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CENTENNIAL REVIEW

Measuring the global burden of disease and epidemiological transitions: 2002–2030

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Any planning process for health development ought to be based on a thorough understanding of the health needs of the population. This should be sufficiently comprehensive to include the causes of premature death and of disability, as well as the major risk factors that underlie disease and injury. To be truly useful to inform health-policy debates, such an assessment is needed across a large number of diseases, injuries and risk factors, in order to guide prioritization. The results of the original Global Burden of Disease Study and, particularly, those of its 2000–2002 update provide a conceptual and methodological framework to quantify and compare the health of populations using a summary measure of both mortality and disability: the disability-adjusted life-year (DALY). Globally, it appears that about 56 million deaths occur each year, 10.5 million (almost all in poor countries) in children. Of the child deaths, about one-fifth result from perinatal causes such as birth asphyxia and birth trauma, and only slightly less from lower respiratory infections. Annually, diarrhoeal diseases kill over 1.5 million children, and malaria, measles and HIV/AIDS each claim between 500,000 and 800,000 children. HIV/AIDS is the fourth leading cause of death world-wide (2.9 million deaths) and the leading cause in Africa. The top three causes of death globally are ischaemic heart disease (7.2 million deaths), stroke (5.5 million) and lower respiratory diseases (3.9 million). Chronic obstructive lung diseases (COPD) cause almost as many deaths as HIV/AIDS (2.7 million). The leading causes of DALY, on the other hand, include causes that are common at young ages [perinatal conditions (7.1% of global DALY), lower respiratory infections (6.7%), and diarrhoeal diseases (4.7%)] as well as depression (4.1%). Ischaemic heart disease and stroke rank sixth and seventh, retrospectively, as causes of global disease burden, followed by road traffic accidents, malaria and tuberculosis. Projections to 2030 indicate that, although these major vascular diseases will remain leading causes of global disease burden, with HIV/AIDS the leading cause, diarrhoeal diseases and lower respiratory infections will be outranked by COPD, in part reflecting the projected increases in death and disability from tobacco use.

This is an era of increasing healthcare costs, numerous and diverse priorities, more sophisticated and informed health consumers, and increasing availability of better health technologies. Governments trying to maximize population health and reduce health inequalities are faced with ever-more critical decisions about their investments in the health sector. Decisions about health spending will always be influenced by a variety of considerations but one of them ought to be a good and comprehensive understanding of the legitimate health needs of the population. This, in turn, requires a detailed assessment of the leading causes of disease and injury burden in populations, incorporating both the causes of death and, particularly, those of premature death, as well as the main causes of (non-fatal) illness. Planning should also be guided by some vision of future health status, based upon accepted and defensible epidemiological methods.

Health planning and decision making also need to be guided by information on the

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availability of cost-effective interventions to reduce disease burden. This, in turn, is predicated on an assessment of the comparative magnitude of disease and injury burden. The first ever global assessment of disease and injury, the Global Burden of Disease (GBD) Study, was carried out by C. J. L. Murray and A. D. Lopez, in collaboration with a global network of over 100 scientists expert in various diseases and injuries (Murray and Lopez, 1996*a*, *b*, *c*). This study was undertaken for the World Bank's pioneering *Report on Investing in Health* (World Bank, 1993), which recommended cost-effective intervention packages for countries at different levels of development. The study not only generated the first comprehensive and consistent set of estimates of mortality and morbidity, split by age, gender and geographical region, but also introduced a new unit of measurement — the disability-adjusted life-year (DALY). The DALY allowed the burden of disease from premature mortality and that from the non-fatal consequences of over 100 diseases and injuries to be quantified simultaneously.

In recent years, the World Health Organization (WHO) has undertaken a progressive re-assessment of the GBD for the years 2000 to 2002, with consecutive revisions and updates published annually in the organization's *World Health Reports*. As in the original study, these updates drew on a wide range of data sources to develop internally consistent estimates of incidence, health-state prevalence, severity and duration, and mortality, for over 130 major causes and 17 sub-regions of the world (Mathers *et al.*, 2003). The participation of the WHO's various programmes in the development and finalization of these estimates, particularly those for the infectious and parasitic diseases, ensured that the estimates reflected all the information and knowledge available at the time.

For the original GBD study, a large volume of information on population health was analysed and synthesised to produce comprehensive and comparable information on the causes of loss of health — globally, regionally, and particularly for the low- and middle-income countries where there are considerable limitations of data availability and comparability. To ensure that the causes of the burdens for which there was very limited information were not implicitly considered to have zero burden (and hence ignored by the makers of health policy), the GBD study developed methods and approaches to make estimates even of the burdens for which there were limited data and considerable uncertainty (Murray *et al.*, 2003).

The basic philosophies guiding the GBD approach are (1) that there is likely to be useful information in almost all sources of health data (provided the data are carefully screened for plausibility and completeness) and (2) that internally consistent estimates of the global descriptive epidemiology of major conditions are possible, given the appropriate tools, investigator commitment and expert opinion. These philosophies remained central to the GBD updates for 2000–2002, which drew on new data and methods developed since the original GBD study.

This article provides a brief overview of the methods used in, and the results of, the updated GBD study for 2000–2002, with a focus on infectious and parasitic diseases. By providing some insight into how disease burden might change over the next 30 or so years, projection models based on the updated results can be used to detect epidemiological transition.

METHODS

In the original GBD study, a comprehensive framework for integrating, validating, analysing and disseminating the fragmented information on the health of populations, so that it becomes truly useful for health policy and planning, was developed (Murray and Lopez, 1996*a*, *c*, 1997*a*, *b*). Features of this framework included the

incorporation of data on non-fatal health outcomes into summary measures of population health, the development of methods and approaches to estimate missing data and to assess the reliability of data, and the use of a common unit of measurement (the DALY) to summarize the disease burden attributable to specific diseases and injuries and the relative importance of the major risk factors that cause those health outcomes.

The 2000–2002 GBD update incorporated a range of new data sources to develop internally consistent estimates of incidence, health-state prevalence, severity and duration, and mortality for 135 major causes, by gender and age-group. The new data sources and methods, which are documented in detail elsewhere (Ezzati *et al.*, 2004; Mathers *et al.*, 2006), are summarized below.

The Disability-adjusted Life-year (DALY)

The disability-adjusted life-year (DALY) is a health-gap measure that extends the concept of the potential years of life lost because of premature death to include equivalent years of 'healthy' life lost by virtue of being in a state of disability or poor health (Murray, 1996). It combines years of life lost because of premature death (YLL) and years of life lived with disabilities (YLD) into a single indicator, allowing an assessment of the total loss of health from different causes. One lost DALY can be thought of as one lost year of 'healthy' life, and the total number of DALY (i.e. the total burden of disease) as a measurement of the gap between the current health of a population and the ideal situation, where everyone in the population lives into old age, in full health.

YLL are calculated from the number of deaths at each age multiplied by a global standard life expectancy for the age at which death occurs. To estimate YLD for a particular cause in a particular time period, the number of incident cases in that period is multiplied by the mean duration of the disease and a weight factor that reflects the severity of the disease, on a scale from 0 (perfect health) to 1 (dead). The weights used in the 2000–2002 GBD updates are listed in detail elsewhere (Mathers *et al.*, 2006). Additionally, 3% time discounting and non-uniform age-weights, which give less weight to years lived at young and older ages, are used in calculating standard DALY. As a result, a death in infancy, for example, corresponds to 33 DALY whereas a death at an age between 5 and 20 years equates to approximately 36 DALY.

Analysis Categories

Diseases and injuries that cause death and burden of disease were classified using a tree structure that was based on the International Classification of Diseases (Murray and Lopez, 1996*c*). The highest level of aggregation consists of three broad cause groups: Group I (communicable, maternal, perinatal and nutritional conditions), Group II (non-communicable diseases), and Group III (injuries). The Group-I causes are those that typically decline at a faster pace than all-cause mortality during epidemiological transition, and occur largely in poor populations.

For each of the 135 disease and injury categories, incidence, prevalence and YLD were originally estimated for more than 500 disabling sequelae in 17 epidemiological regions, which were subdivisions of the six WHO regions (WHO, 2004). Subsequently, estimates were prepared for more homogeneous development regions, as defined by the World Bank and applied in the Disease Control Priorities Project (Jamison *et al.*, 2006). In this categorization, which has been used for the results presented here, high-income countries are treated as one group, with middle- and low-income countries being divided into six geographically contiguous regions (see Figure 1).

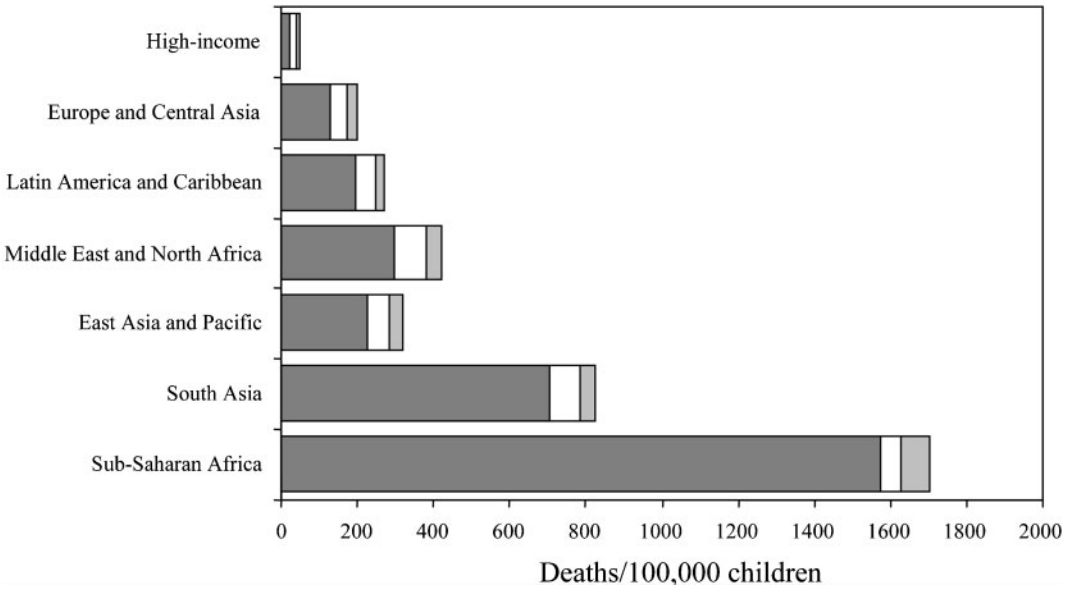

FIG. 1. The regional mortalities in 2002, from causes categorized as Group I (■), Group II (□) or Group III (■), among children aged 0–14 years.

Estimation of Mortality Levels and Causes of Death

Life tables specifying mortality rates by age and gender for 192 of the WHO's member states were developed for 2002, from the available death-registration data (112 states), sample registration systems (India and China), and data on child and adult mortality from censuses and surveys such as the Demographic and Health Surveys (DHS) and the Multiple Indicator Cluster Surveys (MICS) run by the United Nations Children's Fund (UNICEF). The methods used for each country were described by Lopez *et al.* (2002).

Death-registration data containing useable information on cause-of-death distributions were available for 107 countries, the majority of these in the high-income group, 'Latin America and the Caribbean' or 'Europe and Central Asia'. Population-based epidemiological studies, disease registers and notification systems (in excess of 2700 data-sets) also contributed to the estimation of mortality attributable to 21 specific communicable causes of death, including HIV/AIDS, malaria, tuberculosis, childhood immunisable diseases, schistosomiasis, and the African and American trypanosomiases. Almost a third of these data-sets related to sub-Saharan Africa.

In order to address the information gaps relating to other causes of death for the populations without useable death-registration data, models for estimating broad cause-of-death patterns based on the gross domestic product (GDP) and overall mortality levels were used. The approach to cause-of-death modelling used for the 1990 GBD study was substantially revised and enhanced for the 2000–2002 study, to estimate deaths by broad cause-group in regions with limited information on mortality (Salomon and Murray, 2002).

Data and Methods for the Estimation of YLD

Estimating YLD requires systematic assessments of the available evidence on incidence, prevalence, duration and severity of a wide range of conditions, often based on inconsistent, fragmented and partial data available from different studies. The data

sources used included disease registers, the results of epidemiological studies and health surveys, and health-facility data (where relevant). A specific software tool, DisMod, was developed to assist in the development of internally consistent estimates, by enforcing epidemiological consistency across incidence, prevalence, duration and mortality for each disease or injury (Barendregt *et al.*, 2003).

Mathers *et al.* (2006) estimated that around 8700 data-sets were used to quantify the YLD estimates for the 2000–2002 GBD, of which >7000 related to Group-I causes. One-quarter of the data-sets related to populations in sub-Saharan Africa, and around one-fifth to populations in high-income countries. Together with >1370 additional data-sets used for the estimation of YLL, the 2000–2002 GBD study incorporated information from over 10,000 data-sets relating to population health and mortality. This almost certainly represents the largest synthesis of global information on population health ever carried out.

The methods and data sources, for selected infectious and parasitic diseases, are briefly summarized below [more details can be found in Mathers *et al.* (2006)].

TUBERCULOSIS

The WHO's country-specific estimates of tuberculosis incidence, prevalence and mortality were used for most countries (Corbett *et al.*, 2003; WHO, 2003), together with analyses of the available death-registration data.

SEXUALLY-TRANSMITTED INFECTIONS

The results of >300 community- or prenatal-care-based studies on the prevalence and incidence of syphilis, chlamydia and gonorrhea were used to generate corresponding, region-specific estimates (Gerbase *et al.*, 1998; WHO, 2001).

HIV/AIDS

The country-specific estimates of HIV/AIDS prevalence and incidence produced by the Joint United Nations Programme on HIV/AIDS (UNAIDS) or the WHO were used for most countries (Walker *et al.*, 2003), together with analyses of the available death-registration data.

DIARRHOEAL DISEASES

The results of 357 community-based studies and population surveys were used to estimate the incidence of episodes of diarrhoeal disease among children aged <5 years (Bern, 2004). Mortality estimates were derived from regression analyses of the data from >60 community-based studies carried out since 1980 (Boschi-Pinto and Velebit, 2004).

VACCINE-PREVENTABLE CHILDHOOD DISEASES

For the countries that achieve a low (<80%) coverage with their programmes of routine vaccination against measles, data on measles incidence were derived using country-specific reports of vaccine coverage and the attack frequencies estimated in population-based studies (Crowcroft *et al.*, 2003). For countries with higher routine coverage and in the elimination phase, case notifications and country-specific correction factors were used.

Incidences of pertussis and the related mortality were estimated using a natural-history model, reported vaccine coverages, and the levels of age-specific case fatality recorded in community-based studies (Crowcroft *et al.*, 2003).

Incidence estimates for polio and diphtheria were based on country-specific notifications, with adjustments for under-reporting (Stein, 2002*b*; Stein and Robertson, 2002).

HEPATITIS B AND C

The available data on the prevalences of chronic hepatitis B and of infection with the hepatitis C virus were used, together with disease models, to estimate regional incidence and mortality (Anon., 2004; Lavanchy, 2004; WHO, 2002*a*, *b*).

MALARIA

For sub-Saharan Africa, country-specific estimates of malaria-attributable mortality were based on the results of the analyses by Snow *et al.* (1999), updated using the most recent geographical distributions of risks from the Mapping Malaria Risks in Africa International Collaboration.

SCHISTOSOMIASIS

Estimates of the regional prevalences of schistosomiasis (Doumenge *et al.*, 1987; Murray and Lopez, 1996*b*) were updated using country-specific estimates of the populations at risk in 2001 (Van der Werf and de Vlas, 2001).

LYMPHATIC FILARIASIS

The original GBD estimates for lymphatic filariasis (Murray and Lopez, 1996*b*) were updated using country-specific estimates of the populations at risk in 2001, which were provided by the WHO's Lymphatic Filiariasis Elimination Programme.

ONCHOCERCIASIS

Prevalence of blindness from onchocerciasis was re-estimated from the available results of prevalence studies and overall blindness surveys, taking into account the declining trends in prevalence and the coverage and duration of onchocerciasis-control programmes (Alley *et al.*, 2001; Richards *et al.*, 2001; Shibuya and Ezzati, 2003).

LEPROSY

Regional incidences and prevalences of leprosy were based on case reporting and the results of surveillance by 120 of the WHO's member states (Stein, 2002*a*; WHO, 2002*c*).

DENGUE AND DENGUE HAEMORRHAGIC FEVER

For dengue and dengue haemorrhagic fever, regional estimates of incidences and prevalences were based on a review of the results of nearly 300 population-based studies, but data were sparse for regions apart from 'East Asia and the Pacific' and 'Latin America and the Caribbean' (LeDuc *et al.*, 2004).

TRACHOMA

The baseline regional and subregional prevalences of blinding trachoma were first estimated as described elsewhere (Frick *et al.*, 2003; Ranson and Evans, 1995) and then updated using the data collected during several recent population-based studies in sub-Saharan Africa, the Middle East and North Africa (Shibuya and Mathers, 2003).

INTESTINAL NEMATODE INFECTIONS

Updated estimates of the prevalences of intestinal nematode infections were based on the WHO's new global databank on schistosomiasis and soil-transmitted helminths, which contains data derived from community-based, cross-sectional surveys, for subnational administrative regions (Brooker *et al.*, 2000; De Silva *et al.*, 2003). In areas without comprehensive data, predictions of the distribution of soil-transmitted helminths were developed using environmental data derived from satellite remote sensing (Brooker *et al.*, 2002). Incidences and the YLD for the disabling sequelae of helminth infections were estimated using a mathematical model developed by M. S. Chan and others (Chan, 1997; Bundy *et al.*, 2004).

LOWER RESPIRATORY INFECTIONS

The results published since 1980 of community-based studies that had run for at least 1 year were used to estimate the proportional mortality from acute respiratory infections among children aged <5 years, in developing countries (Williams *et al.*, 2002). Estimates of the prevalences and incidences of lower respiratory infections were based on an analysis of data on

the incidence of clinical pneumonia, which came from 95 community-based studies and had been published since 1961 (Rudan *et al.*, 2004).

RESULTS

Global and Regional Mortality in 2002

Slightly over 57 million people died in 2002, 10.5 million (or nearly 20%) of whom were children younger than 5 years of age. Almost all (99%) of these child deaths occurred in low- or middle-income countries. In addition, 30% of all the deaths in the low- and middle-income countries but only 15% of those in the high-income countries occurred at the ages of 15–59 years. The causes of death in 'middle' age, as well as in childhood, are thus important in assessing public-health priorities.

World-wide, one death in every three that occurred in 2002 was from a Group-I cause (i.e. communicable disease, a maternal or perinatal condition, or a nutritional deficiency). This proportion remains almost unchanged from 1990, with one major difference. Whereas HIV/AIDS accounted for only 2% of the Group-I deaths in 1990, it accounted for 14% in 2002. Excluding HIV/AIDS, Group-I deaths have fallen from one-third of all deaths in 1990 to less than one-fifth of all deaths in 2002. Virtually all of the Group-I deaths are in low- and middle-income countries. Mortality attributable to several of the 'traditional' infectious diseases, such as tuberculosis and malaria, did not decline between 1990 and 2002, in part because of weak public-health services and the increasing numbers of people with immune systems weakened by HIV/AIDS.

The extent of the global inequalities in health is illustrated by the large variations in the levels of mortality among young children. Based on the estimates for 2002, the risk of a child dying before the age of 5 years ranges from 17% in sub-Saharan Africa to just 0.7% in the high-income countries. If all countries had the Japanese level of child mortality, which is the lowest in the world, the annual number of child deaths would fall by 90%, to around 1 million. Of all global deaths among children under the age of 5 years, 83% occur in low-income countries and 60% of these can be attributed to just seven preventable conditions — malaria, measles, pertussis, HIV/AIDS, pneumonia, diarrhoeal diseases, and tetanus. A further 23% of these deaths are attributable to causes arising in the perinatal period or to protein-energy malnutrition. The Group-I causes dominate the pattern of child deaths in all regions but especially those in sub-Saharan Africa and South Asia (Fig. 1).

In South Asia and sub-Saharan Africa, fewer than half of the deaths in adults aged 15–59 years are caused by Group-II conditions, and Group-I causes, including HIV/AIDS, remain responsible for one-third and two-thirds of the deaths in this age-group, respectively (Fig. 2). In most developing countries, however, Group-II causes (i.e. non-communicable diseases) are now responsible for $>50\%$ of deaths in the adults aged 15–59 years (Fig. 2). In other words, the epidemiological transition is already well established in most developing countries, and is of major concern for health planning.

Figure 3, which shows the leading causes of deaths and of YLL, highlights the importance of considering the age at which death occurs when interpreting mortality data for policy-making. Although causes such as ischaemic heart disease, cerebrovascular disease and chronic obstructive lung diseases (COPD) are among the leaders in terms of the numbers of deaths, they are ranked much lower in terms of YLL. The converse is true of lower respiratory infections, perinatal conditions such as birth asphyxia and birth trauma, HIV/AIDS, diarrhoeal diseases, measles and malaria, which mostly claim young lives. Compared with simple numbers of deaths, YLL are a much better reflection of the social priorities for avoiding premature death.

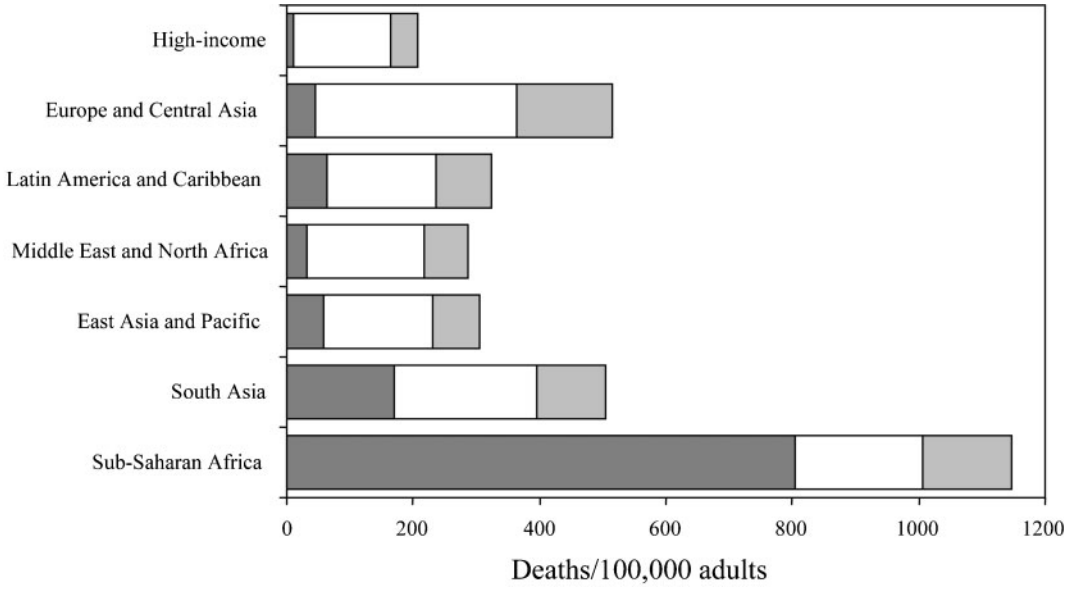

FIG. 2. The regional mortalities in 2002, from causes categorized as Group I (■), Group II (□) or Group III (■), among adults aged 15–59 years.

The leading causes of death in 2002 are shown in Table 1. The extent of the epidemiological transition world-wide is reflected in the dominant role of ischaemic heart disease and stroke (cerebrovascular disease) as the leading killers world-wide, together accounting for >20% of all deaths. HIV/AIDS is estimated to have killed almost 3 million people in 2002, slightly more than COPD. Major communicable diseases, such as lower respiratory infections, diarrhoeal diseases and tuberculosis, are among the top 10 causes of death, as are road traffic accidents and lung cancer.

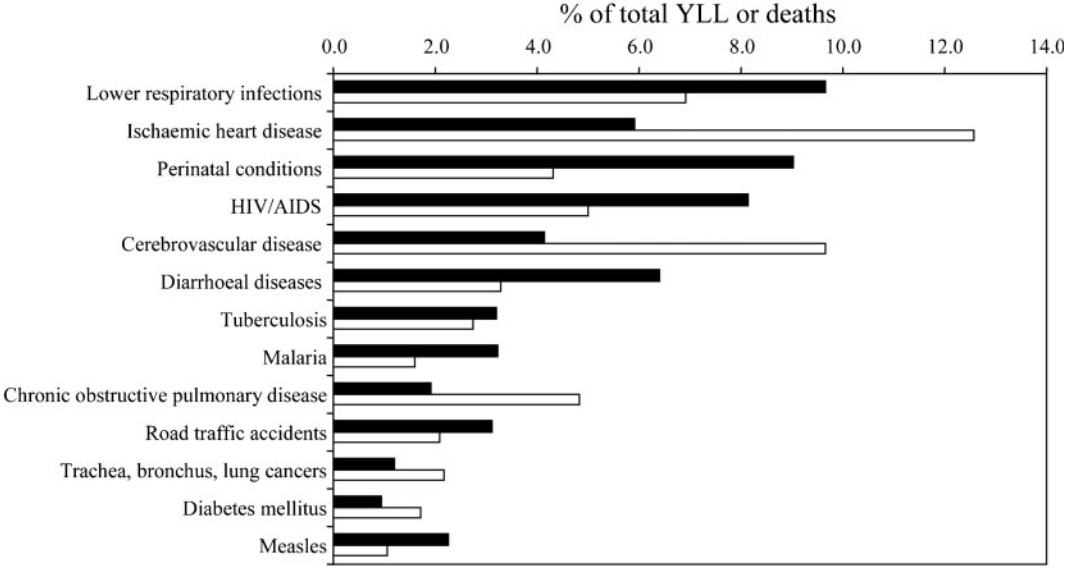

FIG. 3. The leading causes of years of life lost (YLL; ■) and of all deaths (□) world-wide in 2002.

TABLE 1. *The 15 leading causes of death world-wide in 2002*

Rank	Cause	Total deaths(millions)	% of all deaths
	All	57.01	100.0
1	Ischaemic heart disease	7.20	12.6
2	Cerebrovascular disease	5.50	9.7
3	Lower respiratory infections	3.94	6.9
4	HIV/AIDS	2.85	5.0
5	Chronic obstructive pulmonary disease	2.75	4.8
6	Perinatal conditions	2.46	4.3
7	Diarrhoeal diseases	1.87	3.3
8	Tuberculosis	1.56	2.7
9	Trachea, bronchus, lung cancers	1.24	2.2
10	Road traffic accidents	1.19	2.1
11	Diabetes mellitus	0.98	1.7
12	Malaria	0.91	1.6
13	Hypertensive heart disease	0.91	1.6
14	Suicide	0.87	1.5
15	Stomach cancer	0.85	1.5

Table 2 lists the leading causes of child deaths at ages 0–14 years (mostly below the age of 5 years). Apart from those with perinatal causes and the congenital abnormalities, most of such deaths are the result of communicable diseases and are largely preventable. Interestingly, road traffic accidents are the 10th leading cause of child deaths world-wide, something rarely appreciated by health departments.

Leading Causes of Disability

The results of the original GBD study brought the previously largely ignored burden of non-fatal illnesses, particularly mental disorders, to the attention of the makers of health policy. The findings of the 2000–2002 GBD study, based on updated data and analyses, confirm that disability and states of less than full health, caused by diseases and injuries, play a central role in determining the overall health status of populations in all regions of the world.

The overall burden of non-fatal disabling conditions is dominated by a relatively short list of causes — neuro–psychiatric conditions, vision disorders, hearing loss, and alcohol-use disorders. In all regions, neuro–psychiatric conditions are the most important causes of disability, accounting for $>37\%$ of YLD among adults aged $\geqslant 15$ years. Although the disabling burden of

TABLE 2. *The 10 leading causes of death among children aged 0–14 years, world-wide, in 2002*

Rank	Cause	Total deaths (millions)	% of all deaths
	All	11.92	100.0
1	Perinatal conditions	2.46	20.6
2	Lower respiratory infections	2.08	17.5
3	Diarrhoeal diseases	1.69	14.1
4	Malaria	0.83	7.0
5	Measles	0.60	5.1
6	HIV/AIDS	0.45	3.8
7	Congenital anomalies	0.45	3.7
8	Pertussis	0.29	2.5
9	Tetanus	0.20	1.7
10	Road traffic accidents	0.18	1.5

these conditions is almost the same for males and females, the major contributing causes are different. Depression, for example, is the leading cause of the neuropsychiatric disability seen in both males and females but the burden of depression is 50% higher for females than males, and females also have higher burdens from anxiety disorders, migraine and senile dementias. In contrast, the male burden for alcohol- and drug-use disorders is nearly six times higher than that for females, and accounts for one-quarter of the male neuropsychiatric burden.

Surprisingly, >80 percent of global non-fatal health outcomes occur in developing countries. Nearly half of all YLD arise as the result of diseases and injuries in the poorest (developing, high-mortality) countries. Although the prevalence of disabling conditions such as dementia and musculoskeletal disease is higher in countries with relatively long life expectancies, this is offset by lower contributions to disability from conditions such as cardiovascular disease, chronic respiratory diseases and the long-term sequelae of communicable diseases and nutritional deficiencies. In other words, people living in developing countries not only have lower life expectancies (i.e. a higher risk of premature death) than those in developed countries but also live a higher proportion of their lives in poor health.

The Burden of Diseases and Injuries

In indicating the importance of including non-fatal outcomes in a comprehensive assessment of global population health, the GBD results for 2002 reinforce the conclusions of the original GBD study. They have also confirmed the growing importance of non-communicable diseases in low- and middle-income countries. The results also highlight important changes in population health in some regions since 1990, as discussed below.

HIV/AIDS is now the third leading cause of disease burden globally (Table 3). In sub-Saharan Africa it is the leading cause, followed by malaria, and seven other Group-I causes appear in the top 10 causes for this region (Table 4). Between 1990 and 2002, the epidemiological transition in low- and middle-income countries resulted in a 20% reduction in the per-capita disease burden due to Group-I causes. Without the HIV/AIDS epidemic, and the associated lack of decline in the tuberculosis burden,

TABLE 3. *The 10 leading causes of the burden of disease, measured in disability-adjusted life-years (DALY), in low-, middle- and high-income countries in 2002*

Low- and middle-income countries				High-income countries			
Rank	Cause	DALY (millions)	% of all DALY	Rank	Cause	DALY (millions)	% of all DALY
1	Perinatal conditions	96.8	7.1	1	Unipolar depressive disorders	10.6	9.0
2	Lower respiratory infections	92.2	6.7	2	Ischaemic heart disease	7.5	6.4
3	HIV/AIDS	81.8	6.0	3	Cerebrovascular disease	5.7	4.8
4	Diarrhoeal diseases	64.4	4.7	4	Alcohol-use disorders	5.5	4.6
5	Unipolar depressive disorders	56.5	4.1	5	Alzheimer and other dementias	4.1	3.5
6	Ischaemic heart disease	51.6	3.8	6	Hearing loss, adult onset	4.0	3.4
7	Cerebrovascular disease	43.7	3.2	7	Chronic obstructive pulmonary disease	3.9	3.3
8	Road traffic accidents	35.2	2.6	8	Trachea, bronchus, lung cancers	3.5	3.0
9	Malaria	34.8	2.5	9	Diabetes mellitus	3.1	2.6
10	Tuberculosis	34.5	2.5	10	Road traffic accidents	3.1	2.6

this reduction would have been substantially greater — closer to 30%.

The per-capita disease burden in 'Europe and Central Asia' increased by nearly 40% between 1990 and 2002. This change is largely a reflection of the substantial increases seen in adult-male mortality and disability in 'Europe and Central Asia' in the 1990s, which have produced the greatest male–female differential in disease burden in the world (Lopez *et al.*, 2002). A significant factor in this trend is thought to be increasing alcohol abuse, particularly among males, which has led to high incidences of accidents, violence and cardiovascular disease (Shkolnikov *et al.*, 2001). From 1991 to 1994, the risk of premature death at an age of 15–59 years increased by 50% for Russian males. This risk decreased somewhat between 1994 and 1998 but increased again after 1998 (Shkolnikov *et al.*, 2001).

The burden of non-communicable diseases is increasing, accounting for nearly half of the global burden of disease among all ages — a 10% increase from the estimated levels for 1990. Indeed, almost 50% of the adult disease burden in the low- and middle-income countries of the world is now attributable to non-communicable disease (Fig. 4). In many developing countries, the implementation of effective interventions for Group-I diseases, population ageing, and the dynamics of risk for non-communicable disease are the likely causes of this shift. The burden of disease in 'Europe and Central Asia' is dominated by ischaemic heart disease and stroke, which together account for more than one-quarter of the total disease burden. In the countries of Latin America and the Caribbean, in contrast, these conditions account for only 8% of the disease burden, although the burdens posed by diabetes and endocrine disorders in these countries are relatively high.

Violence is the fourth leading cause of burden in 'Latin America and the Caribbean'. Although it is not ranked in the top 10 causes in any other region, it is, nonetheless, globally significant. Injuries primarily affect young adults, often resulting in severe disabling sequelae. All forms of injury accounted for 16% of the adult burden in the world in 2001. Road traffic accidents, violence and self-inflicted injuries are all among the top 10 leading causes of burden. The former Soviet Union and the other countries of Eastern Europe that have relatively high (adult) mortality have levels of injury-attributable death and disability among males that are similar to those seen in sub-Saharan Africa.

Figure 3 illustrates the regional variations in disease burden, in 2002, for adults aged 15–59 years. Group-I conditions account for 70% of the burden of disease in sub-Saharan Africa, and 44% of the burden in

TABLE 4. *The 10 leading causes of the burden of disease, measured in disability-adjusted life-years (DALY), in sub-Saharan Africa in 2002*

Rank	Cause	DALY (millions)	% of all DALY
1	HIV/AIDS	63.4	17.0
2	Lower respiratory infections	37.2	10.0
3	Malaria	31.6	8.5
4	Diarrhoeal diseases	26.4	7.1
5	Perinatal conditions	22.8	6.1
6	Maternal conditions	12.1	3.2
7	Measles	11.5	3.1
8	Tuberculosis	10.0	2.7
9	Road traffic accidents	7.5	2.0
10	Protein-energy malnutrition	6.0	1.6

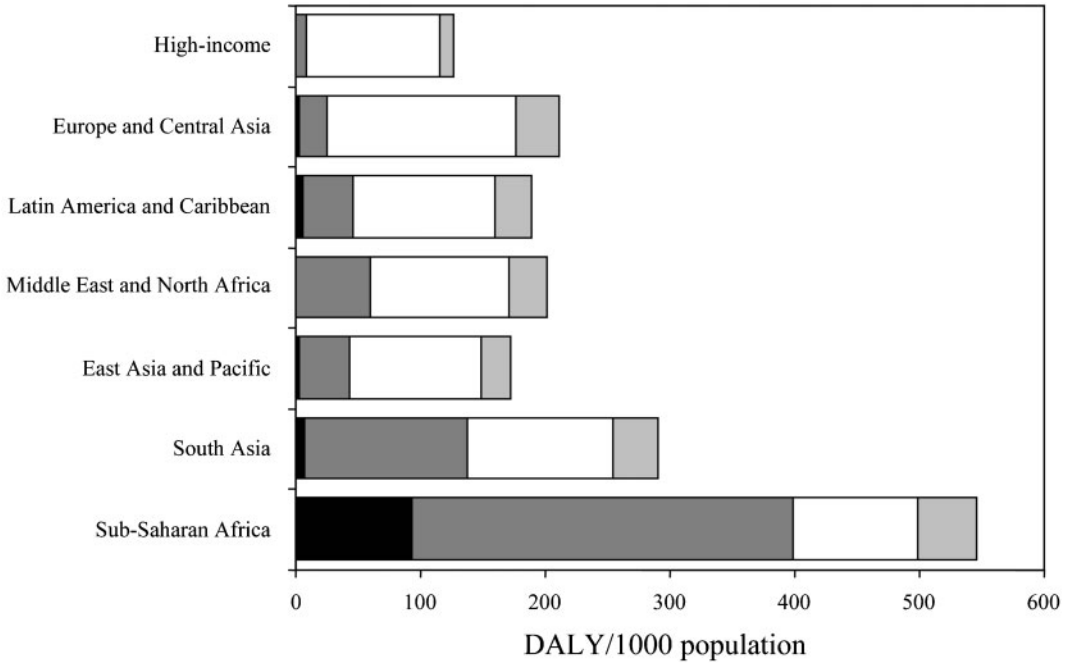

FIG. 4. The regional burden of disease in 2002, from HIV/AIDS (■), other Group-I causes (■), Group-II causes (□) or Group-III causes (■). Burden was measured in disability-adjusted life-years (DALY).

South Asia. In other low- and middle-income countries, Group-I conditions account for around one-quarter of the disease burden. Total disease burden in Europe and Central Asian countries is now higher than for other developing regions of the world apart from South Asia and sub-Saharan Africa. Sense-organ disorders, principally hearing and sight loss, contribute significantly to disability in all regions of the world.

In 'Latin America and the Caribbean' as well as in 'Europe and Central Asia' and 'Middle East and North Africa', >30% of the entire disease and injury burden among male adults aged 15–44 years is attributable to injuries, including road traffic accidents, violence and self-inflicted injuries. Additionally, in some parts of Asia and the Middle East and North Africa, injury deaths are relatively common among women, in part due to high levels of suicide and violence.

Burden of Disease Attributable to Risk Factors

The quantification of the burden of disease attributable to the individual and joint hazards of selected risk factors (Ezzati *et al.*, 2002, 2004) indicates that, although the main risk factors for the Group-I conditions are primarily concentrated in low- and middle-income countries, the main risk factors for non-communicable diseases (smoking, alcohol, high blood pressure and cholesterol, overweight and obesity) are globally wide-spread. In low- and middle-income countries, therefore, the leading causes of the burden of disease not only include the risk factors that affect the poor and/or are associated with the Group-I conditions [e.g. childhood underweight (10.3% of the disease burden in these regions), unsafe water, sanitation, and hygiene (4.0%), indoor smoke from household use of solid fuels (2.9%), and unsafe sex (6.8%)] but also the risk factors

for non-communicable diseases [e.g. high blood pressure (4.2%), smoking (3.4%), and alcohol use (3.8%)]. Across high-income countries, smoking (12.0%), high blood pressure (7.3%), overweight and obesity (6.7%), alcohol use (6.8%) and high cholesterol (5.6%) were the leading causes of loss of healthy life, contributing mainly to non-communicable diseases and injuries.

Estimates of the joint contributions of 20 selected leading global risk factors indicated that, globally, an estimated 48% of mortality and 39% of disease burden were attributable to the 20 selected factors (Ezzati *et al.*, 2004). The joint hazards were even larger in regions where a relatively small number of diseases and their risk factors were responsible for a very large loss of life (such as HIV/AIDS and childhood-disease risk factors in sub-Saharan Africa and cardiovascular risks, smoking and alcohol in 'Europe and Central Asia'). Globally, large fractions of the burden of major diseases such as diarrhoea (93%), lower respiratory infections (58%), HIV/AIDS (96%), lung cancer (74%), COPD (55%), ischaemic heart disease (86%) and stroke (73%) were attributable to the joint effects of the 20 selected risk factors. The joint population-attributable fractions for a number of other important diseases and injuries (e.g. perinatal and maternal conditions, selected other cancers, and intentional and unintentional injuries), which have more diverse risk factors, were smaller but not negligible. This concentration of disease burden in a relatively small number of risk factors further emphasises the contribution of leading risks, such as undernutrition, unsafe sex, smoking and alcohol use, to global loss of healthy life. Policies, programmes and scientific research need to take advantage of interventions that would reduce multiple major risks to health, across and within different levels of causality (Ezzati *et al.*, 2004).

DISCUSSION

Since the publication of the initial results of the first Global Burden of Disease Study in 1993, policy makers with national and international mandates for health development, as well as public-health practitioners and researchers, have shown extensive interest in applying the methods and findings. This interest indicates that there is a very keen latent demand for comprehensive global, regional and national assessments of disease and injury burden, of the factors that are primarily responsible for loss of healthy life, and of the likely impact of health interventions on future health. The 2000–2002 GBD study addresses this need, through a comprehensive update of the original study, applying the same estimation philosophies but drawing on the extensive improvements, since 1990, in the data for several diseases and in the relevant methodologies. The results confirm a progressive reduction in mortality risks for several of the leading causes of child death, particularly measles, diarrhoeal diseases and lower respiratory infections, reflecting progress with some disease-control programmes (Lopez *et al.*, 2006). Little progress, however, appears to have been made since 1990 in reducing mortality from malaria or the broad category of perinatal conditions that, together, currently cause almost one-third of all deaths among children aged <5 years. The recent estimates also indicate that the 'tropical-disease' cluster (including schistosomiasis, leishmaniasis and the trypanosomiases but excluding malaria) causes relatively few deaths and is, like leprosy, dengue and intestinal nematode infections, responsible for a relatively low disease burden. This is not to suggest that research and disease-control efforts for these conditions should receive lower priority but rather that these conditions are no longer major causes of global disease burden. They remain, however, of local importance for some populations.

It is of interest to attempt to quantify how the future of global health might appear if there were to be no major changes to current disease-control efforts and no major research breakthroughs that might lead to

new, affordable and implementable disease-control technologies. Mathers and Loncar (2006) have prepared updated projections of future trends for mortality and burden of disease between 2002 and 2030, using methods similar to those used in the original GBD study (Murray and Lopez, 1997*c*). A set of relatively simple models was used to project future health trends for 'baseline', 'optimistic' and 'pessimistic' scenarios, based largely on projections of economic and social development and on the historically observed relationships between such development and cause-specific mortalities.

The data inputs for the projection models have been updated to take account of the greater number of countries reporting death-registration data to the WHO, particularly from developing regions, and to take into account other recently developed projection models for HIV/AIDS, and projected trends in tobacco smoking and overweight and obesity. In total, 2605 observation years of death-registration data from 106 countries were used — almost double the number available for the original projections by Murray and Lopez (Mathers and Loncar, 2006). Separate projections for the mortality caused by HIV/AIDS were prepared by UNAIDS and the WHO, under a scenario in which coverage with anti-retroviral drugs reaches 80% by 2012 (thereafter remaining constant) and assuming that there are no changes to current transmission rates as a consequence, for example, of increased prevention efforts. The optimistic projections for HIV/AIDS were based on the scenarios modelled by Salomon *et al.* (2005), for sub-Saharan Africa, combining treatment and additional prevention efforts. Projections of the tuberculosis-attributable mortality rates were modified in regions with a high prevalence of HIV, to reflect the detrimental interaction that seems to occur between tuberculosis and HIV (Harries and Dye, 2006).

The results of the projections are summarized in Tables 5 and 6 and Figures 5 and 6. According to these results, overall (age-standardized) mortality rates worldwide are expected to decline by 0.6%–1.0%/year over the next 30 years. For most major communicable diseases, but not HIV/AIDS, the decline is expected to be two to three times this rate. By 2030, the global mortality caused by HIV/AIDS is expected to double from the current annual toll of just under 3 million deaths; the avoidance of this scenario must remain a global health priority. Interestingly, whereas the proportion of deaths from non-communicable diseases is expected to rise everywhere, the death rate from these diseases is expected to decline at 0.6%–0.8%/year. Major failures

TABLE 5. *Projected mean annual rates of change in the age-standardized global mortality for selected causes between 2002 and 2020 (Mathers and Loncar, 2006)*

	Mean annual change (%) among:	
Cause	Males	Females
All	−0.6	−1.0
GROUP-I	−1.0	−1.7
Tuberculosis	−0.7	−0.9
HIV/AIDS	+3.0	+2.1
Malaria	−1.4	−1.7
Other infectious	−2.5	−3.0
Respiratory infections	−2.6	−3.3
Perinatal conditions	−1.6	−1.9
Other	−3.0	−3.5
Group-II	−0.6	−0.8
Group-III	−0.1	−0.2

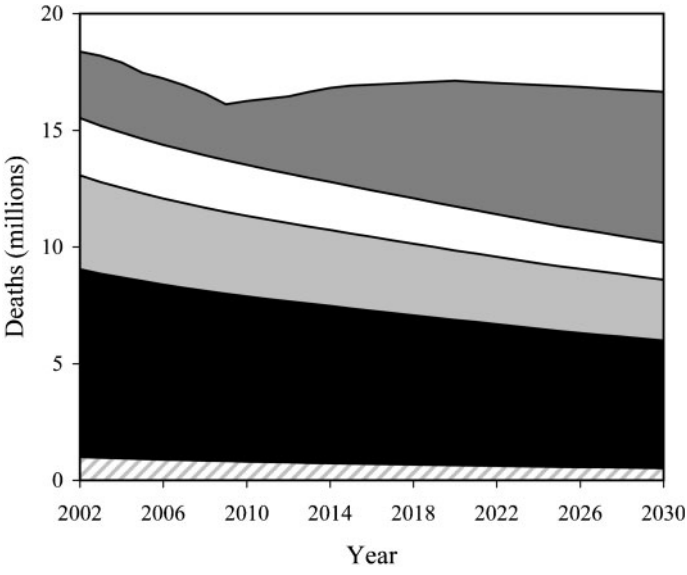

FIG. 5. Changes in the annual numbers of deaths caused by HIV/AIDS (■), perinatal conditions (□), respiratory infections (■), infectious diseases other than HIV/AIDS (■) and other Group-I causes (▨), between 2002 and 2030. The numbers after 2002 were estimated from projections, with a 'baseline scenario' (Mathers and Loncar, 2006).

TABLE 6. *Changes in the rankings for 15 leading causes of disease burden (as measured in disability-adjusted life-years) between 2002 and 2030 (Mathers and Loncar, 2006)*

Disease or injury	Rank in: 2002	2030*	Change in rank
RANKED WITHIN TOP 15 IN 2002			
Perinatal conditions	1	5	−4
Lower respiratory infections	2	9	−7
HIV/AIDS	3	1	+2
Unipolar depressive disorders	4	2	+2
Diarrhoeal diseases	5	13	−8
Ischaemic heart disease	6	3	+3
Cerebrovascular disease	7	6	+1
Road traffic accidents	8	7	+1
Malaria	9	15	−6
Tuberculosis	10	10	0
Chronic obstructive pulmonary disease	11	4	+7
Congenital anomalies	12	22	−10
Hearing loss, adult onset	13	11	+2
Cataracts	14	8	−6
Violence	15	14	+1
RANKED LOWER THAN 15TH IN 2002			
Diabetes mellitus	20	12	+8

*According to projections, with a 'baseline scenario'.

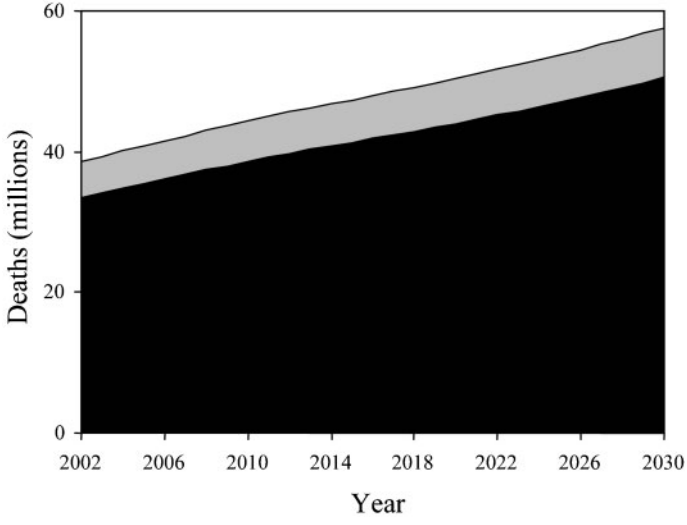

FIG. 6. Changes in the annual numbers of deaths caused by Group-II (■) or Group-III (■) causes between 2002 and 2030. The numbers after 2002 were estimated from projections with a 'baseline scenario' (Mathers and Loncar, 2006).

with tobacco and obesity control, as seen in several western countries in the 1950s and 1960s, could, however, dramatically alter this prediction.

If the projected changes in disease burden over the next 30 years occur, there will be dramatic changes in the global importance of some causes. Lower respiratory infections and diarrhoeal diseases, for example, are expected to fall to ninth and 13th place, respectively, in the global DALY 'league' table (from second and fifth place, respectively, in 2002). Malaria is also expected to decline in relative importance, as are congenital anomalies. Conversely, by 2030, HIV/AIDS is expected to be the leading global cause of DALY, followed by depression, ischaemic heart disease, COPD and perinatal conditions. This rather diverse set of important but largely avoidable or treatable causes will require very flexible and innovative responses from health systems world-wide. Indeed, policy action to accelerate declines in the incidences of these causes, or at least to avoid any further increases, needs to be taken today. Further research will help to focus the necessary control efforts.

By their very nature, projections of the future are highly uncertain and need to be interpreted with caution. Apart from the uncertainties in the baseline data on burden of disease, particularly for low-income regions, the projections of burden are not intended as forecasts of what will happen in the future but as projections of current and past trends, based on certain explicit assumptions and on observed historical relationships between development and mortality levels and patterns. The disease-burden projections are based on broad mortality projections that are driven, to a large extent, by the World Bank's projections of future growth in per-capita income in different regions of the world. The results depend strongly on the assumption that future mortality trends in poor countries will have the same relationship to economic and social development as seen in the higher-income countries in the recent past. If this assumption is not correct, then the projections for low-income countries will probably be over-optimistic in terms of the rate of decline of communicable diseases. The projections have also not taken explicit account of trends in any major risk factor

apart from tobacco smoking and, to a limited extent, overweight and obesity. If the broad trends are for the worsening of risk exposures with development, rather than for the improvements observed in recent decades in many high-income countries, then again the projections for low- and middle-income countries presented here will be too optimistic.

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