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.

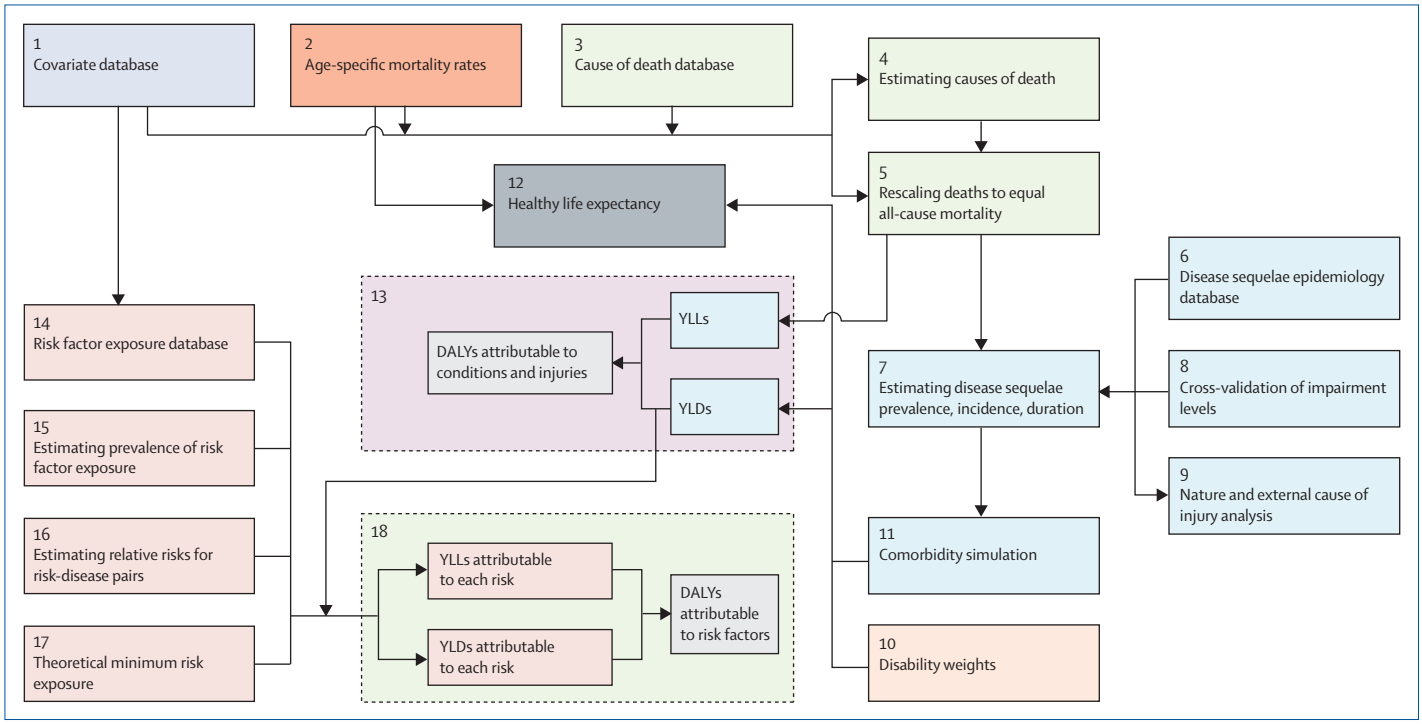

Figure 1: **18 components of the GBD 2010 and their inter-relations**
GBD 2010=Global Burden of Disease Study 2010. DALYs=disability-adjusted life years. YLLs=years of life lost due to premature mortality. YLDs=years lived with disability.

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.

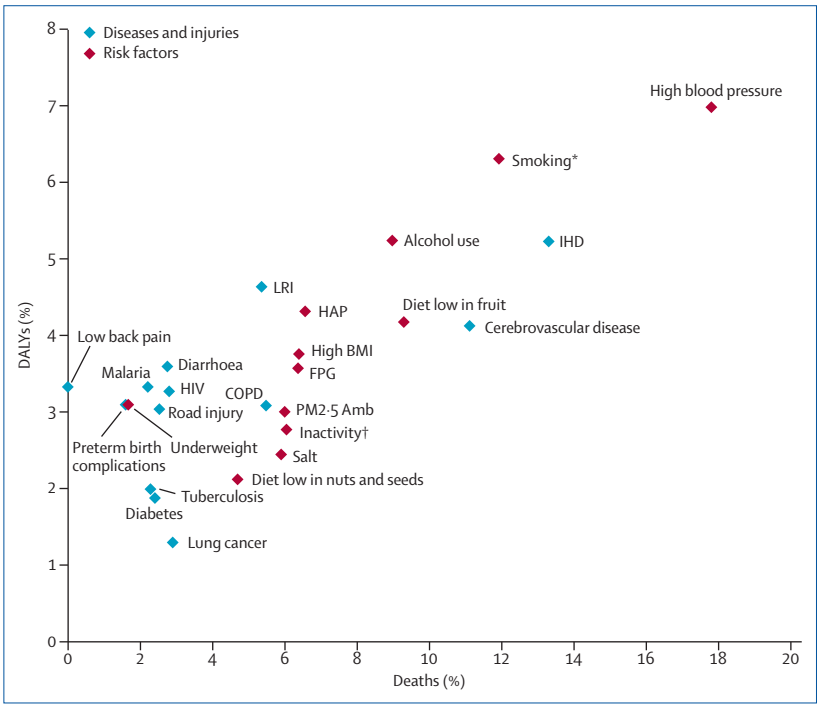

Figure 2: **Comparison of the magnitude of the ten leading diseases and injuries and the ten leading risk factors based on the percentage of global deaths and the percentage of global DALYs, 2010**
The figure shows 25 total diseases, injuries, and risk factors because some of the largest contributors 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.