Global and regional causes of death

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Background: Assessing the causes of death across all regions of the world requires a framework for integrating, and analysing, the fragmentary information that is available on numbers of deaths and their cause distributions. This paper provides an overview of the met and methods used by the World Health Organization to develop global-, regional- and country-level estimates of mortality for a comprehensive set of causes, and provides an overview of global and regional levels and patterns of causes of death for the year 2004. The paper also examines some of the data gaps, uncertainties and limitations in the resulting mortality estimates.

Sources of data: Deaths for 136 disease and injury causes were estimated from available death registration data (111 countries), sample death registration data (India and China), and for the remaining countries from census and survey information, and cause-of-death models. Population-based epidemiological studies and notifications systems also contributed to estimating mortality for 21 of these causes (representing 28% of deaths globally, 58% in Africa).

Areas of agreement: Ischaemic heart disease and cerebrovascular disease are the leading causes of death, followed by lower respiratory infections, chronic obstructive pulmonary disease and diarrhoeal diseases. AIDS and TB are the sixth and seventh most common causes of death, respectively, lower than in previous estimates. One-half of all child deaths are from four preventable and treatable communicable diseases. Globally, around 6 in 10 deaths are from non-communicable diseases, 3 from communicable diseases and 1 from injuries. Injury mortality is highest in South-East Asia, Latin America and the Eastern Mediterranean region. These results illustrate continuing huge disparities in risks and causes of death across the world.

Areas of controversy: Global mortality analyses of the type reported here have been criticized for making estimates of mortality for regions with limited, incomplete and uncertain data. Estimates presented here use a range of techniques depending on the type and quality of evidence. Better evidence on levels of adult mortality is needed for African countries.

Growing points: Considerable gaps and deficiencies remain in the information available on causes of death. Nine of 10 deaths in 2004 occurred in low- and middle-income countries, reinforcing the fundamental importance of improving

Accepted: July 10, 2009
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mortality statistics as a measure of health status in the developing world. Acknowledging the controversies around use of incomplete and uncertain data, systematic assessments and synthesis of the available evidence will continue to provide important inputs for global health planning.

Areas timely for developing research: Innovative methods involving sample registration, and the use of verbal autopsy questionnaires in surveys, are needed to address these gaps. Research on strategies to improve comparability of cause-of-death certification and coding practices across countries is also a high priority.

Keywords: mortality/causes of death/burden of disease

Introduction

An important input to national and international health decision-making and planning processes is a consistent and comparative analysis of the causes of death across different population groups. Assessing the causes of death across all regions of the world requires a framework for integrating, validating, analysing and disseminating the fragmentary, and at times contradictory, information that is available on numbers of deaths and their cause distributions. World Health Organization (WHO) maintains a mortality database\(^1\) that includes detailed annual tabulations of deaths from the death registration systems of Member States, with causes classified in most cases according to the 9th or 10th revision of the International Classification of Diseases (ICD).\(^2\)

Over the last decade, the WHO has intensified efforts to support the collection of vital registration information and other mortality data in developing countries. The number of countries reporting data on recent death registrations to WHO annually has increased from around 65 in 1970, 90 in 1999, to over 110 in 2009 (Table 1). Regional coverage of death registration varies from close to 100% in the European region to around 50% in the Asia-Pacific region and less than 10% in Africa. However, death registration is considered to be essentially 100% complete in only 64 of the countries reporting data, and predominantly these are the developed countries in Europe, the Americas and the Pacific region (Table 1).

In terms of actual deaths recorded by registration systems, data are provided to WHO annually for about 18.6 million deaths, representing one-third of all deaths estimated to be occurring in the world. Taking account of the representative data from multiple registration systems for India and China (described in the following section), population-level information on mortality and causes of death is available for around 72% of the world’s population.\(^3\)
During the last decade, a number of WHO programmes have made substantial investments in the collection and analysis of data to estimate the mortality for specific causes of policy interest, particularly for HIV, tuberculosis (TB), major causes of maternal and child deaths, and more recently, for malaria deaths.4–6 Additionally, the WHO has invested substantial effort, along with other UN Agencies such as UNICEF, in collecting and analysing information on total all-cause mortality levels for children in developing countries drawing on population surveys and censuses. Available information on adult mortality from demographic surveillance systems, sample registration systems (SRSs), surveys and censuses has also been used to improve estimates of adult mortality—all cause, and cause specific.

WHO has recently released an updated assessment of global and regional causes of death, drawing on extensive WHO databases and information provided by Member States, as part of an update of the Global Burden of Disease (GBD) study for the year 2004.7 This update built on previous WHO analyses using methods documented in a book published in 2006 by the Disease Control Priorities project,8 with some revisions and new data as described below.

The purpose of this paper is to provide an overview of the data and methods used by WHO to develop global-, regional- and country-level estimates of mortality for a comprehensive set of causes, and to provide an overview of global and regional levels and patterns of

<table>
<thead>
<tr>
<th>Data/method</th>
<th>Africa</th>
<th>Americas</th>
<th>Eastern Mediterranean</th>
<th>Europe</th>
<th>South-East Asia</th>
<th>Western Pacific</th>
<th>World</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death registration data with coverage of 85% or more</td>
<td>3</td>
<td>21</td>
<td>2</td>
<td>40</td>
<td>1</td>
<td>12</td>
<td>79</td>
</tr>
<tr>
<td>Death registration data with coverage of &lt;85%</td>
<td>–</td>
<td>12</td>
<td>7</td>
<td>11</td>
<td>1</td>
<td>3</td>
<td>34</td>
</tr>
<tr>
<td>SRS*</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>No population level data†</td>
<td>43</td>
<td>2</td>
<td>12</td>
<td>2</td>
<td>8</td>
<td>11</td>
<td>78</td>
</tr>
<tr>
<td>Total countries</td>
<td>46</td>
<td>35</td>
<td>21</td>
<td>52</td>
<td>11</td>
<td>27</td>
<td>193</td>
</tr>
</tbody>
</table>

*China and India both maintain systems in which deaths are recorded in a representative sample of districts across the country. Cause of death for most deaths is attributed using data collected using the VA methods (see text).

†Some of these countries do collect data on deaths in hospitals or urban areas, but these data cannot be considered to provide a representative picture of cause-of-death patterns at the population level.
causes of death. The paper also examines some of the data gaps, uncertainties and limitations in the resulting mortality estimates.

Results are presented here for high-income countries, treated as one group, and for low- and middle-income countries grouped by WHO regions. Results are available on the WHO website for other regional groupings, including World Bank regions and the regions used for monitoring progress to the Millennium Development Goals and for 192 countries. The 2004 estimates discussed here have also been used to prepare updated projections of mortality by cause for all regions of the world to the year 2030; these results are also available on the WHO website.

**Improving and updating global estimates of deaths by cause**

The original GBD study for 1990 was the first attempt to estimate global and regional numbers of deaths due to a comprehensive set of causes while ensuring consistency with death totals provided by death registration and demographic methods. Estimates of numbers of deaths carried out separately for individual causes and that are not constrained to sum to a demographically derived total often result in substantial overestimates of deaths due to each cause for regions without complete death registration data. In part, this occurs because in carrying out analysis for a single cause it is easy to be over-inclusive in counting the deaths attributable to the cause of interest, even if there is not an intention to maximize the size of the specific problem.

The first analytical step in estimating deaths by cause is thus to estimate the age-specific total death rates, by sex. Life tables specifying mortality rates by age and sex for 192 WHO Member States were developed for 2004 from available death registration data (111 Member States), SRSs (India, China, described below) and data on child and adult mortality from censuses and surveys. Surveys such as the Demographic and Health Surveys and UNICEF’s Multiple Indicator Cluster Surveys now provide information on levels of child mortality for most developing countries. For 55 countries, 42 of them in the Sub-Saharan Africa, no information was available on levels of adult mortality in 2004. Based on the estimated level of child mortality in 2004, the most likely level of adult mortality was estimated, based on regression models of child versus adult mortality as observed in a set of almost 2000 life tables judged to be of good quality, including the data for a number of African and other countries with high levels of child mortality. As almost all the life tables were for populations without significant HIV mortality, HIV deaths were excluded, and estimated HIV and conflict deaths (for countries with
war or civil conflict) were added to the predicted adult mortality to obtain the total estimated adult deaths.

For countries with death registration data, demographic techniques known as death distribution methods, which compare the number of registered deaths in an intercensal period with changes in population numbers, were used to assess the level of completeness of the recorded mortality data for adults, where completeness was assessed as less than 100%, death rates above age 5 were adjusted accordingly. Completeness of child death registration was separately assessed, using other available sources of information on child mortality.

We drew on four broad sources of mortality data for assessing causes of death: death registration systems with medically certified cause-of-death information, sample death registrations systems for India and China, epidemiological assessments for specific causes and cause-of-death models (CodMod). We summarize the approach used for the 2004 estimates; more detail is provided elsewhere. Table 2 summarizes the proportions of deaths in each region and in the world in 2004 for which the cause of death was estimated using each of these four data sources or methods.

Death registration data with information on cause-of-death distributions were available for 111 countries, the majority of these in the high-income group, Latin America and the Caribbean, and Europe and

Table 2 Methods used for cause-of-death estimation for 2004, by WHO region.

<table>
<thead>
<tr>
<th>Data/method</th>
<th>Africa</th>
<th>The Americas</th>
<th>Eastern Mediterranean</th>
<th>Europe</th>
<th>South-East Asia</th>
<th>Western Pacific</th>
<th>World</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death registration data with coverage of 85% or more</td>
<td>7</td>
<td>63</td>
<td>0</td>
<td>88</td>
<td>3</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>Death registration data with coverage of &lt;85%—adjusted for bias in cause-of-death distribution</td>
<td>0</td>
<td>30</td>
<td>0</td>
<td>10</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>SRS</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>45</td>
<td>56</td>
<td>23</td>
</tr>
<tr>
<td>Cause-specific estimates*</td>
<td>58</td>
<td>6</td>
<td>38</td>
<td>2</td>
<td>32</td>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>CodMod, regional pattern of causes of death</td>
<td>36</td>
<td>1</td>
<td>42</td>
<td>0</td>
<td>19</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Total deaths (millions)</td>
<td>11.2</td>
<td>6.2</td>
<td>4.3</td>
<td>9.5</td>
<td>15.3</td>
<td>12.2</td>
<td>58.8</td>
</tr>
</tbody>
</table>

*Epidemiological estimates obtained from studies, WHO technical programmes, CHERG and UNAIDS for the following causes: AIDS, TB, diphtheria, measles, pertussis, poliomyelitis, tetanus, dengue, malaria, schistosomiasis, trypanosomiasis, Japanese encephalitis, Chagas, maternal conditions (including abortion), all major causes of death in the neonatal period and in children to age 5, drug use disorders, rheumatoid arthritis and war.
Central Asia (Table 1). Deaths coded to the 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 were re-distributed across defined causes.\(^1\) The percentage of deaths coded to these ill-defined causes varied from 4% in New Zealand to more than 30% in Sri Lanka and Thailand.\(^3\) Cause of death was estimated for one-third of global deaths in 2004 using information from the death registration data (Table 2).

China and India, two countries with large populations (20% and 17% of the global population, respectively), do not have complete vital registration but information on causes of death are available from SRSs. From the mid-1990s until recently, death data for China has been routinely available from a nationally representative system of 145 disease surveillance centres (DSP) covering 1% of the total Chinese population.\(^1\) At each surveillance centre, a team including a physician investigated each death using medical records and interviews with family members to assign a cause of death. Periodic evaluations of the DSP data by re-surveying households at random have suggested a level of underreporting of deaths of about 15%.\(^1\) More recently, the DSP sites were used as the sampling frame for the third National Mortality Survey, which collected the cause of death for 868 000 deaths in 2004–2005.\(^1\)

Data on the age, sex and cause of more than 300 000 deaths are also collected annually from the vital registration system operated by the Chinese Ministry of Health, covering a population of 57 million, (36 million in the urban areas and 21 million in the rural). While the data are not representative of mortality conditions throughout China, they are useful for suggesting trends in mortality, given the number of deaths covered, and also provide valuable information on cause-of-death patterns. A third source of data on mortality in China is the decennial population census that asks about deaths in the household in the past 12 months.\(^2\) From these three data sources, it has been possible to extrapolate to the national level and contribute to estimates of global patterns and causes of death.

In India, the Medical Certificate of Cause of Death provides information for deaths in the urban India. Additionally, an SRS has successfully collected data on rural mortality and fertility since 1965 through continuous recording by resident enumerators as well as retrospective half yearly population surveys. During the early years of the twenty-first century, the methods used in the SRS in India were substantially revised as part of the Million Deaths study (MDS). As of 2002, causes of death have been ascertained using a verbal autopsy (VA) method (see below), with re-sampling, double coding by physicians centrally and other quality control efforts. The MDS is following the lives and
deaths of 1.1 million households throughout India until 2014.\textsuperscript{21,22} Data for a nationally representative sample of 62,553 deaths in 2001–2003 have now been released.\textsuperscript{23}

Both the Chinese and the Indian SRSs use VA methods to assign cause of death for deaths outside hospitals. A questionnaire is administered to care-givers or family members of deceased persons to gather information on signs and symptoms and their durations, and other pertinent information about the decedent in the period before death. Most approaches to date have used panels of physicians to review the data collected and assign a probable cause of death. Such methods naturally produce more uncertain attribution of cause of death than physician diagnosis.\textsuperscript{24} Categorical assignment of cause of death is inherently difficult for diseases without distinctive symptoms, such as malaria in children, or some forms of cardiovascular disease in older adults. WHO is working to standardize VA instruments for use with children and adult deaths.\textsuperscript{25} Cause of death was estimated for just under one-quarter of global deaths in 2004 using the VA and vital registration data for China and India (Table 2).

Population-based epidemiological studies, disease registers and notifications systems (in excess of 2700 data sets) also contributed to the estimation of mortality due to 21 specific causes of death, including HIV/AIDS (acquired immuno-deficiency syndrome), malaria, TB, childhood immunizable diseases, schistosomiasis, trypanosomiasis, Chagas disease, cancers, drug dependence, war and natural disasters. Almost one-third of these data sets was related to sub-Saharan Africa.

Particular attention was paid to the estimation of causes of child death in <5 years of age and in the infant and neonatal (under 28 days) periods. For countries without relatively complete death registration data, cause-specific and multi-cause models for child mortality, developed by the WHO Child Health Epidemiology Reference Group (CHERG) and the WHO Department of Immunization, Biologicals and Vaccines, were used to estimate causes of child deaths <5 years of age (neonatal and postneonatal);\textsuperscript{7,26,27} the resulting cause-specific estimates were adjusted country-by-country for consistency with estimated total deaths for neonates, infants and children aged <5 years.\textsuperscript{28,29} Cause of death was estimated using cause-specific information for just under under 30% of global deaths in 2004; with proportions ranging from 2% of deaths in Europe to 58% of deaths in the African region (Table 2).

Although epidemiological studies, and other data sources described above, allow estimation of deaths for certain causes in populations without death registration data, they do not cover many important causes of death in these populations, such as cardiovascular disease or injuries. In order to address these information gaps, models for
estimating broad cause-of-death patterns can serve as the starting point for indirect methods of estimating attributable mortality for a comprehensive list of detailed causes.

Indirect methods for estimating cause-of-death structure were first developed by Preston,\textsuperscript{30} who modelled the relationship between total mortality and cause-specific mortality for 12 broad groups of causes using the historical vital registration data for industrialized countries and a few developing countries. In the original GBD study for the year 1990, Murray and Lopez\textsuperscript{31} used cause-of-death models to estimate the mortality for three major cause groups: I, II and III, as a function of mortality from all causes, based on the regression analysis of observations on recent mortality patterns from 67 countries. Group I causes comprise communicable, maternal and perinatal conditions and nutritional deficiencies, Group II includes non-communicable diseases and Group III injuries. Group I causes are conditions that occur largely in the poorer populations, and typically decline at a faster pace than all-cause mortality during the epidemiological transition (in which the pattern of mortality shifts from high death rates from Group I causes at younger ages to Group II diseases at older ages).

For WHO updates of global causes of death, the statistical model for cause-of-death composition was estimated using a much larger data set consisting of 1613 country-years of historical death registration data.\textsuperscript{32} Regional patterns for detailed cause distributions within the broad cause groups were based on available death registration data within each region. The regional patterns were updated for African countries using a greater range of information on cause-of-death distributions in Africa than previously. These included the South African 2004 vital registration data, the Zimbabwe National Burden of Disease Study 1997,\textsuperscript{33} INDEPTH VA data from seven sites in Africa for 1999–2002,\textsuperscript{34} data from Antananarivo in Madagascar for 1976–1995,\textsuperscript{34} and Mozambique Maputo Central Hospital Mortuary data for 1993–2004.\textsuperscript{35} Cause of death was assigned using the CodMod for around 40% of deaths, primarily non-communicable diseases and injuries, in Africa and South-East Asia. At a global level, around 16% of deaths were assigned cause using CodMod (Table 2).

For this updated global analysis of causes of death for 2004, a complete analysis of the above sources of data was carried out at a country level for 192 countries. Apart from the specific data sources for China and India, this update also benefited from recent detailed analyses of causes of death drawing on multiple data sources for Iran,\textsuperscript{36} Mexico,\textsuperscript{37} South Africa,\textsuperscript{38} Thailand\textsuperscript{39} and Turkey.\textsuperscript{40}

Mortality estimates for HIV/AIDS were based on the most recent estimates released by WHO and the Joint United Nations Programme on
HIV/AIDS (UNAIDS). Advances in methodology, applied to an increased range of country data, resulted in a substantial reduction in the estimated global deaths due to HIV/AIDS: these were revised downwards from 2.7 million to 2.0 million for 2004.

Updated estimates for vaccine-preventable childhood diseases were prepared by the WHO Department of Immunization, Vaccines and Biologicals using estimates for vaccine coverage in 2004 prepared by WHO and UNICEF (United Nations Children’s Fund).

Revised mortality estimates for malaria were based on the estimates and analyses prepared by the Roll Back Malaria Partnership, CHERG and the Malaria Epidemiology Reference Group (MERG), together with the data from national case reports. Estimates for mortality for ages 5 years and above were revised using a transmission-intensity-based model, resulting in an increased proportion of such deaths (21% globally in 2004, compared with 10% in previous estimates).

Mortality estimates for tropical diseases, including dengue fever and Japanese encephalitis, were revised to take into account the latest WHO data on populations at risk, levels of endemicity, reported cases, treatment coverage and case fatality. Site-specific cancer incidence and mortality estimates were updated using revised estimates of site-specific survival probabilities for 2004, together with the site-specific incidence distributions from the Globocan 2002 database of the International Agency for Research on Cancer. Country-specific estimates of war and conflict deaths were updated to 2004 using information on conflict intensity, time trends and mortality obtained from a variety of published and unpublished war mortality databases. Population estimates for 2004 were based on the latest revisions by the UN Population Division.

**Sensitivity of methods and uncertainty of results**

There remain substantial data gaps and deficiencies, particularly for regions with limited death registration data. The results reported below include estimates of cause-specific deaths even for regions with limited death registration data, based on the best possible assessment of the available evidence. While these estimates will have wider uncertainty ranges than those for regions with more data, their exclusion would result in a potentially biased picture of the patterns of global mortality. 2004 includes results for these regions, albeit with wider uncertainty ranges. Uncertainty ranges for all-cause mortality rates for WHO Member States were published in the *World Health Report 2006*. Uncertainty analysis for the 2004 cause-specific estimates has not been carried out, but the ranges are likely to be similar to those...
assessed previously for 2001, with some reductions in uncertainty for specific countries and causes where improved data have become available.\textsuperscript{43}

Ninety-five per cent uncertainty ranges for regional cause-specific mortality estimates were calculated for 2001 using simulation methods based on the estimated uncertainty ranges for input data.\textsuperscript{43} Uncertainty in estimated all-cause mortality for 2001 ranged from ±1\% for high-income countries to ±15–20\% for sub-Saharan Africa, reflecting differential data availability. Uncertainty ranges were generally larger for deaths from specific causes. For example, the relative uncertainty for deaths from ischaemic heart disease (IHD) ranged from ±12\% for high-income countries to ±25–35\% for sub-Saharan Africa. There is considerable uncertainty in estimates of cause-specific deaths for chronic diseases such as IHD, cerebrovascular disease, diabetes, chronic obstructive pulmonary disease and external causes of injury for sub-Saharan Africa where these estimates depend heavily on cause-of-death modelling.

Results

Life expectancy

Life expectancy at birth in 2004 ranged from 79 years in high-income countries down to 50 years in sub-Saharan Africa. This is a 1.6-fold difference in total life expectancy across major regions of the globe. Overall, for the entire population of the world, average life expectancy at birth in 2004 was 65.6 years, an increase of almost 9 years over the last quarter century. Life expectancy increased during the 1990s for most regions of the world, with the notable exception of Africa and the former Soviet countries of Europe.\textsuperscript{44}

Global deaths: where and at what ages?

We estimated that almost 59 million people died in 2004, 10.4 million (or nearly 20\%) of whom were children <5 years of age. Of these child deaths, 99\% occurred in low- and middle-income countries. Just over 70\% of deaths in high-income countries occur beyond age 70, compared with 32\% in low- and middle-income countries (Fig. 1). A key point is the comparatively high numbers of deaths in poor countries at young adult ages (15–59 years). Just over 30\% of all deaths in low- and middle-income countries occur at younger adult ages (15–59 years), compared with 15\% in wealthy regions.
Among both men and women, most deaths are due to non-communicable conditions (Group II), and they account for about 6 of 10 deaths globally. Communicable diseases, reproductive and nutritional conditions are responsible for just under one-third of deaths in both males and females. The largest difference between the sexes occurs for Group III, with injuries accounting for almost 1 in 8 male deaths and 1 in 14 female deaths.

Figure 2 shows the distribution of deaths at all ages for 12 major cause groups. Cardiovascular diseases are the leading cause of death in the world, particularly among women; such diseases caused almost 32% of all deaths in women and 27% in men in 2004. Infectious and parasitic diseases are the next leading cause, followed by cancers, but these groupings show much smaller overall sex differentials. The largest differences between men and women are observed for intentional injuries (twice as high among men) and unintentional injuries. Maternal conditions account for 1.9% of all female deaths.

Leading causes of death

Table 3 shows the 20 most frequent causes of death, using cause categories at the next level below the broad cause groups shown in Fig. 2. IHD and cerebrovascular disease are the leading causes of death,
Table 3 Leading causes of death, all ages, 2004.

<table>
<thead>
<tr>
<th>Disease or injury</th>
<th>Deaths (millions)</th>
<th>Per cent of total deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 IHD</td>
<td>7.2</td>
<td>12.2</td>
</tr>
<tr>
<td>2 Cerebrovascular disease</td>
<td>5.7</td>
<td>9.7</td>
</tr>
<tr>
<td>3 Lower respiratory infections</td>
<td>4.2</td>
<td>7.1</td>
</tr>
<tr>
<td>4 COPD</td>
<td>3.0</td>
<td>5.1</td>
</tr>
<tr>
<td>5 Diarrhoeal diseases</td>
<td>2.2</td>
<td>3.7</td>
</tr>
<tr>
<td>6 HIV/AIDS</td>
<td>2.0</td>
<td>3.5</td>
</tr>
<tr>
<td>7 TB</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>8 Trachea, bronchus, lung cancers</td>
<td>1.3</td>
<td>2.3</td>
</tr>
<tr>
<td>9 Road traffic accidents</td>
<td>1.3</td>
<td>2.2</td>
</tr>
<tr>
<td>10 Prematurity and low birth weight</td>
<td>1.2</td>
<td>2.0</td>
</tr>
<tr>
<td>11 Neonatal infections*</td>
<td>1.1</td>
<td>1.9</td>
</tr>
<tr>
<td>12 Diabetes mellitus</td>
<td>1.1</td>
<td>1.9</td>
</tr>
<tr>
<td>13 Hypertensive heart disease</td>
<td>1.0</td>
<td>1.7</td>
</tr>
<tr>
<td>14 Malaria</td>
<td>0.9</td>
<td>1.5</td>
</tr>
<tr>
<td>15 Birth asphyxia and birth trauma</td>
<td>0.9</td>
<td>1.5</td>
</tr>
<tr>
<td>16 Self-inflicted injuries†</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>17 Stomach cancer</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>18 Cirrhosis of the liver</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>19 Nephritis and nephrosis</td>
<td>0.7</td>
<td>1.3</td>
</tr>
<tr>
<td>20 Colon and rectum cancers</td>
<td>0.6</td>
<td>1.1</td>
</tr>
<tr>
<td>All causes</td>
<td>58.8</td>
<td>100</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease; TB, tuberculosis.

*This category also includes other non-infectious causes arising in the perinatal period, apart from prematurity, low birth weight, birth trauma and asphyxia. These non-infectious causes are responsible for about 20% of deaths shown in this category.

†Self-inflicted injuries resulting in death can also be referred to as suicides.
followed by lower respiratory infections (including pneumonia), chronic obstructive pulmonary disease and diarrhoeal diseases. HIV/AIDS and TB are the sixth and seventh most common causes of death, respectively, and together caused 3.5 million deaths in 2004.

As may be expected from the very different distributions of deaths by age and sex, there are major differences in the ranking of causes between high- and low-income countries (Table 4). In low-income countries, the dominant causes are infectious and parasitic diseases (including malaria), and neonatal causes. In the high-income countries, 9 of the 10 leading causes of death are non-communicable conditions, including the four types of cancer. In the middle-income countries, the 10 leading causes of death are again dominated by non-communicable conditions; they also include road traffic accidents as the sixth most common cause.

IHD and cerebrovascular disease (stroke) were the leading causes of death in both middle- and high-income countries in 2004, and also in the top five causes for low-income countries. These two causes were together responsible for 22% of all deaths worldwide. Only 1.3 million of the 7.2 million deaths from IHD were in high-income countries. Of the 5.7 million stroke deaths, less than 0.8 million were in high-income countries. Lung cancer was the third leading cause of death in high-income countries, and the fifth leading cause in middle-income countries.

Causes of death among children <5 years of age

Six causes of death accounted for 73% of the 10.4 million deaths among children <5 years in 2004 (Fig. 3): acute respiratory infections, mainly pneumonia (17%), diarrhoeal diseases (17%), prematurity and low birth weight (11%), neonatal infections such as sepsis (9%), birth asphyxia and trauma (8%) and malaria (7%) The four communicable disease categories accounted for one-half (50%) of all child deaths.

Deaths in the neonatal period (0–28 days) account for more than one-third of all deaths in children. Among neonatal deaths, three main causes account for 80% of all neonatal deaths: prematurity and low birth weight (31%), neonatal infections (mainly sepsis and pneumonia and excluding diarrhoeal diseases) (26%) and birth asphyxia and birth trauma (23%).

Forty-five per cent (4.7 million deaths) of all child deaths <5 years in 2004 occurred in the African region, and an additional 30% (3.1 million) in the South-East Asia region. The death rate per 1000 children aged 0–4 years in the African region is almost double that of the region with the next highest rate, the Eastern Mediterranean, and more
### Table 4 Leading causes of death by income group, 2004.

<table>
<thead>
<tr>
<th>Disease or injury</th>
<th>World Low-income countries*</th>
<th>World All causes</th>
<th>Middle-income countries</th>
<th>High-income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Disease or injury</td>
<td>Deaths (millions)</td>
<td>Per cent of total deaths</td>
<td>Disease or injury</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IHD</td>
<td>7.2</td>
<td>12.2</td>
<td>1 Lower respiratory infections</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular disease</td>
<td>5.7</td>
<td>9.7</td>
<td>2 IHD</td>
</tr>
<tr>
<td></td>
<td>Lower respiratory infections</td>
<td>4.2</td>
<td>7.1</td>
<td>3 Diarrhoeal diseases</td>
</tr>
<tr>
<td></td>
<td>COPD</td>
<td>3.0</td>
<td>5.1</td>
<td>4 HIV/AIDS</td>
</tr>
<tr>
<td></td>
<td>Diarrhoeal diseases</td>
<td>2.2</td>
<td>3.7</td>
<td>5 Cerebrovascular disease</td>
</tr>
<tr>
<td></td>
<td>HIV/AIDS</td>
<td>2.0</td>
<td>3.5</td>
<td>6 COPD</td>
</tr>
<tr>
<td></td>
<td>TB</td>
<td>1.5</td>
<td>2.5</td>
<td>7 TB</td>
</tr>
<tr>
<td></td>
<td>Trachea, bronchus, lung cancers</td>
<td>1.3</td>
<td>2.3</td>
<td>8 Neonatal infections†</td>
</tr>
<tr>
<td></td>
<td>Road traffic accidents</td>
<td>1.3</td>
<td>2.2</td>
<td>9 Malaria</td>
</tr>
<tr>
<td></td>
<td>Prematurity and low birth weight</td>
<td>1.2</td>
<td>2.0</td>
<td>10 Prematurity and low birth weight</td>
</tr>
<tr>
<td></td>
<td>All causes</td>
<td>58.8</td>
<td>100</td>
<td>All causes</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease; TB, tuberculosis.

*Countries grouped by gross national income per capita—low income ($825 or less), high income ($10 066 or more).

†This category also includes other non-infectious causes arising in the perinatal period, which are responsible for about 20% of deaths shown in this category.
than double that of any other region (Fig. 4). The two leading communicable disease killers in all the regions are diarrhoeal diseases and respiratory infections. Deaths directly attributable to malaria occur almost entirely in the African region, representing 16% of all under-five deaths in that region.

Fig. 3 Distribution of causes of death among children aged <5 years and within the neonatal period, 2004. *Includes other non-communicable diseases (1%) and injuries (0.3%). †ICD-10 codes Q00-Q99. Another 1.2% of neonatal deaths are due to genetic conditions classified elsewhere. ‡Other non-infectious causes arising in the perinatal period. ‡Includes all neonatal infections except diarrhoeal diseases and neonatal tetanus. Source: Ref. 7.

Fig. 4 Differences in causes of child death, 2004. Note: High-income countries have been excluded for each WHO region and are shown as a single group at the top. Source: Ref. 7.
HIV/AIDS and measles are important causes of death summarized in the ‘other’ category. Globally, estimates suggest that 2.5% of all child deaths are associated with the HIV infection. In the African region, however—where more than 9 of 10 of the total global number of child deaths due to HIV/AIDS in 2004 occurred—5% of all child deaths are associated with HIV. Measles mortality, which has declined considerably in recent years, is estimated to be responsible for 4% of deaths among children aged <5 years worldwide and 5% of such deaths in the African region.

**Causes of death among adults aged 15–59 years**

The ranking of regions by mortality rates among adults aged 15–59 years differs markedly from the rankings by child mortality. The low- and middle-income countries of the European region have the second highest mortality level for adults aged 15–59 years, lower than for the African region but higher than that of the South-East Asia region (Fig. 5).

The mortality rate due to non-communicable diseases is highest in Europe, where nearly two-thirds of all deaths at ages 15–59 years for low- and middle-income countries are associated with cardiovascular diseases, cancers and other non-communicable diseases. Mortality rates due to non-communicable diseases are second highest in the African region.

![Fig. 5 Adult mortality rates by major cause group and region, 2004. Note: Respiratory infections are included in the category ‘Other infectious and parasitic diseases’, and are to be distinguished from chronic respiratory diseases, included in the category ‘Other non-communicable diseases’. Source: Ref. 7.](https://academic.oup.com/bmb/article-abstract/92/1/7/332071)
region, followed by the Eastern Mediterranean and South-East Asia regions, and lowest in the high-income countries. Injury mortality ranges from 0.5 (high-income countries) to 1.5 (European region) per 1000 adults aged 15–59 years. The proportion of deaths in this age group due to injuries ranges from 22% (high-income countries) to 29% (the Americas) of all deaths at ages 15–59, except in Africa, where it is 13%.

Group I causes of death—which include infectious and parasitic diseases, and maternal and nutritional conditions—account for more than one-fifth of all deaths in adults aged 15–59 years in two regions: South-East Asia (29%) and Africa (62%). This includes 35% of deaths due to HIV/AIDS in Africa. In fact, the mortality rate among adults due to HIV/AIDS alone in Africa is higher than mortality at 15–59 years due to all causes in three other regions: high-income countries, the Americas and the Western Pacific region.

**Adult mortality in Africa**

In the African region, mortality among men is slightly higher than among women, entirely due to higher mortality through injuries (Fig. 6). Women have higher mortality due to Group I causes. At ages 15–59 years, women have much higher mortality than men for HIV/AIDS, which causes more than half of all deaths in Group I and 40% of all female deaths. Maternal causes were associated with 14% of all

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**Fig. 6** Adult mortality rates among those aged 15–59 years in the African region, by sex and major cause group, 2004. Source: Ref. 7.
deaths. Maternal causes are causes associated specifically with pregnancy and childbirth and include deaths due to obstructed labour, maternal haemorrhage, sepsis, maternal hypertension, and to unsafe abortion.

**Adult mortality in low- and middle-income countries of Europe**

Figure 7 illustrates the high levels of mortality among men in the low- and middle-income countries of the European region. The main reason is the high mortality rates due to cardiovascular diseases and injuries, each associated with a mortality rate exceeding 2.5 per 1000 adults aged 15–59 years, and together being responsible for almost two-thirds of overall male mortality in this age group.

**Adult mortality in Latin America and the Caribbean**

The most striking data from the low- and middle-income countries of the Americas relate to injury mortality, which is about 1.6 per 1000 men aged 15–59 years, making it the leading cause group (Fig. 8). Intentional injuries account for 57% of adult mortality due to injuries, while motor vehicle accidents account for 25% of adult mortality due to injuries. One-quarter of the 600 000 global homicides occur in Latin America, 8.4% of the world’s population.
Mortality in the Eastern Mediterranean region

Perhaps unsurprisingly given the conflicts in Iraq and Afghanistan, war and violence are responsible for 40% of injury deaths in the Eastern Mediterranean region. Almost 55% of estimated 184 000 global war deaths occurred in this region in 2004. There is considerable uncertainty with estimates of war deaths; the 56 000 estimated conflict deaths in Iraq have an uncertainty range of approximately 45 000–66 000.45

South-East Asia

One-third of the 527 000 global deaths due to pregnancy and childbirth (maternal causes) occurred in South-East Asia in 2004. Accidental fire deaths were high in this region and caused twice as many deaths in women as in men. An extraordinary 80% of global fire-related deaths among adult women occurred in South-East Asia. Many fire deaths are probably related to cooking accidents but this is not the only cause. In India, fire is implicated in an estimated 16% of suicides in women and an unknown number of homicides.46

Western Pacific region

China, with 20% of the world’s population, dominates mortality for the low- and middle-income countries of the Western Pacific region.
Low- and middle-income countries of this region now have a lower child mortality rate than the former Soviet countries of Europe (Fig. 4), and adults aged 15–59 years have the lowest mortality rate for any regional grouping of low- and middle-income countries (Fig. 5), not far behind the mortality rates for high-income countries.

Suicide, arguably the most extreme expression of mental illness, is the sixth leading cause of death globally for adults aged 20–59 years, and the third leading cause of death in low- and middle-income countries of the Western Pacific region. The suicide rate for women aged 15–44 years in these countries is 60% times higher than that for the rest of the world.

Discussion

The original GBD study, initial results of which appeared in the 1993 World Development Report, was the first attempt to provide comprehensive regional and global estimates for mortality by cause for a comprehensive set of more than 130 causes. Earlier attempts to quantify global cause-of-death patterns were largely restricted to broad cause-of-death groups (e.g. all infections and parasitic diseases combined).

In updating global cause-of-death estimates over the last decade, the WHO has focused on individual countries as the unit of analysis, with the systematic application of standardized approaches for countries in each category for mortality data availability as well as drawing much more extensively on the detailed analyses of cause-specific data carried out in priority areas by WHO and other international agencies. This has greatly improved the cross-population comparability of cause-specific death estimates as well as increasing the usefulness of the results for country-level health situation assessment and priority setting. More attention has also been paid to assessing uncertainty in both national and global assessments of cause-specific and all-cause deaths. This uncertainty must be taken into account when making cross-national comparisons, and needs to be carefully communicated and interpreted by epidemiologists and policy-makers alike.

Global patterns of mortality in the early twenty-first century

Communicable diseases remain an important cause of death in low-income countries. Seven of 10 deaths in children <5 years still occur in low-income countries and almost half are due to only four infectious diseases: pneumonia, diarrhoeal diseases, malaria and measles. There
have been impressive reductions in diarrhoeal disease and measles deaths, but malaria, malnutrition and safe water and sanitation systems remain as substantial challenges. A recent study projected that global under-five mortality will decline by 27% from 1990 to 2015, substantially less than the target of Millennium Development Goal 4 of a 67% decrease. Globally, we are not doing a better job of reducing child mortality now than we were three decades ago.

These results incorporate recent revisions to HIV/AIDS mortality, which have used improved methods, applied to an increased range of country data resulting in a significant reduction in estimated HIV prevalence and HIV/AIDS mortality. However, HIV/AIDS remains the leading cause of death in sub-Saharan Africa, causing an estimated 1.7 million deaths (or 15% of all deaths) in 2004.

Our results also confirm the growing importance of non-communicable diseases in most low- and middle-income countries. Population ageing is the most important driver of this trend, but adverse risk factor trends for tobacco and overweight and obesity will exacerbate it. Already more than half of the world’s population >65 years lives in low- and middle-income countries. The proportion of the world’s population >65 years, currently 7%, will be more than double (to 16%) in the next 50 years. In all regions in 2004, except for Africa, non-communicable diseases were responsible for one-half or more of all deaths in low- and middle-income countries. The dramatic reversal in adult mortality decline in Eastern Europe during the 1990s is a stark reminder that epidemiological transitions, and improvements, can be very rapidly reversed.

Controversy

Previous global mortality analyses of the type reported here have been criticized for making estimates of mortality for regions with limited, incomplete and uncertain data, and have even been characterized by some critics as having at best only tenuous links to empirical evidence. Murray et al. have argued systematic assessments and synthesis of the available evidence, which attempt to ensure consistency and adjust for known biases, will almost always provide a better basis for health planning than ideology or special interests. The analytical approach used here has been strongly influenced by demographic and economic traditions of making the best possible estimates of quantities of interest for populations from the available data, using a range of techniques depending on the type and quality of evidence.
Addressing the data limitations and gaps

Although morbidity and disability assessment is of growing significance in all countries, mortality as a health status measure is still of great importance in the poorer countries. Of the estimated 58.8 million deaths worldwide in 2004, 9 of 10 occurred in low- and middle-income countries, reinforcing the fundamental importance of improving mortality statistics as a measure of health status in the developing world.

While there have been noteworthy improvements in the coverage and quality of death registration data, with Iran and South Africa being two success stories in the last decade or so, only one-third of the world’s population is covered by population-level death registration data. China and India, the two most populous nations in the world, have both been redeveloping their VA-based SRSs, and the new data from these systems is now becoming available to improve our understanding of the causes of death in almost 40% of the world’s population.

Apart from the as-yet unsolved problems in obtaining valid cause-of-death information from VA instruments, less than 5% of the African population is covered by functioning death registration systems. There is very little national-level information available on the causes of child mortality or even on levels of adult mortality for most African countries.

Assignment of cause of death is one of the areas that require additional data and research. Mirroring the work on causes of death among children, there is a need to better understand and characterize the role of specific diseases in adult mortality in a consistent and comparable framework. Currently the ICD rules determine the assignment of causes of death, but have shortcomings for diseases such as TB, diabetes and hepatitis B and C, which are both direct causes of death and increase the risk of other diseases such as HIV/AIDS, cirrhosis of the liver, renal failure and cardiovascular diseases.

There remain unresolved methodological and empirical challenges for better global and national estimates of causes of death. Chief among these are the following:

- Development of improved methods for ascertaining levels and causes of mortality using survey and VA methods for populations where it is not yet possible to establish functioning vital registration systems with medically certified causes of death.
- Increasing the coverage of the global population by death registration with medically certified cause of death. WHO is working with other international agencies and partnerships to assist countries in implementing and improving vital registration systems. There have been relatively few
success stories in the last three decades of countries implementing good
civil registration from scratch—considerable country-level political will is
necessary.

- Improving the quality of certification and coding of causes of death using
the ICD and its guidelines and rules. There are unacceptably large propor-
tions of deaths in some countries, which are coded to inappropriate or
invalid codes for underlying cause of death.

Besides the international agencies, non-governmental organizations
such as the Bill and Melinda Gates Foundation are funding research
and capacity building in this area. These networks and research groups
should provide valuable partners for global health agencies, such as
WHO, UNICEF and the World Bank, in improving the measurement
and policy use of information on population health.

Acknowledgements

The views expressed in this paper are entirely those of its authors and
do not necessarily represent the decisions or the stated policy of the
World Health Organization or its Member States. Valuable inputs
were provided by WHO staff from many departments and by experts
outside WHO. While it is not possible to name all those who contribu-
ted to this effort, we would like to particularly note the contributions
of Bob Black, Cynthia Boschi-Pinto, Somnath Chatterji, Richard
Cibulskis, Simon Cousens, Chris Dye, Mercedes de Onis, Majid Ezzati,
Marta Gacic Dobo, Peter Ghys, Kim Iburg, Mie Inoue, Eline
Korenremp, Joy Lawn, Steve Lim, Silvio Mariotti, Erin McLean,
Donatella Pascolini, Juergen Rehm, Serge Resnikoff, Lisa Rogers,
Alexander Rowe, Lale Say, Suzanne Scheele, Kenji Shibuya, Andrew
Smith, Karen Stanecki, Jose Suaya, Jos Vandelaer, Theo Vos and Lara
Wolfson.

Funding

This work was funded by the World Health Organization.

References

Global and regional causes of death

