

Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015



GBD 2015 Mortality and Causes of Death Collaborators*



Summary

Background Improving survival and extending the longevity of life for all populations requires timely, robust evidence on local mortality levels and trends. The Global Burden of Disease 2015 Study (GBD 2015) provides a comprehensive assessment of all-cause and cause-specific mortality for 249 causes in 195 countries and territories from 1980 to 2015. These results informed an in-depth investigation of observed and expected mortality patterns based on sociodemographic measures.

Methods We estimated all-cause mortality by age, sex, geography, and year using an improved analytical approach originally developed for GBD 2013 and GBD 2010. Improvements included refinements to the estimation of child and adult mortality and corresponding uncertainty, parameter selection for under-5 mortality synthesis by spatiotemporal Gaussian process regression, and sibling history data processing. We also expanded the database of vital registration, survey, and census data to 14 294 geography-year datapoints. For GBD 2015, eight causes, including Ebola virus disease, were added to the previous GBD cause list for mortality. We used six modelling approaches to assess cause-specific mortality, with the Cause of Death Ensemble Model (CODEm) generating estimates for most causes. We used a series of novel analyses to systematically quantify the drivers of trends in mortality across geographies. First, we assessed observed and expected levels and trends of cause-specific mortality as they relate to the Socio-demographic Index (SDI), a summary indicator derived from measures of income per capita, educational attainment, and fertility. Second, we examined factors affecting total mortality patterns through a series of counterfactual scenarios, testing the magnitude by which population growth, population age structures, and epidemiological changes contributed to shifts in mortality. Finally, we attributed changes in life expectancy to changes in cause of death. We documented each step of the GBD 2015 estimation processes, as well as data sources, in accordance with Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).

Findings Globally, life expectancy from birth increased from 61·7 years (95% uncertainty interval 61·4–61·9) in 1980 to 71·8 years (71·5–72·2) in 2015. Several countries in sub-Saharan Africa had very large gains in life expectancy from 2005 to 2015, rebounding from an era of exceedingly high loss of life due to HIV/AIDS. At the same time, many geographies saw life expectancy stagnate or decline, particularly for men and in countries with rising mortality from war or interpersonal violence. From 2005 to 2015, male life expectancy in Syria dropped by 11·3 years (3·7–17·4), to 62·6 years (56·5–70·2). Total deaths increased by 4·1% (2·6–5·6) from 2005 to 2015, rising to 55·8 million (54·9 million to 56·6 million) in 2015, but age-standardised death rates fell by 17·0% (15·8–18·1) during this time, underscoring changes in population growth and shifts in global age structures. The result was similar for non-communicable diseases (NCDs), with total deaths from these causes increasing by 14·1% (12·6–16·0) to 39·8 million (39·2 million to 40·5 million) in 2015, whereas age-standardised rates decreased by 13·1% (11·9–14·3). Globally, this mortality pattern emerged for several NCDs, including several types of cancer, ischaemic heart disease, cirrhosis, and Alzheimer's disease and other dementias. By contrast, both total deaths and age-standardised death rates due to communicable, maternal, neonatal, and nutritional conditions significantly declined from 2005 to 2015, gains largely attributable to decreases in mortality rates due to HIV/AIDS (42·1%, 39·1–44·6), malaria (43·1%, 34·7–51·8), neonatal preterm birth complications (29·8%, 24·8–34·9), and maternal disorders (29·1%, 19·3–37·1). Progress was slower for several causes, such as lower respiratory infections and nutritional deficiencies, whereas deaths increased for others, including dengue and drug use disorders. Age-standardised death rates due to injuries significantly declined from 2005 to 2015, yet interpersonal violence and war claimed increasingly more lives in some regions, particularly in the Middle East. In 2015, rotaviral enteritis (rotavirus) was the leading cause of under-5 deaths due to diarrhoea (146 000 deaths, 118 000–183 000) and pneumococcal pneumonia was the leading cause of under-5 deaths due to lower respiratory infections (393 000 deaths, 228 000–532 000), although pathogen-specific mortality varied by region. Globally, the effects of population growth, ageing, and changes in age-standardised death rates substantially differed by cause. Our analyses on the expected associations between cause-specific mortality and SDI show the regular shifts in cause of death composition and population age structure with rising SDI. Country patterns of

Lancet 2016; 388: 1459–544

This online publication has been corrected. The corrected version first appeared at thelancet.com on January 5, 2017

See [Editorial](#) page 1447

See [Comment](#) pages 1448 and 1450

*Collaborators listed at the end of the Article

Correspondence to:

Prof Christopher J L Murray,
2301 5th Avenue, Suite 600,
Seattle, WA 98121, USA
cjlm@uw.edu

See Online for [infographic](#)
<http://www.thelancet.com/gbd>

premature mortality (measured as years of life lost [YLLs]) and how they differ from the level expected on the basis of SDI alone revealed distinct but highly heterogeneous patterns by region and country or territory. Ischaemic heart disease, stroke, and diabetes were among the leading causes of YLLs in most regions, but in many cases, intraregional results sharply diverged for ratios of observed and expected YLLs based on SDI. Communicable, maternal, neonatal, and nutritional diseases caused the most YLLs throughout sub-Saharan Africa, with observed YLLs far exceeding expected YLLs for countries in which malaria or HIV/AIDS remained the leading causes of early death.

Interpretation At the global scale, age-specific mortality has steadily improved over the past 35 years; this pattern of general progress continued in the past decade. Progress has been faster in most countries than expected on the basis of development measured by the SDI. Against this background of progress, some countries have seen falls in life expectancy, and age-standardised death rates for some causes are increasing. Despite progress in reducing age-standardised death rates, population growth and ageing mean that the number of deaths from most non-communicable causes are increasing in most countries, putting increased demands on health systems.

Funding Bill & Melinda Gates Foundation.

Copyright © The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY license.

Introduction

Comparable information about deaths and mortality rates broken down by age, sex, cause, year, and geography provides a starting point for informed health policy debate. However, generating meaningful comparisons of mortality involves addressing many data and estimation challenges, which include reconciling marked discrepancies in cause of death classifications over time and across populations; adjusting for vital registration system data with coverage and quality issues; appropriately synthesising mortality data from cause-specific sources, such as cancer registries, and alternative cause of death

identification tools, such as verbal autopsies; and developing robust analytical strategies to estimate cause-specific mortality amid sparse data.¹⁻⁶ The annual Global Burden of Disease (GBD) analysis provides a standardised approach to addressing these problems, thereby enhancing the capacity to make meaningful comparisons across age, sex, cause, time, and place.

Previous iterations of the GBD study showed substantial reductions in under-5 mortality, largely driven by decreasing rates of death from diarrhoeal diseases, lower respiratory infections, malaria, and, in several countries, neonatal conditions and

Research in context

Evidence before this study

In 2012, the Global Burden of Disease 2010 study was published, providing results from the first complete revision of the Global Burden of Disease (GBD) since the first assessment in 1993. The study reported on mortality and causes of death between 1990 and 2010 in 187 countries. In response to demand for up-to-date information on the health of populations to inform health policy debates, annual updates of the GBD study are now prepared, with the first of these, the GBD 2013 study, published in 2015. For the first time, collaborative teams undertook subnational assessments for China, Mexico, and the UK as part of this study.

Added value of this study

The GBD 2015 assessment of mortality and causes of death provides new and more robust evidence on the health of populations worldwide through the inclusion of subnational data from an expanded group of countries, including Brazil, India, Japan, Kenya, Saudi Arabia, South Africa, Sweden, and the USA, in addition to updates for China, Mexico, and the UK. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations. Estimation of mortality levels, patterns, and distribution for several new causes, including Ebola virus disease, further disaggregations of

carcinoma and leukaemia, motor neuron disease, and mortality attributable to environmental heat and cold exposure have been added for the GBD 2015 study. Furthermore, this analysis extends the concept of sociodemographic status first reported in GBD 2013, with important changes to computational methods, resulting in a new Socio-demographic Index (SDI) for a more robust positioning of countries and territories on the development continuum.

Implications of all the available evidence

This study provides the most comprehensive assessment to date of patterns and levels of mortality worldwide, expanding on previous analyses by further investigating the main determinants of epidemiological patterns and trends across geographies and over time. The GBD 2015 study entails a complete reanalysis of trends for each cause of death from 1990 to 2015; the time series published here supersedes the results of the GBD 2013 study. The expansion of geographic units, from 296 in GBD 2013 to 519 for GBD 2015, is envisaged to continue so as to sustain comparability over time and across all geographies. The comparison of estimates of observed mortality levels with patterns expected based on the SDI provides an in-depth understanding of national health challenges and priority areas for intervention.

malnutrition.⁷⁻¹¹ Non-communicable diseases (NCDs) and injuries claimed increasingly more lives throughout the world, although age-standardised death rates fell for many causes and countries.⁷ Examination of epidemiological convergence among high-income, middle-income, and low-income countries showed the importance of evaluating both absolute and relative changes in mortality, as solely focusing on absolutes can mask rising relative inequality among certain age groups and causes. The GBD 2015 study expands on these analyses by further evaluating the drivers of epidemiological patterns across countries and over time. Such mortality trends are generally shaped by a combination of factors, including changes in income per

capita, educational attainment, fertility, shifts in clinical care and health system responsiveness, emergent health threats such as disease outbreaks or increasing rates of obesity, and geography-specific health contexts. An in-depth understanding of national health gains and priority areas for intervention can be provided by comparing estimates of expected mortality patterns. These results are of particular importance amid debates on financing and policy options for the newly adopted Sustainable Development Goals, which include both ambitious targets for maternal and child health and a much broader health agenda also encompassing NCDs and injuries. The GBD 2010 study presented results for 187 countries, encompassing all those with a population

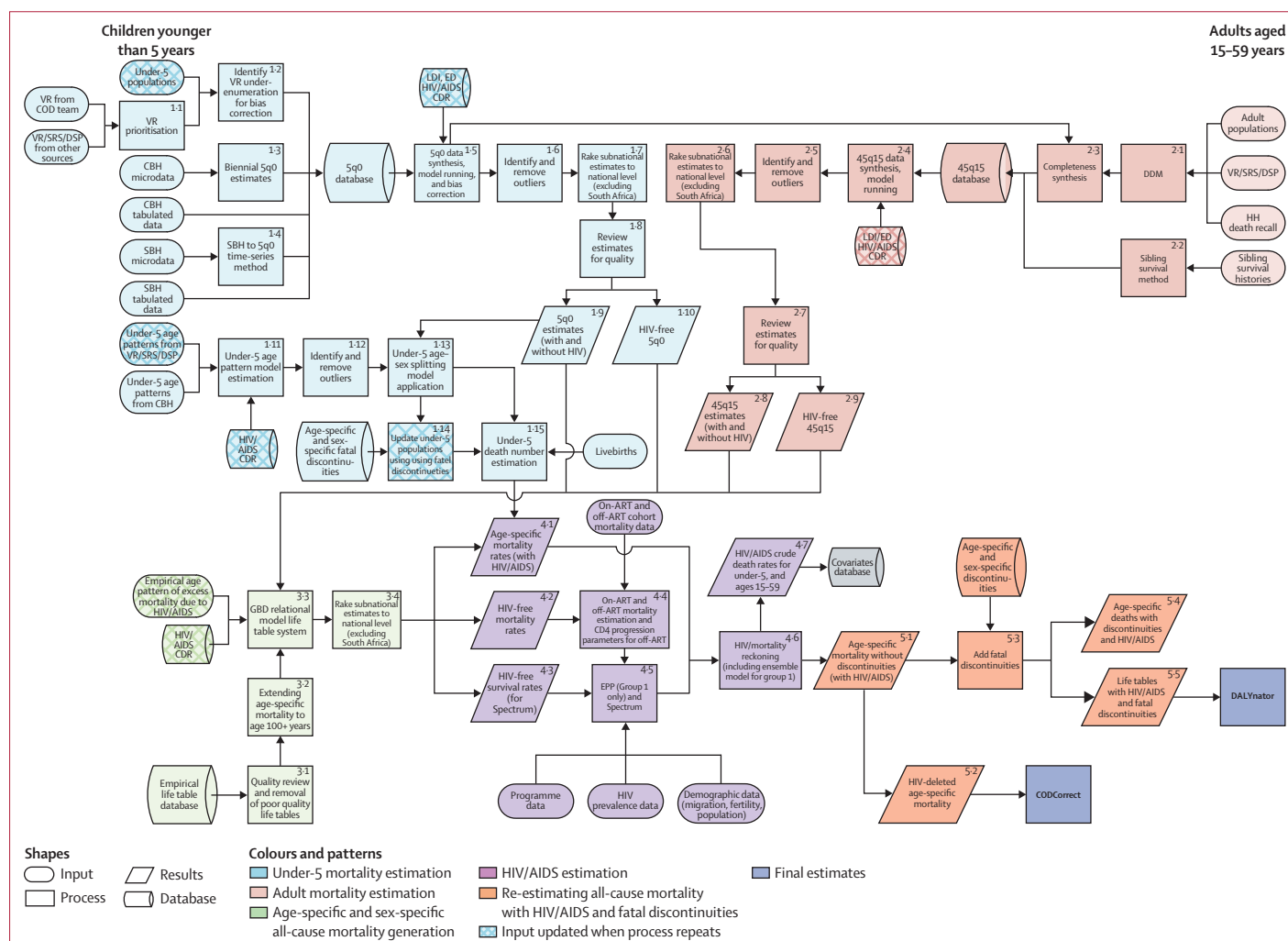


Figure 1: Estimation of all-cause mortality by age and sex and HIV/AIDS incidence, prevalence, and mortality for GBD 2015
 Data and analyses are indicated by shape and the flow chart is colour coded by major estimation component. The process depicted is performed twice to bring in updated under-5 population estimates and crude death rates due to HIV/AIDS. The inputs that are updated in the second run of the process are shown by patterned boxes in this flow chart. Because of the very large and changing effects of HIV/AIDS on all-cause mortality in several countries with large HIV epidemics and limited data on all-cause mortality, the estimation of HIV/AIDS and all-cause mortality are closely linked and are presented jointly here. GBD=Global Burden of Disease. 5q0=probability of death from birth to age 5 years. 45q15=probability of death from age 15 to 60 years. ART=antiretroviral therapy. CBH=complete birth histories. CDR=crude death rate. COD=causes of death. DSP=disease surveillance points. ED=educational attainment in years per capita above age 15 years and mother's educational attainment in years per capita for children younger than 5 years. EPP=Estimation and Projection Package. HIV CDR=crude death rate due to HIV/AIDS. LDI=lagged distributed income per capita. SBH=summary birth history. SRS=Sample Registration System. VR=vital registration.

greater than 50 000 in the year 2000.¹² In the GBD 2013 study, collaborative teams produced subnational assessments for the UK, Mexico, and China, expanding the number of geographies included in the GBD analysis to 296.^{7,13–15} The value of such subnational assessments to local decision makers¹⁶ has driven further geographical disaggregation for GBD 2015 including in Brazil, India, Japan, Kenya, Saudi Arabia, South Africa, Sweden, and the USA, in addition to updates for China, Mexico, and the UK. The expansion of the geographical units in the GBD studies will continue in a way that will sustain the comparability over time for the period 1990 to present and across all geographic entities.

As with all revisions of the GBD, the GBD 2015 study provides an update for the entire time series from 1990 to 2015 based on newly identified data sources released or collected since GBD 2013. In response to published commentaries and unpublished seminars and communications about GBD methods, various methodological refinements have been implemented.^{17,18} Additionally, in the GBD 2015 cycle, a major effort towards data and code transparency has been made. As with each GBD cycle, the full time series published here supersedes previous GBD studies. This detailed assessment of causes of death allows the exploration of key questions including what are the leading causes of deaths in each geography, which causes are increasing or decreasing, what is the expected pattern of change in causes of death with the epidemiological transition and how does this expected pattern over time diverge across geographies.

Methods

Overview

GBD employs various analytical tools and a diverse set of data sources to generate comparable estimates of deaths and mortality rates broken down by age, sex, cause, year, and geography. Multiple publications show more detail on the various aspects of the methods.^{7,8,12,19} Part 1 of the methods appendix (pp 4–51) is a structured and succinct explanation of each step. Figure 1 shows all of the inputs, analytical processes, and outputs from the analysis of all-cause mortality and HIV/AIDS mortality, included because of its important effects on all-cause mortality in countries with large HIV epidemics, and figure 2 does the same for cause-specific mortality. Each input or process is numbered for reference, with part 2 of the methods appendix (pp 52–70) providing explanation for each step. The GBD analytical approach to estimation is guided by standardised solutions to some general analytical problems: inconsistent case definitions or coding over time or across geographies; missing data; conflicting data for the same year and geography; and population groups (eg, the poor, minorities, and vulnerable groups) who are often missed in administrative data sources. In this Article, we provide

only a very high-level summary. This analysis adheres to the new Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) proposed by the World Health Organization (WHO) and others, which includes recommendations on documentation of data sources, estimation methods, and statistical analysis.²⁰ Table 1 shows the precise ways in which we have adhered to each element of the GATHER agreement.

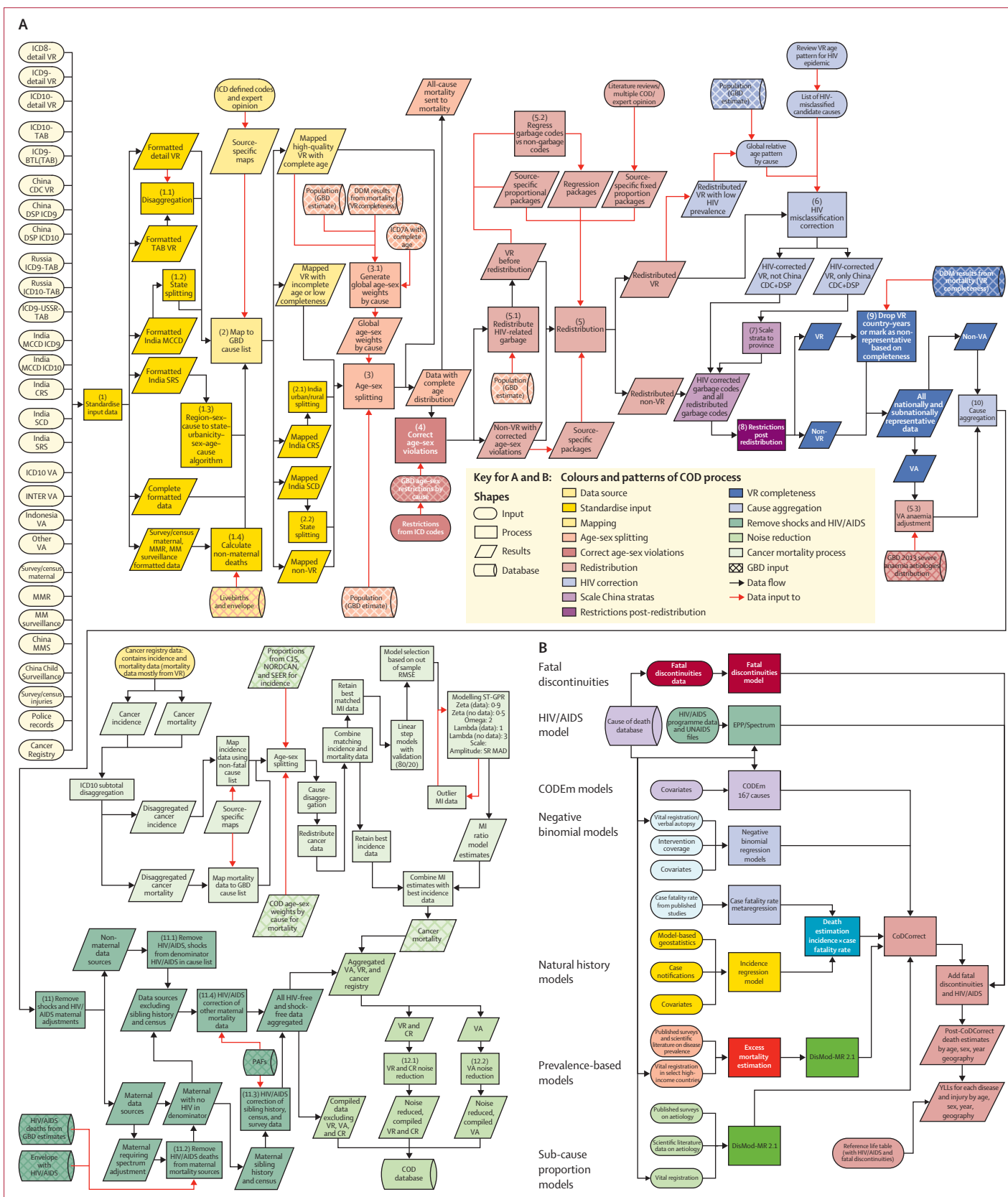
Geographic units

We have organised geographies into a set of hierarchical categories: seven super-regions; 21 regions nested within the seven super-regions; and 195 countries and territories nested within the 21 regions (table 2). Details on the classification of each geographical unit into each level of this hierarchy are provided in the methods appendix (pp 670–83). Compared with GBD 2013, we have added seven territories—American Samoa, Bermuda, Greenland, Guam, the Northern Mariana Islands, Puerto Rico, and the Virgin Islands—because of the availability of high-quality vital registration data. These territories were not previously included in the national totals of the USA, UK, or Denmark, and were included only in GBD 2013 regional totals. We have further disaggregated data for selected countries or territories into subnational units: 26 states and one district for Brazil, 34 provinces and municipalities for China, 31 states and union territory groupings for India that include 62 rural and urban units, 47 prefectures for Japan, 47 counties for Kenya, 32 states and districts for Mexico, 13 regions for Saudi Arabia, nine provinces for South Africa, two regions for Sweden, 13 regions for the UK (Northern Ireland, Scotland, Wales, England, and nine subregions of England), and 51 states and districts for the USA. At the first subnational unit level, we have 256 geographic units. Subnational level 1 geographies in the GBD 2015 analysis include countries that have been subdivided into the first subnational level, such as states or provinces. The subnational level 2 category applies only to India and England. In this Article we present national, territory, and previously published subnational units in the UK.¹³

See Online for appendices

Figure 2: Development of the GBD 2015 cause of death database

Figure shows (A) different strategies used to model different causes and to (B) combine them into a consistent set of cause-specific deaths for each location, age, sex, and year. Data and analytical processes are indicated by shape and the flow chart is colour coded by major estimation component. GBD=Global Burden of Disease. BTL=basic tabulation list. CDC=Center for Disease Control and Prevention. COD=cause of death. CODEm=Cause Of Death Ensemble model. CR=cancer registry. CRS=civil registration system. DSP=disease surveillance points. ICD=International Classification of Diseases. MI=mortality/incidence ratio. MCCD=medical certification of causes of death. MM=maternal mortality. MMR=maternal mortality ratio. MMS=maternal mortality surveillance. PAF=population-attributable fraction. SCD=survey of causes of death. SEER=Surveillance, Epidemiology, and End Results Program. SRS=Sample Registration System. SR MAD=super-region median average deviation. ST-GPR=spatiotemporal Gaussian process regression. VA=verbal autopsy. VR=vital registration. YLL=years of life lost.



GATHER checklist item		Description of compliance	Reference
Objectives and funding			
1	Define the indicators, populations, and time periods for which estimates were made	Narrative provided in paper and methods appendix describing indicators, definitions, and populations	Main text (Methods—Geographic units, GBD cause list, Time periods) and methods appendix (pp 4–70)
2	List the funding sources for the work	Funding sources listed in paper	Summary (Funding)
Data inputs			
For all data inputs from multiple sources that are synthesised as part of the study			
3	Describe how the data were identified and how the data were accessed	Narrative description of data seeking methods provided	Main text (Methods) and methods appendix (pp 4–283)
4	Specify the inclusion and exclusion criteria; identify all ad-hoc exclusions	Narrative about inclusion and exclusion criteria by data type provided	Main text (Methods) and methods appendix (pp 4–283)
5	Provide information on all included data sources and their main characteristics; for each data source used, report reference information or contact name or institution, population represented, data collection method, years of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant	An interactive, online data source tool that provides metadata for data sources by component, geography, cause, risk, or impairment has been developed	Online data citation tools
6	Identify and describe any categories of input data that have potentially important biases (eg, based on characteristics listed in item 5)	Summary of known biases by cause included in methods appendix	Methods appendix (pp 4–283)
For data inputs that contribute to the analysis but were not synthesised as part of the study			
7	Describe and give sources for any other data inputs	Included in online data source tool	Online data citation tools
For all data inputs			
8	Provide all data inputs in a file format from which data can be efficiently extracted (eg, a spreadsheet as opposed to a PDF), including all relevant metadata listed in item 5; for any data inputs that cannot be shared due to ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data	Downloads of input data available through online tools, including data visualisation tools and data query tools; input data not available in tools will be made available upon request	Online data visualisation tools, data query tools, and the Global Health Data Exchange
Data analysis			
9	Provide a conceptual overview of the data analysis method; a diagram may be helpful	Flow diagrams of the overall methodological processes, as well as cause-specific modelling processes, have been provided	Main text (Methods, figures 1 and 2) and methods appendix (pp 4–287)
10	Provide a detailed description of all steps of the analysis, including mathematical formulae; this description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical models	Flow diagrams and corresponding methodological write-ups for each cause, as well as the demographics and causes of death databases and modelling processes, have been provided	Main text (Methods, figures 1 and 2) and methods appendix (pp 4–287)
11	Describe how candidate models were evaluated and how the final models were selected	Provided in the methodological write-ups	Methods appendix (pp 71–283)
12	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis	Provided in the methodological write-ups	Methods appendix (pp 71–283)
13	Describe methods for calculating uncertainty of the estimates; state which sources of uncertainty were, and were not, accounted for in the uncertainty analysis	Provided in the methodological write-ups	Methods appendix (pp 71–283)
14	State how analytic or statistical source code used to generate estimates can be accessed	Access statement provided	Code is provided in an online repository

(Table 1 continues on next page)

For the **data citation tools** see <http://ghdx.healthdata.org/gbd-data-input-sources>

For the **data visualisation tools** see <http://www.healthdata.org/results/data-visualizations>

For the **data query tools** see <http://ghdx.healthdata.org/gbd-data-tool>

For the **Global Health Data Exchange** see <http://ghdx.healthdata.org/>

GBD cause list

The GBD cause list is the crucial organising framework for the analysis of causes of death and premature mortality, as well as disease incidence and prevalence and years lived with disability.²¹ The GBD cause list has evolved during the 25 years of the GBD study to become a list of causes that have public health and medical care importance either because they are major causes of lost health or because of policy relevance.^{7,21–24} Because different levels of cause aggregation are appropriate for different purposes and users, the GBD cause list is organised hierarchically (table 2). At each level of the

cause hierarchy, the set of causes is mutually exclusive and collectively exhaustive.²¹ At the first level of the cause list, there are three broad causes: communicable, maternal, neonatal, and nutritional diseases; NCDs; and injuries. At the second level of the hierarchy, these three causes are broken down into 21 cause groups such as neoplasms (cancers) or cardiovascular diseases. Levels 3 and 4 of the cause list provide more disaggregated causes. Based on policy interest and by approval of the GBD Scientific Council, we have added eight causes to the GBD cause list: Ebola virus disease, motor neuron disease, environmental heat and cold

GATHER checklist item	Description of compliance	Reference
(Continued from previous page)		
Results and discussion		
15	Provide published estimates in a file format from which data can be efficiently extracted	GBD 2015 results are available through online data visualisation tools, the Global Health Data Exchange, and the online data query tool
16	Report a quantitative measure of the uncertainty of the estimates (eg, uncertainty intervals)	Uncertainty intervals are provided with all results
17	Interpret results in light of existing evidence; if updating a previous set of estimates, describe the reasons for changes in estimates	Discussion of methodological changes between GBD rounds provided in the narrative of the Article and methods appendix
18	Discuss limitations of the estimates; include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates	Discussion of limitations provided in the narrative of the main paper, as well as in the methodological write-ups in the methods appendix

GBD 2015=Global Burden of Disease 2015 Study. GATHER=Guidelines for Accurate and Transparent Health Estimates Reporting.

Table 1: GATHER checklist with description of compliance and location of information in the GBD 2015 mortality and causes of death study

exposure, squamous-cell carcinoma, acute lymphoid leukaemia, chronic lymphoid leukaemia, acute myeloid leukaemia, and chronic myeloid leukaemia. Bulimia nervosa has also been added as a cause of death. In total, there are now three causes at Level 1, 21 at Level 2, 166 at Level 3, and 261 at Level 4. Some causes, such as acne, medication overuse headache, and cutaneous leishmaniasis, are not considered causes of death according to the rules of the International Classification of Diseases (ICD), so the number of causes included in this analysis of causes of death is three at Level 1, 21 at Level 2, 144 at Level 3, and 200 at Level 4. The full GBD cause list, including those for which we estimate deaths, is available in the methods appendix (pp 684–90).

Time periods

Because of the greater availability of data on all-cause mortality than cause-specific mortality, the all-cause mortality analysis for GBD 2015 covered 1970 to 2015. The cause of death analysis of GBD 2015 covered 1980 to 2015. A complete set of age-specific, sex-specific, cause-specific, and geography-specific death numbers and rates were generated. We present results covering different periods. However, for the main global and national results, we have focused on trends in the past decade, from 2005 to 2015, and detailed findings in 2015. Data visualisation tools are available online and provide results for each year from 1990 to 2015.

All-cause mortality and HIV/AIDS mortality

Because of the very large and changing effects of HIV/AIDS on all-cause mortality in several countries with large HIV epidemics and scarce data on all-cause mortality, especially in eastern and southern Africa,¹¹ the estimation of HIV/AIDS mortality and all-cause mortality

are closely linked and presented jointly in figure 1. We divided the estimation effort into five distinct components: estimation of under-5 mortality rate (5q0); estimation of the adult mortality rate (45q15); age-specific mortality estimation; HIV/AIDS mortality estimation; and addition of the effects of events such as wars, pandemics, and disasters, which can cause abrupt discontinuities in death numbers (fatal discontinuities). Because of the interdependencies in the estimation of HIV/AIDS incidence, prevalence, and mortality and all-cause mortality, the estimation steps shown in figure 1 were repeated, with the HIV/AIDS crude death rates produced in step 4.7 used as covariates in steps 1.5, 1.11, 2.4, and 3.3 in the flow diagram.

Under-5 mortality estimation

Seven types of primary data contributed to the estimation process (oval shapes in figure 1). The most important set of inputs were the data for estimating the overall level of under-5 mortality (5q0) that were obtained from vital registration systems, surveys, and censuses. Figure 3A provides information about the proportion of the 519 geographies included in the analysis for which data were available in each year from 1980 to 2015. Because of lags in reporting of both vital registration data and the release of household survey or census data, the availability of data was much lower for 2014 and 2015 than for previous years. Different data types, such as summary or complete birth histories, were processed to yield estimates for each year of the under-5 death rate; country-specific and year-specific details of the measurements are provided in the methods appendix (pp 4–19). Figure 3B shows the nature of the data and estimation process for under-5 mortality using the example of Zambia, as well as the uncorrected and bias-adjusted datapoints for each

For the **online repository** see <http://ghdx.healthdata.org/global-burden-disease-study-2015>

For the **online data visualisation tools** see <http://vizhub.healthdata.org/gbd-compare>

	Number of geographies
Geographical levels	
Super-region	7
Regions	21
Nations and territories	195
Subnational level 1	480
Subnational level 2	519
Cause levels	
Level 1	
Total causes	3
YLD causes	3
YLL causes	3
Level 2	
Total	21
YLD	21
YLL	21
Level 3	
Total causes	166
YLD causes	161
YLL causes	144
Level 4	
Total causes	261
YLD causes	256
YLL causes	200

Nations and territories includes countries, territories, and non-sovereign states. Subnational level 1 includes countries that, in the GBD analysis, have been subdivided into the first subnational level such as states or provinces. Subnational level 2 applies only to India and England. In India, states have been divided into urban and rural units. England has been divided into nine regions. For each level, the number of geographies includes the geographies at that level plus the number of most-detailed geographies at each higher level such that at each level of the hierarchy, all geographies create a collectively exhaustive and mutually exclusive set covering the world. Likewise, the GBD cause list is mutually exclusive and collectively exhaustive. The three Level 1 GBD causes consist of communicable, maternal, neonatal, and nutritional disorders; non-communicable diseases; and injuries. Level 2 causes consist of 21 cause groups, such as neoplasms and cardiovascular diseases. Levels 3 and 4 consist of disaggregated causes, such as liver cancer and cerebrovascular disease (Level 3), and liver cancer due to hepatitis C and ischaemic stroke (Level 4). GBD=Global Burden of Disease. YLD=years lived with disability. YLL=years of life lost.

Table 2: Number of geographies and causes at each hierarchical level for GBD 2015

source. We used spatiotemporal Gaussian process regression to synthesise the sources and simultaneously correct for biases in specific source types.⁸ Bias corrections were made by comparison to reference sources, which for Zambia were the Demographic and Health Surveys. Further details of this estimation process are provided in the methods appendix (pp 4–19).

Because there are many sources for measuring under-5 mortality, such as summary birth histories from censuses and surveys, that do not provide sex and specific age group detail, we first estimated under-5 mortality and then split it into mortality for four age groups: early neonatal (0–6 days), late neonatal (7–28 days), post-neonatal (29–364 days), and ages 1–4 years. Splitting into these age groups was based on a statistical model using

the analysis of available data that provide breakdowns by age and sex. Figure 3C shows the availability by country–year of data used to build the model to estimate mortality for specific age–sex groups younger than age 5 years. We modelled the ratio of male-to-female probability of death from birth to age 5 years as a function of both sexes' combined under-5 mortality rate and country and regional random effects. We further disaggregated sex-specific probability of death between birth and age 5 by modelling the ratio between age-and-sex-specific probability of deaths in the early neonatal, late neonatal, post-neonatal, and 1–4 year age groups and sex-specific probability of death between birth and age 5 years. This model allowed for the association between these age-and-sex-specific probabilities and the under-5 death rate to be non-linear, and included other covariates consisting of the death rate due to HIV/AIDS in children younger than 5 years, average years of schooling among females of reproductive age, and country and regional random effects. More details, including the equations are provided in the methods appendix (p 18). Figure 3D shows an example of the empirical fit for the post-neonatal period for Bangladesh. This model was applied to all countries to generate the under-5 estimates for each geography–year.

With the estimated mortality by detailed age group, we generated both deaths and population estimates for the respective age groups for each location, sex, and year.

Adult mortality estimation

Measurements of adult mortality (45q15) were mainly derived from vital registration data and household surveys that ask about the birth and death of siblings.²⁵ In a smaller set of cases, information was obtained from censuses or surveys about household deaths in a defined interval before the interview. Figure 4A shows the number of geographies for which data in each year were available for adult mortality estimation. Vital registration data were assessed for completeness with death distribution methods optimised for performance.^{26,27} We generated a best estimate of the completeness of vital registration in each geography over time by combining estimated completeness of registration for under-5 deaths with the results for different intercensal periods of the application of three death distribution methods. These sources were combined by use of spatiotemporal Gaussian process regression—details are provided in the methods appendix (p 21). Data from sibling histories were corrected for known biases, including selection bias, zero reporter bias, and recall bias.^{7,25} Our sibling history method can also deal with data sparsity in many sibling survival modules (ie, sibling history questions and variables from surveys). The predictive validity of the sibling history analytical methods has been assessed with simulated data and shown to be unbiased.²⁵ Additionally, we compared estimates of adult mortality rates from sibling survival data with completeness-adjusted vital registration data in

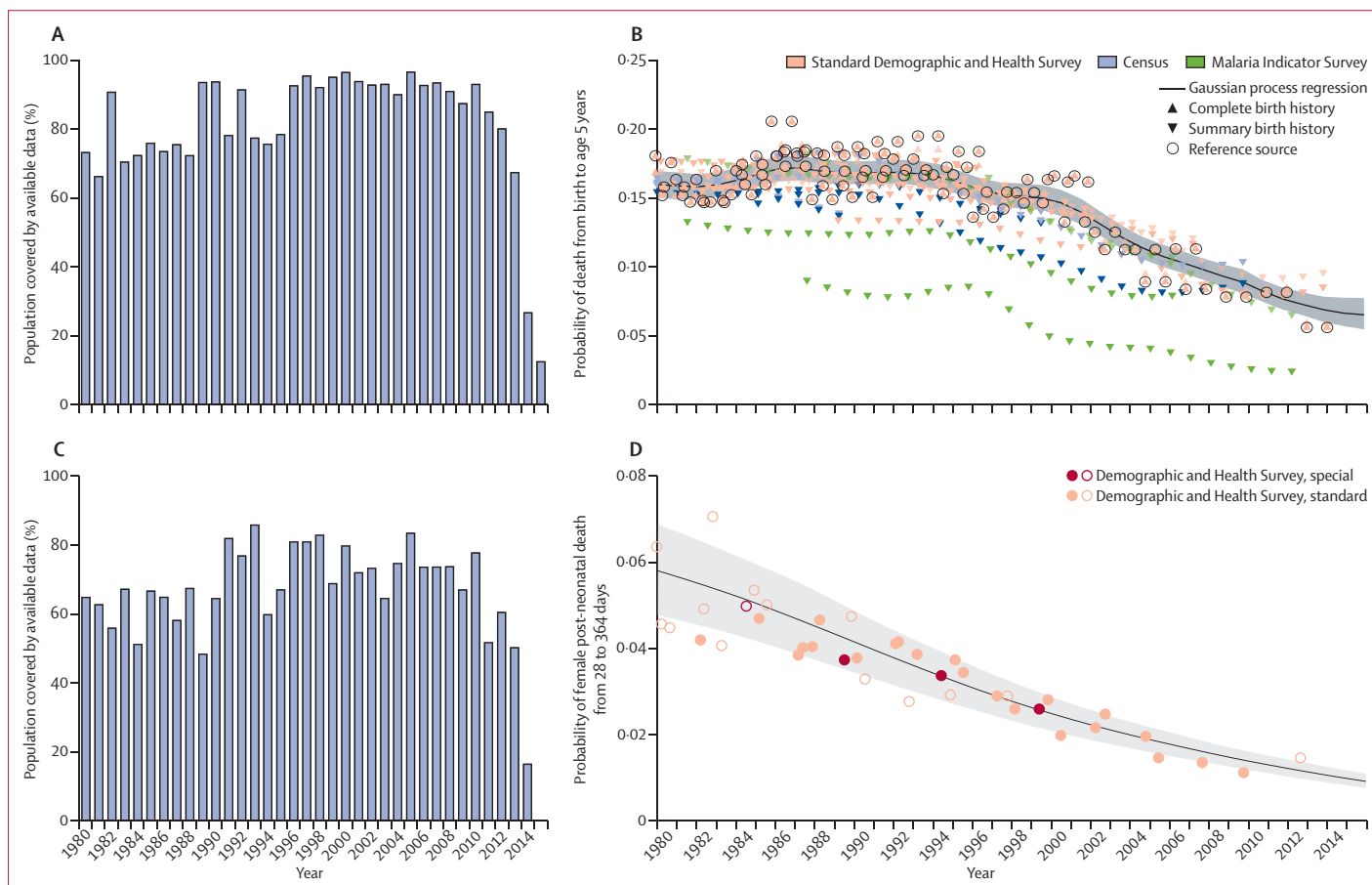


Figure 3: Examples of under-5 mortality data availability and estimation

(A) Percentage of global under-5 population covered by under-5 mortality data for each year, 1980–2015. The percentage of under-5 population covered was calculated by dividing the population of children aged 0–4 years in locations covered by available under-5 mortality data by the total global under-5 population. Because of lags in reporting of both vital registration data and the release of household survey or census data, the availability of data was much lower for 2014 and 2015 than for previous years. (B) Country-specific example of data and under-5 mortality estimates in Zambia, 1980–2015. The black line shows Gaussian process regression fit with 95% uncertainty interval shown in grey. Black circles denote reference data. Triangles denote complete birth history data. Inverted triangles denote summary birth history data. Transparent symbols are the data post-adjustment for non-sampling error. Hollow shapes represent data identified as outliers. (C) Percentage of global under-5 population covered by under-5 age-specific and sex-specific data for each year, 1980–2015. The percentage of under-5 population covered was calculated by dividing the population of children aged 0–4 years in locations covered by available under-5 age-specific and sex-specific data by the total global under-5 population. Because of lags in reporting both vital registration data and the release of household survey or census data, the availability of data was much lower for 2014 than for previous years, and no data existed for 2015. (D) Country-specific example of probability of female post-neonatal mortality in Bangladesh, 1980–2015. Standard Demographic and Health Surveys generally include large population samples and standard sets of questions. Special Demographic and Health Surveys can survey smaller, more targeted populations, such as women who have given birth. The black line shows probability of death, with 95% uncertainty interval shown in grey. Solid circles represent data sources. Hollow circles represent outliers. The post-neonatal period is 28–364 days.

countries from which both sources are available and found no systematic biases from sibling survival method (methods appendix p 292).^{7,25,26} We synthesised vital registration data corrected for completeness and adjusted sibling history data into a best time series estimate of adult 45q15 using spatiotemporal Gaussian process regression. Examples of the application of these steps in three types of settings are shown in figure 4.

The spatiotemporal Gaussian process regression method used to fit the model to the available data included lag distributed income per capita, educational attainment, and the estimated HIV/AIDS death rate as covariates. Because the estimation of the HIV/AIDS death rate used the estimate of HIV-free mortality rate by age and sex as an input, the entire estimation loop was

repeated once, which dealt with this interconnection. Step 2.9 in figure 1 deals with situations in which an inconsistency exists between the spatiotemporal Gaussian process regression-estimated adult mortality rate and the separately estimated crude death rate due to HIV/AIDS. When the HIV/AIDS death rate as estimated from the natural history model is too high compared with demographic sources, there is a risk that HIV-free death rates are depressed to implausibly low levels. In step 2.9, we scaled the HIV/AIDS crude death rate by imposing a maximum proportion of deaths that can be attributed to HIV/AIDS, as shown in our version of UNAIDS' Spectrum model, which estimates HIV/AIDS prevalence and deaths by age and sex. Our adult mortality estimation is for ages 15–60 years (45q15), but other adult

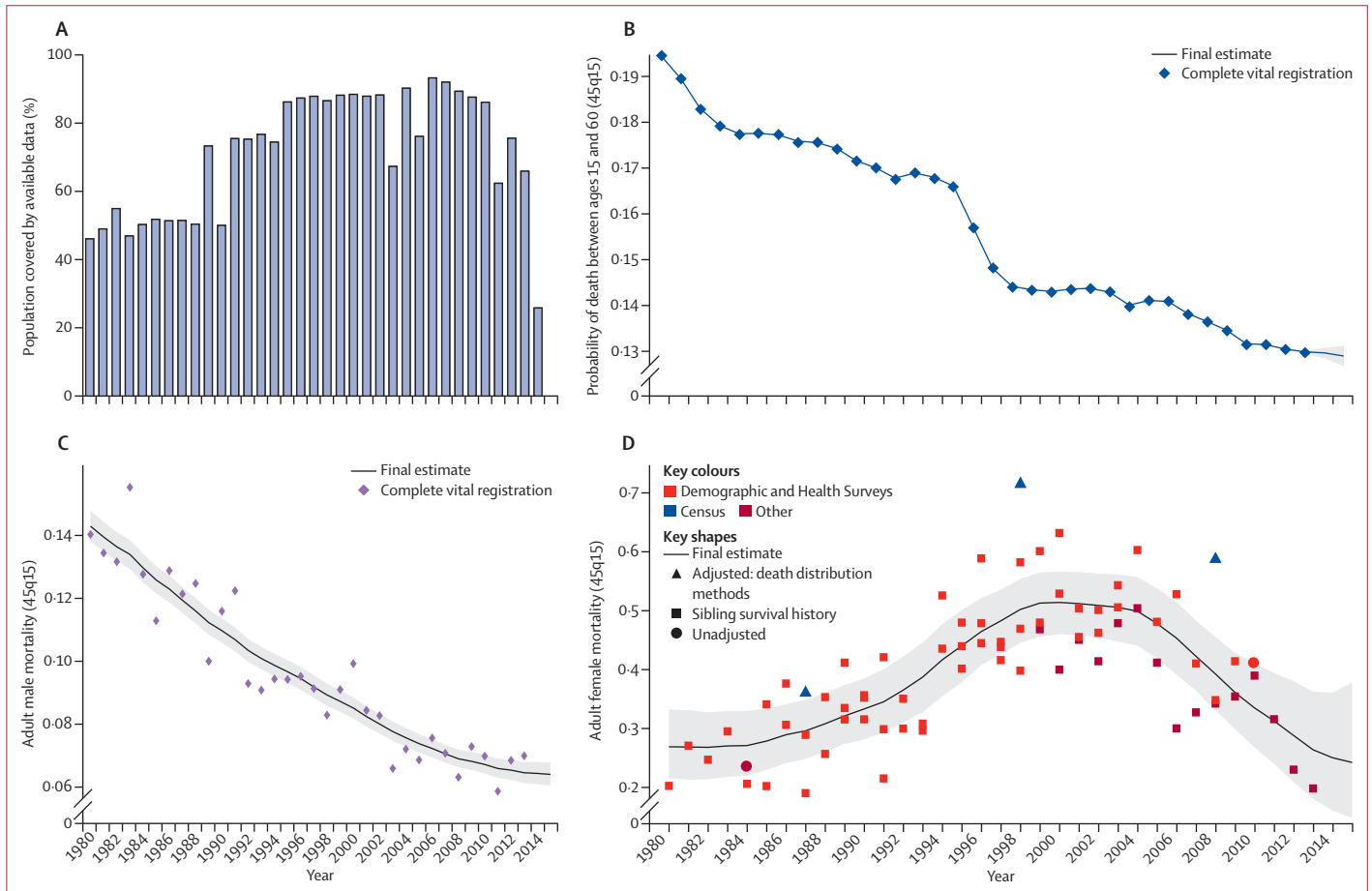


Figure 4: Examples of adult mortality data availability and estimation

(A) Percentage of global adult population covered by adult mortality data from vital registration systems, sibling survival surveys, sample registration systems, or censuses, 1980–2015. The percentage of available data was calculated by dividing the population of adults aged 15–59 years in locations covered by available adult mortality data by the total global population aged 15–49 years. Because of lags in reporting both vital registration data and the release of household survey or census data, the availability of data was much lower for 2014 than for previous years, and no data existed for 2015. Country-specific examples of (B) vital registration data and adult male mortality (45q15) estimation for a country with complete vital registration and large population (USA), 1980–2015; (C) vital registration data and adult male mortality (45q15) estimation for a country with complete vital registration and small population (Iceland), 1980–2015; and (D) sibling survival data and adult female mortality (45q15) estimation (Malawi), 1980–2015. Black line shows final estimates of adult mortality among males or females in each country, with 95% uncertainty interval shown in grey. Squares show sibling survival histories. 45q15=probability of death from age 15 years to 60 years.

age groups that can be calculated for other purposes include 35q15 (ages 15–50 years, corresponding to the reproductive age period), and 20q50 (ages 20–70 years).

Age-specific mortality

In demographic estimation, measures of child mortality, adult mortality, or both are used alongside a model life table system to predict age-specific mortality.^{27–30} The UN mostly still uses the Coale-Demeny model life tables, which were based on 192 empirical tables gathered before 1963, and in a few cases they use the 33-year-old UN Model Life Table for Developing Countries.^{31,32} Murray and colleagues³³ developed the Modified Logit Model Life Table system that is used by WHO to estimate age-specific mortality, which captures a much wider range of age patterns of mortality through the year 2000. The GBD approach uses three inputs to generate age-specific mortality: 5q0, 45q15, and a relevant empirical

reference pattern of mortality by age.⁷ The reference in the GBD system was selected on the basis of empirical age patterns that are closest to the population in space and time.⁷ The reference was developed with a database of 16 507 age patterns of mortality from settings that meet explicit inclusion criteria as described in the methods appendix (pp 34–42). Table 3 shows a summary of the availability of empirical age–sex patterns of mortality in the GBD database.

To account for the effect of HIV/AIDS on the age pattern of mortality, the GBD model life table system for locations affected by HIV/AIDS and without high-quality vital registration data used a two-step process whereby we first estimated an HIV-free age pattern of mortality assuming that deaths due to HIV/AIDS were removed. This was accomplished by use of the HIV-free and without-fatal-discontinuity 5q0 and 45q15 estimates, crude death rates due to HIV/AIDS in age

groups 0–4 and 15–59 years, and the methods detailed in the methods appendix (p 44), which reconcile the potential disconnect between HIV/AIDS mortality implied in the spatiotemporal Gaussian process regression estimates of all-cause mortality and those estimated by the Estimation and Project Package (EPP)-Spectrum. We then added the excess mortality due to HIV/AIDS to specific age groups to match the with-HIV/AIDS 5q0 and 45q15 by using the estimated age pattern of excess mortality due to HIV/AIDS for generalised and concentrated epidemics. These age patterns of excess mortality were based on ICD-10-coded vital registration data from various countries, including high-income countries with good-quality vital registration data and other middle-income nations that are affected by HIV/AIDS such as South Africa, Thailand, and Trinidad and Tobago. A list of country-years for which we obtained the empirical age pattern of HIV/AIDS excess mortality rate is shown in the methods appendix (p 313).

Figure 5 shows examples of the life table system estimates of age-specific mortality compared with observed patterns for males and females in France in 2011. There was a very close fit between the estimated age-specific mortality and the observed mortality.

HIV/AIDS estimation

Because HIV/AIDS estimation is so closely connected to all-cause mortality estimation, we discuss HIV/AIDS estimation separately here rather than in the later section about estimating other causes of death. We divided geographies into two broad groups: countries with larger epidemics and incomplete or non-existent vital registration systems and the remaining geographies. For the first group of geographies for which we had necessary information about the transmission of HIV/AIDS among adults and children and other programme information, we fitted a modified version of EPP-Spectrum^{11,34} to the data on prevalence collated by UNAIDS from antenatal clinic serosurveillance and household surveys. EPP-Spectrum is a natural history model of the HIV/AIDS epidemic that has two distinct components. In the EPP component, data on the prevalence of HIV are used to back-estimate incidence of HIV. In the Spectrum component, the estimated incidence and a set of assumptions are used to estimate prevalence and deaths by age and sex. These assumptions are informed by published or unpublished cohort studies on the initial CD4 distribution of new HIV infections, rates of decline in CD4 counts, death rates on and off antiretroviral therapy (ART) differentiated by age, sex, and CD4 count, and prevention of mother-to-child transmission (PMTCT) coverage data, as well as other demographic assumptions, such as the HIV-free death rate. We have modified EPP-Spectrum to enhance the internal consistency between EPP and Spectrum and to more

	1950–59	1960–69	1970–79	1980–89	1990–2000	2000–14
Central Europe, eastern Europe, and central Asia	61	145	240	386	477	555
High income	434	498	611	2481	2399	3056
Latin America and Caribbean	56	170	280	879	948	1416
North Africa and Middle East	2	5	16	27	32	61
South Asia					45	145
Southeast and east Asia and Oceania	3	30	76	171	148	310
Sub-Saharan Africa				2	60	282
Total	556	848	1223	3946	4109	5825

Numbers show available empirical life tables in the GBD 2015 database. All life tables included in the database meet quality inclusion criteria whereby the observed age-specific mortality rate in an empirical life table conforms to the age pattern of mortality as described by the Gompertz–Makeham law of mortality and that observed in countries with high-quality vital and civil registration systems. GBD=Global Burden of Disease.

Table 3: Distribution of empirical life tables by GBD super-region and decade, 1950–2015

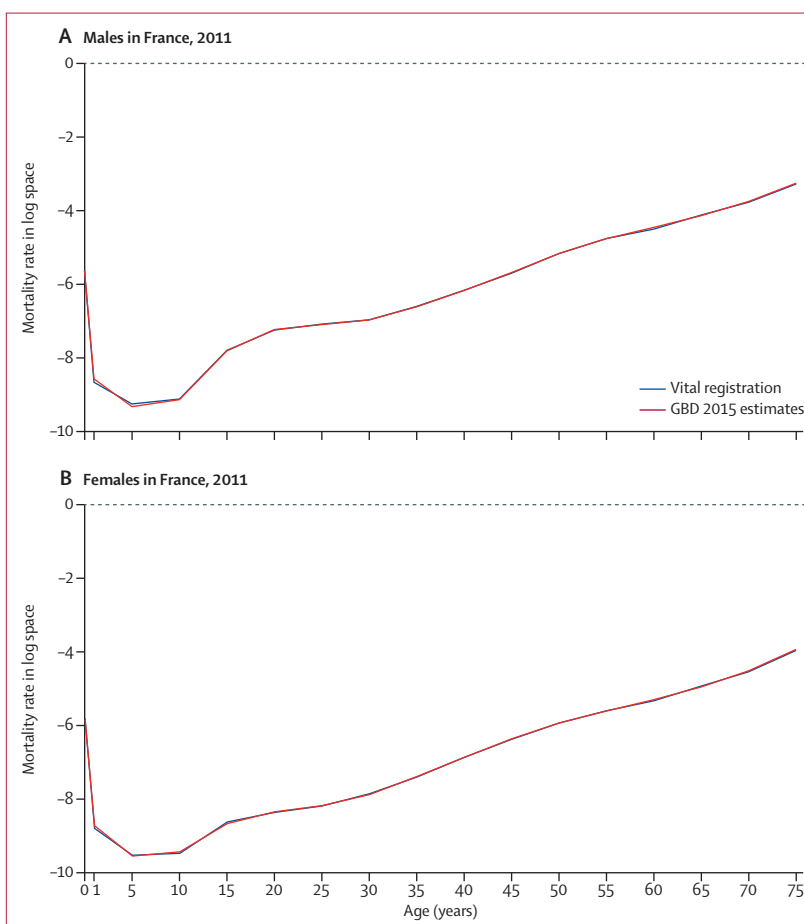


Figure 5: Age-specific mortality estimation with GBD life table method versus observed data excluded from the model

Country-specific examples for (A) males and (B) females in France, 2011. The red line shows the GBD 2015 life table system estimates of age-specific mortality rates from birth through age 75 years in log space, compared with observed age-specific mortality (blue line). Year 2011 selected for illustration purposes. GBD=Global Burden of Disease.

accurately reflect published cohort data on CD4 progression and death rates on and off ART.

At this point in the estimation process for the first group of geographies, we generated two estimates of HIV/AIDS. One is informed by available data on all-cause mortality and the statistically related association between all-cause mortality and the HIV/AIDS crude death rate; the other is the EPP-Spectrum natural history model. In some locations, these estimates can be quite different. Given the inherent uncertainties in both methods, for GBD 2015 we have adopted an ensemble model which is the average of HIV/AIDS deaths for each age–sex–year from the two approaches. Figure 6 shows the results of this process using Zimbabwe as an example for incidence, prevalence, and deaths from HIV/AIDS. For comparison, we provide prevalence data from surveys and the UNAIDS estimates from their 2014 round of estimation.^{35,36}

For the second group of geographies, we estimated mortality due to HIV/AIDS on the basis of vital registration data if available. Estimates of incidence and prevalence for HIV were based on calibrating Spectrum to match the observed numbers of HIV/AIDS deaths after accounting for under-registration of the vital registration system. This calibration method is based on tracking incidence cohorts through Spectrum and adjusting incidence to fit the observed deaths for that cohort in each year in a specific age group (methods appendix p 44). Using the methods discussed in the age-specific mortality section, with-HIV/AIDS all-cause mortality was estimated for these countries. Depending on the subgroup categorisation within the second group of geographies (methods appendix pp 44–45), we generated the HIV/AIDS-specific mortality either by applying spatio-temporal Gaussian process regression to HIV/AIDS cause-specific data from the vital registration system if the quality of vital registration was deemed high (methods appendix pp 21–26) or by using cohort incidence bias-adjusted mortality estimates from Spectrum.

Fatal discontinuities

The fifth stage of estimation (figure 1) re-estimates all-cause mortality by incorporating the effects of HIV/AIDS and fatal discontinuities. To incorporate fatal discontinuities from natural disasters (eg, the 2011 Japan earthquake and tsunami), wars, pandemics, wildfires (eg, the Australian bushfires in 2009), or major transportation accidents (eg, the Al Ayyat train accident in Egypt in 2002), we used death counts reported in a wide range of international databases such as the International Disaster Database, the Uppsala Conflict Data Program, the International Institute for Strategic Studies Armed Conflict Databases, the Robert S Strauss Center, and various internet sources for more recent events such as the ongoing Syrian and Yemeni conflicts (databases are listed in the methods appendix [p 270], and additional sources are downloadable from the online source

tool).^{37–40} When multiple sources for the same fatal discontinuity event exist, we prioritised data from vital registration systems if it had the highest estimate, and gave least priority to data from internet searches. We constructed uncertainty on the basis of high and low estimates when available. We generated regional and cause-specific uncertainty intervals in relative terms and applied them to fatal discontinuities when only the mean estimate was provided by a specific source. The fatal discontinuity section of the methods appendix (pp 270–73) provides more detail on how we assigned fatal discontinuity deaths to different GBD causes as appropriate and how we applied a cause-specific age–sex splitting model to arrive at age-and-sex-specific deaths due to specific fatal discontinuity events.

Given that all-cause mortality analysis requires estimates of crude death rates from HIV/AIDS as initial inputs and that the ensemble model changes the HIV/AIDS-specific and with-HIV/AIDS age-specific mortality rates, the all-cause mortality and HIV/AIDS estimation processes were performed twice. Crude death rates due to HIV/AIDS and under-5 population estimates were generated in the first run of the processes and propagated the second run of the processes to make the HIV/AIDS-specific and all-cause mortality processes more consistent.

Causes of death estimation

The GBD cause list relies on categorical attribution of deaths to a single underlying cause in accordance with the principles outlined in the ICD. The core principle of the ICD is to assign each death to only the underlying cause of death; ie, the cause that initiated the series of events leading to death. We used the ICD principle of underlying cause of death for the primary tabulations in this Article. Data from vital registration sources, verbal autopsy studies, and other sources all adhere to the same principle that one death can only have one cause. The categorical attribution of causes of death differs from a counterfactual approach, which answers the question “in the absence of the disease of interest how many deaths would not have occurred?”, similar to how we estimate burden due to risk factors in GBD. The categorical attribution of causes of death also differs from excess mortality in people with a disease followed up over time in a cohort study or through linkage of a disease registry to vital registration data. The excess mortality in such studies might contain deaths that are assigned as the underlying cause, those that are causally related to the disease, and those that are due to confounding, such as by a common underlying risk that predisposes to the disease but where there are also additional pathways to death. These counterfactual and excess mortality relationships are important and need to be quantified by considering the underlying risk, such as elevated fasting plasma glucose.

Figure 2 shows the steps in the estimation of causes of death, which are divided into seven categories: cause of

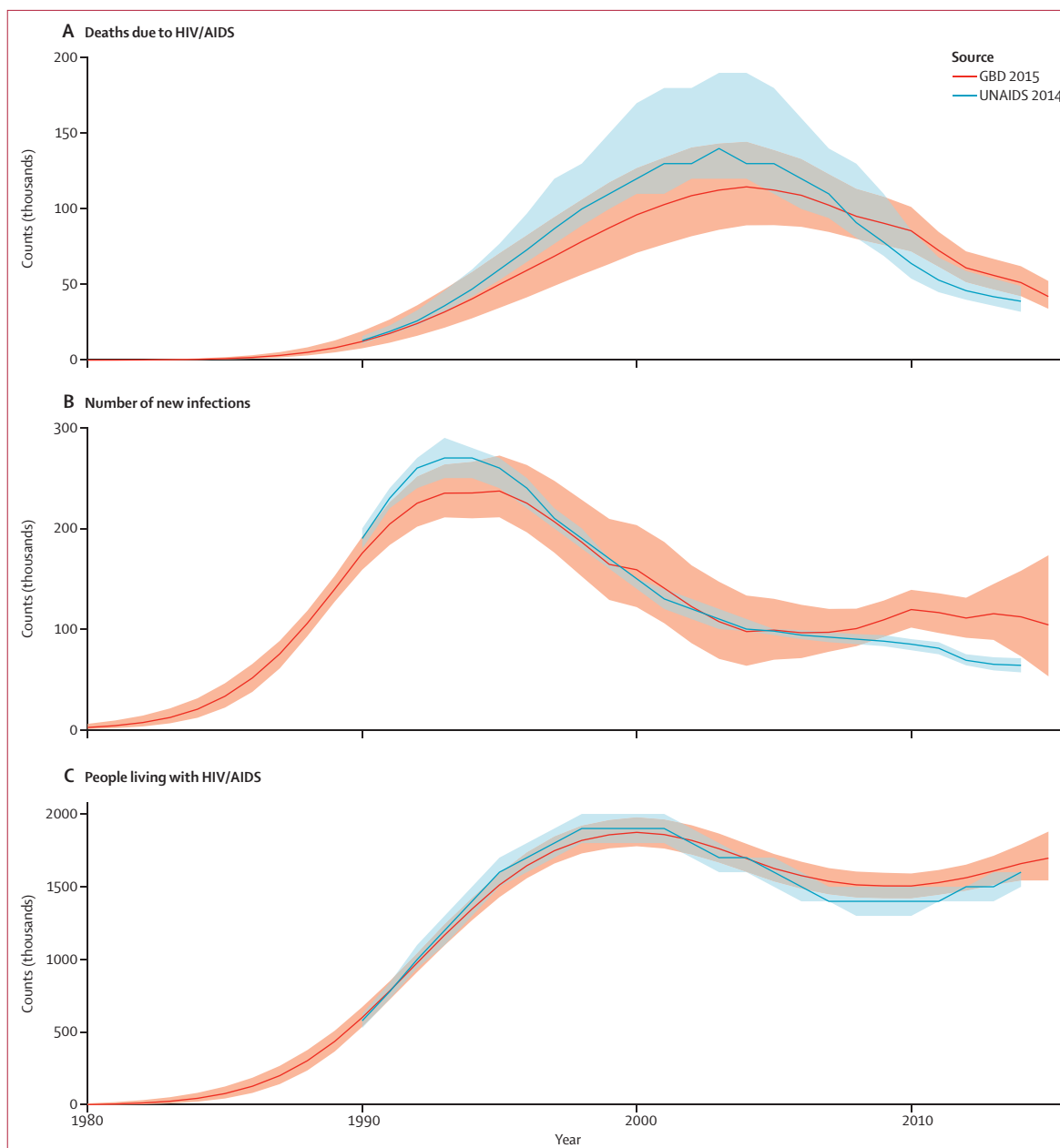


Figure 6: Comparisons of GBD 2015 estimates and UNAIDS 2014 estimates for Zimbabwe

Country-specific example comparing estimates of deaths due to HIV/AIDS (A), new HIV infections (B), and people living with HIV/AIDS (C) in Zimbabwe from GBD 2015 and UNAIDS 2014. Curves show the estimation process of a particular country and highlight the differences in results from the GBD and UNAIDS analysis of the same prevalence data. Numbers are reported in thousands. Uncertainty intervals are shown in red and blue shading. GBD=Global Burden of Disease. UNAIDS=The Joint United Nations Programme on HIV and AIDS.

death database development (figure 2A), Cause of Death Ensemble modelling (CODEm), negative binomial models for rare causes, natural history models, subcause proportion models, prevalence-based models, and CodCorrect (figure 2B). For each component, we discuss the steps, with more extensive detail provided in the methods appendix (pp 52–283). Details about the modelling of HIV/AIDS and fatal discontinuities are

also described in detail in the methods appendix (pp 255–64, 270–73).

Cause of death database development

Figure 2A shows the detailed steps from data inputs and processing to the finalisation of the cause of death database. The methods appendix (pp 52–70) includes details on each step. Cause of death data collected