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# Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010

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## Summary

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

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

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

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

See **Special Report** page 2067

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

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See Online for appendix

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

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

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

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## Introduction

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

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

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

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

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

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

## Methods

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

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## Database development

Over the 5-year duration of the GBD 2010, we sought to identify all published and unpublished data sources relevant to estimating causes of death for 187 countries from 1980 to 2010. Depending on the cause, various sources of data were used. We briefly outline in the following text the main types of data identified and how they were used. The appendix (p 2) provides a summary of the site-years of data identified by broad type of data system and the number of site-years by GBD region (the data presented in the appendix are mapped at the most detailed level for a given study; the aggregate levels are created by combining the detailed levels). Of the GBD regions, central sub-Saharan Africa had the most limited evidence base with data on only 27 causes from at least one country.

For vital registration with medical certification of causes of death, we identified 2798 site-years of data from 130 countries between 1980 and 2010. 3% of the site-years were coded with ICD 8, 44% with ICD 9, 40% with ICD 10, 12% with country-specific tabulations of ICD 8, ICD 9, and ICD 10, and 1% with non-ICD tabulations. Additionally, there is country to country variation in the detail used to report causes of death included in national reporting lists—namely, the basic tabulation list for ICD 9, the ICD 10 tabulation list, three-digit and four-digit detail, and special reporting lists. Overall, we identified 25 variants of cause of death reporting lists in use from 1980 to 2010 across all sources of vital registration.

The verbal autopsy data were collected through sample registration systems, demographic surveillance systems, or surveys. Verbal autopsy is a means for ascertaining the cause of death of individuals and the cause-specific mortality fractions in populations with incomplete vital registration systems. A trained interviewer uses a structured questionnaire to ask about the signs, symptoms, and demographic characteristics of a recently deceased individual from the next of kin. We identified 486 site-years of published and unpublished verbal autopsy data across 66 countries, of which 10% were nationally representative. Verbal autopsy data are highly heterogeneous: studies use different instruments, different cause lists from single causes to full ICD cause lists, different methods for assigning cause of death based on a completed verbal autopsy, different recall periods, and different age groups, quite apart from cultural differences in the interpretation of specific questions. The appendix (p 25) provides a full listing of the sources used for all verbal autopsy and non-vital registration data organised by country.

Population-based cancer registries provide an important source of data on incidence of cancers in various countries. We identified 2715 site-years of cancer registry data across 93 countries. Some registries also track cancer mortality and provide plausible data on the mortality-to-incidence ratio by age, sex, and site. Following the methods developed by Forouzanfar and colleagues,[31] we developed estimated mortality-to-incidence ratios for all major cancers by age, sex, and country. We estimated the log of the mortality-to-incidence ratio as a function of national income per head with random effects for country, year, and age. The estimated mortality-to-incidence ratios were used to map cancer registry data on incidence to expected deaths that have been incorporated into the database. Mortality-to-incidence ratios by country, age, and sex are available on request.

In most countries, police and crime reports are an important source of information for some types of injuries, notably road injuries and interpersonal violence. The police reports used in this analysis were obtained from published studies, national agencies, and institutional surveys such as the UN Crime Trends survey and the WHO Global Status Report on Road Safety Survey.[30,41] By comparing with other sources such as vital registration data, we assessed whether police reports were likely to be complete and cover the entire country. In total, we included in the analysis 1129 site-years of police reports from 122 countries from 1980 to 2010 that met our criteria.

We identified 32 site-years of burial and mortuary data in 11 countries from ministries of health, published reports, and mortuaries themselves. Because of known bias in the epidemiological composition of burial and mortuary data, we only used information on the fraction of injuries due to specific sub-causes from these sources. These proportionate fractions of injury deaths due to specific causes were transformed into fractions of all causes by multiplying by the fraction of all deaths due to injuries estimated from a model for all injuries.

Multiple demographic and health surveys, other surveys, and censuses provide data on the fraction of deaths in the reproductive age groups that are pregnancy-related. We identified 1557 survey years with sibling history data, and a further 52 household survey years or census years of data covering 61 countries. We also identified 56 surveys or censuses with information on injury mortality across 65 survey years or census years.

We identified eight countries with nationally representative maternal mortality surveillance systems covering 83 site-years and five GBD regions. Some surveillance systems were based on prospective verbal autopsy. Surveillance data on the number of maternal deaths, or the maternal mortality ratio multiplied by births, were converted into cause fractions by dividing by the total number of deaths estimated in the reproductive age groups.

Additionally, we included 21 site-years of data based on deaths in health facilities. However, we chose to only incorporate deaths due to injury from this source because of known bias. We adjusted data for bias using a revised version of the hospital adjustment method, which uses more data and is more consistent with the GBD cause list developed by Murray and colleagues in 2007.[42] This method attempts to correct for selection bias in the deaths that occur in hospital. Finally, we used only the fraction of injury deaths due to specific injuries from these sources and converted them to fractions of deaths

from all causes following the method described for burial and mortuary data.

### Assessement and enhancement of data quality and comparability

We assessed and enhanced data quality following six steps outlined in more detail here:

Step 1 consists of the assessment of completeness of death recording in each source. In settings where a data source does not capture all deaths in a population, the cause composition of deaths captured might be different from those that are not. Murray and Lopez[43] postulated in the GBD 1990 that deaths recorded in countries with incomplete vital registration would more likely originate from wealthier sectors of populations for which the cause of death structure was skewed towards non-communicable rather than communicable diseases, communicable diseases being more common in those who cannot afford appropriate treatment. They proposed a correction based on the assumption that this inequality in death rates within a country was uniform across countries. This approach was used in subsequent GBD revisions and in some of the CHERG[19,44] analyses when making use of vital registration data.

There are reasons, however, to also be concerned that deaths recorded in systems with low coverage might be biased towards selected causes that are more likely to occur in hospital. Many vital registration systems begin with in-hospital deaths and progressively capture deaths in the community. Murray and colleagues[42] showed that the fraction of deaths in hospital was higher for acute causes for which death was not immediate but occurred over a matter of days such as for some maternal causes. Further, evidence on subnational mortality patterns[45] clearly shows that the assumption of uniform inequality is unlikely to be true; nor is the assumption that deaths are registered in order, from the richest to the poorest communities. For the GBD 2010, we assessed the completeness of vital registration or sample registration data over age 5 years using the most accurate variants of death distribution methods: synthetic extinct generations, the generalised growth balance method, and a hybrid of the two.[46] We assessed completeness for under age 5 years by comparing registration data with survey and census data on child mortality. More details on how the synthesis of these methods was done are provided by Wang and colleagues.[40] Completeness is often substantially different for child and adult deaths; in some regions such as Latin America, child completeness is usually lower than adult completeness, but other patterns are observed in Asia.[40] Completeness levels must also be interpreted with caution. Some systems, for example in Turkey, capture deaths relatively completely in selected administrative units only. That is, completeness of registration might be high but coverage is not.

For adults, few vital registration or sample registration datapoints exist with completeness lower than 70% in the database. Because completeness is often lower for deaths in children younger than 5 years compared with that in individuals older than 5 years, we investigated the effect of including data on causes of death with completeness lower than 70% (see appendix p 49 for more detail). We re-ran cause of death models for the major causes of death in children younger than 5 years in five different ways: excluding all data with completeness lower than 30%, lower than 40%, lower than 50%, lower than 60%, and lower than 70%. At the global level, the number of deaths estimated in 2010 for acute respiratory infections and diarrhoea, for example, differ by 0·9% and 1·2%, respectively, between models that include all data and those that exclude data where death registration for children younger than 5 years is less than 70% complete. The difference is slightly larger in 1980, for which including all data leads to higher numbers than excluding the incomplete data. Even in the 1980s at the regional or country level, the differences are small enough that we chose to use all available data. These sensitivity analyses suggest that, at least for major causes of child death, no consistent evidence of selection bias towards causes of death in richer populations exists.

To assess completeness is feasible for vital registration and sample registration data but not for small-scale studies on verbal autopsy, which might not detect all deaths through household recall. In fact, household recall often yields a substantial undercount of deaths.[47,48] In the absence of evidence on the cause of death pattern in recalled versus not recalled deaths, we have made the simplifying assumption that verbal autopsy cause fractions are representative of the study population; the CHERG analyses of verbal autopsy data make the same assumption.[19,20]

Step 2 consists of mapping revisions and variants of the ICD (see appendix p 50 for more detail). Vital registration data and some verbal autopsy data for 1980–2010 are reported using several variants of the ICD 8, ICD 9, and ICD 10. We mapped these revisions to the GBD cause list in the appendix. This mapping provides the codes for the detailed list for ICD 9 and ICD 10, as well as the basic tabulation list for ICD 9 (BTL). We identified three national variants of ICD 9 BTL that we also mapped to the GBD cause list. Of note, there were 119 GBD causes not available in the BTL, such as pneumonia and diarrhoea aetiologies, some of the cancers, hepatitis by type, some of the cardiovascular causes, many of the mental and behavioural disorders, some musculoskeletal disorders, and some injury subtypes.

Step 3 relates to the redistribution of deaths assigned to garbage codes. Murray and Lopez[43] introduced the notion of "garbage codes" in the GBD 1990 and proposed methods to redistribute deaths assigned to garbage codes to probable underlying causes of death. Garbage codes are causes of death that should not be identified as underlying causes of death but have been entered as the underlying cause of death on death certificates. Classic examples of garbage codes include senility or cardiopulmonary arrest. In the GBD 1990, major garbage codes were identified and

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