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Diabetes mortality and trends before 25 years of age: an analysis of the Global Burden of Disease Study 2019

*GBD 2019 Diabetes Mortality Collaborators**

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*Collaborators are listed at the end of the Article

Correspondence to: Dr Ewerton Cousin, Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA 98195, USA
ecousin@uw.edu

Summary

Background Diabetes, particularly type 1 diabetes, at younger ages can be a largely preventable cause of death with the correct health care and services. We aimed to evaluate diabetes mortality and trends at ages younger than 25 years globally using data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019.

Methods We used estimates of GBD 2019 to calculate international diabetes mortality at ages younger than 25 years in 1990 and 2019. Data sources for causes of death were obtained from vital registration systems, verbal autopsies, and other surveillance systems for 1990–2019. We estimated death rates for each location using the GBD Cause of Death Ensemble model. We analysed the association of age-standardised death rates per 100 000 population with the Socio-demographic Index (SDI) and a measure of universal health coverage (UHC) and described the variability within SDI quintiles. We present estimates with their 95% uncertainty intervals.

Findings In 2019, 16 300 (95% uncertainty interval 14 200 to 18 900) global deaths due to diabetes (type 1 and 2 combined) occurred in people younger than 25 years and 73·7% (68·3 to 77·4) were classified as due to type 1 diabetes. The age-standardised death rate was 0·50 (0·44 to 0·58) per 100 000 population, and 15 900 (97·5%) of these deaths occurred in low to high-middle SDI countries. The rate was 0·13 (0·12 to 0·14) per 100 000 population in the high SDI quintile, 0·60 (0·51 to 0·70) per 100 000 population in the low-middle SDI quintile, and 0·71 (0·60 to 0·86) per 100 000 population in the low SDI quintile. Within SDI quintiles, we observed large variability in rates across countries, in part explained by the extent of UHC (r^2=0·62). From 1990 to 2019, age-standardised death rates decreased globally by 17·0% (–28·4 to –2·9) for all diabetes, and by 21·0% (–33·0 to –5·9) when considering only type 1 diabetes. However, the low SDI quintile had the lowest decline for both all diabetes (–13·6% [–28·4 to 3·4]) and for type 1 diabetes (–13·6% [–29·3 to 8·9]).

Interpretation Decreasing diabetes mortality at ages younger than 25 years remains an important challenge, especially in low and low-middle SDI countries. Inadequate diagnosis and treatment of diabetes is likely to be major contributor to these early deaths, highlighting the urgent need to provide better access to insulin and basic diabetes education and care. This mortality metric, derived from readily available and frequently updated GBD data, can help to monitor preventable diabetes-related deaths over time globally, aligned with the UN's Sustainable Development Targets, and serve as an indicator of the adequacy of basic diabetes care for type 1 and type 2 diabetes across nations.

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Introduction

Diabetes has been identified by the UN and WHO as one of the five priority non-communicable diseases (NCDs) in their Action Plan to confront the NCDs challenge.[1,2] Prevention and management of the chronic complications in patients with diabetes involve complex, long-lasting, and costly endeavours.[3]

By contrast, deaths due to acute complications (ie, diabetic ketoacidosis, hyperosmolar coma, and severe hypoglycaemia), early-onset renal failure, and acute infections can be prevented through a minimal core set of actions. These include the provision of affordable insulin,[4] access to health care (including glucose monitoring and promptly available services for acute decompensation), and health education (including rapid recognition and detection of type 1 diabetes and ketoacidosis).[5] Since contemporary health care in high-income countries[6–8] has proven to be effective in reducing mortality due to these complications it is reasonable to assume that major reductions could be seen globally if better care, including the availability of affordable insulin, were more widely provided.

Many low-income and middle-income countries (LMICs) have made considerable progress in the provision of a minimal core of actions to prevent mortality due to acute complications of diabetes. For example, Brazil observed a decrease of 74·5% in deaths due to acute complications in people younger than 40 years from 1991 to 2010 following the implementation of the National Health System, which greatly increased access to care for patients with diabetes, including the provision of free insulin.[9]

Since mortality data are the most available health statistics worldwide, they can be used to track levels and

Research in context

Evidence before this study

Deaths due to acute complications of diabetes such as diabetic ketoacidosis, hyperosmolar coma, and severe hypoglycaemia, as well as due to early manifestation of diabetic kidney disease and acute infections, can largely be avoided with adequately functioning basic health care, including ready access to insulin. This has mostly been accomplished in high-income countries. Direct monitoring of progress on this cause of death globally is currently not feasible because details on the type of diabetes and cause of death are frequently incomplete, which makes it difficult to track and reveal disparities in avoidable causes of death related to diabetes around the world. We searched PubMed for research articles published up to Oct 13, 2021, using the terms ["diabetes" AND "mortality" AND ("child" OR "adolescent" OR "youth")]. No language restriction was applied. This search revealed few studies evaluating nationwide diabetes mortality in the initial decades of life, and none considering diabetes type.

Added value of this study

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) collates mortality data of nations around the world, adjusting for incompleteness of death registration and ill-defined causes of death. To produce more accurate estimates for countries with poor data, GBD applies modelling techniques which take advantage of findings from countries with good data. Based on GBD 2019 estimates, we assessed levels and trends of age-standardised diabetes death rates at ages younger than 25 years, considering it as a metric of potential avoidable mortality from diabetes that can be used for comparisons by location and over time. Trends across the world revealed progress in decreasing these deaths from 1990 to 2019 at all levels of development, as indicated by the GBD's Socio-demographic Index. Countries with a lower level of development had lesser declines and much higher mortality in 2019 than those with a higher level of development. However, even at similar levels of development mortality varied widely across countries, in great part related to the level of universal health coverage. Globally, most of the deaths were due to type 1 diabetes. The death rate due to type 2 diabetes at ages younger than 25 years showed less progress over the period.

Implications of all the available evidence

Diabetes-related death among people younger than 25 years, principally due to incomplete or inadequate access to basic health care for type 1 diabetes, can be largely avoided with universal access to insulin and basic diabetes care. However, the task of creating such access is far from accomplished globally. Although disparities were largely related to levels of development of a country, accessibility of health care was also important. The metric of age-standardised mortality due to diabetes at ages younger than 25 years, derived from readily available and frequently updated GBD data, can help to monitor diabetes-related potentially preventable deaths over time globally, aligned with the UN's Sustainable Development Target 3.8 of achieving "universal health coverage, including financial risk protection, access to quality essential health-care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all". The metric mostly reflects potentially avoidable deaths due to type 1 diabetes in the young but also those due to early-onset type 2 diabetes, thus helping to give voice to those advocating better care for diabetes across the globe.

trends in basic care for diabetes. However, deaths due to diabetes (International Classification of Diseases, revision 10 [ICD-10], codes E10–E14) are frequently further classified vaguely as due to multiple (.7) or unspecified (.8) complications, or without complications (.9), making a direct assessment of trends in deaths due to acute complications difficult.[10] For example, from 1996 to 2011 in Brazil, 83·6% of deaths, after removing those due to renal disease (.2) and peripheral arterial disease (.5), were coded with uninformative .7 to .9 codes.[10] However, because mortality in people younger than 25 years is probably mostly due to acute complications,[11] restricting the evaluation to this age range permits a focus on avoidable causes of death.

For **estimates from the GBD 2019 study** see http://ghdx.healthdata.org/gbd-results-tool.

See Online for appendix

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), which systematically collects mortality data, offers estimates of mortality rates by age group and disease for countries around the world.[12] With the goal of developing a simple and up-to-date indicator of potentially preventable diabetes mortality, our objective was to evaluate diabetes mortality in people younger than 25 years and its trends using readily available GBD 2019 data on countries across the world.

Methods

Overview and definition

We used estimates from the GBD 2019 study. The GBD applies a standard methodological approach to generate estimates for mortality and causes of death for diseases for 204 countries and territories. We restricted our country-specific analyses to those with a total population of 1 million or more people in 2019 to minimise the higher variability present in the 45 countries with smaller populations. Estimates for all locations can be found in the appendix (pp 45–52).

We defined deaths occurring at ages younger than 25 years as due to type 1 and type 2 diabetes and due to chronic kidney disease resulting from diabetes based on ICD-9 and ICD-10 codes.

The general methods used to generate these estimates are described in the appendix (pp 5–31), which also includes references to the methodology used in additional GBD publications, which provide further detail. Data

sources for causes of death were obtained from vital registration systems, verbal autopsies, and other surveillance systems for 1990–2019.[12,13] Data inputs used to generate the estimates are available on the Global Health Data exchange website. The appendix (p 13) shows the quality of the national vital registration data over the period 2010–18. An explanation on how to assess the data quality is also provided in the appendix (p 12).

For **data inputs** see http://ghdx.healthdata.org/gbd-2019/data-input-sources

Mortality estimation

Mortality estimates were generated through standardisation of input data and mapping of ICD-10 (and equivalent ICD-9 codes) to type 1 diabetes (ICD-10 codes E10–E10.11, E10.3–E10.9, and P70.2), type 2 diabetes (E11–E11.1 and E11.3–E11.9), and chronic kidney disease due to each type of diabetes (E10.2 for type 1 and E11.2 for type 2). Age-sex splitting was then performed for data from sources providing only overall summaries. After this process, intermediate or poorly defined ICD codes were redistributed to plausible causes using regression or proportion redistribution methods.[12] Deaths reported as due to other or unspecified types of diabetes (E12–E14) were redistributed to type 1 or type 2 diabetes using regression modelling. To estimate the causes of death, GBD uses the Cause of Death Ensemble model (CODEm), which combines results from different statistical models weighted on the basis of their out-of-sample predictive validity.[12] The estimate for each cause of death is the mean of 1000 draws from the set best performing models. 95% uncertainty intervals (UIs) reflect the 25th and 975th values of these 1000 draws, and were calculated for all estimates. CODEm was used to model diabetes overall, both types of diabetes, and chronic kidney disease. However, the distribution of chronic kidney disease deaths due to diabetes into separate type 1 and type 2 diabetes categories was performed with DisMod-MR 2.1, which permits adjustment based on the prevalence of each type. For estimation of deaths due to overall diabetes, the GBD applies two distinct models, one for ages younger than 15 years (calculating deaths assumed to be due only to type 1 diabetes), and the other for ages 15 years and older, representing deaths due to all types of diabetes.[12] For ages 0–14 years, the covariates used in modelling were Healthcare Access and Quality (HAQ) Index, education years per capita, age-standardised fertility rate, geographic latitude, age-standardised underweight (weight-for-age) summary exposure variable, percentage of births occurring in women older than 35 years, percentage of births occurring in women older than 40 years, Socio-demographic Index (SDI), age-standardised stunting (height-for-age) summary exposure variable, and mean birthweight. For ages 15 years and older, the covariates were age-standardised mean fasting plasma glucose (mmol/L), age-standardised prevalence of diabetes, education years per capita, lag-distributed income per capita, mean BMI, mean cholesterol, mean systolic blood pressure, prevalence of obesity, age-specific and sex-specific summary exposure variable for low fruit intake, energy-adjusted grams of sugar, age-specific and sex-specific summary exposure variable for low vegetable intake, HAQ Index, and age-specific and sex-specific summary exposure variable for alcohol use.

For all models generated, GBD then applies a cause of death correction procedure that scales deaths from individual causes to match all-cause mortality for each sex-year-location, as derived from demographic analyses. Further details on these procedures can be found elsewhere.[12,13] For this study, we aggregated deaths from diabetes and from chronic kidney disease due to diabetes in ICD-10. Death rates per 100 000 population were age standardised using the direct method and the GBD standard population.[13]

SDI and universal health coverage index, and diabetes prevalence

The SDI is a composite indicator of development status derived from the total fertility rate in women younger than 25 years, mean education for those 15 years or older, and lag-distributed income per capita,[13] as detailed in the appendix (p 32). We expressed this index for 204 countries and territories, and stratified it into quintiles to explore the difference in age-standardised death rates due to diabetes between countries at different levels of development. We provide a list of countries by SDI quintile and identify the SDI quintile of each country in a map (appendix pp 40–44, 53).

GBD's universal health coverage (UHC) index was constructed by mapping 23 effective coverage indicators against five health service domains, then weighting each indicator relative to its associated potential health gains.[14] We analysed the association between the UHC effective coverage index and age-standardised death rates by linear regression and present r^2 as a measure of how much of the variance in diabetes mortality in people younger than 25 years is explained by the UHC index.

We similarly analysed the association between age-standardised prevalence of diabetes and mortality. Prevalence of diabetes was estimated from surveys of glycaemic values or use of diabetes medication, and for individuals younger than 15 years also from diabetes registries or hospital records. Detailed description of prevalence estimation is found elsewhere.[12]

Analyses in this Article were conducted with Python (version 3.6.2), Stata (version 13), and R (versions 3.5.0 and 3.6.0).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Mortality due to diabetes

In 2019, 16 300 (95% UI 14 200–18 900) deaths were due to diabetes (types 1 and 2 combined) in people younger than

	Deaths, 2019				Age–standardised death rate				
	Number	Percentage due to type 1 diabetes	Percentage due to CKD*	Percentage of total deaths†	Per 100 000, 1990	Per 100 000, 2019	All diabetes percentage change, 1990–2019	Type 1 diabetes percentage change, 1990–2019	Type 2 diabetes percentage change, 1990–2019
Global	16 300 (14 200 to 18 900)	73·7% (68·3 to 77·4)	16·5% (9·8 to 24·6)	0·24% (0·21 to 0·27)	0·60 (0·51 to 0·69)	0·50 (0·44 to 0·58)	–17·0% (–28·4 to –2·9)	–21·0% (–33·0 to –5·9)	–2·5% (–17·7 to 15·8)
Low SDI	4860 (4070 to 5900)	79·3% (74·3 to 82·5)	7·8% (4·1 to 13·3)	0·15% (0·13 to 0·17)	0·83 (0·70 to 0·95)	0·71 (0·60 to 0·86)	–13·6% (–28·4 to 3·4)	–13·6% (–29·3 to 8·9)	–13·7% (–32·2 to 11·1)
Low–middle SDI	5300 (4510 to 6200)	73·7% (66·5 to 77·8)	13·3% (7·6 to 20·7)	0·25% (0·22 to 0·29)	0·71 (0·60 to 0·84)	0·60 (0·51 to 0·70)	–15·4% (–30·9 to 2·6)	–18·4% (–35·9 to 2·9)	–5·0% (–28·9 to 23·9)
Middle SDI	4710 (4000 to 5640)	67·5% (60·9 to 72·6)	29·1% (18·8 to 39·8)	0·42% (0·35 to 0·50)	0·70 (0·56 to 0·83)	0·48 (0·41 to 0·57)	–31·3% (–40·2 to –15·4)	–38·6% (–47·4 to –21·6)	–7·2% (–20·0 to 9·0)
High–middle SDI	1000 (878 to 1140)	72·9% (67·8 to 76·4)	20·8% (12·8 to 29·8)	0·35% (0·31 to 0·40)	0·39 (0·34 to 0·45)	0·22 (0·19 to 0·25)	–44·5% (–52·0 to –36·5)	–48·8% (–56·3 to –41·5)	–26·5% (–37·2 to –11·2)
High SDI	415 (390 to 443)	83·1% (78·2 to 85·2)	4·9% (2·5 to 8·5)	0·35% (0·33 to 0·37)	0·19 (0·17 to 0·20)	0·13 (0·12 to 0·14)	–29·4% (–33·3 to –25·4)	–29·6% (–33·7 to –25·4)	–28·7% (–37·1 to –15·4)

Data in parentheses are 95% uncertainty intervals. CKD=chronic kidney disease· SDI=Socio-demographic Index. *CKD deaths due to type 1 and type 2 diabetes; note that percentages due to type 1 diabetes and those due to CKD are not mutually exclusive. †Number of deaths due to diabetes at ages younger than 25 years divided by the total of deaths from all causes at ages younger than 25 years.

Table 1: **Comparison of mortality due to diabetes at ages younger than 25 years and contribution of CKD according to the SDI**

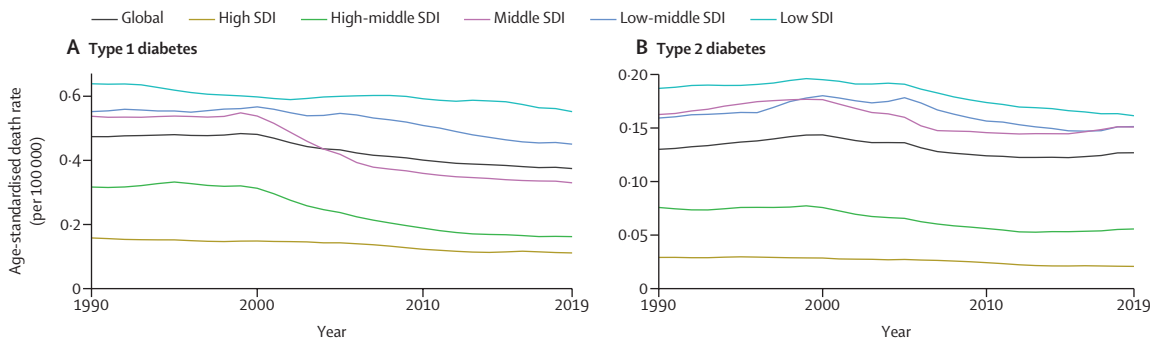
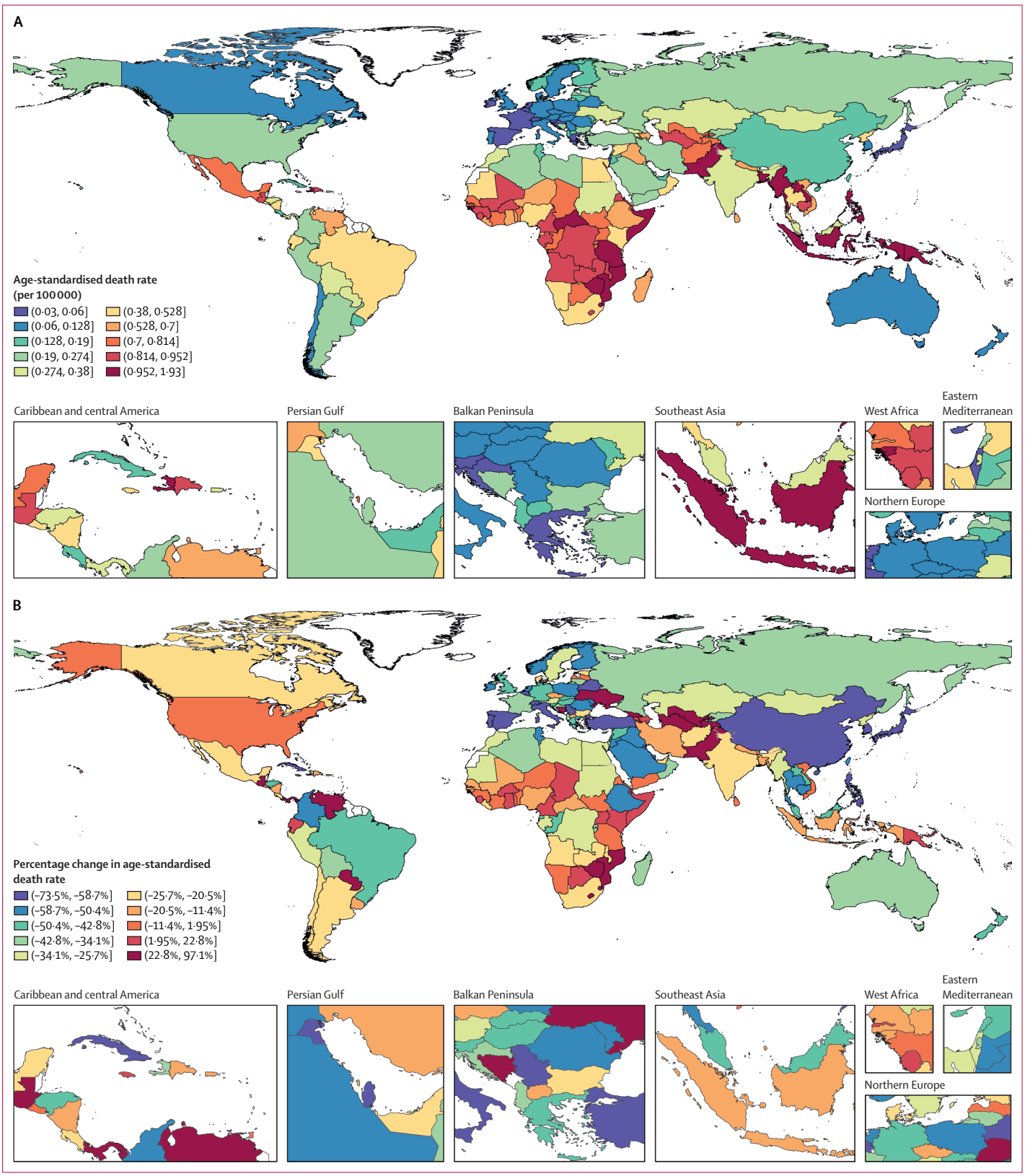


Figure 1: **Trends in age-standardised death rates due to type 1 diabetes (A) and type 2 diabetes (B) at ages younger than 25 years, 1990–2019, by SDI quintiles**
SDI=Socio-demographic Index.

25 years globally, with 15 900 (97·5%) occurring in low to high-middle SDI countries. 415 (390–443) individuals younger than 25 years died from diabetes in 2019 in high SDI countries compared to 4860 (4070–5900) in the low SDI countries and 5300 (4510–6200) in the low-middle SDI countries. Among global deaths, 73·7% (68·3–77·4) were classified as due to type 1 diabetes, and the remainder as due to type 2 diabetes. Chronic kidney disease due to either type of diabetes was responsible for 16·5% (9·8–24·6) of these deaths (varying between 4·9% [2·5–8·5] in the high SDI quintile and 29·1% [18·8–39·8] in the middle SDI quintile). At ages younger than 25 years, diabetes was a rare cause of death, with 16 300 (0·24%) deaths of 6 912 000 total deaths from all causes globally, varying from 4860 (0·15%) of 3 259 000 deaths in the low SDI quintile to 4710 (0·42%) of 1 133 000 deaths in the middle SDI quintile. Data for all-cause mortality are from GBD 2019 results (appendix pp 5–6). The age-standardised death rate in 2019 was 0·50 (0·44–0·58) per 100 000 population, varying from 0·13 (0·12–0·14) per 100 000 population in the high SDI quintile to 0·60 (0·51–0·70) per 100 000 population in the low-middle SDI quintile and 0·71 (0·60–0·86) per 100 000 population in the low SDI quintile (table 1). Age-standardised death rates decreased by 17·0% (–28·4 to –2·9) globally from 1990 to 2019, ranging from –13·6% (–28·4 to 3·4) in the low SDI quintile to –44·5% (–52·0 to –36·5) in the high-middle SDI quintile (table 1).

The appendix presents trends in age-standardised death rates due to diabetes overall by SDI for ages younger than 25 years, from 1990 to 2019 (appendix p 54), as well as data for age-standardised deaths rate, percentage change in rates from 1990 to 2019, percentage of total deaths, number of deaths, and population for all countries grouped into SDI quintiles (appendix pp 45–52).

Figure 2: **Age-standardised mortality due to diabetes at ages younger than 25 years**
(A) Age-standardised death rate per 100 000 population in 2019. (B) Percentage change in age-standardised death rate from 1990 to 2019. Countries with total population of less than 1 million people are excluded.


A
Age-standardised death rate (per 100 000)
(0·03, 0·06]
(0·06, 0·128]
(0·128, 0·19]
(0·19, 0·274]
(0·274, 0·38]
(0·38, 0·528]
(0·528, 0·7]
(0·7, 0·814]
(0·814, 0·952]
(0·952, 1·93]
Caribbean and central America
Persian Gulf
Balkan Peninsula
Southeast Asia
West Africa
Eastern Mediterranean
Northern Europe
B
Percentage change in age-standardised death rate
(−73·5%, −58·7%]
(−58·7%, −50·4%]
(−50·4%, −42·8%]
(−42·8%, −34·1%]
(−34·1%, −25·7%]
(−25·7%, −20·5%]
(−20·5%, −11·4%]
(−11·4%, 1·95%]
(1·95%, 22·8%]
(22·8%, 97·1%]
Caribbean and central America
Persian Gulf
Balkan Peninsula
Southeast Asia
West Africa
Eastern Mediterranean
Northern Europe

	Age-standardised death rate per 100 000, 2019		Percentage change, 1990–2019	
	Highest	Lowest	Least favourable	Most favourable
Low SDI	1·78 (1·29 to 2·39; Papua New Guinea)	0·27 (0·13 to 0·42; Yemen)	91·4% (41·1 to 146·0; Pakistan)	–52·2% (–64·8 to –35·8; Ethiopia)
Low-middle SDI	1·93 (1·30 to 2·68; Myanmar)	0·23 (0·19 to 0·28; Kyrgyzstan)	84·8% (18·1 to 158·2; Guatemala)	–51·1% (–66·2 to –27·0; Cambodia)
Middle SDI	1·35 (1·07 to 1·70; Philippines)	0·15 (0·11 to 0·19; Cuba)	96·3% (57·0 to 137·7; Uzbekistan)	–64·8% (–72·8 to –54·6; Cuba)
High-middle SDI	1·31 (0·98 to 1·74; Mauritius)	0·04 (0·03 to 0·05; Spain)	97·1% (51·0 to 151·2; Mauritius)	–73·1% (–82·8 to –60·9; Turkey)
High SDI	0·45 (0·34 to 0·62; Kuwait)	0·03 (0·02 to 0·04; Cyprus)	–3·5% (–10·5 to 2·0; USA)	–73·5% (–79·6 to –63·2; Singapore)

Data in the parentheses are 95% uncertainty intervals and countries. SDI=Socio-demographic Index.

Table 2: **Highest and lowest age-standardised death rates due to diabetes at ages younger than 25 years in 2019, and most and least favourable percentage changes from 1990 to 2019, by SDI quintile**

Additionally, age-specific mortality before the age of 15 years in 2019, as expected, was very low for all SDI quintiles, except for the low SDI quintile (appendix p 55). Rates then increased, particularly in the low to middle SDI quintiles. At the age range of 20–24 years, rates in the low SDI were almost 3·5 times those of the high SDI quintile (appendix p 55).

Age-standardised death rates by type of diabetes

Because most deaths before the age of 25 years were due to type 1 diabetes, declines seen for this diabetes type resembled those seen for all cases. By contrast, declines for type 2 diabetes were generally smaller globally (–2·5 % [95% UI –17·7 to 15·8]), although variable across SDI quintiles (eg, –28·7% [–37·1 to –15·4] in high SDI countries; table 1).

For type 1 diabetes (figure 1A), the age-standardised death rate decreased by 21·0% (95% UI –33·0 to –5·9) globally when considering only type 1 diabetes, and the greatest decreases from 1990 to 2019, starting at about year 2000, were observed for the high-middle quintile (–48·8% [–56·3 to –41·5]) and middle SDI quintile (–38·6% [–47·4 to –21·6]). In 2019, the high-middle quintile approached the rate of high SDI countries. Lesser decreases were seen in low-middle and low SDI quintiles, leaving them with high rates in 2019. For type 2 diabetes (figure 1B), declines were generally small. Ranking of SDI quintiles by their type 2 diabetes age-standardised death rates in 2019 showed a similar pattern to that seen for type 1 diabetes, except for the middle SDI quintile, the rate of which equalled that of the low-middle SDI quintile (figure 1B).

Differences in age-standardised death rates by location

Important variation in age-standardised death rates due to diabetes before the age of 25 years in 2019 was seen globally (figure 2A). Many countries in sub-Saharan Africa, the Caribbean, and southeast Asia, as well as a cluster of countries in central Asia together with neighbouring Afghanistan and Pakistan, had the highest age-standardised death rates. By contrast, high-income countries of western Europe, Australasia, and Asia Pacific, as well as Chile and Canada, had the lowest age-standardised death rates.

Progress in decreasing this mortality rate from 1990 to 2019 has also varied considerably. Although age-standardised death rates in some countries increased, rates decreased in most countries, frequently by more than half (figure 2B). Many countries in central Asia, Oceania, Latin America and the Caribbean, and eastern, western, and southern sub-Saharan Africa had high increases, and many from Europe, high-income Asia Pacific, and east and southeast Asia had large decreases.

The three countries with the highest age-standardised diabetes death rates in 2019 across all SDI quintiles were Myanmar (1·93 [95% UI 1·30–2·68] per 100 000 population; table 2), Papua New Guinea (1·78 [1·29–2·39] per 100 000 population; table 2), and Haiti (1·57 [1·14–2·10] per 100 000 population; appendix p 48). The three countries with lowest age-standardised diabetes death rates in 2019 regardless of SDI index were Cyprus (0·03 [0·02–0·04] per 100 000 population; table 2), Slovenia (0·03 [0·03–0·04] per 100 000 population; appendix p 46), and Switzerland (0·03 [0·03–0·04] per 100 000 population; appendix p 47). Frequently, the highest rate in each SDI quintile was approximately ten times that of the lowest (table 2). A similar mortality pattern was seen globally when analyses included only type 1 diabetes deaths (appendix p 56).

Differences in age-standardised death rates by SDI and UHC indices

Variability was also seen when considering the extremes of changes within each SDI quintile. For example, in the high SDI quintile, the age-standardised death rate decreased by 73·5% (95% UI –79·6 to –63·2) for Singapore versus 3·5% (–10·5 to 2·0) for the USA; within the low SDI quintile, the rate increased by 91·4% (41·1 to 146·0) for Pakistan and decreased by 52·2% (–64·8 to –35·8) for Ethiopia (table 2).

Death rates in 2019 were unrelated to age-standardised diabetes prevalence at ages younger than 25 years (r^2=0·0004; data not shown). Universal health coverage was inversely associated with age-standardised death rates per 100 000 population explaining 62% of total variance (r^2=0·62; figure 3A). An inverse association was also present within each individual SDI stratum (figure 3B).

Discussion

From 1990 to 2019, we observed general progress in decreasing mortality due to diabetes at ages younger than 25 years, mostly related to type 1 diabetes. However, large disparities persisted across countries, with age-standardised mortality of low and low-middle SDI countries being approximately five times that of high SDI countries and varying more than ten times across countries within SDI quintiles. UHC explains an important part of the variability in rates and highlights

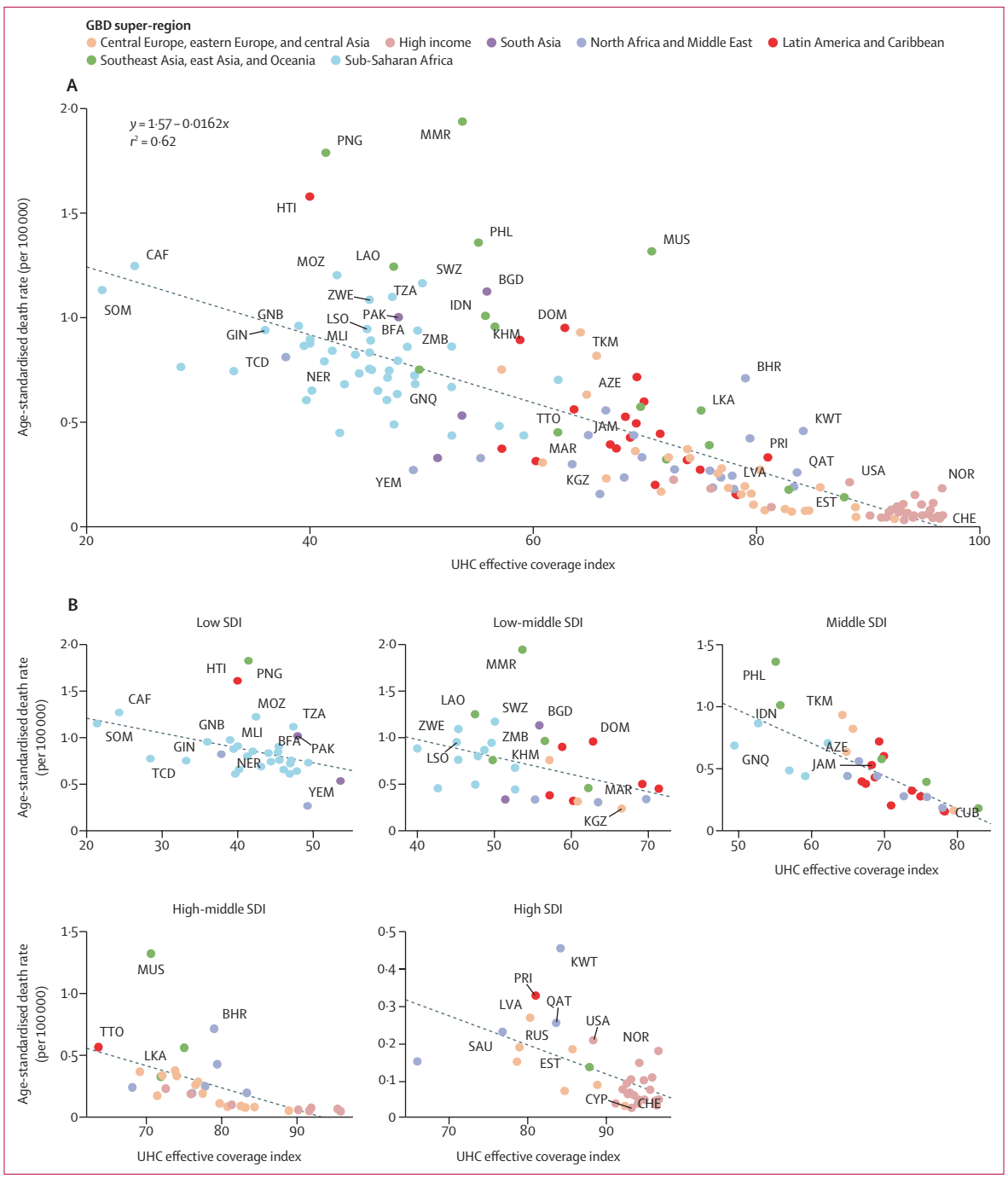


Figure 3: **Scatterplot of age-standardised diabetes death rate at ages younger than 25 years by UHC index in 2019 globally (A) and by SDI quintile (B)**
The diagonal line is the death rate at each UHC index as estimated by linear regression. Country super-regions are indicated by colours. UHC=universal health coverage.

the role of access to care in reducing disparities in mortality in this age group.

Deaths due to acute complications of type 1 diabetes, although usually avoidable, have been rarely used as an indicator of potentially preventable deaths, owing to poor specification on death certificates. By restricting our analyses to ages younger than 25 years, a range in which most deaths are among cases of type 1 diabetes and presumably mostly due to acute complications, this derived indicator minimises the problem of poor reporting in vital registration. Chronic kidney disease, as here reported, represents 16·5% of all diabetes deaths before the age of 25 years. As this cause of death at early ages is likely to be related to extremely poor glycaemic

control, which can be prevented through basic diabetes care, it can logically be considered within this metric of avoidable deaths. Of note, acute infections associated with poor glycaemic control, another potentially avoidable cause of death among people with diabetes at ages younger than 25 years,[15–18] will not be captured by the metric as they are not assigned to diabetes on the death certificate.

Deaths due to chronic complications at ages younger than 25 years also occur in people with early-onset type 2 diabetes, as type 2 diabetes in the young has been recognised as a more severe form of disease than diabetes presenting at older ages.[19] As the epidemic of type 2 diabetes grows, type 2 diabetes in the young is posing new challenges to health care. The small and variable progress in decreasing early deaths due to type 2 diabetes described here highlights the need to monitor this mortality in the years to come.

Our findings of low mortality rates at ages younger than 25 years in high SDI countries attests to the amenability of these deaths and supports the importance of access to diabetes medications and basic diabetes care. Protocols have been successfully implemented in high-income countries over the years.[20] However, many LMICs, while striving to adjust to rapid and incomplete epidemiological transitions, have faced additional obstacles, such as limited technical expertise and political and economic instability, complicating their implementation of similar protocols. The rapid decrease in deaths due to acute complications in Brazil,[9] a country in the middle SDI quintile, with increasingly adequate and accessible primary care and the provision of free insulin, highlights the preventability of such deaths in settings with fewer resources.

Almost 22 million people were living with type 1 diabetes in 2019,[12] needing insulin daily. Insulin access and prices vary widely across countries,[21] and limited government expenditures for health[22] hinder the creation of universal care systems in many LMICs. In settings where individuals are required to pay out-of-pocket for all or part of their diabetes care, which includes insulin as well as syringes, blood glucose meters, and the necessary health education, cost can make insulin treatment unaffordable.[4] This is particularly important in low-income countries, in which insulin prices are frequently higher than in middle-income and high-income countries.[23,24]

By analysing diabetes mortality at ages younger than 25 years, we have mapped areas of the world that need greater action to prevent these avoidable early deaths. Among these areas are sub-Saharan Africa, parts of central and southeast Asia, Oceania, and Latin America and the Caribbean. Countries in these locations have high age-standardised death rates due to diabetes, in comparison to those from the high SDI quintile, and in some, rates are increasing.[12] Although our analyses for these countries frequently depend on modelling, we can postulate that inadequate diagnosis and treatment of diabetes, as highlighted for sub-Saharan Africa,[25] is likely to be a major contributor to these early deaths. The diabetes burden of these countries calls for global action in alignment with the UN Sustainable Development Goal 3, which emphasises the provision of universal access to care and affordable essential medicines, and with WHO's Global Target 9 for confronting NCDs, which focuses on the availability of essential medicines, including insulin.[1,2] The *Lancet Global Health* Commission on high-quality health systems emphasised the importance of developing health systems in LMICs to permit broad access to quality health services.[26] As highlighted by the *Lancet* Diabetes Commission, access to insulin, patient education, and tools for monitoring blood glucose concentration are important to prevent premature deaths and emergencies in young patients with type 1 diabetes.[27] So far, there has been no means of periodic monitoring of this mortality goal globally. The use of the age-standardised death rate from diabetes at ages younger than 25 years can help to track achievements in basic diabetes health care. Additionally, the recently described increased risk of young people with type 2 diabetes[19] could be similarly tracked.

This study has limitations. First, the vital registration data are generally of low quality or absent in many countries, especially in sub-Saharan Africa. However, the GBD, over decades, has developed a comprehensive methodology to address this problem, including yearly searches with in-country collaborators for available data; detailed cleaning, correction, and smoothing routines; and modelling approaches to maximise the use of what data are available. Second, few well established risk factors for type 1 diabetes exist, limiting the ability to extrapolate findings from data-rich countries. Third, our diabetes mortality indicator could have varied, in part, due to differences in the underlying prevalence of diabetes. However, within the age range analysed, prevalence was poorly associated with age-standardised diabetes death rates. Although lack of adjustment for diabetes prevalence could be an issue for a few countries with very high prevalence of type 2 diabetes, to keep the indicator simple we did not make this adjustment. In the future, as the prevalence of type 2 diabetes in the young increases, this adjustment might become indicated.

Within these limitations and recognising that the rates modelled for specific countries are approximations of their true rates, we describe a comprehensive and global overview of the level and trends in age-standardised diabetes mortality at early ages. The metric allows the monitoring of potentially avoidable diabetes deaths—those caused by acute complications and, to a lesser extent, chronic complications resulting from extremely poor glycaemic control—around the world. If meaningful progress on decreasing avoidable diabetes deaths is to be made on a world scale, it must be focused on low to high-middle SDI countries where 97·5% of the deaths due to diabetes in people younger than 25 years occur.

Prevention of diabetes mortality can be improved with the prompt diagnosis and treatment of type 1 diabetes and with the provision of basic care and education to both people with all types of diabetes and their families.[24] It is time for insulin, now 100 years after its discovery, to become available to all in need.

Globally, progress has been made in decreasing diabetes mortality at ages younger than 25 years, although important variability across countries remains. The decreases are less pronounced in low and low-middle SDI countries. Additionally, the large variability of this metric within each SDI quintile and its strong inverse correlation with the GBD's UHC index indicate that factors related to the organisation and quality of health care are important determinants of these outcomes. Diabetes mortality at ages younger than 25 years can serve as a readily available indicator for the surveillance of basic diabetes care and access to insulin around the world.

Contributors

Please see the appendix (pp 37–41) for more detailed information about individual author contributions to the research, divided into the following categories: managing the estimation or publication process; writing the first draft of the manuscript; primary responsibility for applying analytical methods to produce estimates; primary responsibility for seeking, cataloguing, extracting, or cleaning data; designing or coding figures and tables; providing data or critical feedback on data sources; development of methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; extracting, cleaning, or cataloguing data; and designing or coding figures and tables. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. E Cousin and C Stein verified all data in this study.

GBD 2019 Diabetes Mortality Collaborators

Ewerton Cousin, Bruce B Duncan, Caroline Stein, Kanyin Liane Ong, Theo Vos, Cristiana Abbafati, Mohsen Abbasi-Kangevari, Michael Abdelmasseh, Amir Abdoli, Rami Abd-Rabu, Hassan Abolhassani, Eman Abu-Gharbieh, Manfred Mario Kokou Accrombessi, Qorinah Estiningtyas Sakilah Adnani, Muhammad Sohail Afzal, Gina Agarwal, Krishna K Agrawaal, Marcela Agudelo-Botero, Bright Opoku Ahinkorah, Sajjad Ahmad, Tauseef Ahmad, Keivan Ahmadi, Sepideh Ahmadi, Ali Ahmadi, Ali Ahmed, Yusra Ahmed Salih, Wuraola Akande-Sholabi, Tayyaba Akram, Hanadi Al Hamad, Ziyad Al-Aly, Jacqueline Elizabeth Alcalde-Rabanal, Vahid Alipour, Syed Mohamed Aljunid, Rajaa M Al-Raddadi, Nelson Alvis-Guzman, Saeed Amini, Robert Ancuceanu, Tudorel Andrei, Catalina Liliana Andrei, Ranjit Mohan Anjana, Adnan Ansar, Ippazio Cosimo Antonazzo, Benny Antony, Anayochukwu Edward Anyasodor, Jalal Arabloo, Damian Arizmendi, Benedetta Armocida, Anton A Artamonov, Judie Arulappan, Zahra Aryan, Samaneh Asgari, Tahira Ashraf, Thomas Astell-Burt, Prince Atorkey, Maha Moh'd Wahbi Atout, Martin Amogre Ayanore, Ashish D Badiye, Atif Amin Baig, Mohan Bairwa, Jennifer L Baker, Ovidiu Constantin Baltatu, Palash Chandra Banik, Anthony Barnett, Mark Thomaz Ugliara Barone, Francesco Barone-Adesi, Amadou Barrow, Neeraj Bedi, Rebuma Belete, Uzma Iqbal Belgaumi, Arielle Wilder Bell, Derrick A Bennett, Isabela M Bensenor, David Beran, Akshaya Srikanth Bhagavathula, Sonu Bhaskar, Krittika Bhattacharyya, Vijayalakshmi S Bhojaraja, Ali Bijani, Boris Bikbov, Setognal Birara, Virginia Bodolica, Aime Bonny, Hermann Brenner, Nikolay Ivanovich Briko, Zahid A Butt, Florentino Luciano Caetano dos Santos, Luis Alberto Cámera, Ismael R Campos-Nonato, Yin Cao, Chao Cao, Ester Cerin, Promit Ananyo Chakraborty, Joht Singh Chandan, Vijay Kumar Chattu, Simiao Chen, Jee-Young Jasmine Choi, Sonali Gajanan Choudhari, Enayet Karim Chowdhury, Dinh-Toi Chu, Barbara Corso, Omid Dadras, Xiaochen Dai, Albertino Antonio Moura Damasceno, Lalit Dandona, Rakhi Dandona, Claudio Alberto Dávila-Cervantes, Jan-Walter De Neve, Edgar Denova-Gutiérrez, Deepak Dhamnetiya, Daniel Diaz, Sanam Ebtehaj, Hisham Atan Edinur, Sahar Eftekharzadeh, Iman El Sayed, Islam Y Elgendy, Muhammed Elhadi, Mohamed A Elmonem, Mohammed Faisaluddin, Umar Farooque, Xiaoqi Feng, Eduarda Fernandes, Florian Fischer, David Flood, Marisa Freitas, Peter Andras Gaal, Mohamed M Gad, Piyada Gaewkhiew, Lemma Getacher, Mansour Ghafourifard, Reza Ghanei Gheshlagh, Ahmad Ghashghaee, Nermin Ghith, Ghozali Ghozali, Paramjit Singh Gill, Ibrahim Abdelmageed Ginawi, Ekaterina Vladimirovna Glushkova, Mahaveer Golechha, Sameer Vali Gopalani, Rafael Alves Guimarães, Rajat Das Gupta, Rajeev Gupta, Vivek Kumar Gupta, Veer Bala Gupta, Sapna Gupta, Tesfa Dejenie Habtewold, Nima Hafezi-Nejad, Rabih Halwani, Asif Hanif, Graeme J Hankey, Shafiul Haque, Ahmed I Hasaballah, Syed Shahzad Hasan, Abdiwahab Hashi, Soheil Hassanipour, Simon I Hay, Khezar Hayat, Mohammad Heidari, Mohammad Bellal Hossain Hossain, Sahadat Hossain, Mostafa Hosseini, Soodabeh Hoveidamanesh, Junjie Huang, Ayesha Humayun, Rabia Hussain, Bing-Fang Hwang, Segun Emmanuel Ibitoye, Kevin S Ikuta, Leeberk Raja Inbaraj, Usman Iqbal, Md Shariful Islam, Sheikh Mohammed Shariful Islam, Rakibul M Islam, Nahlah Elkudssiah Ismail, Gaetano Isola, Ramaiah Itumalla, Masao Iwagami, Ihoghosa Osamuyi Iyamu, Mohammad Ali Jahani, Mihajlo Jakovljevic, Ranil Jayawardena, Ravi Prakash Jha, Oommen John, Jost B Jonas, Tamas Joo, Ali Kabir, Rohollah Kalhor, Ashwin Kamath, Tanuj Kanchan, Himal Kandel, Neeti Kapoor, Gbenga A Kayode, Sewnet Adem Kebede, Pedram Keshavarz, Mohammad Keykhaei, Yousef Saleh Khader, Himanshu Khajuria, Moien A B Khan, Md Nuruzzaman Khan, Maseer Khan, Amir M Khater, Tawfik Ahmed Muthafer Khoja, Jagdish Khubchandani, Min Seo Kim, Yun Jin Kim, Ruth W Kimokoti, Sezer Kisa, Adnan Kisa, Mika Kivimäki, Vladimir Andreevich Korshunov, Oleksii Korzh, Ai Koyanagi, Kewal Krishan, Barthelemy Kuate Defo, G Anil Kumar, Nithin Kumar, Dian Kusuma, Carlo La Vecchia, Ben Lacey, Anders O Larsson, Savita Lasrado, Wei-Chen Lee, Chiachi Bonnie Lee, Paul H Lee, Shaun Wen Huey Lee, Ming-Chieh Li, Stephen S Lim, Lee-Ling Lim, Giancarlo Lucchetti, Azeem Majeed, Ahmad Azam Malik, Borhan Mansouri, Lorenzo Giovanni Mantovani, Santi Martini, Prashant Mathur, Colm McAlinden, Nafiul Mehedi, Teferi Mekonnen, Ritesh G Menezes, Amanual Getnet Mersha, Junmei Miao Jonasson, Tomasz Miazgowski, Irmina Maria Michalek, Andreea Mirica, Erkin M Mirrakhimov, Agha Zeeshan Mirza, Prasanna Mithra, Abdollah Mohammadian-Hafshejani, Reza Mohammadpourhodki, Arif Mohammed, Ali H Mokdad, Mariam Molokhia, Lorenzo Monasta, Mohammad Ali Moni, Farhad Moradpour, Rahmatollah Moradzadeh, Ebrahim Mostafavi, Ulrich Otto Mueller, Christopher J L Murray, Ahmad Mustafa, Gabriele Nagel, Vinay Nangia, Atta Abbas Naqvi, Biswa Prakash Nayak, Javad Nazari, Rawlance Ndejjo, Ruxandra Irina Negoi, Sandhya Neupane Kandel, Cuong Tat Nguyen, Huong Lan Thi Nguyen, Jean Jacques Noubiap, Christoph Nowak, Bogdan Oancea, Oluwakemi Ololade Odukoya, Ayodipupo Sikiru Oguntade, Temitope T Ojo, Andrew T Olagunju, Obinna E Onwujekwe, Alberto Ortiz, Mayowa O Owolabi, Raffaele Palladino, Songhomitra Panda-Jonas, Seithikurippu R Pandi-Perumal, Shahina Pardhan, Tarang Parekh, Mojtaba Parvizi, Veincent Christian Filipino Pepito, Arokiasamy Perianayagam, Ionela-Roxana Petcu, Manju Pilania, Vivek Podder, Roman V Polibin, Maarten J Postma, Akila Prashant, Navid Rabiee, Mohammad Rabiee, Vafa Rahimi-Movaghar, Muhammad Aziz Rahman, Md. Mosfequr Rahman, Mosiur Rahman, Setyaningrum Rahmawaty, Nazanin Rajai, Pradhum Ram, Juwel Rana, Kamal Ranabhat, Priyanga Ranasinghe, Chythra R Rao, Satish Rao, Salman Rawaf, David Laith Rawaf, Lal Rawal, Andre M N Renzaho, Nima Rezaei, Aziz Rezapour, Seyed Mohammad Riahi, Daniela Ribeiro, Jefferson Antonio Buendia Rodriguez, Leonardo Roever, Peter Rohloff, Godfrey M Rwegerera, Paul MacDaragh Ryan, Maha Mohamed Saber-Ayad, Siamak Sabour, Basema Saddik, Sahar Saeedi Moghaddam, Amirhossein Sahebkar, Harihar Sahoo,

KM Saif-Ur-Rahman, Hamideh Salimzadeh, Mehrnoosh Samaei, Juan Sanabria, Milena M Santric-Milicevic, Brijesh Sathian, Thirunavukkarasu Sathish, Markus P Schlaich, Abdul-Aziz Seidu, Mario Šekerija, Nachimuthu Senthil Kumar, Allen Seylani, Masood Ali Shaikh, Hina Shamshad, Md Shajedur Rahman Shawon, Sara Sheikhbahaei, Jeevan K Shetty, Rahman Shiri, K M Shivakumar, Kerem Shuval, Jasvinder A Singh, Ambrish Singh, Valentin Yurievich Skryabin, Anna Aleksandrovna Skryabina, Ahmad Sofi-Mahmudi, Amin Soheili, Jing Sun, Viktória Szerencsés, Miklós Szócska, Rafael Tabarés-Seisdedos, Hooman Tadbiri, Eyayou Girma Tadesse, Md. Tariqujjaman, Kavumpurathu Raman Thankappan, Rekha Thapar, Nihal Thomas, Binod Timalsina, Ruoyan Tobe-Gai, Marcello Tonelli, Marcos Roberto Tovani-Palone, Bach Xuan Tran, Jaya Prasad Tripathy, Lorainne Tudor Car, Biruk Shalmeno Tusa, Riaz Uddin, Era Upadhyay, Sahel Valadan Tahbaz, Pascual R Valdez, Tommi Juhani Vasankari, Madhur Verma, Victor E Villalobos-Daniel, Sergey Konstantinovitch Vladimirov, Bay Vo, Giang Thu Vu, Rade Vukovic, Yasir Waheed, Richard G Wamai, Andrea Werdecker, Nuwan Darshana Wickramasinghe, Andrea Sylvia Winkler, Befikadu Legesse Wubishet, Xiaoyue Xu, Suowen Xu, Seyed Hossein Yahyazadeh Jabbari, Hiroshi Yatsuya, Sanni Yaya, Taklo Simeneh Yazie Yazie, Siyan Yi, Naohiro Yonemoto, Ismaeel Yunusa, Siddhesh Zadey, Sojib Bin Zaman, Maryam Zamanian, Nelson Zamora, Mikhail Sergeevich Zastrozhin, Anasthasia Zastrozhina, Zhi-Jiang Zhang, Chenwen Zhong, Mohammad Zmaili, Alimuddin Zumla, Mohsen Naghavi, and Maria Inês Schmidt.

Affiliations

Institute for Health Metrics and Evaluation (E Cousin PhD, K L Ong PhD, Prof T Vos PhD, X Dai PhD, Prof L Dandona MD, Prof R Dandona PhD, Prof S I Hay DSc, K S Ikuta MD, Prof S S Lim PhD, A H Mokdad PhD, Prof C J L Murray DPhil, Prof M Naghavi MD), Department of Health Metrics Sciences, School of Medicine (E Cousin PhD, Prof T Vos PhD, X Dai PhD, Prof R Dandona PhD, Prof S I Hay DSc, Prof S S Lim PhD, A H Mokdad PhD, Prof C J L Murray DPhil, Prof M Naghavi MD), Division of Allergy and Infectious Diseases (K S Ikuta MD), University of Washington, Seattle, WA, USA; Postgraduate Program in Epidemiology (E Cousin PhD, Prof B B Duncan MD, C Stein PhD, Prof M I Schmidt PhD), Federal University of Rio Grande do Sul, Porto Alegre, Brazil; Department of Juridical and Economic Studies (C Abbafati PhD), La Sapienza University, Rome, Italy; Social Determinants of Health Research Center (M Abbasi-Kangevari MD), School of Advanced Technologies in Medicine (S Ahmadi PhD), Department of Epidemiology (A Ahmadi PhD, S Sabour PhD), Prevention of Metabolic Disorders Research Center (S Asgari MSc), Shahid Beheshti University of Medical Sciences, Tehran, Iran; Department of Surgery (M Abdelmasseh MD, Prof J Sanabria MD), Marshall University, Huntington, WV, USA; Zoonoses Research Center (A Abdoli PhD), Jahrom University of Medical Sciences, Jahrom, Iran; Evidence-Based Practice Center (R Abd-Rabu MD), Department of Cardiovascular Medicine (S Ebtehaj PhD), Division of Endocrinology (M Parvizi PhD), Mayo Clinic, Rochester, MN, USA; Research Center for Immunodeficiencies (H Abolhassani PhD, Prof N Rezaei PhD), Non-communicable Diseases Research Center (Z Aryan MD, M Keykhaei MD, S Saeedi Moghaddam MSc), Iranian Research Center for HIV/AIDS (IRCHA) (O Dadras DrPH), School of Medicine (N Hafezi-Nejad MD), Department of Epidemiology and Biostatistics (Prof M Hosseini PhD), Pediatric Chronic Kidney Disease Research Center (Prof M Hosseini PhD), Students' Scientific Research Center (SSRC) (M Keykhaei MD), Sina Trauma and Surgery Research Center (Prof V Rahimi-Movaghar MD), Digestive Diseases Research Institute (H Salimzadeh PhD), Tehran University of Medical Sciences, Tehran, Iran; Department of Biosciences and Nutrition (H Abolhassani PhD), Karolinska University Hospital, Huddinge, Sweden; Clinical Sciences Department (E Abu-Gharbieh PhD, Prof R Halwani PhD), College of Medicine (Prof R Halwani PhD), Department of Clinical Sciences (M M Saber-Ayad MD), Sharjah Institute for Medical Research (B Saddik PhD), University of Sharjah, Sharjah, United Arab Emirates; Department of Disease Control (M M K Accrombessi PhD), Department of Non-Communicable Disease Epidemiology (M Iwagami PhD), London School of Hygiene & Tropical Medicine, London, UK; Department of Clinical Research (M M K Accrombessi PhD), Clinical Research Institute of Benin (IRCB), Abomey-Calavi, Benin; Faculty of Medicine (Q E S Adnani PhD), Universitas Padjadjaran (Padjadjaran University), Bandung, Indonesia; Department of Life Sciences (M S Afzal PhD), University of Management and Technology, Lahore, Pakistan; Department of Family Medicine (Prof G Agarwal PhD), Department of Psychiatry and Behavioural Neurosciences (A T Olagunju MD), Population Health Research Institute (T Sathish PhD), McMaster University, Hamilton, ON, Canada; Department of Internal Medicine (K K Agrawaal PhD), Tribhuvan University, Bhairahawa, Nepal; Center for Policy, Population & Health Research (Prof M Agudelo-Botero PhD), Center of Complexity Sciences (Prof D Diaz PhD), National Autonomous University of Mexico, Mexico City, Mexico; The Australian Centre for Public and Population Health Research (ACPPHR) (B O Ahinkorah MPH), School of Computing Sciences (Prof J Sun PhD), University of Technology Sydney, Sydney, NSW, Australia; Department of Health and Biological Sciences (S Ahmad PhD), Abasyn University, Peshawar, Pakistan; Department of Epidemiology and Health Statistics (T Ahmad MS), Southeast University, Nanjing, China; Lincoln Medical School (K Ahmadi PhD), Universities of Nottingham & Lincoln, Lincoln, UK; Department of Epidemiology and Biostatistics (A Ahmadi PhD, A Mohammadian-Hafshejani PhD), Community-Oriented Nursing Midwifery Research Center (M Heidari PhD), Shahrekord University of Medical Sciences, Shahrekord, Iran; School of Pharmacy (A Ahmed MPhil, S W H Lee PhD), Monash University, Bandar Sunway, Malaysia; Department of Pharmacy (A Ahmed MPhil), Quaid I Azam University Islamabad, Islamabad, Pakistan; Database Technology Department (Y Ahmed Salih PhD), College of Informatics (Y Ahmed Salih PhD), Sulaimani Polytechnic University, Sulaymaniyah, Iraq; Department of Clinical Pharmacy and Pharmacy Administration (W Akande-Sholabi PhD), Department of Health Promotion and Education (S E Ibitoye MPH), Department of Medicine (Prof M O Owolabi DrM), University of Ibadan, Ibadan, Nigeria; School of Mathematical Sciences (T Akram PhD), School of Pharmaceutical Sciences (R Hussain PhD), University of Science Malaysia, Penang, Malaysia; Geriatric and Long Term Care Department (H Al Hamad MD, B Sathian PhD), Rumailah Hospital (H Al Hamad MD), Hamad Medical Corporation, Doha, Qatar; John T Milliken Department of Internal Medicine (Z Al-Aly MD), Program in Physical Therapy (C Cao MPH), Washington University in St. Louis, St. Louis, MO, USA; Clinical Epidemiology Center (Z Al-Aly MD), US Department of Veterans Affairs (VA), St Louis, MO, USA; Center for Health Systems Research (J E Alcalde-Rabanal PhD), Health and Nutrition Research Center (I R Campos-Nonato PhD), Center for Nutrition and Health Research (E Denova-Gutiérrez DSc), National Institute of Public Health, Cuernavaca, Mexico; Health Management and Economics Research Center (V Alipour PhD, J Arabloo PhD, A Ghashghaee BSc, A Rezapour PhD), Department of Health Economics (V Alipour PhD), Student Research Committee (A Ghashghaee BSc), Minimally Invasive Surgery Research Center (A Kabir MD), Iran University of Medical Sciences, Tehran, Iran; Department of Health Policy and Management (Prof S M Aljunid PhD), Kuwait University, Safat, Kuwait; International Centre for Casemix and Clinical Coding (Prof S M Aljunid PhD), National University of Malaysia, Bandar Tun Razak, Malaysia; Department of Community Medicine (R M Al-Raddadi PhD), Rabigh Faculty of Medicine (A A Malik PhD), King Abdulaziz University, Jeddah, Saudi Arabia; Research Group in Hospital Management and Health Policies (Prof N Alvis-Guzman PhD), Universidad de la Costa (University of the Coast), Barranquilla, Colombia; Research Group in Health Economics (Prof N Alvis-Guzman PhD), University of Cartagena, Cartagena, Colombia; Department of Health Services Management (S Amini PhD), Khomein University of Medical Sciences, Khomein, Iran; Pharmacy Department (Prof R Ancuceanu PhD), Cardiology Department (C Andrei PhD), Department of Anatomy and Embryology (R I Negoi PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; Department of Statistics and Econometrics (Prof T Andrei PhD, A Mirica PhD, I Petcu PhD), Bucharest University of Economic Studies, Bucharest, Romania; Department of Diabetology (R M Anjana PhD), Madras Diabetes Research Foundation, Chennai,

India; School of Nursing and Midwifery (A Ansar MPH, M Rahman PhD), La Trobe University, Melbourne, VIC, Australia; Special Interest Group International Health (A Ansar MPH), Public Health Association of Australia, Canberra, ACT, Australia; Research Center on Public Health (I Antonazzo PhD), School of Medicine and Surgery (Prof L G Mantovani DSc), University of Milan Bicocca, Monza, Italy; Menzies Institute for Medical Research (B Antony PhD, A Singh MTech), University of Tasmania, Hobart, TAS, Australia; School of Community Health (A E Anyasodor PhD), Charles Sturt University, Orange, NSW, Australia; Faculty of Nutrition (Prof D Arizmendi MSc), Autonomous University of the State of Morelos, Cuernavaca, Morelos, Mexico; Epidemiology Department (B Armocida MSc), Clinical Epidemiology and Public Health Research Unit (L Monasta DSc), Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy; Department of Biophysics (A A Artamonov PhD), Russian Academy of Sciences, Moscow, Russia; Department of Maternal and Child Health (J Arulappan DSc), Sultan Qaboos University, Muscat, Oman; Brigham and Women's Hospital (Z Aryan MD), Department of Global Health and Social Medicine (A W Bell MSW), Division of Cardiology (I Y Elgendy MD), Department of Internal Medicine (N Rajai MD), Department of Global Health and Population (P Rohloff MD), Harvard University, Boston, MA, USA; University Institute of Radiological Sciences and Medical Imaging Technology (T Ashraf MS), University Institute of Public Health (A Hanif PhD, A A Malik PhD), The University of Lahore, Lahore, Pakistan; School of Health and Society (Prof T Astell-Burt PhD), University of Wollongong, Wollongong, NSW, Australia; Menzies Centre for Health Policy (Prof T Astell-Burt PhD), Sydney Medical School (S Islam PhD), Save Sight Institute (H Kandel PhD), University of Sydney, Sydney, NSW, Australia; School of Medicine and Public Health (P Atorkey MPhil, A G Mersha MD), School of Biomedical Sciences and Pharmacy (S Hasan PhD), Research Centre for Generational Health and Ageing (B Wubishet MPH), University of Newcastle, Newcastle, NSW, Australia; Hunter New England Population Health, Wallsend, NSW, Australia (P Atorkey MPhil); Faculty of Nursing (M M W Atout PhD), Philadelphia University, Amman, Jordan; Department of Health Policy Planning and Management (M A Ayanore PhD), University of Health and Allied Sciences, Ho, Ghana; Department of Health Economics (M A Ayanore PhD), Centre for Health Policy Advocacy Innovation & Research in Africa (CHPAIR-Africa), Accra, Ghana; Department of Forensic Science (A D Badiye MSc, N Kapoor MSc), Government Institute of Forensic Science, Nagpur, India; Unit of Biochemistry (A A Baig PhD), Universiti Sultan Zainal Abidin (Sultan Zainal Abidin University), Kuala Terengganu, Malaysia; Centre for Community Medicine (M Bairwa MD), All India Institute of Medical Sciences, New Delhi, India; Center for Clinical Research and Prevention (J L Baker PhD), Bispebjerg University Hospital, Frederiksberg, Denmark; Department of Pharmacology & Therapeutics (Prof O C Baltatu PhD), Khalifa University, Abu Dhabi, United Arab Emirates; Center of Innovation, Technology and Education (CITE) (Prof O C Baltatu PhD), Anhembi Morumbi University, Sao Jose dos Campos, Brazil; Department of Non-communicable Diseases (P C Banik MPhil), Bangladesh University of Health Sciences, Dhaka, Bangladesh; Mary MacKillop Institute for Health Research (A Barnett PhD, Prof E Cerin PhD), Australian Catholic University, Melbourne, VIC, Australia; Programs, Partnerships, Research and Education (M T U Barone PhD), International Diabetes Federation, São Paulo, Brazil; International Diabetes Federation, Brussels, Belgium (M T U Barone PhD); Department of Translational Medicine (F Barone-Adesi PhD), University of Eastern Piedmont, Novara, Italy; Department of Public & Environmental Health (A Barrow MPH), University of The Gambia, Brikama, The Gambia; Epidemiology and Disease Control Unit (A Barrow MPH), Ministry of Health, Kotu, The Gambia; School of Public Health (Prof N Bedi MD), Dr. D. Y. Patil University, Mumbai, India; Research & Scientific Studies Unit (S Haque PhD), Epidemiology Department (M Khan MD), Jazan University, Jazan, Saudi Arabia (Prof N Bedi MD); Department of Medical Laboratory Sciences (R Belete MSc), Haramaya University, Harar, Ethiopia; Department of Oral Pathology and Microbiology (U I Belgaumi MD), Krishna Institute of Medical Sciences "Deemed To Be University", Karad, India; Department of Social Services (A W Bell MSW), Tufts Medical Center, Boston, MA, USA; Nuffield Department of Population Health (D A Bennett PhD, B Lacey PhD), The George Institute for Global Health (Prof S Yaya PhD), University of Oxford, Oxford, UK; Department of Internal Medicine (I M Bensenor PhD), University of São Paulo, São Paulo, Brazil; Division of Tropical and Humanitarian Medicine (D Beran PhD), University of Geneva, Geneva, Switzerland; Department of Social and Clinical Pharmacy (A S Bhagavathula PharmD), Charles University, Hradec Kralova, Czech Republic; Institute of Public Health (A S Bhagavathula PharmD), Family Medicine Department (M A Khan MSc), United Arab Emirates University, Al Ain, United Arab Emirates; Neurovascular Imaging Laboratory (S Bhaskar PhD), NSW Brain Clot Bank, Sydney, NSW, Australia; Department of Neurology and Neurophysiology (S Bhaskar PhD), South West Sydney Local Heath District and Liverpool Hospital, Sydney, NSW, Australia; Department of Statistical and Computational Genomics (K Bhattacharyya MSc), National Institute of Biomedical Genomics, Kalyani, India; Department of Statistics (K Bhattacharyya MSc), University of Calcutta, Kolkata, India; Department of Anatomy (V S Bhojaraja MD), Department of Biochemistry (J K Shetty MD), Manipal University College Melaka, Melaka, Malaysia; Social Determinants of Health Research Center (A Bijani PhD, M A Jahani PhD), Babol University of Medical Sciences, Babol, Iran; Mario Negri Institute for Pharmacological Research, Ranica, Italy (B Bikbov MD); Department of Public Health (S Birara MPH), Samara University, Samara, Ethiopia; School of Business Administration (Prof V Bodolica PhD), American University of Sharjah, Sharjah, United Arab Emirates; Faculty of Medicine and Pharmaceutical Sciences (A Bonny MD), University of Douala, Douala, Cameroon; Department of Cardiology (A Bonny MD), Centre Hospitalier Montfermeil (Montfermeil Hospital Center), Montfermeil, France; Division of Clinical Epidemiology and Aging Research (Prof H Brenner MD), German Cancer Research Center, Heidelberg, Germany; Department of Epidemiology and Evidence-Based Medicine (Prof N I Briko DSc, E V Glushkova PhD, V A Korshunov PhD, R V Polibin PhD), Department of Information and Internet Technologies (S K Vladimirov PhD), I.M. Sechenov First Moscow State Medical University, Moscow, Russia; School of Public Health and Health Systems (Z A Butt PhD), University of Waterloo, Waterloo, ON, Canada; Al Shifa School of Public Health (Z A Butt PhD), Al Shifa Trust Eye Hospital, Rawalpindi, Pakistan; Institute of Microengineering (F Caetano dos Santos PhD), Federal Polytechnic School of Lausanne, Lausanne, Switzerland; Internal Medicine Department (Prof L A Cámera MD), Hospital Italiano de Buenos Aires (Italian Hospital of Buenos Aires), Buenos Aires, Argentina; Board of Directors (Prof L A Cámera MD), Argentine Society of Medicine, Buenos Aires, Argentina (Prof P R Valdez Med); Department of Surgery (Y Cao DSc), Washington University in St. Louis, Saint Louis, MO, USA; School of Public Health (Prof E Cerin PhD), University of Hong Kong, Hong Kong, China; School of Population and Public Health (P A Chakraborty MPH, I O Iyamu MD), University of British Columbia, Vancouver, BC, Canada; Institute of Applied Health Research (J S Chandan MFPH), University of Birmingham, Birmingham, UK; Department of Medicine (V Chattu MD), University of Toronto, Toronto, ON, Canada; Saveetha Medical College (V Chattu MD), Saveetha University, Chennai, India; Heidelberg Institute of Global Health (HIGH) (S Chen DSc, J De Neve MD), Department of Ophthalmology (Prof J B Jonas MD, S Panda-Jonas MD), Heidelberg University, Heidelberg, Germany; Division of Biomedical Informatics (J J Choi PhD), Seoul National University Hospital, Seoul, South Korea; Department of Community Medicine (Prof S G Choudhari MD), Datta Meghe Institute of Medical Sciences, Wardha, India; School of Public Health (E K Chowdhury PhD), Curtin University, Perth, WA, Australia; Department of Epidemiology and Preventative Medicine (E K Chowdhury PhD), Department of Epidemiology and Preventive Medicine (R M Islam PhD), The School of Clinical Sciences at Monash Health (S Zaman MPH), Monash University, Melbourne, VIC, Australia; Center for Biomedicine and Community Health (D Chu PhD), VNU-International School, Hanoi, Vietnam; Institute of Neuroscience (B Corso PhD), National Research Council, Pisa, Italy; School of Public Health (O Dadras DrPH), Walailak University, Nakhon Si Thammarat, Thailand; Faculty of Medicine (Prof A A M Damasceno PhD), Eduardo

Mondlane University, Maputo, Mozambique; Public Health Foundation of India, Gurugram, India (Prof L Dandona MD, Prof R Dandona PhD, G Kumar PhD); Indian Council of Medical Research, New Delhi, India (Prof L Dandona MD); Department of Population and Development (C A Dávila-Cervantes PhD), Latin American Faculty of Social Sciences Mexico, Mexico City, Mexico; Department of Community Medicine (D Dhamnetiya MD, R P Jha MSc), Dr. Baba Saheb Ambedkar Medical College & Hospital, Delhi, India; Faculty of Veterinary Medicine and Zootechnics (Prof D Diaz PhD), Autonomous University of Sinaloa, Culiacán Rosales, Mexico; School of Health Sciences (H A Edinur PhD), Universiti Sains Malaysia (University of Science Malaysia), Kubang Kerian, Malaysia; Division of Urology (S Eftekharzadeh MD), Children's Hospital of Philadelphia, Philadelphia, PA, USA; Biomedical Informatics and Medical Statistics Department (I El Sayed PhD), Alexandria University, Alexandria, Egypt; Division of Cardiology (I Y Elgendy MD), Massachusetts General Hospital, Boston, MA, USA; Faculty of Medicine (M Elhadi MD), University of Tripoli, Tripoli, Libya; Department of Clinical and Chemical Pathology (M A Elmonem PhD), National Hepatology and Tropical Medicine Research Institute (A M Khater MD), Cairo University, Cairo, Egypt; Department of Internal Medicine (M Faisaluddin MD), Rochester General Hospital, Rochester, NY, USA; Department of Internal Medicine (U Farooque MD), Dow University of Health Sciences, Karachi, Pakistan; School of Population Health (X Feng PhD, X Xu PhD), Department of Medicine (O John MD), Centre for Big Data Research in Health (M Shawon PhD), University of New South Wales, Sydney, NSW, Australia; National Institute of Environmental Health (X Feng PhD), Chinese Center for Disease Control and Prevention, Beijing, China; Associated Laboratory for Green Chemistry (LAQV) (Prof E Fernandes PhD, M Freitas PhD, D Ribeiro PhD), University of Porto, Porto, Portugal; Institute of Gerontological Health Services and Nursing Research (F Fischer PhD), Ravensburg-Weingarten University of Applied Sciences, Weingarten, Germany; Center for Research in Indigenous Health (D Flood MD), Maya Health Alliance, Tecpán, Guatemala; Department of Internal Medicine (D Flood MD), University of Michigan, Ann Arbor, MI, USA; Health Services Management Training Centre (P A Gaal PhD, T Joo MSc, V Szerencsés MA), Faculty of Health and Public Administration (M Szócska PhD), Semmelweis University, Budapest, Hungary; Department of Applied Social Sciences (P A Gaal PhD), Sapientia Hungarian University of Transylvania, Târgu-Mureş, Romania; Department of Cardiovascular Medicine (M M Gad MD), Heart and Vascular Institute (M Zmaili MD), Cleveland Clinic, Cleveland, OH, USA; Gillings School of Global Public Health (M M Gad MD), University of North Carolina Chapel Hill, Chapel Hill, NC, USA; Department of Community Dentistry (P Gaewkhiew PhD), Mahidol University, Ratchathewi, Thailand; Population and Patient Health Group (P Gaewkhiew PhD), Faculty of Life Sciences and Medicine (M Molokhia PhD), King's College London, London, UK; Department of Public Health (L Getacher MPH), Debre Berhan University, Debre Berhan, Ethiopia; Department of Medical Surgical Nursing (M Ghafourifard PhD), Tabriz University of Medical Sciences, Tabriz, Iran; Faculty of Nursing and Midwifery (R Ghanei Gheshlagh PhD), Social Determinants of Health Research Center (F Moradpour PhD), Kurdistan University of Medical Sciences, Sanandaj, Iran; Research Group for Genomic Epidemiology (N Ghith PhD), Technical University of Denmark, Copenhagen, Denmark; Department of Public Health (G Ghozali PhD), University of Muhammadiyah Kalimantan Timur, Samarinda, Indonesia; Medical School (Prof P S Gill DM), University of Warwick, Coventry, UK; Family Medicine Research Center (Prof I A Ginawi MD), Ministry of Health, Hail, Saudi Arabia; Health Systems and Policy Research (M Golechha PhD), Indian Institute of Public Health, Gandhinagar, India; Hudson College of Public Health (S V Gopalani MPH), University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; Department of Health and Social Affairs (S V Gopalani MPH), Government of the Federated States of Micronesia, Palikir, Federated States of Micronesia; Institute of Tropical Pathology and Public Health (IPTSP) (R A Guimarães MSc), Federal University of Goias, Goiânia, Brazil; Department of Epidemiology and Biostatistics (R Gupta MPH), Department of Clinical Pharmacy and Outcomes Sciences (I Yunusa PhD), University of South Carolina, Columbia, SC, USA; Centre for Noncommunicable Diseases and Nutrition (R Gupta MPH), BRAC University, Dhaka, Bangladesh; Department of Preventive Cardiology (Prof R Gupta MD), Eternal Heart Care Centre & Research Institute, Jaipur, India; Department of Medicine (Prof R Gupta MD), Mahatma Gandhi University Medical Sciences, Jaipur, India; Department of Clinical Medicine (Prof V K Gupta PhD), Macquarie University, Sydney, NSW, Australia; School of Medicine (V Gupta PhD), Deakin University, Geelong, VIC, Australia; Toxicology Department (S Gupta MSc), Shriram Institute for Industrial Research, Delhi, Delhi, India; Department of Quantitative Economics (T D Habtewold PhD), Maastricht University, Maastricht, Netherlands; Department of Radiology and Radiological Science (N Hafezi-Nejad MD, S Sheikhbahaei MD), Johns Hopkins University, Baltimore, MD, USA (H Tadbiri MD); Medical School (Prof G J Hankey MD), Dobney Hypertension Centre (Prof M P Schlaich MD), University of Western Australia, Perth, WA, Australia; Department of Neurology (Prof G J Hankey MD), Sir Charles Gairdner Hospital, Perth, WA, Australia; Department of Zoology and Entomology (A I Hasaballah PhD), Al Azhar University, Cairo, Egypt; Department of Pharmacy (S Hasan PhD), University of Huddersfield, Huddersfield, UK; Department of Public Health (A Hashi PhD), Jigjiga University, Jijiga, Ethiopia; Gastrointestinal and Liver Diseases Research Center (S Hassanipour PhD), Caspian Digestive Disease Research Center (S Hassanipour PhD), Guilan University of Medical Sciences, Rasht, Iran; Institute of Pharmaceutical Sciences (K Hayat MS), University of Veterinary and Animal Sciences, Lahore, Pakistan; Department of Pharmacy Administration and Clinical Pharmacy (K Hayat MS), Xian Jiaotong University, Xian, China; Department of Population Sciences (Prof M B H Hossain PhD), University of Dhaka, Dhaka, Bangladesh; Department of Public Health and Informatics (S Hossain MS), Jahangirnagar University, Dhaka, Bangladesh; Burn Research Center (S Hoveidamanesh MD), Shahid Motahari Hospital, Tehran, Iran; Jockey Club School of Public Health and Primary Care (J Huang MD, C Zhong MD), The Chinese University of Hong Kong, Hong Kong, China; Department of Public Health and Community Medicine (Prof A Humayun PhD), Shaikh Khalifa Bin Zayed Al-Nahyan Medical College, Lahore, Pakistan; Department of Occupational Safety and Health (Prof B-F Hwang PhD), Department of Health Services Administration (C B Lee PhD), China Medical University, Taichung, Taiwan; Division of Community Health and Family Medicine (L R Inbaraj MD), Bangalore Baptist Hospital, Bangalore, India; College of Public Health (U Iqbal PhD), Taipei Medical University, Taipei, Taiwan; Department of Nutrition Research (M Islam MSc), Institute of Public Health Nutrition, Dhaka, Bangladesh; Institute for Physical Activity and Nutrition (S Islam PhD), Deakin University, Burwood, VIC, Australia; Department of Clinical Pharmacy (Prof N Ismail PhD), MAHSA University, Bandar Saujana Putra, Malaysia; Department of General Surgery and Surgical-Medical Specialties (Prof G Isola PhD), University of Catania, Catania, Italy; Department of Health Management (R Itumalla PhD), University of Hail, Hail, Saudi Arabia; Department of Health Services Research (M Iwagami PhD), University of Tsukuba, Tsukuba, Japan; Knowledge Translation Program (I O Iyamu MD), Centre for Health Evaluation and Outcome Sciences, Vancouver, BC, Canada; Institute of Comparative Economic Studies (Prof M Jakovljevic PhD), Hosei University, Tokyo, Japan; Department of Global Health, Economics and Policy (Prof M Jakovljevic PhD), University of Kragujevac, Kragujevac, Serbia;; Department of Physiology (R Jayawardena PhD), Department of Pharmacology (P Ranasinghe PhD), University of Colombo, Colombo, Sri Lanka; School of Exercise and Nutrition Sciences (R Jayawardena PhD), Queensland University of Technology, Brisbane, QLD, Australia; Department of Community Medicine (R P Jha MSc), Banaras Hindu University, Varanasi, India; Renal and Cardiovascular Division (O John MD), The George Institute for Global Health, New Delhi, India; Beijing Institute of Ophthalmology (Prof J B Jonas MD), Beijing Tongren Hospital, Beijing, China; Institute for Prevention of Non-communicable Diseases (R Kalhor PhD), Health Services Management Department (R Kalhor PhD), Qazvin University of Medical Sciences, Qazvin, Iran; Kasturba Medical College, Mangalore (A Kamath MD), Department of Community Medicine (C R Rao MD), Manipal Academy of Higher Education, Manipal, India (A Kamath MD); Department of Forensic Medicine and Toxicology (T Kanchan MD), All India Institute

of Medical Sciences, Jodhpur, India; Sydney Eye Hospital (H Kandel PhD), South Eastern Sydney Local Health District, Sydney, NSW, Australia; International Research Center of Excellence (G A Kayode PhD), Institute of Human Virology Nigeria, Abuja, Nigeria; Julius Centre for Health Sciences and Primary Care (G A Kayode PhD), Utrecht University, Utrecht, Netherlands; Department of Epidemiology and Biostatistics (S A Kebede MPH), University of Gondar, Gondar, Faroe Islands; School of Science and Technology (P Keshavarz MD), The University of Georgia, Tbilisi, Georgia; Department of Diagnostic & Interventional Radiology (P Keshavarz MD), New Hospitals LTD, Tbilisi, Georgia; Department of Public Health (Prof Y S Khader PhD), Jordan University of Science and Technology, Irbid, Jordan; Amity Institute of Forensic Sciences (H Khajuria PhD, B P Nayak PhD), Amity University, Noida, India; Primary Care Department (M A Khan MSc), NHS North West London, London, UK; Department of Population Science (M Khan PhD), Jatiya Kabi Kazi Nazrul Islam University, Mymensingh, Bangladesh; Executive Board of the Health Ministers' Council for the Gulf Cooperation Council States, Riyadh, Saudi Arabia (Prof T A M Khoja FRCP); Department of Public Health (Prof J Khubchandani PhD), New Mexico State University, Las Cruces, NM, USA; Department of Genomics and Digital Health (M Kim MD), Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Seoul, South Korea; Public Health Center (M Kim MD), Ministry of Health and Welfare, Wando, South Korea; School of Traditional Chinese Medicine (Y Kim PhD), Xiamen University Malaysia, Sepang, Malaysia; Department of Nutrition (R W Kimokoti MD), Simmons University, Boston, MA, USA; Department of Nursing and Health Promotion (S Kisa PhD), Oslo Metropolitan University, Oslo, Norway; School of Health Sciences (Prof A Kisa PhD), Kristiania University College, Oslo, Norway; Department of Global Community Health and Behavioral Sciences (Prof A Kisa PhD), Tulane University, New Orleans, LA, USA; Department of Epidemiology and Public Health (Prof M Kivimäki PhD), Institute of Cardiovascular Science (A S Oguntade MSc), Department of Infection (Prof A Zumla PhD), University College London, London, UK; Department of Public Health (Prof M Kivimäki PhD), University of Helsinki, Helsinki, Finland; Department of General Practice - Family Medicine (Prof O Korzh DSc), Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine; Biomedical Research Networking Center for Mental Health Network (CIBERSAM) (A Koyanagi MD), San Juan de Dios Sanitary Park, Sant Boi de Llobregat, Spain; Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain (A Koyanagi MD); Department of Anthropology (Prof K Krishan PhD), Panjab University, Chandigarh, India; Department of Demography (Prof B Kuate Defo PhD), Department of Social and Preventive Medicine (Prof B Kuate Defo PhD), University of Montreal, Montreal, QC, Canada; Department of Community Medicine (N Kumar MD, P Mithra MD, R Thapar MD), Department of Infectious Disease (S Rao MD), Manipal Academy of Higher Education, Mangalore, India; Imperial College Business School (D Kusuma DSc), Department of Primary Care and Public Health (Prof A Majeed MD, R Palladino MD, Prof S Rawaf MD), WHO Collaborating Centre for Public Health Education and Training (D L Rawaf MD), Imperial College London, London, UK; Faculty of Public Health (D Kusuma DSc), University of Indonesia, Depok, Indonesia; Department of Clinical Sciences and Community Health (Prof C La Vecchia MD), University of Milan, Milan, Italy; National Institute for Health Research (NIHR) Oxford Biomedical Research Centre, Oxford, UK (B Lacey PhD); Department of Medical Sciences (Prof A O Larsson PhD), Uppsala University, Uppsala, Sweden; Department of Clinical Chemistry and Pharmacology (Prof A O Larsson PhD), Uppsala University Hospital, Uppsala, Sweden; Department of Otorhinolaryngology (S Lasrado MS), Father Muller Medical College, Mangalore, India; The Office of Health Policy & Legislative Affairs (W Lee PhD), University of Texas, Galveston, TX, USA; Department of Health Sciences (P H Lee PhD), University of Leicester, Leicester, UK; School of Pharmacy (S W H Lee PhD), Taylor's University Lakeside Campus, Subang Jaya, Malaysia; Department of Health Promotion and Health Education (M Li PhD), National Taiwan Normal University, Taipei, Taiwan; Department of Medicine (L Lim MRCP), University of Malaya, Kuala Lumpur, Malaysia; Department of Medicine and Therapeutics (L Lim MRCP), The Chinese University of Hong Kong, Shatin, N.T., China; School of Medicine (Prof G Lucchetti PhD), Federal University of Juiz de Fora, Juiz de Fora, Brazil; Substance Abuse Prevention Research Center (B Mansouri PhD), Kermanshah University of Medical Sciences, Kermanshah, Iran; Value-Based Healthcare Unit (Prof L G Mantovani DSc), IRCCS MultiMedica, Sesto San Giovanni, Italy; Faculty of Public Health (S Martini PhD), Universitas Airlangga (Airlangga University), Surabaya, Indonesia; Indonesian Public Health Association, Surabaya, Indonesia (S Martini PhD); National Centre for Disease Informatics and Research (P Mathur PhD), Indian Council of Medical Research, Bengaluru, India; Department of Ophthalmology (C McAlinden PhD), Singleton Hospital, Swansea, UK; Department of Social Work (N Mehedi MSS), Shahjalal University of Science and Technology, Sylhet, Bangladesh; Department of Nutrition (T Mekonnen MPH), Institute of Health and Society (Prof A S Winkler PhD), University of Oslo, Oslo, Norway; Forensic Medicine Division (Prof R G Menezes MD), Department of Pharmacy Practice (A Naqvi PhD), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; School of Medicine (A G Mersha MD), University of Gondar, Gondar, Ethiopia; School of Public Health and Community Medicine (J Miao Jonasson PhD), University of Gothenburg, Gothenburg, Sweden; Department of Propedeutics of Internal Diseases & Arterial Hypertension (Prof T Miazgowski MD), Pomeranian Medical University, Szczecin, Poland; Woman-Mother-Child Department (I Michalek PhD), Lausanne University Hospital, Lausanne, Switzerland; Internal Medicine Programme (Prof E M Mirrakhimov PhD), Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan; Department of Atherosclerosis and Coronary Heart Disease (Prof E M Mirrakhimov PhD), National Center of Cardiology and Internal Disease, Bishkek, Kyrgyzstan; Department of Chemistry (A Mirza PhD), Umm Al Qura University, Makkah, Saudi Arabia; Department of Nursing (R Mohammadpourhodki PhD), Applied Biomedical Research Center (A Sahebkar PhD), Biotechnology Research Center (A Sahebkar PhD), Mashhad University of Medical Sciences, Mashhad, Iran; Department of Biology (A Mohammed PhD), University of Jeddah, Jeddah, Saudi Arabia; Department of Computer Science and Engineering (M Moni PhD), Pabna University of Science and Technology, Pabna, Bangladesh; Department of Epidemiology (R Moradzadeh PhD, M Zamanian PhD), Department of Pediatrics (J Nazari MD), Arak University of Medical Sciences, Arak, Iran; Department of Medicine (E Mostafavi PhD), Stanford Cardiovascular Institute (E Mostafavi PhD), Stanford University, Palo Alto, CA, USA; Demographic Change and Aging Research Area (A Werdecker PhD), Federal Institute for Population Research, Wiesbaden, Germany (Prof U O Mueller MD); Center for Population and Health, Wiesbaden, Germany (Prof U O Mueller MD); Department of Internal Medicine (A Mustafa MD), Staten Island University Hospital Northwell Health, Staten Island, NY, USA; Institute of Epidemiology and Medical Biometry (Prof G Nagel PhD), Ulm University, Ulm, Germany; Suraj Eye Institute, Nagpur, India (V Nangia MD); Discipline of Social & Administrative Pharmacy (A Naqvi PhD), University of Science, Malaysia, Penang, Malaysia; Department of Disease Control and Environmental Health (R Ndejjo MSc), Makerere University, Kampala, Uganda; Cardio-Aid, Bucharest, Romania (R I Negoi PhD); Estia Health Blakehurst (S Neupane Kandel BSN), Estia Health, Sydney, NSW, Australia; Institute for Global Health Innovations (C T Nguyen MPH, H L T Nguyen MPH), Duy Tan University, Hanoi, Vietnam; Centre for Heart Rhythm Disorders (J Noubiap MD), School of Public Health (V Podder HSC), University of Adelaide, Adelaide, SA, Australia; Department of Neurobiology, Care Sciences and Society (C Nowak PhD), Karolinska Institute, Huddinge, Sweden; Administrative and Economic Sciences Department (Prof B Oancea PhD), University of Bucharest, Bucharest, Romania; Department of Community Health and Primary Care (O O Odukoya MSc), University of Lagos, Idi Araba, Nigeria; Department of Family and Preventive Medicine (O O Odukoya MSc), University of Utah, Salt Lake City, UT, USA; Department of Medicine (A S Oguntade MSc, Prof M O Owolabi DrM), University College Hospital, Ibadan, Ibadan, Nigeria; Department of Social and Behavioral Sciences (T T Ojo MPH), New York University, New York, NY, USA; Department of Psychiatry (A T Olagunju MD), University of Lagos, Lagos, Nigeria; Department of Pharmacology and Therapeutics (Prof O E Onwujekwe PhD), University of Nigeria Nsukka, Enugu,

Nigeria; Department of Medicine (Prof A Ortiz MD), Autonomous University of Madrid, Madrid, Spain; Department of Nephrology and Hypertension (Prof A Ortiz MD), The Institute for Health Research Foundation Jiménez Díaz University Hospital, Madrid, Spain; Department of Public Health (R Palladino MD), University of Naples Federico II, Naples, Italy; Corporate (S R Pandi-Perumal MSc), Somnogen Canada Inc, Toronto, ON, Canada; Vision and Eye Research Institute (Prof S Pardhan PhD), Anglia Ruskin University, Cambridge, UK; Department of Health Administration and Policy (T Parekh MSc), George Mason University, Fairfax, VA, USA; Center for Research and Innovation (V F Pepito MSc), Ateneo De Manila University, Pasig City, Philippines; Department of Development Studies (Prof A Perianayagam PhD, H Sahoo PhD), International Institute for Population Sciences, Mumbai, India; Department of Community Medicine (M Pilania MD), Mahatma Gandhi Medical College & Hospital, Jaipur, India; Medical College (V Podder HSC), Tairunnessa Memorial Medical College and Hospital, Gazipur, Bangladesh; University Medical Center Groningen (Prof M J Postma PhD), School of Economics and Business (Prof M J Postma PhD), University of Groningen, Groningen, Netherlands; Department of Biochemistry (Prof A Prashant PhD), Jagadguru Sri Shivarathreeswara University, Mysuru, India; Department of Physics (N Rabiee PhD), Sharif University of Technology, Tehran, Iran; Biomedical Engineering Department (Prof M Rabiee PhD), Amirkabir University of Technology, Tehran, Iran; School of Nursing and Healthcare Professions (M Rahman PhD), Federation University Australia, Berwick, VIC, Australia; Department of Population Science and Human Resource Development (Prof M Rahman PhD, M Rahman DrPH), University of Rajshahi, Rajshahi, Bangladesh; Department of Nutrition Science (S Rahmawaty PhD), Muhammadiyah University of Surakarta, Surakarta, Indonesia; Department of Cardiology (P Ram MD), Emory University, Atlanta, GA, USA; Department of Public Health (J Rana MPH), North South University, Dhaka, Bangladesh; Department of Biostatistics and Epidemiology (J Rana MPH), University of Massachusetts Amherst, Amherst, MA, USA; Health Emergency Operation Center (K Ranabhat MPH), Ministry of Health & Population, Kathmandu, Nepal; Central Department of Public Health (K Ranabhat MPH), Institute of Medicine, Kathmandu, Nepal; Academic Public Health England (Prof S Rawaf MD), Public Health England, London, UK; NIHR-Biomedical Research Centre (NIHR-BRC) (Prof A Zumla PhD), University College London Hospitals, London, UK (D L Rawaf MD); School of Health, Medical and Applied Sciences (L Rawal PhD), CQ University, Sydney, NSW, Australia; School of Medicine (Prof A M N Renzaho PhD), Translational Health Research Institute (Prof A M N Renzaho PhD), Western Sydney University, Campbelltown, NSW, Australia; Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA) (Prof N Rezaei PhD), Universal Scientific Education and Research Network (USERN), Tehran, Iran; Cardiovascular Diseases Research Center (S Riahi PhD), Birjand University of Medical Sciences, Birjand, Iran; Faculty of Agrarian Sciences and Environment (D Ribeiro PhD), University of the Azores, Angra do Heroísmo, Portugal; Department of Pharmacology and Toxicology (Prof J A B Rodriguez PhD), University of Antioquia, Medellin, Colombia; Department of Clinical Research (L Roever PhD), Federal University of Uberlândia, Uberlândia, Brazil; Center for Indigenous Health Research (P Rohloff MD), Wuqu' Kawoq Maya Health Alliance, Tecpan, Guatemala; Department of Internal Medicine (G M Rwegerera MD), University of Botswana, Gaborone, Botswana; School of Medicine (P M Ryan PhD), University College Cork, Cork, Ireland; Department of Medical Pharmacology (M M Saber-Ayad MD), Cairo University, Giza, Egypt; Health Systems and Population Studies Division (K Saif-Ur-Rahman MPH), Nutrition and Clinical Services Division (M Tariqujjaman MSc), Maternal and Child Health Division (S Zaman MPH), International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; Department of Public Health and Health Systems (K Saif-Ur-Rahman MPH, Prof H Yatsuya PhD), Nagoya University, Nagoya, Japan; Emergency Department (M Samaei MD), Brown University, Providence, RI, USA; Department of Nutrition and Preventive Medicine (Prof J Sanabria MD), Case Western Reserve University, Cleveland, OH, USA; Faculty of Medicine (Prof M M Santric-Milicevic PhD), School of Public Health and Health Management (Prof M M Santric-Milicevic PhD), School of Medicine (R Vukovic PhD), University of Belgrade, Belgrade, Serbia; Faculty of Health & Social Sciences (B Sathian PhD), Bournemouth University, Bournemouth, UK; Hypertension and Kidney Disease Laboratory (Prof M P Schlaich MD), Baker Heart and Diabetes Institute, Melbourne, VIC, Australia; Department of Population and Health (A Seidu MPhil), University of Cape Coast, Cape Coast, Ghana; College of Public Health, Medical and Veterinary Sciences (A Seidu MPhil), James Cook University, Townsville, QLD, Australia; Department of Medical Statistics, Epidemiology and Medical Informatics (M Šekerija PhD), University of Zagreb, Zagreb, Croatia; Department of Epidemiology and Prevention of Chronic Noncommunicable Diseases (M Šekerija PhD), Croatian Institute of Public Health, Zagreb, Croatia; Department of Biotechnology (Prof N Senthil Kumar PhD), Mizoram University, Aizawl, India; National Heart, Lung, and Blood Institute (A Seylani BS), National Institute of Health, Rockville, MD, USA; Independent Consultant, Karachi, Pakistan (M A Shaikh MD); Research Institute of Pharmaceutical Sciences (H Shamshad PhD), University of Karachi, Karachi, Pakistan; Finnish Institute of Occupational Health, Helsinki, Finland (R Shiri PhD); Public Health Dentistry Department (Prof K M Shivakumar PhD), Krishna Institute of Medical Sciences "Deemed to be University", Karad, India; School of Public Health (K Shuval PhD), University of Haifa, Haifa, Israel; The Cooper Institute, Dallas, TX, USA (K Shuval PhD); School of Medicine (Prof J A Singh MD), University of Alabama at Birmingham, Birmingham, AL, USA; Medicine Service (Prof J A Singh MD), US Department of Veterans Affairs (VA), Birmingham, AL, USA; Department No.16 (V Y Skryabin MD), Laboratory of Genetics and Genomics (Prof M S Zastrozhin PhD), Moscow Research and Practical Centre on Addictions, Moscow, Russia; Therapeutic Department (A A Skryabina MD), Balashiha Central Hospital, Balashikha, Russia; Department of Oral Health (A Sofi-Mahmudi DDS), Non-Communicable Diseases Research Center (NCDRC), Tehran, Iran; Cochrane Iran Associate Centre, National Institute for Medical Research Development (NIMAD) (A Sofi-Mahmudi DDS), Iranian Ministry of Health and Medical Education, Tehran, Iran; Nursing Care Research Center (A Soheili PhD), Semnan University of Medical Sciences, Semnan, Iran; School of Medicine (Prof J Sun PhD), Griffith University, Gold Coast, QLD, Australia; Department of Medicine (Prof R Tabarés-Seisdedos PhD), University of Valencia, Valencia, Spain; Carlos III Health Institute (Prof R Tabarés-Seisdedos PhD), Biomedical Research Networking Center for Mental Health Network (CIBERSAM), Madrid, Spain; Department of Biomedical Sciences (E G Tadesse MSc), Arba Minch University, Arba Minch, Ethiopia; Department of Public Health and Community Medicine (Prof K R Thankappan MD), Central University of Kerala, Kasaragod, India; Department of Endocrinology, Diabetes and Metabolism (Prof N Thomas PhD), Christian Medical College and Hospital (CMC), Vellore, India; Department of Anatomy (B Timalsina MSc), Dongguk University, Geongju-si, South Korea; Department of Social Security Empirical Research (Prof R Tobe-Gai PhD), National Institute of Population and Social Security Research, Tokyo, Japan; Department of Medicine (Prof M Tonelli MD), University of Calgary, Calgary, AB, Canada; Department of Pathology and Legal Medicine (M R Tovani-Palone PhD), University of São Paulo, Ribeirão Preto, Brazil; Modestum LTD, London, UK (M R Tovani-Palone PhD); Department of Health Economics (B X Tran PhD), Hanoi Medical University, Hanoi, Vietnam; Department of Community Medicine (J P Tripathy MD), All India Institute of Medical Sciences, Nagpur, India; Lee Kong Chian School of Medicine (L Tudor Car PhD), Nanyang Technological University, Singapore, Singapore; Department of Epidemiology and Biostatistics (B S Tusa MPH), Haramaya University, Haramaya, Ethiopia; Institute for Physical Activity and Nutrition (R Uddin PhD), Deakin University, Melbourne, VIC, Australia; School of Health and Rehabilitation Sciences (R Uddin PhD), The University of Queensland, Brisbane, QLD, Australia; Amity Institute of Biotechnology (E Upadhyay PhD), Amity University Rajasthan, Jaipur, India; Clinical Cancer Research Center (S Valadan Tahbaz PhD, S Yahyazadeh Jabbari MD), Milad General Hospital, Tehran, Iran; Department of Microbiology (S Valadan Tahbaz PhD), Islamic Azad University, Tehran, Iran; Velez Sarsfield Hospital, Buenos Aires, Argentina (Prof P R Valdez Med); UKK Institute, Tampere, Finland (Prof T J Vasankari MD); Faculty of

Medicine and Health Technology (Prof T J Vasankari MD), Tampere University, Tampere, Finland; Department of Community & Family Medicine (M v Verma MD), All India Institute of Medical Sciences, Bathinda, India; Center for Disease and Control Programs (Prof V E Villalobos-Daniel PhD), Ministry of Health, Mexico City, Mexico; Health Initiative of the Americas (Prof V E Villalobos-Daniel PhD), University of California Berkeley, Berkeley, CA, USA; Laboratory of Public Health Indicators Analysis and Health Digitalization (S K Vladimirov PhD), Moscow Institute of Physics and Technology, Dolgoprudny, Russia; Faculty of Information Technology (B Vo PhD), Ho Chi Minh City University of Technology (HUTECH), Ho Chi Minh City, Vietnam; Center of Excellence in Behavioral Medicine (G T Vu BA), Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam; Department of Pediatric Endocrinology (R Vukovic PhD), Mother and Child Healthcare Institute of Serbia "Dr Vukan Cupic", Belgrade, Serbia; Foundation University Medical College (Prof Y Waheed PhD), Foundation University Islamabad, Islamabad, Pakistan; Cultures, Societies and Global Studies, & Integrated Initiative for Global Health (R G Wamai PhD), Northeastern University, Boston, MA, USA; School of Public Health (R G Wamai PhD), University of Nairobi, Nairobi, Kenya; Department of Community Medicine (N D Wickramasinghe MD), Rajarata University of Sri Lanka, Anuradhapura, Sri Lanka; Department of Neurology (Prof A S Winkler PhD), Technical University of Munich, Munich, Germany; School of Pharmacy (B Wubishet MPH), Mekelle University, Mekelle, Ethiopia; Cardiovascular Program (X Xu PhD), The George Institute for Global Health, Sydney, NSW, Australia; Department of Endocrinology, First Affiliated Hospital (Prof S Xu PhD), University of Science and Technology of China, Hefei, China; Department of Medicine (Prof S Xu PhD), University of Rochester, Rochester, NY, USA; Department of Public Health (Prof H Yatsuya PhD), Fujita Health University, Toyoake, Japan; School of International Development and Global Studies (Prof S Yaya PhD), University of Ottawa, Ottawa, ON, Canada; Department of Pharmacy (T S Y Yazie MSc), Debre Tabor University, Debre Tabor, Ethiopia; Saw Swee Hock School of Public Health (S Yi PhD), National University of Singapore, Singapore, Singapore; KHANA Center for Population Health Research (S Yi PhD), KHANA, Phnom Penh, Cambodia; Department of Neuropsychopharmacology (N Yonemoto PhD), National Center of Neurology and Psychiatry, Kodaira, Japan; Department of Public Health (N Yonemoto PhD), Juntendo University, Tokyo, Japan; Duke Global Health Institute (S Zadey MS), Duke University, Durham, NC, USA; Medical College of La Paz, La Paz, Bolivia (N Zamora MD); Addictology Department (Prof M S Zastrozhin PhD), Russian Medical Academy of Continuous Professional Education, Moscow, Russia; Peoples' Friendship University of Russia, Moscow, Russia (A Zastrozhina PhD); School of Medicine (Z Zhang PhD), Wuhan University, Wuhan, China.

Declaration of interests

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Data sharing

To download the data used in these analyses, please visit the Global Health Data Exchange at http://ghdx.healthdata.org/gbd-2019/data-input-sources.

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