

Mapping geographical inequalities in oral rehydration therapy coverage in low-income and middle-income countries, 2000–17



Local Burden of Disease Diarrhoea Collaborators*



Summary

Background Oral rehydration solution (ORS) is a form of oral rehydration therapy (ORT) for diarrhoea that has the potential to drastically reduce child mortality; yet, according to UNICEF estimates, less than half of children younger than 5 years with diarrhoea in low-income and middle-income countries (LMICs) received ORS in 2016. A variety of recommended home fluids (RHF) exist as alternative forms of ORT; however, it is unclear whether RHF prevent child mortality. Previous studies have shown considerable variation between countries in ORS and RHF use, but subnational variation is unknown. This study aims to produce high-resolution geospatial estimates of relative and absolute coverage of ORS, RHF, and ORT (use of either ORS or RHF) in LMICs.

Methods We used a Bayesian geostatistical model including 15 spatial covariates and data from 385 household surveys across 94 LMICs to estimate annual proportions of children younger than 5 years of age with diarrhoea who received ORS or RHF (or both) on continuous continent-wide surfaces in 2000–17, and aggregated results to policy-relevant administrative units. Additionally, we analysed geographical inequality in coverage across administrative units and estimated the number of diarrhoeal deaths averted by increased coverage over the study period. Uncertainty in the mean coverage estimates was calculated by taking 250 draws from the posterior joint distribution of the model and creating uncertainty intervals (UIs) with the 2·5th and 97·5th percentiles of those 250 draws.

Findings While ORS use among children with diarrhoea increased in some countries from 2000 to 2017, coverage remained below 50% in the majority (62·6%; 12 417 of 19 823) of second administrative-level units and an estimated 6 519 000 children (95% UI 5 254 000–7 733 000) with diarrhoea were not treated with any form of ORT in 2017. Increases in ORS use corresponded with declines in RHF in many locations, resulting in relatively constant overall ORT coverage from 2000 to 2017. Although ORS was uniformly distributed subnationally in some countries, within-country geographical inequalities persisted in others; 11 countries had at least a 50% difference in one of their units compared with the country mean. Increases in ORS use over time were correlated with declines in RHF use and in diarrhoeal mortality in many locations, and an estimated 52 230 diarrhoeal deaths (36 910–68 860) were averted by scaling up of ORS coverage between 2000 and 2017. Finally, we identified key subnational areas in Colombia, Nigeria, and Sudan as examples of where diarrhoeal mortality remains higher than average, while ORS coverage remains lower than average.

Interpretation To our knowledge, this study is the first to produce and map subnational estimates of ORS, RHF, and ORT coverage and attributable child diarrhoeal deaths across LMICs from 2000 to 2017, allowing for tracking progress over time. Our novel results, combined with detailed subnational estimates of diarrhoeal morbidity and mortality, can support subnational needs assessments aimed at furthering policy makers' understanding of within-country disparities. Over 50 years after the discovery that led to this simple, cheap, and life-saving therapy, large gains in reducing mortality could still be made by reducing geographical inequalities in ORS coverage.

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Introduction

Oral rehydration solution (ORS) is a simple treatment that can be prepared and used at home to prevent mortality due to dehydration and undernutrition in children with diarrhoea. This intervention is especially suitable in locations where intravenous fluids are scarce or unavailable,¹ and replaces indiscriminate and unnecessary use of antibiotics to treat diarrhoea.² ORS

was discovered more than 50 years ago when a physician in Dhaka, Bangladesh, found that treating patients with cholera with glucose-electrolyte solutions in equivalent amounts to fluid losses could prevent the need for intravenous liquids in 80% of patients.³ Shortly thereafter, its ability to prevent dehydration was shown in a trial in Kolkata, India,⁴ and during a cholera outbreak among Bangladeshi refugees in India.⁵ Since then,

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*Collaborators listed at the end of the Article

Correspondence to:
Dr Robert C Reiner Jr, Institute for Health Metrics and Evaluation, Department of Health Metrics Science, School of Medicine, University of Washington, Seattle, WA 98121, USA
bcreiner@uw.edu

Research in context

Evidence before this study

WHO's integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea emphasises the need to make resources available to properly prevent and treat these childhood infections, including use of oral rehydration solution (ORS) to treat diarrhoea. In 2016, UNICEF published national-level estimates of the proportion of children with diarrhoea who received ORS or any alternative recommended home fluids (RHF) for countries and years with available household survey data. To understand the full landscape of currently published estimates, we did a literature review on Feb 11, 2019, with no date or language restrictions. We searched the PubMed database for the following terms in titles or abstracts: "ORS", "ORT", "RHF", "oral rehydration solution", "oral rehydration therapy", "oral rehydration salts", and "recommended home fluids", with the necessary inclusion of "coverage". This returned 229 total studies, seven of which presented or reviewed national-level estimates of ORS coverage globally or across multiple countries, and 26 of which estimated ORS or RHF subnational coverage in select countries. None of these studies, however, estimated ORS or RHF coverage subnationally across multiple regions or used geospatial modelling techniques to estimate ORS or RHF coverage in locations with sparse data.

Added value of this study

To our knowledge, this study presents the first high-resolution subnational estimates of the proportion and absolute number of children younger than 5 years with diarrhoea that received ORS or RHF in low-income and middle-income countries (LMICs) from 2000 to 2017. This work supports the examination of how patterns of coverage have changed over time since the establishment of the Millennium Development Goals in 2000, the identification of subnational areas in need of targeted interventions, and the stratification of oral rehydration therapy coverage into ORS and RHF estimates. We used Bayesian

geostatistical modelling techniques and an extensive geolocated dataset to produce these estimates. Wherever possible, we tailored these methods to take into account national or subnational factors that might contribute to variation in ORS coverage, using spatially resolved covariates to estimate for areas with sparse data. These techniques produced estimates on continuous continent-wide surfaces, which we aggregated to policy-relevant administrative units. We show that ORS use has increased over time, and that increases in ORS use often corresponded to declines in RHF use to treat diarrhoea and in diarrhoeal mortality rate. We estimate that scaling up of ORS treatment over the study period prevented an estimated 52 230 deaths (36 910–68 860) across LMICs in 2017. Despite progress, coverage of ORS (ie, the proportion of children with diarrhoea who received ORS) remained below 50% in many locations where diarrhoea prevalence and mortality rates remain high. Importantly, we also show that while within-country geographical inequalities declined over time, large disparities remained in multiple countries with high diarrhoeal burden, including subnational areas of Colombia, Peru, Nigeria, and Sudan.

Implications of all the available evidence

Our mapped estimates identify areas with low ORS usage, which could indicate gaps in access to ORS or knowledge of its efficacy to treat diarrhoea, and illuminate areas where improvements in ORS coverage are needed. Together with maps of other key risk factors, including sanitation and childhood stunting, these results can be used to develop integrated strategies that prevent diarrhoeal morbidity and mortality on a local level. These estimates and corresponding visualisation tools can aid policy makers and public health practitioners in determining where increased efforts to reduce geographical inequalities in ORS coverage are needed to make further strides in reducing mortality with this simple therapy.

WHO, UNICEF, and the US Centers for Disease Control and Prevention have promoted ORS as an essential medicine to treat diarrhoea, the third leading cause of death in children younger than 5 years of age worldwide.⁶ In the 1980s, in response to low ORS coverage (ie, the proportion of children with diarrhoea who received ORS), WHO promoted the use of so-called recommended home fluids (RHF) in addition to ORS, and oral rehydration therapy (ORT) became the phrase used to refer to treatment with ORS or RHF.⁷ Despite its inclusion in the WHO Essential Medicines List and Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea,^{7–9} coverage of ORS remains low. According to UNICEF surveys, only 34% of children younger than 5 years in low-income and middle-income countries (LMICs) in 2000 received ORS to treat diarrhoea; in 2016, the proportion increased to 44%, yet the majority remained untreated.¹⁰

The efficacy of ORS and RHF in preventing child mortality relies on proper preparation of the solutions, which can vary depending on the resources available to a household. ORS is most commonly sold as premade packets with standardised sodium and glucose content, which need to be dissolved in 1 L of clean water and can then be stored for about 48 h.¹¹ The cost of these packets varies by country; in Uganda, a single packet costs approximately 500 Ugandan shillings (about US\$0.15),¹² and in Nigeria in 2012, the cost of three packets ranged from \$0.63 to \$4.38 depending on location.¹³ By contrast, RHF can be made with household items and therefore can be less costly and more widely accessible. The composition of RHF varies by country and can include carefully measured sugar and salt added to clean water, or it can simply include plain juice, rice water, tea, or coconut water.¹⁴ A meta-analysis study in 2010 estimated that 100% coverage of ORS could prevent

93% of diarrhoeal deaths, yet found insufficient evidence on the effectiveness of RHF in preventing mortality, probably due to the broad range in RHF composition.¹⁴

To understand trends in diarrhoeal deaths and ORT coverage across space and time, it is crucial to analyse ORS and RHF treatment separately. A study in Ethiopia found subnational geographical variation in ORT coverage, which was driven primarily by differences in wealth.¹⁵ A recent study including data from 88 LMICs showed an 8 percentage-point difference in ORT coverage on average between the wealthiest and poorest household quintiles, which was low compared with other interventions such as improvements to water and sanitation.¹⁶ These studies, however, did not analyse ORS and RHF separately and might have underestimated variation. Other studies have shown that ORS use can vary broadly between countries, even between those sharing borders.^{11,17} Additionally, studies have shown differences in ORS use between urban and rural populations in Kenya¹⁸ and Mexico.¹⁹ These findings suggest that there are subnational drivers of variation in ORS coverage, and that these drivers can differ between geographical regions. Moreover, previous studies showed subnational variation in diarrhoeal deaths and overall deaths in children younger than 5 years,^{20–22} some of which might be driven by subnational variation in ORS given its efficacy in reducing child mortality.

Furthermore, policies related to diarrhoea treatment set at the national level do not affect all subnational areas equally, and interventions are often implemented at the subnational level, such as those currently done in Nigeria and India.^{23,24} Local-level estimates of ORS and RHF coverage are thus needed to identify vulnerable subpopulations most in need of increased efforts to prevent child mortality. Yet, to our knowledge, no study has estimated ORS coverage subnationally across multiple regions or has used geospatial modelling techniques to estimate ORS coverage in locations with sparse data, and no study has compared ORS coverage to patterns in RHF coverage.

Our aim in this study was to estimate the proportions of children with diarrhoea who were treated with ORS and RHF (ie, ORS and RHF coverage, respectively) over space and time in LMICs and examine geographical inequalities within countries. Here we present, to our knowledge, the first maps of ORS or RHF coverage for second administrative-level units (eg, districts, counties; henceforth referred to as units) in LMICs. We present both relative quantities (proportion of children) and absolute quantities (number of children), as these measures have distinct policy implications. We conclude by highlighting countries with some of the broadest differences in coverage across subnational units, which also have high diarrhoeal burdens and high subnational variation in mortality.

Methods

Definitions

For this study, ORS was defined as a pre-packaged electrolyte solution containing glucose or another form of sugar or starch, as well as sodium, chloride, potassium, and bicarbonate.¹⁴ Survey questions did not allow us to separate RHF into their different formulations; therefore, RHF were defined as all possible home fluid alternatives, including sugar-salt solution, cereal-salt solution, rice-water solution, and additional fluids, such as plain water, juice, tea, or rice water.¹⁴ To account for this variation, we adjusted all non-standard RHF definitions to the most common or standard definition across all surveys, using logistic regression to determine adjustments (appendix 1 p 3). ORT was defined as treatment with either ORS, RHF, or both. Coverage was defined as the proportion of children younger than 5 years of age with diarrhoea who received ORS, RHF, or ORT. Diarrhoea was defined as three or more abnormally loose or watery stools within a 24-h period.

Data

We compiled 385 household surveys (including Demographic and Health Surveys, Multiple Indicator Cluster Surveys, and other country-specific surveys) representing 3 609 000 children with diarrhoea in 94 LMICs from 2000 to 2017, with geocoded information from 120 742 coordinates corresponding to survey clusters and 14 055 subnational polygon boundaries where point-level referencing was not available (appendix 1 p 4). We included surveys that asked if children younger than 5 years with diarrhoea received any kind of ORT, allowed for geolocation below the country level, and were representative of the populations in which they were conducted. We included surveys for countries classified as low income or middle income on the basis of their Socio-demographic Index (SDI) quintile: low SDI, low-middle SDI, or middle SDI.²⁵ SDI, developed as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), indicates the level of development based on a country's average education, fertility, and income, and is on a scale of 0 to 1.²⁵ Only LMICs with relevant and available underlying data were included in subsequent analyses, and island nations with fewer than 1 million inhabitants were excluded (appendix 1 p 4). This study complied with the Guidelines for Accurate and Transparent Health Estimates Reporting recommendations (appendix 1 pp 85–86).²⁶ Further details on data inclusion, coverage, and validation can be found in appendix 1 (pp 4, 8).

We compiled 15 spatial covariates that were indexed at the subnational level for all 94 countries included in the study and that had conceivable relationships with ORT, which were used as predictors in our model. Covariates related to urbanicity or access to cities were night-time lights, population, urban or rural location, urban proportion of the location, and access to cities. Covariates related to child health, support, and nutrition were

See Online for appendix 1

prevalence of under-5 stunting, prevalence of under-5 wasting, ratio of child dependents (ages 0–14 years) to working adults (ages 15–64 years), number of children younger than 5 years per woman of childbearing age, number of people whose daily vitamin A needs could be met, and maternal education. Covariates related to environmental factors that might affect diarrhoeal burden, which might in turn affect ORS supply, were aridity, distance from rivers or lakes, elevation, and irrigation. We also included the Healthcare Access and Quality Index²⁷ and the proportion of pregnant women who received four or more antenatal care visits as national-level covariates. We filtered these covariates for multicollinearity within each modelling region (appendix 1 p 5) using variance inflation factor (VIF) analysis with a VIF threshold of 3.²⁸ Detailed covariate information can be found in appendix 1 (p 5).

Statistical analysis

Analyses were done using R version 3.5.0. ORS, RHF, and ORT coverage were modelled separately using a Bayesian model-based geostatistical framework. Briefly, this framework uses a spatially and temporally explicit hierarchical logistic regression model to predict coverage in all locations, assuming that points that are closer together in space and time and that have similar covariate patterns have similar coverage. Potential non-linear relationships between covariates and coverage were incorporated through the use of a stacked generalisation technique.²⁹ Posterior distributions of all model parameters and hyperparameters were estimated using the statistical package R-INLA (version 19.05.30.9000).^{30,31} Uncertainty in the mean coverage estimates was calculated by taking 250 draws from the posterior joint distribution of the model, and each point value is reported with an uncertainty interval (UI), which represents the 2.5th and 97.5th percentiles of those 250 draws. Maps were produced using ArcGIS Desktop 10.6. Models were run independently in 14 geographically distinct modelling regions based on GBD,³² and an additional nine country-specific models due to distinct temporal patterns of ORS coverage in these countries compared with their surrounding regions. Additional methodological details can be found in appendix 1 (pp 5–7).

Models were validated using five-fold cross-validation. Holdout sets were created by combining randomised sets of datapoints at the second administrative-unit cluster level. Model performance was summarised by the bias (mean error), total variance (root-mean-square error), and 95% data coverage within prediction intervals, and correlation between observed data and predictions. Where possible, estimates from these models were compared against other existing estimates. All validation procedures and corresponding results are provided in appendix 1 (p 8).

We calculated population-weighted aggregations of the 250 draws of ORS, RHF, and ORT coverage estimates at

the country level, first administrative-level unit, and second administrative-level unit. To quantify geographical inequalities within countries over time, we used three different measures of inequality, each with their own strengths. We calculated Gini coefficients as a summary measure of inequality at the country level;³³ in brief, the Gini coefficient summarises the distribution of each indicator across the population, with a value of 0 representing perfect equality and a value of 1 representing maximum inequality (appendix 1 p 9). We quantified absolute percentage-point deviation from the country mean to illustrate the total percentage-point difference in coverage between each unit and its country mean. Finally, we used relative deviation from the country mean to illustrate the difference in ORS coverage between each unit and its country mean.

To investigate the relationship between ORT and diarrhoeal mortality, we used mortality estimates from Reiner and colleagues³⁴ and compared them with ORS coverage at the country and second administrative-unit levels. In addition, we did a counterfactual analysis to determine the estimated number of deaths averted due to changes in ORS coverage between 2000 and 2017, which is described in detail in appendix 1 (pp 9–10). In the counterfactual analysis, we treated ORS coverage as an independent risk factor and did not take into account how changes in demography or other risk factors affect deaths. We additionally did a sensitivity analysis of these results by halving and doubling the estimated lives that could be saved with ORS treatment¹⁴ (appendix 1 pp 82–83).

Role of the funding source

This research was supported by the Bill & Melinda Gates Foundation. The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

In all years from 2000 to 2017, we found both between-country and within-country variation in the proportion of children younger than 5 years with diarrhoea who received ORT. In general, ORS coverage was highest in south Asia, east Asia, central America, and southern sub-Saharan Africa, and lowest in central sub-Saharan Africa, parts of western and eastern sub-Saharan Africa, the Middle East, and South America (figure 1). Within these regions, some countries had fairly uniform subnational distribution of ORS across units, such as Zimbabwe in 2017, where coverage ranged from 35.1% (95% UI 11.8–66.6) in Chivi district, Masvingo province, to 44.6% (16.2–76.7) in Mazowe district, Mashonaland Central province. Other countries had notable subnational variation, such as Peru in 2017, where coverage ranged from 16.1% (12.1–20.6) in Azángaro province, Puno region, to 45.2% (38.2–51.5) in Trujillo province,

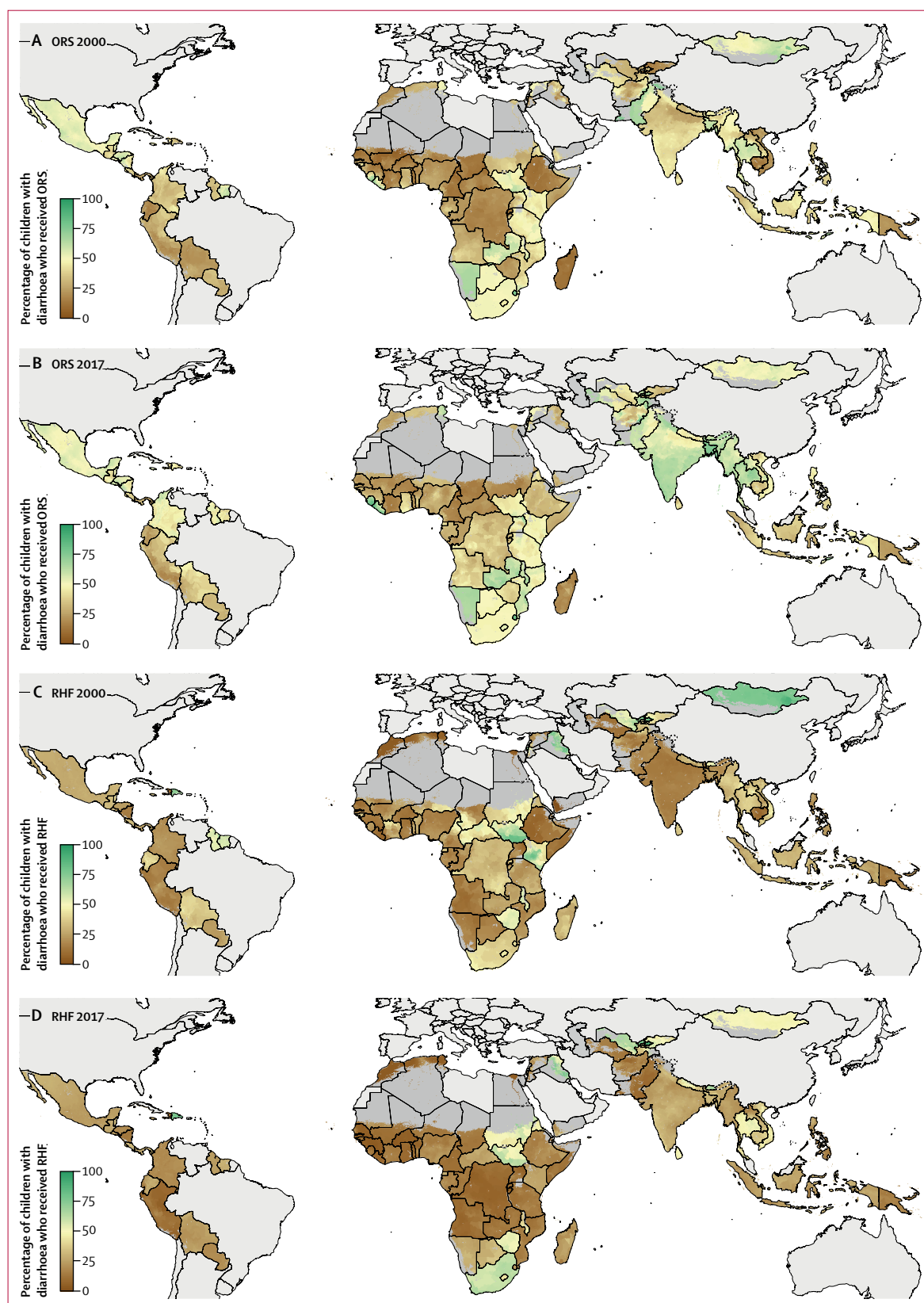


Figure 1: Proportion of children younger than 5 years with diarrhoea who received ORT at the second administrative-unit level, 2000 and 2017

Mean proportion of children with diarrhoea who received ORS in 2000 (A) and 2017 (B) or who received RHF in 2000 (C) and 2017 (D). All countries are aggregated to second administrative units. Maps reflect administrative boundaries, land cover, lakes, and population. Dark grey grid cells were classified as barren or sparsely vegetated and had fewer than ten people per 1 km x 1 km grid cell; light grey countries were not included in these analyses.³⁵⁻⁴⁰ ORS=oral rehydration solution. ORT=oral rehydration therapy. RHF=recommended home fluids.

For full model outputs see
<http://ghdx.healthdata.org/record/ihme-data/lmic-oral-rehydration-therapy-coverage-geospatial-estimates-2000-2017>

For the visualisation tool see
<https://vizhub.healthdata.org/lbd/ort>

See Online for appendix 2

La Libertad region (figure 1B). In terms of absolute coverage, RHF coverage was lower and more evenly distributed in Peru in 2017, with coverage ranging from 5.0% (2.9–8.5) in Coronel Portillo province, Ucayali, to 19.7% (12.3–28.9) in Daniel Alcides Carrión province, Pasco (figure 1D). Across all LMICs, ORS coverage remained below 50% in 62.6% (12 417 of 19 823) of units in 2017.

Although most changes were small, we found that ORS coverage increased while RHF coverage decreased between 2000 and 2017 in many locations (figure 1). We found significant increases in ORS coverage nationally and subnationally in Rwanda, Vietnam, Bolivia, Cambodia, and India (figure 1; appendix 1 p 75; appendix 2 pp 1–8, 25–1615), and significant declines in RHF coverage in Rwanda, Burundi, Bolivia, Niger, Chad, and India (figure 1; appendix 1 p 76; appendix 2 pp 9–16, 1616–3206). In Rwanda, ORS coverage increased from 12.0% (95% UI 9.8 to 14.6) to 33.9% (22.9 to 45.4), with an annualised rate of change (AROC) of 10.7% (3.2 to 17.6). At the same time, RHF coverage decreased from 28.1% (16.1 to 41.6) to 10.7% (3.3 to 25.8), with an AROC of –2.8% (–28.3 to 19.7). Increases in ORS, as measured by AROC, were significant (ie, 95% UIs did not include 0) in 27 of Rwanda's 30 units, while overall ORT coverage remained constant (appendix 1 pp 75–77; appendix 2 pp 1–8, 3207–4797). Kyrgyzstan, Yemen, and Liberia saw the largest increases in RHF coverage; however, uncertainty around these estimates was high, and only Yemen saw significant increases in RHF use (appendix 1 p 76; appendix 2 pp 9–16). Sudan and South Sudan were the only countries where AROC in ORS coverage declined substantially, with coverage decreasing from 32.3% (26.5 to 38.3) to 19.7% (14.6 to 26.2) in Sudan and from 52.0% (41.6 to 62.2) to 48.4% (37.6 to 59.5) in South Sudan. Declines were significant in eight of Sudan's 80 units and four of South Sudan's 45 units (figure 1; appendix 1 p 75; appendix 2 pp 1–8, 25–1615).

In 2017, the highest number of children with diarrhoea who remained untreated by ORS were in parts of eastern sub-Saharan Africa, north Africa, south Asia, and southeast Asia (figure 2). In 2000, we estimated that approximately 6 668 000 children (95% UI 5 330 000–7 673 000) across the 94 LMICs included in this study were untreated with either ORS or RHF, out of a total of 12 873 000 children (12 344 000–13 471 000) with diarrhoea. Although prevalence of untreated children has declined, a substantial number remain in need of treatment; in 2017, we estimated 6 519 000 children (95% UI 5 254 000–7 733 000) with diarrhoea did not receive either ORS or RHF treatment, out of a total of 13 343 000 children (12 709 000–13 944 000) with diarrhoea, and this burden varied substantially within many countries (figure 2).

In addition to the results presented here, the full array of our model outputs for ORS, RHF, or ORT

(either ORS or RHF) is provided in appendix 1 (pp 28–36) and is publicly available online, and can be further explored at various spatial levels via a user-friendly visualisation tool.

We found that inequality in ORS coverage, as measured by the Gini coefficient, decreased in the majority (63 [67%]) of countries from 2000 to 2017. In particular, although there were nine countries (Afghanistan, Cambodia, Cameroon, Côte d'Ivoire, Equatorial Guinea, Guinea, Iraq, Mali, and Mauritania) in 2000 whose Gini coefficient was greater than 0.15, only Afghanistan and Cameroon had coefficients above 0.15 in 2017.

Absolute percentage-point differences between units with the highest and lowest ORS coverage declined in 40 countries, with notable decreases in Equatorial Guinea, Central African Republic, Iraq, Mongolia, Myanmar, and Sierra Leone (figure 3). Absolute inequalities increased in more than half (54 [57%]) of LMICs, with notable increases in Jordan, Colombia, Uzbekistan, Afghanistan, Bolivia, Turkmenistan, Palestine, Benin, and Madagascar (figure 3). By contrast, within-country absolute geographical inequalities in RHF coverage declined in most (55 [59%]) countries, with notable exceptions in Yemen and Tajikistan (appendix 1 p 79).

Analysis of relative deviation from the country mean revealed that 11 LMICs (Afghanistan, Benin, Cameroon, Democratic Republic of the Congo, Colombia, Ethiopia, Guinea, Jordan, Nigeria, Sudan, and Uganda) had at least 50% relative deviation in one of their units in ORS use in 2017 (figure 3). Additionally, as mean national-level ORS coverage increased over time in most (76 [81%]) countries (appendix 1 p 78), within-country relative differences in ORS coverage also declined in 64 (68%) LMICs, with greater than 50% declines in relative deviation in Central African Republic, Equatorial Guinea, Iraq, Mali, Cambodia, Ethiopia, Niger, Senegal, Kyrgyzstan, Togo, Democratic Republic of the Congo, and Côte d'Ivoire (figure 3). Exceptions to this pattern, where relative differences increased more than 20%, included Jordan, Benin, Madagascar, Yemen, Sudan, Suriname, Guatemala, Turkmenistan, and Bolivia. Furthermore, as mean national-level RHF coverage declined over time in most (69 [73%]) countries, within-country relative inequalities in RHF coverage declined in 45 (48%) countries (appendix 1 p 78). In 2017, relative inequalities in RHF coverage remained highest in North Africa and the Middle East (appendix 1 p 78).

We found that mean ORS coverage was less than 50% in 12 of 14 countries where diarrhoeal mortality in 2017 was greater than two children per 1000 (appendix 2 pp 1–8). Furthermore, we found that ORS coverage was negatively correlated with RHF coverage over time in 56.6% (10 786 of 19 064) of units and was negatively correlated with diarrhoeal mortality over time in 74.7% (14 241 of 19 064) of units (appendix 1 p 81).

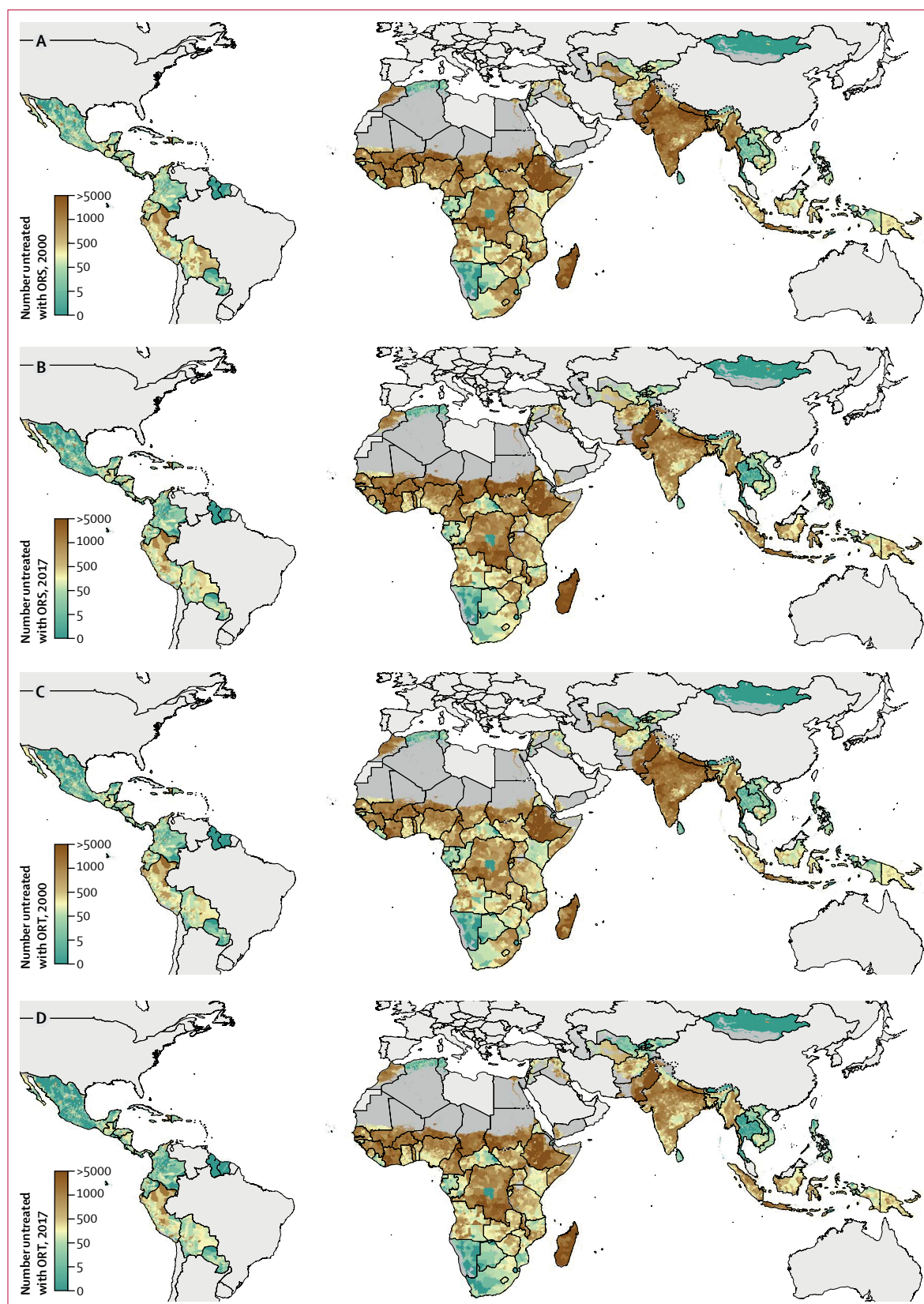


Figure 2: Number of children younger than 5 years with diarrhoea who did not receive ORT at the second administrative-unit level, 2000 and 2017

Number of children younger than 5 years with diarrhoea who did not receive ORS in 2000 (A) and 2017 (B) or did not receive ORT (either ORS or RHF) in 2000 (C) and 2017 (D). Countries are aggregated to second administrative units. Maps reflect administrative boundaries, land cover, lakes, and population. Dark grey grid cells were classified as barren or sparsely vegetated and had fewer than ten people per 1 km × 1 km grid cell; light grey countries were not included in these analyses.^{35–40} ORS=oral rehydration solution. ORT=oral rehydration therapy. RHF=recommended home fluids.

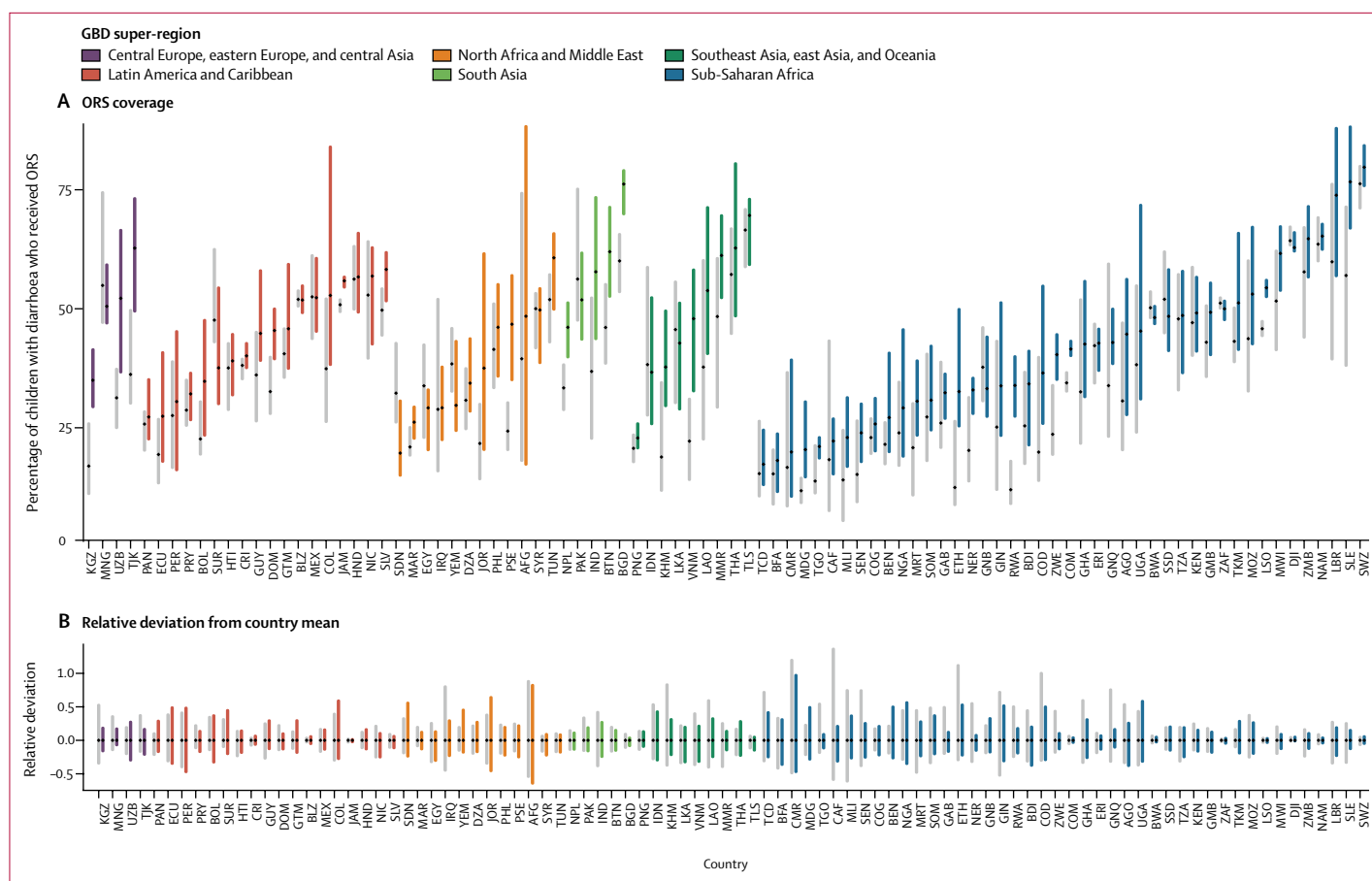


Figure 3: Geographical inequalities within countries in the proportion of children with diarrhoea who received ORS, 2000 and 2017

(A) Bars show range of ORS coverage at the second administrative-unit level for each country in 2000 (shown in grey) and 2017 (coloured by region), with the mean proportion (national-level aggregations) marked with a dot in each bar. (B) Bars show range of relative deviation from the country mean in the proportion of children younger than 5 years with diarrhoea who received ORS in 2000 (shown in grey) and 2017 (coloured by region). Countries are labelled by their ISO 3 codes. Geographical inequality in ORS coverage for each country is shown in detail in appendix 1 (p 78); inequalities in RHF and ORT coverage are shown in appendix 2 (pp 79–80). ORS=oral rehydration solution. ORT=oral rehydration therapy. RHF=recommended home fluids.

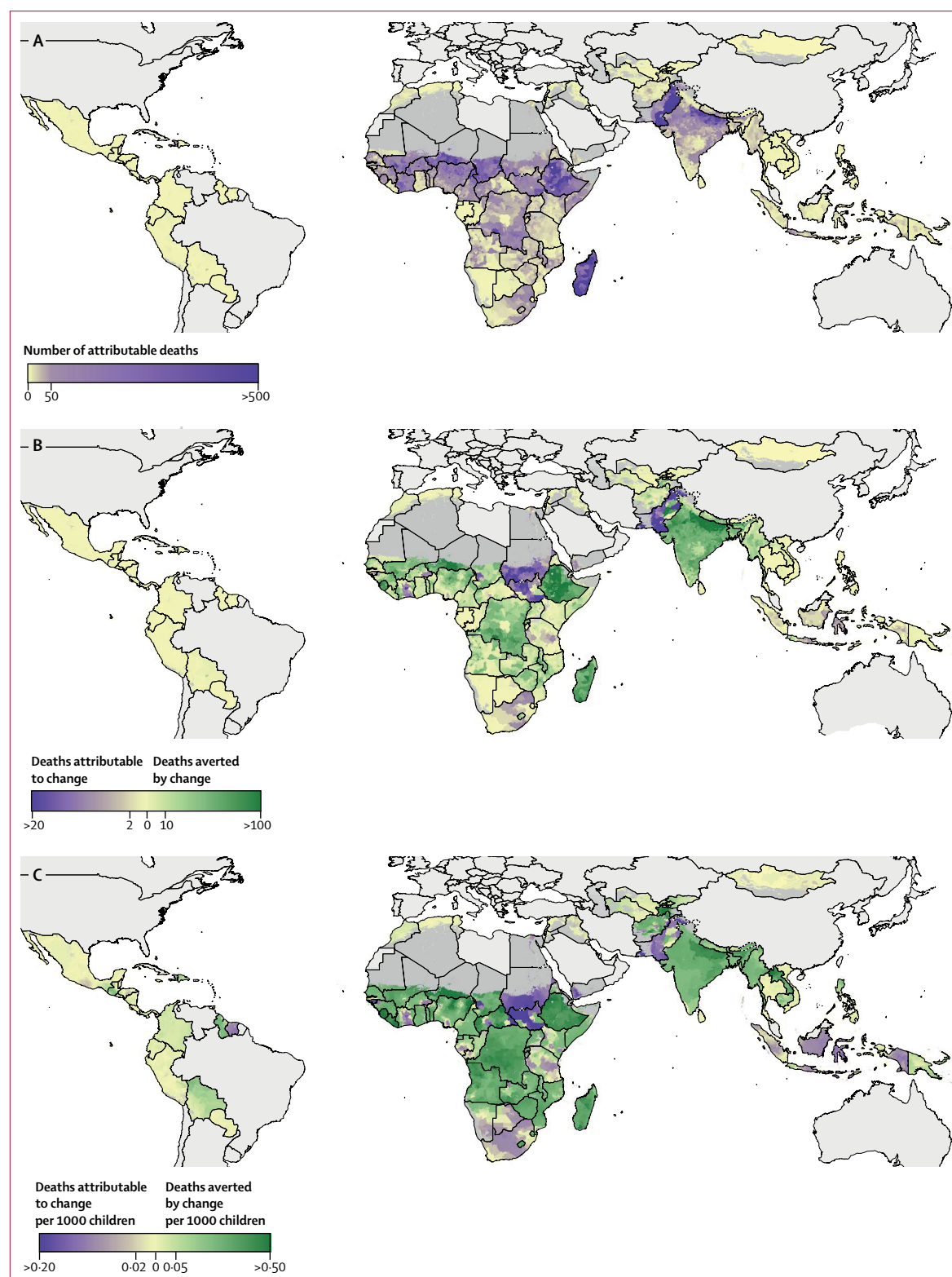
For ISO 3 codes see <https://www.iso.org/obp/ui>

To illustrate how our maps can be used to estimate the number of diarrhoeal deaths that were averted by changes in ORS coverage, we did a counterfactual analysis using a previous estimate that 75% ORS coverage could reduce diarrhoeal deaths by 69%.¹⁴ This estimate is based on a systematic review of three quasi-experimental studies with small sample sizes and that did not adjust for confounding variables (eg, stunting) to examine the risk of death in the absence of ORS treatment; thus, the results of this analysis should be interpreted with some caution. We found that of the 526 800 diarrhoeal deaths (95% UI 485 300–568 900) estimated to have occurred in 2017 in children younger than 5 years across the 94 LMICs included in our analysis, an estimated 299 900 deaths (274 000–324 300) could be attributable to lack of treatment with ORS. We also estimated that increase in ORS coverage during the study period prevented an additional 52 230 deaths (36 910–68 860). Nigeria, India, Ethiopia, Pakistan, Chad, and Madagascar contained units with high numbers of

deaths attributable to lack of ORS treatment in 2017; however, these countries also contained units with the highest numbers of deaths averted by improved ORS coverage in 2017 (figure 4). By contrast, an estimated 4850 deaths (2200–10 080) globally were due to declines in ORS coverage, with some of the highest numbers of deaths attributable to worsening coverage in units of Sudan, South Sudan, and Pakistan (figure 4). Some of the highest rates of deaths averted were in units of Sierra Leone, where 0·9 deaths (0·2–1·9) were averted per 1000 children in Kambia district, Northern Province (figure 4), corresponding to 67 lives (18–141) saved in 2017 in this district alone.

In a sensitivity analysis, we found that, while the geographical patterns in deaths averted remained largely unchanged, the absolute number of averted deaths changed substantially in some places (appendix 1 pp 82–83). Reducing the percentage of diarrhoeal deaths that could be averted with ORS from 69% to 35% reduced the total number of deaths attributable to lack of ORS

coverage in 2017 from 299 900 (95% UI 274 000–324 300) to 143 360 (130 400–156 000), the estimated total deaths averted by increase in ORS coverage from 52 230 (36 910–68 860) to 22 760 (15 600–30 650), and the averted deaths in Kambia district, Sierra Leone, from 67 (18–141) to 26 (8–53; appendix 1 p 82).



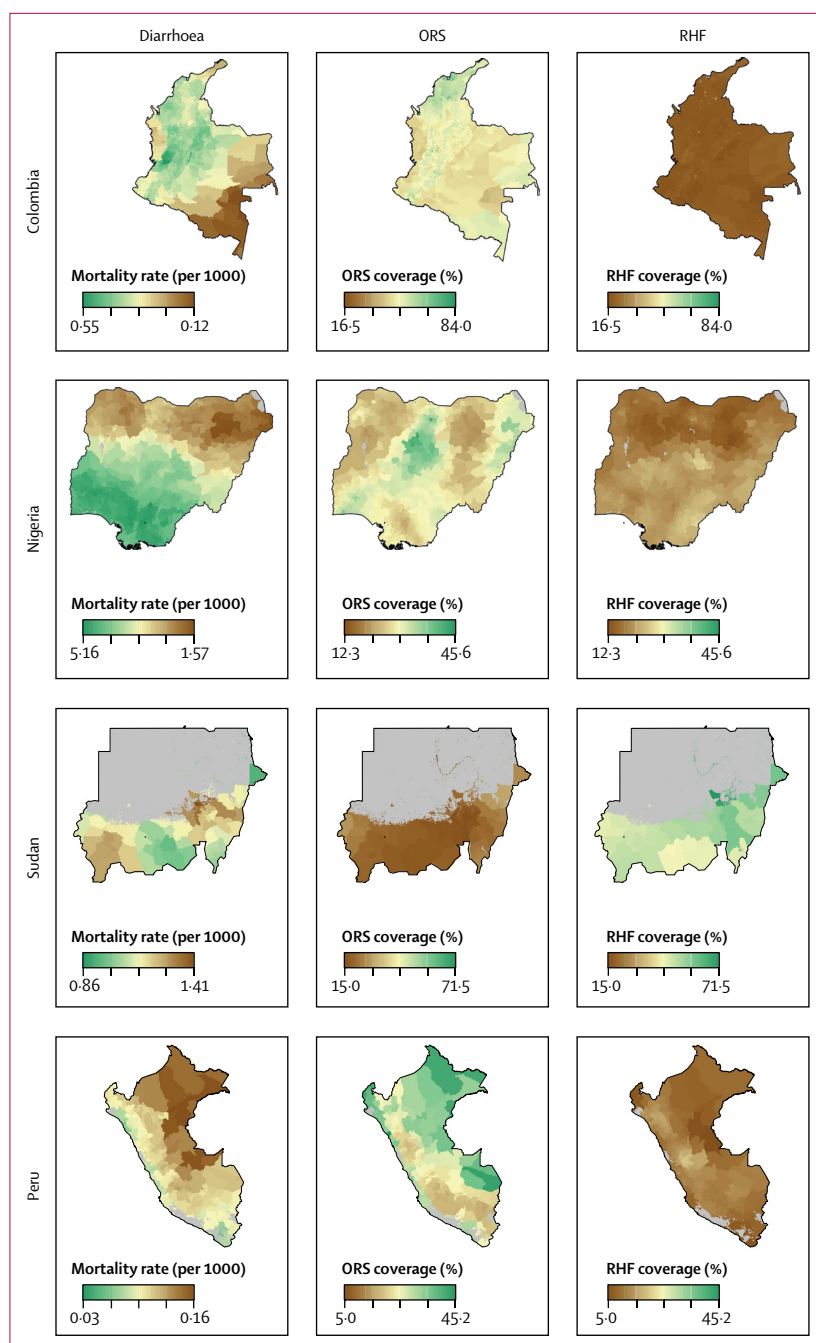


Figure 5: Subnational variation in the 2017 proportions of children who received ORT and diarrhoeal mortality in countries with high diarrhoeal burden at the second administrative-unit level

Subnational variation in ORS, RHF, and diarrhoeal mortality per 1000 children is shown in four countries that had both high diarrhoeal burden and high geographical inequality in ORT in 2017. Results are shown for 2017 at second administrative units. Maps reflect administrative boundaries, land cover, lakes, and population. Dark grey grid cells were classified as barren or sparsely vegetated and had fewer than ten people per 1 km × 1 km grid cell.^{35–40} ORS=oral rehydration solution. ORT=oral rehydration therapy. RHF=recommended home fluids.

Finally, to illustrate how these maps can be used to identify children in need, we present side-by-side maps of diarrhoeal mortality, ORS coverage, and RHF coverage at the unit level for three countries—Colombia, Nigeria,

and Sudan—that had subnational locations with higher-than-average mortality rates and lower-than-average ORS coverage (figure 5). In Colombia, ORS and RHF coverage were lowest in the southern Amazonas region, where diarrhoeal burden was highest. In Nigeria, ORS coverage was lowest in the northern region, where diarrhoeal burden was highest. In Sudan, RHF remains widely used to treat diarrhoea, and there was not a clear trend between ORS, RHF, and diarrhoea distributions, but distinct areas in Darfur, in the southeast of the country, had high diarrhoeal mortality and particularly low ORS coverage. To illustrate that this pattern was not present everywhere, we also present results for Peru, where ORS coverage was relatively high in the Amazon Basin rainforests, which is where diarrhoeal mortality was also highest. There were gaps in coverage in the mountainous and arid regions of central and south Peru, where diarrhoeal mortality was lower (figure 5).

Discussion

The discovery that led to the development of ORS as treatment for diarrhoea was hailed as “potentially the most important medical advancement of the century”.⁴¹ More than 50 years later, ORS is recognised as an important treatment for childhood diarrhoea, as well as a crucial component in treating other forms of dehydration, including dehydration-induced kidney injury and Ebola virus disease.⁴² By providing high-resolution estimates of the use of different forms of ORT—ORS, RHF, and either ORS or RHF—in children younger than 5 years with diarrhoea in LMICs, this study examines where uptake has occurred and which places stand to gain the most. While we show increases in ORS coverage in many locations, it is striking that these increases have been so incremental, given the importance and simplicity of this intervention. These slow changes are reflected in the relatively low number of total deaths estimated to have been averted by increases in ORS coverage between 2000 and 2017, and the substantial number of children with diarrhoea that remained untreated in 2017. ORS coverage remains below 50% in the majority (62.6%) of second administrative units, and there are various locations with high diarrhoeal mortality rates where geographical inequalities in ORS coverage are high. These areas need to be targeted with improved efforts to increase access to and awareness of this life-saving treatment.

We also show that increases in ORS coverage over time were correlated with declines in RHF coverage in many locations. It is possible that these results represent shifts over time in diarrhoea treatment, which might have contributed to declines in diarrhoeal mortality in these locations; ORS has shown effectiveness in preventing child mortality, whereas the effect of RHF on child mortality is unclear.¹⁴ However, if the rates of decline in RHF exceeded the rates of increase in ORS in some locations, this could have left a proportion of children

completely untreated and in need of targeted interventions to prevent diarrhoeal mortality. These results further highlight the importance of reaching these vulnerable populations with targeted interventions to improve ORS coverage. It is important to note that there were also locations where there was apparently no relationship between ORS coverage and diarrhoeal mortality over time. This could, in part, be attributed to other risk factors that affect diarrhoeal mortality, which we did not take into account in this analysis.

Our estimates are comparable with previously published estimates at the national level.^{10,11} We show notable differences in ORS coverage between countries in the same region (eg, Senegal vs Sierra Leone), consistent with a previous review.⁸ We show that ORS use has increased over time, with greater uptake in some regions compared with others (eg, south Asia vs the Horn of Africa), which is consistent with the conclusions of UNICEF's 2016 report.^{8,10} However, we also show that the rates of increase in ORS coverage and decrease in RHF coverage were modest and that uncertainty in these estimates was high, which is consistent with previous studies that showed no substantial increases in ORT coverage between 1990 and 2001⁴³ or between 1996 and 2003.⁴⁴ We also show that relative and absolute geographical inequalities in ORS coverage declined over time in many countries, which is in contrast with a previous study that showed that absolute inequalities in ORT have remained the same over time in all but three LMICs.¹⁶ There are numerous methodological differences between that study and ours; most importantly, the previous study did not separate the effect of ORS from that of RHF. As we show, analysis of ORT (a combined variable) masks spatial and temporal variation in ORS and RHF.

We are surprised to see low use of ORS after so many years of programmes in many countries, especially those with high diarrhoeal burden. Ensuring access to ORS treatment is not only important for treating existing diarrhoea cases, but also in preparing for outbreaks and having supplies ready for emergencies. Moreover, educating caregivers on the causes of diarrhoea mortality—and how ORS can prevent those child deaths—is essential to ensure sustainable uptake. To address shortfalls in coverage, it will be essential to examine the root causes specific to each location. Previous studies have shown that challenges in using ORS include doctor and patient knowledge about ORS; ORS supply, cost, and taste; and access to clean water.^{11,45} Studies have also shown that improvements in ORS coverage can be driven by changes in government policies, media campaigns, and community culture and beliefs.^{2,23,24} According to our results, Sierra Leone had some of the highest ORS coverage in western sub-Saharan Africa in 2017. Sierra Leone has previously been described as an example of how community mobilisation can promote access to and awareness of ORS, even after a devastating civil war.¹¹ Our results also suggest that promotion of RHF over ORS might negatively affect

ORS use and that locations with high RHF use, such as Sudan, can have very low ORS coverage. A previous study has similarly shown that inconsistent and unclear diarrhoea treatment recommendations present challenges in Sudan and Somalia and might have had implications for the recent cholera epidemic in Yemen.⁴⁶ By determining key country-specific drivers of low uptake and subnational inequalities, including various social, cultural, political, and economic factors that might inhibit proper coverage, successful interventions such as those in Sierra Leone could be adapted and applied to similar contexts.

Our study has several limitations. Although we constructed a large database of geolocated ORT coverage data, spatial and temporal gaps remain, and data quality is likely to be variable by source, contributing to uncertainty in our estimates. Thus, results from zones of conflict and political instability, such as Yemen, Syria, Iraq, Afghanistan, and Pakistan, should be interpreted with caution. For RHF modelling, we included a broad range of RHF definitions in the survey data, and the RHF definitions in survey questionnaires do not always correspond to the actual solutions that governments have recommended. In addition, since the denominator of our input data was the proportion of children with diarrhoea (ie, diarrhoea prevalence), sample sizes were very small. Finally, heterogeneity within the data as well as amount of relevant available data varied between countries. Each of these factors probably contributed to uncertainty in our estimates, which varied by indicator and country (appendix 2).

As a further limitation, the modelling framework was optimised for prediction rather than causal inference, and there were overlaps between covariates used to estimate ORS, RHF, and diarrhoeal mortality, so we cannot make any conclusions about causal relationships between them. Additionally, we were unable to incorporate uncertainty into our estimates of the number of children with diarrhoea who were untreated because uncertainty from WorldPop datasets³⁵ was not available. Furthermore, we fit our models using survey data, which depend on recall and are susceptible to biases that could be in the direction of increased or decreased coverage, depending on the context. Lastly, we mapped the reported use of ORS, yet use is not equivalent to proper preparation of the solution.^{47,48}

Future studies should examine the factors that have affected ORS coverage, particularly those that have contributed to shortfalls in efforts to increase coverage, to inform future interventions and implementation studies. Future work should also further investigate coverage of zinc treatment, which has shown effectiveness in reducing undernourishment and diarrhoeal mortality in many countries.⁴⁹ In addition, promoting zinc use has shown a secondary effect of increasing ORS use in some places,^{50,51} thus comprehensive approaches to overcome challenges to uptake and scaling up of coverage are warranted.⁵² Future work could investigate how missing data affect

estimates of ORS coverage and how to account for this, as well as how to incorporate differences between urban and rural populations into the analysis. In addition, we did not map ORS availability, but rather the prevalence of its use, and future studies could map availability distribution patterns. Future work should examine the co-distribution of different interventions to prevent childhood mortality from diarrhoea, such as the co-distributions of ORS, zinc, and access to clean water. Finally, as with any study that involves estimation, the availability and quality of input data influences the certainty of our estimates; as LMICs work to improve their cause-specific vital registration systems, analyses that incorporate diarrhoea-specific cause of death data in estimates of diarrhoea mortality would improve future updates to this work.

In conclusion, our results show that advancement in ORS coverage was slow from 2000 to 2017, and that within-country inequalities in ORS coverage persist in many LMICs. Depending on the local context, low levels of coverage might reflect challenges in access to ORS or the need for education on the efficacy of ORS in preventing diarrhoea mortality. Increased efforts are needed, particularly where childhood deaths from diarrhoea are high yet ORS coverage remains low; in 2017, 12 of 14 LMICs where diarrhoeal mortality exceeded two children per 1000 had less than 50% ORS coverage. The subnational scale of these mapped estimates can aid in identifying where gaps in coverage of this life-saving intervention remain, contributing to the UN Sustainable Development Goals' commitment to address inequalities and leave no one behind.⁵³ Our results illustrate that scaling up of ORS coverage has been insufficient, and that new efforts to improve access are desperately needed.

Local Burden of Disease Diarrhoea Collaborators

Kirsten E Wiens, Paulina A Lindstedt, Brigitte F Blacker, Kimberly B Johnson, Mathew M Baumann, Lauren E Schaeffer, Hedayat Abbastabar, Foad Abd-Allah, Ahmed Abdelalim, Ibrahim Abdollahpour, Kadir Hussein Abegaz, Ayenew Negesse Abejie, Lucas Guimarães Abreu, Michael R M Abrigo, Ahmed Abualhasan, Manfred Mario Kokou Accrombessi, Dilaram Acharya, Maryam Adabi, Abdu A Adamu, Oladimeji M Adebayo, Rufus Adesoji Adedoyin, Victor Adekanmbi, Olatunji O Adetokunboh, Beyene Meressa Adhena, Mohsen Afarideh, Sohail Ahmad, Keivan Ahmadi, Anwar E Ahmed, Muktar Beshir Ahmed, Rushdia Ahmed, Temesgen Yihunie Akalu, Fares Alahdab, Ziyad Al-Aly, Noore Alam, Samiah Alam, Genet Melak Alamene, Turki M Alanzi, Jacqueline Elizabeth Alcalde-Rabanal, Beriwan Abdulqadir Ali, Mehran Alijanzadeh, Yahid Alipour, Syed Mohamed Aljunid, Ali Almasi, Amir Almasi-Hashiani, Hesham M Al-Mekhlafi, Khalid A Altirkawi, Nelson Alvis-Guzman, Nelson J Alvis-Zakzuk, Saeed Amini, Arianna Maeve L Amit, Catalina Liliana Andrei, Mina Anjomshoa, Amir Anoushiravani, Fereshteh Ansari, Carl Abelardo T Antonio, Benny Antony, Ernoiz Antriyandarti, Jalal Arabloo, Hany Mohamed Amin Aref, Olatunde Aremu, Bahram Armoon, Amit Arora, Krishna K Aryal, Afsaneh Arzani, Mehran Asadi-Aliabadi, Hagos Tasew Atalay, Seyyed Shamsadin Athari, Seyyede Masoume Athari, Sachin R Atre, Marcel Ausloos, Nefsu Awoke, Beatriz Paulina Ayala Quintanilla, Getinet Ayano, Martin Amogre Ayanore, Yared Asmare Aynalem, Samad Azari, Peter S Azzopardi, Ebrahim Babae, Tesleem Kayode Babalola, Alaa Badawi, Mohan Bairwa, Shankar M Bakkannavar,

Senthilkumar Balakrishnan, Ayele Geleto Bali, Maciej Banach, Joseph Adel Mattar Banoub, Aleksandra Barac, Till Winfried Bärnighausen, Huda Basaleem, Sanjay Basu, Vo Dinh Bay, Mohsen Bayati, Estifanos Baye, Neeraj Bedi, Mahya Beheshti, Masoud Behzadifar, Meysam Behzadifar, Bayu Begashaw Bekele, Yaschilal Muche Belayneh, Michelle L Bell, Derrick A Bennett, Dessalegn Ajema Berbada, Robert S Bernstein, Anusha Ganapati Bhat, Kritika Bhattacharyya, Suraj Bhattarai, Soumyadeep Bhaumik, Zulfiqar A Bhutta, Ali Bijani, Boris Bikbov, Binyam Minuye Biriha, Raaj Kishore Biswas, Somayeh Bohlouli, Hunduma Amensisa Bojia, Soufiane Boufous, Oliver J Brady, Nicola Luigi Bragazzi, Andrey Nikolaevich Briko, Nikolay Ivanovich Briko, Gabrielle B Britton, Sharath Burugina Nagaraja, Reinhard Busse, Zahid A Butt, Luis Alberto Cámara, Ismael R Campos-Nonato, Jorge Cano, Josip Car, Rosario Cárdenas, Felix Carvalho, Carlos A Castañeda-Orjuela, Franz Castro, Wagaye Fentahun Chanie, Pranab Chatterjee, Vijay Kumar Chattu, Tesfaye Yitna Chichiabellu, Ken Lee Chin, Devasahayam J Christopher, Dinh-Toi Chu, Natalie Maria Cormier, Vera Marisa Costa, Carlos Culquichicon, Matiwo Soboka Daba, Giovanni Damiani, Lalit Dandona, Rakhi Dandona, Anh Kim Dang, Aso Mohammad Darwesh, Amira Hamed Darwish, Ahmad Daryani, Jai K Das, Rajat Das Gupta, Aditya Prasad Dash, Gail Davey, Claudio Alberto Dávila-Cervantes, Adrian C Davis, Dragos Virgil Davitoiu, Fernando Pio De la Hoz, Asmamaw Bizuneh Demis, Dereje Bayissa Demissie, Getu Debalkie Demissie, Gebre Teklemariam Demoz, Edgar Denova-Gutiérrez, Kebede Deribe, Assefa Desalew, Aniruddha Deshpande, Samath Dhamminda Dharmaratne, Preeti Dhillon, Meghnath Dhimel, Govinda Prasad Dhungana, Daniel Diaz, Isaac Oluwafemi Dipeolu, Shirin Djalalinia, Kerrie E Doyle, Eleonora Dubljanin, Bereket Dukko, Andre Rodrigues Duraes, Mohammad Ebrahimi Kalan, Hisham Atan Edinur, Andem Effiong, Aziz Eftekhari, Nevine El Nahas, Iman El Sayed, Maysaa El Sayed Zaki, Maha El Tantawi, Teshome Bekele Elema, Hala Rashad Elhabashy, Shaimaa I El-Jaafari, Hajer Elkout, Aisha Elsharkawy, Iqbal RF El Yazar, Akliu Endalamaw, Daniel Adane Endalew, Sharareh Eskandarieh, Alireza Esteghamati, Sadaf Esteghamati, Arash Etemadi, Oluchi Ezekannagha, Mohammad Fareed, Roghiyeh Faridnia, Farshad Farzadfar, Mehdi Fazlzadeh, Valery L Feigin, Seyed-Mohammad Fereshtehnejad, Eduarda Fernandes, Irina Filip, Florian Fischer, Nataliya A Foigt, Morenike Oluwatoyin Folayan, Masoud Foroutan, Richard Charles Franklin, Takeshi Fukumoto, Mohamed M Gad, Reta Tsegaye Gayesa, Teshome Gebre, Ketema Bizuwork Gebremedhin, Gebreamlak Gebremedhin Gebremeskel, Hailay Abhra Gesesew, Kebede Embaye Gezae, Keyghobad Ghadiri, Ahmad Ghashghae, Pramesh Raj Ghimire, Paramjit Singh Gill, Tiffany K Gill, Themba G Ginindza, Nelson G M Gomes, Sameer Vali Gopalani, Alessandra C Goulart, Bárbara Niegia Garcia Goulart, Ayman Grada, Mohammed Ibrahim Mohialdeen Gubari, Harish Chander Guagnani, Davide Guido, Rafael Alves Guimarães, Yuming Guo, Rajeev Gupta, Nima Hafezi-Nejad, Dessalegn H Haile, Gessesew Bugssa Hailu, Arvin Haj-Mirzaian, Arya Haj-Mirzaian, Randah R Hamadeh, Samer Hamidi, Demelash Woldeyohannes Handiso, Hamidreza Haririan, Ninuk Hariyani, Ahmed I Hasaballah, Md Mehedi Hasan, Edris Hasanpoor, Amir Hasanzadeh, Hadi Hassankhani, Hamid Yimam Hassen, Mohamed I Hegazy, Behzad Heibati, Behnam Heidari, Delia Hendrie, Nathaniel J Henry, Claudiu Herteliu, Fatemeh Heydarpour, Hagos Degefa de Hidru, Thomas R Hird, Chi Linh Hoang, Enayatollah Homaie Rad, Praveen Hoogar, Mohammad Hoseini, Naznin Hossain, Mostafa Hosseini, Mehdi Hosseinzadeh, Mowafa Househ, Mohamed Hsairi, Guoqing Hu, Mohammedaman Mama Hussien, Segun Emmanuel Ibitoye, Ehimario U Igumbor, Olayinka Stephen Ilesanmi, Milena D Ilic, Mohammad Hasan Imani-Nasab, Usman Iqbal, Seyed Sina Naghibi Irvani, Sheikh Mohammed Shariful Islam, Chinwe Juliana Iwu, Neda Izadi, Anelisa Jaca, Nader Jahanmehr, Mihajlo Jakovljevic, Amir Jalali, Achala Upendra Jayatilleke, Ravi Prakash Jha, Vivekanand Jha, John S Ji, Jost B Jonas, Jacek Jerzy Jozwiak, Ali Kabir, Zubair Kabir, Amaha Kahsay,

- Hamed Kalani, Tanuj Kanchan, Behzad Karami Matin, André Karch, Mohd Anisul Karim, Hamidreza Karimi-Sari Surendra Karki, Amir Kasaiean, Gebremicheal Gebresslassie Kasahun, Yawukal Chane Kasahun, Habtamu Kebebe Kasaye, Gebrehiwot G Kassa, Getachew Mullu Kassa, Gbenga A Kayode, Ali Kazemi Karyani, Mihiretu M Kebede, Peter Njenga Keiyoro, Abraham Getachew Kelbore, Andre Pascal Kengne, Daniel Bekele Ketema, Yousef Saleh Khader, Morteza Abdullatif Khafae, Nauman Khalid, Rovshan Khalilov, Ejaz Ahmad Khan, Junaid Khan, Md Nuruzzaman Khan, Muhammad Shahzeb Khan, Khaled Khatab, Amir M Khater, Mona M Khater, Maryam Khayamzadeh, Mohammad Khazaei, Salman Khazaei, Mohammad Hossein Khosravi, Jagdish Khubchandani, Ali Kiadaliri, Yun Jin Kim, Ruth W Kimokoti, Adnan Kisa, Sezer Kisa, Niranjana Kissoon, K M Shivakumar, Sonali Kochhar, Tufa Kolola, Hamidreza Komaki, Soewarta Kosen, Parvaiz A Koul, Ai Koyanagi, Moritz U G Kraemer, Kewal Krishan, Nuworza Kugbey, G Anil Kumar, Manasi Kumar, Pushpendra Kumar, Vivek Kumar, Dian Kusuma, Carlo La Vecchia, Ben Lacey, Sheetal D Lad, Dharmesh Kumar Lal, Felix Lam, Faris Hasan Lami, Prabhat Lamichhane, Van Charles Lansingh, Savita Lasrado, Avula Laxmaiah, Paul H Lee, Kate E LeGrand, Mostafa Leili, Tsegaye Lolaso Lenjebo, Cheru Tesema Leshargie, Aubrey J Levine, Shanshan Li, Shai Linn, Shiwei Liu, Simin Liu, Rakesh Lodha, Joshua Longbottom, Jaifred Christian F Lopez, Hassan Magdy Abd El Razek, Muhammed Magdy Abd El Razek, D R Mahadeshwara Prasad, Phetole Walter Mahasha, Narayan B Mahotra, Azeem Majeed, Reza Malekzadeh, Deborah Carvalho Malta, Abdullah A Mamun, Navid Manafi, Ana Laura Manda, Narendar Dawani Dawanu Manohar, Mohammad Ali Mansournia, Chabila Christopher Mapoma, Joemer C Maravilla, Gabriel Martinez, Santi Martini, Francisco Rogerlândio Martins-Melo, Anthony Masaka, Benjamin Ballard Massenbourg, Manu Raj Mathur, Benjamin K Mayala, Mohsen Mazidi, Colm McAlinden, Birhanu Geta Meharie, Man Mohan Mehndiratta, Kala M Mehta, Tefera Chane Mekonnen, Gebrekios Gebremichael Meles, Peter T N Memiah, Ziad A Memish, Walter Mendoza, Ritesh G Menezes, Seid Tiku Mereta, Tuomo J Meretoja, Tomislav Mestrovic, Bartosz Miazgowski, Keadnew Mulatu Mihretie, Ted R Miller, GK Mini, Erkin M Mirrakhimov, Babak Moazen, Bahram Mohajer, Amjad Mohamadi-Bolbanabad, Dara K Mohammad, Karzan Abdulmuhsin Mohammad, Yousef Mohammad, Naser Mohammad Gholi Mezerji, Roghayeh Mohammadibakhsh, Noushin Mohammadifard, Jemal Abdu Mohammed, Shafiu Mohammed, Farnam Mohebi, Ali H Mokdad, Mariam Molokhia, Lorenzo Monasta, Yoshan Moodley, Catrin E Moore, Ghobad Moradi, Masoud Moradi, Mohammad Moradi-Joo, Maziar Moradi-Lakeh, Paula Moraga, Linda Morales, Ilais Moreno Velásquez, Abbas Mosapour, Simin Mouodi, Seyyed Meysam Mousavi, Milvia Mozaffor, Kindie Fentahun Muchie, Getahun Fentaw Mulaw, Sandra B Munro, Moses K Muriithi, Christopher J L Murray, GVS Murthy, Kamarul Imran Musa, Ghulam Mustafa, Saravanan Muthupandian, Ashraf F Nabhan, Mehdi Naderi, Ahamarshan Jayaraman Nagarajan, Kovin S Naidoo, Gurudatta Naik, Farid Najafi, Vinay Nangia, Jobert Richie Nansseu, Bruno Ramos Nascimento, Javad Nazari, Duduzile Edith Ndawandwe, Ionut Negoi, Henok Biresaw Netsere, Josephine W Ngunjiri, Cuong Tat Nguyen, Huong Lan Thi Nguyen, Trang Huyen Nguyen, Dabere Ngatu, Solomon Gedlu Ngatu, Dina Nur Anggraini Ningrum, Chukwudi A Nnaji, Marzieh Nojomi, Vuong Minh Nong, Ole F Norheim, Jean Jacques Noubiap, Soraya Nouraei Motlagh, Bogdan Oancea, Okechukwu Samuel Ogah, Felix Akpojene Ogbo, In-Hwan Oh, Andrew T Olagunju, Tinuke O Olagunju, Bolajoko Olubukunola Olusanya, Jacob Olusegun Olusanya, Obinna E Onwujekwe, Eyal Oren, Doris V Ortega-Altamirano, Osayomwanbo Osarenotor, Frank B Osei, Mayowa O Owolabi, Mahesh P A, Jagadish Rao Padubidri, Smita Pakhale, Sangram Kishor Patel, Angel J Paternina-Caicedo, Ashish Pathak, George C Patton, Deepak Paudel, Kebreab Paulos, Veincent Christian Filipino Pepito, Alexandre Pereira, Norberto Perico, Aslam Pervaiz, Julia Moreira Pescarini, Bakhtiar Piroozi, Meghdad Pirsaeheb, Maarten J Postma, Hadi Pourjafar, Farshad Pourmalek, Akram Pourshams, Hossein Poustchi, Sergio I Prada, Narayan Prasad, Liliana Preotescu, Hedley Quintana, Navid Rabiee, Amir Radfar, Alireza Rafiei, Fakher Rahim, Afarin Rahimi-Movaghar, Vafa Rahimi-Movaghar, Mohammad Hifz Ur Rahman, Muhammad Aziz Rahman, Shafiur Rahman, Fatemeh Rajati, Saleem Muhammad Rana, Chhabhi Lal Ranabhat, Davide Rasella, David Laith Rawaf, Salman Rawaf, Lal Rawal, Wasiq Faraz Rawasia, Vishnu Renjith, Andre M N Renzaho, Serge Resnikoff, Melese Abate Reta, Negar Rezaei, Mohammad Sadegh Rezai, Seyed Mohammad Riahi, Ana Isabel Ribeiro, Jennifer Rickard, Maria Rios-Blancas, Leonardo Roeber, Luca Ronfani, Elias Merdassa Roro, Jennifer M Ross, Enrico Rubagotti, Salvatore Rubino, Anas M Saad, Yogesh Damodar Sabde, Siamak Sabour, Ehsan Sadeghi, Yahya Safari, Roya Safari-Faramani, Rajesh Sagar, Amirhossein Sahebkar, Mohammad Ali Sahraian, S Mohammad Sajadi, Mohammad Reza Salahshoor, Nasir Salam, Payman Salamati, Hosni Salem, Marwa Rashad Salem, Yahya Salimi, Hamideh Salimzadeh, Abdallah M Samy, Juan Sanabria, Milena M Santric-Milicevic, Bruno Piassi Sao Jose, Sivan Yegnanarayana Iyer Saraswathy, Kaushik Sarkar, Abdur Razzaque Sarker, Nizal Sarrafzadegan, Benn Sartorius, Brijesh Sathian, Thirunavukkarasu Sathish, Monika Sawhney, Sonia Saxena, David C Schwebel, Anbissa Muleta Senbeta, Subramanian Senthilkumaran, Sadaf G Sepanlou, Edson Serván-Mori, Hosein Shabaninejad, Azadeh Shafieesabet, Masood Ali Shaikh, Ali S Shalash, Seifadin Ahmed Shallo, Mehran Shams-Beyranvand, MohammadBagher Shamsi, Morteza Shamsizadeh, Mohammed Shannawaz, Kiomars Sharafi, Hamid Sharifi, Hatem Samir Shehata, Aziz Sheikh, B Suresh Kumar Shetty, Kenji Shibuya, Wondimeneh Shibabaw Shiferaw, Desalegn Markos Shifti, Mika Shigematsu, Jae Il Shin, Rahman Shiri, Reza Shirkoobi, Soraya Siabani, Tariq Jamal Siddiqi, Diego Augusto Santos Silva, Ambrish Singh, Jasvinder A Singh, Narinder Pal Singh, Virender Singh, Malede Mequanent Sisay, Eirini Skiadaresi, Mohammad Reza Sobhiyeh, Anton Sokhan, Shahin Soltani, Ranjani Somayaji, Moslem Soofi, Muluken Bekele Sorrie, Ireneous N Soyiri, Chandrashekhar T Sreeramareddy, Agus Sudaryanto, Mu'awiyah Babale Sufiyan, Hafiz Ansar Rasul Suleria, Marufa Sultana, Bruno Fokas Sunguya, Bryan L Sykes, Rafael Tabarés-Seisdedos, Takahiro Tabuchi, Degena Bahrey Tadesse, Ingan Ukur Tarigan, Aberash Abay Tasew, Yonatal Mesfin Tefera, Merhawi Gebremedhin Tekle, Mohamad-Hani Temsah, Berhe Etsay Tesfay, Fisaha Haile Tesfay, Belay Tessema, Zemenu Tadesse Tessema, Kavumpurathu Raman Thankappan, Nihal Thomas, Alemayehu Toma, Roman Topor-Madry, Marcos Roberto Tovani-Palone, Eugenio Traini, Bach Xuan Tran, Khanh Bao Tran, Irfan Ullah, Bhaskaran Unnikrishnan, Muhammad Shariq Usman, Benjamin S Chudi Uzochukwu, Pascual R Valdez, Santosh Varughese, Francesco S Violante, Sebastian Vollmer, Feleke Gebremeskel W/hawariat, Yasir Waheed, Mitchell Taylor Wallin, Yafeng Wang, Yuan-Pang Wang, Marcia Weaver, Bedilu Girma Weji, Girmay Teklay Weldesamuel, Catherine A Welgan, Andrea Werdecker, Ronny Westerman, Taweewat Wiangkham, Charles Shew Wiysonge, Haileab Fekadu Wolde, Dawit Zewdu Wondafrash, Tewodros Eshete Wonde, Getasew Tadesse Worku, Ai-Min Wu, Gelin Xu, Ali Yadollahpour, Seyed Hossein Yahyazadeh Jabbari, Tomohide Yamada, Hiroshi Yatsuya, Alex Yeshaneh, Christopher Sabo Yilgwan, Mekdes Tigistu Yilma, Paul Yip, Engida Yisma, Naohiro Yonemoto, Seok-Jun Yoon, Mustafa Z Younis, Mahmoud Yousefifard, Hebat-Allah Salah A Yousof, Chuanhua Yu, Hasan Yusefzadeh, Siddhesh Zadey, Zoubida Zaidi, Sojib Bin Zaman, Mohammad Zamani, Hamed Zandian, Nejimu Biza Zepro, Tadesse Alemu Zerfu, Yunquan Zhang, Xiu-Ju George Zhao, Arash Ziapour, Sanjay Zodpey, Yves Miel H Zuniga, Simon I Hay*, Robert C Reiner Jr*.

*Joint senior authors.

Affiliations

Institute for Health Metrics and Evaluation (K E Wiens PhD, P A Lindstedt MPH, B F Blacker MPH, K B Johnson MS, M M Baumann BS, L E Schaeffer MS, N M Cormier MPSA,

- Prof L Dandona MD, Prof R Dandona PhD, A Deshpande MPH, Prof S D Dharmaratne MD, Prof V L Feigin PhD, N J Henry BS, K E LeGrand MPH, A J Levine MSPH, B K Mayala PhD, Prof A H Mokdad PhD, S B Munro PhD, Prof C J L Murray DPhil, J M Ross MD, M Weaver PhD, C A Welgan BS, Prof S I Hay FMedSci, R C Reiner Jr PhD, Department of Health Metrics Sciences, School of Medicine (Prof R Dandona, Prof S D Dharmaratne, Prof A H Mokdad, Prof C J L Murray, Prof B Sartorius PhD, M Weaver, Prof S I Hay, R C Reiner Jr), Department of Global Health (S Kochhar MD, J M Ross), Division of Plastic and Reconstructive Surgery (B B Massenburg MD), Department of Medicine (J M Ross, R Somayaji MD), University of Washington, Seattle, WA, USA (Prof E Oren PhD); Advanced Diagnostic and Interventional Radiology Research Center (H Abbastabar PhD), Endocrinology and Metabolism Research Center (M Afarideh MD, Prof A Esteghamati MD, S Esteghamati MD, B Heidari MD, N Rezaei PhD), Digestive Diseases Research Institute (A Anoushiravani MD, Prof R Malekzadeh MD, Prof A Pourshams MD, H Poustchi PhD, H Salimzadeh PhD, S G Sepanlou MD), Multiple Sclerosis Research Center (S Eskandarieh PhD, B Mohajer MD, Prof M Sahraian MD), Non-communicable Diseases Research Center (Prof F Farzadfar DSc, B Mohajer, F Mohebi MD, N Rezaei), Department of Environmental Health Engineering (M Fazlzadeh PhD), School of Medicine (N Hafezi-Nejad MD), Department of Pharmacology (Arv Haj-Mirzaian MD), Department of Microbiology (A Hasanzadeh PhD), Department of Epidemiology and Biostatistics (Prof M Hosseini PhD, M Mansournia PhD), Pediatric Chronic Kidney Disease Research Center (Prof M Hosseini), Hematology, Oncology and Stem Cell Transplantation Research Center (A Kasaeian PhD), National Institute of Health Research (F Mohebi), Department of Health Policy, Management, and Economics (S Mousavi PhD), Metabolomics and Genomics Research Center (F Rahim PhD), Iranian National Center for Addiction Studies (Prof A Rahimi-Movaghar MD), Sina Trauma and Surgery Research Center (Prof V Rahimi-Movaghar MD, Prof P Salamat MD), Cancer Research Institute (R Shirkoobi PhD), Cancer Biology Research Center (R Shirkoobi), Tehran University of Medical Sciences, Tehran, Iran (A Etemadi PhD); Department of Neurology (Prof F Abd-Allah MD, Prof A Abdelalim MD, A Abualhasan MD, S I El-Jaafary MD, M I Hegazy PhD, Prof H S Shehata MD), Neurophysiology Department (Prof H R Elhabashy MD), Endemic Medicine and Hepatogastroenterology Department (A Elsharkawy MD), National Hepatology and Tropical Medicine Research Institute (A M Khater MD), Department of Medical Parasitology (M M Khater MD, H S A Yousof MD), Urology Department (Prof H Salem MD), Cairo University, Cairo, Egypt; Neuroscience Research Center (I Abdollahpour PhD), Isfahan Cardiovascular Research Institute (N Mohammadiard PhD, Prof N Sarrafzadegan MD), Isfahan University of Medical Sciences, Isfahan, Iran; Department of Biostatistics (K H Abegaz MSc), Near East University, Nicosia, Cyprus; Department of Biostatistics and Health Informatics (K H Abegaz), Department of Public Health (G Alamene MPH), Department of Medical Laboratory Science (M Hussen MSc), Madda Walabu University, Bale Robe, Ethiopia; Department of Nursing (D H Haile MSc), College of Health Sciences (G M Kassa MSc), Department of Public Health (D B Ketema MPH, T E Wonde MPH), Debre Markos University, Debre Markos, Ethiopia (A N Abejie MPH); Department of Pediatric Dentistry (Prof L G Abreu PhD), Department of Maternal and Child Nursing and Public Health (Prof D C Malta PhD), Department of Clinical Medicine (Prof B R Nascimento PhD), Clinical Hospital (Prof B R Nascimento), Department of Infectious Diseases and Tropical Medicine (B P Sao Jose PhD), Federal University of Minas Gerais, Belo Horizonte, Brazil; Department of Research (M R M Abrigo PhD), Philippine Institute for Development Studies, Quezon City, Philippines; Department of Disease Control (M M K Accrombessi PhD, J Cano PhD), Department of Infectious Disease Epidemiology (O J Brady PhD), Faculty of Infectious and Tropical Diseases (Prof B Sartorius), London School of Hygiene & Tropical Medicine, London, UK; Clinical Research and Operations (M M K Accrombessi), Foundation for Scientific Research, Cotonou, Benin; Department of Preventive Medicine (D Acharya MPH), Dongguk University, Gyeongju, South Korea; Department of Community Medicine (D Acharya), Kathmandu University, Devdaha, Nepal; Department of Environmental Health Engineering (M Khazaei PhD, M Leili PhD), Department of Epidemiology (S Khazaei PhD), Neurophysiology Research Center (H Komaki MD), Department of Biostatistics (N Mohammad Gholi Mezerji MSc), Hamadan University of Medical Sciences, Hamadan, Iran (M Adabi PhD, Prof R Mohammadibakhsh PhD); Department of Global Health (A A Adamu PhD, O O Adetokunboh PhD, C J Iwu PhD), Centre for Evidence Based Health Care (A Jaca PhD), Stellenbosch University, Cape Town, South Africa; Cochrane South Africa (A A Adamu, D E Ndwandwe PhD), Grants, Innovation and Product Development Unit (P W Mahasha PhD), South African Medical Research Council, Cape Town, South Africa (C J Iwu, A Jaca, C A Nnaji MPH, Prof C S Wiysonge MD); College of Medicine (O M Adebayo MD), Department of Community Medicine (O S Ilesanmi PhD), Department of Medicine (Prof M O Owolabi DrM), University College Hospital, Ibadan, Ibadan, Nigeria; Department of Medical Rehabilitation (Prof R A Adedoyin PhD), Department of Child Dental Health (Prof M O Folan FWACS), Obafemi Awolowo University, Ile-Ife, Nigeria; School of Medicine (V Adekanmbi PhD), Cardiff University, Cardiff, UK; Centre of Excellence for Epidemiological Modelling and Analysis (O O Adetokunboh), Stellenbosch University, Stellenbosch, South Africa; School of Public Health (B M Adhena MPH, G G Meles MPH, F H Tesfay PhD), Department of Nursing (G G Gebremeskel MSc), Department of Epidemiology (H A Gesesew PhD), Department of Biostatistics (K Gezae MSc, A A Tawse MSc), Department of Medical Parasitology and Entomology (G B Hailu MSc), Department of Nutrition and Dietetics (A Kahsay MPH), Department of Microbiology and Immunology (S Muthupandian PhD), Department of Pharmacology and Toxicology (D Z Wondafrash MSc), Mekelle University, Mekelle, Ethiopia; Department of Dermatology (M Afarideh), Mayo Clinic, Rochester, MN, USA; Faculty of Pharmacy (S Ahmad MSc), Mahsa University, Kuala Langat, Malaysia; Lincoln Medical School (K Ahmadi PhD), Universities of Nottingham and Lincoln, Lincoln, UK; Economics and Rural Development Department (A E Ahmed PhD), University of Gezira, Wad Madani, Sudan; Department of Epidemiology (M B Ahmed MPH), Department of Psychiatry (M S Daba MSc), School of Nursing (A B Demis MSc), Department of Environmental Health Sciences and Technology (S Mereta PhD), Jimma University, Jimma, Ethiopia; Australian Center for Precision Health (M B Ahmed), University of South Australia, Adelaide, SA, Australia; James P Grant School of Public Health (R Ahmed MPH, R Das Gupta MPH), BRAC University, Dhaka, Bangladesh; Health Systems and Population Studies Division (R Ahmed), Nutrition and Clinical Services Division (M Sultana MPH), Maternal and Child Health Division (S Zaman MPH), International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; Department of Epidemiology and Biostatistics (T Y Akalu MPH, S G Nigatu MPH, M M Sisay MPH, Z T Tessema MSc, H F Wolde MPH), Institute of Public Health (W F Chanie MPH, G D Demissie MPH), School of Nursing (H B Netsere MS), Department of Medical Microbiology (B Tessema PhD), University of Gondar, Gondar, Ethiopia; 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-Ally MD), Washington University in St. Louis, St. Louis, MO, USA; Clinical Epidemiology Center (Z Al-Ally), Department of Veterans Affairs, St. Louis, MO, USA; Prevention Division (N Alam MPH), Queensland Health, Brisbane, QLD, Australia; Centre for Environment and Population Health (N Alam), Griffith University, Nathan, Australia; Community Health and Epidemiology (S Alam MSc), Dalhousie University, Halifax, NS, Canada; Health Information Management and Technology Department (T M Alanzi PhD), Forensic Medicine Division (Prof R G Menezes MD), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; Center for Health System Research (J E Alcalde-Rabanal PhD), Health and Nutrition Research Center (I R Campos-Nonato PhD), Center for Nutrition and Health Research (E Denova-Gutiérrez DSc), Center for Population Health Research (L Morales MSc), Center for Health System Research (M Rios-Blancas MPH, E Serván-Mori PhD), Health Systems Research Center (D V Ortega-Altamirano DrPH), National Institute of Public

Health, Cuernavaca, Mexico; Erbil Technical Health College (B A Ali PhD), Erbil Polytechnic University, Erbil, Iraq; School of Pharmacy (B A Ali), Tishk International University, Erbil, Iraq (K A Mohammad PhD); Social Determinants of Health Research Center (M Alijanzadeh PhD), Qazvin University of Medical Sciences, Qazvin, Iran; Health Management and Economics Research Center (V Alipour PhD, J Arabloo PhD, S Azari PhD, A Ghashghaee BSc), Health Economics Department (V Alipour), Preventive Medicine and Public Health Research Center (M Asadi-Aliabadi MSc, E Babae PhD, M Moradi-Lakeh MD, Prof M Nojomi MD), Student Research Committee (A Ghashghaee), Minimally Invasive Surgery Research Center (A Kabir MD), Pars Advanced and Minimally Invasive Medical Manners Research Center (A Kasaeian), Department of Neurosurgery (M Khosravi MD), Department of Ophthalmology (N Manafi MD), Department of Community and Family Medicine (Prof M Nojomi), Department of Health Services Management (H Shabaninejad PhD), Physiology Research Center (M Yousefifard PhD), Iran University of Medical Sciences, Tehran, Iran; Department of Health Policy and Management (Prof S M Aljunid PhD), Kuwait University, Safat, Kuwait; International Centre for Casemix and Clinical Coding (Prof S M Aljunid), National University of Malaysia, Bandar Tun Razak, Malaysia; Department of Environmental Health Engineering (Prof A Almasi PhD), Infectious Disease Research Center (Prof K Ghadiri MD), Pediatric Department (Prof K Ghadiri), Medical Biology Research Center (F Heydarpour PhD), Health Institute (A Jalali PhD), Substance Abuse Prevention Research Center (A Jalali), Research Center for Environmental Determinants of Health (Prof B Karami Matin PhD, A Kazemi Karyani PhD, M Moradi PhD, Prof F Najafi PhD, Prof M Pirsaeheb PhD, F Rajati PhD, Prof E Sadeghi PhD, Y Safari PhD, K Sharafi PhD, S Soltani PhD), Department of Public Health (A Kazemi Karyani), Clinical Research Development Center (M Naderi PhD), Department of Epidemiology and Biostatistics (Prof F Najafi, Y Salimi PhD), Faculty of Public Health (R Safari-Faramani PhD), Department of Anatomical Sciences (M R Salahshoor PhD), Social Development and Health Promotion Research Center (Y Salimi, M Soofi PhD), Department of Sports Medicine and Rehabilitation (M Shamsi PhD), Department of Health Education and Health Promotion (S Siabani PhD, A Ziapour PhD), Department of Vascular and Endovascular Surgery (M Sobhiyeh MD), Kermanshah University of Medical Sciences, Kermanshah, Iran; Department of Epidemiology (A Almasi-Hashiani PhD), Health Services Management Department (S Amini PhD), Department of Pediatrics (J Nazari MD), Arak University of Medical Sciences, Arak, Iran; Medical Research Center (H M Al-Mekhlafi PhD), Jazan University, Jazan, Saudi Arabia (Prof N Bedi MD); Department of Parasitology (H M Al-Mekhlafi), Sana'a University, Sana'a, Yemen; Pediatric Intensive Care Unit (K A Altirkawi MD, M Tamsah MD), Internal Medicine Department (Y Mohammad MD), King Saud University, Riyadh, Saudi Arabia; Research Group in Health Economics (Prof N Alvis-Guzman PhD), University of Cartagena, Cartagena, Colombia; Research Group in Hospital Management and Health Policies (Prof N Alvis-Guzman), Department of Economic Sciences (N J Alvis-Zakzuk MSc), University of the Coast, Barranquilla, Colombia; National Health Observatory (N J Alvis-Zakzuk), Colombian National Health Observatory (C A Castañeda-Orjuela MD), National Institute of Health, Bogota, Colombia; Department of Epidemiology and Biostatistics (A L Amit BS), Department of Health Policy and Administration (C T Antonio MD), Department of Nutrition (J F Lopez MD), University of the Philippines Manila, Manila, Philippines; School of Public Health (A L Amit), Department of Epidemiology (M Bairwa MD), Department of Radiology and Radiological Sciences (N Hafezi-Nejad, Ary Haj-Mirzaian MD), Center for Clinical Global Health Education (S R Atre PhD), Johns Hopkins University, Baltimore, MD, USA; Cardiology Department (C Andrei PhD), Department of General Surgery (D V Davitoiu PhD, A Manda MD, I Negoi PhD), Department of Infectious Diseases (L Preotescu PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; Social Determinants of Health Research Center (M Anjomshoa PhD), Rafsanjan University of Medical Sciences, Rafsanjan, Iran; Research Center for Evidence Based Medicine (F Ansari PhD), School of Nursing and Midwifery

(H Hassankhani PhD), Tabriz University of Medical Sciences, Tabriz, Iran (H Haririan PhD); Razi Vaccine and Serum Research Institute (F Ansari), Agricultural Research, Education, and Extension Organization, Tehran, Iran; Department of Applied Social Sciences (C T Antonio), School of Nursing (P H Lee PhD), Hong Kong Polytechnic University, Hong Kong, China; Menzies Institute for Medical Research (B Antony PhD, A Singh MTech), University of Tasmania, Hobart, TAS, Australia; Agribusiness Study Program (E Antriandarti DrAgrSc), Sebelas Maret University, Surakarta, Indonesia; Neurology Department (Prof H M A Aref PhD, Prof N El Nahas MD, Prof A S Shalash PhD), Department of Obstetrics and Gynecology (Prof A F Nabhan PhD), Department of Entomology (A M Samy PhD), Ain Shams University, Cairo, Egypt; Department of Public Health (O Aremu PhD), Birmingham City University, Birmingham, UK; Social Determinants of Health Research Center (B Armoon PhD), Saveh University of Medical Sciences, Saveh, Iran; Social Determinants of Health Research Center (B Armoon), Yasuj University of Medical Sciences, Yasuj, Iran; School of Health Sciences (A Arora PhD), Western Sydney University, Campbelltown, NSW, Australia; Disciple of Child and Adolescent Health (A Arora), University of Sydney, Westmead, NSW, Australia; Monitoring Evaluation and Operational Research Project (K K Aryal PhD), Abt Associates Nepal, Lalitpur, Nepal; School of Nursing and Midwifery (A Arzani DrPH), Social Determinants of Health Research Center (A Bijani PhD, S Mouodi PhD), Department of Clinical Biochemistry (A Mosapour PhD), Student Research Committee (M Zamani MD), Babol University of Medical Sciences, Babol, Iran (A Arzani); Department of Nursing (H T Atalay MSc, G G Gebremeskel, D B Tadesse MSc, G T Welde Samuel MSc), School of Pharmacy (G T Demoz MSc, G G Kasahun MSc), Department of Biomedical Sciences (G G Kassa MSc), Aksum University, Aksum, Ethiopia; Department of Immunology (S Athari MPH), Zanjan University of Medical Sciences, Iran; Department of Biology (S Athari), Department of Pharmacology and Toxicology (A Eftekhari PhD), Department of Healthcare Management (E Hasanpoor PhD), Department of Microbiology (A Hasanzadeh), Department of Nutrition and Food Sciences (H Pourjafar PhD), Maragheh University of Medical Sciences, Maragheh, Iran; Dr DY Patil Medical College, Hospital and Research Centre (S R Atre), Dr DY Patil Vidyapeeth, Pune, India; School of Business (Prof M Ausloos PhD), University of Leicester, Leicester, UK; Department of Statistics and Econometrics (Prof M Ausloos, Prof C Herteliu PhD), Bucharest University of Economic Studies, Bucharest, Romania; Department of Nursing (N Awoke MSc, T Y Chichiabellu MSc), Department of Dermatology (A G Kelbore MSc), School of Public Health (T L Lenjebo MPH), Department of Midwifery (K Paulos MSc), Wolaita Sodo University, Wolaita Sodo, Ethiopia; The Judith Lumley Centre (B Ayala Quintanilla PhD), School of Nursing and Midwifery (Mu Rahman PhD), La Trobe University, Melbourne, VIC, Australia; General Office for Research and Technological Transfer (B Ayala Quintanilla), Peruvian National Institute of Health, Lima, Peru; School of Public Health (G Ayano MSc, B Duko MPH, D Hendrie PhD, T R Miller PhD), Curtin University, Perth, WA, Australia; Department of Health Policy Planning and Management (M A Ayanore PhD), Department of Family and Community Health (N Kugbey PhD), University of Health and Allied Sciences, Ho, Ghana; Department of Nursing (Y A Aynalem MSc, W S Shiferaw MSc), Debre Berhan University, Debre Berhan, Ethiopia; Global Adolescent Health Group (P S Azzopardi PhD), Burnet Institute, Melbourne, VIC, Australia; Wardliparingga Aboriginal Research Unit (P S Azzopardi), South Australian Health and Medical Research Institute, Adelaide, SA, Australia; Department of Public Health Medicine (T K Babalola MSc), Discipline of Public Health Medicine (T G Ginindza PhD), Department of Psychology and Health Promotion (N Kugbey), Discipline of Optometry (Prof K S Naidoo PhD), University of KwaZulu-Natal, Durban, South Africa (T G Ginindza); Department of Community Health and Primary Care (T K Babalola), Department of Psychiatry (A T Olagunju MD), University of Lagos, Lagos, Nigeria; Public Health Risk Sciences Division (A Badawi PhD), Public Health Agency of Canada, Toronto, ON, Canada; Department of Nutritional Sciences (A Badawi), Centre for Global Child Health (Prof Z A Bhutta PhD), Department of Medicine (V Chattu MD), University of Toronto, Toronto,

- ON, Canada; Centre for Community Medicine (M Bairwa), Department of Paediatrics (Prof R Lodha MD), Department of Psychiatry (Prof R Sagar MD), All India Institute of Medical Sciences, New Delhi, India; Department of Forensic Medicine and Toxicology (S M Bakkannavar MD), Centre for Bio Cultural Studies (P Hoogar PhD), Manipal Academy of Higher Education, Manipal, India (Prof V Jha MD); Department of Medical Microbiology (S Balakrishnan PhD), School of Public Health (A G Bali MPH, W F Chanie, M G Tekle MPH), School of Pharmacy (H A Bojia BPharm), School of Nursing and Midwifery (A Desalew MSc), Haramaya University, Harar, Ethiopia; Department of Hypertension (Prof M Banach PhD), Medical University of Lodz, Lodz, Poland; Polish Mothers' Memorial Hospital Research Institute, Lodz, Poland (Prof M Banach); Department of Internal Medicine (J A M Banoub MRCP), University of London, London, UK; Department of General Medicine (J A M Banoub), Biomedical Informatics and Medical Statistics Department (I El Sayed PhD), Pediatric Dentistry and Dental Public Health Department (Prof M El Tantawi PhD), Alexandria University, Alexandria, Egypt; Clinic for Infectious and Tropical Diseases (A Barac PhD), Clinical Center of Serbia, Belgrade, Serbia; Faculty of Medicine (A Barac, Prof M M Santric-Milicevic PhD), Institute of Microbiology and Immunology (E Dubljanin PhD), School of Public Health and Health Management (Prof M M Santric-Milicevic), University of Belgrade, Belgrade, Serbia; Heidelberg Institute of Global Health (Prof T W Bärnighausen MD, B Moazen MSc, S Mohammed PhD), Heidelberg University, Heidelberg, Germany; T.H. Chan School of Public Health (Prof T W Bärnighausen), Center for Primary Care (S Basu PhD), Harvard Medical School (M U G Kraemer PhD), Brigham and Women's Hospital (V Kumar MD), Department of Global Health and Population (Prof O F Norheim PhD, Prof S Vollmer PhD), Department of Genetics (A Pereira PhD), Division of General Internal Medicine (Prof A Sheikh MD), Harvard University, Boston, MA, USA; School of Public Health and Community Medicine (Prof H Basaleem PhD), Aden College, Aden, Yemen; School of Public Health (S Basu, Prof S Saxena MD), Department of Primary Care and Public Health (J Car PhD, Prof A Majeed MD, Prof S Rawaf MD), Department of Surgery and Cancer (Prof A C Davis PhD), Imperial College Business School (D Kusuma DSc), WHO Collaborating Centre for Public Health Education and Training (D L Rawaf MD), Imperial College London, London, UK; Information Technology (V Bay PhD), Ho Chi Minh City University of Technology, Ho Chi Minh City, Vietnam; Health Human Resources Research Center (M Bayati PhD), Department of Environmental Health (M Hoseini PhD), Research Center for Health Sciences, Institute of Health (M Hoseini), Non-communicable Disease Research Center (Prof R Malekzadeh, S G Sepanlou), Shiraz University of Medical Sciences, Shiraz, Iran; School of Public Health (E Baye PhD), Department of Pharmacy (Y M Belayneh MSc, B Meharie MSc), Department of Public Health (T C Mekonnen MPH), Department of Environmental Health (Y M Tefera MSc), Wollo University, Dessie, Ethiopia; Department of Community Medicine (Prof N Bedi), Gandhi Medical College Bhopal, Bhopal, India; Department of Physical Medicine and Rehabilitation (M Beheshti MD), New York University, New York, NY, USA; Social Determinants of Health Research Center (Ma Behzadifar PhD), Department of Epidemiology and Biostatistics (Me Behzadifar MSc), Department of Public Health (M Imami-Nasab PhD, S Nouraei Motlagh PhD), Lorestan University of Medical Sciences, Khorramabad, Iran; Department of Public Health (B Bekele MPH, H Y Hassen MPH), Mizan-Tepi University, Mizan Teferi, Ethiopia; Doctoral School of Health Sciences (B Bekele), University of Debrecen, Debrecen, Hungary; School of the Environment (Prof M L Bell PhD), Yale University, New Haven, CT, USA; Nuffield Department of Population Health (D A Bennett PhD, M A Karim MD, B Lacey PhD), Department of Zoology (M U G Kraemer), Big Data Institute (C E Moore PhD), University of Oxford, Oxford, UK; Department of Public Health (D A Berbada MPH, M B Sorrie MPH, F G W/hawariat MPH), Faculty of Business and Economics (G T Worku MPH), Arba Minch University, Arba Minch, Ethiopia; Hubert Department of Global Health (R S Bernstein MD), Division of Cardiology (Prof J Shin MD), Emory University, Atlanta, GA, USA; Department of Global Health (R S Bernstein), University of South Florida, Tampa, FL, USA; Division of General Internal Medicine (A G Bhat MD), University of Massachusetts Medical School, Springfield, MA, USA; Department of Statistical and Computational Genomics (K Bhattacharyya MSc), National Institute of Biomedical Genomics, Kalyani, India; Department of Statistics (K Bhattacharyya), University of Calcutta, Kolkata, India; Department of Global Health (S Bhattarai MD), Global Institute for Interdisciplinary Studies, Kathmandu, Nepal; Injury Division (S Bhaumik MBBS), The George Institute for Global Health (Prof V Jha), New Delhi, India; The George Institute for Global Health (S Bhaumik), Transport and Road Safety Research Centre (R Biswas MSc, S Boufous PhD), School of Public Health and Community Medicine (S Karki PhD), School of Optometry and Vision Science (Prof K S Naiddoo, Prof S Resnikoff MD), University of New South Wales, Sydney, NSW, Australia; Centre of Excellence in Women & Child Health (Prof Z A Bhutta), Division of Women and Child Health (J K Das MD), Aga Khan University, Karachi, Pakistan; Mario Negri Institute for Pharmacological Research, Ranica, Italy (B Bikbov MD); Ethiopian Public Health Institute, Addis Ababa, Ethiopia (B M Biriha MSc); Department of Nursing (B M Biriha), Debre Tabor University, Debre Tabor, Ethiopia; School of Health Sciences (R Biswas), Swinburne University of Technology, Melbourne, VIC, Australia; Department of Veterinary Medicine (S Bohloul PhD), Islamic Azad University, Kermanshah, Iran; University of Genoa, Genoa, Italy (N L Bragazzi PhD); Department of Biomedical Technologies (A N Briko MSc), Bauman Moscow State Technical University, Moscow, Russia; Department of Epidemiology and Evidence Based Medicine (Prof N I Briko DSc), N A Semashko Department of Public Health and Healthcare (Prof M Jakovljevic PhD), I.M. Sechenov First Moscow State Medical University, Moscow, Russia; Neuroscience Unit (G B Britton PhD), Institute for Scientific Research and High Technology Services, Panama City, Panama; Gorgas Memorial Institute for Health Studies, Panama City, Panama (G B Britton, F Castro MD, I Moreno Velásquez PhD, H Quintana PhD); Department of Community Medicine (Prof S Burugina Nagaraja MD), Employee State Insurance Post Graduate Institute of Medical Sciences and Research, Bangalore, India; Department of Health Care Management (Prof R Busse PhD), Technical University of Berlin, Berlin, Germany; School of Public Health and Health Systems (Z A Butt PhD), University of Waterloo, Waterloo, ON, Canada; Al Shifa School of Public Health (Z A Butt), Al Shifa Trust Eye Hospital, Rawalpindi, Pakistan; Internal Medicine Department (Prof L L A Cámara MD), Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; Board of Directors (Prof L L A Cámara), Argentine Society of Medicine, Buenos Aires, Argentina (Prof P R Valdez MEd); Centre for Population Health Sciences (J Car), Nanyang Technological University, Singapore, Singapore; Department of Health Care (Prof R Cárdenas DSc), Metropolitan Autonomous University, Mexico City, Mexico; Research Unit on Applied Molecular Biosciences (Prof F Carvalho PhD, V M Costa PhD), Associated Laboratory for Green Chemistry (Prof E Fernandes PhD, N G M Gomes PhD), Department of Chemistry (N G M Gomes), EPIUnit—Public Health Institute University Porto (A Ribeiro PhD), University of Porto, Porto, Portugal; Epidemiology and Public Health Evaluation Group (C A Castañeda-Orjuela), Department of Public Health (Prof F P De la Hoz PhD), National University of Colombia, Bogotá, Colombia; Division of Epidemiology and Communicable Diseases (P Chatterjee MD), Indian Council of Medical Research, New Delhi, India (Prof L Dandona); Department of Epidemiology and Preventive Medicine (K L Chin PhD, Prof Y Guo PhD), School of Public Health and Preventive Medicine (S Li PhD), The School of Clinical Sciences at Monash Health (S Zaman), Monash University, Melbourne, VIC, Australia; Melbourne Medical School (K L Chin), University of Melbourne, Parkville, VIC, Australia; Department of Pulmonary Medicine (Prof D J Christopher MD), Department of Endocrinology, Diabetes and Metabolism (Prof N Thomas PhD), Department of Nephrology (Prof S Varughese FRCP), Christian Medical College and Hospital, Vellore, India; Faculty of Biology (D Chu PhD), Hanoi National University of Education, Hanoi, Vietnam; Research Unit and Training Consortium on Emerging Diseases and Climate Change (C Culquichicon MD), Peruvian University Cayetano Heredia, Lima, Peru; Clinical Dermatology, IRCCS Istituto Ortopedico Galeazzi (G Damiani MD), Department of Clinical Sciences and Community Health (Prof C La Vecchia MD), University of Milan, Milan, Italy;

Department of Dermatology (G Damiani), Department of Nutrition and Preventive Medicine (Prof J Sanabria MD), Case Western Reserve University, Cleveland, OH, USA; Health Policy Research (M R Mathur PhD), Indian Institute of Public Health (Prof S Zodpey PhD), Public Health Foundation of India, Gurugram, India (Prof L Dandona, Prof R Dandona, G Kumar PhD, D K Lal MD); Institute for Global Health Innovations (A K Dang MD, C T Nguyen MPH, H L T Nguyen MPH, V M Nong MPH), Institute of Research and Development (M Hosseinzadeh PhD), Duy Tan University, Da Nang, Vietnam; Department of Information Technology (A M Darwesh PhD), Department of Computer Science (M Hosseinzadeh PhD), University of Human Development, Sulaymaniyah, Iraq; Department of Pediatrics (A H Darwish DipLangStud), Tanta University, Tanta, Egypt; Toxoplasmosis Research Center (Prof A Daryani PhD), Department of Medical Parasitology (Prof R Faridnia PhD), Department of Immunology (Prof A Rafiei PhD), Molecular and Cell Biology Research Center (Prof A Rafiei), Pediatric Infectious Diseases Research Center (Prof M Rezai MD), Mazandaran University of Medical Sciences, Sari, Iran; Department of Epidemiology and Biostatistics (R Das Gupta), University of South Carolina, Columbia, SC, USA; Central University Tami Nadu, Thiruvavur, India (Prof A P Dash DSc); Department of Global Health and Infection (Prof G Davey MD), Wellcome Trust Brighton and Sussex Centre for Global Health Research (K Deribe PhD), Brighton and Sussex Medical School, Brighton, UK; School of Public Health (Prof G Davey, K Deribe, E M Roro MPH), Center for Food Science and Nutrition (T B Elema MA), Department of Nursing and Midwifery (K B Gebremedhin MSc), Department of Pharmacology (D Z Wondafraash), School of Allied Health Sciences (E Yisma MSc), Addis Ababa University, Addis Ababa, Ethiopia (G T Demoz); Department of Population and Development (C A Dávila-Cervantes PhD), Latin American Faculty of Social Sciences Mexico, Mexico City, Mexico; Ear Institute (Prof A C Davis), Division of Psychology and Language Sciences (M Kumar PhD), Institute of Child Health (K Sarkar MD), University College London, London, UK; Department of Surgery (D V Davitoiu), Clinical Emergency Hospital Sf. Pantelimon, Bucharest, Romania; Department of Nursing (A B Demis), Department of Public Health (G F Mulaw MPH), Department of Medical Laboratory Science (M A Reta MSc), Woldia University, Woldia, Ethiopia; Neonatal Nursing Department (D B Demissie MSc), Anesthesia Department (B G Weji MSc), St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia (D Shifti MSc); Department of Public Health (T Kolola MPH, S A Shallo MPH), Ambo University, Ambo, Ethiopia (D B Demissie); Department of Community Medicine (Prof S D Dharmaratne), University of Peradeniya, Peradeniya, Sri Lanka; Department of Mathematical Demography & Statistics (P Dhillion PhD), Department of Population Studies (J Khan MPH), International Institute for Population Sciences, Mumbai, India (P Kumar PhD); Health Research Section (M Dhimal PhD), Nepal Health Research Council, Kathmandu, Nepal; Department of Microbiology (G P Dhungana MSc), Far Western University, Mahendranagar, Nepal; 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), Autonomous University of Sinaloa, Culiacan Rosales, Mexico; Department of Health Promotion and Education (I O Dipeolu PhD, S E Ibitoye MPH), Department of Community Medicine (O S Ilesanmi), Department of Medicine (O S Ogah PhD, Prof M O Owolabi), University of Ibadan, Ibadan, Nigeria; Development of Research and Technology Center (S Djalalinia PhD), Ministry of Health and Medical Education, Tehran, Iran; School of Medicine (Prof K E Doyle PhD), School of Health Sciences (N D D Manohar MPH), Translational Health Research Institute (F A Ogbo PhD), Western Sydney University, Sydney, NSW, Australia; Health Sciences (Prof K E Doyle), Royal Melbourne Institute of Technology University, Melbourne, VIC, Australia; School of Public Health (B Duko, Y C Kasahun MPH), Department of Pharmacy (A Toma PhD), Hawassa University, Hawassa, Ethiopia; School of Medicine (Prof A R Duraes PhD), Institute of Collective Health (Prof D Rasella PhD), Institute of Public Health (Prof D Rasella), Federal University of Bahia, Salvador, Brazil; Department of Internal Medicine

(Prof A R Duraes), Bahiana School of Medicine and Public Health, Salvador, Brazil; Department of Epidemiology (M Ebrahimi Kalan MSc), Florida International University, Miami, FL, USA; School of Health Sciences (H A Edinur PhD), Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia; Centre Clinical Epidemiology and Biostatistics (A Effiong MB), School of Medicine and Public Health (M N Khan MSc), University of Newcastle, Newcastle, NSW, Australia; Department of Pharmacology and Toxicology (A Eftekhari), The John Paul II Catholic University of Lublin, Lublin, Poland; Department of Clinical Pathology (Prof M El Sayed Zaki PhD), Mansoura University, Mansoura, Egypt; Department of Food Science and Nutrition (T B Elema), Arsi University, Asella, Ethiopia; Department of Community Medicine (H Elkout PhD), Tripoli University, Tripoli, Libya; Health Information (H Elkout), WHO, Tripoli, Libya; Eijkman-Oxford Clinical Research Unit (I R Elyazar PhD), Eijkman Institute for Molecular Biology, Jakarta, Indonesia; Department of Pediatrics and Child Health Nursing (A Endalamaw MSc), Department of Epidemiology and Biostatistics (K M Mihretie MPH, K Muchie MSc), Department of Reproductive Health and Population Studies (D Nigatu MPH), Bahir Dar University, Bahir Dar, Ethiopia; Department of Midwifery (D A Endalew MSc, A Yeshaneh MSc), Wolkite University, Wolkite, Ethiopia; Division of Cancer Epidemiology and Genetics (A Etemadi), National Cancer Institute, Bethesda, MD, USA; Independent Consultant, Awka, Nigeria (O Ezekannagha PhD); International Institute for Tropical Agriculture, Ibadan, Nigeria (O Ezekannagha); College of Medicine (M Fareed PhD), Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia; Department of Environmental Health Engineering (M Fazlzadeh), Social Determinants of Health Research Center (H Zandian PhD), Department of Community Medicine (H Zandian), Ardabil University of Medical Science, Ardabil, Iran; National Institute for Stroke and Applied Neurosciences (Prof V L Feigin), Auckland University of Technology, Auckland, New Zealand; Research Center of Neurology, Moscow, Russia (Prof V L Feigin); Department of Neurobiology (S Fereshtehnejad PhD), Department of Medicine-Huddinge (D K Mohammad PhD), Global Public Health-Health Systems and Policy: Medicines Focusing Antibiotics (Prof A Pathak PhD), Karolinska Institutet, Stockholm, Sweden; Division of Neurology (S Fereshtehnejad), University of Ottawa, Ottawa, ON, Canada; Psychiatry Department (I Filip MD), Kaiser Permanente, Fontana, CA, USA; School of Health Sciences (I Filip), College of Graduate Health Sciences (A Radfar MD), AT Still University, Mesa, AZ, USA; Institute of Gerontological Health Services and Nursing Research (F Fischer PhD), Ravensburg-Weingarten University of Applied Sciences, Weingarten, Germany; Institute of Gerontology (N A Foigt PhD), National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine; Abadan Faculty of Medical Sciences (M Foroutan PhD), Abadan School of Medical Sciences, Abadan, Iran; School of Public Health, Medical, and Veterinary Sciences (R C Franklin PhD), James Cook University, Douglas, QLD, Australia; Department of Dermatology (T Fukumoto PhD), Kobe University, Kobe, Japan; Gene Expression & Regulation Program (T Fukumoto), The Wistar Institute, Philadelphia, PA, USA; Department of Cardiovascular Medicine (M M Gad MD), Heart and Vascular Institute (A M Saad MD), Cleveland Clinic, Cleveland, OH, USA; Gillings School of Global Public Health (M M Gad), University of North Carolina Chapel Hill, Chapel Hill, NC, USA; Department of Nursing (R T Gayesa MSc), School of Nursing and Midwifery (H K Kasaye MSc), Department of Public Health (E M Roro), Department of Public Health (M T Yilma MPH), Wollega University, Nekemte, Ethiopia; International Trachoma Initiative (T Gebre PhD), Task Force for Global Health, Decatur, GA, USA; College of Medicine and Public Health (H A Gesesew), Southgate Institute for Health and Society (F H Tesfay), Flinders University, Adelaide, SA, Australia; Population Health (P R Ghimire PhD), New South Wales Health, Queanbeyan, Australia; Medical School (Prof P S Gill DM), University of Warwick, Coventry, UK; Adelaide Medical School (T K Gill PhD), Australian Research Centre for Population Oral Health (N Hariyani PhD), Centre for Heart Rhythm Disorders (J Noubiap MD), School of Public Health (Y M Tefera), University of Adelaide, Adelaide, SA, Australia; Hudson College of Public Health (S V Gopalani MPH), University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; Department of Health and Social Affairs (S V Gopalani), Government of the Federated States of Micronesia, Palikir, Federated

States of Micronesia; Center for Clinical and Epidemiological Research (A C Goulart PhD), Department of Internal Medicine (A C Goulart), Laboratory of Genetics and Molecular Cardiology (A Pereira), Department of Psychiatry (Yu Wang PhD), University of São Paulo, São Paulo, Brazil; Postgraduate Program in Epidemiology (Prof B N G Goulart DSc), Federal University of Rio Grande do Sul, Porto Alegre, Brazil; Department of Dermatology (A Grada MD), Boston University, Boston, MA, USA; Department of Family and Community Medicine (M I M Gubari PhD), University of Sulaimani, Sulaimani, Iraq; Department of Microbiology (Prof H C Gugnani PhD), Department of Epidemiology (Prof H C Gugnani), Saint James School of Medicine, The Valley, Anguilla; Epidemiology Unit (D Guido PhD), Agency for Health Protection, Milan, Italy; Institute of Tropical Pathology and Public Health (R A Guimarães MSc), Federal University of Goiás, Goiânia, Brazil; Department of Epidemiology (Prof Y Guo), Binzhou Medical University, Yantai City, China; Department of Preventive Cardiology (Prof R Gupta MD), Eternal Heart Care Centre & Research Institute, Jaipur, India; Department of Medicine (Prof R Gupta), Mahatma Gandhi University Medical Sciences, Jaipur, India; Obesity Research Center (Arv Haj-Mirzaian), Research Institute for Endocrine Sciences (S N Irvani MD), Department of Epidemiology (N Izadi MSc, S Riahi PhD, S Sabour PhD), School of Management and Medical Education (N Jahanmehr PhD), Safety Promotion and Injury Prevention Research Center (N Jahanmehr), Shahid Beheshti University of Medical Sciences, Tehran, Iran (M Khayamzadeh MD); Department of Family and Community Medicine (Prof R R Hamadeh PhD), Arabian Gulf University, Manama, Bahrain; School of Health and Environmental Studies (Prof S Hamidi DrPH), Hamdan Bin Mohammed Smart University, Dubai, United Arab Emirates; Department of Public Health (D Handiso MPH), Wachemo University, Hossana, Ethiopia; Department of Dental Public Health (N Hariyani), Faculty of Public Health (S Martini PhD), Airlangga University, Surabaya, Indonesia; Department of Zoology and Entomology (A I Hasaballah PhD), Al Azhar University, Cairo, Egypt; Institute for Social Science Research (M Hasan MPH, A A Mamun PhD), ARC Centre of Excellence for Children and Families over the Life Course (M Hasan), The University of Queensland, Indooroopilly, QLD, Australia; Independent Consultant, Tabriz, Iran (H Hassankhani); Department of Primary and Interdisciplinary Care (H Y Hassen), University Hospital Antwerp, Antwerp, Belgium; Center for Environmental and Respiratory Health Research (B Heibati PhD), University of Oulu, Oulu, Finland; School of Business (Prof C Herteliu), London South Bank University, London, UK; Department of Public Health (H D d Hidru MPH, B E Tesfay MPH), Adigrat University, Adigrat, Ethiopia; Department for Health (T R Hird PhD), Department of Mathematical Sciences (P Moraga PhD), University of Bath, Bath, UK; Population Health Domain (T R Hird), Baker Heart and Diabetes Institute, Melbourne, VIC, Australia; Center of Excellence in Behavioral Medicine (C L Hoang BMedSc, T H Nguyen BMedSc), Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam; Guilan Road Trauma Research Center (E Homaie Rad PhD), Social Determinants of Health Research Center (E Homaie Rad), Guilan University of Medical Sciences, Rasht, Iran; Department of Pharmacology (N Hossain MPhil), Bangladesh Industrial Gases Limited, Tangail, Bangladesh; Division of Information and Computing Technology (Prof M Househ PhD), Hamad Bin Khalifa University, Doha, Qatar; Faculty of Medicine of Tunis (Prof M Hsairi MPH), University Tunis El Manar, Tunis, Tunisia; Department of Epidemiology and Health Statistics (Prof G Hu PhD), Central South University, Changsha, China; School of Public Health (Prof E U Igumbor PhD), University of the Western Cape, Bellville, Cape Town, South Africa; Department of Public Health (Prof E U Igumbor), Walter Sisulu University, Mthatha, South Africa; Department of Epidemiology (Prof M D Ilıc PhD), Department of Global Health, Economics and Policy (Prof M Jakovljevic), University of Kragujevac, Kragujevac, Serbia; College of Public Health (U Iqbal PhD), Graduate Institute of Biomedical Informatics (D N A Ningrum MPH), Taipei Medical University, Taipei, Taiwan; Institute for Physical Activity and Nutrition (S Islam PhD), Deakin University, Burwood, VIC, Australia; Sydney Medical School (S Islam), University of Sydney, Sydney, NSW, Australia; Postgraduate Institute of Medicine (A U Jayatilake PhD), University of Colombo, Colombo, Sri Lanka; Faculty of Graduate Studies (A U Jayatilake), Institute for Violence and

Injury Prevention, Colombo, Sri Lanka; Department of Community Medicine (R P Jha MSc), Dr Baba Saheb Ambedkar Medical College & Hospital, Delhi, India; Department of Community Medicine (R P Jha), Banaras Hindu University, Varanasi, India; Environmental Research Center (J S Ji DSc), Duke Kunshan University, Kunshan, China; Nicholas School of the Environment (J S Ji), Duke Global Health Institute (S Zadey MS), Duke University, Durham, NC, USA; Department of Ophthalmology (Prof J B Jonas MD), Heidelberg University, Mannheim, Germany; Beijing Institute of Ophthalmology (Prof J B Jonas), Beijing Tongren Hospital, Beijing, China; Department of Family Medicine and Public Health (J J Jozwiak PhD), University of Opole, Opole, Poland; School of Public Health (Z Kabir PhD), University College Cork, Cork, Ireland; Infectious Diseases Research Center (H Kalani PhD), Golestan University of Medical Sciences, Gorgan, Iran; Department of Forensic Medicine and Toxicology (T Kanchan MD), All India Institute of Medical Sciences, Jodhpur, India; Institute for Epidemiology and Social Medicine (A Karch MD), University of Münster, Münster, Germany; Centre for Therapeutic Target Validation (M A Karim), Wellcome Trust Sanger Institute, Cambridge, UK; Baqiyatallah Research Center for Gastroenterology and Liver Diseases (H Karimi-Sari MD), Batiyatallah University of Medical Sciences, Tehran, Iran; Department of Young Investigators (H Karimi-Sari), Middle East Liver Disease Center, Tehran, Iran; 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), Institute for Risk Assessment Sciences (E Traini MSc), Utrecht University, Utrecht, Netherlands; Department of Cancer Epidemiology (M M Kebede PhD), German Cancer Research Center, Heidelberg, Germany; Department of Prevention and Evaluation (M M Kebede), Leibniz Institute for Prevention Research and Epidemiology, Bremen, Germany; Open, Distance and eLearning Campus (Prof P N Keiyoro PhD), Department of Psychiatry (M Kumar), School of Economics (M K Muriithi PhD), University of Nairobi, Nairobi, Kenya; Non-Communicable Diseases Research Unit (Prof A P Kengne PhD), Medical Research Council South Africa, Cape Town, South Africa; Department of Medicine (Prof A P Kengne), School of Public Health and Family Medicine (C A Nnaji, Prof C S Wiysonge), University of Cape Town, Cape Town, South Africa; Department of Public Health (Prof Y S Khader PhD), Jordan University of Science and Technology, Irbid, Jordan; Social Determinants of Health Research Center (M A Khafaie PhD), Thalassemia and Hemoglobinopathy Research Center (F Rahim), Medical Physics Department (A Yadollahpour PhD), Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; School of Food and Agricultural Sciences (N Khalid PhD), University of Management and Technology, Lahore, Pakistan; Department of Biophysics and Molecular Biology (Prof R Khalilov PhD), Baku State University, Baku, Azerbaijan; Institute of Radiation Problems (Prof R Khalilov), Azerbaijan National Academy of Sciences, Baku, Azerbaijan; Department of Epidemiology and Biostatistics (E A Khan MPH), Health Services Academy, Islamabad, Pakistan; Department of Population Sciences (M N Khan), Jatiya Kabi Kazi Nazrul Islam University, Mymensingh, Bangladesh; Department of Internal Medicine (M S Khan MD), John H. Stroger, Jr. Hospital of Cook County, Chicago, IL, USA; Department of Internal Medicine (M S Khan, M S Usman MB), Department of Medicine (T J Siddiqi MB), Dow University of Health Sciences, Karachi, Pakistan; Faculty of Health and Wellbeing (K Khatab PhD), Sheffield Hallam University, Sheffield, UK; College of Arts and Sciences (K Khatab), Ohio University, Zanesville, OH, USA; The Iranian Academy of Medical Sciences, Tehran, Iran (M Khayamzadeh); Department of Nutrition and Health Science (Prof J Khubchandani PhD), Ball State University, Muncie, IN, USA; Clinical Epidemiology Unit (A Kiadaliri PhD), Lund University, Lund, Sweden; 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; School of Health Sciences (Prof A Kisa PhD), Kristiania University College, Oslo, Norway; Global Community Health and Behavioral Sciences (Prof A Kisa), Tulane University, New Orleans, LA, USA; Department of Nursing and Health Promotion (S Kisa PhD), Oslo Metropolitan University, Oslo, Norway; Department of Pediatrics (Prof N Kisson MD), School of Population and Public Health (F Pourmalek PhD, Prof N Sarrafzadegan), University of British

Columbia, Vancouver, BC, Canada; Public Health Dentistry Department (Prof K M Shivakumar PhD), Krishna Institute of Medical Sciences Deemed to be University, Karad, India; Global Healthcare Consulting, New Delhi, India (S Kochhar); Brain Engineering Research Center (H Komaki), Institute for Research in Fundamental Sciences, Tehran, Iran; Independent Consultant, Jakarta, Indonesia (S Kosen MD); Department of Internal and Pulmonary Medicine (Prof P A Koul MD), Sheri Kashmir Institute of Medical Sciences, Srinagar, India; CIBERSAM (A Koyanagi MD), San Juan de Dios Sanitary Park, Sant Boi de Llobregat, Spain; Catalan Institution for Research and Advanced Studies, Barcelona, Spain (A Koyanagi); Department of Anthropology (K Krishan PhD), Panjab University, Chandigarh, India; Faculty of Public Health (D Kusuma), University of Indonesia, Depok, Indonesia; National Institute for Health Research Oxford Biomedical Research Centre, Oxford, UK (B Lacey); Department of Pediatrics (S D Lad MD), Post Graduate Institute of Medical Education and Research, Chandigarh, India; Department of Essential Medicines and Health Products (F Lam MSc), Clinton Health Access Initiative, Boston, MA, USA; Department of Community and Family Medicine (F H Lami PhD), University of Baghdad, Baghdad, Iraq; School of Medicine (P Lamichhane PhD), Deakin University, Geelong, VIC, Australia; Medical Director (Prof V C Lansingh PhD), HelpMeSee, New York, NY, USA; General Director (Prof V C Lansingh), Mexican Institute of Ophthalmology, Queretaro, Mexico; Department of Otorhinolaryngology (S Lasrado MS), Father Muller Medical College, Mangalore, India; National Institute of Nutrition (Prof A Laxmaiah PhD), Indian Council of Medical Research, Hyderabad, India; School of Public Health (C T Leshargie MPH), Haramaya University, Debre Markos, Ethiopia; School of Public Health (Prof S Linn DrPH), University of Haifa, Haifa, Israel; Chinese Center for Disease Control and Prevention, Beijing, China (Prof Sh Liu PhD); Department of Epidemiology (Si Liu MD), Brown University, Providence, RI, USA; Department of Vector Biology (J Longbottom MSc), Liverpool School of Tropical Medicine, Liverpool, UK; Alliance for Improving Health Outcomes, Quezon City, Philippines (J F Lopez); Radiology Department (H Magdy Abd El Razek MD), Mansoura Faculty of Medicine, Mansoura, Egypt; Ophthalmology Department (M Magdy Abd El Razek MSc), Ministry of Health & Population, Aswan, Egypt; Department of Forensic Medicine & Toxicology (D Mahadeshwara Prasad MD), Mysore Medical College & Research Institute, Mysooru, India; Department of Health & Family Welfare (D Mahadeshwara Prasad), Government of Karnataka, India; Department of Clinical Physiology (N B Mahotra MD), Tribhuvan University, Kathmandu, Nepal; Ophthalmology Department (N Manafi), University of Manitoba, Winnipeg, MB, Canada; General Surgery Department I (A Manda), Emergency University Hospital Bucharest, Bucharest, Romania; Department of Population Studies (C Mapoma PhD), University of Zambia, Lusaka, Zambia; Institute for Social Science Research (J C Maravilla PhD), The University of Queensland, Brisbane, QLD, Australia; Department of Economics (Prof G Martinez PhD), Autonomous Technology Institute of Mexico, Mexico City, Mexico; Indonesian Public Health Association, Surabaya, Indonesia (S Martini); Campus Caucaia (F R Martins-Melo PhD), Federal Institute of Education, Science and Technology of Ceará, Caucaia, Brazil; Faculty of Health and Education (A Masaka MSc), Botho University-Botswana, Gaborone, Botswana; Institute of Population Health Sciences (M R Mathur), University of Liverpool, Liverpool, UK; ICF International (B K Mayala), DHS Program, Rockville, MD, USA; Department of Twin Research and Genetic Epidemiology (M Mazidi PhD), Faculty of Life Sciences and Medicine (M Molokhia PhD), Institute for Population Health (Prof K Shibuya MD), King's College London, London, UK; Department of Ophthalmology (C McAlinden PhD), Singleton Hospital, Swansea, UK; Neurology Department (Prof M Mehndiratta MD), Janakpuri Super Specialty Hospital Society, New Delhi, India; Department of Neurology (Prof M Mehndiratta), Govind Ballabh Institute of Medical Education and Research, New Delhi, India; Department of Epidemiology and Biostatistics (K M Mehta DSc), University of California San Francisco, San Francisco, CA, USA; Institute of Human Virology (P T N Memiah DrPH), School of Medicine (M T Wallin MD), University of Maryland, Baltimore, MD, USA; College of Medicine (Prof Z A Memish MD, M Tamsah), Alfaisal University, Riyadh, Saudi Arabia; Research & Innovation Center (Prof Z A Memish),

Ministry of Health, Riyadh, Saudi Arabia; Peru Country Office (W Mendoza MD), United Nations Population Fund, Lima, Peru; Breast Surgery Unit (T J Meretoja MD), Helsinki University Hospital, Helsinki, Finland; University of Helsinki, Helsinki, Finland (T J Meretoja); Clinical Microbiology and Parasitology Unit (T Mestrovic PhD), Dr Zora Profozic Polyclinic, Zagreb, Croatia; University Centre Varazdin (T Mestrovic), University North, Varazdin, Croatia; Center for Innovation in Medical Education (B Miazgowski MD), Pomeranian Medical University, Szczecin, Poland (B Miazgowski); Pacific Institute for Research & Evaluation, Calverton, MD, USA (T R Miller); Global Institute of Public Health (Prof G Mini PhD), Ananthapuri Hospitals and Research Institute, Trivandrum, India; Women's Institute for Social and Health Studies (Prof G Mini), Women's Social and Health Studies Foundation, Trivandrum, India; Internal Medicine Programme (Prof E M Mirrakhimov PhD), Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan; Department of Atherosclerosis and Coronary Heart Disease (Prof E M Mirrakhimov), National Center of Cardiology and Internal Disease, Bishkek, Kyrgyzstan; Institute of Addiction Research (B Moazen), Frankfurt University of Applied Sciences, Frankfurt, Germany; Social Determinants of Health Research Center (A Mohamadi-Bolbanabad PhD, G Moradi PhD, B Pirooz PhD), Department of Epidemiology and Biostatistics (G Moradi), Kurdistan University of Medical Sciences, Sanandaj, Iran; Department of Forestry (D K Mohammad), Department of Biology (K A Mohammad), Salahaddin University-Erbil, Erbil, Iraq; Department of Public Health (J A Mohammed MPH), Department of Nursing (N B Zepro MSc), Samara University, Semera, Ethiopia; Health Systems and Policy Research Unit (S Mohammed), Department of Community Medicine (M B Sufiyan MD), Ahmadu Bello University, Zaria, Nigeria; Health and Environmental Sciences Department (Y Moodley PhD), Central University of Technology, Bloemfontein, South Africa; National Center for Health Insurance Research (M Moradi-Joo PhD), Iran Health Insurance Organization, Tehran, Iran; Department of Clinical Biochemistry (A Mosapour), Tarbiat Modares University, Tehran, Iran; Department of Biochemistry (M Mozaffar MD), Medical College for Women & Hospital, Dhaka, Bangladesh; Biomedical Research Foundation, Dhaka, Bangladesh (M Mozaffar); Indian Institute of Public Health (Prof G Murthy MD), Public Health Foundation of India, Hyderabad, India; School of Medical Sciences (K Musa PhD), Science University of Malaysia, Kubang Kerian, Malaysia; Department of Pediatric Medicine (Prof G Mustafa MD), The Children's Hospital & The Institute of Child Health, Multan, Pakistan; Department of Pediatrics & Pediatric Pulmonology (Prof G Mustafa), Institute of Mother & Child Care, Multan, Pakistan; Knowledge Translation and Utilization (Prof A F Nabhan), Egyptian Center for Evidence Based Medicine, Egypt; 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), Bioinsilico Technologies, Chennai, India; Comprehensive Cancer Center (G Naik MPH), Department of Psychology (D C Schwebel PhD), School of Medicine (Prof J A Singh MD), University of Alabama at Birmingham, Birmingham, AL, USA; Suraj Eye Institute, Nagpur, India (V Nangia MD); Department for the Control of Disease, Epidemics, and Pandemics (J Nansseu MD), Ministry of Public Health, Yaoundé, Cameroon; Department of Public Health (J Nansseu), University of Yaoundé I, Yaoundé, Cameroon; Department of General Surgery (I Negoj), Emergency Hospital of Bucharest, Bucharest, Romania; School of Health Sciences, Surgical Nursing (H B Netsere), Bahir Dar University, Gondar, Ethiopia; Department of Biological Sciences (J W Ngunjiri DrPH), University of Embu, Embu, Kenya; Public Health Department (D N A Ningrum), Universitas Negeri Semarang, Kota Semarang, Indonesia; Department of Global Public Health and Primary Care (Prof O F Norheim), University of Bergen, Bergen, Norway; Administrative and Economic Sciences Department (Prof B Oancea PhD), University of Bucharest, Bucharest, Romania; Department of Medicine (O S Ogah), Abia State University, Uturu, Nigeria; Department of Preventive Medicine (I Oh PhD), Kyung Hee University, Dongdaemun-gu, South Korea; Department of Psychiatry and Behavioural Neurosciences (A T Olagunju), Department of Pathology and Molecular Medicine (T O Olagunju MD), Population Health Research Institute (T Sathish PhD), McMaster University,

Hamilton, ON, Canada; Centre for Healthy Start Initiative, Lagos, Nigeria (B O Olusanya PhD, J O Olusanya MBA); Department of Pharmacology and Therapeutics (Prof O E Onwujekwe PhD), Department of Community Medicine (Prof B S Uzochukwu MD), University of Nigeria Nsukka, Enugu, Nigeria; Graduate School of Public Health (Prof E Oren), San Diego State University, San Diego, CA, USA; Department of Environmental Management and Toxicology (O Osarenorot MSc), University of Benin, Benin City, Nigeria; Faculty of Geo-Information Science and Earth Observation (F B Osei PhD), University of Twente, Enschede, Netherlands; Department of Mathematics and Statistics (F B Osei), University of Energy and Natural Resources, Sunyani, Ghana; Department of Respiratory Medicine (Prof M P A DNB), Jagadguru Sri Shivarathreeswara Academy of Health Education and Research, Mysore, India; Department of Forensic Medicine (J Padubidri MD), Department of Forensic Medicine and Toxicology (Prof B K Shetty MD), Kasturba Medical College (Prof B Unnikrishnan MD), Manipal Academy of Higher Education, Mangalore, India; Department of Medicine (S Pakhale MD), Ottawa Hospital Research Institute, Ottawa, ON, Canada; Department of Poverty, Gender and Youth (S K Patel PhD), Population Council, New Delhi, India; Indian Institute of Health Management Research University, Jaipur, India (S K Patel); School of Medicine (A J Paternina-Cacedo MSc), University of Sinu, Cartagena, Colombia; Department of Pediatrics (Prof A Pathak), RD Gardi Medical College, Ujjain, India; Department of Pediatrics (Prof G C Patton MD), Department of Agriculture and Food Systems (H Suleria PhD), University of Melbourne, Melbourne, VIC, Australia; Population Health Theme (Prof G C Patton), Murdoch Childrens Research Institute, Melbourne, VIC, Australia; Health, Nutrition, and HIV/AIDS Program (D Paudel PhD), Save the Children, Kathmandu, Nepal; Center for International Health (D Paudel), Ludwig Maximilians University, Munich, Germany; Center for Research and Innovation (V F Pepito MSc), Ateneo De Manila University, Pasig City, Philippines; Mario Negri Institute for Pharmacological Research, Bergamo, Italy (N Perico MD); Field Epidemiology and Laboratory Training Program (A Pervaiz MSc), National Institute of Health Islamabad, Islamabad, Pakistan; Center for Integration of Data and Health Knowledge (J M Pescarini PhD), Oswaldo Cruz Foundation, Salvador, Brazil; University Medical Center Groningen (Prof M J Postma PhD), School of Economics and Business (Prof M J Postma), University of Groningen, Groningen, Netherlands; Dietary Supplements and Probiotic Research Center (H Pourjafar), School of Medicine (M Shams-Beyranvand MSc), Alborz University of Medical Sciences, Karaj, Iran; Clinical Research Center (S I Prada PhD), Fundación Valle del Lili, Cali, Colombia; Center for Studies in Social Protection and Health Economics (S I Prada), ICESI University, Cali, Colombia; Department of Nephrology (Prof N Prasad DM), Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India; National Institute of Infectious Diseases, Bucuresti, Romania (L Preotescu); Department of Chemistry (N Rabiee MSc), Sharif University of Technology, Tehran, Iran; College of Medicine (A Radfar), University of Central Florida, Orlando, FL, USA; Department of Community Medicine (Mo Rahman PhD), Maharishi Markandeshwar Institute of Medical Sciences & Research, Ambala, India; School of Nursing and Healthcare Professions (Mu Rahman), Federation University Australia, Berwick, VIC, Australia; Research Center for Child Mental Development (S Rahman MHS), Hamamatsu University School of Medicine, Hamamatsu, Shizuoka Prefecture, Japan; Department of Global Health Policy (S Rahman), Department of Diabetes and Metabolic Diseases (T Yamada MD), University of Tokyo, Tokyo, Japan; University Institute of Public Health (Prof S M Rana PhD), The University of Lahore, Lahore, Pakistan; Public Health Department (Prof S M Rana), University of Health Sciences, Lahore, Pakistan; Research Department (C L Ranabhat PhD), Policy Research Institute, Kathmandu, Nepal; Health and Public Policy Department (C L Ranabhat), Global Center for Research and Development, Kathmandu, Nepal; University College London Hospitals, London, UK (D L Rawaf); Academic Public Health England (Prof S Rawaf), Public Health England, London, UK; School of Health, Medical and Applied Sciences (L Rawal PhD), CQ University, Sydney, NSW, Australia; River Region Cardiology Associates, Montgomery, WV, USA (W F Rawasia MD); School of Nursing and Midwifery (V Renjith PhD), Royal College of Surgeons in Ireland - Bahrain, Muharraq Governorate, Bahrain; School of Social Sciences and Psychology (Prof A M N Renzaho PhD), Translational Health Research Institute (Prof A M N Renzaho), Western Sydney University, Penrith, NSW, Australia; Brien Holden Vision Institute, Sydney, Australia (Prof S Resnikoff); Department of Medical Microbiology (M A Reta), University of Pretoria, Pretoria, South Africa; Cardiovascular Diseases Research Center (S Riahi), Birjand University of Medical Sciences, Birjand, Iran; Department of Surgery (J Rickard MD), University of Minnesota, Minneapolis, MN, USA; Department of Surgery (J Rickard), University Teaching Hospital of Kigali, Kigali, Rwanda; Department of Clinical Research (L Roever PhD), Federal University of Uberlândia, Uberlândia, Brazil; Clinical Epidemiology and Public Health Research Unit (L Monasta DSc, L Ronfani PhD), Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy; Agrosavia, Palmira, Colombia (E Rubagotti PhD); Department of Ocean Science and Engineering (E Rubagotti), Southern University of Science and Technology, Shenzhen, China; Department of Biomedical Sciences (Prof S Rubino PhD), University of Sassari, Sassari, Italy; Environmental Epidemiology and Public Health (Y D Sabde MD), National Institute for Research in Environmental Health, Bhopal, India; Halal Research Center of IRI (A Sahebkar PhD), Food and Drug Administration of the Islamic Republic of Iran, Tehran, Iran; Neurogenic Inflammation Research Center (A Sahebkar), Mashhad University of Medical Sciences, Mashhad, Iran; Department of Phytochemistry (Prof S Sajadi PhD), Soran University, Soran, Iraq; Department of Nutrition (Prof S Sajadi), Cihan University-Erbil, Kurdistan Region, Iraq; Department of Microbiology (N Salam PhD), Central University of Punjab, Bathinda, India; Public Health and Community Medicine Department (M R Salem MD), Cairo University, Giza, Egypt; Department of Surgery (Prof J Sanabria), Marshall University, Huntington, WV, USA; Department of Community Medicine (S Y Saraswathy PhD), PSG Institute of Medical Sciences and Research, Coimbatore, India; PSG-FAIMER South Asia Regional Institute, Coimbatore, India (S Y Saraswathy); Malaria No More, Delhi, India (K Sarkar); Health Economics Department (A R Sarker PhD), Bangladesh Institute of Development Studies, Dhaka, Bangladesh; Department of Geriatrics and Long Term Care (B Sathian PhD), Hamad Medical Corporation, Doha, Qatar; Faculty of Health & Social Sciences (B Sathian), Bournemouth University, Bournemouth, UK; Department of Public Health Sciences (M Sawhney PhD), University of North Carolina at Charlotte, Charlotte, NC, USA; Department of Food Science and Nutrition (A M Senbeta MSc), Jigjiga University, Jigjiga, Ethiopia (A A Tasew); Emergency Department (S Senthilkumaran MD), Manian Medical Centre, Erode, India; Population Health Sciences Institute (H Shabaninejad), Newcastle University, Newcastle Upon Tyne, UK; Department of Cardiology (A Shafieesabet MD), Charité Medical University Berlin, Berlin, Germany; Center for Stroke Research Berlin, Berlin, Germany (A Shafieesabet); Independent Consultant, Karachi, Pakistan (M A Shaikh MD); Faculty of Caring Science, Work Life, and Social Welfare (M Shamsizadeh MSc), University of Boras, Borås, Sweden; Department of Community Medicine (M Shannawaz PhD), BLDE University, Vijayapur, India; HIV/STI Surveillance Research Center, and WHO Collaborating Center for HIV Surveillance (Prof H Sharifi PhD), Kerman University of Medical Sciences, Kerman, Iran; Centre for Medical Informatics (Prof A Sheikh), Usher Institute of Population Health Sciences and Informatics (I N Soyiri PhD), Public Health Department (T A Zerfu PhD), University of Edinburgh, Edinburgh, UK; Department of Forensic Medicine (Prof B K Shetty), Yenepoya University, Mangalore, India; National Institute of Infectious Diseases, Tokyo, Japan (M Shigematsu PhD); College of Medicine (Prof J Shin), Yonsei University, Seoul, South Korea; Finnish Institute of Occupational Health, Helsinki, Finland (R Shiri PhD); School of Health (S Siabani), University of Technology Sydney, Sydney, NSW, Australia; Department of Physical Education (Prof D A S Silva PhD), Federal University of Santa Catarina, Florianopolis, Brazil; Global Patient Outcome and Real World Evidence (A Singh), Eli Lilly and Company, Indianapolis, IN, USA; Medicine Service (Prof J A Singh), US Department of Veterans Affairs, Birmingham, AL, USA; Max Hospital, Ghaziabad, India (Prof N P Singh MD); Department of Pulmonary Medicine (Prof V Singh MD), Asthma Bhawan, Jaipur, India;

Department of Physiotherapy and Occupational Therapy (M M Sisay), Næstved-Slagelse-Ringsted Hospitals, Slagelse, Denmark; Department of Ophthalmology (E Skiadaresi MD), Hywel Dda University Health Board, Llanelli, UK; Department of Infectious Diseases (A Sokhan PhD), Kharkiv National Medical University, Kharkiv, Ukraine; Department of Medicine (R Somayaji), University of Calgary, Calgary, AB, Canada; Hull York Medical School (I N Soyiri), University of Hull, Hull City, UK; Division of Community Medicine (C T Sreeramareddy MD), International Medical University, Kuala Lumpur, Malaysia; Nursing (A Sudaryanto MPH), Muhammadiyah University of Surakarta, Surakarta, Indonesia; Department of Public Health (A Sudaryanto), China Medical University, Taiwan; Health Economics (M Sultana), Deakin University, Melbourne, VIC, Australia; Department of Community Health (B F Sunguya PhD), Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; Department of Criminology, Law, and Society (Prof B L Sykes PhD), University of California Irvine, Irvine, CA, USA; Department of Medicine (Prof R Tabarés-Seisdedos PhD), University of Valencia, Valencia, Spain; Carlos III Health Institute (Prof R Tabarés-Seisdedos), Biomedical Research Networking Center for Mental Health Network, Madrid, Spain; Cancer Control Center (T Tabuchi MD), Osaka International Cancer Institute, Osaka, Japan; Axum College of Health Science, Mekelle, Ethiopia (D B Tadesse); Research and Development Center for Humanities and Health Management (I U Tarigan PhD), National Institute of Health Research & Development, Jakarta, Indonesia; Department of Public Health and Community Medicine (Prof K R Thankappan MD), Central University of Kerala, Kasaragod, India; Institute of Public Health (R Topor-Madry PhD), Jagiellonian University Medical College, Kraków, Poland; Agency for Health Technology Assessment and Tariff System, Warsaw, Poland (R Topor-Madry); Department of Pathology and Legal Medicine (M R Tovani-Palone PhD), University of São Paulo, Ribeirão Preto, Brazil; Modestum LTD, London, UK (M R Tovani-Palone); Department of Health Economics (B X Tran PhD), Hanoi Medical University, Hanoi, Vietnam; Molecular Medicine and Pathology (K B Tran MD), University of Auckland, Auckland, New Zealand; Clinical Hematology and Toxicology (K B Tran), Maurice Wilkins Centre, Auckland, New Zealand; Department of Microbiology (I Ullah PhD), Iqra National University, Peshawar, Pakistan; TB Culture Laboratory (I Ullah), Mufti Mehmood Memorial Teaching Hospital, Dera Ismail Khan, Pakistan; Velez Sarsfield Hospital, Buenos Aires, Argentina (Prof P R Valdez); Department of Medical and Surgical Sciences (Prof F S Violante MD), University of Bologna, Bologna, Italy; Occupational Health Unit (Prof F S Violante), Sant'Orsola Malpighi Hospital, Bologna, Italy; Department of Economics (Prof S Vollmer), University of Göttingen, Göttingen, Germany; Foundation University Medical College (Prof Y Waheed PhD), Foundation University Islamabad, Islamabad, Pakistan; Department of Neurology (M T Wallin), George Washington University, Washington, DC, USA; Department of Epidemiology and Biostatistics (Ya Wang BSA, Prof C Yu PhD), Global Health Institute (Prof C Yu), School of Health Sciences (X G Zhao PhD), Wuhan University, Wuhan, China; Demographic Change and Aging Research Area (A Werdecker PhD), Competence Center of Mortality-Follow-Up of the German National Cohort (R Westerman DSc), Federal Institute for Population Research, Wiesbaden, Germany; Center for Population and Health, Wiesbaden, Germany (A Werdecker); Department of Physical Therapy (T Wiangkham PhD), Naresuan University, Phitsanulok, Thailand; Department of Health Economics (G T Worku), Addis Continental Institute of Public Health, Addis Ababa, Ethiopia; Department of Orthopaedics (Prof A Wu MD), Wenzhou Medical University, Wenzhou, China; School of Medicine (Prof G Xu MD), Nanjing University, Nanjing, China; Clinical Cancer Research Center (S Yahyazadeh Jabbari MD), Milad General Hospital, Tehran, Iran; Department of Public Health (Prof H Yatsuya PhD), Fujita Health University, Toyooka, Japan; Department of Public Health and Health Systems (Prof H Yatsuya), Nagoya University, Nagoya, Japan; Pediatrics Department (C S Yilgwan MD), University of Jos, Jos, Nigeria; Department of Pediatrics (C S Yilgwan), Jos University Teaching Hospital, Jos, Nigeria; Centre for Suicide Research and Prevention (Prof P Yip PhD), Department of Social Work and Social Administration (Prof P Yip), University of Hong Kong, Hong Kong, China; Department

of Neuropsychopharmacology (N Yonemoto MPH), National Center of Neurology and Psychiatry, Kodaira, Japan; Department of Public Health (N Yonemoto), Juntendo University, Tokyo, Japan; Department of Preventive Medicine (Prof S Yoon PhD), Korea University, Seoul, South Korea; Department of Health Policy and Management (Prof M Z Younis PhD), Jackson State University, Jackson, MS, USA; School of Medicine (Prof M Z Younis), Tsinghua University, Beijing, China; Department of Health Care Management and Economics (H Yusefzadeh PhD), Urmia University of Medical Science, Urmia, Iran; Department of Medicine (Prof Z Zaidi PhD), University Ferhat Abbas of Setif, Sétif, Algeria; Department of Epidemiology and Public Health (N B Zepro), University of Basel, Basel, Switzerland; College of Medicine and Health Sciences (T A Zerfu), Dilla University, Dilla, Ethiopia; School of Public Health (Y Zhang PhD), Hubei Province Key Laboratory of Occupational Hazard Identification and Control (Y Zhang), Wuhan University of Science and Technology, Wuhan, China; School of Biology and Pharmaceutical Engineering (X G Zhao), Wuhan Polytechnic University, Wuhan, China; Health Technology Assessment Unit (Y H Zuniga BS), Department of Health Philippines, Manila, Philippines; #MentalHealthPH, Quezon City, Philippines (Y H Zuniga).

Contributors

P A Lindstedt, M M Baumann, and K E Wiens collected, cleaned, and vetted the data. K E Wiens produced estimates and K E Wiens, R C Reiner Jr, and A Deshpande vetted the models and the results. K E Wiens prepared the first draft of the manuscript. K E Wiens, K B Johnson, M M Baumann, and P A Lindstedt constructed the figures and tables. R C Reiner Jr and S I Hay provided overall direction and guidance. B F Blacker, K E Wiens, and R C Reiner Jr managed the project. K E Wiens, L E Schaeffer, M M Baumann, P A Lindstedt, and B F Blacker finalised the manuscript on the basis of comments from other authors and reviewer feedback. P A Lindstedt managed appendix 1. M M Baumann and C A Welgan created appendix 2. All other authors provided data or developed models for indicators, reviewed results, initiated modelling infrastructure, or reviewed and contributed to the Article; their contributions can be found in appendix 1 (pp 158–162).

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Data sharing

The source code used to generate estimates is available online. The study data, including full sets of estimates at the first and second administrative levels, are available online.

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