



BRIEF REPORT

Qualitative Assessment of Adult Patients' Perception of Atopic Dermatitis Using Natural Language Processing Analysis in a Cross-Sectional Study

Bruno Falissard · Eric L. Simpson · Emma Guttman-Yassky ·
Kim A. Papp · Sebastien Barbarot · Abhijit Gadkari · Grece Saba ·
Laurene Gautier · Adeline Abbe · Laurent Eckert

Received: November 25, 2019 / Published online: January 31, 2020
© The Author(s) 2020

ABSTRACT

Introduction: Atopic dermatitis (AD) is an incurable, inflammatory skin disease characterized by skin barrier disruption and immune dysregulation. Although AD is considered a childhood disease,

Enhanced Digital Features To view enhanced digital features for this article go to <https://doi.org/10.6084/m9.figshare.11547855>.

B. Falissard
Paris Sud University, Paris, France

E. L. Simpson
Department of Dermatology, Oregon Health and Science University, Portland, OR, USA

E. Guttman-Yassky
Department of Dermatology and the Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA

K. A. Papp
Probit Medical Research, Waterloo, ON, Canada

S. Barbarot
Centre Hospitalier Universitaire de Nantes, Nantes, France

A. Gadkari
Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

G. Saba · L. Gautier
Kantar—Health Division, Paris, France

A. Abbe · L. Eckert (✉)
Sanofi, Chilly-Mazarin, France
e-mail: Laurent.Eckert@sanofi.com

adult onset is possible, presenting with daily sleep disturbance and functional impairment associated with itch, neuropsychiatric issues (anxiety and depression), and reduced health-related quality of life. Although such aspects of adult AD disease burden have been measured through standardized assessments and based on population-level data, the understanding of the disease experienced at the patient level remains poor. This text-mining study assessed the impact of AD on the lives of adult patients as described from an experiential perspective.

Methods: Natural language processing (NLP) was applied to qualitative patient response data from two large-scale international cross-sectional surveys conducted in the USA and countries outside of the USA (non-USA; Canada, France, Germany, Italy, Spain, and the UK). Descriptive analysis was conducted on patient responses to an open-ended question on how they felt about their AD and how the disease affected their life. Character length, word count, and stop word (common words) count were evaluated; centrality analysis identified concepts that were most strongly interlinked.

Results: Patients with AD in all countries were most frequently impacted by itch, pain, and embarrassment across all levels of disease severity. Patients with moderate-to-severe AD were more likely than patients with mild AD to describe sleep disturbances, fatigue, and feelings of depression, anxiety, and a lack of hope that were directly associated with AD. Centrality analysis revealed sleep disturbance was strongly

linked with itch. Collectively, these concepts revealed that patients with AD are impacted by both physical and emotional burdens that are intricately connected.

Conclusions: Qualitative data from NLP, being more patient-centric than data from clinical standardized measures, provide a more comprehensive view of the burden of AD to inform disease management.

Keywords: Atopic dermatitis; Natural language processing; Patient perception; Qualitative; Text-mining

Key Summary Points

Why carry out this study?

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease characterized by itch, sleep disturbance, functional impairment, reduced health-related quality of life, depression and anxiety, systemic immune abnormalities, and impairments to work and school productivity

While the current understanding on the burden of AD has only been quantitatively characterized on the basis of clinical, mechanistic, and patient-reported outcome measures in trial and real-world settings, the full understanding of the impact experienced at the patient level is limited and would provide a more comprehensive view of the burden of AD to inform disease management

What was learned from the study?

Through the approach of natural language processing uncovering word patterns and important trends of experiences, the impact of AD on patients' lives as per their personal experience and choice of words was identified; interviewed patients from the USA, Canada, France, Germany, Italy, Spain, and the UK described not only a physical burden but also a substantial emotional burden due to their AD

Patients were most frequently impacted by itch, pain, and embarrassment across all levels of disease severity. Patients with moderate-to-severe AD were more likely than patients with mild AD to describe sleep disturbances, fatigue, and feelings of depression, anxiety, and a lack of hope that were directly associated with AD

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease characterized by intense itch, disruption of the skin barrier, and upregulation of type 2 immune responses [1]. AD most often presents in early childhood but can continue throughout, or first appear in adulthood, with an estimated adult prevalence of 2–10% across the USA and Europe [2, 3].

The burden of AD has been quantitatively characterized on the basis of clinical, mechanistic, and patient-reported outcome measures in trial and real-world settings. Manifestations of burden, such as itch, sleep disturbance, functional impairment, reduced health-related quality of life, depression and anxiety [4], systemic immune abnormalities [5–7], and impairments to work and school productivity, have all been reported with high prevalence [8]. However, these assessments only capture AD burden at the population level and, as such, the full understanding of the impacts experienced at the patient level is limited. Qualitative data may facilitate our understanding of the totality of the patient experience [9], providing important patterns and themes of AD from an individual patient perspective.

One approach to evaluating qualitative data is through using natural language processing (NLP) (Table 1), an innovative method to analyze text to derive implicit knowledge to inform the research objective. The approach has been applied in healthcare research, from biomedicine [10] uncovering valuable information on prostate cancer biomarkers [11] to psychiatry

Table 1 Terminology explained

Terminology	Definition
Natural language processing	The application of computational techniques to the analysis and synthesis of natural language and speech
Text-mining analysis	The process of exploring and analyzing large amounts of unstructured text data aided by software to identify concepts, patterns, topics, and keywords

[12, 13] exploring patient perceptions on antidepressant withdrawal [13]. To our knowledge, the use of NLP to assess the patient experience in AD is limited. This study assessed the impact of AD on the lives of adult patients with AD through NLP.

METHODS

NLP analysis was conducted on patient responses to an open-ended question that was included in two multinational surveys on the burden of AD.

Population

Patients in the USA (at least 18 years of age) were selected from electronic medical records from six geographically diverse academic medical centers. Participants were included if they were diagnosed with AD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 691.8 or 692.9) by a physician and had at least one visit for AD between January 1, 2013 and December 31, 2014.

Outside of the USA (non-USA), patients (18–65 years of age) from Canada, France, Germany, Italy, Spain, and the UK were selected if they had not participated in a randomized controlled trial for AD treatment in the past 12 months. Participants were included if they

were diagnosed with AD by a dermatologist (all countries), general practitioner (France and the UK), or allergist (France and Canada), and had at least one visit for AD between May 15, 2016 and November 21, 2017.

All patients provided informed consent and were stratified according to disease severity (mild or moderate-to-severe AD) based on the Investigator's Global Assessment (IGA) scale. Data were collected in accordance with ethical codes of the British Healthcare Business Intelligence Association, European Society for Opinion and Marketing Research (ESOMAR) and European Pharmaceutical Market Research Association (EphMRA), and was compliant with the US Health Insurance Portability and Accountability Act (HIPAA) of 1996. The study was approved at country level by the appropriate ethics committees (Canada: Research Review Board INC [07 June 2016] and Health Research Ethics Board of Alberta [04 January 2017]; France: Advisory Committee on Information Processing in Material Research in the Field of Health [12 July 2016] and National Commission for Computing and Liberties [26 October 2016]; Germany: Medizinische Hochschule Hannover [6 June 2016]; Spain: Hospital de la Santa Creu I Sant Pau [8 June 2016]; UK: Research Ethics Committee [29 September 2016] and Health Research Authority [9 December 2016]).

Data Collection

Qualitative data were derived from the international, cross-sectional, observational survey AWARE (Adults With Atopic Dermatitis Reporting on their Experience) studies of patients with AD. Patients provided a written response to the following question: Please take a few minutes to think about your atopic dermatitis, its effect on your life, and how you feel about it. What are some words that best describe the impact of atopic dermatitis on your life?

Prior to administration, the question was translated to the local language in each country; responses were then translated to English to facilitate the analysis.

Natural Language Processing

Single words that described the impact of AD on the patient's life were extracted from the open-ended responses; a corpus (collection of words) was created with word occurrence frequency using a tagging and lemmatization (headword identification) tool (WinTreeTagger for the USA and R Software for non-USA). Descriptive analysis evaluated character length, word count, and stop word (common words) count (Excel in the USA and R Software in non-USA). Using a stop word to total words ratio, keywords were extracted for analysis and a term-document matrix (TDM) was created. A word cloud was generated using R software (USA and non-USA). Co-occurrence identified words with the highest degree of centrality (TreeCloud and IramutQ software for the USA and R Software for non-USA). Centrality analysis was based on words with a frequency of more than 12 for the USA and more than 20 for non-USA.

RESULTS

USA

Of the 1519 survey participants recruited in the USA, 639 responded (Table 2). The most frequently used words describing the impact of AD included itch (37%), embarrassed (37%), annoyed (35%), pain (25%), and frustration (22%), as shown in Fig. 1a, b. The words annoyed and itch had the highest centrality (Fig. 1c). Concepts linked to annoyed included itch, embarrassed, distracted, inconvenient, and frustration. Concepts linked to itch included ugly, dryness, and red. Patients with moderate-to-severe AD commonly used the words depressed, anxious, worry, and hopeless to describe the impact of AD (Fig. 1d).

Non-USA

Of the 1444 survey participants in non-US countries, 592 responded (Table 2). The most frequently used words for describing the impact of AD included itch (24%),

Table 2 Baseline demographics

	Total	Mild AD	Moderate-to-severe AD
USA			
Number of respondents, <i>n</i>	639	260	379
Age, years, mean (SD)	42.2 (16.9)	42.8 (17.7)	41.9 (16.4)
Female, %	65.4	61.2	68.3
Non-USA			
Number of respondents, <i>n</i>	592	196	396
Age, years, mean (SD)	38.1 (13.5)	38.7 (14.4)	37.8 (13.0)
Female, %	57.9	66.8	53.5

AD atopic dermatitis, SD standard deviation

uncomfortable (17%), annoyed (15%), pain (14%), life (12%), and embarrassed (11%), as shown in Fig. 2a, b. Itch and pain had the highest centrality (Fig. 2c). Concepts linked to itch included pain, frustration, sleep, feel, dry, and red. Concepts linked to pain included uncomfortable, embarrassed, annoyed, frustration, and tired. Words commonly used by patients with moderate-to-severe AD included itch, tired, pain, uncomfortable, and annoyed (Fig. 2d).

DISCUSSION

Although a large body of quantitative evidence measuring AD burden on patients is available, the impact of disease, as described by patients from the experiential level, has not yet been fully explored. This study, through the approach of NLP, evaluated the impact of AD on patients' lives as per their personal experience and choice of words. By uncovering word patterns and important trends of experiences, we found that patients not only face a physical burden but also a substantial emotional burden due to their AD.

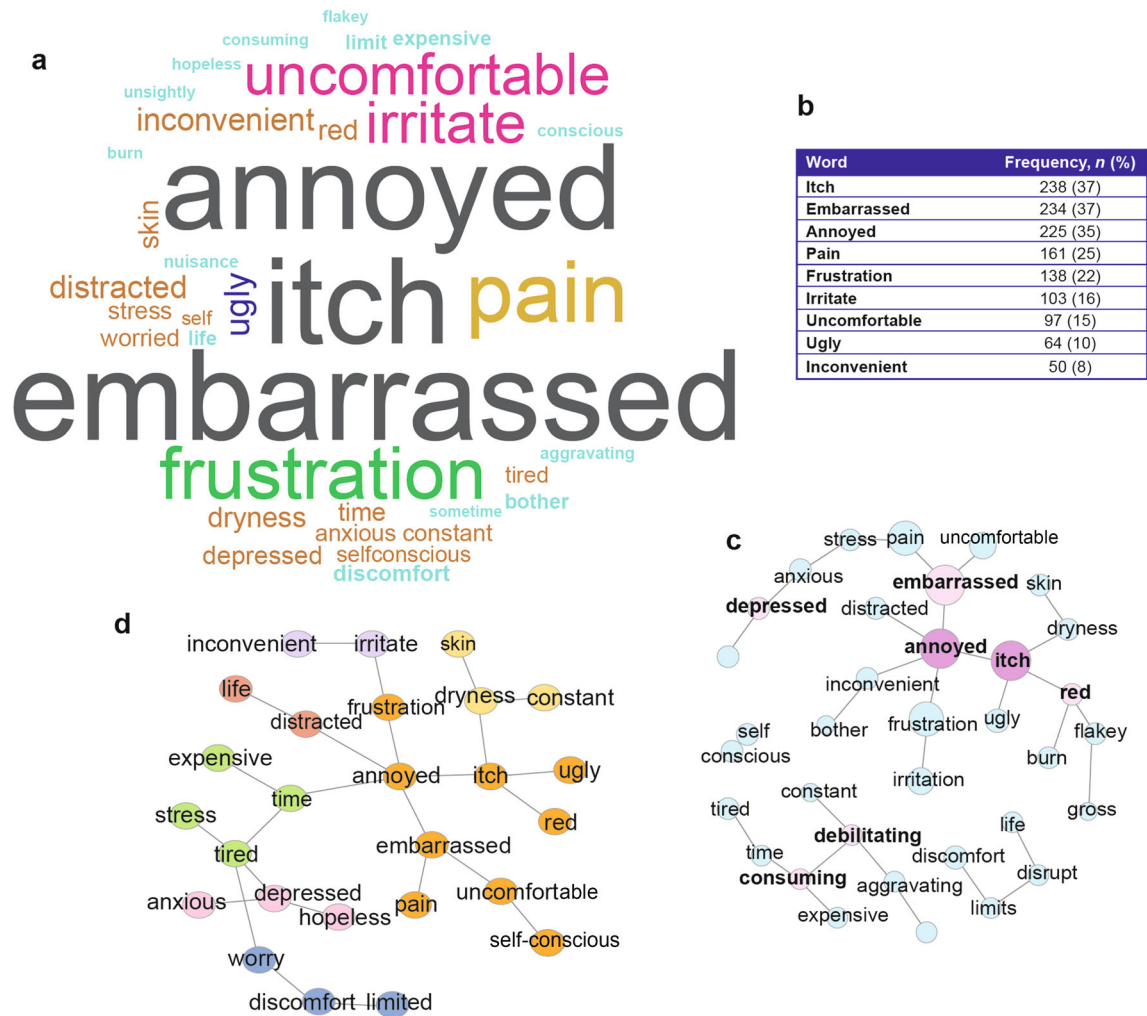


Fig. 2 Text-mining analysis of global data from France, Germany, Italy, Spain, the UK, and Canada. **a** Word cloud. **b** Frequency of words used by patients to describe AD. **c** Tree cloud showing centrality based on words with frequency greater than 20 in all AD severity groups. **d** Tree

cloud for patients in moderate-to-severe AD group (size of circle denotes word frequency, red denotes words with higher centrality, width of links denotes number of co-occurrences). *AD* atopic dermatitis

The use of ugly was linked to itch in US (Fig. 1c, d) and non-US (Fig. 2c, d) patients; this reflects the negative self-image that AD induces in patients. While previous studies have recognized itch as a physical burden [14], this emotional burden of itch was not captured. Pain was linked to itch in non-US patients (Fig. 2c, d), but also strongly linked to embarrassment and annoyance in both US and non-US patients (Fig. 1c, d and Fig. 2c, d), suggesting that pain is not only a physical characteristic of AD [14] but also distinctly associated with emotional

distress. Of note, despite the US and non-US studies being conducted sequentially with different analytical tools, the concepts elicited were similar.

The importance of patient-reported outcomes in optimizing disease management is well established [15]. NLP and centrality analysis assisted in uncovering an otherwise implicit and overlooked pool of knowledge on the patient experience that cannot be fully captured with standardized outcome measures such as the SCORing Atopic Dermatitis (SCORAD) tool

[16], Dermatology Life Quality Index (DLQI) [17], Patient-Oriented Eczema Measure (POEM) [18], and Eczema Area and Severity Index (EASI) [19]; these measures are better applied in assessing AD severity [20]. Specifically, SCORAD and POEM focus on itch and sleep, whereas our approach has shown that pain is also a symptom of AD that greatly impacts patients' lives. Although DLQI assesses pain, it is only assessed in relation to itch; our results support the notion that pain should also be evaluated distinctly from itch. These findings urge the need to incorporate patients' perceptions in AD assessment tools, such as the Atopic Dermatitis Control Tool [21]. Although our study did not identify all patient-reported consequences of AD, such as the known impact of AD on sexual health [22], our qualitative approach has provided an understanding of patient perceptions and the underlying range of physical and emotional consequences of AD, which can inform shared decision-making. These findings suggest the need for broader assessment of the impact of AD on patients' lives.

CONCLUSIONS

Through the approach of NLP, we have been able to identify the far-reaching consequences of AD on patients' lives, beyond the outcomes reported in standardized patient-reported and clinical measures. It is anticipated that a better understanding of the patient experience will enhance patient–physician communication and, ultimately, the management of AD.

ACKNOWLEDGEMENTS

The authors thank the patients, their families and all physicians involved in this study.

Funding. The study, as well as the journal's Rapid Service Fee, was funded by Sanofi (Bridgewater, NJ, USA) and Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA).

Medical Writing Assistance. Medical writing support was provided by Saba Choudhary,

PhD, of Prime (New York, USA), according to Good Publication Practice guidelines (Link) and was funded by Sanofi and Regeneron Pharmaceuticals, Inc. The authors were responsible for all content and editorial decisions, and received no honoraria related to the development of this publication.

Authorship. All authors had full access to all the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosures. Bruno Falissard has received consultancy honoraria from Actelion, Allergan, Almirall, Astellas, AstraZeneca, Bayer, Biotronik, BMS, Boeringer Ingelheim, Daiichi-Sankyo, Eli Lilly, Genzyme, Gilead, Grunenthal, GSK, HRA, Janssen, Lundbeck, MSD, Novartis, Otsuka, Pierre Fabre, Roche, Sanofi, Servier, Stallergene, UCB, and ViiV. Eric L. Simpson has received grants/research support from Amgen, Celgene, Chugai, Galderma, and Regeneron Pharmaceuticals, Inc., and is a consultant for Anacor, Asubio, Celgene, Galderma, Genentech, Medicis, and Merck. Emma Guttman-Yassky has acted as a consultant for and received grants/honoraria from AbbVie, Anacor, Celgene, Celsus Therapeutics, Dermira, Galderma, Glenmark, Janssen Biotech, LEO Pharmaceuticals MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, Stiefel/GlaxoSmithKline, Vitae, Mitsubishi Tanabe, Eli Lilly, Asana Biosciences, Kiowa Kirin; has acted as an investigator for Celgene, Glenmark, LEO Pharmaceuticals, MedImmune, Regeneron Pharmaceuticals, Inc., Eli Lilly; and has participated in advisory boards for Celgene, Celsus Therapeutics, Dermira, Galderma, Glenmark, MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, Stiefel/GlaxoSmithKline, Vitae and Asana Biosciences. Kim A. Papp has been a consultant and investigator for Akros, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Dermira, Dow

Pharma, Genentech, Merck Serono, Mylan, Roche, Sanofi-Aventis/Genzyme, Takeda and UCB; a speaker, consultant, and investigator for AbbVie, Amgen, Astellas, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, LEO Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., and Valeant; an investigator for Allergan, Anacor, Coherus, GlaxoSmithKline, and MedImmune; a consultant for AstraZeneca, Baxter, CanFite, Meiji Seika Pharma, and Mitsubishi Pharma; and a speaker and consultant for Devonian. Sebastien Barbarot has received research grants from Pierre Fabre Laboratory and Fondation pour la dermatite atopique, and received personal fees from Bioderma, Laboratoire La Roche Posay, Sanofi-Genzyme, Abbvie, Novartis, Janssen, and LEO Pharma. Abhijit Gadkari was an employee of and stockholder in Regeneron Pharmaceuticals, Inc. at the time of the study, and is currently an employee of Boehringer Ingelheim. Grèce Saba and Laurène Gautier are employees of Kantar–Health Division, who received funding from Sanofi to conduct the non-US study. Adeline Abbe and Laurent Eckert are employees of and stockholders in Sanofi.

Compliance with Ethics Guidelines. Data collection was according to ethical codes of the British Healthcare Business Intelligence Association, European Society for Opinion and Marketing Research (ESOMAR) and European Pharmaceutical Market Research Association (EphMRA), and was compliant with the US Health Insurance Portability and Accountability Act (HIPAA) of 1996. The study was approved at country level by the appropriate ethics committees (Canada: Research Review Board INC [07 June 2016] and Health Research Ethics Board of Alberta [04 January 2017]; France: Advisory Committee on Information Processing in Material Research in the Field of Health [12 July 2016] and National Commission for Computing and Liberties [26 October 2016]; Germany: Medizinische Hochschule Hannover [6 June 2016]; Spain: Hospital de la Santa Creu I Sant Pau [8 June 2016]; UK: Research Ethics Committee [29 September 2016] and Health Research Authority [9 December 2016]). All participants provided informed consent.

Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. Czarnewicki T, He H, Krueger JG, et al. Atopic dermatitis endotypes and implications for targeted therapeutics. *J Allergy Clin Immunol.* 2019;143(1):1–11.
2. Barbarot S, Auziere S, Gadkari A, et al. Epidemiology of atopic dermatitis in adults: results from an international survey. *Allergy.* 2018;73:1284–93.
3. Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. *J Allergy Clin Immunol.* 2013;132(5):1132–8.
4. Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): insights from a phase 2b clinical trial of dupilumab in adults. *J Am Acad Dermatol.* 2016;74(3):491–8.
5. Brunner PM, Suarez-Farinas M, He H, et al. The atopic dermatitis blood signature is characterized by increases in inflammatory and cardiovascular risk proteins. *Sci Rep.* 2017;7(1):8707.

6. Ungar B, Garcet S, Gonzalez J, et al. An integrated model of atopic dermatitis biomarkers highlights the systemic nature of the disease. *J Invest Dermatol*. 2017;137(3):603–13.
7. Brunner PM, He H, Pavel AB, et al. The blood proteomic signature of early-onset pediatric atopic dermatitis shows systemic inflammation and is distinct from adult long-standing disease. *J Am Acad Dermatol*. 2019;81(2):510–9.
8. Eckert L, Gupta S, Amand C, et al. Impact of atopic dermatitis on health-related quality of life and productivity in adults in the United States: an analysis using the National Health and Wellness Survey. *J Am Acad Dermatol*. 2017;77:274–9.
9. Denzin N, Lincoln Y. *Handbook of qualitative research*. Thousand Oaks: Sage; 1994.
10. Zhu F, Patumcharoenpol P, Zhang C, et al. Biomedical text mining and its applications in cancer research. *J Biomed Inform*. 2013;46(2):200–11.
11. Deng X, Geng H, Bastola DR, et al. Link test—a statistical method for finding prostate cancer biomarkers. *Comput Biol Chem*. 2006;30(6):425–33.
12. Abbe A, Grouin C, Zweigenbaum P, et al. Text mining applications in psychiatry: a systematic literature review. *Int J Methods Psychiatr Res*. 2016;25(2):86–100.
13. Abbe A, Falissard B. Stopping antidepressants and anxiolytics as major concerns reported in online health communities: a text mining approach. *JMIR Ment Health*. 2017;4(4):e48.
14. Simpson EL, Guttman-Yassky E, Margolis DJ, et al. Association of inadequately controlled disease and disease severity with patient-reported disease burden in adults with atopic dermatitis. *JAMA Dermatol*. 2018;154(8):903–12.
15. Wensing M, Elwyn G. Methods for incorporating patients' views in health care. *BMJ*. 2003;326(7394):877–9.
16. European Task Force on Atopic Dermatitis. Severity scoring of atopic dermatitis: the SCORAD index. Consensus report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1993;186(1):23–31.
17. Finlay AY, Khan GK. Dermatology life quality index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210–6.
18. Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Arch Dermatol*. 2004;140(12):1513–9.
19. Hanifin JM, Thurston M, Omoto M, et al. The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis EASI Evaluator Group. *Exp Dermatol*. 2001;10(1):11–8.
20. Chopra R, Vakharia PP, Sacotte R, et al. Severity strata for eczema area and severity index (EASI), modified EASI, scoring atopic dermatitis (SCORAD), objective SCORAD, atopic dermatitis severity index and body surface area in adolescents and adults with atopic dermatitis. *Br J Dermatol*. 2017;177(5):1316–21.
21. Simpson E, Eckert L, Gadkari A, et al. Validation of the atopic dermatitis control tool (ADCT©) using a longitudinal survey of biologic-treated patients with atopic dermatitis. *BMC Dermatol*. 2019;19(1):15.
22. Misery L, Seneschal J, Reguiai Z, et al. The impact of atopic dermatitis on sexual health. *J Eur Acad Dermatol Venereol*. 2019;33(2):428–32.