Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data

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Summary

Background Our aim was to calculate the global burden of disease and risk factors for 2001, to examine regional trends from 1990 to 2001, and to provide a starting point for the analysis of the Disease Control Priorities Project (DCPP).

Methods We calculated mortality, incidence, prevalence, and disability adjusted life years (DALYs) for 136 diseases and injuries, for seven income/geographic country groups. To assess trends, we re-estimated all-cause mortality for 1990 with the same methods as for 2001. We estimated mortality and disease burden attributable to 19 risk factors.

Findings About 56 million people died in 2001. Of these, 10·6 million were children, 99% of whom lived in low-and-middle-income countries. More than half of child deaths in 2001 were attributable to acute respiratory infections, measles, diarrhoea, malaria, and HIV/AIDS. The ten leading diseases for global disease burden were perinatal conditions, lower respiratory infections, ischaemic heart disease, cerebrovascular disease, HIV/AIDS, diarrhoeal diseases, unipolar major depression, malaria, chronic obstructive pulmonary disease, and tuberculosis. There was a 20% reduction in global disease burden per head due to communicable, maternal, perinatal, and nutritional conditions between 1990 and 2001. Almost half the disease burden in low-and-middle-income countries is now from non-communicable diseases (disease burden per head in Sub-Saharan Africa and the low-and-middle-income countries of Europe and Central Asia increased between 1990 and 2001). Undernutrition remains the leading risk factor for health loss. An estimated 45% of global mortality and 36% of global disease burden are attributable to the joint hazardous effects of the 19 risk factors studied. Uncertainty in all-cause mortality estimates ranged from around 1% in high-income countries to 15–20% in Sub-Saharan Africa. Uncertainty was larger for mortality from specific diseases, and for incidence and prevalence of non-fatal outcomes.

Interpretation Despite uncertainties about mortality and burden of disease estimates, our findings suggest that substantial gains in health have been achieved in most populations, countered by the HIV/AIDS epidemic in Sub-Saharan Africa and setbacks in adult mortality in countries of the former Soviet Union. Our results on major disease, injury, and risk factor causes of loss of health, together with information on the cost-effectiveness of interventions, can assist in accelerating progress towards better health and reducing the persistent differentials in health between poor and rich countries.

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Introduction

An important input to decision-making and planning processes in health is a consistent and comparative description of the burden of diseases and injuries and their associated risk factors. Assessment of the comparative importance of risks to health and their outcomes in different populations depends on a framework for integrating, validating, analysing, and disseminating the fragmentary, and at times contradictory, information that is available on a population's health, along with some understanding of how that population's health is changing. The Global Burden of Disease (GBD) study quantified the health effects of more than 100 diseases and injuries and ten selected risk factors for the world as a whole and for eight regions in 1990.[1–3] As well as generating comprehensive and internally consistent estimates of mortality and morbidity by age, sex, and region,[4] the 1990 GBD study used a new metric—disability-adjusted life years (DALYs)—to quantify the burden of diseases, injuries, and risk factors with a single currency based on years of life lost due to premature mortality (YLL) and years of life lived in less than full health.[5]

Between 1998 and 2004, WHO invested in improving the conceptual, methodological, and empirical basis of assessments of burden of disease and of the disease and injury burden attributable to major risk factors.[6–9] The summaries of consecutive revisions and updates were published yearly in WHO's *World Health Reports*. National applications of the burden of disease framework[10–12] have also led to new data sources. Here, we present the results of the GBD study for 2001.

In addition to including improved methods and new and more extensive data, we incorporated three features into the 2001 assessment of the global burden of disease. First, we estimated changes in cause-specific mortality and burden of disease, to assess progress and setbacks, overall and for specific diseases, since 1990. Second, we examined the uncertainty of mortality and burden-of-disease estimates due to data limitations, and their sensitivity to social value choices built into the DALY metric. Third, researchers used the estimates of disease burden as the starting point for a comprehensive analysis of intervention cost-effectiveness in the Disease Control Priorities Project (DCPP).[13] A joint initiative of the Fogarty International

Center (FIC) of the US National Institutes of Health, the World Bank, WHO, and the Bill & Melinda Gates Foundation, the DCPP aims to provide a comprehensive assessment of health-system development priorities in developing countries. Such an assessment depends on an understanding of the need for various health interventions—ie, comparative magnitude of the burden of disease and risk factors—as well as the effectiveness or cost-effectiveness of interventions. We chose 2001 as the base year for analysis for consistency with the DCPP cost-effectiveness analyses. Here, we provide an overview of our methods and results; further information on data sources, methods, and detailed results are provided in the two DCPP volumes.[13,14]

Methods

Mortality and cause of death estimates

We developed life tables for 192 WHO member states from available death registration data, sample registration systems (India, China), and data on child and adult mortality from censuses and surveys, such as the Demographic and Health Surveys (DHS) and UNICEF's Multiple Indicator Cluster Surveys (MICS). We calculated age-specific and sex-specific death rates for countries with one of three standard approaches:[7] routine life-table methods for countries with complete vital registration; standard demographic methods to correct for under-registration of deaths; or model life tables, if no vital registration data on adult mortality were available.[8]

Death registration data, containing useable information on cause of death distributions, were available for 107 countries, most of which are in the high-income group, Latin America and the Caribbean, and Europe and Central Asia. The proportion of deaths coded to ill-defined causes varied from 4% in New Zealand to more than 40% in Sri Lanka and Thailand.[16] For 55 countries, 42 of them in Sub-Saharan Africa, no information was available on levels of adult mortality.

We redistributed deaths coded to International Classification of Diseases (ICD) codes for "symptoms, signs, and ill-defined conditions", as well as certain ill-defined codes within the cancer, cardiovascular disease, and injury chapters of ICD across defined causes.[15,16] We used population-based epidemiological studies, disease registers, and notification systems (more than 2700 sources) to estimate mortality from 21 specific diseases.[15] Almost one third of these sources were from Sub-Saharan Africa. Following the rules and conventions of the ICD, in cases for which several contributing causes might co-exist, we categorically attributed deaths to one underlying cause.[17] In some cases, for which the ICD rules are ambiguous, we followed the conventions used for the 1990 GBD study, itself designed to be broadly consistent with the ICD rules—eg, all deaths caused by cirrhosis of the liver or from renal failure are classified as such, irrespective of whether they were a consequence of hepatitis infection or diabetes.[2]

For countries without usable death registration data, we applied the estimated levels of child and adult mortality to a modified logit life-table model, using a global standard, to estimate the full life table for 2001.[7,8] For countries for which no information was available on levels of adult mortality, we selected the most likely level based on the predicted level of child mortality in 2001 (excluding HIV/AIDS deaths where necessary), along with uncertainty ranges, based on regression models of child versus adult mortality as noted in a set of almost 2000 life tables judged to be of good quality.[7,8]

To estimate deaths by cause for populations without usable death registration data,[16] we applied models at country level for assessment of the proportion of deaths in communicable, maternal, and perinatal conditions and nutritional deficiencies (group I conditions), non-communicable diseases (group II conditions), and injuries (group III conditions). The statistical model for cause of death composition was estimated with a dataset consisting of 1613 country-years, larger than that used for the 1990 GBD study.[18] We used the estimates of mortality by age to calculate YLL, a time-based measure that gives greater weight to deaths at younger ages.

Because of improvements in methods and data availability both for all-cause mortality and cause-specific incidence, prevalence, or mortality for some diseases, cause-specific results for 2001 might not be completely comparable with those for 1990. We re-estimated all-cause mortality levels for 1990 for children and adults, using data for years around 1990, which are now available, and consistent model-life tables for countries without usable death registration data.[19] We used the new estimates to revise 1990 cause-specific estimates, and presented them in the regions used for the 2001 assessment.

Non-fatal disease burden

To assess non-fatal disease burden, by sex and eight age groups (0–4, 5–14, 15–29, 30–44, 45–59, 60–69, 70–79, and ≥80 years), we incorporated a range of data sources, including disease registers, epidemiological studies, health surveys, and health facility data, to develop internally consistent estimates of incidence, health state prevalence, severity, duration, and mortality for almost 500 disabling sequelae for 136 disease and injury cause categories. Overall, we used about 8700 data sources to analyse the epidemiology of non-fatal health outcomes, of which more than 7000 related to communicable, maternal, perinatal, and nutritional conditions.[15] One-quarter of the data sources related to populations in Sub-Saharan Africa, and around one-fifth to populations in high-income countries. Neuropsychiatric conditions, vision disorders, hearing loss, osteoarthritis, and cerebrovascular disease dominated the overall burden of non-fatal, disabling conditions. Although depression was the leading cause of years of life lived with disability (YLD) for both males and females, the burden of depression was 50% higher for females than for males;
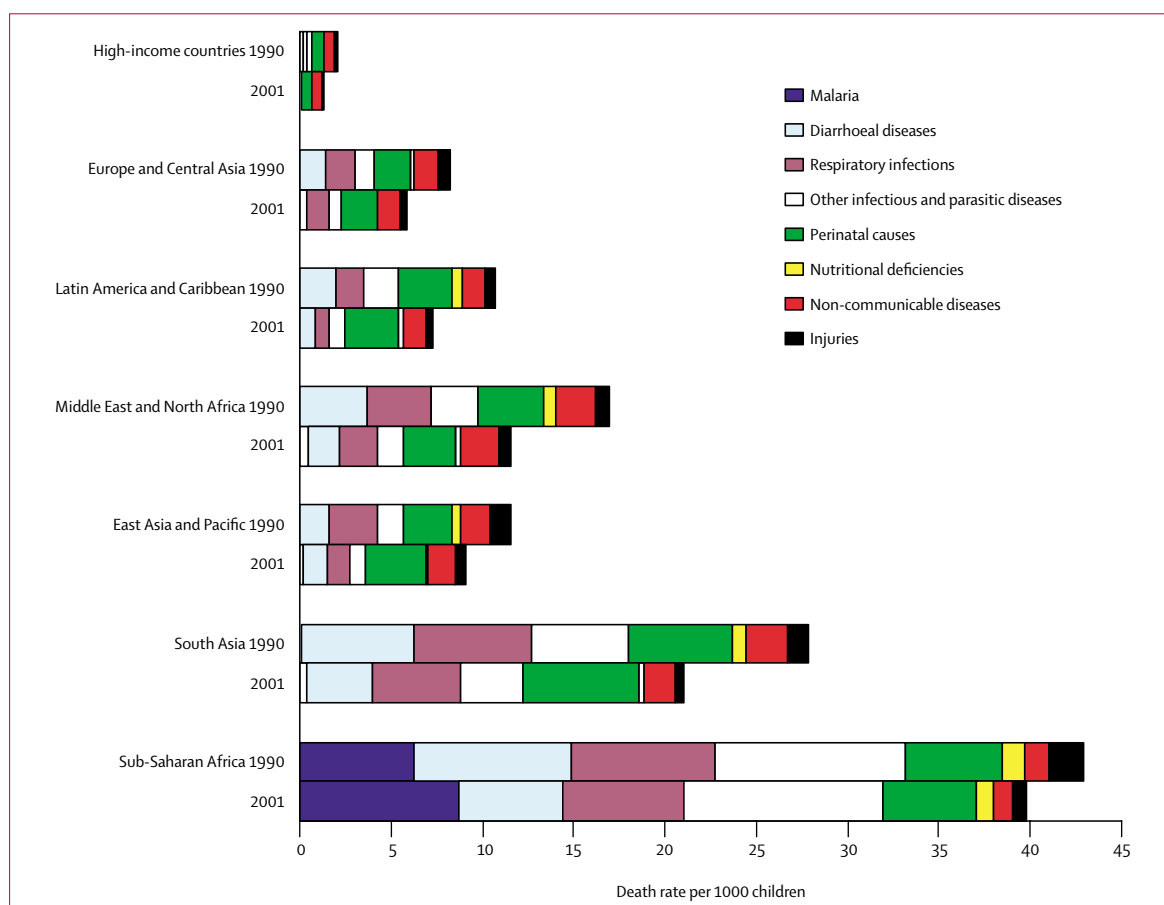
Figure 1: Death rates by disease group and region in 1990 and 2001 for children aged 0–4 years
Cause-specific death rates for 1990 estimated from Murray and Lopez[2] might not be completely comparable to those for 2001 because of changes in data availability and methods, plus some approximations in mapping 1990 estimates to the 2001 regions East Asia and Pacific, South Asia, and Europe and Central Asia. For all geographical regions, high-income countries excluded and shown as single group at top of graph. The geographical regions therefore refer to low-and-middle-income countries only.

females also had a higher burden from anxiety disorders, migraine, and senile dementias. By contrast, the male burden for disorders associated with alcohol and drug use was nearly six times higher than that for females and accounted for one-quarter of the male neuropsychiatric burden. We used a mathematical model (DisMod) to convert partial, often non-specific, data on disease and injury occurrence into consistent estimates of incidence, prevalence, duration, and mortality.[20] We used the estimates of incidence and duration, together with severity weights, to calculate YLD. The disability weights used for GBD 2001 are largely based on the GBD 1990 disability weights and are described elsewhere.[15]

Disease burden from risk factors
The 1990 GBD study quantified the population health effects of ten risk factors, but there were concerns about the comparability of the methods and estimates used[21,22] because of the different epidemiological traditions for various risk factors with regard to the definitions of hazardous exposure, the strength of the evidence on

causality, and the availability of epidemiological data on exposure and hazard. For the GBD 2001 study, we defined a new framework for risk factor assessment that quantified changes in mortality or disease burden that would be expected if the population distribution of exposure to a risk factor or group of risk factors were changed to an alternative (counterfactual) distribution. For comparability, we defined the counterfactual exposure distribution as the distribution that would lead to the lowest levels of disease burden.[21,22] For some risks, limitations of exposure or relative risk data limited complete comparability of counterfactuals across risk factors.[21–23]

Expert working groups collated data on risk factor exposure and the hazardous effects of exposure for a selected group of risk factors through comprehensive and systematic reviews of: published work, government reports, and international databases; collection of primary data; re-analyses of original data sources; and meta-analyses of epidemiological studies. The disease burden attributable to the combined hazards of multiple risk factors was also estimated, as described elsewhere.[24]
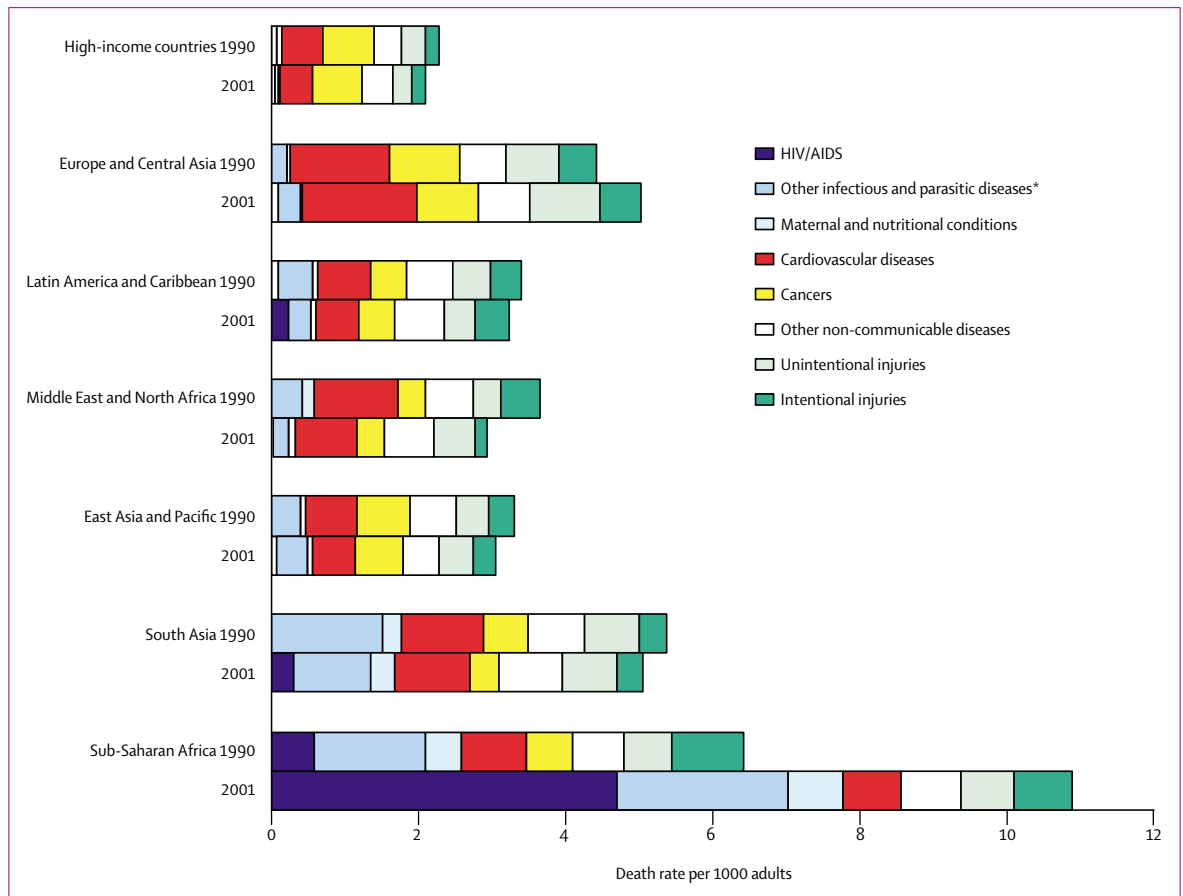
Figure 2: **Death rates by disease group and region in 1990 and 2001 for adults aged 15–59 years**
*Includes respiratory infections. Cause-specific death rates for 1990 estimated from Murray and Lopez[2] might not be completely comparable to those for 2001 because of changes in data availability and methods, plus some approximations in mapping 1990 estimates to the 2001 regions East Asia and Pacific, South Asia, and Europe and Central Asia. For all geographical regions, high-income countries excluded and shown as single group at top of graph. The geographical regions therefore refer to low-and-middle-income countries only.

Sensitivity analyses

Much of the comment on, and criticism of, the 1990 GBD study focused on the construction of DALYs,[25,26] particularly the social choices pertaining to placing differential weights on years of life at different ages (referred to as age weights), severity scores for disabilities, and discounting the future stream of life years. Little attention was directed at the uncertainty of the basic descriptive epidemiology for some populations, especially in Sub-Saharan Africa, which is likely to be far more consequential for the application of results.[27] To examine sensitivity to discounting and age weighting, we calculated DALY estimates for 2001 with alternative choices of discount rate (0% and 3%) and age weighting (uniform or non-uniform). Results reported here use a discount rate of 3% and uniform age weights. We included an analysis of stillbirths in the 2001 GBD study to examine the sensitivity of the results to this inclusion and to modifications of the DALY formulation so that YLL could be assigned to the deaths that occurred near the time of birth.[28]

See **Online** for webtable 1

In addition to these sensitivity analyses, we assessed uncertainty in the results at regional level that arose from data limitations. We calculated 95% uncertainty ranges for regional cause-specific mortality estimates with simulation methods based on estimated uncertainty ranges for input data.[29]

We present the results for World Bank regions as used in the DCPP. We treat high-income countries as one group and divide low-and-middle-income countries into six geographical regions (see webtable 1).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Worldwide, slightly more than 56 million people died in 2001. One-third of these deaths were from communicable,

maternal, and perinatal conditions and nutritional deficiencies (group I). This proportion has remained almost unchanged since 1990. Among these diseases, HIV/AIDS accounted for only 2% of deaths in 1990, but for 14% in 2001. Excluding HIV/AIDS, deaths due to group I conditions fell from one-third of total deaths in 1990 to less than one-fifth in 2001. 97% of the group I deaths not associated with HIV were in low-and-middle-income countries (figures 1 and 2).

Webtable 2 summarises estimated numbers of deaths in 2001 for high-income and low-and-middle-income countries, for diseases and injuries causing more than 1% of global deaths or global DALYs. Ischaemic heart disease and cerebrovascular disease (stroke) were the leading causes of death in both groups of countries, together responsible for more than a fifth of all deaths worldwide (table 1). Only 1·4 million of the 7·1 million deaths from ischaemic heart disease were in high-income countries. 5·4 million individuals died of stroke, of whom fewer than 1·0 million lived in high-income countries. Lung cancer was the third leading cause of death in high-income countries, but was not among the leading causes of death in low-and-middle-income countries, where five of the leading ten causes of death remain infectious diseases, including lower respiratory infections, HIV/AIDS, diarrhoeal diseases, tuberculosis, and malaria.

Nearly 20% of deaths (10·5 million) in 2001 were among children younger than age 5 years.[7] 99% of these deaths occurred in low-and-middle-income countries and more than 40% in Sub-Saharan Africa. If stillbirths are included in death totals, then 13·5 million children died before reaching their fifth birthday in 2001, and nearly half of these deaths occurred before the age of 1 month.[28] Table 2 shows in more detail the estimated age distribution of deaths among children younger than age 5 years. The main causes of neonatal death include low birthweight, respiratory infections, birth asphyxia, and birth trauma.

Child mortality (age 0–4 years) declined between 1990 and 2001 in all regions of the world (figure 1). It fell by 30% or more in high-income countries, in Latin America and the Caribbean, in the Middle East and North Africa region, and in the low-and-middle-income countries of Europe and Central Asia. Death rates from communicable diseases and injuries fell substantially in these regions, especially for diarrhoeal and respiratory diseases. More than half of child deaths in 2001 were from five preventable and treatable conditions: acute respiratory infection, measles, diarrhoea, malaria, and HIV/AIDS. Mortality from diarrhoeal diseases fell from 2·4 million deaths in 1990 to about 1·6 million deaths in 2001 as a result of efforts in diarrhoea case management—eg, use of oral rehydration therapy; diarrhoea now accounts for 15% of all deaths among children younger than age 5 years. Deaths from measles also declined, probably because of higher measles vaccination coverage, although more than 0·5 million children younger than age 5 years still died from this disease in 2001. Death rates from acute respiratory infections declined less in South Asia (by 25%) and Sub-Saharan Africa (15%) than in other regions, where the decline was 40% or more.

See **Online** for webtable 2

	Low-and-middle-income countries			High-income countries		
	Cause	Deaths (millions)	% of total deaths	Cause	Deaths (millions)	% of total deaths
1	Ischaemic heart disease	5·70	11·8%	Ischaemic heart disease	1·36	17·3%
2	Cerebrovascular disease	4·61	9·5%	Cerebrovascular disease	0·78	9·9%
3	Lower respiratory infections	3·41	7·0%	Trachea, bronchus, lung cancers	0·46	5·8%
4	HIV/AIDS	2·55	5·3%	Lower respiratory infections	0·34	4·4%
5	Perinatal conditions	2·49	5·1%	Chronic obstructive pulmonary disease	0·30	3·8%
6	Chronic obstructive pulmonary disease	2·38	4·9%	Colon and rectum cancers	0·26	3·3%
7	Diarrhoeal diseases	1·78	3·7%	Alzheimer's disease and other dementias	0·21	2·6%
8	Tuberculosis	1·59	3·3%	Diabetes mellitus	0·20	2·6%
9	Malaria	1·21	2·5%	Breast cancer	0·16	2·0%
10	Road traffic accidents	1·07	2·2%	Stomach cancer	0·15	1·9%

Table 1: **Ten leading causes of death by income group, 2001**

	Stillbirths*			Neonatal†			Post-neonatal‡	Infant	Death at younger than age 5 years		
	Antepartum	Intrapartum	Total	Early	Late	Total	Total	Total	1–4 years	0–4 years	Total including stillbirths
Low-and-middle-income countries	2152	1077	3228	2889	965	3854	3745	7599	2935	10530	13758
High-income countries	40	5	45	32	9	41	41	58	13	73	119
Worldwide	2192	1082	3274	2921	974	3896	3762	7658	2948	10602	13876

*Birth of dead fetus weighing >1000 g up to 13 weeks before expected date of birth (27 weeks' gestation). Stillbirths conventionally divided into two categories: antepartum stillbirths, when a fetus dies before onset of labour, and intrapartum stillbirths, when fetal death occurs during labour. The estimated number of livebirths in 2001 was 129·9 million (118·5 in low-and-middle-income countries and 11·4 million in high-income countries). †Early neonatal period extends from birth to <7 days; late neonatal period extends from 7 days to <28 days. ‡28 days to <1 year. Together, neonatal and postneonatal periods comprise infant period.

Table 2: **Age distribution of deaths (thousands) among children younger than age 5 years including stillbirths, 2001[28]**
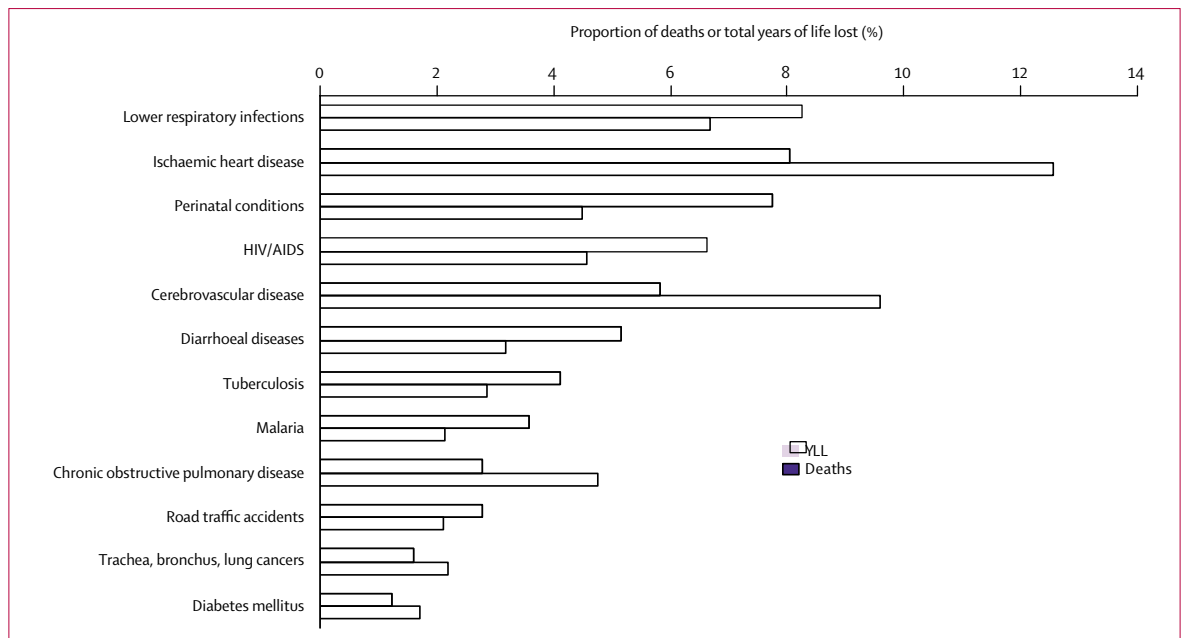
Proportion of deaths or total years of life lost (%)

Figure 3: **Leading causes of premature death (YLL) and of deaths worldwide, 2001**

The malaria mortality rate seems to have increased during the 1990s, primarily in Sub-Saharan Africa, with the proportion of deaths in children younger than 5 years old increasing from 15% to 22% (figure 1). There were more than a million deaths from malaria in 2001. HIV/AIDS is the only other disease for which child death rates increased. Death rates from perinatal conditions seem to have risen in both East Asia and the Pacific and South Asia, but remained unchanged in Latin America and the Caribbean and Europe and Central Asia. There is substantial uncertainty about levels, trends, and causal composition from these conditions, which are highly dependent on prenatal care and delivery conditions. Similarly, the large suggested decline in child death from injuries in South Asia and Sub-Saharan Africa might be a result of better data rather than actual trends. Death rates among children aged 5–14 years were only 7% of those of children younger than 5 years. More than 98% of child deaths occurred in low-and-middle-income countries. The leading causes of death at age 5–14 years included selected infectious diseases, unintentional injuries, and cancers.

A large number of the deaths at age 15–59 years also arose in low-and-middle-income countries in 2001 (30% *vs* 15% in high-income countries). Non-communicable diseases are responsible for more than half of deaths in adults aged 15–59 in all regions except South Asia and Sub-Saharan Africa, where group I conditions, including HIV/AIDS, remain responsible for one-third and two-thirds of deaths, respectively (figure 2). 15–59-year old adults in low-and-middle-income countries face a 30% greater risk of death from non-communicable diseases than their counterparts in high-income countries.

Injuries were a disproportionately important cause of death in adults aged 15–59 years, and accounted for one-quarter of deaths, one-third in Europe and Central Asia (figure 2). Violence and war accounted for a disproportionate share of injury deaths in this age group in Sub-Saharan Africa (47%) and Latin America and the Caribbean (45%).

Death rates among adults aged 15–59 years have declined in all regions except Europe and Central Asia, and Sub-Saharan Africa (figure 2). HIV/AIDS has been a major factor in the rise in mortality in Sub-Saharan Africa; the increase in Europe and Central Asia is attributable to cardiovascular diseases and injuries.[30] Death rates from cardiovascular disease among adults aged 15–59 years have fallen in all regions except the low-and-middle-income countries of Europe and Central Asia (16% increase), although the declines are lower in South Asia and Sub-Saharan Africa than elsewhere. Similarly, Europe and Central Asia was the only region where death rates from injury increased (22% increase).

Non-communicable diseases accounted for nearly 60% of deaths globally in 2001, but for only 40% of YLL; conversely, injuries accounted for 12% of YLL and 9% of deaths. Figure 3 compares the ten leading causes of YLL and death for 2001. Measuring mortality with YLL gives relatively greater importance to HIV/AIDS, perinatal conditions, and diarrhoeal diseases, whereas simple counts of deaths give relatively greater importance to ischaemic heart disease, stroke, and chronic obstructive pulmonary disease, which primarily affect middle-aged and older adults. Sex differences in mortality were also better delineated with time-based measures. Globally, the male all-cause death rate was 11% higher than that for

females, but the male rate of YLL was 15% higher, indicating the earlier ages of male deaths on average. YLL also varied greatly across regions, with rates nearly five times higher in Sub-Saharan Africa than in high-income countries.

YLD rates were higher in low-and-middle-income countries than in high-income countries in 2001 although their variation across regions was much lower than for YLL rates. The prevalence of disabling conditions, such as dementia and musculoskeletal disease, was higher in high-income countries than in low-and-middle-income countries because of the higher proportions of older people in their populations. The contributions to disability in high-income countries from conditions such as cardiovascular and chronic respiratory diseases, and long-term sequelae of communicable diseases and nutritional deficiencies are, however, lower than in low-and-middle-income countries. In other words, people living in developing countries not only face shorter life expectancies than those in developed countries, but also live a higher proportion of their lives in poor health.

In 2001, the ten leading causes of the burden of disease in low-and-middle-income countries were broadly similar to those for the world as a whole (table 3), and included five communicable diseases. The leading causes in high-income countries were all non-communicable diseases, including three conditions (unipolar depressive disorders, adult-onset hearing loss, and disorders associated with alcohol use) with few direct deaths but large disability. Webtable 2 summarises estimated DALYs in 2001 for high-income and low-and-middle-income countries, for diseases and injuries that cause more than 1% of deaths or DALYs.

HIV/AIDS was the fourth leading cause of the burden of disease globally in 2001, and the leading cause in Sub-Saharan Africa, where it was followed by malaria. Worldwide, there was a 20% reduction in the per head disease burden due to communicable, maternal, perinatal, and nutritional conditions between 1990 and 2001. Without

the HIV/AIDS epidemic and the associated persistence of the burden of tuberculosis, this reduction would have been closer to 30%.

South Asia and Sub-Saharan Africa together bore 45% of the global burden of disease in 2001, even though they accounted for only one-third of the world's population (figure 4). East Asia and the Pacific was the healthiest of the low-and-middle-income regions: China now has DALY rates similar to those of many Latin American countries and lower than those in some low-and-middle-income European countries. Per head disease burden in Europe and Central Asia increased by nearly 40% between 1990 and 2001; the disease burden in this region is now worse than in all other regions except South Asia and Sub-Saharan Africa (figure 4). This deterioration indicates the sharp increase in adult male mortality and disability from injuries and non-communicable diseases, particularly cardiovascular diseases, in the 1990s, leading to the highest male-female differential in disease burden worldwide.

Almost half of disease burden in low-and-middle-income countries is now from non-communicable diseases, a rise of 10% in its relative share since 1990. Ischaemic heart disease and stroke are the largest sources of this burden, especially in the low-and-middle-income countries of Europe and Central Asia, where they account for more than a quarter of the total disease burden. Injuries accounted for 17% of the disease burden in adults aged 15–59 years in 2001. In Latin America and the Caribbean, and the Middle East and North Africa, more than one-quarter of the entire disease and injury burden among men aged 15–44 years was from injuries, 31% in Europe and Central Asia. Road traffic accidents, violence, and self-inflicted injuries were also among the ten leading causes of burden of disease in these regions.

Among the selected risk factors in low-and-middle-income countries, the leading causes of disease burden included risk factors prevalent among the poor and associated with communicable, maternal, perinatal, and

	Low-and-middle-income countries			High-income countries		
	Cause	DALYs (millions of years)*	% of total DALYs	Cause	DALYs (millions of years)*	% of total DALYs
1	Perinatal conditions	89·07	6·4%	Ischaemic heart disease	12·39	8·3%
2	Lower respiratory infections	83·61	6·0%	Cerebrovascular disease	9·35	6·3%
3	Ischaemic heart disease	71·88	5·2%	Unipolar depressive disorders	8·41	5·6%
4	HIV/AIDS	70·80	5·1%	Alzheimer's disease and other dementias	7·47	5·0%
5	Cerebrovascular disease	62·67	4·5%	Trachea, bronchus, lung cancers	5·40	3·6%
6	Diarrhoeal diseases	58·70	4·2%	Hearing loss, adult onset	5·39	3·6%
7	Unipolar depressive disorders	43·43	3·1%	Chronic obstructive pulmonary disease	5·28	3·5%
8	Malaria	39·96	2·9%	Diabetes mellitus	4·19	2·8%
9	Tuberculosis	35·87	2·6%	Alcohol use disorders	4·17	2·8%
10	Chronic obstructive pulmonary disease	33·45	2·4%	Osteoarthritis	3·79	2·5%

*Constructed with 3% yearly discount rate and uniform age weights.

Table 3: Ten leading causes of burden of disease (DALYs) by income group, 2001

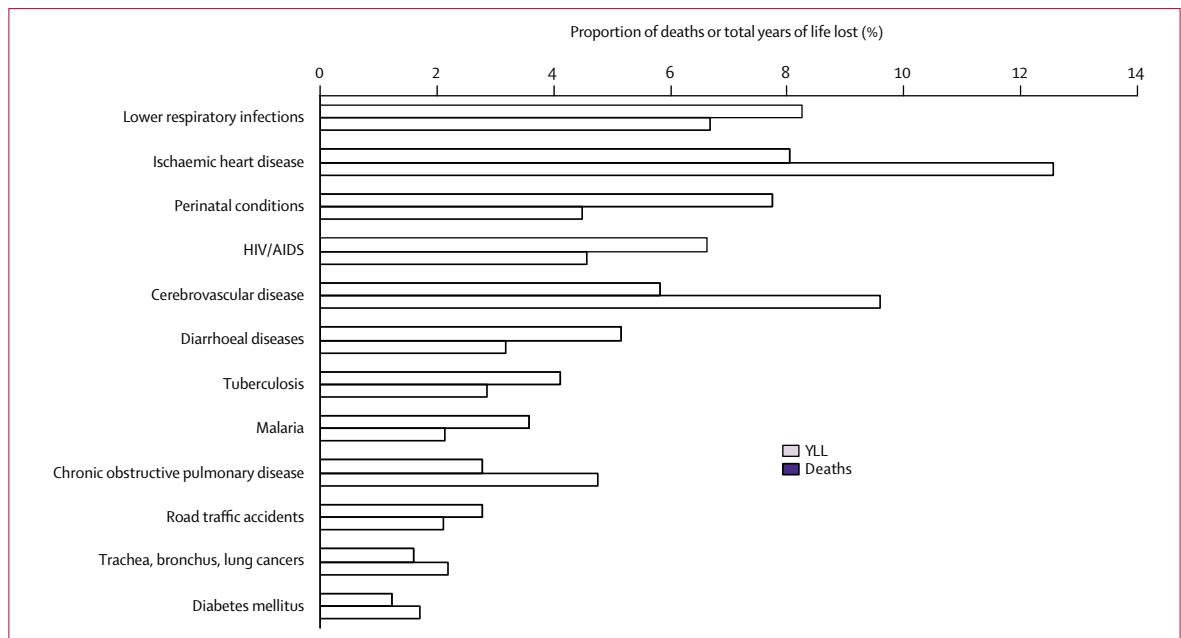Proportion of deaths or total years of life lost (%)

Figure 3: Leading causes of premature death (YLL) and of deaths worldwide, 2001

The malaria mortality rate seems to have increased during the 1990s, primarily in Sub-Saharan Africa, with the proportion of deaths in children younger than 5 years old increasing from 15% to 22% (figure 1). There were more than a million deaths from malaria in 2001. HIV/AIDS is the only other disease for which child death rates increased. Death rates from perinatal conditions seem to have risen in both East Asia and the Pacific and South Asia, but remained unchanged in Latin America and the Caribbean and Europe and Central Asia. There is substantial uncertainty about levels, trends, and causal composition from these conditions, which are highly dependent on prenatal care and delivery conditions. Similarly, the large suggested decline in child death from injuries in South Asia and Sub-Saharan Africa might be a result of better data rather than actual trends. Death rates among children aged 5–14 years were only 7% of those of children younger than 5 years. More than 98% of child deaths occurred in low-and-middle-income countries. The leading causes of death at age 5–14 years included selected infectious diseases, unintentional injuries, and cancers.

A large number of the deaths at age 15–59 years also arose in low-and-middle-income countries in 2001 (30% *vs* 15% in high-income countries). Non-communicable diseases are responsible for more than half of deaths in adults aged 15–59 in all regions except South Asia and Sub-Saharan Africa, where group I conditions, including HIV/AIDS, remain responsible for one-third and two-thirds of deaths, respectively (figure 2). 15–59-year old adults in low-and-middle-income countries face a 30% greater risk of death from non-communicable diseases than their counterparts in high-income countries.

Injuries were a disproportionately important cause of death in adults aged 15–59 years, and accounted for one-quarter of deaths, one-third in Europe and Central Asia (figure 2). Violence and war accounted for a disproportionate share of injury deaths in this age group in Sub-Saharan Africa (47%) and Latin America and the Caribbean (45%).

Death rates among adults aged 15–59 years have declined in all regions except Europe and Central Asia, and Sub-Saharan Africa (figure 2). HIV/AIDS has been a major factor in the rise in mortality in Sub-Saharan Africa; the increase in Europe and Central Asia is attributable to cardiovascular diseases and injuries.[30] Death rates from cardiovascular disease among adults aged 15–59 years have fallen in all regions except the low-and-middle-income countries of Europe and Central Asia (16% increase), although the declines are lower in South Asia and Sub-Saharan Africa than elsewhere. Similarly, Europe and Central Asia was the only region where death rates from injury increased (22% increase).

Non-communicable diseases accounted for nearly 60% of deaths globally in 2001, but for only 40% of YLL; conversely, injuries accounted for 12% of YLL and 9% of deaths. Figure 3 compares the ten leading causes of YLL and death for 2001. Measuring mortality with YLL gives relatively greater importance to HIV/AIDS, perinatal conditions, and diarrhoeal diseases, whereas simple counts of deaths give relatively greater importance to ischaemic heart disease, stroke, and chronic obstructive pulmonary disease, which primarily affect middle-aged and older adults. Sex differences in mortality were also better delineated with time-based measures. Globally, the male all-cause death rate was 11% higher than that for
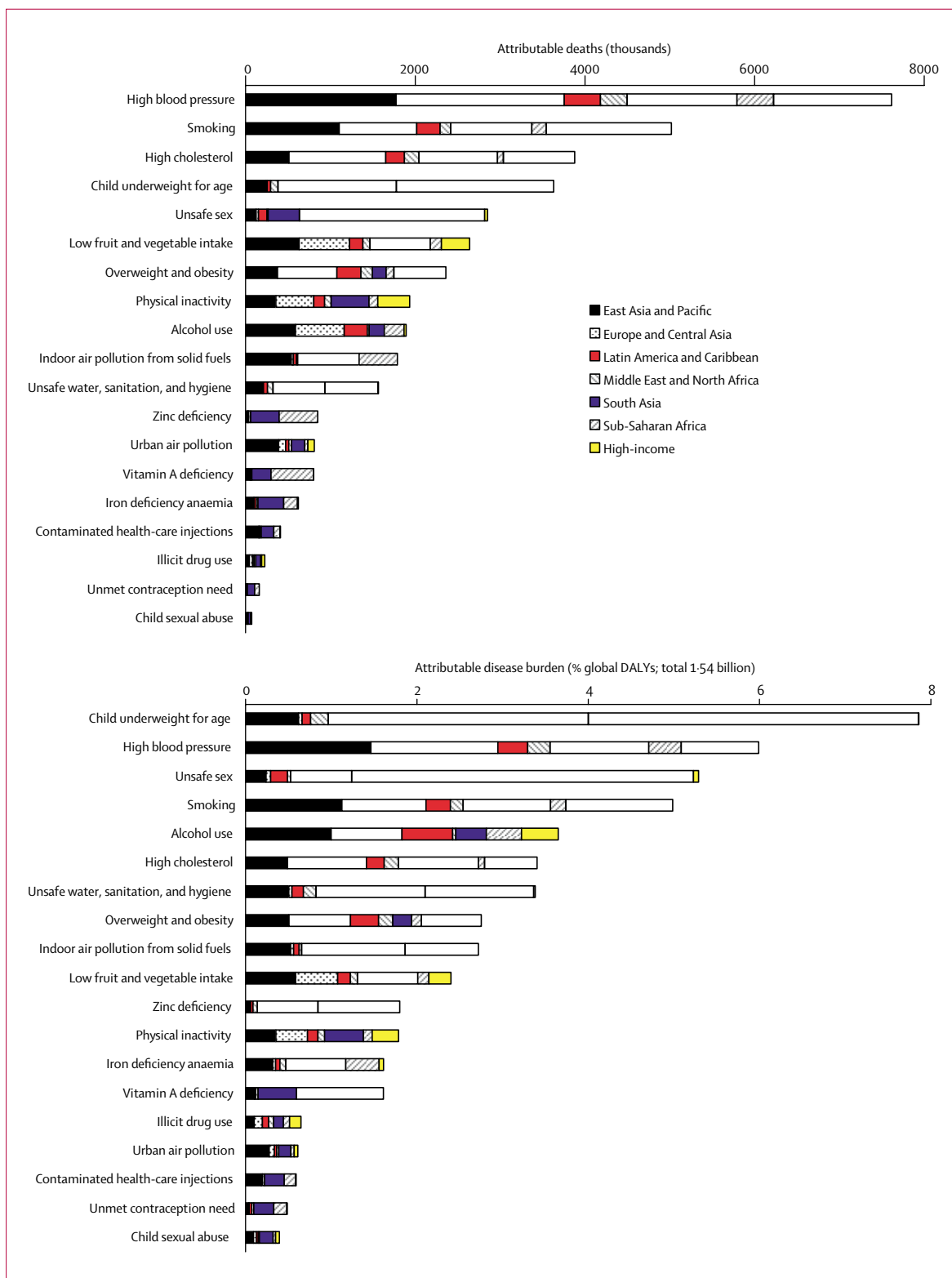
Attributable deaths (thousands)

High blood pressure
Smoking
High cholesterol
Child underweight for age
Unsafe sex
Low fruit and vegetable intake
Overweight and obesity
Physical inactivity
Alcohol use
Indoor air pollution from solid fuels
Unsafe water, sanitation, and hygiene
Zinc deficiency
Urban air pollution
Vitamin A deficiency
Iron deficiency anaemia
Contaminated health-care injections
Illicit drug use
Unmet contraception need
Child sexual abuse

■ East Asia and Pacific
▨ Europe and Central Asia
■ Latin America and Caribbean
▨ Middle East and North Africa
■ South Asia
▨ Sub-Saharan Africa
■ High-income

Attributable disease burden (% global DALYs; total 1·54 billion)

Child underweight for age
High blood pressure
Unsafe sex
Smoking
Alcohol use
High cholesterol
Unsafe water, sanitation, and hygiene
Overweight and obesity
Indoor air pollution from solid fuels
Low fruit and vegetable intake
Zinc deficiency
Physical inactivity
Iron deficiency anaemia
Vitamin A deficiency
Illicit drug use
Urban air pollution
Contaminated health-care injections
Unmet contraception need
Child sexual abuse

Figure 5: **Mortality (upper) and burden of disease (lower) due to leading global risk factors**
Figure shows estimated mortality and disease burden for each risk factor considered individually, divided by World Bank regions. These risks act in part though other risks and act jointly with other risks. Consequently, burden due to groups of risk factors will usually be less than sum of individual risks. For all geographical regions, high-income countries excluded and shown as single group at right-hand side of graph (yellow).

with disability for an incident case, discounting has a greater effect on reducing YLL than YLD. Different choices of discount rates and age weights do not cause any large changes in the rank ordering of diseases and injuries.

Uncertainty in estimated all-cause mortality ranged from 1% either way for high-income countries to 15–20% for Sub-Saharan Africa, reflecting differential data availability.[16] Uncertainty ranges were generally larger for deaths from specific diseases. For example, the relative uncertainty for deaths from ischaemic heart disease ranged from 12% for high-income countries to 25–35% for Sub-Saharan Africa.[29] The seemingly large uncertainty for high-income countries indicates a combination of uncertainty in overall mortality levels, in cause of death assignment, and in the attribution of deaths coded to ill-defined causes.

Assessments of the uncertainty of YLD for specific causes took into account not only typical levels of measurement error in the input datasets, but also expert judgment about the degree of uncertainty arising from the lack of representativeness of the available data for each region. The resulting uncertainty varied considerably across causes, ranging from relatively certain estimates for diseases such as polio, for which intensive surveillance systems are in place, to highly uncertain estimates for those like osteoarthritis, where for some regions no usable data source was found, and for others the latest available data were decades old. Typical uncertainty for regional prevalence estimates ranged from 10% to 90%, with a median value of 41%, among a subset of diseases for which uncertainty analysis was undertaken.[29]

Discussion

As programmes and policies to improve health worldwide become more widespread, so too will the need for more comprehensive, credible, and critical assessments to periodically monitor population health and the success, or otherwise, of these policies and programmes. The 1990 GBD study highlighted the importance of some conditions, particularly mental health disorders, and drew global public-health attention to the unrecognised burden of injuries. The results of the 2001 GBD study reinforce the conclusions of the 1990 GBD study about the importance of including non-fatal outcomes in a comprehensive assessment of global population health. They also confirm the growing importance of non-communicable diseases in most low-and-middle-income countries. Additionally, the 2001 study emphasises the important changes in population health in some regions since 1990 and suggests the importance of explicit attention to stillbirths and neonatal deaths. The intervening period was clearly one of mixed progress, when reductions in child mortality in many regions were countered by the HIV/AIDS epidemic and setbacks in adult mortality in countries of the former Soviet Union.

Worldwide, HIV/AIDS and malaria are large and growing causes of death and disease burden, especially in Sub-Saharan Africa, where they have negated gains in reducing child mortality in Africa from measles, acute respiratory infections, and diarrhoea. We did not undertake an analysis of trends in risk factors, but smoking is likely to be the cause of disease burden that has increased the most since 1990. The striking reversal in adult mortality decline in Eastern Europe during the 1990s is a stark reminder that epidemiological transitions, and improvements, can be reversed in the absence of sustained health monitoring and policies.

Methodological and data developments over the past decade, especially in the availability of information on causes of death, together with inputs from national and subnational studies of burden of disease, have greatly improved the empirical base for assessment of disease burden, and the comparability of the estimated contributions of diseases, injuries, and risk factors. Progress in knowledge about the disease burden for the specific causes has been uneven, although advances have been made in the data for and epidemiological understanding of major causes of ill health, such as HIV/AIDS and diabetes mellitus. Nevertheless, many methodological and empirical challenges remain and need to be addressed systematically if the burden of disease framework is to have greater use as the method for health accounting. For example, recent efforts at estimating the leading causes of child deaths, using approaches other than those described here, lead to differences for some causes, especially in the neonatal period, and indicate that substantial uncertainty remains about some causes of child mortality, requiring new evidence.[32] Results of our analysis of the levels of uncertainty in the GBD 2001 estimates reinforce the need for considerable caution when interpreting global comparative epidemiological assessments, and the need for increased investment in population health measurement systems.

Assignment of cause of death is one of the areas that requires additional data and research. Mirroring the work on causes of death among children,[32] there is a need to better understand and characterise the role of specific diseases in adult mortality in a consistent and comparable framework. The ICD rules determine the assignment of causes of death, but have shortcomings for diseases such as HIV/AIDS, diabetes, and hepatitis B and C, which are direct causes of death and increase the risk of other diseases such as tuberculosis, cirrhosis of the liver, renal failure, and cardiovascular diseases. Future work should both increase the comparability of cause of death assignment across populations and aim to develop methods for estimating what proportions of deaths from one disease are causally attributable to another disease.

Further work is also needed to improve data on risk factor exposure and to extend the analysis from the selected group of risk factors presented here to other important risks—eg, non-breastfeeding and salt and fat intake—and to estimate trends in exposure to risk factors. Such research will improve our understanding of the comparative importance of exposure to individual or multiple

environmental, nutritional, and life-style risk factors in different populations for major causes of disease burden, and of their role in observed disease trends over time—eg, trends in cardiovascular disease mortality.

Despite these uncertainties, the results of the 2001 GBD study suggest that further gains in health in poor countries could be achieved in relatively short time. Intervention choices can be better guided by information about potential costs and gains, including a comprehensive understanding of disease burden. Such guidance is available[13] and more rational application of it would accelerate progress towards the Millennium Development Goals and reduce the persistent differentials in health that show little tendency to narrow under current health policies.

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