Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990–2021: findings from the Global Burden of Disease Study 2021

*GBD 2021 Anaemia Collaborators**

Summary

Background Anaemia is a major health problem worldwide. Global estimates of anaemia burden are crucial for developing appropriate interventions to meet current international targets for disease mitigation. We describe the prevalence, years lived with disability, and trends of anaemia and its underlying causes in 204 countries and territories.

Methods We estimated population-level distributions of haemoglobin concentration by age and sex for each location from 1990 to 2021. We then calculated anaemia burden by severity and associated years lived with disability (YLDs). With data on prevalence of the causes of anaemia and associated cause-specific shifts in haemoglobin concentrations, we modelled the proportion of anaemia attributed to 37 underlying causes for all locations, years, and demographics in the Global Burden of Disease Study 2021.

Findings In 2021, the global prevalence of anaemia across all ages was 24·3% (95% uncertainty interval [UI] 23·9–24·7), corresponding to 1·92 billion (1·89–1·95) prevalent cases, compared with a prevalence of 28·2% (27·8–28·5) and 1·50 billion (1·48–1·52) prevalent cases in 1990. Large variations were observed in anaemia burden by age, sex, and geography, with children younger than 5 years, women, and countries in sub-Saharan Africa and south Asia being particularly affected. Anaemia caused 52·0 million (35·1–75·1) YLDs in 2021, and the YLD rate due to anaemia declined with increasing Socio-demographic Index. The most common causes of anaemia YLDs in 2021 were dietary iron deficiency (cause-specific anaemia YLD rate per 100 000 population: 422·4 [95% UI 286·1–612·9]), haemoglobinopathies and haemolytic anaemias (89·0 [58·2–123·7]), and other neglected tropical diseases (36·3 [24·4–52·8]), collectively accounting for 84·7% (84·1–85·2) of anaemia YLDs.

Interpretation Anaemia remains a substantial global health challenge, with persistent disparities according to age, sex, and geography. Estimates of cause-specific anaemia burden can be used to design locally relevant health interventions aimed at improving anaemia management and prevention.

Funding Bill & Melinda Gates Foundation.

Lancet Haematol 2023

Published Online
July 31, 2023
https://doi.org/10.1016/S2352-3026(23)00160-6

See Online/Comment
https://doi.org/10.1016/S2352-3026(23)00171-0

*Collaborators are listed at the end of the Article

Correspondence to:
Prof Nicholas J Kassebaum, Institute for Health Metrics and Evaluation, Seattle, WA 98195, USA
nickjk@uw.edu

Introduction

Anaemia is a widespread global health problem associated with poor health outcomes, increased morbidity and mortality, and substantial health and economic costs.[1] Anaemia in pregnancy is associated with increased rates of preterm labour, postpartum haemorrhage, low birthweight, short gestation, stillbirth, and infections for both child and mother.[2] Anaemia in children is linked with impaired cognitive and motor development and susceptibility to infections, potentially increasing the risk of mortality during childhood from severe infections, such as those due to malaria.[3,4] Symptoms of anaemia in adults include weakness, fatigue, difficulty concentrating, and challenges with work and activities of daily life.[5] Anaemia in older adults (>65 years) is an identified risk factor for hospitalisation, poorer surgical outcomes,[6] and increased all-cause mortality.[7]

Anaemia can be caused by numerous conditions that result in blood loss, reduce the lifespan of red blood cells, or trigger reductions in the synthesis of haemoglobin or red blood cells. Chronic inflammation can lead to hepcidin-mediated inhibition of iron absorption that renders oral iron administration ineffective,[8,9] and some data suggest that iron supplementation could increase susceptibility to malaria[8] and potentially to other acute inflammatory conditions. Despite the complexity of underlying causes of anaemia, most anaemia reduction strategies have focused only on iron delivery, probably because iron deficiency is a common manifestation of anaemia in most countries and dietary interventions are comparatively simple.[10,11] However, iron administration alone is likely to be insufficient because inadequate iron intake is only one of numerous underlying reasons for an individual to be iron-deficient or anaemic.[12] Fewer than half of individuals with anaemia will respond to iron interventions if the causes of anaemia that are unrelated to inadequate iron intake are not addressed,[13] and it should therefore not be surprising that progress in reducing the burden of anaemia has been slow and uneven in regions around the world.[14,15]

Research in context

Evidence before this study

The Global Burden of Disease, Injuries, and Risk Factors Study (GBD) is a comprehensive effort to systematically measure the causes and risk factors of death and disability. Anaemia-specific manuscripts relating to the 2010 and 2013 GBDs have previously been published. Other studies examining trends in anaemia burden at the global level have often been limited to particular demographic groups (eg, children or women of reproductive age), geographies (eg, low-income settings), or specific underlying causes (eg, iron deficiency), and therefore do not capture the full extent of the anaemia burden. For example, 2022 WHO estimates present anaemia burden among children aged 6–59 months and women aged 15–49 years from 2000 to 2019. In this context, the GBD provides an ideal framework to comprehensively quantify the prevalence, years lived with disability, and trends of anaemia burden across all geographies, demographics, and causes. To estimate total anaemia prevalence, we used individual-level and tabulated survey and report data from the Global Health Data Exchange, identified using the keywords "anemia" and "hemoglobin", supplemented with sources from the WHO Vitamin and Mineral Nutrition Information System, a comprehensive database including measurements of haemoglobin concentration and anaemia prevalence collected from systematic reviews of scientific literature databases; WHO regional and country offices; other research, governmental and non-governmental organisations; and manual searches of non-indexed journals. Inclusion criteria were quantitative measurement of haemoglobin concentrations in either a population-based sample or a group judged to adequately represent the sex, age groups, and location of the study.

Added value of this study

To our knowledge, this study presents the most up-to-date and complete estimates of global anaemia burden, covering 204 countries and territories, 25 age groups, and male and female sexes from 1990 to 2021. We provide a comprehensive account of anaemia prevalence, associated years lived with disability, and the trends in these values, including an examination of underlying causes of anaemia and associations with Socio-demographic Index. We have improved on previous estimates through the addition of numerous data sources, enhanced data processing algorithms for pregnancy adjustment, and revised modelling techniques to strengthen estimates in locations and populations in which data are sparse. Our causal attribution models included additional causes of anaemia, amended methods for estimating cause-specific anaemia burden, and optimised redistribution algorithms to account for the varied effect of different diseases on haemoglobin concentrations.

Implications of all the available evidence

We show that progress towards alleviating the anaemia burden across age, sex, and geography is varied and often slow. Our analysis of the underlying causes of anaemia provides insights for the design of effective, contextualised disease surveillance programmes and public health interventions. Although iron deficiency is often the most frequent cause of anaemia, much of the iron-related anaemia burden could be unresponsive to iron treatments if the underlying issues relating to iron deficiency are not addressed. Interventions to deal with major causes of anaemia—such as chronic kidney disease, gastrointestinal disorders, malaria, and, where prevalent, neglected tropical diseases such as schistosomiasis and hookworm disease—are necessary to substantially reduce anaemia burden. Important gaps in data and knowledge remain, necessitating the development of evidence-based definitions of anaemia centred on actual health loss, quantification of morbidity and mortality associated with low haemoglobin concentrations as a risk factor for other illnesses, and analysis of the effect of comorbid diseases on the incidence and severity of anaemia. Investments in closing these gaps will improve future estimates of the burden of anaemia and will provide policy makers, stakeholders, and health practitioners with the comprehensive data needed to reduce persistently high anaemia prevalence and associated health loss.

WHO's Global Nutrition Target calls for a 50% reduction in anaemia prevalence among women of reproductive age (15–49 years) by 2030[16] to meet the targets of Sustainable Development Goals 2 and 3, which relate to improved nutrition, good health, and wellbeing.[17] Accordingly, many organisations—including WHO, UNICEF, the United States Agency for International Development (USAID), and the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project—have called for a comprehensive anaemia monitoring framework.[18] Estimates from WHO of the overall anaemia prevalence in women of reproductive age and children were published in 2022,[15] and other studies highlight anaemia burden in low-income and middle-income countries.[19]

High-quality, internally consistent, and comprehensive estimates of the distribution of anaemia and its underlying causes are essential for policy makers and health practitioners to develop interventions that are contextually appropriate and likely to reduce anaemia-associated morbidity and mortality.[13] This study aims to update and expand on our previous estimates of global anaemia burden.[20,21] This manuscript was produced as part of the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) Collaborator Network and in accordance with the GBD Protocol.[22]

Methods

Overview and definitions

Anaemia is defined by decreased blood concentration of haemoglobin.[23] We estimated unique, continuous

distributions of elevation-adjusted haemoglobin concentrations (g/L), anaemia prevalence, and years lived with disability (YLDs) by severity and 37 underlying causes of anaemia annually from 1990 to 2021 for 204 countries and territories, 21 GBD regions, male and female sexes, and 25 age groups (0–6 days, 7–27 days, 1–5 months, 6–11 months, 12–23 months, 2–4 years, 5–94 years in five-year age bins, and ≥95 years). Anaemia severity levels (mild, moderate, and severe) were defined using specific haemoglobin concentration thresholds that vary by age, sex, and pregnancy status (table). This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (appendix pp 3–4).[24]

Anaemia prevalence estimation

Input data and data processing

We used representative data on mean haemoglobin concentrations and severity-specific anaemia prevalence from population surveys, published studies, and government reports. All input sources are listed in the appendix (pp 888–923) and at the Global Health Data Exchange. Each input datum was assigned to a specific GBD location, age, sex, and pregnancy status. Elevation-adjusted or elevation-adjusted and smoking-adjusted data were used in the model directly, raw data were adjusted using the WHO elevation-adjustment formula (appendix p 8), and no additional adjustments were made for smoking status, method of haemoglobin sampling (eg, whole blood *vs* capillary), or analysis method (eg, Coulter counter *vs* point-of-care testing).

Spatiotemporal Gaussian process regression

We estimated log-transformed mean haemoglobin concentration and logit-transformed prevalence of severe, moderate plus severe, and total anaemia using spatiotemporal Gaussian process regression models.[25] The first-stage prediction was an ensemble of linear mixed-effects models (for a list of all covariates considered in submodels, see appendix pp 10–11), for which we retained only those submodels with significant covariate coefficients in the expected direction and each retained submodel was weighted inversely proportionally to its out-of-sample root mean squared error.[26] In stage two, we calculated the residuals between our ensemble model and our input data and smoothed these residuals over space, age, and time, producing a revised estimate for every location, year, age, and sex. The final step was a Gaussian process regression that further smoothed the residuals between our data and step two estimates, from which we quantified uncertainty in our final model estimates by taking 1000 draws from the posterior Gaussian process. More detailed information on the spatiotemporal Gaussian process regression modelling process can be found in the appendix (pp 10–11, 32–36).

Ensemble distribution modelling and calculation of prevalence

We estimated final distributions of haemoglobin concentration using ensemble modelling in three phases (appendix pp 11–13). First, to identify which distribution families to use, we tested both single candidate two-parameter distributions (gamma, mirrored gamma, Weibull, mirrored lognormal, and mirrored Gumbel) and weighted ensembles of those same candidate distributions, fitting to individual-level data on haemoglobin concentration from population surveys, and evaluating the fit using a loss function of severity-specific prediction error weighted by the severity-specific GBD disability weights for anaemia. We selected the combination that minimised test set error, defined as the absolute difference between the observed severity-specific prevalence in a given survey and the prevalence predicted by a given combination of distributions, with the severity-specific errors summed and weighted proportionally to the disability weights for mild, moderate, and severe anaemia (appendix pp 11–12).

See **Online** for appendix

Second, we estimated the variance in haemoglobin concentration distributions for each GBD demographic by using mean haemoglobin concentration and anaemia prevalence estimates from spatiotemporal Gaussian process regression modelling and pairing with the selected distributions from phase one. To calculate variance, we anchored each distribution at the modelled mean estimate of haemoglobin concentration, then used an optimisation algorithm to find the variance value that minimised the distance between our modelled anaemia prevalence estimates and those

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

	Mild anaemia	Moderate anaemia	Severe anaemia
0–6 days			
Males	145–159	100–144	<100
Females	145–159	100–144	<100
7–27 days			
Males	120–134	85–119	<85
Females	120–134	85–119	<85
1 month–4 years			
Males	100–109	70–99	<70
Females	100–109	70–99	<70
5 – 14 years			
Males	110–114	80–109	<80
Females	110–114	80–109	<80
≥15 years			
Males	110 –129	80–109	<80
Females, non–pregnant	110–119	80–109	<80
Females, pregnant	100–109	70–99	<70

Published WHO thresholds[23] were used for males and females aged 6 months and older; thresholds for those younger than 6 months were imputed as described in the appendix (p 6).

Table: **Haemoglobin concentration thresholds (g/L) for classification of anaemia severity by age, sex, and pregnancy status**

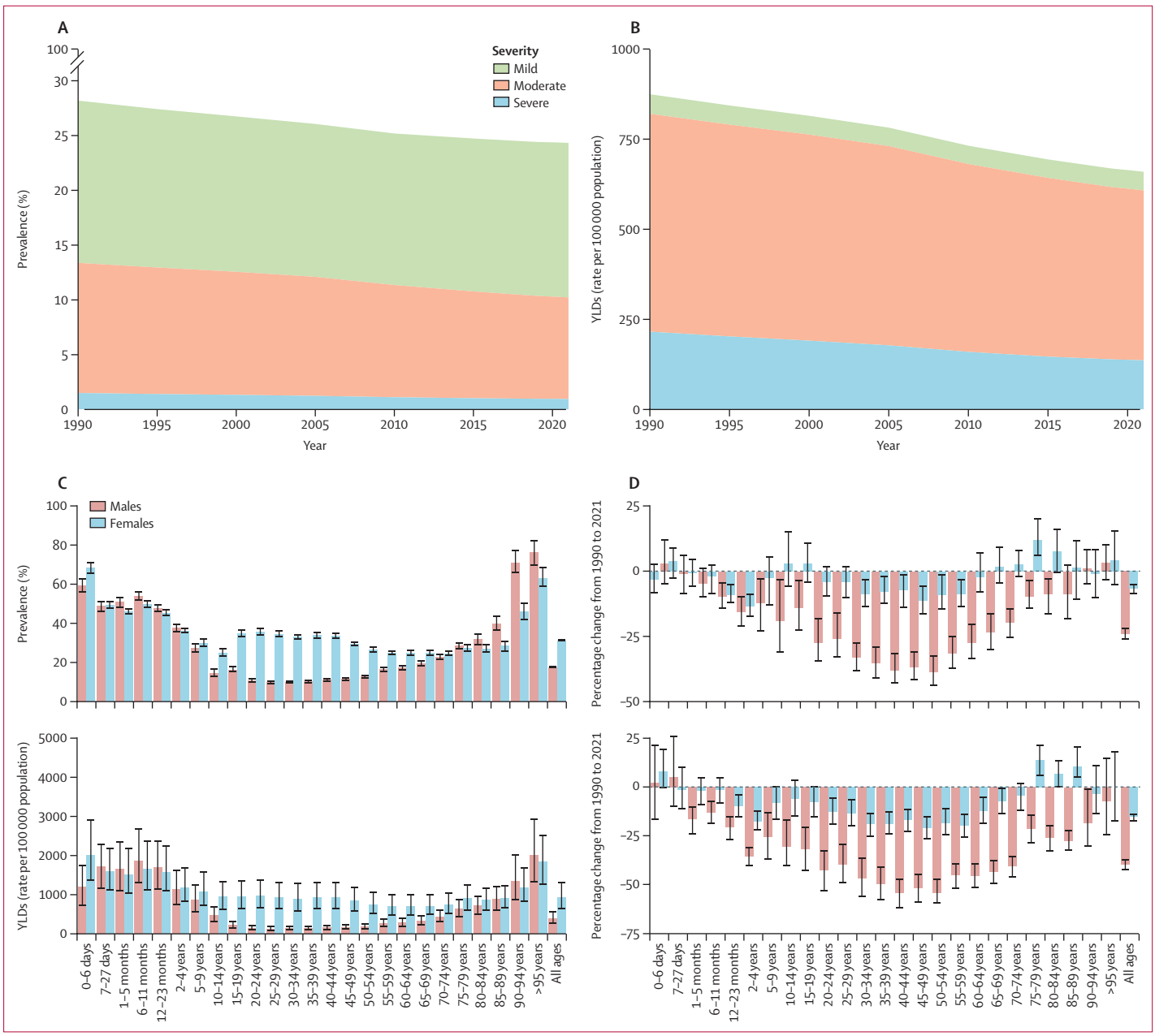


Figure 1: **Anaemia prevalence and YLDs (rate per 100 000 population)**
(A) Global anaemia prevalence by severity for all ages and male and female sexes, 1990–2021. (B) YLDs (rate per 100 000 population) by severity for all ages and male and female sexes, 1990–2021. (C) Global anaemia prevalence (top) and YLDs (rate per 100 000 population; bottom) for all ages and male and female sexes in 2021. Error bars are 95% CI. (D) Percentage change between 1990 and 2021 in anaemia prevalence (top) and YLDs (rate per 100 000 population; bottom) for all ages and male and female sexes. Error bars are 95% CI. YLDs=years lived with disability.

implied by the given mean haemoglobin and variance combination. We again weighted severity-specific errors proportionally to severity-specific disability weights, such that errors for more severe anaemia were more heavily penalised.

Third, we derived haemoglobin distributions for every location, year, age group, and sex using mean haemoglobin concentrations from spatiotemporal Gaussian process regression modelling, optimised variance, and ensemble distribution weights, with separate distributions by pregnancy status for females aged 10–54 years. Final anaemia prevalence was calculated by finding the area under the probability density curve between the corresponding haemoglobin concentration thresholds for each severity by age, sex, and pregnancy status. Separate prevalence estimates by pregnancy status were aggregated into final combined estimates for all females aged 10–54 years.

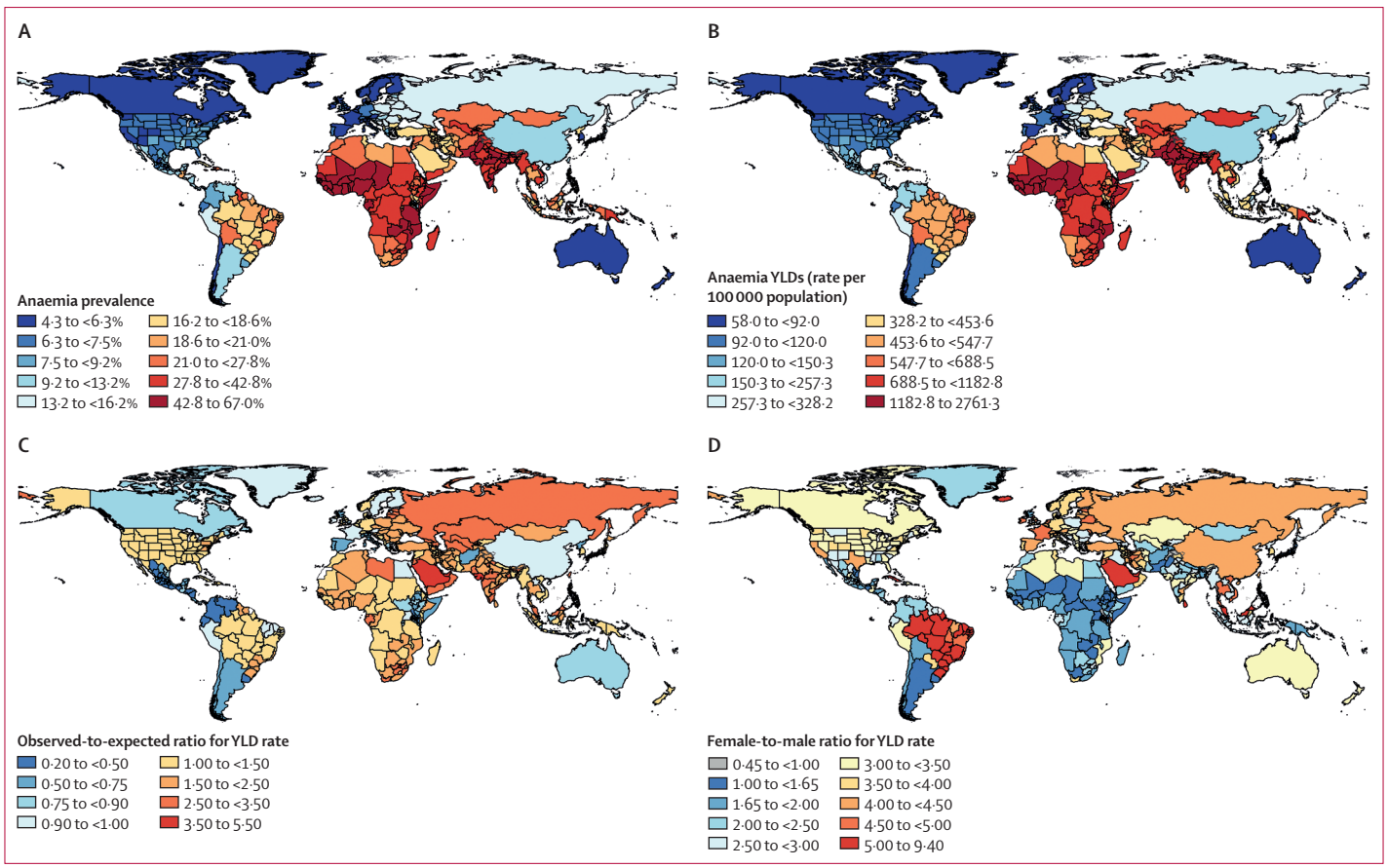


Figure 2: **All-ages anaemia burden, 2021**
(A) Anaemia prevalence for all ages and male and female sexes, 2021. (B) Anaemia YLDs (rate per 100 000 population) for all ages and male and female sexes, 2021. (C) Observed-to-expected ratio for YLD rate per 100 000 population for all ages and male and female sexes, 2021. Expected values were based on Socio-demographic Index. (D) Male-to-female ratio for YLD rate per 100,000 population, 2021. YLDs=years lived with disability.

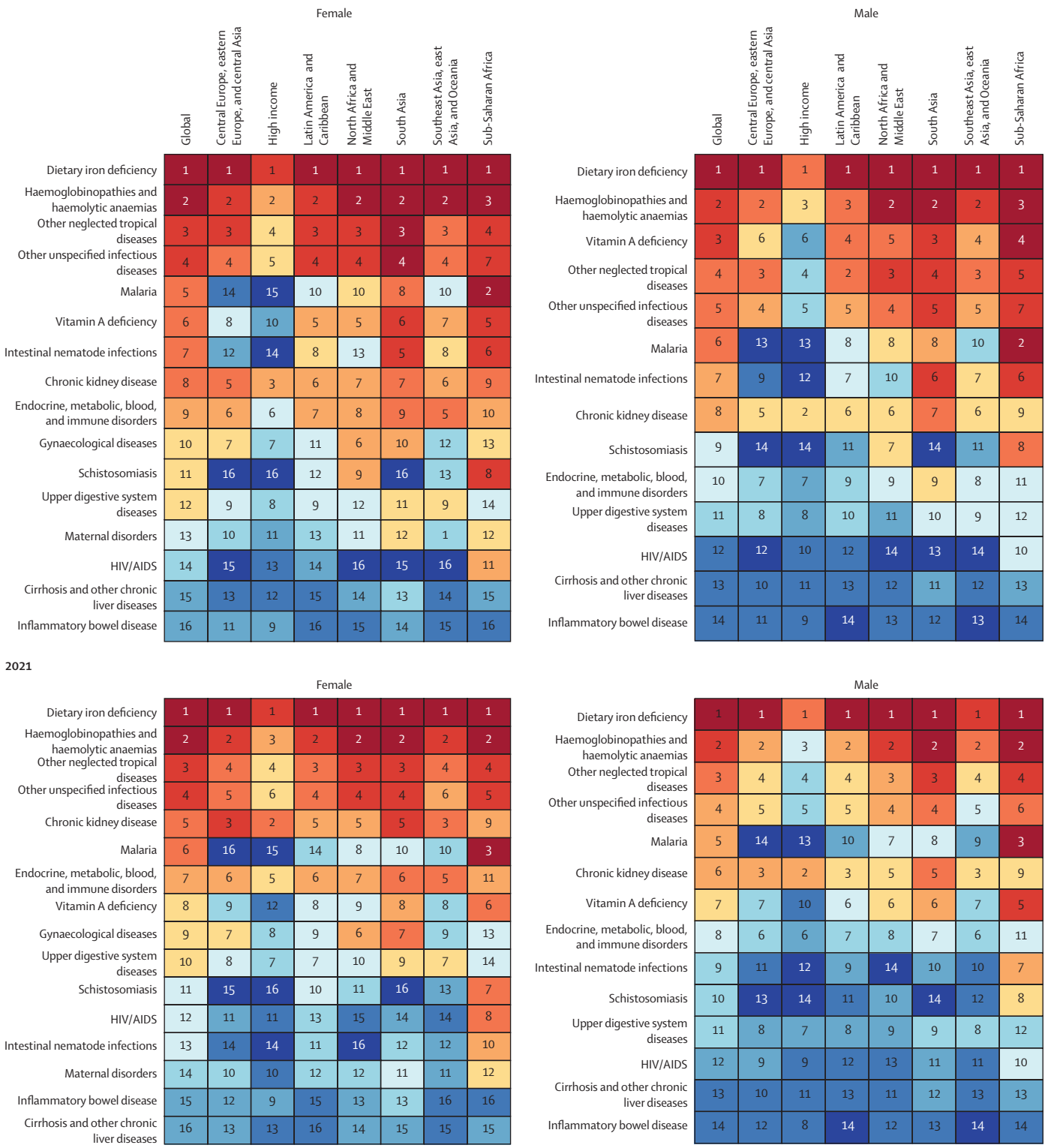
Causal attribution of anaemia

Each case of anaemia was assigned to a single cause in a mutually exclusive, collectively exhaustive manner for each of 37 underlying GBD causes considered in this analysis (appendix pp 13–16). We used four inputs for this process: haemoglobin concentration distributions including mean and variance; overall anaemia prevalence by severity; prevalence or incidence of each disease from the GBD 2021 study; and cause-specific haemoglobin shifts. Haemoglobin shifts represent mean difference in haemoglobin concentration associated with a given cause. These values were derived from published cohort studies, case-control studies, and intervention trials and have been described previously.[20] A minimum of 10% of prevalent anaemia cases were reserved for five residual causes for which haemoglobin shift information, estimates of cause-specific prevalence, or both were absent. Anaemia cases due to these causes were assigned using fixed-proportion redistribution, with most assigned to dietary iron deficiency (appendix p 15).

We multiplied each cause-specific haemoglobin shift by the prevalence of that cause, giving a prevalence-weighted haemoglobin shift for every location, year, age, sex, and cause. We added this shift to our estimate of mean haemoglobin concentration and recalculated a counterfactual haemoglobin concentration distribution (assuming unchanged variance) that represents a theoretical population distribution that would exist in the absence of each underlying cause. We then calculated the difference in anaemia prevalence by severity between the counterfactual and original haemoglobin distributions and assigned the difference to a specific cause and severity combination (eg, moderate anaemia due to clinical malaria). We scaled the results to ensure that cause-specific prevalence of anaemia could not exceed the total prevalence of a given cause and that all estimated cases of anaemia were attributed to an underlying cause.

YLDs

The YLD metric allows for standardised comparisons of non-fatal health burden between diseases.[27] We calculated YLDs by multiplying our estimates of severity-specific anaemia cases by associated severity-specific


1990
Female
Male
Global
Central Europe, eastern Europe, and central Asia
High income
Latin America and Caribbean
North Africa and Middle East
South Asia
Southeast Asia, east Asia, and Oceania
Sub-Saharan Africa
Dietary iron deficiency 1 1 1 1 1 1 1 1
Haemoglobinopathies and haemolytic anaemias 2 2 2 2 2 2 2 3
Other neglected tropical diseases 3 3 4 3 3 3 3 4
Other unspecified infectious diseases 4 4 5 4 4 4 4 7
Malaria 5 14 15 10 10 8 10 2
Vitamin A deficiency 6 8 10 5 5 6 7 5
Intestinal nematode infections 7 12 14 8 13 5 8 6
Chronic kidney disease 8 5 3 6 7 7 6 9
Endocrine, metabolic, blood, and immune disorders 9 6 6 7 8 9 5 10
Gynaecological diseases 10 7 7 11 6 10 12 13
Schistosomiasis 11 16 16 12 9 16 13 8
Upper digestive system diseases 12 9 8 9 12 11 9 14
Maternal disorders 13 10 11 13 11 12 1 12
HIV/AIDS 14 15 13 14 16 15 16 11
Cirrhosis and other chronic liver diseases 15 13 12 15 14 13 14 15
Inflammatory bowel disease 16 11 9 16 15 14 15 16
Dietary iron deficiency 1 1 1 1 1 1 1 1
Haemoglobinopathies and haemolytic anaemias 2 2 3 3 2 2 2 3
Vitamin A deficiency 3 6 6 4 5 3 4 4
Other neglected tropical diseases 4 3 4 2 3 4 3 5
Other unspecified infectious diseases 5 4 5 5 4 5 5 7
Malaria 6 13 13 8 8 8 10 2
Intestinal nematode infections 7 9 12 7 10 6 7 6
Chronic kidney disease 8 5 2 6 6 7 6 9
Schistosomiasis 9 14 14 11 7 14 11 8
Endocrine, metabolic, blood, and immune disorders 10 7 7 9 9 9 8 11
Upper digestive system diseases 11 8 8 10 11 10 9 12
HIV/AIDS 12 12 10 12 14 13 14 10
Cirrhosis and other chronic liver diseases 13 10 11 13 12 11 12 13
Inflammatory bowel disease 14 11 9 14 13 12 13 14
2021
Female
Male
Dietary iron deficiency 1 1 1 1 1 1 1 1
Haemoglobinopathies and haemolytic anaemias 2 2 3 2 2 2 2 2
Other neglected tropical diseases 3 4 4 3 3 3 4 4
Other unspecified infectious diseases 4 5 6 4 4 4 6 5
Chronic kidney disease 5 3 2 5 5 5 3 9
Malaria 6 16 15 14 8 10 10 3
Endocrine, metabolic, blood, and immune disorders 7 6 5 6 7 6 5 11
Vitamin A deficiency 8 9 12 8 9 8 8 6
Gynaecological diseases 9 7 8 9 6 7 9 13
Upper digestive system diseases 10 8 7 7 10 9 7 14
Schistosomiasis 11 15 16 10 11 16 13 7
HIV/AIDS 12 11 11 13 15 14 14 8
Intestinal nematode infections 13 14 14 11 16 12 12 10
Maternal disorders 14 10 10 12 12 11 11 12
Inflammatory bowel disease 15 12 9 15 13 13 16 16
Cirrhosis and other chronic liver diseases 16 13 13 16 14 15 15 15
Dietary iron deficiency 1 1 1 1 1 1 1 1
Haemoglobinopathies and haemolytic anaemias 2 2 3 2 2 2 2 2
Other neglected tropical diseases 3 4 4 4 3 3 4 4
Other unspecified infectious diseases 4 5 5 5 4 4 5 6
Malaria 5 14 13 10 7 8 9 3
Chronic kidney disease 6 3 2 3 5 5 3 9
Vitamin A deficiency 7 7 10 6 6 6 7 5
Endocrine, metabolic, blood, and immune disorders 8 6 6 7 8 7 6 11
Intestinal nematode infections 9 11 12 9 14 10 10 7
Schistosomiasis 10 13 14 11 10 14 12 8
Upper digestive system diseases 11 8 7 8 9 9 8 12
HIV/AIDS 12 9 9 12 13 11 11 10
Cirrhosis and other chronic liver diseases 13 10 11 13 11 12 13 13
Inflammatory bowel disease 14 12 8 14 12 13 14 14
YLDs per 100 000 population
103·24 to 1676·3
38·59 to <103·24
20·54 to <38·59
12·16 to <20·54
5·57 to <12·16
2·57 to <5·57
1·02 to <2·57
0·39 to <1·02
0·05 to <0·39
0 to <0·05

disability weights, which represent the level of health loss associated with a given disease state, where 0 is no health loss and 1 is death. The disability weights were 0·004 (95% uncertainty interval [UI] 0·001–0·008) for mild anaemia, 0.052 (0·034–0·076) for moderate anaemia, and 0·149 (0·101–0·209) for severe anaemia (for more information on this calculation see appendix pp 16–17).

Epidemiological transition and annualised rates of change

As secondary analyses, we explored the association between anaemia and socioeconomic development by analysing the relationship between anaemia burden (prevalence and YLDs) and the Socio-demographic Index (SDI) for each location in the analysis. SDI is a composite indicator based on estimates of total fertility rate in those younger than 25 years, mean years of education in individuals older than 15 years, and lag-distributed income per capita.[28] We conducted a meta-analysis of the relationship between country-level logit-transformed anaemia prevalence and log-transformed YLDs and SDI using meta-regression—Bayesian, regularised, trimmed models,[29] fitting restricted cubic splines that allowed for estimation of non-linear associations between anaemia burden and SDI. The splines contained two internal knots: one placed at the 33·33rd percentile and one at the 66·66th percentile of observed SDI values. From these models, we predicted expected values of anaemia prevalence and YLDs for each SDI value and calculated observed-to-expected ratios of anaemia burden for each location to identify countries with an anaemia burden substantially larger or smaller than expected on the basis of each country's level of socioeconomic development. Results stratified by SDI are based on each country's 2021 SDI value. To supplement trend assessments, we calculated annualised rate of change between two years as log-transformed difference in anaemia prevalence or YLD rate divided by the total number of years between the two values (for more information on this analysis see appendix p 17).

Uncertainty

We propagated uncertainty through each step of the estimation process by sampling draws from the posterior distribution of each estimated quantity. Uncertainty was not captured for population size, covariates used in spatiotemporal Gaussian process regression models, pregnancy prevalence, or haemoglobin shifts. Aggregations by geography, age, sex, and cause were made at the draw level, assuming uncorrelated uncertainty. The 95% UIs for each quantity correspond to the 2·5th and 97·5th percentiles of the draws.

Figure 3: **Causes of anaemia ranked by all-ages YLD rate, globally and by super-region, in males and females in 1990 and 2021**
YLDs=years lived with disability.

Role of the funding source

The funder had no role in study design, data collection, analysis, interpretation, or manuscript preparation.

Results

Overview

In 2021, the global prevalence of anaemia across all ages was 24·3% (95% UI 23·9–24·7), a decrease from 28·2% (27·8–28·5) in 1990 (figure 1A). The prevalence of severe anaemia was 0·9% (0·9–1·0), moderate anaemia was 9·3% (9·1–9·4), and mild anaemia was 14·1% (13·8–14·5; appendix pp 38–43). Despite a decrease in prevalence, the total number of people with anaemia increased from 1·50 billion (95% UI 1·48–1·52) in 1990 to 1·92 billion (1·89–1·95) in 2021, a difference attributable primarily to population growth. Total anaemia YLDs increased from 46·6 million (31·6–65·7) in 1990 to 52·0 million (35·1–75·1) in 2021, while YLD rate per 100 000 population decreased from 874·2 (591·7–1232·6) in 1990 to 659·2 (444·9–952·3) in 2021 (figure 1B; appendix pp 38–43). Country profiles and additional results can be found in the appendix (p 48–887).

Age and sex trends

Across all ages, males had a lower prevalence of anaemia than females (figure 1C). The 2021 all-ages prevalence was 17·5% (95% UI 17·0–18·0) in males and 31·2% (30·7–31·7) in females. Differences by sex were particularly large among adolescents and adults (aged 10–64 years); whereas children younger than 5 years had a comparatively high anaemia prevalence of 41·4% (40·7–42·2), the differences between males and females were smaller for that age group. Prevalence and YLDs in males and females began to increasingly diverge after age 5 years and did not begin to reconverge until age 80 years (figure 1C). For females aged 15–49 years the anaemia prevalence in 2021 was 33·7% (33·0–34·4), compared with 11·3% (10·9–11·8) for males. The corresponding YLD rates per 100 000 population were 926·8 (628·3–1328·7) for females and 151·8 (97·5–230·2) for males. In every region, females had a higher anaemia YLD rate than males. Regions with the largest female-to-male YLD ratio in 2021 were tropical Latin America (6·0 [4·5–7·6]), east Asia (4·2 [3·7–4·5]), and eastern Europe (4·2 [3·5–5·2]; figure 2D). The decrease in anaemia prevalence over time was also larger for males (reduction of 24·1% [21·8–26·3] from 1990 to 2021) than for females (reduction of 6·6% [4·9–8·6]; figure 1D). This disparity was similar in the YLD results, with males having a reduction of 40·2% (37·2–43·1) and females having a reduction of 15·4% (13·6–17·7) between 1990 and 2021. The reduction in anaemia burden over this period was

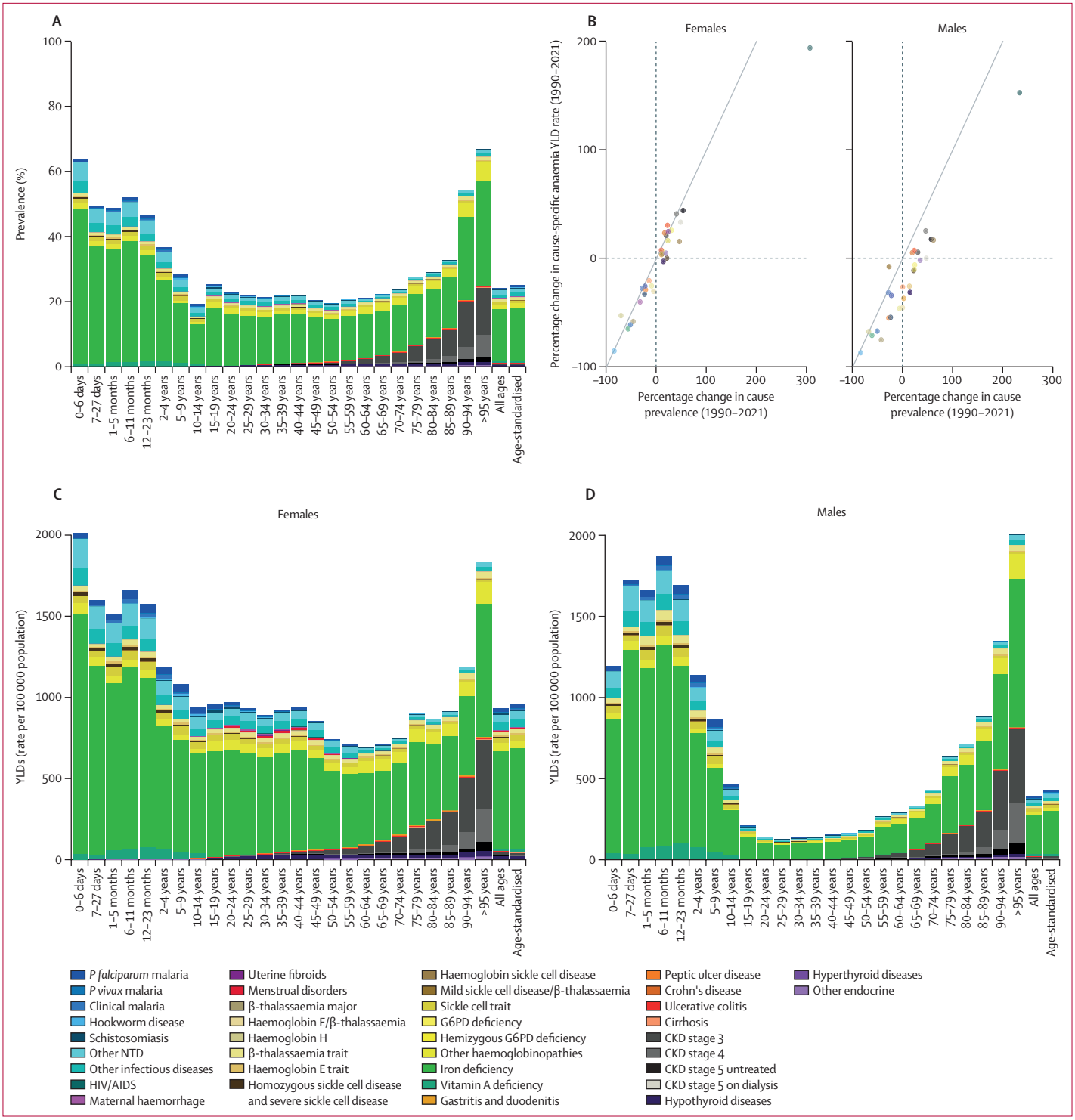


Figure 4: **Global distribution of anaemia causes**
(A) Cause-specific anaemia prevalence by age, for male and female sexes, 2021. (B) Percentage change in YLDs versus the percentage change in cause prevalence, all ages, for male and female sexes, 1990–2021. (C) Cause-specific anaemia YLD rate per 100 000 population by age, for males, 2021. (D) Cause-specific anaemia YLD rate per 100 000 population by age, for females, 2021. CKD=chronic kidney disease. Endocrine=endocrine, metabolic, blood, and immune disorders. G6PD=glucose-6-phosphate dehydrogenase. NTD=neglected tropical diseases. *P falciparum*=*Plasmodium falciparum*. *P vivax*=*Plasmodium vivax*. YLDs=years lived with disability.

greatest in adults, particularly those aged 20–74 years, for both males and females.

Geographical trends

We found large geographical disparities in anaemia burden (figure 2). Total anaemia prevalence in 2021 was greatest in western sub-Saharan Africa (47·4% [95% UI 45·1–49·5]), south Asia (43·0% [41·9–44·0), and central sub-Saharan Africa (35·7% [33·1–39·3]; figure 2A). These regions had the largest YLD rates per 100 000 population in 2021 (western sub-Saharan Africa 1540·8 [1042·1–2202·4], south Asia 1264·5 [856·5–1821·7], and central sub-Saharan Africa 962·6 [635·6–1429·6]; figure 2B). These regions also had the greatest anaemia burden in 1990 (appendix pp 38–43). By contrast, the regions with the lowest prevalence in 2021 were Australasia (5·7% [5·1–6·9]), western Europe (6·0% [5·7–6·4]), and high-income North America (6·8% [6·2–7·6]; figure 2A). Disparities in anaemia prevalence were more pronounced at the country level. In 2021, the three countries with the highest burden (Mali, Zambia, and Togo) all had an anaemia prevalence of greater than 50%, whereas the three countries with the lowest burden (Iceland, Norway, and Monaco) all had an anaemia prevalence of less than 5%. Whereas 22 countries had an anaemia prevalence of greater than 50% in 1990, only four countries (Mali, Zambia, Togo, and Senegal) had such a high prevalence in 2021.

Epidemiological transition

We observed a large negative association between SDI and anaemia burden (appendix p 17); countries at higher SDI levels tended to have lower anaemia prevalence and YLD rates. Expected anaemia prevalence based on SDI varied from 52·9% at the lowest observed SDI value to 3·5% at the highest observed SDI value; the equivalent range for anaemia YLD rates per 100 000 population was 1735·2 to 42·1. Substantial variation in anaemia YLD rates were also observed within SDI levels. Countries with the highest observed-to-expected ratios for YLDs based on SDI in 2021 were the United Arab Emirates (ratio 5·3), Saudi Arabia (4·1), and the Bahamas (4·1), and those with the lowest ratios were El Salvador (0·3), Ecuador (0·4), and Nicaragua (0·4; figure 2C).

Trends in causes of anaemia

Across all ages and male and female sexes, the leading causes of anaemia YLDs globally in 2021 were dietary iron deficiency (cause-specific anaemia YLD rate per 100 000 population: 422·4 [95% UI 286·1–612·9]), haemoglobinopathies and haemolytic anaemias (89·0 [58·2–123·7]), and other neglected tropical diseases (36·3 [24·4–52·8]; figure 3), collectively accounting for 84·7% (84·1–85·2) of anaemia YLDs. The burden due to dietary iron deficiency anaemia was particularly large, comprising 66·2% (65·5–66·8) of total anaemia cases with 444 million (433–455) cases among males and 825 million (811–839) cases among females globally in 2021. Dietary iron deficiency was the leading cause of all-ages anaemia YLDs in every GBD super-region (figure 3). Compared with prevalence, dietary iron deficiency was responsible for a smaller share of anaemia YLDs (64·0% [63·3–64·9]), reflective of dietary iron deficiency being associated with comparatively less severe forms of anaemia.

We observed variation in the relative contribution of causes of anaemia by age and sex that mirrored the underlying epidemiology of the causes. For example, in the oldest age groups, anaemia due to chronic kidney disease increased considerably, accounting for the second-largest share of anaemia YLDs globally for people older than 80 years (figure 4). Among children younger than 5 years, the most frequent cause of anaemia was dietary iron deficiency, but haemoglobinopathies, other infectious diseases, and malaria were also important contributors in locations where these diseases were prevalent. Gynaecological disorders and maternal haemorrhage were important contributors to anaemia burden among women of reproductive age, although dietary iron deficiency was the largest contributor for females in this age group and accounted for a substantial portion of the difference in anaemia burden between males and females (figure 4C, D). In general, changes in the epidemiology and prevalence of underlying causes over time were similarly reflected in changes in anaemia burden (figure 4B).

Regional variation in disease distribution was also reflected in cause-specific anaemia burden. For example, HIV/AIDS was the second largest contributor to anaemia YLDs in southern sub-Saharan Africa. Anaemia due to malaria was most prominent in the central, eastern, and western sub-Saharan Africa regions, and this cause ranked second or third in YLD burden in each of these regions. Chronic illnesses—particularly chronic kidney disease—contributed the second-largest share of anaemia YLDs across all ages in western Europe, high-income North America, and high-income Asia Pacific, whereas infections caused less anaemia in these than in other regions (figure 3).

Discussion

Anaemia affected more than 1·9 billion people and caused 52·0 million YLDs in 2021. This massive burden represented 5·7% of all YLDs in 2021, with only two level 3 GBD causes (low back pain and depressive disorders) responsible for more disability. Reductions in anaemia YLDs outpaced prevalence changes between 1990 and 2021, reflecting a global shift towards less severe anaemia,[30] but progress was variable and comparatively slow. The largest decreases were among males and adults aged 20–74 years and not the young children (<5 years) and women of reproductive age that

are the focus of international targets on anaemia and nutrition. All but one region saw decreases at the aggregate level, but considerable geographical disparities within regions remain and the range in prevalence between countries with the highest and lowest burdens is more than 50 percentage points.

Preventing diseases and injuries that cause anaemia is a crucial component of any public health strategy for anaemia. For example, antiretroviral therapy can help to reverse anaemia and improve survival in people living with HIV.[31] Malaria control methods (eg, mosquito vector management and treatment of bed nets with insecticide), malaria vaccination,[32] and increased access to antimalarial medications[47] can reduce the incidence of malaria and subsequently reduce anaemia.[39] Curing parasitic infections with antihelminthics can reverse chronic inflammation and blood loss due to conditions such as hookworm,[33] schistosomiasis,[34] and other neglected tropical diseases. Chronic kidney disease and other diseases that lead to chronic inflammation, decreased erythropoietin production, or both are an important cause of anaemia among older populations;[35] monitoring and preventing the onset and progression of these diseases can substantially reduce the anaemia burden in these groups.[36] Because of the importance of considering underlying causes, cause-specific anaemia YLD estimates are the most informative view of underlying epidemiology, especially with our approach, which assigns each prevalent case of anaemia to a single underlying cause.

A substantial component of the higher prevalence of anaemia in women of reproductive age is probably related to unmet needs for family planning services. Hormonal contraception has shown to be effective[37] as both prevention and treatment for anaemia caused by abnormal uterine bleeding,[38,39] as its use has been associated with lower anaemia rates in the community.[40] Gender inequalities related to household food consumption and division of labour probably exacerbate disparities in conditions such as anaemia, because women might be the most likely among household members to be affected by food insecurity[41,42] and to lack access to sufficient quantities of iron-rich foods,[43] and be less likely to receive health screening and care, whether due to domestic work demands, lack of autonomy, or prioritisation of other family members' care.[44,45] Social interventions, including education for girls and women[46] and expanded agricultural empowerment (eg, access to productive resources, self-managed time, decision-making power, and financial control) of women,[47] could help to reduce these disparities. Further research into gender inequalities is needed to evaluate the relative contributions of each of these factors in different contexts and to target interventions aimed at reducing the enormous anaemia burden among women of reproductive age.

Dietary iron deficiency was the leading cause of anaemia in most demographics, including children and women of reproductive age, and iron delivery interventions remain a mainstay of public health programmes. Iron delivery approaches include large-scale food fortification,[48] oral iron supplements,[49] and intravenous iron (depending on context and severity).[50] In addition to reducing iron-deficiency anaemia directly, iron delivery can have other positive effects. As part of a multiple micronutrient supplementation regimen, iron administration during the antenatal period is associated with improved birth outcomes and improved maternal and infant health.[51] Iron repletion might improve cognition,[52] although benefits are not uniform across age groups and have not been shown in children younger than 5 years.[53,54] Delayed cord clamping, breastfeeding, and vitamin A supplementation for severe vitamin A deficiency[55] could also reduce the anaemia burden in newborn babies, especially those born preterm who might also benefit from early erythropoietin administration.[56] However, iron delivery alone is unlikely to prevent or treat all iron deficiency, and a growing body of evidence suggests that iron supplementation could be harmful to some children with acute or chronic infections.[38] Population-level interventions for anaemia in children should therefore consider the infectious status of the community and the individual.[57,58]

Several fundamental unknowns remain in our collective understanding of anaemia; many researchers worldwide are working on these problems and that focus must be sustained. First and foremost, we do not truly know what the ideal definition of anaemia should be. Although many health conditions are defined on the basis of empirical assessments of increased rates of poor health outcomes (eg, diabetes, hypertension, obesity, and chronic kidney disease) or statistical deviations in representative populations (eg, childhood growth standards), WHO anaemia definitions do not have a similar rigorous clinical basis.[18] Evidence-based definitions of anaemia according to health loss associated with low haemoglobin concentrations are urgently needed to guide updated burden assessments, clinical standards,[59] and subsequent prioritisation of this public health problem.[60] Work from the BRINDA team suggests that existing formulae for altitude adjustment could lead to underestimation of anaemia at lower altitudes (<2000 m) and overestimation at higher altitudes (>3000 m), with differences in total anaemia prevalence ranging from three to 22 percentage points in the locations studied.[61] Second, methods of haemoglobin sampling (eg, whole *vs* capillary blood) and analysis (eg, laboratory *vs* point-of-care testing) vary considerably; the effect of this heterogeneity on estimates of anaemia burden and trends requires further exploration, as some evaluations have suggested up to a 28% variation between sampling methods.[62] Third, although we assess the direct disability burden of anaemia in the form of YLDs, this measure probably represents only a small part of the full health effects of low haemoglobin concentrations.

In addition to anaemia-related risks of preterm labour, low birthweight, short gestation, stillbirth, and impaired motor and cognitive development, anaemia has been associated with increased risk of several conditions including stroke,[63] cardiovascular disease,[64] dementia,[65] vision problems,[66] low bone mineral density,[67] and increased all-cause mortality after surgery[68] and in older adults.[7] A rigorous assessment of the evidence for low haemoglobin concentrations as an upstream risk factor for morbidity and mortality is necessary to close this knowledge gap. Similarly, although acute and chronic anaemia are common comorbidities in the hours and days preceding death, and blood transfusion is universally regarded as a life-saving intervention, there has been no comprehensive accounting for anaemia-associated mortality during this period.[69] Furthermore, disability weights and YLDs do not account for changes in health loss associated with adaptation and chronicity of illness. As such, these and similar analyses capture disease burden before longer-term compensatory changes.

This study has a number of limitations. First, data availability varied considerably by age and sex. Although comparatively many haemoglobin surveys exist for children older than 6 months and women of reproductive age, data are much sparser for younger children, adult males, and males and females older than 60 years. In addition, high-quality data at more granular levels to inform subnational estimation, including those subnational locations included in this analysis, are comparatively sparse. Second, WHO anaemia definitions are not available for children younger than 6 months, so we imputed thresholds based on median haemoglobin concentrations for older children; this probably imparted additional uncertainty in burden estimates beyond what is presented. Third, in our causal analysis, we assumed a linear cause-specific haemoglobin shift for any starting haemoglobin value, and we assumed that the shape of the population haemoglobin distribution was constant, which might not capture the true variation in cause-specific effects on haemoglobin distributions across geography and cause. Fourth, because the amount of data available to inform haemoglobin shifts varied substantially by cause (appendix pp 18–25) we were not able to capture uncertainty in the shifts themselves. Fifth, the assumption that each anaemia case has only a single underlying cause, although reflecting a sparsity of data to inform the interplay between diseases, nonetheless is a limitation in that many people with anaemia are likely to have multiple comorbid conditions contributing to their anaemia. Additional data on the combined effects of comorbid conditions on haemoglobin concentrations are needed to fully account for the multiple causes underlying many cases of anaemia. Finally, we were unable to capture all potential causes of anaemia in our causal analysis, owing to an absence of either estimates of disease prevalence or associated haemoglobin shifts. These potential causes include cancers, injuries, some micronutrient deficiencies (eg, folate and cobalamin), causes of inflammation not already captured in this analysis, and drug reactions. In addition, we had to estimate some causes as residual causes, again because either cause prevalence estimates or haemoglobin shifts were not available; this includes dietary iron deficiency, the largest cause of anaemia in our analyses.

Anaemia remains a major public health issue across the life course. The persistently high anaemia burden—particularly in women of reproductive age and young children—underscores the need for renewed attention on accurately measuring the prevalence of anaemia and its underlying causes, and using these data to design comprehensive policies and interventions that reflect the context-specific epidemiology of the disease and its determinants. Analyses of population-level anaemia burden can provide the insights required to appropriately tailor interventions at the country and subnational levels in an effort to reduce the prevalence of anaemia across all ages and sexes. Although probably not obtainable for most countries, multifaceted and contextual approaches will be necessary to ensure substantive progress towards Sustainable Development Goals 2 and 3 and WHO Global Nutrition Targets.

GBD 2021 Anaemia Collaborators

William M Gardner, Christian Razo, Theresa A McHugh, Hailey Hagins, Victor M Vilchis-Tella, Conor Hennessy, Heather Jean Taylor, Nandita Perumal, Kia Fuller, Kelly M Cercy, Leo Zucker Zoeckler, Catherine S Chen, Stephen S Lim, Amirali Aali, Kalkidan Hassen Abate, Sherief Abd-Elsalam, Ame Mehadi Abdurehman, Getachew Abebe, Hassan Abidi, Richard Gyan Aboagye, Hassan Abolhassani, Girma Beressa Aboye, Yonas Derso Abtew, Manfred Mario Kokou Accrombessi, Denberu Eshetie Adane, Tigist Demssew Adane, Isaac Yeboah Addo, Miracle Ayomikun Adesina, Daniel Adedayo Adeyinka, Qorinah Estiningtyas Sakilah Adnani, Muhammad Sohail Afzal, Saira Afzal, Rina Agustina, Bright Opoku Ahinkorah, Aqeel Ahmad, Sajjad Ahmad, Sepideh Ahmadi, Ayman Ahmed, Tarik Ahmed Rashid, Wajeeha Aiman, Marjan Ajami, Hossein Akbarialiabad, Fares Alahdab, Ziyad Al-Aly, Nazmul Alam, Astawus Alemayehu, Robert Kaba Alhassan, Muhammad Ashar Ali, Sami Almustanyir, Rajaa M Al-Raddadi, Rami H Al-Rifai, Khalid A Altirkawi, Saba Alvand, Nelson Alvis-Guzman, Yasser Sami Abdel Dayem Amer, Edward Kwabena Ameyaw, Hubert Amu, Tadele Fentabil Anagaw, Robert Ancuceanu, Ali Arash Anoushirvani, Maxwell Hubert Antwi, Davood Anvari, Jalal Arabloo, Aleksandr Y Aravkin, Hany Ariffin, Timur Aripov, Asrat Arja, Michael Benjamin Arndt, Judie Arulappan, Raphael Taiwo Aruleba, Tahira Ashraf, Melash Belachew Asresie, Seyyed Shamsadin Athari, Daniel Atlaw, Avinash Aujayeb, Andargie Abate Awoke, Mamaru Ayenew Awoke, Sina Azadnajafabad, Mohammadreza Azangou-Khyavy, Darshan B B, Alaa Badawi, Ashish D Badiye, Nayereh Baghcheghi, Nasser Bagheri, Sara Bagherieh, Atif Amin Baig, Maciej Banach, Palash Chandra Banik, Abere Tilahun Bantie, Ronald D Barr, Amadou Barrow, Azadeh Bashiri, Saurav Basu, Abdul-Monim Mohammad Batiha, Tahmina Begum, Melaku Ashagrie Belete, Luis Belo, Isabela M Bensenor, Alemshet Yirga Berhie, Akshaya Srikanth Bhagavathula, Nikha Bhardwaj, Pankaj Bhardwaj, Ajay Nagesh Bhat, Zulfiqar A Bhutta, Boris Bikbov, Sk Masum Billah, Setognal Birara, Jessica Devin Bishai, Saeid Bitaraf, Archith Boloor, João Silva Botelho, Katrin Burkart, Daniela Calina, Francieli Cembranel, Promit Ananyo Chakraborty, Gashaw Sisay Chanie, Vijay Kumar Chattu, Ju-Huei Chien, Isaac Sunday Chukwu, Eunice Chung, Michael H Criqui,

Natália Cruz-Martins, Omid Dadras, Gizachew Worku Dagnew, Xiaochen Dai, Hadi A Danawi, Lalit Dandona, Rakhi Dandona, Aso Mohammad Darwesh, Jai K Das, Saswati Das, Vanessa De la Cruz-Góngora, Fitsum Wolde Demisse, Solomon Demissie, Desalegn Getnet Demsie, Hardik Dineshbhai Desai, Markos Desalegn, Fikadu Nugusu Dessalegn, Gashaw Dessie, Samath Dhamminda Dharmaratne, Meghnath Dhimal, Sameer Dhingra, Daniel Diaz, Mojtaba Didehdar, M Ashworth Dirac, Mengistie Diress, Saeid Doaei, Milad Dodangeh, Paul Narh Doku, Deepa Dongarwar, Bezabih Terefe Dora, Haneil Larson Dsouza, Hisham Atan Edinur, Michael Ekholuenetale, Ahmed Elabbas Mustafa Elagali, Mostafa Ahmed Elbahnasawy, Iffat Elbarazi, Ghada Metwally Tawfik ElGohary, Muhammed Elhadi, Waseem El-Huneidi, Mohamed A Elmonem, Daniel Berhanie Enyew, Habitu Birhan Eshetu, Samuel B Ewald, Rana Ezzeddini, Adeniyi Francis Fagbamigbe, Abidemi Omolara Fasanmi, Ali Fatehizadeh, Ginenus Fekadu, Bikila Regassa Feyisa, Florian Fischer, Ryan Fitzgerald, Masoud Foroutan, Kayode Raphael Fowobaje, Muktar A Gadanya, Abhay Motiramji Gaidhane, Santosh Gaihre, Abduzhappar Gaipov, Yaseen Galali, Nasrin Galehdar, Priyanka Garg, Tushar Garg, Yosef Haile Gebremariam, Ketema Bizuwork Gebremedhin, Berhe Gebremichael, Yibeltal Yismaw Gela, Urge Gerema, Lemma Getacher, Kazem Ghaffari, Mansour Ghafourifard, Seyyed-Hadi Ghamari, Mohammad Ghasemi Nour, Ahmad Ghashghaee, Maryam Gholamalizadeh, Sherief Ghozy, Abraham Tamirat T Gizaw, James C Glasbey, Mahaveer Golechha, Pouya Goleij, Mohamad Golitaleb, Alessandra C Goulart, Girma Garedew Goyomsa, Habtamu Alganeh Guadie, Mohammed Ibrahim Mohialdeen Gubari, Zewdie Gudisa, Damitha Asanga Gunawardane, Rahul Gupta, Rajat Das Gupta, Sapna Gupta, Vivek Kumar Gupta, Alemu Guta, Parham Habibzadeh, Samer Hamidi, Alexis J Handal, Asif Hanif, Md Abdul Hannan, Harapan Harapan, Mehdi Harorani, Ahmed I Hasaballah, Md Mehedi Hasan, Hamidreza Hasani, Hadi Hassankhani, Mohammed Bheser Hassen, Khezar Hayat, Golnaz Heidari, Sonja Y Hess, Demisu Zenbaba Heyi, Kamal Hezam, Yuta Hiraike, Ramesh Holla, Sheikh Jamal Hossain, Kaveh Hosseini, Mohammad-Salar Hosseini, Mehdi Hosseinzadeh, Mihaela Hostiuc, Sorin Hostiuc, Junjie Huang, Salman Hussain, Foziya Mohammed Hussien, Segun Emmanuel Ibitoye, Olayinka Stephen Ilesanmi, Irena M Ilic, Mustapha Immurana, Leeberk Raja Inbaraj, Sheikh Mohammed Shariful Islam, Nahlah Elkudssiah Ismail, Linda Merin J, Elham Jamshidi, Manthan Dilipkumar Janodia, Umesh Jayarajah, Shubha Jayaram, Rime Jebai, Bedru Jemal, Angeline Jeyakumar, Ravi Prakash Jha, Jost B Jonas, Nitin Joseph, Jacek Jerzy Jozwiak, Ali Kabir, Laleh R Kalankesh, Rohollah Kalhor, Vineet Kumar Kamal, Himal Kandel, Tesfaye K Kanko, Ibraheem M Karaye, Faizan Zaffar Kashoo, Patrick D M C Katoto, Joonas H Kauppila, Harkiran Kaur, Gbenga A Kayode, Adera Debella Kebede, Vikash Ranjan Keshri, Mohammad Keykhaei, Yousef Saleh Khader, Himanshu Khajuria, Nauman Khalid, Mohammad Khammarnia, Imteyaz A Khan, Moien AB Khan, Khaled Khatab, Zaher Khazaei, Jagdish Khubchandani, Yun Jin Kim, Ruth W Kimokoti, Sezer Kisa, Farzad Kompani, Soewarta Kosen, Sindhura Lakshmi Koulmane Laxminarayana, Kewal Krishan, Barthelemy Kuate Defo, Mohammed Kuddus, G Anil Kumar, Naveen Kumar, Nithin Kumar, Om P Kurmi, Oluwatosin Kuti, Dharmesh Kumar Lal, Iván Landires, Anders O Larsson, Zohra S Lassi, Kamaluddin Latief, Avula Laxmaiah, Caterina Ledda, Sang-woong Lee, Samson Mideksa Legesse, Xuefeng Liu, László Lorenzovici, Vanessa Sintra Machado, Preetam Bhalchandra Mahajan, Soleiman Mahjoub, Ata Mahmoodpoor, Elham Mahmoudi, Elaheh Malakan Rad, Tauqeer Hussain Mallhi, Deborah Carvalho Malta, Sahar Masoudi, Seyedeh Zahra Masoumi, John Robert Carabeo Medina, Fabiola Mejia-Rodriguez, José João Mendes, Walter Mendoza, Oliver Mendoza-Cano, Alexios-Fotios A Mentis, Haftu Asmerom Meresa, Tomislav Mestrovic, Tomasz Miazgowski, Mojgan Mirghafourvand, Andreea Mirica, Moonis Mirza, Awoke Misganaw, Sanjeev Misra, Dara K Mohammad, Shadieh Mohammadi, Shafiu Mohammed, Syam Mohan, Nagabhishek Moka, Ali H Mokdad, Sara Momtazmanesh, Lorenzo Monasta, Mohammad Ali Moni, Delaram Moosavi, Maryam Moradi, Abbas Mosapour, Ebrahim Mostafavi, Temesgen Muche, Francesk Mulita, Getaneh Baye Mulu, Ana-Maria Musina, Ghulam Mustafa, Ahamarshan Jayaraman Nagarajan, Tapas Sadasivan Nair, Sreenivas Narasimha Swamy, Hasan Nassereldine, Zuhair S Natto, Biswa Prakash Nayak, Shumaila Naz, Ionut Negoi, Ruxandra Irina Negoi, Georges Nguefack-Tsague, Josephine W Ngunjiri, Robina Khan Niazi, Maryam Noori, Ali Nowroozi, Dieta Nurrika, Khan M Nuruzzaman, Ogochukwu Janet Nzoputam, Bogdan Oancea, Rahman Md Obaidur, Mohammed Suleiman Obsa, Julius Nyerere Odhiambo, Ropo Ebenezer Ogunsakin, Hassan Okati-Aliabad, Osaretin Christabel Okonji, Adeolu Olufunso Oladunjoye, Olubunmi Omotola Oladunjoye, Andrew T Olagunju, Isaac Iyinoluwa Olufadewa, Ahmed Omar Bali, Abidemi E Emmanuel Omonisi, Alberto Ortiz, Mayowa O Owolabi, Jagadish Rao Padubidri, Reza Pakzad, Tamás Palicz, Anamika Pandey, Apurva Kumar Pandya, Paraskevi Papadopoulou, Shahina Pardhan, Jay Patel, Ashish Pathak, Aslam Ramjan Pathan, Rajan Paudel, Uttam Paudel, Shrikant Pawar, Gavin Pereira, Norberto Perico, Simone Perna, Navaraj Perumalsamy, Ionela-Roxana Petcu, Brandon V Pickering, Zahra Zahid Piracha, Richard Charles G Pollok, Pranil Man Singh Pradhan, Akila Prashant, Ibrahim Qattea, Zahiruddin Quazi Syed, Fakher Rahim, Mehran Rahimi, Azizur Rahman, Mohammad Hifz Ur Rahman, Mosiur Rahman, Amir Masoud Rahmani, Shayan Rahmani, Rajesh Kumar Rai, Ivano Raimondo, Sathish Rajaa, Pradhum Ram, Juwel Rana, Muhammad Modassar Ali Nawaz Ranjha, Chythra R Rao, Sowmya J Rao, Sina Rashedi, Mohammad-Mahdi Rashidi, Salman Rawaf, Lal Rawal, Rabail Zehra Raza, Elrashdy Moustafa Mohamed Redwan, Giuseppe Remuzzi, Maryam Rezaei, Nazila Rezaei, Negar Rezaei, Toby Richards, Jennifer Rickard, Jefferson Antonio Buendia Rodriguez, Leonardo Roever, Gholamreza Roshandel, Bedanta Roy, Godfrey M Rwegerera, Aly M A Saad, Siamak Sabour, Basema Saddik, Malihe Sadeghi, Saeid Sadeghian, Umar Saeed, Amirhossein Sahebkar, Harihar Sahoo, Marwa Rashad Salem, Abdallah M Samy, Senthilkumar Sankararaman, Rocco Santoro, Itamar S Santos, Maheswar Satpathy, Ganesh Kumar Saya, Binyam Tariku Seboka, Anbissa Muleta Senbeta, Subramanian Senthilkumaran, Allen Seylani, Melika Shafeghat, Pritik A Shah, Masood Ali Shaikh, Mohd Shanawaz, Mohammed Shannawaz, Mequannent Melaku Sharew, Purva Sharma, Rahim Ali Sheikhi, Suchitra M Shenoy, Adithi Shetty, B Suresh Kumar Shetty, Jeevan K Shetty, Pavanchand H Shetty, Jae Il Shin, Siddharudha Shivalli, Velizar Shivarov, Parnian Shobeiri, Seyed Afshin Shorofi, Mustafa Kamal Sikder, Ali Reza Sima, Wudneh Simegn, Jasvinder A Singh, Narinder Pal Singh, Paramdeep Singh, Surjit Singh, Md Shahjahan Siraj, Yordanos Sisay, Anna Aleksandrovna Skryabina, Yonatan Solomon, Yi Song, Reed J D Sorensen, Jeffrey D Stanaway, Parminder S Suchdev, Mu'awiyyah Babale Sufiyan, Saima Sultana, Mindy D Szeto, Seidamir Pasha Tabaeian, Alireza Tahamtan, Majid Taheri, Moslem Taheri Soodejani, Zemenu Tamir, Ker-Kan Tan, Md Tariqujjaman, Elvis Enowbeyang Tarkang, Nathan Y Tat, Yibekal Manaye Tefera, Mohamad-Hani Temsah, Rekha Thapar, Arulmani Thiyagarajan, Jansje Henny Vera Ticoalu, Bereket M Tigabu, Amir Tiyuri, Ruoyan Tobe-Gai, Marcos Roberto Tovani-Palone, Mai Thi Ngoc Tran, Biruk Shalmeno Tusa, Irfan Ullah, Abdurezak Adem Umer, Bhaskaran Unnikrishnan, Marco Vacante, Sahel Valadan Tahbaz, Pascual R Valdez, Priya Vart, Shoban Babu Varthya, Siavash Vaziri, Madhur Verma, Massimiliano Veroux, Dominique Vervoort, Linh Gia Vu, Birhanu Wagaye, Fitsum Weldegebreal, Nuwan Darshana Wickramasinghe, Melat Woldemariam, Tewodros Eshete Wonde, Gedif Ashebir Wubetie, Xiaoyue Xu, Kheirollah Yari, Fereshteh Yazdanpanah, Sisay Shewasinad Yehualashet, Arzu Yigit, Vahit Yiğit, Eshetu Yisihak, Dong Keon Yon, Naohiro Yonemoto, Melissa F Young, Chuanhua Yu, Ismaeel Yunusa, Mazyar Zahir, Leila Zaki, Burhan Abdullah Zaman, Nelson Zamora, Iman Zare, Zahra Zareshahrabadi, Getachew Assefa Zenebe, Zhi-Jiang Zhang, Peng Zheng, Mohammad Zoladl, Simon I Hay, Christopher J L Murray, Nicholas J Kassebaum

Affiliations
Institute for Health Metrics and Evaluation (W M Gardner MPH, C Razo PhD, T A McHugh PhD, H Hagins MSPH, V M Vilchis-Tella MSc, C Hennessy MPA, H J Taylor BA, N Perumal PhD, K Fuller PhD, K M Cercy BS, L Z Zoeckler BA, C S Chen BA, Prof S S Lim PhD, A Y Aravkin PhD, M B Arndt PhD, J D Bishai BA, K Burkart PhD, E Chung MSc, X Dai PhD, Prof L Dandona MD, Prof R Dandona PhD, Prof S D Dharmaratne MD, M A Dirac MD, S B Ewald MS, R Fitzgerald MPH, M Hassen BSc, T Mestrovic PhD, A H Mokdad PhD, H Nassereldine MD, B V Pickering, R J D Sorensen PhD, J D Stanaway PhD, P Zheng PhD, Prof S I Hay FMedSci, Prof C J L Murray DPhil, Prof N J Kassebaum MD), Department of Health Metrics Sciences, School of Medicine (Prof S S Lim PhD, A Y Aravkin PhD, K Burkart PhD, X Dai PhD, Prof R Dandona PhD, Prof S D Dharmaratne MD, M A Dirac MD, Prof S I Hay FMedSci, A Misganaw PhD, A H Mokdad PhD, Prof C J L Murray DPhil, J D Stanaway PhD, P Zheng PhD, Prof N J Kassebaum MD), Department of Applied Mathematics (A Y Aravkin PhD), Department of Global Health (M B Arndt PhD, R J D Sorensen PhD), Department of Family Medicine (M A Dirac MD), Department of Anesthesiology and Pain Medicine (Prof N J Kassebaum MD), University of Washington, Seattle, WA, USA; Center for Health System Effectiveness (C Hennessy MPA), Oregon Health and Science University, Portland, OR, USA; Faculty of Medicine (A Aali MD), E-Learning Center (M Ghasemi Nour MD), Applied Biomedical Research Center (A Sahebkar PhD), Biotechnology Research Center (A Sahebkar PhD), Mashhad University of Medical Sciences, Mashhad, Iran; Department of Nutrition and Dietetics (K H Abate PhD), Department of Public Health (U Gerema MSc), Department of Health, Behavior and Society (A T T Gizaw MPH), Jimma University, Jimma, Ethiopia; Tropical Medicine Department (S Abd-Elsalam PhD), Tanta University, Tanta, Egypt; Department of Emergency and Critical Care Nursing (A M Abdurehman MSc), Department of Health Informatics (D B Enyew MSc), Department of Public Health (B Gebremichael MPH), School of Nursing and Midwifery (A D Kebede MSc), Department of Medical Laboratory Science (H A Meresa MSc, F Weldegebreal MSc), Haramaya University, Harar, Ethiopia; Department of Medical Anatomy (G Abebe MSc), Department of Biomedical Sciences (Y D Abtew MSc, T K Kanko MSc), Department of Midwifery (F W Demisse MSc, B T Dora MSc, E Yisihak MSc), Department of Anatomy (S Demissie MSc), Department of Public Health (Y H Gebremariam MPH, G A Wubetie MPH), Department of Medical Laboratory Science (M Woldemariam MSc), Arba Minch University, Arba Minch, Ethiopia; Laboratory Technology Sciences Department (H Abidi PhD), Department of Nursing (M Zoladl PhD), Yasuj University of Medical Sciences, Yasuj, Iran; Department of Family and Community Health (R G Aboagye MPH), Institute of Health Research (R K Alhassan PhD, M Immurana PhD), Department of Population and Behavioural Sciences (H Amu PhD, E E Tarkang PhD), University of Health and Allied Sciences, Ho, Ghana; Research Center for Immunodeficiencies (H Abolhassani PhD), Liver and Pancreatobiliary Diseases Research Center (S Alvand MD), Non-communicable Diseases Research Center (S Azadnajafabad MD, M Azangou-Khyavy MD, S Ghamari MD, M Keykhaei MD, S Momtazmanesh MD, S Rahmani MD, M Rashidi MD, N Rezaei MD, N Rezaei PhD), Tehran Heart Center (K Hosseini MD), Department of Cardiology (K Hosseini MD, E Mahmoudi MD, S Rashedi MD), Students' Scientific Research Center (M Keykhaei MD), Children's Medical Center (F Kompani MD), Department of Pediatric Cardiology (Prof E Malakan Rad MD), Digestive Diseases Research Institute (S Masoudi MSc, A Sima MD), School of Medicine (S Momtazmanesh MD, A Nowroozi BMedSc, M Shafeghat MD), Endocrinology and Metabolism Research Institute (N Rezaei PhD), Faculty of Medicine (P Shobeiri MD), Shariati Hospital (A Sima MD), Department of Pediatric Allergy and Immunology (F Yazdanpanah MD), Tehran University of Medical Sciences, Tehran, Iran; Department of Biosciences and Nutrition (H Abolhassani PhD), Karolinska University Hospital, Huddinge, Sweden; Department of Public Health (G B Aboye MSc), Madda Walabu University, Addis Ababa, Ethiopia; Department of Nutrition and Dietetics (G B Aboye MSc), Jimma University, Addis Ababa, Ethiopia; Department of Disease Control (M M K Accrombessi PhD), Medical Statistics Department (S Shivalli MD), London School of Hygiene and Tropical Medicine, London, UK; Department of Clinical Research (M M K Accrombessi PhD), Clinical Research Institute of Benin, Abomey-Calavi, Benin; Department of Anesthesia and Critical Care (D E Adane MSc), Debre Tabor University, Debre Tabor, Ethiopia; Department of Clinical and Psychosocial Epidemiology (T D Adane MSc), Department of Internal Medicine (P Vart PhD), University of Groningen, Groningen, Netherlands; Centre for Social Research in Health (I Y Addo PhD), Faculty of Medicine (V R Keshri MD), School of Population Health (X Xu PhD), University of New South Wales, Sydney, NSW, Australia; Quality and Systems Performance Unit (I Y Addo PhD), Cancer Institute NSW, Sydney, NSW, Australia; Slum and Rural Health Initiative Research Academy (M A Adesina BPT, I I Olufadewa MHS), Slum and Rural Health Initiative, Ibadan, Nigeria; Department of Physiotherapy (M A Adesina BPT), Department of Epidemiology and Medical Statistics (M Ekholuenetale MSc, A F Fagbamigbe PhD, K R Fowobaje MSc), Faculty of Public Health (M Ekholuenetale MSc, I I Olufadewa MHS), Department of Health Promotion and Education (S E Ibitoye MPH), Department of Community Medicine (O S Ilesanmi PhD), Department of Medicine (Prof M O Owolabi DrM), University of Ibadan, Ibadan, Nigeria; Department of Community Health and Epidemiology (D A Adeyinka PhD), University of Saskatchewan, Saskatoon, SK, Canada; Department of Public Health (D A Adeyinka PhD), Federal Ministry of Health, Abuja, Nigeria; Faculty of Medicine (Q E S Adnani PhD), Universitas Padjadjaran (Padjadjaran University), Bandung, Indonesia; Department of Life Sciences (M S Afzal PhD, I Ullah PhD), School of Food and Agricultural Sciences (N Khalid PhD), University of Management and Technology, Lahore, Pakistan; Department of Community Medicine (Prof S Afzal PhD), King Edward Memorial Hospital, Lahore, Pakistan; Department of Public Health (Prof S Afzal PhD), Public Health Institute, Lahore, Pakistan; Department of Nutrition (R Agustina PhD), Human Nutrition Research Center (R Agustina PhD), University of Indonesia, Jakarta, Indonesia; School of Public Health (B O Ahinkorah MPhil), University of Technology Sydney, Sydney, NSW, Australia; Department of Medical Biochemistry (A Ahmad PhD), Department of Pediatrics (Prof G Mustafa MD), Shaqra University, Shaqra, Saudi Arabia; Department of Health and Biological Sciences (S Ahmad PhD), Abasyn University, Peshawar, Pakistan; School of Advanced Technologies in Medicine (S Ahmadi PhD), National Nutrition and Food Technology Research Institute (M Ajami PhD), Social Determinants of Health Research Center (M Azangou-Khyavy MD, S Ghamari MD, M Rashidi MD), Department of Community Nutrition (S Doaei PhD), Cancer Research Center (M Gholamalizadeh PhD), Functional Neurosurgery Research Center (E Jamshidi PharmD), School of Medicine (S Rahmani MD), Department of Epidemiology (S Sabour PhD), Medical Ethics and Law Research Center (M Taheri PhD), Urology and Nephrology Research Center (M Zahir MD), Shahid Beheshti University of Medical Sciences, Tehran, Iran; Institute of Endemic Diseases (A Ahmed MSc), University of Khartoum, Khartoum, Sudan; Swiss Tropical and Public Health Institute (A Ahmed MSc), University of Basel, Basel, Switzerland; Department of Computer Science and Engineering (T Ahmed Rashid PhD), University of Kurdistan Hewler, Erbil, Iraq; Department of Neurology (W Aiman MD), Nishtar Medical University, Multan, Pakistan; Department of Food and Nutrition Policy and Planning Research (M Ajami PhD), National Institute of Nutrition, Tehran, Iran; Department of Public Health and Community Medicine (H Akbarialiabad MD), Department of Health Information Management (A Bashiri PhD), Department of Medical Mycology and Parasitology (Z Zareshahrabadi PhD), Shiraz University of Medical Sciences, Shiraz, Iran; Mayo Evidence-based Practice Center (F Alahdab MSc), Mayo Clinic Foundation for Medical Education and Research, Rochester, MN, USA; John T Milliken Department of Internal Medicine (Z Al-Aly MD), 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; Department of Public Health (Prof N Alam DrPH), Asian University for Women, Chittagong, Bangladesh; Department of Public Health (A Alemayehu MPH), Harar

Health Science College, Harar, Ethiopia; Department of Public Health (A Alemayehu MPH), Rift Valley University, Harar, Ethiopia; Department of Medicine (M Ali MD), King Edward Medical University, Lahore, Pakistan; College of Medicine (S Almustanyir MD), Alfaisal University, Riyadh, Saudi Arabia; Ministry of Health, Riyadh, Saudi Arabia (S Almustanyir MD); Department of Community Medicine (R M Al-Raddadi PhD), Department of Dental Public Health (Z S Natto DrPH), King Abdulaziz University, Jeddah, Saudi Arabia; Institute of Public Health (R H Al-Rifai PhD, I Elbarazi DrPH), Family Medicine Department (M A Khan MSc), United Arab Emirates University, Al Ain, United Arab Emirates; Pediatric Intensive Care Unit (K A Altirkawi MD, M Temsah MD), Quality Management Department (Y S A Amer MSc), Section of Adult Hematology (Prof G M T ElGohary MD), King Saud University, Riyadh, 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; Alexandria Center for Evidence-based Clinical Practice Guidelines (Y S A Amer MSc), Alexandria University, Alexandria, Egypt; School of Graduate Studies (E K Ameyaw MPhil), Lingnan University, Hong Kong Special Administrative Region, China; Department of Health Promotion (T F Anagaw MPH), School of Public Health (M B Asresie MPH), College of Medicine and Health Sciences (A A Awoke MSc, D G Demsie MSc), School of Health Science (A Y Berhie MSc), Department of Reproductive Health (G W Dagnew MPH), Department of Health Informatics (H A Guadie MPH), Bahir Dar University, Bahir Dar, Ethiopia; Faculty of Pharmacy (Prof R Ancuceanu PhD), Internal Medicine Department (M Hostiuc PhD), Department of Legal Medicine and Bioethics (S Hostiuc PhD), Department of General Surgery (I Negoi PhD), Department of Anatomy and Embryology (R I Negoi PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; Department of Internal Medicine (A Anoushirvani MD, S Tabaeian MD), Health Management and Economics Research Center (J Arabloo PhD), School of Medicine (M Dodangeh MD, D Moosavi MD), Minimally Invasive Surgery Research Center (A Kabir MD), Student Research Committee (M Noori MD), Trauma and Injury Research Center (M Taheri PhD), Department of Epidemiology and Biostatistics (A Tiyuri MSc), Iran University of Medical Sciences, Tehran, Iran (M Moradi MD); Department of Medical Laboratory Science (M Antwi MPhil), Koforidua Technical University, Koforidua, Ghana; Department of Parasitology (D Anvari PhD), Department of Medical-Surgical Nursing (S Shorofi PhD), Mazandaran University of Medical Sciences, Sari, Iran; Department of Parasitology (D Anvari PhD), Iranshahr University of Medical Sciences, Iranshahr, Iran; Department of Paediatrics (Prof H Ariffin MD), University of Malaya Medical Centre (Prof H Ariffin MD), University of Malaya, Kuala Lumpur, Malaysia; Public Health and Healthcare Management (T Aripov PhD), Tashkent Institute of Postgraduate Medical Education, Tashkent, Uzbekistan; Medicine Critical Care (A O Oladunjoye MD), Boston Children's Hospital, Boston, MA, USA (T Aripov PhD); National Data Management Center for Health (A Arja MPH, M Hassen BSc, A Misganaw PhD), Knowledge Translation Directorate (S M Legesse PhD), Water, Sanitation and Hygiene Unit (B Wagaye MPH), Ethiopian Public Health Institute, Addis Ababa, Ethiopia; Department of Maternal and Child Health (J Arulappan DSc), Sultan Qaboos University, Muscat, Oman; Department of Molecular and Cell Biology (R T Aruleba MSc), University of Cape Town, Cape Town, South Africa; University Institute of Radiological Sciences and Medical Imaging Technology (T Ashraf MS), University Institute of Public Health (A A Baig PhD, A Hanif PhD), The University of Lahore, Lahore, Pakistan; Department of Immunology (S Athari PhD), Zanjan University of Medical Sciences, Zanjan, Iran; Department of Biomedical Science (D Atlaw MSc), Madda Walabu University, Bale Robe, Ethiopia; Northumbria HealthCare NHS Foundation Trust (A Aujayeb MBBS), Newcastle upon Tyne, UK; Department of Epidemiology and Preventive Medicine (M A Awoke MPH), University of Melbourne, Melbourne, VIC, Australia; Kasturba Medical College, Mangalore (D B B MD, R Holla MD), Manipal College of Pharmaceutical Sciences (Prof M D Janodia PhD), Manipal TATA Medical College (M Rahman PhD), Department of Community Medicine (C R Rao MD), Manipal Academy of Higher Education, Manipal, India; Public Health Risk Sciences Division (A Badawi PhD), Public Health Agency of Canada, Toronto, ON, Canada; Department of Nutritional Sciences (A Badawi PhD), Centre for Global Child Health (Prof Z A Bhutta PhD), University of Toronto, Toronto, ON, Canada; Department of Forensic Science (A D Badiye PhD), Government Institute of Forensic Science, Nagpur, India; Department of Nursing (N Baghcheghi PhD), Saveh University of Medical Sciences, Saveh, Iran; Research School of Population Health (N Bagheri PhD), Australian National University, Canberra, ACT, Australia; Health Research Institute (N Bagheri PhD), University of Canberra, Canberra, ACT, Australia; School of Medicine (S Bagherieh BSc), Department of Environmental Health Engineering (A Fatehizadeh PhD), Isfahan University of Medical Sciences, Isfahan, Iran; Department of Hypertension (Prof M Banach PhD), Medical University of Lodz, Lodz, Poland; Polish Mothers' Memorial Hospital Research Institute, Lodz, Poland (Prof M Banach PhD); Department of Non-communicable Diseases (P C Banik MPhil), Bangladesh University of Health Sciences, Dhaka, Bangladesh; Department of Anesthesiology (A T Bantie MSc), Adigrat University, Adigrat, Ethiopia; Department of Pediatrics (Prof R D Barr MD), Department of Medicine (O P Kurmi PhD), Department of Psychiatry and Behavioural Neurosciences (A T Olagunju MD), McMaster University, Hamilton, ON, Canada; Department of Public and 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; Academics Department (S Basu MD), Indian Institute of Public Health, Gurgaon, India; Faculty of Nursing (Prof A M Batiha PhD), Philadelphia University, Amman, Jordan; Center of Research Excellence in Stillbirth (T Begum MPH), School of Health and Rehabilitation Sciences (M Moni PhD), The University of Queensland, Brisbane, QLD, Australia; Health System and Population Studies Division (T Begum MPH), Maternal and Child Health Division (S M Billah MPH, S J Hossain MPH, M Siraj MSc), Nutrition and Clinical Services Division (M Tariqujjaman MSc), International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; Medical Laboratory Science (M A Belete MSc), Department of Public Health (F M Hussien MPH, F M Hussien MPH), Department of Public Health Nutrition (B Wagaye MPH), Wollo University, Dessie, Ethiopia; Biological Sciences Department (L Belo PhD), Research Unit on Applied Molecular Biosciences (L Belo PhD), Institute for Research and Innovation in Health (Prof N Cruz-Martins PhD), University of Porto, Porto, Portugal; Department of Internal Medicine (I M Bensenor PhD, A C Goulart PhD, I S Santos PhD), Center for Clinical and Epidemiological Research (A C Goulart PhD, I S Santos PhD), University of São Paulo, São Paulo, Brazil; Department of Health, Human Performance and Recreation (A S Bhagavathula PhD), University of Arkansas, Fayetteville, AR, USA; Department of Anatomy (Prof N Bhardwaj MD), Department of Community Medicine and Family Medicine (P Bhardwaj MD), School of Public Health (P Bhardwaj MD), Department of Surgical Oncology (Prof S Misra MCh), Department of Pharmacology (S Singh DM, S B Varthya MD), All India Institute of Medical Sciences, Jodhpur, India; Department of General Medicine (A N Bhat MD), Department of Internal Medicine (A Boloor MD), Department of Forensic Medicine and Toxicology (H L Dsouza MD, J Padubidri MD, Prof B K Shetty MD, P H Shetty MD), Department of Community Medicine (N Joseph MD, N Kumar MD, R Thapar MD), Department of Obstetrics and Gynaecology (A Shetty MS), Kasturba Medical College (Prof B Unnikrishnan MD), Manipal Academy of Higher Education, Mangalore, India; Centre of Excellence in Women and Child Health (Prof Z A Bhutta PhD), Division of Women and Child Health (J K Das MD), Department of Pediatrics (Z S Lassi PhD), Aga Khan University, Karachi, Pakistan; Scientific Tools, Bergamo, Italy (B Bikbov MD); Sydney School of Public Health (S M Billah MPH), Sydney Medical School (S Islam PhD), Save Sight Institute (H Kandel PhD), Department of Public Health (K Nuruzzaman PhD), University of Sydney, Sydney, NSW, Australia; Department of Public Health (S Birara MPH), Samara University, Samara, Ethiopia; Department of Biostatistics and Epidemiology (Prof S Bitaraf PhD), Department of Pediatric Neurology (S Sadeghian MD), Ahvaz

Jundishapur University of Medical Sciences, Ahvaz, Iran; Clinical Research Unit (Prof J S Botelho PhD), Centro de Investigação Interdisciplinar Egas Moniz (Interdisciplinary Research Center of Egas Moniz), Almada, Portugal; Clinical Pharmacy (Prof D Calina PhD), University of Medicine and Pharmacy of Craiova, Romania, Craiova, Romania; Department of Nutrition (Prof F Cembranel DSc), Federal University of Santa Catarina, Florianópolis, Brazil; School of Population and Public Health (P A Chakraborty MPH), University of British Columbia, Vancouver, BC, Canada; Department of Clinical Pharmacy (G S Chanie MSc), Biochemistry Department (G Dessie MSc), Department of Human Physiology (M Diress MSc, Y Gela MSc), Department of Health Education and Behavioral Sciences (H B Eshetu MPH), Institute of Public Health (M M Sharew MPH), Department of Social and Administrative Pharmacy (W Simegn MSc), University of Gondar, Gondar, Ethiopia; Department of Community Medicine (V Chattu MD), Datta Meghe Institute of Medical Sciences, Sawangi, India; Saveetha Medical College and Hospitals (V Chattu MD), Saveetha University, Chennai, India; Department of Laboratory Medicine (J Chien PhD), Taichung Tzu-Chi Hospital Buddhist Tzu-Chi Medical Foundation, Tanzih, Taiwan; Department of Medical Laboratory Science and Biotechnology (J Chien PhD), Central Taiwan University of Science and Technology, Taichung, Taiwan; Department of Paediatric Surgery (I S Chukwu BMedSc), Federal Medical Centre, Umuahia, Nigeria; Department of Family Medicine and Public Health (Prof M H Criqui MD), University of California San Diego, La Jolla, CA, USA; Therapeutic and Diagnostic Technologies (Prof N Cruz-Martins PhD), Cooperativa de Ensino Superior Politécnico e Universitário (Polytechnic and University Higher Education Cooperative), Gandra, Portugal; Section Global Health and Rehabilitation (O Dadras DrPH), Western Norway University of Applied Sciences, Bergen, Norway; Department of Global Public Health and Primary Care (O Dadras DrPH), University of Bergen, Bergen, Norway; Walden University, Minneapolis, MN, USA (H A Danawi PhD); Research Division (H Kaur MPH), Department of Research (A Pandey PhD), Public Health Foundation of India, Gurugram, India (Prof L Dandona MD, Prof R Dandona PhD, G Kumar PhD, D K Lal MD); Biostatistics (V K Kamal PhD), Indian Council of Medical Research, New Delhi, India (Prof L Dandona MD); Department of Information Technology (A M Darwesh PhD), Department of Computer Science (M Hosseinzadeh PhD), Diplomacy and Public Relations Department (A Omar Bali PhD), University of Human Development, Sulaymaniyah, Iraq; Department of Biochemistry (S Das MD), Ministry of Health and Welfare, New Delhi, India; Center for Evaluation and Surveys Research (V De la Cruz-Góngora PhD), Research in Nutrition and Health (F Mejia-Rodriguez MSc), National Institute of Public Health, Cuernavaca, Mexico; Graduate Medical Education (H D Desai MD), Gujarat Adani Institute of Medical Sciences, Bhuj, India; Department of Public Health (M Desalegn MPH, B R Feyisa MPH), Department of Pharmacy (G Fekadu MSc), Wollega University, Nekemte, Ethiopia; Department of Public Health (F N Dessalegn MPH), Madda Walabu University, Bale Goba, Ethiopia; Department of Community Medicine (Prof S D Dharmaratne MD), University of Peradeniya, Peradeniya, Sri Lanka; Health Research Section (M Dhimal PhD, U Paudel PhD), Nepal Health Research Council, Kathmandu, Nepal; Department of Pharmacy Practice (S Dhingra PhD), National Institute of Pharmaceutical Education and Research, Hajipur, India; Center of Complexity Sciences (Prof D Diaz PhD), National Autonomous University of Mexico, Mexico City, Mexico; Faculty of Veterinary Medicine and Zootechnics (Prof D Diaz PhD), Autonomous University of Sinaloa, Culiacán Rosales, Mexico; Department of Parasitology and Mycology (M Didehdar PhD), Department of Nursing (M Golitaleb PhD, M Harorani MSc), Arak University of Medical Sciences, Arak, Iran; School of Health (S Doaei PhD), Guilan University of Medical Sciences, Rasht, Iran; School of Nursing and Midwifery (P N Doku PhD), University of Cape Coast, Cape Coast, Ghana; Health Science Center (D Dongarwar MS), University of Texas, Houston, TX, USA; Department of Forensic Medicine and Toxicology (H L Dsouza MD), Kasturba Medical College, Mangalore, Mangalore, India; School of Health Sciences (H A Edinur PhD), Universiti Sains Malaysia (University of Science Malaysia), Kubang Kerian, Malaysia; Minderoo Foundation, Perth, WA, Australia (A E M Elagali PhD); School of Biological Sciences (A E M Elagali PhD), The University of Western Australia, Crawley, WA, Australia; Microbiology Department (M A Elbahnasawy PhD), Department of Zoology and Entomology (A I Hasaballah PhD), Al Azhar University, Cairo, Egypt; Department of Internal Medicine and Hematology Unit (Prof G M T ElGohary MD), Department of Entomology (A M Samy PhD), Medical Ain Shams Research Institute (A M Samy PhD), Ain Shams University, Cairo, Egypt; Faculty of Medicine (M Elhadi MD), University of Tripoli, Tripoli, Libya; Department of Basic Medical Sciences (W El-Huneidi PhD), Sharjah Institute for Medical Research (B Saddik PhD), University of Sharjah, Sharjah, United Arab Emirates; Egypt Center for Research and Regenerative Medicine, Cairo, Egypt (M A Elmonem PhD); Department of Clinical Biochemistry (R Ezzeddini PhD, A Mosapour PhD), Department of Parasitology and Entomology (L Zaki PhD), Tarbiat Modares University, Tehran, Iran; Institute of Applied Health Sciences (A F Fagbamigbe PhD, S Gaihre PhD), University of Aberdeen, Aberdeen, UK; Satcher Health Leadership Institute (A O Fasanmi PhD), Morehouse School of Medicine, Atlanta, GA, USA; School of Medicine (A O Fasanmi PhD), Department of Cardiology (P Ram MD), Department of Pediatrics (Prof P S Suchdev MD), Hubert Department of Global Health (M F Young PhD), Emory University, Atlanta, GA, USA; School of Pharmacy (G Fekadu MSc), Jockey Club School of Public Health and Primary Care (J Huang MD), The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China; Institute of Public Health (F Fischer PhD), Charité Universitätsmedizin Berlin (Charité Medical University Berlin), Berlin, Germany; Department of Medical Parasitology (M Foroutan PhD), Faculty of Medicine (M Foroutan PhD), Abadan University of Medical Sciences, Abadan, Iran; Child Survival Unit (K R Fowobaje MSc), Centre for African Newborn Health and Nutrition, Ibadan, Nigeria; Community Medicine Department (Prof M A Gadanya FMCPH), Bayero University, Kano, Kano, Nigeria; Department of Community Medicine (Prof M A Gadanya FMCPH), Aminu Kano Teaching Hospital, Kano, Nigeria; Department of Community Medicine (Prof A M Gaidhane MD, Prof Z Quazi Syed PhD), Datta Meghe Institute of Medical Sciences, Wardha, India; Department of Medicine (A Gaipov PhD), Nazarbayev University School of Medicine, Nur-Sultan, Kazakhstan; Food Technology Department (Y Galali ResM), Department of Forestry (D K Mohammad PhD), Salahaddin University-Erbil, Erbil, Iraq; Department of Nutrition and Dietetics (Y Galali ResM), Cihan University-Erbil, Erbil, Iraq; Department of Surgical Technology (N Galehdar PhD), Lorestan University of Medical Sciences, Khorramabad, Iran; Department of Obstetrics and Gynaecology (P Garg MD), Department of Hospital Administration (M Mirza MD), Department of Radiodiagnosis (P Singh MD), Department of Community Medicine and Family Medicine (M Verma MD), All India Institute of Medical Sciences, Bathinda, India; Department of Radiology (T Garg MBBS), King Edward Memorial Hospital, Mumbai, India; Department of Nursing and Midwifery (K B Gebremedhin MSc), Department of Medical Laboratory Science (Z Tamir MSc), Addis Ababa University, Addis Ababa, Ethiopia; Department of Public Health (L Getacher MPH), Department of Pediatrics and Child Health Nursing (G B Mulu MSc, S S Yehualashet MSc), Debre Berhan University, Debre Berhan, Ethiopia; Department of Laboratory Sciences (K Ghaffari MSc), Khomein University of Medical Sciences, Khomein, Iran; Department of Medical Surgical Nursing (M Ghafourifard PhD), School of Nursing and Midwifery (H Hassankhani PhD), Student Research Committee (M Hosseini MD), Department of Anesthesiology and Critical Care (Prof A Mahmoodpoor MD), Department of Midwifery (Prof M Mirghafourvand PhD), Cardiovascular Research Center (M Rahimi MD), Department of Pediatric Allergy and Immunology (F Yazdanpanah MD), Tabriz University of Medical Sciences, Tabriz, Iran; School of Public Health (A Ghashghaee BSc), Institute for Prevention of Non-communicable Diseases (R Kalhor PhD), Health Services Management Department (R Kalhor PhD), Qazvin University of Medical Sciences, Qazvin, Iran; Department of Radiology (S Ghozy MD), Mayo Clinic, Rochester, MN, USA; NIHR Global Health Research Unit on Global Surgery (J C Glasbey MSc), University of Birmingham, Birmingham, UK; Health Systems and Policy Research (M Golechha PhD), Indian Institute of Public Health, Gandhinagar,

India; Department of Genetics (P Goleij MSc), Sana Institute of Higher Education, Sari, Iran; Public Health Department (G G Goyomsa MPH), Salale University, Fitche, Ethiopia; Department of Family and Community Medicine (M I M Gubari PhD), University Of Sulaimani, Sulaimani, Iraq; Department of Anesthesia (Z Gudisa MSc), Madda Walabu University, Goba, Ethiopia; Department of Community Medicine (D A Gunawardane MD), University of Peradeniya, Kandy, Sri Lanka; Department of Cardiology (R Gupta MD), Lehigh Valley Health Network, Allentown, PA, USA; 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 Non-communicable Diseases and Nutrition (R Gupta MPH), BRAC University, Dhaka, Bangladesh; Toxicology Department (S Gupta MSc), Shriram Institute for Industrial Research, Delhi, India; Faculty of Medicine Health and Human Sciences (Prof V K Gupta PhD), Macquarie University, Sydney, NSW, Australia; Department of Midwifery (A Guta MSc), Department of Nursing (Y Solomon MSc), Department of Public Health (A A Umer MPH), Dire Dawa University, Dire Dawa, Ethiopia; School of Medicine (P Habibzadeh MD), University of Maryland, Baltimore, MD, USA; School of Health and Environmental Studies (Prof S Hamidi DrPH), Hamdan Bin Mohammed Smart University, Dubai, United Arab Emirates; Department of Epidemiology (A J Handal PhD), University of Michigan, Ann Arbor, MI, USA; Department of Biochemistry and Molecular Biology (Prof M Hannan PhD), Bangladesh Agricultural University, Mymensingh, Bangladesh; Department of Anatomy (Prof M Hannan PhD), Dongguk University, Gyeongju, South Korea; Medical Research Unit (H Harapan PhD), Universitas Syiah Kuala (Syiah Kuala University), Banda Aceh, Indonesia; Institute for Social Science Research (M Hasan MPH), ARC Centre of Excellence for Children and Families over the Life Course (M Hasan MPH), The University of Queensland, Indooroopilly, QLD, Australia; Department of Ophthalmology (H Hasani MD), Iran University of Medical Sciences, Karaj, Iran; Independent Consultant, Tabriz, Iran (H Hassankhani PhD); 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), Xi'an Jiaotong University, Xi'an, China; Independent Consultant, Santa Clara, CA, USA (G Heidari MD); Department of Nutrition (S Y Hess PhD), University of California Davis, Davis, CA, USA; Micronutrient Forum, Washington, DC, USA (S Y Hess PhD); Department of Public Health (D Z Heyi MPH), Madda Walabu University, Robe, Ethiopia; Department of Applied Microbiology (K Hezam PhD), Taiz University, Taiz, Yemen; Department of Microbiology (K Hezam PhD), Nankai University, Tianjin, China; Division for Health Service Promotion (Y Hiraike PhD), University of Tokyo, Tokyo, Japan; Institute of Research and Development (M Hosseinzadeh PhD), Institute for Global Health Innovations (L G Vu MSc), Faculty of Medicine (L G Vu MSc), Duy Tan University, Da Nang, Viet Nam; Clinical Legal Medicine Department (S Hostiuc PhD), National Institute of Legal Medicine Mina Minovici, Bucharest, Romania; Czech National Centre for Evidence-Based Healthcare and Knowledge Translation (S Hussain PhD), Institute of Biostatistics and Analyses (S Hussain PhD), Masaryk University, Brno, Czech Republic; Department of Community Medicine (O S Ilesanmi PhD), Department of Medicine (Prof M O Owolabi DrM), University College Hospital, Ibadan, Ibadan, Nigeria; Faculty of Medicine (I M Ilic PhD), University of Belgrade, Belgrade, Serbia; Division of Community Health and Family Medicine (L R Inbaraj MD), Bangalore Baptist Hospital, Bangalore, India; 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 Orthodontics and Dentofacial Orthopedics (L J BDS), Dr D Y Patil University, Pune, India; Division of Pulmonary Medicine (E Jamshidi PharmD), Lausanne University Hospital (CHUV), Lausanne, Switzerland; Postgraduate Institute of Medicine (U Jayarajah MD), University of Colombo, Colombo, Sri Lanka; Department of Surgery (U Jayarajah MD), National Hospital, Colombo, Sri Lanka; Department of Biochemistry (Prof S Jayaram MD), Government Medical College, Mysuru, India; Department of Epidemiology (R Jebai MPH), Florida International University, Miami, FL, USA; Department of Anesthesiology (B Jemal MSc), Department of Human Nutrition (T Muche MPH), School of Public Health (B Seboka MPH), Department of Public Health (G A Zenebe MPH), Dilla University, Dilla, Ethiopia; Interdisciplinary School of Health Sciences (A Jeyakumar PhD), Savitribai Phule Pune University, Pune, India; Food Evolution Research Laboratory (A Jeyakumar PhD), School of Tourism and Hospitality Management, Johannesburg, South Africa; Department of Community Medicine (R P Jha MSc), Dr Baba Saheb Ambedkar Medical College and Hospital, Delhi, India; Department of Community Medicine (R P Jha MSc), Banaras Hindu University, Varanasi, India; Institute of Molecular and Clinical Ophthalmology Basel, Basel, Switzerland (Prof J B Jonas MD); Department of Ophthalmology (Prof J B Jonas MD), Heidelberg University, Mannheim, Germany; Department of Family Medicine and Public Health (J J Jozwiak PhD), University of Opole, Opole, Poland; Social Determinants of Health Research Center (L R Kalankesh PhD), Gonabad University of Medical Sciences, Gonabad, Iran; Division of Epidemiology and Biostatistics (V K Kamal PhD), National Institute of Epidemiology, Chennai, India; Sydney Eye Hospital (H Kandel PhD), South Eastern Sydney Local Health District, Sydney, NSW, Australia; School of Health Professions and Human Services (I M Karaye MD), Hofstra University, Hempstead, NY, USA; Department of Physical Therapy and Health Rehabilitation (F Z Kashoo MSc), Majmaah University, Majmaah, Saudi Arabia; Centre for Tropical Diseases and Global Health (P D Katoto PhD), Catholic University of Bukavu, Bukavu, Democratic Republic of the Congo; Department of Global Health (P D Katoto PhD), Stellenbosch University, Cape Town, South Africa; Surgery Research Unit (J H Kauppila MD), University of Oulu, Oulu, Finland; Department of Molecular Medicine and Surgery (J H Kauppila MD), Department of Medicine (D K Mohammad PhD), Department of Global Public Health (Prof A Pathak PhD), Karolinska Institute, Stockholm, Sweden; 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; Injury Division (V R Keshri MD), The George Institute for Global Health, New Delhi, India; 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 Institute of Public Health (M Shannawaz PhD), Amity University, Noida, India; Health Promotion Research Center (M Khammarnia PhD, H Okati-Aliabad PhD), Zahedan University of Medical Sciences, Zahedan, Iran; Department of Pediatrics (I A Khan MD), Rutgers University, New Brunswick, NJ, USA; Primary Care Department (M A Khan MSc), NHS North West London, London, UK; Department of Health and Wellbeing (Prof K Khatab PhD), Sheffield Hallam University, Sheffield, UK; Department of Epidemiology and Statistics (Z Khazaei MSc), Department of Biostatistics and Epidemiology (M Taheri Soodejani PhD), Shahid Sadoughi University of Medical Sciences, Yazd, Iran; Iranian Research Center on Healthy Aging (Z Khazaei MSc), Sabzevar University of Medical Sciences, Sabzevar, Iran; Department of Public Health (Prof J Khubchandani PhD), New Mexico State University, Las Cruces, NM, USA; 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; Independent Consultant, Jakarta, Indonesia (S Kosen MD); Kasturba Medical College, Udupi, India (S Koulmane Laxminarayana 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 Biochemistry (Prof M Kuddus PhD), University of Hail, Hail, Saudi Arabia; Amity Institute of Biotechnology (N Kumar PhD), Amity University Rajasthan, Jaipur, India; Faculty of Health and Life Sciences (O P Kurmi PhD), Coventry University, Coventry, UK; Health and Nutrition Section (O Kuti MSc), United Nations Children's Fund, Accra, Ghana; Unit of Genetics and Public Health (Prof I Landires MD), Institute of Medical Sciences, Las Tablas, Panama; Ministry of Health, Herrera, Panama (Prof I Landires MD); 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; Robinson Research Institute (Z S Lassi PhD), University of Adelaide, Adelaide, SA, Australia; Centre for Family Welfare (K Latief MSE), University of Indonesia, Depok, Indonesia; Global Health and Health Security (K Latief MSE), Taipei Medical University, Taipei, Taiwan; National Institute of Nutrition (Prof A Laxmaiah PhD), Indian Council of Medical Research, Hyderabad, India; Clinical and Experimental Medicine (C Ledda PhD), Department of General Surgery and Medical-Surgical Specialties (M Vacante PhD), Department of Medical and Surgical Sciences and Advanced Technologies (Prof M Veroux PhD), University of Catania, Catania, Italy; Pattern Recognition and Machine Learning Lab (Prof S Lee PhD), Gachon University, Seongnam, South Korea; Lerner Research Institute (X Liu PhD), Cleveland Clinic, Cleveland, OH, USA; Department of Quantitative Health Science (X Liu PhD), Department of Neonatology (I Qattea MD), Department of Pediatrics (S Sankararaman MD), Case Western Reserve University, Cleveland, OH, USA; Department of Health Economics (L Lorenzovici MSc), Syreon Research Romania, Targu Mures, Romania; Department of Doctoral Studies (L Lorenzovici MSc), George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureș, Tirgu Mures, Romania; Clinical Research Unit (Prof V S Machado PhD, Prof J Mendes PhD), Centro de Investigação Interdisciplinar Egas Moniz (Egas Moniz Interdisciplinary Research Center), Monte da Caparica, Portugal; Department of Community Medicine (P B Mahajan MD), Jawaharlal Institute of Postgraduate Medical Education and Research, Karaikal, India; Cellular and Molecular Biology Research Center (Prof S Mahjoub PhD), Department of Clinical Biochemistry (Prof S Mahjoub PhD, A Mosapour PhD), Babol University of Medical Sciences, Babol, Iran; Department of Clinical Pharmacy (T Mallhi PhD), Jouf University, Sakaka, Saudi Arabia; Department of Maternal and Child Nursing and Public Health (Prof D C Malta PhD), Federal University of Minas Gerais, Belo Horizonte, Brazil; Department of Midwifery (S Masoumi PhD), Hamadan University of Medical Sciences, Hamadan, Iran; Department of Epidemiology and Biostatistics (J C Medina MD), University of the Philippines Manila, Manila, Philippines; Department of Global Health (J C Medina MD), University of the Ryukyus, Nishihara, Japan; Peru Country Office (W Mendoza MD), United Nations Population Fund, Lima, Peru; Faculty of Civil Engineering (Prof O Mendoza-Cano PhD), University of Colima, Colima, Mexico; International Dx Department (A A Mentis MD), BGI Genomics, Copenhagen, Denmark; University Centre Varazdin (T Mestrovic PhD), University North, Varazdin, Croatia; Department of Propedeutics of Internal Diseases and Arterial Hypertension (Prof T Miazgowski MD), Pomeranian Medical University, Szczecin, Poland; Department of Statistics and Econometrics (A Mirica PhD, I Petcu PhD), Bucharest University of Economic Studies, Bucharest, Romania; Environmental Health Research Center (S Mohammadi PhD), Research Institute for Health Development (S Mohammadi PhD), Kurdistan University of Medical Sciences, Sanandaj, Iran; Health Systems and Policy Research Unit (S Mohammed PhD), Department of Community Medicine (M B Sufiyan MD), Ahmadu Bello University, Zaria, Nigeria; Department of Health Care Management (S Mohammed PhD), Technical University of Berlin, Berlin, Germany; Substance Abuse and Toxicology Research Center (S Mohan PhD), Department of Health Education and Promotion (M Shanawaz MD), Jazan University, Jazan, Saudi Arabia; Center for Transdisciplinary Research (S Mohan PhD), Saveetha Institute of Medical and Technical Science, Chennai, India; Oncology Department (N Moka MD), Appalachian Regional Healthcare, Hazard, KY, USA; Department of Internal Medicine (N Moka MD), University of Kentucky, Lexington, KY, USA; Clinical Epidemiology and Public Health Research Unit (L Monasta DSc), Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy; Department of Medicine (E Mostafavi PhD), Stanford Cardiovascular Institute (E Mostafavi PhD), Stanford University, Palo Alto, CA, USA; Department of Surgery (F Mulita PhD), General University Hospital of Patras, Patras, Greece; Medical School (F Mulita PhD), University of Thessaly, Larissa, Greece; Surgery Department (A Musina MD), University of Medicine and Pharmacy Grigore T Popa, Iasi, Romania; Second Surgical Unit (A Musina MD), Regional Institute of Oncology Iasi, Iasi, Romania; Department of Pediatrics and Pediatric Pulmonology (Prof G Mustafa MD), Institute of Mother and Child Care, Multan, Pakistan; Research and Analytics Department (A J Nagarajan Mtech), Initiative for Financing Health and Human Development, Chennai, India; Department of Research and Analytics (A J Nagarajan Mtech), Bioinsilico Technologies, Chennai, India; Health Workforce Department (T S Nair MD), World Health Organisation, Geneva, Switzerland; Mysore Medical College and Research Institute (Prof S Narasimha Swamy MD), Government Medical College, Mysore, India; Department of Health Policy and Oral Epidemiology (Z S Natto DrPH), Harvard T H Chan School of Public Health (P M S Pradhan MD), Harvard University, Boston, MA, USA; Department of Biological Sciences (S Naz PhD, R Z Raza PhD), National University of Medical Sciences, Rawalpindi, Pakistan; Department of General Surgery (I Negoi PhD), Emergency Hospital of Bucharest, Bucharest, Romania; Department of Cardiology (R I Negoi PhD), Cardio-Aid, Bucharest, Romania; Department of Public Health (G Nguefack-Tsague PhD), University of Yaoundé I, Yaoundé, Cameroon; Department of Biological Sciences (J W Ngunjiri DrPH), University of Embu, Embu, Kenya; International Islamic University Islamabad, Islamabad, Pakistan (R K Niazi PhD); Public Health Department (D Nurrika PhD), Banten School of Health Science, South Tangerang, Indonesia; Higher Education Service Institutions (LL-DIKTI) Region IV (D Nurrika PhD), Ministry of Research, Technology and Higher Education, Bandung, Indonesia; Population Science Department (K Nuruzzaman PhD), Jatiya Kabi Kazi Nazrul Islam University, Mymensingh, Bangladesh; Department of Physiology (O J Nzoputam PhD), University of Benin, Edo, Nigeria; Department of Physiology (O J Nzoputam PhD), Benson Idahosa University, Benin City, Nigeria; Department of Applied Economics and Quantitative Analysis (Prof B Oancea PhD), University of Bucharest, Bucharest, Romania; National Institute of Infectious Diseases (R M Obaidur PhD), Center for Surveillance, Immunization, and Epidemiologic Research, Tokyo, Japan; Center for Evidence-Based Medicine and Clinical Research, Dhaka, Bangladesh (R M Obaidur PhD); Department of Anesthesia (M S Obsa BhlthSci), College of Health Sciences and Medicine (M S Obsa BhlthSci), Department of Public Health (Y Sisay MPH), Wolaita Sodo University, Wolaita Sodo, Ethiopia; Discipline of Public Health Medicine (J N Odhiambo MSc, R E Ogunsakin PhD), School of Nursing and Public Health (E E Tarkang PhD), University of KwaZulu-Natal, Durban, South Africa; Department of Management Science and Technology (J N Odhiambo MSc), Technical University of Kenya, Nairobi, Kenya; School of Pharmacy (O C Okonji MSc), University of the Western Cape, Cape Town, South Africa; Department of Psychiatry and Behavioral Sciences (A O Oladunjoye MD), General Internal Medicine (O O Oladunjoye MD), Baylor College of Medicine, Houston, TX, USA; Department of Psychiatry (A T Olagunju MD), University of Lagos, Lagos, Nigeria; Department of Anatomic Pathology (A E E Omonisi FWACP), Ekiti State University, Ado Ekiti, Nigeria; Department of Anatomic Pathology (A E E Omonisi FWACP), Ekiti State University Teaching Hospital, Ado Ekiti, 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 Epidemiology (R Pakzad PhD), Ilam University of Medical Sciences, Ilam, Iran; Health Services Management Training Centre (T Palicz MD), Semmelweis University, Budapest, Hungary; Hungarian Health Management Association, Budapest, Hungary (T Palicz MD); Parul Institute of Public Health (A Pandya PhD), Parul University, Vadodara, India; Department of Science and Mathematics (Prof P Papadopoulou PhD), Deree – The American College of Greece, Athens, Greece; Department of Biophysics (Prof P Papadopoulou PhD), University of Athens, Athens, Greece; Vision and Eye Research Institute (Prof S Pardhan PhD), Anglia Ruskin University, Cambridge, UK; Global Health Governance Programme (J Patel BSc), University of Edinburgh, Edinburgh, UK; School of Dentistry (J Patel BSc), University of Leeds, Leeds, UK; Department of Pediatrics (Prof A Pathak PhD), RD Gardi Medical College, Ujjain, India; Department of Pharmacology (A R Pathan PhD), Shaqra University, Shaqra, Saudi Arabia; Research Consultancy (A R Pathan PhD), Author Gate Publications, Malegaon, India; Central Department of Public

Health (R Paudel MPH), Faculty of Humanities and Social Sciences (U Paudel PhD), Department of Community Medicine (P M S Pradhan MD), Tribhuvan University, Kathmandu, Nepal; Department of Genetics (S Pawar PhD), Yale University, New Haven, CT, USA; Curtin School of Population Health (Prof G Pereira PhD), Curtin University, Bentley, WA, Australia; Centre for Fertility and Health (Prof G Pereira PhD), Norwegian Institute of Public Health, Oslo, Norway; Mario Negri Institute for Pharmacological Research, Bergamo, Italy (N Perico MD, Prof G Remuzzi MD); Department of Biology (Prof S Perna PhD), University of Bahrain, Sakir, Bahrain; Department of Zoology (Prof N Perumalsamy PhD), Yadava College, Madurai, India; Department of Zoology (Prof N Perumalsamy PhD), Annai Fathima College, Madurai, India; International Center of Medical Sciences Research, Islamabad, Pakistan (Z Z Piracha PhD); Institute of Infection and Immunity (R C G Pollok FRCP), St George's University of London, London, UK; Department of Biochemistry (Prof A Prashant PhD), Jagadguru Sri Shivarathreeswara University, Mysuru, India; Department of Anesthesia (F Rahim PhD), Cihan University of Sulaimaniya, Sulaimaniya, Iraq; Data Mining Research Unit (A Rahman PhD), Charles Sturt University, Wagga Wagga, NSW, Australia; Department of Population Science and Human Resource Development (M Rahman DrPH), University of Rajshahi, Rajshahi, Bangladesh; Future Technology Research Center (A Rahmani PhD), National Yunlin University of Science and Technology, Yunlin, Taiwan; Society for Health and Demographic Surveillance, Suri, India (R Rai MPH); Department of Economics (R Rai MPH), University of Göttingen, Göttingen, Germany; Department of Medical, Surgical and Experimental Sciences (I Raimondo MD), University of Sassari, Sassari, Italy; Gynecology and Breast Care Center (I Raimondo MD), Mater Olbia Hospital, Olbia, Italy; Department of Community Medicine (S Rajaa MD), Employees' State Insurance Model Hospital, Chennai, India; Department of Epidemiology, Biostatistics and Occupational Health (J Rana MPH), McGill University, Montreal, QC, Canada; Research and Innovation Division (J Rana MPH), South Asian Institute for Social Transformation, Dhaka, Bangladesh; Institute of Food Science and Nutrition (M A Ranjha BSc), University of Sargodha, Sargodha, Pakistan; Department of Oral Pathology (S Rao MDS), Sharavathi Dental College and Hospital, Shimogga, India; Department of Epidemiology (S Rashedi MD), Department of International Studies (P Shobeiri MD), Non-Communicable Diseases Research Center, Tehran, Iran; Department of Primary Care and Public Health (Prof S Rawaf MD), Imperial College London, London, UK; Academic Public Health England (Prof S Rawaf MD), Public Health England, London, UK; School of Health, Medical and Applied Sciences (L Rawal PhD), CQ University, Sydney, NSW, Australia; Department Biological Sciences (Prof E M M Redwan PhD), King Abdulaziz University, Jeddah, Egypt; Department of Protein Research (Prof E M M Redwan PhD), Research and Academic Institution, Alexandria, Egypt; Medical Toxicology and Drug Abuse Research Center (M Rezaei MD), Department of Epidemiology and Biostatistics (A Tiyuri MSc), Birjand University of Medical Sciences, Birjand, Iran; Surgery Division (Prof T Richards MD), University of Western Australia, Perth, WA, Australia; Anaesthesia and Perioperative Medicine (Prof T Richards MD), Monash Health, Melbourne, VIC, Australia; Department of Surgery (J Rickard MD), University of Minnesota, Minneapolis, MN, USA; Department of Surgery (J Rickard MD), University Teaching Hospital of Kigali, Kigali, Rwanda; 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; Golestan Research Center of Gastroenterology and Hepatology (G Roshandel PhD), Department of Microbiology (A Tahamtan PhD), Golestan University of Medical Sciences, Gorgan, Iran; Faculty of Medicine (B Roy PhD), Quest International University Perak, Ipoh, Malaysia; Department of Internal Medicine (G M Rwegerera MD), University of Botswana, Gaborone, Botswana; Cardiovascular Department (Prof A M A Saad MD), Zagazig University, Zagazig, Egypt; Health Information Management (M Sadeghi PhD), Semnan University of Medical Sciences, Semnan, Iran; Multidisciplinary Laboratory Foundation University School of Health Sciences (Prof U Saeed PhD), Foundation University, Islamabad, Pakistan; Department of Development Studies (H Sahoo PhD), International Institute for Population Sciences, Mumbai, India; Public Health and Community Medicine Department (M R Salem MD), Cairo University, Giza, Egypt; Department of Pediatrics (S Sankararaman MD), University Hospitals Rainbow Babies and Children's Hospital, Cleveland, OH, USA; Daccude, Todi, Italy (R Santoro MA); UGC Centre of Advanced Study in Psychology (M Satpathy PhD), Utkal University, Bhubaneswar, India; Udyam-Global Association for Sustainable Development, Bhubaneswar, India (M Satpathy PhD); Department of Preventive and Social Medicine (G Saya MD), Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India; Department of Food Science and Nutrition (A M Senbeta MSc), Jigjiga University, Jigjiga, Ethiopia; Emergency Department (S Senthilkumaran MD), Manian Medical Centre, Erode, India; National Heart, Lung, and Blood Institute (A Seylani BS), National Institutes of Health, Rockville, MD, USA; Infectious Diseases and Microbiology (P A Shah MBBS), Rajiv Gandhi University of Health Sciences, Bangalore, India; HepatoPancreatoBiliary Surgery and Liver Transplant (P A Shah MBBS), HealthCare Global Limited Cancer Care Hospital, Bangalore, India; Independent Consultant, Karachi, Pakistan (M A Shaikh MD); Department of Medical Oncology (P Sharma MD), Kent Hospital, Warwick, RI, USA; Department of Health in Disasters and Emergencies (R Sheikhi BHlthSci), Shahrekord University of Medical Sciences, Shahrekord, Iran; Department of Microbiology (S M Shenoy MD), Kasturba Medical College, Mangalore, India; Department of Biochemistry (J K Shetty MD), Royal College of Surgeons in Ireland - Medical University of Bahrain, Busaiteen, Bahrain; College of Medicine (Prof J Shin MD), Yonsei University, Seoul, South Korea; Clinical Immunology and Hematology (V Shivarov PhD), Sofiamed University Hospital, Sofia, Bulgaria; Department of Genetics (V Shivarov PhD), Sofia University "St Kliment Ohridiski", Sofia, Bulgaria; Nursing and Health Sciences (S Shorofi PhD), Flinders University, Adelaide, SA, Australia; Department of International Health (M K Sikder Phd), Department of Health Policy and Management (D Vervoort MD), Johns Hopkins University, Baltimore, MD, USA; 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, Birmingham, AL, USA; Faculty of Medicine and Health Sciences (Prof N P Singh MD), Shree Guru Gobind Singh Tricentenary University, Gurugram, India; Department of Infectious Diseases and Epidemiology (A A Skryabina MD), Pirogov Russian National Research Medical University, Moscow, Russia; Institute of Child and Adolescent Health (Y Song PhD), Peking University, Beijing, China; Maternal and Child Health Division (S Sultana MPH), Projahnmo Research Foundation, Dhaka, Bangladesh; Department of Dermatology (M D Szeto BS), University of Colorado, Aurora, CO, USA; Department of Surgery (K Tan PhD), National University of Singapore, Singapore; Department of Economics (N Y Tat MS), Rice University, Houston, TX, USA; Research and Innovation (N Y Tat MS), Enventure Medical Innovation, Houston, TX, USA; Department of Public Health (Y M Tefera MPH), Dire Dawa University, Dire Dawa, Ethiopia; Department of Clinical Epidemiology (A Thiyagarajan MPH), Leibniz Institute for Prevention Research and Epidemiology, Bremen, Germany; Faculty of Public Health (J H V Ticoalu MPH), Universitas Sam Ratulangi, Manado, Indonesia; Department of Pharmacy (B M Tigabu PhD), Komar University of Science and Technology, Sulaymaniyah, Iraq; Department of Social Security Empirical Research (Prof R Tobe-Gai PhD), National Institute of Population and Social Security Research, Tokyo, Japan; Saveetha Dental College and Hospitals (M R Tovani-Palone PhD), Saveetha Institute of Medical and Technical Sciences, Chennai, India; Modestum, Eastbourne, UK (M R Tovani-Palone PhD); School of Public Health and Social Work (M T N Tran PhD), Queensland University of Technology, Brisbane, QLD, Australia; Health Informatics Department (M T N Tran PhD), Hanoi Medical University, Ha Noi, Viet Nam; Department of Epidemiology and Biostatistics (B S Tusa MPH), Haramaya University, Haramaya, Ethiopia; Clinical Cancer Research Center (S Valadan Tahbaz PhD), Milad General Hospital, Tehran, Iran; Department of Microbiology

(S Valadan Tahbaz PhD), Islamic Azad University, Tehran, Iran; Argentine Society of Medicine, Buenos Aires, Argentina (Prof P R Valdez MEd); Velez Sarsfield Hospital, Buenos Aires, Argentina (Prof P R Valdez MEd); Department of Infectious Disease (Prof S Vaziri MD), Medical Biology Research Center (K Yari BDM), Kermanshah University of Medical Sciences, Kermanshah, Iran; Department of Community Medicine (N D Wickramasinghe MD), Rajarata University of Sri Lanka, Anuradhapura, Sri Lanka; Department of Public Health (T E Wonde MPH), Debre Markos University, Debre Markos, Ethiopia; Cardiovascular Program (X Xu PhD), The George Institute for Global Health, Sydney, NSW, Australia; Department of Health Management (A Yigit PhD, V Yiğit PhD), Süleyman Demirel Üniversitesi (Süleyman Demirel University), Isparta, Türkiye; Department of Pediatrics (D Yon MD), Kyung Hee University, Seoul, South Korea; 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; Department of Epidemiology and Biostatistics (Prof C Yu PhD), School of Medicine (Z Zhang PhD), Wuhan University, Wuhan, China; Department of Pharmacology (B A Zaman MSc), University of Duhok, Duhok, Iraq; Medical College of La Paz, La Paz, Bolivia (N Zamora MD); Research and Development Department (I Zare BSc), Sina Medical Biochemistry Technologies, Shiraz, Iran.

Contributors

Please see appendix (pp 924–929) for more detailed information about individual author contributions to the research, divided into the following categories: managing the overall research enterprise; 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; developing methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the estimation or publications process. W M Gardner and N J Kassebaum verified the underlying raw data and were responsible for the decision to submit the manuscript for publication. All other authors had access to and reviewed estimates as part of the research evaluation process, which included additional stages of formal review.

Declaration of interests

S Afzal reports participation on a data safety monitoring board or advisory board with the National Bioethics Committee of Pakistan, King Edward Medical University Institutional Review Board, and the Ethics Review Board in Board of Studies; a leadership or fiduciary role with the Pakistan Association of Medical Editors, as a Fellow of Faculty of Public Health (FFPH) Royal Colleges UK, and an advocacy role in the Society of Prevention and Advocacy Research with King Edward Medical University, Lahore, Pakistan, all outside the submitted work. R Agustina reports leadership or fiduciary roles with the Multiple Micronutrient Supplementation Technical Advisory Group of the New York Academy of Sciences and with the Indonesia Technical Advisory Board for Multimicronutrient Supplemenation, outside the submitted work. R Ancuceanu reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from AbbVie, Sandoz, B Braun, and Laropharm, outside the submitted work. S Das is a member of the Personalized Medicine Division of the American Association of Clinical Chemistry and a member of the Royal College of Biology; and reports other financial interests through a research grant of 1·6 million INR from the Department of Science and Technology, Government of India; all outside the submitted work. C Hennessy reports support for the present work from the Institute for Health Metrics and Evaluation and the Center for Health System Effectiveness. N E Ismail is a council member of the Malaysian Academy of Pharmacy, outside the submitted work. J J Jozwiak reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Novartis and Adamed as personal payments, outside the submitted work. N J Kassebaum reports support for this manuscript from the Bill & Melinda Gates Foundation as grant payments to their institution (Institute of Health Metrics and Evaluation, University of Washington, Seattle, WA, USA). K Krishan reports non-financial support from UGC Centre of Advanced Study, CAS II, Department of Anthropology, Panjab University, Chandigarh, India, outside the submitted work. W Mendoza is a staff member at the UNFPA Peru Country Office, which does not necessarily endorse these results. A-F A Mentis reports grants or contracts from MilkSafe: a novel pipeline to enrich formula milk using omics technologies, a project co-financed by the European Regional Development Fund of the European Union and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH – CREATE – INNOVATE (project code T2EDK-02222) and from ELIDEK (Hellenic Foundation for Research and Innovation, MIMS-860); has received payment for expert testimony as a peer-reviewer for Fondazione Cariplo, Italy; serves as an editorial board member for the journals *Systematic Reviews* and *Annals of Epidemiology*, and as an Associate Editor for *Translational Psychiatry*; and is a scientific officer with the BGI Group; all outside the submitted work. N Moka is Treasurer of the Kentucky Society of Clinical Oncology, outside the submitted work. A Ortiz reports grants or contracts from Sanofi as payments to their institution (IIS-Fundacion Jiménez Díaz UAM, Madrid, Spain); consulting fees from Advicienne, Astellas Pharma, AstraZeneca, Amicus Therapeutics, Amgen, Boehringer Ingelheim, Fresenius Medical Care, GSK, Bayer, Sanofi-Genzyme, Menarini, Mundipharma, Kyowa Kirin, Lilly, Alexion Pharmaceuticals, Freeline Therapeutics, Idorsia, Chiesi, Otsuka Pharmaceutical, Novo Nordisk, Sysmex, and Vifor Fresenius Medical Care Renal Pharma; support for travel from Advicienne, Astellas Pharma, AstraZeneca, Amicus Therapeutics, Amgen, Boehringer Ingelheim, Fresenius Medical Care, GSK, Bayer, Sanofi-Genzyme, Menarini, Mundipharma, Kyowa Kirin, Lilly, Alexion Pharmaceuticals, Freeline Therapeutics, Idorsia, Chiesi, Otsuka Pharmaceutical, Novo Nordisk, Sysmex, and Vifor Fresenius Medical Care Renal Pharma; a leadership or fiduciary role with the European Renal Association, a role as Director of the Catedra Mundipharma-UAM of diabetic kidney disease and the Catedra AstraZeneca-UAM of chronic kidney disease and electrolytes; and stock or stock options in Telara Pharma; all outside the submitted work. Z Quazi Syed reports support for this manuscript from the South Asia Infant Feeding Research Network and Datta Meghe Institute of Higher Education and Research, Wardha, India; grants or contracts from the Global Consortium for Public Health and Research and Datta Meghe Institute of Higher Education and Research; support for attending meetings and/or travel from the Division of Evidence Synthesis, Jawaharlal Nehru Medical College, Wardha, India, and Datta Meghe Institute of Medical Sciences, Wardha, India, outside the submitted work. T Richards reports grants or contracts from Vifor Pharma for PREVENT laboratory analysis; consulting fees from BioAge Labs for a clinical trial design; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Pharmacosmos through the CAVIAR education grant and from Pfizer for the IRONWOMAN trial; support for attending meetings from Pfizer, Pharmacosmos, and Vifor Pharma; a role as treasurer with NATA; and a role as Director of The Iron Clinic; all outside the submitted work. V Shivarov is an employee of ICON and reports stock or stock options in the company, all outside the submitted work. J A Singh reports consulting fees from Crealta/Horizon, MediSys, Fidia Farmaceutici, PK Med, Two Labs, Adept Field Solutions, Clinical Care Options, Clearview Healthcare Partners, Putnam Associates, Focus Forward, Navigant Consulting, Spherix Global Insights, Mediq, Jupiter Life Science, UBM, Trio Health, Medscape, WebMD, and Practice Point Communications, the National Institutes of Health, and the American College of Rheumatology; payment or honoraria for speakers bureaus from Simply Speaking; support for attending meetings or travel from the steering committee of OMERACT; participation on a data safety monitoring board or advisory board with the US Food and Drug Administration Arthritis Advisory Committee; membership of the steering committee of OMERACT, a role as Chair (unpaid) of the Veterans Affairs Rheumatology Field Advisory Committee, and roles as Editor and Director (unpaid) with the UAB Cochrane Musculoskeletal Group Satellite Center on Network

Meta-analysis; stock or stock options in TPT Global Tech, Vaxart Pharmaceuticals, Aytu BioPharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics, Seres Therapeutics, Tonix Pharmaceuticals, and Charlotte's Web Holdings, and previous stock options in Amarin, Viking Therapeutics, and Moderna Pharmaceuticals; all outside the submitted work. J D Stanaway reports support for this manuscript from the Bill & Melinda Gates Foundation as grants to their institution (Institute of Health Metrics and Evaluation, University of Washington, Seattle, WA, USA). P S Suchdev reports grants or contracts from the Centers for Disease Control and Prevention (CDC) and the Bill & Melinda Gates Foundation, all outside the submitted work. M F Young reports grants from the Bill & Melinda Gates Foundation and the CDC for a project titled Biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) and from the National Institutes of Health for a project titled Mother–child hemoglobin at preconception and first 1000 days and child development at 6 years; roles in the *Lancet Haematology* Commission on anaemia, the Anaemia Evidence Gap Map Advisory Group, as a subject matter expert on the advisory committee related to the Improving Estimates of Anemia in Global Burden of Disease research project, as a member of the technical advisory group for the Redefining Maternal Anaemia in Pregnancy and Postpartum project and a member of the WHO Guideline Development Group for Anemia; all outside the submitted work. All other authors declare no competing interests.

Data sharing

To download the data used in these analyses and corresponding results, please visit the Global Health Data Exchange at http://ghdx.healthdata.org.

Acknowledgments

This project was supported by the Bill & Melinda Gates Foundation. S Afzal acknowledges support from the Department of Community Medicine and Epidemiology, King Edward Medical University, Lahore, Pakistan. A Ahmad acknowledges Shaqra University, Shaqra, Saudi Arabia for supporting this work. A Badawi is supported by the Public Health Agency of Canada. L Belo acknowledges the support from Fundação para a Ciência e a Tecnologia in the scope of the project UIDP/04378/2020 and UIDB/04378/2020 of UCIBIO and the project LA/P/0140/2020 of i4HB. A Fatehizadeh acknowledges support from the Department of Environmental Health Engineering, Isfahan University of Medical Sciences, Isfahan, Iran. S Gaihre acknowledges the Institute of Applied Health Sciences, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, UK for their institutional support. J C Glasbey is supported by a National Institute for Health and Care Research Doctoral Research Fellowship (NIHR300175). V K Gupta acknowledges funding support from the National Health and Medical Research Council (NHMRC), Australia. S Hussain was supported by Operational Program Research, Development and Education project Postdoc2MUNI (number CZ.02.2.69/0.0/0.0/18_053/0016952). S M S Islam is funded by the NHMRC and has received funding from the National Heart Foundation of Australia. N Joseph acknowledges support from the Department of Community Medicine, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, India. H Kandel is supported by a Kornhauser Research Fellowship at The University of Sydney, Sydney, NSW, Australia. Y J Kim was supported by the Research Management Centre, Xiamen University Malaysia, Sepang, Malaysia (grant numbers XMUMRF/2020-C6/ITCM/0004). S L Koulmane Laxminarayana acknowledges institutional support from Manipal Academy of Higher Education, Manipal, India. K Krishan acknowledges non-financial support from UGC Centre of Advanced Study, CAS II, Department of Anthropology, Panjab University, Chandigarh, India. I Landires acknowledges support from Sistema Nacional de Investigación, which is supported by Panama's Secretaría Nacional de Ciencia, Tecnología e Innovación. K Latief acknowledges funding from Taipei Medical University, Taipei, Taiwan for doctoral education during the conduct of this review. D C Malta acknowledges support from Conselho Nacional de Pesquisas (CNPq), Brazil. L Monasta received support from the Italian Ministry of Health (Ricerca Corrente 34/2017) as payments made to the Institute for Maternal and Child Health - IRCCS Burlo Garofolo, Trieste, Italy. A Ortiz was supported by Instituto de Salud Carlos III RICORS programme to RICORS2040 (RD21/0005/0001) funded by European Union – NextGenerationEU, Mecanismo para la Recuperación y la Resiliencia and SPACKDc PMP21/00109, FEDER funds. J R Padubidri, A Shetty, B S K Shetty, P H Shetty, and B Unnikrishnan acknowledge the support given by Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, India. T Palicz acknowledges support from the National Research, Development and Innovation Office in Hungary (RRF-2.3.1-21-2022-00006, Data-Driven Health Division of National Laboratory for Health Security). G Pereira was supported with funding from NHMRC Project and Investigator Grants (1099655 and 1173991). Z Z Piracha acknowledges the International Center of Medical Sciences Research, Islamabad, Pakistan. Z Quazi Syed acknowledges support from the South Asia Infant Feeding Research Network and Datta Meghe Institute of Higher Education and Research, Wardha, India. A Rahman acknowledges Charles Sturt University, Wagga Wagga, NSW, Australia. U Saeed acknowledges the International Center of Medical Sciences Research, Islamabad, Pakistan. A M Samy acknowledges the support from Ain Shams University, Cairo, Egypt and the Egyptian Fulbright Mission Program. P A Shah acknowledges the support from Bangalore Medical College and Research Institute, part of the Rajiv Gandhi University of Health Sciences, Bangalore, India. M R Tovani-Palone acknowledges support from Saveetha Institute of Medical and Technical Sciences, Chennai, India. D Vervoort is supported by the Canadian Institutes of Health Research Vanier Canada Graduate Scholarship. X Xu is supported by a postdoctoral fellowship funded by the Heart Foundation of Australia (award number 102597) and Scientia Program at the University of New South Wales, Sydney, NSW, Australia. C Yu acknowledges support from the National Natural Science Foundation of China (grant number 82173626).

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