(*Continued*)

20 December 2006	New search has been performed	Search updated. Nine new studies have been added to the original seven included studies, plus one previously excluded study (USA 1985) has now been included, making a total of 17 studies included in the 2006 update. A total of 11 studies have been excluded in this update and two studies have been placed in Studies awaiting classification. The Background and Methods sections have been expanded in this update, and additional outcomes have been added. The title has been changed from 'Zinc supplementation in pregnancy' to 'Zinc supplementation for improving pregnancy and infant outcome'. The conclusions regarding the effect of zinc supplementation on reducing preterm birth have been slightly strengthened

CONTRIBUTIONS OF AUTHORS

R Mori (RM) prepared the first version of this update. RM, R Tobe-Gai, E Ota and P Middleton applied study selection criteria and extracted data from the included studies. Z Bhutta and K Mahomed and all the other authors commented on drafts of the update.

DECLARATIONS OF INTEREST

Kassam Mahomed was principal investigator in a trial included in this review.

SOURCES OF SUPPORT

Internal sources

- Discipline of Obstetrics and Gynaecology, The University of Adelaide, Australia.
- Collaboration for Research in Global Women's and Children's Health, Japan.
- The University of Tokyo, Japan.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have updated our methods to reflect the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Outcomes have been separated into 'Primary' and 'Secondary' outcomes.

We have added 'congenital malformation' to our secondary outcomes.

GIven the number of trials identified and the standard methods for the Cochrane Pregnancy and Childbirthbirth Group, quasi-randomised controlled trials have been excluded.

INDEX TERMS

Medical Subject Headings (MeSH)

*Dietary Supplements; *Infant, Low Birth Weight; Infant, Newborn; Pregnancy Outcome; Premature Birth [*prevention & control]; Randomized Controlled Trials as Topic; Zinc [*administration & dosage]

MeSH check words

Female; Humans; Pregnancy

5 The CRASH-2 collaborators. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. *Lancet* 2011; **377:** 1096–101.
6 Guerriero C, Cairns J, Perel P, et al. Cost-effectiveness analysis of administering tranexamic acid to bleeding trauma patients using evidence from the CRASH-2 trial. *PLoS One* 2011; **6:** e18987.
7 Ker K, Kiriya J, Perel P, Edwards P, Shakur H, Roberts I. Avoidable mortality from giving tranexamic acid to bleeding trauma patients: an estimation based on WHO mortality data, a systematic literature review and data from the CRASH-2 trial. *BMC Emerg Med* 2012; **12:** 3.
8 Roberts I, Shakur H, Ker K, Coats T, CRASH-2 trial collaborators. Antifibrinolytic drugs for acute traumatic injury. *Cochrane Database Syst Rev* 2011; **1:** CD004896.
9 Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. *J R Soc Med* 2011; **104:** 510–20.

GBD 2010: design, definitions, and metrics

See Comment pages 2053, 2054, 2055, 2058, 2060, and 2062
See Special Report page 2067
See Articles pages 2071, 2095, 2129, 2144, 2163, 2197, and 2224

The Global Burden of Diseases, Injuries, and Risk Factors (GBD) enterprise is a systematic, scientific effort to quantify the comparative magnitude of health loss due to diseases, injuries, and risk factors by age, sex, and geography for specific points in time. The GBD construct of the burden of disease is health loss, not income or productivity loss.[1] For decision makers, health-sector leaders, researchers, and informed citizens, the GBD approach provides an opportunity to see the big picture, to compare diseases, injuries, and risk factors, and to understand in a given place, time, and age-sex group what are the most important contributors to health loss.

The Global Burden of Disease Study 2010 (GBD 2010) builds on the earlier versions for 1990, 1999–2002, and 2004 sponsored by the World Bank and WHO.[2–10] A more thorough description of the context, objectives, key definitions, and metrics used in GBD 2010 is provided in the appendix. Previous GBD studies have led to national burden of disease studies in at least 37 countries and subnational studies in eight countries. GBD 2010 was implemented as a collaboration between seven institutions: the Institute for Health Metrics and Evaluation as the coordinating centre, the University of Queensland School of Population Health, the Harvard School of Public Health, the Johns Hopkins Bloomberg School of Public Health, the University of Tokyo, Imperial College London, and WHO. The study was designed to address key limitations of previous studies, such as the absence of uncertainty intervals, and to solicit the input of many expert advisers across the spectrum of diseases and risk factors. This study represents a great expansion in the scope of work from previous GBD revisions, including a larger disease and injury cause list, more risk factors, many more age groups, and an assessment for three time periods. Furthermore, a completely revised and improved set of estimation methods has been developed; most notably, the prevalence of diseases and their sequelae is estimated using statistical inference on all available data.

A key aspect of the study is the hierarchical cause list for 291 diseases and injuries. This list has four levels of diseases and injuries and a fifth level for sequelae (appendix p 6). The 1160 sequelae are designed to capture the direct consequences of disease or injury that are not otherwise captured elsewhere in the cause list. Across sequelae, there are 220 common sequelae called health states in GBD 2010. For example, anaemia is identified as a sequela of 19 diseases in the cause list. Three health states are associated with anaemia: mild anaemia, moderate anaemia, and severe anaemia. For each of the health states, a lay description was developed for use in the empirical assessment of disability weights. As with diseases, we have developed a hierarchical list of 69 risk factors for which we have developed estimates for 67 (appendix p 6).

See Online for appendix

We divided countries into 21 regions on the basis of two criteria: epidemiological homogeneity, and geographical contiguity (appendix pp 6–7). For some statistical analyses, we grouped regions into seven super-regions. To facilitate various detailed analyses, we estimate the burden of disease in 20 age groups for each sex separately: early neonatal, late neonatal, postneonatal, 5 year age groups from 1–4 years to 75–79 years, and 80 years and older. Using strictly comparable data and methods, we have estimated the burden of disease for 1990, 2005, and 2010 to allow meaningful estimation of time trends. This study supersedes all previously published GBD study results.

Figure 1 summarises the overall analytical strategy for GBD 2010 and identifies 18 distinct components. The strong interconnections between components mean that changes in one component require the

re-estimation of multiple components. For example, changes in the estimation of age-specific mortality rates (component 2) leads to changes in the rescaled deaths for each cause (component 5), changes in healthy life expectancy (component 12), changes in years of life lost due to premature mortality (YLLs; component 13), and changes in risk factor-attributable YLLs (component 18). Details on each component are provided in appendix pp 8–13 and accompanying articles in *The Lancet*.[11–17] Uncertainty in each component is propagated through to the results with simulation methods.

Comparisons require the use of summary metrics that allow meaningful juxtaposition of deaths and non-fatal health outcomes. The basic unit of measurement for these summary measures is lost years of healthy life. The construction of time-based summary metrics requires making a series of value choices.[18] These value choices are either explicit or implicit in all summary measures of population health. Since the publication of GBD 1990, there has been extensive debate on these value choices;[18–23] for GBD 2010, we therefore convened a consultation of 21 philosophers, ethicists, and economists to advise on current thought with regard to these value choices (appendix pp 13–16). In summary, we have chosen to simplify the calculation of disability-adjusted life years (DALYs). First, we developed a new normative standard life table for males and females to compute YLLs at each age by identifying the lowest observed death rate for any age group in countries of more than 5 million in population. The new reference life table has a life expectancy at birth of 86·0 years for males and females. Second, years lived with disability (YLDs) have been estimated taking into account comorbidity in individuals. Third, we have computed YLDs simply as the prevalence of each sequela multiplied by the relevant disability weight adjusted for comorbidity. Fourth, on the basis of many arguments,[24–26] we have chosen not to discount YLLs, YLDs, or DALYs for time. Fifth, we conclude that we should treat a year of healthy life as equal irrespective of the age at which it is lived. The simpler version of YLLs, YLDs, and DALYs is thus conceptually grounded and easier to explain. It does, however, imply a substantial shift towards greater weight being given to deaths at younger ages, especially younger than 5 years, and greater weight to deaths compared to non-fatal health loss.

Summary measures such as DALYs combine complex information across a wide range of health outcomes.

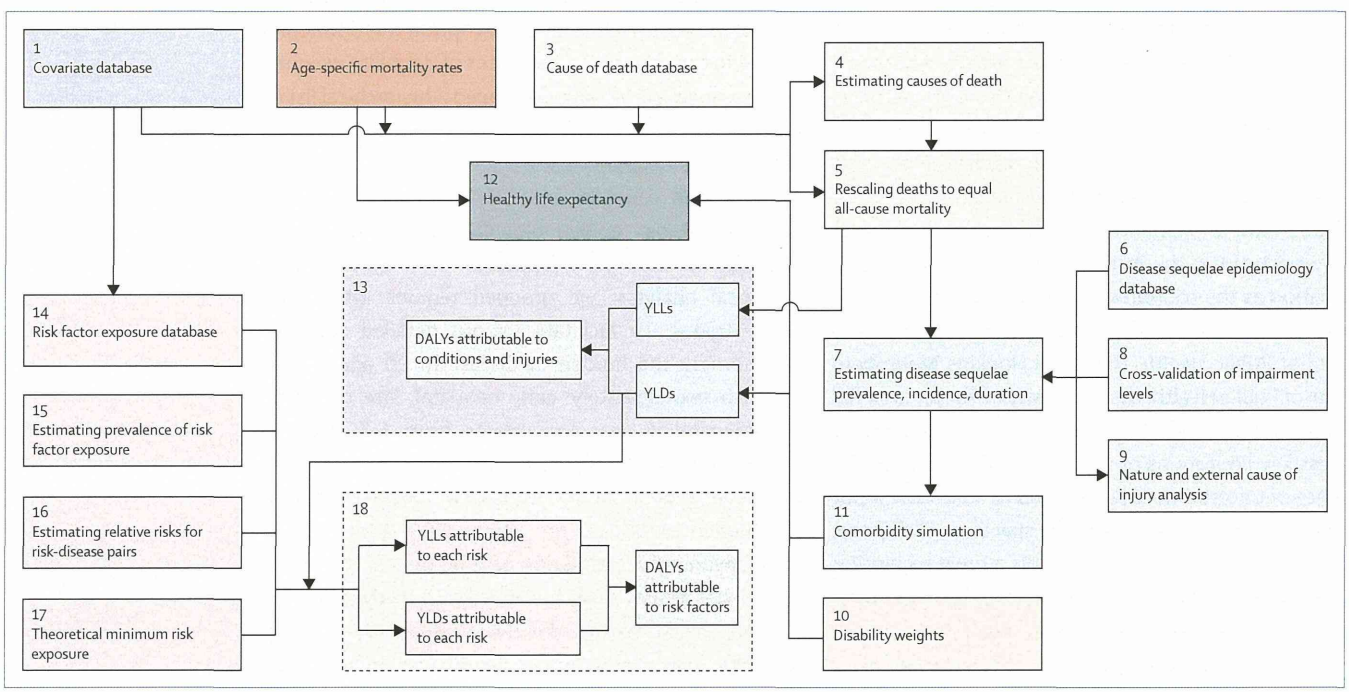

Figure 1: **18 components of the GBD 2010 and their inter-relations**
GBD 2010=Global Burden of Disease Study 2010. DALYs=disability-adjusted life years. YLLs=years of life lost due to premature mortality. YLDs=years lived with disability.

Figure 2 shows the power of comparison of these burden measures using the results of GBD 2010; it illustrates how leading risk factors compare with leading diseases and injuries and how changing the metric from deaths to DALYs alters the comparative importance of health problems. Because the assessment of burden for diseases and injuries is governed by the rules of the International Classification of Diseases and Injuries (ICD), which assigns every outcome to one cause among a set of mutually exclusive and collectively exhaustive causes, the interpretation of the fraction of deaths or DALYs from diseases is different than for risk factors, which are not so constrained. For some diseases and risk factors the fraction of DALYs is higher than the fraction of deaths. For example, this is the case for low back pain, malaria, underweight, preterm birth, diarrhoea, road injury, and HIV/AIDS. These disorders stand out as causing more burden measured in DALYs than deaths, because of either their effect on YLDs or deaths at young ages, or both.

Compared with previous efforts, GBD 2010 represents a major step towards a replicable scientific approach to global descriptive epidemiology. The discipline of propagating uncertainty across all components of the study has required a coherent approach to identifying sources of uncertainty and their objective quantification. An important emphasis on quantifying uncertainty has revealed that our knowledge of some disorders is limited. The width of 95% uncertainty intervals provides a mechanism of communicating to users the limitations of estimates for different diseases, injuries, and risk factors.

Modelling strategies that capture spatial and temporal patterns in the data have reduced estimation error. Where possible, objective tests of model performance through out-of-sample predictive validity have been included. These out-of-sample predictive validity tests have been designed to test how well prediction models perform even in settings where no data are available for a country. Efforts at cross-validation have been implemented not only for age-specific all-cause mortality and cause of death estimates, but also for several impairments that are caused by more than one disease. This study represents a major shift from subjective inputs to more replicable approaches. These approaches will foster further innovation in the future and will facilitate burden assessment for analysts, especially as versions that work on less sophisticated computational platforms become available.

GBD 2010 is the largest systematic effort to describe the epidemiology of a wide array of major diseases, injuries, and risk factors ever undertaken. Millions of observations on mortality, causes of death, disease and injury prevalence and incidence, and risk factors have been collected, assessed, and collated. The effort has taken 5 years with hundreds of contributing experts. Our understanding of global descriptive epidemiology has advanced but GBD 2010 has also identified huge lacunae in our knowledge. New data on all-cause mortality, cause-specific mortality, or disease sequelae prevalence will improve our understanding of priority health challenges as they become available, as will new multicountry studies on disease epidemiology. Meanwhile, we expect that this study will provide the essential health intelligence, with uncertainty, to guide policy debates about the most urgent global health challenges, and how well we are addressing them.

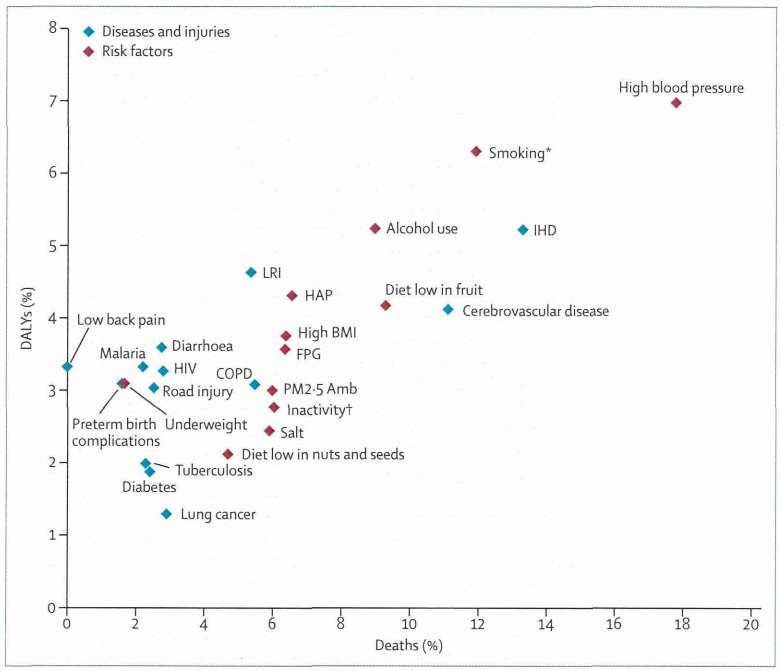

Figure 2: Comparison of the magnitude of the ten leading diseases and injuries and the ten leading risk factors based on the percentage of global deaths and the percentage of global DALYs, 2010
The figure shows 25 total diseases, injuries, and risk factors because some of the largest contributors to disability-adjusted life years (DALYs) were not in the top ten for deaths, and vice versa. DALYs=disability-adjusted life years. IHD=ischaemic heart disease. LRI=lower respiratory infections. COPD=chronic obstructive pulmonary disease. HAP=household air pollution from solid fuels. BMI=body-mass index. FPG=fasting plasma glucose. PM2.5 Amb=ambient particulate matter pollution. *Tobacco smoking, including second-hand smoke. †Physical inactivity and low physical activity.

*Christopher J L Murray†, Majid Ezzati‡, Abraham D Flaxman‡, Stephen Lim‡, Rafael Lozano‡, Catherine Michaud‡, Mohsen Naghavi‡, Joshua A Salomon‡, Kenji Shibuya‡, Theo Vos‡, Daniel Wikler‡, Alan D Lopez†
Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA 98121, USA (CJLM, ADF, SL, RL, MN); MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK (ME); China Medical Board, Boston, MA, USA (CM); School of Public Health, Harvard University, Boston, MA, USA (JAS, DW); School of Population Health, University of Queensland, Brisbane, Australia (TV, ADL); and Department of Global Health Policy, University of Tokyo, Tokyo, Japan (KS)
cjlm@uw.edu

†Joint senior authors. ‡Authors listed alphabetically.

ME chaired a session and gave a talk at the World Cardiology Congress (WCC) with travel cost reimbursed by the World Heart Federation. At the WCC, he also gave a talk at a session organised by PepsiCo with no financial or other remuneration. The other authors declare that they have no conflicts of interest. We would like to thank the countless individuals who have contributed to the Global Burden of Disease Study 2010 in various capacities. We would also like to specifically acknowledge the important contribution to this work from multiple staff members of WHO. We would like to thank the Pan American Health Organization, the Eastern Mediterranean Regional Office of WHO, the Ministry of Health of Brazil, the Chinese Center for Disease Control and Prevention, UNAIDS, and the University of Zambia for organising review meetings and workshops. Many individuals have helped in this overall effort over the multiple years of the study. We would like to thank Nick Beckstead, Michael Blake, Greg Bognar, Dan Brock, John Broome, Tom Dougherty, Nir Eyal, Marc Fleurbaey, Johann Frick, Daniel Hausman, Iwao Hirose, Frances Kamm, Jeff McMahan, Paul Menzel, Ole Norheim, Kristi Olson, Toby Ord, Thomas Pogge, Wlodek Rabinowicz, John Roemer, Andrew Schroeder, and Larry Temkin for their contributions to the consultation on the simplification of DALYs, which was an important source of input into shaping the philosophical underpinnings of its methodological approach. We would like to thank Kate Jackson, Lesley Baker, Rebecca Cooley, Melissa Stewart, Deborah Bentzel, and Abigail Donner for their crucial assistance facilitating communication and coordination between expert groups, the Core Team, and other important collaborators throughout the study to help achieve the final results. Robert Black and Dean Jamison served on the Core Team for GBD 2010 and contributed to the conceptualisation of the effort and the early phase of its implementation. JAS acknowledges the support he received from the Burke Global Health Fellowship. Finally, we would like to acknowledge the extensive support from staff members at the Institute for Health Metrics and Evaluation and specifically thank: James Bullard, Andrew Ernst, and Serkan Yalcin for their tireless support of the computational infrastructure required to produce the results; Linda A Ettinger for her expert administrative support to facilitate communication and coordination among the authors; Evan Laurie for designing several of the data visualisations that help to illustrate for readers results from the accompanying papers; Brandon Loo for responding to the needs of multiple researchers for software and data access to reach the study's goals; Peter Speyer, Abigail McLain, Katherine Leach-Kemon, and Eden Stork for their persistent and valuable work to gain access to and catalogue as much data as possible to inform the estimates; and Erin C Mullany for her systematic efforts in organising drafts of papers, formatting correspondence with expert groups, and preparing the final manuscript.

1 Murray CJL, Lopez AD. The Global Burden of Disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Boston, MA: Harvard University Press on behalf of the World Health Organization and The World Bank, 1996.
2 World Bank. World Development Report 1993. Investing in health: world development indicators. Oxford: Oxford University Press, 1993.
3 Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet* 1997; **349:** 1269–76.
4 Murray CJL, Lopez AD. Regional patterns of disability-free life expectancy and disability-adjusted life expectancy: Global Burden of Disease Study. *Lancet* 1997; **349:** 1347–52.
5 Murray CJL, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 1997; **349:** 1436–42.
6 Murray CJL, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet* 1997; **349:** 1498–504.
7 Murray CJL, Ferguson BD, Lopez AD, Guillot M, Salomon JA, Ahmad O. Modified logit life table system: principles, empirical validation, and application. *Popul Stud* 2003; **57:** 165–82.
8 Salomon JA, Murray CJL. The epidemiologic transition revisited: compositional models for causes of death by age and sex. *Popul Dev Rev* 2002; **28:** 205–28.
9 Salomon JA, Tandon A, Murray CJL. Comparability of self rated health: cross sectional multi-country survey using anchoring vignettes. *BMJ* 2004; **328:** 258.
10 WHO. The World Health Report 2000—health systems: improving performance. Geneva: World Health Organization, 2000.
11 Wang H, Dwyer-Lindgren L, Lofgren KT, et al. Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2071–94.
12 Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2095–128.
13 Salomon JA, Vos T, Hogan DR, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2129–43.
14 Salomon JA, Wang H, Freeman MK, et al. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2144–62.
15 Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLD) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2163–96.
16 Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2197–223.
17 Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2224–60.
18 Murray CJL, Salomon JA, Mathers CD, Lopez AD. Summary measures of population health: concepts, ethics, measurement and applications. Geneva: World Health Organization, 2002.
19 Anand S, Hanson K. Disability-adjusted life years: a critical review. *J Health Econ* 1997; **16:** 685–702.
20 Bognar G. Age-weighting. *Econ Philos* 2008; **24:** 167–89.
21 Tsuchiya A. The value of health at different ages. Working paper 184. York: Centre for Health Economics, University of York, 2001.
22 Arnesen T, Kapiriri L. Can the value choices in DALYs influence global priority-setting? *Health Policy* 2004; **70:** 137–49.
23 Airoldi M, Morton A. Adjusting life for quality or disability: stylistic difference or substantial dispute? *Health Econ* 2009; **18:** 1237–47.
24 Parsonage M, Neuburger H. Discounting and health benefits. *Health Econ* 1992; **1:** 71–76.
25 Brouwer WB, Niessen LW, Postma MJ, Rutten FF. Need for differential discounting of costs and health effects in cost effectiveness analyses. *BMJ* 2005; **331:** 446–48.
26 Murray CJL, Acharya AK. Understanding DALYs (disability-adjusted life years). *J Health Econ* 1997; **16:** 703–30.

Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010

Christopher J L Murray†‡, Theo Vos, Rafael Lozano, Mohsen Naghavi, Abraham D Flaxman, Catherine Michaud, Majid Ezzati, Kenji Shibuya, Joshua A Salomon, Safa Abdalla*, Victor Aboyans*, Jerry Abraham*, Ilana Ackerman*, Rakesh Aggarwal*, Stephanie Y Ahn*, Mohammed K Ali*, Mohammad A AlMazroa*, Miriam Alvarado*, H Ross Anderson*, Laurie M Anderson*, Kathryn G Andrews*, Charles Atkinson*, Larry M Baddour*, Adil N Bahalim*, Suzanne Barker-Collo*, Lope H Barrero*, David H Bartels*, Maria-Gloria Basáñez*, Amanda Baxter*, Michelle L Bell*, Emelia J Benjamin*, Derrick Bennett*, Eduardo Bernabé*, Kavi Bhalla*, Bishal Bhandari*, Boris Bikbov*, Aref Bin Abdulhak*, Gretchen Birbeck*, James A Black*, Hannah Blencowe*, Jed D Blore*, Fiona Blyth*, Ian Bolliger*, Audrey Bonaventure*, Soufiane Boufous*, Rupert Bourne*, Michel Boussinesq*, Tasanee Braithwaite*, Carol Brayne*, Lisa Bridgett*, Simon Brooker*, Peter Brooks*, Traolach S Brugha*, Claire Bryan-Hancock*, Chiara Bucello*, Rachelle Buchbinder*, Geoffrey Buckle*, Christine M Budke*, Michael Burch*, Peter Burney*, Roy Burstein*, Bianca Calabria*, Benjamin Campbell*, Charles E Canter*, Hélène Carabin*, Jonathan Carapetis*, Loreto Carmona*, Claudia Cella*, Fiona Charlson*, Honglei Chen*, Andrew Tai-Ann Cheng*, David Chou*, Sumeet S Chugh*, Luc E Coffeng*, Steven D Colan*, Samantha Colquhoun*, K Ellicott Colson*, John Condon*, Myles D Connor*, Leslie T Cooper*, Matthew Corriere*, Monica Cortinovis*, Karen Courville de Vaccaro*, William Couser*, Benjamin C Cowie*, Michael H Criqui*, Marita Cross*, Kaustubh C Dabhadkar*, Manu Dahiya*, Nabila Dahodwala*, James Damsere-Derry*, Goodarz Danaei*, Adrian Davis*, Diego De Leo*, Louisa Degenhardt*, Robert Dellavalle*, Allyne Delossantos*, Julie Denenberg*, Sarah Derrett*, Don C Des Jarlais*, Samath D Dharmaratne*, Mukesh Dherani*, Cesar Diaz-Torne*, Helen Dolk*, E Ray Dorsey*, Tim Driscoll*, Herbert Duber*, Beth Ebel*, Karen Edmond*, Alexis Elbaz*, Suad Eltahir Ali*, Holly Erskine*, Patricia J Erwin*, Patricia Espindola*, Stalin E Ewoigbokhan*, Farshad Farzadfar*, Valery Feigin*, David T Felson*, Alize Ferrari*, Cleusa P Ferri*, Eric M Fèvre*, Mariel M Finucane*, Seth Flaxman*, Louise Flood*, Kyle Foreman*, Mohammad H Forouzanfar*, Francis Gerry R Fowkes*, Marlene Fransen*, Michael K Freeman*, Belinda J Gabbe*, Sherine E Gabriel*, Emmanuela Gakidou*, Hammad A Ganatra*, Bianca Garcia*, Flavio Gaspari*, Richard F Gillum*, Gerhard Gmel*, Diego Gonzalez-Medina*, Richard Gosselin*, Rebecca Grainger*, Bridget Grant*, Justina Groeger*, Francis Guillemin*, David Gunnell*, Ramyani Gupta*, Juanita Haagsma*, Holly Hagan*, Yara A Halasa*, Wayne Hall*, Diana Haring*, Josep Maria Haro*, James E Harrison*, Rasmus Havmoeller*, Roderick J Hay*, Hideki Higashi*, Catherine Hill*, Bruno Hoen*, Howard Hoffman*, Peter J Hotez*, Damian Hoy*, John J Huang*, Sydney E Ibeanusi*, Kathryn H Jacobsen*, Spencer L James*, Deborah Jarvis*, Rashmi Jasrasaria*, Sudha Jayaraman*, Nicole Johns*, Jost B Jonas*, Ganesan Karthikeyan*, Nicholas Kassebaum*, Norito Kawakami*, Andre Keren*, Jon-Paul Khoo*, Charles H King*, Lisa Marie Knowlton*, Olive Kobusingye*, Adofo Koranteng*, Rita Krishnamurthi*, Francine Laden*, Ratilal Lalloo*, Laura L Laslett*, Tim Lathlean*, Janet L Leasher*, Yong Yi Lee*, James Leigh*, Daphna Levinson*, Stephen S Lim*, Elizabeth Limb*, John Kent Lin*, Michael Lipnick*, Steven E Lipshultz*, Wei Liu*, Maria Loane*, Summer Lockett Ohno*, Ronan Lyons*, Jacqueline Mabweijano*, Michael F MacIntyre*, Reza Malekzadeh*, Leslie Mallinger*, Sivabalan Manivannan*, Wagner Marcenes*, Lyn March*, David J Margolis*, Guy B Marks*, Robin Marks*, Akira Matsumori*, Richard Matzopoulos*, Bongani M Mayosi*, John H McAnulty*, Mary M McDermott*, Neil McGill*, John McGrath*, Maria Elena Medina-Mora*, Michele Meltzer*, Ziad A Memish*, George A Mensah*, Tony R Merriman*, Ana-Claire Meyer*, Valeria Miglioli*, Matthew Miller*, Ted R Miller*, Philip B Mitchell*, Charles Mock*, Ana Olga Mocumbi*, Terrie E Moffitt*, Ali A Mokdad*, Lorenzo Monasta*, Marcella Montico*, Maziar Moradi-Lakeh*, Andrew Moran*, Lidia Morawska*, Rintaro Mori*, Michele E Murdoch*, Michael K Mwaniki*, Kovin Naidoo*, M Nathan Nair*, Luigi Naldi*, K M Venkat Narayan*, Paul K Nelson*, Robert G Nelson*, Michael C Nevitt*, Charles R Newton*, Sandra Nolte*, Paul Norman*, Rosana Norman*, Martin O'Donnell*, Simon O'Hanlon*, Casey Olives*, Saad B Omer*, Katrina Ortblad*, Richard Osborne*, Doruk Ozgediz*, Andrew Page*, Bishnu Pahari*, Jeyaraj Durai Pandian*, Andrea Panozo Rivero*, Scott B Patten*, Neil Pearce*, Rogelio Perez Padilla*, Fernando Perez-Ruiz*, Norberto Perico*, Konrad Pesudovs*, David Phillips*, Michael R Phillips*, Kelsey Pierce*, Sébastien Pion*, Guilherme V Polanczyk*, Suzanne Polinder*, C Arden Pope III*, Svetlana Popova*, Esteban Porrini*, Farshad Pourmalek*, Martin Prince*, Rachel L Pullan*, Kapa D Ramaiah*, Dharani Ranganathan*, Homie Razavi*, Mathilda Regan*, Jürgen T Rehm*, David B Rein*, Guiseppe Remuzzi*, Kathryn Richardson*, Frederick P Rivara*, Thomas Roberts*, Carolyn Robinson*, Felipe Rodriguez De Leòn*, Luca Ronfani*, Robin Room*, Lisa C Rosenfeld*, Lesley Rushton*, Ralph L Sacco*, Sukanta Saha*, Uchechukwu Sampson*, Lidia Sanchez-Riera*, Ella Sanman*, David C Schwebel*, James Graham Scott*, Maria Segui-Gomez*, Saeid Shahraz*, Donald S Shepard*, Hwashin Shin*, Rupak Shivakoti*, David Singh*, Gitanjali M Singh*, Jasvinder A Singh*, Jessica Singleton*, David A Sleet*, Karen Sliwa*, Emma Smith*, Jennifer L Smith*, Nicolas J C Stapelberg*, Andrew Steer*, Timothy Steiner*, Wilma A Stolk*, Lars Jacob Stovner*, Christopher Sudfeld*, Sana Syed*, Giorgio Tamburlini*, Mohammad Tavakkoli*, Hugh R Taylor*, Jennifer A Taylor*, William J Taylor*, Bernadette Thomas*, W Murray Thomson*, George D Thurston*, Imad M Tleyjeh*, Marcello Tonelli*, Jeffrey A Towbin*, Thomas Truelsen*, Miltiadis K Tsilimbaris*, Clotilde Ubeda*, Eduardo A Undurraga*, Marieke J van der Werf*, Jim van Os*, Monica S Vavilala*, N Venketasubramanian*, Mengru Wang*, Wenzhi Wang*, Kerrianne Watt*, David J Weatherall*, Martin A Weinstock*, Robert Weintraub*, Marc G Weisskopf*, Myrna M Weissman*, Richard A White*, Harvey Whiteford*, Natasha Wiebe*, Steven T Wiersma*, James D Wilkinson*, Hywel C Williams*, Sean R M Williams*, Emma Witt*, Frederick Wolfe*, Anthony D Woolf*, Sarah Wulf*, Pon-Hsiu Yeh*, Anita K M Zaidi*, Zhi-Jie Zheng*, David Zonies*, Alan D Lopez†

Summary

Background Measuring disease and injury burden in populations requires a composite metric that captures both premature mortality and the prevalence and severity of ill-health. The 1990 Global Burden of Disease study proposed disability-adjusted life years (DALYs) to measure disease burden. No comprehensive update of disease burden worldwide incorporating a systematic reassessment of disease and injury-specific epidemiology has been done since the 1990 study. We aimed to calculate disease burden worldwide and for 21 regions for 1990, 2005, and 2010 with methods to enable meaningful comparisons over time.

Methods We calculated DALYs as the sum of years of life lost (YLLs) and years lived with disability (YLDs). DALYs were calculated for 291 causes, 20 age groups, both sexes, and for 187 countries, and aggregated to regional and global estimates of disease burden for three points in time with strictly comparable definitions and methods. YLLs were calculated from age-sex-country-time-specific estimates of mortality by cause, with death by standardised lost

Lancet 2012; 380: 2197–223

This online publication has been corrected. The corrected version first appeared at thelancet.com on February 22, 2013

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

See Special Report page 2067

See Articles pages 2071, 2095, 2129, 2144, 2163, and 2224

*Authors listed alphabetically

†Joint senior authors
‡Corresponding author
See Online for appendix
For **interactive versions of figures 2, 3, 5, 7, and 10** see http://healthmetricsandevaluation.org/gbd/visualizations/regional
Queensland Centre for Mental Health Research (A Baxter MPH, H Erskine BPsySc, A Ferrari BPsySc, J-P Khoo MBBS, S Saha PhD, Prof H Whiteford MBBS), **School of Population Health** (Prof T Vos PhD, J D Blore PhD, F Charlson MPH, H Higashi PhD, Y Y Lee MHEcon, R Norman PhD, A Page PhD, Prof A D Lopez PhD), **Centre for Clinical Research** (J G Scott PhD), **Queensland Brain Institute** (Prof J McGrath MD), **University of Queensland, Brisbane, QLD, Australia** (B Garcia MPH, Prof W Hall PhD); **Institute for Health Metrics and Evaluation** (A D Flaxman PhD, M Naghavi PhD, Prof R Lozano MD, S Y Ahn MPH, M Alvarado BA, K G Andrews MPH, C Atkinson BS, I Bolliger AB, R Burstein BA, B Campbell BA, D Chou BA, K E Colson BA, Prof S D Dharmaratne MBBS, A Delossantos BS, *M H Forouzanfar MD*, M K Freeman BA, E Gakidou PhD, D Gonzalez-Medina BA, D Haring BS, S L James MPH, R Jasrasaria BA, N Johns BA, S S Lim PhD, S Lockett Ohno BA, M F MacIntyre EdM, L Mallinger MPH, A A Mokdad MD, M N Nair MD, K Ortblad BA, D Phillips BS, K Pierce BA, D Ranganathan BS, T Roberts BA, L C Rosenfeld MPH, E Sanman BS, M Wang MPH, S Wulf MPH, Prof C J L Murray MD), **Department of Epidemiology, School of Public Health** (L M Anderson PhD), **Department of Anesthesiology and Pain Medicine** (N Kassebaum MD), **University of Washington, Seattle, WA, USA** (Prof W Couser MD, H Duber MD, B Ebel MD, Prof C Mock MD, C Olives PhD, Prof F P Rivara MD, B Thomas MD, Prof M S Vavilala MD); **China Medical Board, Boston, MA, USA** (C Michaud MD); **MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health** (Prof M Ezzati PhD), **Imperial College London, London,**

life expectancy at each age. YLDs were calculated as prevalence of 1160 disabling sequelae, by age, sex, and cause, and weighted by new disability weights for each health state. Neither YLLs nor YLDs were age-weighted or discounted. Uncertainty around cause-specific DALYs was calculated incorporating uncertainty in levels of all-cause mortality, cause-specific mortality, prevalence, and disability weights.

Findings Global DALYs remained stable from 1990 (2·503 billion) to 2010 (2·490 billion). Crude DALYs per 1000 decreased by 23% (472 per 1000 to 361 per 1000). An important shift has occurred in DALY composition with the contribution of deaths and disability among children (younger than 5 years of age) declining from 41% of global DALYs in 1990 to 25% in 2010. YLLs typically account for about half of disease burden in more developed regions (high-income Asia Pacific, western Europe, high-income North America, and Australasia), rising to over 80% of DALYs in sub-Saharan Africa. In 1990, 47% of DALYs worldwide were from communicable, maternal, neonatal, and nutritional disorders, 43% from non-communicable diseases, and 10% from injuries. By 2010, this had shifted to 35%, 54%, and 11%, respectively. Ischaemic heart disease was the leading cause of DALYs worldwide in 2010 (up from fourth rank in 1990, increasing by 29%), followed by lower respiratory infections (top rank in 1990; 44% decline in DALYs), stroke (fifth in 1990; 19% increase), diarrhoeal diseases (second in 1990; 51% decrease), and HIV/AIDS (33rd in 1990; 351% increase). Major depressive disorder increased from 15th to 11th rank (37% increase) and road injury from 12th to 10th rank (34% increase). Substantial heterogeneity exists in rankings of leading causes of disease burden among regions.

Interpretation Global disease burden has continued to shift away from communicable to non-communicable diseases and from premature death to years lived with disability. In sub-Saharan Africa, however, many communicable, maternal, neonatal, and nutritional disorders remain the dominant causes of disease burden. The rising burden from mental and behavioural disorders, musculoskeletal disorders, and diabetes will impose new challenges on health systems. Regional heterogeneity highlights the importance of understanding local burden of disease and setting goals and targets for the post-2015 agenda taking such patterns into account. Because of improved definitions, methods, and data, these results for 1990 and 2010 supersede all previously published Global Burden of Disease results.

Funding Bill & Melinda Gates Foundation.

Introduction

Summary measures of population health combine information on mortality and non-fatal health outcomes to provide unique perspectives on levels of health and key contributing causes to loss of health.[1] There are three related but distinct uses of summary measures of population health at the global, regional, national, or subnational levels. Summary measures can be used, first, to compare overall population health across communities and over time; for example, national estimates of healthy life expectancy (HALE) have been published for 191 countries.[2] The second and more common use of summary measures is to provide a coherent overall picture as to which diseases, injuries, and risk factors contribute the most to health loss in a given population. The comparative view provided by summary measures helps decision-makers, researchers, and citizens understand what the most important problems are and whether they are getting better or worse. This information, along with information on the costs, intervention effectiveness, and equity implications of health interventions and policy options, lays the foundation for a debate on priorities for health policy action and research that is clearly informed by the best available evidence. Third, summary measures can help guide an assessment of where health information systems are strong or weak by identifying which data sources required for their calculation are missing, of low quality, or highly uncertain. Different users in different contexts will make use of summary measures for any of the three purposes.

The only comprehensive effort to date to estimate summary measures of population health for the world, by cause, is the ongoing Global Burden of Diseases, Injuries, and Risk Factors (GBD) enterprise. For a summary measure of population health, the GBD study uses disability-adjusted life years (DALYs), which are the sum of years of life lost due to premature mortality (YLL) and years lived with disability (YLD). While the term disability has taken on many different meanings in different settings,[3–7] in the GBD lexicon it refers to any short-term or long-term health loss, other than death. The construct of health in the GBD study is defined in terms of functioning, which encompasses multiple domains of health such as mobility, pain, affect, and cognition.[8] Final GBD results for 1990 were published in 1996 and 1997.[9–14] GBD estimates were produced for 1999, 2000, 2001, 2002, and 2004 by WHO.[15–19] Although GBD results have been estimated by WHO for 1999–2004, and incorporated new approaches to mortality measurement,[20] these updates undertook systematic analysis of the epidemiological data for only a subset of disease sequelae.[21] DALY results have been referenced extensively in global health debates and decision-making. The first results from the GBD study for 1990 were published in the *World Development Report 1993: Investing in Health*.[22] The study has led to many national burden of disease studies in developed and developing countries using similar methods.[23–75] Subnational studies

have also been done in many countries.[76–81] Quantifying health loss in terms of DALYs has led to increased attention to mental health problems[82] and injuries,[83] non-fatal health effects of neglected tropical diseases,[84] and more generally non-communicable diseases (NCDs).[85]

The Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010)[86] has been implemented as a collaboration of seven institutions: the Institute for Health Metrics and Evaluation (IHME) as the coordinating centre providing academic leadership; the University of Queensland School of Population Health; WHO; the Johns Hopkins Bloomberg School of Public Health; the Harvard School of Public Health; Imperial College London; and the University of Tokyo. The GBD 2010 has been undertaken to apply comparable, systematic, and rigorous epidemiological assessment of all diseases and injuries. The number of disease and injury sequelae has expanded from 483 to 1160. The study also uses a much more detailed set of age groups, 20 instead of eight; and 21 regions instead of the 14 used in the GBD 2000 study.[86]

In the GBD 1990 study, results were computed with several variants of DALYs reflecting different social-value choices for discounting and age-weighting. The base case reported for DALYs used a 3% discount rate and age weights that placed the greatest emphasis on health outcomes in young adults. WHO has continued in its updates for 1999, 2000, 2001, 2002, and 2004 to use this base case set of social-value choices although other variants have been calculated. One publication for 2001 reported discounted DALYs without age-weighting.[87] On the basis of broad consultation,[86] the base case for DALYs in GBD 2010 has been simplified to omit both discounting and age-weighting. YLLs are calculated with reference to a new reference-standard life expectancy at each age; for example, a death at age 5 years counts as 81·4 YLLs and a death at age 60 counts as 27·8 YLLs.[86] The reference standard has been computed on the basis of the lowest age-specific death rates recorded across countries in 2010. YLDs are based on the product of the prevalence of a sequela and its associated disability weight. Of note, the empirical basis for disability weights in the GBD 2010 derives from judgments of the general public about health severity, by contrast with the GBD 1990 study that relied on judgments of health-care professionals.[3] A key tenet of the GBD analytical philosophy is not to allow advocates for the importance of specific diseases to choose the disability weights associated with specific disorders (panel).

The goal of the GBD 2010 has been to synthesise available data on the epidemiology of all major diseases and injuries to provide a comprehensive and comparable assessment of the magnitude of 291 diseases and injuries and their associated sequelae in 1990, 2005, and 2010. In this Article, we summarise the results of a large and complex study involving hundreds of researchers. The findings draw on millions of observations of epidemiological parameters over the past three decades. By

***Panel:* Disability-adjusted life years and Global Burden of Disease definitions**

1. Disability-adjusted life years (DALYs) are a summary metric of population health. DALYs represent a health gap; they measure the state of a population's health compared to a normative goal. The goal is for individuals to live the standard life expectancy in full health.
2. DALYs are the sum of two components: years of life lost due to premature mortality (YLLs) and years lived with disability (YLDs).
3. YLLs are computed by multiplying the number of deaths at each age x by a standard life expectancy at age x. The standard selected represents the normative goal for survival and has been computed based on the lowest recorded death rates across countries in 2010.
4. YLDs are computed as the prevalence of different disease-sequelae and injury-sequelae multiplied by the disability weight for that sequela. Disability weights are selected on the basis of surveys of the general population about the loss of health associated with the health state related to the disease sequela.
5. DALYs are an absolute measure of health loss; they count how many years of healthy life are lost due to death and non-fatal illness or impairment. They reflect the number of individuals who are ill or die in each age-sex group and location. Population size and composition influences the number of DALYs in a population.
6. The GBD 2010 disease-and-injury-cause list is a hierarchical list of 291 diseases and injuries. At the first level of disaggregation causes are divided into three broad groups: communicable, maternal, neonatal, and nutritional disorders; non-communicable diseases; and injuries. At each level in the hierarchy, the cause list provides a set of mutually exclusive and collectively exhaustive categories.
7. Sequelae—in total, we have identified 1160 sequelae of the 291 diseases and injuries. For example, diabetic neuropathy is a sequela of diabetes mellitus. To avoid double counting, a sequela can only appear in the cause-sequela list once even if the same outcome might be claimed by more than one disease.
8. Health states—across the 1160 sequelae, 220 unique health states were identified. 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: (a) to allow assessment of the total burden of some health states such as anaemia across various causes; and (b) to simplify the task of measuring disability weights for sequelae.
9. DALYs presented in this study are not age-weighted and are not discounted for time preference. Base case tabulations for the GBD 1990 and GBD 2000 studies used age-weighting and a 3% discount rate.
10. Because of improved data and methods, comparisons between 1990 and 2010 should be based exclusively on the results of this study.

UK (Prof M-G Basáñez PhD, Prof P Burney MD, K Foreman MPH, D Jarvis FFPH, S O'Hanlon MSc, L Rushton PhD); **Department of Global Health Policy** (Prof K Shibuya MD), **University of Tokyo, Tokyo, Japan** (Prof N Kawakami MD); **Department of Biostatistics** (M M Finucane PhD), **School of Public Health** (Prof J A Salomon PhD, G Danaei MD, F Laden ScD, J K Lin AB, M Miller MD, G M Singh PhD, C Sudfeld ScM, M Tavakkoli MD, M G Weisskopf PhD, R A White MA), **Department of Epidemiology** (W Liu MD), **Harvard Humanitarian Initiative** (L M Knowlton MD), **Boston Children's Hospital** (Prof S D Colan MD), **Brigham and Women's Hospital** (S Jayaraman MD), **Harvard Medical School, Harvard University, Boston, MA, USA** (D H Bartels BA, K Bhalla PhD); **Sudanese Public Health Consultancy Group, Sudan** (S Abdalla MBBS); **Department of Cardiology, Dupuytren University Hospital, Limoges, France** (Prof V Aboyans MD); **University of Texas, San Antonio, TX, USA** (J Abraham MPH); **Centre for International Child Health** (A Steer MBBS), **Department of Pediatrics** (R Weintraub MBBS), **Centre for Health Policy, Programs and Economics** (Prof L Degenhardt PhD), **School of Population Health** (Prof R Room PhD), **University of Melbourne, Melbourne, VIC, Australia** (I Ackerman PhD, Prof P Brooks MD, Prof R Marks MBBS, Prof H R Taylor MD); **Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India** (Prof R Aggarwal MD); **Schools of Public Health and Medicine** (S B Omer MBBS), **Emory University, Atlanta, GA, USA** (M K Ali MBChB, K C Dabhadkar MBBS, K M V Narayan MD, H A Ganatra MBBS); **Ministry of Health, Riyadh, Saudi Arabia** (M A AlMazroa MD, Prof Z A Memish MD); **St George's University of London, London, UK** (Prof H R Anderson MD, R Gupta MSc, E Limb MSc); **Mayo Clinic, Rochester, MN, USA** (Prof L M Baddour MD, P J Erwin MLS, Prof S E Gabriel MD); **Independent Consultant,**

Geneva, Switzerland (A N Bahalim MEng); University of Auckland, Auckland, New Zealand (S Barker-Collo PhD); Department of Industrial Engineering, School of Engineering, Pontificia Universidad Javeriana, Bogota, Colombia (L H Barrero ScD); Global Partners in Anesthesia and Surgery (D Ozgediz MD), Yale University, New Haven, CT, USA (Prof M L Bell PhD, J J Huang MD); School of Medicine (Prof D T Felson MD), Boston University, Boston, MA, USA (Prof E J Benjamin MD); Clinical Trial Service Unit and Epidemiological Studies Unit (D Bennett PhD), University of Oxford, Oxford, UK (Prof C R Newton MD, D J Weatherall MD); Dental Institute (E Bernabé PhD), Hospital NHS Trust (Prof R J Hay DM), Institute of Psychiatry, King's College London, London, UK (Prof M Prince MD); Institute of Dentistry (M Dahiya BDS), Queen Mary University of London, London, UK (B Bhandari MSc, Prof W Marcenes PhD); Moscow State University of Medicine and Dentistry, Research Institute of Transplantology and Artificial Organs, Moscow, Russia (B Bikbov MD); King Fahad Medical City, Riyadh, Saudi Arabia (A Bin Abdulhak MD, I M Tleyjeh MD); Michigan State University, East Lansing, MI, USA (Prof G Birbeck MD); MRC Epidemiology Unit, Cambridge, UK (J A Black MPhil); London School of Hygiene and Tropical Medicine, London, UK (Prof S Brooker DPhil, H Blencowe MBChB, K Edmond PhD, Prof N Pearce PhD, R L Pullan PhD, J L Smith MSc); Department of Rheumatolology, Northern Clinical School (E Smith PhD), Faculty of Health Sciences (M Fransen PhD), Institute of Bone and Joint Research (Prof L March MD, L Sanchez-Riera MD), Sydney School of Public Health (T Driscoll PhD, J Leigh MBBS), University of Sydney, Sydney, NSW, Australia (F Blyth PhD, L Bridgett PhD, M Cross PhD, Prof G B Marks PhD, N McGill FRACP); Inserm, Paris, France (A Bonaventure MD, A Elbaz MD); Transport and Road Safety Research (S Boufous PhD), National

the synthetic nature of the work, we provide a high-level overview of key findings. Because this study uses consistent definitions and improved methods to assess the GBD over two decades, the findings supersede all previously published GBD results.

Methods

Study design

The division of countries into 21 epidemiological regions, the choice of 20 age groups, and the primary methods for each of the 18 components of the study are described by Murray and colleagues.[86] We provide only a brief description here. The GBD cause list has 291 diseases and injuries, which are organised in a hierarchy with up to four levels of disaggregation. For each cause, there are from one to 24 sequelae. In total, the study includes 1160 sequelae. The expansion of the cause list and the criteria used to add causes and sequelae across various revisions of the GBD study is described elsewhere.[86]

Causes of death

YLLs have been computed on the basis of cause-of-death estimates for 235 of 291 causes of death for 20 age groups, both sexes, and 187 countries. Two disorders, sudden infant death syndrome (SIDS) and aortic aneurysm, cause only YLLs. Cause of death estimates have been developed with a comprehensive database of vital registration, verbal autopsy, surveillance, and other sources covering 187 countries from 1980 to 2010. Quality of each observation has been assessed, and various revisions of the International Classification of Diseases and Injuries (ICD) have been mapped. Deaths assigned to causes that are not likely to underlie causes of death have been reassigned with standardised algorithms.[88,89] All observations were converted to the 20 standard GBD age groups. For 133 causes, including all major causes of death excluding HIV/AIDS, we used the Cause of Death Ensemble model (CODEm) strategy to develop ensembles of the best performing models that meet two plausibility criteria. The first criterion is that the direction of the regression coefficient for a covariate is in the expected direction, and the second is that the coefficient has a p value less than 0·05. Performance is assessed in terms of rigorous out-of-sample predictive validity testing based on the root-mean-squared error of the log of the age-specific death rates, the percentage of time that trend is accurately predicted, and the coverage of the uncertainty intervals (UIs). For HIV/AIDS, we have used CODEm for countries with high-quality vital registration systems and the UNAIDS 2012 revision estimates by age and sex for the remaining countries. Natural history models have been used for African trypanosomiasis, measles, whooping cough, hepatitis E, typhoid and paratyphoid fevers, leishmaniasis, HIV/AIDS, and congenital syphilis. Aetiologies or subcauses for diarrhoea, lower respiratory infections, meningitis, chronic kidney diseases, maternal disorders, cirrhosis, and liver cancer have been based on meta-regression of published studies on aetiology, disease registry data, and, where appropriate, vital registration data. For some rarer causes such as diphtheria or varicella, negative binomial regression has been used; for a few causes that rarely account for mortality, fixed proportions of the parent cause in the hierarchy have been used by age, sex, and region. A key aspect of the GBD method is to enforce consistency between the sum of cause-specific mortality and independently assessed levels of all-cause mortality derived from demographic sources (see Wang and colleagues[90] for details on the all-cause-mortality analysis). Uncertainty in cause-of-death model predictions has been captured with standard simulation methods by taking 1000 draws[91] for each age, sex, country, year, and cause (see Lozano and colleagues[92] for more details on causes-of-death methods). Consistency with all-cause mortality is enforced at the draw level. Final uncertainty for YLLs reflects uncertainty in the levels of all-cause mortality in each age-sex-country-year as well as uncertainty in the estimation of each cause of death for that age-sex-country-year.

Years lived with disability

The second component of DALYs is YLDs. YLDs have been estimated for 1160 sequelae of the diseases and injuries in the hierarchical cause list. YLDs are the product of prevalence times the disability weight for a sequela. Prevalence estimation for each sequela begins with a systematic analysis of published and available unpublished data sources for prevalence, incidence, remission, and excess mortality. For most sequelae, estimates have been made based on the database for all age-sex-country-year groups, with a Bayesian meta-regression method developed for the GBD 2010 (DisMod-MR). The meta-regression can handle data reported for any age interval and can use two types of covariates: those that explain true variation in prevalence; and those that explain variation across studies due to study design, case definitions, or diagnostic technology. Nested super-region, region, and country random intercepts are also included. A map of regions and super-regions is published elsewhere.[86] Where appropriate, DisMod-MR uses data on incidence, prevalence, remission, excess mortality, and cause-specific mortality to generate prevalence estimates assuming these rates are stable over time. Using data on multiple epidemiological parameters to estimate prevalence is especially important when prevalence data are sparse. Where rates are changing rapidly, DisMod-MR can be used to undertake meta-regression without assuming equilibrium rates. Alternative strategies have been used for the prevalence of selected sequelae (see elsewhere for details).[93] DisMod-MR and alternative methods generate uncertainty distributions for the prevalence of each sequela by age, sex, country, and year. For nine residual cause categories such as other mental and behavioural disorders, YLDs have been approximated with the relation between YLLs and YLDs reported for similar disease groupings.