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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

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Original Paper

# Exploring Acceptability, Barriers, and Facilitators for Digital Health in Dermatology: Qualitative Focus Groups With Dermatologists, Nurses, and Patients

Patrick Reinders<sup>1</sup>, MA; Matthias Augustin<sup>1</sup>, Prof Dr Med; Anastasia Fleyder<sup>1</sup>, BA; Marina Otten<sup>1</sup>, PhD

Institute for Health Services Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany

**Corresponding Author:**

Marina Otten, PhD

Institute for Health Services Research in Dermatology and Nursing (IVDP)

University Medical Center Hamburg-Eppendorf (UKE)

Martinistraße 52

Hamburg, 20246

Germany

Phone: 49 40 7410 ext 24723

Email: [m.otten@uke.de](mailto:m.otten@uke.de)

## Abstract

**Background:** Although several digital health interventions (DHIs) have shown promise in the care of skin diseases their uptake in Germany has been limited. To fully understand the reasons for the low uptake, an in-depth analysis of patients' and health care providers' barriers and facilitators in dermatology is needed.

**Objective:** The objective of this study was to explore and compare attitudes, acceptability, barriers, and facilitators of patients, dermatologists, and nurses toward DHIs in dermatology.

**Methods:** We conducted 6 web-based focus groups each with patients (n=34), dermatologists (n=30), and nurses (n=30) using a semistructured interview guide with short descriptions of DHIs described in the literature. A content analysis was performed using deductive constructs, following the unified theory of acceptance and use of technology framework, and inductive categories.

**Results:** Patients identified many positive performance expectancies, such as reduced travel times and improvement in follow-up appointments. Dermatologists also stated positive effects (eg, promotion of standardized care), but also negative implications of health care digitalization (eg, increased workload). All stakeholders reported that a DHI should bring additional value to all stakeholders. A lack of digital competence among patients was identified as the major barrier to adoption by all 3 groups. Nurses and dermatologists want apps that are easy to use and easy to implement into their daily routines. Trust in selected institutions, colleagues, and physicians was identified as a facilitator. Patients reported their dependence on the dermatologists' acceptance. All groups expressed concerns about data privacy risks and dermatologists stated insecurities toward data privacy laws.

**Conclusions:** To ensure successful digitalization in dermatology, apps should be user-friendly, adapted to users' skill levels, and beneficial for all stakeholders. The incorporation of dermatologists' perspectives is especially important as their acceptance may impact use among patients and nurses. DHIs should ensure and be transparent about data privacy. The found barriers and facilitators can be used for implementation strategies.

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## KEYWORDS

digitalization; digital health interventions; UTAUT; unified theory of acceptance and use of technology; barriers and facilitators; dermatology; qualitative research; focus groups; mobile phone

## Introduction

Skin diseases, such as atopic dermatitis, psoriasis, acne, skin cancer, and urticaria, are among the most frequent medical conditions in Europe [1,2]. In Germany, about 26.75% (11,291/42,215) of adults have a dermatological condition that requires

further examination by a dermatologist, causing high use of health care services [2-4]. The resulting time constraints restrict possibilities for shared decision-making and impair timely access to care [5,6]. Demographic change will put additional pressure on the system in the near future [7].

Digital health interventions (DHIs) through information and communication technologies can support the provision of care [8]. In dermatology, a wide array of DHIs is available to patients and health care providers across numerous indications, each offering various features [9]. Given the visual nature of many dermatological assessments, the integration of telemedicine and artificial intelligence can support diagnoses [10,11]. Digitally supported self-management strategies may be beneficial, as many chronic dermatological conditions such as atopic dermatitis and psoriasis exist, where lifestyle adjustments can lead to positive outcomes [12]. Disease monitoring apps could also become essential in dermatology. These apps support both patients and physicians by enabling them to track disease progression through image documentation, patient-reported outcomes, and access to digital medical records, including laboratory results [13,14]. All apps can improve communication, data availability, efficiency, patient-centered care [15], and treatment adherence in dermatology [16].

Despite the variety of DHIs in the literature, their adoption in the field of dermatology remains limited. Although a guideline and reimbursement for teledermatological services exist, only 40% of dermatologists offered these services during the height of the COVID-19 pandemic in Germany [17-19]. In other countries, the number exceeded 80% [19,20]. When considering actual usage, published data indicate that only 7.6% (60/792) of dermatologists frequently used real-time teledermatology, with more precise statistics currently unavailable. Other DHIs are used more commonly, such as the electronic appointment reminder ("frequently used" by 212/792, 27% of dermatologists), but still used by a minority of dermatologists [21].

A recent systematic literature analysis identified key barriers to the implementation of DHIs in general health care worldwide including limited knowledge of DHIs among physicians and patients, unclear benefits for participants, and financing issues related to reimbursement and cost coverage for patients [22]. Acceptability and attitude of stakeholders, including patients, nurses, and dermatologists, play an important role in the adoption of DHIs. Whereas patients in Germany have a general interest in digital health and a willingness to share their data with dermatologists [23,24] the acceptability of German dermatologists on electronic health records is lower [25]. Nurses' acceptability and competencies are vital for the successful implementation of DHIs because they play a pivotal role in assisting physicians by processing patient data, coordinating, and communicating with patients, educating them on DHIs, preparing data for consultations, and seamlessly integrating DHIs into clinical workflows [26]. Yet they are frequently overlooked and inadequately addressed in the literature [26]. To gain a deeper understanding of the acceptability of the 3 groups, an in-depth analysis of patients' and health care providers' barriers and facilitators in dermatology is needed. The perspectives identified can then be used to develop tailored interventions and implementation strategies for DHIs [27].

The objective of this study was to explore and exploratively compare attitudes, acceptability, barriers, and facilitators of

patients, dermatologists, and nurses toward DHIs in dermatology.

## Methods

### Study Design

We conducted web-based focus groups with dermatologists, dermatology nurses, and patients with skin conditions via a video conference platform Cisco Webex (Cisco Systems). Focus groups are a qualitative research method that provides a deeper understanding of shared experiences and opinions by facilitating an interaction between participants [28]. We ensured the quality of the web-based focus groups by following the STEER (Stability of Group Numbers, Technology, Environment, Evaluation, and Recruitment) guidelines [29]. The COREQ (consolidated criteria for reporting qualitative research) was followed in this study reporting when applicable ([Multimedia Appendix 1](#)) [30].

### Material

The focus groups were conducted using a semistructured interview guide based on literature research and developed among a team of health scientists and dermatologists ([Multimedia Appendix 2](#)). First, questions were asked on the current status and issues in providing or receiving dermatological care. After that, a short description of five common DHIs was given (1) treatment reminders for adherence [16], (2) self-support tools and webpages [12], (3) store-and-forward teledermatology in different settings (with known and unknown dermatologists) [31,32], (4) eHealth portals for disease monitoring via active data collection (including patient-reported outcomes) [13], and (5) live-interactive video consultations [10].

In all focus groups, participants were asked to express whether they could imagine using the presented DHI, identify additional features they deemed necessary from their perspective, and pinpoint any aspects that might deter them from using the DHI ([Multimedia Appendix 2](#)). In addition, general aspects of DHIs were investigated with questions on data security, data ownership, evidence, and their impact on the patient-physician relationship.

### Participant Selection and Recruiting

To gather a broad range of perspectives on DHIs, we purposefully selected participants: dermatologists and nurses (German: Medizinische Fachangestellte or Gesundheits- und Krankenpfleger\*innen) were selected based on type of workplace (clinic or practice), location of workplace (East, West, North, or South Germany and urban or rural), age group (<39, 40-49, and +50 years), and gender. Participants were invited to participate by field managers of Novartis Pharma GmbH and were compensated for their participation. A total of 33 dermatologists and 34 nurses were willing to participate, out of which 7 did not attend a focus group and without providing a specific reason.

Patients were selected based on diagnosis: psoriasis, atopic dermatitis, skin cancer, acne, hidradenitis suppurativa, and chronic wounds. Decision on indications was made to cover a

wide range of dermatological care from chronic inflammatory skin diseases (eg, psoriasis and atopic dermatitis) via chronic wounds to skin cancer. Patients were invited from two sources: (1) offline via the dermatological outpatient clinic at the University Medical Center Hamburg-Eppendorf (UKE) and rural dermatological practice in the Hamburg area and (2) web-based via a patient association (Deutscher Psoriasisbund eV) by sending out an email to members. Inclusion criteria were aged  $\geq 18$  years and proficiency in German and technical equipment to participate in a video conference. Patients received an allowance for their participation. We enlisted 41 patients willing to participate, out of which 7 patients did not participate in the focus groups. Of those, 3 cited scheduling conflicts and 4 did not state any specific reason.

The researchers had no personal acquaintance with any of the participants before the focus groups.

### Ethical Considerations

The local psychological ethics committee at the UKE (Lokale Psychologische Ethikkommission am Zentrum für Psychosoziale Medizin des University Medical Center Hamburg-Eppendorf) approved this study (LPEK-0250). Participants received study information via email and gave their informed consent in a mandatory 1:1 video call before the respective focus group. Their anonymity was ensured by a personally chosen acronym during the video conference. The study was conducted following the Declaration of Helsinki.

### Data Collection

Preceding the focus groups, we conducted a mandatory 1:1 video call to (1) introduce the researcher and explain their motivation for the research project, (2) ensure participants' technical proficiency, (3) provide information about the research project, (4) answer any questions, (5) record oral consent as described above, (6) explain ground rules for the web-based focus groups, and (7) collect sociodemographic data.

In total, 2 researchers of the UKE (health scientists) participated in each focus group: one to moderate the session and guide the discussion; the other to ensure a smooth organizational procedure and take field notes. MO (PhD and lead of research group telemedicine and digital health at UKE) or PR (PhD student and research associate in research group telemedicine and digital health at UKE) moderated the focus groups. All focus groups were scheduled with 5 to 7 participants for 1.5

hours and were conducted between February and April 2021. The recordings had an average length of 1:28 hours (SD 0.19) with a range from 0:49 hours and 1:59 hours.

We initially planned at least 6 focus groups per stakeholder group with the option to conduct further groups until data saturation would have been reached. The data saturation was discussed among the researchers during the analysis and was defined as "the degree to which new data repeat what was expressed in previous data" [33]. After the fourth focus group, approximately 70%-80% of topics were repeated within all 3 stakeholder groups, resulting in the conduction of 6 focus groups each.

### Data Analysis

All focus groups were fully recorded via audio and transcribed for qualitative content analysis. Data analysis was conducted following the recommendations by Elo and Kyngäs [34] using content analysis and the software NVivo (version 12; Lumivero). Overarching constructs were deductively based on the unified theory of acceptance and use of technology (UTAUT) model (Textbox 1). The UTAUT model aims to explain the acceptance and usage of technology and is based on 4 major constructs: performance expectancy, effort expectancy, facilitating conditions, and social influence. Another relevant construct associated with the model is the attitude toward using technology [35]. The UTAUT was chosen, as the model is one of the most frequently applied theories to explain acceptance toward technology [36] in the health care context and has proven itself in qualitative research (Textbox 1) [37,38]. Main categories and subcategories were initially derived inductively on an individual DHI (eg, treatment reminder) or topic level (eg, evidence or data privacy). In a subsequent step, a category system was developed (constructs deductively based on UTAUT), where individual DHI and topic-specific inductive categories were abstracted to identify attitudes, acceptability, barriers, and facilitators. For this study, the main and subcategories for the individual DHIs were not further analyzed, categories were formed across all. Constructs, main categories, subcategories, and quotations were openly discussed in multiple sessions between researchers (MO, PR, and AF). Similar main categories and subcategories across the 3 stakeholder groups were aligned in wording to allow for comparison between groups. The coding was carried out by PR supported by AF and MO.

**Textbox 1.** Description of deductive constructs according to the unified theory of acceptance and use of technology model.

**Attitudes toward technology**

- Liking or disliking digital health interventions (DHIs), seeing the need for DHI, and willingness to use DHI in the future.

**Performance expectancy**

- Expected usefulness of technology, productivity, and career prospects.

**Effort expectancy**

- Expected ease or difficulty of use from an individual perspective.

**Facilitating conditions**

- Facilitator or barrier associated with resources, knowledge, compatibility with current routines, availability of assistance, and special features of the DHI.

**Social influence**

- Opinion of important others, organizational support, trust in recommendations of colleagues, societies (eg, patient or medical societies), or patients.

## Results

### Characteristics of Participants

The number of participants per focus group ranged between 4 and 7 participants. The 30 dermatologists who participated in 1 of the 6 focus groups were between 34 and 69 (mean 51.3, SD 8.4) years, and 12/30 (40%) were women (Table 1). Dermatologists predominantly worked in an outpatient practice (23/30, 77%), a minority in both settings (6/30, 20%), or in an outpatient clinic (1/30, 3%). All 4 regions were represented with a range from 12 (40%) dermatologists from western German states to 5/30 (17%) dermatologists from eastern German states. The 30 nurses were between 23 and 60 (mean

37.5, SD 12.2) years, almost entirely women (29/30, 98%), working in an outpatient practice (29/30, 98%), and mainly having a medium school education (21/30, 68%). Nurses from all 4 regions were included with a range of 9 (30%) nurses from northern and 5 (16.7%) nurses from southern Germany. Patients (n=34) had a mean age of 47.7 (SD 16.8) years with a range between 20 and 77 years, 47% (16/34) were female. The majority of patients had a high school education (24/34, 71%) and were from northern federal states (29/34, 85%). Patients from eastern Germany did not participate. Each targeted indication was covered. The indications hidradenitis suppurativa, atopic dermatitis, and acne were represented by 4 participants, respectively. Psoriasis was represented by 10, chronic wounds by 6, and skin cancer by 5 participants (Table 1).

**Table 1.** Demographic characteristics of participants.

	Dermatologists (n=30)	Nurses (n=30)	Patients (n=34)
<b>Range of participants per focus group</b>			
Minimum	5	4	5
Maximum	6	7	6
<b>Age (years)</b>			
Minimum	34	23	20
Maximum	69	60	77
Mean (SD)	51.3 (8.4)	37.5 (12.2)	47.7 (16.8)
Female participants, n (%)	12 (40)	29 (98)	16 (47)
<b>Regional variation, n (%)</b>			
West	12 (40)	7 (23.3)	3 (8.8)
North	6 (20)	9 (30)	29 (85.3)
South	7 (23)	5 (17)	2 (6)
East	5 (17)	7 (23)	0 (0)
Rural area, n (%)	7 (23)	10 (33)	11 (32)
<b>Health care sector, n (%)</b>			
Outpatient practices	23 (77)	29 (98)	— <sup>a</sup>
Outpatient clinic	1 (3.3)	1 (3.3)	—
Both	6 (20)	0 (0)	—
<b>School education, n (%)</b>			
Low	—	0 (0)	2 (3)
Medium	—	21 (68)	8 (23)
High	—	9 (32)	24 (71)
<b>Use of digital devices at least once a week, n (%)</b>			
PC	29 (97)	28 (93)	30 (88)
Tablet	15 (50)	15 (50)	15 (44)
Smartwatch	6 (20)	8 (27)	6 (18)
Smartphone	30 (100)	30 (100)	33 (97)
<b>Use of digital apps, n (%)</b>			
Search engine	30 (100)	30 (100)	34 (100)
Social media	13 (43)	24 (80)	23 (68)
Instant messenger	29 (97)	30 (100)	32 (94)
Podcasts	16 (53)	13 (43)	10 (30)
Videos (eg, YouTube or Netflix)	29 (97)	21 (70)	31 (91)
Encyclopedia (eg, Wikipedia)	28 (93)	19 (63)	28 (82)
Online banking	27 (90)	26 (87)	30 (88)
Sports and fitness apps (eg, Strava or Garmin)	14 (47)	18 (60)	23 (70)
Use of DHIs <sup>b</sup> , yes	17 (57)	14 (47)	2 (6)
Recommendation of DHIs, yes	17 (57)	9 (33)	2 (6)
<b>Indications, n (%)</b>			
Psoriasis	—	—	11 (32)
Hidradenitis suppurativa	—	—	4 (12)



	Dermatologists (n=30)	Nurses (n=30)	Patients (n=34)
Chronic wounds	—	—	6 (15)
Atopic dermatitis	—	—	4 (12)
Acne	—	—	4 (12)
Skin cancer	—	—	5 (18)

<sup>a</sup>Not applicable.

<sup>b</sup>DHI: digital health intervention.

Nearly every participant of each stakeholder group used a personal computer or smartphone at least once a week and digital apps such as online banking, instant messengers, and search engines (Table 1). Every second dermatologist had used or recommended DHI within the last 12 months before participating in the focus groups (17/30; 57%). Among nurses, 47% (14/30) worked in practices that had used DHIs within the last 12 months, but only a minority of patients had any experiences with DHIs (2/34; 6%).

### Categories of the Focus Groups

The following section describes all deductively used constructs and inductively identified main and subcategories. For some subcategories, we provide representative quotes. All constructs (A-E), main categories, and subcategories are presented in Tables 2-6. Further, 1 representative quote per subcategory is presented in Multimedia Appendix 3. The letters and numbers in front of the quotes indicate the focus group (G1 to G6) and participant number in the respective stakeholder group (P1 to P6: patient, D1 to D6: dermatologist, and N1 to N6: nurse).

**Table 2.** Construct A: attitude toward technology.

Main and subcategories	Physicians	Nurse	Patients
<b>Positive</b>			
Interest in using digital health interventions	— <sup>a</sup>	—	✓ <sup>b</sup>
Digitalization in the medical field is deemed necessary	—	✓	—
Dermatologists are required to participate in digitalization to have a voice in shaping the system	✓	—	—
Higher acceptability among younger patients	✓	—	—
Acceptability of digital health intervention if used complementary to in-person consultation	✓	✓	✓
<b>Negative</b>			
Not willing to switch dermatologists for lack of offering digital health interventions	—	—	✓
Fast pace of digitalization makes life more difficult	✓	—	—
Fear of being replaced by digital health intervention	✓	—	—
Older patients prefer personal consultation	—	✓	—
Nurses prefer personal consultation	—	✓	—
Fear of data misuse by third parties	✓	✓	✓
<b>Neutral</b>			
Patients are unrestrained toward their data privacy	✓	—	—
Economic concerns are important for decision-making	—	✓	—
Physicians rate personal impressions over evidence	✓	—	—
The dermatologist sees no need for adjustments	✓	—	—

<sup>a</sup>“—”: statement related to this subcategory did not occur for this group.

<sup>b</sup>“✓”: statement related to this subcategory did occur in this group.

**Table 3.** Construct B: performance expectancy.

Main and subcategories	Physicians	Nurse	Patients
<b>Positive</b>			
Greater involvement of patient in treatment	✓ <sup>a</sup>	✓	✓
Improvement of patient-physician relationship	✓	— <sup>b</sup>	✓
Promotion of need-based care	✓	—	—
Promotion of standardized care	✓	—	—
Improvement of follow-up consultations	—	—	✓
Support of treatment process through digitized patient data	—	✓	—
Reduction of unnecessary travel to medical appointments	—	—	✓
Time savings during the treatment process	—	✓	—
Usefulness of data for research purposes	—	—	✓
<b>Negative</b>			
Impersonal patient-physician relationship	✓	✓	✓
Additional workload	✓	✓	—
Overload of information	✓	—	—
<b>Requirement</b>			
Technical functionality should result in an added value	✓	—	—
Additional value for both patient and physician	✓	✓	✓

<sup>a</sup>“✓”: statement related to this subcategory did occur in this group.

<sup>b</sup>“—”: statement related to this subcategory did not occur for this group.

**Table 4.** Construct C: effort expectancy.

Main and subcategories	Physicians	Nurse	Patients
<b>Positive</b>			
High digital competencies among nurses	✓ <sup>a</sup>	— <sup>b</sup>	—
High digital competencies among younger patients	—	✓	—
Decreasing proportion of patients with low digital competencies over time	—	✓	—
<b>Negative</b>			
Low digital competencies among older patients	✓	✓	✓
Difficulties in assessing the integrity of apps	✓	—	—
Low digital competencies among nurses	✓	—	—
Initial high effort to implement digital health interventions	—	✓	—
Low digital competencies among older physicians	—	✓	—
Exclusion of digital illiterate patient groups from care	✓	—	—
<b>Requirements</b>			
Easy-to-use apps	✓	✓	—
Easy integration into daily routines	—	✓	—

<sup>a</sup>“✓”: statement related to this subcategory did occur in this group.

<sup>b</sup>“—”: statement related to this subcategory did not occur for this group.



**Table 5.** Construct D: social influence.

Main and subcategories	Physicians	Nurse	Patients
<b>Positive</b>			
Trust in physicians' recommendations	— <sup>a</sup>	✓ <sup>b</sup>	✓
Trust in colleagues' recommendations	✓	✓	—
Physicians rate colleagues' recommendations over evidence	✓	—	—
Trust in recommendations or digital health developments of or by trustworthy institutions	—	—	✓
Trust in recommendations of physician associations	✓	—	—
<b>Negative</b>			
Dependence on physicians' acceptance	—	✓	✓
Dependence on patients' acceptance	✓	—	—
No trust in nurses' recommendations by patients	—	✓	—

<sup>a</sup>“—”: statement related to this subcategory did not occur for this group.

<sup>b</sup>“✓”: statement related to this subcategory did occur in this group.

**Table 6.** Construct E: facilitating conditions.

Main and subcategories	Physicians	Nurse	Patients
<b>Facilitators</b>			
A single app for different purposes	— <sup>a</sup>	✓ <sup>b</sup>	✓
A single app for the same purpose used by all physicians	✓	—	—
Clear data access permissions	—	—	✓
Possibility to choose between analog and digital health intervention	—	—	✓
Engagement of nurses in digital processes	—	✓	—
Patients possess digital devices	—	✓	—
General trust in data protection and security	✓	—	—
Sufficient reimbursement	✓	✓	✓
Pandemic has accelerated the progress of digitalization	—	✓	—
<b>Barriers</b>			
Difficult to integrate digital health interventions into busy daily routines	✓	✓	—
Use of outdated technology in practices	—	—	✓
High-maintenance of IT infrastructure	✓	—	—
Current data protection regulations impede the functionality of digital health interventions	✓	—	✓
Insecurity toward data privacy laws	✓	—	—
<b>Neutral</b>			
Data privacy is very important in medical practices	—	✓	—

<sup>a</sup>“—”: statement related to this subcategory did not occur for this group.

<sup>b</sup>“✓”: statement related to this subcategory did occur in this group.

### Attitude Toward Technology

In general, all groups found DHIs acceptable if they serve as a complement to rather than a replacement of in-person consultations with dermatologists (Table 2):

*So I would find such an app good, but it must be complementary to the physicians' consultation and not that a doctor would say, "Just look on the app,"*

*so to speak, in order to shorten parts of the consultation or the treatment time. [G2, P2]*

In addition, patients stated a general interest in using DHI in the future but would not change dermatologists for not offering DHIs at their practice (Table 2). Dermatologists also saw acceptability among patients but mainly in younger patients. Nurses emphasized the necessity of digitalization due to the limited availability of time and resources. However, some nurses

underscored the preference for in-person consultations from their own and older patients' perspectives. They additionally highlighted the importance of economic concerns for a decision on a DHI.

All groups expressed a fear of data misuse by third parties, but dermatologists also observed patients having low standards for their own data protection practices.

*So patients are self-indulgent when it comes to privacy. Of their own accord. They send you naked photos via WhatsApp. When you get a cell phone, everyone thinks I'm a child pornographer, because there are so many baby bums from vacation with diaper dermatitis on it. So, they are completely, completely uninhibited.* [G5, D1]

Furthermore, for some dermatologists, their personal impression of a DHI is more important than the scientific evidence. Some dermatologists thought they were required to participate in the digitalization process to have a say in shaping the health care system (Table 2). Other dermatologists expressed pessimism regarding the digitalization process and emphasized how the rapid pace of digitalization makes their work more challenging.

They even voiced concerns about digitalization leading to the replacement of health care professionals.

*On the other hand, even as a doctor, you must worry that this digitalization will eventually replace us. For example, we know that rheumatologists and radiologists will soon no longer be able to work properly because artificial intelligence can make much better assessments than radiologists.* [G6, D4]

### Performance Expectancy

Nurses, dermatologists, and patients collectively mentioned positive performance expectations regarding greater patient engagement in their treatment and care:

*But if it goes the other way, as we just discussed that we as patients then take a little more responsibility, and then you can present a condensed summary to the doctor, then maybe it will make sense.* [G5, P2]

All groups also required that DHIs should result in an additional value for both patients and physicians. On one hand, all 3 stakeholders expected a more impersonal patient-physician relationship whereas on the other hand, an improvement of the relationship was discussed by some patients and dermatologists. Patients mentioned other positive performance expectations such as reduced unnecessary travel, improved follow-up sessions (eg, better-prepared patients and practitioners), and the usefulness of data for additional purposes, such as research. Although dermatologists recognized potential positive impacts of DHIs, such as enabling standardized treatment and promoting need-based care, they stressed the need for technical functionalities to result in added value. For them, existing functionalities did not consistently meet this requirement. Negative effects on dermatologists' daily work were also anticipated by this group. For instance, they indicated the potential overload of information and additional workload associated with DHIs:

*So I think, that will not be a relief. There will be additional work. For example, most of the patients with a video consultation, must come into the office afterwards [...]. So, it costs more time and maybe you could do it in the evening when you really need to relax. I already have an (exhausting) day anyway, and then a video consultation in the evening?* [G3, D6]

This additional workload was also mentioned by some nurses. Other nurses noted the potential for time savings for both physicians and patients:

*... when it's digital, the doctor can immediately write in the medical history, I can prepare the prescription, the doctor is sitting in the treatment room, I'm sitting at the reception. He writes it in the medical history, and I can prepare it at the same time, so ... For the patient, too, it's much, much, much shorter in terms of time.* [G5, N5]

The potential of digitized patient data to support a patient's treatment process, for example through optimized therapy decisions, was also identified by nurses.

### Effort Expectancy

All 3 stakeholder groups articulated the existence of low digital competencies among older patients. Dermatologists even concluded that digitalization would result in the exclusion of digitally illiterate patient groups from care (Table 4):

*In my opinion, 20-30 percent of humanity is still digitally illiterate. That includes people like my mother, who somehow managed to crash the Internet I think three times by now. Not the computer, the Internet.* [G6, D2]

Some dermatologists believe that nurses possess high digital competencies which are crucial for implementing DHIs, while others perceive nurses to have low digital competencies. Nurses, in turn, observed that physicians also exhibited low digital competencies. Another barrier to the adoption of DHIs, as stated by some dermatologists, is the challenge of assessing the credibility and trustworthiness of apps. Nurses described the high effort that is required to adapt to a DHI in a practice, yet they emphasized the considerable advantage once the DHI is successfully implemented:

*As with everything that is new at first, it is of course a lot of work, a huge amount of work for those involved, but then I think there is also a great benefit underneath. [...]at the beginning, of course, it was new and incredibly difficult, and everyone said, "oh God, oh God, oh God," and now everyone expresses their gratitude, saying, "thank God, we have it better now."* [G6, N6]

According to nurses, DHIs should be easy to integrate into daily routines. Dermatologists and nurses agreed on the importance of ease of use for DHIs.

### Social Influence

Social influence played a role in discussing DHIs for all stakeholder groups, especially regarding trust (Table 5).

Dermatologists expressed their trust in recommendations from their physician associations as well as colleagues. Dermatologists even emphasized trusting the opinions of their colleagues over scientific evidence:

*The most important evidence is still colleagues you trust and who also have experience, and there you listen to three, four opinions, and if that goes in one direction, then you try that. [G2, D5]*

Patients place their trust in the opinions of trustworthy institutions (eg, patient organizations) and dermatologists. Patients and nurses shared the viewpoint that usage of DHI is highly dependent on dermatologists' acceptance:

*The physicians [...] play the main role. Because with him is the main interaction and he is the main person to whom one would turn, be it digital or otherwise. So, if the- if the doctor rejects digitalization, then there's no point in any of this. So, then it's a side event. [G2, P2]*

This is supported by patients' lack of reliance on nurses' recommendations:

*It doesn't matter if it's a recommendation for something, if it's just a cream for something, if it's something I say at the front, it's only something she says. But ...uh... if the doctor says it in the treatment room, then, then it's great and then it's like that and then we'll definitely buy it. [G3, N2]*

### Facilitating Conditions

Sufficient reimbursement of DHIs emerged as an important facilitator for all stakeholder groups. As additional facilitators patients and nurses stated that they would like to have a single app for multiple purposes:

*The described applications are all scattered pieces. I can make a constellation here, I can get a second opinion here, I can at best download my prescription to my cell phone instead of in paper form. Um, I have to lug doctor's letters from A to B, then there's faxing, so I would prefer an integrated solution, whether that's for dermatology or anything else. [G1, P3]*

Patients identified technical barriers as hindrances to the implementation of DHIs such as outdated technology in medical practices (Table 6). They also emphasized the importance of clear access permissions to transfer data between physicians. Nurses were willing to participate in digital processes to support an easy integration of DHIs in their practices:

*I would have liked to offer video consultation hours. You can also really do it in such a way that a doctor is present, a nurse is present, and that all the other things, i.e., writing and doing, i.e., writing materials, etc., are taken over by the nurse, that's not a problem. And so that the communication of doctor and patient takes place, that could have worked. But it shouldn't be. So yes, too bad. [G3, N3]*

The nurses positively pointed out that nearly all patients possess digital devices, and they described how the pandemic has accelerated the digitalization in their practices. Dermatologists

preferred a single, standardized app for a specific purpose that would be used by all physicians instead of several platforms with diverse accounts and handling. They identified the considerable effort required for the IT infrastructure as a key barrier to the implementation of DHIs. Additionally, both dermatologists and nurses highlighted the challenge of integrating DHIs into their already demanding daily workloads in medical practices:

*Well, I haven't done it [store-and-forward telemedicine] either. I won't do it either. But that's usually because of the time factor. If you have so many functions in addition to your work in the practice, then you think: Do I still sit down there in the evening and answer something like that? [G5, D2]*

Nurses generally describe that data privacy is very important in medical practices. Some dermatologists generally trust whereas others feel insecure about data protection and security. Moreover, dermatologists highlighted the negative effect of current data regulations on the functionality of DHIs.

## Discussion

### Principal Findings

The current use of DHIs in Germany, both in general and dermatological care, remains low. Therefore, we conducted a qualitative focus group study to explore and exploratively compare patients', nurses', and dermatologists' attitudes, acceptability, barriers, and facilitators on the implementation of DHIs in dermatology. Additionally, we exploratively compared their perspectives. Patients and nurses had a generally positive stance and optimistic attitude toward digitalization and assumed largely positive performance expectancies. In contrast, dermatologists showed more different opinions with some expressing positive performance expectations, while others anticipated increased workload and information overload with the implementation of DHIs. While sufficient reimbursement and patients owning digital devices were identified facilitators, insecurity regarding data privacy laws and the difficulty of integrating DHIs into an already busy day were identified barriers.

Although our research identified a more negative stance of dermatologists toward DHIs in comparison to patients and nurses, quantitative research yielded mixed results [23,39]. It is important to consider that the acceptability of DHIs is influenced by the context in which they are used. For instance, willingness to use tele dermatology is lower for severe and acute conditions compared to minor problems [39].

Independent of the context, dermatologists' acceptability is crucial for actual usage, as patients and nurses also pointed out, and can mitigate barriers, including low patient demand, problems with the technology, and lack of financial resources [33,40]. The influential role of dermatologists stems from their function as gatekeepers in introducing medical innovations, including DHIs, into care. Additionally, their positive stand on a DHI can signal credibility to patients, nurses, and colleagues. The low acceptability by dermatologists seems to be a barrier

to the implementation of many DHIs. However, improving physicians' acceptability could become a facilitator, particularly as they trust their colleagues' recommendations and patients trust their health care providers. To increase acceptability among physicians, reimbursements should be clarified, and patient benefits should be aligned with an added value for dermatologists as proposed by all stakeholder groups in our study and as found in the literature [41].

In recent years, physicians were required to make financial investments in the IT infrastructure without a clear perceived benefit leading to hesitance in adopting new DHIs in clinical practice [42,43]. Both, the missing positive financial perspective and missing benefits are established barriers to the introduction of eHealth interventions [22]. While 98% of outpatient medical practices are connected to the nationwide telematic infrastructure, only a minority are satisfied with its services [44]. Other countries, especially Estonia and Canada were more successful in establishing an eHealth-infrastructure that allowed a fast uptake of DHI services by physicians and other health care providers [45,46]. In addition, physicians in both countries were financially incentivized to adopt DHIs [45,46].

The infrastructure in Germany is therefore considered a barrier to the seamless adoption of many DHIs [41]. This resonates with the cautious perspectives of dermatologists on DHIs in our study. In addition, the economic and resource advantages for society, health insurance, or patients, such as reduced follow-up appointments or travel costs, may not necessarily translate into added value for dermatologists [47]. These concerns should be addressed so that physicians are more likely to adopt and recommend new technologies [48].

Dermatologists and nurses expressed concerns about an increased workload. Other nurses also identified time savings as an effect of DHIs. Both perspectives were identified across other medical fields [22]. The potential increased workload for dermatologists may be explained by the DHIs not aligning with working routines or dermatologists needing additional time for patient care, such as explaining DHI to patients [49]. From another angle, even successfully implemented DHIs may result in additional workload as technological progress enables faster completion of tasks (eg, accelerated patient consultation per store-and-forward teledermatology), but increases in the number of tasks (eg, more patients per day). Consequently, actual time being spent inactive is reduced and time pressure is amplified (theory of social acceleration) [50]. Yet, the ability to complete tasks faster may also result in a reduced workload for dermatologists and nurses.

The true impact of DHIs on the patient-physician relationship remains uncertain and will largely depend on the extent and the specific context in which the DHI is introduced [51]. Following the social acceleration theory, using DHIs can result in increased but less relationship-building communication between dermatologists and patients [50]. Time savings, possibly leading to more available time for individual patients, can also foster a trusting patient-physician relationship.

An identified barrier to using DHIs in dermatology is the lack of digital competencies and knowledge among patients, practitioners, and nurses. Although internet use and

competencies have increased in the last decade [52,53], a recent European survey estimated that 22% (Norway) to 58% (Germany) of Europeans have inadequate digital health literacy levels. Among older and less educated individuals, the percentage is even higher [54]. To avoid the exclusion of patient groups (digital divide) [55], participants in our study even emphasized the need for analog alternatives to DHIs. To increase adoption rates, digital health literacy skills need to be improved and services must be adapted to the digital competency levels of intended users and should always be easy to use [56]. For physicians, knowledge of DHIs and their evidence base should be incorporated into medical curricula and continued medical education [57].

Participants in our study discussed data privacy and security from different perspectives. For some, data privacy risk was a reason for the nonusage of DHIs, consistent with findings in the literature [58]. Conversely, others noted that the enforcement of data privacy laws hindered the development of effective DHIs. This might not be generalizable to other countries, as German citizens have generally stronger concerns regarding data privacy and protection [59,60].

Furthermore, dermatologists complained about the considerable maintenance burden of the IT infrastructure, partially driven by data privacy regulations. Increasing IT costs and dissatisfaction with IT were also identified in the literature [43,61]. The difficulties assessing the integrity of DHIs may be explained by the missing transparency of data privacy policies of many DHIs [62]. Health data are one of the most sensitive data requiring an enforced data privacy regulation. However, the enforcement of data security policies should be balanced in the sense that data are protected while the usage of the app remains convenient and useful. Other European countries under the same regulatory framework, including Estonia, seem to have achieved this balance [45].

While our study provided valuable insights into the attitudes toward DHIs from patients', dermatologists', and nurses' perspectives, it is important to acknowledge several limitations when interpreting our findings. The digital conduction of our focus groups may have excluded individuals with limited or no digital competencies. To at least mitigate this limitation, we followed the STEER recommendations by conducting test calls to enable individuals with limited competencies to participate [29]. Furthermore, we established ground rules to ensure a comfortable and private setting for all participants [29]. Thereby, we also ensured a smooth discussion. The possibility of social desirability cannot be completely excluded, but it may have been low due to the private setting, ensured confidentiality, and anonymity of the focus groups, as well as the nonsensitive topic of digital health [63]. Moreover, participants with a digital background or interest in the topic may have been more motivated to join the web-based focus groups. Despite efforts to recruit a diverse range of participants through purposeful sampling [42], it should be noted that the majority of patients in our study were well-educated. Additionally, it is important to mention that the apps discussed in our study were hypothetical limiting participants' ability to fully assess the practical implications of using these interventions in real-life scenarios, as only a minority of patients had actual experience with a DHI.



Considering all limitations, including the general qualitative nature of this study and the fact that it was carried out in Germany only, the results may not be completely generalizable to other medical fields and health care systems. However, as shown, many aspects are also described in the international literature and the findings may, therefore, be relevant to a wider audience.

### Conclusions

To ensure a successful digitalization process in dermatology, it is essential to develop easy-to-use apps that bring additional value to all stakeholders involved. Dermatologists' acceptance is crucial as dermatologists can serve as a facilitator in their role. Incorporating their perspectives during the development phase can help align future digital interventions with clinical practices, increasing acceptance and usage.

Due to the lack of digital health literacy among the population DHIs should be designed to accommodate different levels. Analog access options should be provided to prevent the exclusion of less digitally literate patient groups in the near future.

Data privacy and security concerns must be taken seriously, as they are crucial for maintaining trust in digital interventions. They can function as barriers to interventions' effectiveness and cause users' insecurities. Successful digitalization in dermatology requires striking a balance on data privacy to allow for the development of effective interventions.

In summary, our findings can aid researchers, developers, and decision makers in comprehending diverse stakeholder perspectives. This can help create successful DHIs and subsequent implementation strategies, thereby enhancing the acceptability and uptake of DHIs.

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### Conflicts of Interest

PR and AF declare no conflicts of interest. MA is a scientific advisor for the tele dermatology platform derma2go AG, A+ Videoclinic GmbH, and Novartis, and author of the German guideline on tele dermatology. MO is a coauthor of the German guideline on tele dermatology.

#### Multimedia Appendix 1

COREQ (consolidated criteria for reporting qualitative research) checklist.

[PDF File (Adobe PDF File), 486 KB - [derma\\_v7i1e57172\\_app1.pdf](#) ]

#### Multimedia Appendix 2

Semistructured interview guide (German version and English translation).

[DOCX File , 56 KB - [derma\\_v7i1e57172\\_app2.docx](#) ]

#### Multimedia Appendix 3

Overview of categories per stakeholder group and representative quote for the category.

[DOCX File , 44 KB - [derma\\_v7i1e57172\\_app3.docx](#) ]

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## Abbreviations

**COREQ:** consolidated criteria for reporting qualitative research

**DHI:** digital health intervention

**STEER:** Stability of Group Number, Technology, Environment, Evaluation, and Recruitment

**UKE:** University Medical Center Hamburg-Eppendorf

**UTAUT:** unified theory of acceptance and use of technology

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Original Paper

# Development, Feasibility, and Acceptability of the Electronic Patient Benefit Index for Psoriasis in Clinical Practice: Mixed Methods Study

Marina Otten<sup>1</sup>, Dr phil; Vahid Djamei<sup>2</sup>, MSc; Matthias Augustin<sup>1</sup>, Prof Dr Med

<sup>1</sup>German Center for Health Services Research in Dermatology (CVderm), Institute for Health Services Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany

<sup>2</sup>Department of Dermatology, University Hospital Zurich, Zurich, Switzerland

**Corresponding Author:**

Marina Otten, Dr phil

German Center for Health Services Research in Dermatology (CVderm)

Institute for Health Services Research in Dermatology and Nursing (IVDP)

University Medical Center Hamburg-Eppendorf (UKE)

Martinstraße 52

Hamburg, 20246

Germany

Phone: 49 40741059369

Fax: 49 40741024723

Email: [m.otten@uke.de](mailto:m.otten@uke.de)

## Abstract

**Background:** Patient-reported outcomes are relevant in clinical practice showing patient benefits, supporting clinicians' decision-making, and contributing to the delivery of high standards of care. Digital monitoring of patient-reported outcomes is still rare. The Patient Benefit Index (PBI) measures benefits and goals from patients' views and may be relevant for regular documentation and shared decision-making.

**Objective:** This study aimed to develop electronic versions of the PBI to examine their feasibility and acceptability in clinical practice for patients with psoriasis.

**Methods:** We developed an app and a web version of the existing, valid PBI using focus groups and cognitive debriefings with patients before conducting a quantitative survey on its feasibility and acceptability. Conduction took part in an outpatient dermatology care unit in Germany. Descriptive and subgroup analyses were conducted.

**Results:** A total of 139 patients completed the electronic PBIs (ePBIs) and took part in the survey. The ePBI was understandable (n=129-137, 92.8%-98.6%) and feasible, for example, easy to read (n=135, 97.1%) and simple to handle (n=137, 98.5%). Acceptability was also high, for example, patients can imagine using and discussing the ePBI data in practice (n=91, 65.5%) and documenting it regularly (n=88, 63.3%). They believe it could support treatment decisions (n=118, 84.9%) and improve communication with their physician (n=112, 81.3%). They can imagine filling in electronic questionnaires regularly (n=118, 84.9%), even preferring electronic over paper versions (n=113, 81.2%). Older and less educated people show less feasibility, but the latter expected the relationship with their physician to improve and would be more willing to invest time or effort.

**Conclusions:** The app and web version of the PBI are usable and acceptable for patients offering comprehensive documentation and patient participation in practice. An implementation strategy should consider patients' needs, barriers, and facilitators but also physicians' attitudes and requirements from the health care system.

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**KEYWORDS**

patient-reported outcomes; Patient Benefit Index; dermatology; psoriasis; feasibility; acceptability; eHealth; digital health; dermatologist; dermatologists; skin; mobile health; app; apps; application; applications; digital technology; digital intervention; digital interventions; smartphone; smartphones; mobile phone

## Introduction

Studies already showed the relevance of patient-reported outcomes (PROs) in clinical practice [1]. PROs can provide information on the effectiveness and benefits of treatments and on changes in patient functional status over time [2] and can support patient referrals [3]. PROs can also be used to evaluate and compare health care providers and systems and can inform quality improvement efforts [2].

The National Health Service Outcomes Framework cites enhancing quality of life (QoL) for people with long-term conditions as a key domain for improvements [4]. The European Academy of Dermatology and Venereology Task Force on QoL considers that there are several ways in which the measurement of QoL in clinical practice may benefit patients, support clinicians' decision-making, and contribute to the delivery of high standards of care [5]. PROs in dermatology include, for example, QoL, patient benefit and goal measures, treatment harm assessment, and treatment response adequacy [4,6,7]. They all enhance the management of psoriasis and, thereby, improve patients' lives [8].

Many PROs are already included in data sets for documenting psoriasis in clinical practice [9], for example, the Patient Benefit Index (PBI) by assessing patients' treatment goals and benefits [10]. Analyzing patient needs on an individual level facilitates shared decisions by patients and physicians and optimizes personalized treatment [11]. Furthermore, the World Health Organization [6] and the Techniker health insurance [12] emphasize the importance of patient-defined treatment goals.

The PBI (Multimedia Appendix 1) is a valid instrument suitable for the assessment of patient-reported goals and benefits in dermatological studies and practice. In the first part of the questionnaire (Patient Needs Questionnaire; PNQ), patients state how relevant 25 goals are for them on a 5-point Likert scale (0=not important at all to 4=very important). In the second part of the questionnaire (Patient Benefit Questionnaire; PBQ),

they state how the identical items detect the extent to which the current therapy has contributed to attaining the therapy goals (scaled from 0=treatment did not help at all to 4=treatment helped a lot). Patients can also tick the option "does not apply to me." The PBI total score is derived from the ratings on both questionnaires, as the PBI score is the arithmetic mean of all rated benefits (PBQ items) weighted by the relative importance of each corresponding need item (PNQ) for each patient [10,13]. The PBI has already widely been used in research.

With improved access to the internet and increased use of electronic devices, the digital health care sector gained importance. This makes the collection of electronic PROs more feasible [14,15]. Many benefits were detected by the digitalization of PROs such as error reductions, automatic scoring calculations, management of data security measures, and better access to data [16]. Furthermore, electronic PROs turned out to be feasible and acceptable to dermatologists and patient groups with different indications [3,17,18], but burdens remain [18,19]. In dermatology, digital monitoring is still rarely used [6,20] and is not evaluated in practice and for shared decision-making. The aim of this study was (1) to develop the electronic PBI (ePBI), (2) to examine its feasibility, and (3) acceptability for patients with psoriasis.

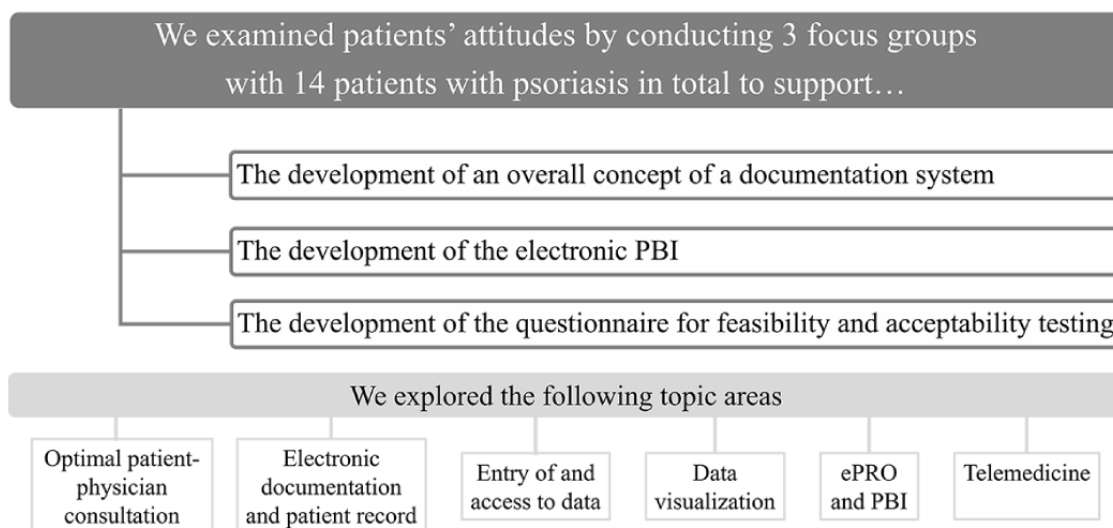
## Methods

This paper follows STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines where applicable. To develop and test the ePBI, we followed 3 steps.

### Step 1: Conceptualization Phase

We conducted 3 focus groups with 14 patients with psoriasis (Figure 1). The goal was to develop a basis for the conceptualization of an electronic documentation system as well as for the development of the ePBI and the questionnaire. The focus groups were recorded, fully transcribed, and subjected to content analysis [21].

**Figure 1.** Goals and content of focus groups (besides the development of a data set for documenting psoriasis). ePRO: electronic patient-reported outcome; PBI: Patient Benefit Index.



### Step 2: Development of ePBI

We developed an app and a web version of the PBI [22]. For better feasibility and use in practice, adaptations were necessary:

- App: We included a first screen showing a link to PNQ and PBQ.
- App: We developed 1 page for the introduction text and each item.
- App and web: We included the calculation and presentation of resulting scores.
- App and web: We changed some words within the introduction of the PBQ and deleted or adapted the last

sentence (“Please check once more if you have exactly marked each statement ...”).

Due to the PBI being a complex outcome measure and to the adaptations described earlier, we conducted further steps in developing and testing the electronic version as recommended by the Professional Society for Health Economics and Outcome Research (ISPOR) [15,23]. Cognitive debriefing allowed adaptations and iterative development of both electronic versions. Altogether, we conducted 3 rounds with 11 patients in total and used different techniques testing different parts of the ePBI until no further adjustments were necessary (Table 1). Thereby, the items of PNQ and PBQ themselves were not open for discussion.

**Table 1.** Cognitive debriefing to develop the electronic PBI<sup>a</sup> versions iteratively.

Subject of investigation	PBI (app version) <sup>b</sup>		PBI (web version) <sup>c</sup>		Paper-based graphs and charts <sup>d,e</sup>
	Usability of PNQ <sup>f</sup> and PBQ <sup>g</sup>	Understanding of resulting scores	Usability of PNQ and PBQ	Understanding resulting scores	Understanding and usability of paper-based graphs and charts
Technique: Think aloud	Applied	Applied	Applied	Applied	Applied
Technique: Observation	Applied	Applied	Applied	Applied	Applied
Technique: Comment options	Applied	Applied	Applied	Applied	Applied
Technique: Predefined questions <sup>h</sup>	Not applied	Applied	Not applied	Applied	Applied
Technique: Ad hoc questions <sup>i</sup>	Not applied	Applied	Not applied	Applied	Applied

<sup>a</sup>PBI: Patient Benefit Index.

<sup>b</sup>Test rounds: 2 and patient sampling: 7.

<sup>c</sup>Test rounds: 1 and patient sampling: 4.

<sup>d</sup>Test rounds: 3 and patient sampling: 11.

<sup>e</sup>Exemplary nondigitalized graphics were developed and discussed for future development steps.

<sup>f</sup>PNQ: Patient Needs Questionnaire.

<sup>g</sup>PBQ: Patient Benefit Questionnaire.

<sup>h</sup>Example: Can you describe that with your own words? Where can you find yourself on the scale?

<sup>i</sup>Example: When patients took a long time or showed difficulties to answer.

### Step 3: Feasibility and Acceptability Testing of ePBI

An observational study was conducted using a standardized questionnaire on patients’ demography and health status as well as on the feasibility and acceptability for both ePBI versions. We used nominal, ordinal, interval, and ratio scales. Mainly, participants answered items on 5-point Likert scales.

#### Patients and Conduction

Patients were recruited at an outpatient dermatology care unit of the University Medical Center Hamburg-Eppendorf and were eligible to participate if they were German-speaking and diagnosed with psoriasis. One-half of patients filled in the app version on a smartphone. The other half filled in the web version on a laptop. After that, both groups filled in the questionnaire described earlier [15,23]. The interviewer stopped the time when each patient needed to fill out the ePBI.

### Ethical Considerations

According to the ethics commission of the Medical Association of Hamburg, there was no ethics vote required because of anonymous and noninterventonal data collection for both the qualitative and quantitative parts of the study (WF-053/19). All participants gave written informed consent before participation. They were informed that they could cancel participation at any time. No compensation was provided for participation.

### Analysis

The quantitative data were analyzed using descriptive statistics. For bivariate analysis, we classified metric variables and variables with 5-point Likert scales into 3 categories. Comparison of response behaviors was conducted using cross tables, chi-square test, and Fisher exact test if cross tables had more than 20% of cells with expected counts below 5. A significance level of  $\alpha=.05$  was applied. For investigating the

direction of the association, adjusted standardized residuals were calculated with values below  $-1.96$  and above  $1.96$  revealing significance. Subgroup comparison was conducted for sex, age, education, and ePBI version (app vs web). We used SPSS (version 25.0; IBM Corp).

## Results

In total, 139 patients participated, and all filled in the questionnaire on demography, feasibility, and acceptability: 52.5% ( $n=73$ ) completed the app, and 47.5% ( $n=66$ ) completed the web version.

### Participants

The sample encompassed 67.6% ( $n=94$ ) of male participants and had a mean age of 47 (SD 13.95; median 49; range 18-84)

years. On average, the first psoriasis symptoms appeared 22 (SD 14.66; median 19; range 0-65) years ago, and the first diagnoses had been made 21 (SD 15.15; median 19; range 0-65) years ago. The mean Dermatology Life Quality Index score was 4.57 (SD 5.50; median 3; range 0-22), the mean EQ-5D-5L score was 83.05 (SD 21.92; median 88; range 8.83-100), the mean European Quality Visual Analogue Scale score was 73.93 (SD 20.43; median 80; range 1-100), and the mean PBI score 2.77 (SD 1.13; median 3.11; range 0.10-4.0). Most participants were of higher education (intermediate and high:  $n=107$ , 76.9%), and had several comorbidities (eg,  $n=58$ , 41.7% had psoriasis arthritis; on average, a patient had 0.98 comorbidities; [Tables 2 and 3](#)).

The majority was experienced in using internet-ready devices (eg,  $n=124$ , 89.9% used smartphones frequently; [Table 4](#)).

**Table 2.** Descriptive results of demographic and clinical information I (N=139).

	Mean (SD)	Median	Mode	Minimum	Maximum
Age ( $n=139$ )	47 (13.95)	49	50	18	84
First symptoms appeared/years ago ( $n=132$ )	22 (14.66)	19	20	0	65
Diagnosis made/years ago ( $n=130$ )	21 (15.15)	19	10	0	65
Number of comorbidities ( $n=135$ )	0.98 (0.99)	1	1	0	5
Dermatology Life Quality Index; range 0-30 ( $n=135$ )	4.57 (5.50)	3	0	0	22
EQ-5D-5L; range 0-100 ( $n=134$ )	83.05 (21.92)	88	100	8.83	100
EQ VAS <sup>a</sup> ; range 0-100 ( $n=125$ )	73.93 (20.43)	80	90	1	100
Electronic Patient Benefit Index; range 0-100 ( $n=89$ <sup>b</sup> )	2.77 (1.13)	3.11	4	0.1	4

<sup>a</sup>EQ VAS: European Quality Visual Analogue Scale.

<sup>b</sup>Patient Benefit Index global score and subscales may only be computed if the patient has provided valid data on importance (Patient Needs Questionnaire) and benefit (Patient Benefit Questionnaire) for at least 75% of the respective treatment goals.

**Table 3.** Descriptive results of demographic and clinical information II (N=139).

	Values, n (%)
<b>Sex</b>	
Male	94 (67.6)
Female	44 (31.7)
Missing	1 (0.7)
<b>Highest school diploma</b>	
No degree	2 (1.4)
Lower or general secondary degree	23 (16.5)
Intermediate secondary degree	42 (30.2)
Polytechnic high school degree	5 (3.6)
University of applied sciences entrance qualification	22 (15.8)
Higher education entrance qualification	38 (27.3)
Missing	3 (2.2)
Other degree	4 (2.9)
<b>Comorbidities</b>	
Psoriasis arthritis	58 (41.7)
Diseases of the cardiovascular system (eg, high blood pressure and arteriosclerosis)	21 (15.2)
Diabetes mellitus type 2	6 (4.3)
Obesity	15 (10.8)
Lipometabolic disorders	3 (2.2)
Depression	18 (12.9)
Nonalcoholic steatohepatitis (fatty liver disease)	4 (2.9)
Chronic inflammatory bowel diseases (eg, Morbus Crohn)	1 (0.7)
Alcohol abuse	0 (0)
Nicotine abuse	7 (5)
None	48 (34.5)

**Table 4.** Descriptive results of the use of internet-ready devices (N=139).

	Computer, n (%)	Laptop, n (%)	Tablet-PC, n (%)	Smartphone, n (%)
Not at all	39 (28.3)	30 (21.7)	44 (31.9)	11 (8)
Rarer than 1 time a week	11 (8)	21 (15.2)	16 (11.6)	1 (0.7)
1-3 times a week	9 (6.5)	15 (10.9)	12 (8.7)	0 (0)
4-6 times a week	3 (2.2)	14 (10.1)	5 (3.6)	3 (2.2)
Daily	63 (45.7)	44 (31.9)	44 (31.9)	120 (87)
Missing	13 (9.4)	14 (10.1)	17 (12.3)	3 (2.2)

### Feasibility

Most participants (“rather” or “totally”) agreed on the ePBI being usable (Table 5), stating that the questions and texts were easy to read (n=135, 97.1%), the questions (n=133, 95.7%) or instructions (n=137, 98.6%) or information (n=129, 92.8%) understandable, the handling simple (n=137, 98.5%), the questionnaire easy to complete (n=136, 97.8%), and the

information on individual results satisfying (n=122, 87.8%). A small number of participants declared that they needed help filling in the ePBI (n=24, 17.3%) and found it too long (n=30, 21.6%) but visually appealing (n=117, 84.2%; Table 3). On average, they needed 6.92 (SD 2.49; median 7; range 2.75-14) minutes to fill in the electronic PNQ and PBQ, read the results, and the last page including the PBI score (Table 5).

**Table 5.** Descriptive results on usability (N=139)<sup>a</sup>.

	Totally disagree, n (%)	Rather not agree, n (%)	Partly agree, n (%)	Rather agree, n (%)	Totally agree, n (%)	Missing, n (%)
The questions and texts are easy to read.	0 (0)	1 (0.7)	2 (1.4)	10 (7.2)	125 (89.9)	1 (0.7)
The questions are understandable.	0 (0)	1 (0.7)	5 (3.6)	14 (10.1)	119 (85.6)	0 (0)
The handling is simple.	0 (0)	0 (0)	1 (0.7)	12 (8.6)	125 (89.9)	1 (0.7)
The instructions on how to complete the questionnaire are understandable.	0 (0)	0 (0)	1 (0.7)	16 (11.5)	121 (87.1)	1 (0.7)
In general, the questionnaire is easy to complete.	0 (0)	1 (0.7)	2 (1.4)	12 (8.6)	124 (89.2)	0 (0)
The information about my individual results is understandable.	0 (0)	1 (0.7)	6 (4.3)	35 (25.2)	94 (67.6)	3 (2.2)
I am satisfied with the content of the information about my individual results.	0 (0)	5 (3.6)	9 (6.5)	37 (26.6)	85 (61.2)	3 (2.2)
I need help filling in the questionnaires.	77 (55.4)	27 (19.4)	9 (6.5)	5 (3.6)	19 (13.7)	2 (1.4)
The questionnaire seems too long to me.	42 (30.2)	51 (36.7)	16 (11.5)	19 (13.7)	11 (7.9)	0 (0)
The questionnaire is visually appealing.	0 (0)	4 (2.9)	17 (12.2)	56 (40.3)	61 (43.9)	1 (0.7)

<sup>a</sup>Completion time (n=138): mean 6.92, SD 2.49; median 7; mode 6; range 2.75-14 minutes.

### Acceptability

Acceptability of the ePBI was also very high (Tables 6-9) but with more participants being indecisive (between n=7, 5% and n=41, 29.5%). Most participants (“rather” or “totally agreed”) could imagine filling in the ePBI on a regular basis (n=88, 63.3%), but less so if the documentation would be only for their own use (n=55, 39.5% and n=34, 24.5% being indecisive). They could imagine to discuss the content with their physician (n=91, 65.5%). They thought the ePBI could form a good basis for a patient-physician consultation (n=98, 70.5%), support treatment decisions (n=118, 84.9%), improve communication with the physician (n=113, 81.3%), and improve the relationship with

the physician (n=78, 56.1%). In addition, it would help them to remember their symptoms and well-being better during patient-physician consultation (n=94, 67.7%). It would also help them to manage their condition (n=90, 64.7%; over periods of time: n=129, 92.8%). In general, patients could imagine filling in electronic questionnaires (n=118, 84.9%). They did not agree that regular completion might make them feel sad (n=120, 86.3%) and they would not prefer filling in the questionnaires on paper (n=113, 81.2%; Table 6). The majority of participants could imagine filling in the ePBI at every patient-physician consultation (n=85, 61.2%; Table 7). However, they accepted much greater effort for documenting their data regarding frequency, length, and device (Tables 7-9).



**Table 6.** Descriptive results on acceptability I (N=139).

	Totally disagree, n (%)	Rather not agree, n (%)	Partly agree, n (%)	Rather agree, n (%)	Totally agree, n (%)	Missing, n (%)
I can imagine filling in the questionnaire regularly.	5 (3.6)	16 (11.5)	29 (20.9)	42 (30.2)	46 (33.1)	1 (0.7)
The regular answering of the questions would make me feel sad.	84 (60.4)	36 (25.9)	10 (7.2)	2 (1.4)	7 (5)	0 (0)
I would rather answer the questions on paper.	78 (56.1)	35 (25.1)	12 (8.6)	6 (4.3)	7 (5)	1 (0.7)
I can imagine discussing my personal goals and benefits from the questionnaires with my physician.	10 (7.2)	7 (5)	31 (22.3)	47 (33.8)	44 (31.7)	0 (0)
The questionnaires on my personal goals and benefits form a good basis for a patient-physician consultation.	3 (2.2)	9 (6.5)	28 (20.1)	46 (33.1)	52 (37.4)	1 (0.7)
I can imagine filling out and documenting the questionnaires for myself.	20 (14.4)	29 (20.9)	34 (24.5)	23 (16.5)	32 (23)	1 (0.7)
I can basically imagine filling out electronic questionnaires.	5 (3.6)	4 (2.9)	11 (7.9)	35 (25.2)	83 (59.7)	1 (0.7)
By filling out and storing the data on my goals and benefits, treatment decisions can be supported.	0 (0)	1 (0.7)	20 (14.4)	51 (36.7)	67 (48.2)	0 (0)
By filling out and storing the data on my goals and benefits, communication with my physician can be improved.	0 (0)	5 (3.6)	21 (15.1)	38 (27.3)	75 (54)	0 (0)
By filling in and storing the data on my goals and benefits, the relationship with my physician can be improved.	4 (2.9)	16 (11.5)	41 (29.5)	28 (20.1)	50 (36)	0 (0)
By filling in and saving the data on my goals and benefits, the course of my disease can be observed over a long period of time.	1 (0.7)	2 (1.4)	7 (5)	42 (30.2)	87 (62.6)	0 (0)
By filling in and saving the data on my goals and benefits, I can better remember my symptoms and well-being during patient-physician consultation.	6 (4.3)	12 (8.6)	27 (19.4)	34 (24.5)	60 (43.2)	0 (0)
By filling in and storing the data on my goals and benefits, I can gain more control over my condition.	4 (2.9)	14 (10.1)	31 (22.3)	38 (27.3)	52 (37.4)	0 (0)

**Table 7.** Descriptive results on acceptability II (N=139).

	Values, n (%)
<b>How often would you be willing to fill in the questionnaires on your personal goals and benefits?</b>	
Not at all	1 (0.7)
Rarer than at each patient-physician consultation	33 (23.7)
At every patient-physician consultation	85 (61.2)
More frequently than at each patient-physician consultation	14 (10.1)
Missing	6 (4.3)

**Table 8.** Descriptive results on acceptability III (N=139).

	Daily, n (%)	Weekly, n (%)	Monthly, n (%)
<b>What is the maximum amount of minutes it may take, that you would fill in the data ...</b>			
That would be too often for me	79 (56.8)	31 (22.3)	1 (0.7)
1 minute	10 (7.2)	6 (4.3)	2 (1.4)
5 minutes	29 (20.9)	50 (36)	27 (19.4)
10 minutes	15 (10.8)	35 (25.2)	69 (49.6)
20 minutes	0 (0)	9 (6.5)	22 (15.8)
30 minutes	1 (0.7)	2 (1.4)	11 (7.9)
Over 30 minutes	1 (0.7)	1 (0.7)	4 (2.9)
Missing	4 (2.9)	5 (3.6)	3 (2.2)

**Table 9.** Descriptive results on acceptability IV (N=139).

	From home, n (%)	In the waiting room, n (%)	Via my own smartphone or tablet, n (%)	Via my own laptop or PC, n (%)	Via a device provided to me by the physician (eg, smartphone, tablet, and laptop), n (%)
<b>How could you imagine filling in the questionnaires about your personal goals and benefits?</b>					
Totally disagree	16 (11.5)	3 (2.2)	23 (16.5)	31 (22.3)	23 (16.5)
Rather not agree	7 (5)	14 (10.1)	19 (13)	20 (14.4)	13 (9.4)
Neither	13 (9.4)	26 (18.7)	12 (8.7)	9 (6.5)	14 (10.1)
Rather agree	16 (11.5)	23 (16.5)	17 (13.7)	15 (10.8)	18 (12.9)
Totally agree	87 (62.6)	71 (51.1)	68 (48.9)	60 (43.2)	70 (50.4)
Missing	0 (0)	2 (1.4)	0 (0)	4 (2.9)	1 (0.7)

## Subgroup Comparison

Subgroup comparison showed some significant differences regarding sex, age, education, and ePBI version (web or app; [Multimedia Appendix 2](#)). Female participants disagreed more often than male participants that data collection of ePBI can improve communication between physician and patient. They were more often of the opinion that they could gain more control over their disease and showed significantly more missing values on the question if they could imagine filling in the ePBI via their own laptop or PC (see adjusted residuals in [Multimedia Appendix 2](#)).

Patients older than 60 years were less likely to think that filling in e-surveys daily was too frequent. They were willing to spend more time on completing (long) questionnaires although it took them more time. The younger group even needed less assistance. Anyway, the older groups still preferred completion on paper, respectively, less often to fill in electronic questionnaires in comparison to the younger groups.

Patients with low or no school degrees expected the relationship with their physician to improve by filling in the ePBI. They were less willing to spend a lot of time on questionnaire completion than the higher education groups, as it also took them longer to complete an ePBI.

Only one significant difference was found between the opinions of patients filling in the app in comparison to the web version: patients who filled in the web version more often thought that

the questionnaire would form a good basis for a patient-physician consultation than the patients who used the app (see adjusted residuals in [Multimedia Appendix 2](#)).

## Discussion

### Summary

We developed an app and a web version of the existing and valid PBI using the results of focus groups for conceptualization and cognitive debriefing to adapt the preliminary versions as recommended by the ISPOR. The results of the subsequent survey showed a high understanding and feasibility of the ePBI. Moreover, the acceptability was also very high: patients can imagine using and discussing the ePBI in practice and documenting it regularly, expecting improvements, for example, better treatment decisions and communication with their physician, as well as gaining more control over their disease. Importantly, they can imagine filling in the ePBI and other electronic questionnaires regularly, even preferring the electronic over the paper versions. Other studies also showed high feasibility and acceptability of electronic data collection [19,24,25]. These results show that the basis for an implementation is in place. However, the acceptability of patients with dermatological diseases is higher compared to dermatologists' acceptability [19,24], indicating barriers for implementation as physicians play a key role in disseminating [26].



## Principal Findings

The frequent values of the “partly agree” answers (Likert scale) to the acceptability questions show that some patients may have difficulties in imagining the use of an electronic PRO in clinical practice. We assume that the more experiences people gain with electronic devices, the more usable and acceptable it will become.

We did not find fundamental differences in sex. Merely, female participants in our study would use the ePBI more often than male participants to gain more control over their disease, which goes in line with previous findings showing that female participants are more health-conscious than male participants [27]. According to male participants, the ePBI could help to improve communication with their physician, which may be more important for them to improve than for female participants.

We detected several differences in age, which are reinforced by other studies, after which older adults use technologies at lower rates than other age groups [28]. In this study, the older participants had more problems filling in the ePBI and would more often prefer paper versions over digital ones. This may indicate a digital divide. However, they were willing to spend more time documenting data digitally, probably reflecting their higher needs. Existing data also reveal that internet use by older people is increasing, expecting a less digital divide in the future [28].

Participants with lower school degrees had more difficulties filling in the ePBI and were less willing to spend time documenting their data than those with higher education. We assume that it takes them longer to understand the concept of and get used to such digital applications. Again, this may indicate a digital divide. Nevertheless, our data reveal that it may be especially promising for this group to use the ePBI, as participants with lower school degrees more often expected an improved relationship with their physicians.

We only found one difference between the participants’ opinions using the different modes of data collection. They thought the web version would be more suitable to form a good basis for a patient-physician consultation than the app. In the web version, the questionnaire looks more familiar, as the structure is similar to a paper version. It is also easier to discuss data on a big screen than on a mobile phone. However, as soon as data are digitalized, there are several opportunities to display and store them on different electronic devices. Again, we assume that gaining more experience in data collection and use will increase usability and acceptability.

Due to its many years of proven use in research and practice, we have conducted various qualitative studies on the development of the ePBI. We followed guidelines on research, implementation, and validation processes. The sampling size was chosen based on statistical necessity and therefore appropriate to answer the present research question. As recruitment was conducted in a specified outpatient ward, the sample mainly includes patients who are moderately and severely affected. Digital applications especially aim to support these patient groups, as they have more issues dealing with their disease. Our sample consists of many patients who are well-educated and experienced regarding internet-ready devices, possibly resulting in more positive attitudes on feasibility and acceptability as our results show with respect to the subgroup analysis. The digitalization rate is only slightly higher than within the general population, for example, in Germany [29]. As nearly everybody within our sample had great experiences with digital devices, we did not expect significant differences between low or high users within our sample. Unfortunately, we did not capture the number of patients who were asked to participate but declined. Therefore, we have no information about that group.

## Conclusions

The app and web version of the ePBI are usable and acceptable for patients. The results show that the basis for an implementation is in place. This offers many advantages not only for research but also for documenting and more comprehensively using patient data in practice, such as in eHealth records or other documentation applications, for shared decision-making and patient participation. Thereby, a focus should be placed on the digital divide with special attention on age and education. People with higher age and lower education seem to have more difficulties using and understanding digital applications. In contrast, they are willing to put more effort into documentation and see other important advantages, which may increase successful use. Information on and experiences with digital applications, such as the ePBI or other digital monitoring solutions, will increase usability and acceptability.

Our results can support other researchers, developers, and decision makers. Physicians need to be better informed and included in processes, as their low acceptability and use may form a barrier for future implementations. In Germany, some political barriers also hinder digitalization in medicine, for example, no unified telematics infrastructure, reimbursement, and data security issues.

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## Data Availability

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

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## Conflicts of Interest

None declared.

### Multimedia Appendix 1

Patient Benefit Index questionnaire.

[PDF File (Adobe PDF File), 238 KB - [derma\\_v7i1e54762\\_app1.pdf](#) ]

### Multimedia Appendix 2

Significant results of subgroup analysis.

[DOCX File , 56 KB - [derma\\_v7i1e54762\\_app2.docx](#) ]

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## Abbreviations

**ePBI:** electronic Patient Benefit Index

**ISPOR:** Professional Society for Health Economics and Outcome Research

**PBI:** Patient Benefit Index

**PBQ:** Patient Benefit Questionnaire

**PNQ:** Patient Needs Questionnaire

**PRO:** patient-reported outcome

**QoL:** quality of life

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

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Original Paper

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

Laurie Groshon<sup>1</sup>, MS; Molly E Waring<sup>2</sup>, PhD; Aaron J Blashill<sup>3</sup>, PhD; Kristen Dean<sup>2</sup>; Sanaya Bankwalla<sup>2</sup>, BSc (Marketing); Lindsay Palmer<sup>4</sup>, PhD; Sherry Pagoto<sup>2</sup>, PhD

<sup>1</sup>University of Florida, Gainesville, FL, United States

<sup>2</sup>University of Connecticut, Storrs, CT, United States

<sup>3</sup>San Diego State University, San Diego, CA, United States

<sup>4</sup>UMass Chan Medical School, Worcester, MA, United States

**Corresponding Author:**

Sherry Pagoto, PhD

University of Connecticut

2006 Hillside Road, Unit 1248, Room 22

Storrs, CT, 06268

United States

Phone: 1 4344654162

Email: [sherry.pagoto@uconn.edu](mailto:sherry.pagoto@uconn.edu)

## 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.

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## 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

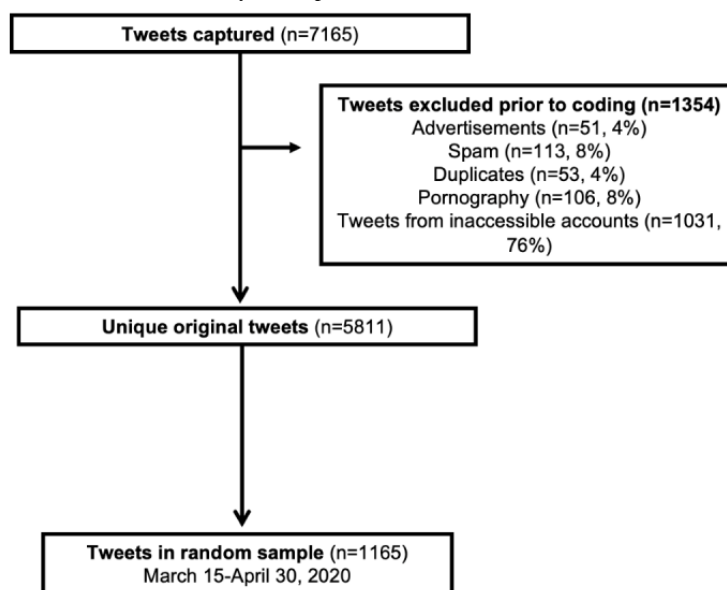
median population movement immediately after the start dates of the stay-at-home orders [10]. We were interested in whether tanners found alternative means of accessing tanning beds if they discussed interest in UV tanning alternatives (eg, sunless tanners), and their reactions to having no access to 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 pre-pandemic 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.

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## 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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Original Paper

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

Isaac Weber<sup>1\*</sup>, MD; Caterina Zagona-Prizio<sup>2\*</sup>, BS; Torunn E Sivesind<sup>2\*</sup>, MD; Madeline Adelman<sup>2\*</sup>, MD; Mindy D Szeto<sup>2</sup>, MS; Ying Liu<sup>3</sup>, PhD; Stefan H Sillau<sup>3</sup>, PhD; Jacquelyn Bainbridge<sup>3</sup>, PharmD; Jost Klawitter<sup>3</sup>, PhD; Cristina Sempio<sup>3</sup>, PhD; Cory A Dunnick<sup>2</sup>, MD; Maureen A Leehey<sup>3</sup>, MD; Robert P Dellavalle<sup>2,4,5</sup>, MSPH, MD, PhD

<sup>1</sup>Mercy Hospital St. Louis, St. Louis, MO, United States

<sup>2</sup>Department of Dermatology, University of Colorado School of Medicine, Aurora, CO, United States

<sup>3</sup>Department of Neurology, University of Colorado School of Medicine, Aurora, CO, United States

<sup>4</sup>Dermatology Service, Rocky Mountain Regional Veterans Affairs Medical Center, Aurora, CO, United States

<sup>5</sup>Colorado School of Public Health, Aurora, CO, United States

\* these authors contributed equally

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Dermatology Service

Rocky Mountain Regional Veterans Affairs Medical Center

1700 N Wheeling St, Rm E1-342

Aurora, CO, 80045

United States

Phone: 1 720 857 5562

Email: [Robert.dellavalle@ucdenver.edu](mailto:Robert.dellavalle@ucdenver.edu)

## 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)	P 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.

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## 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

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Original Paper

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

Yiwen Li<sup>1</sup>, MS; Charlene Pope<sup>2</sup>, PhD; Jennifer Damonte<sup>3</sup>, MA; Tanika Spates<sup>3</sup>, MPH; April Maa<sup>3,4</sup>, MD; Suephy Chen<sup>5</sup>, MS, MD; Howa Yeung<sup>1,3</sup>, MSc, MD

<sup>1</sup>Department of Dermatology, Emory University School of Medicine, Atlanta, GA, United States

<sup>2</sup>Charleston Veterans Affairs Health Equity and Rural Outreach Innovation Center, Ralph H. Johnson Veterans Affairs Health Care System, Charleston, SC, United States

<sup>3</sup>Clinical Resource Hub, Veterans Affairs Veterans Integrated Service Network 7, Atlanta, GA, United States

<sup>4</sup>Department of Ophthalmology, Emory University School of Medicine, Atlanta, GA, United States

<sup>5</sup>Department of Dermatology, Duke University School of Medicine, Durham, NC, United States

**Corresponding Author:**

Howa Yeung, MSc, MD

Department of Dermatology

Emory University School of Medicine

Suite 100

1525 Clifton Road NE

Atlanta, GA, 30322

United States

Phone: 1 404 727 9838

Fax: 1 404 727 5878

Email: [howa.yeung@emory.edu](mailto:howa.yeung@emory.edu)

## 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 (tele dermatology 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.

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## KEYWORDS

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

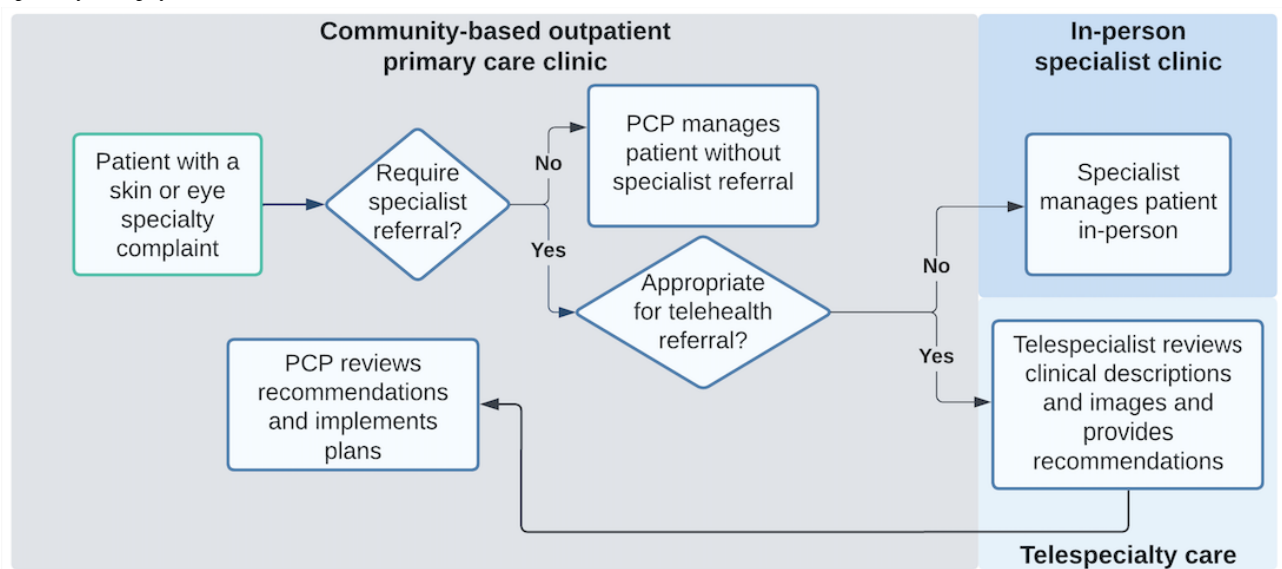
## Introduction

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 Tele dermatology 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 interviewees 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 Tele dermatology 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.

#### Staffing

- Ensure telespecialty care technicians are not simultaneously assigned regular clinical duties.
- Train additional telehealth technicians and standardize backup plans for staff absences.

#### Scheduling

- Implement real-time scheduling to optimize time use with appointment cancellations.
- Streamline referral process from primary care providers to reduce redundant appointments.
- Review patient suitability for telespecialty care.

#### Equipment

- Standardize plan for maintaining software access, reporting and troubleshooting equipment failure, and purchasing new equipment.
- Identify backup plans for care continuation during equipment or software downtime.

#### Protocol

- Standardize personnel delegation in telespecialty care.

#### Training

- Train all staff regularly on the scope and practices of telespecialty care.
- Promote awareness of telespecialty care across departments.

#### Others

- Implement a feedback system using patient and staff surveys to identify areas for improvement.
- Develop and iterate for regular communication and feedback mechanisms within the program.

### 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 tele dermatology 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 tele dermatology 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 Tele dermatology 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.

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### 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

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Research Letter

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

Sofie Mylle<sup>1,2\*</sup>, MD; Jorien Papeleu<sup>1,2\*</sup>, MD; Isabelle Hoorens<sup>1,2</sup>, MD, PhD; Evelien Verhaeghe<sup>1,2</sup>, MD, PhD; Lieve Brochez<sup>1,2</sup>, MD, PhD

<sup>1</sup>Dermatology Department, Ghent University Hospital, Ghent, Belgium

<sup>2</sup>Cancer Research Institute Ghent, Ghent, Belgium

\* these authors contributed equally

**Corresponding Author:**

Lieve Brochez, MD, PhD

Dermatology Department

Ghent University Hospital

Corneel Heymanslaan 10

Ghent, 9000

Belgium

Phone: 32 9 332 21 11

Fax: 32 9 332 21 11

Email: [lieve.brochez@ugent.be](mailto:lieve.brochez@ugent.be)

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**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

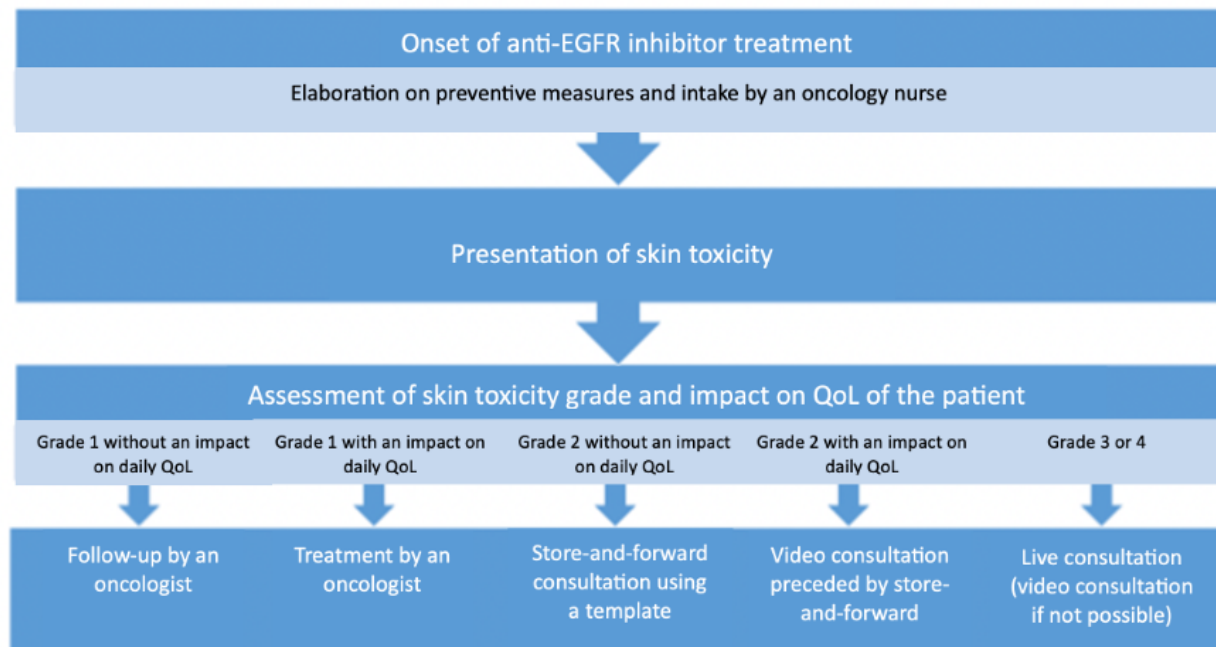
Although skin toxicity during anti-EGFR treatment might be considered a minor, non-life-threatening side effect, it is known to markedly impact patients' QoL. This may lead to dose tapering or early treatment discontinuation, thereby potentially interfering with its anticancer effects [1-4]. Skin toxicity 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.



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## 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

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Original Paper

# An Exploration of Dutch Dermatologists' Experience and Satisfaction With Tele dermatology: Sociotechnical and Complex Adaptive System Perspective

Femke van Sinderen<sup>1,2,3</sup>, MSc; Craig Kuziemsy<sup>4</sup>, PhD; Monique W Jaspers<sup>1,2</sup>, PhD; Linda W Peute<sup>1,2</sup>, PhD

<sup>1</sup>Department of Medical Informatics, Amsterdam UMC location University of Amsterdam, Amsterdam, Netherlands

<sup>2</sup>Amsterdam Public Health, Digital Health, Amsterdam, Netherlands

<sup>3</sup>Ksyos Health Management Research, Amsterdam, Netherlands

<sup>4</sup>Office of Research Services, MacEwan University, Edmonton, AB, Canada

**Corresponding Author:**

Femke van Sinderen, MSc

Department of Medical Informatics

Amsterdam UMC location University of Amsterdam

Meibergdreef 9

Amsterdam, 1105AZ

Netherlands

Phone: 31 20 5666204

Email: [f.vansinderen@amsterdamumc.nl](mailto:f.vansinderen@amsterdamumc.nl)

## Abstract

**Background:** Despite the global upscale of tele dermatology during the COVID-19 pandemic, persistent barriers, such as the poor anamnesis and photo quality, hinder its effective use in practice. Understanding Dutch dermatologists' experiences and satisfaction with using the tele dermatology system in the Dutch health care system is needed. A holistic evaluation may provide valuable insight to understand how barriers interrelate which is deemed necessary for the innovation of tele dermatology in practice.

**Objective:** Guided by a complex adaptive system perspective, this study aims to understand Dutch dermatologists' experience and satisfaction with their training, support communication, interaction, and usage of a tele dermatology platform of a Dutch digital hospital during the COVID-19 pandemic, uncovering insights to improve tele dermatology services for the future.

**Methods:** A web-based questionnaire was sent in December 2021 to Dutch dermatologists who (1) had an active tele dermatology platform account, and (2) responded to a tele dermatology consultation between October 1, 2019, and September 30, 2021. The questionnaire consisted of the validated Store-and-Forward Telemedicine Service User-satisfaction Questionnaire (SAF-TSUQ) questionnaire, and new questions regarding; demographics of tele dermatologists, the use of tele dermatology during the COVID-19 pandemic, the performance of tele dermatology by general practitioners (GP), and the role of dermatologists in the tele dermatology process. The open-ended questions were analyzed by a grounded theory approach guided by a sociotechnical model and complemented by a complex adaptive system perspective. A panel discussion with 3 dermatologists was performed to provide additional insight into the responses to the questionnaire.

**Results:** We obtained responses from 25 out of the 249 (10%) invited dermatologists. Overall, dermatologists had a positive experience with tele dermatology. Interestingly, tele dermatology use frequency remained unaffected by the COVID-19 pandemic. However, the insufficient quality and incompleteness of the clinical content (photos and anamneses information) of the tele dermatology consultation impacted the efficiency of the tele dermatology workflow. Dermatologists expressed the need for improvement to avoid time-consuming processes or physical referrals. The panel discussion enriched and confirmed the responses, suggesting solutions like mandatory fields for the GPs for a complete anamnesis.

**Conclusions:** Dutch Dermatologists view tele dermatology as a valuable tool to provide access to dermatology care. However, improvements regarding the quality and completeness of the provided clinical content are necessary for the effectiveness and efficiency of the complex tele dermatology system in Dutch health care. This could increase both the dermatologists' satisfaction and the quality of tele dermatology services. Managing trade-offs, such as time investments versus image quality, is crucial for tele dermatology implementation and should be assessed from a complexity perspective to understand trade-offs and prevent unintended consequences.

**KEYWORDS**

tele dermatology; teledermoscopy; provider satisfaction; dermatologist; dermatology; telemedicine; e-health; COVID-19; telehealth; general practitioner; quality; sociotechnical model

## Introduction

Telemedicine is a method to deliver health care remotely by use of digital technologies and is applied in several medical disciplines such as in the dermatology field [1,2]. Through tele dermatology, photos and anamnesis information of different types of skin disorders of patients are digitally submitted by a primary care provider and reviewed by a remote dermatologist [3,4]. In the Dutch health care system, this facilitates the guidance of a general practitioner (GP) in primary care by a remote dermatologist from secondary care on the management of the skin disorder. GPs play a central role in the Dutch health care system in coordinating the patients' health care needs, including referrals to secondary care. Tele dermatology has been used since 1995 [5], but challenges still exist worldwide [6,7], including the inability of dermatologists to conduct a full body skin check and palpation of the lesion. Consequently, dermatologists rely on the information provided by the GP for a diagnosis, emphasizing the need for high-quality photos and anamnesis details. This is illustrated by the Danish studies of Vestergaard et al. In these studies, 9.5%-10% of the images were deemed of poor quality, assessed as "useless" due to issues such as out-of-focus images or missing dermoscopic or overview images [4,8]. Another known barrier is reimbursement issues, such as that in the United States, where patients and dermatologists are not always reimbursed for requesting or providing a tele dermatology consultation, respectively [9,10].

An increase of dermatology referrals to secondary care in the Netherlands [11,12] underscores the growing demand for the effective use of tele dermatology. This surge is partly driven by the aging Dutch population and increasing skin cancer incidence [13,14]. Within the next decade, incidences of basal cell carcinoma are expected to increase [15], potentially leading to a heightened demand for referrals to secondary dermatological care. Despite these barriers, studies demonstrate the potential of tele dermatology for general practice in the Netherlands, particularly in preventing unnecessary referrals and minimizing environmental impact [3,16-18].

The COVID-19 pandemic [19] had a massive impact on dermatology practice, as face-to-face care delivery became limited [20]. This led to a global, sudden upscale of tele dermatology use to ensure that dermatologists could continue to provide essential dermatology care while still adhering to public health guidelines [21-25]. This required a steep learning curve from some dermatologists as they had to use tele dermatology without adequate training or implementation of the service into their practice. These issues have led to increased support requests from dermatologists to the tele dermatology provider [23-25]. Despite progress being made, known barriers to effective tele dermatology use and implementation still existed after COVID-19 restrictions were stopped. How dermatologists experienced this need and delivery

of training, support communication, interaction, and usage of a Dutch tele dermatology platform by service providers and whether the COVID-19 pandemic impacted these perceptions positively or negatively is yet unknown. A holistic evaluation may provide valuable insight to understand how barriers interrelate which is deemed necessary for the innovation of tele dermatology in practice and to inform strategies to optimize tele dermatology services.

Guided by a complex adaptive system perspective, this study aims to understand Dutch dermatologists' experience and satisfaction with their training, support communication, interaction, and usage of a tele dermatology platform of a Dutch digital hospital during the COVID-19 pandemic, uncovering insights to improve tele dermatology services for the future [26,27].

## Methods

### The Questionnaire

The Store-and-Forward Telemedicine Service User-satisfaction Questionnaire (SAF-TSUQ) [28], a Dutch validated questionnaire, consists of 29 closed-ended questions within the following themes: Training (eg, offered training to work with tele dermatology), Support Communication (eg, preferred way to communicate with Ksyos), Interaction (eg, tele dermatology is easy to use), and Use (eg, tele dermatology improves access to dermatology care) with the telemedicine platform (Multimedia Appendix 1). The responses are rated on a 5-point Likert scale (1=strongly disagree to 5=strongly agree) with 2 additional options "I do not know" and "not applicable." On the basis of this questionnaire, the tele dermatology service of Ksyos was evaluated [29]. Ksyos is a digital hospital and the largest tele dermatology provider in the Netherlands [29].

We added 21 closed- and 6 open-ended questions to tailor the generic SAF-TSUQ questionnaire to specifically address the nuances of tele dermatology use. These additional questions were added for the following themes: demographic information of dermatologists, the use of tele dermatology (during the COVID-19 pandemic, eg, experience and frequency of use before or during the COVID-19 pandemic), the use of tele dermatology by GPs (eg, photo quality), and to evaluate tele dermatology as experienced by the dermatologists (eg, not able to perform a full body skin check; Multimedia Appendix 1). All questions were mandatory, except the optional free text fields at the end of each theme. These new questions were discussed in a focus group with tele dermatology experts of Ksyos and reviewed by a dermatologist via email.

### Participants

The supplemented questionnaire was sent by email to dermatologists who (1) had an active tele dermatology platform account at the moment of sending the questionnaire, and (2)



responded to a teledermatology consultation between October 1, 2019, and September 30, 2021.

The questionnaire was sent out in December 2021. Dermatologists gained access to the questionnaire via a unique link in the email. The link became inactive after the questionnaire was filled in so the questionnaire could only be filled in once. This link only allowed tracking if a questionnaire was filled in, thus the individual responses were not visible for the researchers. We sent reminders once to nonresponders 1 week after sending the questionnaire. Informed consent was requested in the questionnaire for the use of their responses for research purposes.

Participation was voluntary and anonymous. Four gift cards were raffled among respondents who completed the questionnaire in a larger study. The LimeSurvey questionnaire tool was used to store the questionnaire and its responses. The Medical Ethical Committee of the Amsterdam University Medical Center (location AMC) provided a waiver.

### Analysis of the Responses

The responses to the closed-ended questions of the SAF-TSUQ questionnaire were analyzed descriptively per questionnaire theme with RStudio.

The Sittig and Singh sociotechnical model was used for the analysis of the open-ended questions [30]. This sociotechnical model has been previously used to understand sociotechnical barriers and facilitators of digital health use after its implementation [31-34], and consists of eight interrelated dimensions: (1) hardware and software; (2) clinical content; (3) human-computer interface; (4) people; (5) workflow and communication; (6) internal organizational policies, procedures and culture; (7) external rules, regulations, and pressures; and (8) system measurement and monitoring (Table 1).

The open-ended questionnaire responses were analyzed by combining an inductive and a deductive approach. First, during a content analysis with an inductive approach, 2 researchers (LWP, Bibiche Groenhuijzen) systematically and independently reviewed the open-ended questionnaire responses to identify patterns and themes using a grounded theory approach [35]. Secondly, a deductive approach was applied to map the identified themes onto the sociotechnical model. The combined deductive and inductive approach allowed for the potential extension of the Sittig and Singh [30] model.

During the content analysis, the data were ordered into discrete responses during the open coding phase. Responses consisting of multiple sentences were split into smaller units of meaning, if necessary. An inductive coding approach was applied by one researcher (LWP) and one coder (Bibiche Groenhuijzen), meaning that the first codes emerged from the prior content analysis. This is an iterative approach whereby the data are reread and the first codes are refined and, if required, new codes

can be created. These refined and new codes were (re)applied to the data until saturation of codes was reached and all responses were coded. This final set of codes is referred to as our set of "subcodes." The subcode "not applicable" was assigned to responses that could not be interpreted by the researchers, and those responses were, therefore, assigned with the maincode "not able to code" and were not assigned to a dimension. The subcodes represented the rich details of the responses. Patterns emerged from these subcodes from which maincodes were formulated. The maincodes represented higher-level categories of the data compared to the subcodes. During axial coding [36,37], sets of subcodes were grouped by one maincode. The open and inductive coding phase resulted in a codebook of sub- and maincodes (Tables S1 and S2 in [Multimedia Appendix 2](#)). The coders (Bibiche Groenhuijzen, FvS) independently assigned sub- and maincodes and were blinded to each other's codes. Continuous discussion meetings took place between the two coders (BG, FvS) and a researcher (LWP) to discuss the content of the responses and to refine the sub- and maincodes. In addition, the dimensions of the sociotechnical model were discussed. Small adaptations to the definition of the dimensions were made to fit them to the teledermatology evaluation. This was done during the inductive phase of coding [30], since at this moment, we got insights into the meaning and application of the dimensions (Table 1).

Finally with a deductive approach, 1 of the 8 interrelated dimensions of the sociotechnical model [30] was independently assigned by the 2 coders to a response. There was a discussion meeting (Bibiche Groenhuijzen, FvS) until consensus was reached regarding the assigned sub- and maincodes and dimensions. A third researcher (LWP) was involved in the discussion meeting if no consensus was reached.

As part of our comprehensive evaluation, we will discuss teledermatology as a complex adaptive system (CAS) [26,27], characterized by several components that interact with each other as part of achieving broader system outcomes. Tenets of a CAS include emergent behavior (system interactions may result in an outcome that is unpredictable) and nonlinearity (a small change in one part of the system may lead to a large change in another part of the system) [38,39]. The components must be meaningfully integrated to achieve desired outcomes such as accurate diagnostic outcomes, improved patient care, and user satisfaction [9,40]. Teledermatology exhibits characteristics of a CAS where users (eg, patients, GPs, dermatologists) are separated by system concepts (eg, time and space), and different technologies (eg, digital systems and photography equipment). A CAS-guided evaluation allows us to understand how various system subcomponents interact within system operations, supplementing the sociotechnical approach by elucidating the relationship between multiple interacting components in a system.

**Table 1.** Definition of the dimensions adapted to the tele dermatology situation [30].

Dimension	Definition
Hardware and software	All technical remarks on hardware and the software used on the (tele dermatology) consultation platform, for example, (the ease of use of) the photo equipment, (the ease of) uploading photos, and interoperability issues.
Clinical content	All remarks on the (un)structured, textual or numeric data; information, and knowledge that are stored on the (tele dermatology) consultation platform. Also remarks on the (feedback of dermatologist on) quality of the photos provided by GP in the consultation.
Human computer interface	All remarks on the software interaction with the user, for example, on the system layout or front-end features.
People	All remarks on individuals that interact with the system or remarks related to training and learnability.
Workflow and communication	All remarks on how tele dermatology is used in the workflow, the impact on workload, and the tasks required to provide appropriate care, and communication with the telemedicine provider.
Organizational policies and procedures	All remarks on structures, policies, financials, and procedures of the telemedicine organization that influence technology management.
External rules, regulations, and pressures	All remarks on external factors outside the telemedicine organization that facilitate or impede efforts to design, implement, use, and evaluate technology, as well as remarks indicating that the use of tele dermatology by health care providers has changed due to the COVID-19 pandemic.
System measurement and monitoring	All remarks including system availability, its use by stakeholders, its effectiveness, and associated (un)intended consequences (by the COVID-19 pandemic).
Not able to code	All remarks that were insufficiently specific or not comprehensive to be assigned to a dimension. This dimension also includes remarks about the questionnaire itself.

### Dermatologist Panel Discussion

After the questionnaire study, there was an open, unstructured panel discussion with 3 dermatologists (10, 12, and 13 years' experience with Ksyos tele dermatology platform) where one researcher (FvS) presented the questionnaire outcomes. The interpretation and perspectives of the dermatologists on the questionnaire results, and their experience with tele dermatology was discussed. The remarks of the dermatologists were noted and directly mapped onto the adapted dimensions (Table 1).

### Ethical Considerations

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

## Results

### Demographics Respondents

A total of 25 dermatologists (10%) completed the questionnaire, including informed consent (Table 2). We received 3 hard bouncers, 6 out-of-office emails (for an extended period of time), and 2 dermatologists who indicated that they did not want to receive the questionnaire and reminders. The median time to fill in the questionnaire was 11.50 (average 16.49) minutes.

**Table 2.** Demographics respondents.

	Dermatologists, n (%)
<b>Gender</b>	
Male	13 (52)
Female	12 (48)
<b>Age (years)</b>	
25-34	2 (8)
35-44	7 (28)
45-54	6 (24)
55-64	9 (36)
≥65	1 (4)
<b>Computer skills</b>	
Excellent	7 (28)
Good	13 (52)
Sufficient	5 (20)
Bad	0 (0)
<b>Technical knowledge</b>	
I am an innovator who is eager to try out new technology	0 (0)
I am a pioneer and one of the first to experiment with new technology	6 (24)
I am a frontrunner; if others are adopting new technology, I want to do the same	16 (64)
I am a laggard and usually one of the last to try out new technology	3 (12)
<b>How many times using the Ksyos platform</b>	
Daily	12 (48)
Weekly	3 (12)
Monthly	8 (32)
A few times per year	2 (8)
<b>Duration of use of the Ksyos platform</b>	
6-12 months	1 (4)
1-3 years	1 (4)
3-5 years	4 (16)
5-10 years	6 (24)
More than 10 years	13 (52)

### SAF-TSUQ Question Analysis

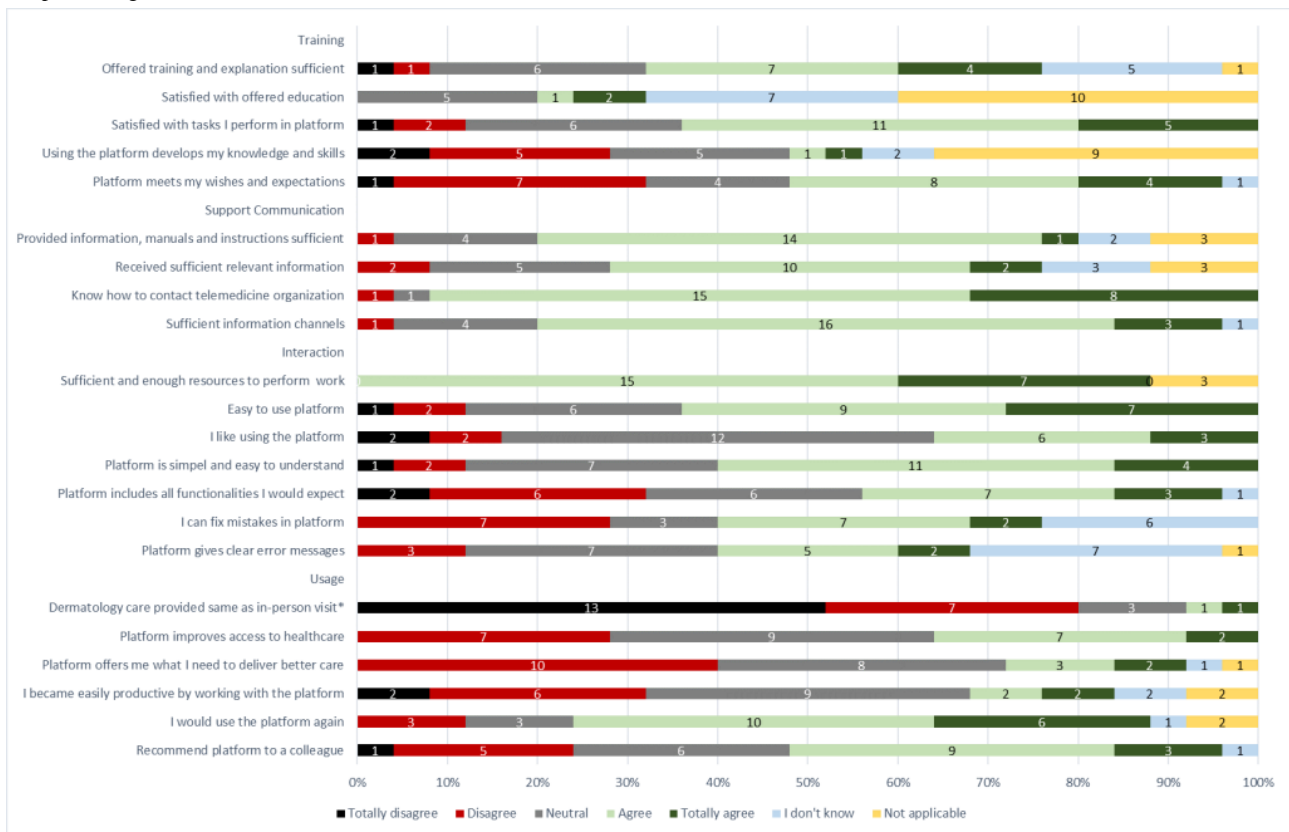
Overall, dermatologists found that the training, support communication, and information provided by Ksyos was sufficient to work with the platform. However, they were more critical that tele dermatology care is not considered the same as providing physical care (Figure 1).

Dermatologists were satisfied with performing the tele dermatology tasks. They knew how to contact Ksyos, and if support communication with Ksyos was needed, they preferred to do this via email.

While they found that performing tele dermatology did not help them to increase their dermatology knowledge, dermatologists expressed that the platform is easy to use and understandable. Despite this positive feedback, one-third of the dermatologists mentioned that the platform did yet not contain all functionalities to provide tele dermatology care (eg, they expressed their preference to provide a diagnosis in a free text field).

The majority of dermatologists acknowledged that tele dermatology serves as a valuable medium to provide the GP with advice, recommended the platform and stated that they would use it again.

**Figure 1.** Responses on the Store-and-Forward Telemedicine Service User-satisfaction Questionnaire (SAF-TSUQ) regarding the themes Training, Interaction, Support Communication, and Usage. TD: teledermatology. \*Additional explanation in the questionnaire: we meant that a digital consultation could replace a regular consultation.



### Teledermatology During the COVID-19 Pandemic

Some dermatologists reported that teledermatology use slightly increased during the first COVID-19 wave, compared to prepandemic levels (Table 3). During this time, they noted that sufficient support from Ksyos on how to use teledermatology

was received. Dermatologists observed that the type of questions asked by GPs in the teledermatology consultation did not change. They reported difficulties in evaluating teledermatology consultations with poor photo quality and anamnesis information.

**Table 3.** Responses COVID-19 questions.

	Dermatologists, n (%)
<b>Frequency of using the platform in the first COVID-19 wave vs before the COVID-19 pandemic</b>	
More often used	7 (28)
Used about as often	17 (68)
Used less often	0 (0)
Not applicable	1 (4)
<b>How often do you use the platform at this moment?</b>	
More frequently than before the COVID-19 pandemic	6 (24)
About the same as before the COVID-19 pandemic	16 (64)
Less frequently than before the COVID-19 pandemic	2 (8)
Not applicable	1 (4)
<b>Did you receive enough support to perform teledermatology during the COVID-19 pandemic?</b>	
Yes	22 (88)
No	3 (12)

### The Sociotechnical Analysis

A codebook consisting of 13 maincodes and 113 subcodes was developed (Tables S1 and S2 in [Multimedia Appendix 2](#)). Two coders (FvS, Bibiche Groenhuijzen) had a 65.5% and 71.4%

agreement after coding the responses with the sub- and maincodes, respectively. Out of the 247 responses that were coded, the 2 coders were not able to code 35 responses ([Table 4](#)). We were able to map all responses on an existing dimension of the Sittig and Sing model ([Multimedia Appendix 3](#)).



**Table 4.** Dimensions with related maincodes and exemplary quotes (Q).

Dimension, maincode	Quotes, n	Exemplary Quotes
<b>System measurement and monitoring</b>	63	— <sup>a</sup>
Conditions for use	2	<ul style="list-style-type: none"> <li>• Teledermatology is only suitable for lesions that are on body parts that can be (easily) photographed.</li> </ul>
Effect on care	3	<ul style="list-style-type: none"> <li>• Q1—The patient doesn't need to visit the hospital and has therefore less risk of a COVID-19 infection.</li> </ul>
General	8	<ul style="list-style-type: none"> <li>• Teledermatology is mostly going fine.</li> </ul>
Learnability	3	<ul style="list-style-type: none"> <li>• I did not learn anything new.</li> </ul>
Need for	3	<ul style="list-style-type: none"> <li>• Teledermatology should be applied on a larger scale.</li> </ul>
Quality of care	22	<ul style="list-style-type: none"> <li>• Q3—The overall picture of the skin is always important when assessing atypical lesions.</li> <li>• Q4—It's about the assessment of only this lesion. I cannot look at other lesions.</li> </ul>
System use	19	<ul style="list-style-type: none"> <li>• Q2—It's difficult to obtain a diagnosis based on only photos. I miss information about the skin condition and the story of the patient.</li> </ul>
User-friendliness	1	<ul style="list-style-type: none"> <li>• The system is not very user-friendly, although it has improved a bit</li> </ul>
Workload	2	<ul style="list-style-type: none"> <li>• Teledermatology is time-consuming</li> </ul>
<b>Clinical content</b>	49	—
Photo quality	35	<ul style="list-style-type: none"> <li>• Q5—The photo quality is insufficient and the specific location of the lesion on the body is sometimes unclear from the photos.</li> </ul>
Quality of care	11	<ul style="list-style-type: none"> <li>• It happens often that a teledermatology consultation contains insufficient information about the patient</li> </ul>
System failure/improvement	2	<ul style="list-style-type: none"> <li>• It would be great if more photos per teledermatology consultation can be added</li> </ul>
Workload	1	<ul style="list-style-type: none"> <li>• It increases my workload if the teledermatology consultation contains photos of insufficient quality</li> </ul>
<b>Organizational policies and procedures</b>	41	—
Effect on care	1	<ul style="list-style-type: none"> <li>• There are no restrictions (e.g. certain diagnosis) on when a GP can or cannot send a teledermatology consultation.</li> </ul>
System use	41	<ul style="list-style-type: none"> <li>• Q6—I prefer not to use teledermoscopy, but it is useful for patients for whom it is difficult to visit the hospital</li> </ul>
<b>People</b>	22	—
Conditions for use	2	<ul style="list-style-type: none"> <li>• Teledermatology should only be used by specialized GPs</li> </ul>
General	1	<ul style="list-style-type: none"> <li>• The GP is responsible for performing a full-body skin check</li> </ul>
Learnability	2	<ul style="list-style-type: none"> <li>• Q7—The GP can learn from the teledermatology consultations because for me it's only sharing my knowledge</li> </ul>
Photo quality	1	<ul style="list-style-type: none"> <li>• We should not accept that patients take their own photos due to the low quality</li> </ul>
System use	4	<ul style="list-style-type: none"> <li>• The use of teledermatology during the COVID-19 pandemic did not change</li> </ul>

Dimension, maincode	Quotes, n	Exemplary Quotes
Training	11	<ul style="list-style-type: none"> <li>Q8—I provide tips for future consultations. That's one of my tasks as a specialist; inform the GP what you need to be able to obtain a diagnosis.</li> <li>Q9—GPs should be taught what is needed to make high-quality photographs.</li> </ul>
User-friendliness	1	<ul style="list-style-type: none"> <li>It is difficult for a lot of patients to upload photos</li> </ul>
<b>Workflow and communication</b>	21	—
Conditions for use	2	<ul style="list-style-type: none"> <li>Certain processes should be faster and more efficient</li> </ul>
Need for	1	<ul style="list-style-type: none"> <li>Teledermatology is essential</li> </ul>
Quality of care	6	<ul style="list-style-type: none"> <li>A photo or video cannot replace a physical consultation</li> </ul>
System failure/improvement	1	<ul style="list-style-type: none"> <li>I use a lot of different platforms which all have different credentials. This should be replaced by one system for digital care.</li> </ul>
System use	7	<ul style="list-style-type: none"> <li>Sometimes, the patient hasn't even visited the GP, and thus photos are sent by the GP that the patient has taken themselves.</li> </ul>
Workload	3	<ul style="list-style-type: none"> <li>Teledermatology requires a lot of time compared to a physical consultation</li> </ul>
<b>Human computer interface</b>	9	—
System failure/improvement	4	<ul style="list-style-type: none"> <li>There are too many fixed, mandatory fields</li> </ul>
System use	2	<ul style="list-style-type: none"> <li>The new layout of the platform has improved</li> </ul>
User-friendliness	3	<ul style="list-style-type: none"> <li>The platform should be more user-friendly</li> </ul>
<b>Hardware and software</b>	5	—
System failure/improvement	5	<ul style="list-style-type: none"> <li>There should be an app so that I can respond quickly to the GP</li> </ul>
<b>External rules, regulations, and pressures</b>	2	—
System use	2	<ul style="list-style-type: none"> <li>GPs started using teledermatology due to the urgency during the COVID-19 pandemic</li> </ul>
Not able to code	35	—
Total	247	—

<sup>a</sup>Not applicable.

## System Measurement and Monitoring

Most dermatologists had a positive experience with teledermatology, especially during the COVID-19 pandemic where they could continue to provide care without seeing the patient at the hospital (Table 4, Q1).

Dermatologists (56%) noted that GPs generally provided complete information in the teledermatology consultations with the required types of photos and anamnesis. However, they were more critical regarding the use of teledermoscopy for diagnosing potential malignant skin lesions. The inability to perform a full body skin check of the patient is a barrier (Table 4, Q2). This underscores the need to receive (overview) pictures of the skin lesion, along with the patient anamnesis information. Dermatologists emphasized the importance of accurately selecting lesions for evaluation, given the ability of GPs to

perform a full-body skin check (*quality of care*) (Table 4; Q3, Q4).

## Clinical Content

Dermatologists (44%) expressed their concerns about the low quality of the photos taken by the GP; these are often blurry and assessment (*photo quality*). Also, overview and dermoscopic photos are mostly lacking (*quality of care*), hindering the assessment of the skin type and number of lesions. Consequently, most dermatologists (76%) advise physical referrals (Table 4; Q5).

## Organizational Policies and Procedures

The accurate assessment of potential malignant skin lesions relies heavily on high-quality (dermoscopic) photos [41]. Seven dermatologists considered that teledermoscopy is unsuitable for this purpose, and prefer live dermoscopy for a clearer view

of the skin (*system use*). Twelve dermatologists find teledermoscopy suitable and 5 dermatologists preferred not to use teledermoscopy, (Table 4; Q6) indicating different viewpoints for diagnostic suitability for different lesions (*system use*).

### People

Several dermatologists indicate the importance of training GPs in providing high-quality photos and complete patient information (*training*, Table 4; Q9). They believe such training will help GPs understand which information is required for accurate assessment by dermatologists. Dermatologists assert that they feel adequately trained in using teledermatology due to provided instructions, and emphasize that teledermatology does not enhance their dermatological knowledge but assists GPs in diagnosing skin lesions (Table 4; Q7, Q8).

### Workflow and Communication

Three dermatologists find teledermatology more time-consuming than a physical consultation (*workload*), especially with poor-quality photos (*quality of care*). For these reasons, dermatologists prefer a physical consultation as they cannot replace the full body skin check (*quality of care*). Dermatologists believe that teledermatology is, therefore, only useful for dermatologists who have sufficient time. Other dermatologists indicate that teledermatology is indispensable, for example, to monitor patients with a known diagnosis and to supervise the GP.

### Human-Computer Interface

Dermatologists differ in their viewpoint about the usability of the platform. While some believe that improvements have been made in the last years (*system use*), others mention that there are too many fixed, mandatory fields in the teledermatology consultation form which decreases their possibility to enter free text (*System failure/improvement*).

### Hardware and Software

Dermatologists provide suggestions for system improvements, for example, that the photography equipment of the GP should automatically focus to yield better photos, or a mobile app to respond to teledermatology consultations (*System failure/improvement*).

### External Rules, Regulations, and Pressures

Three dermatologists observed that GPs used teledermatology more often during the COVID-19 pandemic than before, driven by the urgency to be able to provide dermatological care.

### Dermatologist Panel Discussion

Comments of the dermatologists mostly matched the questionnaire responses (Table 5). We obtained additional insight into the experiences of dermatologists with teledermatology, since also new findings compared to the questionnaire responses were mentioned. Dermatologists gave possible explanations for critical responses on the use of teledermoscopy provided by dermatologists in the questionnaire (*Organizational policies and procedures, External rules, regulations, and pressures*). There were no comments made regarding the dimension "System measurement and monitoring."

**Table 5.** Comments panel discussion mapped on the adapted dimensions and compared to questionnaire results.

Dimension	Comments panel discussion	Compared to questionnaire results
Hardware and software	Preference for dedicated fields related to the question and suspected diagnosis of the GP, instead of 1 set of fixed, generic questions in the teledermatology consultation.	Known from questionnaire
Clinical content	The photo quality must be improved.	Known from questionnaire
Human-computer interface	More fields regarding the anamnesis should be mandatory so that the GP will provide more anamnesis information. The provided information by filling in those fields is necessary to be able to diagnose the lesion of the teledermatology consultation.	New result
Human-computer interface	Dermatologists prefer a free text entry field to fill in the diagnosis, instead of a field where a diagnosis is filled in based on a thesaurus. This is too restrictive.	Known from questionnaire
People	GPs must be instructed on the importance of anamnesis information as well as how to obtain high-quality images that dermatologists will require to diagnose the lesion.	Known from questionnaire
Workflow and communication	An option for GPs to request an urgent consultation.	New result
Workflow and communication	Currently, GPs can react to the dermatologists' response to the teledermatology consultation. GPs mostly use this to thank dermatologists, which is confusing for dermatologists because they expect additional questions.	New result
Organizational policies and procedures	The use of teledermoscopy is discouraged, because the Dutch GP guidelines (" <i>Nederlands HuisartsenGenootschap</i> ") advice to physically refer patients with suspicious lesions.	New result
External rules, regulations, and pressures	The Dutch Board of Dermatologists (" <i>Nederlandse Vereniging voor Dermatologie en Venereologie</i> ") is cautious regarding the application of teledermoscopy for the diagnosis of potential malignant skin lesions, since they believe that there is yet insufficient evidence regarding the diagnostic accuracy of teledermoscopy. As a result, there are different viewpoints on the use of teledermoscopy which discourages the use.	New result
System measurement and monitoring	No comments	N/A <sup>a</sup>

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

## Discussion

### Main Findings

Dermatologists showed overall satisfaction with the teledermatology service, and considered it a valuable addition to dermatology care, rather than a replacement of face-to-face consultations. Dermatologists find supervising GPs in patient and lesion management especially valuable. Teledermatology facilitates efficient triage, aiding in prioritizing appointments in secondary care, and thus, streamlines the referral assessment process for dermatologists, ultimately saving time in dermatology practice. Despite reported preferences for face-to-face consultations, dermatologists consistently reported high satisfaction rates with teledermatology [3,42,43]. Teledermatology provides appropriate low-complex diagnostic care at the right place, although acknowledging limitations. The current health care landscape is marked by challenges, including rising health care costs and long hospital waiting times. Teledermatology emerges as a solution to enhance efficient dermatology care [44]. However, barriers were also identified through qualitative analysis of the open-ended responses. Further, this discussion also explores factors that intricately influenced the dermatologists' experience and satisfaction with the use of teledermatology.

First, dermatologists reported that incomplete anamnesis information or low-quality (dermoscopic) photos (eg, blurry, bad lightning), from GPs hinders an accurate diagnosis, as they

heavily rely on this, due to the inability to conduct a full body skin check (*System measurement and monitoring* [45,46]. From the study's holistic perspective, the trade-off between the convenience of teledermatology (saving patient travel time and less unnecessary physical referrals) and the dermatologists' preference for physical consultations (depending on lesion complexity) is influenced by the quality of the provided clinical content.

The suboptimal quality of photos and anamnesis information may lead to more time-consuming teledermatology assessments (*Workflow and communication*), emphasizing the need for adequate clinical content quality. However, this illustrates a trade-off in teledermatology use, namely the balance between the photo quality and the time a GP spent on taking photos. High-quality photos will likely increase the workload of the GP, but will save dermatologists' time during assessment and improve the dermatologists' confidence and diagnostic performance [47,48]. In contrast, a consultation with low quality images will likely be considered ineligible for assessment by the dermatologists [3,49]. These barriers were acknowledged during the panel discussion. The poor image quality barrier was already identified in 2011 in the United States [9], making it remarkable that this continues to exist in 2020 in Denmark [4] and in our study. Despite the time-efficiency of teledermatology [3], this study did not assess how quality of the clinical content affects the time needed for assessment by dermatologists.

Teledermatology was already widely implemented in Dutch general practice prior to the pandemic, leading to a more gradual uptake compared to other countries [20]. Dermatologists did not observe a massive increase in the number of teledermatology consultations during or after the pandemic, which indicates its well-established use in the Netherlands. Despite the global forced uptake of teledermatology during the COVID-19 pandemic, both patients and their treating practitioners viewed the experience positively [50].

Our findings demonstrated how barriers impacted different aspects of care delivery. Exclusively analyzing the closed-ended questions of the SAF-TSUQ questionnaire would not have unveiled these findings, as those specifically focused only on the platform usage and omitted other aspects of teledermatology (eg, workload, clinical content). Applying a user-centered approach by surveying the dermatologists gave a better understanding of the dermatologists' experiences and satisfaction with using teledermatology. This emphasizes the need for improvements to ensure that teledermatology remains of added value, facilitating its acceptance and implementation in general health care, rather than viewing it solely as a separate digital system [51].

From a sociotechnical CAS perspective, we aimed to understand the impact of interacting system components (eg, photo quality vs workload). While acknowledging that this study is limited in identifying all complex relationships of teledermatology use and that poor photo quality is not a new result, we provide a different perspective on how to think about those barriers and how they present trade-offs in managing these issues. The interrelated nature of digital health implementation means that we cannot view barriers as isolated entities but rather we must think of them as an interrelated system [30]. Our integrated sociotechnical-CAS perspective can be used to study digital health in other settings.

### Future Research

Future research could address the refinement of training methods for GPs to optimize their dermatology knowledge and use of the advanced photography equipment (*People*). The training should be time-efficient and flexible, given the high workload of GPs. We suggest that accreditation would be a nice incentive for participation. Second, automatic focus of camera equipment (*Hardware and software*), and artificial intelligence assisted (image) analysis tools to improve the quality of the provided clinical content should be investigated. The critical attitude of dermatologists toward teledermatology should be investigated. Despite advancements of photography equipment over the past decade and the widespread use of teledermatology, dermatologists remain critical. However, caution is needed when making aforementioned changes in teledermatology systems, since the barriers resulting from this study cannot be evaluated as an isolated entity. Changes could result in unintended consequences on various parts of the system. This underscores the complexity of teledermatology innovation. By looking through a complex system perspective, we could not only identify the barriers but also support the investigation of the consequential impacts on various aspects when modifying one simple factor to a CAS [26,27].

### Strengths and Limitations

We achieved an acceptable response rate of 10%, considering the fact that the questionnaire was distributed during a lockdown. A comparable response rate (13%) was achieved in the study of Kennedy et al [52]. The panel discussion enriched perspectives, thereby balancing diverse viewpoints. This study is part of a larger investigation into teledermatology, wherein also the experiences of GPs were investigated [53]. Through the additional open-ended questions and panel discussion, we were able to provide in-depth insight into the responses of closed-ended questions of the SAF-TSUQ questionnaire. We thus believe that we obtained valid responses. This study was the first step to investigate the experiences of dermatologists with the use of teledermatology in the Netherlands. Follow-up research among a larger group of dermatologists is needed to enrich our results.

Secondly, we used a sociotechnical model as a theoretical framework to thematically analyze the responses on the questionnaire, ensuring a consistency and reliability across the data evaluation process. Through structured coding, we were able to systematically explore the responses, revealing interconnected themes such as that "workload," which could be related to "Clinical content" (poor photo quality), "Workflow and communication" (time-consuming), and "System measurement and monitoring" (unable to conduct a full body skin check). More information could be gathered from research in practice in addition to the questionnaire responses (eg, observing and interviewing how dermatologists and GPs use the teledermatology service). While various frameworks exist, such as Rogers' diffusion of innovations theory [54] and Reason's Swiss Cheese Model [55], they may have a limited scope for the evaluation of complex systems. In this study, we chose the sociotechnical model of Sittig and Singh [30] that integrates technological and sociotechnical (eg, people, processes) factors. This sociotechnical model helped us to examine the experiences of dermatologists with teledermatology services in a systematic manner [56]. Given the fact that this teledermatology service is implemented since 1995 [5], this sociotechnical model accounts for long-term perspectives, allowing for a thorough analysis of the open responses per dimensions of the model.

We experienced the expected limitations of a questionnaire study. Some incomplete responses were excluded. Since this study was the first step in understanding the dermatologists' experiences with teledermatology, we believe that a questionnaire combined with a panel discussion was an appropriate method. Follow-up research among a larger group of dermatologists within focus groups could provide a deeper understanding of the experiences. Using a sociotechnical model supported a consistent approach, but the sentiment of responses might be lost [57,58]. However, steps were taken to mitigate this through blinded coding and researcher discussions (FvS, LWP, and BG).

Another limitation included the focus on a single teledermatology service which may restrict the generalizability of our findings. It was unknown if the dermatologists also had experiences with other teledermatology services, and avoided



this in the questionnaire for clarity purposes. It should be addressed in follow-up research if the experiences of Dutch dermatologists with the Ksyos teledermatology service are shared across different teledermatology services. This could be achieved by investigating a broader range of teledermatology services across different countries through surveying dermatologists or conducting panel discussions, with a similar methodology used in our study. We acknowledge that the teledermatology system in the unique Dutch health care setting, including our results, may not be generalizable to other health care systems. Additionally, only experienced dermatologists responded to the questionnaire, thus a selection bias may exist. Including dermatologists who use teledermatology less frequent in follow-up research could reveal broader perceptions. Finally, the questionnaire did not address reimbursement and legal aspects, which are important considerations for teledermatology adoption [9,10,56].

### Conclusions

Our study sheds light on the use of teledermatology in the Dutch health care system. Dermatologists generally view

teledermatology as a valuable tool to provide access to dermatology care as alternative or decision-making prior to a physical consultation. However, their feedback highlights its challenges in providing effective and convenient care via teledermatology. Currently, trade-offs exist between the convenience of saving patient travel time and the preference for a physical consultation, and the need for high-quality photos versus the time spent by GPs on taking pictures. Improving the photo quality and the completeness of the anamnesis information is crucial. Innovative solutions such as artificial intelligence–assisted analysis tools, and not only GP training, are deemed necessary. Complete teledermatology consultations are a prerequisite for dermatologists to provide added value to the GPs and patients. Addressing barriers and implementing solutions will facilitate the continuous use of teledermatology; however, we emphasize the need to address this from a complexity perspective to understand trade-offs as a means of preventing unintended consequences.

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### Authors' Contributions

FvS conceptualized the study, was responsible for the data acquisition, and wrote the manuscript from the first version onward. FvS and LWP were involved in the study design, the analysis, and interpretation of data. CK and MWJ were further involved in critical revision of the manuscript. All authors approved the final version of the manuscript.

### Conflicts of Interest

FvS is a PhD researcher at the Amsterdam University Medical Center (UMC) and is employed by Ksyos and the Amsterdam UMC. The remaining authors state no conflicts of interest.

#### Multimedia Appendix 1

The questionnaire sent to dermatologists, including English translation.

[[DOCX File, 92 KB - derma\\_v7i1e56723\\_app1.docx](#)]

#### Multimedia Appendix 2

Codebook consisting of maincodes and subcodes (Table S1), including the number of dimensions with corresponding maincodes and subcodes (Table S2).

[[DOCX File, 37 KB - derma\\_v7i1e56723\\_app2.docx](#)]

#### Multimedia Appendix 3

Distribution of coded responses on the dimensions.

[[PNG File, 27 KB - derma\\_v7i1e56723\\_app3.png](#)]

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## Abbreviations

**CAS:** complex adaptive system

**GP:** general practitioner

**SAF-TSUQ:** Store-and-Forward Telemedicine Service User-satisfaction Questionnaire

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Original Paper

# Public Interest in Acetyl Hexapeptide-8: Longitudinal Analysis

Sofia Eva Olsson<sup>1</sup>, BS; Bhavana Sreepad<sup>1</sup>, BS; Trevor Lee<sup>1</sup>, BS; Manal Fasih<sup>1</sup>, BS; Arman Fijany<sup>1</sup>, MD

Anne Burnett Marion School of Medicine, Fort Worth, TX, United States

**Corresponding Author:**

Sofia Eva Olsson, BS

Anne Burnett Marion School of Medicine

2800 S University Dr

Fort Worth, TX, 76109

United States

Phone: 1 817 257 4212

Email: [sofia.olsson@tcu.edu](mailto:sofia.olsson@tcu.edu)

## 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.

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## 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.

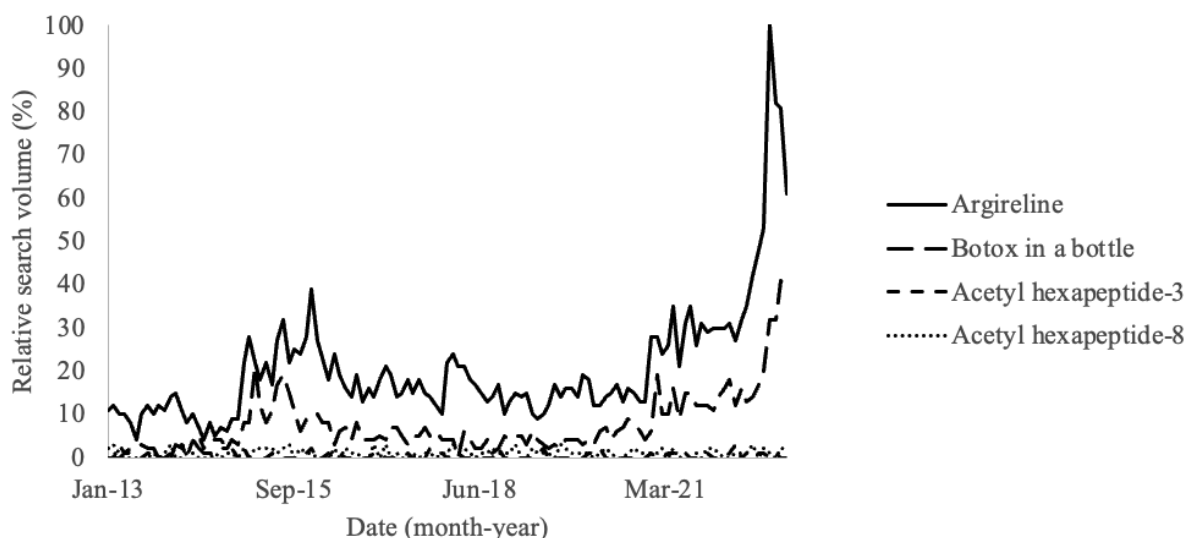
Monthly search volumes for each of these terms were obtained from Google Trends as normalized values on a relative search index. The index scale used for analysis ranged from 0, representing minimal search volume, to 100, indicating maximal search volume.

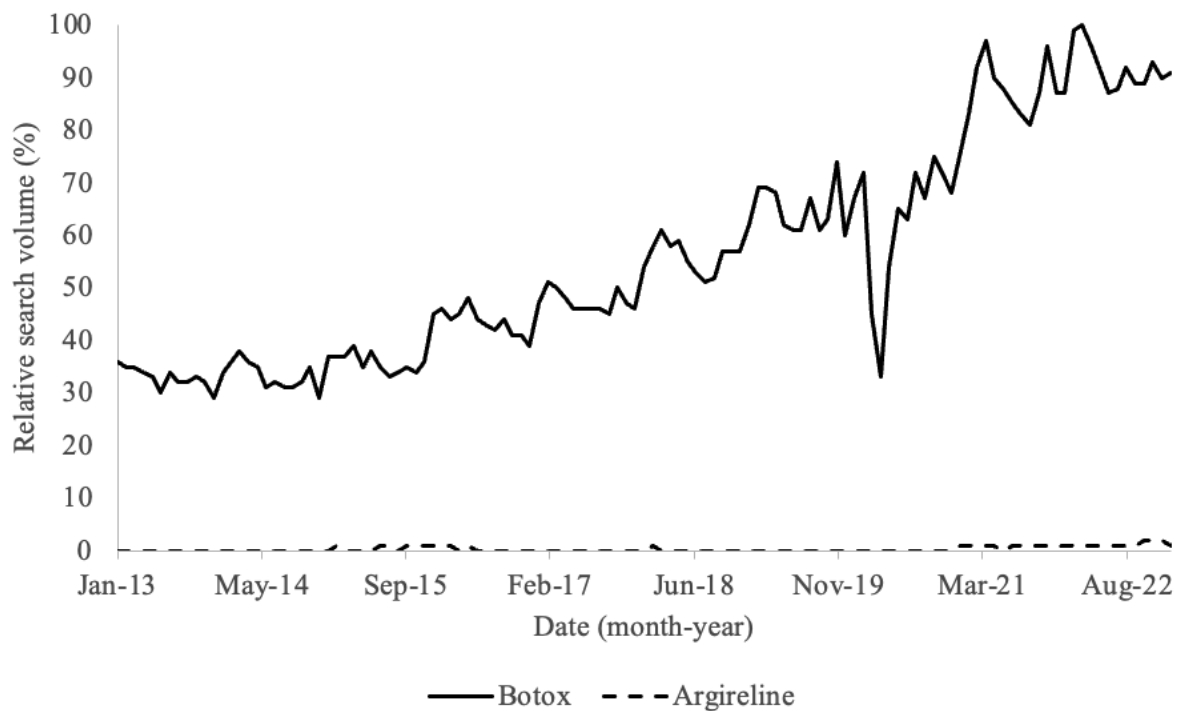
## Results

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

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Original Paper

# Assessing the Relationship Between Vitiligo and Major Depressive Disorder Severity: Cross-Sectional Study

Amr Molla<sup>1</sup>, MD; Raed Jannadi<sup>2</sup>, MD, PhD; Hamza Alayoubi<sup>3</sup>; Haya Altouri<sup>3</sup>; Maryam Balkhair<sup>3</sup>; Dareen Hafez<sup>4</sup>, MD

<sup>1</sup>Department of Medicine, College of Medicine, Taibah University, Madinah, Saudi Arabia

<sup>2</sup>Department of Family, Community Medicine, & Medical Education, College of Medicine, Taibah University, Madinah, Saudi Arabia

<sup>3</sup>Internship Unit, College of Medicine, Taibah University, Madinah, Saudi Arabia

<sup>4</sup>Department of Psychiatry, Al-Amal Complex for Mental Health, Madinah, Saudi Arabia

**Corresponding Author:**

Amr Molla, MD

Department of Medicine

College of Medicine

Taibah University

Universities Road, P.O. Box: 344, Taibah

Madinah, 42353

Saudi Arabia

Phone: 966 504342992

Email: [molladerm@outlook.com](mailto:molladerm@outlook.com)

## Abstract

**Background:** Vitiligo, a common dermatological disorder in Saudi Arabia, is associated with significant psychological impacts. This study explores the relationship between vitiligo and the severity of major depressive disorder (MDD), highlighting the broader implications on mental health among affected individuals.

**Objective:** We aim to assess the prevalence and predictors of depression among adult patients with vitiligo, and to examine the relationship between MDD severity and vitiligo.

**Methods:** Using a cross-sectional design, the research used the vitiligo area severity index and the Patient Health Questionnaire-9 to measure the extent of vitiligo and depression severity, respectively. This study involved 340 diagnosed patients with vitiligo from various health care settings. Logistic and ordinal regression analysis were applied to evaluate the impact of sociodemographic variables and vitiligo types on MDD severity.

**Results:** The prevalence of MDD was 58.8% (200/340) of participants. Depression severity varied notably: 18.2% (62/340) of patients experienced mild depression, 17.9% (61/340) moderate, 11.8% (40/340) moderately severe, and 10.9% (37/340) severe depression. Female patients had higher odds of severe depression than male patients (adjusted odds ratio [aOR] 3.14, 95% CI 1.93-5.1;  $P < .001$ ). Age was inversely related to depression severity, with patients aged older than 60 years showing significantly lower odds (aOR 0.1, 95% CI 0.03-0.39;  $P < .001$ ). Lower income was associated with higher depression severity (aOR 10.2, 95% CI 3.25-31.8;  $P < .001$ ). Vitiligo types also influenced depression severity; vulgaris (aOR 5.3, 95% CI 2.6-10.9;  $P < .001$ ) and acrofacial vitiligo (aOR 2.8, 95% CI 1.5-5.1;  $P < .001$ ) were significantly associated with higher depression levels compared to focal vitiligo.

**Conclusions:** The findings suggest that vitiligo contributes to an increased risk of severe depression, highlighting the need for integrated dermatological and psychological treatment approaches to address both the physical and mental health aspects of the disease.

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**KEYWORDS**

vitiligo; major depressive disorder (MDD); PHQ-9; Patient Health Questionnaire-9; depression severity; Saudi Arabia; cross-sectional study



## Introduction

Skin, the largest organ of the human body, serves as the visible exterior that covers internal structures. Vitiligo is a chronic, relapsing skin disorder characterized by well-defined milky-white, depigmented macules and patches resulting from the destruction of melanocytes [1]. This condition is often associated with other autoimmune disorders, particularly thyroid autoimmune diseases. Beyond the physical manifestations, vitiligo imposes a significant psychological burden due to its impact on cosmetic appearance, leading to potential stigmatization and misconceptions within social interactions. Consequently, individuals with vitiligo are at an elevated risk of developing major depressive disorder (MDD) [2].

MDD is marked by persistent sadness, loneliness, and disinterest, typically triggered by fear, trauma, or other significant stressors. This condition not only affects mood and interest but also impairs cognitive functions, influencing emotions, sleep, and appetite. These changes can alter behavior, making individuals appear irritable or despondent, with severe cases potentially leading to suicidal ideation [3]. The prevalence of MDD for life is 16.2% [4]. According to a meta-analysis study, the prevalence of depression among patients with vitiligo is 25.3% [5].

Patients with vitiligo often exhibit a dysregulated immune system, which may be exacerbated by concomitant depression. Clinical and animal studies suggest that depression can aggravate vitiligo, as both conditions share similar leukocyte signatures and inflammatory genetic mechanisms associated with systemic autoimmune inflammation. This overlap suggests a shared pathophysiological pathway, potentially increasing the risk of an inflammatory brain-skin axis, offering new insights into their bidirectional relationship and their classification within a socially stress-stigmatized model [6].

Recent studies have highlighted specific gene expression profiles associated with vitiligo, revealing significant molecular mechanisms underlying the condition. Changes in the expression of interleukin (IL)-10 family cytokines (IL26, IL-28A, IL28B, and IL29) and their receptor subunits (IL20RB, IL22RA2, and IL28RA), along with other genes related to melanocyte function such as *MDM1*, *IFNA1*, *IFNB1*, *IFNG*, and *ICAM1*, have been observed in the skin and peripheral blood mononuclear cells of patients with vitiligo. These genes are implicated in pathways regulating melanocyte survival, apoptosis, development, migration, and melanogenesis, suggesting their role in vitiligo pathogenesis [7]. Additionally, increased dopamine levels and altered expression of enzymes in the dopamine pathway, including DOPA decarboxylase, monoamine oxidase A, and monoamine oxidase B, have been noted in vitiligo patients' skin and blood. This suggests that the dopamine pathway may influence melanogenesis directly or through the melanocortin pathway [8]. Furthermore, another study supports the role of IL-10 family cytokines in vitiligo pathogenesis, particularly emphasizing the involvement of IL-22. Altered expression patterns of IL20RB, IL22RA2, IL-28A, IL28B, IL28RA, *MDM1*, *IFNA1*, *IFNB1*, *IFNG*, and *ICAM1* in vitiligo skin and

peripheral blood mononuclear cells further underscore their significance in the disease [9].

Global studies indicate that vitiligo significantly affects mental health, often leading individuals to self-isolation and avoidance of social gatherings, thereby severely affecting quality of life. Acceptance and active coping can mitigate stress and anxiety; however, the appearance-related impacts of vitiligo and MDD can lead to social withdrawal, sensitivity to perceived societal judgments, and overall deterioration in personal and professional life, culminating in diminished self-esteem and confidence [10,11].

Inspired by the PASI (psoriasis area and severity index), the vitiligo area severity index (VASI) uses hand units to quantify affected skin areas, where 1 hand unit approximates 1% of total body skin. The VASI score is calculated by multiplying the area of vitiligo (in hand units) by the degree of depigmentation within each measured patch [12].

This study aims to assess the prevalence and predictors of depression among adult patients with vitiligo. Moreover, examining the relationship between MDD severity and vitiligo, using the VASI and Patient Health Questionnaire-9 (PHQ-9) scales to assess the extent and severity of both conditions.

## Methods

### Study Design and Sample

This is a cross-sectional study aimed to investigate the relationship between MDD and vitiligo in Saudi Arabia. This study targeted adult patients diagnosed with vitiligo based on VASI and Wood's lamp examination, which revealed depigmented patches or macules that occur at typical vitiligo sites. A total of 340 adult patients with vitiligo were selected by simple random sampling method for this study, which was conducted from April 2023 to April 2024 at participating hospitals across Saudi Arabia.

The inclusion and exclusion criteria for participation were as follows:

Inclusion criteria: (1) patients diagnosed with vitiligo, as determined by the VASI, (2) ages ranging from 18 to 85 years, (3) resident in Saudi Arabia during this study's period, and (4) able to provide informed consent and complete this study's assessments.

VASI score measures the extent and severity of vitiligo by evaluating the body's surface area affected by vitiligo and quantifies the degree of skin depigmentation. The index divides the body into segments, with each segment's depigmentation severity scored on a scale from 0% (no depigmentation) to 100% (complete depigmentation). The score for each segment is calculated by multiplying the affected body surface area percentage by the depigmentation level, which provides a comprehensive measure of the disease's severity [13].

Exclusion criteria: (1) known preexisting mental health disorders before the diagnosis of vitiligo (eg, diagnosed MDD, bipolar disorder, and schizophrenia); (2) other forms of skin depigmentation not classified as vitiligo, such as albinism or

chemical leukoderma; (3) cognitive impairments or any conditions that might hinder comprehension of the questionnaire or informed consent process; and (4) pregnant or lactating women, due to potential hormonal effects on skin condition and mood.

### Data Collection

Data were collected by using a web-based questionnaire conducted through social media of the patient contact number or email, phone call, or interview clinic during the period of this study. The questionnaire was divided into 2 parts. The first part captured sociodemographic information such as sex, age, marital status, nationality, job, and monthly income, while the second part consisted of the PHQ-9 to assess symptoms of depression.

### Study Variables

#### *Independent Variable: Vitiligo Type*

In this study, the independent variable was the type of vitiligo, categorized according to the revised classification from the Vitiligo Global Issues Consensus Conference (2012) [14]. This system classifies vitiligo into 3 primary clinical forms. Nonsegmental vitiligo encompasses generalized vitiligo (formerly known as vulgaris), acrofacial vitiligo with its subtype referred to as “lip-tip” vitiligo, and vitiligo universalis. Segmental vitiligo is characterized by a unilateral, asymmetric distribution. Unclassified vitiligo includes cases that do not evolve into either segmental or nonsegmental forms within a long period, such as focal vitiligo and single mucosal vitiligo affecting either genital areas or the oral cavity.

#### *Dependent Variable: MDD*

PHQ-9 score was used to assess the severity of depressive symptoms. The PHQ-9 is a clinician-administered instrument that screens for depression and grades symptom severity based on the criteria from the *DSM-IV (Diagnostic and Statistical Manual of Mental Disorders [Fourth Edition])* [15,16]. Respondents rate how often they have experienced each of the 9 *DSM-IV* criteria for depression over the past 2 weeks on a scale from 0 (“not at all”) to 3 (“nearly every day”). The total possible score ranges from 0 to 27, with higher scores indicating greater depression severity. The depression severity categories are none to minimal depression (0-4), mild depression (5-9), moderate depression (10-14), moderately severe depression (15-19), and severe depression (20-27).

Further, 2 variables were created based on the PHQ-9 score. First, the depression severity variable was coded as follows: 0=non, 1=mild, 2=moderate, 3=moderately severe, and 4=severe depression. The binary depression variable was categorized into 2 groups whether the patient has depression (mild to severe) or not (none or minimal).

### Covariates

In this study, the covariates include gender, age, nationality, marital status, job, and monthly income. Gender was categorized as male or female. Age was divided into 3 groups: 18-25 years, 26-60 years, and older than 60 years, with the 26-60 age group serving as the reference category in multivariate analysis. Nationality was classified as either Saudi or non-Saudi. Income

levels were categorized into 4 groups, ranging from less than US \$810 per month for the low-income group to over US \$5265 per month for the high-income group, with the moderately high-income group (ranging from US \$2430 to US \$5265 per month) used as the reference in regression analysis. Marital status was classified as single, married, or divorced, with married participants considered the reference group. Job status was divided into 3 categories: employed, unemployed, or student.

### Data Management and Analysis

Data were collected electronically and analyzed using SPSS software (version 29; IBM Corp). For bivariate analysis, the chi-square test was used to investigate the association between categorical variables. The Monte Carlo simulation method was applied when indicated as an alternative to the standard chi-square test. Logistic regression analysis was conducted to explain the variability of depression occurrence by including sex, age, nationality, marital status, income, employment status, and vitiligo types in the final model. Similarly, the same model was applied in ordinal logistic regression analysis to predict depression severity. A *P* value less than .05 was considered statistically significant.

### Ethical Considerations

This paper is original, unpublished, and not under consideration elsewhere. All content, unless cited, is based on our unique research. We adhered to Saudi ethical standards, obtaining Taibah University institutional review board approval (TU-039-22) on June 5, 2023, and participant consent, respecting confidentiality and the Declaration of Helsinki.

## Results

### Sociodemographic Characteristics

Table 1 shows the sociodemographic characteristics of this study's sample stratified by depression status. The prevalence of depression among patients with vitiligo was 58.8%, with 200 of 340 participants having depression. A significant gender difference in depression prevalence was observed. Women showed a higher prevalence, with 109 of 156 (69.9%) women experiencing depression compared to 91 of 184 (49.5%) men, and this difference was statistically significant ( $P<.001$ ). Moreover, age played a significant role in depression among patients with vitiligo. The 18- to 25-year age group had the highest depression rate, with 51 of 69 (73.9%) participants experiencing depression, followed by the 26- to 60-year age group with 146 of 248 (58.9%) participants experiencing depression, while those older than 60 years had a much lower rate of 3 of 23 (13%) participants experiencing depression ( $P<.001$ ). Marital status was significantly associated with depression development, where divorced and single individuals were more likely to be depressed, with 34 of 41 (82.9%) divorced participants and 115 of 153 (75.2%) single participants experiencing depression, compared to 51 of 146 (34.9%;  $P<.001$ ) married patients. Depression development varied significantly across income levels. The lowest income group had a higher depression proportion, with 181 of 253 (71.5%) participants experiencing depression. In contrast, individuals

in the high-moderate income category showed a much lower depression prevalence, with 6 of 43 (14%) participants experiencing depression ( $P<.001$ ; Table 1).

**Table 1.** Demographic and socioeconomic influences on depression status among patients with vitiligo.

Variables	Depression		P value
	Total (N=340), n (%)	Yes (n=200), n (%)	
<b>Gender</b>			<.001
Male	184 (54.1)	91 (49.5)	93 (50.5)
Female	156 (45.9)	109 (69.9)	47 (30.1)
<b>Age groups (years)</b>			<.001
18-25	69 (20.3)	51 (73.9)	18 (26.1)
26-60	248 (72.9)	146 (58.9)	102 (41.1)
>60	23 (6.8)	3 (13)	20 (87)
<b>Nationality</b>			.17
Saudi	290 (85.3)	175 (60.3)	115 (39.7)
Non-Saudi	50 (14.7)	25 (50)	25 (25)
<b>Marital status</b>			<.001
Single	153 (45)	115 (75.2)	38 (24.8)
Divorced	41 (12.1)	34 (82.9)	7 (17.1)
Married	146 (42.9)	51 (34.9)	95 (65.1)
<b>Income</b>			<.001 <sup>a</sup>
Low	253 (74.4)	181 (71.5)	72 (28.5)
Low-moderate	32 (9.4)	10 (31.3)	22 (68.8)
High-moderate	43 (12.6)	6 (14)	37 (86)
High	12 (3.5)	3 (25)	9 (75)
<b>Job</b>			<.001
Yes	128 (37.6)	46 (35.9)	82 (64.1)
No	183 (53.8)	133 (72.7)	50 (27.3)
Student	29 (8.5)	21 (72.4)	8 (27.6)

<sup>a</sup>P value calculated by using the Monte Carlo simulation.

### Bivariate Association of Depression Severity With Sociodemographic Characteristics

Table 2 illustrates the bivariate association of depression severity and various sociodemographic characteristics of this study's sample. Men were less likely to experience severe depression than women, with 2 of 184 (1.1%) men experiencing severe depression versus 35 of 156 (22.4%;  $P<.001$ ) women. Furthermore, age group analysis reveals that most (20/23, 87%) of the older patients with vitiligo (>60 years) did not have depression, while the youngest age group (18-25 years) had more representation in the moderate and moderately severe categories, with 18 of 69 (26.1%) experiencing moderate

depression and 12 of 69 (17.4%) experiencing moderately severe depression ( $P<.001$ ). Marital status was significantly associated with depression severity, where divorced individuals exhibited higher rates of severe depression, with 13 of 41 (31.7%) experiencing severe depression compared to 22 of 153 (14.4%) singles and 2 of 146 (1.4%;  $P<.001$ ) married individuals. Moreover, the low-income group notably had higher rates of moderate to severe depression compared to higher-income groups. For instance, in the low-income group, 91 of 253 (36%) participants experienced moderate to severe depression, whereas in the high-moderate income group, only 2 of 43 (4.7%) participants experienced moderate to severe depression ( $P<.001$ ; Table 2).

**Table 2.** Variation in depression severity across demographic and socioeconomic characteristics of patients with vitiligo.

Variables	Depression severity						P value
	Total(N=340), n (%)	None (n=140), n (%)	Mild (n=62), n (%)	Moderate (n=61), N (%)	Moderately severe (n=40), N (%)	Severe (n=37), N (%)	
<b>Gender</b>							<.001
Male	184 (54.1)	93 (50.5)	44 (23.9)	32 (17.4)	13 (7.1)	2 (1.1)	
Female	156 (45.9)	47 (30.1)	18 (11.5)	29 (18.6)	27 (17.3)	35 (22.4)	
<b>Age groups (years)</b>							<.001 <sup>a</sup>
18-25	69 (20.3)	18 (26.1)	14 (20.3)	18 (26.1)	12 (17.4)	7 (10.1)	
26-60	248 (72.9)	102 (41.1)	48 (19.4)	40 (16.1)	28 (11.3)	30 (12.1)	
>60	23 (6.8)	20 (87)	0 (0)	3 (13)	0 (0)	0 (0)	
<b>Nationality</b>							.11
Saudi	290 (85.3)	115 (39.7)	49 (16.9)	55 (19)	36 (12.4)	35 (12.1)	
Non-Saudi	50 (14.7)	25 (50)	13 (26)	6 (12)	4 (8)	2 (4)	
<b>Marital status</b>							<.001 <sup>a</sup>
Single	153 (45)	38 (24.8)	36 (23.5)	36 (23.5)	21 (13.7)	22 (14.4)	
Divorced	41 (12.1)	7 (17.1)	2 (4.9)	7 (17.1)	12 (29.3)	13 (31.7)	
Married	146 (42.9)	95 (65.1)	24 (16.4)	18 (12.3)	7 (4.8)	2 (1.4)	
<b>Income</b>							<.001 <sup>a</sup>
Low	253 (74.4)	72 (28.5)	54 (21.3)	52 (20.6)	39 (15.4)	36 (14.2)	
Low-moderate	32 (9.4)	22 (68.8)	3 (9.4)	5 (15.6)	1 (3.1)	1 (3.1)	
High-moderate	43 (12.6)	73 (86)	4 (9.3)	2 (4.7)	0 (0)	0 (0)	
High	12 (3.5)	9 (75)	1 (8.3)	2 (16.7)	0 (0)	0 (0)	
<b>Job</b>							<.001 <sup>a</sup>
Yes	128 (37.6)	82 (64.1)	20 (15.6)	15 (11.7)	6 (4.7)	5 (3.9)	
No	183 (53.8)	50 (27.3)	34 (18.6)	39 (21.3)	29 (15.8)	31 (16.9)	
Student	29 (8.5)	8 (27.6)	8 (27.6)	7 (24.1)	5 (17.2)	1 (3.4)	

<sup>a</sup>P value calculated by using the Monte Carlo simulation.

### Association of Vitiligo Types With Depression Severity

Vitiligo types varied significantly in their association with depression severity. Acrofacial vitiligo was the most common type, affecting 165 (48.5%) patients. This group showed a higher proportion of moderate to severe depression, with 73 of 165 (44.2%) patients experiencing moderate to severe depression compared to a more localized focal vitiligo, with 16 of 65 (24.7%) patients experiencing moderate to severe depression. Vulgaris vitiligo was observed in 73 (21.5%) patients and revealed the highest proportion of moderate to severe depression,

with 42 of 73 (57.6%) patients experiencing moderate to severe depression. On the other hand, universalis vitiligo appeared in 11 (3.2%) patients, with a majority, 10 of 11 (90.9%) patients, having no depression, and the remaining proportion, 1 of 11 (9.1%) patients, experienced mild depression. Similarly, genital vitiligo affected 16 (4.7%) patients, mostly with no depression, with 10 of 16 (62.5%) patients having no depression, and lesser extents of mild depression, with 3 of 16 (18.8%) patients, moderate depression with 2 of 16 (12.5%) patients, and moderately severe depression, with 1 of 16 (6.3%) patients (Table 3).

**Table 3.** Correlation between vitiligo types and depression severity among patients.

	Depression severity					Total (N=340), n (%)	P value
	None (n=140), n (%)	Mild (n=62), n (%)	Moderate (n=61), n (%)	Moderately severe (n=40), n (%)	Severe (n=37), n (%)		
<b>Vitiligo types</b>							.01 <sup>a</sup>
Acrofacial	61 (37)	31 (18.8)	34 (20.6)	20 (12.1)	19 (11.5)	165 (48.5)	
Vulgaris	24 (32.9)	7 (9.6)	18 (24.7)	14 (19.2)	10 (13.7)	73 (21.5)	
Focal	33 (50.8)	16 (24.6)	7 (10.8)	4 (6.2)	5 (7.7)	65 (19.1)	
Universalis	10 (90.9)	1 (9.1)	0 (0)	0 (0)	0 (0)	11 (3.2)	
Segmental	2 (20)	4 (40)	0 (0)	1 (10)	3 (30)	10 (2.9)	
Genital	10 (62.5)	3 (18.8)	2 (12.5)	1 (6.3)	0 (0)	16 (4.7)	

<sup>a</sup>P value calculated by using the Monte Carlo simulation.

### Logistic Regression Analysis of Depression Risk Factors

Logistic regression analysis indicates that the age group over 60 years is significantly less likely to develop MDD compared to the reference group (aged 26-60 years), with an adjusted odds ratio (aOR) of 0.12 (95% CI 0.03-0.48;  $P=.002$ ). Women did not have a statistically significant higher risk of developing depression than men, with an aOR of 1.29 (95% CI 0.7-2.39;  $P=.42$ ). Individuals with a low income had a significantly higher risk of developing MDD, with an aOR of 9.5 (95% CI 2.9-30.9;  $P<.001$ ) compared to the moderately high-income reference

group. Additionally, single patients had an aOR of 2.78 (95% CI 1.29-5.98;  $P=.01$ ), and divorced individuals had an aOR of 3.86 (95% CI 1.28-11.67;  $P=.02$ ) of having depression compared to married patients. Compared to localized focal vitiligo, segmental vitiligo showed the highest risk of depression development, with an aOR of 6.37 (95% CI 1.04-38.8;  $P=.045$ ), followed by vulgaris and acrofacial types that showed significantly increased risks, with aORs of 3.5 (95% CI 1.46-8.38;  $P=.005$ ) and 2.45 (95% CI 1.2-4.98;  $P=.01$ ), respectively. In contrast, universalis vitiligo was associated with a significantly lower depression risk, with an aOR of 0.07 (95% CI 0.01-0.59;  $P=.02$ ; [Table 4](#)).



**Table 4.** Logistic regression analysis of study variables influencing major depressive disorder development among patients with vitiligo.

Variables	aOR <sup>a</sup> (95% CI)	P value
<b>Age groups (years)</b>		
26-60 (reference)	1	— <sup>b</sup>
18-25	0.67 (0.27-1.65)	.38
>60	0.12 (0.03-0.48)	.002
<b>Gender</b>		
Male (reference)	1	—
Female	1.29 (0.7-2.39)	.42
<b>Income</b>		
Moderately high (reference)	1	—
High	2.95 (0.51-17.1)	.23
Moderate	2.61 (0.78-8.78)	.12
Low	9.5 (2.9-30.9)	<.001
<b>Marital status</b>		
Married (reference)	1	—
Single	2.78 (1.29-5.98)	.01
Divorced	3.86 (1.28-11.67)	.02
<b>Vitiligo types</b>		
Focal (reference)	1	—
Universalis	0.07 (0.01-0.59)	.02
Genital	1.24 (0.29-5.27)	.77
Acrofacial	2.45 (1.2-4.98)	.01
Vulgaris	3.5 (1.46-8.38)	.005
Segmental	6.37 (1.04-38.8)	.045

<sup>a</sup>aOR was calculated by including age, gender, nationality, marital status, income, job, and vitiligo types.

<sup>b</sup>Not applicable.

### Ordinal Logistic Regression Analysis of Depression Severity

**Table 5** demonstrates the ordinal logistic regression of depression severity by modeling depression in an ascending severity direction ranging from minimal to severe depression. Gender significantly influences the severity of depression, with women having a higher risk (aOR 3.14, 95% CI 1.93-5.1;  $P<.001$ ) than men. Moreover, the age group of >60 years has a significantly lower risk of developing severe depression than the reference group (aged 26-60 years; aOR 0.1, 95% CI 0.03-0.39;  $P<.001$ ). Being divorced is associated with a higher

risk of having severe depression (aOR 5.8, 95% CI 2.6-12.9;  $P<.001$ ) than married patients. Low-income patients were linked to a higher severity of depression, showing an aOR of 10.2 (95% CI 3.25-31.8;  $P<.001$ ), than the moderately high-income group. The type of vitiligo shows a significant role in depression severity, with vulgaris (aOR 5.3, 95% CI 2.6-10.9;  $P<.001$ ) and acrofacial (aOR 2.8, 95% CI 1.5-5.1;  $P<.001$ ) types associated with a higher depression severity than focal vitiligo. On the other hand, universalis vitiligo shows a significantly lower association with severe depression (aOR 0.05, 95% CI 0.01-0.5;  $P=.01$ ; **Table 5**).

**Table 5.** Ordinal logistic regression of factors affecting depression severity in patients with vitiligo.

Variables	aOR <sup>a</sup> (95% CI)	P value
<b>Age groups (years)</b>		
26-60 (reference)	1	— <sup>b</sup>
18-25	0.97 (0.51-1.86)	.93
>60	0.1 (0.03-0.39)	<.001
<b>Gender</b>		
Male (reference)	1	—
Female	3.14 (1.93-5.1)	<.001
<b>Income</b>		
Moderately high (reference)	1	—
High	4.1 (0.71-23)	.12
Moderate	3.1 (0.91-10.6)	.07
Low	10.2 (3.25-31.8)	<.001
<b>Marital status</b>		
Married (reference)	1	—
Single	2.7 (1.5-5.1)	.001
Divorced	5.8 (2.6-12.9)	<.001
<b>Vitiligo types</b>		
Focal (reference)	1	—
Universalis	0.05 (0.01-0.5)	.01
Acrofacial	2.8 (1.5-5.1)	<.001
Vulgaris	5.3 (2.6-10.9)	<.001
Segmental	4.4 (1.2-15.9)	.02
Genital	1.7 (0.5-6.2)	.43

<sup>a</sup>aOR was calculated by including age, gender, nationality, marital status, income, job, and vitiligo types.

<sup>b</sup>Not applicable.

## Discussion

### Principal Findings

This study quantitatively assessed the prevalence and predictors of depression among patients with vitiligo in Saudi Arabia, using the VASI and PHQ-9. Our findings revealed a significant association between vitiligo and increased severity of MDD, with a prevalence of 58.8% (200/340) participants among the vitiligo population, substantially higher than the 16.2% lifetime prevalence reported for the general population [3,4]. Notably, MDD exhibits a higher severity among certain subgroups within the patients with vitiligo population. Specifically, women, divorced individuals, and those with lower income levels tend to experience more severe forms of depression. Additionally, the type of vitiligo also influences the severity of MDD, with acrofacial and vulgaris vitiligo associated with higher depression levels. These insights are crucial for tailoring more effective, targeted interventions for these vulnerable subgroups.

This study's strengths include the use of validated tools such as the VASI and the PHQ-9, which enhance the reliability of our depression severity assessments. Additionally, our

significant sample size and random sampling methodology provide a robust statistical basis for generalization within the target population. In addition, the PHQ-9 was administered by professional psychiatrists to assess MDD severity. However, this study also faces limitations. Being a cross-sectional study, it does not support causal inferences between vitiligo and the onset of MDD. Our findings might also not apply to other regions or ethnic groups since this study was geographically confined to Saudi Arabia. Moreover, excluding individuals with preexisting mental health conditions might lead to an underestimation of the actual psychological impact of vitiligo, as it does not consider those who might have developed MDD before the onset of vitiligo.

The observed high prevalence of MDD among patients with vitiligo supports the hypothesis that chronic skin diseases are significantly associated with psychiatric morbidities. This correlation is likely due to the visible and stigmatizing nature of vitiligo, which can lead to social withdrawal and significant psychological stress, thereby increasing the risk of depression. The results are consistent with findings from similar studies, which reported depression prevalence rates of 80% and 51.5%

respectively [17,18], emphasizing the need for a multidisciplinary approach to managing patients with vitiligo, considering both dermatological and psychological aspects.

The findings from this study are primarily applicable to the adult population with vitiligo in Saudi Arabia. While these results provide valuable insights into the psychological impact of vitiligo, caution should be used when generalizing to populations in different settings or with different cultural backgrounds. Further research in varied demographic and ethnic groups is necessary to understand fully the global implications of these findings.

Recent studies have identified genetic associations related to immune-regulating genes in MDD. A case-control genetic association study involving the *IKBKE* gene, which encodes the IKK $\epsilon$  protein involved in innate immunity and proinflammatory responses, revealed significant associations between *IKBKE* single-nucleotide polymorphism and MDD, as well as suggestive associations with panic disorder [19]. Additionally, polymorphisms in the limbic system-associated membrane protein (*LSAMP*) gene have shown strong associations with MDD and suggestive associations with panic disorder, suggesting a potential role for *LSAMP* in mood and anxiety disorders [20]. These genetic findings are particularly relevant to the immune dysregulation observed in patients with vitiligo, where immune-related genes play a crucial role in the pathogenesis of the disease. The proinflammatory properties of the *IKBKE* gene and its involvement in innate immunity could provide a mechanistic link between the immune responses in vitiligo and the increased susceptibility to mood disorders such as MDD. Similarly, the *LSAMP* gene's association with mood disorders highlights the potential overlap in genetic pathways

that may contribute to both vitiligo and MDD. The shared genetic markers and pathways between vitiligo and MDD suggest that immune dysregulation may be a common underlying factor. For instance, the involvement of proinflammatory cytokines and immune-modulating genes in both conditions underscores the importance of understanding how immune system alterations can influence both skin pathology and psychiatric outcomes. Further research into these shared genetic and molecular pathways could provide deeper insights into the comorbidity of vitiligo and mood disorders, potentially leading to more integrated therapeutic approaches targeting both the immune system and mental health.

Future research should use longitudinal designs to explore the causal relationships between vitiligo and depression. Studies testing the effectiveness of integrated treatment approaches for the physical and psychological aspects of vitiligo would also be beneficial. Expanding research to include diverse populations can help determine the broader applicability of these findings and explore cultural influences on the psychological impacts of vitiligo.

## Conclusion

In summary, this cross-sectional study has highlighted a significant association between vitiligo and the severity of MDD among patients, with a notably high prevalence of depression observed. The findings underscore the profound psychological impact of vitiligo, reinforcing the need for comprehensive treatment approaches that address both the dermatological and psychological aspects of the disorder. Future research should focus on longitudinal studies to explore the causative mechanisms between vitiligo and depression and evaluate the effectiveness of integrated treatment strategies.

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## Data Availability

The data that support the findings of this research are available from the corresponding author upon reasonable request. Due to legal and ethical considerations, the data cannot be made publicly available. Requests for data access should be directed to AM.

## Authors' Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing this paper; gave final approval of the version to be published; have agreed on the journal to which this paper has been submitted; and agree to be accountable for all aspects of the work.

## Conflicts of Interest

None declared.

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## Abbreviations

- aOR:** adjusted odds ratio
- DSM-IV:** Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition)
- IL:** interleukin
- LSAMP:** limbic system-associated membrane protein
- MDD:** major depressive disorder
- PASI:** psoriasis area and severity index

**PHQ-9:** Patient Health Questionnaire-9

**VASI:** vitiligo area severity index

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Research Letter

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

Ramiro Rodriguez<sup>1</sup>, MD; Lachlan Anderson<sup>2</sup>, BSc; Emily Woolhiser<sup>3</sup>, BSc; Timothy Balmorez<sup>4</sup>, BSc; Bailey Cook<sup>5</sup>, BSc, MBA; Megan Hauptman<sup>6</sup>, BSc; Jessica Kirk<sup>5</sup>, BSc; Noah Keime<sup>1</sup>, BSc; Robert P Dellavalle<sup>1,7,8</sup>, MD, PhD, MSPH

<sup>1</sup>Department of Dermatology, University of Colorado School of Medicine, Aurora, CO, United States

<sup>2</sup>Boston College, Boston, MA, United States

<sup>3</sup>College of Osteopathic Medicine, Kansas City University, Kansas, KS, United States

<sup>4</sup>College of Osteopathic Medicine, Touro University California, Vallejo, CA, United States

<sup>5</sup>Rocky Vista University College of Osteopathic Medicine, Parker, CO, United States

<sup>6</sup>College of Medicine, University of Arizona, Tucson, AZ, United States

<sup>7</sup>Dermatology Service, US Department of Veterans Affairs Rocky Mountain Regional Medical Center, Aurora, CO, United States

<sup>8</sup>Department of Epidemiology, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

**Corresponding Author:**

Robert P Dellavalle, MD, PhD, MSPH

Dermatology Service

US Department of Veterans Affairs Rocky Mountain Regional Medical Center

Rm E1-342

1700 N Wheeling St

Aurora, CO, 80045

United States

Phone: 1 303 399 8020

Email: [robert.dellavalle@cuanschutz.edu](mailto:robert.dellavalle@cuanschutz.edu)

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**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.

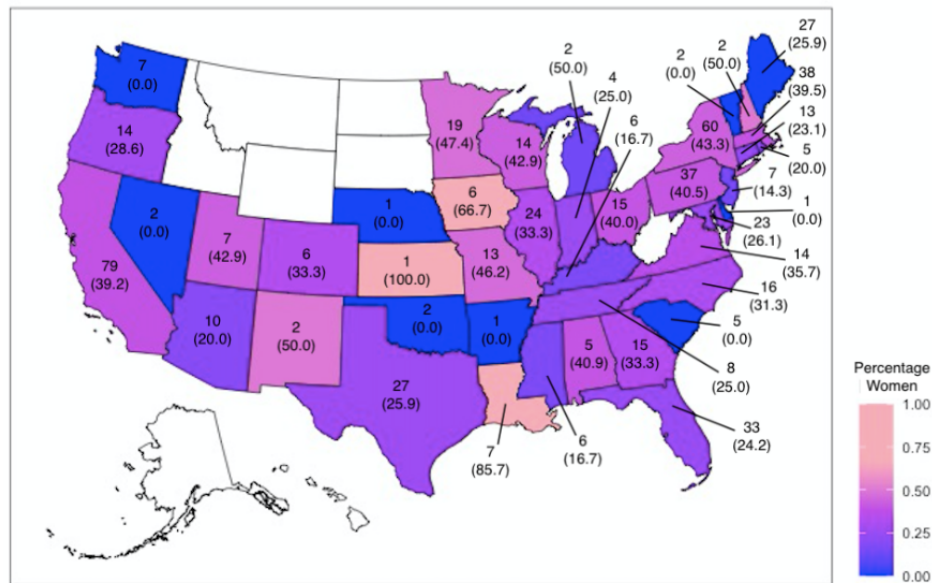
## Results

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

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Original Paper

# Participant Motivators and Expectations in the MEL-SELF Randomized Clinical Trial of Patient-Led Surveillance for Recurrent Melanoma: Content Analysis of Survey Responses

Deonna Ackermann<sup>1</sup>, MPH, MBBS; Jolyn Hersch<sup>1</sup>, PhD; Dana Jordan<sup>1</sup>, MPH; Emily Clinton-Gray<sup>1</sup>, MPH; Karen Bracken<sup>2</sup>, PhD; Monika Janda<sup>3</sup>, PhD; Robin Turner<sup>4</sup>, PhD; Katy Bell<sup>1</sup>, PhD

<sup>1</sup>School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

<sup>2</sup>Kolling Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

<sup>3</sup>Centre for Health Services Research, The University of Queensland, Brisbane, Australia

<sup>4</sup>Biostatistics Centre, University of Otago, Dunedin, New Zealand

**Corresponding Author:**

Deonna Ackermann, MPH, MBBS

School of Public Health

Faculty of Medicine and Health

The University of Sydney

Camperdown NSW

Sydney, 2050

Australia

Phone: 61 418219923

Email: [deonna.ackermann@sydney.edu.au](mailto:deonna.ackermann@sydney.edu.au)

## Abstract

**Background:** Limited data exist on the motivations and expectations of participants when enrolling in dermatology clinical trials, including melanoma early detection trials. Understanding participant motivators for research engagement has been identified as a prioritized area for trial methodology research.

**Objective:** The study aimed to determine motivators of participation and expectations from trial involvement among patients enrolled in the MEL-SELF randomized clinical trial of patient-led surveillance for new or recurrent melanoma.

**Methods:** The MEL-SELF trial is recruiting patients previously treated for localized melanoma, who own a smartphone, have a partner to assist with skin self-examination (SSE), and attend routinely scheduled follow-up at specialist and primary care skin clinics in Australia. We evaluated responses from the first 100 randomized participants to 2 open-ended questions about their motivations and expectations for participating in the trial, administered through the internet-based baseline questionnaire. A total of 3 coders independently coded the free-text responses and resolved discrepancies through consensus. Qualitative content analysis by an iterative process was used to group responses into themes. Responses from potential participants who were not randomized and the 404 participants randomized subsequently into the trial, were also checked for new themes. Coding and analysis were conducted in Microsoft Excel.

**Results:** Out of the 100 survey participants, 98 (98%) answered at least 1 of the 2 questions. Overall, responses across the motivation and expectation items indicated 3 broad themes: community benefit, perceived personal benefit, and trusting relationship with their health care provider. The most common motivators for participation were related to community benefit. These included progressing medical research, benefitting future melanoma patients who may have similar experiences, and broader altruistic sentiments such as “helping others” or “giving back.” The most common expectations from the trial related to personal benefit. These included perceived improved outcomes such as earlier diagnosis and treatment, access to additional care, and increased self-empowerment to take actions themselves that benefit their health. Patients expressed a desire to gain health-related knowledge and skills and were interested in the potential advantages of teledermatology. There were no new themes in responses from those who were not randomized or were randomized subsequent to the first 100.

**Conclusions:** We report a tailorable, patient-focused approach to identify drivers of research engagement in clinical research. Clinical trials offer an opportunity to collate a substantial evidence base on determinants of research participation and to identify context-specific factors. Results from the MEL-SELF trial emphasized notable altruism, self-empowerment, and perceived



advantages of teledermatology as specific motivators. These findings informed consent processes, recruitment, retention, response to trial tasks, and intervention adherence for the MEL-SELF host trial.

**Trial Registration:** Australian New Zealand Clinical Trials Registry (ANZCTR): ACTRN12621000176864. <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379527&>

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## KEYWORDS

teledermatology; melanoma; randomized controlled trial; trial recruitment and retention; studies within a trial; SWATs; dermatology; cancer; early detection; dermatology clinical trials; clinical trials; mobile phone

## Introduction

Participants' willingness to engage with research is an important determinant of study feasibility. Research engagement in randomized clinical trials (RCTs) involves successful recruitment, consenting, retention, response to trial tasks, and adherence to intervention and control conditions. Challenges are often reported across these participation components, resulting in research waste (suboptimal recruitment, response to trial tasks, and adherence can result in underpowered and inconclusive studies), increased costs, and delayed availability of potentially effective interventions for patients [1]. However, the evidence base for effective strategies to improve research engagement, including in dermatology research, is sparse [2-4].

Identification and understanding of the motivators and expectations of participants in clinical trials may provide trialists with the knowledge required to develop strategies that facilitate research engagement [5]. The PRioRiTty (Prioritizing recruitment and retention in randomized trials) study, a James Lind Alliance Priority Setting Partnership, concluded that one of the most pressing recruitment questions is to determine what motivates trial participation [6] and that the top retention priority is to understand what motivates participants to complete a clinical trial [7].

A recent overview of systematic reviews highlighted perceived personal benefits as the most commonly reported motivator for research participation, with other key motivators including altruism, trust in the clinician, low burden, and financial incentives [8]. The included reviews were from specific clinical specialties, including advanced cancer management, HIV, mental health, chronic obstructive pulmonary disease, and emergency medicine. Some focused on specific populations such as children, pregnant women, older adults, and ethnic minority groups. However, a gap exists in the determinants of research participation in dermatology trials and melanoma surveillance in particular.

The MEL-SELF RCT aims to assess whether patient-led surveillance (comprising smartphone-supported skin self-examination, teledermatology, fast-tracked unscheduled clinic visits in addition to routinely scheduled clinic visits) compared with clinician-led surveillance (usual care) leads to increased diagnoses of a new primary or recurrent melanoma ahead of routinely scheduled clinic visits [9]. The intervention was tested in a pilot RCT, which identified difficulties with participant engagement across a variety of trial processes [10].

To inform the design of strategies to improve participant engagement in the larger ongoing MEL-SELF trial, we asked participants to provide free text responses about why they wanted to participate in the trial and what they hoped to get out of it. The questions were administered as part of the internet-based baseline questionnaire before randomization into the trial. This Study Within A Trial (SWAT, an embedded research study within a clinical trial aimed at evaluating and optimizing trial design, processes, or interventions) [2] aimed to identify relevant information to optimize ongoing recruitment, retention, trial task response, and adherence processes both within the current MEL-SELF trial and future dermatology clinical trials. Furthermore, we aimed to determine whether research engagement motivators are consistent with previously identified themes in other disease areas [8] and whether there are important context-specific factors.

## Methods

### Participants and Setting

The MEL-SELF RCT recruits patients attending routine melanoma follow-up from specialist-led and primary care skin cancer clinics in Australia [10]. Eligible participants have been previously treated for localized melanoma (American Joint Committee on Cancer stage 0, I or II), own a smartphone, have a partner to assist with skin self-examination (SSE), are able to understand English, and have no documented history of cognitive impairment. Patients are provided with information about the trial by their doctor, and permission is given to researchers to contact them. Researchers email additional information, including a patient information sheet and a link to sign an electronic informed consent form. Potential participants enter an active run-in phase, which requires them to complete the internet-based baseline questionnaire, view instructional videos, complete electronic reporting of their SSE findings, and upload macroscopic digital photos of 1 melanocytic skin lesion to the study's web-based platform. Participants who complete these tasks are randomized into the trial. Approval to conduct the study was granted by the Sydney Local Health District (RPAH zone) Ethics Review Committee.

This embedded SWAT includes the first 100 participants randomized into the MEL-SELF trial who were recruited from 3 skin cancer clinics in Sydney and Newcastle, New South Wales, Australia (2 specialist-led clinics and 1 primary care skin clinic). The protocol is available on the SWAT repository [11].

## Data Collection and Analysis

A total of 2 open-ended questions about motivations and expectations were included in the internet-based baseline questionnaire delivered through the REDCap (Research Electronic Data Capture; Vanderbilt University) survey software: “Please tell us why you decided to participate in this study?” and “Please tell us what you are hoping to get out of this study?” To avoid prompting participants to respond in a certain way, we only included these 2 open-ended questions without an accompanying participation motivation scale (as has been used in other clinical areas) [12,13]. Content analysis, which combines qualitative and quantitative methods to analyze text data, was used to identify common themes in the responses [14]. A stepwise process that combined conventional and directed content analysis was used to identify both common and context-specific elements [15].

1. Initial conventional approach: after familiarization through reading and rereading the responses from both questions, an initial sample (n=50, first 50 patients completing the baseline questionnaire during the active run-in phase) was coded by DA to identify preliminary themes and subthemes.
2. Directed approach: in parallel to this, potential coding categories were derived from a review of existing literature [8].
3. Comparison and synthesis: the themes that emerged from the data itself and those derived from existing literature were examined by members of the research team (DA, Bell K) to create an initial coding framework that incorporated both common and context-specific elements.
4. Integration and application: this framework was applied to SWAT participant responses (first 100 randomized participants), and a final framework was iteratively developed and used to examine the data for themes and subthemes. Themes were concluded through discussions

among 3 authors (DA, EC, and DJ, with conflicts resolved by a fourth author, Bell K).

DA coded all data, while DJ and EC checked half each. No new subthemes emerged so the sample size of 100 was retained. Coding and analysis were conducted in Excel, discrepancies were resolved through discussion, and theme frequencies were calculated. In addition, responses from participants (n=49) who did not successfully complete the active run-in phase and were not enrolled in the trial were reviewed by DA using the developed framework. These 49 participants completed the baseline questionnaire during the same period as the 100 participants who did complete the active run-in and were enrolled. This was done to identify potential differences between those who did and did not complete the active run-in, as completing this required significant motivation and effort from the patients. Finally, we also reviewed responses from the 404 trial participants who were randomized subsequent to the first 100 to check for any new themes in the full trial sample.

## Ethical Considerations

This study was approved by the Sydney Local Health District (RPAH zone) Ethics Review Committee (2019/ETH13612).

## Results

The first 100 participants enrolled in the MEL-SELF RCT completed the baseline survey from November 4, 2021, to March 28, 2022, with 98 providing a response on participation and 97 on expectations. Patient characteristics are presented in [Table 1](#). Respondents had a mean age of 56 years (SD 13.01, range 28-83 years), were more likely to be female (59, 59%), reside in a major city (88, 88%), and have post high school or higher education (87, 87%). Half of the participants resided in areas that were in the most advantaged socioeconomic status quintile.

**Table 1.** Baseline characteristics.

Characteristic	Total (N=100)
<b>Age (years)</b>	
Mean (SD)	56.4 (13.01)
Minimum, maximum	28, 83
<b>Sex, n (%)</b>	
Male	41 (41)
Female	59 (59)
<b>Study site, n (%)</b>	
Primary care skin clinic	13 (13)
Specialist-led clinic	87 (87)
<b>Highest melanoma substage, n (%)</b>	
0	34 (34)
IA	52 (52)
IB	12 (12)
II combined	2 (2)
<b>Country of birth, n (%)</b>	
Australia	78 (78)
Other: English speaking	15 (15)
Other: non-English speaking	7 (7)
<b>Indigenous status, n (%)</b>	
Neither Aboriginal nor Torres Strait Islander	96 (96)
Aboriginal or Torres Strait Islander	1 (1)
Unknown	3 (3)
<b>Marital status, n (%)</b>	
Never married	4 (4)
Married	74 (74)
De facto or in a committed relationship	15 (15)
Separated or divorced	6 (6)
Widowed	1 (1)
<b>Any children, n (%)</b>	
Yes	82 (82)
No	18 (18)
<b>Level of education, n (%)</b>	
High school or leaving certificate	13 (13)
TAFE <sup>a</sup> advanced diploma or certificate	33 (33)
Bachelor degree	27 (27)
Postgraduate degree or higher	27 (27)
<b>Remoteness (based on area of residence), n (%)</b>	
Major city	88 (88)
Inner regional	11 (11)
Outer regional	1 (1)
<b>Socioeconomic status (based on area of residence), n (%)</b>	
1 (most disadvantaged)	4 (4)

Characteristic	Total (N=100)
2	9 (9)
3	18 (18)
4	19 (19)
5 (least disadvantaged)	50 (50)

<sup>a</sup>TAFE is a government-run system in Australia that provides education after high school in vocational areas like beauty, childcare, accounting, business, and computing.

Participant responses to both questions mapped to 3 dominant themes as outlined in [Table 2](#) and [Figure 1](#): community benefit, personal benefit, and trust in their health care provider. Subthemes were more likely to be context-specific. [Table 3](#) displays the frequencies of these themes and subthemes, organized by question. Participants most commonly identified community benefit as the reason for their participation, while perceived personal benefit was most commonly expressed for what they hoped to get out of the trial. A notable majority (67/100, 67%) identified community benefit as their primary motivation, followed by personal benefit (38/100, 38%) and trust in their health care provider (21/100, 21%). Regarding expectations, a significant number of participants (78/100, 78%) expressed interest in personal health benefits or insights from the trial, while community benefit was expected by 33%

(33/100) participants. An additional 49 participants completed the baseline questionnaire between November 2021 and March 2022 but did not complete the active run-in phase. Out of these 100 participants, 47 (95%) provided responses to the participation and expectation questions with similar themes identified. For the participation question, 26 (53%) suggested community benefit, 17 (35%) personal benefit, and 11 (22%) trust in their health care provider. After recruitment closed (June 3, 2024), the responses from all 504 trial participants were reviewed, and no new themes emerged.

We highlight some illustrative quotes from the SWAT participants (first 100 randomized) in the sections below and present additional comments in [Table S1](#) in [Multimedia Appendix 1](#).

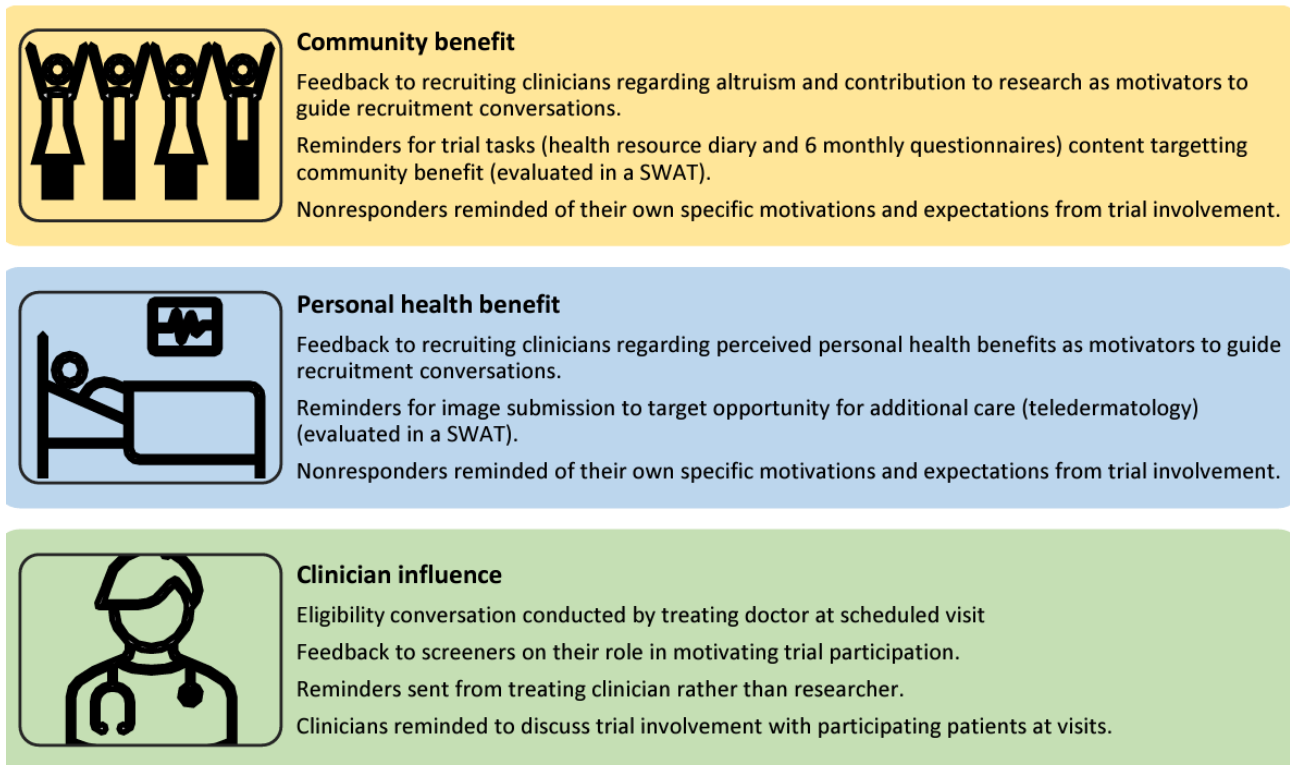
**Table 2.** Identified themes and subthemes for research engagement in the MEL-SELF randomized clinical trial (RCT).

Category and themes	Description
<b>Community benefit</b>	
Contribution to medical research	<ul style="list-style-type: none"> <li>• Participants broadly recognize the importance of medical research</li> <li>• Participants link research to improved health outcomes</li> <li>• “Sense of duty”</li> <li>• May express personal satisfaction arising from their contribution</li> <li>• Participants specify a wish to contribute to advances in melanoma-related research</li> <li>• Feel that their personal experience may particularly benefit others</li> </ul>
Specific merits of the intervention	<ul style="list-style-type: none"> <li>• Telehealth and digital technology research</li> <li>• Benefits people who live in remote areas</li> <li>• General</li> </ul>
Altruism	<ul style="list-style-type: none"> <li>• The trial results may benefit future melanoma patients (ie, people with a similar experience to themselves)</li> <li>• May specify future generations of their own family</li> <li>• Broader altruistic comments</li> <li>• Sometimes expressed together with “nothing for me” in expectation question</li> </ul>
<b>Personal health benefits</b>	
Melanoma history	<ul style="list-style-type: none"> <li>• Beneficial due to high-risk status</li> </ul>
Empowerment	<ul style="list-style-type: none"> <li>• Increased melanoma knowledge and opportunity for learning</li> <li>• SSE<sup>a</sup></li> <li>• Improved skills</li> <li>• Increased awareness of skin</li> <li>• Increased self-confidence in SSE skills</li> <li>• Increased self-management role: <ul style="list-style-type: none"> <li>• More active role in own health care</li> <li>• Motivation</li> <li>• Discipline</li> <li>• Routine</li> </ul> </li> </ul>
Additional care: telehealth	<ul style="list-style-type: none"> <li>• Access to a new intervention before it is widely available</li> <li>• Additional access to medical services (teledermatologist review)</li> <li>• Specific advantages of intervention for themselves</li> <li>• Rural patients</li> </ul>
Improved outcomes	<ul style="list-style-type: none"> <li>• Earlier diagnosis and treatment</li> <li>• Survival and quality of life</li> </ul>
Reassurance	<ul style="list-style-type: none"> <li>• Reassurance due to perceived personal health benefits</li> </ul>
<b>Doctor or health facility</b>	
Relationship	<ul style="list-style-type: none"> <li>• Clinician influence</li> <li>• Trust in the clinician</li> <li>• Reciprocity</li> </ul>

<sup>a</sup>SSE: skin self-examination



**Figure 1.** Strategies to improve trial processes implemented in the MEL-SELF trial by identified motivators of research engagement. SWAT: Study Within A Trial.



**Table 3.** Frequency of identified themes and subthemes for research engagement identified in 100 MEL-SELF randomized clinical trial participants<sup>a</sup>.

Themes	Motivators <sup>b</sup>	Expectations <sup>c</sup>
Community benefit	67	33
Contribution to medical research	30	16
Specific merits of the intervention	6	0
Altruism	36	17
Personal benefit	38	78
Perceived melanoma risk	5	0
Empowerment	18	54
Additional care	9	7
Improved outcomes	11	14
Reassurance	0	7
Trust in health care provider or facility	21	0

<sup>a</sup>Participants may have expressed more than 1 motivator or expectation.

<sup>b</sup>A total of 2 participants did not respond to the motivator question, "Please tell us why you decided to participate in this study?"

<sup>c</sup>A total of 3 participants did not respond to the expectations question, "Please tell us what you are hoping to get out of this study?"

### Theme 1: Community Benefit

We identified community benefit as a reason to participate in the MEL-SELF RCT in 67 responses to the first question and as a potential beneficial outcome of trial involvement in 33 responses to the second question. Subthemes included a desire to contribute to the advancement of medical research, a belief in the specific merits of patient-led surveillance, and altruism.

### Contribution to Scientific Research

Some participants broadly recognized the importance of research and expressed a desire to advance medical knowledge. As one participant noted:

*Scientific research and evidence is important for the whole community. It is important to try new techniques to improve treatments. [P56, female, age 64 years]*

Support for medical research was frequently voiced, with several participants commenting that they “believe in” research. Participants often expressed an understanding that the research process is necessary for advancing medical knowledge, and they expected clinical trial results to be translated into improved medical practice.

*I believe it is important to be a part of research as this will lead to better health outcomes for future patients.* [P32, female, age 62 years]

For some, participation was linked to a “sense of duty”:

*I feel that if I qualify for a medical study, it is my duty to participate.* [P78, female, age 73] *and as an ex-health services researcher I am interested and feel some responsibility to support research* [P85, male, age 73 years]

Others characterized a sense of fulfillment from trial involvement, describing it as “pleasing,” “satisfying,” and “something to be grateful for.” For many participants, the desire to contribute was directly expressed as a commitment to advancing melanoma-related research:

*“Anything to help researchers [find] out more about melanoma and treatments.”* [P95, male, age 57 years]

Some participants felt uniquely qualified to add value to the research project due to their personal experience.

*With my unusual number of melanomas, my experience may provide a clue or two that may lead to greater understanding of skin cancers.* [P7, male, age 66 years]

Others linked their desire to further melanoma research to their personal experience, as described by a participant who wanted “to actively support research into a health issue which has directly impacted me and could again in the future” [P18, female, age 49 years].

### **Specific Merits of the Intervention**

A total of 6 participants identified that the MEL-SELF intervention had specific merits that could benefit the community, including furthering telehealth and digital technology research.

*If I can be a part of something that is going [to] drive technology and innovation in this space forward, then I want to be a part of it.* [P38, male, age 38 years]

Regarding providing options for people living in remote areas,

*Seems like a great way to improve the identification of melanoma, especially for those who live remotely.* [P65, male, age 50 years]

### **Altruism**

The ability to help others at a community level is featured in many participants’ responses. Broad altruistic reasons for participation, such as “*in the hope I will help others*” [P75, female, age 57 years], were frequently shared and were sometimes expressed together with “nothing for me” in the expectation question. “*Nothing personally other than looking to assist.*” [P40, male, age 67 years]. Participants commonly

expressed a desire to benefit future melanoma patients (ie, people with a similar experience as themselves). As 1 participant noted,

*If it helps others who get/have melanoma and their timely diagnosis and treatment is afforded, then I have done something.* [P6, male, age 63 years]

The desire to help was sometimes linked to future generations of their own family.

*Taking part in the study and knowing the results may help others in the future is something I am happy to do. I have a red-headed granddaughter, and who knows, she may benefit in the future.* [P63, female, age 79 years]

### **Theme 2: Personal Health Benefit**

Personal benefit was identified as a reason to participate in the MEL-SELF RCT in 38 participant responses to the first question and as a potentially beneficial outcome of trial involvement in 78 responses to the second question. Subthemes included a perception of benefit related to their high-risk status, empowerment, access to additional care in the form of a novel telehealth intervention, improved health outcomes, and reassurance.

#### **Perceived Risk of Melanoma**

Some participants acknowledged that their high-risk status due to their personal or family history of melanoma motivated them to contribute to the research. As a participant described:

*I believe I have a real risk of developing melanoma - both my father and older brother had multiple melanomas removed; we spent a lot of time in the sun, unprotected, as children, and I have a lot of moles.* [P86, female, age 57 years]

#### **Empowerment**

A significant number of participants expressed a desire to enhance their knowledge, understanding, and autonomy regarding their personal health. They frequently perceived participation in the trial as an opportunity to learn about melanoma, which they considered both a motivator (eg, P1, female, age 47 years: “*I would like to be more educated*”) and an expectation (eg, P41, male, 34 years: “*better knowledge of melanoma*”). Participants anticipated improving and gaining confidence in their SSE skills. They believed that by enhancing these skills, they would become more aware of their skin and potential changes, ultimately leading to greater confidence in their ability to perform SSE effectively. As one participant explained:

*I hope to learn to recognise the signs of a changing mole or spots...and be more confident about it.* [P29, female, age 54 years]

Many participants described a desire to take a more active role in managing their own health care. For example, a participant commented,

*I’m all for further advancement in the ability to do things better for myself - If I can be more in tune with*

*my body and what's happening to it, good or bad, it can only be a good thing.* [P10, female, age 48 years]

Meanwhile, P20, female, age 50, wanted “*to do the most I can to manage my own health.*” Some patients hoped to become more motivated to check their own skin and to develop a more disciplined routine, such as a participant who said, “[*This is a good way for me to make regular home checking a part [of] my routine,*” and P99, male, age 40 years, shared, “[*Perhaps it may lead to a more diligent skin check regime by moi?*” [P17 female, age 57 years].

### **Additional Care: Access to Telehealth**

Some participants recognized the potential benefits of gaining access to a novel telehealth intervention that would have been otherwise unavailable to them. They appreciated the opportunity for more frequent skin monitoring and the additional access to medical services, such as teledermatologist reviews. A participant (P14, male, age 49 years) shared, “I am hoping it will provide a way of getting suspicious spots checked between my regular visits,” while P37 (male, age 59 years) viewed the intervention as “another tool in the prevention of serious melanoma issues going unchecked.” The potential for closer monitoring was identified by P28, male, aged 65 years, who was drawn to the trial due to the opportunity to have “several sets of eyes on my changing spots & skin issues.” Rural participants identified specific advantages of the intervention for their personal circumstances. For instance, a participant expressed:

*Due to the distance I live from the [Hospital] in Sydney, it makes sense to perform a self-diagnosis and be able to update it to the app for a professional doctor to examine and determine if there is a reason for me to travel to the [Hospital] for further investigations.* [P42, male, age 46 years]

### **Better Health Outcomes**

Many participants viewed trial involvement as an opportunity for earlier diagnosis and prompt treatment of recurrent melanoma. A participant (P6, female, age 63 years) explained that the intervention “may assist in identifying any further lesions needing attention in a timely manner.” This sentiment was shared by others who valued the possibility of early detection:

*To increase the possibility of finding melanoma early” and “To have more chance of early detection and treatment if I get more melanoma.”* [P45, female, age 62 years]

Many patients, such as P27 (female, age 35 years), were determined to “do whatever I can to prevent further melanomas or catch them early.” Participants perceived that the intervention may facilitate “a more timely response to new skin cancers,” as noted by P14 (male, age 49 years), and assist patients, like P88 (male, age 74 years), to “get early treatment if I found anything suspicious.” Furthermore, the perceived benefits of the intervention extended beyond early detection and treatment to include improved survival rates and overall quality of life for patients. As a participant expressed, “I hope to catch melanomas before they kill me” [P13, female, age 61 years].

### **Reassurance**

For some participants, trial participation offered a sense of reassurance, which was closely related to themes such as receiving additional care and achieving improved health outcomes. They believed that engaging in the trial would give them “peace of mind” as they had taken additional measures to minimize the risk of recurrence. As a participant (P18, female, age 49 years) stated, “[I will feel] more confident that I have not had a recurrence.” This was echoed by P3 (male, age 84 years), who sought “peace of mind regarding ...any future melanomas.” In addition, the trial offered participants such as P65 (male, age 50 years) an opportunity to quickly address potential concerns, such as “Ease of mind that if I do identify something, I can send it through for assessment.” Overall, trial participation was seen as a means to instill confidence and reassurance in the pursuit of better health outcomes.

### **Theme 3: Trust in Health Practitioner or Facility**

Physician influence was identified as a major determinant for trial participation, as illustrated by 21 responses to the first question. Notably, this theme was not present in the expectations voiced in response to the second question. Often, patients enrolled in the trial due to their doctor’s request or recommendation, emphasizing the significance of trust in their treating clinician. For instance, P3 (male, age 84 years) mentioned, “I hold my doctor in high regard, and he recommended it.”

In addition, several respondents with positive experiences conveyed gratitude and a desire to “give back” to the health care facility where they had received treatment.

A participant described trial participation as:

*One way for me to give back to the team that have cared for me at [Facility] as they have always demonstrated care, compassion, and empathy.* [P32, female, age 62 years]

This underscores the impact of personal experiences and trust in medical professionals on patients’ willingness to participate in clinical trials.

## **Discussion**

### **Principal Findings**

This SWAT provides valuable insights into patients’ motivations for and expectations from participating in the MEL-SELF RCT of patient-led melanoma surveillance using patient-performed mobile teledermoscopy. Common overarching themes related to benefitting the community by contributing to medical research or helping others, personal benefit through improved health outcomes, and trust in the clinician’s request. These themes were consistently voiced by participants with diverse sociodemographic and clinical characteristics, including those who completed the baseline questionnaire but did not complete the active run-in. While in keeping with identified motivators for trial participation in other conditions [8], this sample of melanoma patients reported distinct, notable influencing factors. Community benefit was the most frequently cited reason for participation (n=67), highlighting a significant yet

underappreciated desire among this population to contribute positively to their community. Subthemes specific to the MEL-SELF trial context included a strong emphasis on self-empowerment and a specific interest in the merits of patient-led surveillance, particularly related to telehealth and increasing health care access for people living in rural and remote areas. Understanding motivators in a specific trial context is useful, as factors influencing participation may vary based on patient population, setting, intervention, and disease. The proportions of participants expressing the common overarching themes may also differ according to context. For example, patients with advanced melanoma may be more willing to join clinical trials seeking improved treatment options, while early-stage melanoma patients, as in our trial, were primarily motivated by the desire to help others with melanoma.

Most participants acknowledged the importance of research and expressed motivation to help others, often referencing a sense of social responsibility. In addition, participants demonstrated a clear understanding that medical practice relies on clinical trial outcomes and anticipated direct translation of results into clinical practice. Consequently, many opted to participate with the intention of contributing to the development of new management options for melanoma in the hope this will benefit future patients. Participants identified personal health benefits from taking part in the trial, including increased melanoma knowledge and SSE skills, a more active role in their health care, increased self-efficacy, potentially earlier diagnosis and treatment of subsequent melanomas, and early access to an innovative intervention. It is important to note that most of these perceived personal benefits would only be available to those subsequently randomized into the intervention group. To ensure awareness of equal allocation chances, a final step where participants explicitly acknowledge this was implemented before randomization.

The strengths of our study include conducting the survey prospectively at the point of enrolment, which minimized recall bias and allowed for an accurate assessment of participants' initial motivations and expectations. In addition, enrolling consecutive patients prevented selection bias, ensuring a representative sample of trial participants. We used rigorous methods in accordance with best practices in qualitative research. There are also several limitations. While our sample is representative of the MEL-SELF population and helps answer our research question within this context, it is primarily composed of highly educated individuals, a majority of whom are women from metropolitan areas with high socioeconomic status. Consequently, our findings may not be generalizable to other populations. In addition, our findings may not apply to other settings, such as higher-risk pharmaceutical trials, but our adaptable methodology could be used in these settings. Furthermore, the extent to which stated motivators and expectations at trial commencement translate into long-term adherence to trial processes remains uncertain. A lengthy trial with a significant participant burden for insufficient gains may lead to diminishing motivation and retention. Finally, our data collection was limited to participants, precluding insights into reasons for nonparticipation. Although our analysis of people who completed the baseline questionnaire but not the active

run-in indicated similar findings to the included sample, these may differ for people who did not participate at all. Future research could include interviews with patients who did not participate, particularly those from regional and remote areas and those with indicators of lower socioeconomic status, to identify what would motivate them to engage in research.

### Key Practice Implications

Understanding the factors influencing patient engagement in clinical trials may enable trialists to develop more effective, patient-centered strategies to improve recruitment, response to trial tasks, retention, and adherence to trial interventions. Our SWAT approach, easily implementable in other clinical trials, provides evidence to guide the development of targeted strategies for enhancing trial tasks and processes. The framework of commonly identified motivators could serve as a starting point for other trialists, who may either adopt the existing framework or conduct a SWAT themselves to uncover context-specific themes. Qualitative research is increasingly recognized as a valuable complement to other research methods in dermatology [16]. Although it may seem time-consuming and daunting to some trialists, understanding the underlying factors driving patient participation could ultimately boost trial efficiency and effectiveness.

The findings of this study, together with those of 2 scoping reviews [17,18], have informed refined communication with participants and improved study materials in the MEL-SELF trial, which may, in turn, improve recruitment and consent processes, response rates, retention, and adherence (Figure 1, Table S2 in Multimedia Appendix 1). We implemented strategies targeting clinician influence, such as providing feedback to clinicians on their role in motivating trial participation, sending participant reminders to complete trial tasks from the treating clinician rather than the researcher, and reminding clinicians to discuss trial involvement with participating patients at follow-up visits. In addition, feeding back to recruiting clinicians the diverse reasons reported for trial participation presents an opportunity to enhance recruitment and the consent process by explaining the perceived benefits of participation in alignment with value statements summarized by health agencies [19,20]. Mapping determinants to behavior change theory, such as the Theoretical Domains Framework (TDF) and Capability, Opportunity, Motivation-Behavior (COM-B) model may improve understanding of decision-making and offer guidance for strategies to improve trial processes [21]. We have tailored ongoing MEL-SELF trial communication strategies (participant conversations and reminders) to address patient motivations and will evaluate the effects of these in a future SWAT.

### Conclusion

This SWAT revealed context-specific motivators for trial engagement (a prevalent desire to benefit the community, empowerment, and perceived telehealth benefits), which can be used to tailor communication and study materials in the current MEL-SELF trial and future trials.



Assessing participant motivations through surveys may refine clinical research settings.  
research planning and enhance trial processes in different

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## Data Availability

The data that support the findings of this study are available on request from the corresponding author.

## Conflicts of Interest

None declared.

Multimedia Appendix 1

Supplementary tables.

[DOCX File, 34 KB - [derma\\_v7i1e58136\\_app1.docx](#)]

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## Abbreviations

- COM-B:** Capability, Opportunity, Motivation-Behavior model  
**PRioRiTy:** Prioritising recruitment and retention in randomised trials  
**RCT:** randomized clinical trial  
**REDCap:** Research Electronic Data Capture  
**SSE:** skin self-examination  
**SWAT:** Study Within A Trial  
**TDF:** Theoretical Domains Framework

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**Editorial**

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

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Ramiro Rodriguez<sup>1</sup>, MD; Karima M Osman<sup>1</sup>, BSc; Lachlan Anderson<sup>2</sup>, BSc; Micah Pascual<sup>1</sup>, BSc; Robert P Dellavalle<sup>1,3,4</sup>, MD, MSPH, PhD

<sup>1</sup>Department of Dermatology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

<sup>2</sup>Texas Christian University School of Medicine, Fort Worth, TX, United States

<sup>3</sup>Dermatology Service, US Department of Veterans Affairs Rocky Mountain Regional Medical Center, Aurora, CO, United States

<sup>4</sup>Department of Epidemiology, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

**Corresponding Author:**

Robert P Dellavalle, MD, MSPH, PhD

Dermatology Service

US Department of Veterans Affairs Rocky Mountain Regional Medical Center

1700 N Wheeling St

Aurora, CO, 80045-7211

United States

Phone: 1 303 399 8020

Email: [robert.dellavalle@cuanschutz.edu](mailto:robert.dellavalle@cuanschutz.edu)

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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.

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**KEYWORDS**

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

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**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.

#### Keywords

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

#### Diversity

The practice of including many communities, identities, races, ethnicities, backgrounds, abilities, cultures, and beliefs of people, including underserved communities.

#### Equity

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.

#### Inclusion

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

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### 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

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Research Letter

# Visibility of Board-Certified Dermatologists on TikTok

Chaitra Subramanyam<sup>1</sup>, MSc; Alyssa Becker<sup>2</sup>, BSc; Julianne Rizzo<sup>3</sup>, BA; Najiba Afzal<sup>3</sup>, BSc; Yvonne Nong<sup>4</sup>, MSc; Raja Sivamani<sup>5</sup>, AP, MSc, MD

<sup>1</sup>College of Osteopathic Medicine of the Pacific Northwest, Western University of Health Sciences, Lebanon, OR, United States

<sup>2</sup>John A Burns School of Medicine, University of Hawaii at Manoa, Honolulu, HI, United States

<sup>3</sup>College of Medicine, University of California Davis, Sacramento, CA, United States

<sup>4</sup>College of Human Medicine, Michigan State University, Flint, MI, United States

<sup>5</sup>Pacific Skin Institute, Sacramento, CA, United States

**Corresponding Author:**

Raja Sivamani, AP, MSc, MD

Pacific Skin Institute

1495 River Park Dr

Suite 200

Sacramento, CA, 95815

United States

Phone: 1 (916) 925 7020

Email: [raja.sivamani.md@gmail.com](mailto:raja.sivamani.md@gmail.com)

## 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.

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## 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

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Viewpoint

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

Ayşe Serap Karadag<sup>1\*</sup>, MD; Basak Kandi<sup>2\*</sup>, MD; Berna Sanlı<sup>3\*</sup>, MD; Hande Ulusal<sup>4\*</sup>, MD; Hasan Basusta<sup>5\*</sup>, MHRM; Seray Sener<sup>6\*</sup>, MPharm; Sinem Calıka<sup>6\*</sup>, Pharm

<sup>1</sup>Department of Dermatology, Medical School of Istanbul Arel University, Istanbul, Turkey

<sup>2</sup>Private Clinic, Ankara, Turkey

<sup>3</sup>Department of Dermatology, Medical School of Pamukkale University, Denizli, Turkey

<sup>4</sup>Department of Dermatology, Medical School of Biruni University, Istanbul, Turkey

<sup>5</sup>Başusta Training and Consultancy, Istanbul, Turkey

<sup>6</sup>Pfizer Biopharmaceuticals, Istanbul, Turkey

\*all authors contributed equally

**Corresponding Author:**

Ayşe Serap Karadag, MD

Department of Dermatology

Medical School of Istanbul Arel University

Türkoba, Erguvan Sk No: 26

Istanbul, 34537

Turkey

Phone: 90 533 655 22 60

Email: [karadagaserap@gmail.com](mailto:karadagaserap@gmail.com)

## 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 diagnosers" [13]. Strikingly, 38% of these online diagnosers 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.

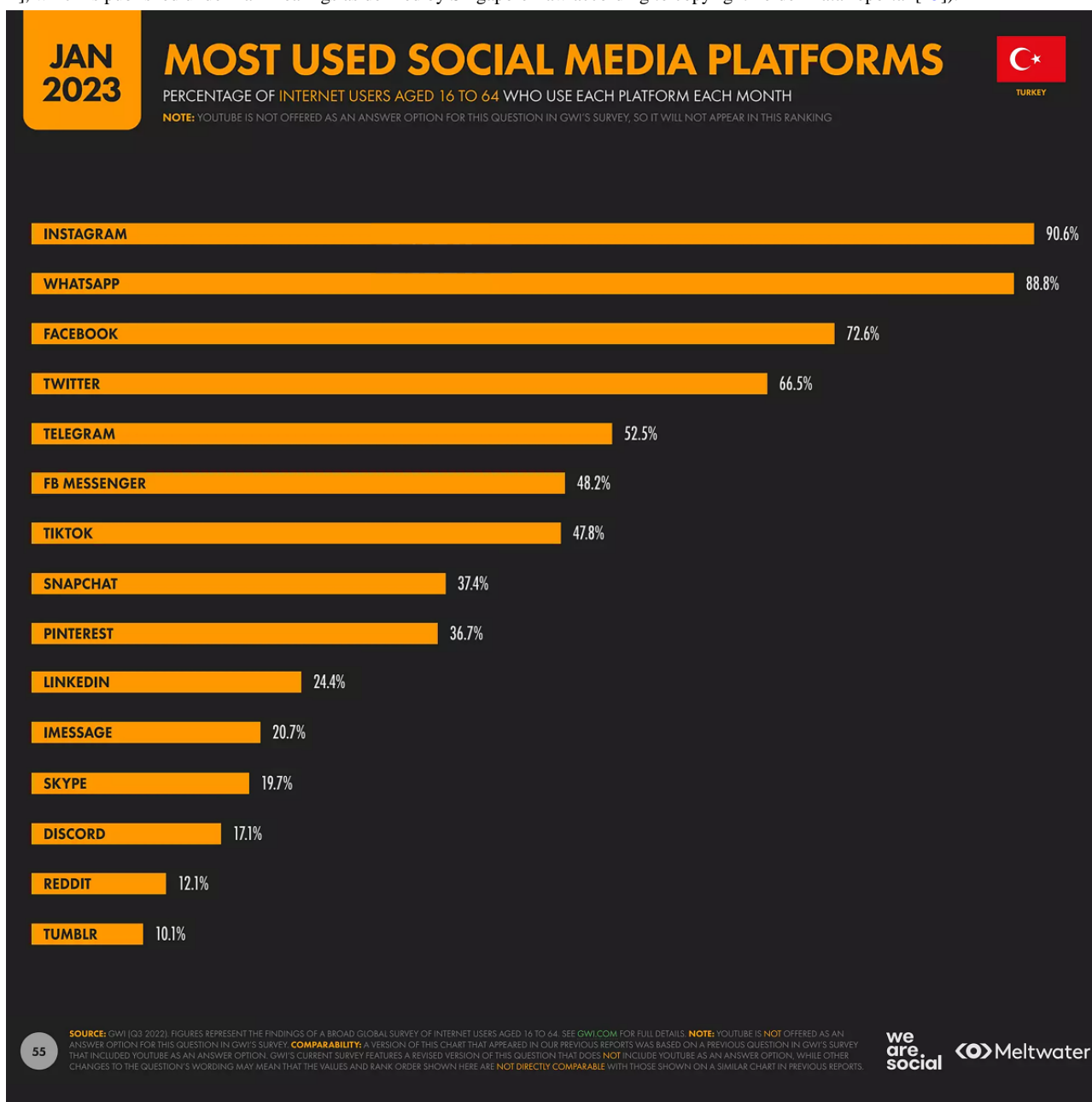
Since dermatology patients on social media are a subset of internet users in Turkey, it is imperative to delineate the essential

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].

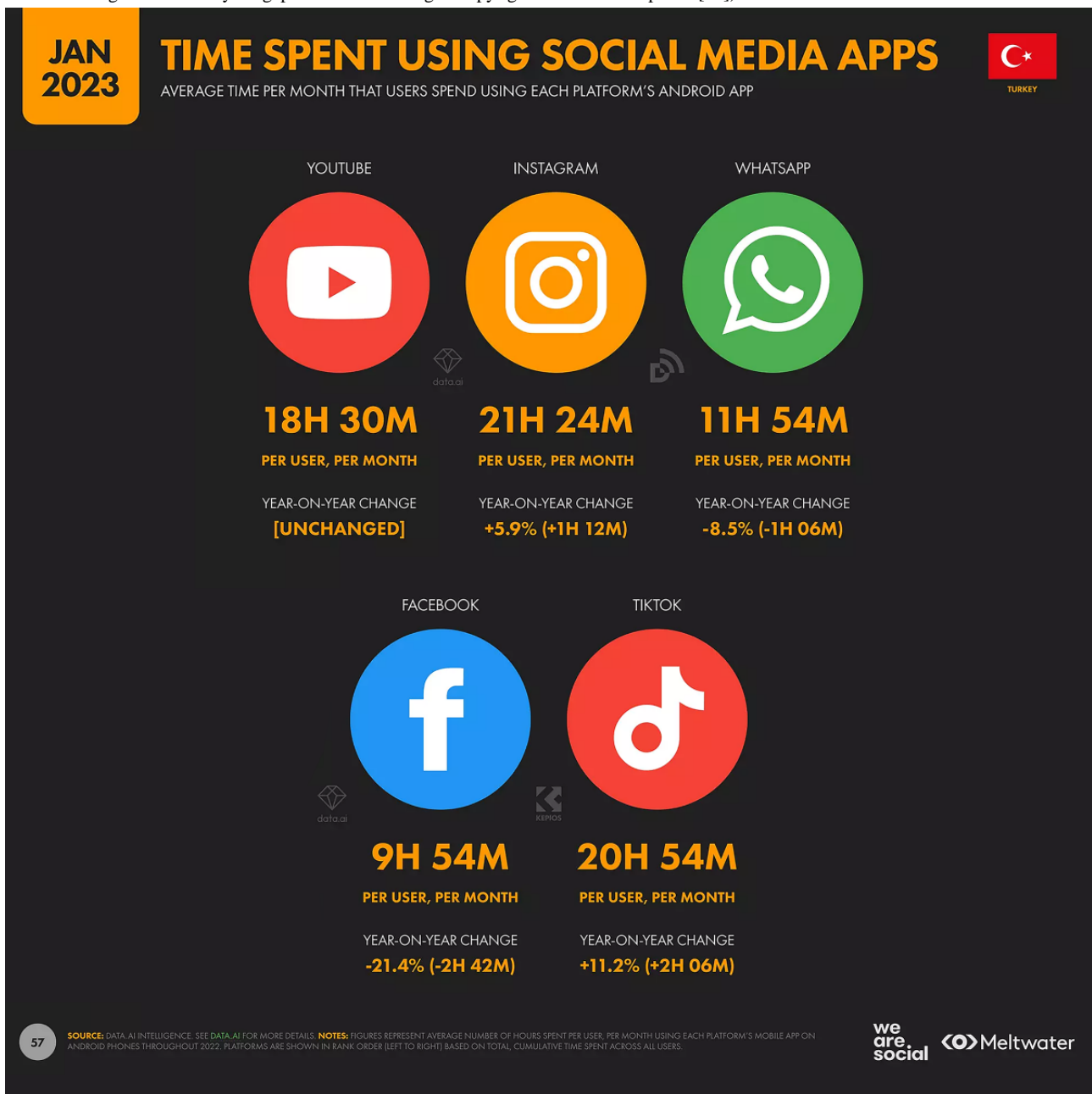
The average time spent on Instagram per capita in Turkey was 20.2 hours per month in 2022, but it increased to 21 hours and 24 minutes in 2023 (Figure 2) [21].

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.

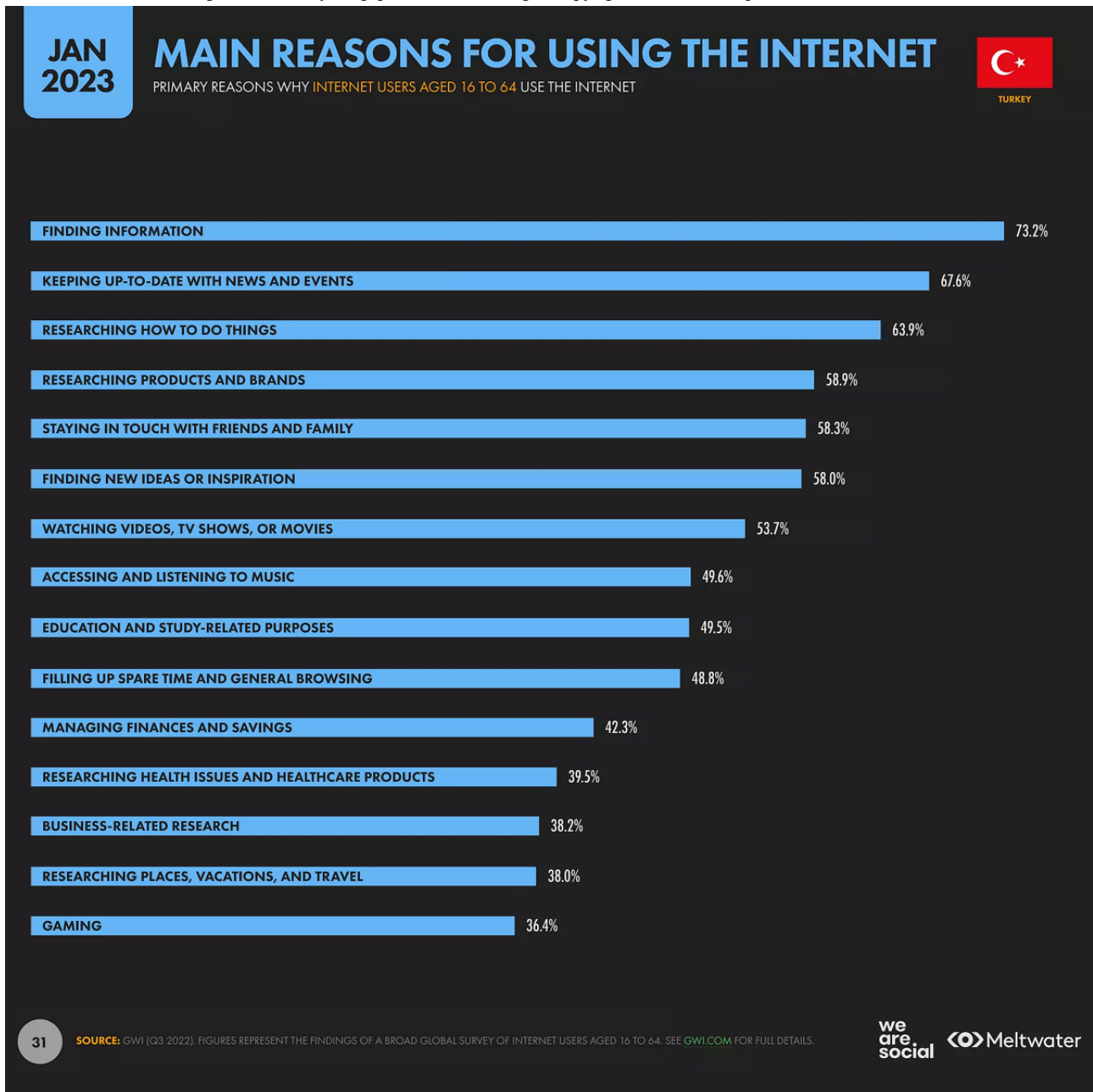
**Figure 1.** The most used social media platforms among the population aged 16-64 years in Turkey (reproduced from We Are Social & Meltwater et al [24], which is published under Fair Dealings as defined by Singapore Law according to copyright holder DataReportal [25]).



**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**

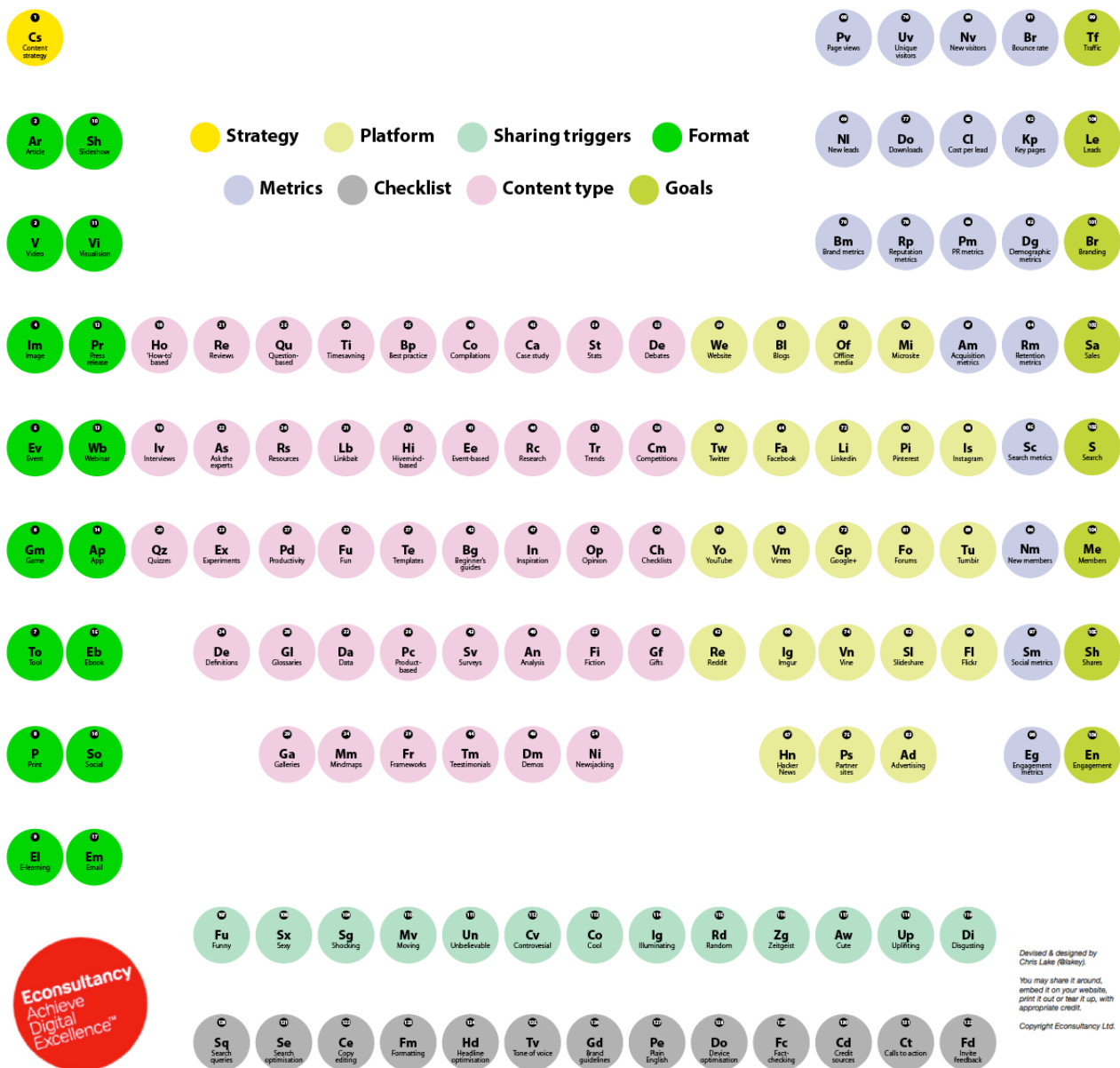
The underlying essential elements of effective communication on social media include a well-structured strategy, content creation, and engagement metrics. When creating content, the device(s) on which the content will be shared should also be considered; for instance, if most website traffic comes from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

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## 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

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Review

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

Priscilla L Haff<sup>1,2</sup>, BS; Alli Jacobson<sup>3</sup>; Madison M Taylor<sup>1,4</sup>, BSA; Hayden P Schandua<sup>1,2</sup>, BS; David P Farris<sup>4</sup>, MSIS; Hung Q Doan<sup>4</sup>, MD, PhD; Kelly C Nelson<sup>4</sup>, MD

<sup>1</sup>McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, United States

<sup>2</sup>Cancer Prevention Research Training Program, Houston, TX, United States

<sup>3</sup>Davidson College, Davidson, NC, United States

<sup>4</sup>University of Texas MD Anderson Cancer Center, Houston, TX, United States

**Corresponding Author:**

Priscilla L Haff, BS

McGovern Medical School

The University of Texas Health Science Center at Houston

6431 Fannin

Houston, TX, 77030

United States

Phone: 1 2108678712

Email: [priscilla.l.haff@uth.tmc.edu](mailto:priscilla.l.haff@uth.tmc.edu)

## 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.

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**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.

#### Inclusion criteria

- Melanoma
- Keratinocyte cancer (Basal cell carcinoma, Squamous cell carcinoma)
- X (Twitter)
- Facebook
- Instagram
- TikTok
- YouTube
- Pinterest
- Other forms of new media
- Tanning ideation
- Skin cancer prevention

#### Exclusion criteria

- Conference abstracts
- No full-text availability
- No translation to English language
- Unfinished study
- Artificial intelligence technology rather than social media
- Teledermatology rather than social media
- Not dermatologic information
- No skin cancer information
- No social media information

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.

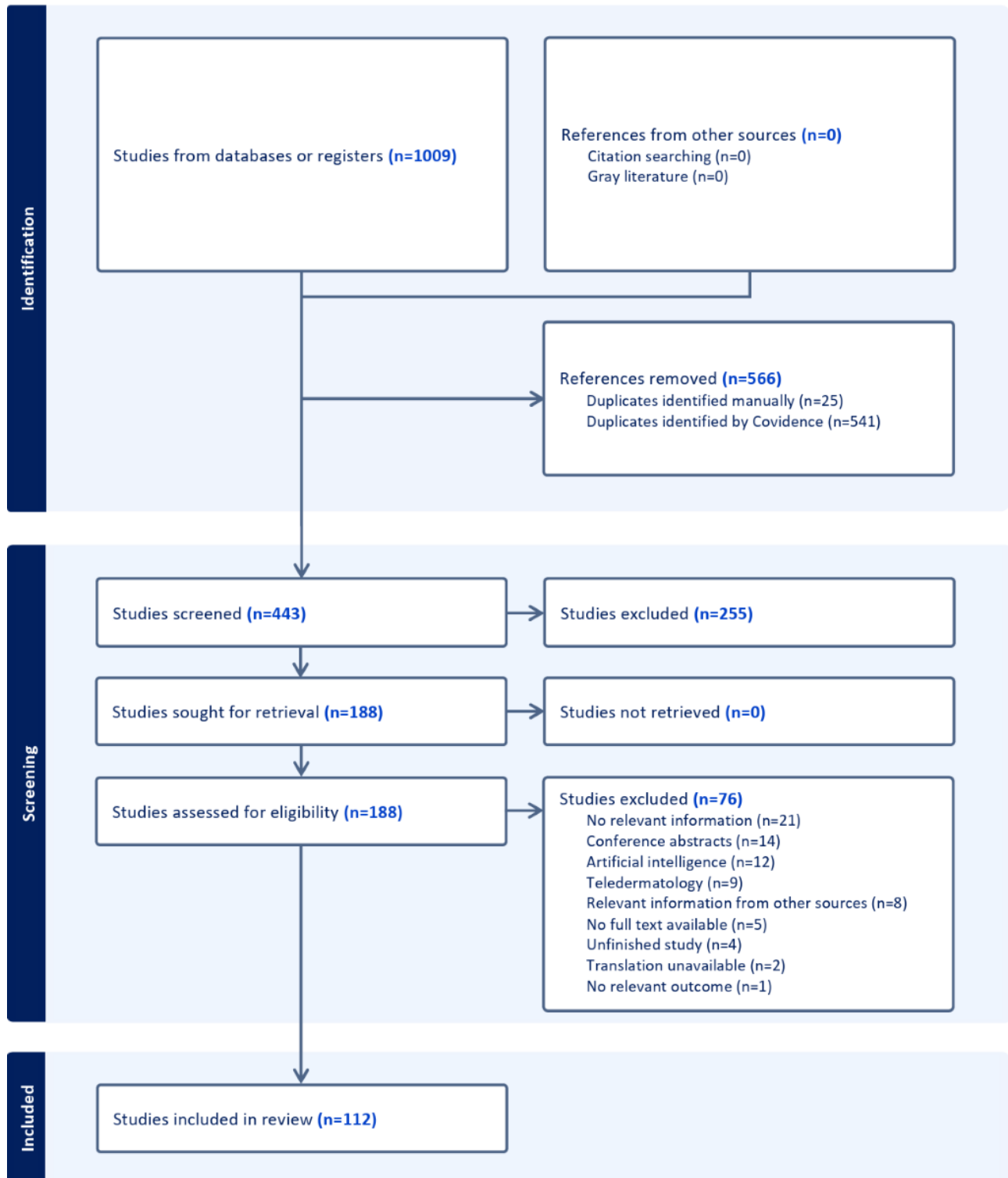
The included publications were divided into 7 categories based on the primary evaluated aspect of the study: engagement, campaigns, demographics, research, education, patient support, and misinformation. To be included in the engagement category, a publication must discuss an attribute of interaction, 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.

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## 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

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Research Letter

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

Camille M Powers<sup>1</sup>, BS; Andrew K Yang<sup>1</sup>, AB, BE; Hannah Verma<sup>1</sup>, BA; Jeremy Orloff<sup>1</sup>, BA; Austin J Piontkowski<sup>1</sup>, BS; Nicholas Gulati<sup>1</sup>, MD, PhD

Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, United States

**Corresponding Author:**

Nicholas Gulati, MD, PhD

Department of Dermatology

Icahn School of Medicine at Mount Sinai

5th Floor

5 E 98th Street

New York, NY, 10029

United States

Phone: 1 212 241 9728

Email: [nicholas.gulati@mssm.edu](mailto:nicholas.gulati@mssm.edu)

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**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

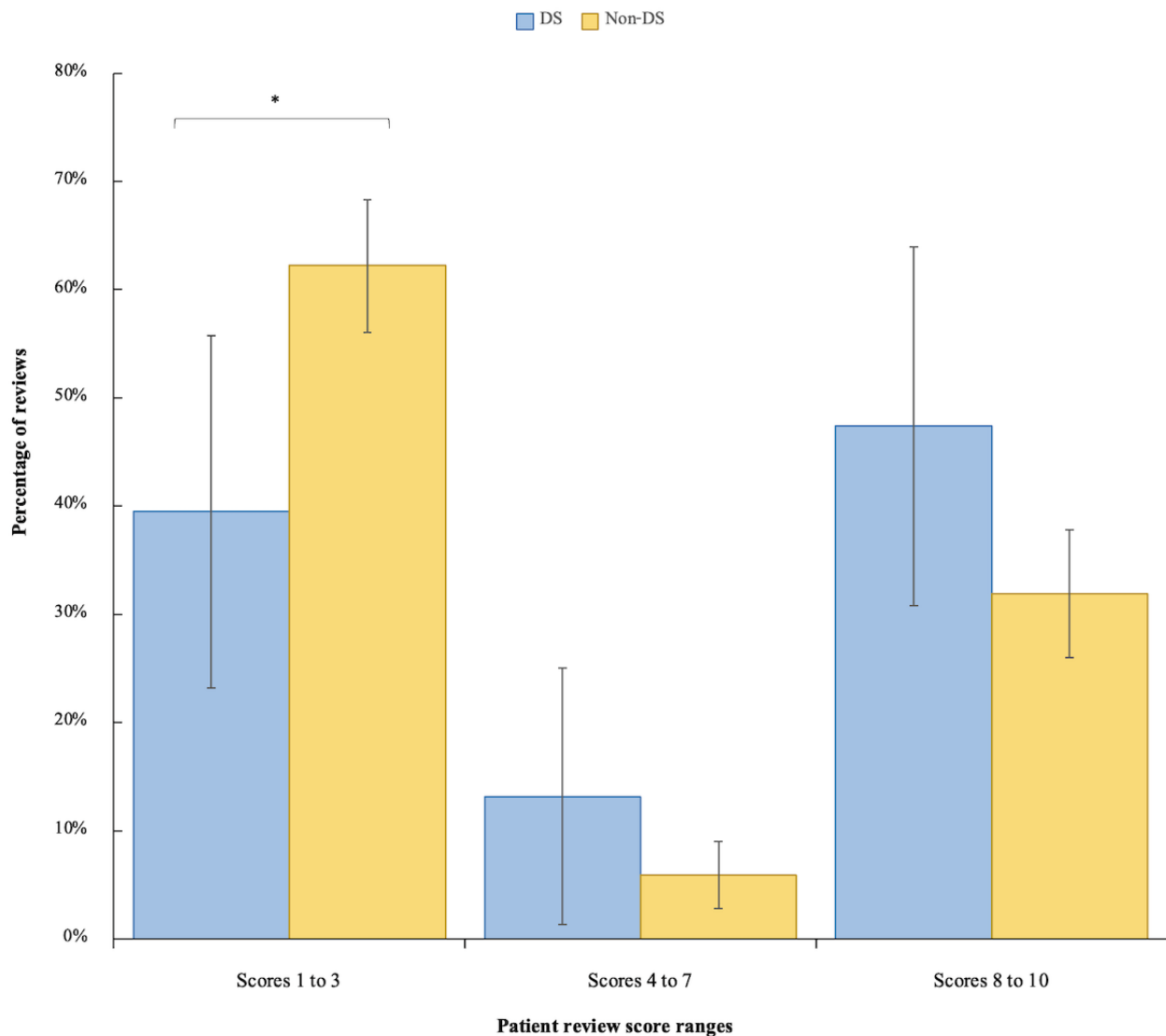
Given the publicly available nature of the data, no institutional review board approval was warranted for this study. We prioritized patient privacy and minimized potential harms by anonymizing data, analyzing all reviews, transparently documenting our methods, and comparing findings to existing literature.

### 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, and 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.

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## 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\\_app1.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



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Review

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

George Kroumpouzou<sup>1,2</sup>, MD, PhD; Patrick Treacy<sup>3</sup>, MD

<sup>1</sup>GK Dermatology, PC, South Weymouth, MA, United States

<sup>2</sup>Department of Dermatology, Warren Alpert Medical School at Brown University, Providence, RI, United States

<sup>3</sup>Ailesbury Clinics Ltd, Dublin, Ireland

**Corresponding Author:**

George Kroumpouzou, MD, PhD

GK Dermatology, PC

541 Main St

Suite 320

South Weymouth, MA, 02190

United States

Phone: 1 7818121078

Fax: 1 7818122748

Email: [gk@gkderm.com](mailto:gk@gkderm.com)

## 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.

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## 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 (Vitrax) 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

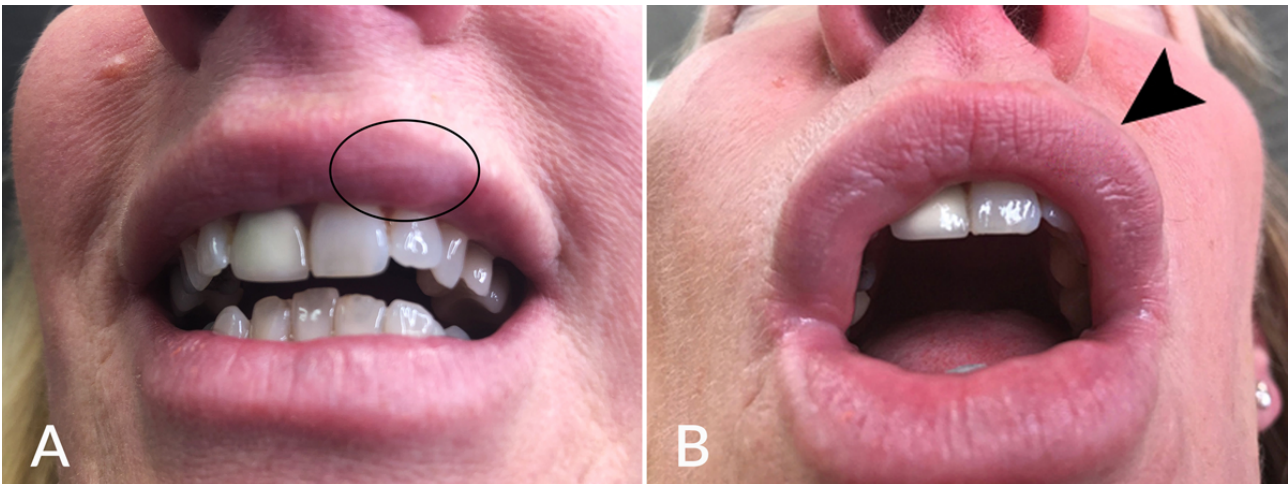
When particulate HA fillers are inappropriately injected too superficially, a bluish discoloration (Tyndall effect) can result and may persist for a long time [1]. Treatment with 30-75 iu Hyal can be effective [34]—a smaller number (10-20 iu) may be used if a small amount of HA needs to be degraded [2]. 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 Tyndall 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

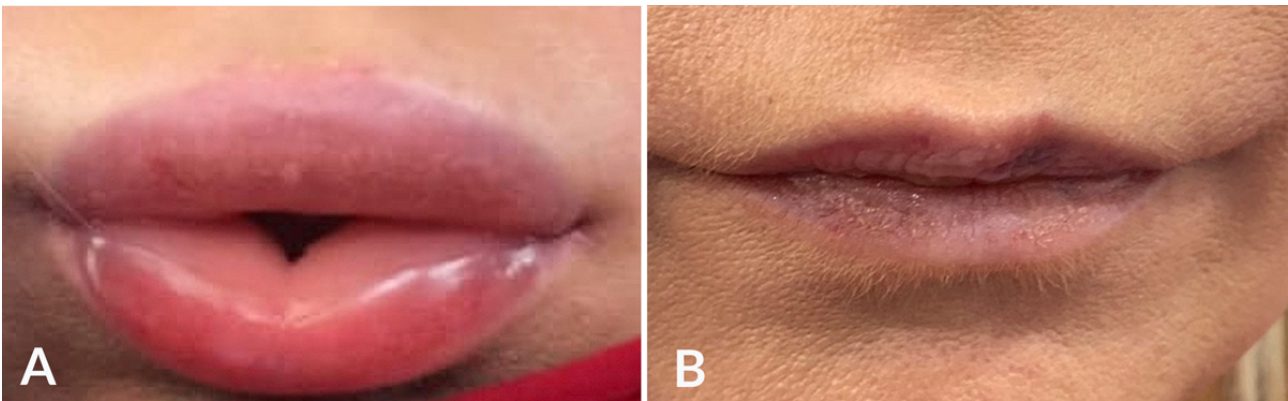
Noninflamed nodules are typically firm, feel rubbery, and tend to be painless. They are not usually associated with redness or significant discoloration. Their incidence is unknown.

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].

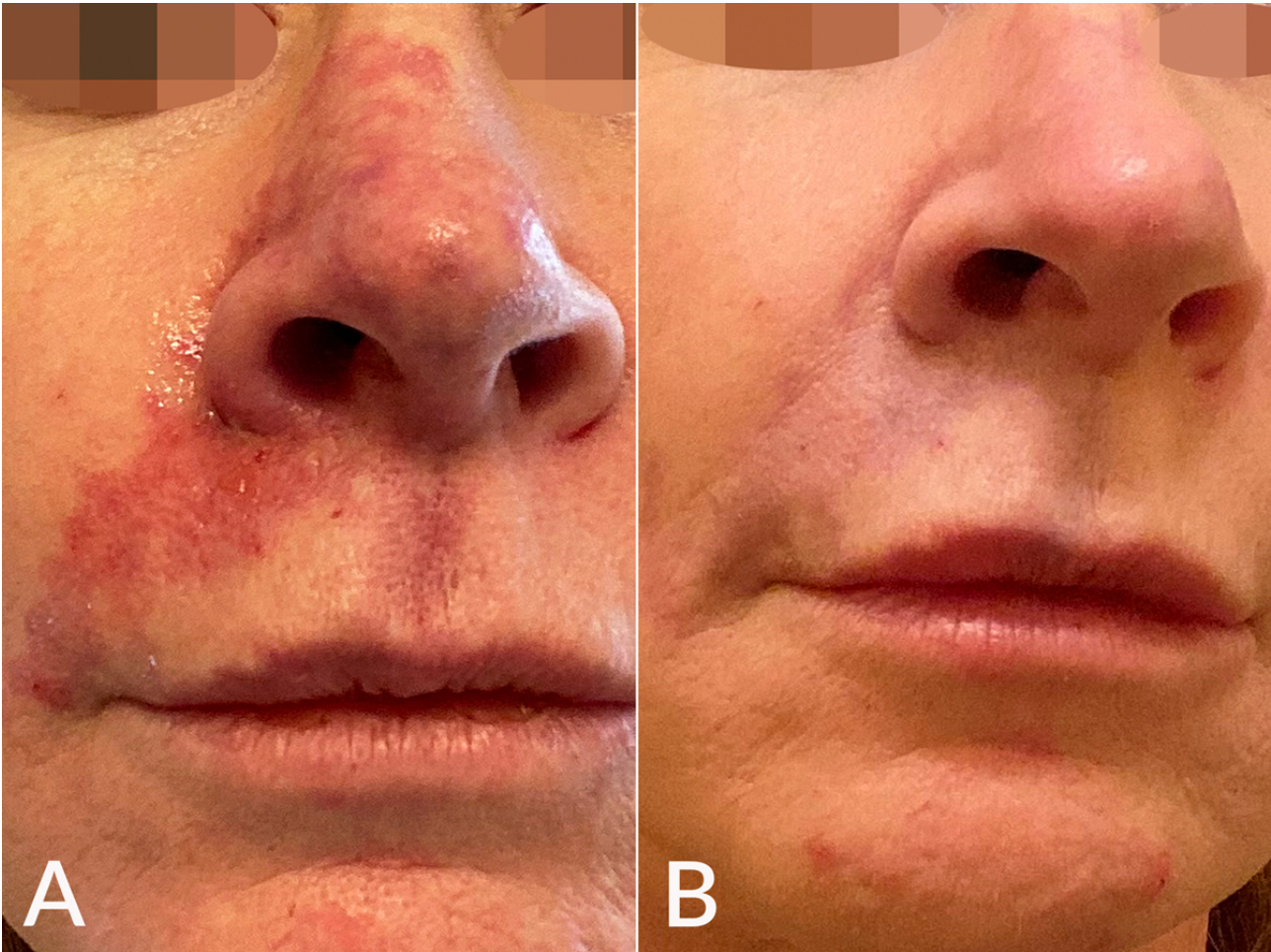
Type I reactions typically respond to oral antihistamines with or without intralesional or oral steroids [1,48,50]. Epinephrine should be administered in systemic reactions such as anaphylaxis or other severe cases. Providers should have an emergency kit containing epinephrine pens, oral steroids, and 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

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Review

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

Blair W Harris<sup>1</sup>, DO; Luke Maxfield<sup>1</sup>, DO; Abigail Hunter<sup>1</sup>, DO; Mandy Alhadjj<sup>2</sup>, DO; Byung Ban<sup>3</sup>, DO; Kayd J Pulsipher<sup>1</sup>, DO

<sup>1</sup>Department of Dermatology, Sampson Regional Medical Center, Campbell University, Clinton, NC, United States

<sup>2</sup>Department of Dermatology, Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH, United States

<sup>3</sup>Department of Rheumatology, MedStar Georgetown University Hospital, Washington, DC, United States

**Corresponding Author:**

Kayd J Pulsipher, DO

Department of Dermatology

Sampson Regional Medical Center

Campbell University

607 Beaman Street

Clinton, NC, 28328

United States

Phone: 1 4355356888

Email: [kpulsipher@sampsonrmc.org](mailto:kpulsipher@sampsonrmc.org)

## 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.

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## 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.

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## 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

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Review

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

Ryosuke Oizumi<sup>1</sup>, PhD; Yoshie Sugimoto<sup>2</sup>, PhD; Hiromi Aibara<sup>3</sup>, PhD

<sup>1</sup>Faculty of Nursing, Shijonawate gakuen University, Daito-shi, Japan

<sup>2</sup>Osaka Metropolitan University, Habikino-shi, Japan

<sup>3</sup>Ehime University, Toon-shi, Japan

**Corresponding Author:**

Ryosuke Oizumi, PhD

Faculty of Nursing

Shijonawate gakuen University

Gakuen-cyo, 6-45

Osaka

Daito-shi, 574-0001

Japan

Phone: 81 72 813 2601

Email: [r-oizumi@un.shijonawate-gakuen.ac.jp](mailto:r-oizumi@un.shijonawate-gakuen.ac.jp)

## 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.

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## 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.

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## Conflicts of Interest

None declared.

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## Abbreviations

**ROS:** reactive oxygen species

**TEWL:** transepidermal water loss

**UVR:** ultraviolet radiation

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Review

# Nutrition, Obesity, and Seborrheic Dermatitis: Systematic Review

Emily Woolhiser<sup>1</sup>, BS; Noah Keime<sup>2</sup>, BS; Arya Patel<sup>3</sup>; Isaac Weber<sup>4</sup>, MD; Madeline Adelman<sup>5</sup>, MD; Robert P Dellavalle<sup>5</sup>, MSPH, MD, PhD

<sup>1</sup>College of Osteopathic Medicine, Kansas City University, Kansas City, MO, United States

<sup>2</sup>School of Medicine, University of Colorado, Aurora, CO, United States

<sup>3</sup>School of Medicine, Case Western Reserve University, Cleveland, OH, United States

<sup>4</sup>Mercy Hospital St. Louis, St Louis, MO, United States

<sup>5</sup>Department of Dermatology, University of Minnesota, Minneapolis, MN, United States

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Department of Dermatology

University of Minnesota

420 Delaware St SE

Minneapolis, MN, 55455

United States

Phone: 1 7208480500

Email: [robert.dellavalle@cuanschutz.edu](mailto:robert.dellavalle@cuanschutz.edu)

## Abstract

**Background:** Pathogenesis of seborrheic dermatitis involves lipid secretion by sebaceous glands, *Malassezia* colonization, and an inflammatory response with skin barrier disruption. Each of these pathways could be modulated by diet, obesity, and nutritional supplements. Current treatment options provide only temporary control of the condition; thus, it is essential to recognize modifiable lifestyle factors that may play a role in determining disease severity.

**Objective:** This study aimed to summarize published evidence on diet, nutritional supplements, alcohol, obesity, and micronutrients in patients with seborrheic dermatitis and to provide useful insights into areas of further research.

**Methods:** A literature search of Scopus, PubMed, and MEDLINE (Ovid interface) for English language papers published between 1993 and 2023 was conducted on April 16, 2023. Case-control studies, cohort studies, and randomized controlled trials with 5 or more subjects conducted on adult participants (>14 years) were included, case reports, case series, and review papers were excluded due to insufficient level of evidence.

**Results:** A total of 13 studies, 8 case-control, 3 cross-sectional, and 2 randomized controlled trials, involving 13,906 patients were included. Seborrheic dermatitis was correlated with significantly increased copper, manganese, iron, calcium, and magnesium concentrations and significantly lower serum zinc and vitamin D and E concentrations. Adherence to the Western diet was associated with a higher risk for seborrheic dermatitis in female patients and an increased consumption of fruit was associated with a lower risk of seborrheic dermatitis in all patients. The probiotic *Triphala* improved patient satisfaction and decreased scalp sebum levels over 8 weeks. Most studies find associations between regular alcohol use and seborrheic dermatitis, but the association between BMI and obesity on seborrheic dermatitis severity and prevalence is mixed.

**Conclusions:** This review sheds light on specific promising areas of research that require further study, including the need for interventional studies evaluating serum zinc, vitamin D, and vitamin E supplementation for seborrheic dermatitis. The negative consequences of a Western diet, alcohol use, obesity, and the benefits of fruit consumption are well known; however, to fully understand their specific relationships to seborrheic dermatitis, further cohort or interventional studies are needed.

**Trial Registration:** PROSPERO CRD42023417768; <https://tinyurl.com/bdcta893>

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**KEYWORDS**

seborrheic dermatitis; systematic review; diet; nutritional supplements; alcohol; BMI; body mass index; skin; review methods; review methodology; nutrition; nutritional; supplement; supplements; dermatology; dermatitis; skin; nutrient; nutrients; micronutrient; micronutrients; vitamin; vitamins; mineral; minerals; obesity; obese; weight



## Introduction

Seborrheic dermatitis is a chronic inflammatory skin disease that commonly presents on the face, scalp, and chest [1]. Seborrheic dermatitis affects approximately 5% of the global population, while its noninflammatory form affects closer to 50% of individuals [2]. Seborrheic dermatitis prefers males of all ethnicities and peaks in the first 3 months of life and again at puberty, where it then reaches an apex at 40-60 years and later declines [3,4]. Risk factors for seborrheic dermatitis include immunodeficiency, neurological diseases including Alzheimer and Parkinson disease, increased sebaceous gland activity, and exposures to drug treatment, including lithium, immunosuppressants, and dopamine antagonists [5]. Seborrheic dermatitis has no definitive cause; however, evidence suggests that pathogenesis begins with androgens and adrenal corticosteroids that stimulate sebaceous gland activity [4]. These hormones are modulated by obesity; therefore, nutrition and BMI may play a role in influencing the seborrheic dermatitis clinical course. Several studies suggest that nutrition can influence other inflammatory skin diseases, such as acne vulgaris, hidradenitis suppurativa, and psoriasis [6-8]. However, the magnitude of the effect on each disease may be small, and nutritional studies are inherently limited by recall bias. Typical treatment includes antifungals in combination with anti-inflammatories including topical corticosteroids and calcineurin inhibitors. However, long-term use of these corticosteroids can cause adverse effects, such as telangiectasia, and current treatments cannot eliminate this chronic disease. Therefore, other options like dietary modifications could assist with management and prevent recurrence [9]. Currently, there is no review evaluating the effects of nutrition and obesity on seborrheic dermatitis disease severity.

The goal of this review is to incorporate studies looking at diet, nutritional supplements, alcohol, obesity, and micronutrients in patients with seborrheic dermatitis into an organized framework that can be used by clinicians to make evidence-based recommendations and to provide useful insights into specific areas of further study. We aimed to answer the question of how diet, nutritional supplements, alcohol, obesity, and micronutrients affect seborrheic dermatitis prevalence, clinical course, severity, and subjective improvement in patients.

## Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement was used to create this study. Case-control studies, cross-sectional studies, cohort studies, and randomized controlled trials with 5 or more subjects conducted on adult participants (>14 years) were included. Exclusion criteria were no case reports, case series, and review papers, as those did not provide a sufficiently high level of evidence. We also excluded studies that included any dietary or supplement intervention evaluated in the context of purposeful concurrent medication use. Eligible literature was any study evaluating BMI, waist circumference, micronutrients, alcohol use, or diet in relation to seborrheic dermatitis and any

dietary or nutritional supplement intervention for seborrheic dermatitis. Eligible methodology to measure changes in seborrheic dermatitis severity included the Seborrheic Dermatitis Area and Severity Index (SEDASI) score, sebum levels, subjective seborrheic dermatitis severity, or seborrheic dermatitis severity evaluated by a physician.

We searched Scopus, PubMed, and MEDLINE (Ovid interface) for English language papers published between 1993 and 2023. The final search was conducted on April 16, 2023. The search terms consisted of (seborrheic dermatitis OR seborrheic eczema) AND (diet OR dietary patterns OR dietary activities OR nutrition OR supplements OR fruit OR vegetables OR gluten OR dairy OR sugars OR meat OR carbohydrates OR protein OR fats OR vitamin OR micronutrients OR minerals OR alcohol OR calorie OR weight loss OR weight changes OR obesity OR obesity reduction OR waist circumference OR body mass index OR BMI). Refer to [Textbox 1](#) for full search strategy.

Literature search results were conducted by one person and exported to CADIMA to remove duplicates and review papers. This tool was used to ensure papers were uploaded to one place and so that reviewers could independently review included papers. In total, 455 unique studies were screened and assessed for eligibility by 2 reviewers working independently. Disagreements were resolved by a third reviewer's decision. After applying inclusion and exclusion criteria, 13 studies (8 case-control, 3 cross-sectional, and 2 randomized control trials) involving 13,906 patients were selected for inclusion. Multiple studies included results that fit into more than 1 category, including 3 studies evaluating both BMI and alcohol use ([Figure 1](#)).

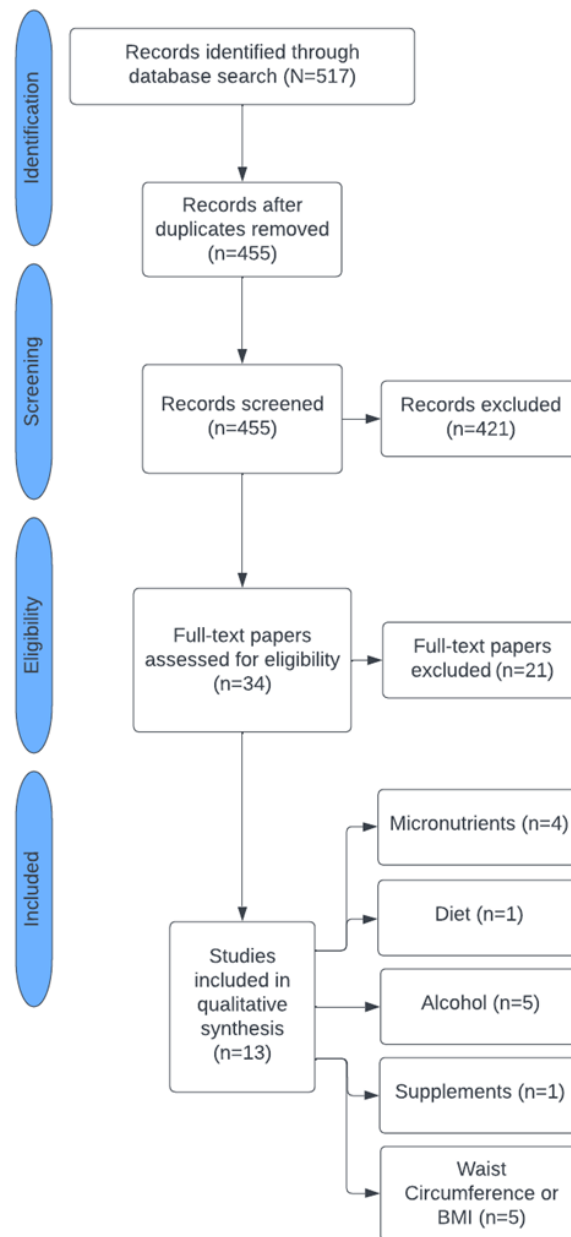
Table S1 in [Multimedia Appendix 1](#) summarizes the included studies' findings and evidence levels according to the ratings of the Oxford Centre for Evidence-based Medicine [10]. Levels of evidence are defined as (1) level 1, randomized trials or systematic reviews of randomized trials, cross-sectional studies, inception cohort studies, or nested case-control studies; (2) level 2, a systematic review of surveys, randomized trials, individual cross-sectional studies with consistent reference standards and blinding, inception cohort studies, or (exceptional) observational studies with dramatic effect; (3) level 3, Cohort studies, local nonrandom sample, nonconsecutive studies or studies without a consistently applied reference standard; (4) level 4, case series, case-control study, or historically controlled studies; and (5) level 5, mechanism-based reasoning. Level 1 represents evidence generally considered to be stronger, and level 5 represents evidence generally considered to be weaker. The Cochrane Collaboration's tool for assessing the risk of bias was used to evaluate randomized control trials [11].

Although these tools intend to reduce bias in selected studies, bias can be transferred from the tools themselves. The Cochrane collaboration's tool specifically assesses for the risk of bias, rather than for bias itself, and is more likely to miss bias associated with incomplete data and selective reporting [11]. Oxford-based Medicine levels of evidence help readers prioritize studies, but they should be used as a guide, rather than absolute, when determining the validity of a study [10].

**Textbox 1.** Search strategy for systematic review.

- Database
  - Scopus, PubMed, and Ovid (MEDLINE interface)
- Search strategy
  - (seborrheic dermatitis OR seborrheic eczema) AND (diet OR dietary patterns OR dietary activities OR nutrition OR supplements OR fruit OR vegetables OR gluten OR dairy OR sugars OR meat OR carbohydrates OR protein OR fats OR vitamin OR micronutrients OR minerals OR alcohol OR calorie OR weight loss OR weight changes OR obesity OR obesity reduction OR waist circumference OR body mass index OR BMI)

**Figure 1.** Study selection. All full-text papers were excluded due to a lack of inclusion criteria eligibility. A total of 3 studies included results that evaluated both BMI and alcohol use.



## Results

### Micronutrients

A total of 3 studies evaluated micronutrient concentrations in patients with seborrheic dermatitis. Jahan et al [12] measured the levels of vitamins and minerals in patients with seborrheic dermatitis (n=75) compared with controls (n=76) in a case-control study, and concluded patients with seborrheic dermatitis had increased copper, manganese, iron, calcium, and magnesium concentrations ( $P<.001$ ) and lower vitamin E concentrations ( $P=.009$ ). Unfortunately, the study did not remeasure micronutrient concentrations after remission of seborrheic dermatitis, so it is not possible to conclude whether normalizing them is clinically beneficial. Another 10-week, randomized double-blind, placebo-controlled trial by Smith et al [13] (n=41) studied the impact of supplementation with weight-based, low-dose oral potassium bromide (3.5 mg/mL), sodium bromide (2.0 mg/mL), nickel sulfate (0.6 mg/mL), and sodium chloride (0.6 mg/mL) in a vehicle of purified water and 20% ethyl alcohol on seborrheic dermatitis severity measured by SEDASI. This study found an improvement in participants' SEDASI score at 10 weeks of treatment ( $P=.03$ ), with no significant difference in the frequency of adverse events between active and placebo groups [13].

Rahimi et al [14] evaluated serum levels of 25-hydroxyvitamin D (25(OH)D) in patients with seborrheic dermatitis (n=118) compared with healthy controls (n=171) in another case-control study [14]. They found that vitamin D deficiency was more prevalent in patients with seborrheic dermatitis than in controls ( $P=.01$ ). This team neither obtained follow-up serum levels of vitamin D nor determined if subsequent supplementation resulted in seborrheic dermatitis improvement, thus it is difficult to conclude if supplementation is clinically beneficial. A separate case-control study evaluated serum zinc levels in patients with seborrheic dermatitis (n=43) compared with age and sex-matched, healthy controls (n=41) [15]. This study found lower serum zinc levels in patients with seborrheic dermatitis ( $P=.05$ ); however, there was no correlation between serum zinc levels and seborrheic dermatitis duration or SEDASI score [15]. Although it evaluated the relationship between micronutrients and disease duration and severity, the study is limited by a small sample size and exclusion of severe patients with seborrheic dermatitis, limiting the generalizability of the data.

One study in the literature evaluates the association between seborrheic dermatitis and diet. This cross-sectional study by Sanders et al [16] (n=4379) examined if specific dietary patterns were associated with seborrheic dermatitis using participants of the Rotterdam Study (a prospective population-based cohort study of chronic diseases in the middle-aged and elderly population in the Netherlands) with a skin exam performed by a dermatology trained physician and a food frequency questionnaire with 389 questions evaluating the consumption of food over the past month. They found that the Western diet, characterized by meat, potato, and alcohol consumption, was associated with a higher risk for seborrheic dermatitis (adjusted odds ratio 1.34;  $P=.07$ ) but only in female patients [16]. They also found that an increased amount of fruit in the diet was

associated with a lower risk of seborrheic dermatitis (adjusted odds ratio 0.75;  $P=.03$ ) [16]. Both associations compared the highest quartile of those most adherent to the dietary pattern with the lowest quartile of adherent participants [16]. Despite the popularity in recommending dietary changes, it is difficult to establish concrete conclusions about the viability of dietary manipulation as an adjunctive treatment due to limited data.

### Alcohol

Numerous studies found significant associations between regular alcohol use and an increased prevalence of seborrheic dermatitis [17-20]. Furthermore, increased alcohol consumption is associated with a greater risk of seborrheic dermatitis flares (odds ratio 5.4;  $P=.08$ ) [20]. Sharma et al [17] evaluated the quantity of alcohol consumed in a week, duration of alcohol intake, and seborrheic dermatitis duration in 196 males, who reported drinking  $\geq 200$  mL of pure alcohol weekly, that were referred for a dermatologic consult. They found an inverse relationship between seborrheic dermatitis prevalence and duration of alcohol intake, seborrheic dermatitis prevalence is inversely related to the duration of alcohol intake, meaning those with fewer years of alcohol use ( $P<.001$ ) were more likely to have seborrheic dermatitis [17].

One cross-sectional study by Sanders et al [3] (n=5498) used Rotterdam study participants who underwent a full-body skin exam by dermatologists, and it compared patient characteristics for those with and without seborrheic dermatitis. They found no association between alcohol and seborrheic dermatitis; however, this study only included middle-aged and elderly patients, making it difficult to generalize to younger patients [3]. In addition, according to the findings by Sharma et al [17], seborrheic dermatitis would be more prevalent in younger patients who use alcohol, and this could account for the lack of association found by Sanders et al [3] when looking at an older population.

These studies are limited by their survey-based design, which inherently include self-reported alcohol intake, which may be unreliable. In addition, there are numerous uncontrolled, confounding factors, including smoking, tobacco use, and HIV, making it difficult to draw accurate conclusions about the effects of alcohol alone. Data related to alcohol and seborrheic dermatitis found in this review have weak and contradictory evidence, warranting further study.

### Supplements

Few nutritional supplements have been evaluated as an intervention for seborrheic dermatitis. One was evaluated in an 8-week, randomized, placebo-controlled trial by Zaeie et al [21] (n=80) was Triphala: a prebiotic. Patients with seborrheic dermatitis received 1 gram of Triphala twice a day for 8 weeks, then rated subjective symptomatic improvement from 1 to 100 [21]. Researchers assessed scalp sebum levels using a Sebumeter [21]. The Triphala group experienced both improvement in patient satisfaction (mean percentage of patients' satisfaction was 37.91 in the Triphala group and 17.89 in the placebo group,  $P=.001$ ) and scalp sebum levels (Triphala group: mean 103.67, SD 70.37; placebo group: mean 128.45, SD 73.90;  $P=.047$ ) [21].

This study is limited by a small sample size, which prevents generalizability to broader populations and introduces doubt surrounding data reproducibility. More trials are necessary to elucidate if there is true efficacy of oral nutritional supplements on seborrheic dermatitis.

### Obesity

Some studies demonstrate no relationship between seborrheic dermatitis and BMI [10,19,20]; however, a case-control study by Akbaş et al [22] (n=101) compared patients with seborrheic dermatitis with age and sex-matched controls and found that seborrheic dermatitis was associated with higher BMI when compared with controls ( $P=.002$ ). Savaş Erdoğan et al [23] (n=103) also evaluated the relationship between BMI, subjective seborrheic dermatitis severity, and SEDASI score in a case-control study with patients with seborrheic dermatitis and age, sex, and BMI-matched controls. Results showed a positive relationship between the SEDASI score and BMI ( $r=0.298$ ;  $P=.03$ ) but no relationship between subjective disease severity score and BMI ( $P=.62$ ) [23]. Although there are studies to the contrary, most evidence indicates no relationship between BMI and seborrheic dermatitis severity [10,19,20,24]. Studies that suggest a causal relationship between the 2 are limited by numerous confounders, including ethnic background, socioeconomic status, and lifestyle factors.

Erdogan et al [23] (n=103) and Akbas et al [22] (n=101) conducted case-control studies comparing waist circumference in patients with seborrheic dermatitis to age, sex, and BMI-matched healthy controls. Both found that waist circumference was higher in the seborrheic dermatitis groups ( $P=.007$  and  $P=.001$ , respectively). These studies are limited by small sample size [24].

### Discussion

The pathophysiology of seborrheic dermatitis is still not entirely understood; however, colonization of *Malassezia*, a fungus present on normal skin, is strongly associated with this condition [25]. *Malassezia* is found on sebum-rich skin and functions as a lipophilic yeast [25]. The metabolites of *Malassezia* induce inflammation, causing infiltration of natural killer cells and macrophages, and increased inflammatory cytokines such as interleukin 1 $\alpha$ , 1 $\beta$ , and 6, and tumor necrosis factor  $\alpha$  [26]. These inflammatory mediators can stimulate keratinocyte differentiation, resulting in dysfunction in the stratum corneum, disruption of the epidermal barrier, and perpetuation of an inflammatory response. This creates a cycle of skin barrier disruption that manifests the clinical features of seborrheic dermatitis [15,25].

Inflammation and oxidative stress are closely linked—oxidative stress causes inflammation, and inflammation precipitates oxidative stress [27]. Increased serum iron, copper, and manganese cause oxidative stress by catalyzing the creation of reactive oxygen species, which in turn leads to the development of inflammatory skin diseases like atopic dermatitis and psoriasis [28-30]. Systemic oxidative stress is also higher in patients with seborrheic dermatitis than in healthy subjects, suggesting a role in the pathogenesis of this disease [31]. Thus, the findings of

Jahan et al [12] regarding elevated levels of serum iron, copper, and manganese in patients with seborrheic dermatitis may contribute to the cycle of oxidative stress, inflammation, and skin barrier disruption.

One study found dietary supplementation with low-dose oral potassium bromide, sodium bromide, nickel sulfate, and sodium chloride, reduced seborrheic dermatitis severity [13]. This compound consists of inorganic soluble mineral salts, but no evidence exists in the literature to explain this compound's mechanism of action. More research is needed to determine the function these mineral salts play in modulating the epidermal barrier.

Zinc is an essential trace element that assists in cell growth, development, and differentiation and plays catalytic and structural roles in transcription factors, receptors, growth factors, cytokines, and enzymes [32]. It also possesses anti-inflammatory properties, including inhibiting polynuclear neutrophils chemotaxis and altering the production of interleukin-6 and tumor necrosis factor  $\alpha$ , 2 proinflammatory cytokines produced by keratinocytes [33,34]. It also possesses antiandrogen activity by inhibiting 5 alpha-reductase type I expression [35]. These inflammatory and androgenic pathways are essential to the pathogenesis of seborrheic dermatitis, therefore lower serum zinc levels in patients with seborrheic dermatitis may represent a precipitating factor to disease development [15]. Importantly, there was no correlation between serum zinc levels and disease severity graded by SEDASI, so it may only be involved in the development of the disease rather than progression [15]. The authors postulated that this is due to the study's small sample size and their inclusion of only mild seborrheic dermatitis. More studies are needed to identify if this relationship holds true for severe seborrheic dermatitis and if oral zinc supplementation is of clinical benefit.

Vitamin E is a fat-soluble vitamin and an important antioxidant that helps protect cell membranes from lipid peroxidation, minimizing oxidative damage [36]. Therefore, the low levels of vitamin E in patients with seborrheic dermatitis may contribute to an increased oxidative burden [12]. Supplementation with oral vitamin E showed early promising results in improving other inflammatory skin diseases, including atopic dermatitis and psoriasis [36]. Further research is needed to elucidate the role of vitamin E supplementation as an adjunctive therapy in seborrheic dermatitis.

Vitamin D plays a role in multiple skin processes, ranging from keratinocyte proliferation, differentiation, and apoptosis to immunoregulatory processes and barrier maintenance [37]. Vitamin D enhances the synthesis of structural proteins and mediates immunosuppressive action in the skin [37]. Thus, the lower 25-hydroxyvitamin D levels in patients with seborrheic dermatitis found by Rahimi et al [14] and Borda and Wikramanayake [25] may decrease these protective functions, generating epidermal barrier dysfunction in seborrheic dermatitis. Vitamin D deficiency also plays a role in other inflammatory skin pathologies, such as psoriasis and atopic dermatitis; supplementation of vitamin D3 and vitamin D analogs is effective against psoriasis [37]. Further research is needed to determine the significance of vitamin D deficiency



in seborrheic dermatitis and the efficacy of interventional supplementation.

Prebiotics and probiotics possess antimicrobial properties and play a role in the inflammatory response and skin barrier function [38]. Probiotics are live microorganisms while prebiotics are nondigestible carbohydrates that induce the growth of probiotic bacteria [38]. Pre- and probiotics are beneficial for several dermatologic conditions, including dandruff and seborrhea, but their use in seborrheic dermatitis is limited [39]. Triphala, a polyphenol-rich prebiotic, is one of the few dietary supplements that has been tested as a seborrheic dermatitis treatment [21]. It has antioxidant properties and acts as a skin protectant for human skin cells in vitro [40]. The study was limited by a small sample size, but Triphala is a potential adjunctive treatment for seborrheic dermatitis, but more extensive clinical trials are necessary to fully understand its efficacy and safety.

Through assessment with the Cochrane tool for assessing risk bias, a tool validated for randomized controlled trials, some biases were observed [11]. Authors denoted a small sample size as a limitation that could inherently give the trial attrition bias. Of the 81 patients originally starting the trial, 80 completed it as participants could abandon it at any time. Patients were blinded due to placebo intervention being used in half of the group. Assessors were blinded to the fact whether the subject received the active treatment or the placebo. The authors stated that the use of a Sebumeter made the data objective, which could have led to some detection bias to overestimate the validity of the results. In addition, performance bias could be at risk due to overconfidence in blinding of the capsules. Researchers claimed that capsules were matched to size, color, and consistency [21].

The Western diet includes a high volume of meat, potato, and alcohol, and a low volume of foods rich in fiber, vitamins, and minerals; its popularity has grown substantially over the past few decades. Long-term consumption of foods popular in the Western diet can negatively impact health by promoting weight gain, activating the immune system, and causing pathological changes in lipids and metabolism [41]. Only 1 study evaluates adherence to specific dietary patterns and their association with seborrheic dermatitis. This study found that patients with higher fruit intake had a decreased likelihood of seborrheic dermatitis [16]. These results align with research on other inflammatory skin diseases, including eczema incidence, which is negatively associated with increased fruit intake [42]. Fruits contain high levels of vitamins and flavonoids, which reduce inflammation and may modulate the inflammatory response in seborrheic dermatitis that contributes to skin barrier dysfunction [42].

This same study found that higher adherence to the Western diet in females was associated with an increased prevalence of seborrheic dermatitis, possibly due to increased chronic inflammation associated with the diet [16,43]. This association was not present in males, which may be explained by known differences in dietary response between the sexes [44,45].

It should be further highlighted that the use of diet to mitigate disease severity is popular in the mainstream, but existing

literature suggests a tenuous relationship. A 2015 study assessed the validity of memory-based dietary assessment methods on informing dietary policies and found that they are inherently flawed, as they necessarily involve subjective memory recall with no objective data [46]. Therefore, retrospective studies of food consumption are prone to bias and are generally limited.

Chronic alcohol use is linked to a variety of skin conditions and the earliest clinical manifestations of alcohol use disorder are cutaneous [47]. There is a known association between regular alcohol use and seborrheic dermatitis, likely resulting from immunosuppression, malnutrition, poor hygiene, vitamin B deficiency, and other confounders [17-20]. One study did not find an association between regular alcohol use and seborrheic dermatitis adjusted for possible confounders, including demographic, socioeconomic, and medical information, calling into doubt conclusions drawn from unadjusted studies [10]. A separate crossover study found that more recent consumption of alcohol was associated with seborrheic dermatitis flares; however, this also correlated with increased reported stress levels, introducing an additional confounder [20]. Given the conflicting nature of these data, it is unclear whether alcohol is an independent determinant of seborrheic dermatitis clinical course, thus controlled interventional studies are necessary.

Current literature on the association between BMI and seborrheic dermatitis is mixed, although larger studies indicate no association [10,19,20,22,23]. The conflicting nature of these data may reflect BMI's poor predictive value in judging metabolic health, which is associated with seborrheic dermatitis [22,48,49].

An arguably more accurate indicator of obesity is waist circumference, with multiple case-control studies showing waist circumference significantly higher in patients with seborrheic dermatitis compared with controls [22-24]. Numerous inflammatory markers are higher in those with obesity, which may contribute to initiating or aggravating seborrheic dermatitis [46]. Abdominal obesity can also lead to dyslipidemia, another factor associated with seborrheic dermatitis [22,23,48].

## Conclusions

More studies are needed to determine how micronutrients, diet, supplements, and obesity affect seborrheic dermatitis. This review sheds light on promising areas of research that require further study but highlights that current data are limited. Low levels of serum zinc, vitamin D, and vitamin E in patients with seborrheic dermatitis suggest a role for interventional studies evaluating the benefits of supplementation. The prebiotic Triphala may also improve seborrheic dermatitis; however, larger studies with more severe seborrheic dermatitis are needed to evaluate its true potential.

The negative consequences of a Western diet, alcohol use, obesity, and the benefits of fruit consumption are well known; however, to fully understand their specific relationships to seborrheic dermatitis, further cohort or interventional studies are needed. As it stands, information on diet-based therapy for seborrheic dermatitis is conflicting and limited, thus future studies are warranted.



## Data Availability

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

## Authors' Contributions

IW conceived the presented idea, synthesized the data, and wrote the preliminary manuscript. IW and MA verified the search terms and methods. IW and EW screened and assessed all studies for eligibility. NK, AP, MA, and RPD provided feedback and edited the manuscript. All authors discussed the results and contributed to the final manuscript.

## Conflicts of Interest

RPD is the editor-in-chief of JMIR Dermatology.

### Multimedia Appendix 1

Summary of included studies.

[DOCX File, 28 KB - [derma\\_v7i1e50143\\_app1.docx](#)]

### Multimedia Appendix 2

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Checklist.

[PDF File (Adobe PDF File), 67 KB - [derma\\_v7i1e50143\\_app2.pdf](#)]

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## Abbreviations

**SEDASI:** SEborrheic Dermatitis Area and Severity Index.

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

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Review

# Association of Cellulitis With Obesity: Systematic Review and Meta-Analysis

Kimi Gabriella Taira<sup>1,2\*</sup>, MD; Madelyn Wang<sup>1\*</sup>, MD; William Guo<sup>3</sup>, MD; Olivia Kam<sup>1</sup>, BA; Tara Kaufmann<sup>3</sup>, MD

<sup>1</sup>Renaissance School of Medicine, Stony Brook University, Stony Brook, NY, United States

<sup>2</sup>Mayo Clinic School of Graduate Medical Education, Rochester, MN, United States

<sup>3</sup>Department of Dermatology, Stony Brook University Hospital, Stony Brook, NY, United States

\*these authors contributed equally

**Corresponding Author:**

Kimi Gabriella Taira, MD

Mayo Clinic School of Graduate Medical Education

Siebens Building, Floor 12

200 First Street SW

Rochester, MN, 55905

United States

Phone: 1 6314444200

Email: [taira.kimi@mayo.edu](mailto:taira.kimi@mayo.edu)

## Abstract

**Background:** Cellulitis is a bacterial skin infection that tends to recur. Previous studies have identified several risk factors that may contribute to its pathogenesis. Obesity is an increasingly prevalent worldwide disease that has been associated with skin and soft tissue infections.

**Objective:** The aim of our systematic review and meta-analysis was to investigate the association of cellulitis with obesity.

**Methods:** The Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Web of Science databases were searched for the relevant studies from the inception of each respective database to March 13, 2021. Case-control, cross-sectional, or cohort studies that examined the odds or risk of increased BMI in patients with cellulitis were included. This study was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The Newcastle-Ottawa scale (NOS) was used to evaluate the risk of bias in included studies.

**Results:** In total, 9 case-control studies were included in our quantitative meta-analysis with a total of 68,148 study participants. A significant association was found between cellulitis and obesity (pooled odds ratio [OR] 2.67, 95% CI 1.91-3.71). No significant association was observed between cellulitis and being overweight (pooled OR 1.69, 95% CI 0.99-2.88). Patients with cellulitis were also found to have 1.63-fold increased odds of being male (pooled OR 1.63, 95% CI 1.12-2.38).

**Conclusions:** Our findings suggest that cellulitis is significantly associated with obesity. Maintaining a healthy BMI may be indicated for patients presenting with cellulitis.

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**KEYWORDS**

cellulitis; obesity; overweight; systematic review; meta-analysis; skin infection; body mass index; BMI

## Introduction

Cellulitis is an acute skin infection commonly caused by the gram-positive bacteria *Staphylococcus aureus* and *Streptococcus* species [1]. Cellulitis results from the entry of bacteria through a breached epidermis into the dermal and subcutaneous layers of the skin, causing an infection that most frequently affects the lower limb, but may involve any part of the body [2]. The clinical findings that characterize cellulitis include erythema,

warmth, edema, and pain, in addition to systemic symptoms such as the acute onset (typically within 48 hours) of fever or chills. The severity of cellulitis varies widely, ranging from a well-demarcated erythematous area on the skin with raised borders to a rapidly spreading erythema and possible sepsis [3]. The former definition is widely known as erysipelas and is argued to be a more superficial type of cellulitis. Previous studies have shown that recurrent cellulitis is common, with up to 35%-49% of patients with cellulitis reporting a previous



history of cellulitis [4,5]. Several local and general risk factors that may contribute to the development of primary and recurrent cellulitis have been studied, the most prevalent ones being disruption of the skin barrier (such as ulcers, trauma, infection of the toe webs, and dermatomycosis), lymphedema, saphenectomy, history of cellulitis, varicose veins, alcohol abuse, cardiovascular disease, smoking, diabetes, and malignancy [4-12].

Obesity is becoming increasingly prevalent, with over 1.9 billion adults worldwide considered overweight, and of those, 650 million people considered obese [13]. Obesity has been associated with an increased risk of systemic diseases such as cardiovascular disease, type 2 diabetes mellitus, and cancer, as well as infections, particularly of the skin and soft tissue [14-18]. Given the global popularity of various physical exercise programs, it is reasonable to consider the role of physical exercise in decreasing adipose tissue, thereby potentially decreasing the risk of such diseases, including skin and soft-tissue infections [19]. There have been several proposed mechanisms to explain the role by which increased adipose tissue in obese individuals leads to their susceptibility to infections. One is that adipose tissue exerts immunosuppressive effects on the body through key adipokines, and another is that impeded lymphatic flow causes increased bacterial growth, decreased tissue oxygenation, and lymphedema commonly seen in individuals with high BMI [20-22].

There remains some controversy regarding whether systemic factors, such as obesity, play a significant role in the development of cellulitis. Several previous studies have reported no significant association between cellulitis and increased BMI [8,9]; however, other recent studies demonstrate that patients with cellulitis are more likely to be overweight or obese [5,6,10,11]. In 2016, Quirke et al [23] analyzed the risk factors for cellulitis of the lower limbs and found a significant association between being overweight or obese and having cellulitis. However, their review included patients who are obese into their definition of overweight, which may have skewed the association between being overweight and cellulitis toward a more positive direction. As new studies reporting on cellulitis have emerged in the past 5 years [6,10,11], we aim to incorporate the current literature into our analysis to determine whether there is a significant association between cellulitis and obesity. In addition, we aim to explore the potential mechanisms that underlie the association between skin infections and increased BMI and identify possible risk factors that may contribute to the development of cellulitis, such as previous history of skin infections and associated pathogens.

## Methods

### Overview

We conducted a systematic review and meta-analysis of observational studies (including case-control and cohort studies) on the association of cellulitis and obesity. This study was done in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [24].

The Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Web of Science databases were searched for the relevant studies from the inception of each respective database to March 13, 2021. No geographic or language restriction was imposed on our search. Our search strategy is detailed in Table S1 in [Multimedia Appendix 1](#).

### Study Selection

Included studies met the following criteria: (1) observational studies examining the association of cellulitis and BMI, including cross-sectional, case-control, or cohort studies; (2) studies including overweight (25 to 29.9 kg/m<sup>2</sup> or >120% of the ideal weight as calculated by Lorentz formula) or any class of obesity including class I (30 to 34.9 kg/m<sup>2</sup>), class II (35 to 39.9 kg/m<sup>2</sup>), or class III (≥40 kg/m<sup>2</sup>); (3) the case group was composed of patients with acute or recurrent cellulitis and the control group was composed of individuals without acute or recurrent cellulitis; and (4) the study contained control groups of n>3.

Excluded studies met the following criteria: (1) studies with nonhuman participants, (2) studies not available in English, (3) conference abstracts with no corresponding full-text paper, and (4) studies with case patients who developed cellulitis as a postoperative complication of surgery. Authors MW and KT independently screened the search results to assess their eligibility by reading the titles and abstracts of all citations. Full texts of potentially eligible studies and studies that met the inclusion criteria were read by both authors. Disagreement regarding the eligibility of a study was resolved by a third author, WG.

### Data Extraction and Risk of Bias Assessment

We extracted the following data from the included studies: first author, year of publication, country, study design, diagnosis method of cellulitis, selection criteria of cases and controls, location of cellulitis, definition of obesity/overweight, cultured microbes, and alcohol usage. Quantitative data that were extracted include total number of participants, number of cases and controls, age of participants, percentage of female participants, and univariate and multivariate odds ratios (ORs) with 95% CI on the association of cellulitis with obesity. We used the Newcastle-Ottawa scale (NOS) to assess the risk of bias in included studies [25].

### Statistical Analysis

A pooled OR on the association between cellulitis and obesity, being overweight, as well as sex prevalence, were calculated and depicted in forest plots using the Review Manager software (version 5.4; Cochrane) [26]. Raw patient data were used to calculate available unadjusted pooled ORs. A random effects model of Mantel-Haenszel was used for the OR due to high heterogeneity, as determined by  $I^2$  values greater than 50%. Calculations for pooled multivariate ORs were calculated using an inverse variance method that included adjusted ORs with a random effects model as determined by the  $I^2$  degree of heterogeneity. All calculations were performed with a 95% CI.  $P$  values less than .05 were considered significant.



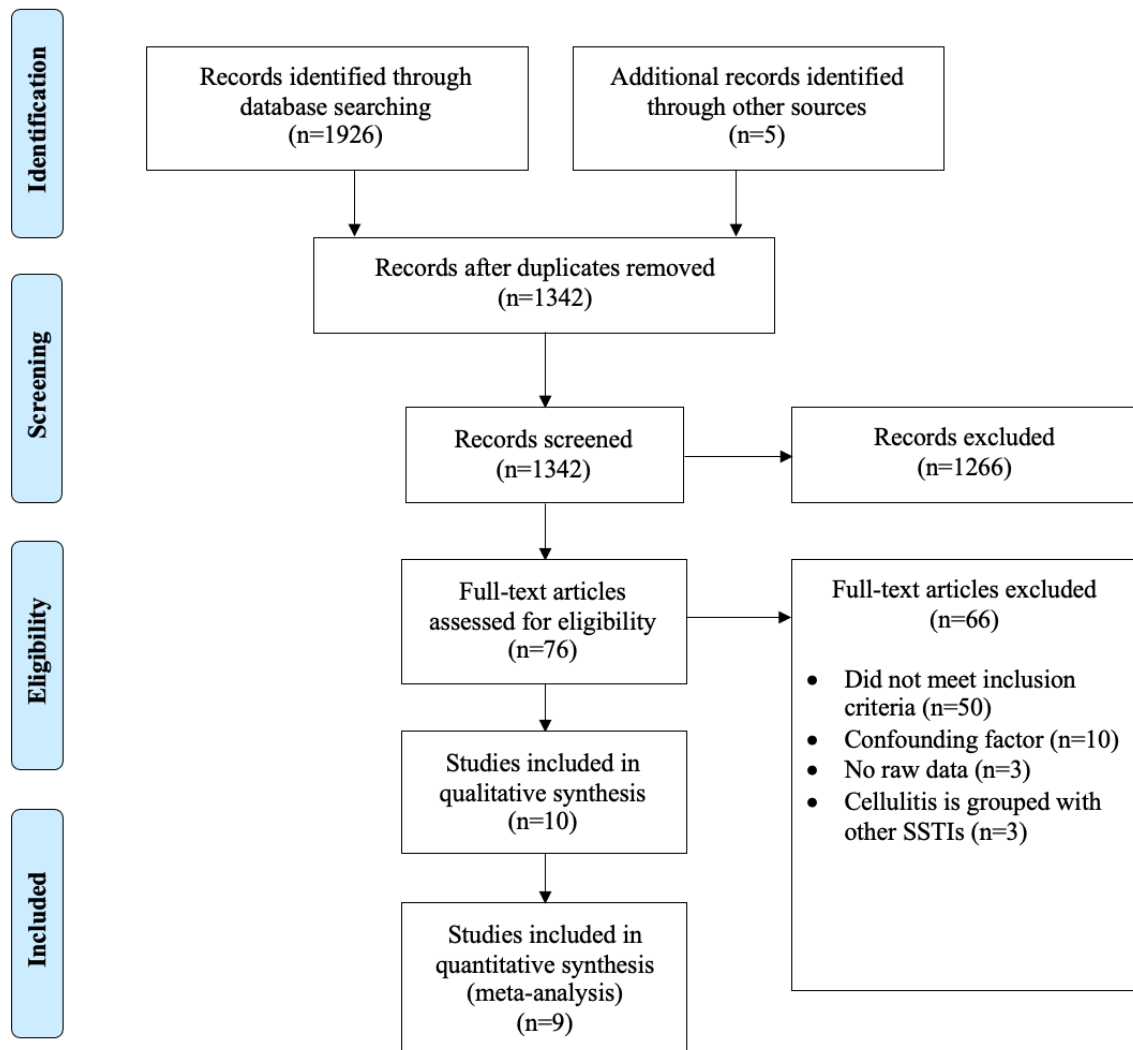
## Results

### Search Results

The PRISMA study flow chart is shown in [Figure 1](#). Our search yielded 1342 citations after removing duplicates. An additional 1266 citations were excluded after reading titles and abstracts. After assessing 76 full-text studies, we excluded 66 studies due to reasons, such as studies not meeting our inclusion criteria (n=50), studies containing confounding factors (n=10), studies

not providing raw data (n=3), and studies grouping cellulitis together with other skin and soft tissue infections (n=3). A study by Roujeau et al [12] contained adequate patient data for analysis but was ultimately not included in the quantitative meta-analysis for overweight as it did not meet the inclusion criteria of overweight, which is defined as BMI  $\geq 25$  and  $< 30$  kg/m<sup>2</sup>. The study did not include data on obesity. A total of 8 studies were ultimately included in our meta-analysis on cellulitis and obesity, and 9 studies were included in our meta-analysis on cellulitis and sex.

**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) study flow chart. SSTI: skin and soft tissue infection.



### Characteristics of Included Studies

A summary of the characteristics of included case-control studies is listed in [Table 1](#). Our meta-analysis incorporated 9 case-control studies consisting of 68,148 total participants. Out of the total, 37,303 participants were patients with cellulitis, and 30,845 participants were individuals who served as controls. In total, 5 studies used controls matched for age and sex; 2 studies used controls matched for age, sex, and location; and 2 studies used controls matched for age, sex, location, and timing of case. In addition, 6 studies used hospitalized patients as

controls, 2 studies used community controls, and 1 study had no description regarding controls. The majority of studies used clinical findings to identify case patients except for 1, which used the *ICD-10 (International and Statistical Classification of Diseases, Tenth Revision)* codes. A total of 7 studies examined cellulitis solely located on the lower limbs. The study locations included Africa (n=2), Australia (n=1), Europe (n=5), and the Middle East (n=1). Additional characteristics of included case-control studies can be found in [Table S2 in Multimedia Appendix 2](#).

**Table 1.** Characteristics of included case-control studies including study design, description of case and control groups, and odds ratios [4-12].

Source	Study design	Case group patients			Control group patients			OR <sup>a</sup> (95% CI)
		Total	Overweight, n	Obese, n	Total	Overweight, n	Obese, n	
Dupuy et al 1999 [7]	Case-control	167 patients with cellulitis (80 females and 87 males)	68	— <sup>b</sup>	294 hospital controls matched for age, sex, and hospital (140 females and 154 males)	97	—	1.39 (0.94-2.07)
Roujeau et al 2004 [12]	Case-control	243 patients with cellulitis (50:50 M/F <sup>c</sup> )	152	—	467 hospital controls matched for age, gender, hospital, and date of admission (50:50 M/F)	174	—	—
Mokni et al 2006 [9]	Case-control	114 patients with cellulitis (1.6 M/F)	64	—	208 hospital controls matched for age, sex, and hospital (79 females and 129 males)	89	—	1.71 (1.08-2.71)
Björnsdóttir et al 2005 [4]	Case-control	100 patients with cellulitis (29 females and 71 males)	37	39	200 hospital controls matched for age and sex	86	36	2.91 (1.70-5.00)
Halpern et al 2008 [8]	Case-control	150 patients with cellulitis (78 females and 72 males)	—	47	300 age and sex-matched controls (156 females and 144 males)	—	70	1.50 (0.97-2.32)
Karppelin et al 2010 [5]	Case-control	90 patients with cellulitis (32 females and 58 males)	—	37	90 community controls matched for age and sex	—	15	3.49 (1.74-7.00)
Nassaji et al 2016 [10]	Case-control	102 patients with cellulitis (38 females and 64 males)	37	20	102 community controls matched for age and gender (35 females and 67 males)	17	1	24.63 (3.24-187.45)
Njim et al 2017 [11]	Case-control	61 patients with cellulitis (40 females and 21 males)	—	27	122 hospital controls matched for age and sex (80 females and 42 males)	—	21	3.82 (1.92-7.62)
Cannon et al 2018 [6]	Case-control	36,276 patients with cellulitis	—	1192	29,062 hospital controls matched for age, sex, location (postcode), and timing of within 1 month of case	—	401	3.06 (2.73-3.43)

<sup>a</sup>OR: odds ratio.<sup>b</sup>Not applicable.<sup>c</sup>M/F: male to female sex ratio.

### Risk of Bias of Included Studies

Overall, all 9 studies were rated as low risk of bias according to the NOS. Of the 9 included case-control studies, 8 studies were listed as high risk in ascertainment of exposure. The main reason underlying a high risk in ascertainment of exposure was

that most studies did not include a description regarding how obesity status was ascertained among study participants beyond a reporting of ICD codes. In total, 7 case-control studies were listed as high risk of bias in the definition of controls because there was no description regarding the history of disease

(cellulitis). In addition, 7 of 9 included case-control studies were listed as high risk in the selection of controls due to the use of hospital controls. We rated the study by Cannon et al [6] as high risk in the adequacy of case definition because ICD diagnosis codes were used to define the case group. All other studies used clinicians to independently validate the definition of case

patients. Finally, we rated the study by Karppelin et al [5] as high risk in nonresponse rate because the respondent rate differed between the case group and control group. The risk of bias in included case-control studies is summarized in Figure 2.

Figure 2. Risk of bias of included case-control studies [4-12]. A green dot denotes low risk of bias and a red dot denotes high risk of bias.

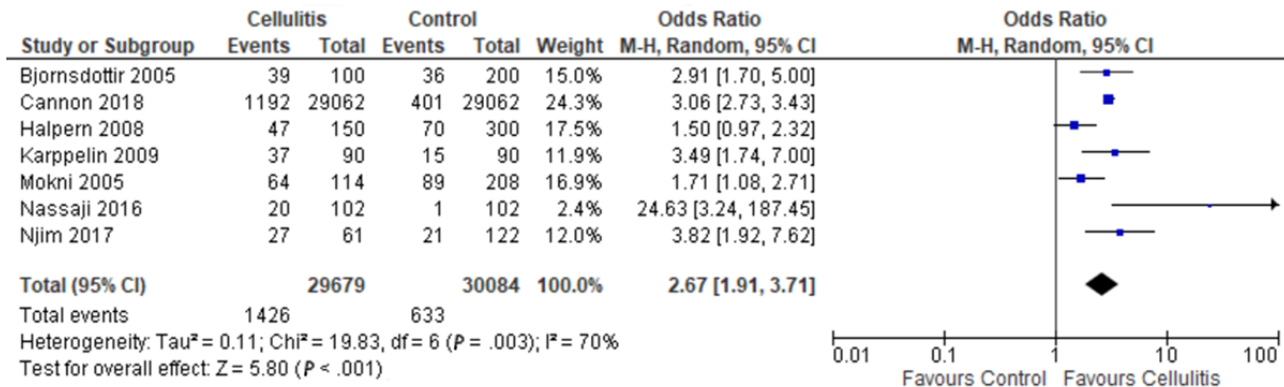
	Adequacy of case definition	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases & controls	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate
<b>BJörnsdóttir 2005</b>	+	+	-	-	+	-	+	+
<b>Cannon 2018</b>	-	+	-	-	+	+	+	+
<b>Dupuy 1999</b>	+	+	-	-	+	-	+	+
<b>Halpern 2008</b>	+	+	-	-	+	-	+	+
<b>Karppelin 2009</b>	+	+	+	+	+	-	+	-
<b>Mokni 2005</b>	+	+	-	-	+	-	+	+
<b>Nassaji 2016</b>	+	+	+	+	+	-	+	+
<b>NJlm 2017</b>	+	+	-	-	+	-	+	+
<b>Roujeau 2004</b>	+	+	-	-	+	-	+	+

### Univariate Pooled Odds Ratio of Cellulitis With Obesity

Pooling data from 7 case-control studies, our meta-analysis demonstrates a significant association between cellulitis and

obesity (pooled OR 2.67, 95% CI 1.91-3.71; Figure 3). With the exception of Halpern et al [8], 6 case-control studies showed a significant association between cellulitis and obesity. There was considerable statistical heterogeneity across all 8 studies ( $I^2=70%$ ).

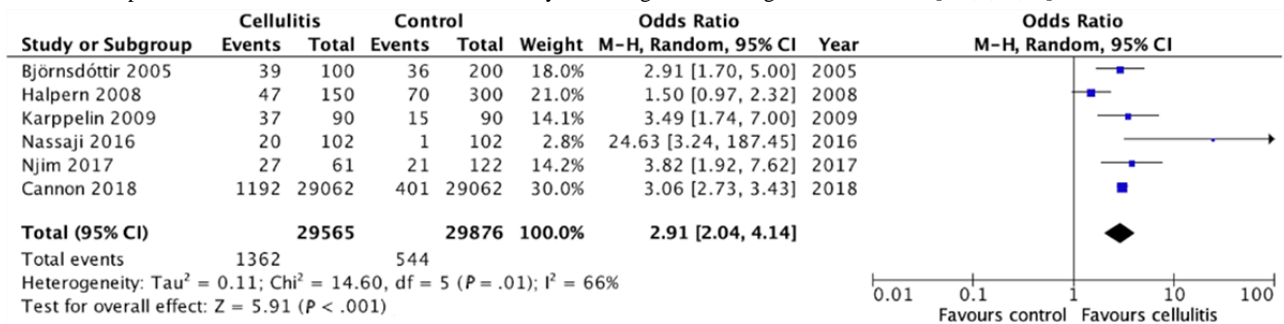
**Figure 3.** Forest plot on the association of cellulitis with obesity [4-6,8-11]. M-H: Mantel-Haenszel.



A separate meta-analysis was conducted on the 6 case-control studies that used BMI to identify patients who were overweight and obese. The study that was excluded, Mokni et al [9], used Lorentz formula (>120% of ideal body weight) to identify

patients with obesity. In this subgroup analysis, we identified increased odds of obesity in association with cellulitis (pooled OR 2.91, 95% CI 2.04-4.14; Figure 4). Substantial statistical heterogeneity was found across the 6 studies (I<sup>2</sup>=66%).

**Figure 4.** Forest plot on the association of cellulitis with obesity excluding studies using Lorentz formula [4-6,8,10,11]. M-H: Mantel-Haenszel.

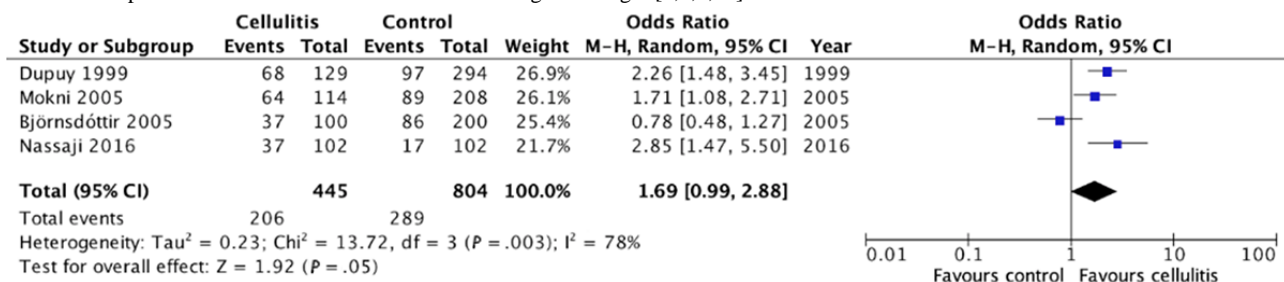


### Association of Cellulitis With Being Overweight

In total, 4 case-control studies provided data on the association between cellulitis and being overweight. Out of these 4, Björnsdóttir et al [4] was the only study that showed no association between cellulitis and being overweight while the

other 3 suggested that patients with cellulitis had an increased odds of being overweight. This meta-analysis illustrates that there is no significant association between cellulitis and being overweight (pooled OR 1.69, 95% CI 0.99-2.88; Figure 5). Across the 4 studies, substantial statistical heterogeneity was found (I<sup>2</sup>=78%).

**Figure 5.** Forest plot on the association of cellulitis with being overweight [4,7,9,10]. M-H: Mantel-Haenszel.

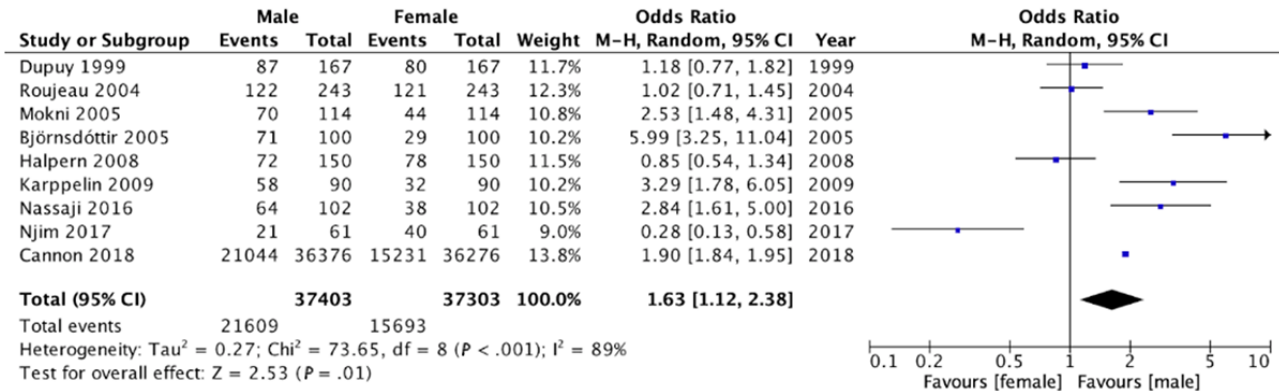


### Association of Cellulitis With Sex

We conducted a meta-analysis on 9 case-control studies that reported data on the association between cellulitis and sex. Of these, 3 case-control studies found no significant association between cellulitis and either sex, while 1 case-control study found a significant association between cellulitis and female

sex. The remaining 5 case-control studies demonstrated significantly increased odds of being male and having cellulitis. Substantial statistical heterogeneity was observed across these 9 studies (I<sup>2</sup>=89%). When data was pooled from all 9 case-control studies, there was a significant association between cellulitis and male sex (pooled OR 1.63, 95% CI 1.12-2.38; Figure 6).

Figure 6. Forest plot on the association of cellulitis with sex [4-12]. M-H: Mantel-Haenszel.



### Multivariate Analysis on the Association of Cellulitis With Obesity

In total, 6 case-control studies conducted multivariate analyses on the association between cellulitis and obesity. There was significant statistical heterogeneity across these 6 studies (I<sup>2</sup>=78%). As shown in Figure 7, the meta-analysis demonstrated

a significant association between cellulitis and obesity (pooled OR 1.91, 95% CI 1.08-3.39). When excluding studies that used the Lorentz formula, we did not observe a significant association between cellulitis and obesity on a meta-analysis of the remaining 5 studies (pooled OR 1.68, 95% CI 0.90-3.13; Figure 8). These 5 studies had high statistical heterogeneity (I<sup>2</sup>=81%).

Figure 7. Multivariate analysis on the association of cellulitis with obesity [4-6,8,9,11]. IV: instrumental variable.

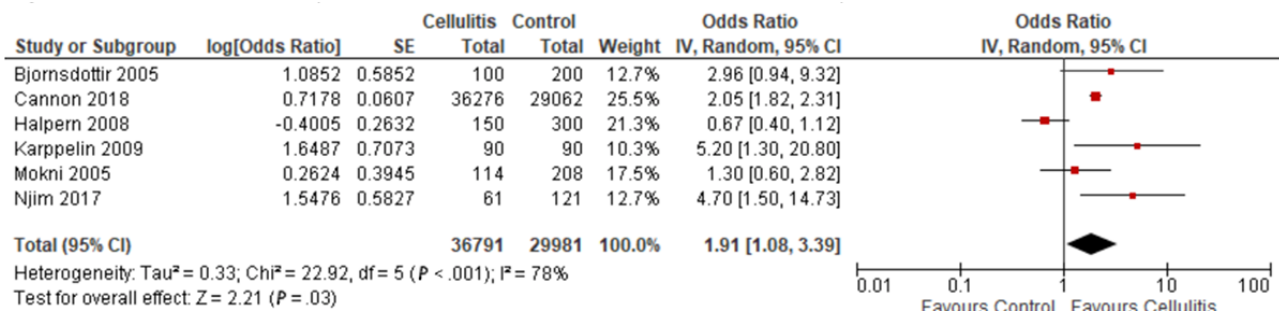
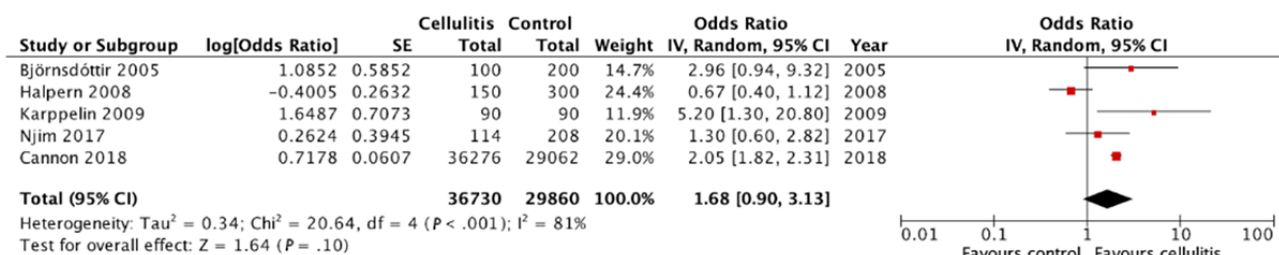


Figure 8. Multivariate analysis on the association of cellulitis with obesity excluding studies using Lorentz formula [4-6,8,11]. IV: instrumental variable.



## Discussion

### Analysis

In this study, we found that patients with cellulitis are more likely to be obese. The findings from our meta-analysis demonstrate that patients with cellulitis have 2.67-fold increased odds of being obese when compared with controls. Interestingly, our results show that there is no significant association between cellulitis and being overweight. While most studies used BMI to determine overweight and obesity status, Dupuy et al [7] and Mokni et al [9] used the Lorentz formula. When these 2 studies are excluded from the primary analysis, our findings show that patients with cellulitis are still more prone to being obese.

Finally, our analysis on the association between cellulitis and sex showed that patients with cellulitis have 1.63-fold increased odds of being male.

In accordance with the NOS, our included studies were ranked as relatively low risk of bias. Of the 9 included case-control studies, 7 studies were scored 6/9, while 2 studies were scored 7/9 and 8/9. The most common reasons for high risk of bias included use of hospitalized patients as controls, absent description regarding how obesity status was obtained, and absent history of the disease (cellulitis).

The results from our analysis on the association of cellulitis with obesity align with those observed by Quirke et al [23] in their previous systematic review. While Quirke et al [23]



included studies that exclusively analyzed patients with cellulitis of the leg, 2 of our studies included patients with cellulitis in other areas of the body, such as the upper extremities, trunk, head, face, and genitals [5,10]. Their analysis found a significant association between obesity and having nonpurulent leg cellulitis (OR 2.37, 95% CI 1.39-4.05) [26]. Our results reinforce these findings, as we observed an even stronger association of cellulitis in patients with obesity, with a pooled OR of 2.67 (95% CI 1.91-3.71).

However, our findings differ from Quirke et al [23] regarding the association between cellulitis and being overweight. Their analysis found an association of nonpurulent leg cellulitis in patients who were overweight (OR 1.87, 95% CI 1.26-2.79) while our results demonstrate no significant association between cellulitis and being overweight. This discrepancy may be attributed to our different definition of overweight. Quirke et al defined overweight as a BMI of greater than 25 kg/m<sup>2</sup>, which included patients with obesity in their analysis, and thus may skew the results toward a more positive association. In contrast, we defined overweight as a BMI between 25 and 29.9 kg/m<sup>2</sup>. Due to our narrower definition of overweight, we believe that our findings suggest a more accurate representation of the association between cellulitis and being overweight. However, it is possible that there is a greater association between nonpurulent leg cellulitis and being overweight when compared with cellulitis of other parts of the body. In addition, being overweight may not be associated with cellulitis because overweight individuals have a decreased proportion of adipose tissue compared with obese individuals. Thus, they may experience less immunosuppressive effects from adipokines released by adipose tissue and may have greater lymphatic flow compared with obese individuals [22,27]. Finally, since our study was performed 5 years after the previous analysis, it includes 3 more studies in our analysis on obesity and also includes pooled multivariate and univariate data.

In addition to investigating the association between cellulitis and obesity, we explored certain risk factors that may contribute to the development of cellulitis. One of these factors is having a positive history of cellulitis. Several studies reported this finding. Overall, 183 patients of 685 (26%) with cellulitis had a previous history of cellulitis [4,5,8,10-12]. Karpelin et al [5] also performed an analysis of risk factors between patients with and without a history of cellulitis. They found that patients with a positive history of cellulitis were more likely to have had a previous operation and were likely to stay in the hospital longer than those without a previous history of cellulitis [5]. These patients were also found to have a greater inflammatory response than patients without a history of cellulitis, as demonstrated by a higher peak C-reactive protein level, higher peak leukocyte count, and longer duration of fever after hospital admission.

Some studies also reported on the dermatophytes and bacteria found in interdigital spaces in patients with cellulitis [4,9,11,12]. In cases with foot dermatomycosis, *Trichophyton rubrum* was the most common, followed by *Trichophyton mentagrophytes* and *Epidermophyton floccosum*. In swabs of toe-web spaces with bacteriological culture, beta-hemolytic streptococci and staphylococci were commonly found, while few gram-negative bacilli were identified. Björnsdóttir et al [4] reported that the

presence of *Staphylococcus aureus* or beta-hemolytic streptococci in the toe webs was strongly associated with cellulitis. When removing the presence of bacteria from their multivariate model, they found that toe-web dermatophytosis was also strongly associated with cellulitis [4].

Interestingly, some studies described a relationship between cellulitis and patient ethnicity. Halpern et al [8] suggested that patients of White ethnicity are at higher risk of developing cellulitis compared with Asian or Afro-Caribbean patients. In addition, Cannon et al [6] found that Indigenous Australians were more likely than non-Indigenous Australians to develop cellulitis. Explanations for these observed differences are largely speculative, as currently there is little research done in this area. Previous studies have identified that the structure and function of darker skin have properties that may serve as a barrier to bacterial entry, which can influence the risk of developing cellulitis. These properties include greater transepidermal water loss, a greater spontaneous desquamation rate, a lower pH, greater variation in blood vessel reactivity, larger mast cell granules, differences in melanin content and melanosome dispersion, hair structure, fibroblast size, and a more compact stratum corneum, which has greater strength to chemical and mechanical challenges [27-30]. Studies carried out in the United Kingdom have also shown that patients of Caribbean and Asian descent are more likely to seek care from primary care physicians, which may lead to earlier identification and treatment of cellulitis [31-33].

Erysipelas is another acute skin infection, commonly caused by beta-hemolytic group A streptococci, and is often referred to as a superficial type of cellulitis. It affects the upper layer of the skin and is characterized by a warm, slightly painful erythema with a well-demarcated margin, along with an acute systemic response such as fever [34,35]. In contrast, cellulitis is thought to affect the deep dermis and subcutaneous tissue. Erysipelas and cellulitis were historically differentiated because they were thought to be caused by different bacteria; however, a growing body of literature has suggested that they overlap in etiology [34]. Thus, we conducted a review of 5 case series and 1 case-control study which explored the incidence of high BMI in patients with erysipelas. In total, there were 2019 patients with erysipelas, of which 487 (24.1%) were overweight or obese [34-40].

The link between obesity and developing skin infections has been investigated in previous cohort studies [36,41,42]. Among Danish blood donors, Kaspersen et al [36] found that obese men were at a 2-fold increased risk of developing skin and subcutaneous tissue infections. In contrast, Harpsøe et al [41] found that overweight and obese women were at an increased risk of skin and subcutaneous tissue infections. In particular, obese women had a 5-fold increased risk of developing erysipelas. Similarly, a Korean cohort study conducted by Cheong et al [42] demonstrated an increased risk of cellulitis and cellulitis-related hospitalization in metabolically healthy and unhealthy obese men and women. However, it is important to note that Kaspersen et al [36], Harpsøe et al [41], and Cheong et al [42] used select individuals in their cohorts (healthy Danish blood donors, Danish women of reproductive age, and healthy, young, and middle-aged educated Koreans, respectively). Thus,

the findings may not be generalizable to other populations. Nevertheless, these results suggest that adiposity itself may be an important contributor to the development of skin infections.

Currently, the pathogenesis underlying the association between obesity and cellulitis is unclear. However, several mechanisms have been proposed to explain the relationship between increased BMI and infection. One possible mechanism involves the effect of excess adipose tissue on the immune system. It is suggested that obesity disrupts the balance between existing adipocytes and immune cells through adipocyte secretion of various adipokines, such as adiponectin and leptin [20-22]. This dysregulation results in impaired macrophage differentiation, chemotaxis, and immune response, all of which may predispose an obese individual to being more susceptible to infections [27]. Obesity may also impair the immune system by contributing to leptin resistance. Leptin plays an important role in regulating immune function through proper signaling in the central nervous system [43,44]. Thus, obese individuals may be more vulnerable to infections because of decreased leptin signaling. Another mechanism provides a more anatomical perspective, citing that the increased skin folds present in obese individuals contribute to decreased blood perfusion of peripheral tissues, thereby increasing the likelihood of abscesses and skin infections [36]. Patient behavior, specifically physical exercise, can play a role in decreasing both body adiposity and hormonal dysregulation, factors that are implicated in the development of cellulitis. Previous studies have shown that exercise that engages both the cardiovascular and the musculoskeletal systems improves anthropometric and body composition, as seen by a decrease in BMI, body fat, and fat-free mass [45]. Recommendation of multicomponent exercise to obese adults can therefore be used as an additional intervention to potentially decrease the likelihood of developing cellulitis.

## Limitations

Our study has several limitations. First, none of our included studies were conducted in Asia or North or South America. Thus, the findings from our meta-analysis may not be generalizable to different ethnic populations, or individuals living in those areas. Second, we were unable to find cohort studies that provided the appropriate data on the association between cellulitis and obesity. More cohort studies are warranted in this area to assess the risk of developing cellulitis in patients who are obese more comprehensively. Finally, the majority of our included studies included hospitalized patients for the case group, control group, or both. The use of hospitalized patients may introduce selection bias, as these patients tend to have more severe sickness, more comorbidities, and older age [5]. Furthermore, community-based studies are needed to investigate cellulitis treated in outpatient settings, as these findings may be more applicable to the general public.

## Future Areas of Research

Future research should be conducted in Asia and North and South America. Given the increased prevalence of obesity in the United States compared with other regions of the world, it would be interesting to explore how studies in the United States may influence the strength of the association between cellulitis and obesity. In addition, it would be beneficial to incorporate cohort studies into future analyses, to strengthen the definitive relationship between cellulitis and obesity. Finally, as cellulitis is also commonly seen in outpatient clinics and in the emergency department, research should focus on the association of cellulitis and obesity in patients from more diverse clinical practices.

## Conclusions

We found that cellulitis is associated with obesity but not with being overweight. Given that the prevalence of obesity continues to increase globally, emphasis on maintaining a healthy BMI may be indicated for patients presenting with cellulitis.

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KGT was affiliated with the Renaissance School of Medicine and Stony Brook University at the time of the study and is currently affiliated with the Mayo Clinic School of Graduate Medical Education.

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## Conflicts of Interest

None declared.

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### Multimedia Appendix 1

Supplementary tables illustrating search strategy and additional characteristics of included studies.

[DOCX File, 26 KB - [derma\\_v7i1e54302\\_app1.docx](#) ]

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### Multimedia Appendix 2

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

[DOCX File, 31 KB - [derma\\_v7i1e54302\\_app2.docx](#) ]

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## Abbreviations

**ICD-10:** International and Statistical Classification of Diseases, Tenth Revision

**NOS:** Newcastle-Ottawa scale

**OR:** odds ratio

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



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Research Letter

# From the Cochrane Library: Leukotriene Receptor Antagonists for Eczema

Lauren Marie Toledo<sup>1</sup>, BS; Ramiro Rodriguez<sup>2</sup>, MD; Torunn E Sivesind<sup>2</sup>, MD; Efstratios Vakirlis<sup>3</sup>, MD, PhD; Reiji Kojima<sup>4</sup>, MD, PhD; Robert P Dellavalle<sup>5,6</sup>, MSPH, MD, PhD

<sup>1</sup>Lake Erie College of Osteopathic Medicine, Bradenton, FL, United States

<sup>2</sup>University of Colorado Anschutz Medical Campus, Aurora, CO, United States

<sup>3</sup>Department of Dermatology and Venereology, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

<sup>4</sup>Department of Health Sciences, School of Medicine, University of Yamanashi, Yamanashi, Japan

<sup>5</sup>University of Colorado School of Medicine, Aurora, CO, United States

<sup>6</sup>Rocky Mountain Regional VA Medical Center, Aurora, CO, United States

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD  
University of Colorado School of Medicine  
1700 N Wheeling St  
Rm E1-342  
Aurora, CO, 80045  
United States  
Phone: 1 720 857 5562  
Fax: 1 720 723 7877  
Email: [robert.dellavalle@gmail.com](mailto:robert.dellavalle@gmail.com)

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**KEYWORDS**

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## 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

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## 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.

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## Abbreviations

**AD:** atopic dermatitis

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

**LTRA:** leukotriene receptor antagonist

**RCT:** randomized controlled trial

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Research Letter

# From the Cochrane Library: Interventions for Chronic Pruritus of Unknown Origin

Pritika Parmar<sup>1</sup>, BA, BS; Amit Singal<sup>2</sup>, BA; Mindy D Szeto<sup>1</sup>, MS; Gaurav N Pathak<sup>3</sup>, PharmD; Viktoria Taranto<sup>4</sup>, MD; Thu M Truong<sup>2,3</sup>, PharmD; Babar Rao<sup>3,5</sup>, MD; Andrea Andrade Miranda<sup>6</sup>, MD; Juan VA Franco<sup>7</sup>, MD, MSc, PhD; Robert P Dellavalle<sup>1</sup>, MSPH, MD, PhD

<sup>1</sup>Department of Dermatology, University of Minnesota Medical School, Minneapolis, MN, United States

<sup>2</sup>Rutgers New Jersey Medical School, Newark, NJ, United States

<sup>3</sup>Department of Dermatology, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, United States

<sup>4</sup>New York Institute of Technology College of Osteopathic Medicine, Glen Head, NY, United States

<sup>5</sup>Department of Dermatology, Weill Cornell Medicine, New York, NY, United States

<sup>6</sup>Department of Dermatology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

<sup>7</sup>Institute of General Practice, Heinrich Heine University, Düsseldorf, Germany

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Department of Dermatology

University of Minnesota Medical School

Phillips-Wangensteen Building, 516 Delaware St SE Suite 1-400

Minneapolis, MN, 55455

United States

Phone: 1 612 625 8625

Email: [della056@umn.edu](mailto:della056@umn.edu)

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Cochrane; systematic review; randomized controlled trial; RCT; pruritus; chronic pruritus; chronic pruritus of unknown origin; CPUO; serlopitant; dupilumab; pregabalin

## Introduction

Chronic pruritus of unknown origin (CPUO) is characterized by pruritus lasting longer than 6 weeks and is a diagnosis of exclusion with no identifiable cause; the estimated prevalence ranges between 7% and 45.9% and is the highest in the older population [1]. Affected individuals experience a significant disruption to quality of life, including sleep disturbances and psychological concerns, which can further contribute to itching [2]. Treatment of patients with CPUO is particularly challenging due to its unclear pathophysiology [3]. No Food and Drug Administration–approved treatment for CPUO currently exists. First-line treatment can consist of antihistamines and topical steroids; unfortunately, treatments for CPUO show only variable responsiveness [4]. Research on interventions for CPUO is sparse, including assessments of safety and efficacy. A Cochrane systematic review, “Interventions for chronic pruritus of unknown origin,” assessed interventions for CPUO in adults and children by examining the available evidence from randomized controlled trials (RCTs) and quasi-RCTs for the efficacy of CPUO interventions [2].

## Methods

A total of 7148 records published up to July 2019 were obtained in a literature search with only 1 eligible RCT meeting the Cochrane review’s inclusion criteria based on participant population, study design, and interventions [2]. The included multicenter RCT’s participants (N=257) had a 6-week minimum complaint of pruritus unresponsive to first-line treatment and ≥7 cm on the visual analog scale (VAS) at baseline, which is considered to indicate a severe case of chronic pruritus. The RCT’s exclusion criteria were based on serum creatinine, aspartate aminotransferase, or alanine aminotransferase levels >2 times the upper limit of the reference range or previous diagnoses suggestive of secondary pruritus causes. The RCT quantified the therapeutic impact (via percentage change in VAS) of 3 different dosing levels of serlopitant, a novel neurokinin 1 (NK1) receptor antagonist that acts to inhibit the NK1-mediated itch signaling pathway. The primary endpoints of the included RCT were evaluation of VAS itch severity and adverse events. Secondary endpoints considered by the Cochrane search included health-related quality of life, sleep disturbances, depression, and patient satisfaction. The GRADE (Grading of



Recommendations, Assessment, Development, and Evaluations) approach was applied to interpret the certainty of the RCT findings [5].

## Results

The primary and secondary outcomes of the RCT are summarized in Table 1.

Compared to placebo, patients who received 5 mg serlopitant orally once daily for 6 weeks showed significant improvements

in VAS (relative risk [RR] 2.06, 95% CI 1.27-3.35) and reduced patient-reported numerical rating scale (NRS) itch intensity (mean difference -10.30, 95% CI -20.01 to -0.59); the number needed to treat was approximately 4. The potential for an increased risk of adverse events was unclear (RR 1.48, 95% CI 0.87-2.50). According to the GRADE assessment, the certainty of the evidence was low to very low, with risk-of-bias concerns due to missing outcome data and presence of potential underlying diagnoses in many RCT participants. Depression and patient satisfaction were not addressed in this RCT.

**Table 1.** Primary and secondary endpoint findings compared to placebo in a randomized controlled trial evaluating different doses of serlopitant for chronic pruritus.

Serlopitant dose <sup>a</sup>	Primary endpoints		Secondary endpoints	
	Reduction ( $\geq 4$ cm) in VAS <sup>b</sup> , RR <sup>c</sup> (95% CI)	Adverse events <sup>d</sup> , RR (95% CI)	Quality of life <sup>e</sup> , MD <sup>f</sup> (95% CI)	Sleep disturbance <sup>g</sup> , RR (95% CI)
0.25 mg (N=64)	1.66 (1.00 to 2.77), n=127 <sup>h</sup>	1.29 (0.75 to 2.24), n=127	-5.70 (-13.18 to 1.78), n=127	0.60 (0.31 to 1.17), n=127
1 mg (N=65)	1.50 (0.89 to 2.54), n=126	1.45 (0.86 to 2.47), n=128	-6.90 (-14.38 to 0.58), n=128	0.38 (0.17 to 0.84), n=128
5 mg (N=64)	2.06 (1.27 to 3.35), n=126	1.48 (0.87 to 2.50), n=127	-4.20 (-11.68 to 3.28), n=127	0.49 (0.24 to 1.01), n=128

<sup>a</sup>All doses (including the placebo) were administered orally once a day for 6 weeks.

<sup>b</sup>VAS: visual analog scale (range 0-10 cm).

<sup>c</sup>RR: relative risk.

<sup>d</sup>Adverse events were defined as the number of participants with any adverse event.

<sup>e</sup>Health-related quality of life was assessed with the Dermatology Life Quality Index score (range 0-30). A higher score indicates greater impairment" so it's clear these are quality of life improvements.

<sup>f</sup>MD: mean difference.

<sup>g</sup>Sleep disturbances were defined as the number of participants with insomnia (assessed with the Pittsburgh Sleep Symptom Questionnaire).

<sup>h</sup>n=total number of participants included in the analysis (placebo+serlopitant groups).

## Discussion

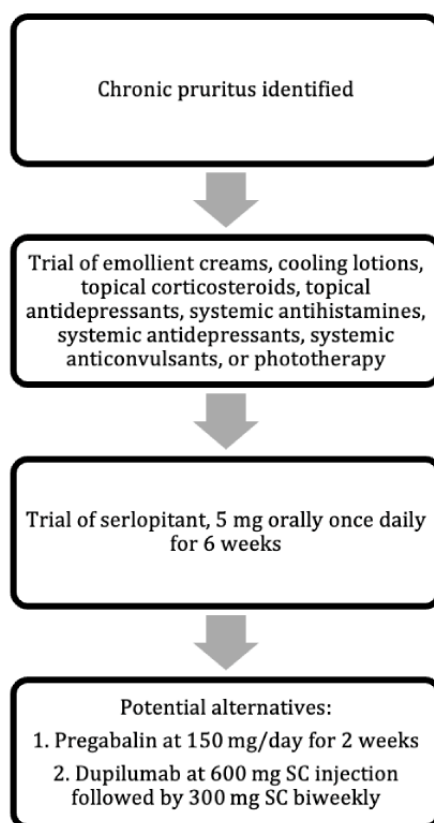
Findings from smaller-scale studies conducted after publication of the Cochrane review suggest that new therapeutic approaches, including pregabalin and dupilumab, may be more effective at reducing VAS and NRS scores in patients with treatment-resistant CPUO [3,4]. Pregabalin is considered to alleviate CPUO through modulating thresholds of the C-fibers shown to transmit itch signals by suppressing the release of several neurotransmitters such as substance P, which may be chronically elevated in patients with CPUO [4]. Dupilumab, which can inhibit interleukin (IL)-4 and IL-13, with well-known anti-inflammatory properties, may help to alleviate CPUO through cytokine-neural interactions [3]. Pregabalin decreased VAS scores for 70% of patients with CPUO refractory to antihistamine therapy [4]. Likewise, treatment with dupilumab resulted in a substantial mean decrease in the NRS itch score by 7 [3]. These findings suggest potential alternative treatment approaches for patients who have treatment-refractory CPUO, which remains a diagnosis of exclusion with unclear etiology. Current treatments, including emollient creams, cooling lotions,

topical corticosteroids, topical antidepressants, systemic antihistamines, systemic antidepressants, systemic anticonvulsants, and phototherapy, lack extensive study, especially in RCTs [2].

Taken together, these studies suggest that after current treatment approaches fail, serlopitant (5 mg orally once daily for 6 weeks), pregabalin (150 mg daily for 2 weeks), or dupilumab (600 mg subcutaneous injection followed by 300 mg subcutaneous injection biweekly) are potential treatment options for CPUO (Figure 1).

Poorly understood pruritic cutaneous manifestations related to COVID-19, along with the frequent handwashing, personal protective equipment use, and psychosocial stress during the pandemic, have presented difficulties in determining the root causes of itch in many patients, likely exacerbated by reduced access to health care and a heightened fear of infection [6]. Postpandemic recovery may require further research to reconsider ideal CPUO management approaches given interruptions to care; ultimately, additional investigation is needed to characterize the various molecular underpinnings of CPUO and may aid in more effective and targeted therapeutics.

**Figure 1.** Practical algorithmic treatment options once chronic pruritus is identified in a patient based on current treatment approaches and recent studies. SC: subcutaneous.



### Conflicts of Interest

RPD is a Joint Coordinating Editor for Cochrane Skin, a dermatology section editor for UpToDate, a Social Media Editor for the Journal of the American Academy of Dermatology (JAAD), a Podcast Editor for the Journal of Investigative Dermatology (JID), Editor-in-Chief of JMIR Dermatology, and is a coordinating editor representative on the Cochrane Council. RPD receives editorial stipends (JAAD, JID), royalties (UpToDate), and expense reimbursement from Cochrane Skin. The other authors have no conflicts to declare.

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## Abbreviations

**CPUO:** chronic pruritus of unknown origin

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

**IL:** interleukin

**NK1:** neurokinin 1

**NRS:** numerical rating scale

**RCT:** randomized controlled trial

**RR:** relative risk

**VAS:** visual analog scale

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Research Letter

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

Emily Eachus<sup>1\*</sup>, BSc; Kayla Schwartz<sup>1\*</sup>, BSc; Taha Rasul<sup>1</sup>, MD; Daniel Bergholz<sup>1</sup>, MD; Jonette Keri<sup>1</sup>, MD, PhD; Armen Henderson<sup>1</sup>, MD

Miami Street Medicine, University of Miami Miller School of Medicine, Miami, FL, United States

\* these authors contributed equally

**Corresponding Author:**

Emily Eachus, BSc  
Miami Street Medicine  
University of Miami Miller School of Medicine  
Suite 1149  
1600 NW 10th Avenue  
Miami, FL, 33136  
United States  
Phone: 1 954 610 8779  
Email: [eachus@med.miami.edu](mailto:eachus@med.miami.edu)

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**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.

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.

## 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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## Abbreviations

**EMR:** electronic medical record

**MSM:** Miami Street Medicine

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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

Gaurav Nitin Pathak<sup>1</sup>, PharmD; Thu Minh Truong<sup>1,2</sup>, PharmD; Amit Singal<sup>2</sup>, BA; Viktoria Taranto<sup>3</sup>, MD; Babar K Rao<sup>1,4</sup>, MD; Audrey A Jacobsen<sup>5,6,7</sup>, MD, MPH

<sup>1</sup>Department of Dermatology, Rutgers Robert Wood Johnson Medical School, Somerset, NJ, United States

<sup>2</sup>Department of Dermatology, Rutgers New Jersey Medical School, Newark, NJ, United States

<sup>3</sup>Department of Dermatology, New York Institute of Technology, Glenhead, NY, United States

<sup>4</sup>Department of Dermatology, Rao Dermatology, Atlantic Highlands, NJ, United States

<sup>5</sup>Department of Dermatology, Hennepin Healthcare, Minneapolis, MN, United States

<sup>6</sup>Department of Dermatology, University of Minnesota, Minneapolis, MN, United States

<sup>7</sup>Department of Dermatology, Veterans Affairs Medical Center, Minneapolis, MN, United States

**Corresponding Author:**

Gaurav Nitin Pathak, PharmD

Department of Dermatology

Rutgers Robert Wood Johnson Medical School

1 World's Fair Drive

Somerset, NJ, 08873

United States

Phone: 1 732235 9895

Email: [gnp28@rwjms.rutgers.edu](mailto:gnp28@rwjms.rutgers.edu)

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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



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Research Letter

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

Winnie Fan<sup>1\*</sup>, BS; Gunnar Mattson<sup>1\*</sup>, BS, MPH; Amanda Twigg<sup>1,2</sup>, MD

<sup>1</sup>Department of Dermatology, School of Medicine, University of California San Francisco, San Francisco, CA, United States

<sup>2</sup>Department of Dermatology, San Francisco Veterans Affairs Health Care System, San Francisco, CA, United States

\*these authors contributed equally

**Corresponding Author:**

Amanda Twigg, MD

Department of Dermatology

School of Medicine

University of California San Francisco

1701 Divisadero St

3rd Floor

San Francisco, CA, 94115

United States

Phone: 1 415 353 7800

Email: [amanda.twigg@ucsf.edu](mailto:amanda.twigg@ucsf.edu)

## 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.

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**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

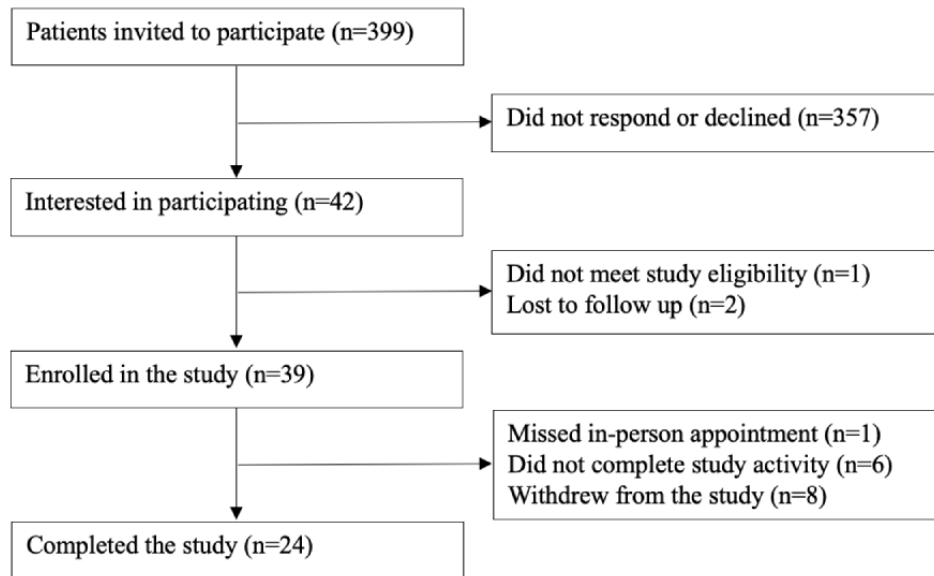
## Introduction

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.

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### 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

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Research Letter

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

Marco Costanza<sup>1</sup>, BS; Jeffrey Sobieraj<sup>1</sup>, MD; Frank Wang<sup>1,2</sup>, MD

<sup>1</sup>University of Michigan Medical School, Ann Arbor, MI, United States

<sup>2</sup>Department of Dermatology, Michigan Medicine, University of Michigan, Ann Arbor, MI, United States

**Corresponding Author:**

Frank Wang, MD

Department of Dermatology

Michigan Medicine

University of Michigan

1500 E Medical Center Drive

Ann Arbor, MI, 48109

United States

Phone: 1 734 936 4054

Email: [fawang@med.umich.edu](mailto:fawang@med.umich.edu)

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**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).

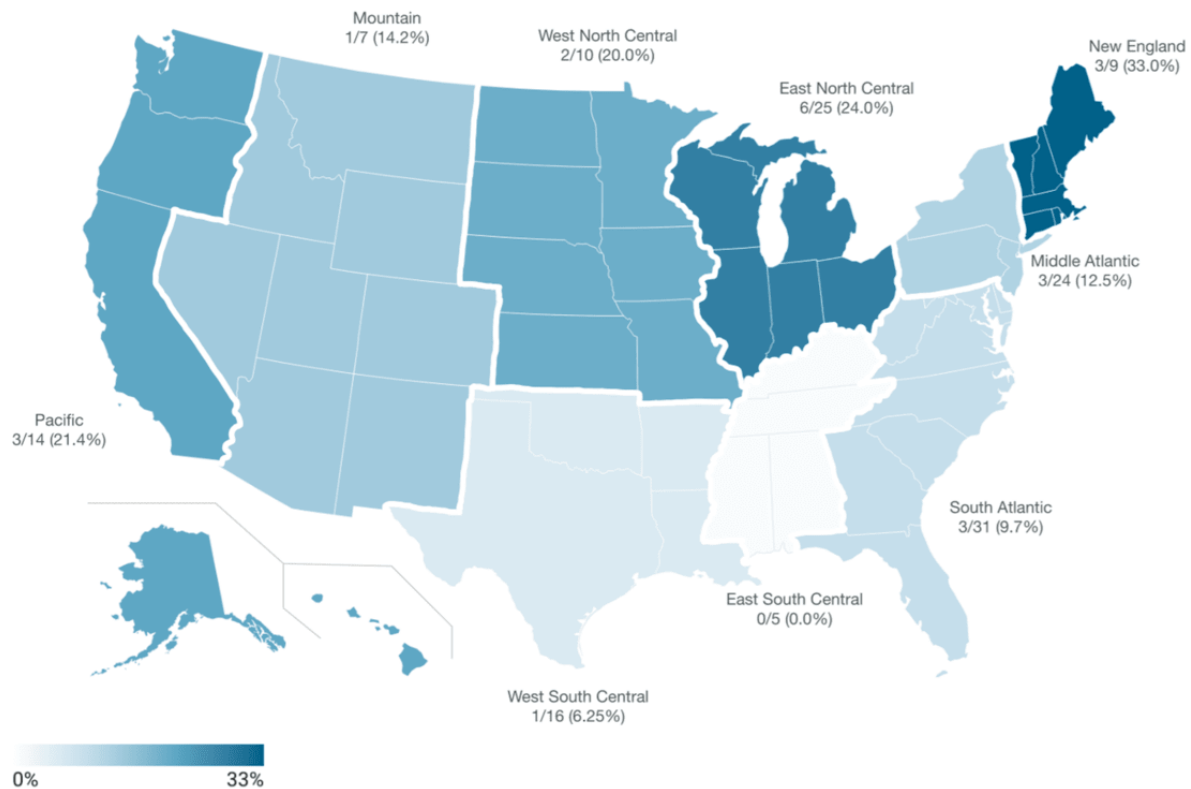
**Table 1.** US dermatology residency programs mentioning involvement in gender-affirming care (GAC).

	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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## Research Letter

# Risk Factors Associated With Burden of Disease of Psoriasis From 1990 to 2019: Epidemiological Analysis

Vishnutheertha Kulkarni<sup>1</sup>, MS; David Liu<sup>2</sup>, MS; Vahram Gamsarian<sup>3</sup>, BE; Tjinder Grewal<sup>1</sup>, BS; Torunn Sivesind<sup>4</sup>, MD

<sup>1</sup>University of Queensland, Woolongabba, Australia

<sup>2</sup>University of Toledo, Toledo, OH, United States

<sup>3</sup>University of Michigan Medical School, Ann Arbor, MI, United States

<sup>4</sup>Department of Dermatology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

**Corresponding Author:**

Vishnutheertha Kulkarni, MS

University of Queensland

The University of Queensland Diamantina Institute Level 5, West Wing, Translational Research Institute

37 Kent Street

Woolongabba, 4102

Australia

Phone: 61 7 3443 7399

Email: [vishnutheertha96@gmail.com](mailto:vishnutheertha96@gmail.com)

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**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.

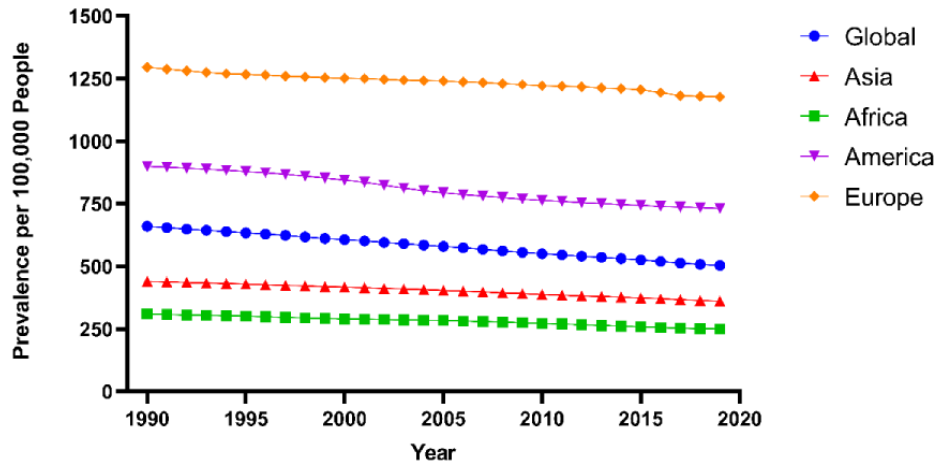
## Results

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

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### Abbreviations

**GBD:** Global Burden of Disease

**SDI:** sociodemographic index

**YLD:** years lost to disability

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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

Colleen M Klein<sup>1</sup>, BA; Torunn E Sivesind<sup>2</sup>, MD; Robert P Dellavalle<sup>2</sup>, MSPH, MD, PhD

<sup>1</sup>Austin Skin Physicians, Austin, TX, United States

<sup>2</sup>Department of Dermatology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Department of Dermatology

University of Colorado Anschutz Medical Campus

Rocky Mountain Regional VA Medical Center

1700 N Wheeling St, Rm E1-342

Aurora, CO, 80045

United States

Phone: 1 720 857 5562

Email: [robert.dellavalle@cuanschutz.edu](mailto:robert.dellavalle@cuanschutz.edu)

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**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 positive, n	False negative, n	False positive, n	True negative, n	True positive, n	False negative, n	False positive, n	True negative, 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

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 12, DOI: 10.1002/14651858.CD011901.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

**BCC:** basal cell carcinoma

**CNN:** convolutional neural network

**KC:** keratinocyte carcinoma

**SROC:** summary receiver operating characteristic

**VI:** visual inspection

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Research Letter

# Does Male Skin Care Content on Instagram Neglect Skin Cancer Prevention?

Alexa Carboni<sup>1</sup>, BS; Olnita Martini<sup>1</sup>, MS; Jessica Kirk<sup>1</sup>, BS; Nathaniel A Marroquin<sup>1</sup>, BS; Corinne Ricci<sup>1</sup>, BS; Melissa Cheng<sup>2</sup>, BS; Mindy D Szeto<sup>3</sup>, MS; Kayd J Pulsipher<sup>4</sup>, DO; Robert P Dellavalle<sup>3,5,6</sup>, MSPH, MD, PhD

<sup>1</sup>College of Osteopathic Medicine, Rocky Vista University, Greenwood Village, CO, United States

<sup>2</sup>Western University of Health Sciences College of Osteopathic Medicine of the Pacific, Pomona, CA, United States

<sup>3</sup>Department of Dermatology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

<sup>4</sup>Department of Dermatology, Campbell University at Sampson Regional Medical Center, Wilmington, NC, United States

<sup>5</sup>Dermatology Service, US Department of Veterans Affairs Rocky Mountain Regional Medical Center, Aurora, CO, United States

<sup>6</sup>Colorado School of Public Health, Aurora, CO, United States

**Corresponding Author:**

Nathaniel A Marroquin, BS

College of Osteopathic Medicine

Rocky Vista University

8401 S Chambers Rd

Greenwood Village, CO, 80112

United States

Phone: 1 3033732008

Email: [Nathaniel.Marroquin@rvu.edu](mailto:Nathaniel.Marroquin@rvu.edu)

## 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.

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**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	#maleskincareproducts 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 educational 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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Research Letter

# Inequities in Technology Access and Digital Health Literacy Among Patients With Dermatologic Conditions: Cross-Sectional Analysis of the National Health Interview Survey

Danny Linggonegoro<sup>1,2</sup>, MD; Kathryn Williams<sup>3</sup>, MS; Madeline Hlobik<sup>1</sup>, BS; Jennifer Huang<sup>1,4</sup>, MD

<sup>1</sup>Dermatology Section, Division of Immunology, Boston Children's Hospital, Boston, MA, United States

<sup>2</sup>Harvard Medical School, Boston, MA, United States

<sup>3</sup>Biostatistics and Research Design Center, ICCTR, Boston Children's Hospital, Boston, MA, United States

<sup>4</sup>Department of Dermatology, Harvard Medical School, Boston, MA, United States

**Corresponding Author:**

Jennifer Huang, MD

Dermatology Section

Division of Immunology

Boston Children's Hospital

300 Longwood Avenue

Boston, MA, 02115

United States

Phone: 1 6173556117

Email: [jennifer.huang@childrens.harvard.edu](mailto:jennifer.huang@childrens.harvard.edu)

## Abstract

Certain sociodemographic factors are associated with low technology access and digital healthy literacy.

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**KEYWORDS**

tele dermatology; 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 tele dermatology 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

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Research Letter

# A Survey of Demographics and Treatments in Melanoma Case Reports: Retrospective Bibliometric Analysis

Ross O'Hagan<sup>1,2</sup>, MD; Jessie Ngandjui<sup>2</sup>, BS; Benjamin Ungar<sup>1</sup>, MD; Jonathan Ungar<sup>1</sup>, MD; Nicholas Gulati<sup>1</sup>, MD, PhD

<sup>1</sup>Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, United States

<sup>2</sup>Department of Medical Education, Garnet Health, Middletown, NY, United States

**Corresponding Author:**

Nicholas Gulati, MD, PhD

Department of Dermatology

Icahn School of Medicine at Mount Sinai

5 East 98th St, 5th floor

New York, NY, 10029

United States

Phone: 1 212 241 9728

Email: [nicholas.gulati@mssm.edu](mailto:nicholas.gulati@mssm.edu)

## Abstract

Melanoma case reports show variations in treatment by age and sex.

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**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

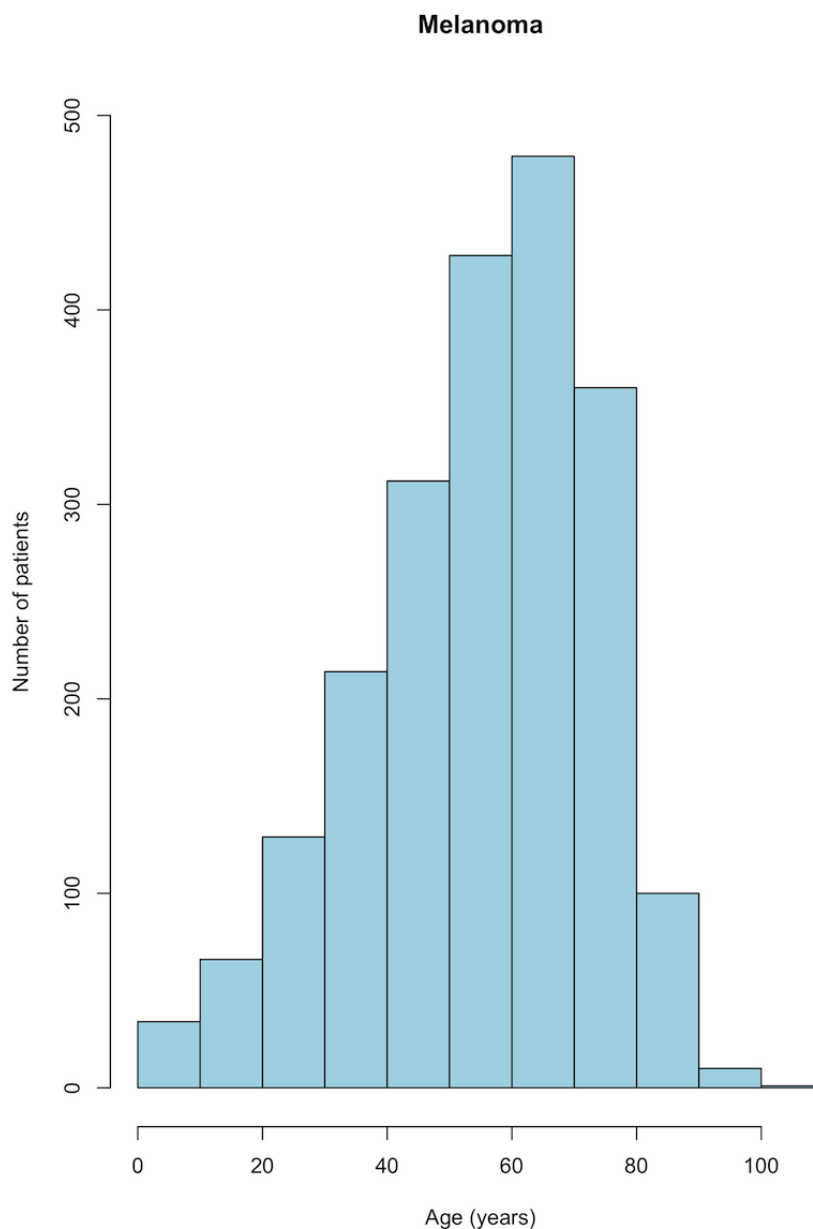
To explore the demographics of patients in PubMed-listed case reports, we used techniques previously described [1,4]. Patients

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

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Research Letter

# Geographic Disparities in Online Searches for Psoriasis Biologics in the United States: Google Trends Analysis

Annie Chang<sup>1</sup>, MS; Ross O'Hagan<sup>1</sup>, MD; Jade N Young<sup>1</sup>, MD; Nancy Wei<sup>1</sup>, MD; Nicholas Gulati<sup>1</sup>, MD, PhD

Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, United States

**Corresponding Author:**

Nicholas Gulati, MD, PhD

Department of Dermatology

Icahn School of Medicine at Mount Sinai

5 East 98th St, 5th Floor

New York, NY, 10029

United States

Phone: 1 212 241 9728

Email: [nicholas.gulati@mssm.edu](mailto:nicholas.gulati@mssm.edu)

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**KEYWORDS**

psoriasis; biologics; health disparities; Google Trends; online search; web-based search; USA; United States; Google; awareness; skin; patient awareness; psoriasis treatment; US; psoriasis medication; patient education

## Introduction

Twelve biologics targeting cytokines TNF- $\alpha$  (tumor necrosis factor alpha), IL-12/23 (interleukin 12/23), IL-17 (interleukin 17), and IL-23 (interleukin 23) have been approved for the treatment of moderate to severe psoriasis in the United States, including most recently bimekizumab in October 2023 [1,2]. In this study, we used publicly available Google Trends data to monitor search volumes for psoriasis biologics, a methodology that has been used in prior studies [3,4].

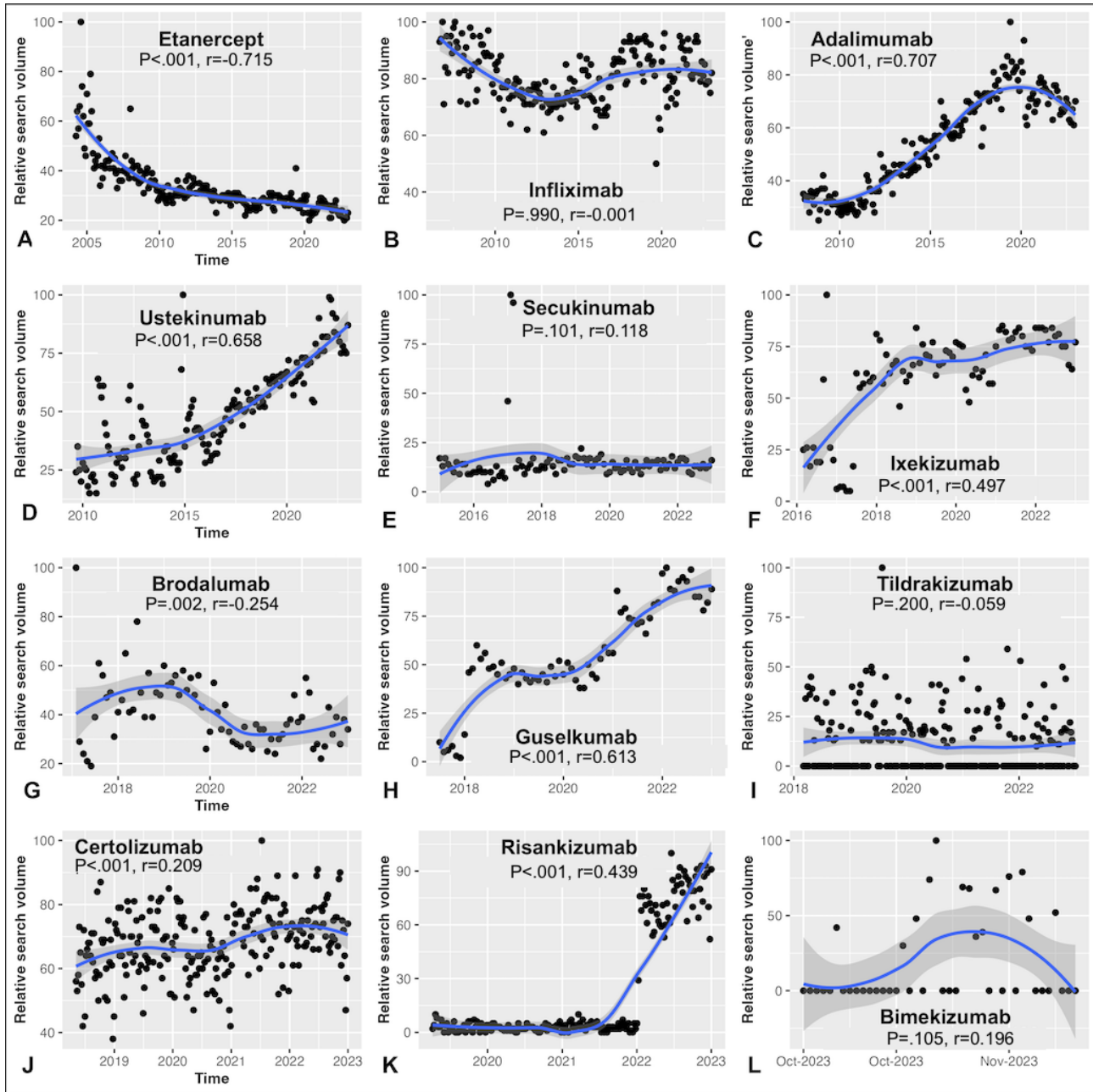
## Methods

All 12 US Food and Drug Administration (FDA)-approved psoriasis biologics were included in our analysis. We examined temporal search volume data from each biologic's approval date for plaque psoriasis until November 1, 2023, and geographic search volume data over the past 12 months (November 2022 to November 2023). Search volume was indicated by a relative search volume (RSV) index, scaling from 0 (no searches for that medication) to 100 (peak search volume for that medication). This index is calibrated in relation to each state's total search volume within the United States and specified time range. Trend analysis was conducted using the Mann-Kendall test in R software (version 4.3.1; The R Foundation).

## Results

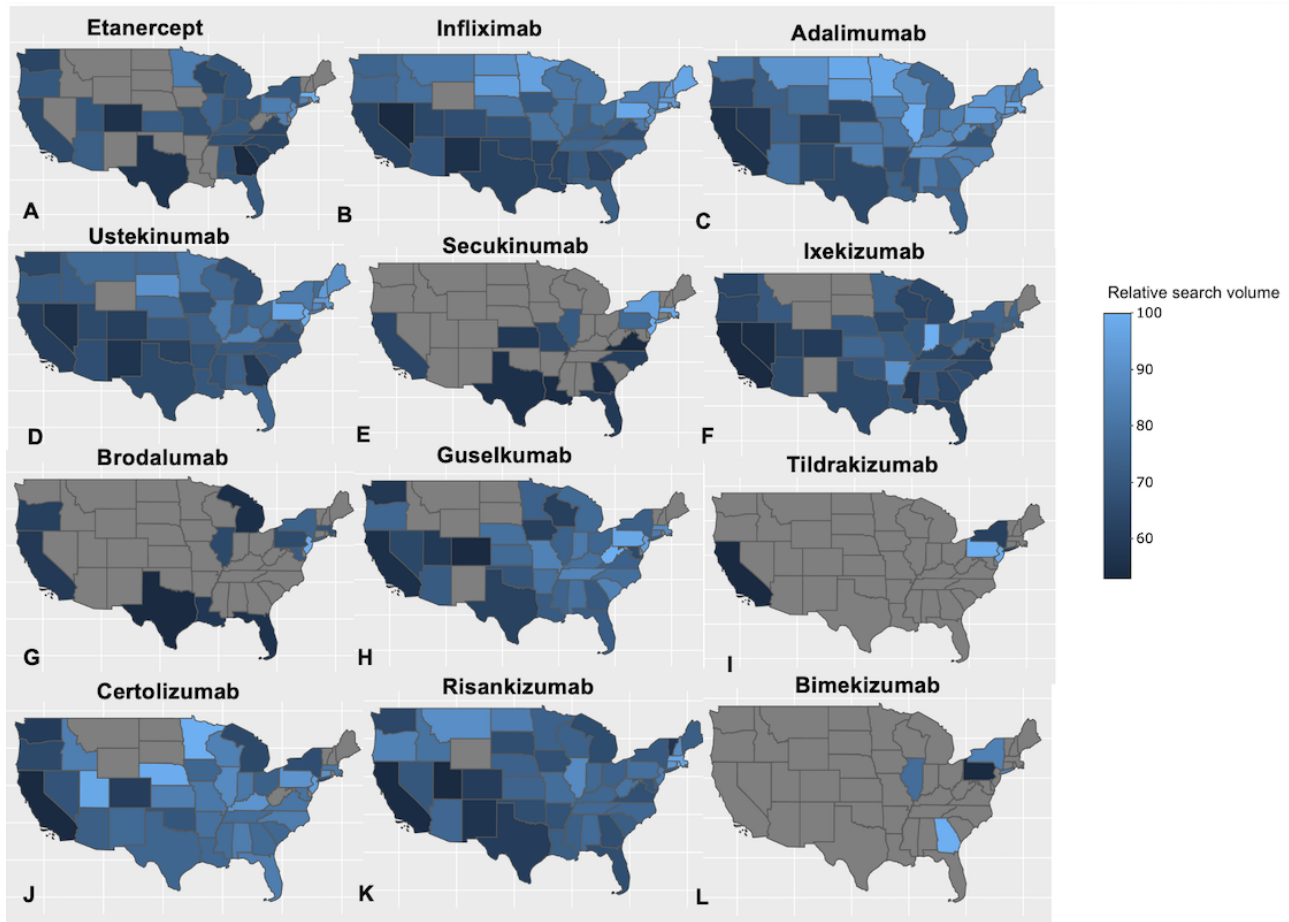
Overall, our analysis of search trends over time revealed increasing public interest in most psoriasis biologics (Figure 1) based on RSVs. Rising trends in RSVs since FDA approval were observed for adalimumab, ustekinumab, ixekizumab, guselkumab, certolizumab, and risankizumab. Declining RSVs were observed for etanercept and brodalumab, while search volumes were generally stable for infliximab, secukinumab, tildrakizumab, and bimekizumab. For detailed RSV ranges, please refer to [Multimedia Appendix 1](#). It is important to note that these RSVs represent the search interest in each medication relative to the total search volume within the specified region and time period rather than absolute search volumes. Therefore, while risankizumab has shown increased relative popularity, this does not necessarily imply that its absolute search volume surpasses that of older medications like infliximab. Over the past year, geographic analysis revealed heterogeneous public interest patterns across biologics in the United States (Figure 2). Coastal states, particularly California and the Eastern seaboard, had higher RSVs, whereas Midwestern states had the lowest. In many areas of the United States, IL-17 and IL-23 inhibitors remain among the lesser-searched psoriasis treatments. Notably, risankizumab demonstrated a rapid rise in nationwide search volume from mid-2021 ( $P < .001$ ).

**Figure 1.** Temporal trends in relative search volume for psoriasis biologics after approval by the US Food and Drug Administration.





**Figure 2.** Geographic distribution of relative search volume for psoriasis biologics in the past 12 months (November 2022 to November 2023) across the United States. The relative search volumes are based on each state's total search volume within the designated geography and time frame. The color scale ranges from 0 (no searches) to 100 (peak search volume), with the gray in the maps representing no data available.



## Discussion

Our results highlight consistently low Google search volumes for many standard-of-care psoriasis biologics across the United States, indicating disparities in patient awareness regarding these treatments. These findings add to previous studies showing regional disparities in psoriasis medication use and treatment outcomes in the United States, including research indicating that Southern states had the highest proportion of patients receiving psoriasis biologics per year based on the 1996-2015 Medicare Expenditure Panel Survey [5,6]. Furthermore, while risankizumab has shown increased popularity, it does not necessarily correlate with clinical superiority. A recent meta-analysis of psoriasis randomized controlled trials found no significant difference in efficacy, defined as the proportion of patients who achieved Psoriasis Area and Severity Index (PASI) 90, 8 to 24 weeks following treatment onset, between risankizumab, infliximab, bimekizumab, and ixekizumab [7].

To our knowledge, this study is the first to examine disparities in patient awareness of psoriasis medications both

geographically and longitudinally. While an RSV analysis does not provide information on absolute search volumes, it offers valuable insights into the relative popularity and public interest in different psoriasis medications across regions and over time. By analyzing relative trends for each medication, we can identify medications that are gaining or declining in awareness, which can inform efforts to improve patient education.

A limitation of our study is the nonspecific nature of search queries, which may not relate exclusively to psoriasis (eg, “etanercept” searches could include other indications). This likely underestimates the disparity in searches between TNF- $\alpha$  agents and newer biologics, suggesting that the observed decline in etanercept searches could be more pronounced than indicated. Incorporating per capita search data in future research could improve our understanding by providing a normalized metric that reflects search interest adjusted for population size. This study serves as an initial investigation into the utility of online search trends as a proxy for public awareness of psoriasis biologics, underscoring the need for comprehensive patient education on the wide array of available psoriasis treatments.

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## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Minimum and maximum relative search volumes for each biologic.

[[DOCX File, 15 KB - derma\\_v7i1e56406\\_app1.docx](#)]

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## Abbreviations

**FDA:** Food and Drug Administration

**IL-12/23:** interleukin 12/23

**IL-17:** interleukin 17

**IL-23:** interleukin 23

**PASI:** Psoriasis Area and Severity Index

**RSV:** relative search volume

**TNF- $\alpha$ :** tumor necrosis factor alpha

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Research Letter

# Prevalence of Musculoskeletal Symptoms in Patients With Hidradenitis Suppurativa and Associated Factors: Cross-Sectional Study

Hayley McKee<sup>1</sup>, MSc; Lihi Eder<sup>2,3</sup>, MD, PhD; Dana Jerome<sup>2,3</sup>, MD; Reza D Mirza<sup>4,5,6</sup>, MSc, MD; Chikaodili Obetta<sup>1</sup>, BMSc; Elisabeth Pek<sup>4</sup>, MD; Vincent Piguet<sup>7,8</sup>, MD, PhD; Raed Alhusayen<sup>7,9</sup>, MBBS, MSc

<sup>1</sup>Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

<sup>2</sup>Division of Rheumatology, Department of Medicine, University of Toronto, Toronto, ON, Canada

<sup>3</sup>Women's College Research Institute, Toronto, ON, Canada

<sup>4</sup>Division of Rheumatology, Sunnybrook Hospital, Toronto, ON, Canada

<sup>5</sup>Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada

<sup>6</sup>Department of Medicine, McMaster University, Hamilton, ON, Canada

<sup>7</sup>Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada

<sup>8</sup>Division of Dermatology, Department of Medicine, Women's College Hospital, Toronto, ON, Canada

<sup>9</sup>Sunnybrook Research Institute, Toronto, ON, Canada

**Corresponding Author:**

Hayley McKee, MSc

Temerty Faculty of Medicine

University of Toronto

Medical Sciences Building

1 King's College Circle

Toronto, ON, M5S 1A8

Canada

Email: [hayley.mckee@mail.utoronto.ca](mailto:hayley.mckee@mail.utoronto.ca)

## Abstract

The prevalence of and factors associated with musculoskeletal (MSK) symptoms in patients with hidradenitis suppurativa (HS) have yet to be elucidated. Given the association between HS and inflammatory comorbidities, understanding the burden of MSK symptoms in patients with HS is crucial for patient-centered care. Our objective was to describe the prevalence of and factors associated with MSK symptoms in patients with HS. A cross-sectional study of 78 consecutive patients recruited between November 2021 and February 2023 with a dermatology-confirmed diagnosis of HS, irrespective of MSK symptoms, was performed. The average age of participants (n=78) was 37 (SD 12.2) years, and the average age at symptom onset was 23 (SD 12.1) years; 54% (n=42) of participants identified as women, and 46% (n=36) as men. The most common comorbidities included depression (n=17, 22%) and preexisting arthritis (n=12, 16%). Approximately 24% (n=18) of participants reported prolonged morning stiffness. In a multivariate regression, depression was significantly associated with morning stiffness (odds ratio [OR] 6.1, 95% CI 1.4-26.1;  $P=.02$ ), while female sex was significantly associated with arthralgia (OR 19.1, 95% CI 1.6-235.2;  $P=.02$ ). Every patient with depression reported arthralgia. We highlight the high prevalence of MSK symptoms among patients with HS and note the interplay between depression and MSK symptoms, with each one potentially contributing to the other.

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**KEYWORDS**

hidradenitis suppurativa; cross sectional; skin; musculoskeletal symptoms; morning stiffness; arthralgia; comorbidities; musculoskeletal; comorbidity; stiff; stiffness; muscle; muscles; muscular; prevalence; incidence; epidemiology; epidemiological; factor; factors; dermatology; dermatological

## Introduction

Hidradenitis suppurativa (HS) is a chronic, suppurating inflammatory condition that characterizes the potential link between cutaneous and systemic disease. Currently, the underlying pathogenesis is unclear; however, follicular occlusion in the folliculopilosebaceous unit followed by follicular rupture and dysregulated immune response is widely proposed [1]. HS prevalence is 1%-4% worldwide and is higher in women [2].

Increasingly, evidence links HS, an inflammatory condition, with systemic comorbidities, such as cardiovascular disease, inflammatory bowel disease, diabetes mellitus, and depression [1]. A meta-analysis of more than 200,300 patients with HS found they had a higher prevalence of inflammatory arthritis, including spondyloarthritis and rheumatoid arthritis, than the general population [3]. Thus, this study investigated the prevalence of musculoskeletal (MSK) symptoms in patients with HS and associated factors.

## Methods

### Participants

Patients were recruited between November 2021 and February 2023 from one dermatology clinic in a tertiary hospital. All patients had dermatologist-diagnosed HS, irrespective of MSK symptoms. Of 106 patients approached, 18 declined participation and 10 withdrew; the final analysis included 78 patients. Patient information was collected via standard questionnaires, including age at first symptoms, family history, lifestyle habits, length of morning stiffness (minutes), Hurley stage, presence of arthralgia, and comorbidities including depression, diabetes mellitus, inflammatory bowel disease, hypertension, and cardiovascular disease. Rheumatic disease was investigated with follow-up X-rays, bloodwork, and rheumatology assessment.

### Statistical Analysis

Continuous variables were summarized as means, SDs, and minimums/maximums. Categorical variables were summarized using counts and percentages. Independent variables were identified a priori and examined for collinearity with the Pearson rank. Multivariable logistic regression models were built for morning stiffness (defined as stiffness and reduced mobility in the joints lasting >30 minutes after waking) and arthralgia (defined as joint pain without necessarily implying an underlying inflammatory process). Confounding was assessed by >10% change on variable removal. Odds ratios (ORs) and 95% CIs are reported in final models, with statistical significance at  $P<.05$ . Analyses were performed with Stata (version 17.0; StataCorp).

### Ethical Considerations

This study has been approved by the research ethics board at Sunnybrook Research Institute (1829). Informed consent was obtained from patients. Data were anonymized.

## Results

The mean age of the 78 patients with HS was 37 (SD 12.2) years at recruitment and 23 (SD 12.1) years at symptom onset; 54% (42/78) were women and 46% (36/78) were men. Most participants identified as South Asian ( $n=23$ ), White ( $n=19$ ), or Black ( $n=14$ ). There was a family history of HS in 14% (11/78) and of rheumatic disease in 53% (41/78) of participants. The most common comorbidities included depression ( $n=17$ ) and arthritis ( $n=12$ ) (Table 1).

Prolonged morning stiffness was reported by 24% (18/78) of participants, while a majority of reported arthralgia (41). In a multivariate regression, depression was significantly associated with prolonged morning stiffness (OR 6.1, 95% CI 1.4-26.1;  $P=.02$ ), while female sex was significantly associated with arthralgia (OR 19.1, 95% CI 1.6-235.2;  $P=.02$ ). Every patient with depression reported arthralgia (Table 2).

**Table 1.** Baseline characteristics of study participants (n=78) with hidradenitis suppurativa inflammatory and musculoskeletal symptoms.

Variables	Values
<b>Age (years) at recruitment</b>	
Mean (SD)	36.949 (12.2)
Range	19-67
<b>Age (years) at symptom onset (n=77)</b>	
Mean (SD)	23.442 (12.1)
Range	7-60
<b>Age (years) at diagnosis</b>	
Mean (SD)	29.603 (12.7)
Range	12-64
<b>Sex, n (%)</b>	
Women	42 (54)
Men	36 (46)
<b>Ethnicity, n (%)</b>	
South Asian	23 (30)
White	19 (24)
Black	14 (18)
Other	22 (28)
<b>Employment status, n (%)</b>	
Not working because of disability	10 (13)
Working full-time	44 (56)
Other	24 (31)
<b>Social history, n (%)</b>	
<b>Smoking</b>	
Current smoker	16 (21)
Previous smoker	6 (8)
Never smoked	55 (71)
<b>Alcohol (n=77)</b>	
Yes	26 (34)
No	51 (66)
<b>Family history of hidradenitis suppurativa, n (%)</b>	
Yes	11 (14)
No	67 (86)
<b>Family history of rheumatic disease, n (%)</b>	
Yes	41 (53)
No	37 (47)
<b>Biologic treatment, n (%)</b>	
Yes	21 (33)
No	43 (67)
<b>Comorbidities, n (%)</b>	
Arthritis	12 (16)
Irritable bowel disease	8 (10)
Diabetes mellitus	9 (12)



Variables	Values
Hypertension	9 (12)
Cardiovascular disease	4 (5)
Dyslipidemia	1 (1)
Depression	17 (22)
<b>Hidradenitis suppurativa disease severity, n (%)</b>	
Hurley stage 1 or 2 (mild, moderate)	60 (79)
Hurley stage 3 (severe)	16 (21)
<b>Musculoskeletal symptoms, n (%)</b>	
>30 min morning stiffness	18 (24)
≤30 min morning stiffness	57 (76)
Arthralgia present	41 (84)
Arthralgia absent	8 (16)

**Table 2.** Multivariate logistic regressions for participants with hidradenitis suppurativa (n=78) for symptoms of prolonged morning stiffness (>30 min) and arthralgia.

	Odds ratio (95% CI)	SE	P value
<b>Multivariate logistic regression for morning stiffness &gt;30 min based on IBD<sup>a</sup>, biologic therapy, Hurley stage, depression, and age at symptom onset</b>			
Depression	6.10 (1.43-26.12)	4.53	.02
IBD	1.08 (0.13-8.86)	1.16	.94
Biologic treatment	0.71 (0.16-3.23)	0.55	.66
Hurley stage <3	0.84 (0.17-4.09)	0.67	.83
Age >25 years at symptom onset	0.84 (0.20-3.52)	0.62	.81
<b>Multivariate logistic regression for arthralgia based on IBD, sex, biologic therapy, Hurley stage, depression, and age at symptom onset<sup>b</sup></b>			
Female sex	19.14 (1.56-235.24)	24.51	.02
Biologic treatment	0.30 (0.30-3.04)	0.35	.31
Hurley stage <3	0.33 (0.17-6.60)	0.51	.47
Age >25 years at symptom onset	6.06 (0.41-90.57)	8.37	.19

<sup>a</sup>IBD: inflammatory bowel disease.

<sup>b</sup>Depression and IBD were omitted from these rows given the perfect correlation with the predictor.

## Discussion

This cross-sectional study including 78 patients with HS demonstrates a significant association between MSK symptom severity, depression, and female sex. In a multivariate analysis, patients with depression had 6-fold greater odds of prolonged morning stiffness, while women had 19-fold greater odds of arthralgia. All patients with depression reported arthralgia.

A correlation between depression and HS has been reported [4]. The prevalence of depression in our study was 22% (17/78), comparable to 16.9% in a meta-analysis of 40,307 patients with HS [4]. World Health Organization survey data reported 69% of patients with depression present primarily with somatic symptoms, such as joint pain and back pain [5]. Proinflammatory cytokines tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin-1  $\beta$  (IL-1 $\beta$ ), and interleukin-10 (IL-10) are elevated in major

depressive disorder [6] and HS [7], suggesting a possible pathophysiological process for increased inflammatory symptoms in comorbid patients. Alternatively, prolonged morning stiffness might limit activities of daily living, such as dressing and getting out of bed, leading to feelings of loss of independence and comorbid depression [8]. Women were more likely to report arthralgia, consistent with population-based findings of higher chronic MSK pain prevalence and inflammatory arthritis-associated pain [9] in women. Still, men may be more likely to have severe HS [10]. Further research into sex-based experiences of MSK symptoms in HS is recommended.

This cross-sectional study cannot show causality. Patients came from a single center, introducing possible selection bias. Associations between depression and arthralgia could not be assessed in the regression due to perfect correlation.

We highlight the importance of managing depression in patients with HS to lessen its potential effects on pain processing and worsened MSK symptoms. Larger cohort studies exploring the impacts of sex and depression on MSK symptoms are recommended.

## Acknowledgments

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## Conflicts of Interest

LE has received educational and research grants and consulting fees from Janssen, AbbVie, Pfizer, Novartis, Eli Lilly, UCB, and Sandoz. VP has served as a consultant for Pfizer, AbbVie, Janssen, UCB, Novartis, Amgen, and Celgene; has received honoraria from Kyowa Kirin Co Ltd, AbbVie, and Novartis; has received grants from AbbVie, Bausch Health, Celgene, Janssen, LEO Pharma, Lilly, NAOS, Novartis, Pfizer, Pierre-Fabre, and Sanofi; and has received a donation of medical equipment from La Roche-Posay. RA has served as a consultant and received honoraria from AbbVie, Janssen, Novartis, Incyte, UCB, Pfizer, Amgen, and Boehringer Ingelheim. All other authors declare no conflicts of interest.

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## Abbreviations

**HS:** hidradenitis suppurativa  
**IBD:** inflammatory bowel disease  
**IL-10:** interleukin-10  
**IL-1 $\beta$ :** interleukin-1  $\beta$   
**MSK:** musculoskeletal  
**TNF- $\alpha$ :** tumor necrosis factor  $\alpha$

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## Research Letter

# Google Search Trends About Systemic Psoriasis Treatment: What Do People Want to Know About Biologics and Janus Kinase Inhibitors?

Subin Lim<sup>1</sup>, BA; Sarah Kooper-Johnson<sup>1</sup>, BA; Courtney A Chau<sup>2</sup>, BS; Claire Chen<sup>1</sup>, BS; Fei-Shiuann Clarissa Yang<sup>1</sup>, MBA, MD; Gabriela Cobos<sup>1</sup>, MD

<sup>1</sup>Department of Dermatology, Tufts Medical Center, Boston, MA, United States

<sup>2</sup>Icahn School of Medicine at Mount Sinai, New York, NY, United States

**Corresponding Author:**

Subin Lim, BA

Department of Dermatology

Tufts Medical Center

260 Tremont Street

Boston, MA, 02116

United States

Phone: 1 6176360156

Email: [subin.lim@tuftsmedicalcenter.org](mailto:subin.lim@tuftsmedicalcenter.org)

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**KEYWORDS**

Google; psoriasis vulgaris; psoriasis; systemic treatment; biologics; small molecule inhibitors; adalimumab; apremilast; methotrexate; health care delivery; skin; dermatologist; medication

## Introduction

Google is the most widely used search engine worldwide [1]. While previous studies have utilized Google machine learning algorithms to assess commonly asked questions about various medical topics [2,3], no studies have employed these tools to explore queries surrounding dermatological conditions. Recognizing the internet's profound influence on patients, our study aimed to examine the most frequently asked questions concerning systemic treatment for psoriasis vulgaris and evaluate the quality of medical information available online.

## Methods

The Google Trends tool was utilized to compare the relative search volume (RSV) of traditional disease-modifying antirheumatic drugs, biologics, and small molecule inhibitors used to treat psoriasis between January 31, 2019, and January 31, 2024. Trade names were used. For example, "Enbrel for psoriasis" was compared with "Humira for Psoriasis." Subsequently, the People AlsoAsked tool was utilized to generate the most asked questions about the most searched medication in each of the three categories. The questions were checked for relevance and classified based on Rothwell's criteria (Multimedia Appendix 1). Cohen  $\kappa$  coefficient was calculated to determine the level of interrater agreement. Additionally, the People AlsoAsked tool was employed to extract internet sources

sought by the readers. The quality of these information sources was determined based on the *The Journal of the American Medical Association (JAMA)* benchmark criteria [4]. Statistical analyses were performed in R 4.1.2 (R Foundation for Statistical Computing).

## Results

Adalimumab exhibited the highest search volume among all medications (RSV 1). Apremilast was the most searched among small molecule inhibitors and methotrexate among disease-modifying antirheumatic drugs (RSV 1). Adalimumab garnered the most fact-based questions overall when compared with apremilast and methotrexate (68/147, 46.3% vs 42/125, 33.6%;  $P=.04$ ; 68/147, 46.3% vs 59/180, 32.7%;  $P=.01$  for  $t$  tests, respectively), with the majority falling into the subcategories of technical details (36/147, 24.5%) and cost (18/147, 12.2%; Table 1).

Inquiries specifically revolved around scheduling of adalimumab administration, dietary restrictions linked to medication usage (eg, concurrent use with alcohol), and concerns about affording adalimumab.

Between apremilast and methotrexate, apremilast drew more cost-related questions (13/125, 10.4% vs 1/180, 0.5%;  $P<.001$  for  $t$  tests), whereas methotrexate attracted more questions about its risks when compared with adalimumab (72/180, 40% vs

35/147, 23.8%;  $P=.002$  for  $t$  tests). The interrater agreement indicated a strong agreement in question categorization ( $\kappa=0.96$ ).

Our findings on adalimumab suggest that it has the most public awareness, possibly due in part to direct-to-patient marketing. According to data on advertisement expenses, AbbVie allocated almost US \$500 million toward advertising adalimumab in 2020, while roughly half of that amount (US \$202 million) was dedicated to promoting risankizumab. In the same period, Amgen invested US \$150.4 million in advertising for apremilast [5].

Nonetheless, most inquiries about adalimumab centered around its cost and objective details rather than its safety. This aligns with trends observed in similar studies on rheumatoid arthritis and spinal surgeries, where individuals sought more factual information about these topics, such as the timeline for treating rheumatoid arthritis and activity restrictions related to spine surgeries [2,3]. The lower frequency of value-based questions

on systemic psoriasis treatment may be due to a lack of patient understanding about the value of these medications, underscoring the need for comprehensive patient education on this topic. Alternatively, patients may be finding adequate information on these subjects from other sources, such as their dermatologists.

Furthermore, 782 websites were classified, with the majority (362/782, 46.3%) consisting of commercial sites such as Healthline. Social media websites accounted for 24.4% (191/782), government-based websites such as PubMed accounted for 15.2% (119/782), academic websites for 12.6% (98/782), and medical practice websites for 1.5% (12/782). In assessing the quality of these sources, commercial and government websites scored the highest average based on the *JAMA* benchmark criteria, with 3.1 and 3.2 points out of 4, respectively. Medical practice websites scored the lowest, with an average of 1.0 points (Table 2).

**Table 1.** Relative proportion of question type for apremilast, adalimumab, and methotrexate and significance of difference.

Question category	Apremilast (n=125), n (%)	Adalimumab (n=147), n (%)	MTX <sup>a</sup> (n=180), n (%)	Apremilast vs adalimumab, $P$ value ( $t$ test)	Apremilast vs MTX, $P$ value ( $t$ test)	Adalimumab vs MTX, $P$ value ( $t$ test)
<b>Fact</b>	42 (33.6)	68 (46.3)	59 (32.7)	.04 <sup>b</sup>	.88	.01 <sup>b</sup>
Cost	13 (10.4)	18 (12.2)	1 (0.5)	.64	<.001 <sup>b</sup>	<.001 <sup>b</sup>
Mechanism	6 (2.4)	6 (4.1)	6 (3.3)	.44	.64	.72
Technical	15 (12.0)	36 (24.5)	44 (24.4)	.01 <sup>b</sup>	.007 <sup>b</sup>	.98
Timeline of treatment	8 (6.4)	8 (5.4)	8 (4.4)	.73	.45	.68
<b>Policy</b>	44 (35.2)	37 (25.2)	75 (41.7)	.07	.26	.002 <sup>b</sup>
Risks	42 (33.6)	35 (23.8)	72 (40.0)	.07	.26	.002 <sup>b</sup>
Indications	2 (1.6)	2 (1.4)	3 (1.7)	.84	.96	.86
<b>Value</b>	39 (31.2)	46 (29.2)	46 (25.5)	.72	.28	.45
Evaluation	22 (17.6)	31 (17.7)	31 (17.2)	.98	.93	.91
Prognosis	6 (4.8)	7 (4.8)	8 (4.4)	.97	.88	.89
Timeline of clinical course	11 (8.8)	9 (6.1)	7 (3.8)	.40	.07	.35

<sup>a</sup>MTX: methotrexate.

<sup>b</sup>Statistical significance.

**Table 2.** Evaluation of internet source categories and quality according to *The Journal of the American Medical Association (JAMA)* benchmark criteria.

Category	Description	Internet sources (n=782), n (%)	Average source quality score (out of 4)
Commercial	Commercial organization that positions itself as a source of health information, includes medical device and pharmaceutical companies (eg, Healthline, WebMD)	362 (46.3)	3.1
Academic	Institution with a clear academic mandate, including universities, academic medical centers, academic societies, and journals (eg, Mayo Clinic)	98 (12.5)	2.3
Government	Websites ending in .gov or maintained by a national government (eg, PubMed)	119 (15.2)	3.2
Medical practice	Local hospital or dermatology practices without an academic affiliation	12 (1.5)	1
Social media	Websites maintained by nonmedical organizations primarily designed for information sharing between internet users, including health blogs, internet forums, and support groups	191 (24.4)	2.1



## Discussion

Our analyses indicate that users are being directed to commercial and government-based websites most often when seeking information about psoriasis treatment. This is reassuring, as these websites received the highest scores based on source quality criteria. Surprisingly, academic websites scored lower on average, similar to social media websites. Finally, although individual medical practice websites were not referred to as often, they scored only 1 out of 4 on average, indicating an area for improvement both for these practices and the search engine. Enhancing the visibility and content quality of medical practice websites as determined by the *JAMA* benchmark criteria and optimizing search engine algorithms to prioritize higher-quality

sources could improve patient access to reliable health information.

In summary, given that the internet has a substantial impact on the dissemination and understanding of health-related information, dermatologists should consider tailoring their discussions when counseling patients on systemic medications for psoriasis. Emphasis should be placed on addressing a medication's administration schedule, dietary restrictions associated with its use, cost considerations, and side effect profile relative to alternative options. Additionally, dermatologists can guide patients on how to identify and access high-quality online resources, empowering them to make more informed decisions about their health. Study limitations include potential question comprehensiveness and the evolving nature of medication concerns over time.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Question classification based on Rothwell's criteria and subcategories specific to the dataset.

[[PNG File , 300 KB - derma\\_v7i1e62948\\_app1.png](#) ]

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## Abbreviations

**JAMA:** *The Journal of the American Medical Association*

**RSV:** relative search volume

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Letter to the Editor

# Strengthening TikTok Content Analysis in Academia Using Follower Count and Engagement

Serena Ramjee<sup>1</sup>, MBBS; Zeeshaan-ul Hasan<sup>2</sup>, MBBS, BSc

<sup>1</sup>Urology Department, Darent Valley Hospital, Dartford, United Kingdom

<sup>2</sup>Dermatology Department, Barts Health NHS Trust, London, United Kingdom

**Corresponding Author:**

Serena Ramjee, MBBS

Urology Department

Darent Valley Hospital

Darenth Wood Road

Dartford, DA2 8DA

United Kingdom

Phone: 44 1322 428100

Email: [serena.ramjee1@nhs.net](mailto:serena.ramjee1@nhs.net)

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**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

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## Case Report

# An Unusual Case of Anderson-Fabry Disease: Case Report

Alpana Mohta<sup>1</sup>, MD; Achala Mohta<sup>2</sup>, MBBS; Pramila Kumari<sup>3</sup>, MD

<sup>1</sup>Department of Dermatology, Venereology and Leprosy, Sardar Patel Medical College, Bikaner, India

<sup>2</sup>Department of Preventive and Social Medicine, Sardar Patel Medical College, Bikaner, India

<sup>3</sup>Department of Dermatology, Era's Lucknow Medical College, Lucknow, India

### Corresponding Author:

Alpana Mohta, MD

Department of Dermatology, Venereology and Leprosy

Sardar Patel Medical College

SP Medical College Rd

Bikaner, 334001

India

Phone: 91 8769036292

Email: [dralpanamohta10@gmail.com](mailto:dralpanamohta10@gmail.com)

## 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.

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### 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.

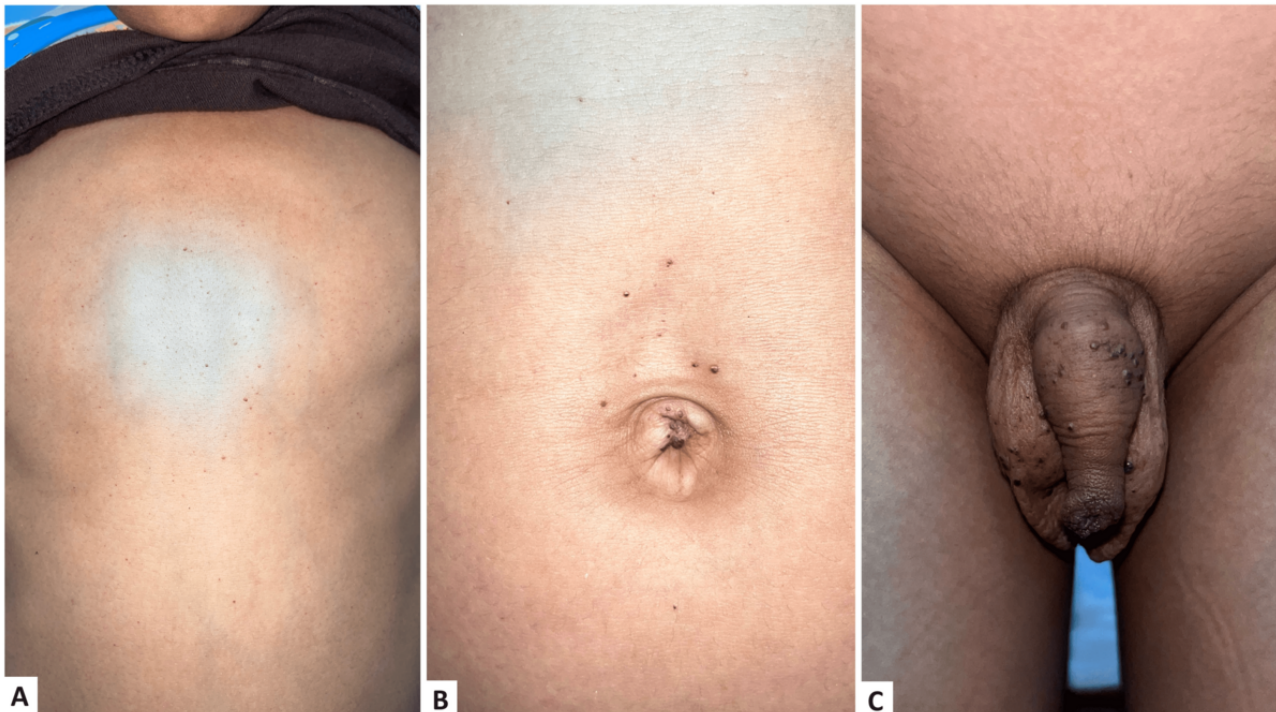


The child had no history of seizures, visual disturbances, hearing loss, or atypical facial features. There was no history of similar skin lesions or associated features in any family members. The child also had bilateral cervical lymphadenopathy. On pure tone audiometry, there was sensorineural hearing 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.

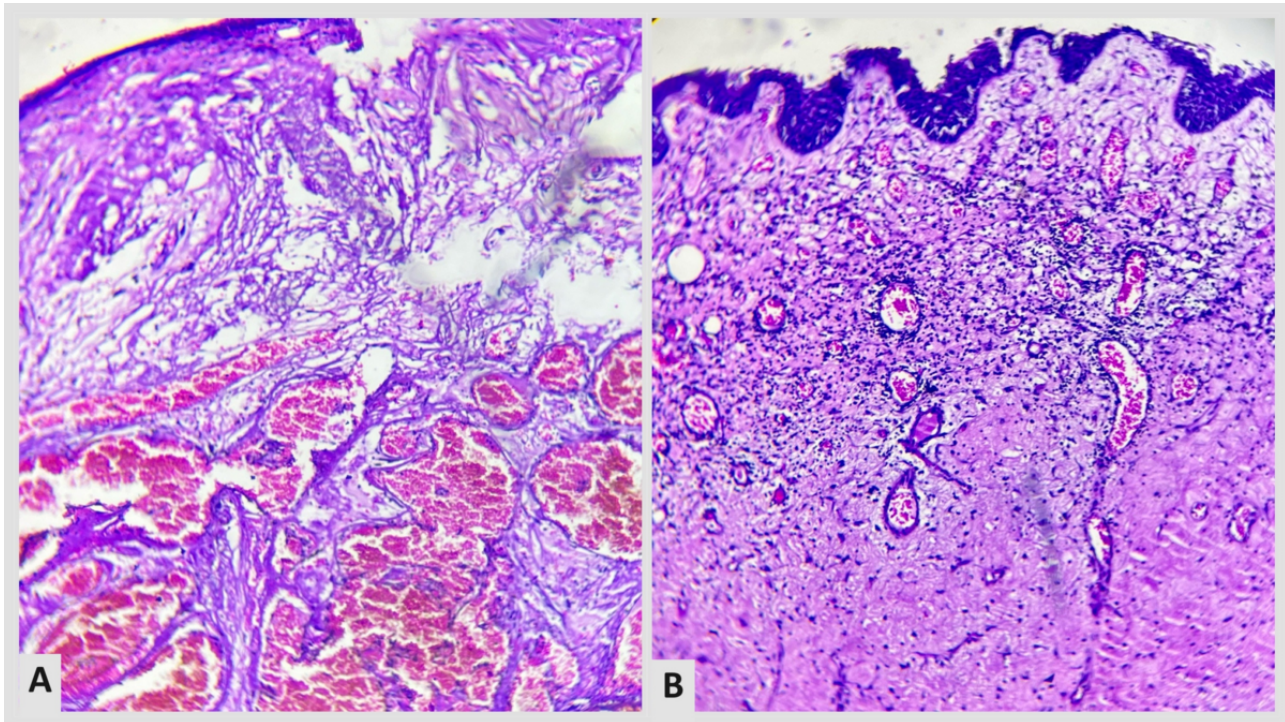
Due to the patient's low socioeconomic status, a genetic study could not be carried out for the rest of the family members.

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

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Case Report

# Merkel Cell Carcinoma on the Face: Case Report

Shaikha Salah Alhaj<sup>1</sup>, MBBS; Fatma Abdulghaffar Qaderi<sup>2</sup>, MBBS; Tarek Ibrahim<sup>2</sup>, MD; Maha Almohammad<sup>1</sup>, MD

<sup>1</sup>Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates

<sup>2</sup>Dermatology, Dubai Academic Healthcare Corporation, Dubai, United Arab Emirates

**Corresponding Author:**

Shaikha Salah Alhaj, MBBS

Mohammed Bin Rashid University of Medicine and Health Sciences

Dubai Health

Dubai

United Arab Emirates

Phone: 971 507000711

Email: [shawa5i1@hotmail.com](mailto:shawa5i1@hotmail.com)

## 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.

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**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, $n \times 10^3/uL$	16.4	3.6-11.0
Hemoglobin, g/dL	8.1	13.0-17.0
Hematocrit, %	25.2	40-50
Platelets, $n \times 10^3/uL$	850	150-410
Lactate dehydrogenase, U/L	167	105-222
Creatinine, mg/dL	1.67	0.70-1.20

**Table 2.** Immunohistochemistry results.

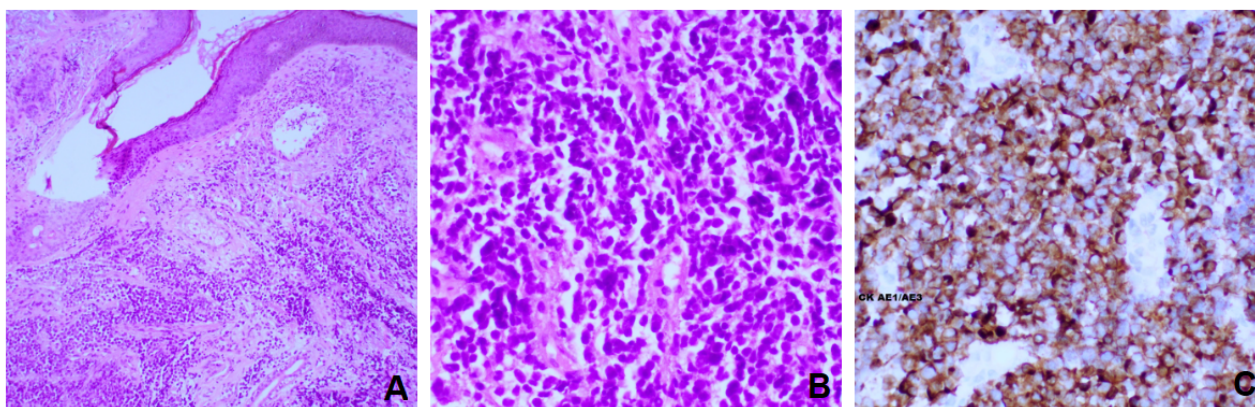
Name	Results
Synaptophysin	Diffusely positive in tumor cells
Chromogranin	Diffusely positive in tumor cells
CD <sup>a</sup> 56	Diffusely positive in tumor cells
Ki67 <sup>b</sup>	Shows a high proliferative index
CK <sup>c</sup> (AE 1/AE 3)	Positive with focal paranuclear staining
CD45	Negative in tumor 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-programed cell death protein 1/anti-programed 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-programed cell death protein 1/anti-programed 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

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Case Report

# Ichthyosiform Lichen Planus Pigmentosus in a 19-Year-Old Male Patient: Case Report

Audi Sugiharto<sup>1</sup>, MD; Julius Gatmaitan<sup>2</sup>, MD; Johannes Dayrit<sup>1,3</sup>, MD

<sup>1</sup>Department of Dermatology, Research Institute for Tropical Medicine, Muntinlupa City, Philippines

<sup>2</sup>Skines Aesthetic and Laser Center, Bulacan, Philippines

<sup>3</sup>Department of Internal Medicine, De La Salle University Medical Center, Dasmariñas City, Philippines

**Corresponding Author:**

Audi Sugiharto, MD

Department of Dermatology

Research Institute for Tropical Medicine

9002 Research Drive, Filinvest Corporate City

Muntinlupa City, 1781

Philippines

Phone: 63 288072631

Email: [sugihartoaudi@gmail.com](mailto:sugihartoaudi@gmail.com)

## 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.

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**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).

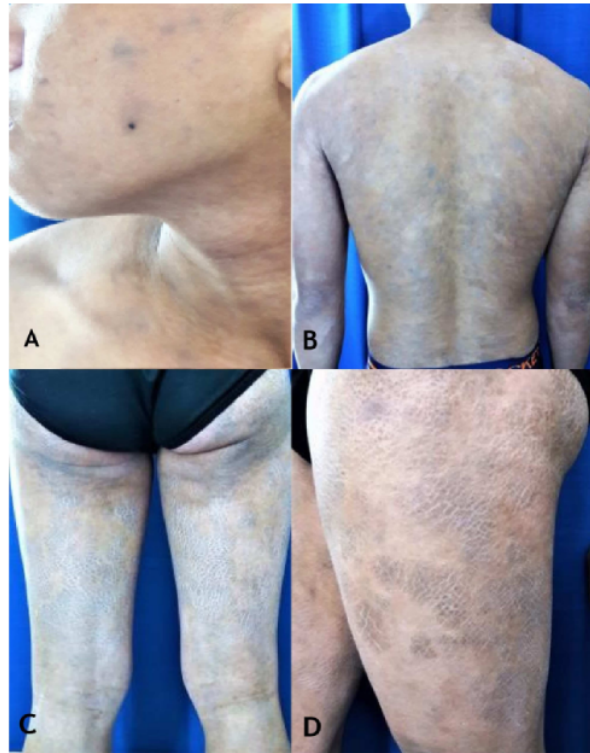
We used a manual polarized light device (Dermlite DL3x10, 3Gen). The dermoscopic finding shows dots and globules in a “hem-like” and reticular pattern, which spares the follicular opening (Figure 2).

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

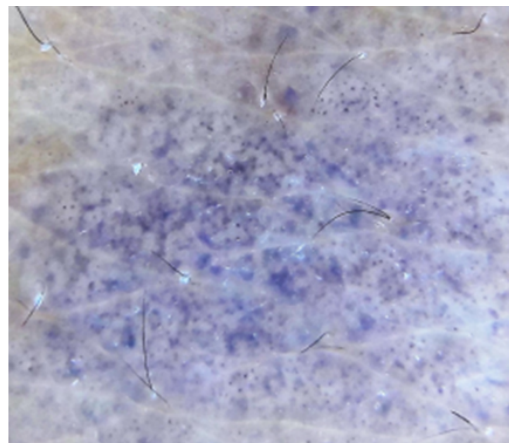
multifocal areas of vacuolar alteration of the basal cell layer. Histopathology results of both specimens presented with numerous pigment-laden macrophages and mild perivascular inflammatory infiltrate of lymphocytes in the dermis (Figure 3A and 3B). Cluster differentiation (CD) 68 immunostaining highlights 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.

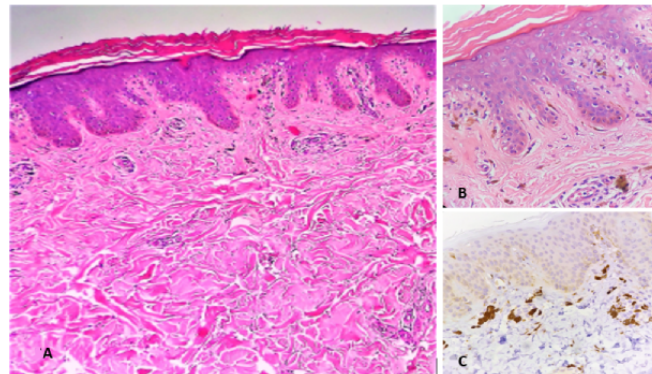
**Figure 1.** Clinical findings: “asymptomatic grayish macules; patches with fine scales on the face (A), trunk, and upper extremities (B); and grayish plaques with thick “ichthyosiform” scales on the lower extremities (C and D).



**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 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

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Case Report

# Epithelioid Hemangioendothelioma as a Dangerous, Easy to Miss, and Nearly Impossible to Clinically Diagnose Condition: Case Report

Kayd Pulsipher<sup>1</sup>, DO; Samantha Mills<sup>2</sup>, BS; Blair Harris<sup>1</sup>, DO; Rene Bermudez<sup>1</sup>, DO; Muammar Arida<sup>1</sup>, MD; Jonathan Crane<sup>1</sup>, DO

<sup>1</sup>Department of Dermatology, Campbell University, Sampson Regional Center, Clinton, NC, United States

<sup>2</sup>Campbell University School of Osteopathic Medicine, Lillington, NC, United States

**Corresponding Author:**

Kayd Pulsipher, DO

Department of Dermatology

Campbell University

Sampson Regional Center

607 Beaman Street

Clinton, NC, 28328

United States

Phone: 1 (910) 592 8511

Email: [kpulsipher@sampsonrhc.org](mailto:kpulsipher@sampsonrhc.org)

## Abstract

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor with metastatic potential. EHE can have single- or multiorgan involvement, with presentations ranging from asymptomatic disease to pain and systemic symptoms. The extremely heterogeneous clinical presentation and disease progression complicates EHE diagnosis and management. We present the case of a 24-year-old woman with two periauricular erythematous papules, leading to the discovery of metastatic EHE through routine biopsy, despite a noncontributory medical history. Histology revealed the dermal proliferation of epithelioid cells and vacuoles containing red blood cells. Immunohistochemistry markers consistent with EHE solidified the diagnosis. Although extremely rare, prompt diagnosis of EHE is essential for informed decision-making and favorable outcomes. Key clinical and histopathological findings are highlighted to aid dermatologists in diagnosing and managing this uncommon condition.

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**KEYWORDS**

epithelioid hemangioendothelioma; EHE; vascular tumor; tumor; vascular; blood vessel; cutaneous; skin; lesion; histopathology; case report; metastatic; dermatology; dermatological; diagnose; diagnosis; rare cancer; oncology

## Introduction

Epithelioid hemangioendothelioma (EHE) is an extremely rare cancer, accounting for less than 1% of all vascular tumors, demonstrating features between those of hemangioma and angiosarcoma [1]. Although first described by Dail and Liebow in 1975, the term EHE was only first proposed by Weiss and Enzinger in 1982 [1]. These tumors can occur at any age, with 38 years being the median age at diagnosis [2]. The most common presenting symptom is pain, along with less commonly reported symptoms such as cough, palpable mass, or fatigue. Nearly one-third of patients with EHE are asymptomatic and tumors are discovered incidentally [2]. While likely endothelial in origin, EHE is extremely heterogeneous in presentation and

prognosis, complicating diagnosis and clinical decisions [3]. EHE can occur nearly anywhere in the body. Primary cutaneous EHE is rare and should prompt suspicion of metastatic disease, especially if multifocal in the skin [4]. Owing to their rarity and similarities to other diagnoses, cutaneous EHE lesions are commonly misdiagnosed [5]. Previous studies suggest the diagnosis of strictly cutaneous EHE incurs a 17% mortality rate at 3 years, highlighting its relatively aggressive nature [6]. It is paramount for dermatologists and dermatopathologists to be aware of EHE and its defining characteristics to minimize the risk of missing this crucial diagnosis.

We report a case of two periauricular lesions with dermal proliferation consistent with EHE, leading to the discovery of underlying metastatic EHE with pulmonary and hepatic



involvement in a 24-year-old woman. The aim of presenting this case is to enhance understanding of EHE, an uncommon cancer that is not well studied.

## Case Report

A 24-year-old woman presented to our dermatology clinic with a left posterior auricular papule and left preauricular papule present for 8 and 4 months, respectively (Figure 1). The patient had no significant medical or social history, including no tobacco or heavy alcohol use. Both lesions were painful and progressively enlarging. The patient denied any other symptoms.

Shave biopsy was taken of both lesions. The histology of both lesions demonstrated cellular dermal proliferations of epithelioid cells with the eosinophilic cytoplasm arranged in cords within

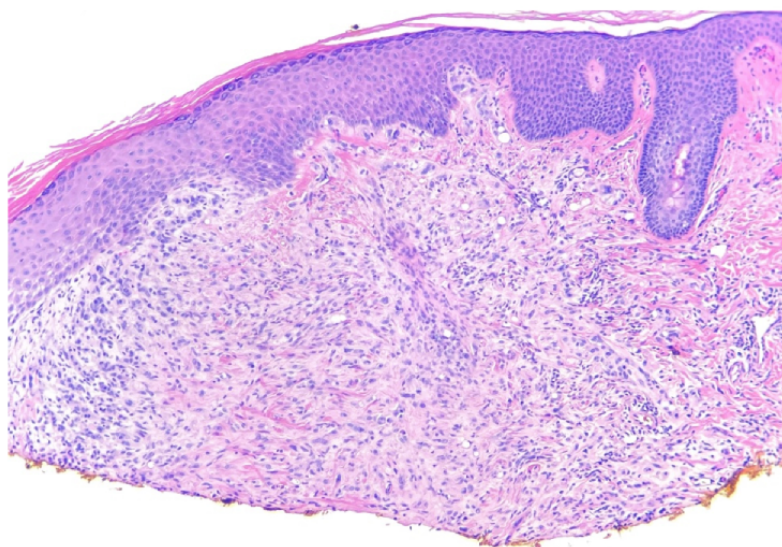
a myxohyaline stroma (Figure 2). Subtle vacuoles containing red blood cells were present within some of the cells (Figure 3). Histological and immunohistochemical findings were consistent with the diagnosis of EHE (Table 1).

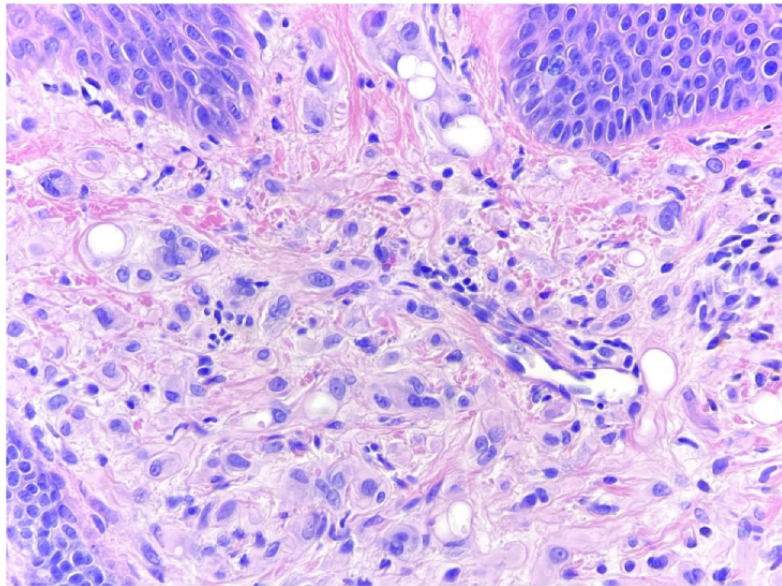
Due to multifocal cutaneous disease, there was high clinical suspicion of metastatic disease. Our patient was referred to medical and surgical oncology for further evaluation, and computed tomography (CT) scans of the head, neck, chest, abdomen, and pelvis were performed. Innumerable bilateral pulmonary nodules, a 1.8-cm hypoattenuated hepatic lesion, and prominent bilateral axillary lymph nodes were noted, all consistent with metastatic disease. After seeking multiple opinions from oncology, our patient elected the watchful waiting approach. Serial CT scans every 3 months were recommended to monitor disease progression.

**Figure 1.** A 3-mm umbilicated, skin-colored papule on the post auricular neck (left) and a 2-mm hyperpigmented papule with surrounding erythema on the preauricular cheek (right).



**Figure 2.** Dense proliferation of dermal epithelioid cells with no attachment to the epidermis.



**Figure 3.** Dermal epithelioid cells with eosinophilic cytoplasm and red blood cells in vacuolations identifying them as vascular spaces.**Table 1.** Immunohistochemistry patterns characteristic of epithelioid hemangioendothelioma (EHE) and the staining results of the patient.

EHE immunohistochemistry markers	Result in patient
ERG	Positive (diffuse)
CD31	Positive (diffuse)
$\alpha$ -SMA <sup>a</sup>	Negative
FVIII Ag <sup>b</sup>	— <sup>c</sup>
CAMTA1/TFE3	Positive (diffuse)
Focal cytokeratin (<30% <sup>d</sup> )	Positive
SOX10	Negative

<sup>a</sup>SMA: smooth muscle actin.

<sup>b</sup>FVIII Ag: factor VIII-related antigen.

<sup>c</sup>Not tested.

<sup>d</sup>Percentages refer to the estimated prevalence in EHE tumors [3,6,7].

## Ethical Considerations

The patient provided consent to publish information regarding her case, including photographs and relevant findings. Identifiable patient information has been appropriately masked or omitted to comply with ethical standards and patient privacy.

## Discussion

### Prior Reports of EHE

Literature pertaining to EHE is limited with case reports and case series comprising the majority. This can largely be attributed to the low prevalence of EHE, reported as approximately 1 in 1 million [1]. Sites of primary and metastatic involvement in EHE most commonly involve the liver, lung, and bone; however, the disease has been reported in nearly every part of the body. When cutaneous EHE is discovered, it typically represents metastatic disease rather than primary malignancy. The appearance, location, and characteristics of cutaneous EHE vary immensely from case to case, with no clear consensus

available [4,7,8]. The extreme heterogeneity of this disease complicates detection and diagnosis [2].

Histopathology and immunohistochemistry are often crucial for diagnosis of cutaneous disease. Histologically, tumors typically show circumscribed nodules with an overlying acanthotic epidermis. A mixture of pleomorphic spindle and epithelioid cells with sharply eosinophilic cytoplasm will be present, typically embedded in a myxoid or hyaline matrix [8]. Cells typically stain positive for CD31, CD34, factor VIII-related antigen,  $\alpha$ -smooth muscle actin, and cytokeratin [6,7]. When unable to be clearly differentiated from other vascular tumors, the presence of the *WWTR1-CAMTA1* translocation can aid the diagnosis of EHE [3]. This translocation dysregulates the Hippo pathway, promoting cancer proliferation and survival [9].

The prognosis of strictly cutaneous EHE is not readily available. In a small case series of 30 patients with cutaneous EHE, at 36 months follow-up, 21% of cases had metastatic disease, 13% had local recurrence, and 17% had died from the disease [6].

In all cases of EHE irrespective of site, 1-year overall survival is 90% with a 5-year overall survival of 73% [2].

Given the low prevalence of EHE, no randomized clinical trials exist regarding the optimal treatment strategy [7]. Patients with cutaneous EHE should receive additional imaging to evaluate for metastatic disease. When no metastatic disease is found, the

treatment is surgical resection [3]. A variety of treatments such as cytotoxic chemotherapy, immunotherapy, targeted therapies, and organ transplantation have been used for metastatic disease (Table 2). With reports of spontaneous disease regression [10], watchful waiting can also be proposed as a reasonable course following EHE diagnosis, especially if the nature of the disease is not yet understood or the risks of treatment outweigh benefits.

**Table 2.** Possible treatment options for epithelioid hemangioendothelioma based on retrospective studies of tumor involvement and case outcomes [9].

Involvement and considerations	Treatment
<b>Unifocal involvement</b>	
R0 <sup>a</sup> margins	Surgical resection (70%-80% cure rate)
R1 <sup>b</sup> margins	Surgical resection ± radiation therapy
Severe morbidity or R0/R1 not possible	Radiation therapy/ ablative procedure/ isolated limb perfusion
Not surgical candidate (comorbidities or technical challenges)	Active surveillance
<b>Locoregional</b>	
Resection possible	Surgical resection ± radiation therapy
Asymptomatic	Active surveillance
Symptomatic (surgery not possible)	Radiation therapy/ ablative procedure/ isolated limb perfusion
<b>Systemic</b>	
Resection possible	Surgical resection ± radiation therapy
Asymptomatic	Active surveillance
Symptomatic (systemic) or serosal effusion	Systemic therapy (limited evidence)
Organ involvement	Surgical resection/transplant (unresectable)

<sup>a</sup>R0: microscopic negative margins.

<sup>b</sup>R1: gross negative margins.

## Conclusion

The heterogeneity of EHE is also demonstrated in its variable course; EHE can be unpredictable, at times being indolent and at other times very aggressive [7]. Given the uncertain course of the disease, joint decision-making between the patient and physician is necessary. Active surveillance includes monitoring progression, and the decision to treat with radiation or surgery

often follows once the nature of the tumor is better understood [9]. Systemic treatments have been recorded, but not enough data are currently available to determine a standard approach [9]. Regardless of the course of management, close follow-up for local recurrence and metastatic disease is essential. Future studies should focus on early detection and a standardized approach for the treatment EHE.

## Conflicts of Interest

None declared.

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## Abbreviations

**CT:** computed tomography

**EHE:** epithelioid hemangioendothelioma

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Research Letter

# Reflecting on Decades of Data: The Global Burden of Disease—Cochrane Project

Madeline Adelman<sup>1\*</sup>, MD; Isaac Weber<sup>2\*</sup>, MD

<sup>1</sup>Department of Dermatology, University of Colorado, Aurora, CO, United States

<sup>2</sup>Mercy Hospital St. Louis, St. Louis, MO, United States

\* all authors contributed equally

**Corresponding Author:**

Isaac Weber, MD

Mercy Hospital St. Louis

615 S New Ballas Rd

St. Louis, MO, 63141

United States

Phone: 1 (314) 251 6000

Email: [isaac.weber@mercy.net](mailto:isaac.weber@mercy.net)

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**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.

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## Conflicts of Interest

None declared.

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## Abbreviations

**CDSR:** Cochrane Database of Systematic Reviews

**GBD:** Global Burden of Disease

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**Editorial**

# NVIDIA's "Chat with RTX" Custom Large Language Model and Personalized AI Chatbot Augments the Value of Electronic Dermatology Reference Material

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Maged N Kamel Boulos<sup>1</sup>, MBBCh, MSc, PhD; Robert Dellavalle<sup>2</sup>, MSPH, MD, PhD

<sup>1</sup>School of Medicine, University of Lisbon, Lisbon, Portugal

<sup>2</sup>Department of Dermatology, University of Minnesota Medical School, Minneapolis, MN, United States

**Corresponding Author:**

Maged N Kamel Boulos, MBBCh, MSc, PhD

School of Medicine

University of Lisbon

Av Prof Egas Moniz MB

Lisbon, 1649-028

Portugal

Phone: 351 920531573

Email: [mnkboulos@ieeee.org](mailto:mnkboulos@ieeee.org)

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**Abstract**

This paper demonstrates a new, promising method using generative artificial intelligence (AI) to augment the educational value of electronic textbooks and research papers (locally stored on user's machine) and maximize their potential for self-study, in a way that goes beyond the standard electronic search and indexing that is already available in all of these textbooks and files. The presented method runs fully locally on the user's machine, is generally affordable, and does not require high technical expertise to set up and customize with the user's own content.

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**KEYWORDS**

AI chatbots; artificial intelligence; AI; generative AI; large language models; dermatology; education; self-study; NVIDIA RTX; retrieval-augmented generation; RAG

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**Introduction**

Artificial intelligence (AI) chatbots powered by large language models (LLMs) can potentially improve clinical learning experiences and promote self-paced study—for example, by summarizing large amounts of text data, such as a collection of research articles—thus helping users to instantly identify key information in large bodies of literature [1]. However, uploading copyrighted and other sensitive content for processing by web-based (externally hosted) chatbots may prove to be problematic; for example, it may violate applicable license agreements and regulations.

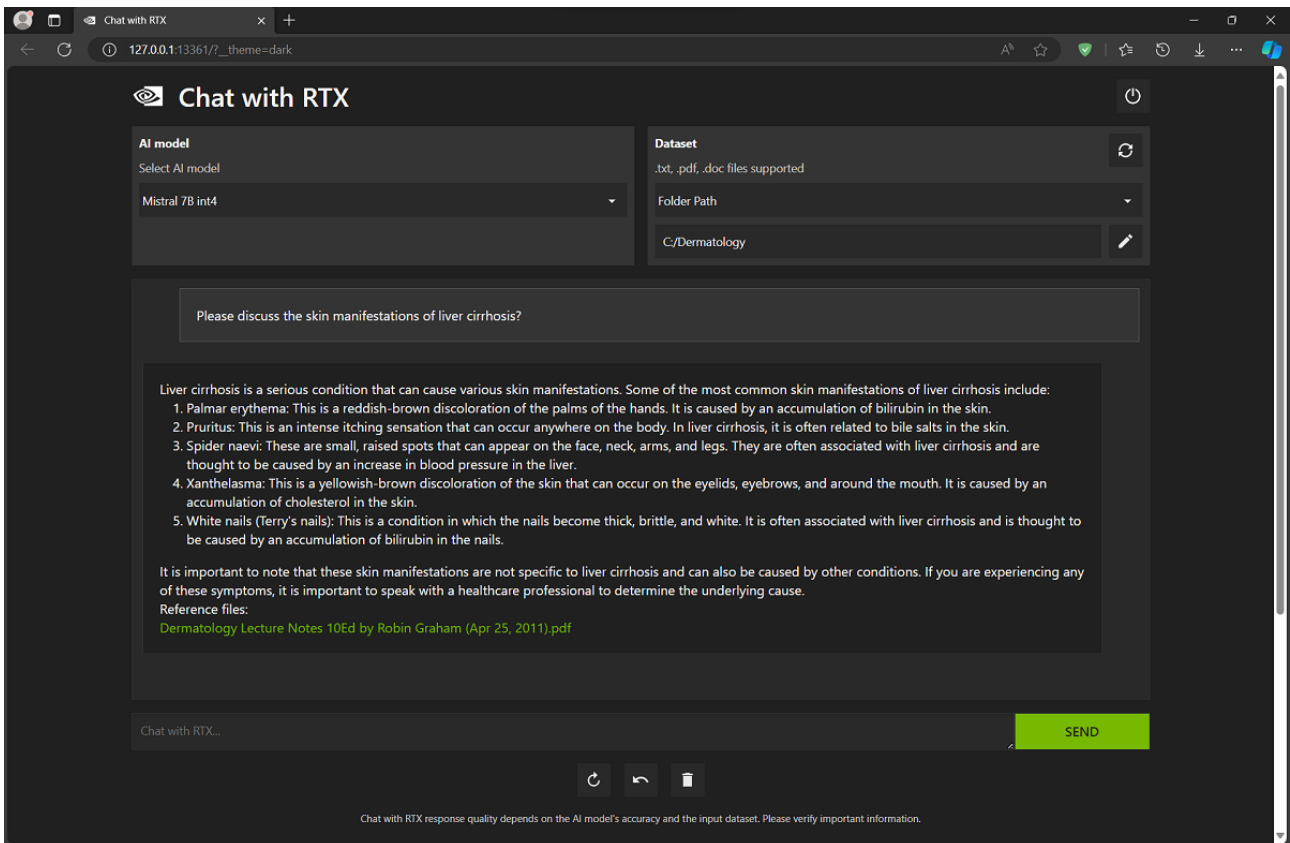
On the other hand, running fully locally hosted and managed instances of LLMs and their associated end-user interfaces (eg, ChatGPT [OpenAI]) requires very large investments (starting at tens of thousands of US dollars) in hardware and infrastructure [2]. This cost has decreased with the launch of NVIDIA's free "Chat with RTX" tech demo download in February 2024 [3], which can be used to build custom LLMs and personalized AI chatbots. "Chat with RTX" runs fully

locally on relatively inexpensive laptops and does not require high technical expertise to set up and customize with the user's own content.

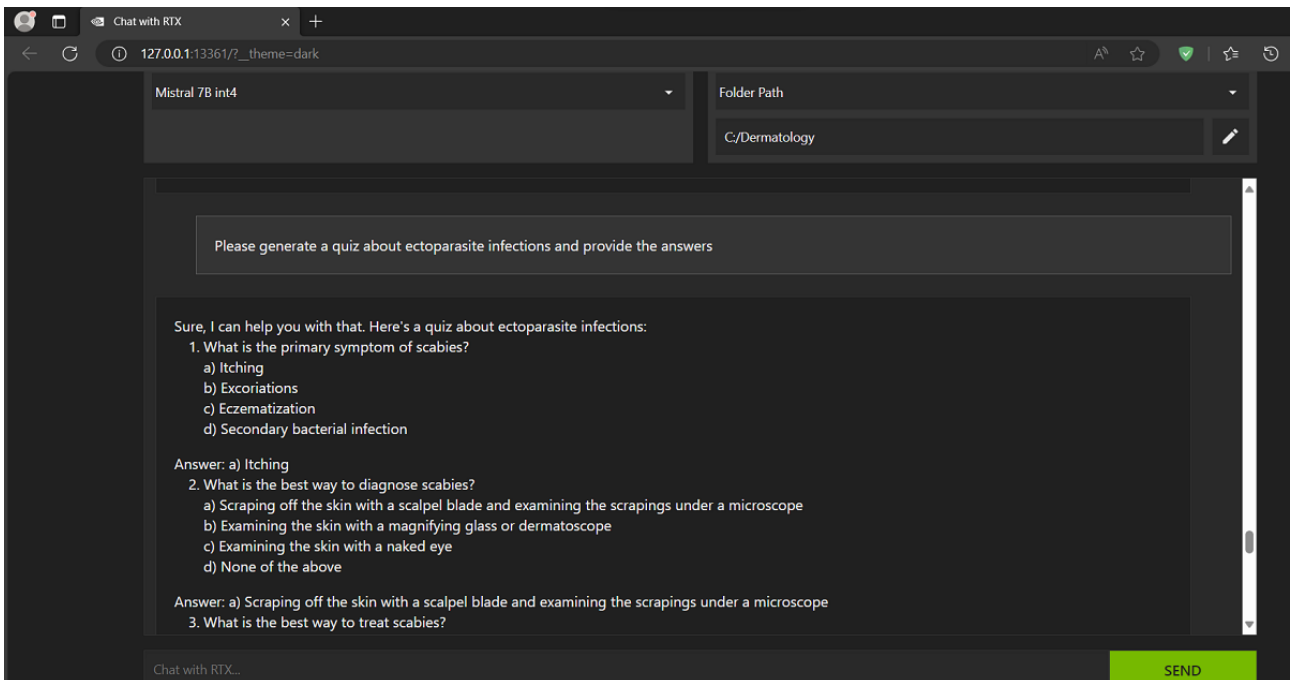
This paper describes a novel use of "Chat with RTX" to build a cloud-independent, dermatology self-study AI chatbot that can work with, and enhance the educational value of, electronic textbooks and research papers locally stored on the user's computer without uploading them to any remote server. Electronic textbooks and research papers are often acquired in .pdf format. The presented AI chatbot offers additional functionality beyond that of the standard electronic search and indexing that is already available in .pdf files, such as the abilities (1) to link, synthesize, and summarize at a single location related information scattered across different book chapters and multiple papers and (2) to generate knowledge-testing quizzes with answers.



**Figure 2.** NVIDIA's "Chat with RTX" response to prompt to discuss the skin manifestations of liver cirrhosis. Note the cited source listed at the bottom of the chatbot answer.



**Figure 3.** NVIDIA's "Chat with RTX" (customized with a local copy of a dermatology textbook) was prompted to generate a quiz (with answers) about ectoparasite infections.



### Current Limitations

“Chat with RTX” is still an early tech demo with rough edges and limitations, such as (at the time of writing) its currently less than ideal user interface for importing and parsing user content and its relatively costly consumer hardware requirements, which

may put it out of reach for some users [10,11]. It is also prone to hallucinations (albeit to a lesser degree than non-RAG systems) and other inconsistencies of generative AI [12,13]. However, as is the case with other digital technologies, this emerging consumer technology (software and hardware) will



continue to improve and become increasingly more affordable over time.

## Discussion and Future Directions

The goal of this exercise was not to compare “Chat with RTX” answers with those of a human dermatology expert, but rather to demonstrate a new, promising way to increase the educational value of electronic textbooks and research papers (locally stored on the user’s machine) and maximize their potential for self-study, in a way that goes beyond the standard electronic search and indexing that is already available in all of these textbooks and .pdf files. “Chat with RTX” does this by serving as an intelligent personal clinical tutor, for example, by summarizing important facts, linking and synthesizing related bits across different book chapters and papers, developing study themes spanning multiple chapters, and generating quizzes (and answers for marking them) for the user to test their own knowledge and understanding of a subject, as briefly demonstrated in this paper (Figures 2 and 3).

General purpose LLMs such as OpenAI’s GPT-4o are not optimized for clinical use and are prone to generating hallucinatory information. RAG as used in “Chat with RTX”

enables the creation of custom LLMs and personalized AI chatbots that are specifically and comprehensively trained using handpicked corpora of quality, evidence-based medical texts that sufficiently cover a given clinical area of specialism [12,13].

Cloud independence is another notable feature of AI chatbot implementation using “Chat with RTX.” The ability to run fully offline not only protects copyrighted and other sensitive data but also offers more flexibility to users, by allowing them to run the software in places and situations where there is no internet connection.

Although promising, a dermatology self-study AI chatbot such as the one presented in this paper will need to undergo formal testing, evaluation, and refining or fine-tuning as necessary before it can be signed off for mainstream use. Testing and evaluation should cover critical aspects of these chatbots such as accuracy and impact on student learning outcomes [1], among others, and should be revisited whenever the underlying software implementation or medical content are updated.

In the future, publishers might consider bundling electronic dermatology (and other clinical specialty) textbooks with custom self-study AI chatbots to offer a superior service to their readers.

## Conflicts of Interest

RD is the editor-in-chief of *JMIR Dermatology*. MNKB declares no conflicts of interest.

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**Abbreviations**

**AI:** artificial intelligence

**LLM:** large language model

**RAG:** retrieval-augmented generation

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Editorial

# JMIR Dermatology's 2023 Year in Review

Ramiro Rodriguez<sup>1</sup>, MD; Robert P Dellavalle<sup>1,2,3</sup>, MSPH, MD, PhD

<sup>1</sup>Department of Dermatology, University of Colorado School of Medicine, Aurora, CO, United States

<sup>2</sup>Department of Dermatology, Minneapolis VA Medical Center, US Department of Veterans Affairs, Minneapolis, MN, United States

<sup>3</sup>Department of Dermatology, University of Minnesota School of Medicine, Minneapolis, MN, United States

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Department of Dermatology

Minneapolis VA Medical Center

US Department of Veterans Affairs

1 Veterans Drive

Minneapolis, MN, 55417

United States

Phone: 1 720 289 0247

Email: [robert.dellavalle@va.gov](mailto:robert.dellavalle@va.gov)

## Abstract

In 2023, *JMIR Dermatology* embraced papers treating all topics related to diseases of the skin, hair, and nails. This editorial aims to bring attention and recognize reviewers, staff, and authors for their contributions to the journal. *JMIR Dermatology* updated the Research Letter format and introduced the In Memoriam article type to feature and celebrate highly accomplished and internationally recognized leaders in dermatology. We also summarize the 3 *JMIR Dermatology* publications from 2023 with the highest Altmetric scores and share what we look forward to in the coming year.

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**KEYWORDS**

rural; teledermatology; neglected tropical diseases; NTD; melanoma; PubMed; review; diversity; editorial; dermatology; review; JMIR

In 2023, *JMIR Dermatology* embraced papers treating all topics related to diseases of the skin, hair, and nails. This editorial aims to bring attention to and recognize reviewers, staff, and authors for their contributions to the journal. *JMIR Dermatology* published more than 78 papers exploring clinical information exchange, education, and efforts to facilitate the diagnosis and delivery of dermatologic care. These publications included Original Articles (n=29), Reviews (n=9), Research Letters (n=31), Viewpoints (n=3), a Short Paper (n=1), Case Reports (n=2), Editorials (n=2), and an In Memoriam article (n=1), which have provided room for authors to showcase their research.

Research Letters were a popular article type; this article type is “optimal for presenting new, early, or sometimes preliminary research findings, including interesting observations from ongoing research with significant implications that justify concise and rapid communication” [1]. The Research Letter article type is also conducive to JMIR Publications' cascading peer review policy [2].

The In Memoriam article type was added to feature and celebrate highly accomplished and internationally recognized leaders in dermatology. Dr William Weston was featured in this year's In Memoriam article to recognize his accomplishments as a clinician and educator and for inspiring the careers of many academic dermatologists [3].

The 3 publications with the highest Altmetric scores (as of December 4, 2023) examined the strengths of teledermatology applications and areas for improving care delivery. Drabarek et al [4] provided qualitative data capturing patient impressions of a participant-led skin self-examination (SSE) model using smartphone app reminders, patient-performed dermoscopy, and teledermatology assessments. Implementation barriers revolved around participants' perceptions of melanoma recurrence risk. Concerns included the short time interval between melanoma diagnosis, treatment, and the introduction of the SSE model; medical provider availability for urgencies; and the need for evidence on the efficacy of SSE relative to usual care. Follow-up studies could explore underserved communities where access to dermatologic care is a preexisting limitation. Yotsu et al [5] exemplified studies exploring the use of phone apps in rural,

underserved communities; they evaluated how teledermatology can diagnose skin-related neglected tropical diseases. Over 3 months in rural Côte d'Ivoire, the investigators trained local practitioners and implemented an app-based electronic medical record and teledermatology workflow. The study design assigned providers to an interventional group and a usual care group. It was found that the group who used the app-based electronic medical record and teledermatology workflow identified 79 cases of different neglected tropical diseases (Buruli ulcer, leprosy, lymphatic filariasis, mycetoma, scabies, and yaws), compared to the 8 identified cases among practitioners not using the system. Difficulties with the system were reported to revolve around internet connectivity and initial challenges with using the system. Challenges with teledermatology were not only limited by internet connectivity but also by target diseases, as described by Long et al [6]. Specifically, teledermatology posed unique challenges for treating hidradenitis suppurativa. These challenges involved the sensitive location of lesions and the limited nature of a teledermatology exam.

Overall, teledermatology offers an opportunity to bring health equity to diverse populations, and *JMIR Dermatology* embraced

these topics [7]. With new technological advances, *JMIR Dermatology* looks forward to improving the understanding of teledermatology applications in the coming years. Through the contributions of authors, the editorial team, and reviewers, the Library Operations Division of the US National Library of Medicine decided to include *JMIR Dermatology* for indexing in PubMed Central after a rigorous scientific and technical evaluation. This indexing will be in addition to the journal appearing in the Sherpa Romeo, Scopus, Directory of Open Access Journals, and Centre for Agriculture and Biosciences International databases. These platforms will help increase the visibility of the authors' work and help advance clinical information exchange and education.

Beyond our 3 highlighted papers, our PubMed indexing has made 2023 a big year for *JMIR Dermatology*. We are proud to be open access and to be the number 1 academic dermatology journal published in Canada per the Scimago Journal & Country Rank. We sincerely thank the International Society of Digital Health in Dermatology, formerly known as The International Teledermatology Society, and all of our editorial board members [8], staff, and reviewers (Multimedia Appendix 1), without whom our success would not have been possible.

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## Conflicts of Interest

RPD is the editor-in-chief of *JMIR Dermatology*. RR declared no conflicts of interest.

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## Multimedia Appendix 1

*JMIR Dermatology* reviewers in 2023.

[DOCX File, 37 KB - [derma\\_v7i1e57007\\_app1.docx](#) ]

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## Abbreviations

**SSE:** skin self-examination

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Review

# AI in Psoriatic Disease: Scoping Review

Richard Barlow<sup>1</sup>, BSc, MBBS; Anthony Bewley<sup>2</sup>, BA (hons), MB ChB; Maria Angeliki Gkini<sup>2</sup>, PhD

<sup>1</sup>Dermatology Department, University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom

<sup>2</sup>Department of Dermatology, The Royal London Hospital, Barts Health NHS Trust, London, United Kingdom

**Corresponding Author:**

Maria Angeliki Gkini, PhD  
Department of Dermatology  
The Royal London Hospital  
Barts Health NHS Trust  
Whitechapel Road  
London, E1 1FR  
United Kingdom  
Phone: 44 020 7377 700  
Email: [gkinimargo@gmail.com](mailto:gkinimargo@gmail.com)

## Abstract

**Background:** Artificial intelligence (AI) has many applications in numerous medical fields, including dermatology. Although the majority of AI studies in dermatology focus on skin cancer, there is growing interest in the applicability of AI models in inflammatory diseases, such as psoriasis. Psoriatic disease is a chronic, inflammatory, immune-mediated systemic condition with multiple comorbidities and a significant impact on patients' quality of life. Advanced treatments, including biologics and small molecules, have transformed the management of psoriatic disease. Nevertheless, there are still considerable unmet needs. Globally, delays in the diagnosis of the disease and its severity are common due to poor access to health care systems. Moreover, despite the abundance of treatments, we are unable to predict which is the right medication for the right patient, especially in resource-limited settings. AI could be an additional tool to address those needs. In this way, we can improve rates of diagnosis, accurately assess severity, and predict outcomes of treatment.

**Objective:** This study aims to provide an up-to-date literature review on the use of AI in psoriatic disease, including diagnostics and clinical management as well as addressing the limitations in applicability.

**Methods:** We searched the databases MEDLINE, PubMed, and Embase using the keywords "AI AND psoriasis OR psoriatic arthritis OR psoriatic disease," "machine learning AND psoriasis OR psoriatic arthritis OR psoriatic disease," and "prognostic model AND psoriasis OR psoriatic arthritis OR psoriatic disease" until June 1, 2023. Reference lists of relevant papers were also cross-examined for other papers not detected in the initial search.

**Results:** Our literature search yielded 38 relevant papers. AI has been identified as a key component in digital health technologies. Within this field, there is the potential to apply specific techniques such as machine learning and deep learning to address several aspects of managing psoriatic disease. This includes diagnosis, particularly useful for remote teledermatology via photographs taken by patients as well as monitoring and estimating severity. Similarly, AI can be used to synthesize the vast data sets already in place through patient registries which can help identify appropriate biologic treatments for future cohorts and those individuals most likely to develop complications.

**Conclusions:** There are multiple advantageous uses for AI and digital health technologies in psoriatic disease. With wider implementation of AI, we need to be mindful of potential limitations, such as validation and standardization or generalizability of results in specific populations, such as patients with darker skin phototypes.

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**KEYWORDS**

artificial intelligence; machine learning; psoriasis; psoriatic arthritis; psoriatic disease; biologics; prognostic models; mobile phone

## Introduction

Artificial intelligence (AI) is generally regarded as the ability of machines to simulate human intelligence, and typically refers to computers or software. Although the term AI is used daily, a standard definition is lacking. In 1950, Alan Turing [1] suggested a method to examine machine intelligence via an exercise now termed the Turing test. In this exercise, an impartial observer deemed a machine intelligent if it was indistinguishable from a human in conversation [1]. Nowadays, AI refers to the ability of a machine to communicate, reason, and operate independently in both familiar and novel scenarios in a similar manner to a human and that is not indistinguishable [2].

**Textbox 1.** Essential terminology in the field of machine learning and artificial intelligence.

- Artificial intelligence: The ability of machines, such as computers, to simulate human intelligence.
- Machine learning: Algorithms and statistical models that are programmed to learn from data, therefore recognizing and inferring patterns within them. This enables computers to perform specific tasks without explicit instructions from a human operator.
- Deep learning: Refers to a neural network with multiple layers of “neurons” that have adjustable weights (mathematical functions), with machine learning to train or test data across its network for improved accuracy and performance.

Both the US Department of Health and Human Services [3] and the European Union [4] have outlined potential future roles and implementation of AI within health care. The National Health Service in the United Kingdom has also identified AI as a current and future priority; the 2019 Topol review [5] published

AI is distinct from machine learning (ML), although the 2 terms are often used interchangeably (Textbox 1) [2]. ML is a subset of AI that is related to teaching machines to automatically learn tasks from data by recognizing and inferring patterns within them [2]. Due to the growth in available patients’ medical data, ML’s potential to comprehend medical tasks has significantly increased. Algorithms can also be learned via deep learning (DL), which can be performed without labeled data sets. DL refers to a neural network with multiple layers of “neurons” that have adjustable weights (mathematical functions) [2], with ML to train or test data across its network for improved accuracy and performance.

by Health Education England includes AI as one of 3 key digital health technologies. The report also details how to prepare the health care workforce to deliver a digital future as a response to keeping up with the increasing demands of our expanding population (Textbox 2) [5].

**Textbox 2.** Digital health technologies.

- Genomics (reading and writing the genome)
- Digital medicine (telemedicine, apps, sensors and wearables, and virtual reality)
- Artificial intelligence (speech recognition, natural language processing, and robotics)

AI has broad applications within medical settings (Textbox 3), all of which need careful consideration regarding appropriate clinical governance [6]. Many of these applications naturally lend themselves to dermatology given the visual nature of the specialty and the large data sets already established (Textbox 4) [7,8]. Further steps forward have been taken in screening and

diagnosing of melanoma and nonmelanoma skin cancers. Numerous apps and digital platforms, using dermoscopic or clinical images, have been already available although their sensitivities and specificities vary. More recently, there is growing interest in the use of AI in inflammatory skin diseases [9].

**Textbox 3.** Artificial intelligence (AI) in health care.

- AI-assisted robotic surgery
- Virtual nursing assistants
- AI-assisted medical diagnoses
- Medical image analysis
- Drug discovery
- Automated workflow assistance
- Fraud detection
- Medical data security
- Medical risk prediction
- Clinical trials
- Personalized treatment
- Improve gene editing

**Textbox 4.** Uses of artificial intelligence in dermatology.

- Skin cancer diagnosis
- Onychomycosis assessment
- Ulcer assessment
- Predicting skin sensitization substances
- Novel applications in pathology and gene expression profiling
- Psoriasis disease and other inflammatory skin diseases

Psoriatic disease is a common, chronic, systemic inflammatory condition with a significant impact on a patient's quality of life. Common comorbidities include psoriatic arthritis, cardiovascular disease, metabolic syndrome, and psychiatric or psychosocial impact. More recently researched comorbidities such as liver fibrosis and renal disease also exist [10]. Concerning is the fact that these comorbidities can be found also in the US pediatric population [11]. Advanced systemic treatments, including biologics and small molecules can improve comorbidities [12].

Globally, the problem of delayed and or incorrect diagnosis of psoriasis remains. Long waiting lists and pressure to prioritize potential malignant lesions also prolong patients accessing appropriate specialist dermatology care. In areas of limited resources, access to dermatology can also be a challenge. Identifying the most appropriate treatment for each individual remains an unmet goal, although recently there have been updates in the field of genomics and personalized medicine [13,14]. Therefore, AI offers progress in both directions, diagnostics and management (Textbox 5).

**Textbox 5.** Roles for artificial intelligence in psoriasis evaluation using skin images.**Diagnosis**

- Identification and differential diagnosis of psoriasis lesions
- Assessment of severity

**Clinical management**

- Prediction of complications
- Treatment
- Discovery of new biomarkers and drug targets

Our objective was to provide an up-to-date literature review on the use of AI in psoriatic disease, including diagnostics and clinical management as well as addressing the limitations in applicability.

## Methods

We conducted a literature search from the databases MEDLINE, PubMed, and Embase using the keywords "AI AND psoriasis OR psoriatic arthritis OR psoriatic disease," "ML AND psoriasis

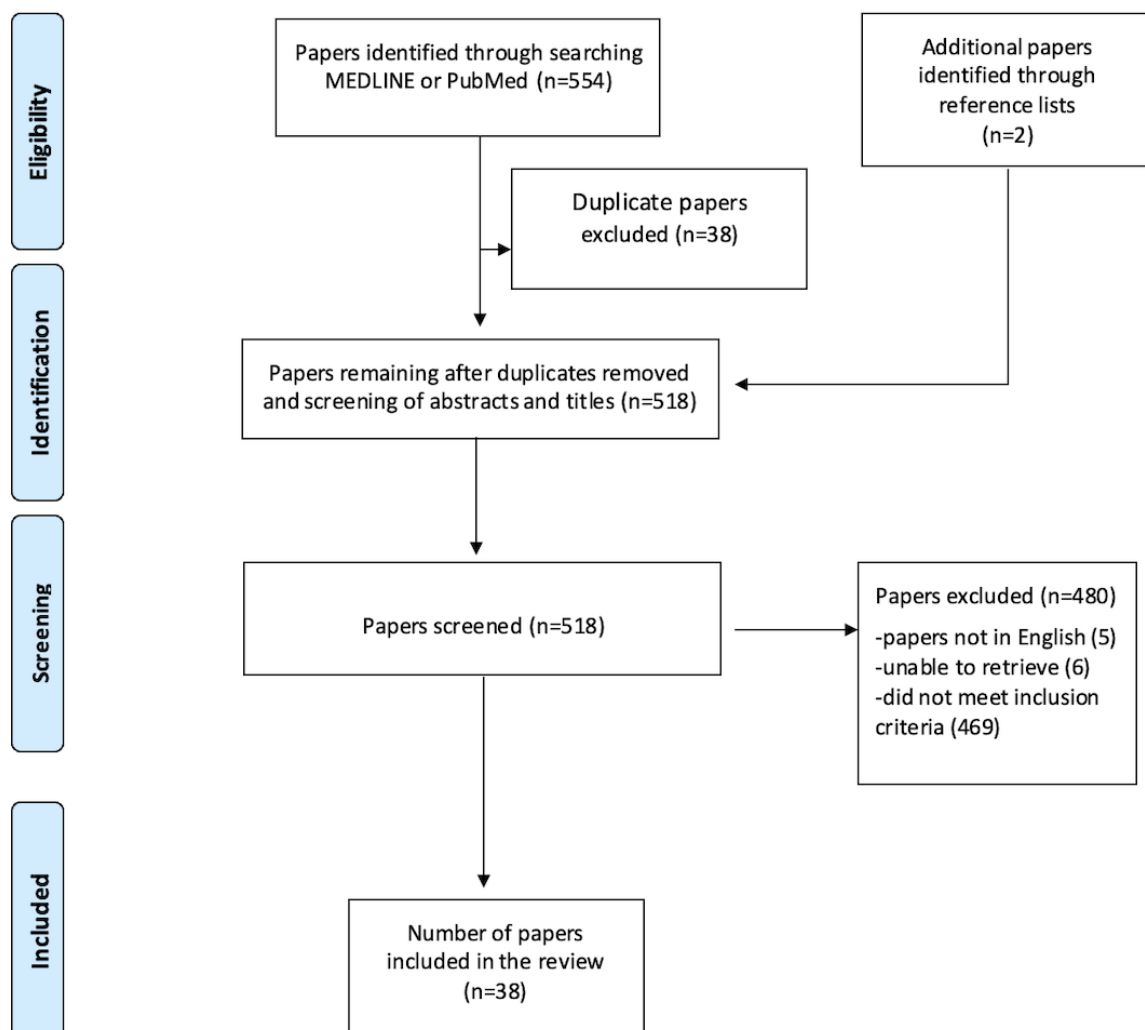
OR psoriatic arthritis OR psoriatic disease,” and “prognostic model AND psoriasis OR psoriatic arthritis OR psoriatic disease” until June 1, 2023. Reference lists of relevant papers were also cross-examined for other papers not detected in the initial search. RB and MAG screened papers and discrepancies were reviewed by AB. For articles that met our inclusion criteria, the study characteristics and outcomes were abstracted using a spreadsheet developed by the research team. The data abstraction was conducted by RB. The spreadsheet was reviewed and discussed by RB, MAG and AB with key findings categorized

under ‘Diagnosis and assessment of severity’ and ‘Clinical management’.

## Results

Figure 1 demonstrates the flowchart of methodology. The search strategy and screening yielded a total of 38 relevant papers. These included a range of observational, interventional and descriptive studies across a multitude of populations and datasets.

**Figure 1.** PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flowchart of methodology to identify included studies.



### Diagnosis and Assessment of Severity

Correct, timely diagnosis is the first step of management in psoriasis; distinguishing it from other similar disorders can be particularly challenging for clinicians and AI alike.

Google has recently launched its own AI-tool for differentiating between 288 conditions and is undergoing validation. Users can upload 3 well-lit images of the skin, hair, or nail of concern from different angles. The tool then asks questions related to personal history, and combining this with the image, it suggests a list of possible causative conditions. The user is then signposted to similar matching images and

dermatologist-reviewed information [15]. This system is underpinned by a DL system formed from a data set containing over 16,000 pictures of skin disorders. The system was shown to be noninferior to 6 board-certified US dermatologists and superior to 6 general practitioners [16].

On the scalp, psoriasis and seborrheic dermatitis can look very similar. Multispectral imaging allows pictographic data to be collected from regions of the electromagnetic spectrum not visible to the human eye. Historically speaking, processing such vast data can be time-consuming, with the equipment being bulky and cumbersome. A smartphone-based multispectral imaging system in conjunction with ML has been used in South

Korea to differentiate between psoriasis and seborrheic dermatitis of the scalp—allowing for swifter data interpretation and AI-based diagnosis. The authors used a small handheld multispectral camera, which displayed results on a smartphone screen for diagnosis and monitoring. Kim et al [17] achieved a sensitivity of 65% to 75% and specificity of 70% to 80% in psoriasis diagnosis of the scalp versus seborrheic dermatitis. Moreover, the ML methods yielded better outcomes versus conventional methods.

Psoriasis can also be differentiated from other similar looking inflammatory disorders. Zhao et al [18] classified 8021 images of 9 skin conditions using convolutional neural networks in psoriasis versus nonpsoriasis. Images included were lichen planus, lupus erythematosus, basal cell carcinoma, squamous cell carcinoma, atopic dermatitis, pemphigus, seborrheic keratosis, and psoriasis from a cohort of patients from a Chinese hospital. Their algorithm was superior to 25 Chinese dermatologists when tested on 100 new images. They reported a misdiagnosis rate of 3% compared to 27% by dermatologists.

Further to diagnosis, severity assessment is key to disease monitoring as well as determining which treatments are indicated. Shrivastava et al [19] used ML to analyze 540 images of skin (270 affected and 270 nonaffected images) in a cohort of 30 patients of Indian heritage with psoriasis. Principal component analysis was used to condense the data without losing important data points. This, in combination with computer-aided diagnosis, was used to define 3 main components of each image: higher order spectra features, texture features, and color features. This type of ML, when combining the 3 features, was proven to be highly effective with a classification accuracy of approximately 99% [19].

More sophisticated assessments such as psoriasis area and severity index (PASI) is widely used and present an additional challenge for AI with textural changes and thickness featuring in the scoring. This is further complicated by the regional scores, which require AI to determine which part of an image is unaffected as a percentage of overall body surface area. Huang et al [20] used a database of 14,096 images from a cohort of 2367 Chinese patients with psoriasis to estimate PASI. Multiview enhancement block (images from different angles) was implemented to allow all facets of the PASI score to be estimated. These images were then processed with convolutional neural network to extract specific features. Despite the large subjectivity of PASI scoring in clinical practice, the DL method used by the authors was comparable to PASI scores calculated by 43 dermatologists and has been successfully used in 18 different sites via the use of an app [20]. This has important ramifications for how we may deal with patients in more remote settings and those patients with less flexibility, where severity needs to be objectively scored.

Okamoto et al [21] developed this concept further via a technique termed “single-shot” PASI. The authors used 705 images of psoriasis, expanded with data augmentation techniques. Expert scoring was used as teacher data for the system to learn from. This DL system was then able to accurately assess psoriasis severity from a single photograph

only, reducing interuser variability and increasing efficiency [21].

### Clinical Management

Despite an abundance of classic and novel treatments for psoriasis, including biologics and small molecules, there are vast unmet needs in the management of psoriatic disease. A significant number of patients may not respond to a specific treatment primarily or secondarily or may develop adverse events. Therefore, we are still unable to predict the right treatment for the right patient. Available guidelines can help us select an appropriate biologic agent [22], although understanding and predicting outcomes is much more challenging. Biomarkers that could predict response to biologic therapy would be ideal for clinical care, although a lack of robust experimental data means no consensus exists yet toward application in clinical practice [23]. The use of AI to combine genotypic and phenotypic characteristics of patients with psoriasis to identify the most appropriate treatment is starting to emerge.

Emam et al [24], a Danish group in 2020, analyzed data from 681 patients with psoriasis from a national registry. A total of 6 different ML techniques were used to identify patterns from demographic and clinical data: generalized linear model, support vector machine, decision tree, random forest, gradient-boosted trees, and DL. Treatment outcomes were able to be predicted with high accuracy and less than 18% classification error, with data that are routinely available to clinicians. The generalized linear model was found to be the most accurate. Additionally, the model was able to identify characteristics associated with prolonged successful treatment, including but not limited to the age of 23 years and older at the time of diagnosis, baseline dermatology life quality index  $\geq 16$ , baseline PASI  $\geq 94$ , and weight  $\leq 98.9$  kg [24]. The study was limited by its retrospective nature, and it did not take into account access to medication, which could have limited duration of treatment.

Nielsen et al [25] used the same registry to retrospectively predict the most suitable biological therapy for patients with psoriasis. The authors found that gradient-boosted decision trees, a specific type of ML, performed significantly better than logistic regression for the prediction of specific biologic therapy. This technique was able to predict discontinuation of a given biologic within the first year of treatment with an accuracy of 62.9% to 67.6% [25].

AI is a natural fit to interpret the considerable amount of data that naturally accumulates as health care becomes more digitalized, which can often be dynamic through real-time capture. “Big data” is therefore well suited to interpretation via ML to draw patterns that may deepen our understanding of treatment trajectories and pathophysiology, taking health care one step closer to personalized medicine.

Bragazzi et al [26] performed a systemic review to map the current use of ML for big data analysis in psoriatic disease; 26 papers met the inclusion criteria. ML algorithms were shown to accurately extract patterns on predicting psoriatic arthritis from epidemiological registries, molecular databases, and different smartphone health applications. The authors did



however highlight that we should be mindful of data protection, confidentiality, and association biases [26].

Furthering genetic understanding of psoriasis paves the way for future treatment options as well as aiding in diagnosis and prediction of progression. Genetic medicine provides an enormous amount of data which can also benefit from ML interpretation. Using genetic markers to select those who are at the most risk of developing psoriatic arthritis could have a large potential for reducing long-term morbidity. With each new gene identified comes possible new targets for therapy—more of these are being identified through increasingly sophisticated data analysis [27]. Encouragingly, AI has also been shown to predict psoriasis highly accurately from microarray-based gene expression profiles [27].

Genome-wide association studies provide enormous amounts of complex data that can be swiftly interpreted via ML

**Textbox 6.** Advantages and disadvantages of artificial intelligence (AI).

#### Advantages

- Use in repetitive and time-consuming tasks
- Use in tasks with poor interobserver reliability
- Creative diagnostics via AI
- Applications for resource-limited settings
- Interpretation of big data

#### Disadvantages

- Choice of predictive model
- Generalizability
- Standardization
- Interpretability
- Data requirements
- Acceptance
- Liability

## Discussion

### Overview

In the future, AI will certainly take health care closer to personalized medicine. As research interests continue to grow, we will see an increase in application of AI, and this will translate to greater benefits to our patients. As described in [Textbox 6](#), AI can be used to reach greater numbers of patients—particularly those in remote and resource-limited settings.

Gaps do remain in the literature and there is a need for robust clinical governance when handling large volumes of patient data, which limits AI's applicability to current clinical practice. Fortunately, the International Psoriasis Council has agreed upon 36 statements around psoriasis and telemedicine relating to diagnosis and treatment, which will continue to progress the frontier [32].

techniques. Patrick et al [28] used ML (including random forest, conditional inference forest, shrinkage discriminant analysis, and elastic net regression) to identify 9 novel loci for psoriasis following evaluation of more than 7000 genotyped patients with psoriasis provided by genome-wide association studies. Love et al [29] analyzed data on 2318 patients with psoriatic arthritis to identify 31 psoriatic arthritis-related predictors. A single psoriatic arthritis code had a positive predictive value of 57% (95% CI 0.55-0.58), which increased to 90%-93% following natural language processing.

We should be mindful that AI is susceptible to various bias, and ethical aspects need to be considered with the patient as reference. [Textbox 6](#) [30,31] outlines broader disadvantages of AI applicable to psoriasis, and by contrast some of the advantages as well.

Despite the advances in the field of AI and psoriatic disease, AI is still not a panacea. Further validated models are needed to assess its role in both the diagnosis and the management of psoriatic disease. Dermatologists can play a crucial role in the evolution of AI and relevant training is required as well as cooperation with other specialties, such as data scientists. In the future, AI and ML may be able to predict the clinical course of the disease and, in combination with molecular studies, may even be able to guide our choice of treatment although acceptance by patients will need to be considered.

Moreover, teledermatology has gained significant popularity after the COVID-19 pandemic. Combining teledermatology with AI in psoriatic disease could indeed transform our current practice, as suggested by the International Psoriasis Council in their statements concerning remote monitoring of patients [32].

### Limitations

One of the challenges of AI in psoriatic disease resides with interpreting 3D aspects missed in imaging, such as thickness

of plaques for calculating the PASI. While multiview enhancement block may combat this to some extent, most algorithms only assess area, erythema, and/or scale [33], making an accurate PASI assessment difficult to achieve.

Additionally, AI diagnostics seem to be less accurate on dark skin color than lighter skin, even when trained on equal numbers of images [34,35]. More work is needed to optimize accuracy when using AI as a diagnostic tool in individuals with darker skin phototypes. Of note, most data sets are based on European and Australian teaching sets, which limits the ability of ML to perform on individuals with darker skin phototypes [36].

An Australian survey of over 4000 individuals demonstrated that people experiencing accuracy was consistently the most important factor in using AI and reducing costs the least important. Notably, 3558 (80%) responders valued continued human contact more than other factors [37]. Another international survey of dermatologists found that only 292 (23%) had good knowledge on the subject while 116 (17%) of 680 hospital-based dermatologist were fearful of the technology, although most agreed that dermatology would provide benefit overall [38].

Further, issues of choice regarding the right predictive model exist. These include small sample size of studies and variation in systems used, which make comparisons of studies challenging.

There are multiple guidelines and recommendations in the literature, which give suggestions on how to use AI safely, including methodologies for reporting on studies that use AI [39]. Interestingly, there is little mention of any such adherence in many AI and ML studies, although this likely represents unawareness rather than poor methodology.

AI is coming to the forefront of governing bodies. In June 2023, the European Parliament began negotiations on the AI Act; a framework for incorporating AI safely into health care [40].

## Conclusions

Future management of psoriatic disease will use diagnostic and therapeutic tools that are tailored to a group of patients with common characteristics, taking health care closer to precision medicine. As for dermatologists, it is crucial to embrace these new technologies and familiarize with them, in order to provide the best possible care to our patients, although we should be mindful that there remains a demand for human-human, face-to-face interaction.

## Conflicts of Interest

AB was involved in ad hoc consultancy, travel bursary, and lecturing fees with AbbVie, Almirall, Bristol Myers Squib, Galderma, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, and UCB. MAG has served as an investigator for Abbvie, Amgen, Argenx, Pfizer, Leo, Janssen Cilag, and UCB; and has received honoraria from Abbvie, Novartis, Janssen-Cilag, Almirall, Leo, UCB, Eli-Lilly, Bristol Myers Squib, Pfizer, Galderma, Faran, Pierre Fabre, Frezyderm, Galenica, Intramed, and Soterius as an advisory board member, as a speaker, or for support of educational activities or travel bursaries.

MAG has served as an investigator for Abbvie, Amgen, Argenx, Pfizer, Leo, Janssen Cilag, and UCB; and has received honoraria from Abbvie, Novartis, Janssen-Cilag, Almirall, Leo, UCB, Eli-Lilly, Bristol Myers Squib, Pfizer, Galderma, Faran, Pierre Fabre, Frezyderm, Galenica, Intramed, and Soterius as an advisory board member, as a speaker, or for support of educational activities or travel bursaries.

## Multimedia Appendix 1

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

[DOCX File, 109 KB - [derma\\_v7i1e50451\\_app1.docx](#)]

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## Abbreviations

**AI:** artificial intelligence

**DL:** deep learning

**ML:** machine learning

**PASI:** psoriasis area and severity index

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Viewpoint

# Potential Use of ChatGPT in Responding to Patient Questions and Creating Patient Resources

Kelly Reynolds<sup>1</sup>, MD; Trilokraj Tejasvi<sup>1</sup>, MBBS

Department of Dermatology, University of Michigan, Ann Arbor, MI, United States

**Corresponding Author:**

Trilokraj Tejasvi, MBBS  
Department of Dermatology  
University of Michigan  
1500 East Medical Center Drive  
Ann Arbor, MI, 48109  
United States  
Phone: 1 7349364054  
Fax: 1 7346476593  
Email: [ttejasvi@med.umich.edu](mailto:ttejasvi@med.umich.edu)

## 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.

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## 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

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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

Katie Roster<sup>1</sup>, MS; Rebecca B Kann<sup>1</sup>, BA; Banu Farabi<sup>2</sup>, MD; Christian Gronbeck<sup>3</sup>, MD; Nicholas Brownstone<sup>4</sup>, MD; Shari R Lipner<sup>5</sup>, MD, PhD

<sup>1</sup>New York Medical College, New York, NY, United States

<sup>2</sup>Dermatology Department, NYC Health + Hospital/Metropolitan, New York, NY, United States

<sup>3</sup>Department of Dermatology, University of Connecticut HealthCenter, Framington, CT, United States

<sup>4</sup>Department of Dermatology, Temple University Hospital, Philadelphia, PA, United States

<sup>5</sup>Department of Dermatology, Weill Cornell Medicine, New York, NY, United States

**Corresponding Author:**

Shari R Lipner, MD, PhD

Department of Dermatology

Weill Cornell Medicine

1305 York Ave 9th Floor

New York, NY, 10021

United States

Phone: 1 646 962 3376

Email: [shl9032@med.cornell.edu](mailto:shl9032@med.cornell.edu)

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**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

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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

Katrina Cirone<sup>1,2</sup>, HBSc; Mohamed Akrouf<sup>2,3</sup>, BSCEN, MScAC; Latif Abid<sup>2</sup>, BEng, HBA; Amanda Oakley<sup>4,5</sup>, MBChB

<sup>1</sup>Schulich School of Medicine and Dentistry, Western University, London, ON, Canada

<sup>2</sup>AIPLabs, Budapest, Hungary

<sup>3</sup>Department of Computer Science, University of Toronto, Toronto, ON, Canada

<sup>4</sup>Department of Dermatology, Health New Zealand Te Whatu Ora Waikato, Hamilton, New Zealand

<sup>5</sup>Department of Medicine, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

**Corresponding Author:**

Katrina Cirone, HBSc

Schulich School of Medicine and Dentistry

Western University

1151 Richmond Street

London, ON, N6A 5C1

Canada

Phone: 1 6475324596

Email: [kcirone2024@meds.uwo.ca](mailto:kcirone2024@meds.uwo.ca)

## 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.

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**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
<b>Feature conditioning</b>		
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
<b>Color bias</b>		
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
<b>Skin of color</b>		
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
<b>Image manipulation</b>		
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.

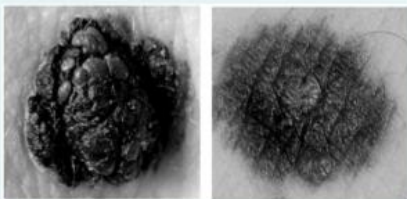
**Figure 1.** Melanoma detection when conditioned on color and diameter. GPT-4V: GPT-4 Vision; LLaVA: Large Language and Vision Assistant.

## 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\\_v7i1e55508\\_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

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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

Raphaella Lambert<sup>1</sup>, BA; Zi-Yi Choo<sup>1</sup>, BS; Kelsey Gradwohl<sup>2</sup>, MD; Liesl Schroedl<sup>2</sup>, MD; Arlene Ruiz De Luzuriaga<sup>2</sup>, MBA, MPH, MD

<sup>1</sup>Pritzker School of Medicine, University of Chicago, Chicago, IL, United States

<sup>2</sup>Section of Dermatology, University of Chicago Medical Center, Chicago, IL, United States

**Corresponding Author:**

Raphaella Lambert, BA  
Pritzker School of Medicine  
University of Chicago  
924 East 57th Street #104  
Chicago, IL, 60637  
United States  
Phone: 1 7737021937  
Email: [aleksalambert@uchicagomedicine.org](mailto:aleksalambert@uchicagomedicine.org)

## 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 specified <sup>c</sup>	Fifth grade <sup>d</sup>	Seventh grade <sup>e</sup>	Not specified	Fifth grade	Seventh grade	Not specified	Fifth grade	Seventh grade	Not specified	Fifth grade	Seventh grade
<b>Common conditions</b>													
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 dermatitis	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 conditions	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)
<b>Rare conditions</b>													
Bullous pemphigoid	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 conditions	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.

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## 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

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Original Paper

# Efficacy of an Artificial Intelligence App (Aysa) in Dermatological Diagnosis: Cross-Sectional Analysis

Shiva Shankar Marri<sup>1</sup>, MD; Warood Albadri<sup>1</sup>, MD; Mohammed Salman Hyder<sup>1</sup>, MBBS; Ajit B Janagond<sup>1</sup>, MD; Arun C Inamadar<sup>1</sup>, MD

Department of Dermatology, Venereology and Leprosy, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be) University, Vijayapura, Karnataka, India

**Corresponding Author:**

Arun C Inamadar, MD

Department of Dermatology, Venereology and Leprosy

Shri B M Patil Medical College, Hospital and Research Centre

BLDE (Deemed to be) University

Bangaramma Sajjan Campus

Vijayapura, Karnataka, 586103

India

Phone: 91 9448102920

Email: [aruninamadar@gmail.com](mailto:aruninamadar@gmail.com)

## 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.

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**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.

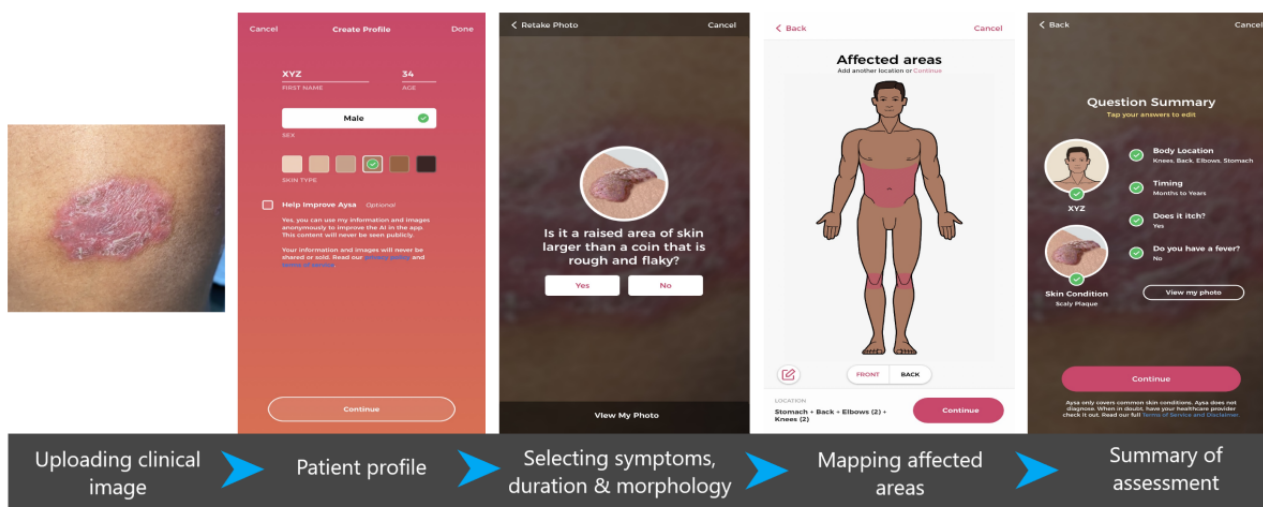
**Methodology**

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 (74.3-89.3)	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.





**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 pyoderma 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.

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### Data Availability

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

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### Conflicts of Interest

None declared.

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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

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Research Letter

# Readability of Information Generated by ChatGPT for Hidradenitis Suppurativa

Lauren Gawey<sup>1</sup>, MD; Caitlyn B Dagenet<sup>2</sup>, BS; Khiem A Tran<sup>3</sup>, MD, PhD; Sarah Park<sup>4</sup>, BA; Jennifer L Hsiao<sup>5</sup>, MD; Vivian Shi<sup>3</sup>, MD

<sup>1</sup>University of Arkansas for Medical Sciences, Little Rock, AR, United States

<sup>2</sup>College of Medicine, The University of Arizona, Tucson, AZ, United States

<sup>3</sup>Department of Dermatology, University of Arkansas for Medical Sciences, Little Rock, AR, United States

<sup>4</sup>David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, United States

<sup>5</sup>Department of Dermatology, University of Southern California, Los Angeles, CA, United States

**Corresponding Author:**

Vivian Shi, MD

Department of Dermatology

University of Arkansas for Medical Sciences

4301 W Markham St

#576

Little Rock, AR, 72205

United States

Phone: 1 8148022747

Email: [vivian.shi.publications@gmail.com](mailto:vivian.shi.publications@gmail.com)

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**KEYWORDS**

hidradenitis suppurativa; ChatGPT; Chat-GPT; chatbot; chatbots; chat-bot; chat-bots; machine learning; ML; artificial intelligence; AI; algorithm; algorithms; predictive model; predictive models; predictive analytics; predictive system; practical model; practical models; deep learning; patient resources; readability

## Introduction

ChatGPT is an artificial intelligence (AI) language model that has emerged as a resource for patient education, with over 100 million general users worldwide [1]. Despite its popularity, the readability of information provided by ChatGPT on dermatological conditions, such as hidradenitis suppurativa (HS), has yet to be explored. Patients with HS wait an average of 7 years after their initial symptoms appear to seek medical attention, which is largely attributed to insufficient awareness of the condition [2]. Effective patient education is vital for informed decision-making and self-management of medical conditions. The American Medical Association and the National Institutes of Health recommend that patient educational materials should be written at a sixth- and eighth-grade reading level, respectively [3]. This study aimed to assess the readability of ChatGPT-generated responses in comparison to established HS educational materials and web-based resources.

## Methods

We compared the readability of responses to frequently asked questions from the HS Foundation (HSF), HS Patient Guide (HSPG) [4], and ChatGPT-3.5, along with HS-related websites

(Google, Yahoo, and Bing were searched using the term “hidradenitis suppurativa”). The top 50 web pages from each search engine were reviewed, of which, 55 met inclusion criteria for further analysis. Readability was determined by average readability grade level and Flesch Reading Ease, which is scored from 0 to 100, with a higher score indicating that the material is easier to read. These readability formulas take into account the number of characters, syllables, words, and sentences to determine their score. Lexical density—a measure of linguistic complexity—and other text readability metrics were also recorded. While reviewers did not directly participate in the scoring process, the use of standardized software from [online-utility.org](http://online-utility.org) facilitated objective evaluations aligned with established criteria for readability assessment. The 2-tailed Student *t* test was used for bivariate analysis, with significance set at  $P < .05$ .

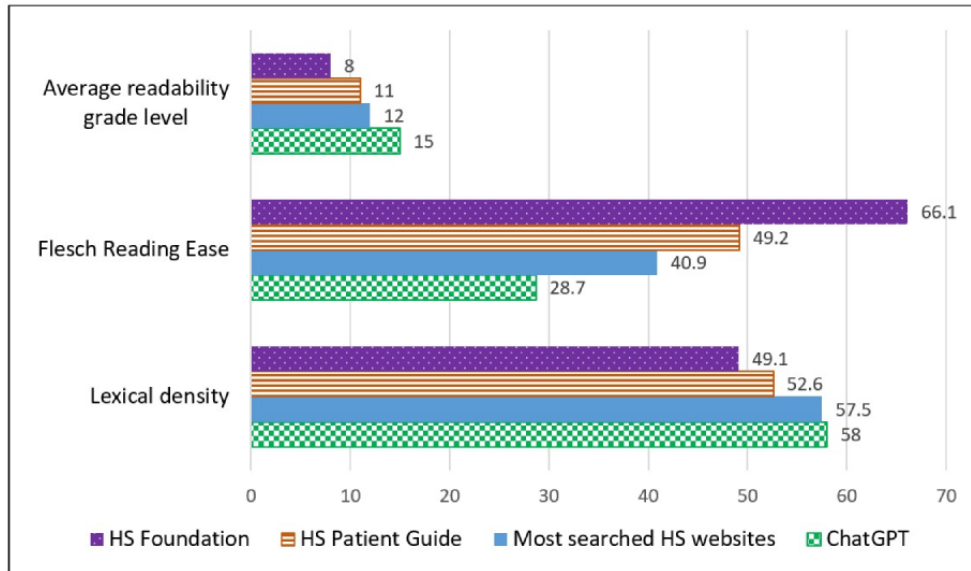
## Results

ChatGPT-generated responses had an average readability grade level of 15.0, which was significantly higher than that of the HSF (8.0), the HSPG (11.0), and HS-related websites (12.0;  $P < .001$ ). Flesch Reading Ease was significantly lower for ChatGPT-generated responses (28.7) than for the HSF (66.1),

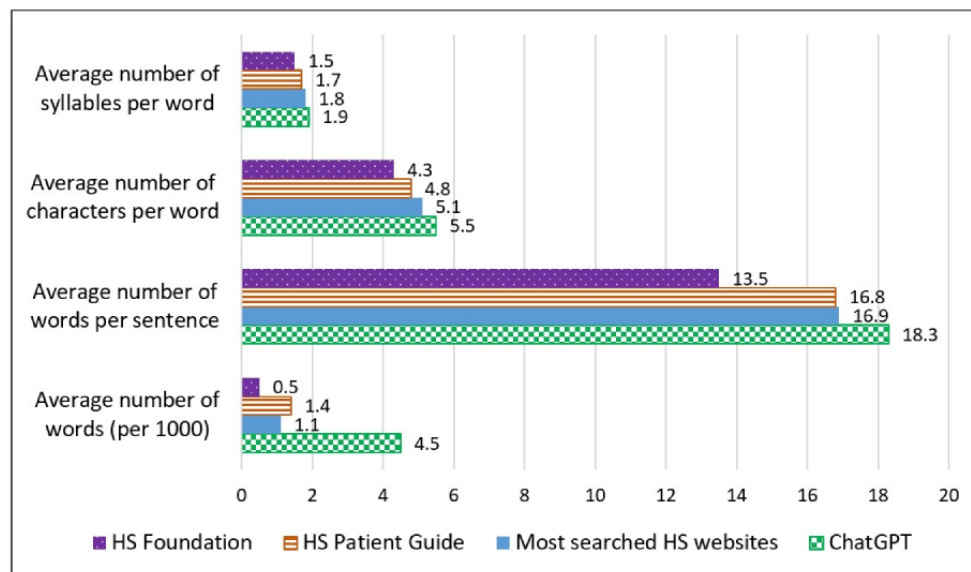
the HSPG (49.2), and HS-related websites (40.9;  $P < .001$ ; Figure 1). Both ChatGPT and HS-related websites had a higher lexical density of 58.0 and 57.47 respectively, indicating higher

linguistic complexity than that for the HSF (49.1) and the HSPG (52.6; Figure 2).

**Figure 1.** Readability of information for patients with hidradenitis suppurativa (HS) based on the average readability grade level, Flesch Reading Ease, and lexical density. The average readability grade level is calculated by averaging the Flesch Kincaid Grade Level, Gunning Fog Index, Simple Measure of Gobbledygook index, Coleman–Liau index, and automated readability index scores. Flesch Reading Ease is scored between 0 and 100, with a higher score indicating that the article is easier to read. Lexical density estimates linguistic complexity in a composition from the functional words (grammatical units) and content words (lexical units), calculated by comparing the ratio of lexical items to the total number of words.



**Figure 2.** Text readability metrics of information for patients with hidradenitis suppurativa (HS). These values represent an average of text readability metrics for each specified source.



## Discussion

Our results show that ChatGPT-generated responses were 7-9 grade levels above the recommended reading level and had a higher linguistic complexity than other HS-related web-based resources. These findings underscore the limitations of ChatGPT as a patient resource for HS, as the higher reading level and linguistic complexity of ChatGPT could hinder patient comprehension. The potential of AI-driven resources, such as ChatGPT, to transform health care communication hinges on their ability to align with recommended readability standards.

One study showed that when prompting AI to convert patient educational material to an easier grade level, AI could improve the readability of input material [5]. However, without prompting, the baseline reading level of ChatGPT-generated information is much higher than is recommended for patient educational materials. It is important to note that the practice of prompting AI systems for readability adjustments is currently not commonplace among the general public user base. As AI integration becomes more commonplace, future studies can explore and compare the effectiveness of prompting strategies to make consistent adjustments in readability. Educating health

care providers about the availability of options to prompt ChatGPT responses for enhanced readability can allow them to counsel their patients on adjusting readability levels that are most suitable for their preferences.

While the readability formulas used in this study offer a useful quantitative measure of text complexity, they focus primarily on surface-level features such as sentence length and syllable count, neglecting the structural complexity of texts, such as

coherence, organization, and language context, which also influence readability. Additionally, AI-generated texts may exhibit variations in tone, style, and content that traditional readability formulas may struggle to evaluate accurately.

Future directions should work toward improving not only the readability of AI, but also the quality and accuracy of generated information. The findings of this study serve as a foundational reference for future AI resource development in dermatology.

## Conflicts of Interest

VS is on the board of directors for the Hidradenitis Suppurativa Foundation; is a shareholder in Learn Health; and has served as an advisory board member, investigator, speaker, and received research funding from Genzyme (Sanofi), Regeneron Pharmaceuticals, AbbVie, Eli Lilly, Novartis, Sun Pharmaceutical Industries Limited, LEO Pharma Inc, Pfizer, Incyte Corporation, Boehringer Ingelheim, Aristeia Therapeutics, VYNE Therapeutics (formerly Menlo Therapeutics), Dermira, Inc (Eli Lilly), Burt's Bees, Galderma, Kiniksa Pharmaceuticals, UCB, TARGET PharmaSolutions, Altus Lab/cQuell, MYOR, Polyfins Technology, GPSkin, Skin Actives Scientific, and the National Eczema Association. JLH is on the board of directors for the Hidradenitis Suppurativa Foundation, a consultant for Novartis, and speaker for AbbVie. LG, CBD, KAT, and SP have nothing to declare.

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## Abbreviations

**AI:** artificial intelligence

**HS:** hidradenitis suppurativa

**HSF:** Hidradenitis Suppurativa Foundation

**HSPG:** Hidradenitis Suppurativa Patient Guide

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Viewpoint

# Atrophic Postacne Scar Treatment: Narrative Review

Enas Attia<sup>1,2</sup>, MD

<sup>1</sup>Department of Dermatology, Venereology, and Andrology, Faculty of Medicine, Ain Shams University, Cairo, Egypt

<sup>2</sup>Department of Dermatology, Ain Al Khaleej Hospital, Abu Dhabi, United Arab Emirates

**Corresponding Author:**

Enas Attia, MD

Department of Dermatology, Venereology, and Andrology, Faculty of Medicine

Ain Shams University

Abbaseya square

Cairo, 11566

Egypt

Phone: 20 224346709

Fax: 20 224346709

Email: [annosah1974@yahoo.com](mailto:annosah1974@yahoo.com)

## 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.

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**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  $\mu\text{m}$  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  $\mu\text{m}$  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. Intra-dermal 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 intra-dermal 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

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Viewpoint

# PatientsLikeMe and Online Patient Support Communities in Dermatology

Mindy D Szeto<sup>1</sup>, MS; Michelle Hook Sobotka<sup>2</sup>, MS; Emily Woolhiser<sup>3</sup>, BS; Pritika Parmar<sup>4</sup>, BS; Jieying Wu<sup>5</sup>, MS; Lina Alhanshali<sup>6</sup>, BA; Robert P Dellavalle<sup>1,7</sup>, MSPH, MD, PhD

<sup>1</sup>Department of Dermatology, University of Minnesota Medical School, Minneapolis, MN, United States

<sup>2</sup>Arizona College of Osteopathic Medicine, Midwestern University, Glendale, AZ, United States

<sup>3</sup>College of Osteopathic Medicine, Kansas City University, Kansas City, MO, United States

<sup>4</sup>Department of Dermatology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

<sup>5</sup>School of Medicine, Rocky Vista University College of Osteopathic Medicine, Parker, CO, United States

<sup>6</sup>Department of Dermatology, SUNY Downstate College of Medicine Brooklyn, New York, NY, United States

<sup>7</sup>Dermatology National Executive Program Director, Dermatology Service, Minneapolis VA Medical Center, Minneapolis, MN, United States

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Department of Dermatology

University of Minnesota Medical School

1-411 Phillips-Wangensteen Building

516 Delaware St SE, MMC 98

Minneapolis, MN, 55455

United States

Phone: 1 612 625 8625

Email: [della056@umn.edu](mailto:della056@umn.edu)

## 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.

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**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.

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## 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

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Original Paper

# Effectiveness of 675-nm Wavelength Laser Therapy in the Treatment of Androgenetic Alopecia Among Indian Patients: Clinical Experimental Study

BS Chandrashekar<sup>1</sup>, MD; Oliver Clement Lobo<sup>1</sup>, MD; Irene Fusco<sup>2</sup>, PhD; Francesca Madeddu<sup>2</sup>, MSc; Tiziano Zingoni<sup>2</sup>, MSc

<sup>1</sup>Cutis Academy of Cutaneous Sciences, Bengaluru, India

<sup>2</sup>El.En. Group, Calenzano, Italy

**Corresponding Author:**

Irene Fusco, PhD

El.En. Group

Via Baldanzese 17

Calenzano, 50041

Italy

Phone: 39 3286853105

Email: [i.fusco@deka.it](mailto:i.fusco@deka.it)

## Abstract

**Background:** Androgenetic alopecia (AGA) is the most prevalent cause of hair loss around the world.

**Objective:** The purpose of this study was to evaluate the efficacy of laser stimulation with a 675-nm wavelength for the treatment of AGA in male and female Indian patients.

**Methods:** A total of 20 Indian healthy patients aged 23-57 years who presented a grade of alopecia stage I to stage V underwent one single pass with a 675-nm laser to the scalp area twice a week for a total of 8 sessions, followed by once a week for 4 sessions and once in 2 weeks for 2 sessions. There are 14 laser treatments in total. Macro- and dermatoscopic images have been acquired at T0 (baseline) and T1 (4 months). The vertex, frontal, and parietal areas of the scalp were evaluated. Many parameters were analyzed including hair count and hair density of terminal; mean thickness; vellus follicles; total follicular units; units with 1 hair, 2 hairs, 3 hairs, 4 hairs, and >4 hairs; unit density; and average hair/unit.

**Results:** The macroimages and dermatoscopic evaluations showed good improvement over the entire treated area, with a clear increase in the number of hairs and hair thickness. General parameters such as hair count and hair density showed a percentage increase of around 17%. The hair mean thickness parameters showed a significant ( $P<.001$ ) percentage increase of 13.91%. Similar results were obtained for terminal and vellus hair: terminal hair count and hair density significantly ( $P=.04$  and  $P=.01$ , respectively) increased by 17.45%, vellus hair count increased by 16.67% ( $P=.06$ ), and the density of vellus hair increased by 16.61% ( $P=.06$ ).

**Conclusions:** The study findings demonstrate that the 675-nm laser system improved AGA in Indian patients, facilitating the anagen phase and improving hair density and other positive hair parameters.

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## KEYWORDS

androgenetic alopecia; AGA; 675-nm laser; Indian patients; hair restoration; effectiveness; laser therapy; therapy; treatment; Indian; patients; patient; India; hair loss; hair; laser stimulation; hair density

## Introduction

Worldwide, androgenetic alopecia (AGA) represents the most common cause of hair loss. Up to 70% of men and 40% of women are affected, primarily affecting the frontal and parietal regions of the scalp.

AGA can affect all races, but the prevalence rates vary. Prevalence is considered to be highest in White men [1,2]. Male AGA phenotypic variants are graded using the universally accepted modified Norwood-Hamilton classification. AGA grade scores range from I to III for men according to the Norwood-Hamilton scale [3] and from I to II for women according to the Ludwig scale [4].

According to statistics, at least 50% of male individuals by age 50 years and a similar proportion of female individuals by age 60 years will experience this medical disorder [5]. A new community-based study in Singapore found that 87% of Indian individuals are affected, compared to more than 61% of Chinese individuals [6].

In the Indian context, a population-based study of 1005 patients showed a 58% prevalence of AGA in male individuals aged 30-50 years [7], and a large study also reported that stage II was the most common presentation of AGA in the Indian population [8]. Another study conducted on the Indian population found stage II and III as the most common presentations [9].

Affected individuals experience psychological and emotional consequences [10]. Androgens, including testosterone and its derivatives, frequently cause AGA in genetically predisposed individuals [11]. It manifests as a gradually shorter anagen phase in terminal hair follicles (HFs) and a final hair cycle transition from terminal to intermediate to vellus hair on the scalp in a characteristic pattern [12].

Receptor activation pathways play a role in the development of AGA in mini complex organs. In this setting, the increased sensitivity to androgenic hormones in individuals with AGA negatively impacts the Wnt/ $\beta$ -catenin signaling pathway, which is crucial for stimulating the anagen phase [13]. The HFs in areas affected by AGA have an oval dermal papilla, a very thin matrix, low levels of melanin in the catagen phase, and often exhibit recurring nondestructive perifollicular microinflammation along with the deposition of mastocytes, macrophages, and lymphocytes. This condition leads to progressive follicular fibrosis and thickening of the fibrocollagenous sheath [14].

Currently, the US Food and Drug Administration has approved three therapies for AGA: topical minoxidil, topical finasteride, and lower-level laser therapy. However, some of these treatments are associated with several side effects and unsatisfactory outcomes.

Minoxidil is associated with a number of adverse reactions, including pruritus, scalp irritation, irritant and allergic contact dermatitis, cardiovascular system symptoms/signs in a dose-dependent manner, and facial hypertrichosis [15-17]. Although primarily utilized in dermatologic applications, finasteride has been associated with hepatic dysfunction, unilateral breast enlargement and palpitations, libido reduction, head pain, fever, sexual dysfunction, and neuropsychiatric side effects [18-20]. In clinical practice, various medication treatments like progesterone, azelaic acid, zinc salts, flutamide, dutasteride, and spironolactone, as well as invasive techniques like platelet-rich plasma, scalp microneedling, and hair transplantation, are commonly employed, but they have not demonstrated conclusive outcomes or promising prospects [16]. For this reason, research into specific treatments for AGA is needed.

Devices based on light-emitting diodes (LEDs) represent the most innovative and secure therapy solution for a range of diseases, such as aging, dysfunctional hair development, and skin inflammatory illnesses [21]. Numerous research studies

have documented the efficacy of photodynamic treatment (PDT) in the management of hair loss [22]. When compared to alternative treatments, PDT provides patients with numerous advantages. It has a good safety profile and is noninvasive, affordable, and convenient for patients. Pharmacotherapy and other treatment methods can be combined or substituted with PDT [23].

The most common light source mentioned in studies is represented by low-level laser therapy [22,24-26]. A recently published study [27] conducted on Indian patients demonstrated that the application of low-level laser therapy in combination with a minoxidil topical solution can successfully raise the percentage of patients who recover from AGA and enhance patients' satisfaction with treatments received for hair regrowth.

The efficacy of LED therapy with visible light has additionally been accepted as a valid adjuvant treatment in the recalcitrant form of alopecia areata [28]. Furthermore, real effectiveness in treating hair loss has recently been shown with LED therapy, especially with treatments that use red and infrared wavelengths.

Palma and colleagues [29] reported the first case in which photobiomodulation therapy with a continuous wavered laser (660 nm) was successfully used as monotherapy for AGA. It has been demonstrated that the anagen phase, which is the active growth phase of HFs, can be stimulated with great success at a wavelength of 660 nm. Studies conducted in vitro demonstrate how red light can prolong the anagen phase and postpone the catagen transition [30]. Specifically, near-infrared light has been used to stimulate cell proliferation and differentiation of stem cells [31]. The effect was established in vitro by the degree of expression of Ki-67, an indicative biomarker of cell proliferation in the hair matrix [32].

The recent published investigation of Sorbellini et al [33] assessed the efficacy of 675-nm laser emissions for the management of androgenetic alopecia in female and male patients. The results showed a significant increase in the density of the hair shafts, resulting in a 60% reduction of the miniaturization process in the treated areas without side effects.

Based on these scientific findings, the purpose of this study was to evaluate the efficacy of laser stimulation with a 675-nm wavelength for the treatment of AGA in male and female Indian patients, which currently has limited research.

## Methods

### Recruitment

From August 2023 to March 2024, a total of 20 Indian healthy patients (7 female and 13 male) aged 23-57 years and who presented with Alopecia stage I to stage V were enrolled. AGA severity ranges from stage I to V for men according to the Norwood-Hamilton scale and from stage I to III for women according to the Ludwig scale.

AGA was diagnosed based on dermatologic and clinical examinations. The following exclusion criteria were used: topical or systemic treatments for AGA in the 3 months preceding the study, systemic or cutaneous comorbidities on an autoimmune basis or involving connective tissue, and pregnancy.



## Ethical Considerations

The study received ethics approval from the Cutis Institutional Ethics Committee (CIEC) on July 14, 2023. It was conducted in accordance with the Declaration of Helsinki on ethical principles for medical research involving human subjects. All data utilized in this study were managed securely and deidentified to ensure the rights and privacy of the participants. Informed consent was obtained from all patients involved in the study. This research received no external funding. No compensation was provided to participants for their time participating in this research.

## Device Description

The RedTouch laser (Deka M.E.L.A, Calenzano, Italy) device was used. The study device emits a wavelength of 675 nm, and it is equipped with a 13 × 13 mm scanning system able to generate fractional microzones with a width of 0.7 mm (DOT area) of subablative and selective thermal damage on the skin. The presence of an integrated skin cooling system and the possibility to add a contact sensor minimizes downtime and possible adverse effects, and protects the epidermal layer. This laser can have different effects on the skin. At low energies, it creates a reversible thermal area that biostimulates to a depth of 3-6 mm while increasing the energy results in the formation of a coagulation column to a depth of 0.5-1 mm and deeper reversible heating.

## Study Protocol and Clinical Photographic Assessment

All patients underwent one single pass of the 675-nm laser to the scalp area twice a week for a total of 8 sessions, followed by once a week for 4 sessions and once every 2 weeks for 2 sessions. The duration time of each session was 20 minutes, and the following parameters were selected: power 1 W, dwell time 100 ms, stack 1, spacing of 1000 µm, and a cooling temperature set at 15 °C. At the end of the treatment protocol, patients completed 14 laser sessions.

Macro- and dermatoscopic images were acquired at T0 (baseline) and T1 (4 months). For the dermatoscopy analysis, the Fotofinder device (FotoFinder Trichoscale System, GmbH 1000, Bad Birnbach, Germany) was used at T0 (baseline) and

T1 (4 months). The dermatoscopic analysis of each patient was compared at baseline and after 4 months to quantitatively assess the hair. The vertex, frontal, and parietal areas of the scalp were evaluated.

Many parameters were analyzed including hair count and hair density of terminal; mean thickness; vellus follicles; total follicular units; units with 1 hair, 2 hairs, 3 hairs, 4 hairs, or more than 4 hairs; unit density; and average hair/unit.

Hair count and hair density indicate the number of hairs in the analyzed area without distinguishing between terminal hairs and vellus (which are analyzed with the next two parameters). Finally, the total number of follicular units, the density of the units, the number of hairs per follicular unit, and the average number of hairs per unit were analyzed. An increase in the number of follicular units, mean thickness, and number of hairs per follicular unit was considered a positive outcome at the end of 4 months (T1).

## Side Effects

Possible side effects such as hair burn, blistering, scarring, burns, hypopigmentation, or hyperpigmentation that may result from the use of given energy levels are monitored for the entire treatment period.

## Pretreatment Procedure

To prevent light reflections and to keep the handpiece's cooling temperature uniform, the patient's skin and hair were soaked with water prior to the treatment. To increase patient comfort and allow the patient to leave easily after the treatment, hair gel was not used.

## Statistical Analysis

All clinical data were reported as means and SDs. The statistical analysis was carried out using a Student *t* test (1-tailed). A *P* value of .05 was selected as the cutoff for significance.

## Results

Macro- and dermatoscopic images of patients' scalp areas taken at T0 and T1 were quantitatively evaluated (Table 1).

**Table 1.** Mean clinical parameters for 20 patients at baseline (T0) and follow-up (T1), and the percentage difference

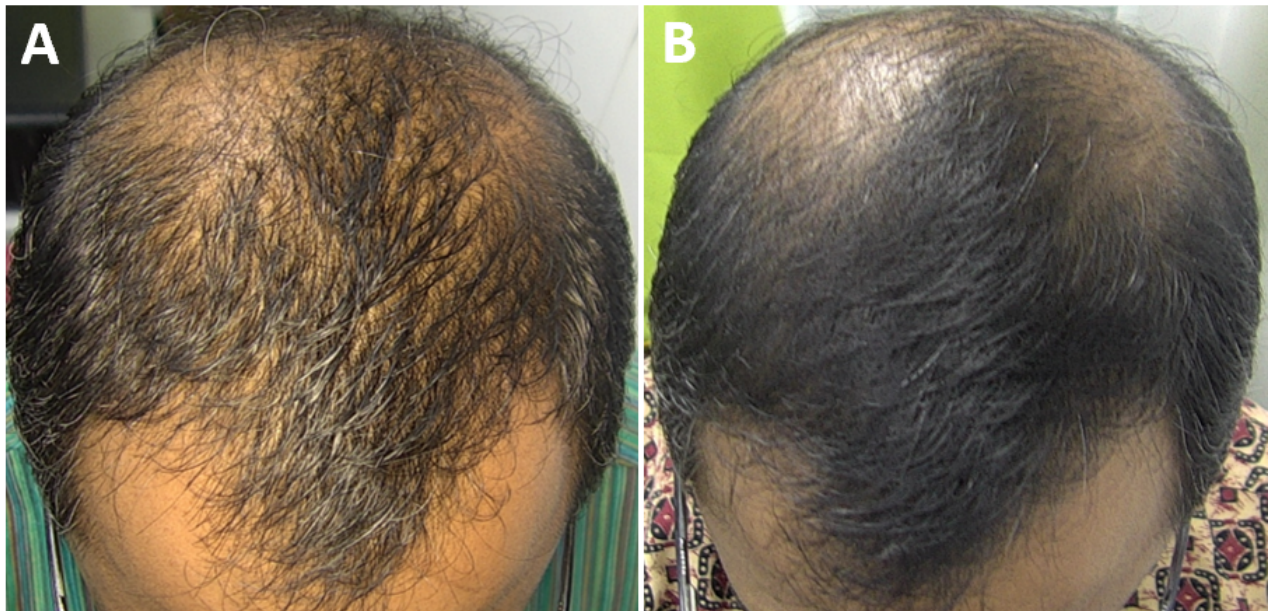
	T0, mean (SD)	T1, mean (SD)	Percentage difference (%)	P value
Hair count <sup>a</sup>	104.62 (23.71)	122.60 (30.19)	+17.19	<.001
Hair density (cm <sup>2</sup> ) <sup>a</sup>	115.82 (26.24)	135.72 (33.42)	+17.18	<.001
Hair count terminal <sup>a</sup>	69.58 (18.37)	81.72 (19.00)	+17.45	.04
Hair count vellus	35.04 (19.83)	40.88 (16.67)	+16.67	.06
Hair density terminal (cm <sup>2</sup> ) <sup>a</sup>	77.03 (20.33)	90.47 (21.03)	+17.45	.01
Hair density vellus (cm <sup>2</sup> )	38.81 (21.93)	45.26 (23.58)	+16.61	.06
Mean thickness (mm) <sup>a</sup>	0.05 (0.01)	0.06 (0.01)	+13.91	<.001
Total follicular units <sup>a</sup>	91.36 (11.69)	100.85 (12.45)	+10.39	<.001
Units (1 hair)	50.71 (3.44)	51.90 (4.34)	+2.35	.16
Units (2 hairs) <sup>a</sup>	27.62 (5.37)	32.01 (5.29)	+15.89	<.001
Units (3 hairs) <sup>a</sup>	9.89 (3.33)	11.71 (3.60)	+18.40	.01
Units (4 + >4 hairs) <sup>a</sup>	3.14 (2.21)	5.21 (2.09)	+69.92	<.001
Units density (cm <sup>2</sup> ) <sup>a</sup>	101.24 (13.10)	109.64 (16.03)	+8.30	.004
Average hair/unit <sup>a</sup>	1.61 (0.12)	1.71 (0.10)	+5.97	<.001

<sup>a</sup>Statistically significant clinical data ( $P < .05$ ).

The macro- and dermatoscopic images showed good improvement over the entire treated area, with a clear increase in the number of hairs and thickened hair (Figures 1-7). These

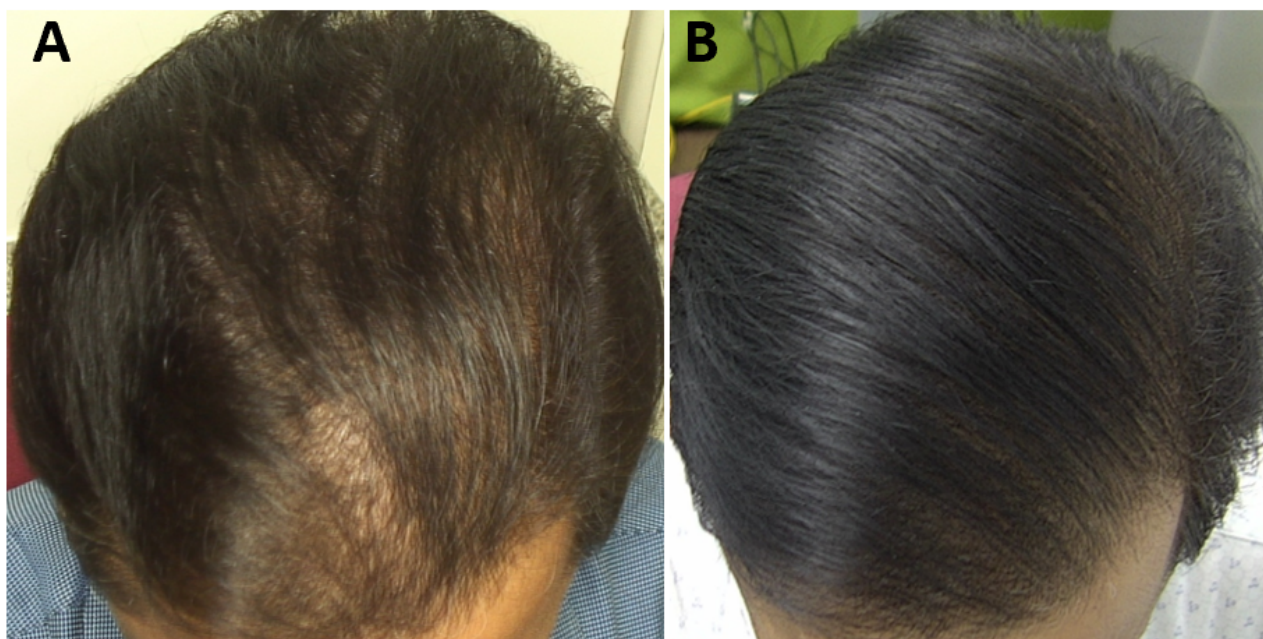
data were confirmed by the quantitative dermatoscopic evaluation. General parameters such as hair count and hair density showed a percentage increase of around 17%.

**Figure 1.** Scalp area of Indian male patient before (A) and after 14 sessions with 675-nm laser (B). A clinical improvement and restoration of the scalp's central hairline hairs from baseline (T0) to the 4-month follow-up (T1) were observed.

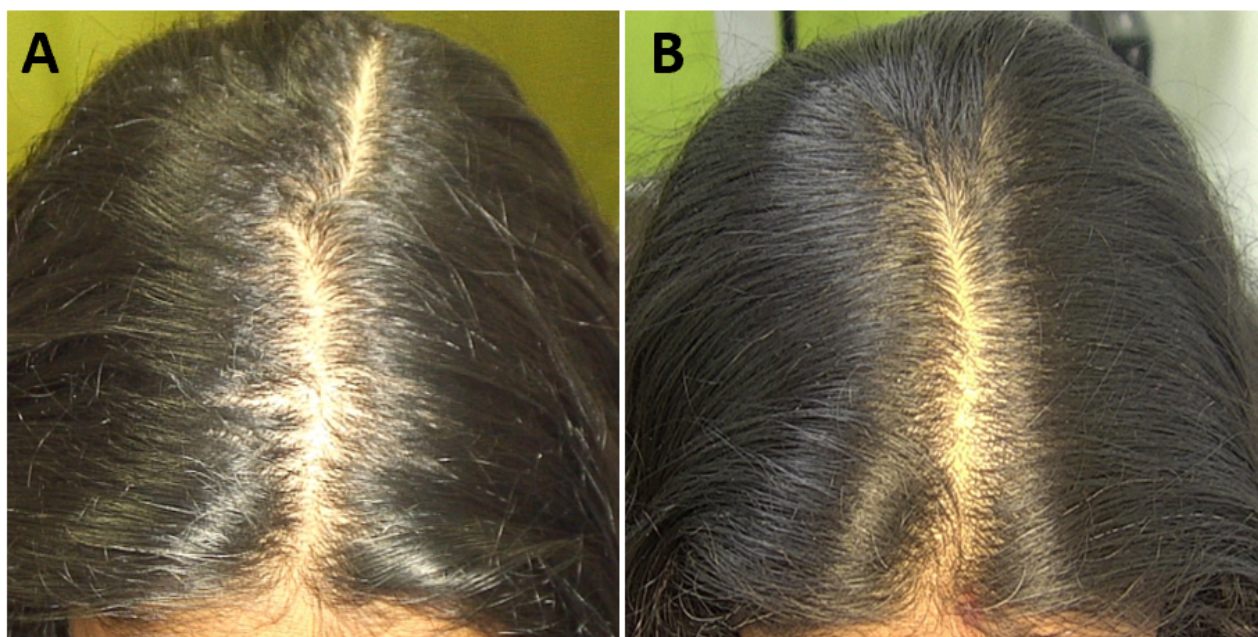




**Figure 2.** Scalp area of Indian male patient before (A) and after 14 sessions with 675-nm laser (B). A clinical improvement and restoration of the scalp's central hairline hairs from baseline (T0) to 4-month follow-up (T1) were observed.

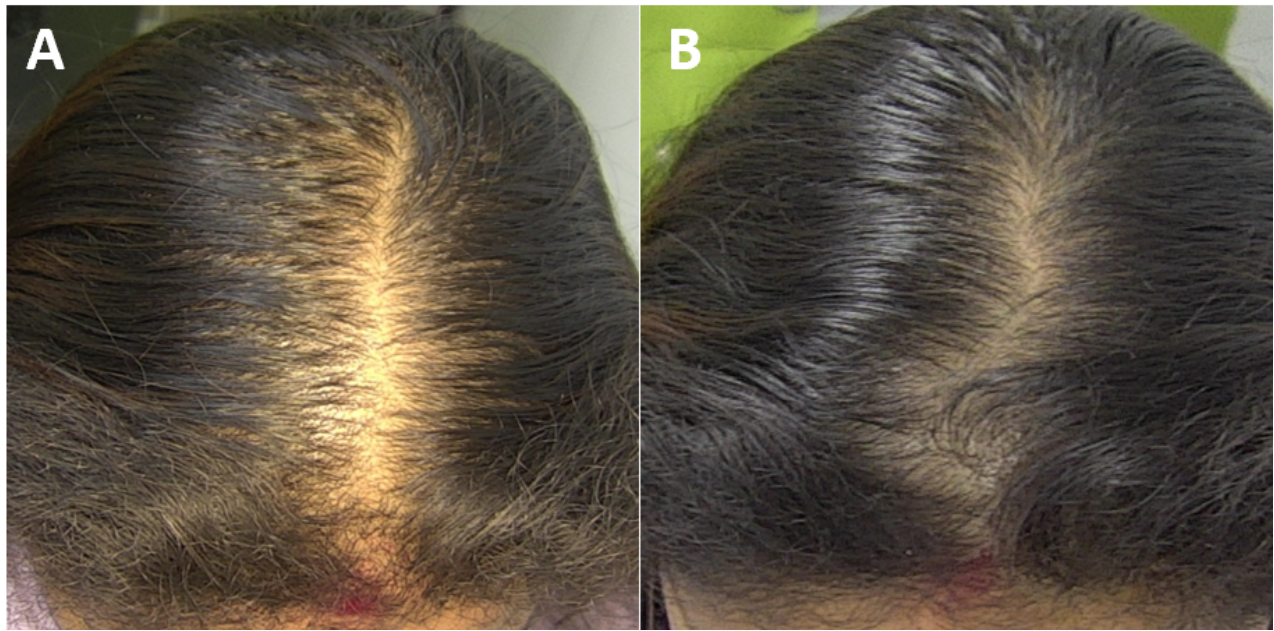


**Figure 3.** Scalp area of Indian female patient before (A) and after 14 sessions with 675-nm laser (B). A clinical improvement and restoration of the scalp's central hairline hairs from baseline (T0) to 4-month follow-up (T1) were observed.

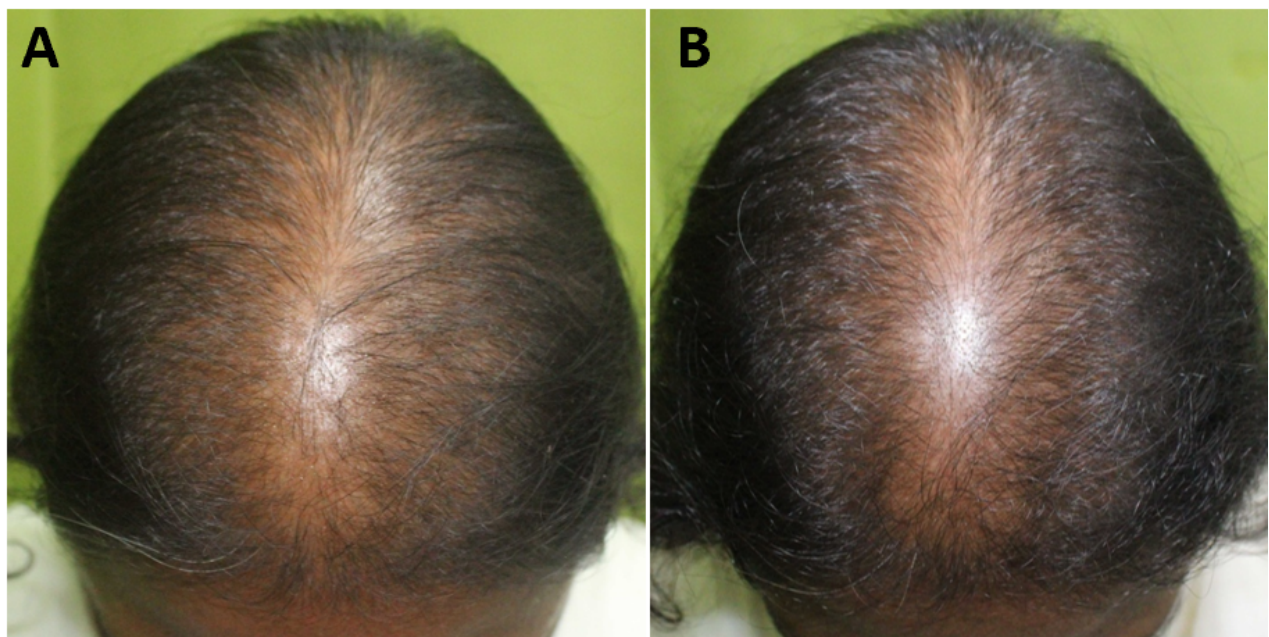




**Figure 4.** Scalp area of Indian female patient before (A) and after 14 sessions with 675-nm laser (B). A clinical improvement and restoration of the scalp's central hairline hairs from baseline (T0) to 4-month follow-up (T1) were observed.

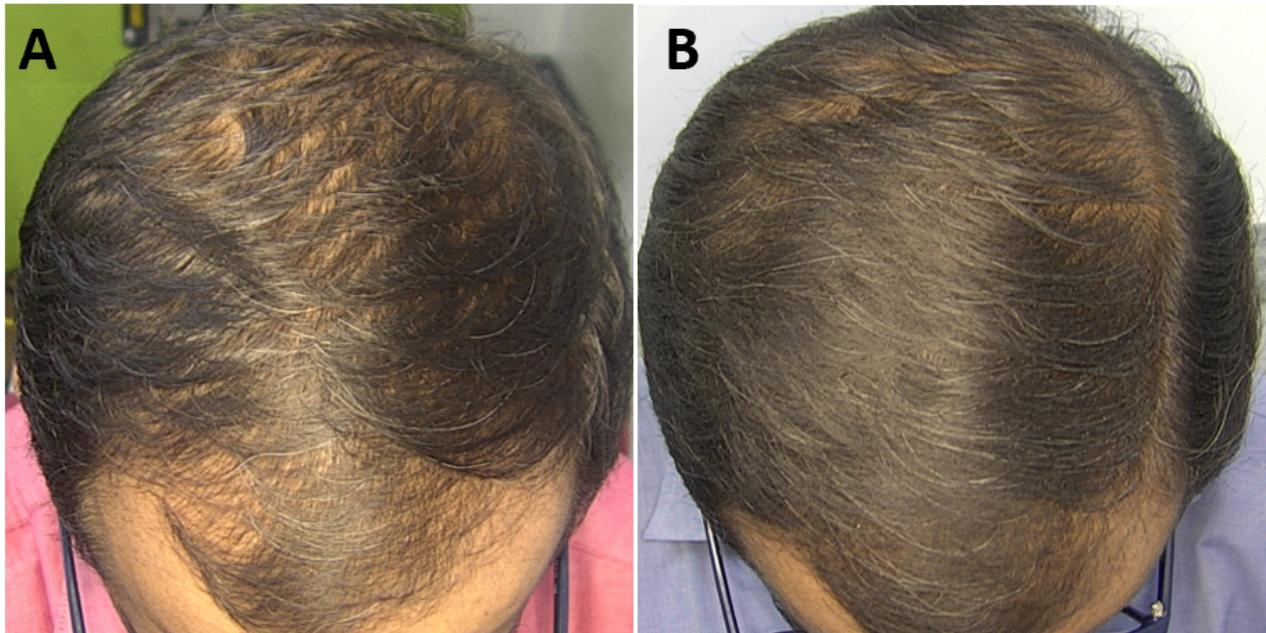


**Figure 5.** Scalp area of Indian female patient before (A) and after 14 sessions with 675-nm laser (B). A clinical improvement and restoration of the scalp's central hairline hairs from baseline (T0) to the 4-month follow-up (T1) were observed.

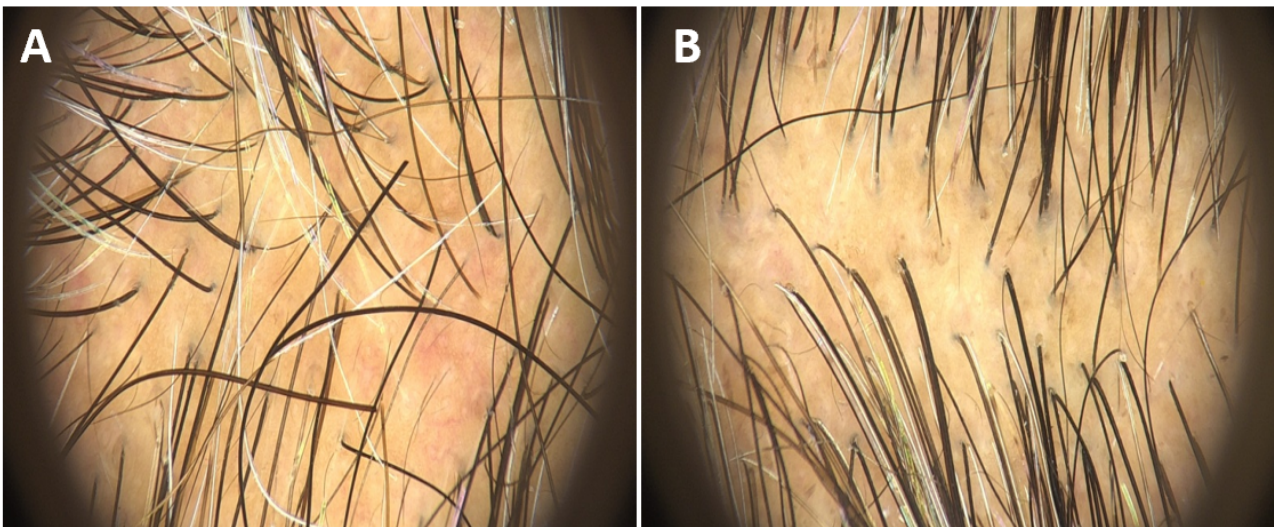




**Figure 6.** Scalp area of Indian male patient before (A) and after 14 sessions with 675-nm laser (B). A clinical improvement and restoration of the scalp's central hairline hairs from baseline (T0) to the 4-month follow-up (T1) were observed.



**Figure 7.** Dermatoscopy imaging of the patient's scalp area before (A) and at the 4-month follow-up (B). A clinical improvement and restoration of the scalp's central hairline hairs were observed.



The mean hair thickness parameters showed a significant ( $P<.001$ ) percentage increase of 13.91%. Similar results were obtained for terminal hair and vellus hair: terminal hair count and hair density significantly ( $P=.04$  and  $P=.01$ , respectively) increased by 17.45%, vellus hair count increased by 16.67% ( $P=.06$ ), and vellus hair density increased by 16.61% ( $P=.06$ ). Confirming the improvements, a significant ( $P<.001$ ) increase in follicular units with 4 or more hairs was observed. This is a crucial aspect, since having more hair per follicular unit corresponds to greater hair density, giving the appearance of a thicker scalp, which is a sign of young and healthy hair.

## Discussion

When standard and established treatments are less effective or less productive, laser therapy offers an extra therapeutic option and is a useful adjunct to traditional therapies. For patients who

are unable or unwilling to take drugs or inject platelet-rich plasma, laser therapy may be the ideal option for growing hair and preventing future progression. There are various medications available for the management of AGA. Other minimally invasive methods like the use of pulsed electromagnetic field therapy also have shown a positive biological effect on hair regrowth and were used in combination with laser therapy for the clinical treatment of AGA [34]. Among laser treatment modalities, red light, which has a skin penetration depth of 1-6 mm, improves blood circulation, promotes cell metabolism and nutrition supply to capillaries, and strengthens hair strands, anchoring follicles and pain relief (seen as an additional advantage in cases of trichodynia). The other techniques, unlike laser therapy, achieved good results but required a greater number of sessions at the same time, and the injected substances and needle pricks are not always tolerated by the patient. Red and near-infrared lasers can prolong the anagen growth phase of the HFs,



promoting an increase in hair count in patients without significant side effects [35]. Indeed, laser phototherapy is assumed to facilitate anagen reentry in telogen HF in the anagen phase, boost active anagen HF proliferation, and prevent premature catagen growth [25].

Among the laser treatment modalities, red light, with its 1- to 6-mm skin penetration depth, is the most effective in promoting cell metabolism, blood circulation, capillary nourishment delivery, cuticle anchorage, and pain relief.

The study's findings showed that 675-nm laser technology represents a secure and efficient therapeutic approach for AGA, particularly when telogen effluvium is present. Potential mechanisms of action for this laser technology include promoting and lengthening the anagen phase of follicle hair, enhancing blood microcirculation, and stimulating fibroblasts to produce collagen and elastin.

The mechanisms through which red light acts include photobiochemical reactions with an upregulation of intracellular oxidative stress and an increment of adenosine triphosphate production (through absorption of mitochondrial protoporphyrin IX). This cellular pathway leads to an increase in reactive oxygen species and increases in transcription factors like hypoxia-inducible factor-1 and nuclear factor  $\kappa$ B [36]. Further consequences, such as increased cell motility and proliferation; changes in the levels of cytokines, growth factors, and inflammatory mediators; and increased oxygenation of the tissue are triggered downstream by these transcription factors that regulate protein synthesis.

This mechanism has significant roles in HF growth-stimulating collagen synthesis through fibroblast growth factor activation, increasing type 1 procollagen, increasing the metalloproteinase-9 (MMP-9) matrix, decreasing MMP-1, stimulating angiogenesis, and increasing blood flow [11]. Furthermore, published data on cultured human HF have demonstrated that red light enhances Ki-67-positive cells, which represents a typical marker of HF cell proliferation [32].

The data reported in our study showed that there has been a 17% increase in hair length measurable parameters such as hair count, hair density, and hair thickness. Similar results were obtained for terminal and vellus hair.

Additionally, follicular units containing 4 or more hairs increased, suggesting hair revival leading to improvement in hair density and the appearance of a fuller scalp.

The study device interacts with water and the vascular component minimally while having a strong affinity for collagen and melanin. In contrast to laser systems that use wavelengths

<650 nm, which are highly absorbed by hemoglobin, and wavelengths >950 nm, which are primarily absorbed by water, the wavelength of 675 nm operates directly on the collagen component based on its spectrum absorption coefficient. In this manner, the heat reaches the collagen fibers directly, bypassing other chromophores. Consequently, a thermal column was formed that diffuses heat to the surrounding areas causing immediate shrinkage and denaturation of the collagen with subsequent neocollagenogenesis [37].

Within 3 months of the treatment sessions, the qualitative and quantitative results demonstrated a significant increase in the number of vellus hairs compared with terminal hairs, indicating the revival of dormant follicles resulting in hair restoration.

The main study limitation was the small population sample and short follow-up. Additional investigations on a larger population sample will be required to standardize the criteria employed. A longer follow-up period will be expected to see whether the laser's effects on hair growth are lasting. As a future goal, we plan to execute immunohistochemical or histological analyses.

Comparable to previous scientific research, this study looked at different parameters of accuracy like, a better hair count/density, length, thickness and follicular ratio, a photographic evaluation, and dermatoscopic analysis. Additionally, dermatoscopy helps physicians examine the skin post therapy and observe an optimal end point.

The 675-nm wavelength treatment is easy to administer and produces a minimally invasive therapy for patients, as it does not burn preexisting hair, requires no recovery period for the patient, and avoids needles and pain.

According to the research by Sorbellini et al [33], 675-nm laser treatment has proven effective in improving AGA in young patients, managing to preserve the intact epidermis and hair shaft. Indeed, the biostimulation parameters selected in this study did not damage the HF, performing the procedure with intact hair length.

As confirmed by the results of this study and those previously published, the 675-nm laser device promises a uniform, rapid, safe, and effective method of treatment for AGA, with minimal discomfort to the patients and the potential to be combined with other treatment options.

In conclusion, the 675-nm laser system improved AGA in Indian patients, facilitating the anagen phase and improving hair density and other positive hair parameters while minimizing the risks of side effects when compared to other conventional interventions.

## Authors' Contributions

BSC, OCL, and TZ conceptualized the study, validated the data, conducted the investigation, and contributed toward project administration and funding acquisition. BSC and OCL contributed toward the methodology, software, and resources. BSC, FM, and OCL conducted the formal analysis. BSC, OCL, FM, and TZ curated the data. IF and FM prepared the original draft. BSC, OCL, IF, FM, and TZ reviewed and edited the manuscript, contributed to the visualization, and supervised the study. All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

TZ, FM, and IF were employed by El.En. Group. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Abbreviations

**AGA:** androgenetic alopecia

**HF:** hair follicle

**LED:** light-emitting diode

**MMP-9:** metalloproteinase-9

**PDT:** photodynamic treatment

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# Gender Representation in Authorship of Academic Dermatology Publications During the COVID-19 Pandemic: Cross-Sectional Study

Mindy D Szeto<sup>1</sup>, MS; Melissa R Laughter<sup>2</sup>, MD, PhD; Mayra B C Maymone<sup>3</sup>, MD, DSc; Payal M Patel<sup>4</sup>, MD; Torunn E Sivesind<sup>5</sup>, MD; Colby L Presley<sup>6</sup>, DO; Steven M Lada<sup>7</sup>, MD; Kayd J Pulsipher<sup>8</sup>, DO; Henriette De La Garza<sup>9</sup>, MD; Robert P Dellavalle<sup>1</sup>, MSPH, MD, PhD

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## Corresponding Author:

Robert P Dellavalle, MSPH, MD, PhD

## Abstract

Analyses of women dermatology literature authorship from 2018 to 2022 reveal a slight increase in total female authors, female first authors, and female senior authors with no substantial immediate impact of COVID-19 on current trends, encouraging future examination of long-term effects and ongoing promotion of systemic initiatives to support gender equity.

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## KEYWORDS

women; gender; representation; authorship; academic; leadership; diversity; equity; inclusion; dermatology; journals; publications; COVID-19; pandemic; bibliometric

## Introduction

Early examination of the COVID-19 pandemic's impact on academic productivity affirmed that female academics were disproportionately affected relative to their male counterparts, likely due to differential burdens including childcare and domestic demands [1]. These differences were particularly pronounced in academic medicine, where publications by women authors decreased substantially [2]. This trend has yet to be examined in-depth within dermatology. We, therefore, surveyed the representation of total female authors, female first authors (FFAs), and female senior or last authors (FSAs; a potential indicator of academics more advanced in their careers [3]) in the recent dermatologic literature.

## Methods

Dermatology articles, letters, reviews, and editorials published in 2018 through 2022 were searched on June 21, 2023, in Clarivate's Web of Science and filtered for the top five dermatology journals by the 2022 h-index [4]. The *Journal of*

*the American Academy of Dermatology*, the *Journal of Investigative Dermatology*, and *JAMA Dermatology* were included in the analysis, while the *British Journal of Dermatology* was excluded due to the unavailability of authors' full first names in database citations. Binary (women vs men) gender estimation by authors' first names was performed by genderize.io, a popular probabilistic gender inference service built on a large international database of gender-name associations collected from various web sources. The percentages of total female authors, FFAs, and FSAs were calculated for each year to allow comparisons before and during the pandemic-affected time frame.

## Results

The total proportion of female authorship increased from 41.7% (3896/9344) in 2018 to 45.2% (5214/11,536) in 2022 ( $r=0.92$ ; [Table 1](#)). The percentages of FFAs fluctuated but slightly increased from 45.1% (771/1710) to 47% (924/1964;  $r=0.61$ ), while the percentage of FSAs trended weakly upward over time, with a peak in 2021 at 36.4% (920/2526) and falling to 34.5%



(678/1964) in 2022 ( $r=0.76$ ). Notably, the number of total publications and authors increased each year within the four journals analyzed until peaking in 2021 ( $n=2526$  publications totaling  $n=14,247$  authors).

**Table .** Frequencies and percentages of first, senior, and total authors by gender from 2018 to 2022 in the top h-index dermatology journals.

Year	Total publications, n	Female authors, n (%)	Male authors, n (%)	Unknown authors, n (%)
<b>First authors</b>				
2018	1710	771 (45.1)	905 (52.9)	34 (2.0)
2019	1753	828 (47.2)	882 (50.3)	43 (2.5)
2020	2169	991 (45.7)	1118 (51.5)	60 (2.8)
2021	2526	1187 (47.0)	1286 (50.9)	53 (2.1)
2022	1964	924 (47.0)	996 (50.7)	44 (2.2)
<b>Senior authors</b>				
2018	1710	542 (31.7)	1121 (65.6)	47 (2.7)
2019	1753	576 (32.9)	1117 (63.7)	60 (3.4)
2020	2169	771 (35.5)	1339 (61.7)	59 (2.7)
2021	2526	920 (36.4)	1531 (60.6)	75 (3.0)
2022	1964	678 (34.5)	1219 (62.1)	67 (3.4)
<b>Total authors</b>				
2018	9344	3896 (41.7)	5222 (55.9)	226 (2.4)
2019	10,424	4321 (41.5)	5811 (55.7)	292 (2.8)
2020	12,341	5470 (44.3)	6592 (53.4)	279 (2.3)
2021	14,247	6399 (44.9)	7485 (52.5)	363 (2.5)
2022	11,536	5214 (45.2)	6025 (52.2)	297 (2.6)

## Discussion

Many possible explanations exist for this trend, which differs from observations in other fields [5]. The proportion of women in dermatology who are board-certified has grown substantially, from 24% in 1992 to 53% in 2017 [6], a growth rate possibly exceeding any negative impact of COVID-19. Decreased patient capacity at dermatology clinics, suspension of elective procedures, and a prominent shift to telemedicine may be providing more time for research. However, our study was limited to certain article types from four journals, which may be influential but not fully representative of dermatology publishing. Additionally, high-throughput inference of binary gender using genderize.io's predictive database was used due to the thousands of author names queried, but we recognize that this is a limited approach with lower accuracy for many gender-neutral names and cultural or regional differences in naming. Furthermore, given the delayed nature of the publication process and indexing, some included works may have been completed before the pandemic, compelling the need for subsequent assessment of future trajectories.

It is promising that FFA data currently suggests proportional contributions from female lead authors, but FSA percentages are still far from gender parity, corroborating patterns of female underrepresentation in senior faculty positions and ongoing inequities in research funding and academic promotion. While COVID-19 does not appear to have immediately impacted

female author contributions in dermatology beyond current trends, increased analysis and discussion will be necessary to assess the long-term effects of the pandemic, determine implications surrounding author position, and strengthen support for female academic dermatologists throughout a highly varied and interdisciplinary field. Recent investigations have revealed that only 4 of the top 50 individual most cited dermatology authors by h-index in 2020 were women, though increases in overall percentages of top women authors were also observed in prior decades [7]. Given these findings, detailed characterization of the higher representation of women in dermatology and broader trends compared to other specialties could therefore identify factors contributing to the prevention or evolution of these gender disparities over time. As initial steps, increasing the number of women in academic leadership, prioritizing family-friendly work hour flexibility, and preventing burnout have been recommended as possible strategies to retain women dermatologists [8]. The need for women in leadership has been recognized by journals such as *JMIR Dermatology*, which has emphasized inviting women dermatologists to its editorial board to achieve gender parity [9]. Senior editors have considerable influence over journals and editorial procedures, and could help ensure diversity, equity, and inclusion in the publication process [10]. We hope that dermatology could therefore serve as a role model and set a precedent in demonstrating how proactive and intentional initiatives could address persistent systemic challenges in reaching gender equity.

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## Conflicts of Interest

RPD is editor in chief of *JMIR Dermatology*. RPD receives editorial stipends and meeting expense reimbursement from *JMIR Dermatology*, and royalties from *UpToDate*.

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## Abbreviations

**FFA:** female first author

**FSA:** female senior or last author

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Research Letter

# Gender Parity Analysis of the Editorial Boards of Influential Dermatology Journals: Cross-Sectional Study

Mindy D Szeto<sup>1</sup>, MS; Torunn E Sivesind<sup>2</sup>, MD; Lori S Kim<sup>3</sup>, MD; Katie A O'Connell<sup>4</sup>, MD; Kathryn A Sprague<sup>5</sup>, BA; Yvonne Nong<sup>6</sup>, MS; Daniel M Strock<sup>7</sup>, BS; Annie L Cao<sup>2</sup>, BS; Jieying Wu<sup>8</sup>, MS; Lauren M Toledo<sup>9</sup>, BS; Sophia M Wolfe<sup>2</sup>, MD; Wyatt Boothby-Shoemaker<sup>10</sup>, MD; Robert P Dellavalle<sup>1</sup>, MSPH, MD, PhD

<sup>1</sup>Department of Dermatology, University of Minnesota Medical School, Minneapolis, MN, United States

<sup>2</sup>Department of Dermatology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

<sup>3</sup>Department of Dermatology, Boston University School of Medicine, Boston, MA, United States

<sup>4</sup>Department of Dermatology, Vanderbilt University Medical Center, Nashville, TN, United States

<sup>5</sup>Chicago College of Osteopathic Medicine, Downers Grove, IL, United States

<sup>6</sup>Michigan State University College of Human Medicine, Flint, MI, United States

<sup>7</sup>Eastern Virginia Medical School, Norfolk, VA, United States

<sup>8</sup>College of Osteopathic Medicine, Rocky Vista University, Parker, CO, United States

<sup>9</sup>Lake Erie College of Osteopathic Medicine, Bradenton, FL, United States

<sup>10</sup>Department of Dermatology, Henry Ford Hospital, Detroit, MI, United States

**Corresponding Author:**

Robert P Dellavalle, MSPH, MD, PhD

Department of Dermatology

University of Minnesota Medical School

1-411 Phillips-Wangensteen Building

516 Delaware St SE, MMC 98

Minneapolis, MN, 55455

United States

Phone: 1 612 625 8625

Email: [della056@umn.edu](mailto:della056@umn.edu)

## 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.

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**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

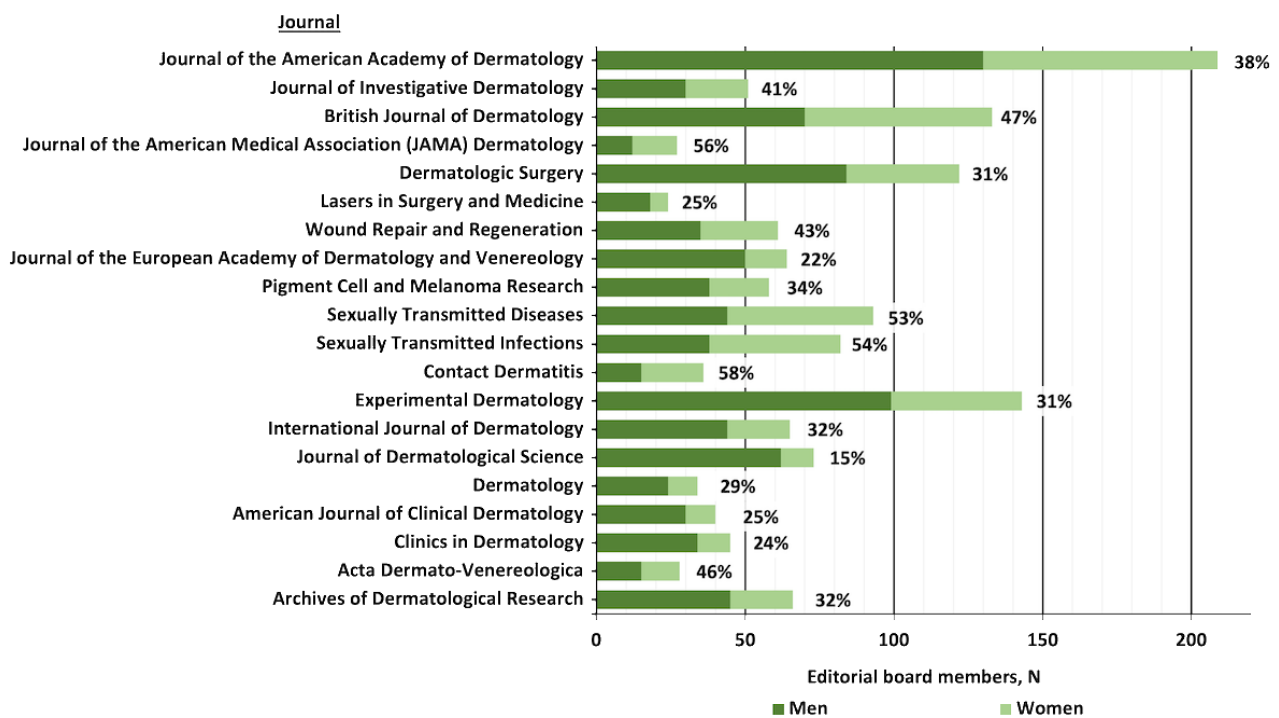
API [4], a popular gender inference service based on querying large multifactorial databases and name repositories. Estimations were corroborated by web-based searches of professional photographs and biographies by 2 independent researchers, with in-depth discussion and consensus meetings to resolve 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.

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## Conflicts of Interest

RPD is a joint coordinating editor for *Cochrane Skin*, a dermatology section editor for *UpToDate*, a social media editor for the *Journal of the American Academy of Dermatology (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

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