On top of a general pattern of the demographic and epidemiological transition associated with both mortality decline and fertility decline, substantial regional heterogeneity exists in the diseases and injuries that cause burden. HIV/AIDS is one vivid example that has come to be the dominant cause of burden in eastern and southern sub-Saharan Africa. Interpersonal violence is a leading cause in central Latin America (rank 1) and tropical Latin America (rank 2), and in southern sub-Saharan Africa (rank 5); the pattern of interpersonal violence across regions is unrelated to metrics of the epidemiological and demographic transition. Self-harm is a top ten cause of burden in high-income Asia Pacific (rank 5), eastern Europe (rank 6) and central Europe (rank 11). Cirrhosis is an important cause in central Asia (rank 9), central Europe (rank 10), eastern Europe (rank 11), and central Latin America (rank 12). Drug use disorders are especially important in Australasia (rank 11) and high-income North America (rank 11). Site-specific cancers show substantial regional heterogeneity. The leading cancer across regions ranges from lung to liver to stomach and colon and rectum.

Some diseases show a strong relation between prevalence and mortality with age. As the number of individuals aged 75 years and older in the world increased from 119 million in 1990 to 206 million in 2010, it has driven up the burden of these diseases substantially. The most notable diseases include the various causes of blindness and low vision but also several neurological disorders. The rise of dementia and Parkinson's disease is almost entirely attributable to population ageing because age-specific rates have remained constant. In view of the global shifts in fertility and declines in age-specific mortality, we can expect the numbers of individuals with age-related disorders to increase substantially in coming decades. This shift in numbers of people with certain disorders will have substantial implications for health-service planning.

At least partly viewed through the lens of the Millennium Development Goals (MDGs), the world has paid increased attention to the mortality of children younger than 5 years of age, maternal mortality, HIV/AIDS, tuberculosis, and malaria. Collectively the MDG-related causes of burden account for 742 million DALYs in 2010, or 29·8% of the total burden of disease—this burden includes YLLs from all causes in children younger than 5 years of age and DALYs from maternal disorders, HIV/AIDS, tuberculosis, and malaria. Progress has clearly been made. In 1990 these disorders accounted for 1096 million DALYs or 43·8% of the total burden. Although we are unlikely to achieve most of the health-related MDG targets by 2015, the burden of these disorders has declined by nearly 32·0% from 1990 to 2010 and will probably decline further by 2015 in view of current trends. More than two-thirds of global DALYs now arise from disorders not targeted in the MDGs. As 2015 nears and the world is discussing goals for the post-MDG period, addressing the leading, and often largely preventable, causes of the non-MDG health spectrum, especially NCDs and injuries, should be given greater priority than hitherto. When examined at a regional level (figure 11), the issue is even starker. In 2010, the fraction of the burden of disease that is related to disorders targeted in the MDGs ranges from 68·9% in western sub-Saharan Africa to 1·7% in high-income Asia Pacific. In five of 21 regions, the burden of MDG-related disorders exceeds a third of regional DALYs: the four sub-Saharan Africa regions, and south Asia. This regional heterogeneity shows how it will be important for post-2015 development goals to reflect the widely differing disorders across regions in setting targets.

The findings from this study have implications for health system investment decisions, including health manpower needs and the content of medical education. Many systems are already grappling with the challenges posed by rising numbers of cardiovascular events and cancers; these findings also highlight the importance of health-care professionals who will service the specialties of trauma, rehabilitation, mental health, musculoskeletal disorders, and diabetes. More generally, the shifting burden of disease driven by population ageing and differential rates of decline in age-specific rates that are greater for communicable, maternal, neonatal, and nutritional disorders than for NCDs also has implications for any health system's capital investments. These investments will often be used over decades so that they need to reflect future burden. Within professions, the shifting burden should also be reflected in the content of education for health professionals. The pace of demographic and epidemiological change is fast enough that a forward-looking assessment of the burden should be incorporated in the reform of health professional education on a region-by-region basis.[95]

The burden of musculoskeletal disorders is much larger than in previous GBD assessments. In the 2004 revision of the GBD study, this group of disorders was estimated to

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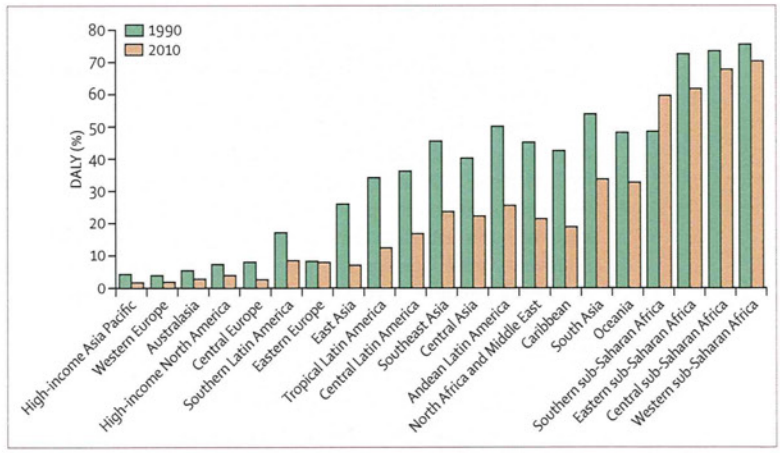

Figure 11: **Disability-adjusted life years (DALYs) related to Millennium Development Goals 4, 5, and 6 as a proportion of the total burden, by region, 1990 and 2010**

account for 2·0%, compared with 6·8% in this study. This much higher share relates to three factors. First, there has been a much more comprehensive and systematic assessment of the epidemiological data. These data show that low back pain, neck pain, osteoarthritis, and other musculoskeletal disorders are extremely common in nearly all populations. Second, the disability weights assigned to these disorders—which cause pain, discomfort, lack of mobility, anxiety, and sleeplessness—in the population-based surveys are higher than those based on the judgment of health-care professionals. Finally, in previous assessments that focused on incidence, the duration of symptoms was probably systematically underestimated. These disorders account for a substantial number of health-care visits and cost in populations with access to medical care.[96,97] The burden is likely to grow steadily because of rising rates with age, little change over time, and an ageing world population. In view of the epidemiological pattern and associated costs, health-care systems will need to develop a coherent policy for dealing with musculoskeletal disorders. Prioritisation of research on the most effective and affordable strategies is urgently needed to deal with these disorders.

A key finding of the GBD 1990 and 2000 studies was the large unrecognised burden of mental illness in developed and developing countries—8·5% of DALYs in the GBD 1990 study and 10·1% in the GBD 2000 study. These results were reported for DALYs with discounting and age-weighting. Age-weighting assigns maximum value to young and middle-aged adults in whom the prevalence of mental illness is high. Without age-weighting and discounting, the burden of mental illness in the GBD 1990 study was 5·7%. Despite the switch in the GBD 2010 study to a base case for DALY computation of no discounting and no age-weighting, mental and behavioural disorders account for 7·4% of global DALYs in 2010. This study has expanded the set of disorders carefully assessed to include many disorders previously crudely estimated in a residual category. Newly added disorders include all anxiety disorders compared with only three in the earlier studies, childhood disorders, and eating disorders. Some disorders such as major depressive disorder have a higher prevalence than previously estimated. Using consistent definitions in this study over time for the mental and behavioural disorders, the number of DALYs for this group increased by 38% from 1990 to 2010. The drivers of the increase are the combination of population growth, shift in age structure towards the age groups at highest risk, and relatively stable age-specific prevalence rates—although notable fluctuations exist in drug use disorders over time. We can expect that the absolute number and share of burden attributable to mental and behavioural disorders, already substantial, will probably steadily increase in the future. Despite increased global attention to mental health in the past decade,[17] practical strategies for managing these disorders in low-income and middle-income countries are urgently needed.

Road injury accounts for 75·5 million DALYs in 2010, up from 56·7 million in 1990. To put road injury in context, it accounts for 53% more burden than tuberculosis. Road injury shows a classic inverted U-shaped pattern with the largest DALY rates and highest rank as a cause of burden in regions that are upper low-income or middle-income. Nevertheless, even in the demographically and epidemiologically advanced regions, road injury is in the top 16 causes. The distribution of road injury by specific subcause is also important for policy: in seven developing regions more than 40% of road injury deaths are in pedestrians including all sub-Saharan African regions, south and east Asia, and Andean Latin America. Motorised two-wheel vehicles account for more than 20% of road injury deaths in southeast and east Asia and tropical Latin America. The local patterns of road injury and publications on road safety[98,99] argue that most road injury is preventable. Some high-income countries such as Australia have been able to reduce the death rate from road injuries by 43·7% since 1990, providing a population level demonstration that many deaths are preventable. Various global initiatives on road safety have been launched[100,101] but they remain relatively weakly funded and are yet to have a demonstrable effect on the rising burden from road injury globally. Continued attention from both the health sector and the transport sector will be needed to address this growing challenge.

Interpersonal violence in 2010 ranks 27th across causes at the global level; in view of the fact that 81% of the DALYs due to interpersonal violence are in male individuals, it is the 21st ranked cause in male individuals and 49th in female individuals. This global figure masks enormous inter-regional variation in the extent of interpersonal violence. Three regions—central and tropical Latin America and southern sub-Saharan Africa—have violence as a top five cause of burden. Ecological analyses of the root causes of violence[102–106] have helped elucidate risk factors for different forms of violence and have been useful for exploring the determinants of within-country variation.[107] Few studies, however, help to explain why violence is such a dominant factor in population health in specific countries and regions. More robust research on this topic, as well as its relation to social and political changes and drug markets, would be a valuable addition to the public health literature. Increased links between public health researchers and social scientists working in this complex field could make this research more productive. A key challenge for this area, nevertheless, will be proposing, testing, and assessing effective policy interventions that stem from increased understanding of the broader determinants.

Among the top cancer causes of DALYs, liver cancer and pancreatic cancer DALYs have increased the most. Stomach cancer is declining, and lung, colon and rectum, breast, and brain cancer increased by about 35% from 1990 to 2010. For smaller causes, kidney cancer, prostate cancer, liver cancer secondary to

hepatitis C, and non-melanoma skin cancer are the only causes of cancer that have increased by more than 50% from 1990 to 2010. Many researchers might have expected the burden of liver cancer secondary to hepatitis B to decrease because of expansion of hepatitis B vaccine coverage. Burden, however, has increased from 1990 to 2010 by over 45%. The increase can be understood in terms of population growth in areas with substantial prevalence of hepatitis B and the long lag between childhood immunisation for hepatitis B and reductions in adult liver cancer deaths some 30–50 years later. Increases are also in part related to other causes of liver cancer, including hepatitis C and alcohol.

The downward trend in COPD rates in east Asia and upward trend in lung cancer in this region need explanation. In addition to tobacco consumption, other factors probably contribute to levels and trends in COPD possibly including exposure to particulates from biomass and coal fuels.[108–110] Relations might exist between exposure to respiratory infections as a child and adult COPD that can also alter secular trends.[111] Historical analysis, for example, for the UK and Australia also suggests that cause of death declined from 1900 to 1940 then increased until the 1980s from rising tobacco consumption.[112,113] The same set of determinants that account for the downward trend in high-income countries could be occurring in Asia.

In a study covering 291 diseases and injuries, 1160 sequelae, 20 age groups, both sexes, and 21 regions, many limitations reflect the availability, representativeness, and broad quality of the data. It is beyond the scope of this summary article to describe all the specific limitations associated with data availability, efforts to enhance quality and comparability of data, and model specification for estimation. More detail is provided in accompanying articles on all-cause mortality, causes of death, disability weights, and YLDs.[3,11,90,92] Future cause-specific publications will also provide a forum for exploring disease or injury-specific limitations. More generally, we have tried for the first time to quantify uncertainty as a way to inform the user of the strength of the evidence on the burden of a given disease or injury. Relative uncertainty varies widely across causes. For example, only four studies are available on onchocercal skin disease but for epilepsy there are 353 studies. For some causes of death like ischaemic heart disease, the models have very small prediction error whereas for others like dengue or rabies it is very large. The width of the UIs is a useful guide to where the limitations of the analysis are greatest. Of course, we might be missing sources of uncertainty for some disease and injury sequelae. As with any systematic analysis, selection bias in data collection can lead to systematic biases in the results that are not reflected in the statistical UIs. In computing UIs, we assumed that uncertainty distributions for YLLs and YLDs were independent; this assumption, however, could be incorrect. Countries with poor data on mortality and causes of death might be more likely to have poor data on the prevalence of sequelae. Empirical information to establish the correlation, however, is extremely limited. If data quality between causes of death and prevalence are correlated, our UIs could be underestimated. For the YLD component, disability weights play a crucial role; to the extent that lay descriptions used in the measurement of disability weights do not reflect the average experience of an individual with a sequela then the YLDs could be overestimated or underestimated. The shift in burden towards YLDs from 1990 to 2010 is not a function of the disability weights because the same weights are used for computing 1990 and 2010 burden. However, since the disability weights for this study are on average somewhat lower than the GBD 1990 disability weights, this shift would have seemed greater with the older, larger weights. For the first time in the GBD study, we have taken into account comorbidity. These corrections have reduced the number of YLDs that would be estimated without taking into account comorbidity. Because of limitations of data, we have only been able to take into account independent comorbidity within an age-sex group.

The heterogeneity across the 21 regions in the burden of disease highlights how important it will be to make estimates at the national level. Two strategies exist for national estimation: using the information collected in the GBD 2010 to report national burden results, and national burden of disease studies that start with collection and analysis of all local sources. Both strategies are useful. The wealth of data on causes of death and within-region variation in prevalence of disease and injury sequelae can be used to generate informed national estimates building on the GBD 2010 results. These estimates can be immediately useful for enriching a range of national policy debates but can also serve as an informative starting point for an in-depth national burden of disease study. Many countries will also be keenly interested in estimating disease burden for subpopulations on the basis of geography, ethnic group, and socioeconomic status. Capacity and methods to undertake this type of analysis need to be created or strengthened through appropriate training. The new generation methods and standardisation of approaches will make it easier than in the past to undertake comparable, comprehensive, and consistent national assessments.

The results of the GBD study show a truism known to everyone trained in clinical practice that also applies to population health: that individuals and communities suffer from a wide range of disorders. Clinical subspecialties have emerged in modern medicine to deal with some of this complexity at the level of individual patients. One of the fundamental challenges for the global health system and for national health systems is responding to the diversity of urgent health needs for communities. The GBD study provides quantification of this diversity and reminds us that the organised social

response to health problems must deal with a wide array of medical and public health priorities for action. Regular updating of the GBD study is an important way that the world can track many different health problems without the risk of a limited set of temporary priorities capturing all of our attention. Regular updates would provide a mechanism both to assess the latest evidence but also to promote accountability of health systems for achieving reductions in the burden of disease. Furthermore, despite this complexity and diversity, important health challenges are readily identifiable for which technologies and knowledge exist to substantially reduce or eliminate their impact on burden of disease rankings. The sustained commitment of governments, donors, and the public health community to do so is crucial, on the basis of the essential health intelligence that regular burden of disease updates can provide.

Contributors

CJLM and ADL prepared the first draft. CJLM, TV, RL, MN, AF, CM, ME, KS, JS, and ADL finalised the draft based on comments from other authors and reviewer feedback. CJLM and ADL conceived the study and provided overall guidance. CJLM, TV, RL, MN, AF, CM, ME, KS, JS, and ADL oversaw the implementation of the work. All other authors developed cause-specific models, reviewed results, provided guidance on the selection of key covariates, and reviewed the manuscript.

Conflicts of interest

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References

1 Murray CJ, Salomon JA, Mathers CD, Lopez AD. Summary measures of population health: concepts, ethics, measurement and applications. Geneva: WHO, 2002.
2 Mathers CD, Sadana R, Salomon JA, Murray CJ, Lopez AD. Healthy life expectancy in 191 countries, 1999. *Lancet* 2001; **357:** 1685–91.
3 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.
4 Chamie M. What does morbidity have to do with disability? *Disabil Rehabil* 1995; **17:** 323–37.
5 Grosse SD, Lollar DJ, Campbell VA, Chamie M. Disability and disability-adjusted life years: not the same. *Public Health Rep* 2009; **124:** 197–202.
6 Leonardi M, Bickenbach J, Ustun TB, Kostanjsek N, Chatterji S, and the MHADIE Consortium. The definition of disability: what is in a name? *Lancet* 2006; **368:** 1219–21.
7 Thomas C. How is disability understood? An examination of sociological approaches. *Disabil Soc* 2004; **19:** 569–83.
8 Murray C, Evans D. Quantifying individual levels of health: definitions, concepts, and measurement issues. In: Health systems performance assessment: debates, methods and empiricism. Geneva: World Health Organization, 2003: 301–18.
9 Murray CJ, 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: Harvard School of Public Health on behalf of the World Health Organization and the World Bank, 1996.
10 Murray CJ, Lopez AD. Global Health Statistics: A compendium of incidence, prevalence and mortality estimates for over 200 conditions. Boston: Harvard School of Public Health on behalf of the World Health Organization and the World Bank, 1996.
11 Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease study. *Lancet* 1997; **349:** 1269–76.
12 Murray CJ, Lopez AD. Regional patterns of disability-free life expectancy and disability-adjusted life expectancy: Global Burden of Disease Study. *Lancet* 1997; **349:** 1347–52.
13 Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 1997; **349:** 1436–42.
14 Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997; **349:** 1498–504.
15 World Health Organization. The world health report 1999—making a difference. http://www.who.int/whr/1999/en/whr99_en.pdf (accessed July 9, 2012).
16 World Health Organization. The world health report 2000—health systems: improving performance. http://www.who.int/whr/2000/en/whr00_en.pdf (accessed July 9, 2012).
17 World Health Organization. The world health report 2001—mental health: new understanding, new hope. http://www.who.int/whr/2001/en/whr01_en.pdf (accessed June 25, 2012).
18 World Health Organization. The world health report 2002—reducing risks, promoting healthy life. http://www.who.int/whr/2002/en/whr02_en.pdf (accessed July 9, 2012).
19 World Health Organization. The world health report 2004—changing history http://www.who.int/whr/2002/en/whr02_en.pdf (accessed July 9, 2012).
20 Lopez AD, Ahmad OB, Guillot M, et al. World mortality in 2000: life tables for 191 countries. Geneva: World Health Organization, 2002.
21 World Health Organization. Regional burden of disease estimates for 2004. http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html (accessed July 5, 2012).
22 World Bank. World Development Report 1993. Investing in health: world development indicators. Oxford: Oxford University Press, 1993.
23 Mathers CD, Vos ET, Stevenson CE, Begg SJ. The burden of disease and injury in Australia. *Bull World Health Organ* 2001; **79:** 1076–84.
24 Mathers CD, Vos ET, Stevenson CE, Begg SJ. The Australian Burden of Disease Study: measuring the loss of health from diseases, injuries and risk factors. *Med J Aust* 2000; **172:** 592–96.
25 Begg SJ, Vos T, Barker B, Stanley L, Lopez AD. The burden of disease and injury in Australia in the new millennium: measuring health loss from diseases, injuries and risk factors. *Med J Aust* 2008; **188:** 36–40.
26 Gadelha AMJ, Leite I da C, Valente JG, Schramm JM de A, Portela MC, Campos MR. Projeto Carga de Doenca: relatorio final do projeto—estimativa da carga de doenca do Brasilù, 1998. http://www.scribd.com/doc/2350704/Projeto-Carga-de-Doenca-Fiocruz (accessed June 26, 2012).

27 Concha Barrientos M, Aguilera Sanhueza X, Salas Vergara J. Estudio de Carga de Enfermedad, Informe final. Estudio Prioridades de Inversión en Salud. República de Chile: Ministerio de Salud, 1996.

28 Ministerio de Salud. Estudio de carga de enfermedad y carga atribuible, Chile. Informe Final. Chile: Ministerio de Salud, 2007.

29 Escobar M, Gallardo H, Giraldo G, Londoño J, Rodríguez J. La carga de la enfermedad en Colombia. Santa Fé: Ministerio de Salud de Bogotá, 1994.

30 Rodríguez J, Gallardo H. Carga Global de Enfermedad. Colombia, 1985–1995. República de Colombia: Ministerio de Salud, Imprenta Nacional, 2000.

31 Rodríguez J, Peñaloza E, Acosta N. Carga de Enfermedad Colombia. Resultados alcanzados. Bogotá: Pontifica Universidad Javeriana. Centro de Proyectos para el Desarrollo, 2008.

32 Ministerio de Salud de Costa Rica. Medición de la carga de enfermedad en Costa Rica, 2005. En: Programa de Desarrollo del Sector Salud. Componente Fortalecimiento Institucional del Ministerio de Salud. Costa Rica: Ministerio de Salud, 2008.

33 Seuc AH, Domínguez E. Evolution of disease mortality burden in Cuba: 1990-2005. *Cad Saude Publica* 2010; **26:** 615–23.

34 Lozada P, Aguinaga L, Páez R, Olmedo C, Pozo A. El Peso de la Enfermedad en el Ecuador. Quito: Partnerships for Health Reform, 1999.

35 Fouad D, El-Essawy OM. Egypt disability-adjusted life years and life expectation models and human development. EcoMod2007 Conference, 2007. http://www.ecomod.net/sites/default/files/document-conference/ecomod2007/18.doc (accessed July 27, 2012).

36 Lai T, Habicht J, Kiivet R-A. Measuring burden of disease in Estonia to support public health policy. *Eur J Public Health* 2009; **19:** 541–47.

37 Highlights on health in Estonia 2005. Estonia, WHO Country Office: World Health Organization, 2006.

38 Lapostolle A, Lefranc A, Gremy I, Spira A. Sensitivity analysis in summary measure of population health in France. *Eur J Public Health* 2008; **18:** 195–200.

39 Hyder AA, Rotllant G, Morrow RH. Measuring the burden of disease: healthy life-years. *Am J Public Health* 1998; **88:** 196–202.

40 NCMH Background Papers—Burden of Disease in India. New Delhi: Ministry of Health & Family Welfare, 2005.

41 Kosen S, Sidharta Y. Estimation of national burden of disease in Indonesia: a challenge of epidemiological transition. Jakarta: Health Services Research and Development Center, National Institute of Health Research and Development, Ministry of Health, 1998.

42 Mariotti S, D'Errigo P, Mastroeni S, Freeman K. Years of life lost due to premature mortality in Italy. *Eur J Epidemiol* 2003; **18:** 513–21.

43 Ikeda S, Tabata K. Estimation of disability-adjusted life years (DALYs) in Japan using a simplified method. *J Health Care Soc* 1998; **8:** 83–99.

44 Fukuda Y, Hasegawa T, Yatsuya H, Tabata K. Disease burden and disability-adjusted life years (DALYs) in Japan. *J Health Welfare Stat* 1999; **46:** 28–33.

45 Yoon S-J, Bae S-C, Lee S-I, et al. Measuring the burden of disease in Korea. *J Korean Med Sci* 2007; **22:** 518–23.

46 Oh IH, Yoon SJ, Kim EJ. The burden of disease in Korea. *J Korean Med Assoc* 2011; **54:** 646–52.

47 Bowie C. The burden of disease in Malawi. *Malawi Med J* 2007; **18:** 104–10.

48 Yusoff AF, Mustafa AN, Kaur GK, et al. Malaysian Burden of Disease and Injury Study. http://espace.uq.edu.au/view/UQ:172329 (accessed June 26, 2012).

49 Stevens G, Dias RH, Thomas KJA, et al. Characterizing the epidemiological transition in Mexico: national and subnational burden of diseases, injuries, and risk factors. *PLoS Med* 2008; **5:** e125.

50 Lozano R, Gómez-Dantés H, Franco M, Rodríguez A. Carga de la enfermedad en municipios urbanos marginados, México 2004–2008, BID, Observatorio de la Salud para América Latina y el Caribe. México: Funsalud, 2009.

51 Lozano R. El peso de la enfermedad en México: avances y desafíos. In: Observatorio de la Salud. Necesidades, servicios y políticas. México: Funsalud, 1997: 23–61.

52 Lozano R, Murray CJL, Frenk J, Bobadilla J-L. Burden of disease assessment and health system reform: results of a study in Mexico. *J Int Dev* 1995; **7:** 555–63.

53 Dgedge M, Novoa A, Macassa G, et al. The burden of disease in Maputo City, Mozambique: registered and autopsied deaths in 1994. *Bull World Health Organ* 2001; **79:** 546–52.

54 Melse JM, Essink-Bot ML, Kramers PG, Hoeymans N, and the Dutch Burden of Disease Group. A national burden of disease calculation: Dutch disability-adjusted life-years. *Am J Public Health* 2000; **90:** 1241–47.

55 Ministry of Health. The burden of disease and injury in New Zealand—Public Health Intelligence Occasional Bulletin No. 1. New Zealand: Ministry of Health, 2001.

56 Hyder AA, Morrow RH. Applying burden of disease methods in developing countries: a case study from Pakistan. *Am J Public Health* 2000; **90:** 1235–40.

57 Velásquez Valdivia A. Análisis del Estudio de Carga de Enfermedad en el Perú-MINSA 2004 y Propuesta Metodológica para el Ajuste con Datos Nacionales de Morbilidad. Lima: Promoviendo alianzas y estrategias, Abt Associates Inc, 2006.

58 de Salud M. Estudio de Carga de Enfermedad en el Perú, 2004. Lima, Perú: DGE, 2006.

59 Janković S, Vlajinac H, Bjegović V, et al. The burden of disease and injury in Serbia. *Eur J Public Health* 2007; **17:** 80–85.

60 Phua HP, Chua AV, Ma S, Heng D, Chew SK. Singapore's burden of disease and injury 2004. *Singapore Med J* 2009; **50:** 468–78.

61 Bradshaw D, Groenewald P, Laubscher R, et al. Initial burden of disease estimates for South Africa, 2000. *S Afr Med J* 2003; **93:** 682–88.

62 Norman R, Bradshaw D, Schneider M, Pieterse D, Groenewald P. Revised burden of disease estimates for the comparative risk factor assessment, South Africa 2000. South African Medical Research Council, 2006.

63 Gènova-Maleras R, Alvarez-Martín E, Morant-Ginestar C, Fernández de Larrea-Baz N, Catalá-López F. Measuring the burden of disease and injury in Spain using disability-adjusted life years: an updated and policy-oriented overview. *Public Health* 2012; published online Oct 9. DOI:S0033-3506(12)00318-6.10.1016/j.puhe.2012.08.012.

64 Catalá López F, Alvarez Martín E, Gènova Maleras R, Morant Ginestar C. Relationship between research funding in the Spanish National Health System and the burden of disease. *Rev Esp Salud Publica* 2009; **83:** 137–51.

65 Peterson S, Backlund I, Diderichsen F. Sjukdomsbördan i Sverige: en svensk DALY-kalkyl [Burden of disease in Sweden—a Swedish DALY calculation]. Stockholm: National Public Health Institute, 1998.

66 Bundhamcharoen K, Odton P, Phulkerd S, Tangcharoensathien V. Burden of disease in Thailand: changes in health gap between 1999 and 2004. *BMC Public Health* 2011; **11:** 53.

67 Bundhamcharoen K, Teerawattananon Y, Vos T, Begg S. Thai Working Group on Burden of Disease and Injuries: burden of disease and injuries in Thailand: priority setting for policy. Thainland: Ministry of Public Health, 2002.

68 The Thai Working Group on Burden of Disease and Injury. Burden of disease for priority of health problems in Thailand 1999. *J Health Sci* 2004; **13:** 239–56.

69 Samutharuk B, Vecharuk P, Kongkamnerd R, Sitthiamorn C. Measurement of disease burden on Thai society: guideline of health problem prioritisation. Nonthaburi: Health System Research Institute, 1999.

70 Ministry of Health. Baskent University. Burden of disease final report. Ankara: Refik Saydam Hygiene Center Presidency Refik Saydam School of Public Health Directorate, 2004.

71 Green S, Miles R. The burden of disease and illness in the UK: a preliminary assessment to inform the development of UK health research and development priorities. Oxford: Healthcare Associates, 2007.

72 Michaud CM, McKenna MT, Begg S, et al. The burden of disease and injury in the United States 1996. *Popul Health Metr* 2006; **4:** 11.

73 McKenna MT, Michaud CM, Murray CJL, Marks JS. Assessing the burden of disease in the United States using disability-adjusted life years. *Am J Prev Med* 2005; **28:** 415–23.

74 Viet Nam Burden of Disease and Injury Study 2008. Viet Nam burden of disease and injury study 2008. Hanoi: Medical Publishing House, 2011.

75 Chapman G, Hansen KS, Jelsma J, et al. The burden of disease in Zimbabwe in 1997 as measured by disability-adjusted life years lost. *Trop Med Int Health* 2006; **11:** 660–71.

76 Schopper D, Pereira J, Torres A, et al. Estimating the burden of disease in one Swiss canton: what do disability adjusted life years (DALY) tell us? *Int J Epidemiol* 2000; **29:** 871–77.

77 Kominski GF, Simon PA, Ho A, Luck J, Lim Y-W, Fielding JE. Assessing the burden of disease and injury in Los Angeles County using disability-adjusted life years. *Public Health Rep* 2002; **117:** 185–91.

78 Zhou S-C, Cai L, Wan C-H, Lv Y-L, Fang P-Q. Assessing the disease burden of Yi people by years of life lost in Shilin county of Yunnan province, China. *BMC Public Health* 2009; **9:** 188.

79 Friedman C, McKenna MT, Ahmed F, et al. Assessing the burden of disease among an employed population: implications for employer-sponsored prevention programs. *J Occup Environ Med* 2004; **46:** 3–9.

80 Hsairi M, Fekih H, Fakhfakh R, Kassis M, Achour N, Dammak J. Années de vie perdues et transition épidémiologique dans le gouvernorat de Sfax (Tunisie). *Sante Publique* 2003; **15:** 25–37.

81 Dodhia H, Phillips K. Measuring burden of disease in two inner London boroughs using Disability Adjusted Life Years. *J Public Health (Oxf)* 2008; **30:** 313–21.

82 Prince M, Patel V, Saxena S, et al. No health without mental health. *Lancet* 2007; **370:** 859–77.

83 Polinder S, Haagsma JA, Lyons RA, et al. Measuring the population burden of fatal and nonfatal injury. *Epidemiol Rev* 2012; **34:** 17–31.

84 Mathers CD, Ezzati M, Lopez AD. Measuring the burden of neglected tropical diseases: the global burden of disease framework. *PLoS Negl Trop Dis* 2007; **1:** e114.

85 Mathur P, Shah B. Research priorities for prevention and control of noncommunicable diseases in India. *Indian J Community Med* 2011; **36** (suppl 1): S72–77.

86 Murray CJL, Ezzati M, Flaxman AD, et al. The Global Burden of Disease Study 2010: design, definitions, and metrics. *Lancet* 2012; **380:** 2063–66.

87 Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ, eds. Global burden of disease and risk factors. Washington, DC: Oxford University Press and The World Bank, 2006.

88 Naghavi M, Makela S, Foreman K, O'Brien J, Pourmalek F, Lozano R. Algorithms for enhancing public health utility of national causes-of-death data. *Popul Health Metr* 2010; **8:** 9.

89 Ahern RM, Lozano R, Naghavi M, Foreman K, Gakidou E, Murray CJ. Improving the public health utility of global cardiovascular mortality data: the rise of ischemic heart disease. *Popul Health Metr* 2011; **9:** 8.

90 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.

91 King G, Tomz M, Wittenberg J. Making the most of statistical analyses: improving interpretation and presentation. *Am J Pol Sci* 2000; **44:** 347–61.

92 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.

93 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.

94 Murray CJL, Rosenfeld LC, Lim SS, et al. Global malaria mortality between 1980 and 2010: a systematic analysis. *Lancet* 2012; **379:** 413–31.

95 Frenk J, Chen L, Bhutta ZA, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. *Lancet* 2010; **376:** 1923–58.

96 Yelin E, Callahan LF, Group TNADW, and the National Arthritis Data Work Groups. The economic cost and social and psychological impact of musculoskeletal conditions. *Arthritis Rheum* 1995; **38:** 1351–62.

97 Coyte PC, Asche CV, Croxford R, Chan B. The economic cost of musculoskeletal disorders in Canada. *Arthritis Care Res* 1998; **11:** 315–25.

98 Peden M, Scurfield R, Sleet D, et al. World report on road traffic injury prevention. Geneva: World Health Organization, 2004.

99 Hyder AA, Allen KA, Di Pietro G, et al. Addressing the implementation gap in global road safety: exploring features of an effective response and introducing a 10-country program. *Am J Public Health* 2012; **102:** 1061–67.

100 World Health Organization, and the United Nations Road Safety Collaboration. http://www.who.int/roadsafety/en/ (accessed June 28, 2012).

101 United Nations. The United Nations and Road Safety. http://www.un.org/en/roadsafety/background.shtml (accessed June 28).

102 Reiss A, Roth J, eds. Violence in families: understanding and preventing violence. Panel on the understanding and control of violent behavior. Washington, DC: National Academy Press, 1993.

103 Carp FM. Elder abuse in the family: an interdisciplinary model for research. New York: Springer, 2000.

104 Schiamberg LB, Gans D. An ecological framework for contextual risk factors in elder abuse by adult children. *J Elder Abuse Negl* 1999; **11:** 79–103.

105 Heise LL. Violence against women: an integrated, ecological framework. *Violence Against Women* 1998; **4:** 262–90.

106 Chalk RA, King P. Violence in families: assessing prevention and treatment programs. Washington, DC: National Academies Press, 1998.

107 World Health Organization. Violence prevention: the evidence, 2010 http://www.who.int/violence_injury_prevention/violence/4th_milestones_meeting/publications/en/ (accessed July 21, 2012).

108 Kurmi OP, Semple S, Simkhada P, Smith WCS, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. *Thorax* 2010; **65:** 221–28.

109 Hu G, Zhou Y, Tian J, et al. Risk of COPD from exposure to biomass smoke: a metaanalysis. *Chest* 2010; **138:** 20–31.

110 Marks G, Burney P. Diseases of the respiratory system. In: The health of adult britain 1841–1994. London: HM Stationery Office, 1997.

111 Hurley SF, Matthews JP. The Quit Benefits Model: a Markov model for assessing the health benefits and health care cost savings of quitting smoking. *Cost Eff Resour Alloc* 2007; **5:** 2.

112 Logan WPD. Mortality in England and Wales from 1848 to 1947. *Popul Stud* 1950; **4:** 132–78.

113 Adair T, Hoy D, Dettrick Z, Lopez AD. 100 years of Chronic Obstructive Pulmonary Disease (COPD) mortality in Australia: the role of tobacco consumption. *Int J Tuberc Lung Dis* 2012; **16:** 1699–705.

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

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Summary

Background Reliable and timely information on the leading causes of death in populations, and how these are changing, is a crucial input into health policy debates. In the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010), we aimed to estimate annual deaths for the world and 21 regions between 1980 and 2010 for 235 causes, with uncertainty intervals (UIs), separately by age and sex.

Methods We attempted to identify all available data on causes of death for 187 countries from 1980 to 2010 from vital registration, verbal autopsy, mortality surveillance, censuses, surveys, hospitals, police records, and mortuaries. We assessed data quality for completeness, diagnostic accuracy, missing data, stochastic variations, and probable causes of death. We applied six different modelling strategies to estimate cause-specific mortality trends depending on the strength of the data. For 133 causes and three special aggregates we used the Cause of Death Ensemble model (CODEm) approach, which uses four families of statistical models testing a large set of different models using different permutations of covariates. Model ensembles were developed from these component models. We assessed model performance with rigorous out-of-sample testing of prediction error and the validity of 95% UIs. For 13 causes with low observed numbers of deaths, we developed negative binomial models with plausible covariates. For 27 causes for which death is rare, we modelled the higher level cause in the cause hierarchy of the GBD 2010 and then allocated deaths across component causes proportionately, estimated from all available data in the database. For selected causes (African trypanosomiasis, congenital syphilis, whooping cough, measles, typhoid and parathyroid, leishmaniasis, acute hepatitis E, and HIV/AIDS), we used natural history models based on information on incidence, prevalence, and case-fatality. We separately estimated cause fractions by aetiology for diarrhoea, lower respiratory infections, and meningitis, as well as disaggregations by subcause for chronic kidney disease, maternal disorders, cirrhosis, and liver cancer. For deaths due to collective violence and natural disasters, we used mortality shock regressions. For every cause, we estimated 95% UIs that captured both parameter estimation uncertainty and uncertainty due to model specification where CODEm was used. We constrained cause-specific fractions within every age-sex group to sum to total mortality based on draws from the uncertainty distributions.

Findings In 2010, there were 52·8 million deaths globally. At the most aggregate level, communicable, maternal, neonatal, and nutritional causes were 24·9% of deaths worldwide in 2010, down from 15·9 million (34·1%) of

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

See Special Report page 2067

See Articles pages 2071, 2129, 2144, 2163, 2197, and 2224

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See Online for appendix

For **interactive versions of figures 1, 4, and 6–9** see http://healthmetricsandevaluation.org/gbd/visualizations/regional

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46·5 million in 1990. This decrease was largely due to decreases in mortality from diarrhoeal disease (from 2·5 to 1·4 million), lower respiratory infections (from 3·4 to 2·8 million), neonatal disorders (from 3·1 to 2·2 million), measles (from 0·63 to 0·13 million), and tetanus (from 0·27 to 0·06 million). Deaths from HIV/AIDS increased from 0·30 million in 1990 to 1·5 million in 2010, reaching a peak of 1·7 million in 2006. Malaria mortality also rose by an estimated 19·9% since 1990 to 1·17 million deaths in 2010. Tuberculosis killed 1·2 million people in 2010. Deaths from non-communicable diseases rose by just under 8 million between 1990 and 2010, accounting for two of every three deaths (34·5 million) worldwide by 2010. 8 million people died from cancer in 2010, 38% more than two decades ago; of these, 1·5 million (19%) were from trachea, bronchus, and lung cancer. Ischaemic heart disease and stroke collectively killed 12·9 million people in 2010, or one in four deaths worldwide, compared with one in five in 1990; 1·3 million deaths were due to diabetes, twice as many as in 1990. The fraction of global deaths due to injuries (5·1 million deaths) was marginally higher in 2010 (9·6%) compared with two decades earlier (8·8%). This was driven by a 46% rise in deaths worldwide due to road traffic accidents (1·3 million in 2010) and a rise in deaths from falls. Ischaemic heart disease, stroke, chronic obstructive pulmonary disease (COPD), lower respiratory infections, lung cancer, and HIV/AIDS were the leading causes of death in 2010. Ischaemic heart disease, lower respiratory infections, stroke, diarrhoeal disease, malaria, and HIV/AIDS were the leading causes of years of life lost due to premature mortality (YLLs) in 2010, similar to what was estimated for 1990, except for HIV/AIDS and preterm birth complications. YLLs from lower respiratory infections and diarrhoea decreased by 45–54% since 1990; ischaemic heart disease and stroke YLLs increased by 17–28%. Regional variations in leading causes of death were substantial. Communicable, maternal, neonatal, and nutritional causes still accounted for 76% of premature mortality in sub-Saharan Africa in 2010. Age standardised death rates from some key disorders rose (HIV/AIDS, Alzheimer's disease, diabetes mellitus, and chronic kidney disease in particular), but for most diseases, death rates fell in the past two decades; including major vascular diseases, COPD, most forms of cancer, liver cirrhosis, and maternal disorders. For other conditions, notably malaria, prostate cancer, and injuries, little change was noted.

Interpretation Population growth, increased average age of the world's population, and largely decreasing age-specific, sex-specific, and cause-specific death rates combine to drive a broad shift from communicable, maternal, neonatal, and nutritional causes towards non-communicable diseases. Nevertheless, communicable, maternal, neonatal, and nutritional causes remain the dominant causes of YLLs in sub-Saharan Africa. Overlaid on this general pattern of the epidemiological transition, marked regional variation exists in many causes, such as interpersonal violence, suicide, liver cancer, diabetes, cirrhosis, Chagas disease, African trypanosomiasis, melanoma, and others. Regional heterogeneity highlights the importance of sound epidemiological assessments of the causes of death on a regular basis.

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Introduction

Cause-specific mortality is arguably one of the most fundamental metrics of population health. The rates and numbers of people who die, where, at what age, and from what, is a crucial input into policy debates, planning interventions, and prioritising research for new health technologies. Trends in causes of death provide an important geographical summary of whether society is or is not making progress in reducing the burden of premature (and especially avoidable) mortality and where renewed efforts are needed. If a health information system is not providing timely and accurate information on causes of death by age and sex, major reforms are required to provide health planners with this essential health intelligence.

Despite the importance of tracking causes of death and the tradition since 1893 of standardisation of definitions and coding for causes of death in the International Classification of Diseases and Injuries (ICD), global assessments of causes of death are a major analytical challenge. Vital registration systems that include medical certification of the cause of death captured about 18·8 million deaths of an estimated annual total of 51·7 million deaths in 2005, which is the latest year for which the largest number of countries (100) reported deaths from a vital registration system. Even for these deaths, the comparability of findings on the leading causes of death is affected by variation in certification skills among physicians, the diagnostic and pathological data available at the time of completing a death certificate, variations in medical culture in choosing the underlying cause, and legal and institutional frameworks for governing mortality reporting.[1–5] For the remaining deaths that are not medically certified, many different data sources and diagnostic approaches must be used from surveillance systems, demographic research sites, surveys, censuses, disease registries, and police records to construct a consolidated picture of causes of death in various populations. Because of the variety of data sources and their associated biases, cause of death assessments are inherently uncertain and subject to vigorous debate.[6–8]

Efforts to develop global assessments for selected causes began in the 1980s.[9–11] These efforts were motivated partly because the sum of various disease-specific estimates substantially exceeded the estimated number of deaths in

the world, particularly for children.[12] Lopez and Hull[11] attempted to develop a set of estimates of mortality in children younger than 5 years (under-5 mortality) by cause consistent with all-cause mortality data in 1983. The Global Burden of Disease study 1990 (GBD 1990) was the first comprehensive attempt to do so, and included 134 causes covering all age groups. The GBD 1990 cause of death approach was applied with some refinements to yield estimates of causes of death for 1999, 2000, 2001, 2002, 2004, and 2008.[13–17] Over this period, special attention was paid to priority diseases such as malaria, HIV/AIDS, and tuberculosis. The Child Health Epidemiology Reference Group (CHERG) also produced estimates of under-5 mortality from 16 causes that summed to estimates of deaths in children younger than 5 years for 2000–03, 2008, and 2010,[18–20] partly using the GBD 1990 approach combined with other methods, and putting special emphasis on the use of verbal autopsy as a source of data in low-income settings. Additionally to these comprehensive approaches, the tradition of disease-specific analyses that began in the 1980s with global cancer mortality has continued and intensified. In the past 5 years, for example, articles and reports have been published on global mortality from maternal causes,[21–24] malaria,[25,26] tuberculosis,[27,28] HIV/AIDS,[29] road traffic accidents,[30] site-specific cancers,[31,32] and diabetes,[33] among others.[34,35] These assessments of individual causes are based on diverse epidemiological approaches of varying scientific rigour, and, moreover, are not constrained to sum to estimates of all-cause mortality from demographic sources.

Global cause of death assessments can be characterised in four dimensions: the universe of raw data identified and examined, efforts to evaluate and enhance quality and comparability of data, the statistical modelling strategy, and whether causes of death are constrained to sum to all-cause mortality. First, in terms of the universe of data, the various iterations of the GBD and CHERG analysis of deaths in children younger than 5 years have made substantial use of data on causes of death from systems that attempt to capture the event of death. Other single-cause analyses, such as the annual UNAIDS efforts to estimate HIV-related deaths, measles estimates,[34] the World Malaria Report,[26] the WHO Global TB Control Report,[28] and many others have used data on disease incidence or prevalence and on case-fatality rates combined in a model of natural history progression. Second, perhaps the area of greatest variation in the published studies is the efforts to assess and enhance the quality and comparability of available data. These efforts often include very specific steps undertaken for different data sources and are frequently poorly documented. Third, in the past two decades, efforts to develop statistical models for causes of death have become more sophisticated. Compositional models that estimate cause fractions for several causes at once were first applied to global health by Salomon and Murray[36] and have been used extensively by CHERG but only for a subset of causes. GBD revisions for 1999, 2000, 2001, 2002, 2004, and 2008 have used these compositional models to allocate deaths according to three broad cause groups: communicable, maternal, neonatal, and nutritional causes; non-communicable diseases; and injuries. More recently, the array of modelling strategies used for causes of death has been broadened to include spatial-temporal Gaussian process regression,[22,37] mixed effects hierarchical models, and ensemble models.[38] Given the profusion of statistical modelling options, an important innovation has been the reporting of out-of-sample predictive validity to document the performance of complex models.[22,38]

Finally, in view of the developments in the field of mortality and cause of death estimation, for the GBD 2010 we completely re-evaluated all aspects of the GBD analytical strategy, including demographic estimation of all-cause mortality.[39,40] Because of the huge increase in published verbal autopsy studies and the availability in the public domain of cause of death data from government vital registration sources (130 countries), the universe of data has expanded substantially. Assessing and enhancing the quality and comparability of data can now take into account time trends in cause of death data from 1980 to 2010 that provide important insights into changes in certification and coding. Borrowing from other scientific fields, we have changed our analytical approach (see below) to an ensemble modelling strategy to generate more realistic uncertainty intervals (UIs) and more accurate predictions.[38] These innovations have been used in estimating mortality for an expanded GBD 2010 cause list of 291 causes compared with 134 in the GBD 1990 Study; of the 291 causes, 235 are causes of mortality, whereas the remaining causes account for years lived with disability (YLDs) but not deaths. We use a unified framework for all causes such that the sum of cause-specific estimates equals the number of deaths from all causes in each country or region, period, age group, and sex. This creates a link between the systematic analysis of data on all-cause mortality reported by Wang and colleagues[40] and results by cause presented here. In this Article, we provide a summary overview of the vast array of data and methods that have gone into this revision of the GBD, as well as what we believe are the key global and regional findings of importance for health priority debates.

Methods

Some general aspects of the analytical framework such as the creation of the 21 GBD regions and the full hierarchical cause list including the mapping of the ICD to the GBD 2010 cause list are reported elsewhere.[39] Although results are reported in this Article at the regional level for 1990 and 2010, the cause of death analysis has been undertaken at the country level for 187 countries from 1980 to 2010. Use of longer time series improves the performance of many types of estimation models; data from before 1980, however, are much sparser for developing countries so we restricted the analysis to 1980–2010.

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