Global Burden of Eye and Vision Disease as Reflected in the Cochrane Database of Systematic Reviews

Lindsay N. Boyers, BA; Chante Karimkhani, BA; John Hilton, MSc, MPhil; William Richheimer, MD; Robert P. Dellavalle, MD, PhD, MSPH

IMPORTANCE  Eye and vision disease burden should help guide ophthalmologic research prioritization. The Global Burden of Disease (GBD) Study 2010 compiled data from 1990 to 2010 on 291 diseases and injuries, 1160 disease and injury sequelae, and 67 risk factors in 187 countries. The Cochrane Database of Systematic Reviews (CDSR) is a resource for systematic reviews in health care, with peer-reviewed systematic reviews that are published by Cochrane Review Groups.

OBJECTIVE  To determine whether systematic review and protocol topics in the CDSR reflect disease burden, measured by disability-adjusted life-years (DALYs), from the GBD 2010 project. This is one of a series of projects mapping GBD 2010 medical field disease burdens to corresponding systematic reviews in the CDSR.

DESIGN AND SETTING  Two investigators independently assessed 8 ophthalmologic conditions in the CDSR for systematic review and protocol representation according to subject content. The 8 diseases were matched to their respective DALYs from the GBD 2010 project.

MAIN OUTCOMES AND MEASURES  Cochrane Database of Systematic Reviews systematic review and protocol representation and percentage of total 2010 DALYs.

RESULTS  All 8 ophthalmologic conditions were represented by at least 1 systematic review in the CDSR. A total of 91.4% of systematic reviews and protocols focused on these conditions were from the Cochrane Eyes and Vision Group. Comparing the number of reviews and protocols with disability, only cataract was well matched; glaucoma, macular degeneration, and other vision loss were overrepresented. In comparison, trachoma, onchocerciasis, vitamin A deficiency, and refraction and accommodation disorders were underrepresented.

CONCLUSIONS AND RELEVANCE  These results prompt further investigation into why certain diseases are overrepresented or underrepresented in the CDSR relative to their DALY. With regard to ophthalmologic conditions, this study encourages that certain conditions get more focus to create a better representation of what is causing the most disability and mortality within this research database. These results provide high-quality and transparent data to inform future prioritization decisions.

Published online September 18, 2014.
The process of setting research agendas and priorities is complex and multifactorial, with the aim to provide the greatest public health benefit. While a uniform approach to establishing health research priorities is not appropriate for the unique situation and context in which agendas are set, 9 common themes of good practice have been identified including, but not limited to, determination of criteria that will guide prioritization decisions, minimization of bias, keeping up to date, striving for relevance, promoting access, ensuring quality, continuity, and enabling wide participation.

Within the Cochrane Library, the Cochrane Database of Systematic Reviews (CDSR) contains reviews produced by 53 Cochrane Review Groups. The CDSR serves as a source of peer-reviewed systematic reviews in health care. It aims to provide evidence-based information to inform decision making for individuals, health care professionals, and policy makers alike. Until now, Cochrane reviews have mainly focused on treatment effectiveness assessed in randomized clinical trials, although guidance on incorporating evidence from studies with other designs is being developed.

One of the Cochrane Review Groups, the Eyes and Vision Group, registered with Cochrane in 1997 and has 200 members from 30 countries. This group seeks to create, sustain, and encourage access to systematic reviews that synthesize information regarding all aspects of prevention and treatment of eye disease and visual impairment. Its scope extends to aid those affected by visual impairment or blindness in the adjustment to their disability. Prioritization strategies for the Cochrane Eyes and Vision Group specifically emphasize chief causes of blindness worldwide and regions with a large range of clinical practices and outcomes. The compiled systematic reviews rely on data from randomized and quasi-randomized clinical trials and create descriptive compilations where such information is scarce. Primary outcome measurements are visual function such as visual acuity, assessment of visual field, and assessment of vision-related quality of life.

There are various efforts underway to help drive agendas and priorities within the field of ophthalmology. For instance, the Sight Loss and Vision Priority Setting project, initiated in 2011, is supported and guided by the James Lind Alliance. The priorities set by this group are within the context of the UK National Health Service. This organization uses the input of patients, caregivers, and health care professionals to identify and prioritize unanswered questions or overlooked issues regarding ophthalmology treatment, diagnosis, and prevention. The results are publicized to research commissioning bodies to be considered for funding. Li et al conducted an eye and vision prioritization exercise on the topic of open-angle glaucoma. This study focused on creating and evaluating a framework to determine evidence gaps and prioritize clinical questions by using clinical practice guidelines and systematic reviews. Unlike the Sight Loss and Vision Priority Setting project, this work aimed to respond to clinicians’ needs and was thus limited to the professionals’ perspective.

When it comes to research prioritization, burden of disease is one of many factors that may be considered. In particular, the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2010 is the result of a worldwide collaboration of 500 researchers that scientifically and systematically quantified various health metrics of loss to diseases, injuries, and risk factors by age and sex. The GBD 2010 included 291 diseases and injuries, 67 risk factors, 1160 sequelae (nonfatal health consequences) for 21 regions, 187 countries, and 20 age groups. The GBD 2010 uses improved methods for the estimation of disability weights, which quantify the severity of health loss associated with a particular disease state. Disability-adjusted life-years (DALYs) are a metric established by the GBD to analyze and compare years of healthy life lost. The DALY is a combination of years lost owing to premature death and years lived with disability. These data metrics enable comparison of health data across boundaries of geography and time in a way that is more comprehensive, internally consistent, and comparable than previous data sources.

The aim of the current study was to assess representation of 8 ophthalmologic categories studied by the GBD 2010 within the CDSR and whether representation corresponds to GBD 2010 disability estimates for each category. The current study is part of a larger series intending to map all 291 diseases studied by the GBD 2010 to representation in major research databases.

**Methods**

The following 8 ophthalmologic categories were studied by the GBD 2010: refraction and accommodation disorders, cataracts, macular degeneration, glaucoma, trachoma, onchodiasis, vitamin A deficiency, and other vision loss. The other vision loss category included a total of 57 eye conditions including choroidal degeneration, central retinal artery occlusion and diplopia (see eTable 1 in the Supplement for a complete list of conditions in the other vision loss category). Each ophthalmologic category was explored in the CDSR by searching the condition name under title, abstract, keywords (see Table 1 and eTable 1 in the Supplement for International Statistical Classification of Diseases, 10th Revision [ICD-10] definitions and search terms for each ophthalmologic category). Both systematic reviews and protocols were considered to assess ophthalmologic disease representation in the database.

Certain GBD categories were ultimately excluded because ophthalmologic conditions were not the focus and GBD metrics could not be attributed solely to the ophthalmologic conditions. These categories included sense organ diseases, other sense organ diseases, and other noncommunicable diseases. The category of vitamin A deficiency was predominantly eye conditions (ICD codes of nonophthalmologic conditions were E50.8, E50.9, and E64.1); thus, it was included.
A systematic review or protocol was matched to 1 of the 8 ophthalmologic categories according to its subject content, and the particular Cochrane Review Group that published each review and date of publication were determined. For a review or protocol to be classified under a disease, the disease was required to be a predominant focus of the abstract objectives and main results. If the systematic review or protocol included the search term in the title, it was automatically included. Reviews or protocols with more than 1 category as a predominant focus were counted once within each respective category. For instance, if a review pertained to both cataracts and glaucoma, it was counted twice.

Methods used by the GBD 2010 to generate DALY estimates have been previously described. As previously mentioned, the DALY metric combines years of life lost owing to premature mortality and years lived with a disability. Disabilty-adjusted life-year metrics for each of the 8 ophthalmologic categories, expressed as the percentage of total DALYs of 291 conditions measured in the GBD 2010, were obtained from the GBD Compare interactive time plot. Using this tool, search parameters of time plot, DALYs metric, global place, all ages, both sexes, and % units were selected for each ophthalmologic condition. The DALY rankings for the 8 ophthalmologic categories compared with 176 conditions measured in the GBD 2010 were obtained from the GBD interactive arrow diagram. Although the GBD project studied 291 conditions, rankings only include 176 conditions, excluding conditions for which the project made no explicit estimates such as etiologies 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. The DALY percentage change from 1990 to 2010 was also obtained from the GBD interactive arrow diagram for each ophthalmologic condition. Age standardization was used in the interactive arrow diagram for DALY ranking and percentage change to eliminate effects of population growth and aging over the 20-year span.

Matching of the CDSR representation with GBD disability estimates was accomplished by creating a data plot of representation vs disability to generate a linear line of best fit with a coefficient of determination (R²) and qualitatively determining whether conditions were well matched or not well matched. Because research prioritization of a major database, such as the CDSR, was not expected to solely correlate with a single factor, qualitative rather than quantitative methods were used to match funding with disability.

Two authors (L.N.B. and C.K.) collected data independently, with consensus review during March 2014. Because the current study solely involved nonhuman subjects, institutional review board approval was not necessary.

### Table 1. GBD 2010 Ophthalmologic Conditions, the ICD-10 Codes That Define Them, and Terms Searched on the Cochrane Library

<table>
<thead>
<tr>
<th>Ophthalmologic Condition</th>
<th>ICD-10 Codes Populating Ophthalmologic Category in GBD 2010[^1]</th>
<th>Terms Entered Into Search Query</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refraction and accommodation disorders</td>
<td>H49-H52</td>
<td>Refraction, accommodation disorders, paresis of accommodation, span of accommodation, paralytic strabismus, third nerve palsy, oculomotor nerve palsy, fourth nerve palsy, trochlear nerve palsy, sixth nerve palsy, abducens nerve palsy, ophthalmoplegia, Keane-Sayre syndrome, strabismus, esotropia, exotropia, hypertropia, hypermetropia, heterotropia, cycloplegia, microtropia, monocular deviation, hypermetropia, myopia, astigmatism, anisometropia, aniseikonia, presbyopia, internal ophthalmoplegia</td>
</tr>
<tr>
<td>Cataracts</td>
<td>H25-H26</td>
<td>Cataracts, senile cataract, senile incipient cataract, subcapsular polar senile cataract, water clefs, senile nuclear cataract, cataracta brunescens, nuclear sclerosis cataract, Morgagnian type, senile hypermature cataract, infantile cataract, presenile cataract, traumatic cataract, complicated cataract, cataract in chronic iridocyclitis, glaucomatous flecks, drug-induced cataract, secondary cataract, Soemmerring ring</td>
</tr>
<tr>
<td>Macular degeneration</td>
<td>H35.3</td>
<td>Macular degeneration, angiod streaks of macula, cyst of macula, drusen of macula, degeneration of macula, hole of macula, puckering of macula, Kuhnt-Junius degeneration, senile macular degeneration, toxic maculopathy</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>H40</td>
<td>Glaucoma, glaucoma suspect, ocular hypertension, primary open-angle glaucoma, primary angle-closure glaucoma, glaucoma secondary to eye trauma, glaucoma secondary to eye inflammation, glaucoma secondary to other eye disorders, glaucoma secondary to drugs</td>
</tr>
<tr>
<td>Trachoma</td>
<td>A71, A74.0, and B94.0</td>
<td>Trachoma, trachoma dubium, trachomatous, chlamydial conjunctivitis, paratrachoma</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>B73</td>
<td>Onchocerciasis, Onchocerca volvulus infection, Onchocercosis, river blindness, Robles disease</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>E50.0-50.7 (E50.8, E50.9, and E64.1 excluded because not ophthalmologic conditions)</td>
<td>Vitamin A deficiency with conjunctival xerosis, vitamin A deficiency with Bitot spot, vitamin A deficiency with corneal xerosis, vitamin A deficiency with corneal ulceration, vitamin A deficiency with keratomalacia, vitamin A deficiency with night blindness, vitamin A deficiency with xerophthalic scars of cornea, ocular manifestations of vitamin A deficiency, cataract due to vitamin A deficiency, vitamin A eye, vitamin A blindness, vitamin A ocular</td>
</tr>
</tbody>
</table>

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

[^1]: Specific ICD-10 codes used by GBD 2010 are published in a study by Lozano et al. (2015).
Table 2. Representation in the CDSR and DALY Metrics for 8 Ophthalmologic Conditions Studied by GBD 2010*

<table>
<thead>
<tr>
<th>Ophthalmologic Condition</th>
<th>No. of Systematic Reviews and Protocols in the CDSR</th>
<th>Cochrane Group Contributions</th>
<th>% of Total 2010 DALY (Of 291 Conditions)</th>
<th>DALY % Change of DALY From 1990 to 2010</th>
<th>2010 DALY Rank (Of 176 Conditions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other vision loss</td>
<td>26 (23 reviews, 3 protocols)</td>
<td>19 Eyes and Vision, 5 Neonatal, and 2 Stroke</td>
<td>0.23</td>
<td>+2</td>
<td>67</td>
</tr>
<tr>
<td>Refraction and accommodation disorders</td>
<td>15 (12 reviews, 3 protocols)</td>
<td>15 Eyes and Vision</td>
<td>0.23</td>
<td>+1</td>
<td>68</td>
</tr>
<tr>
<td>Cataracts</td>
<td>19 (16 reviews, 3 protocols)</td>
<td>16 Eyes and Vision and 3 Anesthesia</td>
<td>0.19</td>
<td>−30</td>
<td>74</td>
</tr>
<tr>
<td>Macular degeneration</td>
<td>20 (19 reviews, 1 protocol)</td>
<td>20 Eyes and Vision</td>
<td>0.054</td>
<td>+56</td>
<td>132</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>30 (20 reviews, 10 protocols)</td>
<td>30 Eyes and Vision</td>
<td>0.038</td>
<td>+31</td>
<td>147</td>
</tr>
<tr>
<td>Trachoma</td>
<td>4 (4 reviews, 0 protocols)</td>
<td>4 Eyes and Vision</td>
<td>0.013</td>
<td>+48</td>
<td>165</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>1 (1 review, 0 protocols)</td>
<td>1 Eyes and Vision</td>
<td>0.02</td>
<td>−31</td>
<td>163</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>1 (1 review, 0 protocols)</td>
<td>1 Acute Respiratory Infections</td>
<td>0.032</td>
<td>−9</td>
<td>153</td>
</tr>
</tbody>
</table>

Abbreviations: CDSR, Cochrane Database of Systematic Reviews; DALY, disability-adjusted life-year; GBD, Global Burden of Disease; * Arranged in order of decreasing percentage of total 2010 DALY.

**Results**

A total of 116 reviews and protocols represented the 8 ophthalmologic categories, with 106 (91.4%) of these being from the Cochrane Eyes and Vision Group (Table 2). Glaucoma had the greatest representation in the CDSR, with 30 reviews and protocols, followed closely by the other vision loss category, with 26 reviews and protocols, and macular degeneration, with 20 reviews and protocols. Those categories with lower representation were trachoma, with 4 reviews, and onchocerciasis and vitamin A deficiency, both with only 1 review. A list of all included review and protocol titles for each condition is available in eTables 2 and 3 in the Supplement and a list of all excluded titles in eTables 4 and 5 in the Supplement. The range of review and protocol publication year was from 1999 to 2014, with 73.3% occurring from 2010 to 2014; the median and mode year was 2012.

Looking at the global GBD 2010 DALY metrics, other vision loss had the greatest percentage of total DALY (0.25%), followed by refraction and accommodation disorders (0.23%) (Table 2). Vitamin A deficiency had the lowest percentage of total DALY (0.032%) of the conditions assessed. The conditions that experienced an increase in DALY from 1990 to 2010 listed from greatest to least were macular degeneration (percentage change in DALY from 1990 to 2010 was +56%), trachoma (+48%), glaucoma (+31%), other vision loss (+2%), and refraction and accommodation disorders (+1%). The conditions that experienced a decrease in DALY from 1990 to 2010 listed from greatest to least were onchocerciasis (percentage change in DALY from 1990 to 2010 was −31%), cataracts (−30%), and vitamin A deficiency (−9%). The 2010 DALY ranks for the 8 ophthalmic conditions assessed ranged from 67 for other vision loss to 153 for vitamin A deficiency.

Comparing the CDSR representation with DALY metrics, the overall $R^2$ was 0.23, indicating an overall poor correlation between these variables (Figure). Specifically, cataract was the only category that was well matched (Table 2). Glaucoma, macular degeneration, and other vision loss were overrepresented when matched with corresponding DALYs. Conversely, trachoma, onchocerciasis, vitamin A deficiency, and refraction and accommodation disorders were underrepresented in the CDSR relative to corresponding DALYs.

Twenty-six systematic reviews and protocols covered 57 ophthalmic conditions defined by the GBD 2010 other vision loss category (see eTable 1 in the Supplement for ICD codes and conditions that comprise the other category; see eTable 3 in the Supplement for included titles and eTable 5 for excluded titles). The Cochrane Eyes and Vision Group was responsible for 73.1% of the systematic reviews in the CDSR for these 57 ophthalmologic conditions.

**Discussion**

The 8 ophthalmologic categories assessed were represented by a total of 116 reviews and protocols in the CDSR, with most (91.4%) published by the Eyes and Vision Group. While the CDSR covers a broad diversity of ophthalmologic conditions, prioritization is not solely guided by burden of disease data. This was exemplified by the poor correlation between the CDSR representation and DALYs for the ophthalmologic categories, which yielded an $R^2$ of 0.23. Other factors and considerations play critical roles in the prioritization process by the CDSR. In addition, the fact that most reviews and protocols were published from 2010 to 2014 provided evidence of the current and frequently updated nature of the CDSR content.

**Conditions for Which CDSR Representation Appeared Well Matched With Disability Metrics**

Cataract was the only category that was well matched with respect to DALY and CDSR representation. Although cataracts had the third highest DALY, the condition experienced the greatest decrease in DALY from 1990 to 2010 of the conditions stud-
ied. Age-related cataracts are the leading cause of blindness, causing an estimated 51% of all blindness and affecting 19.7 million people worldwide. In addition, surgery for cataracts and refractive errors are among the most cost-effective interventions in health care.

**Conditions for Which CDSR Representation Appeared Overmatched With Disability Metrics**

Glucoma, macular degeneration, and other vision loss were overrepresented when compared with their DALY metrics. Glaucoma not only had the greatest number of CDSR reviews and protocols, but also experienced a 31% increase in DALY from 1990 to 2010. Similarly, macular degeneration experienced the greatest increase in DALY (+56%) of all the categories. The apparent overrepresentation of these 2 conditions in the CDSR is more accurately reflected by their 20-year disability trends.

Representing 57 eye conditions, the other vision loss category was second in terms of CDSR representation, with 29 reviews and protocols and has the greatest DALY and highest DALY ranking of all the categories. This category experienced a DALY percentage change increase of 2%, the smallest of the 3 conditions that were overmatched.

**Conditions for Which CDSR Representation Appeared Undermatched With Disability Metrics**

Trachoma, onchocerciasis, vitamin A deficiency, and refractive errors were among the most cost-effective interventions in health care. In contrast, trachoma was underrepresented in the CDSR but experienced the second greatest 20-year increase in DALY (+48%) of all the conditions assessed. While trachoma is the leading cause of infectious blindness in the world, the condition is irreversible and highly contagious. Active efforts, such as those led by the World Health Organization’s Alliance for the Global Elimination of Trachoma, predominantly focus on prevention at the population level.

**Limitations and Future Directions**

Limitations of this study were related to synthesizing ophthalmologic presence in the CDSR and the use of GBD metrics. First, quantification of reviews and protocols in the CDSR was subject to how the reviews and protocols were compiled. For instance, multiple conditions may be covered in one review with a broader focus, referred to as lumping. Alternatively, several reviews may cover the same information, each with a more narrow focus, referred to as splitting. Hence, consideration of a systematic review as one unit of representation may not be appropriate for certain topics. In addition, the CDSR reviews synthesize studies and the best evidence in the literature. For this
reason, meta-analyses for topics that lack studies in the literature are generally not possible in the CDSR. Variables beyond Cochrane research prioritization determine database presence. Additionally, the assignment of a particular review or protocol by the study authors to a particular ophthalmologic category was not completely objective; the use of independent data collection by 2 authors with consensus review strove to minimize this source of error.

Second, this study was also subject to limitations of the GBD 2010 such as inconsistent or scarce data sources. The ICD codes comprising disease categories were established by GBD collaborator consensus. These ICD codes were used to generate search terms and may not have generated all search results pertaining to each topic. Several GBD categories were excluded from the current study that did not focus exclusively on ophthalmologic conditions because the DALYs could not be solely attributed to the ophthalmologic condition. In addition, the GBD 2010 does not provide disability estimates for individual diseases in the other vision loss category. Further breakdown of this category would enable a more in-depth and inclusive study of disease impact. As GBD data become available on an annual basis, analysis of the relationship and trends between database representation and GBD disability over time can be explored further. Finally, this study did not explore the contributions of disease inclusion in the CDSR other than global disease burden such as the skewed financial burden of diseases that disproportionately cause vision impairment in developed populations.

Conclusions

Overall, the global burden of ophthalmic conditions was poorly proportioned to the reviews and protocol representation in the CDSR. There are likely a variety of factors contributing to the lack of correlation. Diseases with known cures, but with significant public health and economic barriers to treatment, such as vitamin A deficiency, were underrepresented in the CDSR. Furthermore, economic impact of diseases disproportionately affecting wealthy populations may contribute to overrepresentation in the CDSR. This article highlighted ophthalmic diseases where global burden fails to correlate with current research and reviews. We suggest that considerations be taken of such underrepresented and overrepresented ophthalmic conditions in pursuit of future research, reviews, and funding.

Overall, global burden of disease comprises one of many factors guiding research prioritization of ophthalmic conditions by Cochrane Review Groups. The process of mapping systematic reviews with disability metrics, such as DALY, provides reproducible, transparent, and valuable data for use in future research prioritization discussions. Certainly, the allocation of research funds and topic prioritization is an intricate process guided by many factors. Within Cochrane, prioritization processes are largely determined and maintained by individual Cochrane Review Groups.

This study is part of a series that aims to map all conditions studied by the GBD to representation in various major databases such as the CDSR. In the future, we hope that this initial manual mapping will become automated, using the advanced and large-scale methods possible with computer programs and technological advances. Global burden of disease is a useful metric that may guide prioritization decisions. The GBD has created unprecedented public access of electronic information. As GBD metrics become increasingly used by health care professionals, policy makers, and individuals alike, the global burden of disease may ultimately help to reduce research gaps and profoundly impact the human population.
Global Burden of Eye and Vision Disease


