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# DISABILITY BURDEN OF SKIN DISEASES

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"SKIN DISEASES ARE THE FOURTH LARGEST CAUSE OF DISABILITY WORLDWIDE".  
DISCUSS THE VERACITY OF THIS STATEMENT.

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## Introduction

The Global Burden of Diseases, Injury, and Risk Factors Study (GBD) is a study that aims to quantify the worldwide health impacts of diseases and risk factors [1]. An article by Karimkhani *et al.* from the 2013 iteration of the GBD study claimed that skin disease was the 'fourth leading cause of nonfatal burden' worldwide; in other words, the fourth largest cause of disability. At 41.0 million disability-adjusted life-years (DALYs), the impact of skin diseases ranked behind iron deficiency anaemia at 43.7 million DALYs, tuberculosis at 49.8 million DALYs, and sense organ diseases at 54.4 million DALYs [2]. This was in agreement with an article by Hay *et al.* from the 2010 iteration of the GBD study, where skin diseases were the fourth largest cause of disability in terms of years lost to disability (YLDs) at 33.7 million YLDs, behind iron-deficiency anaemia at 42.5 million YLDs, major depressive disorder at 63.3 million YLDs, and low back pain at 80.7 million YLDs.[3]. In this essay, I will aim to verify and discuss the accuracy of these assertions that skin diseases are the fourth largest cause of disability worldwide.

## Metrics and Quantitative Analysis

The GBD study uses a number of metrics in order to estimate the health impact of diseases. Disability-adjusted life-years, an innovation of the first 1990 GBD study, is calculated by summing two components: years of life lost (YLLs) and years lived with disability (YLDs). YLLs estimates the impact of mortality caused by a particular disease, with reference to a standard life expectancy. YLDs estimates the impact of disability caused by a disease by weighting the prevalence of disabling sequelae by a 'disability weight' determined by the estimated severity of each disabling sequela [4]. Disabling sequela relevant to skin disease include disfigurement (with or without itch or pain), and acute fever [2]. In this essay, I have chosen to use YLDs as the primary measure of disease burden due to disability; it excludes the impact of mortality and weights disabilities by their severity.

The GBD Compare Tool, available online courtesy of the Institute for Health Metrics and Evaluation (IHME), was

used to determine the where skin diseases ranked in terms of YLDs [5]. Data from the most recent iteration of the GBD study (2017), was used with diseases grouped at Level 2 of the GBD cause hierarchy. The result was that skin diseases were the ninth largest cause of disability in terms of YLDs, with a burden of 41.6 million YLDs (95% confidence interval: 27.4 million - 61.9 million). This is equivalent to 545 YLDs per 100,000 (95% confidence interval: 358 - 810). Ahead of skin diseases were nutritional deficiencies (42.4 million), chronic respiratory diseases (44.3 million), diabetes and kidney disease (45.9 million), other non-communicable diseases (53.6 million), sense organ diseases (66.6 million), neurological disorders (73.2 million), mental disorders (122.7 million), and musculoskeletal disorders (135.9 million).

Worldwide, YLD rates for skin diseases have remained relatively constant over time, with a rate of 551 YLDs per 100,000 in the first iteration of the GBD study in 1990 (ranked seventh), although absolute YLDs have been increasing due to worldwide population growth. This ninth place ranking has remained consistent over the years of the GBD study since 2010, including the 2013 iteration. In terms of trends by country, countries with low to middle social development indices (SDI) had a lower rate of skin disease disability burden compared to countries with high SDI. For instance, in 2017, YLDs for skin disease were 852 per 100,000 in the United States and 726 per 100,000 in New Zealand, compared to just 574 in Nigeria and 545 in China.

The skin disease with the highest disability burden in the 2017 GBD study was dermatitis (11.1 million YLDs). This was followed by psoriasis (5.57 million), urticaria (5.01 million), scabies (4.53 million), fungal skin diseases (4.15 million), viral skin diseases (2.60 million), and acne vulgaris (2.55 million).

## Discussion

There is evidently a discrepancy between the claim of skin diseases as being the fourth largest cause of disability by Karimkhani *et al.* and Hay *et al.* when skin diseases have consistently ranked in ninth place in YLDs according to

the GBD Compare Tool. It is likely that this difference has occurred due to differences in metrics and disease groupings for calculating disease burden. Firstly, Karimkhani *et al.* and Hay *et al.* compare skin disease against Level 3 groupings on the GBD hierarchy (such as iron deficiency anaemia and tuberculosis), rather than broader Level 2 groupings (such as chronic respiratory diseases and musculoskeletal disorders) [2][3]. Level 3 groupings are more specific descriptors than Level 2 groupings, thus they will naturally have smaller total burdens of disease, making it easier for skin disease to rank higher. It is also important to note that 'skin and subcutaneous diseases' is, in itself, a Level 2 grouping, and the Level 3 descriptors are specific skin diseases such as dermatitis and psoriasis [5]. I am therefore of the opinion that it is most appropriate to compare skin diseases against Level 2 groupings.

Furthermore, Karimkhani *et al.* have used DALYs as their primary metric for measuring the impact of skin disease, claiming that skin disease is the eighteenth largest cause of DALYs and fourth largest when considering only 'nonfatal burden'. It is unclear how nonfatal burden was calculated, but it appears to be measured in DALYs and appears to be distinct to YLDs [2]. I believe that, in the context of ranking causes of disability, it is more simple and appropriate to consider YLDs. Other authors who have ranked causes of disability, such as Hay *et al.* and Steiner *et al.*, have used YLDs as their metric of disability [3] [6].

There are several other issues to consider when attempting to definitively rank the disability burden of skin disease. Metrics such as DALYs and YLDs come with 95% confidence intervals which are often relatively wide [4]; the confidence interval for YLDs due to skin disease in the 2017 GBD ranges from 27.4 million to 61.9 million. This confidence interval overlaps with the confidence intervals of many other disease classifications. This includes third placed neurological disorders on the high end (50.7 million - 100.4 million) and fourteenth placed digestive diseases on the low end (13.9 million - 27.9 million). There is therefore a large amount of variability when it comes to estimating the precise ranking of the disability burden of skin diseases: the 95% confidence interval could place it anywhere between third and fourteenth place.

Another issue that exists with the classification system used by the GBD study is the mutually exclusive classification of disease states. For instance, systemic lupus erythematosus (SLE) is solely classified under 'other musculoskeletal disease' and is not classified as a skin disease, despite the fact that it often has cutaneous manifestations that will contribute to the overall disability burden of SLE [3]. The result of this is that the GBD study likely underestimates the impact of skin disease. In fact, it is plausible that skin disease has a number of hidden impacts and contributions to other disease classifications.

For instance, mental disorders (ranked as the second highest cause of disability with 122.7 million YLDs) [5] have a strong association with skin disease. According to Dalgard *et al.*, patients with skin diseases are significantly more

likely to have depression (adjusted odds ratio (OR): 2.40; 95% CI: 1.67 - 3.47), anxiety (adjusted OR: 2.18; 95% CI: 1.68 - 2.82), and suicidal ideation (adjusted OR: 1.24; 95% CI: 0.95 - 1.62) compared to controls [7]. This suggests a hidden psychological burden of skin diseases that needs to be taken into account when performing a full assessment of the disease burden of skin diseases.

Another significant association of skin disease is the association with diabetes mellitus; 'diabetes and kidney disease' was ranked as the sixth highest cause of disability with 45.9 million YLDs [5]. A significant contribution of this is likely to be attributable to the cutaneous sequelae of diabetes, such as foot ulcers and infection (as well as amputation, which may be necessary due to ulcers or skin infection). According to data from the 2016 iteration of the GBD, there were 2.5 million YLDs from diabetic foot ulcers, as well as an additional 1.5 million YLDs due to amputation [8]. This suggests a further burden of disease associated with skin disease that will not be strictly counted as skin disease in the GBD classification. Furthermore, leg ulcers have a particularly strong and well-established association with depression: Dalgard *et al.* found patients with leg ulcers to have the highest odds of depression (adjusted OR: 10.17; 95% CI: 4.07 - 25.41) [7].

There are also a number of infectious sequelae of skin disease that may lead to further disability. For instance, streptococcal skin diseases such as impetigo can lead to poststreptococcal glomerulonephritis, which creates a significant disease burden in developing countries [9]. In the 2017 iteration of the GBD, there were 1.05 million YLDs due to chronic kidney disease caused by glomerulonephritis [5]; it is likely a significant portion of this would have had a poststreptococcal aetiology. Additionally, skin diseases such as atopic dermatitis can predispose to a number of infections that may spread beyond the skin due to impaired barrier function. For instance, Belden *et al.* found that patients with inflammatory skin diseases such as dermatitis and psoriasis were more likely to develop musculoskeletal infection [10].

Another issue that may lead to underestimation of the disease burden of skin disease is related to the method used to calculate the weightings of diseases. The disability weighting of diseases in the GBD study is determined by via large surveys of members of the public, rather than the experiences of people who have the disease [11]. Many skin diseases (such as psoriasis) are highly stigmatised, and it has been established the quality of life impact of diseases with high levels of stigma are often underestimated by members of the public [12], which will lead to an underestimation of the disability weighting of skin diseases such as psoriasis. It is also likely the stigmatisation will also lead to an underestimation of the prevalence of skin diseases due to under-reporting [13].

Limitations in the geographic coverage of studies may also contribute to a global underestimation of the prevalence of skin diseases. For instance, when estimating the disability burden of skin disease in Sub-Saharan Africa, the

GBD study used only 53 studies, compared to the 62 studies used to estimate the disability burden of skin in the United States, which has only a third of the population as Sub-Saharan Africa [13].

## Conclusion

The process of ranking worldwide causes of disability is highly dependent on the metric and disease groupings chosen; it almost becomes an arbitrary task because of this. According to Karimkhani *et al.* and Hay *et al.*, who compared skin diseases collectively against a number of Level 3 disease descriptors, skin diseases were indeed the fourth largest cause of disability worldwide [2] [3]. However, according to the 2017 iteration of the GBD, based on Level 2 groupings of the GBD hierarchy only, and using YLDs as the primary metric, skin and subcutaneous diseases are in fact the ninth largest cause of disability worldwide, with a 95% confidence interval that could place skin diseases anywhere between third and fourteenth place.

Due to the limitations of the GBD study, it is probable that the disability burden of skin diseases is underestimated, and the true ranking is likely on the higher end of the confidence interval. A number of other disease classifications with high burdens of disease are either strongly influenced by skin diseases (most notably mental disorders) [7], or have skin diseases as a major complication (most notably diabetes) [8], and these are not counted by the GBD study. Furthermore, the prevalence of skin diseases is likely underestimated, particularly in developing countries [13], and the quality of life impact of skin diseases is also likely to be understated [12]. More study needs to be done to accurately quantify the burden of disability of skin disease worldwide, particularly in developing countries, and particularly focusing on lesser recognised complications of skin disease, such as depression. This will be valuable for developing stronger public health policy internationally.

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