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Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010

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Summary

Background Non-fatal health outcomes from diseases and injuries are a crucial consideration in the promotion and monitoring of individual and population health. The Global Burden of Disease (GBD) studies done in 1990 and 2000 have been the only studies to quantify non-fatal health outcomes across an exhaustive set of disorders at the global and regional level. Neither effort quantified uncertainty in prevalence or years lived with disability (YLDs).

Methods Of the 291 diseases and injuries in the GBD cause list, 289 cause disability. For 1160 sequelae of the 289 diseases and injuries, we undertook a systematic analysis of prevalence, incidence, remission, duration, and excess mortality. Sources included published studies, case notification, population-based cancer registries, other disease registries, antenatal clinic serosurveillance, hospital discharge data, ambulatory care data, household surveys, other surveys, and cohort studies. For most sequelae, we used a Bayesian meta-regression method, DisMod-MR,

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See **Comment** pages 2053, 2054, 2055, 2058, 2060, 2062, and 2063

See **Special Report** page 2067

See **Articles** pages 2071, 2095, 2129, 2144, 2197, and 2224

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See Online for appendix

For interactive versions of figures 2, 4, 5, and 6 see http://healthmetricsandevaluation.org/gbd/visualizations/regional

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designed to address key limitations in descriptive epidemiological data, including missing data, inconsistency, and large methodological variation between data sources. For some disorders, we used natural history models, geospatial models, back-calculation models (models calculating incidence from population mortality rates and case fatality), or registration completeness models (models adjusting for incomplete registration with health-system access and other covariates). Disability weights for 220 unique health states were used to capture the severity of health loss. YLDs by cause at age, sex, country, and year levels were adjusted for comorbidity with simulation methods. We included uncertainty estimates at all stages of the analysis.

Findings **Global prevalence for all ages combined in 2010 across the 1160 sequelae ranged from fewer than one case per 1 million people to 350 000 cases per 1 million people. Prevalence and severity of health loss were weakly correlated (correlation coefficient −0·37). In 2010, there were 777 million YLDs from all causes, up from 583 million in 1990. The main contributors to global YLDs were mental and behavioural disorders, musculoskeletal disorders, and diabetes or endocrine diseases. The leading specific causes of YLDs were much the same in 2010 as they were in 1990: low back pain, major depressive disorder, iron-deficiency anaemia, neck pain, chronic obstructive pulmonary disease, anxiety disorders, migraine, diabetes, and falls. Age-specific prevalence of YLDs increased with age in all regions and has decreased slightly from 1990 to 2010. Regional patterns of the leading causes of YLDs were more similar compared with years of life lost due to premature mortality. Neglected tropical diseases, HIV/AIDS, tuberculosis, malaria, and anaemia were important causes of YLDs in sub-Saharan Africa.**

Interpretation **Rates of YLDs per 100 000 people have remained largely constant over time but rise steadily with age. Population growth and ageing have increased YLD numbers and crude rates over the past two decades. Prevalences of the most common causes of YLDs, such as mental and behavioural disorders and musculoskeletal disorders, have not decreased. Health systems will need to address the needs of the rising numbers of individuals with a range of disorders that largely cause disability but not mortality. Quantification of the burden of non-fatal health outcomes will be crucial to understand how well health systems are responding to these challenges. Effective and affordable strategies to deal with this rising burden are an urgent priority for health systems in most parts of the world.**

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Introduction

Non-fatal health outcomes from diseases and injuries are a crucial consideration in the promotion and monitoring of individual and population health. In an era in which the Millennium Development Goals (MDGs) have refocused global health attention on prevention of mortality from selected disorders, it is important to emphasise that health is about more than avoiding death. Individuals, households, and health systems devote enormous resources to the cure, prevention, and amelioration of non-fatal sequelae of diseases and injuries. Some form of periodic accounting about the burden of non-fatal illness in populations, and how it is changing, should therefore be available for policy making and planning. Quantification of the burden of non-fatal health outcomes was one of the main goals in launching the Global Burden of Disease study (GBD) in the 1990s.[1] The study introduced the disability-adjusted life-year (DALY) as a time-based measure of health that enables commensurable measurement of years of life lost due to premature mortality (YLLs) with years of life lived in less than ideal health (years lived with disability [YLDs]). The amalgamation of both components of individual and population health under a comprehensive framework for measuring population health can provide important insights into a broader set of causes of disease burden than can consideration of mortality alone.

To our knowledge, the various revisions of the GBD are the only effort to quantify non-fatal health outcomes across an exhaustive set of disorders at the global and regional level.[2–8] Many national burden of disease studies and subnational studies have analysed local patterns of YLDs as well.[9–16] Publication of the GBD 1990 results raised awareness about a range of disorders that primarily cause ill health and not death, such as unipolar major depression, bipolar disorder, asthma, and osteoarthritis.[17–19] This attention has led to greater policy debate and action on mental health and other non-communicable diseases at WHO,[4,20,21] in non-governmental organisations, and in many countries.[22] The burden of non-fatal illness attributed to some parasitic diseases has also been an important issue highlighted by the GBD findings.[23–26]

Despite the unique role of the GBD in provision of comparative quantification of the burden of non-fatal health outcomes, there have been important limitations. The evidence on MDG-related diseases has been regularly revised and incorporated into updates of the GBD, but many disorders have not been systematically analysed since 1990. *Global Health Statistics*, a companion volume to the original *Global Burden of Disease and Injuries* book, provided estimates of incidence, prevalence, remission, and case fatality for 483 sequelae, by age and sex, for eight regions of the world.[27] The GBD 2000 revisions included 474 sequelae. A substantial number, but not all, of these sequelae were revised since GBD 1990. Those that were not revised were approximated with constant relations between YLLs and YLDs or YLD rates estimated from the GBD 1990. Even when revisions were undertaken, however, many were not based on systematic analyses of published studies and unpublished sources. The epidemiological inputs to YLD estimates such as prevalence have been released for only 40 sequelae. The most important limitation of both the GBD 1990 and 2000 efforts is that YLDs have not been estimated with uncertainty. Uncertainty can come from many sources, including heterogeneity in the empirical data that are available and uncertainty in the indirect estimation models used to make predictions for populations with little or no data. Because the empirical basis for estimating prevalence or incidence is much weaker for some sequelae than it is for others, uncertainty is likely to vary substantially across sequelae and across countries and regions for the same sequelae.[8,28]

The Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) provided an important opportunity to address the key limitations of past burden of disease assessments, including a more standardised approach to evidence synthesis, epidemiological estimation with uncertainty, and assessment of comorbidity. In this Article, we describe the approach to undertaking these analyses with the available evidence, and discuss key comparative results. Subsequent disease-specific and injury-specific papers are planned that will provide much more detail on data, methods, and results for various disorders of interest.

Methods

Overview

Details of the GBD 2010 hierarchical cause list, the 21 epidemiological regions (and combinations of these into seven super-regions), the 20 age groups, and the relation between different components of GBD 2010 are published elsewhere.[29] For the GBD 2010, YLDs are computed as the prevalence of a sequela multiplied by the disability weight for that sequela without age weighting or discounting. The YLDs arising from a disease or injury are the sum of the YLDs for each of the sequelae associated with that disease. Across the 291 diseases and injury causes in the study, 289 cause disability—for these causes there were 1160 sequelae that captured the major outcomes of these diseases and injuries.[29,30] The key analytical task for the study was to estimate the prevalence with uncertainty of each of the 1160 sequelae for 20 age groups, both sexes, and 21 regions for 1990, 2005, and 2010. See panel for terminology used in GBD 2010.

For each disease or injury, we identified the key sequelae from that cause. Sequelae could include the disease itself, such as diabetes, or the outcomes associated with that disease such as diabetic foot, neuropathy, or retinopathy. Some clinical disorders were classified as a disease but also can be a consequence of another disease—eg, chronic kidney disease secondary to diabetes is a consequence of diabetes but was classified as a disease. Any given outcome appears in the GBD cause and sequela list only once to avoid double counting of the associated burden. Across the 1160 sequelae, we identified 220 unique health states, representing a parsimonious list providing enough detail to describe the large variations between health states while still a manageable number for which we were able to derive disability weights by survey. In principle, we estimated YLDs at the level of an individual and then assigned individual health loss to all the contributing sequelae present in an individual. The analysis can be divided into seven specific steps (figure 1) which are briefly described below.

Panel: Terminology used in the Global Burden of Disease study (GBD)

Disability

Disability refers to any short-term or long-term health loss. Many other definitions of disability are in use such as those in the WHO World Report on Disabilities.[31] These definitions often stress moderate to severe health loss and the role of the environment in the loss of individuals' wellbeing.

Sequelae

In the GBD 2010 cause list there are 291 diseases and injuries, of which 289 cause disability. In total, we have identified 1160 sequelae of these diseases and injuries. For example, diabetic neuropathy is a sequela of diabetes mellitus. To avoid double counting, a sequela can only be counted in the cause list once even if the same outcome might be caused by more than one disease.

Health state

Across the 1160 sequelae, we identified 220 unique health states. For example, both malaria and hookworm have mild anaemia as a sequela. Mild anaemia is a unique health state. The list of unique health states serves two purposes: to allow assessment of the total burden of some health states such as anaemia across various causes, and to simplify the task of measuring disability weights for sequelae.

Disability weights

A quantification of the severity of health loss associated with the 220 unique health states on a scale from 0 to 1, when 0 is commensurate with perfect health and 1 is commensurate with death. In the GBD 2010, disability weights for health states are measured based on survey respondents representing the general public.

Years lived with disability (YLDs)

For the GBD 2010, YLDs per person from a sequela are equal to the prevalence of the sequela multiplied by the disability weight for the health state associated with that sequela. YLDs for a disease or injury are the sum of the YLDs for each sequela associated with the disease or injury.

Impairments

In the GBD 2010 we estimated the prevalence and burden of several unique health states that are sequelae for multiple diseases including anaemia, heart failure, vision loss, seizures, hearing loss, infertility, and intellectual disability. These are referred to as impairments.

Identification and documentation of data sources

The analysis for each sequela began with the identification and documentation of sources of data for incidence, prevalence, remission, duration, and excess mortality. We used nine types of data sources. First, contributors to the GBD have undertaken systematic reviews for disease sequelae. For example, for epilepsy we retrieved:

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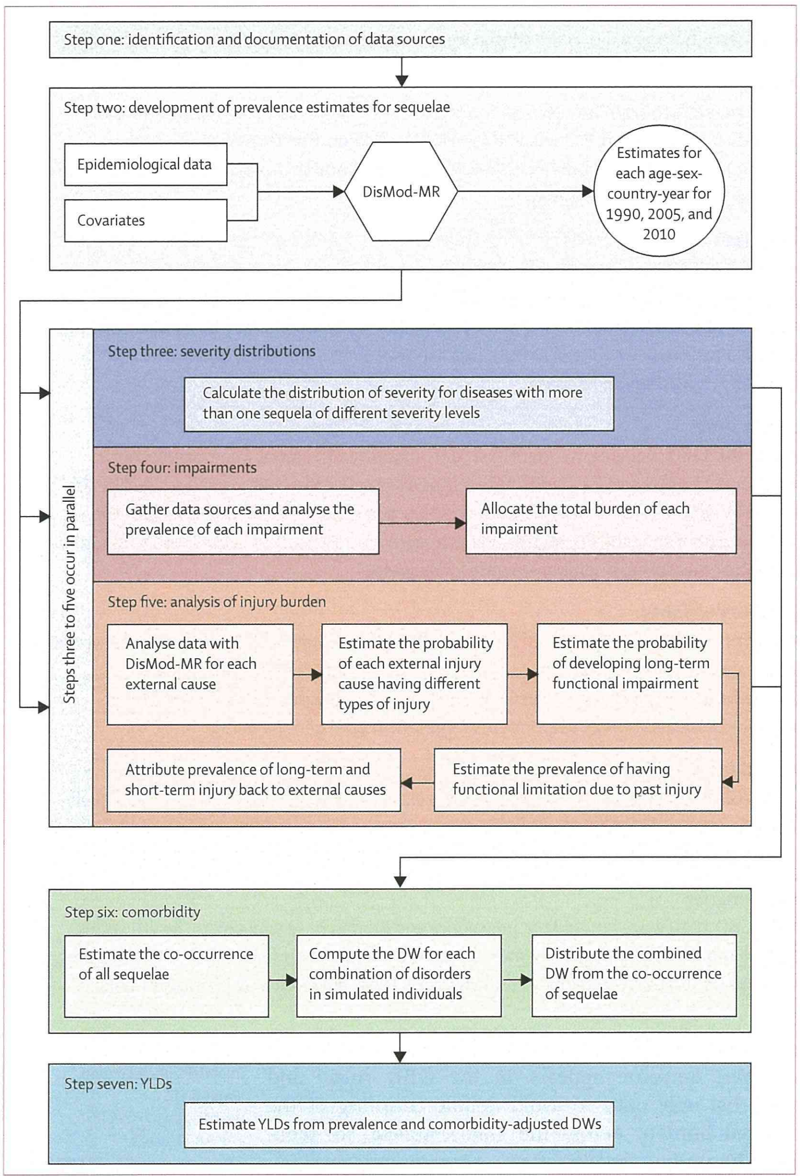

Figure 1: **Overview of the seven steps in the estimation of prevalence and years lived with disability (YLDs)**
DW=disability weight.

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230 prevalence studies from 83 countries in all 21 world regions, a further 97 studies of incidence, 25 studies of the mortality risk in people with epilepsy, and only one study on remission meeting inclusion criteria. For other disease sequelae, only a small fraction of the existing data appear in the published literature, and other sources predominate such as local surveys of schistosomiasis prevalence or antenatal clinic serosurveillance for HIV/AIDS. Second, reports to governments of cases have been used for African trypanosomiasis, measles, pertussis, tuberculosis, leprosy, dengue, cholera, and yellow fever. Use of these data for burden of disease assessment required explicit modelling of the case detection rate for every disease. Third, we used population-based disease registry data for cancers,[32–40] chronic kidney diseases, multiple sclerosis,[41] Parkinson's disease,[42,43] and congenital anomalies.[44] Cancer registries have been established in many developed countries and are being rapidly established in developing countries. For example, by the end of 2010, cancer registries had expanded in China to 149 registries covering 31 provinces;[45] India now has 23 registries.[46] Fourth, many countries, in collaboration with UNAIDS and WHO, have established networks of antenatal clinics that test women presenting for antenatal care for HIV, syphilis, and other disorders. Fifth, for 43 countries, we obtained hospital discharge data coded to ICD9 or ICD10. Use of these data required an explicit model of selection bias to take into account variations in access to care. Additionally, for chronic diseases, we had to estimate the average number of admissions to hospital per person per year with a disease to interpret the results. We analysed datasets with unique identifiers for every patient for seven US states from 2003 to 2007 for cirrhosis and pneumoconiosis. Hospital discharge data were an important source for acute disorders such as stroke, myocardial infarction, appendicitis, or pancreatitis, and for injuries. Sixth, for skin diseases and other mental and behavioural disorders, outpatient data collected in health systems with nearly complete or at least representative samples of ambulatory data[47–55] have also been used after taking into account selection bias. Seventh, we used interview questions, direct measurements (eg, hearing, vision, and lung function testing), serological measurements, and anthropometry from the re-analysis of multiple household surveys. Surveys of selected populations such as school children for intellectual disability,[56] nursing home residents for dementia,[57] or mental health clinic attendees for schizophrenia[58] have also been used after taking into consideration selection bias. Eighth, re-analysis of cohort or follow-up studies has been used for some causes such as impairment due to injury. We also used cohort studies to provide information about remission rates, duration, and mortality risks for many chronic disorders. Finally, we used indirect prevalence studies as an input to estimate the total number of drug users.[59] These estimates were produced from a combination of multiplier, capture-recapture, and back-projection methods combining data from treatment centres, police records, court records, and survey data.

Developing prevalence estimates for sequelae

Meta-analysis or meta-regression of descriptive epidemiological studies[60–63] poses many challenges. First, for many regions and for many sequelae data are scarce. Predictions of prevalence need to take advantage of relations with covariates in a meta-regression or default to the average of a region, super-region, or the world. Second, in settings with multiple measurements, study results can be highly heterogeneous because of much non-sampling error. Sources of non-sampling error include selection bias in the population studied, study design, implementation issues in data collection, widely varying case definitions across studies, and the use of different diagnostic technologies or laboratory techniques. Third, available studies have often used diverse age groups like 17–38 years or 15 years and above. Fourth, data for various disorders were collected for many different outcomes such as incidence, prevalence, remission, excess mortality, or cause-specific mortality. The mix of data varies across diseases and across regions for a disease. All of these sources provide some relevant information for the estimation of prevalence. Fifth, within regions or countries, the true prevalence of a sequela can vary enormously. Sixth, on the basis of biology or clinical series, there might be strong prior views on the age pattern of incidence or prevalence for a disorder that should be reflected in the results. For instance, we would not expect prevalence of Alzheimer's disease before age 40 years and diagnostic rules stipulate that the onset of attention deficit and hyperactivity disorder cannot occur before age 4 years or after age 8 years.[64]

To address these challenges, we have developed a Bayesian meta-regression method, DisMod-MR, which estimates a generalised negative binomial model for all epidemiological data. The model includes the following: covariates that predict variation in true rates; covariates that predict variation across studies because of measurement bias; super-region, region, and country random intercepts; and age-specific fixed effects. When appropriate, the rates were assumed to have been constant over time, which allowed data for incidence, prevalence, excess mortality, and cause-specific mortality to inform prevalence estimates. The differential equations governing the relation between the parameters of incidence, remission, mortality, prevalence, and duration are well characterised.[65,66] DisMod-MR can use data reported for any age group to inform the maximum likelihood estimate. We used a large set of 179 covariates that have been appropriately imputed so that the data provide a complete time series for all 187 countries in the analysis (see the appendix for details of the estimation equations used for DisMod-MR and the approach to numerical solution, as well as an example of its application).[29]

For cancer incidence and prevalence, we used the approach applied by Forouzanfar and colleagues[67] to breast and cervical cancers. We estimated the mortality-to-incidence ratio for each cancer for all country, age, and sex groups using data from all high-quality registries that reported on both incidence and mortality. We developed separate models for both sexes. Cause of death estimates for each cancer by country, year, age, and sex[68] were divided by the predicted mortality-to-incidence ratio to generate incidence estimates. To estimate the prevalence of each of four sequelae of cancer including: diagnosis or treatment phase, remission, recurrence, and terminal phase, we estimated the natural history of incident cases using a calculated 5 year survival and relative duration of each cancer phase. We also used a variant of this approach to estimate incidence and prevalence for visceral leishmaniasis.

We used four sets of alternative methods for some disorders because of variation in the types of data available and the complexity of their spatial and temporal distributions (see appendix for further details). For HIV/AIDS, we used the UNAIDS natural history model developed with the Spectrum platform.[69,70] Detailed estimates of prevalence and mortality with uncertainty by age and sex have been provided based on the 2012 revision of HIV/AIDS epidemiology. We developed natural history models for measles and pertussis. For ascariasis, trichuriasis, hookworm, and schistosomiasis, prevalence of the disease has been estimated with geospatial estimation methods.[71–73] For diphtheria, tetanus, and rabies, we have used systematic reviews of data for case-fatality rates with estimates of mortality to estimate incidence—the mortality estimates for these diseases are described elsewhere.[68] For these disorders, DisMod-MR was used as a meta-regression method to estimate the case-fatality rate by age, sex, and region. For tuberculosis and dengue, the key source of information was registered cases. We developed statistical models that simultaneously model the expected rates as a function of covariates and the undercount of cases as a function of health system access.

Severity distributions

For 41 diseases, the sequelae of the disease have been linked to more than one health state including stroke, anxiety, major depressive disorder, symptomatic heart failure, and chronic obstructive pulmonary disease (COPD). After analysing the prevalence of the overall disorder, we estimated the distribution of these prevalent cases across severity levels. Disability weights were measured in population surveys[30] for individuals without comorbidity. Two estimates are needed to calculate YLDs: the disability weight for individuals with a single sequela and the disability weight for individuals with multiple sequelae, which is a common occurrence. The prevalence of comorbid disorders can be estimated with micro-simulation. However, we needed to estimate the distribution of severity controlling for comorbidity, otherwise the severity distribution would be systematically biased towards more severe symptoms caused by comorbidity. For example, if individuals with depression are also likely to have anxiety and substance-use disorders, the reported distribution of functional health status would be shifted towards the more severe end.

Data for severity distributions are often scarcer and of poorer quality than are data for prevalence of disorders, with some exceptions.[74,75] Approaches to severity classification are inconsistent across disorders.[76] Because of the heterogeneity of the available evidence for disease severity, we supplemented disease specific reviews with an analysis of three data sources: the US Medical Expenditure Panel Survey (MEPS) 2000–09,[77] the US National Epidemiological Survey on Alcohol and Related Conditions (NESARC) 2000–01 and 2004–05,[78] and the Australian National Survey of Mental Health and Wellbeing of Adults (AHS) 1997.[79]

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These sources allow the assessment of the severity distributions taking into account comorbidity (see appendix for more details of this analysis). For some diseases for which data are available for the distribution of severity by age, sex, and region, we pooled proportions in each health state using DisMod-MR or simple meta-analysis methods.

Impairments

For selected impairments, we have constrained the estimates for sequelae related to that impairment to sum to estimates of the impairment prevalence from independent sources of data. For example, nine disorders have blindness as a sequela. We have analysed all available blindness survey data and we constrain the prevalence of all blindness sequelae to sum to blindness prevalence. We did this impairment prevalence analysis for anaemia, blindness, low vision, hearing impairment, infertility, heart failure, epilepsy, and intellectual disability (appendix).

Analysis of injury burden

The analysis of YLDs from injuries needed careful consideration because injuries are classified in the cause list according to the external cause such as a road injury, animal bite, or drowning, whereas the functional

	Prevalence (both sexes)		Male prevalence		Female prevalence	
	Total (thousands)	Proportion of population (%)	Total (thousands)	Proportion of population (%)	Total (thousands)	Proportion of population (%)
Dental caries of permanent teeth	2 431 636	35·29%	1 194 051	34·37%	1 237 585	36·23%
Tension-type headache	1 431 067	20·77%	655 937	18·88%	775 131	22·69%
Migraine	1 012 944	14·70%	371 072	10·68%	641 873	18·79%
Fungal skin diseases	985 457	14·30%	516 167	14·86%	469 291	13·74%
Other skin and subcutaneous diseases	803 597	11·66%	417 129	12·01%	386 468	11·32%
Chronic periodontitis	743 187	10·79%	378 407	10·89%	364 780	10·68%
Mild hearing loss with perinatal onset due to other hearing loss	724 689	10·52%	386 147	11·11%	338 543	9·91%
Acne vulgaris	646 488	9·38%	311 349	8·96%	335 140	9·81%
Low back pain	632 045	9·17%	334 793	9·64%	297 252	8·70%
Dental caries of baby teeth	621 507	9·02%	352 085	10·13%	269 421	7·89%
Moderate iron-deficiency anaemia	608 915	8·84%	269 596	7·76%	339 319	9·93%
Other musculoskeletal disorders	560 978	8·14%	262 779	7·56%	298 199	8·73%
Near sighted due to other vision loss	459 646	6·67%	235 052	6·77%	224 593	6·58%
Mild iron-deficiency anaemia	375 438	5·45%	152 523	4·39%	222 915	6·53%
Asthma	334 247	4·85%	160 346	4·61%	173 901	5·09%
Neck pain	332 049	4·82%	135 134	3·89%	196 915	5·77%
Chronic obstructive pulmonary disease	328 615	4·77%	168 445	4·85%	160 170	4·69%
Genital prolapse	316 897	4·55%	..	..	316 897	9·28%
Major depressive disorder	298 441	4·33%	111 441	3·21%	187 000	5·48%
Pruritus	280 229	4·07%	117 758	3·39%	162 471	4·76%
Anxiety disorders	272 777	3·96%	95 731	2·76%	177 046	5·18%
Mild anaemia due to hookworm disease	260 254	3·78%	149 572	4·30%	110 681	3·24%
Osteoarthritis of the knee	250 785	3·64%	88 885	2·56%	161 900	4·74%
Schistosomiasis	238 366	3·46%	124 289	3·58%	114 077	3·34%
Eczema	229 761	3·33%	104 259	3·00%	125 502	3·67%
Uncomplicated diabetes mellitus	227 588	3·30%	114 817	3·30%	112 771	3·30%
Uterine fibroids	225 259	3·23%	..	..	225 259	6·60%
Sexually transmitted chlamydial diseases	215 621	3·13%	85 675	2·47%	129 946	3·80%
Benign prostatic hyperplasia	210 142	3·05%	210 142	6·05%	..	..
Premenstrual syndrome	199 072	2·89%	..	..	199 072	5·83%
Moderate hearing loss with perinatal onset due to other hearing loss	189 919	2·76%	103 629	2·98%	86 290	2·53%
Goitre due to iodine deficiency	187 181	2·72%	69 752	2·01%	117 429	3·44%
Lacerations, multiple wounds, other dislocations, and eye injuries due to falls	185 700	2·70%	110 263	3·17%	75 438	2·21%
Upper respiratory infections	183 137	2·66%	92 394	2·66%	90 743	2·66%
Lacerations, multiple wounds, other dislocations, and eye injuries due to road injury	180 683	2·62%	118 964	3·42%	61 719	1·81%

(Continues on next page)

	Prevalence (both sexes)		Male prevalence		Female prevalence	
	Total (thousands)	Proportion of population (%)	Total (thousands)	Proportion of population (%)	Total (thousands)	Proportion of population (%)
(Continued from previous page)						
Edentulism	158 284	2·30%	67 264	1·94%	91 020	2·66%
Trichomoniasis	152 232	2·21%	49 731	1·43%	102 501	3·00%
Chronic urolithiasis	144 346	2·10%	90 446	2·60%	53 901	1·58%
Mild hearing loss due to otitis media	141 600	2·06%	79 359	2·28%	62 241	1·82%
Mild anaemia due to sickle cell disorders	141 419	2·05%	64 343	1·85%	77 075	2·26%
Impetigo	140 495	2·04%	67 464	1·94%	73 031	2·14%
Diabetic neuropathy	131 930	1·91%	63 509	1·83%	68 421	2·00%
Other cardiovascular and circulatory diseases	127 990	1·86%	48 040	1·38%	79 950	2·34%
Molluscum contagiosum	122 601	1·78%	65 841	1·89%	56 760	1·66%
Otitis media (chronic)	117 881	1·71%	55 891	1·61%	61 989	1·81%
Polycystic ovarian syndrome	116 730	1·68%	..	..	116 730	3·42%
Angina due to ischaemic heart disease	111 705	1·62%	59 683	1·72%	52 022	1·52%
Dysthymia	105 520	1·53%	43 863	1·26%	61 657	1·81%
Scabies	100 625	1·46%	51 736	1·49%	48 889	1·43%
Mild anaemia due to thalassaemias	95 731	1·39%	44 362	1·28%	51 370	1·50%

Table 1: **Global prevalence of the 50 most common sequelae**

limitations after injury are determined by the nature of injury such as brain trauma, femur fracture, or spinal cord transection. We did the injuries analysis in five steps, which are briefly outlined here with further details in the appendix. First, we analysed household survey and hospital discharge data using DisMod-MR for each external cause to generate estimates of incidence by age, sex, country, and year. Survey data included recall of injuries warranting admission to hospital as well as injuries that warranted medical attention but not admission to hospital. The meta-regression included a covariate for whether an individual was admitted to hospital or not, which we used to generate predictions both for injury warranting hospital admission and injury warranting outpatient care. Second, we analysed hospital data from 28 countries that had dual coding of discharges by external cause and nature of injury after ICD9 and ICD10, using negative binomial models to estimate the probability of different groups of nature of injury as a function of age, sex, and an indicator variable for developed versus developing countries. Separate models were created for injury warranting hospital admission and injury warranting other health care. Third, for each nature of injury we estimated the probability of individuals developing long-term functional impairment. We re-analysed follow-up data from four studies using data from the Dutch Injury Surveillance system (LIS),[80] the South Carolina Traumatic Brain Injury Follow-up Registry (SCTBIFR),[81] the National Study on Costs and Outcomes of Trauma (NSCOT),[82] and MEPS.[77] Fourth, we used DisMod-MR to estimate the prevalence of individuals in the population who are likely to have functional limitation because of a previous injury. Prevalence was estimated from incidence assuming zero remission and a relative risk of death compared with the general population based on available studies. In the fifth step, the YLDs due to prevalent cases of long-term injury were attributed back to external causes in proportion with the contributions of these causes to every type of injury.

Comorbidity

Comorbidity was taken into account in the calculation of YLDs, which needed three analytical steps (appendix). First, we estimated the co-occurrence of all the sequelae for each age, sex, country, and year. Co-occurrence is a function of the prevalence of each sequela and whether the probabilities of co-occurrence are independent of, or dependent on, each other.[83] We could not identify sufficiently large datasets to estimate these dependent probabilities reliably within age groups. We therefore adopted the simplifying assumption of independence. For each age-sex-country-year, we used a Monte Carlo simulation of 20 000 individuals to estimate the co-occurrence of sequelae. To capture uncertainty in the prevalences of each of the sequelae, for each age-sex-country-year, we ran 1000 different micro-simulations of 20 000 individuals.

Second, we calculated the combined disability weight for the estimated individuals with every combination of disorders. For all combinations of disorders generated in the micro-simulation, the combined disability weight for a simulated individual with two or more disorders is one minus the product of one minus each disability weight. Tests on real data such as MEPS as well as other studies suggest that this multiplicative model was the most appropriate.[84,85] To propagate uncertainty in disability weights into the YLD estimates, each computation was based on a draw from the uncertainty distribution of each disability weight. Third, the combined disability weight

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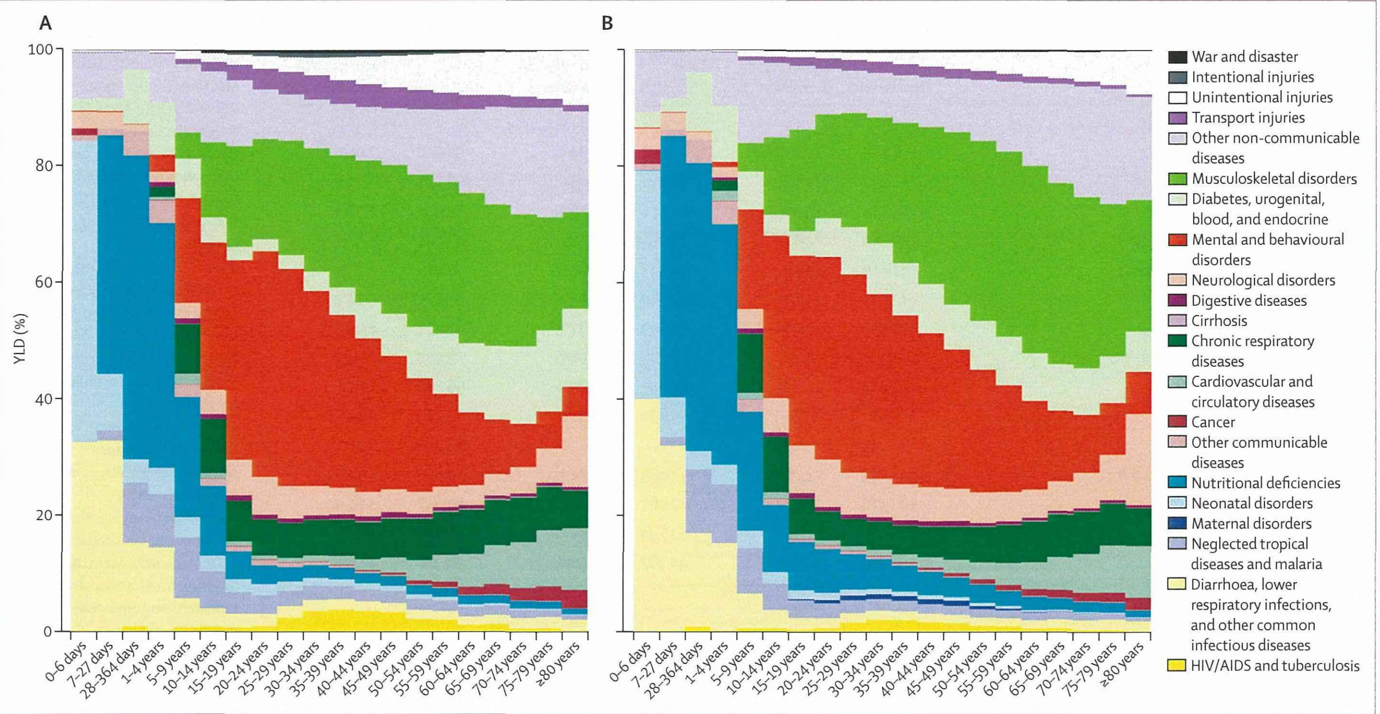

Figure 2: **Percentage of years lived with disability (YLDs) in 2010, by cause and age**
(A) In male individuals. (B) In female individuals. An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

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from the co-occurrence of sequelae was apportioned to each of the contributing sequelae in proportion to the disability weight of a sequela on its own.

We tested the validity of our assumption of independence within an age-sex-country-year using the MEPS data (described above), which includes both individual-level measurement of functional status using SF-12 and ICD-coded diagnoses. We applied the GBD approach assuming multiplicative disability weights and independent disorder probabilities to estimate YLDs and we computed directly from the MEPS data taking into account actual comorbid patterns at the individual level. The correlation coefficient for the two approaches was 0·999.

YLDs from residual categories

There are nine causes on the cause list such as other neglected tropical diseases, other neurological disorders, or other congenital anomalies that are groupings of a large number of often rare disorders. We approximate the YLDs for these disorders using the ratio of YLDs to YLLs for similar or related disorders to then estimate YLDs for these residual categories from YLLs that have been directly estimated.[68]

Ranking lists

For the presentation of leading causes of YLDs, the level at which causes are ranked is subject to debate. We have opted to use the level of disaggregation that seems most relevant for public health decision making. For example, we have chosen to include diarrhoeal diseases, lower respiratory infections, maternal disorders, stroke, liver cancer, cirrhosis, drug use, road injury, exposure to mechanical forces, animal contact, interpersonal violence, and congenital anomalies in the ranking list.

Decomposing changes in YLDs into demographic and epidemiological factors

To help understand the drivers of change in the number of YLDs by cause or region, we have estimated the proportion of the change from 1990 to 2010 due to growth in total population, change in population age-structure and sex-structure, and change in age-specific and sex-specific rates. We computed two counterfactual sets of YLDs. First, a population growth scenario computed as the number of YLDs expected in 2010 if only total population numbers increased to the level of 2010 but the age-sex structure of population stayed the same as in 1990 and age-sex specific rates remained at 1990 levels. Second, a population growth and population ageing scenario computed as the number of YLDs expected in 2010, using 1990 age-specific and sex-specific rates and 2010 age-specific and sex-specific population numbers. The difference between 1990 numbers and the population growth scenario is the change in YLDs due strictly to the growth in total population. The change from the population growth scenario to the population growth and ageing scenario is the number of YLDs due to ageing of the population. The difference between 2010 YLDs and the population growth

	All ages YLDs (thousands)			YLDs (per 100 000)		
	1990	2010	%Δ	1990	2010	%Δ
All causes	**583 393 (484 649–694 406)**	**777 401 (648 158–921 711)**	**33·3%**	**11 004 (9142–13 098)**	**11 283 (9407–13 378)**	**2·5%**
Communicable, maternal, neonatal, and nutritional disorders	**113 925 (85 875–148 463)**	**119 164 (91 399–152 096)**	**4·6%**	**2149 (1620–2800)**	**1730 (1327–2207)**	**–19·5%**
HIV/AIDS and tuberculosis	7681 (5222–10 722)	11 117 (7718–15 187)	44·7%	145 (99–202)	161 (112–220)	11·4%
Tuberculosis	6085 (4020–8737)	6774 (4500–9756)	11·3%	115 (76–165)	98 (65–142)	–14·3%
HIV/AIDS	1596 (1132–2125)	4342 (3142–5629)	172·2%	30 (21–40)	63 (46–82)	109·4%
HIV disease resulting in mycobacterial infection	220 (143–314)	1224 (793–1746)	456·8%	4 (3–6)	18 (12–25)	328·4%
HIV disease resulting in other specified or unspecified diseases	1376 (967–1857)	3119 (2241–4107)	126·7%	26 (18–35)	45 (33–60)	74·4%
HIV pre-AIDS asymptomatic	376 (227–569)	889 (546–1338)	136·8%	7 (4–11)	13 (8–19)	82·2%
HIV pre-AIDS symptomatic	289 (193–411)	531 (350–756)	83·6%	5 (4–8)	8 (5–11)	41·3%
AIDS with antiretroviral treatment	0 (0–0)	389 (251–578)	..	0 (0–0)	6 (4–8)	..
AIDS without antiretroviral treatment	711 (483–958)	1309 (913–1758)	84·2%	13 (9–18)	19 (13–26)	41·7%
Diarrhoea, lower respiratory infections, meningitis, and other common infectious diseases	18 579 (13 419–25 301)	19 921 (14 241–27 439)	7·2%	350 (253–477)	289 (207–398)	–17·5%
Diarrhoeal diseases	7654 (5135–10 855)	8045 (5371–11 366)	5·1%	144 (97–205)	117 (78–165)	–19·1%
Cholera	115 (59–188)	80 (42–134)	–30·1%	2 (1–4)	1 (1–2)	–46·2%
Other salmonella infections	263 (150–410)	341 (202–523)	29·8%	5 (3–8)	5 (3–8)	–0·1%
Shigellosis	703 (391–1111)	744 (440–1147)	5·8%	13 (7–21)	11 (6–17)	–18·6%
Enteropathogenic *E coli* infection	972 (438–1652)	845 (387–1416)	–13·0%	18 (8–31)	12 (6–21)	–33·1%
Enterotoxigenic *E coli* infection	889 (520–1409)	1065 (649–1643)	19·8%	17 (10–27)	15 (9–24)	–7·8%
Campylobacter enteritis	753 (407–1211)	746 (416–1180)	–1·0%	14 (8–23)	11 (6–17)	–23·8%
Campylobacter enteritis	753 (406–1211)	746 (415–1181)	–0·9%	14 (8–23)	11 (6–17)	–23·8%
Guillain-Barré syndrome due to *C enteritis*	1 (0–1)	1 (1–2)	35·7%	<0·5 (0–0·5)	<0·5 (0–0·5)	4·4%
Amoebiasis	142 (84–217)	205 (126–314)	44·1%	3 (2–4)	3 (2–5)	10·9%
Cryptosporidiosis	651 (312–1101)	661 (316–1096)	1·6%	12 (6–21)	10 (5–16)	–21·8%
Rotaviral enteritis	1159 (624–1885)	1269 (701–2006)	9·5%	22 (12–36)	18 (10–29)	–15·8%
Other diarrhoeal diseases	2007 (1027–3412)	2089 (1054–3521)	4·1%	38 (19–64)	30 (15–51)	–19·9%
Typhoid and paratyphoid fevers	134 (25–348)	172 (33–435)	27·8%	3 (0–7)	2 (0–6)	–1·7%
Typhoid and paratyphoid fevers	124 (16–337)	159 (20–423)	27·8%	2 (0–6)	2 (0–6)	–1·6%
Liver abscess and cysts due to typhoid and paratyphoid fevers	10 (7–15)	13 (8–20)	27·4%	<0·5 (0–0·5)	<0·5 (0–0·5)	–1·9%
Lower respiratory infections	2113 (1444–2941)	2331 (1592–3240)	10·3%	40 (27–55)	34 (23–47)	–15·1%
Influenza	510 (344–714)	583 (393–815)	14·2%	10 (6–13)	8 (6–12)	–12·1%
Influenza	510 (343–713)	582 (392–814)	14·2%	10 (6–13)	8 (6–12)	–12·1%
Guillain-Barré syndrome due to influenza	1 (1–2)	2 (1–3)	34·3%	<0·5 (0–0·5)	<0·5 (0–0·5)	3·3%
Pneumococcal pneumonia	298 (203–414)	367 (248–509)	23·2%	6 (4–8)	5 (4–7)	–5·2%
H influenzae type B pneumonia	216 (145–306)	201 (134–286)	–6·6%	4 (3–6)	3 (2–4)	–28·2%
Respiratory syncytial virus pneumonia	52 (31–82)	36 (21–55)	–31·3%	1 (1–2)	1 (0–1)	–47·2%
Other lower respiratory infections	1037 (702–1459)	1144 (779–1589)	10·2%	20 (13–28)	17 (11–23)	–15·2%
Upper respiratory infections	1438 (755–2542)	1728 (911–3050)	20·2%	27 (14–48)	25 (13–44)	–7·5%
Upper respiratory infections	1437 (753–2541)	1727 (910–3048)	20·2%	27 (14–48)	25 (13–44)	–7·5%
Guillain-Barré syndrome due to upper respiratory infections	1 (1–2)	2 (1–3)	33·8%	<0·5 (0–0·5)	<0·5 (0–0·5)	3·0%
Otitis media	3794 (2456–5829)	4436 (2887–6668)	16·9%	72 (46–110)	64 (42–97)	–10·0%
Otitis media	1359 (819–2150)	1613 (979–2594)	18·7%	26 (15–41)	23 (14–38)	–8·7%
Hearing loss due to otitis media	2435 (1423–3929)	2824 (1669–4533)	16·0%	46 (27–74)	41 (24–66)	–10·8%
Meningitis	2757 (1973–3732)	2628 (1857–3643)	–4·7%	52 (37–70)	38 (27–53)	–26·7%
Pneumococcal meningitis	920 (624–1298)	886 (595–1254)	–3·7%	17 (12–24)	13 (9–18)	–25·9%
S pneumoniae meningitis	9 (5–14)	11 (6–17)	19·6%	<0·5 (0–0·5)	<0·5 (0–0·5)	–8·0%
Long term sequelae due to *S pneumoniae* meningitis	571 (324–899)	488 (261–806)	–14·5%	11 (6–17)	7 (4–12)	–34·2%
Seizures due to *S pneumoniae* meningitis	80 (52–118)	79 (55–113)	–0·4%	2 (1–2)	1 (1–2)	–23·4%

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