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Limitations of generalizability and reproducibility of systematic reviews in dermatology



To the Editor: High-quality systematic reviews (SRs) are needed to synthesize the results of multiple studies and inform evidence-based practice. SRs must critically evaluate studies and highlight knowledge gaps to advance dermatology. High-quality SRs are required to avoid the problem of “garbage in...garbage out.” Literature searches are arguably the most fundamental and often overlooked components of SRs. Comprehensive and globally representative search strategies are essential.

Atopic dermatitis (AD) and other inflammatory skin diseases are heterogeneous. Variable presentations by

region and race/ethnicity may be attributable to genetic, environmental, and behavioral factors, or a combination of these. Yet, the most commonly reported literature searches in SRs are limited to English language and Western literature.¹ This may exclude foreign language publications from studies conducted in Asia and other global regions,¹ thereby limiting the generalizability and validity of SR results. Some studies suggested that MEDLINE searches are sufficiently complete.² Others indicated that many other search engines are needed.^{3,4}

We sought to illustrate the impact of incomplete literature searches in dermatology using a post hoc analysis of an SR and meta-analysis that showed considerable regional and age-related differences of AD clinical characteristics.⁵ We used an exhaustive search strategy across multiple languages and search engines with broad global reach, yielding 101 studies. Had we not done so, the results would have been vastly different and arguably incorrect. MEDLINE yielded 32 studies, Embase yielded 22 more studies, and MEDLINE, Embase, Cochrane, Scopus, and LILACS yielded 87 studies, of which 58.7% were prospective and 63.6% high quality (≥ 3 stars for Newcastle-Ottawa Scale study design score). Asian language databases (China National Knowledge Infrastructure, Taiwan Electronic Periodical Services, and CiNii [Scholarly and Academic Information Navigator]) yielded another 9 studies, of which 88.9% were prospective and were high quality. We identified 5 studies from references of included articles.

We repeated the meta-analysis using search results from various combinations of databases. Some characteristics (eg, pruritus, xerosis) showed similar results regardless of the search engines used. Most other characteristics showed considerably different results, and some would have been entirely missed, depending on the search engines used (Fig 1; full results are available in Supplemental Fig 1, available at <https://data.mendeley.com/datasets/5vc2xrfjtp/1>). These results highlight the importance of using comprehensive and globally representative search strategies to reduce bias and improve accuracy of results.

Much of the current dogma about AD is driven by Western literature and may not reflect AD in diverse populations. Our findings have important clinical ramifications given population diversification in the United States and other regions. We are seeing increasingly more ethnically diverse patients, and clinicians need to properly assess AD in diverse populations. These results also have important ramifications for assessing therapeutic efficacy. Most

Clinical Features	Proportion (%)					
	All	Western Engines	Asian Engines	SCOPUS	Pubmed& EMBASE	Pubmed/ MEDLINE
Lichenification	66%	66%		74%	82%	84%
Early onset disease	57%	58%	52%	54%	73%	78%
Ichthyosis/palmar hyperlinearity/keratosis pilar	38%	37%	44%	25%	15%	7%
White dermographism/delayed blanch	35%	35%	38%	27%	30%	17%
Urticaria	27%	27%		50%	30%	50%
Extensor involvement (lower limbs)	25%	25%		17%	8%	
Papular lichenoid lesions	22%	26%	10%	16%	23%	26%
Photophobia	22%	26%	11%	11%	24%	11%
Dyshidrosis / pompholyx	14%	14%		12%	10%	7%
Knuckle dermatitis of hands	14%	21%		15%	24%	31%
Erythroderma	11%	11%		1%	2%	2%

Fig 1. Random-effects proportions of selected clinical characteristics occurring in atopic dermatitis overall and stratified by different regions are presented using a color-coded heat map (0% = dark green; 100% = dark red).

drugs developed for AD are studied in international studies across many regions. Yet, the results are pooled together, presuming homogeneity across regions. Our results suggest that such presumptions are problematic and that ethnic and regional differences should be considered when analyzing trial data.

We strongly recommend searching all of the abovementioned databases in SRs, especially those representing Asian and other non-English languages. Finally, clinicians should cautiously interpret SRs that were limited to English language and Western literature and recognize their potential biases and limited generalizability.

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Prison malpractice litigation involving dermatologists: A cross-sectional analysis of dermatologic medical malpractice cases involving incarcerated patients during 1970-2018



To the Editor: Over 75% of dermatologists are projected to face malpractice litigation by the age of 65 years.¹ Moreover, 28.7% of malpractice claims against dermatologists during 2006-2015 were decided in favor of the plaintiff, with an average indemnity payment of \$238,145.00 USD.² Although >1 in 110 Americans are incarcerated, limited information exists regarding malpractice litigation in the setting of dermatologic care for incarcerated patients.³ Incarcerated patients experience unique exposures, and pharmacologic formularies are often