrit, %	25.2	40-50
Platelets, n×10 <sup>3</sup> /uL	850	150-410
Lactate dehydrogenase, U/L	167	105-222
Creatinine, mg/dL	1.67	0.70-1.20



**Table 2.** Immunohistochemistry results.

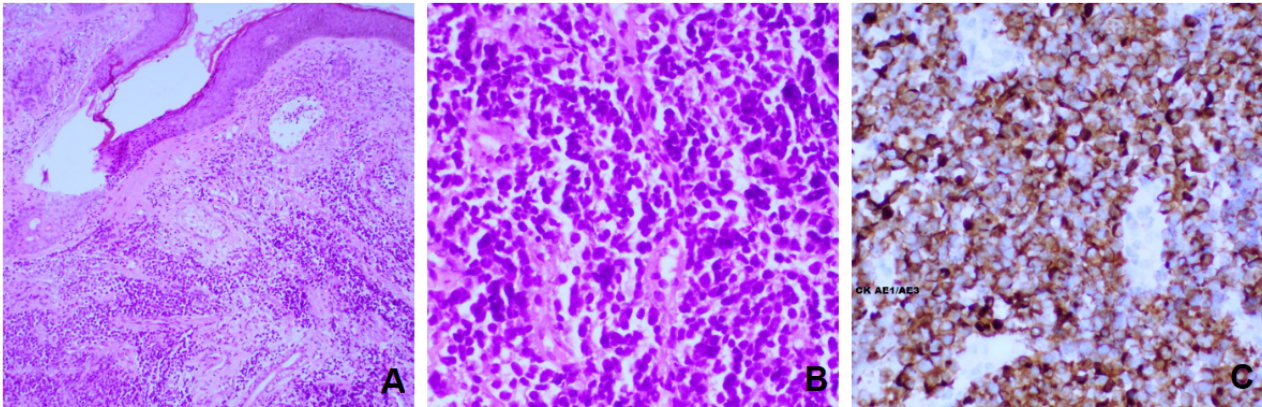
Name	Results
Synaptophysin	Diffusely positive in tumor cells
Chromogranin	Diffusely positive in tumor cells
CD <sup>a</sup> 56	Diffusely positive in tumor cells
Ki67 <sup>b</sup>	Shows a high proliferative index
CK <sup>c</sup> (AE 1/AE 3)	Positive with focal paranuclear staining
CD45	Negative in tumor cells
CD20	Negative in tumor cells
CD3	Negative in tumor cells
CD38	Negative in tumor cells
CD30	Negative in tumor cells
Melanin-A	Negative in tumor cells

<sup>a</sup>CD: cluster of differentiation.

<sup>b</sup>Ki67: Kiel 67.

<sup>c</sup>CK: cytokeratin.

**Figure 2.** (A) Lower power hematoxylin and eosin staining revealed skin with diffusely infiltrative tumor within the dermis. Prominent solar elastosis and telangiectatic blood vessels are seen in the superficial dermis. (B) On higher magnification, tumor cells can be seen to be composed of small round blue cells with a high nucleus to cytoplasm ratio, round/oval hyperchromatic nuclei with a finely stippled salt and pepper chromatic pattern, indistinct nuclei, and scant cytoplasm. Mitoses and apoptotic bodies are seen in between. Nuclear molding and crush artifacts are noted. (C) Positive cytokeratin (AE 1/AE 3) with focal paranuclear staining.



Discussion

MCC is a cutaneous neuroendocrine carcinoma that is aggressive and has a high tendency for metastasis. Because of the lack of symptoms, it is difficult to make an early diagnosis of MCC, which is often misinterpreted as a subcutaneous benign tumor, squamous cell carcinoma, or melanoma [5]. Some uncommon skin lesions, including MCC, require a high index of suspicion to be diagnosed. It is an uncommon and aggressive neuroendocrine skin tumor that accounts for fewer than 1% of all cutaneous malignancies. It often manifests as a red, purple, or violaceous firm, painless nodule or plaque. Because of its rarity, it is frequently confused with more common skin tumors [6]. The clinical differential diagnosis of MCC includes basal cell carcinoma, squamous cell carcinoma, melanoma, metastatic neuroendocrine carcinoma, lymphoma, and sebaceous carcinoma.

UV exposure and immunosuppression are the 2 primary etiological factors besides polyomavirus linked to an elevated risk of MCC. As determined by the UVB solar index, the regional incidence of MCC increases with increasing sun exposure. Most MCC cases are found in the skull, face, and neck regions, which are the most sun-exposed parts of the body [7]. Furthermore, many people who are diagnosed with MCC have a history of other sun-induced skin malignancies. Patients with suppressed or disordered immunity, such as those on immunosuppressive therapy for organ transplantation, hepatitis, or HIV infection, or those with B-cell malignancies such as multiple myeloma, non-Hodgkin lymphoma, and chronic lymphocytic leukemia, have a higher incidence of MCC [8]. Another similar case was reported in 2023 in an immunocompromised patient with diabetes and hepatitis B, suggesting that decreased immune surveillance in these patients results in increased viral replication and integration in the progenitor cells of MCC [9].

Surgical therapy is the foundation of treatment. It is normal practice to do a wide local excision with a clearance margin of 3 cm to 5 cm [10]. Lymph node dissection is generally recommended for patients with regional node metastases. In stage I and II illnesses, adjuvant radiation therapy is often suggested for the main site and lymph node basin. Chemotherapy is often reserved for patients with stage III illness [11]. Anti-programmed cell death protein 1/anti-programmed cell death ligand 1 (anti-PD-1/PD-L1) blocking immunotherapeutic drugs, such as pembrolizumab and avelumab, when administered as first-line treatment, lead to an objective response (ie, a partial response or a complete response) in as many as 50% to 70% of cases, making immunotherapy a promising new therapeutic option for advanced MCC [12]. Prompt management and

treatment of MCC is essential because if left untreated, it can spread to other parts of the body and can also metastasize to lymph nodes and other organs [13].

## Conclusion

MCC is distinguished by violaceous, red intradermal nodules in sun-exposed locations. MCC of the skin is an aggressive lesion with a high risk of metastasis and recurrence; long-term (5-year) survival rates range from 18% to 57% [14]. The primary goal of presenting this case is to bring MCC, which is a diagnostic challenge, to the notice of dermatologists and oncologists, as early detection and prompt treatment are important.

## Conflicts of Interest

None declared.

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## Abbreviations

**Anti-PD-1/PD-L1:** anti-programmed cell death protein 1/anti-programmed cell death ligand 1  
**CK20:** cytokeratin 20  
**Ki67:** Kiel 67  
**MCC:** Merkel cell carcinoma

**TTF-1:** thyroid transcription factor-1

**UV:** ultraviolet

**UVB:** ultraviolet B

**WBC:** white blood cell

*Edited by R Dellavalle, G Eysenbach; submitted 23.01.24; peer-reviewed by T Dicker, V Narayan; comments to author 06.02.24; revised version received 27.02.24; accepted 17.03.24; published 08.04.24.*

*Please cite as:*

*Alhaj SS, Qaderi FA, Ibrahim T, Almohammad M*

*Merkel Cell Carcinoma on the Face: Case Report*

*JMIR Dermatol 2024;7:e56658*

URL: <https://derma.jmir.org/2024/1/e56658>

doi: [10.2196/56658](https://doi.org/10.2196/56658)

PMID: [38512218](https://pubmed.ncbi.nlm.nih.gov/38512218/)

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Case Report

# Ichthyosiform Lichen Planus Pigmentosus in a 19-Year-Old Male Patient: Case Report

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## Abstract

Lichen planus pigmentosus (LPP) is a condition characterized by persistent and asymptomatic brownish-black-to-blue or purple-gray pigmentation, predominantly in the face and sun-exposed areas, commonly in dark-skinned individuals. Several clinical variants of LPP have been reported. However, the ichthyosiform type of LPP has not been reported. We present a 19-year-old male patient who presented with a 7-year history of asymptomatic grayish macules; patches with fine scales on the face, trunk, and upper extremities; and grayish plaques with thick “ichthyosiform” scales on the lower extremities. The diagnosis of LPP was proven by histopathological findings on both the macular and ichthyosiform plaques. Cluster differentiation (CD) 68 stain highlights the same density of pigment-laden macrophages in both the gray macule and the ichthyosiform plaque. The cause of LPP is unknown. Transcription factor anomalies may play a role in increased keratinization of lichen planus lesions. It can be assumed that the mechanism of the altered distribution of keratinization may occur on the ichthyosiform lesions in this patient. The terminology “ichthyosiform lichen planus pigmentosus” is hereby proposed to be added to the clinical variants of LPP.

(*JMIR Dermatol* 2024;7:e50429) doi:[10.2196/50429](https://doi.org/10.2196/50429)

**KEYWORDS**

pigmentary disorder; lichen planus pigmentosus; ichthyosiform; asymptomatic; pigmentation; sun exposed; hypersensitivity; diffuse; hyperpigmentation; clinical; skin; dermatologist; dermatology; Filipino; Pacific Island; sun; sunburn

## Introduction

Lichen planus (LP) is an inflammatory disorder affecting skin, mucous membranes, nails, and hair with prototypic “lichenoid” papules. LP has a worldwide distribution with incidence varying from 0.22% to 1% depending on the geographic location [1]. LP can involve the skin or mucous membranes (oral, vulvovaginal, esophageal, laryngeal, and conjunctival mucosa). This condition has different variants based on the morphology of the lesions and the site of involvement [2].

Subtypes based on the configuration or morphology of the lesions include the following: popular (classic), hypertrophic, vesiculobullous, actinic, annular, atrophic, linear, follicular, and LP pigmentosus (LPP) [2]. LPP is a variant of LP characterized

by hyperpigmented macules in sun-exposed areas and flexures of dark-skinned individuals [3]. The pigmentation is dermal and occurs without any clinical evidence of inflammation [3].

The cause of LPP is unknown. The diffuse and symmetric classical type, linear unilateral hyperpigmentation in the extremities (Blaschkoid), and segmental patterns on the trunk have been documented. Reticular, blotchy, perifollicular, annular, and gyrate patterns are also encountered [4]. Another rare variant of LPP, that is, LPP inversus located on skinfold areas, has also been reported [5]. However, ichthyosiform variant of LPP has not been reported.



## Case Report

A 19-year-old Filipino male patient presented with a 7-year history of asymptomatic grayish macules; patches with fine scales on the face, trunk, and upper extremities (Figure 1A and 1B); and grayish plaques with “ichthyosiform” scales on the lower extremities (Figure 1C and 1D).

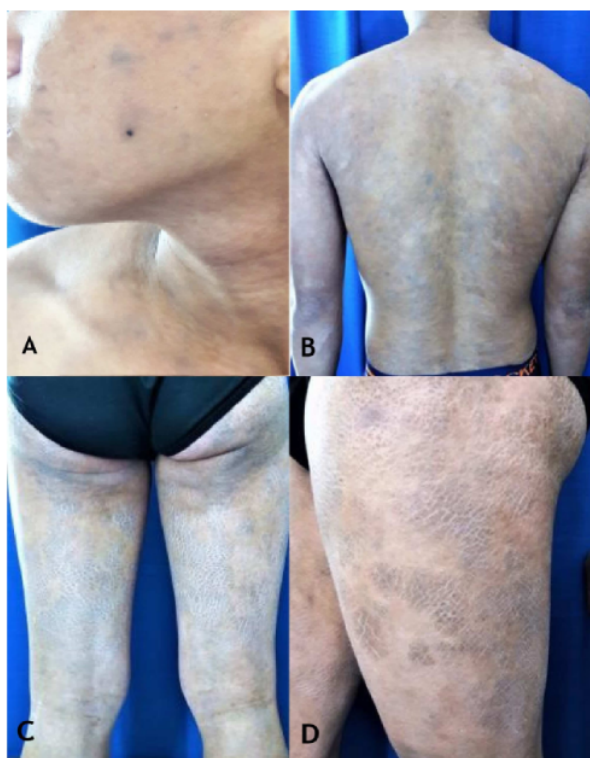
We used a manual polarized light device (DermLite DL3x10, 3Gen). The dermoscopic finding shows dots and globules in a “hem-like” and reticular pattern, which spares the follicular opening (Figure 2).

A 4-mm skin punch biopsy was performed on 2 separate sites (the macule and the ichthyosiform plaque). Histopathology of the ichthyosiform plaque revealed hyperkeratosis and hypergranulosis of the stratum corneum with acanthosis and

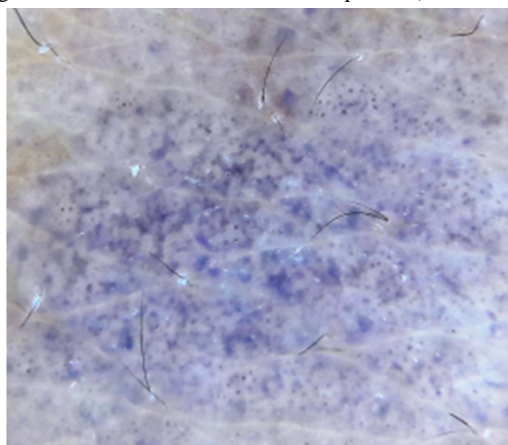
multifocal areas of vacuolar alteration of the basal cell layer. Histopathology results of both specimens presented with numerous pigment-laden macrophages and mild perivascular inflammatory infiltrate of lymphocytes in the dermis (Figure 3A and 3B). Cluster differentiation (CD) 68 immunostaining highlights the same density of pigment-laden macrophages in both the gray macule and the ichthyosiform plaque (Figure 3C). Definitive diagnosis of LPP was proven by histopathological findings on both the macule and ichthyosiform plaque.

Direct immunofluorescence of the 4-mm skin punch biopsy from the lesional area of the right arm revealed negative results. Serial sections showed no immunofluorescence for immunoglobulin (Ig) A, IgG, IgM, and complement C3 and fibrinogen for epidermis, basement membrane zone, and vascular areas.

**Figure 1.** Clinical findings: “asymptomatic grayish macules; patches with fine scales on the face (A), trunk, and upper extremities (B); and grayish plaques with thick “ichthyosiform” scales on the lower extremities (C and D).

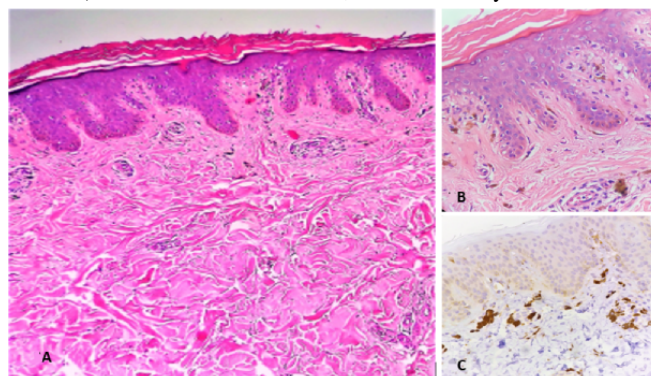


**Figure 2.** Dermoscopy shows black dots and globules in a “hem-like” and reticular pattern (DermLite DL3 polarized dermoscopy).





**Figure 3.** Histopathology of the ichthyosiform gray plaque shows (A) epidermal hyperkeratosis and hypergranulosis with acanthosis and multifocal areas of vacuolar alteration of the basal cell layer (H&E×100). (B) Numerous pigment-laden macrophages and mild perivascular inflammatory infiltrate of lymphocytes can be appreciated from the dermis (H&E×400). (C) CD68 immunostaining highlights the large pigment-laden macrophages on the biopsy of the ichthyosiform plaque (CD68×400). CD: cluster differentiation; H&E: hematoxylin and eosin.



## Discussion

LPP is a rare variant of LP that is seen in individuals with darker pigmented skin [3,4]. The etiology of this condition still remains unknown, but a number of agents have been reported to act as predisposing factors [4]. In 2014, a global consensus statement on acquired macular pigmentation of uncertain etiology concluded that LPP is unlikely to be caused by sociocultural practices or particular dietary ingredients [6].

The occurrence of this condition primarily in sun-exposed areas in numerous patients has led to the proposition that sunlight may be a principal etiological agent [4]. Clinical manifestations of LPP lesions can be found in sun-exposed areas as well as non-sun-exposed areas [6]. For the sites of predilection, LPP involves the head and neck region in most cases followed by the involvement of flexural area, particularly the axillae [6]. Although rare, the involvement of sun-protected areas such as trunk and thigh has also been reported [3,7], similar to our patient.

A number of other variants such as localized LPP (on thigh), segmental LPP, LPP inversus at the skinfold area, linear LPP, LPP in zosteriform distribution, LPP along lines of Blaschko, and LPP of oral mucosa have been reported [4]. Reticular, blotchy, perifollicular, annular, and gyrate patterns were also encountered [4]. LPP with an ichthyosiform pattern similar to our patient has not been reported.

LPP manifests as pigmentation of insidious onset without any features of inflammation or preceding raised lesions. It is typically asymptomatic and may occasionally be accompanied by mild pruritus. The course is variable, with some cases showing spontaneous resolution within weeks to months. It may be persistent over the years in many [3].

Dermoscopy of LPP lesions revealed pigmentation in different nonspecific patterns. These dotted patterns described as fine or coarse blue-gray dots correspond to melanophages in the dermis. Mixed patterns correspond to lesions showing both epidermal and dermal components. In our case, dermoscopy shows dots and globules in a “hem-like” and reticular pattern similar to the findings of Mathews et al [3].

Histologic features of LPP and LP are similar [3,8]. LPP is characterized by interface dermatitis with dense lichenoid reaction in the dermis with pigmentary incontinence and the presence of melanophages [3,7]. The inflammatory phase is characterized by a dense band of lymphohistiocytic inflammatory infiltrate in the upper dermis with prominent basal vacuolar degeneration. Some melanin incontinence is seen with scattered dermal melanophages [3]. These findings are compatible with our patient’s histopathological findings that are more compatible with LPP. In classic LP, additional findings of wedge-shaped hypergranulosis, saw-toothing of the rete ridges, colloid bodies, and a more prominent lichenoid inflammatory infiltrate of lymphocytes are further observed [9].

LPP is considered as a variant of LP [3]. It has a well-described association with classical lesions of LP [3,8]. The pathogenesis of LPP is not yet widely known but postulated to be secondary to type IV hypersensitivity reaction or T-lymphocyte-mediated cytotoxic activity against basal keratinocytes [3,5]. It has been proposed that barrier impairment may be a preceding event in the pathogenesis of LP, or it may occur as a secondary effect resulting from a disturbance in keratinocyte differentiation. A number of studies also revealed that certain transcription factors in LP increased expression of the differentiation-related genes involucrin, filaggrin, and loricrin, which play a role in the keratinization of cutaneous LP lesions [10]. Altered distribution of filaggrin was also observed in patients with LP in other cited literatures [11]. Taking into consideration all the possible pathogenesis of the condition, it is safe to assume that the mechanism of the altered distribution of keratinization in ichthyosiform LPP is similar to what we found in this patient.

The complex relationship between keratinization abnormalities and cutaneous inflammatory illnesses is highlighted by the appearance of ichthyosiform plaques in LPP lesions. Rigid clinicopathological connection and increased dermatologist awareness of this rare clinical presentation are necessary for an accurate diagnosis. In conclusion, the terminology “ichthyosiform lichen planus pigmentosus” is hereby proposed to be added to the clinical variants of LPP. A case series of ichthyosiform LPP is further recommended to confirm this new terminology.

## Declaration of Patient Consent

The patient has given informed consent for the their images and other clinical information to be published in a medical journal. The patient understands that their name and initials will not be published and due efforts will be made to conceal his identity, but complete anonymity cannot be guaranteed.

## Conflicts of Interest

None declared.

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## Abbreviations

**CD:** cluster differentiation

**Ig:** immunoglobulin

**LP:** lichen planus

**LPP:** lichen planus pigmentosus

*Edited by R Dellavalle; submitted 30.06.23; peer-reviewed by S Ps, M Gasmi ; comments to author 01.10.23; revised version received 10.12.23; accepted 02.03.24; published 19.04.24.*

*Please cite as:*

Sugiharto A, Gatmaitan J, Dayrit J

Ichthyosiform Lichen Planus Pigmentosus in a 19-Year-Old Male Patient: Case Report

JMIR Dermatol 2024;7:e50429

URL: <https://derma.jmir.org/2024/1/e50429>

doi:[10.2196/50429](https://doi.org/10.2196/50429)

PMID:[38640470](https://pubmed.ncbi.nlm.nih.gov/38640470/)

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Research Letter

# Reflecting on Decades of Data: The Global Burden of Disease—Cochrane Project

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(*JMIR Dermatol* 2024;7:e41323) doi:[10.2196/41323](https://doi.org/10.2196/41323)

**KEYWORDS**

Global Burden of Disease; Cochrane Library; review; trachoma; onchocerciasis; vitamin A deficiency; data; glaucoma; macular degeneration; vision loss; disorders; disease burden

## Introduction

The Global Burden of Disease (GBD) 2010 study was a systemic epidemiological collaboration between seven institutions to quantify health loss due to diseases, injuries, and risk factors [1]. Its purpose was to develop a platform to compare the magnitude of these health metrics across age groups, countries, sexes, and times, producing comparative metrics for hundreds of causes of premature death and disability. Participating institutions included the “Institute for Health Metrics and Evaluation as the coordinating center, the University of Queensland School of Population Health, the Harvard School of Public Health, the Johns Hopkins Bloomberg School of Public Health, the University of Tokyo, Imperial College London, and the World Health Organization (WHO)” [1].

This project set out to broadly expand the previous GBD 1990 study, conducted primarily by researchers at the World Health Organization and Harvard, to include nearly 500 experts from around the world [2]. In addition, it generated estimates for more than double the number of diseases and sequelae, and improved methods for estimating disability weights. GBD 2010 resulted in estimated disease risk factors, morbidity, and mortality for 291 diseases and injuries and 1160 sequelae [2].

The Cochrane Database of Systematic Reviews (CDSR) is the leading resource for systemic reviews in health care. The GBD-Cochrane project works to assess the representation of different conditions studied in GBD 2010 within CDSR and determine if CDSR accurately reflects GBD disability-adjusted life year metrics.

## Methods

The GBD 2010 study used all available data on cause of death from 187 countries; this included data on vital registration, verbal autopsy, mortality surveillance, censuses, surveys, hospitals, police records, and mortuaries. This data was used to quantify disease burden, disability-adjusted life years, and years of life lost to premature mortality [3].

The GBD-Cochrane project maps the cause-specific disease burden as established by the GBD study to associated systematic reviews of interventions evaluating the same diseases in CDSR. There are seven completed GBD-Cochrane projects and three active projects [4].

## Results

These projects provide high-quality data on systematic reviews and help determine if they poorly or strongly correlate with disease burden. For example, a review of ophthalmologic conditions showed that trachoma, onchocerciasis, vitamin A deficiency, and refraction and accommodation disorders were all underrepresented in the CDSR, while glaucoma, macular degeneration, and other vision loss disorders were overrepresented [5]. Other completed projects have shown poor representation of tropical diseases, while mental health and behavioral conditions are overrepresented [6,7].

## Discussion

There are a plethora of reasons a condition might be overrepresented in the CDSR. Overrepresentation might reflect the high prevalence of these conditions and, therefore, greater availability for randomized clinical trials. Alternatively, overrepresentation may reflect a disparity in funding, the disparity in research in high- versus low-income countries, or the prioritized interest of the public and pharmaceutical companies. Underrepresentation may reflect a decreasing disease

burden, existing effective interventions for those conditions, or a lack of researchers in low- and middle-income nations where certain conditions are more prevalent.

The active GBD-Cochrane projects include conditions in the realm of heart disease, cancer, and infectious disease. As the GBD-Cochrane project continues to map systematic reviews and protocols against disease burden, we will continue to identify research gaps and opportunities to make informed decisions with future research.

## Acknowledgments

MA receives fellowship funding from the Pfizer Global Medical Grant (65894351 and 58858477) Dermatology Fellowship 2022 (principal investigator: RP Dellavalle).

## Conflicts of Interest

None declared.

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## Abbreviations

**CDSR:** Cochrane Database of Systematic Reviews

**GBD:** Global Burden of Disease

*Edited by J Solomon; submitted 21.07.22; peer-reviewed by WD Dotson, E Stallings; comments to author 23.02.23; revised version received 29.06.23; accepted 27.11.23; published 05.01.24.*

*Please cite as:*

Adelman M, Weber I

*Reflecting on Decades of Data: The Global Burden of Disease—Cochrane Project*

*JMIR Dermatol* 2024;7:e41323

URL: <https://derma.jmir.org/2024/1/e41323>

doi: [10.2196/41323](https://doi.org/10.2196/41323)

PMID: [38180789](https://pubmed.ncbi.nlm.nih.gov/38180789/)



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Viewpoint

# Potential Use of ChatGPT in Responding to Patient Questions and Creating Patient Resources

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## Abstract

ChatGPT (OpenAI) is an artificial intelligence–based free natural language processing model that generates complex responses to user-generated prompts. The advent of this tool comes at a time when physician burnout is at an all-time high, which is attributed at least in part to time spent outside of the patient encounter within the electronic medical record (documenting the encounter, responding to patient messages, etc). Although ChatGPT is not specifically designed to provide medical information, it can generate preliminary responses to patients' questions about their medical conditions and can precipitately create educational patient resources, which do inevitably require rigorous editing and fact-checking on the part of the health care provider to ensure accuracy. In this way, this assistive technology has the potential to not only enhance a physician's efficiency and work-life balance but also enrich the patient-physician relationship and ultimately improve patient outcomes.

(*JMIR Dermatol* 2024;7:e48451) doi:[10.2196/48451](https://doi.org/10.2196/48451)

## KEYWORDS

artificial intelligence; AI; ChatGPT; patient resources; patient handouts; natural language processing software; language model; language models; natural language processing; chatbot; chatbots; conversational agent; conversational agents; patient education; educational resource; educational

## Introduction

ChatGPT (OpenAI) is an artificial intelligence (AI)–based natural language processing model that leverages data via complex deep learning algorithms to generate human-like text responses to user-generated prompts [1,2]. This tool is able to quickly, and often remarkably and accurately, generate responses to complex prompts across an infinite array of topics [1,2]. Since the rollout of ChatGPT in November 2022, it has garnered a significant amount of attention for its ability to create remarkably astute prompts for complex inquiries, making it an incredible tool not only for personal use but also for professional and commercial use [1-3].

It is difficult to overstate how the application of ChatGPT and other AI assistive technologies will revolutionize so many aspects of our day-to-day lives. Specifically for health care providers, it seems that there are myriad ways in which this

writing-assistant technology has the potential to not only enhance a physician's efficiency and work-life balance but also enrich the patient-physician relationship and ultimately improve patient outcomes. The advent of this assistive technology has come at a dire time for health care providers, as burnout is at an all-time high [4]. A study funded by the Agency for Healthcare Research and Quality found that the electronic medical record (EMR) is a key player in promoting stress and physician burnout, specifically time spent in the EMR outside of the patient encounter. The Agency for Healthcare Research and Quality [5] has proposed a variety of interventions to mitigate this issue, including offloading of physicians' workload as well as implementation of simplified, standardized, and automated workflow operations within the EMR, and preliminary applications of AI in these processes have shown promise [6]. Specifically, we propose that ChatGPT may be a promising tool to help reduce time spent outside of the patient encounter for dermatologists and other outpatient health care

providers by helping to generate first drafts of written information for patients—for example, instructions for patients and responses to questions in the “patient portal”—which seems to be a relatively underexplored application of this technology.

Although there is a buzz of excitement regarding the application of ChatGPT and other algorithmic or AI technologies in science and medicine [2,7], this excitement is balanced by important concerns about the limitations of this technology or fears about these algorithmic technologies outperforming or replacing health care providers. Importantly, although algorithms have their rightful place in the practice of medicine, the use of algorithms does not substitute for clinical judgment and does not capture the nuances of individualized medicine. This speaks to the importance of the patient-physician relationship, which is based on subtleties in human interactions that AI technologies cannot capture [6]. There are also important ongoing conversations regarding the ethical, privacy, and regulatory concerns about the use of AI technology in health care, although an in-depth conversation on these apprehensions is beyond the scope of this paper [6,7].

An obvious but important caveat is that ChatGPT in its current form is not designed to provide medical information. If, as a patient, you ask a medical question, ChatGPT implements a stock phrase: “As an AI language model, I am not authorized to provide personalized medical advice or recommendations. It is important to consult with a qualified healthcare professional...” [1]. This new technology is still “learning” and may occasionally “hallucinate,” that is, make up false information. Additionally, in generating its responses, ChatGPT may reference poor-quality studies or those with disproven conclusions and may not account for recently published research. This potentially dangerous limitation has been a focus of many

critics of this technology, as ChatGPT-generated false medical information could be misleading, and broader dissemination thereof has the potential to create widespread confusion and potentially foster distrust of medical providers [6]. While solely relying on AI-generated health information without human oversight does indeed have dangerous potential, we propose that if ChatGPT-generated responses are edited and fact-checked by a human health care provider, the ChatGPT-based synthesis of information can be an incredibly useful tool to generate a first draft for patient-based resources.

For example, a patient sends a message to his dermatologist inquiring about whether he should stop his bexarotene for treatment of his cutaneous T-cell lymphoma after having been diagnosed with COVID-19. Inputting this question into ChatGPT generates an accurate response; of course, the caveat is that the chatbot is “not authorized to give medical advice.” Adding more specificity to the prompt specifying that the response should be at a “fifth-grade reading level” or should “cite scientific papers” creates an even better response (Textbox 1 [1]).

After reviewing and making edits to the ChatGPT output, this thorough response may be as good or superior to the response that many dermatologists would have been able to generate de novo.

This same approach can also be applied to drafting written resources for patients. For example, prompting ChatGPT to “create a resource for a patient at a fifth-grade reading level regarding the special considerations of topical steroid application in patients with autism” yields a response (Textbox 2 [1]) in seconds, which would have otherwise required a fair amount of effort to create from scratch.

**Textbox 1.** ChatGPT’s response to a patient question regarding the discontinuation of bexarotene in the setting of active COVID-19 infection.

“If you have been diagnosed with COVID-19, it’s important to talk to your doctor before stopping any medication. There is currently no scientific evidence suggesting that bexarotene should be stopped if you have COVID-19.

A study published in the Pharmacological Research journal found that bexarotene may have antiviral effects against COVID-19 [8]. However, more research is needed.

In conclusion, if you have been diagnosed with COVID-19 and are taking bexarotene, it’s important to talk to your doctor before stopping the medication. There is currently no scientific evidence suggesting that bexarotene should be stopped if you have COVID-19, and it may even have some potential benefits.”

**Textbox 2.** ChatGPT's response to a patient question regarding topical steroid application considerations in patients on the autism spectrum.

"Title: Understanding Topical Steroid Application in Patients with Autism

Introduction: If you or a loved one has autism and needs to use topical steroids, there are a few things you should know. Topical steroids are medicines that are applied to the skin to reduce inflammation and itching. This resource will explain the special considerations that people with autism should keep in mind when using topical steroids.

What are Topical Steroids? Topical steroids are medicines that are applied to the skin to reduce inflammation and itching. They are often used to treat skin conditions like eczema, psoriasis, and allergic reactions. Topical steroids come in many forms, including creams, ointments, and lotions.

Special Considerations for People with Autism: If you or your loved one has autism and needs to use topical steroids, here are some things to keep in mind:

Communication: People with autism may have difficulty communicating their symptoms or the effects of the medication. It is important to communicate any changes in symptoms or side effects to your doctor.

Sensory Issues: People with autism may be sensitive to touch, texture, or smell. They may have difficulty with the feel or smell of the medication. Talk to your doctor about any sensory issues you or your loved one may have.

Routine: People with autism often thrive on routine. Applying medication at the same time each day can help establish a routine and make the medication easier to manage.

Education: Educate yourself and your loved one about the medication. Explain why the medication is necessary and what it is intended to do. Use simple language and visuals if needed.

Conclusion: Topical steroids can be a helpful treatment for skin conditions, but special considerations need to be taken for people with autism. If you or your loved one has autism and needs to use topical steroids, communicate any changes in symptoms or side effects to your doctor, address any sensory issues, establish a routine, and educate yourself and your loved one about the medication. Talk to your doctor if you have any questions or concerns."

## Conclusions

In conclusion, ChatGPT is a tool that may show promise in assisting dermatologists and other outpatient health care providers in generating information for patients to address their questions and concerns, which may help patients better understand and manage their condition and ultimately may help to promote treatment compliance and enhance the patient-physician relationship. The use of ChatGPT has important implications as it pertains to reducing physician burnout by assisting with and automating tasks outside of the patient encounter. Although there are important limitations to this technology, by ensuring the prompt is specific and using

this output as a "first draft" and editing for accuracy, this technology can be used to generate exceptionally high-quality patient resources. Importantly, ensuring the accuracy and appropriateness of the medical information generated by ChatGPT requires rigorous evaluation and validation against trusted sources as well as adherence to current regulatory guidelines. There are seemingly endless ways in which natural language processing tools such as ChatGPT may be used to streamline health care providers' workflow, thereby reducing burnout. However, more research is needed regarding patients' perceptions of chatbot-generated resources as well as the potential implications of AI on the patient-physician relationship.

## Conflicts of Interest

None declared.

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## Abbreviations

**AI:** artificial intelligence

**EMR:** electronic medical record

*Edited by J Solomon, I Brooks; submitted 24.04.23; peer-reviewed by S Kim, Y Zhuang, Y Xie; comments to author 25.05.23; revised version received 11.08.23; accepted 22.02.24; published 06.03.24.*

*Please cite as:*

*Reynolds K, Tejasvi T*

*Potential Use of ChatGPT in Responding to Patient Questions and Creating Patient Resources*

*JMIR Dermatol* 2024;7:e48451

URL: <https://derma.jmir.org/2024/1/e48451>

doi: [10.2196/48451](https://doi.org/10.2196/48451)

PMID: [38446541](https://pubmed.ncbi.nlm.nih.gov/38446541/)

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## Research Letter

# Readability and Health Literacy Scores for ChatGPT-Generated Dermatology Public Education Materials: Cross-Sectional Analysis of Sunscreen and Melanoma Questions

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(*JMIR Dermatol* 2024;7:e50163) doi:[10.2196/50163](https://doi.org/10.2196/50163)

**KEYWORDS**

ChatGPT; artificial intelligence; AI; LLM; LLMs; large language model; language model; language models; generative; NLP; natural language processing; health disparities; health literacy; readability; disparities; disparity; dermatology; health information; comprehensible; comprehensibility; understandability; patient education; public education; health education; online information

## Introduction

A study of 402 randomly selected Medicaid enrollees reported an average of a 5th-grade reading level, which is lower than the average 8th-grade level of US adults [1,2]. Therefore, the American Medical Association (AMA) recommends developing health materials at a 6th-grade reading level or lower [3]. However, a 2018 systematic review of 7891 health websites reported that educational health materials are often at 10th- to 15th-grade reading levels [4].

In a study evaluating ChatGPT-generated materials for 14 dermatological diseases, content was at a 10th-grade reading level [5]. We hypothesized that ChatGPT could be prompted to generate rewritten health materials at a lower grade level and in line with AMA recommendations. The readability of ChatGPT-generated dermatology information and public educational resources on the American Academy of Dermatology Association's (AAD) website was assessed and determined whether strategic prompting would enhance the material's readability.

## Methods

We inputted the AAD website's sunscreen and melanoma FAQs individually into ChatGPT, then compiled corresponding outputs, with the supplemental prompts: "I don't understand, please clarify" and "I still don't understand, please clarify." We used well-established readability and health literacy assessment tools and a single web-based readability calculator to calculate 7 different scores [6,7], and computed an "average readability" score with these grade level outputs. A 2-sample *t* test was used for comparisons ( $P < .05$ ). To determine information accuracy before and after prompting, 3 dermatology residents blindly evaluated the education materials using a numerical scale: 1 (not accurate), 2 (somewhat accurate), and 3 (accurate).

## Results

The AAD's sunscreen FAQs and melanoma FAQs had Flesch Reading Ease scores of 60.9 (standard/average) and 56.2 (fairly difficult), respectively. The initial ChatGPT output had readability scores of 60.5 (standard/average) and 46.5 (difficult) for sunscreen and melanoma questions, respectively. Subsequent prompting resulted in readability levels of 69.4

(standard/average) and 80.2 (easy) for sunscreen questions and 58.9 (fairly difficult) and 59.3 (fairly difficult) for melanoma questions (Table 1).

**Table 1.** Readability and health literacy measures of American Academy of Dermatology Association (AAD) text, ChatGPT output, ChatGPT output with 1 prompt, and ChatGPT output with 2 prompts.

	AAD	ChatGPT	ChatGPT with 1 prompt	ChatGPT with 2 prompts
<b>Sunscreen FAQs</b>				
Flesch Reading Ease score	60.9 (standard/average)	60.5 (standard/average)	69.4 (standard/average)	80.2 (easy)
Gunning Fog	11.1 (hard)	11.7 (hard)	8.0 (fairly easy)	6.2 (fairly easy)
Flesch-Kincaid Grade Level	8.9 (9th grade)	9.1 (9th grade)	5.6 (6th grade)	3.8 (4th grade)
Coleman-Liau Index	10.0 (10th grade)	10.0 (10th grade)	10.0 (10th grade)	8.0 (8th grade)
SMOG <sup>a</sup> Index	8.2 (8th grade)	8.6 (9th grade)	6.0 (6th grade)	4.9 (5th grade)
Automated Readability Index	9.4 (9th grade)	9.4 (9th grade)	4.6 (5th grade)	2.5 (3rd grade)
Linsear Write Formula	9.3 (9th grade)	10.8 (11th grade)	4.0 (4th grade)	2.8 (3rd grade)
Average readability <sup>b</sup>	9.2 (9th grade)	9.6 (10th grade)	6.0 (6th grade)	4.4 (4th grade)
<b>Melanoma FAQs</b>				
Flesch Reading Ease score	56.2 (fairly difficult)	46.5 (difficult)	58.9 (fairly difficult)	59.3 (fairly difficult)
Gunning Fog	12.5 (hard to read)	13.7 (hard to read)	11.0 (hard to read)	10.9 (hard to read)
Flesch-Kincaid Grade Level	9.5 (10th grade)	10.5 (11th grade)	8.0 (8th grade)	7.9 (8th grade)
Coleman-Liau Index	9.0 (9th grade)	12.0 (12th grade)	10.0 (10th grade)	8.0 (8th grade)
SMOG Index	9.4 (9th grade)	10.1 (10th grade)	8.3 (8th grade)	8.2 (8th grade)
Automated Readability Index	8.4 (8th grade)	9.7 (10th grade)	6.9 (7th grade)	6.3 (6th grade)
Linsear Write Formula	10.8 (11th grade)	9.5 (10th grade)	7.0 (7th grade)	6.8 (7th grade)
Average readability	9.4 (9th grade)	10.4 (10th grade)	8.0 (8th grade)	7.4 (7th grade)
Accuracy score <sup>c</sup> , mean (SD)	2.82 (0.25)	2.89 (0.19)	2.63 (0.41)	2.62 (0.37)

<sup>a</sup>SMOG: Simple Measure of Gobbledygook.  
<sup>b</sup>The average readability score was computed by averaging the tests with grade levels as outputs: Flesch-Kincaid Grade Level, Coleman-Liau Index, SMOG Index, Automated Readability Index, and Linsear Write Formula.  
<sup>c</sup>The accuracy score represents the mean score of 3 dermatology residents who assessed the educational materials using a numeric scale: 1 (not accurate), 2 (somewhat accurate), and 3 (accurate).

The AAD’s sunscreen FAQs and melanoma FAQs had readability levels of 9.2 and 9.4 (both 9th grade), respectively, and the original ChatGPT sunscreen and melanoma output readability levels were 9.6 and 10.4 (9th grade and 10th grade), respectively, with no differences in readability between AAD and ChatGPT for both question sets ( $P=.32$  and  $P=.15$ , respectively). The first and second prompting of the sunscreen FAQs output generated material at lower reading levels than AAD-generated material (6.0,  $P=.005$ ; 4.4,  $P<.001$ , respectively). Melanoma FAQs, after prompting, achieved lower reading levels versus AAD material, with scores of 8.0 (8th grade;  $P=.08$ ) and 7.4 (7th grade;  $P=.007$ ) (see Table 1).

The AAD material scored an average of 2.82 in accuracy, while the original ChatGPT material scored 2.89. All of the material (42/42, 100%) averaged within the 2-3 range. Initial and

secondary prompting resulted in generated material with average scores of 2.63 and 2.62, respectively. Of the 42 materials generated from prompting, 42 (95.2%) averaged within the 2-3 range.

### Discussion

The AAD’s sunscreen FAQs and melanoma FAQs had readability scores below the recommended threshold of 80 (Flesch Reading Ease scale) and above the recommended 6th-grade reading level, consistent with a study showing that 27 subungual melanoma websites had poor readability overall, with only 22% having readability lower than the 7th-grade reading level [8]. Taken together, these findings emphasize the need to enhance readability of dermatology public education information.



Our study demonstrated that ChatGPT may be a solution to this problem. Prompting ChatGPT following initial inputs improved health information readability versus AAD materials and was closer to or within recommended guidelines. Our findings are similar to a 2023 study assessing 9 uveitis web pages with an average Flesch-Kincaid Grade Level of 11.0 (SD 1.4); ChatGPT improved the readability, with a mean Flesch-Kincaid Grade Level of 8.0 (SD 1.0) [9]. Therefore, the use of ChatGPT to adapt output to enhance readability might have applicability in dermatology and other medical fields.

Most of the ChatGPT-generated material was rated as accurate to somewhat accurate. However, additional prompting resulted

in a slight trend toward less accuracy, with 2 responses below the 2-3 (accurate to somewhat accurate) range. This observation may highlight a potential limitation to the applicability of ChatGPT in this context. Additionally, only a small number of questions were assessed. We analyzed the ChatGPT-3.5 version, which includes information up until September 2021.

In conclusion, ChatGPT could be used to enhance the readability of dermatology health information and lower it to the 6th-grade reading level recommended by the AMA. Larger studies are needed to corroborate our data and evaluate the utility of ChatGPT for dermatology public education materials.

## Conflicts of Interest

SRL has served as a consultant for Eli Lilly, Ortho Dermatologics, Moberg Pharmaceuticals, and BelleTorus Corporation.

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## Abbreviations

**AAD:** American Academy of Dermatology Association

**AMA:** American Medical Association

*Edited by J Solomon, I Brooks; submitted 21.06.23; peer-reviewed by O Tarawneh, H Mondal, S Friedman; comments to author 27.08.23; revised version received 02.01.24; accepted 06.02.24; published 06.03.24.*

*Please cite as:*

Roster K, Kann RB, Farabi B, Gronbeck C, Brownstone N, Lipner SR

Readability and Health Literacy Scores for ChatGPT-Generated Dermatology Public Education Materials: Cross-Sectional Analysis of Sunscreen and Melanoma Questions

*JMIR Dermatol* 2024;7:e50163

URL: <https://derma.jmir.org/2024/1/e50163>

doi: [10.2196/50163](https://doi.org/10.2196/50163)

PMID: [38446502](https://pubmed.ncbi.nlm.nih.gov/38446502/)

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Research Letter

# Assessing the Utility of Multimodal Large Language Models (GPT-4 Vision and Large Language and Vision Assistant) in Identifying Melanoma Across Different Skin Tones

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## Abstract

The large language models GPT-4 Vision and Large Language and Vision Assistant are capable of understanding and accurately differentiating between benign lesions and melanoma, indicating potential incorporation into dermatologic care, medical research, and education.

(*JMIR Dermatol* 2024;7:e55508) doi:[10.2196/55508](https://doi.org/10.2196/55508)

**KEYWORDS**

melanoma; nevus; skin pigmentation; artificial intelligence; AI; multimodal large language models; large language model; large language models; LLM; LLMs; machine learning; expert systems; natural language processing; NLP; GPT; GPT-4V; dermatology; skin; lesion; lesions; cancer; oncology; visual

## Introduction

Large language models (LLMs), artificial intelligence (AI) tools trained on large quantities of human-generated text, are adept at processing and synthesizing text and mimicking human capabilities, making the distinction between them nearly imperceptible [1]. The versatility of LLMs in addressing various requests, coupled with their capabilities in handling complex concepts and engaging in real-time user interactions, indicates their potential integration into health care and dermatology [1,2]. Within dermatology, studies have found LLMs can retrieve, analyze, and summarize information to facilitate decision-making [3].

Multimodal LLMs with visual understanding, such as GPT-4 Vision (GPT-4V) [4] and Large Language and Vision Assistant (LLaVA) [5], can also analyze images, videos, and speech, a significant evolution. They can solve novel, intricate tasks that

language-only systems cannot, due to their unique capabilities combining language and vision with inherent intelligence and reasoning [4,5]. This study assesses the ability of publicly available multimodal LLMs to accurately recognize and differentiate between melanoma and benign melanocytic nevi across all skin tones.

## Methods

Our data set comprised macroscopic images (900 × 1100 pixels; 96-dpi resolution) of melanomas (malignant) and melanocytic nevi (benign) obtained from the publicly available and validated MClass-D data set [6], Dermnet NZ [7], and dermatology textbooks [8]. Each LLM was provided with 20 unique text-based prompts that were each tested on 3 images (n=60 unique image-prompt combinations) consisting of questions about “moles” (the term used for benign and malignant lesions), instructions, and image-based prompts where the image was



annotated to alter the focus. Our prompts represented potential users, such as general physicians, providers in remote areas, or educational users and residents. The chat content was deleted before each submitted prompt to prevent repeat images influencing responses, and testing was performed over a 1-hour timespan, which is insufficient for learning to take place. Prompts were designed to either involve conditioning of ABCDE (asymmetry, border irregularity, color variation, diameter >6 mm, evolution) melanoma features or to assess effects of background skin color on predictions. Conditioning involved asking the LLM to differentiate between benign and malignant lesions where one feature (eg, symmetry, border irregularity, color, diameter) remained constant in both images to determine whether the fixed element was involved in overall reasoning. To assess the impact of color on melanoma

recognition, color distributions of nevi and melanoma were manipulated by decolorizing images or altering their colors.

Results

Analysis revealed GPT-4V outperformed LLaVA in all examined areas, with overall accuracy of 85% compared to 45% for LLaVA, and consistently provided thorough descriptions of relevant ABCDE features of melanoma (Table 1 and Multimedia Appendix 1). While both LLMs were able to identify melanoma in lighter skin tones and recognize that dermatologists should be consulted for diagnostic confirmation, LLaVA was unable to confidently recognize melanoma in skin of color nor comment on suspicious features, such as ulceration and bleeding.

Table 1. Performance of Large Language and Vision Assistant (LLaVA) and GPT-4 Vision (GPT-4V) for melanoma recognition.

Feature	LLaVA	GPT-4V
Melanoma detection	Melanoma identified—referenced shape and color	Melanoma identified—referenced the other ABCDEs <sup>a</sup> of melanoma
Feature conditioning		
Asymmetry	Melanoma identified—referenced size and color	Melanoma identified—referenced the other ABCDEs of melanoma
Border irregularity	Melanoma identified—referenced size and color	Melanoma identified—referenced the other ABCDEs of melanoma
Color	Melanoma identified—incorrectly commented on color distribution	Melanoma identified—referenced the other ABCDEs of melanoma
Diameter	Melanoma missed—confused by the darker color	Melanoma identified—referenced the other ABCDEs of melanoma
Color + diameter	Melanoma missed—confused by the darker color and morphology	Melanoma identified—referenced morphology, complexity, color, and border
Evolution	Melanoma identified—referenced size and color	Melanoma identified—referenced the other ABCDEs of melanoma
Color bias		
Benign—darkened pigment	Darkened lesion classified as melanoma, became confused about other melanoma features	Darkened lesion classified as melanoma, became confused about other melanoma features
Melanoma—darkened pigment	Darkened lesion classified as melanoma, became confused about the other ABCDEs of melanoma	Darkened lesion classified as melanoma, became confused about the other ABCDEs of melanoma
Melanoma—lightened pigment	Unable to recognize malignancy and to identify that the image had been altered	Melanoma identified—referenced the other ABCDEs of melanoma and recognized that the altered image had been lightened
Skin of color		
Melanoma detection	Diagnostic uncertainty—unsure of lesion severity and diagnosis	Melanoma identified—referenced the other ABCDEs of melanoma
Suspicious features	Did not identify suspicious features	Identified suspicious features and recommended medical evaluation—ulceration, bleeding, and skin distortion
Image manipulation		
Visual referring	Tricked into thinking the annotations indicated sunburned skin	Correctly identified that the annotations were artificially added and could be used to monitor skin lesion evolution or to communicate concerns between providers
Rotation	Tricked into thinking an altered image orientation constituted a novel image	Correctly indicated it could not differentiate between the 2 images and accurately referenced the ABCDEs of melanoma

<sup>a</sup>ABCDE: asymmetry, border irregularity, color variation, diameter >6 mm, evolution.

## Discussion

Across all prompts analyzing feature conditioning, GPT-4V correctly identified the melanoma, while LLaVA did not, when color, diameter, or both were held constant (Figure 1). This suggests these features influence melanoma detection in LLaVA, with less importance placed on symmetry and border. Both LLMs were susceptible to color bias, as when a pigment was darkened with all other features held constant, the lesion was believed to be malignant. Alternatively, when pigments were

lightened, GPT-4V appropriately recognized this alteration, while LLaVA did not. Finally, image manipulation did not impact GPT-4V's diagnostic abilities; however, LLaVA was unable to detect these manipulations and was vulnerable to visual referring associated with melanoma manifestations. The red lines added around the nevus's edges were identified as sunburned skin when presented to LLaVA, while GPT-4V correctly recognized these annotations as useful for monitoring lesion evolution or communicating specific concerns between health care providers.

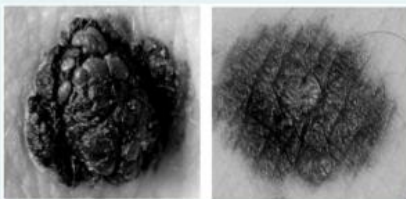
**Figure 1.** Melanoma detection when conditioned on color and diameter. GPT-4V: GPT-4 Vision; LLaVA: Large Language and Vision Assistant.

### Melanoma vs Melanocytic Nevus

#### Classification conditioned on diameter and color

**Prompt:**

Both these lesions have a similar diameter size. Which one is most likely to be malignant and why ?



**LLaVA:**

The mole on the right is more likely to be malignant. This is because it appears to be darker and more irregular in shape compared to the mole on the left. The darker color and irregular shape are often indicators of a malignant mole, as they can be signs of melanoma or other skin cancers. In contrast, the mole on the left appears to be lighter in color and has a more regular shape, which could suggest a benign mole. However, it is essential to consult a dermatologist for a proper diagnosis and to ensure the safety of the individual.

**GPT-4V:**

The image you've provided shows two different moles. When evaluating moles for potential malignancy using the ABCDE rule mentioned earlier, several characteristics are considered, not just diameter. From what can be observed:

**Left Mole:**

- This mole appears to have a more complex structure, with what seems like multiple nodules or a clustered growth pattern.
- The color, although the image is in black and white, seems to be very dark and possibly varied in tone throughout the mole.
- The borders look irregular and notched.
- The texture seems uneven and raised.

**Right Mole:**

- The mole is less raised than the left one, appearing flatter against the skin.
- The border, while somewhat irregular, seems less notched or ragged than the left mole.
- The color appears more uniform across the mole, even though variations in tone are still present.

Based on these observations, the mole on the left may be more concerning for malignancy due to its more irregular border, varied texture, and complex surface characteristics. The mole on the right, while it has some irregularity, appears less complex in structure.

Although limitations are present, GPT-4V can accurately differentiate between benign and melanoma lesions. Performing additional training of these LLMs on specific conditions can improve their overall performance. Despite our findings, it is

critical to account for and address limitations such as reproduction of existing biases, hallucinations, and visual prompt injection vulnerabilities and incorporate validation checks before clinical uptake [9]. Recently, the integration of technology

within medicine has accelerated, and AI has been used in dermatology to augment the diagnostic process and improve clinical decision-making [10]. There is an urgent global need to address high volumes of skin conditions posing health

concerns, and the integration of multimodal LLMs, such as GPT-4V, into health care has the potential to deliver material increases in efficiency and improve education and patient care.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

The 20 unique text-based prompts provided to GPT-4 Vision and Large Language and Vision Assistant and the responses of both large language models depicted side by side.

[DOCX File, 5509 KB - [derma\\_v7ile55508\\_app1.docx](#)]

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## Abbreviations

**ABCDE:** asymmetry, border irregularity, color variation, diameter >6 mm, evolution

**AI:** artificial intelligence

**GPT-4V:** GPT-4 Vision

**LLaVA:** Large Language and Vision Assistant

**LLM:** large language model

*Edited by R Dellavalle; submitted 19.12.23; peer-reviewed by F Liu, E Ko, G Mattson, A Sodhi; comments to author 30.01.24; revised version received 16.02.24; accepted 01.03.24; published 13.03.24.*

*Please cite as:*

Cirone K, Akrouf M, Abid L, Oakley A

*Assessing the Utility of Multimodal Large Language Models (GPT-4 Vision and Large Language and Vision Assistant) in Identifying Melanoma Across Different Skin Tones*

*JMIR Dermatol* 2024;7:e55508

URL: <https://derma.jmir.org/2024/1/e55508>

doi: [10.2196/55508](#)

PMID: [38477960](#)

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Original Paper

# Assessing the Application of Large Language Models in Generating Dermatologic Patient Education Materials According to Reading Level: Qualitative Study

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## Abstract

**Background:** Dermatologic patient education materials (PEMs) are often written above the national average seventh- to eighth-grade reading level. ChatGPT-3.5, GPT-4, DermGPT, and DocsGPT are large language models (LLMs) that are responsive to user prompts. Our project assesses their use in generating dermatologic PEMs at specified reading levels.

**Objective:** This study aims to assess the ability of select LLMs to generate PEMs for common and rare dermatologic conditions at unspecified and specified reading levels. Further, the study aims to assess the preservation of meaning across such LLM-generated PEMs, as assessed by dermatology resident trainees.

**Methods:** The Flesch-Kincaid reading level (FKRL) of current American Academy of Dermatology PEMs was evaluated for 4 common (atopic dermatitis, acne vulgaris, psoriasis, and herpes zoster) and 4 rare (epidermolysis bullosa, bullous pemphigoid, lamellar ichthyosis, and lichen planus) dermatologic conditions. We prompted ChatGPT-3.5, GPT-4, DermGPT, and DocsGPT to “Create a patient education handout about [condition] at a [FKRL]” to iteratively generate 10 PEMs per condition at unspecified fifth- and seventh-grade FKRLs, evaluated with Microsoft Word readability statistics. The preservation of meaning across LLMs was assessed by 2 dermatology resident trainees.

**Results:** The current American Academy of Dermatology PEMs had an average (SD) FKRL of 9.35 (1.26) and 9.50 (2.3) for common and rare diseases, respectively. For common diseases, the FKRLs of LLM-produced PEMs ranged between 9.8 and 11.21 (unspecified prompt), between 4.22 and 7.43 (fifth-grade prompt), and between 5.98 and 7.28 (seventh-grade prompt). For rare diseases, the FKRLs of LLM-produced PEMs ranged between 9.85 and 11.45 (unspecified prompt), between 4.22 and 7.43 (fifth-grade prompt), and between 5.98 and 7.28 (seventh-grade prompt). At the fifth-grade reading level, GPT-4 was better at producing PEMs for both common and rare conditions than ChatGPT-3.5 ( $P=.001$  and  $P=.01$ , respectively), DermGPT ( $P<.001$  and  $P=.03$ , respectively), and DocsGPT ( $P<.001$  and  $P=.02$ , respectively). At the seventh-grade reading level, no significant difference was found between ChatGPT-3.5, GPT-4, DocsGPT, or DermGPT in producing PEMs for common conditions (all  $P>.05$ ); however, for rare conditions, ChatGPT-3.5 and DocsGPT outperformed GPT-4 ( $P=.003$  and  $P<.001$ , respectively). The preservation of meaning analysis revealed that for common conditions, DermGPT ranked the highest for overall ease of reading, patient understandability, and accuracy (14.75/15, 98%); for rare conditions, handouts generated by GPT-4 ranked the highest (14.5/15, 97%).

**Conclusions:** GPT-4 appeared to outperform ChatGPT-3.5, DocsGPT, and DermGPT at the fifth-grade FKRL for both common and rare conditions, although both ChatGPT-3.5 and DocsGPT performed better than GPT-4 at the seventh-grade FKRL for rare conditions. LLM-produced PEMs may reliably meet seventh-grade FKRLs for select common and rare dermatologic conditions and are easy to read, understandable for patients, and mostly accurate. LLMs may play a role in enhancing health literacy and disseminating accessible, understandable PEMs in dermatology.



**KEYWORDS**

artificial intelligence; large language models; large language model; LLM; LLMs; machine learning; natural language processing; deep learning; ChatGPT; health literacy; health knowledge; health information; patient education; dermatology; dermatologist; dermatologists; dermatology resident; dermatology residents; dermatologic patient education material; dermatologic patient education materials; patient education material; patient education materials; education material; education materials

## Introduction

Health literacy has been well-explored to be a predictor of health outcomes. Differences in health literacy levels have been associated with increased hospitalization and emergency care use, as well as decreased mammography, vaccinations, and medication compliance. Importantly, health literacy has been shown to be implicated in widening existing disparities [1]. However, improving written materials can increase health knowledge, especially when used in combination with brief in-office counseling [2].

Medical professionals play a key role in developing and distributing accurate, readable, and comprehensible medical information to patients across different communities. The current reading level in the United States is rated at a seventh- to eighth-grade level, with the latest assessment results available through the Program for the International Assessment of Adult Competencies for each US state and county. However, because up to 20% of individuals read below the fifth-grade level, the Agency for Healthcare Research and Quality (AHRQ) recommends producing written health care materials at a fourth- to sixth-grade level to maximize readability [3]. Readability in the United States is most commonly assessed with the Flesch-Kincaid reading level (FKRL), a formula that approximates the reading grade level of a given text taking into account sentence, word, and syllable counts [4].

Within dermatology, an evaluation of 706 patient-oriented materials of dermatology was shown to be written at a mean 12th-grade reading level [5]. Further, previous analysis of dermatologic patient education materials (PEMs) available through the American Academy of Dermatology (AAD), WebMD, and Wikipedia had average FKRLs of 9.6, 9.3, and 11.8, respectively [6]. When looking at specific dermatologic diseases, there are studies regarding patient-oriented materials of acne keloidalis nuchae, pemphigus vulgaris, bullous pemphigoid, and epidermolysis bullosa, which showed that most handouts are difficult to read and have a reading level above an eighth-grade level [7-9]. Similar results have been seen with the assessment of dermatologic materials written in Spanish [10]. As such, the average patient may struggle to sufficiently understand and process the dermatologic information available on the web or in the office.

ChatGPT is a large language model (LLM) that uses deep learning algorithms trained on vast amounts of data to generate humanlike responses to user prompts [11]. It is currently being explored as a tool across professions including medicine. When challenged, it performed above the passing score on the National Board of Medical Examiners-Free-Step-1 data set and the United Kingdom Dermatology Specialty Certificate Examination [12].

It has also performed satisfactorily in answering physician-generated medical queries across 12 distinct specialties, including ophthalmology, dermatology, oncology, infectious disease, neurosurgery, gastroenterology, radiation oncology, trauma surgery, cardiology, anesthesiology, pulmonology, and surgical oncology [9]. Since the mainstream introduction of ChatGPT in fall 2022, additional natural language processing models such as GPT-4, DocsGPT (a Doximity and OpenAI collaboration), and the dermatology-specific DermGPT have also been made available, although research on their performance and applications remains lacking [13,14]. While ChatGPT has been shown to appropriately answer patient queries in dermatology, generated answers have not yet been assessed for patient readability [15]. Given their functionality, LLMs have the potential to be a tool to help the clinician workflow and improve patient care [16]. Regarding health literacy, LLMs could be applied to generating PEMs at a specified reading level. When prompted, LLMs attempt to generate documents according to the specifications given. However, whether the generated documents meet the specifications requested must be verified. In this way, the application of LLMs as tools for generating patient handouts at specific reading levels has yet to be explored. Additionally, with the choice between numerous LLMs, it is essential to objectively evaluate the functionality of each.

Here, we assess the application of ChatGPT-3.5, GPT-4, DocsGPT, and DermGPT in generating dermatologic PEMs at specified reading levels at or below the average US adult reading level for both common and rare dermatologic conditions. In addition to assessing the readability of each PEM, we also assess the preservation of meaning between LLM-generated PEMs and AAD PEMs for a given condition. This work may inform future clinician workflows both within and outside of dermatology and allow clinics to efficiently create PEMs that are readable and comprehensible to all patient populations.

## Methods

### Ethical Considerations

No ethics board review was sought as this project does not involve human participants or ethically sensitive materials.

### Study Design

The FKRL of current AAD PEMs was evaluated using Microsoft Word (Microsoft Corp) readability statistics for 4 common (atopic dermatitis [AD], acne vulgaris, psoriasis, and herpes zoster) and 4 rare (epidermolysis bullosa, lichen planus, bullous pemphigoid, and lamellar ichthyosis) dermatologic conditions. Next, ChatGPT-3.5, GPT-4, DermGPT, and DocsGPT were independently prompted to "Create a patient education handout about [common or rare condition] at a [FKRL]" to iteratively

generate 10 PEMs per condition at unspecified fifth- and seventh-grade FKRLs. The same prompt was used for each iteration across each LLM. The FKRL of the LLM-generated PEMs was also evaluated using Microsoft Word readability statistics. The preservation of meaning across LLM-generated PEMs was assessed by 2 blinded dermatology resident trainees (LS and KG) using a standardized scoring rubric that assessed a copy of each LLM-generated document at unspecified FKRLs for both common and rare diseases for ease of reading, understandability for patients, and overall accuracy (5 points per domain for an overall total of 15 possible points; [Multimedia Appendix 1](#)). Rubrics also provided space for free-response comments. Additionally, members of the University of Chicago Health Literacy Department reviewed representative AAD PEMs and LLM-produced PEMs to provide qualitative feedback on the readability of such documents in line with their plain language guidelines ([Multimedia Appendix 2](#)).

### Statistical Analysis

Simple descriptive statistics were performed using Microsoft Excel (Microsoft Corp) and RStudio (Posit PBC). Fisher exact tests were performed in RStudio (Posit) at the  $P=.05$  significance level.

## Results

In total, 960 PEMs were generated across 4 LLMs and 8 dermatologic conditions. The average FKRL for each common and rare condition across each LLM and prompt category is shown in [Table 1](#). ChatGPT-3.5 created materials at or below the specified fifth- or seventh-grade FKRL in 53% (43/80) and 65% (52/80) of iterations, respectively; GPT-4 created materials at or below the fifth- or seventh-grade FKRL in 86% (69/80) and 45% (36/80) of iterations, respectively; DocsGPT created materials at or below the specified fifth- or seventh-grade FKRL in 48% (38/80) and 75% (60/80) of iterations, respectively; and DermGPT created materials at or below the specified fifth- or seventh-grade FKRL in 5% (4/80) and 40% (32/80) of iterations, respectively ([Tables 2-4](#)).

When prompted to generate PEMs at a fifth-grade reading level, there were no significant differences between DocsGPT and ChatGPT-3.5; both LLMs were able to generate appropriate handouts for common and rare conditions ( $P=.92$ ). However, when compared to DermGPT, both DocsGPT ( $P<.001$ ) and ChatGPT-3.5 ( $P<.001$ ) were better able to generate PEMs at a fifth-grade reading level for common and rare conditions,

respectively. When prompted to generate PEMs at a seventh-grade reading level, DocsGPT was better than DermGPT for common conditions ( $P=.04$ ).

Finally, we compared the individual LLM's ability to generate PEMs about common and rare conditions at either a fifth-grade reading level or a seventh-grade reading level. No difference was observed in the ability of ChatGPT-3.5 or GPT-4 to create PEMs meeting either a fifth-grade or seventh-grade reading level for both common and rare conditions ( $P<.001$ ). DocsGPT, however, was better at creating PEMs meeting a seventh-grade than fifth-grade reading level for both common ( $P=.01$ ) and rare ( $P=.03$ ) conditions. Likewise, DermGPT was better at creating PEMs meeting a seventh-grade than fifth-grade reading level for both common ( $P<.001$ ) and rare ( $P<.001$ ) conditions.

Results from the preservation of meaning analysis revealed that for common conditions, handouts generated by DermGPT ranked the highest for overall ease of reading, patient understandability, and accuracy (14.75/15, 98%), followed by DocsGPT (14.25/15, 95%), ChatGPT-3.5 (13.5/15, 90%), and GPT-4 (13/15, 87%). For rare conditions, handouts generated by GPT-4 ranked the highest (14/15, 93%), followed by ChatGPT-3.5 (13.5/15, 90%), DermGPT (13/15, 87%), and DocsGPT (13/15, 87%). Resident reviewers commented on several key issues present throughout the LLM-generated PEMs. References were often included in PEMs that were left blank or not in alignment with the main purpose of the PEM (eg, a psoriasis PEM citing acne literature). Some references cited by LLMs were also found to be untraceable after a thorough literature search.

Qualitative analysis of AAD PEMs and select LLM-generated PEMs by the University of Chicago Urban Health Initiative Office of Diversity, Equity, and Inclusion's Health Literacy team was notable for the frequent use of multisyllable, "high-literacy" words across PEMs. Such words, including "permanently," "whether," and "environment," may be difficult for the average reader to understand. Further, individual sentences and paragraphs were often found to be too long for the average reader. Most documents' content was found to require prior medical knowledge to sufficiently comprehend, as many medical terms were frequently not defined within the handout. Formatting issues, including headings posed as questions and inconsistent bullet-point use, were other commonly encountered issues in both AAD and LLM-produced PEMs that may further limit their readability.

**Table 1.** Average Flesch-Kincaid reading levels (FKRLs) for patient education handouts generated by ChatGPT-3.5, GPT-4, DocsGPT, and DermGPT.

FKRLs	AAD <sup>ab</sup>	ChatGPT-3.5, mean (SD)			GPT-4, mean (SD)			DocsGPT, mean (SD)			DermGPT, mean (SD)			
		Not speci-fied <sup>c</sup>	Fifth grade <sup>d</sup>	Seventh grade <sup>e</sup>	Not speci-fied	Fifth grade	Seventh grade	Not speci-fied	Fifth grade	Seventh grade	Not speci-fied	Fifth grade	Seventh grade	
Common conditions														
Acne vulgaris	8.5	11.77 (0.13)	5.13 (0.43)	5.99 (0.85)	9.95 (0.98)	3.91 (0.43)	5.65 (1.03)	10.0 (1.02)	3.76 (0.51)	4.56 (0.26)	9.23 (0.5)	7.22 (0.46)	7.19 (0.34)	
Atopic der-matitis	9.1	11.73 (0.13)	4.94 (0.68)	7.25 (0.17)	10.19 (0.56)	4.26 (0.33)	7.03 (0.83)	10.06 (0.96)	5.78 (0.47)	7.2 (0.88)	12.74 (0.19)	6.9 (0.95)	6.6 (0)	
Herpes zoster	8.6	9.59 (0.14)	5.47 (0.63)	6.3 (1.1)	9.12 (0.88)	3.65 (0.25)	6.94 (0.68)	10.01 (0.68)	4.96 (0.28)	5.28 (0.49)	11.38 (0.93)	8.98 (0.17)	8.9 (0)	
Psoriasis	11.2	11.75 (0.32)	4.55 (1.15)	6.71 (0.95)	9.92 (0.57)	5.06 (0.2)	8.05 (0.76)	10.63 (0.89)	5.68 (0.43)	6.87 (1.08)	11.2 (0.86)	6.63 (1.36)	6.68 (0.62)	
Average FKRL across common con-ditions	9.35 (1.26) <sup>f</sup>	11.21 (1.08)	5.02 (0.38)	6.56 (0.55)	9.795 (0.47)	4.22 (0.61)	6.92 (0.98)	10.18 (0.3)	5.01 (0.93)	5.98 (1.26)	11.14 (1.45)	7.43 (1.06)	7.27 (1.15)	
Rare conditions														
Bullous pem-phigoid	8.4	12.09 (0.19)	4.57 (1.14)	6.91 (1.06)	9.65 (0.77)	4.24 (0.29)	7.37 (0.53)	9.98 (0.52)	6.11 (0.47)	6.86 (1.09)	11.67 (0.05)	7.34 (0.92)	9.39 (1.2)	
Epidermolysis bullosa	12.3	11.36 (0.23)	5.54 (0.79)	7.62 (0.88)	11.32 (0.65)	5.42 (0.51)	9.62 (0.94)	10.8 (0.44)	4.55 (0.4)	6.1 (0.7)	13.77 (0.09)	8.68 (0.82)	8.54 (0.13)	
Lamellar ichthyosis	10.3	11.63 (0.34)	5.19 (1.0)	5.92 (0.98)	9.51 (0.57)	4.08 (0.27)	5.77 (1.27)	11.08 (0.61)	5.66 (0.72)	6.75 (0.91)	11.68 (0.55)	6.6 (0)	6.6 (0)	
Lichen planus	7	10.73 (0.52)	5.21 (0.35)	6.53 (0.51)	8.92 (0.27)	4.08 (0.37)	7.06 (0.79)	9.77 (0.78)	4.88 (0.23)	6.01 (0.93)	10.6 (0.32)	5.95 (0.2)	5.77 (0.13)	
Average FKRL across common con-ditions	9.50 (2.3) <sup>f</sup>	11.45 (0.57)	5.13 (0.4)	6.75 (0.71)	9.85 (1.03)	4.46 (0.65)	7.46 (1.6)	10.41 (0.63)	5.30 (0.71)	6.43 (0.44)	11.93 (1.33)	7.14 (1.17)	7.58 (1.68)	

<sup>a</sup>AAD: American Academy of Dermatology.

<sup>b</sup>Values are expressed as handouts per disease or condition.

<sup>c</sup>When prompted to create patient education handouts without specifying reading level.

<sup>d</sup>When prompted to create patient education handouts at a fifth-grade reading level.

<sup>e</sup>When prompted to create patient education handouts at a seventh-grade reading level.

<sup>f</sup>Values are expressed in mean (SD).

**Table 2.** Handouts generated by ChatGPT-3.5, GPT-4, DocsGPT, and DermGPT that meet the prompted reading level.

Handouts generated at or below the specified reading level	ChatGPT-3.5, n (%)		GPT-4, n (%)		DocsGPT, n (%)		DermGPT, n (%)	
	Fifth-grade reading level <sup>a</sup>	Seventh-grade reading level <sup>b</sup>	Fifth-grade reading level	Seventh-grade reading level	Fifth-grade reading level	Seventh-grade reading level	Fifth-grade reading level	Seventh-grade reading level
<b>Common conditions</b>								
Acne vulgaris (n=10)	6 (60)	9 (90)	10 (100)	9 (90)	10 (100)	10 (100)	0 (0)	3 (30)
Atopic dermatitis (n=10)	7 (70)	0 (0)	10 (100)	5 (50)	1 (10)	3 (30)	0 (0)	10 (100)
Herpes zoster (n=10)	1 (10)	8 (80)	10 (100)	7 (70)	6 (60)	10 (100)	0 (0)	0 (0)
Psoriasis (n=10)	9 (90)	7 (70)	6 (60)	1 (10)	0 (0)	6 (60)	0 (0)	6 (60)
Total (n=40)	23 (57)	24 (60)	36 (90)	22 (55)	17 (42)	29 (72)	0 (0)	19 (47)
<b>Rare conditions</b>								
Bullous pemphigoid (n=10)	9 (90)	9 (90)	10 (100)	2 (20)	0 (0)	5 (50)	0 (0)	2 (20)
Epidermolysis bullosa (n=10)	1(10)	1 (10)	3 (30)	0 (0)	9 (90)	10 (100)	0 (0)	0 (0)
Lamellar ichthyosis (n=10)	8 (80)	9 (90)	10 (100)	9 (90)	4 (40)	7 (70)	0 (0)	10 (100)
Lichen planus (n=10)	2 (20)	9 (90)	10 (100)	3 (30)	8 (80)	9 (90)	4 (40)	10 (100)
Total (n=40)	20 (50)	28 (70)	33 (82)	14 (35)	21 (52)	31 (77)	4 (10)	22 (55)

<sup>a</sup>When prompted to create patient education handouts at a fifth-grade reading level.  
<sup>b</sup>When prompted to create patient education handouts at a seventh-grade reading level.

**Table 3.** LLM<sup>a</sup>-generated handouts meeting a prompted fifth- or seventh-grade reading level for common dermatoses.

LLM	Handouts meeting prompted fifth-grade reading level (n=40), n (%)	Handouts meeting prompted seventh-grade reading level (n=40), n (%)
ChatGPT-3.5	23 (58)	24 (60)
GPT-4	36 (90)	22 (55)
DocsGPT	17 (43)	29 (73)
DermGPT	0 (0)	19 (48)

<sup>a</sup>LLM: large language model.

**Table 4.** LLM<sup>a</sup>-generated handouts meeting a prompted fifth- or seventh-grade reading level for rare dermatoses.

LLM	Handouts meeting prompted fifth-grade reading level (n=40), n (%)	Handouts meeting prompted seventh-grade reading level (n=40), n (%)
ChatGPT-3.5	20 (50)	28 (70)
GPT-4	33 (83)	14 (35)
DocsGPT	21 (53)	32 (78)
DermGPT	4 (10)	22 (55)

<sup>a</sup>LLM: large language model.

## Discussion

### Principal Findings

Studies on interventions to improve care for patients with limited health literacy show that it is important to [17] improve

patient-centered communication, use clear communication techniques, reinforce teaching with confirmation of understanding, use visual aids, use clear medication labeling, develop clear health education materials, and use specialized health educators.

Patient education initiatives have been shown to be effective in dermatology, particularly for common dermatologic conditions such as AD and acne vulgaris. Specific to AD, patient educational initiatives implemented to improve the management of AD have resulted in a significant improvement in severity and quality of life for pediatric and adult patients [18-20]. Similarly, for patients with acne vulgaris, those who received audiovisual education materials regarding their condition showed significant improvements of their acne as well as increased treatment adherence and overall patient satisfaction [21,22]. One study focusing on written eczema action plans for parents whose children have AD showed improvements in child eczema based on this intervention [23]. Despite these successes, educational initiatives and interventions can be time-consuming and challenging to incorporate to a clinic workflow.

Few initiatives have focused on improving the readability of dermatologic PEMs that can easily be distributed at the end of a clinic visit. Studies demonstrate the association of low health literacy with worsened health outcomes and the success of educational interventions on patient outcomes [1,2]. As such, tools that help clinics create patient handouts at an appropriate US reading level (seventh- to eighth-grade level) may be an important factor in patient outcomes.

Larger academic institutions such as the University of Chicago have ancillary support through the Urban Health Initiative Office of Diversity, Equity, and Inclusion that offers services to review and edit existing patient handouts to meet health literacy standards. These standards strictly follow the Patient Education Materials Assessment Tool prepared by the AHRQ of the US Department of Health and Human Services [24]. Unlike standard readability software, human assessment of readability allows for a more nuanced, qualitative review that may be better able to assess how sentence structure, document formatting, and the inclusion of figures or images impact readability. However, these resources are not widely available and require considerable human effort, leaving smaller groups and independent practices largely unsupported. Further, such review may be subject to human error or bias, particularly if standardized rubrics or guidelines are not available.

This work is the first to assess the application of LLMs in generating dermatologic PEMs at specified reading levels. Our analysis suggests that LLM-produced PEMs may reliably meet seventh-grade FKRLs for select common and rare dermatologic conditions and are easy to read, understandable for patients, and mostly accurate. More specifically, GPT-4 appeared to outperform ChatGPT-3.5, DocsGPT, and DermGPT at the fifth-grade FKRL, although both ChatGPT-3.5 and DocsGPT performed better at the seventh-grade FKRL for rare conditions. Although the seventh-grade reading level is slightly outside that recommended by AHRQ for PEMs (fourth- to sixth-grade FKRL), LLMs consistently produced PEMs at lower reading

levels compared to currently available AAD PEMs for the same conditions. As such, LLMs may play a role in enhancing health literacy and disseminating accessible, understandable PEMs in dermatology. Importantly, if using LLMs to create PEMs, this study demonstrates the importance of specifying an FKRL in the prompt. Without specification, all LLMs consistently generate handouts above the average US reading level.

## Limitations

Key limitations of this work include the limited number of iterations per LLM prompt (n=10) as well as the limited number of common (n=4) and rare (n=4) diseases selected to study. Further, reliability assessment may be subject to reviewer bias and is limited by a small sample (n=2) of reviewers. The ability of LLMs to appropriately cite sources and produce factual information remains an area of continued improvement. Recently, novel LLMs using retrieval-augmented capabilities have been designed specifically for clinical practice to help enhance the ability of LLMs to produce factual, clinically relevant information [25]. However, the ability of these newer LLMs to sound human has limited their use [25]. Further, LLMs may benefit from prompt optimization techniques to produce the best outputs, which may require more time and effort than is feasible for clinician users [26]. Together, these issues may hinder the ability of LLMs to produce ready-to-share PEMs, which may result in extra time spent by clinical staff in fact-checking or formatting materials for dissemination. Some platforms, including GPT-4, DocsGPT, and DermGPT, require memberships or paid subscriptions or may have waitlists, which may limit their accessibility. The accuracy and readability of LLM-generated PEMs in multiple languages may present additional hurdles and warrant further investigation. Further, building trust by patients and providers in materials generated by LLMs remains to be explored. Ethical dilemmas surrounding the use of LLMs in dermatology must also consider whether the benefit of more accessible dermatologic information outweighs the risks of sharing potentially inaccurate or incomplete information [27,28]. To this effect, recent literature demonstrates that ChatGPT-3.5's responses to queries about common dermatologic skin conditions may be lacking in both accuracy and comprehensiveness [15]. As such, it is important to emphasize the use of LLMs in producing PEMs as a tool and not as a replacement to physician-written PEMs.

## Conclusions

LLMs such as ChatGPT-3.5, GPT-4, DocsGPT, and DermGPT may be useful in generating dermatology PEMs for select common and rare diseases at the seventh-grade FKRL. With prompting, LLMs consistently produce PEMs at lower reading levels than AAD PEMs for the same conditions and may be a useful supplementary tool in sharing appropriately readable dermatologic information with patients.

## Acknowledgments

The authors are grateful to Lisa Sandos, Shane Desautels, and Claudia Duffy of the University of Chicago Urban Health Initiative Office of Diversity, Equity, and Inclusion for their assistance with this project. This work would not be feasible without their time and dedication to health literacy.



## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Scoring rubric for preservation of meaning analysis.

[DOCX File, 12 KB - [derma\\_v7i1e55898\\_app1.docx](#)]

## Multimedia Appendix 2

Plain language guidelines.

[PDF File (Adobe PDF File), 158 KB - [derma\\_v7i1e55898\\_app2.pdf](#)]

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## Abbreviations

**AAD:** American Academy of Dermatology  
**AD:** atopic dermatitis  
**AHRQ:** Agency for Healthcare Research and Quality  
**FKRL:** Flesch-Kincaid reading level  
**LLM:** large language model  
**PEM:** patient education material

*Edited by W Guo; submitted 29.12.23; peer-reviewed by B Li, S Markham; comments to author 22.01.24; revised version received 01.03.24; accepted 06.03.24; published 16.05.24.*

*Please cite as:*

Lambert R, Choo ZY, Gradwohl K, Schroedl L, Ruiz De Luzuriaga A

Assessing the Application of Large Language Models in Generating Dermatologic Patient Education Materials According to Reading Level: Qualitative Study

*JMIR Dermatol* 2024;7:e55898

URL: <https://derma.jmir.org/2024/1/e55898>

doi: [10.2196/55898](https://doi.org/10.2196/55898)

PMID: [38754096](https://pubmed.ncbi.nlm.nih.gov/38754096/)

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Original Paper

# Efficacy of an Artificial Intelligence App (Aysa) in Dermatological Diagnosis: Cross-Sectional Analysis

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## Abstract

**Background:** Dermatology is an ideal specialty for artificial intelligence (AI)-driven image recognition to improve diagnostic accuracy and patient care. Lack of dermatologists in many parts of the world and the high frequency of cutaneous disorders and malignancies highlight the increasing need for AI-aided diagnosis. Although AI-based applications for the identification of dermatological conditions are widely available, research assessing their reliability and accuracy is lacking.

**Objective:** The aim of this study was to analyze the efficacy of the Aysa AI app as a preliminary diagnostic tool for various dermatological conditions in a semiurban town in India.

**Methods:** This observational cross-sectional study included patients over the age of 2 years who visited the dermatology clinic. Images of lesions from individuals with various skin disorders were uploaded to the app after obtaining informed consent. The app was used to make a patient profile, identify lesion morphology, plot the location on a human model, and answer questions regarding duration and symptoms. The app presented eight differential diagnoses, which were compared with the clinical diagnosis. The model's performance was evaluated using sensitivity, specificity, accuracy, positive predictive value, negative predictive value, and  $F_1$ -score. Comparison of categorical variables was performed with the  $\chi^2$  test and statistical significance was considered at  $P < .05$ .

**Results:** A total of 700 patients were part of the study. A wide variety of skin conditions were grouped into 12 categories. The AI model had a mean top-1 sensitivity of 71% (95% CI 61.5%-74.3%), top-3 sensitivity of 86.1% (95% CI 83.4%-88.6%), and all-8 sensitivity of 95.1% (95% CI 93.3%-96.6%). The top-1 sensitivities for diagnosis of skin infestations, disorders of keratinization, other inflammatory conditions, and bacterial infections were 85.7%, 85.7%, 82.7%, and 81.8%, respectively. In the case of photodermatoses and malignant tumors, the top-1 sensitivities were 33.3% and 10%, respectively. Each category had a strong correlation between the clinical diagnosis and the probable diagnoses ( $P < .001$ ).

**Conclusions:** The Aysa app showed promising results in identifying most dermatoses.

(JMIR Dermatol 2024;7:e48811) doi:[10.2196/48811](https://doi.org/10.2196/48811)

## KEYWORDS

artificial intelligence; AI; AI-aided diagnosis; dermatology; mobile app; application; neural network; machine learning; dermatological; skin; computer-aided diagnosis; diagnostic; imaging; lesion

## Introduction

### Background

Diagnostic and therapeutic decisions in dermatology are heavily influenced by the morphology of diverse skin lesions. Traditionally, dermatological diagnoses are established by integrating the patient's medical history, clinical examination, and, in some instances, dermoscopic and histopathologic analyses [1]. As it is predominantly a morphological feature-dependent specialty, dermatology is a field best suited for incorporating artificial intelligence (AI) image detection and recognition capabilities for aided diagnosis [2-5].

Given the discrepancy in access to dermatologists around the world, it is extremely crucial to be able to address patients' medical needs [6]. Less than 1 dermatologist is available for every 100,000 individuals in India, and the majority of these specialists work in urban areas [7,8]. The diversity of cutaneous disorders and their striking resemblance to each other make accurate and efficient diagnosis challenging for general physicians. A delayed diagnosis due to a lack of specialists might significantly impact the patient's quality of life [9,10]. Moreover, the high frequency of complicated inflammatory skin illnesses and the rising incidence of skin cancer have contributed to a surge in demand for dermatologists that is anticipated to continue growing in the future. Considering the potential for future pandemics, the capacity to deliver high-quality care virtually will likely continue to play a significant role in medicine [6,11]. AI-driven image diagnosis may be the solution to resolving these issues, allowing general practitioners to accurately detect common dermatological disorders by feeding a clinical image to a smartphone app [7,12,13].

Several AI-based applications have been created to assist in interpreting clinical pictures for various skin disorders, which are available for general use. By using these applications to examine concerning lesions, users may be prompted to schedule a telemedicine consultation or visit a dermatologist in person [6]. Medical personnel should have a thorough understanding of the merits and limitations of AI to promote its safe and efficient implementation [3,14]. Some of its merits include automating redundant assignments, performing constrained tasks, addressing spectator dependability issues, and ability to think outside the box. Conversely, there are unresolved legal, ethical, privacy, and liability issues associated with AI, and the inability to understand the decision-making process (ie, the "blackbox" nature) may limit its acceptability [2].

Despite the abundance of AI-integrated health apps accessible to the general public, there is limited research on their reliability, precision, and safety [6,15,16].

### The Aysa AI App

Aysa is an AI-enabled symptom-checker app developed by VisualDx. Aysa combines a problem-oriented clinical search with a well-curated medical image database comprising more

than 120,000 medical images pertaining to 200 skin conditions in all Fitzpatrick skin types, expert medical knowledge, and cutting-edge machine learning (ML) techniques. The app uses the in-device framework such as Apple's CoreML in iOS to accelerate ML tasks. Aysa can modify its results based on a user's medical history, further personalizing the experience for consumers. The Aysa app is commercially available for download on iOS and Android devices [17].

By analyzing clinical images, patient demographic details, skin type, the morphology of the lesions, and associated symptoms, the app provides probable diagnoses for skin conditions and gives a detailed overview of the condition along with the urgency of consultation. This enables the user to learn more about their skin issues and make informed decisions, although it is not intended for diagnostic purposes. Image recognition and analysis occur on the device itself using the in-device AI framework. However, there is a lack of information regarding the type of neural network the app uses. Privacy is ensured by encrypting images during transit, which are then discarded after analysis. Patient profiles, associated cases, and images are in complete control of the user [17].

Although the app is marketed as a symptom-checker app and not for diagnostic purposes, it is imperative to determine its accuracy and reliability, as the general public might be misled by the results.

### Objective

The aim of this study was to validate an AI-based app (Aysa) as a preliminary diagnostic tool for Asian users with Fitzpatrick skin types III-V living in a semiurban town in India seeking consultation in a tertiary-care hospital for common skin conditions such as dermatitis, disorders of keratinization, papulosquamous disorders, pigmentary disorders, photodermatoses, skin infections and infestations, tumors, and other inflammatory conditions.

## Methods

### Source of Data

This observational cross-sectional study included 700 participants older than 2 years who consulted the dermatology outpatient department of a tertiary-care facility [Shri B M Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be) University, Vijayapura, Karnataka, India] for common skin conditions between January 2023 and March 2023. All included patients were of Asian ethnicity with Fitzpatrick skin types III-V and presented with various skin conditions, which were grouped into the categories listed in Table 1. Malignant tumors were histopathologically confirmed. Hair and nail disorders and bullous disorders were excluded as the app is not designed to identify these conditions. Patients who had received prior treatment for their conditions and those who refused to authorize the inclusion of their images for the study were excluded.

**Table 1.** Various skin conditions included in the study grouped into broad categories.

Clinical category	Clinical conditions
Bacterial infections	Cellulitis, folliculitis, impetigo
Benign tumors	Acrochordon, dermatosis papulosa nigra, nevus, pyogenic granuloma, seborrheic keratosis, syringoma
Dermatitis	Atopic dermatitis, dyshidrotic dermatitis, hand dermatitis, nummular dermatitis, pityriasis alba
Disorders of keratinization	Acanthosis nigricans, ichthyosis, keratosis pilaris
Fungal infections	Candidiasis, dermatophytosis, pityriasis versicolor
Malignant tumors	Basal cell carcinoma, cutaneous lymphoma, squamous cell carcinoma
Other inflammatory disorders	Acne keloidalis nuchae, acne vulgaris, granuloma annulare, insect bite reaction, spider bite reaction, urticaria, vasculitis
Papulosquamous disorders	Lichen planus, psoriasis
Photodermatoses	Favre-Racouchot syndrome, polymorphous light eruption
Pigmentary disorders	Café-au-lait macule, freckles, melasma, vitiligo
Skin infestations	Pediculosis, scabies
Viral infections	Hand, foot, and mouth disease; herpes simplex 1 and 2 infections; herpes zoster; molluscum contagiosum; varicella; warts

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethics Committee of BLDE (Deemed to be University; IEC/No. 09/2021). Informed consent was obtained from all individual participants and data were anonymized. No compensation was provided for study participation.

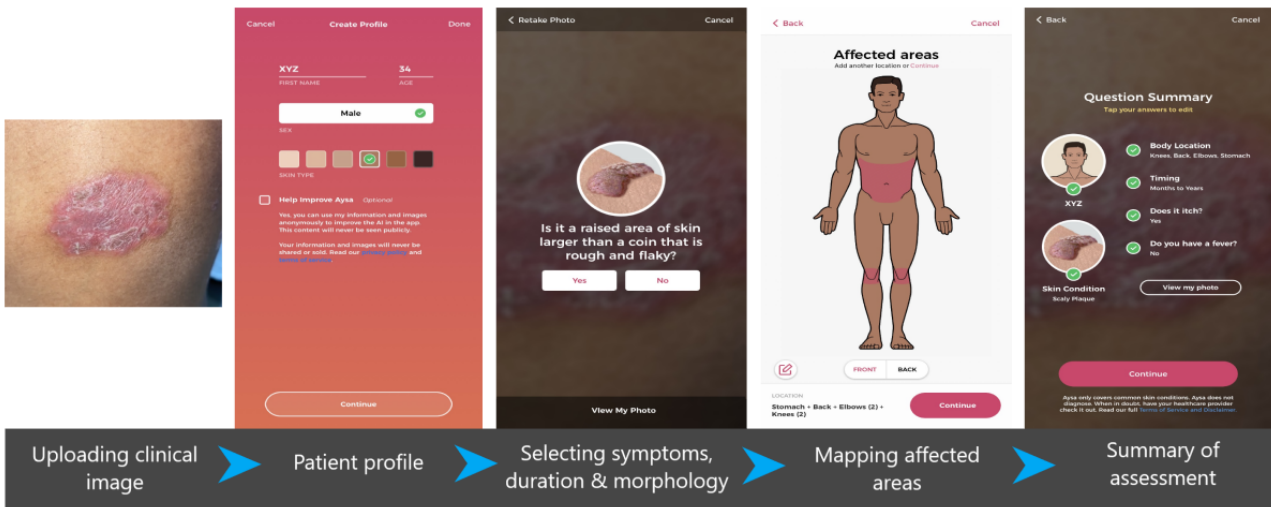
Methodology

This manuscript has been prepared following the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) checklist [18]. After detailed history and examination of the patients, the clinical diagnosis was established and verified by two expert dermatologists.

Histopathological confirmation was obtained for suspicious lesions. Images of the skin lesions were captured on an iPhone 11 with a 12-megapixel sensor in a well-lit environment ensuring privacy. These images were then uploaded onto the Aysa app. A patient profile pertaining to age, sex, and skin type was created. Following this, the app identified the morphology of the skin lesions and ascertained the lesions by providing a description in colloquial language with pictorial representations. The location of the lesions was plotted on a human model put forward by the app, and certain questions relating to the duration of the skin lesions and associated symptoms were answered. Figure 1 provides images from the app depicting the workflow.

The app identifies 8 probable differential diagnoses for every skin condition. These were compared with the clinical diagnosis established by dermatologists.

**Figure 1.** Images from the app depicting the workflow.



Statistical Analysis

Performance criteria such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV),

accuracy, and  $F_1$ -score were used to assess the model's performance. Disease-specific sensitivity; specificity; PPV; NPV; accuracy;  $F_1$ -score; and overall top-1, top-3, and all-8 sensitivities of the model were determined and represented as



percentages with 95% CIs. The clinical diagnosis had to be predicted among the top one, top three, and all probable diagnoses to be eligible for top-1, top-3, and all-8 sensitivities, respectively. Data were analyzed using JMP Pro 16 software version 16 (SAS Institute). Categorical variables were compared with the  $\chi^2$  test and statistical significance was considered at  $P<.05$ .

## Results

### Demographics and Basic Characteristics

This study involved a total of 700 patients. More than half the sample comprised male patients ( $n=418$ , 59.7%) and the greatest proportion of patients were in the age range of 10-19 years ( $n=178$ , 25.4%). Patients presented with a wide range of conditions, which were grouped into 12 categories: bacterial infections ( $n=22$ , 3.1%), benign tumors ( $n=40$ , 5.7%), dermatitis ( $n=55$ , 7.8%), disorders of keratinization ( $n=28$ , 4.0%), fungal infections ( $n=97$ , 13.8%), malignant tumors ( $n=20$ , 2.8%), other inflammatory disorders ( $n=110$ , 15.7%), papulosquamous disorders ( $n=70$ , 10.0%), photodermatoses ( $n=21$ , 3.0%), pigmentary disorders ( $n=101$ , 14.4%), skin infestations ( $n=28$ , 4.0%), and viral infections ( $n=108$ , 15.4%).

### Performance of the App

The AI model demonstrated an aggregate top-1 sensitivity of 71% (95% CI 61.5%-74.3%), top-3 sensitivity of 86.1% (95% CI 83.4%-88.6%), and all-8 sensitivity of 95.1% (95% CI 93.3%-96.6%). The top-1, top-3, and all-8 sensitivities; specificity; PPV; NPV; accuracy; and  $F_1$ -score of the grouped skin conditions are provided in Table 2. The top-1 sensitivities of skin infestations, disorders of keratinization, other inflammatory conditions, and bacterial infections were 85.7%, 85.7%, 82.7%, and 81.8%, respectively. All the classes displayed high specificity, accuracy, and NPV. All categories showed a significant association between clinical and probable top-1, top-3, and all-8 diagnoses ( $P<.001$ ).

Table 3 shows the top-1, top-3, and all-8 sensitivities; specificity; PPV; NPV; accuracy; and  $F_1$ -score of the most common individual skin conditions found among the broader categories. The top-1 sensitivities of acne, dermatophytosis, psoriasis, lichen planus, and vitiligo were 93.2%, 72.2%, 81%, 27.7%, and 97%, respectively. The confusion matrix between probable top-1 diagnoses and clinical diagnoses is illustrated in Figure 2. Figure 3 depicts representative clinical images with their corresponding clinical and predicted diagnoses.

**Table 2.** Performance metrics of the probable diagnoses of the app compared to clinical diagnoses grouped according to skin condition category (N=700).

Clinical category	Cases, n (%)	Sensitivity, % (95% CI)			Specificity, % (95% CI)	PPV <sup>a</sup> , % (95% CI)	NPV <sup>b</sup> , % (95% CI)	Accuracy, % (95% CI)	F <sub>1</sub> -score	P value
		Top-1	Top-3	All-8						
Bacterial infections	22 (3.1)	81.8 (59.7-94.8)	90.9 (70.8-98.9)	100 (84.6-100)	99.7 (98.9-99.9)	90 (68.9-97.3)	99.4 (98.6-99.8)	99.1 (98.1-99.7)	0.857	<.001
Benign tumors	40 (5.7)	62.5 (45.8-77.3)	85 (91.2-100)	92.5 (79.6-98.4)	99.5 (98.7-99.9)	89.3 (72.4-96.3)	97.8 (96.7-98.5)	97.4 (95.9-98.5)	0.735	<.001
Dermatitis	55 (7.8)	52.7 (38.8-66.3)	78.1 (64.9-88.1)	98.1(90.3-99.9)	94.3 (92.2-95.9)	43.9 (34.3-53.9)	95.9 (94.6-96.9)	91 (88.6-93)	0.479	<.001
Disorders of keratinization	28 (4)	85.7 (67.3-95.9)	96.4 (81.6-99.9)	100 (87.7-100)	100 (99.4-100)	100	99.4 (98.5-99.8)	99.4 (98.5-99.8)	0.923	<.001
Fungal infections	97 (13.8)	71.1 (61-79.9)	86.6 (78.2-92.7)	96.9 (91.2-99.4)	98.1 (96.8-99)	86.2 (77.5-91.9)	95.5 (93.9-96.7)	94.4 (92.5-96)	0.779	<.001
Malignant tumors	20 (2.8)	10 (1.2-31.7)	10 (1.2-31.7)	25 (8.6-49.1)	99.8 (99.2-100)	66.7 (15.9-95.5)	97.4 (97-97.8)	97.3 (95.8-98.4)	0.173	<.001
Other inflammatory conditions	110 (15.7)	82.7 (743-89.3)	95.4 (89.7-98.5)	100 (96.7-100)	82.7 (74.3-89.9)	91 (84-95.1)	96.8 (95.3-97.9)	96 (94.3-97.3)	0.866	<.001
Papulosquamous disorders	70 (10)	68.6 (56.4-79.1)	80 (68.7-88.6)	98.6 (92.3-99.9)	99.8 (99.1-100)	97.9 (87-99.7)	96.6 (95.3-97.6)	96.7 (95.1-97.9)	0.806	<.001
Photodermatoses	21 (3)	33.3 (14.6-56.9)	61.9 (38.4-81.9)	100 (83.9-100)	95.6 (93.7-97)	18.9 (10.4-31.9)	97.9 (97.1-98.4)	93.7 (91.6-95.4)	0.241	<.001
Pigmentary disorders	101 (14.4)	77.2 (67.8-84.9)	97 (91.6-99.4)	97 (91.6-99.4)	99.7 (98.8-99.9)	97.5 (90.7-99.4)	96.3 (94.8-97.4)	96.4 (94.8-97.7)	0.861	<.001
Skin infestations	28 (4)	85.7 (67.3-95.9)	100 (87.7-100)	100 (87.7-100)	98.9 (97.9-99.6)	77.4 (61.8-87.9)	99.4 (98.5-99.7)	98.4 (97.2-99)	0.813	<.001
Viral infections	108 (15.4)	75.9 (66.7-83.6)	86.1 (78.1-92)	92.6 (85.9-96.7)	98.6 (97.3-99.4)	91.1 (83.6-95.3)	95.7 (94.1-96.9)	95.1 (93.3-96.6)	0.828	<.001

<sup>a</sup>PPV: positive predictive value.  
<sup>b</sup>NPV: negative predictive value.

Individual skin conditions	Cases, n (%)	Sensitivity, % (95% CI)			Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Accuracy, % (95% CI)	<i>F</i> <sub>1</sub> -score	<i>P</i> value
		Top-1	Top-3	All-8						
Acne	88 (12.6)	93.2 (85.7-97.5)	100 (95.8-100)	100 (95.8-100)	99.8 (99-100)	98.8 (92-99.8)	99 (97.9-99.5)	99 (97.9-99.6)	0.959	<.001
Dermatophytosis	90 (12.9)	72.2 (61.8-81.1)	88.9 (80.5-94.5)	100 (95.9-100)	97.9 (96.4-98.9)	83.3 (74.2-89.7)	95.9 (94.5-97)	94.6 (92.6-96.1)	0.773	<.001
Psoriasis	58 (8.3)	81 (68.6-90.1)	91.4 (81-97.1)	100 (93.8-100)	99.8 (99.1-100)	97.9 (86.9-99.7)	98.3 (97.1-99)	98.3 (97-99.1)	0.886	<.001
Lichen planus	12 (1.7)	8.3 (0.2-38.5)	25 (5.5-57.1)	91.7 (61.5-99.8)	99.9 (99.1-100)	50 (6.2-93.8)	98.4 (98.1-98.7)	98.3 (97-99.1)	0.142	<.001
Vitiligo	68 (9.7)	97 (89.8-99.6)	100 (94.7-100)	100 (94.7-100)	100 (99.4-100)	100	99.68 (98.8-99.9)	99.7 (98.9-99.9)	0.985	<.001

[illegible]

**Figure 3.** Clinical images with clinical and predicted diagnoses. AD: actual diagnosis; BCC: basal cell carcinoma; CALM: café-au-lait macule; PD: predicted diagnosis.



Discussion

Key Findings

This study analyzed the diagnostic accuracy of a commercially available AI-based health care app for various skin conditions. The app uses ML to analyze the clinical images, predict the probable diagnoses, and provide personalized guidance to the user.

Most of the patients included in this study had inflammatory conditions, pigmentary disorders, and infectious diseases. The top-1, top-3, and all-8 sensitivities for the AI model were collectively 71% (95% CI 61.5%-74.3%), 86.1% (95% CI 83.4%-88.6%), and 95.1% (95% CI 93.3%-96.6%), respectively. The app demonstrated high sensitivities in most categories in top-1 probable diagnoses, except in benign tumors, dermatitis, malignant tumors, and photodermatoses. When the top-3 probable diagnoses were considered, the sensitivities increased in all the categories except malignant disorders. In the case of photodermatoses, the sensitivity increased from 33.3% to 61.9% and subsequently to 100% when top-3 and all-8 probable diagnoses were considered, respectively. However, in the case of malignant disorders, the sensitivity remained the same and only increased to 25% when all 8 probable diagnoses were taken into account.

When considering specific skin conditions, the app could diagnose acne, dermatophytosis, psoriasis, and vitiligo with good sensitivity. Among papulosquamous disorders, the top-1 sensitivities of psoriasis and lichen planus were 81% and 27.7%, respectively. Among other inflammatory disorders, the top-1 sensitivity of acne was 93.2%, which increased to 100% when top-3 diagnoses were included.

Examination of the confusion matrix showed that the number of false negatives for herpes zoster was equal to the number of true positives, with herpes simplex being the most predicted diagnosis among false negatives (predicted in 43.7% of all patients with herpes zoster). This can likely be attributed to the

morphology and location of the lesions. Most basal cell carcinoma cases (76.9%) were predicted as melanoma in the top-1 diagnosis.

**Comparison With Similar Studies**

We further sought to compare the diagnostic accuracy of the Aysa app with similar algorithms under comparable study conditions. However, direct comparison would only be possible if the same image sets were used in the evaluation of various algorithms.

Marri et al [2] assessed the Tibot AI app in diagnosing skin conditions in 600 patients. For the predicted top-3 diagnoses given by the app, the mean prediction accuracy was 96.1% (95% CI 94.3%-97.5%) and for the exact diagnosis it was 80.6% (95% CI 77.2%-83.7%).

Using clinical photos of skin lesions from patients with verified COVID-19, healthy individuals, and 18 common dermatoses, Mathur et al [19] developed a convolutional neural network (CNN)-based algorithm. The top-1 overall sensitivity for the diagnosis of 20 skin disorders was 87.65%, while the top-3 sensitivity was 96.72%.

Table 4 provides a comparison of the sensitivities, specificity, and PPV of AI algorithms of this study and the studies by Marri et al [2] and Mathur et al [19] in diagnosing various skin disorders. The sensitivity in the majority of the conditions was comparable in all the studies except for lichen planus and malignant tumors. Although the Tibot app evaluated by Marri et al [2] demonstrated higher sensitivity in diagnosing malignant tumors, it only gives a broad diagnosis, unlike the Aysa app, which predicts a specific diagnosis. In the study by Mathur et al [19], the CNN model predicted lichen planus with better sensitivity than achieved with the Aysa app.

Wu et al [20] evaluated the accuracy of a CNN model in diagnosing inflammatory skin conditions. The sensitivity and specificity of the model were found to be 94.4% and 97.2%, respectively, and the overall accuracy was 95.8%. For eczema and atopic dermatitis, the accuracy was 92.57%, with a



sensitivity and specificity of 94.56% and 94.4%, respectively. The accuracy for psoriasis was 89.46%, with a sensitivity and specificity of 91.4% and 95.48%, respectively. In this study, the Aysa app showed an accuracy of 98.3% with a top-1 sensitivity of 81% and a specificity of 99.8% in the case of psoriasis. For atopic dermatitis, the accuracy was 91%, with a top-1 sensitivity and specificity of 52.7% and 94.3%, respectively.

Other studies have demonstrated the efficacy of AI in diagnosing benign and malignant dermatoses [21-23]. The performance of the CNN models evaluated by Esteva et al [22] and Han et al [23] was comparable to or better than the diagnostic ability of dermatologists. In this study, the Aysa app demonstrated a top-1 sensitivity of 62.5% and a specificity of 99.5% in identifying benign tumors. For malignant conditions, the top-1 sensitivity was 10% with a specificity of 99.8%.

**Table 4.** Comparison of the sensitivities, specificities, and positive predictive values (PPVs) of various artificial intelligence algorithms evaluated in this study and previous studies.

Skin conditions	This study				Marri et al [2]				Mathur et al [19]			
	Sensitivity, %		Specificity, %	PPV, %	Sensitivity, %		Specificity, %	PPV, %	Sensitivity, %		Specificity, %	PPV, %
	Top-1	Top-3			Top-1	Top-3			Top-1	Top-3		
Acne	93.2	100	99.8	98.8	92	99	99	91	92.3	97.9	99.1	91
Bacterial infections	81.8	90.9	99.7	90	50	83	99	43	88.6 <sup>a</sup>	95.3	99.2	89.6
Benign tumors	62.5	85	99.5	89.3	71	100	98	69	— <sup>b</sup>	—	—	—
Dermatitis	52.7	78.1	94.3	43.9	75	100	95	37	—	—	—	—
Fungal infections	71.1	86.6	98.1	86.2	83	97	96	80	90 <sup>c</sup>	98.3	97.9	89.2
Lichen planus	8.3	25	99.9	50	—	—	—	—	81.2	96.2	99	84.7
Malignant tumors	10	10	99.8	66.7	82	100	99	75	—	—	—	—
Psoriasis	81	91.4	99.8	97.9	70	91	99	87	85.3	96.9	97.9	86
Pigmentary disorders	77.2	97	99.7	97.5	89	99	99	96	—	—	—	—
Skin infestations	85.7	100	98.9	77.4	69	94	99	75	—	—	—	—
Viral infections	75.9	86.1	98.6	91.1	63	95	98	90	86.4 <sup>d</sup>	95.3	99.4	85.2

<sup>a</sup>Included impetigo and pyodermas only.  
<sup>b</sup>These conditions were not included in the respective studies.  
<sup>c</sup>Included tinea cruris, corporis, or faciei only.  
<sup>d</sup>Included herpes zoster only.

Implications

The Aysa app has proven to be effective in predicting most of the common dermatoses encountered in a population. In addition to skin analysis, the app provides in-depth details on the conditions in the form of an overview comprising the causes, symptoms, risk factors, course, prognosis, and treatment information; preconsultation advice; when to see a doctor; and differential diagnoses. Materials adapted from renowned textbooks, journal papers, PubMed, the World Health Organization, the Infectious Diseases Society of America, and the US Centers for Disease Control and Prevention are included in the content [17]. Notifying the patient of the urgency index is practical because skin disorders are typically ignored until they cause significant inconvenience. Thus, the Aysa app has the potential to motivate patients to seek medical care, improve patient engagement and participation, improve the efficiency and productivity of physicians, and reduce health care expenditure [24,25].

Health care practices can be enhanced by integrating advanced diagnostic knowledge using these AI-based health care systems. For a skin condition, images can be uploaded to a specialized dermatological AI system from a general practitioner’s office, and prompt analysis can be performed if the uploaded image is sufficient to reach a conclusion. This would help patients with low-risk conditions receive immediate reassurance about their concerns, while those with high-risk conditions can have a speedy referral to a specialist clinic [12]. Finding a balance that optimizes the advantages of AI while maintaining the humanistic touch is crucial for patient care.

Limitations

Absence of image consistency in terms of focus, angle, and illumination is one of the main limitations of our study. Although the app can identify almost 200 skin disorders, this study included only 46 common conditions. The majority of the study population had infections, pigmentary disorders, and inflammatory illnesses. Photodermatoses and tumors were relatively less frequent in this population, which may account for the app’s poor performance in these categories. Additional





research focusing on these conditions and others not included in this study may be required to validate the app's performance. For simplicity of comprehension, specific skin conditions were categorized into broad groups. This could have given an impression of relatively consistent performance, as in the case of papulosquamous disorders, where the app showed good sensitivity to diagnose psoriasis but failed to diagnose lichen planus with the same sensitivity. Dermatological conditions have a diverse morphology based on various factors, including severity of the disease. This might hinder the ability of the app to provide an accurate diagnosis. Further studies correlating severity of the disease and other factors with the app's diagnostic ability might be required.

There are certain drawbacks to the app. As it is designed for users above the age of 2 years, certain conditions such as infantile hemangioma, commonly encountered in clinical

practice, could not be diagnosed. As the app is intended for assessing skin conditions, hair and nail disorders could not be included in the study. The preconsultation advice provided by the app contains information regarding over-the-counter medications appropriate for the condition. This may encourage the patient to self-medicate rather than seek consultation. Another limitation is the lack of transparency regarding the type of neural network used by the app despite our efforts to obtain that information.

## Conclusions

The Aysa app has demonstrated promising outcomes in the diagnosis of prevalent dermatological issues such as infections, inflammatory disorders, infestations, and pigmentary disorders. However, the app is unreliable at detecting photodermatoses and malignant tumors. Further improvement might be required for the app to be implemented in clinical practice.

## Data Availability

The data sets generated and analyzed during this study are available from the corresponding author on reasonable request.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

TRIPOD checklist.

[[PDF File \(Adobe PDF File\), 34 KB - derma\\_v7i1e48811\\_app1.pdf](#)]

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## Abbreviations

**AI:** artificial intelligence

**CNN:** convolutional neural network

**ML:** machine learning

**NPV:** negative predictive value

**PPV:** positive predictive value

**TRIPOD:** Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis

*Edited by J Solomon, I Brooks; submitted 08.05.23; peer-reviewed by JC Hernández-Rodríguez, JA Benítez-Andrades, D Chrimes, Y Zhuang; comments to author 19.07.23; revised version received 12.08.23; accepted 08.06.24; published 02.07.24.*

*Please cite as:*

Marri SS, Albadri W, Hyder MS, Janagond AB, Inamadar AC

Efficacy of an Artificial Intelligence App (Aysa) in Dermatological Diagnosis: Cross-Sectional Analysis

*JMIR Dermatol* 2024;7:e48811

URL: <https://derma.jmir.org/2024/1/e48811>

doi: [10.2196/48811](#)

PMID:

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Viewpoint

# Atrophic Postacne Scar Treatment: Narrative Review

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## Abstract

Acne scarring is a frequent complication of acne. Scars negatively impact psychosocial and physical well-being. Optimal treatments significantly improve the appearance, quality of life, and self-esteem of people with scarring. A wide range of interventions have been proposed for acne scars. This narrative review aimed to focus on facial atrophic scarring interventions. The management of acne scarring includes various types of resurfacing (chemical peels, lasers, and dermabrasion); the use of injectable fillers; and surgical methods, such as needling, punch excision, punch elevation, or subcision. Since the scarred tissue has impaired regeneration abilities, the future implementation of stem or progenitor regenerative medical techniques is likely to add considerable value. There are limited randomized controlled trials that aimed to determine which treatment options should be considered the gold standard. Combining interventions would likely produce more benefit compared to the implementation of a single method.

(*JMIR Dermatol* 2024;7:e49954) doi:[10.2196/49954](https://doi.org/10.2196/49954)

## KEYWORDS

acne; atrophic scars; treatment; acne scarring; scars; scarring; well-being; psychosocial well-being; psychosocial; physical well-being; self-esteem; face; facial scarring; implications; skin; dermatology; dermatologist

## Introduction

Atrophic scars present clinically as indentations in the skin due to destructive inflammation in the deep dermis as a result of delayed or inadequate acne treatment. Atrophic postacne scars are further classified into ice-pick scars (V-shaped epithelial tracts with a sharp margin that can extend deeper in the skin), boxcar scars (a round-to-oval scar with sharp vertical sides that can extend deeper in the skin), and rolling scars (irregular scars with a rolling or undulating shape) [1]. Atrophic postacne scar risk assessment depends on the worst-ever severity of acne, the duration of acne, family history of atrophic postacne scars, and lesion manipulation behaviors. This provides a dichotomous outcome: lower versus higher risk of developing scars [2].

Early effective treatment of acne is the best strategy to prevent or limit postacne scarring. Different factors influence the treatment choice for acne scars, for example, color, texture, distensibility, and morphology. For example, the selection of

the chemical peeling agent and concentration depends on the patient's skin type and severity of scarring. Moreover, considering the flexibility and low cost, chemical peels, in general, play an important role in the management of all grades of acne scars. However, trichloroacetic acid (TCA) chemical peeling carries the risk of postinflammatory hyperpigmentation (PIH), particularly in darker skin phototypes [3]. Regarding lasers, choosing the type and appropriate settings while taking into consideration the depth of the scar, skin type, and tendency to develop PIH is of utmost importance [4]. Nevertheless, severe scars are poorly treated and do not improve greatly with resurfacing procedures, where punch excision and punch elevation can be tried instead [3].

Preprocedure considerations include the acne-free period, isotretinoin-free period, history of skin infections (eg, herpes virus), history of general or local skin disorders affecting healing, history of keloids or hypertrophic scarring, history of tanning, skin phototype, and sun exposure habits, as well as

history of systemic or local therapies affecting healing [5]. The management of acne scarring includes various types of resurfacing (chemical peels, lasers, and dermabrasion); the use of injectable fillers; and surgical methods, such as needling, subcision, punch excision, or punch elevation [6].

This narrative review aimed to focus on facial atrophic scarring interventions in brief. The outcomes, including adverse events, participant satisfaction, and postprocedure downtime, are reviewed.

## Methods

A PubMed literature review was conducted, and the search keywords included a combination of the following keywords: “acne,” “scars,” and “treatment.” The synonyms “management,” “modalities,” and “therapy” were also considered, along with the names of different modalities such as “laser,” “radiofrequency,” “needling, microneedle, micro needling or microneedling,” “dermaroller,” “dermabrasion, microdermabrasion or micro dermabrasion,” “chemical peel, chemical peeling or chemical peels,” “platelet rich plasma,” “stem cells,” “fillers,” “subcision,” “punch,” “growth factor,” “ozone,” and “botulinum toxin.”

The articles regarding clinical trials, meta-analyses, and systematic reviews with at least an English abstract that were published before June 1, 2023, were included.

Articles discussing interventions for nonfacial or other types of scars were excluded.

## Results

### Scars-Associated Erythema Management

Treating scars-associated erythema (SAE) can be an initial and dramatic step toward improving acne scarring. Pulsed dye laser (PDL) is the gold standard. It uses selective thermolysis to destroy vascular components of the dermis, leading to clinical improvement of erythema. The major chromophore is oxyhemoglobin, which absorbs light in the yellow and green range, with peaks at 418, 542, and 577 nm. The long-pulsed PDL (595–600 nm) slowly heats target vessels with less risk of postprocedure purpura. In addition to treating SAE, PDL also induces collagen remodeling, thus improving the depressed appearance of scars [7].

Other laser and light devices include the potassium titanyl phosphate laser, also known as the frequency-doubled neodymium-doped yttrium aluminum garnet (Nd:YAG) laser; 1550-nm erbium-doped fractional laser (EDL); and intense pulsed light (IPL) [8]. The use of the potassium titanyl phosphate laser leads to significant improvement in the vascular component without significant effects on collagen remodeling [9].

In addition to being a frontline agent for atrophic scars, the 1550-nm wavelength emitted by EDL penetrates approximately 1000 µm into the skin to target tissue water, allowing for the improvement of erythema through microvascular destruction of vessels deeper in the dermis [10].

IPL does not typically produce purpura, and larger spot sizes allow for a greater surface area to be treated deeper and more quickly. However, given the range of wavelengths that may be used; adjacent, competing chromophore absorption peaks; and poor specificity, drawing conclusions regarding efficacy in treating SAE with IPL is difficult. Moreover, care must also be taken to avoid postinflammatory hypopigmentation and PIH in darker skin phototypes [7].

### Ablative Laser Resurfacing

Traditional ablative laser resurfacing removes the epidermis and part of the dermis of the scars, allowing collagen remodeling and re-epithelialization. Ablative 10,600-nm carbon dioxide (CO<sub>2</sub>) lasers and 2940-nm erbium-doped yttrium aluminum garnet (Er:YAG) lasers are the most commonly used ablative lasers for acne scars. CO<sub>2</sub> lasers cause denaturation and thermal stimulus in the tissues surrounding ablation, promoting wound healing and the production of myofibroblasts and matrix proteins [11]. Adverse effects include persistent erythema, hypopigmentation, PIH, infection, scarring, and a relatively long recovery period (weeks) [12].

Fractional laser resurfacing acts, as the name indicates, on regularly spaced arrays over a fraction of the skin surface to induce thermal ablation of microscopic columns of epidermal and dermal tissue. Microscopic columns of light or microthermal zones (MTZs) leave the intervening skin unaffected and minimize damage to the epidermis. The skin adjacent to sites of laser injury remains intact, allowing for rapid postprocedural re-epithelialization due to the migration of intact cells into the damaged microcolumns [13]. This approach provides a faster recovery when compared with conventional ablative resurfacing [14].

Fractional 10,600-nm CO<sub>2</sub> laser; 2940-nm Er:YAG laser; 2790-nm erbium-doped yttrium scandium gallium garnet laser; 1540-nm erbium glass (Er:glass) laser; and 1550-nm EDL produce comparable rates of improvement in atrophic acne scars after multiple treatments. The least responsive scar type is ice-pick scars [7]. Adverse effects include erythema that lasts for days to weeks, PIH that lasts for weeks, and procedural discomfort. These lasers are safer in darker skin phototypes, with less dyschromia than ablative lasers. Lower densities have been associated with less risk for hyperpigmentation [15]. The deeper penetration of the laser might lead to contraction of the underlying muscle, so lower energy and densities should be used on the periocular region [7]. Fractional 1540 - nm Er:glass laser treatment for 3 sessions at 4 - week intervals improved scar texture and severity [16].

### Nonablative Laser Resurfacing

Nonablative laser resurfacing, such as the short- and long-pulsed and Q-switched Nd:YAG lasers and diode lasers, produces dermal thermal injury while preserving the epidermis; this promotes collagen remodeling, which leads to improvement in scarring [17]. Results are accordingly modest (20%–30%), and multiple treatment sessions are required to achieve typically less impressive results. Postprocedure side effects are minimal, with erythema lasting less than 2 hours and no reports of pain, swelling, oozing, or scarring. Using the 532-nm Nd:YAG laser



for an average of 3 treatments improved scars by an average of 53.6%, with a range from 10% to 90% [18]. The use of the nonfractional, nonablative Q-switched 1064-nm Nd:YAG laser (4 sessions at 4 - week intervals) resulted in a more than 50% improvement in 3 out of 32 patients with acne scarring [19].

The picosecond 755-nm Alexandrite laser delivers shorter pulse durations with lower fluences of energy and, therefore, leads to fewer adverse effects. With the aid of a diffractive lens array, which delivers pulses 500 µm apart, it permits the treatment of a greater surface area, improving the appearance and texture of atrophic rolling scars similar to fractional ablative lasers. This technology has a favorable safety profile for darker skin phototypes; the mean pain score is mild; and downtime is minimal, with transient erythema and edema and no exfoliation, vesiculation, crusting, scarring, hypopigmentation, or PIH [20].

### Radiofrequency

Nonablative radiofrequency (RF) treatments deliver a current through the dermis that stimulates dermal remodeling. With traditional unipolar or monopolar RF, a single electrode allows for penetration deep into the dermis, but this is associated with increased pain and discomfort [21]. Bipolar RF allows for the delivery of a more focused current to the dermis. Fractional RF uses an array of electrodes to create zones of thermal wounds that stimulate dermal remodeling. Microneedles can be used to deliver RF to a particular depth within the dermis. Microneedle bipolar RF and fractional RF treatments offer the best results for acne scarring, particularly ice-pick and boxcar scars [22]. Needling and ablative fractional lasers are tolerable and safe procedures with no significant difference in the treatment of skin scars in 60% of previous studies [23]. The adverse reactions associated with RF include transient pain, erythema, and scabbing that resolve within days [7]. Zhang et al [24] found that fractional RF sessions resulted in comparable improvement of acne scars after fractional lasers, with no PIH observed on the areas treated with fractional RF.

### Skin Needling

Skin needling procedures may diminish the appearance of acne scars. A needling device is rolled over the surface of the skin to form numerous perforations in the epidermis and dermis, with the goal of stimulating new collagen [25]. The advantages of skin needling include low cost, a relatively short recovery period (2-3 days), and a very low risk for PIH [26].

Skin needling treatment is well tolerated by most people and the pain is minimal. The full result may take 8 to 12 months as the deposition of new collagen takes place slowly [25].

One important advantage is that the epidermis remains intact, eliminating most of the risks of chemical peeling or laser resurfacing. Furthermore, microneedling provides a clear channel for the efficient absorption of topical agents, including platelet-rich plasma (PRP), which can improve cosmetic results [27].

### Dermabrasion and Microdermabrasion

Dermabrasion involves the use of tools (eg, high - speed brush, diamond cylinder, fraise, or silicon carbide sandpaper) to remove the epidermis or the epidermis and part of the dermis. An

advantage of the procedure is that it allows the clinician to target scar edges precisely without thermal injury. It may be effective for some acne scars but is usually not used for ice-pick or deep boxcar scars. Adverse effects include significant pain, a considerable recovery time, scarring, pigment alterations, and milia formation [28].

Microdermabrasion (MDA) is a minimally invasive epidermal resurfacing procedure, in which abrasive crystals are propelled against the skin under the control of a handheld vacuum system. The crystals cause gentle mechanical abrasion to the skin, which ultimately removes the stratum corneum layer of the epidermis. As part of the wound healing process, new epidermis forms with enhanced cosmesis [29]. Half-side comparison between combined MDA plus aminolevulinic acid–photodynamic therapy (PDT) versus combined MDA plus placebo - PDT for 5 sessions (4 - week intervals) showed more improvement of scarring on the combined MDA plus aminolevulinic acid–PDT split - face than the combined MDA plus placebo - PDT split - face using the Physician's Global Assessment of Acne Scarring scale [30].

### Chemical Peels

Chemical peels (using glycolic acid, lactic acid, salicylic acid, mandelic acid, TCA, or phenol) are used in treating small, depressed scars but not ice-pick or deep boxcar scars [31,32]. They induce injury to the skin that stimulates collagen remodeling and are categorized as superficial, medium, and deep based on the depth of the injury [7].

Superficial peels, such as lactic acid, salicylic acid, glycolic acid, Jessner solution, and 10% to 20% TCA, only affect the epidermis. Medium depth peels, such as combined Jessner solution with 25% to 35% TCA, affect the epidermis and papillary dermis. Deep peels, such as 50% or higher TCA and phenol (carbolic acid), injure skin to the midreticular dermis. Complications, including prolonged erythema, infection, PIH, and scarring, are more common in darker skin phototypes, deeper peels, and sun exposure. Phenol has been associated with cardiac toxicity related to systemic absorption [7].

Serial biweekly application of glycolic acid peels with different concentrations in a gradually increasing manner (2 - week intervals) is better than 15% glycolic acid cream applied daily for 24 weeks [33]. The chemical reconstruction of skin scars (CROSS) chemical peeling method applied twice every 12 weeks had comparable results to the use of the 1550-nm Er:glass fractional laser for 3 sessions (6 - week intervals) [34]. Four sessions (4 - week intervals) of chemical peeling using full - strength TCA (100% TCA) CROSS showed equivalent improvement as 4 sessions (4 - week intervals) of skin needling using a dermaroller, with reported transient PIH in the peeling group [35]. Six sessions (4 weeks apart) of chemical peeling with 20% TCA combined with skin needling showed comparable improvement as 6 sessions (4 weeks apart) of fractional nonablative 1540-nm Er:glass laser treatment, with more than 50% improvement in acne scars [36]. Ultrapulsed CO<sub>2</sub> fractional laser combined with 30% supramolecular salicylic acid has better efficacy in the treatment of acne scars than laser alone, and according to patient self-assessment, the combined treatment has a greater degree of improvement in acne scars and does not increase patient pain scores and related

adverse reactions [37]. Four sessions (6 - week intervals) of chemical peeling with 20% TCA combined with skin needling is superior to deep peeling using a non-hydro - alcoholic solution of oil phenol in 60% concentration formula [38].

### PRP and Stem Cell Therapy

Autologous PRP can enhance wound healing by accelerating tissue repair through the release of growth factors, cytokines, and chemokines from their granules. Intradermal injections of PRP were first noted to improve acne scarring when used for skin rejuvenation. Topical PRP has a synergistic effect with skin needling in atrophic acne scars, as skin needling creates a way for PRP absorption and allows platelets to contribute to wound healing. PRP as both an intradermal injection and topical application in fluid or gel form after fractional ablative CO<sub>2</sub> laser therapy enhanced the recovery of laser-damaged skin and improved the clinical appearance of acne scars [39-41].

Mesenchymal stem cells (MSCs) are capable of differentiation into various cell lineages and have been shown to promote wound healing [42]. MSCs can be isolated from umbilical cord blood and expanded [43]. In contrast to umbilical cord MSCs, adipose tissue-derived MSCs are relatively easy to obtain. One injection of autologous adipose tissue-derived adult stem cells is as effective as 3 sessions of fractional CO<sub>2</sub> laser in the treatment of atrophic acne scars [44].

### Filler

Injectable fillers have been proposed to improve the appearance of atrophic acne scars, including collagen, autologous fat transfer, and artificial injectable fillers [45]. Hyaluronic acid (HA) fillers typically last for a few months, making repeated treatments necessary, which increases cost [7]. Semipermanent fillers can last up to 2 years and are biostimulatory; they include poly-L-lactic acid and calcium hydroxylapatite [46,47]. Permanent fillers comprise larger particles that cannot be phagocytosed. They can last from several years to lifelong but can be displaced over time due to changes in the adjacent connective tissue. Silicone is relatively cheap and is stable for 10 to 20 years. Polymethylmethacrylate is a synthetic permanent filler suspended in bovine collagen and lidocaine [7]. Solomon et al [48] injected 96 patients with acne scars with polymethylmethacrylate, resulting in 99.0% improvement, high patient satisfaction, and a good safety profile.

O'Daniel [49] implemented an individualized multimodal approach in patients with atrophic acne scars and aging. Resurfacing techniques were used to correct surface irregularities, long-lasting dermal fillers were used to address the volume loss resulting from acne scars, and subsuperficial musculoaponeurotic system face-lift procedures were used to counter the soft tissue laxity and ptosis associated with aging. In the author's clinical practice, multimodal approaches incorporating fractionated laser, injectable poly-L- lactic acid, and subsuperficial musculoaponeurotic system face-lift procedures have achieved optimal aesthetic outcomes, high patient satisfaction, and durability of aesthetic effect over time.

Autologous fat grafting, PRP, and stromal vascular fraction are effective and safe for the treatment of acne scars. Autologous fat grafting and stromal vascular fraction may be a better

treatment for acne scars than PRP. However, this hypothesis still needs to be tested in the future in large randomized controlled trials [50].

### Individual Atrophic Scars Surgical Management

Punch excision may be an effective treatment for ice-pick scars and small (<3 mm) boxcar scars. A punch biopsy instrument of equal or slightly greater diameter than the scar is used to incise the tissue to the subcutaneous fat layer and excise the scar. Some authors espouse punch excision followed by secondary intention healing, in which a scar is created but is less noticeable because of change at the depth of the base. It has been associated with good results, but secondary widening of the scar may occur [28]. The defect should be closed by sutures along relaxed skin tension lines. Placing a single nonabsorbable suture for punch holes 2.5 mm or larger might facilitate wound healing and minimize spreading [7]. For scars larger than 3.5 mm, elliptical excision may be more favorable than punch excision [51].

Punch elevation is best suited for boxcar scars. The scar border is excised, leaving the deepest part of the scar that is adherent to the fat layer. The scar is raised higher than the surrounding skin; it then retracts during healing to become level with the surface [28].

Fractional CO<sub>2</sub> laser preceded by punch elevation produced a more than 50% improvement in acne scars after 2 sessions [52].

Subcision is used for the management of rolling or depressed scars; a blade inserted parallel to the skin surface is used to cut fibrotic strands tethering the scar to the underlying tissue [53]. Reported adverse effects include bruising, swelling, bleeding, and infection [54]. RF-assisted subcision was found to be comparable to convention subcision with no risk of hematoma, but entry point burn can occur [55]. Using microplasma RF technology combined with subcision to treat depressed scars obtained relatively satisfactory results with no adverse effects [56].

It is of note that blunt cannula subcision is more effective than Nokor needle subcision for acne scars treatment [57]. Injectable fillers showed comparable results to 18 - gauge Nokor needle subcision [58], yet bruising from subcision was significantly worse than that from injection, whereas lumpiness from fillers was significantly worse than that from subcision. Significant and persistent improvement of acne scars, without considerable complications, was noted after the combined protocol of subcision, followed by HA filler initially, and then followed by fractional CO<sub>2</sub> laser 2 weeks later [59]. Subcision combined with HA or threads could offer a more significant, clinical improvement of acne scars than subcision alone [60].

Subcision with autologous fat grafting showed better yet nonsignificant results versus subcision with PRP injection in the treatment of postacne scars [61]. However, one study comparing subcision with PRP injection versus normal saline showed similar efficacy, denoting that subcision, similar to the mechanical effect of injecting solution, is more important than the nature of the solution in the treatment of atrophic acne scars [62].

## Other Treatments

Treatment with topical epidermal growth factor after ablative fractional CO<sub>2</sub> laser is safe and improves the clinical appearance of atrophic acne scars. Epidermal growth factor may help decrease skin pigmentation after laser treatment [63].

Botulinum toxin type A microtoxin, when injected intradermally as microdroplets, can be used to reduce pore size, sebum production, rosacea, acne, scars, and fine lines. Intradermal injection can also be used for the safe prevention and management of scars [64].

Ozone has been gaining greater visibility for its possible antioxidant effects when used in human dermatological pathologies, including skin scarring. However, more studies with better methodological standards and longer-term assessments of side effects should be conducted to achieve better standards and safety in ozone therapy for dermatological conditions [65].

The main treatments for atrophic postacne scars discussed in this review are summarized in [Table 1](#).

**Table 1.** Procedures for atrophic postacne scars.

Procedure and techniques	Advantages	Disadvantages
<b>Vascular lasers or light</b>		
PDL <sup>a</sup> , KTP <sup>b</sup> , EDL <sup>c</sup> , and IPL <sup>d</sup>	Improve SAE <sup>e</sup> and may induce collagen remodeling	PIH <sup>f</sup>
<b>Ablative lasers</b>		
Ablative CO <sub>2</sub> <sup>g</sup> and Er:YAG <sup>h</sup>	Remove epidermis and part of the dermis, allowing collagen remodeling and re-epithelialization	Persistent erythema, hypopigmentation, PIH, infection, scarring, and long recovery period
<b>Fractional ablative lasers</b>		
Fractional CO <sub>2</sub> , 2940-nm Er:YAG, 2790-nm Er:YSGG <sup>i</sup> , 1540-nm Er:glass <sup>j</sup> , and 1550-nm EDL	Faster recovery, safer in darker skin phototypes, and less dyschromia	Poor results for ice-pick scars, erythema, PIH, and procedural discomfort
<b>Nonablative lasers</b>		
Q-switched Nd:YAG <sup>k</sup> , diode, and picosecond 755-nm Alexandrite	Dermal thermal injury while preserving epidermis; minimal side effects: short erythema and minimal pain, swelling, oozing, scarring, or downtime	Results are modest and less impressive
<b>RF<sup>l</sup></b>		
Fractional RF +/- needling	Create zones of thermal wounds to stimulate dermal remodeling; microneedle bipolar RF and fractional RF offer the best results for ice-pick and boxcar scars with no PIH	Transient pain, erythema, and scabbing
<b>Needling</b>		
Needling device rolled over skin	Low cost, well tolerated, increase transepidermal absorption of topical agents, short recovery period, and low PIH	The full result may take 8 to 12 months as the deposition of new collagen takes place slowly
<b>Dermabrasion and microdermabrasion</b>		
High-speed brush, diamond cylinder, fraise, silicon carbide sandpaper, and abrasive crystals	Mechanical resurfacing procedures target scar edges precisely without thermal injury	Not effective for ice-pick or deep boxcar scars
<b>Chemical peels</b>		
Glycolic acid, lactic acid, salicylic acid, mandelic acid, TCA <sup>m</sup> , and phenol	Induce chemical injury to the skin that stimulates collagen remodeling	Prolonged erythema, infection, PIH, and scarring in darker skin phototypes, deeper peels, and sun exposure; phenol has cardiac toxicity related to systemic absorption
<b>PRP and stem cell therapy</b>		
Autologous PRP <sup>n</sup> , MSCs <sup>o</sup> , and adipose tissue-derived MSCs	Enhance wound healing through the release of growth factors, cytokines, and chemokines	Better when combined with skin needling or fractional laser
<b>Filler</b>		
HA <sup>p</sup> fillers, PLL <sup>q</sup> , and CaHA <sup>r</sup>	Address the volume loss resulting from atrophic acne scars	Lumpiness and temporary results, making repeated treatments necessary, which increases cost
<b>Individual atrophic scars surgical management</b>		
Punch excision	Suitable for ice-pick scars and small (<3 mm) boxcar scars +/- sutures along relaxed skin tension lines	Secondary widening of the scar may occur
Elliptical excision	More favorable than punch excision in larger scars	Secondary scar may occur
Punch elevation	For boxcar scars	Better when followed by fractional CO <sub>2</sub> laser
Subcision	A blade is used to cut fibrotic strands tethering the scar	Bruising, swelling, bleeding, and infection
RF-assisted subcision	Comparable to convention subcision with no hematoma	Entry point burn
Microplasma RF technology combined with subcision	Satisfactory results with relatively no adverse effects	Short-term pain, edema, erythema, scaling, and effusion

<sup>a</sup>PDL: pulsed dye laser.<sup>b</sup>KTP: potassium titanyl phosphate.<sup>c</sup>EDL: erbium-doped fractional laser.

<sup>d</sup>IPL: intense pulsed light.

<sup>e</sup>SAE: scars-associated erythema.

<sup>f</sup>PIH: postinflammatory hyperpigmentation.

<sup>g</sup>CO<sub>2</sub>: carbon dioxide.

<sup>h</sup>Er:YAG: erbium-doped yttrium aluminum garnet.

<sup>i</sup>Er:YSGG: erbium-doped yttrium scandium gallium garnet.

<sup>j</sup>Er:glass: erbium glass.

<sup>k</sup>Nd:YAG: neodymium-doped yttrium aluminum garnet.

<sup>l</sup>RF: radiofrequency.

<sup>m</sup>TCA: trichloroacetic acid.

<sup>n</sup>PRP: platelet-rich plasma.

<sup>o</sup>MSC: mesenchymal stem cell.

<sup>p</sup>HA: hyaluronic acid.

<sup>q</sup>PLL: poly-L-lactic acid.

<sup>r</sup>CaHA: calcium hydroxylapatite.

## Discussion

### Principal Findings

Acne scarring is a frequent complication of acne. Early effective treatment of acne is the best strategy to prevent or limit postacne scarring. Treating SAE is the gold-standard, initial, and dramatic step toward improving acne scarring.

The management of acne scarring includes various types of resurfacing (chemical peels, lasers, and dermabrasion); the use of injectable fillers; and surgical methods, such as needling, punch excision, punch elevation, or subcision. There are limited randomized controlled trials that aimed to determine which treatment should be considered the gold standard.

Less invasive, less traumatizing procedures are more appreciated with less side effects and less downtime. Injectable fillers improve atrophic acne scars; however, the impermanence of their effect and their minimal utility for fine, shallow, and sharply depressed scars should be also considered.

The *Energy-Based Devices for the Treatment of Acne Scars: 2022 International Consensus Recommendations* considered energy-based devices to be a first-line treatment for a variety of acne scar types and stated that patients without access to these treatments may not be receiving the best available care for optimal cosmetic results [66]. The consensus recommended future high-quality research and updated international treatment guidelines and reimbursement schemes to reflect this status.

Combining interventions likely produce more benefit compared with the implementation of a single method. Since the scarred

tissue has impaired regeneration abilities, the future implementation of stem or progenitor regenerative medical techniques is likely to add considerable value. One readily available strategy is PRP, which appears to be a safe and effective treatment for various types of atrophic scars. In addition, when added to ablative lasers or microneedling, it seems to considerably add to the efficacy of treatment and reduce the side effects [67]. Platelet-rich fibrin (PRF), a second-generation platelet concentrate, was developed for the purpose of overcoming the limitations of PRP. PRF can produce a higher cumulative release of growth factors than PRP. The therapeutic response was significantly higher in PRF than PRP either alone or combined with needling [68].

### Conclusions

Early effective treatment of acne is the best strategy to prevent or limit postacne scarring. Treating SAE is the gold-standard, initial, and dramatic step toward improving acne scarring. Combining less invasive, less traumatizing procedures is more beneficial and more appreciated with less side effects and less downtime.

Future studies should recruit sufficient participants for blinded trials and include combined therapies versus placebo. Trials should collect baseline variables (participant demographics, acne lesions and extent, skin phototype, scar duration, and depth of scars) to ensure that they are balanced. Trials outcomes should be assessed by both participants and investigators, including adverse events, participant satisfaction, and quality of life, as well as cost and postprocedure downtime.

### Conflicts of Interest

None declared.

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## Abbreviations

**CO<sub>2</sub>**: carbon dioxide  
**CROSS**: chemical reconstruction of skin scars  
**EDL**: erbium-doped fractional laser  
**Er glass**: erbium glass  
**Er YAG**: erbium-doped yttrium aluminum garnet  
**HA**: hyaluronic acid  
**IPL**: intense pulsed light  
**MDA**: microdermabrasion  
**MSC**: mesenchymal stem cell  
**MTZ**: microthermal zone  
**Nd YAG**: neodymium-doped yttrium aluminum garnet  
**PDL**: pulsed dye laser  
**PDT**: photodynamic therapy  
**PIH**: postinflammatory hyperpigmentation  
**PRF**: platelet-rich fibrin  
**PRP**: platelet-rich plasma  
**RF**: radiofrequency  
**SAE**: scars-associated erythema  
**TCA**: trichloroacetic acid

*Edited by R Dellavalle; submitted 21.06.23; peer-reviewed by M Gasmi, T Simonart; comments to author 01.10.23; revised version received 16.11.23; accepted 28.01.24; published 21.02.24.*

*Please cite as:*

Attia E

Atrophic Postacne Scar Treatment: Narrative Review

JMIR Dermatol 2024;7:e49954

URL: <https://derma.jmir.org/2024/1/e49954>

doi: [10.2196/49954](https://doi.org/10.2196/49954)

PMID: [38381492](https://pubmed.ncbi.nlm.nih.gov/38381492/)

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Viewpoint

# PatientsLikeMe and Online Patient Support Communities in Dermatology

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## Abstract

Online patient-oriented platforms such as PatientsLikeMe (PLM) offer a venue for individuals with various diagnoses to share experiences and build community, though they may not be representative of the larger patient population. This potentially limits generalizability and raises concerns about the spread of misinformation, emphasizing the need for informed use and health care provider engagement.

(*JMIR Dermatol* 2024;7:e50453) doi:[10.2196/50453](https://doi.org/10.2196/50453)

**KEYWORDS**

PatientsLikeMe; PLM; online support communities; social media; forums; discussion boards; internet; misinformation; community engagement; representation; demographics; lived experience; atopic dermatitis; prevalence

Receiving a diagnosis can transform a patient's lifestyle, quality of life, and even their identity. Online patient-oriented platforms, such as PatientsLikeMe (PLM), can provide a medium for patients to interact with those who have similar diagnoses. PLM launched in 2005 and was originally focused on patients with amyotrophic lateral sclerosis (ALS); it has since expanded to over 850,000 members with more than 2800 health conditions, and has been featured in over 100 peer-reviewed studies [1].

PLM remains popular among patients who wish to share personal stories about their individual experiences and treatments in order to connect and learn from each other about symptom timing and onset, severity and resolution, medication effectiveness, side effects, and adherence [1]. A 2018 retrospective study assessed characteristics of PLM users with

atopic dermatitis (AD) [2]. As of April 2018, 410 PLM users reported having AD; 90.45% were diagnosed by a medical professional, while 9.55% were self-diagnosed. AD was the primary condition in 61.46% of users; 32.01% of AD PLM users were in the 30-39-year age group and more were women (61%). Common symptoms reported included stress, fatigue, pain, anxious mood, and depressed mood at different levels of patient-defined severity. Users discussed experiences with successful management and nonpharmacological interventions, ranging from modafinil for insomnia to music therapy for anxiety.

However, due to the small number of PLM users reporting AD, especially for treatment data (N=28), profiles may not be representative compared to AD as described in the scientific



literature. For example, some studies report a female predominance of AD, as observed in PLM, while others find no gender association [2]. Conversely, a larger study (N=21,101) of PLM users with systemic lupus erythematosus (SLE) reported similarities in age, socioeconomic status, symptom frequency, and medication use patterns when compared to the greater population of patients with SLE in the United States [3], patterns largely concordant with claims data in other diseases [4]. However, as expected, slightly more PLM users reporting SLE were female (97%, higher than 82%-93% in real-world samples) and White (68%, compared to 22%-63% in population studies) [3]. Discrepancies when comparing demographics of disease prevalence may be rooted in the self-selected nature of PLM use, where users predominantly identified as female and non-Hispanic White, and were generally younger and more highly educated than even those of other online platforms [5]. Women are also more likely to use internet sources for health information compared to men [3]. Internet experience and higher incomes have additionally been associated with the use of online tools, which may be reflective of social determinants that affect other aspects of health care delivery. Attempts to expand the accessibility and benefits of PLM to a wider audience may be worthwhile, as it has been highly valuable in promoting connections among patients, where hearing from those with similar symptoms aided others in comparable situations and forged strong relationships based on shared lived experiences and exchange of knowledge [6].

To help understand and expand the benefits of PLM to a wider audience, a cross-sectional retrospective survey in 2016-2017

investigated the potential of a customized condition-specific versus generalized PLM platform and examined the impact of community-focused upgrades sponsored by pharmaceutical partnerships [7]. A total of 377,625 PLM members were invited to take the survey with 7434 completions (5344 with community upgrades, 2045 without). The generalized platform was observed to improve knowledge, symptom management, and patient activation, with further increases in knowledge for those with upgrades. However, results were potentially biased due to respondent selection and demographics, varying levels of use, and the cross-sectional study design [7].

Despite efforts to improve utility and knowledge, PLM comes with challenges. While it can encourage patient advocacy and data-driven discussions [8], it may not be representative or generalizable to all patients, as previously mentioned, and those willing to share their experiences may already be more active and engaged in their health, with better health care access [4]. There is also a risk of spreading misinformation, as content is not reviewed by medical professionals, which may be particularly dangerous for patients with complex comorbidities (which are underreported on PLM) [3]. PLM information regarding standard of care or interventions to avoid is also lacking [2]. Encouraging health care provider acknowledgment of and engagement on these forums with patients can play an important role in promoting community-building and health literacy and developing trust and rapport while cautioning users on the potential for misinformation. While extremely beneficial to many, online platforms like PLM should not be all-encompassing resources, and informed use is paramount.

## Acknowledgments

RPD receives editorial stipends (*JMIR Dermatology*), royalties (UpToDate), and expense reimbursement from Cochrane.

## Conflicts of Interest

RPD is editor-in-chief of *JMIR Dermatology*, an editor of *Cochrane Skin*, a dermatology section editor for UpToDate, a social media editor for the *Journal of the American Academy of Dermatology*, and a Cochrane Council cochair.

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## Abbreviations

**AD:** atopic dermatitis

**ALS:** amyotrophic lateral sclerosis

**PLM:** PatientsLikeMe

**SLE:** systemic lupus erythematosus

*Edited by J Solomon; submitted 30.06.23; peer-reviewed by E Nyman, A AL-Asadi; comments to author 22.10.23; revised version received 03.05.24; accepted 09.06.24; published 26.06.24.*

*Please cite as:*

*Szeto MD, Hook Sobotka M, Woolhiser E, Parmar P, Wu J, Alhanshali L, Dellavalle RP*

*PatientsLikeMe and Online Patient Support Communities in Dermatology*

*JMIR Dermatol 2024;7:e50453*

*URL: <https://derma.jmir.org/2024/1/e50453>*

*doi: [10.2196/50453](https://doi.org/10.2196/50453)*

*PMID:*

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## Research Letter

# Gender Parity Analysis of the Editorial Boards of Influential Dermatology Journals: Cross-Sectional Study

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## Abstract

This study underscores the persistent underrepresentation of women in academic dermatology leadership positions by examining the gender composition of editorial boards across top dermatology journals, emphasizing the urgent need for proactive strategies to promote diversity, equity, and inclusion.

(*JMIR Dermatol* 2024;7:e40819) doi:[10.2196/40819](https://doi.org/10.2196/40819)

**KEYWORDS**

diversity; equity; inclusion; editors; journals; publications; editorial board; women; gender; underrepresentation

## Introduction

Women continue to be underrepresented in academic leadership positions, especially in dermatology [1]. Although women account for more than half of all board-certified dermatologists in the United States, academic dermatology leadership roles, such as department chair and fellowship director positions, remain disproportionately occupied by men [2]. This inequity extends to medical journals, with substantial gender gaps reported in editorial board composition across multiple specialties; previously published data from 2018 suggested that women accounted for the minority of dermatology editors in

all positions [1]. To provide an evaluation of current trends, the composition of dermatology editorial boards by gender was assessed in 2021, making comparisons among highly indexed dermatology journals.

## Methods

The top 20 most impactful dermatology journals by the 2020 *h*-index were identified on Scimago [3]. Journal editorial board websites were searched in November 2021 for lists of editor names and roles, and journal-defined editorial board members were identified and tabulated. Binary (women vs men) gender estimation by author first name was performed with Gender

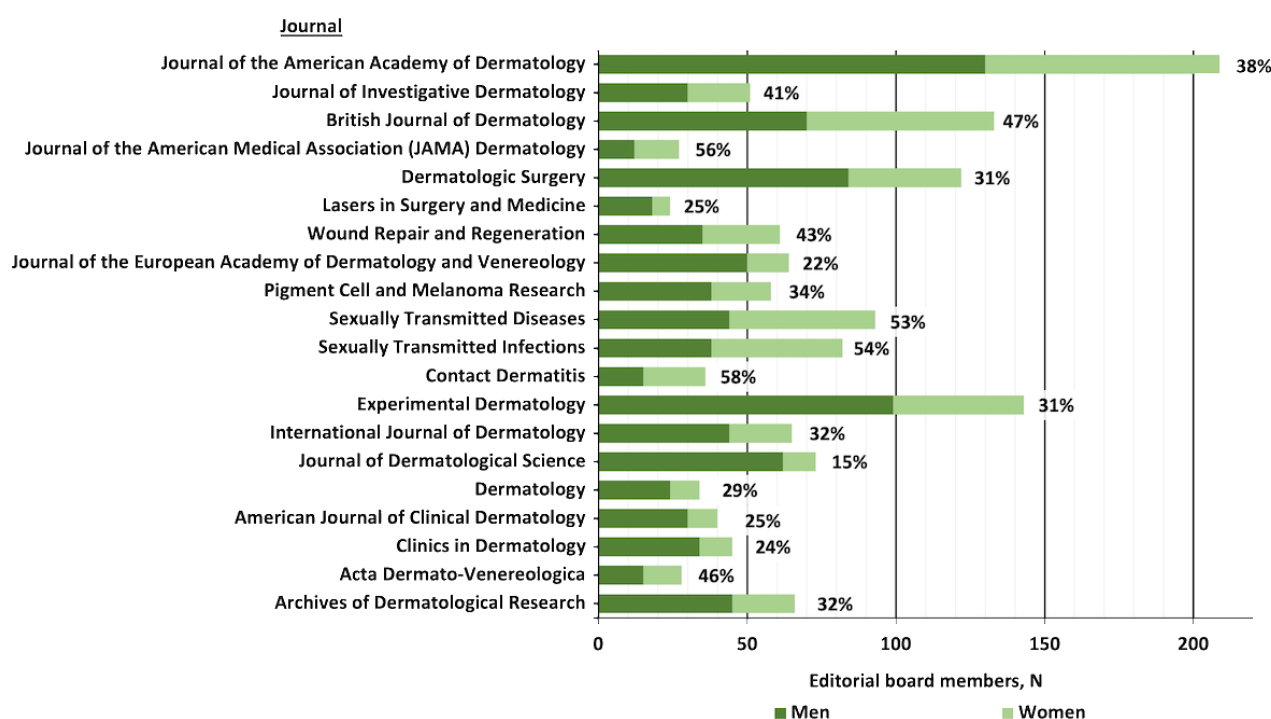
API [4], a popular gender inference service based on querying large multifactorial databases and name repositories. Estimations were corroborated by web-based searches of professional photographs and biographies by 2 independent researchers, with in-depth discussion and consensus meetings to resolve discrepancies.

## Results

Editorial board membership averaged 37% (SD 12%) women, with a median of 33% (IQR 18%) women across the journals

analyzed (Figure 1 and Table 1). The *Journal of Dermatological Science* (11/73, 15%) and *Journal of the European Academy of Dermatology and Venereology* (14/64, 22%) had the lowest proportions of women editors, whereas *Contact Dermatitis* (21/36, 58%), *Sexually Transmitted Infections* (44/82, 54%), and *Sexually Transmitted Diseases* (49/93, 53%) had among the highest. The editorial board of *Journal of the American Medical Association (JAMA) Dermatology* was observed to be 56% (15/27) women after excluding International Advisory Committee members. Of the 20 journals, only 5 (25%) had women editors-in-chief.

**Figure 1.** Numbers of men and women on editorial boards for the top 20 dermatology journals by h-index. Percentages of women editorial board members are indicated.



**Table 1.** Women editorial board members and editors-in-chief for the top 20 dermatology journals by the 2020 h-index.

Dermatology journal	<i>h</i> -index rank	<i>h</i> -index in 2020	Editorial board members, N	Women, n (%)	Woman editor-in-chief
<i>Journal of the American Academy of Dermatology</i>	1	208	209	79 (38)	No
<i>Journal of Investigative Dermatology</i>	2	201	51	21 (41)	No
<i>British Journal of Dermatology</i>	3	179	133	63 (47)	No
<i>JAMA<sup>a</sup> Dermatology<sup>b</sup></i>	4	166	27	15 (56)	Yes
<i>Dermatologic Surgery</i>	5	125	122	38 (31)	No
<i>Lasers in Surgery and Medicine</i>	6	112	24	6 (25)	No
<i>Wound Repair and Regeneration</i>	7	109	61	26 (43)	No
<i>Journal of the European Academy of Dermatology and Venereology</i>	8	107	64	14 (22)	No
<i>Pigment Cell and Melanoma Research</i>	9	105	58	20 (34)	No
<i>Sexually Transmitted Diseases</i>	10	105	93	49 (53)	No
<i>Sexually Transmitted Infections</i>	11	98	82	44 (54)	Yes
<i>Contact Dermatitis</i>	12	96	36	21 (58)	Yes
<i>Experimental Dermatology</i>	13	96	143	44 (31)	No
<i>International Journal of Dermatology</i>	14	93	65	21 (32)	Yes
<i>Journal of Dermatological Science</i>	15	93	73	11 (15)	No
<i>Dermatology</i>	16	92	34	10 (29)	No
<i>American Journal of Clinical Dermatology</i>	17	89	40	10 (25)	Yes
<i>Clinics in Dermatology</i>	18	88	45	11 (24)	No
<i>Acta Dermato-Venereologica</i>	19	83	28	13 (46)	No
<i>Archives of Dermatological Research</i>	20	80	66	21 (32)	No
<b>All journals</b>					
Total	— <sup>c</sup>	—	1454	537 (37)	5/20 (25) <sup>d</sup>
Mean (SD)	—	—	73 (47)	37 (12)	—
Median (IQR)	—	—	63 (46)	33 (18)	—

<sup>a</sup>JAMA: *Journal of the American Medical Association*.  
<sup>b</sup>JAMA Dermatology’s editorial board was observed to be 36% (19/53) women when including International Advisory Committee Members.  
<sup>c</sup>Not applicable.  
<sup>d</sup>Reported as n/N (%).

Discussion

Our findings suggest that an underrepresentation of women on dermatology editorial boards concerningly persists across multiple top journals, recapitulating earlier findings by Lobl and colleagues [1] while highlighting potential ongoing challenges in addressing gender disparities within editorial boards. However, limitations of our study include reliance on high-throughput software examining first names only and estimating binary gender, which may lead to misclassification and lacks acknowledgment of individuals identifying as nonbinary or transgender. Indeed, it has been recognized that Gender API may not be accurate when performing estimations on first names considered to be gender neutral [4]. Future work analyzing self-reported sex and gender identity to ensure true concordance with the individual’s identity is needed.

Abating the gender gap among editorial boards may improve the editorial review process and the diversity of perspectives offered, along with expanding the use of inclusive language and encouraging diverse author representation. Editors-in-chief and academic journal leadership should evaluate board member recruitment with the goal of gender parity, where having 50% women on editorial boards could more accurately represent the dermatology workforce [1]. Furthermore, those serving in senior editor positions may wield considerable influence over the journal and editorial procedures, emphasizing the need for a careful and nuanced approach to fostering overall inclusivity. Subsequent analysis by editor roles, credentials, backgrounds, and experience across different journals may assist with driving meaningful change. As part of *JMIR Dermatology*’s commitment to diversity, equity, and inclusion (DEI) in the publication and peer-review process, a recent editorial uncovered additional areas for improvement in DEI [5]. Very few dermatology journals explicitly include statements about DEI,



have DEI-dedicated editorial board members, or present any information about how the peer-review process ensures DEI. Clear commitments and mission statements from journals could assist with formalizing processes and bolstering transparency. *JMIR Dermatology* has now invited >50% women dermatologists to its editorial board [6]. If the journal's goals are not ultimately reached, conducting investigations into the reasons underlying lower acceptances among applications from women will be important [6]. Given current data trends,

proactive strategies such as these are urgently needed to recruit, promote, and retain women dermatologists in academic settings. Regular monitoring and assessment can help identify foci for improvement and demand accountability. Thus, intentional work to establish expanded frameworks, criteria, and recommending actionable strategies across journals will be a crucial component of broadening DEI and presents a worthwhile goal for further research.

## Acknowledgments

This work was presented at the Ninth International Congress on Peer Review and Scientific Publication in Chicago, Illinois, on September 9, 2022.

## Conflicts of Interest

RPD is a joint coordinating editor for *Cochrane Skin*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology (JAAD)*, a podcast editor for the *Journal of Investigative Dermatology (JID)*, the editor-in-chief of the *JMIR Dermatology*, and a coordinating editor representative on the *Cochrane Council*. DMS is a social media editor for *JMIR Dermatology*. RPD receives editorial stipends (*JAAD* and *JID*), royalties (*UpToDate*), and expense reimbursement (*Cochrane Skin*).

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## Abbreviations

**DEI:** diversity, equity, and inclusion

**JAMA:** Journal of the American Medical Association

*Edited by R Alhusayen; submitted 20.04.23; peer-reviewed by D Verran, R Rodriguez; comments to author 23.07.23; revised version received 26.04.24; accepted 09.05.24; published 21.05.24.*

*Please cite as:*

Szeto MD, Sivesind TE, Kim LS, O'Connell KA, Sprague KA, Nong Y, Strock DM, Cao AL, Wu J, Toledo LM, Wolfe SM, Boothby-Shoemaker W, Dellavalle RP

Gender Parity Analysis of the Editorial Boards of Influential Dermatology Journals: Cross-Sectional Study

*JMIR Dermatol* 2024;7:e40819

URL: <https://derma.jmir.org/2024/1/e40819>

doi:[10.2196/40819](https://doi.org/10.2196/40819)

PMID:[38772024](https://pubmed.ncbi.nlm.nih.gov/38772024/)

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JMIR Publications  
130 Queens Quay East.  
Toronto, ON, M5A 3Y5  
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