Global Burden of Skin Disease as Reflected in Cochrane Database of Systematic Reviews

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**IMPORTANCE** Research prioritization should be guided by impact of disease.

**OBJECTIVE** To determine whether systematic reviews and protocol topics in Cochrane Database of Systematic Reviews (CDSR) reflect disease burden, measured by disability-adjusted life years (DALYs) from the Global Burden of Disease (GBD) 2010 project.

**DESIGN, SETTING, AND PARTICIPANTS** Two investigators independently assessed 15 skin conditions in the CDSR for systematic review and protocol representation from November 1, 2013, to December 6, 2013. The 15 skin diseases were matched to their respective DALYs from GBD 2010. An official publication report of all reviews and protocols published by the Cochrane Skin Group (CSG) was also obtained to ensure that no titles were missed. There were no study participants other than the researchers, who worked with databases evaluating CDSR and GBD 2010 skin condition disability data.

**MAIN OUTCOMES AND MEASURES** Relationship of CDSR topic coverage (systematic reviews and protocols) with percentage of total 2010 DALYs, 2010 DALY rank, and DALY percentage change from 1990 to 2010 for 15 skin conditions.

**RESULTS** All 15 skin conditions were represented by at least 1 systematic review in CDSR; 69% of systematic reviews and 67% of protocols by the CSG covered the 15 skin conditions. Comparing the number of reviews/protocols and disability, dermatitis, melanoma, nonmelanoma skin cancer, viral skin diseases, and fungal skin diseases were well matched. Decubitus ulcer, psoriasis, and leprosy demonstrated review/protocol overrepresentation when matched with corresponding DALYs. In comparison, acne vulgaris, bacterial skin diseases, urticaria, pruritus, scabies, cellulitis, and alopecia areata were underrepresented in CDSR when matched with corresponding DALYs.

**CONCLUSIONS AND RELEVANCE** Degree of representation in CDSR is partly correlated with DALY metrics. The number of published reviews/protocols was well matched with disability metrics for 5 of the 15 studied skin diseases, while 3 skin diseases were overrepresented, and 7 were underrepresented. Our results provide high-quality and transparent data to inform future prioritization decisions.

While many motivations drive research agendas, recent efforts highlight the need to develop accountable and transparent approaches for setting research priorities while best using scarce research funds. Research prioritization must establish objectives, engage key stakeholders, and define criteria for determining priorities. Data synthesis accounting for individual study biases best informs priority-setting decisions. While burden of disease data inform prioritization, other criteria include influence on vulnerable populations (equity), cost, availability and lack of cost-effectiveness interventions, interest-group advocacy (charity revenue), disease transmissibility, public interest, opportunity for scientific innovation, and infrastructure building. The Global Burden of Disease (GBD) 2010 project is a systematic, epidemiological collaboration that estimated disease mortality, morbidity, and risk factors for 291 diseases and injuries in 187 countries from 1990 to 2010. Led by the Institute of Health Metrics and Evaluation (IHME), GBD 2010 measured disease burden using the metrics of years of life lost due to premature mortality and years lived with a disability, which combine to equal disability-adjusted life years (DALYs). Global Burden of Disease 2010 specifically analyzed 15 skin conditions and an other skin and subcutaneous diseases category on the basis of prevalence, common case definitions, and data availability, providing disability estimates for skin conditions on a global scale.

### Methods

Since the study did not involve human subjects but only data review, institutional review board approval was waived.

The following 15 dermatologic conditions were studied in the GBD 2010 study: dermatitis including eczema, acne vulgaris, bacterial skin diseases, viral skin diseases, urticaria, fungal skin diseases, pruritus, scabies, alopecia areata, cellulitis, decubitus ulcer, melanoma, psoriasis, nonmelanoma skin cancer, and leprosy. The GBD 2010 also identified an other skin and subcutaneous diseases category (see Table 1 in the Supplement for International Statistical Classification of Diseases, 10th Revision, definitions and skin condition search terms). Each skin condition was searched in CDSR by searching the condition name under “title, abstract, keywords” (see Table 1 for search terms used for each skin condition). Both systematic reviews and protocols were considered to assess skin disease representation in the database.

A systematic review or protocol was matched to 1 of the 15 skin conditions or the other skin and subcutaneous diseases category according to its subject content, and the particular Cochrane group that published each review was determined. If the systematic review or protocol included the search term in the title, it was automatically included. To ensure that no reviews or protocols were missed, an official publication report of all reviews and protocols published by the Cochrane Skin Group (CSG) as of May 11, 2013, was obtained via e-mail communication with the CSG by one of us (L.P.). If appropriate, reviews or protocols were assigned more than 1 category.

### Table 1. Terms Entered Into Search Query for 15 Skin Conditions With GBD 2010 ICD-10 Code Definitions

<table>
<thead>
<tr>
<th>Skin Condition</th>
<th>ICD-10 Codes</th>
<th>Terms Entered Into Search Query</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis</td>
<td>L20-L28</td>
<td>Eczema, atop dermatitis, seborheic dermatitis, diaper dermatitis, contact dermatitis, dermatitis</td>
</tr>
<tr>
<td>Acne vulgaris</td>
<td>L70</td>
<td>Acne vulgaris, acne</td>
</tr>
<tr>
<td>Bacterial skin diseases</td>
<td>L00, L01, L02, L04, L08, L88, L97, L98.0-198.4</td>
<td>Staphylococcal scalded skin syndrome, impetigo, cutaneous abscess/furuncle/carbuncle, lymphadentitis, pyoderma, erythrasma, bacterial skin</td>
</tr>
<tr>
<td>Viral skin diseases</td>
<td>B00, B07-80</td>
<td>Herpes, viral warts, molluscum contagiosum, exanthema subitum, viral skin</td>
</tr>
<tr>
<td>Urticaria</td>
<td>L50</td>
<td>Urticaria</td>
</tr>
<tr>
<td>Fungal skin diseases</td>
<td>B35, B36.0, B36.1, B36.2, B36.3, B36.8</td>
<td>Candidiasis, tinea, fungal skin</td>
</tr>
<tr>
<td>Pruritus</td>
<td>L29</td>
<td>Pruritus, itch</td>
</tr>
<tr>
<td>Scabies</td>
<td>B66</td>
<td>Scabies</td>
</tr>
<tr>
<td>Alopecia areata</td>
<td>L63.0, L63.1, L63.8, L63.9</td>
<td>Alopecia areata</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>L03.0, L03.1, L03.2-L03.9</td>
<td>Cellulitis</td>
</tr>
<tr>
<td>Decubitus ulcer</td>
<td>L89</td>
<td>Decubitus ulcer, pressure wound</td>
</tr>
<tr>
<td>Melanoma</td>
<td>C43, D03, D48.5</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>L40-L41</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>Nonmelanoma skin cancer</td>
<td>C44, D04</td>
<td>Nonmelanoma skin cancer, basal cell carcinoma, squamous cell carcinoma</td>
</tr>
<tr>
<td>Leprosy</td>
<td>A30, B92</td>
<td>Leprosy</td>
</tr>
</tbody>
</table>

Abbreviations: GBD, Global Burden of Disease; ICD-10, International Statistical Classification of Diseases, 10th Revision.

* Specific ICD-10 codes used by GBD 2010 have been published previously.25
Table 2. Systematic Reviews and Protocols in CDSR, Group Contributions, and DALY Characteristics

<table>
<thead>
<tr>
<th>Skin Condition</th>
<th>CDSR Systematic Reviews and Protocols (No.) (N = 105)</th>
<th>Percentage of Total 2010 DALYs (of 291 Conditions</th>
<th>Median DALY Change, 1990 to 2010, %</th>
<th>2010 DALY Rank (of 176 Conditions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis</td>
<td>26 (18 reviews, 8 protocols)</td>
<td>Skin Group (20), Neonatal Group (4), Pregnancy and Childbirth Group (1), Eyes and Vision Group (1)</td>
<td>0.35</td>
<td>2</td>
</tr>
<tr>
<td>Other skin and subcutaneous diseases</td>
<td>33 (23 reviews, 10 protocols)</td>
<td>Skin Group (24), Menstrual Disorders and Subfertility Group (5), Infectious Diseases Group (1), Oral Health Group (1), Wounds Group (1), Pain, Palliative, and Supportive Care Group (1)</td>
<td>0.20</td>
<td>NA</td>
</tr>
<tr>
<td>Acne vulgaris</td>
<td>10 (6 reviews, 4 protocols)</td>
<td>Skin Group (5), Menstrual Disorders and Subfertility Group (4), Fertility Regulation Group (1)</td>
<td>0.16</td>
<td>1</td>
</tr>
<tr>
<td>Bacterial skin diseases</td>
<td>5 (4 reviews, 1 protocol)</td>
<td>Skin Group (4), Infectious Diseases Group (1)</td>
<td>0.12</td>
<td>−24</td>
</tr>
<tr>
<td>Viral skin diseases</td>
<td>9 (6 reviews, 3 protocols)</td>
<td>Skin Group (4), Acute Respiratory Infections (2), Colorectal Cancer Group (1), Gynaecological Cancer Group (1), HIV/AIDS Group (1)</td>
<td>0.11</td>
<td>−5</td>
</tr>
<tr>
<td>Urticaria</td>
<td>2 (1 review, 1 protocol)</td>
<td>Skin Group (2)</td>
<td>0.10</td>
<td>0</td>
</tr>
<tr>
<td>Fungal skin diseases</td>
<td>6 (4 reviews, 2 protocols)</td>
<td>Skin Group (6)</td>
<td>0.093</td>
<td>6</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2 (1 review, 1 protocol)</td>
<td>Pain, Palliative, and Supportive Care Group (1), Anaesthesia Group (1)</td>
<td>0.085</td>
<td>−1</td>
</tr>
<tr>
<td>Scabies</td>
<td>2 (1 review, 1 protocol)</td>
<td>Infectious Diseases Group (1), Occupational Safety and Health Group (1)</td>
<td>0.063</td>
<td>−31</td>
</tr>
<tr>
<td>Alopecia areata</td>
<td>1 (1 review)</td>
<td>Skin Group (1)</td>
<td>0.054</td>
<td>0</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>2 (1 review, 1 protocol)</td>
<td>Skin Group (2)</td>
<td>0.052</td>
<td>−30</td>
</tr>
<tr>
<td>Decubitus ulcer</td>
<td>15 (10 reviews, 5 protocols)</td>
<td>Wounds Group (15)</td>
<td>0.049</td>
<td>−20</td>
</tr>
<tr>
<td>Melanoma</td>
<td>7 (5 reviews, 2 protocols)</td>
<td>Skin Group (7)</td>
<td>0.047</td>
<td>−10</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>11 (7 reviews, 4 protocols)</td>
<td>Skin Group (10), Musculoskeletal Group (1)</td>
<td>0.042</td>
<td>−2</td>
</tr>
<tr>
<td>Nonmelanoma skin cancer</td>
<td>6 (6 reviews)</td>
<td>Skin Group (4), Eyes and Vision Group (1), Gynaecological Group (1)</td>
<td>0.032</td>
<td>−2</td>
</tr>
<tr>
<td>Leprosy</td>
<td>4 (4 reviews)</td>
<td>Skin Group (2), Neuromuscular Disease Group (2)</td>
<td>0.00024</td>
<td>−82</td>
</tr>
</tbody>
</table>

Abbreviations: CDSR, Cochrane Database Systematic Reviews; DALY, disability-adjusted life years; GBD, Global Burden of Disease; HIV, human immunodeficiency virus; NA, not applicable.

| Listed in descending order of percentage of total 2010 DALYs.

Results

Dermatitis was the leading skin disease represented in CDSR (Table 2) and was also the skin disease with the highest percentage of total DALYs and highest DALY rank (Figure). Decubitus ulcer was the second most represented skin condition, followed by psoriasis, acne vulgaris, and viral skin diseases (Table 2). Melanoma, nonmelanoma skin cancer, bacterial skin diseases, and leprosy had intermediate CDSR representation.

ages of total DALYs of all 291 conditions measured in GBD 2010, were obtained from the GBD Compare interactive time plot. Using this tool, we selected search parameters of “time plot,” “DALYs” metric, “global” place, “all ages,” “both” sexes, and “%” units for each skin condition. DALY rankings for the 15 skin conditions compared with 176 conditions measured in GBD 2010 were obtained from the GBD interactive arrow diagram.

It should be noted that while the GBD project studied 291 conditions, rankings include only 176 conditions, excluding conditions for which the project made no explicit estimates such as causes of diarrhea, pneumonia, and more specific conditions under maternal or congenital. Search parameters of “global” place, “all” conditions, “both” sexes, “DALY” metric, and “age-standardized” were used. Median percentage change of global DALYs from 1990 to 2010 was also obtained from the GBD interactive arrow diagram for each skin condition. Age standardization was used in the interactive arrow diagram for DALY ranking and median percentage change to eliminate effects of population growth and aging over the 20-year time span.

Two of us (C.K. and L.N.B.) collected data independently from November to December 2013 with consensus review by the senior author (R.P.D.) to resolve discrepancies.
Low representation was observed for urticaria, pruritus, scabies, cellulitis, and alopecia areata. A list of all included review and protocol titles for each skin condition is available in eTable 2 in the Supplement; a list of all excluded titles can be found in eTable 3 in the Supplement.

Thirty-three systematic reviews and protocols covered 22 skin conditions defined by the GBD 2010 other skin and subcutaneous diseases category: pediculosis, pityriasis rosea, lichen planus, toxic epidermal necrolysis, vitiligo, melasma, ingrown nail, hypertrichosis, androgenic alopecia, rosacea, hidradenitis suppurativa, eccrine sweat disorder unspecified, lupus erythematosus, localized scleroderma, lichen sclerosis, keloid scar, pemphigoid, pemphigus, polymorphic light eruption, actinic keratosis, photodamage, and radiodermatitis (see eTable 4 in the Supplement for included titles and eTable 5 in Supplement for excluded titles). The CSG in CDSR was responsible for 73% of the systematic reviews for these 22 skin conditions.

**Discussion**

All 15 skin conditions studied in GBD 2010 were represented by at least 1 systematic review, and 13 of the skin conditions also had 1 protocol published by CDSR. Furthermore, 61% of systematic reviews and protocols covering the 15 skin conditions were published by the CSG in CDSR. Sixty-nine percent of all systematic reviews and 67% of all protocols published by the CSG covered the GBD 2010 15 skin conditions. While CDSR covers a broad diversity of skin conditions, prioritization is not solely guided by burden of disease disability data.

**Conditions for Which CDSR Representation Was Appropriate for Associated Disability**

Dermatitis had both the greatest CDSR representation and the highest DALY ranking. Of interest, dermatitis representation in CDSR exceeded that of 2 nonskin diseases with similar GBD 2010 DALY ranking, poisonings and encephalitis, which are represented by 13 and 5 systematic reviews and protocols, respectively.18

The CDSR representation of melanoma and nonmelanoma skin cancer (7 and 6 systematic reviews and protocols, respectively) correlates with their relatively low percentage of total 2010 DALYs and DALY rankings. Similarly, disability and review and protocol representation appear well-matched for viral skin diseases and fungal skin diseases, which have intermediate representation in CDSR (9 and 6 systematic reviews and protocols, respectively) and intermediate percentage total 2010 DALYs (0.11% and 0.093%, respectively). Of note, fungal skin disease showed the highest median percentage change in DALYs from 1990 to 2010 of all 15 skin conditions (6%).

**Conditions for Which CDSR Representation Were Too High for Associated Disability**

Decubitus ulcer was represented by 10 systematic reviews and 5 protocols but had the fifth lowest percentage of total 2010 DALYs of the 15 skin conditions. Similarly, psoriasis had the
third highest review and protocol representation (n = 11) but the third lowest percentage of total 2010 DALYs. Leprosy was also overrepresented in CDSR by 4 systematic reviews, while this condition demonstrated a significant 82% decrease in global DALYs, ranking 175th in 2010 of all 176 conditions ranked by GBD 2010.

**Conditions for Which CDSR Representation Was Too Low for Associated Disability**

At the lower end of the representation spectrum, acne vulgaris and bacterial skin diseases had 10 and 5 reviews and protocols, respectively, but the second and third highest percentage of total 2010 DALYs. The GBD 2010 disability data for these 2 conditions demonstrate similar global disability “hot spots” in Africa, particularly Nigeria for acne vulgaris and Mozambique for bacterial skin diseases.27 The validity of this country-specific disease burden begs further investigation.

The most common dermatologic disorder seen in emergency departments, urticaria, was underrepresented in CDSR when matched with its fifth highest percentage of total 2010 DALYs of the 15 skin conditions.19 Pruritus was similarly underrepresented. Perhaps these may be topics for future expansion in CDSR. However, DALY rates for both conditions remained constant (0% and ~2%, respectively) from 1990 to 2010, which may partially explain their low CDSR representation. It should be noted that while the symptom of pruritus is associated with many systemic diseases, the GBD 2010 DALY estimate corresponds solely to pruritus without underlying systemic disease.20

Scabies was also underrepresented in CDSR compared with its associated disability (0.063% of total DALYs). This condition has recently been classified by the World Health Organization as a neglected disease because it is a surrogate for poverty, causes significant stigmatization, and is associated with nephritis and rheumatic heart disease in tropical settings.21,22

**Limitations and Future Directions**

Several limitations to the current study will be addressed as well as areas for further investigation. The GBD 2010 project employs disability weights for skin diseases that are solely described by the disability that affects the skin, such as disfigurement and itch and/or discomfort, and do not include impact on other organ systems. For example, 1 of the 15 skin conditions studied by GBD 2010 was psoriasis, a chronic and multifactorial condition commonly presenting with erythematous and scaly skin patches.23 However, other debilitating manifestations of the disease are not considered in the GBD 2010 disability data for psoriasis, including psoriatic arthritis, which manifests in 30% of patients with psoriasis; ocular disease, most commonly blepharitis; and a greatly increased risk for chronic kidney disease.24-26

Systematic reviews published by CDSR are sophisticated syntheses of evidence in the published literature meeting pre-specified eligibility criteria regarding a particular topic; thus, meta-analyses cannot be performed for topics that lack research-based evidence in the literature.27 Additionally, reviews can be broad or narrow in scope, particularly from different Cochrane review groups. For a given set of interventions, authors may prepare a single large review of multiple interventions (lumping) or several reviews of individual interventions (splitting). Thus, considering a systematic review or protocol as 1 unit of representation may not be entirely accurate. While 2 of us independently performed the current analysis with consensus review provided by a third author, the classification of a particular review or protocol to a certain skin condition involved some degree of subjectivity. For reference, listings of all review and protocol inclusions and exclusions are provided in eTables 2-5 in the Supplement.

While beyond the scope of our study, the influence of other factors in addition to burden of disease on CDSR prioritization, such as surveying policy makers for their priorities, undertaking a formal prioritization process with the James Lind Alliance, and involving a variety of key stakeholders in prioritization, merit further investigation.28 As mentioned in the Methods section, 33 systematic reviews and protocols in CDSR represented 22 skin conditions in the GBD 2010 other skin and subcutaneous diseases category (see eTables 3 and 4 in the Supplement). A future exploration of the relationship between representation in CDSR and the DALY metric for these “other” conditions, not yet described by the GBD project, would be extremely valuable. Finally, the mapping exercise used in the present study would be helpful to investigate and compare other review databases within The Cochrane Library such as The DARE Database as well non-Cochrane databases such as Medline, Health Systems Evidence, and Web of Science.10 As GBD project data are now to be updated on an annual basis, more information will be available regarding disease disability changes over time.29

**Conclusions**

There is a lack of transparency in many publications on the availability and quality of data and criteria that are used to inform prioritization decisions.29 Although our results do not set the final priorities for Cochrane reviews, we provide high-quality and transparent data to inform these decisions in the future. Our study demonstrates that systematic reviews can be mapped against burden of disease and that this could be a factor to guide prioritization of future systematic review topics. It may be entirely appropriate to have overrepresentation of a topic if, for example, the disease disproportionately affects disadvantaged populations and health equity becomes a high priority in research allocation. This was noted herein to be the case for leprosy, but it is also particularly relevant for neglected tropical diseases for which the World Health Organization has called for allocation of additional research funds to “promote equity in the distribution of resources.”30 As an example, factors considered by the CSG to accept and prioritize topics for future Cochrane reviews include their impact on people’s lives (surrogate for burden of disease), knowledge gap, existence of other systematic reviews, availability of public funding, and whether the topics are of great current interest or public health importance.30 Cochrane Skin Group editors then vote to determine the priority topics for the upcoming year.
As the medical and scientific communities continue to learn more about the global implications of diseases that affect the human population, specifically disability and mortality, it is imperative that information regarding these diseases is available to health care professionals. Large-scale efforts to mitigate the disparity between disease prevalence, disability impact, and availability of electronic information are under way, such as the Research-Disease Disparity (ReDD) Observatory, which seeks to provide “a simple mechanism for publishing and interlinking structured information on the Web,”13 and the Link discovery framework for MeTric Spaces (LIMES) which applies algorithmic models for “novel time-efficient approaches for link discovery in metric spaces.”34 While our study involved the manual linking of skin diseases with Cochrane reviews, tools such as LIMES and the ReDD Observatory will help to automate the process on a much larger scale. As science and mathematics, tempered by humanity, grant us an unprecedented understanding of human disease at a global level, technology provides the means to minimize research disparity and significantly improve the lives of the populations affected by these diseases.

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