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ORIGINAL PAPER

What are the highest yielding search strategy terms for systematic reviews in atopic dermatitis? A systematic review

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Abstract

The impact of search strategies on systematic reviews (SR) of atopic dermatitis (AD) is unknown. The purpose of this review was to evaluate search strategies used in SR of AD and their impact on the frequency of manuscripts identified. MEDLINE and EMBASE were searched for SR related to AD. Simulations were performed by running combinations of search terms in MEDLINE and EMBASE. Overall, 250 SR met inclusion criteria, of which 225 specified search strategies. SR using 5–6 terms (20.0% to 12.1%) or ≥ 7 (40.0% to 18.8%) terms decreased, whereas SR using 3–4 terms numerically increased (18.8% to 30.2%) and 1–2 terms remained similar (37.5% to 38.9%) from 1999–2009 to 2015–2019. The most commonly searched terms were "atopic dermatitis" ($n = 166$), followed by "eczema" ($n = 156$), "dermatitis atopic'" ($n = 81$), "atopic eczema" ($n = 74$), "neurodermatitis" ($n = 59$), "Besniers prurigo" ($n = 29$), "infantile eczema" ($n = 27$), and "childhood eczema" ($n = 19$). Simulations revealed that "eczema" and "atopic dermatitis" yielded the most hits. The number of search terms that maximized hits in MEDLINE and EMBASE was 5 and 4, respectively. Search strategies for AD were heterogeneous, with high proportions of search strategies providing few search hits. Future studies should use standardized and optimized search terms.

Keywords Atopic dermatitis · Eczema · Evidence-based medicine · Neurodermatitis · Meta-analysis

Abbreviations

AD Atopic dermatitis
SR Systematic review

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with heterogeneous symptoms (including itch, pain, sleep disturbance, psychosocial distress, anxiety, depression and cognitive dysfunction), triggers (including heat, sweat, climate and pollutants), lesional distribution (including flexural, extensor, hand and foot, head and neck), and associated signs (including prurigo nodules and nummular lesions) and comorbidities (including asthma, hay fever, anxiety, depression, attention deficit disorder and infections) [1–28]. Many of these symptoms and signs vary by age and geographic location [29]. The variable presentation of disease and therapeutic response may vary depending on geographic location, demographic considerations, and socioeconomic factors.

Systematic reviews (SR) are the cornerstone of evidence-based medicine. High-quality SR are particularly needed to harmonize potentially conflicting data for a heterogeneous disease such as AD. However, the methods used in SR and quality of SR vary widely. A sensitive and appropriate search strategy is necessary to capture as many potentially

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relevant studies as possible and minimize bias in conclusions [30]. Previous research demonstrated that SR search strategies have high amounts of error (92.7%); and 78.1% of these errors, specifically missing terms (synonyms, variation in terms) and search mode for descriptors, negatively affect search results [31].

Dermatology is replete with disparate nomenclature and terminology, with many disease synonyms and eponyms, all of which may pose obstacles in conducting comprehensive literature research [32]. In particular, the terminology for AD changed over the past 40 years and varies by region and stakeholder, such as eczema, atopic eczema, neurodermatitis, flexural eczema and childhood eczema among others. The varied terminology potentially creates confusion among AD patients, clinicians and researchers [33].

It is imperative that search strategies used in SR for AD incorporate the disparate terminology. Incomplete search strategies with few search terms or poorly constructed strategies might result in spurious results. Moreover, poor documentation of search strategies limits the interpretability and reproducibility of SR. We sought to analyze the search strategies used in SR of AD. In this study, we conducted a SR to explore the methodology of SR in the field of AD and identify the highest yielding search strategy terminology for SR in AD.

Methods

Search strategy

This review was registered in PROSPERO (ID# 151673). Medline (via OVID) and EMBASE (via embase.com) were searched for AD, and synonyms, limited to systematic reviews published on-line, in print and in press through September 13, 2019. Supplemental table 1 shows the detailed search strategy. All search results with titles and abstracts written in any language were considered. No date or subject (i.e. humans or animals) restrictions were applied. Institutional review board approval was not required as these data were collected from the published literature.

Selection and data extraction

SR were included in this review if there was a clear indication that they searched for AD. Exclusion criteria included: 1. SR that searched only databases designed solely for AD (e.g. GREAT); 2. SR of other forms of dermatitis, such as chronic hand, contact or seborrheic dermatitis; 3. original research, abstracts, conference proceedings, unpublished studies and retracted articles. If duplicate studies were identified, the paper with the most complete methodology section or the most recent was included. Search strategies that were cited from other SR were also included.

Two reviewers (MA and MY) independently performed title and abstract screen, followed by a full-text review and data extraction (MA and AA). Discrepancies were resolved through discussion. Data extracted from the 250 articles that met inclusion criteria were: region where the review was conducted determined by listed authors affiliations, journal specialty, the purpose of the study, restrictions imposed on searches (including age, language, subjects included), and search strategies used in the reviews including wildcards (truncation search strategies that incorporate symbols, "wildcard characters," that replace one or more characters in a term that allow searches to pick up spelling variants or similar terms in a search), different language translations of search terms, and commonly used search terms.

Simulations

AD specific search terms were extracted from documented search strategies. Search strategies were re-run using OVID MEDLINE and EMBASE over the course of two days (12/3/19-12/4/19). Searches were conducted as closely as possible to the original SR strategy, including headings and wildcards; though, search limitations were not applied. Search strategies provided by SR's that did not specify database used or did not provide search strategies specific for MEDLINE or EMBASE were tailored to suit the databases as closely as possible to the strategy provided. Only components of strategies relating to AD were attempted to be reproduced. The number of hits each search strategy yielded was determined.

After reviewing the search terms provided by the SR, the most frequently used search terms were identified across all SR and various combinations of these terms were searched in MEDLINE and EMBASE (2/23/2020-2/25/2020). Combinations of between 2 and 8 terms were tested, to determine the strategy that provided the highest number of search hits (most articles retrieved). Eight AD-related terms (atopic dermatitis, eczema, atopic eczema, neurodermatitis, dermatitis atopic, besniers prurigo, infantile eczema, and childhood eczema) were identified during data extraction that were found to be the most frequently used terms across the papers specific to the disease. Given that the terms were all synonymous with "AD" the strategies with the highest number of search hits was documented as "optimal."

Results

Literature search

Overall, 1086 non-duplicate potential SRs were identified in the database search; 868 and 80 were excluded during title/

abstract and full-text review, respectively. Two hundred and fifty SR met inclusion/exclusion criteria and were included in this review (Fig. 1).

Study characteristics

The 250 studies were published from 1999 to 2019 [12, 29, 34–281], including 244 (97.6%) written in English language, 3 in Chinese (1.2%), 2 (0.8%) in German, and 1 (0.4%) in Spanish. One hundred and twenty-four SR imposed language restrictions for manuscripts, of which 42 (16.8%) limited their search to the English language, 50 (20.0%) limited their inclusion criteria to English, and 31 (12.4%) papers did not specify whether they imposed language restrictions. The number of reviews published per year increased from 0 in 2002 to 42 in 2018 (Supplemental Figure 1A).

Forty-two SR (16.8%) included studies of children (ages 0–18 years), 24 (9.6%) included studies of pregnant women and their offspring, 7 (2.8%) included studies of adults (ages ≥ 18 years), 3 (1.2%) had other age limitations, and 174 (69.6%) had no age limits. Additional characteristics are presented in Supplemental Results.

Search terms

Search terms were documented in 225 (90.0%) SR (mean ± SD: 4.5 ± 3.8, median: 3). The most commonly used searched terms were "atopic dermatitis" ($n = 166$, 73.7%) and "eczema" ($n = 156$, 69.3%), followed by "dermatitis atopic'" ($n = 81$, 36%), "atopic eczema" ($n = 74$, 32.9%), "neurodermatitis" ($n = 59$, 26.2%), "Besniers prurigo" ($n = 29$, 12.9%), "infantile eczema" ($n = 27$, 12.0%), and "childhood eczema" ($n = 19$, 8.4%). Fourteen SR (6.2%) incorporated different language translations of search terms. Other literature search methods used in the SRs included explode, which searches a subject heading and its narrower terms (Exp $n = 65$, 28.9%), multi-purpose combined search fields (.mp $n = 48$, 21.3%), medical subject heading (MeSH $n = 30$, 13.3%), and text word (tw $n = 12$, 5.3%).

Twenty-eight (12.4%) SR searched for only 1 term, 119 (52.8%) for 2–4 terms, and 78 (35.7%) searched ≥ 5 terms

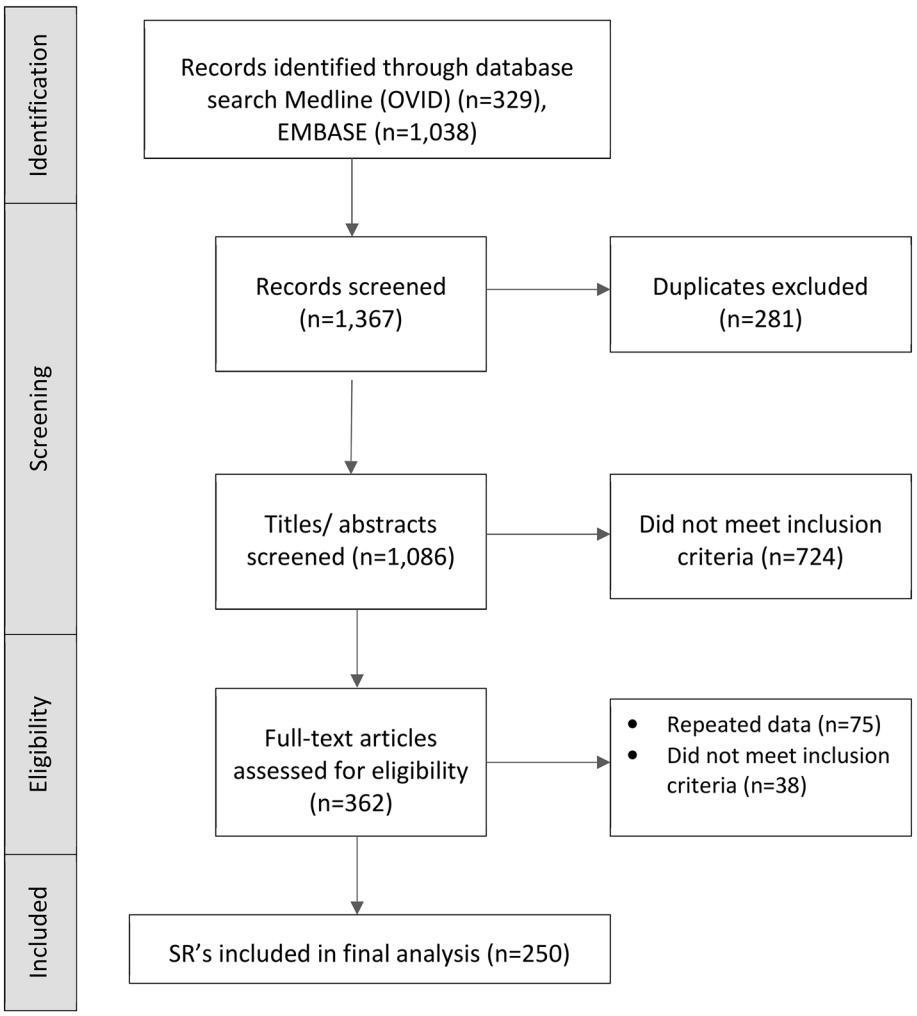

Fig. 1 PRISMA diagram

pertaining to AD. Over time, SR using 5–6 [1999–2009: 20.0% to 2015–2019: 12.1%; OR (95% CI) 0.24 (0.09–0.62)] or ≥ 7 (40.0% to 18.8%; 0.37 [0.14–0.97]) search terms decreased, whereas SR using 3–4 terms numerically increased [18.8–30.2%; 0.77 (0.30–1.94)], and SR using only 1–2 terms (37.5% to 38.9%) were similar (Fig. 2).

Use of specific search terms varied over time. The term "atopic dermatitis" increased from 1999–2004 (20%) to 2005–2009 (79%) and continued at similar rates in 2010–2014 and 2015–2019. The terms "dermatitis, atopic" (often used as the MeSH term of the term AD) (60% to 32.43%), "Besniers prurigo" (20% to 11.49%), "infantile eczema" (20% to 12.16%), "childhood eczema" (20% to 7.43%) were all used less frequently over time (Fig. 3a). Similar search terms were used in SR with or without the use of wildcard characters to identify spelling variants.

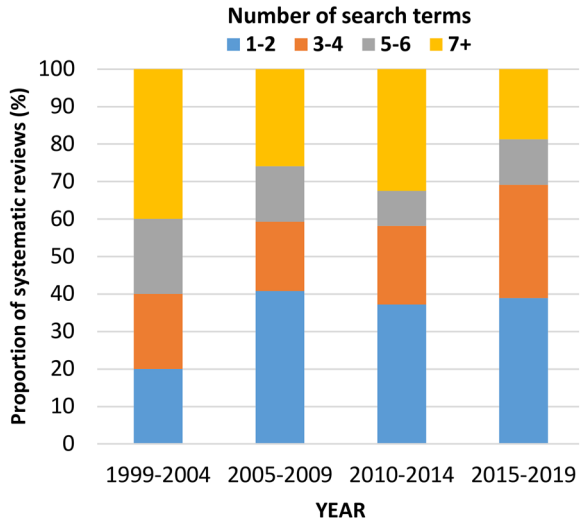

Fig. 2 Proportion of systematic reviews with 1–2, 3–4, 5–6 or ≥ 7 search terms grouped by years

Of studies restricted to a particular age group, "atopic dermatitis" was most commonly searched in SR restricted to adults (85.7%), followed by children (61.9%), and pregnancy/child outcomes (37.5%). "Eczema" was most commonly searched in SR restricted to pregnancy/child outcomes (75.0%), followed by children (64.3%) and adults (57.1%). "Atopic eczema" was most commonly searched in SR restricted to adults (57.1%), followed by children (19.0%) and pregnancy/child outcomes (8.3%).

Proportionally, SR that focused on the methodology of AD research had higher rates of use for each search term. SR focused on AD treatment generally had the lowest proportion of each search term (Fig. 3b). The mean ± SD number of search terms were similar in SR published in journals specializing in dermatology (4.2 ± 4.33, $n = 110$), allergy/immunology (4.4 ± 3.97, $n = 58$), medicine/pediatrics (4.3 ± 3.54, $n = 23$). SR published in SR journals (mean ± SD number of terms 7.1 ± 2.5. $n = 14$) had the highest proportion of all search terms (Fig. 3b).

Of 110 papers published in dermatology journals, 84 (76.4%) searched "atopic dermatitis", 60 (54.5%) searched "eczema", 41 (37.3%) searched "atopic eczema", 36 (32.7%) searched "dermatitis, atopic", 30 (27.3%) searched "neurodermatitis", 14 (12.7%) searched "besniers prurigo", 18 (16.4%) searched "infantile eczema", and 12 (10.9%) searched "childhood eczema" (Fig. 3c). Of the 58 papers published in allergy/immunology journals 32 (55.2%) searched "atopic dermatitis", 41 (70.7%) searched "eczema", 11(19%) searched "atopic eczema", 17 (29.3%) searched "dermatitis, atopic", 11 (19%) searched "neurodermatitis", 3 (5.2%) searched "besniers prurigo", 4 (6.9%) searched "infantile eczema", and 3 (5.2%) searched "childhood eczema." Of the 23 papers published in medicine/pediatric journals 17 (73.9%) searched "atopic dermatitis", 16 (69.6%) searched "eczema", 6 (26.1%) searched "atopic eczema", 7 (30.4%) searched "dermatitis, atopic", 5 (21.7%) searched

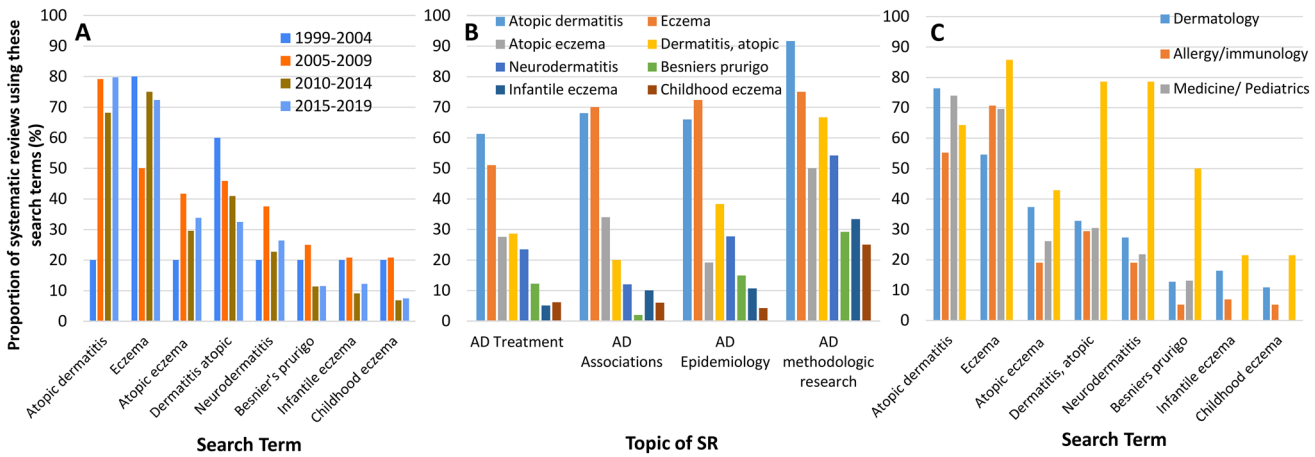

Fig. 3 Proportion of systematic reviews using specific search term **a** over time, **b** by topic and (C) and journal specialty

"neurodermatitis", 3 (13%) searched "besniers prurigo", and no papers searched "infantile eczema", or "childhood eczema."

Simulations

Search strategies were extracted and rerun in MEDLINE and EMBASE. Search results ranged from 1,043 to 481,311 hits (mean ± SD: 59,995 ± 66,228; median: 37,786) articles in MEDLINE, and 347 to 890,144 hits (mean ± SD: 117,557 ± 130,673; median 80,262) articles in EMBASE (Fig. 4).

Using a single search term, the most hits were obtained with the terms "eczema" (MEDLINE: 21,197; EMBASE: 45,493) and "atopic dermatitis" (MEDLINE: 20,238; EMBASE: 47,037). In combination, these two terms yielded 38,220 hits in MEDLINE and 81,216 in EMBASE. Additional terms were tested in combination with "eczema" or "atopic dermatitis". "Dermatitis, atopic" yielded the most additional hits in MEDLINE ($n = 42{,}323$). Whereas, "neurodermatitis" yielded the most additional hits in EMBASE ($n = 83{,}154$). The four-term combination of "atopic dermatitis", "eczema", "neurodermatitis", and "dermatitis, atopic" yielded the most hits (MEDLINE: 43,308; EMBASE: 83,162). "Besniers prurigo" yielded the highest number of hits among fifth search terms in MEDLINE ($n = 43{,}315$) but did not yield additional hits in EMBASE ($n = 83{,}162$). Six-, seven-, or eight-term combinations did not result in a higher number of search hits in either MEDLINE or EMBASE (Fig. 5). The number of search terms that yielded the highest search hits in MEDLINE was 5 and in EMBASE was 4 (Supplemental Table 2).

Discussion

This SR found considerable variability of the search strategies used in SR for AD. The most commonly used search terms were "atopic dermatitis" and "eczema". In simulations, searches with only these two terms captured 88–97% of the maximum number of hits, which was captured by our simulations using 5 or 4 terms in MEDLINE and EMBASE, respectively. SR using 1–4 search terms, particularly those that searched "atopic dermatitis" and "eczema", likely

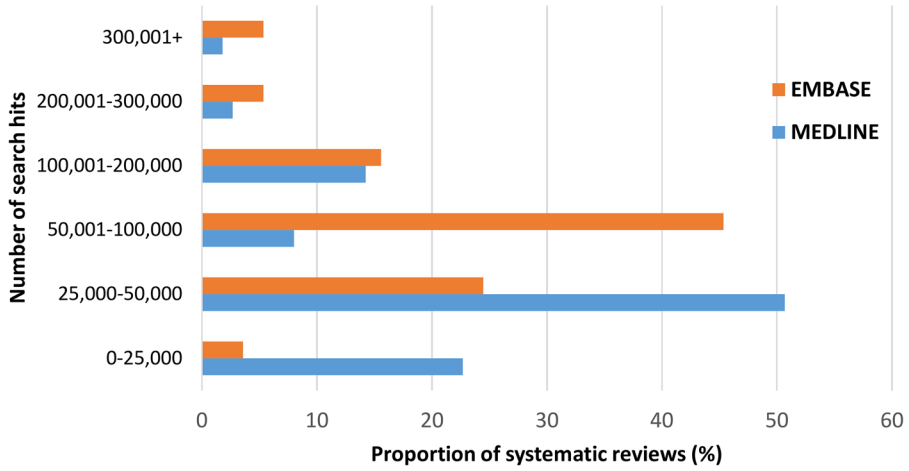

Fig. 4 Proportion of systematic reviews with different frequencies of search hits in EMBASE (orange) and MEDLINE (blue)

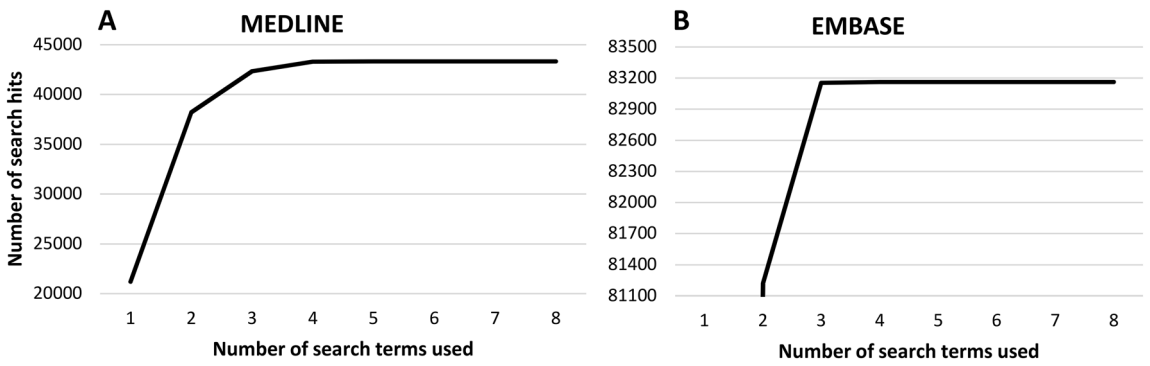

Fig. 5 Maximum frequency of search hits by the number of search terms used in **a** MEDLINE and **b** EMBASE

identified most potentially relevant articles. However, they may have also missed potentially relevant articles. One in seven SR only searched for a single term, which would miss approximately half of the hits from strategies with more search terms that we found in our simulations. While the number of SR of AD increased over time, an increasing proportion of these used fewer search terms that may lead to incomplete identification of relevant manuscripts. This may account for the reason the term "dermatitis, atopic" was used less frequently over time. Another possibility is the decline of well-constructed searches that do not incorporate MeSH terms such as "dermatitis, atopic." Despite the fewer terms being used, most SR still assessed more than one search term, and there was increasing use of the term "atopic dermatitis". There were differences in search terms used by the target age of the SR. "Atopic dermatitis" and "atopic eczema" were most commonly searched in adult studies, whereas "eczema" was most commonly searched in pediatric and pregnancy/child outcomes.

Based on these results, we recommend that all SR include the terms "atopic dermatitis" and "eczema" as a bare minimum. Furthermore, 4–5 search terms would be needed to maximize the sensitivity of searches. Of course, the need for comprehensive search strategies should be balanced with resource allocation. In addition, we recommend extreme caution when interpreting the results of SR with only one search term, which would miss a large proportion of potentially relevant manuscripts.

Surprisingly, 10% of SR did not specify details for their search strategy and related methodology. The lack of details limits the critical assessment and potential reproducibility of these SR. It is probable that many of the included studies used a reasonable search strategy. However, if these issues are not documented, the clinician, peer-reviewer, editor and authors of subsequent SR have limited ability to assess the validity and conclusions of a SR. While this study specifically addresses AD, it is crucial that these details be clearly documented for all other topics as well.

Several tools may be employed to improve the reporting of SR, including A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2), [282]. Quality of Reporting of Meta-Analyses (QUOROM) [283] and PRISMA [284]. These checklists have evolved and added more specifications over the years on the features required in high-quality SR. AMSTAR 2 provides the most critical assessment of search terms by imploring the use of at least 2 databases and the inclusion of "keyword and search strategy." However, there is no mention regarding the minimum number of search terms needed or an explanation for search terms chosen, as this differs per topic [282]. We recommend all SR clearly describe the following details: database names, all search terms and the strategy, range of years searched, and all inclusion and exclusion criteria employed, adhering to the PRISMA standards [284]. Finally, a full description of search strategies must be presented. We acknowledge the growing constraints that journals face with respect to page limits and publication costs, which may preclude the inclusion of this vital information in all circumstances. However, such checklists could be published as online supplementary material, which are increasingly being utilized by journals.

This study has several strengths, including a rigorous search strategy, multiple sensitivity analyses and simulation to compare the results of search strategies. The main limitation is that we were unable to determine the relevancy of search terms and/or strategies on the capture rate of articles for a particular topic. In addition, some papers may have presented the terms they searched, which may not have been their true strategy. We were unable to determine if the methodology sections of the review were conducted as reported. We were also unable to determine if there were undocumented strategies. Thus, it is possible that a larger proportion of articles actually used more search terms or more sensitive search techniques.

In conclusion, we recommend standardizing the presentation of SR, in general, and for AD in particular, and for peer reviewers to employ checklists like AMSTAR2 or other tools in SR submissions. We recommend that the set of terms ("atopic dermatitis" and "eczema") be included in SR search strategies created for SRs focused on AD at minimum, with preferably, 4–5 search terms to obtain more sensitive searches.

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Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interest.

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