

# UCSF

## UC San Francisco Previously Published Works

### Title

Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019

### Permalink

<https://escholarship.org/uc/item/5z66v85v>

### Journal

The Lancet, 400(10369)

### ISSN

0140-6736

### Authors

Collaborators, GBD 2019 Antimicrobial Resistance  
Ikuta, Kevin S  
Swetschinski, Lucien R  
et al.

### Publication Date

2022-12-01

### DOI

10.1016/s0140-6736(22)02185-7

### Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

# Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019



GBD 2019 Antimicrobial Resistance Collaborators\*

## Summary

**Background** Reducing the burden of death due to infection is an urgent global public health priority. Previous studies have estimated the number of deaths associated with drug-resistant infections and sepsis and found that infections remain a leading cause of death globally. Understanding the global burden of common bacterial pathogens (both susceptible and resistant to antimicrobials) is essential to identify the greatest threats to public health. To our knowledge, this is the first study to present global comprehensive estimates of deaths associated with 33 bacterial pathogens across 11 major infectious syndromes.

**Methods** We estimated deaths associated with 33 bacterial genera or species across 11 infectious syndromes in 2019 using methods from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, in addition to a subset of the input data described in the Global Burden of Antimicrobial Resistance 2019 study. This study included 343 million individual records or isolates covering 11361 study-location-years. We used three modelling steps to estimate the number of deaths associated with each pathogen: deaths in which infection had a role, the fraction of deaths due to infection that are attributable to a given infectious syndrome, and the fraction of deaths due to an infectious syndrome that are attributable to a given pathogen. Estimates were produced for all ages and for males and females across 204 countries and territories in 2019. 95% uncertainty intervals (UIs) were calculated for final estimates of deaths and infections associated with the 33 bacterial pathogens following standard GBD methods by taking the 2.5th and 97.5th percentiles across 1000 posterior draws for each quantity of interest.

**Findings** From an estimated 13.7 million (95% UI 10.9–17.1) infection-related deaths in 2019, there were 7.7 million deaths (5.7–10.2) associated with the 33 bacterial pathogens (both resistant and susceptible to antimicrobials) across the 11 infectious syndromes estimated in this study. We estimated deaths associated with the 33 bacterial pathogens to comprise 13.6% (10.2–18.1) of all global deaths and 56.2% (52.1–60.1) of all sepsis-related deaths in 2019. Five leading pathogens—*Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*—were responsible for 54.9% (52.9–56.9) of deaths among the investigated bacteria. The deadliest infectious syndromes and pathogens varied by location and age. The age-standardised mortality rate associated with these bacterial pathogens was highest in the sub-Saharan Africa super-region, with 230 deaths (185–285) per 100 000 population, and lowest in the high-income super-region, with 52.2 deaths (37.4–71.5) per 100 000 population. *S aureus* was the leading bacterial cause of death in 135 countries and was also associated with the most deaths in individuals older than 15 years, globally. Among children younger than 5 years, *S pneumoniae* was the pathogen associated with the most deaths. In 2019, more than 6 million deaths occurred as a result of three bacterial infectious syndromes, with lower respiratory infections and bloodstream infections each causing more than 2 million deaths and peritoneal and intra-abdominal infections causing more than 1 million deaths.

**Interpretation** The 33 bacterial pathogens that we investigated in this study are a substantial source of health loss globally, with considerable variation in their distribution across infectious syndromes and locations. Compared with GBD Level 3 underlying causes of death, deaths associated with these bacteria would rank as the second leading cause of death globally in 2019; hence, they should be considered an urgent priority for intervention within the global health community. Strategies to address the burden of bacterial infections include infection prevention, optimised use of antibiotics, improved capacity for microbiological analysis, vaccine development, and improved and more pervasive use of available vaccines. These estimates can be used to help set priorities for vaccine need, demand, and development.

**Funding** Bill & Melinda Gates Foundation, Wellcome Trust, and Department of Health and Social Care, using UK aid funding managed by the Fleming Fund.

**Copyright** © 2022 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

Lancet 2022; 400: 2221–48

Published Online  
November 21, 2022  
[https://doi.org/10.1016/S0140-6736\(22\)02185-7](https://doi.org/10.1016/S0140-6736(22)02185-7)

See [Comment](#) page 2161

\*Listed at the end of the Article

Correspondence to:  
Prof Mohsen Naghavi,  
Department of Health Metrics  
Sciences, Institute for Health  
Metrics and Evaluation, School  
of Medicine, University of  
Washington, Seattle,  
WA 98195, USA  
[nagham@uw.edu](mailto:nagham@uw.edu)

### Research in context

#### Evidence before this study

Communicable diseases have long been recognised as a cause of substantial health loss globally, but few studies to date have concentrated on pathogen-specific mortality caused by common bacterial pathogens. Many estimates exist for pathogens like *Mycobacterium tuberculosis*, *Plasmodium* spp, and HIV but estimates of the burden of bacterial infections have been restricted to either a small number of locations, specific populations (such as invasive pneumococcal disease in children younger than 5 years), or a small number of bacteria in the context of the scope of infectious syndromes (eg, *Streptococcus pneumoniae* and *Neisseria meningitidis* as a cause of meningitis). The US Centers for Disease Control and Prevention (CDC) Active Bacterial Core surveillance and Emerging Infections Program, and the European CDC's European Antimicrobial Resistance Surveillance Network have provided crucial estimates of selected invasive bacterial infections in high-income countries. These estimates are important first steps in building our understanding of the burden of specific bacterial infections but they provide an incomplete picture: within the locations with the greatest infectious burden, the mortality associated with these pathogens remains unknown, making it difficult to set global public health priorities.

#### Added value of this study

To our knowledge, this is the first study to produce global estimates of mortality associated with 33 clinically significant bacterial pathogens (including those susceptible to antibacterial compounds) across 11 infectious syndromes, and to provide these estimates for all ages and for males and females across 204 countries and territories in 2019. This analysis is intended to provide an audit of the mortality associated with common bacterial pathogens. We estimated the number of deaths

associated with each of these bacterial pathogens using three modelling steps: deaths where infection had a role, the fraction of deaths due to infection attributable to a given infectious syndrome, and the fraction of deaths due to infectious syndromes attributable to a given pathogen. Deaths in which infection had a role were estimated using the number of deaths for which either the underlying cause of death was infectious or the pathway of death was through sepsis. The fraction of deaths due to infection attributable to a given infectious syndrome was estimated using data to determine the infectious syndrome responsible for sepsis by underlying cause of death, age, sex, and geographical location. The fraction of deaths due to an infectious syndrome attributable to a given pathogen was estimated by integrating estimates of pathogen-specific and syndrome-specific case-fatality ratios with modelled pathogen distributions for each infectious syndrome that varied by age and geographical location.

#### Implications of all the available evidence

Our findings show that more than half of all global bacterial deaths in 2019 were due to five bacterial pathogens: *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. The substantial burden of health loss associated with these five pathogens requires increased attention from the global health community and collaborative intervention approaches. Understanding the leading infectious syndromes and pathogens for each region is of the utmost importance so that targeted prevention efforts can be implemented. This study can be used to guide strategies for reducing the burden of bacterial infectious diseases, including infection prevention and control measures, vaccine development and implementation, and the availability of basic acute care services.

## Introduction

Communicable diseases have long been highlighted as a global public health priority and are recognised as a leading cause of health loss globally.<sup>1-3</sup> A recent study estimated that there were more than 10 million sepsis-related deaths in 2017, indicating that infections were involved in more than 20% of deaths globally for that year.<sup>4</sup> Reducing the number of deaths due to infections is a foundational principle in moving towards health equity<sup>5</sup> because there is a disproportionate infectious burden in low-income and middle-income countries (LMICs).<sup>4,6</sup> Preventing and effectively treating infections is also essential to achieving Sustainable Development Goal (SDG) 3: ensure healthy lives and promote wellbeing for all at all ages.<sup>7</sup> Although the contribution of non-bacterial causes (eg, fungal infections, malaria, and HIV) to the overall infection burden must be acknowledged, reducing the number of cases and health impact of bacterial infectious diseases is a priority area that necessitates a multipronged approach with infection prevention and

control measures;<sup>8</sup> vaccine development, deployment, and uptake;<sup>9,10</sup> and early and effective case management.<sup>11,12</sup> Detailed estimates of the number of deaths related to bacterial infections and their causes are an important step in tracking progress towards global health goals and are essential to inform priorities for vaccine and drug development.

To date, no global burden estimates exist for many common bacterial pathogens, making establishment of public health priorities difficult. The few estimates that do exist are often constrained to specific pathogens,<sup>13</sup> infectious syndromes,<sup>14</sup> or high-income countries.<sup>15</sup> For example, global estimates of the burden of *Streptococcus pneumoniae* are available; however, these estimates are mostly restricted to children younger than 5 years<sup>13</sup> or as a cause of pneumonia or meningitis<sup>3</sup> and do not reflect the total burden across all populations and all infectious syndromes.<sup>16</sup> Estimates of selected invasive bacterial infections exist in high-income countries that use passive surveillance systems, such as the US Centers

for Disease Control (CDC) Active Bacterial Core surveillance and Emerging Infections Program<sup>17</sup> and the European CDC's European Antimicrobial Resistance Surveillance Network.<sup>18</sup> Although such estimates offer important insights, no comprehensive estimates exist covering all locations for a broad range of bacteria across major infectious syndromes. Notably absent are country-level estimates for LMICs, which have the greatest burden of infectious diseases,<sup>4</sup> as also emphasised by the recent Global Burden of Antimicrobial Resistance 2019 study.<sup>19</sup> For this reason, there has been profound neglect of these pathogens, and relevant infectious syndromes, in global advocacy campaigns aiming to maximise life-saving interventions.

In this study, we present, to our knowledge, the first global estimates of deaths associated with 33 clinically significant bacterial pathogens (both susceptible and resistant to antimicrobials), across 11 infectious syndromes in 2019. We used data obtained from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019<sup>3</sup> and the Global Burden of Antimicrobial Resistance 2019 study<sup>19</sup> to estimate global, regional, and national mortality and years of life lost (YLLs) associated with these 33 bacterial pathogens across 204 countries and territories and 286 underlying causes of death, by age and sex, in 2019. This manuscript was produced as part of the GBD Collaborator Network and in accordance with the GBD Protocol.<sup>20</sup>

## Methods

### Overview

In this study, we estimated the fatal burden associated with infection caused by 33 bacterial species or genera across 11 infectious syndromes using methods and data from the GBD 2019 and Global Burden of Antimicrobial Resistance studies.<sup>3,19</sup> Detailed methods have been published elsewhere.<sup>19</sup> Briefly, using 343 million individual records or isolates covering 11 361 study-location-years, we implemented three modelling steps to estimate the number of deaths associated with each bacterial pathogen across 204 countries and territories for 2019. First, we estimated the overall number of deaths in which infection had a role using methods described in the Global Burden of Antimicrobial Resistance study.<sup>19</sup> Second, we determined the infectious syndrome responsible for each death due to an infection. Finally, for each infectious syndrome we estimated the distribution of pathogens responsible. With the use of these components, we estimated the number of deaths associated with each of the 33 bacterial pathogens of interest in this study. A summarising flowchart and detailed approach description for each step of the estimation process are in appendix 1 (section 10). All estimates were produced by age, for males and females, and for 204 countries and territories.

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>21</sup>

throughout the study (detailed in appendix 1 [section 7]). This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations.<sup>22</sup> The complete GATHER checklist is provided in appendix 1 (section 8).

### Input data

We used a subset of the input data described in the Global Burden of Antimicrobial Resistance study to estimate mortality burden by pathogen.<sup>19</sup> We selected data inputs only if they were based on a representative sampling framework that would not bias the aetiology estimation towards a specific pathogen (eg, we did not deliberately sample 100 cases of every pathogen). The input data source types that met these criteria were: multiple-cause-of-death and vital registration data; hospital discharge data; linkage data sources; mortality surveillance in the Child Health and Mortality Prevention Surveillance (CHAMPS) study; literature reviews of the microbial cause of meningitis, neonatal sepsis, lower respiratory infections, urinary tract infections, skin infections, peritonitis, and bone and joint infections; and laboratory-based passive surveillance data. We used multiple-cause-of-death and vital registration data, hospital discharge data, CHAMPS, and linkage data sources to estimate the number of deaths for which infection had a role and the distribution of infectious syndromes (appendix 1 [section 4]). We used data from CHAMPS, literature reviews, and laboratory-based passive surveillance systems to estimate the pathogen distribution for each infectious syndrome (appendix 1 [section 6]). The number of individual records or isolates used in each step for each of the GBD regions is shown in appendix 1 (p 62).

### Deaths in which infection played a role

Detailed methods on how the number of deaths in which infection played a role were estimated have been published previously.<sup>4</sup> Briefly, we estimated the number of deaths for which either the underlying cause of death was infectious (using GBD 2019 estimates) or for which a contributing factor in the death was sepsis and the underlying cause was non-infectious. For the identification of sepsis in non-infectious underlying causes of death, we used the following data inputs: 121 million cause-of-death records with multiple-cause-of-death data from eight countries and territories; 192 million hospital records with patient discharge status from seven countries and territories; 264 000 multiple-cause-of-death records linked to hospital records from ten countries and territories; and 849 deaths from CHAMPS sites across six countries. We developed a random-effects logistic regression model to predict the fraction of deaths involving sepsis for each underlying cause of death, age, sex, and geographical location using methods described previously.<sup>4,19</sup> Using this cause-fraction, we estimated the number of deaths for which the underlying cause was non-infectious and sepsis occurred. We then added this to the number of deaths in which the

See Online for appendix 1

underlying cause was infectious from GBD 2019 to estimate the number of deaths in which infection had a role.

### Infectious syndrome estimates

Detailed methods on the estimation process for infectious syndromes have been published previously<sup>19</sup> and are in appendix 1 (section 4). Briefly, we used the available data described in the Input data section (multiple cause of death, hospital data with patient discharge status, linkage data, and CHAMPS) to determine the infectious syndrome responsible for sepsis by underlying cause, age, sex, and geographical location. Within our modelling framework, an infectious syndrome is the infection directly responsible for sepsis and serves as the bridge between the underlying cause of death and sepsis. We estimated 11 infectious syndromes: meningitis and other bacterial CNS infections; cardiac infections; peritoneal and intra-abdominal infections; lower respiratory infections and all related infections in the thorax; bacterial infections of the skin and subcutaneous systems; infections of bones, joints, and related organs; typhoid, paratyphoid, and invasive non-typhoidal *Salmonella*; diarrhoea; urinary tract infections and pyelonephritis; bloodstream infections; and gonorrhoea and chlamydia. We then used syndrome- and age-specific mixed effects logistic regression models (using sex, Healthcare Access and Quality Index, and syndrome-specific bias covariates and a nested random effect on underlying cause) to estimate the fraction of sepsis-related deaths that were caused by each infectious syndrome for each underlying cause of death, age, sex, and geographical location. Applying this fraction to the estimate of number of infection-related deaths from the previous step, we determined the number of deaths that occurred due to a given infectious syndrome by underlying cause of death, age, sex, and geographical location. We estimated deaths with an infectious syndrome as the sum of deaths with the syndrome as an underlying cause of death (ie, for those syndromes considered to be underlying causes) plus deaths with a non-infectious underlying cause where the syndrome was estimated to occur (eg, all deaths where the underlying cause was meningitis plus all road traffic injury deaths in which meningitis occurred). Bloodstream infections; infections of bones, joints, and related organs; and peritoneal and intra-abdominal infections are not estimated in GBD, so for these three infectious syndromes, we assumed they had a non-infectious underlying cause to estimate deaths.

### Pathogen distribution

Detailed methods on the estimation process for pathogen distribution have been published previously<sup>19</sup> and are in appendix 1 (sections 5 and 6), including exceptions and special handling decisions. Briefly, we used data from 343 million isolates covering 11 361 study-location-years to estimate pathogen distributions for each infectious syndrome that varied by age and location, with a subset of

this data adapted to calculate pathogen-specific and syndrome-specific case-fatality ratios (CFRs). We selected a set of pathogens to be explicitly estimated as part of the cause of each infectious syndrome. This selection was based on several factors. First, selection was influenced by the prevalence of each pathogen in the raw data, because the amount of available data restricts the number of pathogens that can be estimated successfully. Second, we aimed to produce estimates for the combination of pathogens that, collectively, represented at least 85% of the aetiological causes of a given infectious syndrome. We included three residual categories: (1) other bacteria and (2) polymicrobial—for bacteria that did not meet these criteria or had two or more bacteria isolated from a single isolate—and (3) non-bacterial pathogen, for pathogens that were not bacteria (ie, viruses, fungi, or parasites).

Much of the input data on pathogen distribution were only reported on a subset of pathogens, such that they did not have a complete denominator for all possible pathogens. For example, many surveillance systems for meningitis only monitor *S pneumoniae* and *Neisseria meningitidis* as the causative pathogen. To account for this partial distribution, we used a network meta-analysis, which allowed us to include any dataset reporting on two or more pathogens. We implemented this network meta-analysis using the multinomial estimation with partial and composite observations (MEPCO) modelling environment. This approach allowed us to include covariates in the network analysis, incorporate Bayesian priors (ie, prior probability distributions), and use data that compared one pathogen with all other pathogens. Input data for the MEPCO process consisted of ratios of sums of cases within a study (with each sum representing a specific pathogen or combination of pathogens). The model was fit by minimising the sum of the residuals between log-transformed observed ratios and predictions using a non-linear likelihood minimisation problem optimised using the Gauss-Newton method<sup>23</sup> (appendix 1 [section 6.3.1]). The resultant MEPCO estimate was the non-fatal pathogen distribution for each infectious syndrome.

To estimate the fatal pathogen distribution, we calculated syndrome-specific and pathogen-specific CFRs using data that linked pathogen-specific disease incidence to deaths and the meta-regression–Bayesian regularised, trimmed (MR-BRT) tool. We estimated CFRs as a function of age, Healthcare Access and Quality Index, and various bias covariates that were specific to the nuances of the data for each infectious syndrome (appendix 1 [section 5]). We then used the pathogen-specific and syndrome-specific CFRs to produce a pathogen distribution of number of deaths estimated for each infectious syndrome by age and location. Our modelling framework accounted for both data-rich and data-sparse pathogens (appendix 1 [section 5.3]). In this analysis we do not report estimates for *Mycobacterium tuberculosis* because this specific pathogen is already part of a global strategy with well

	All 11 infectious syndromes	Lower respiratory infections and all related infections of the thorax	Meningitis and other bacterial CNS infections	Bloodstream infections	Skin and subcutaneous bacterial infections	Urinary tract infections and pyelonephritis	Peritoneal and intra-abdominal infections	Bone, joint, and related organ infections	Cardiac infections	Diarrhoea	Typhoid, paratyphoid, and INTS	Chlamydia and gonorrhoea
<b>Staphylococcus aureus</b>												
All-cause all-age death counts	1 105 000 (816 000–1 470 000)	532 000 (440 000–648 000)	18 400 (13 400–26 000)	299 000 (166 000–485 000)	37 500 (15 700–78 400)	21 300 (15 100–30 800)	169 000 (105 000–253 000)	9490 (2910–21 600)	19 000 (13 200–26 500)	..	..	..
All-cause age-standardised mortality rate	14.6 (10.8–19.4)	7.3 (6.0–8.8)	0.2 (0.2–0.4)	3.9 (2.1–6.3)	0.5 (0.2–1.0)	0.3 (0.2–0.4)	2.1 (1.3–3.2)	0.1 (0.0–0.3)	0.3 (0.2–0.3)	..	..	..
<b>Escherichia coli</b>												
All-age death counts	950 000 (685 000–1 290 000)	181 000 (142 000–230 000)	23 000 (16 200–33 200)	242 000 (133 000–398 000)	18 000 (6190–40 900)	120 000 (96 400–154 000)	290 000 (188 000–423 000)	3370 (1030–7770)	17 700 (12 000–24 500)	54 100 (27 500–95 100)	..	..
Age-standardised mortality rate	12.6 (9.1–16.9)	2.6 (2.0–3.2)	0.3 (0.2–0.5)	3.2 (1.7–5.2)	0.2 (0.1–0.5)	1.6 (1.3–2.0)	3.7 (2.4–5.4)	0.0 (0.0–0.1)	0.2 (0.2–0.3)	0.8 (0.4–1.3)	..	..
<b>Streptococcus pneumoniae</b>												
All-age death counts	829 000 (682 000–1 010 000)	653 000 (553 000–777 000)	44 500 (34 700–59 800)	125 000 (72 600–199 000)	..	..	..	..	6070 (4430–8470)	..	..	..
Age-standardised mortality rate	11.4 (9.4–13.9)	9.1 (7.7–10.8)	0.6 (0.5–0.8)	1.6 (1.0–2.6)	..	..	..	..	0.1 (0.1–0.1)	..	..	..
<b>Klebsiella pneumoniae</b>												
All-age death counts	790 000 (571 000–1 060 000)	276 000 (220 000–343 000)	33 400 (23 600–47 000)	265 000 (157 000–416 000)	7000 (1070–25 800)	38 700 (26 900–55 800)	158 000 (103 000–234 000)	1370 (389–3200)	11 200 (8090–15 400)	..	..	..
Age-standardised mortality rate	10.6 (7.7–14.2)	3.8 (3.1–4.8)	0.5 (0.3–0.7)	3.5 (2.1–5.5)	0.1 (0.0–0.3)	0.5 (0.4–0.7)	2.0 (1.3–2.9)	0.0 (0.0–0.0)	0.1 (0.1–0.2)	..	..	..
<b>Pseudomonas aeruginosa</b>												
All-age death counts	559 000 (390 000–769 000)	233 000 (181 000–302 000)	..	163 000 (94 200–255 000)	22 400 (7320–54 000)	29 900 (17 200–49 600)	103 000 (65 700–151 000)	1360 (368–3330)	7070 (5160–9840)	..	..	..
Age-standardised mortality rate	7.4 (5.2–10.2)	3.2 (2.5–4.1)	..	2.1 (1.2–3.3)	0.3 (0.1–0.7)	0.4 (0.2–0.6)	1.3 (0.8–1.9)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	..	..	..
<b>Acinetobacter baumannii</b>												
All-age death counts	452 000 (269 000–693 000)	166 000 (91 800–267 000)	..	247 000 (138 000–405 000)	12 000 (671–52 900)	16 200 (6350–31 100)	..	..	10 700 (7570–15 200)	..	..	..
Age-standardised mortality rate	5.8 (3.5–8.9)	2.2 (1.2–3.5)	..	3.2 (1.8–5.2)	0.2 (0.0–0.7)	0.2 (0.1–0.4)	..	..	0.1 (0.1–0.2)	..	..	..
<b>Enterobacter spp</b>												
All-age death counts	324 000 (211 000–468 000)	64 700 (46 400–89 600)	..	156 000 (90 400–243 000)	7780 (2380–18 600)	13 100 (8350–20 300)	75 500 (47 200–115 000)	1680 (490–3710)	5460 (3770–7980)	..	..	..
Age-standardised mortality rate	4.2 (2.8–6.1)	0.9 (0.6–1.2)	..	2.0 (1.2–3.2)	0.1 (0.0–0.2)	0.2 (0.1–0.3)	0.9 (0.6–1.4)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	..	..	..

(Table continues on next page)

	All 11 infectious syndromes	Lower respiratory infections and all related infections of the thorax	Meningitis and other bacterial CNS infections	Bloodstream infections	Skin and subcutaneous bacterial infections	Urinary tract infections and pyelonephritis	Peritoneal and intra-abdominal infections	Bone, joint, and related organ infections	Cardiac infections	Diarrhoea	Typhoid, paratyphoid, and INTS	Chlamydia and gonorrhoea
(Continued from previous page)												
<b>Group B Streptococcus</b>												
All-age death counts	320 000 (235 000–420 000)	182 000 (140 000–234 000)	19 800 (14 800–27 200)	75 900 (43 900–119 000)	26 500 (6620–70 100)	8870 (6680–12 000)	..	2970 (668–8250)	3940 (2790–5450)	..	..	..
Age-standardised mortality rate	4.4 (3.3–5.8)	2.6 (2.0–3.4)	0.3 (0.2–0.4)	1.0 (0.6–1.6)	0.3 (0.1–0.9)	0.1 (0.1–0.2)	..	0.0 (0.0–0.1)	0.1 (0.0–0.1)	..	..	..
<b>Enterococcus faecalis</b>												
All-age death counts	220 000 (135 000–332 000)	..	..	74 600 (43 900–118 000)	7460 (549–34 300)	19 700 (16 100–23 700)	113 000 (60 500–186 000)	2010 (589–4760)	3380 (2390–4710)	..	..	..
Age-standardised mortality rate	2.8 (1.7–4.3)	..	..	1.0 (0.6–1.6)	0.1 (0.0–0.4)	0.3 (0.2–0.3)	1.4 (0.7–2.3)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	..	..	..
<b>Enterococcus faecium</b>												
All-age death counts	219 000 (134 000–333 000)	..	..	78 200 (44 200–126 000)	..	17 800 (9390–30 600)	118 000 (72 000–185 000)	647 (185–1530)	4480 (3150–6250)	..	..	..
Age-standardised mortality rate	2.8 (1.7–4.2)	..	..	1.0 (0.6–1.6)	..	0.2 (0.1–0.4)	1.5 (0.9–2.3)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	..	..	..
<b>Non-typhoidal Salmonella</b>												
All-age death counts	215 000 (135 000–327 000)	..	..	87 100 (53 800–131 000)	..	..	..	..	2430 (1800–3320)	46 300 (3130–139 000)	79 100 (43 000–124 000)	..
Age-standardised mortality rate	3.0 (1.9–4.6)	..	..	1.2 (0.7–1.8)	..	..	..	..	0.0 (0.0–0.0)	0.7 (0.0–1.9)	1.1 (0.6–1.8)	..
<b>Group A Streptococcus</b>												
All-age death counts	198 000 (108 000–360 000)	..	..	56 400 (35 000–85 600)	134 000 (53 400–281 000)	..	..	5770 (1740–13 200)	2280 (1680–3150)	..	..	..
Age-standardised mortality rate	2.6 (1.4–4.7)	..	..	0.8 (0.5–1.2)	1.7 (0.7–3.6)	..	..	0.1 (0.0–0.2)	0.0 (0.0–0.0)	..	..	..
<b>Salmonella Typhi</b>												
All-age death counts	182 000 (118 000–271 000)	..	..	70 500 (44 600–105 000)	..	..	..	..	1330 (973–1810)	..	110 000 (52 800–191 000)	..
Age-standardised mortality rate	2.6 (1.7–3.8)	..	..	1.0 (0.6–1.5)	..	..	..	..	0.0 (0.0–0.0)	..	1.5 (0.7–2.7)	..
<b>Neisseria meningitidis</b>												
All-age death counts	141 000 (96 800–203 000)	..	31 100 (24 200–41 700)	110 000 (67 600–168 000)	..	..	..	..	..	..	..	..
Age-standardised mortality rate	2.0 (1.3–2.8)	..	0.4 (0.3–0.6)	1.5 (1.0–2.3)	..	..	..	..	..	..	..	..

(Table continues on next page)

	All 11 infectious syndromes	Lower respiratory infections and all related infections of the thorax	Meningitis and other bacterial CNS infections	Bloodstream infections	Skin and subcutaneous bacterial infections	Urinary tract infections and pyelonephritis	Peritoneal and intra-abdominal infections	Bone, joint, and related organ infections	Cardiac infections	Diarrhoea	Typhoid, paratyphoid, and iNTS	Chlamydia and gonorrhoea
(Continued from previous page)												
<b>Campylobacter spp</b>												
	All-age death counts	123 000 (39 300–266 000)	..	..	..	..	..	..	..	123 000 (39 300–266 000)	..	..
	Age-standardised mortality rate	17 (0.6–3.7)	..	..	..	..	..	..	..	17 (0.6–3.7)	..	..
<b>Shigella spp</b>												
	All-age death counts	113 000 (49 800–214 000)	..	..	..	..	..	..	..	113 000 (49 800–214 000)	..	..
	Age-standardised mortality rate	16 (0.7–3.0)	..	..	..	..	..	..	..	16 (0.7–3.0)	..	..
<b>Proteus spp</b>												
	All-age death counts	109 000 (72 200–157 000)	..	37 600 (21 100–61 900)	9770 (2990–23 600)	23 500 (17 900–31 700)	36 400 (21 700–57 200)	..	1990 (1410–2800)	..	..	..
	Age-standardised mortality rate	1.4 (0.9–2.0)	..	0.5 (0.3–0.8)	0.1 (0.0–0.3)	0.3 (0.2–0.4)	0.5 (0.3–0.7)	..	0.0 (0.0–0.0)	..	..	..
<b>Haemophilus influenzae</b>												
	All-age death counts	101 000 (82 800–124 000)	91 300 (74 700–112 000)	9700 (7080–13 500)	..	..	..	..	..	..	..	..
	Age-standardised mortality rate	1.4 (1.2–1.7)	1.3 (1.0–1.6)	0.1 (0.1–0.2)	..	..	..	..	..	..	..	..
<b>Serratia spp</b>												
	All-age death counts	100 000 (62 100–154 000)	..	76 700 (46 300–123 000)	..	4150 (2460–6730)	17 000 (10 200–26 400)	..	2540 (1830–3510)	..	..	..
	Age-standardised mortality rate	1.3 (0.8–2.0)	..	1.0 (0.6–1.6)	..	0.1 (0.0–0.1)	0.2 (0.1–0.3)	..	0.0 (0.0–0.0)	..	..	..
<b>Other enterococci</b>												
	All-age death counts	100 000 (65 800–145 000)	..	57 000 (32 600–91 000)	14 000 (4560–32 500)	26 600 (19 300–36 900)	..	..	2460 (1670–3440)	..	..	..
	Age-standardised mortality rate	1.3 (0.9–1.9)	..	0.8 (0.4–1.2)	0.2 (0.1–0.4)	0.4 (0.3–0.5)	..	..	0.0 (0.0–0.0)	..	..	..
<b>Vibrio cholerae</b>												
	All-age death counts	96 400 (52 700–159 000)	..	..	..	..	..	..	..	96 400 (52 700–159 000)	..	..
	Age-standardised mortality rate	1.3 (0.7–2.2)	..	..	..	..	..	..	..	1.3 (0.7–2.2)	..	..

(Table continues on next page)



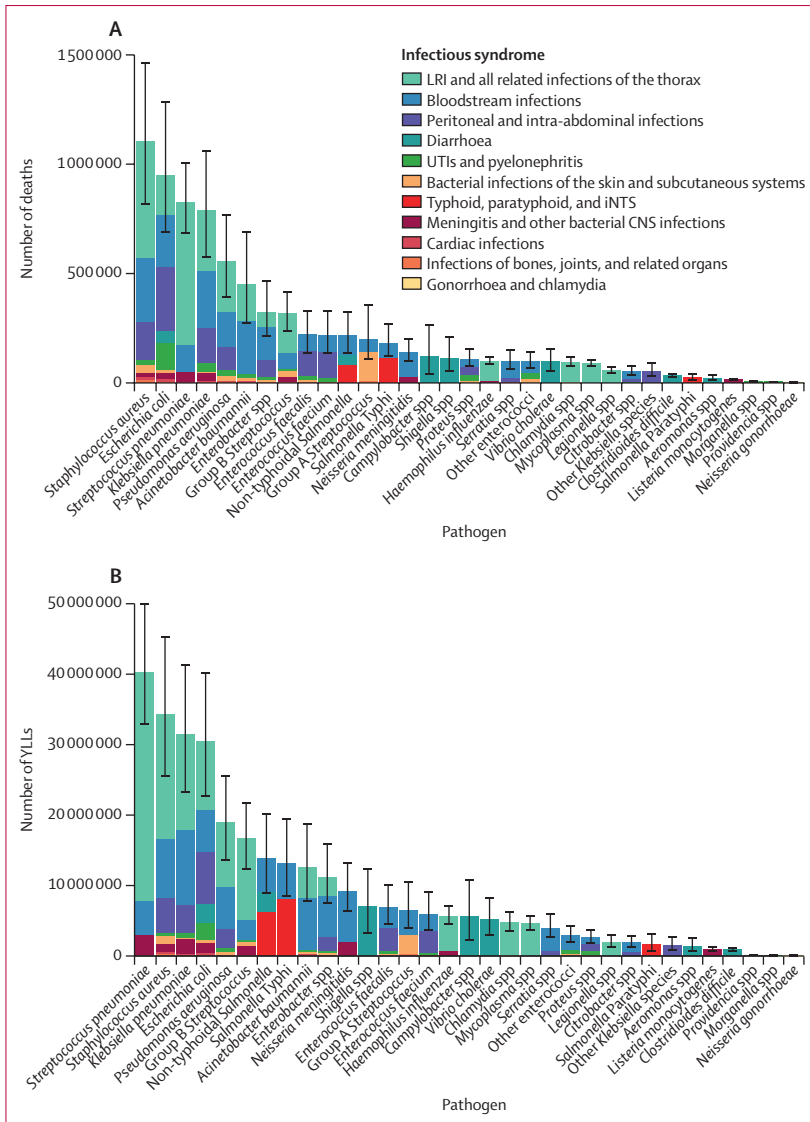
	All 11 infectious syndromes	Lower respiratory infections and all related infections of the thorax	Meningitis and other bacterial CNS infections	Bloodstream infections	Skin and subcutaneous bacterial infections	Urinary tract infections and pyelonephritis	Peritoneal and intra-abdominal infections	Bone, joint, and related organ infections	Cardiac infections	Diarrhoea	Typhoid, paratyphoid, and INTS	Chlamydia and gonorrhoea
(Continued from previous page)												
<b>Chlamydia spp</b>												
All-age death counts	95 300 (74 300–122 000)	94 300 (73 200–121 000)	..	..	..	..	..	..	..	..	..	972 (757–1110)
Age-standardised mortality rate	1.3 (1.0–1.7)	1.3 (1.0–1.7)	..	..	..	..	..	..	..	..	..	0.0 (0.0–0.0)
<b>Mycoplasma spp</b>												
All-age death counts	89 400 (74 400–108 000)	89 400 (74 400–108 000)	..	..	..	..	..	..	..	..	..	..
Age-standardised mortality rate	1.2 (1.0–1.5)	1.2 (1.0–1.5)	..	..	..	..	..	..	..	..	..	..
<b>Legionella spp</b>												
All-age death counts	56 400 (44 200–74 400)	56 400 (44 200–74 400)	..	..	..	..	..	..	..	..	..	..
Age-standardised mortality rate	0.8 (0.6–1.0)	0.8 (0.6–1.0)	..	..	..	..	..	..	..	..	..	..
<b>Citrobacter spp</b>												
All-age death counts	54 100 (33 200–80 400)	..	..	32 600 (18 000–51 700)	..	5210 (3580–7530)	16 300 (9590–25 300)	..	..	..	..	..
Age-standardised mortality rate	0.7 (0.4–1.0)	..	..	0.4 (0.2–0.7)	..	0.1 (0.0–0.1)	0.2 (0.1–0.3)	..	..	..	..	..
<b>Other Klebsiella species</b>												
All-age death counts	53 900 (28 600–92 700)	..	..	..	..	..	53 900 (28 600–92 700)	..	..	..	..	..
Age-standardised mortality rate	0.7 (0.4–1.2)	..	..	..	..	..	0.7 (0.4–1.2)	..	..	..	..	..
<b>Clostridioides difficile</b>												
All-age death counts	33 200 (25 300–44 900)	..	..	..	..	..	..	..	..	33 200 (25 300–44 900)	..	..
Age-standardised mortality rate	0.4 (0.3–0.6)	..	..	..	..	..	..	..	..	0.4 (0.3–0.6)	..	..
<b>Salmonella Paratyphi</b>												
All-age death counts	23 300 (9810–45 700)	..	..	..	..	..	..	..	..	..	23 300 (9810–45 700)	..
Age-standardised mortality rate	0.3 (0.1–0.6)	..	..	..	..	..	..	..	..	..	0.3 (0.1–0.6)	..

(Table continues on next page)

	All 11 infectious syndromes	Lower respiratory infections and all related infections of the thorax	Meningitis and other bacterial CNS infections	Bloodstream infections	Skin and subcutaneous bacterial infections	Urinary tract infections and pyelonephritis	Peritoneal and intra-abdominal infections	Bone, joint, and related organ infections	Cardiac infections	Diarrhoea	Typhoid, paratyphoid, and iNTS	Chlamydia and gonorrhoea
(Continued from previous page)												
<b>Aeromonas spp</b>												
All-age death counts	21300 (9920–38100)	..	..	..	..	..	..	..	..	21300 (9920–38100)	..	..
Age-standardised mortality rate	0.3 (0.1–0.6)	..	..	..	..	..	..	..	..	0.3 (0.1–0.6)	..	..
<b>Listeria monocytogenes</b>												
All-age death counts	14900 (10100–21600)	..	14900 (10100–21600)	..	..	..	..	..	..	..	..	..
Age-standardised mortality rate	0.2 (0.1–0.3)	..	0.2 (0.1–0.3)	..	..	..	..	..	..	..	..	..
<b>Morganella spp</b>												
All-age death counts	5510 (3600–8200)	..	..	..	..	5510 (3600–8200)	..	..	..	..	..	..
Age-standardised mortality rate	0.1 (0.0–0.1)	..	..	..	..	0.1 (0.0–0.1)	..	..	..	..	..	..
<b>Providencia spp</b>												
All-age death counts	5030 (3110–7720)	..	..	..	..	5030 (3110–7720)	..	..	..	..	..	..
Age-standardised mortality rate	0.1 (0.0–0.1)	..	..	..	..	0.1 (0.0–0.1)	..	..	..	..	..	..
<b>Neisseria gonorrhoeae</b>												
All-age death counts	2960 (2320–3360)	..	..	..	..	..	..	..	..	..	..	2960 (2320–3360)
Age-standardised mortality rate	0.0 (0.0–0.0)	..	..	..	..	..	..	..	..	..	..	0.0 (0.0–0.0)

95% uncertainty intervals are shown in parentheses. Death counts are shown to three significant figures and age-standardised mortality rates are shown to one decimal place. iNTS=invasive non-typhoidal *Salmonella*. *Salmonella* Typhi=*Salmonella enterica* serotype Typhi. *Salmonella* Paratyphi=*Salmonella enterica* serotype Paratyphi.

**Table: Global number of deaths and age-standardised mortality rate per 100 000 population by bacterial pathogen and infectious syndrome, 2019**



**Figure 1: Global number of deaths (A) and YLLs (B), by pathogen and infectious syndrome, 2019**  
 Columns show total number of deaths for each pathogen, with error bars showing 95% uncertainty intervals, with the bars split into infectious syndromes. LRI=lower respiratory infection. iNTS=invasive non-typhoidal *Salmonella*. *Salmonella* Typhi=*Salmonella enterica* serotype Typhi. *Salmonella* Paratyphi=*Salmonella enterica* serotype Paratyphi. UTI=urinary tract infection. YLLs=years of life lost.

delineated surveillance and data-driven control plans, and the motivation for the current study was to provide insight into the public health burden of less well studied pathogens.

**Estimating mortality and YLLs**

To estimate the number of deaths due to the pathogens of interest, we multiplied the number of deaths for each underlying cause, age, sex, and location by the fraction of deaths in which infection had a role, the fatal infectious syndrome fraction, and the pathogen fraction, and summed across all underlying causes of death and infectious syndromes to estimate the number of deaths

due to a given pathogen by age, sex, and location. We estimated YLLs associated with each pathogen using previously published methods<sup>3</sup> that convert age-specific deaths into YLLs using the standard counterfactual life expectancy at each age.

**Uncertainty and validity analysis**

Following standard GBD methods,<sup>16</sup> we propagated uncertainty from each step of the analysis into the final estimates of deaths associated with each pathogen by taking the 2·5th and 97·5th percentiles of 1000 draws from the posterior distribution of each quantity of interest. To assess model validity, we calculated the root mean square error and coefficient of determination (*R*<sup>2</sup>) for each pathogen distribution model in proportion space for both in-sample and out-of-sample predictions (appendix 1 [section 6.5]).

**Role of the funding source**

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

**Results**

In 2019, there were an estimated 13·7 million (95% UI 10·9–17·1) infection-related deaths globally, with 7·7 million (5·7–10·2) deaths associated with the 33 bacterial pathogens we investigated. These bacteria altogether were associated with 13·6% (10·2–18·1) of all global deaths in 2019 and 56·2% (52·1–60·1) of all infection-related deaths for that year. The all-age mortality rate was 99·6 deaths (74·2–132) per 100 000 population collectively for these pathogens. Only one organism, *Staphylococcus aureus*, was associated with more than 1 million deaths in 2019 (1 105 000 deaths [816 000–1 470 000]; table). Four additional pathogens were associated with more than 500 000 deaths each in 2019; these were *Escherichia coli*, *S pneumoniae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* (table, figure 1A). These five leading pathogens were associated with 30·9% (28·6–33·1) of all infection-related deaths and were responsible for 54·9% (52·9–56·9) of all deaths among the investigated bacterial pathogens. Of the bacteria estimated, *Morganella* spp, *Providencia* spp, and *Neisseria gonorrhoeae* had the fewest associated deaths (table). There were 304 million (234–392) YLLs associated with the 33 bacterial pathogens globally in 2019, representing 18·1% (14·1–22·8) of the global YLLs for the year. The leading five organisms by YLL burden were similar to the mortality estimates but the order changed: *S pneumoniae* was associated with the greatest YLL burden with 40·3 million (32·8–50·0) YLLs, followed by *S aureus* with 34·3 million (25·5–45·3), *K pneumoniae* with 31·4 million (23·2–41·5), *E coli* with 30·4 million (22·7–40·2), and *P aeruginosa* with 18·9 million (13·6–25·7; figure 1B; appendix 1 [section 10]). The age-standardised mortality rate associated with these 33 bacterial pathogens varied by super-region

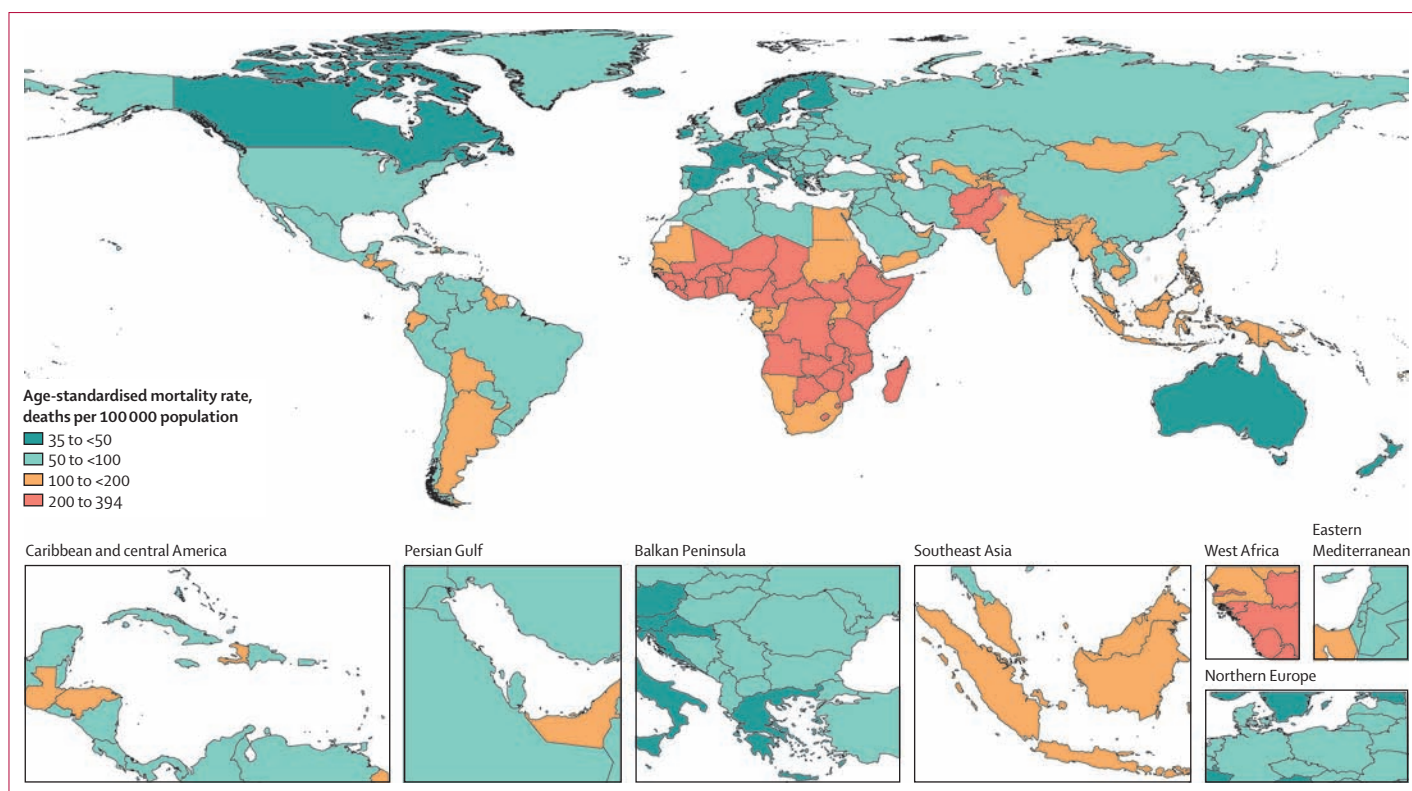


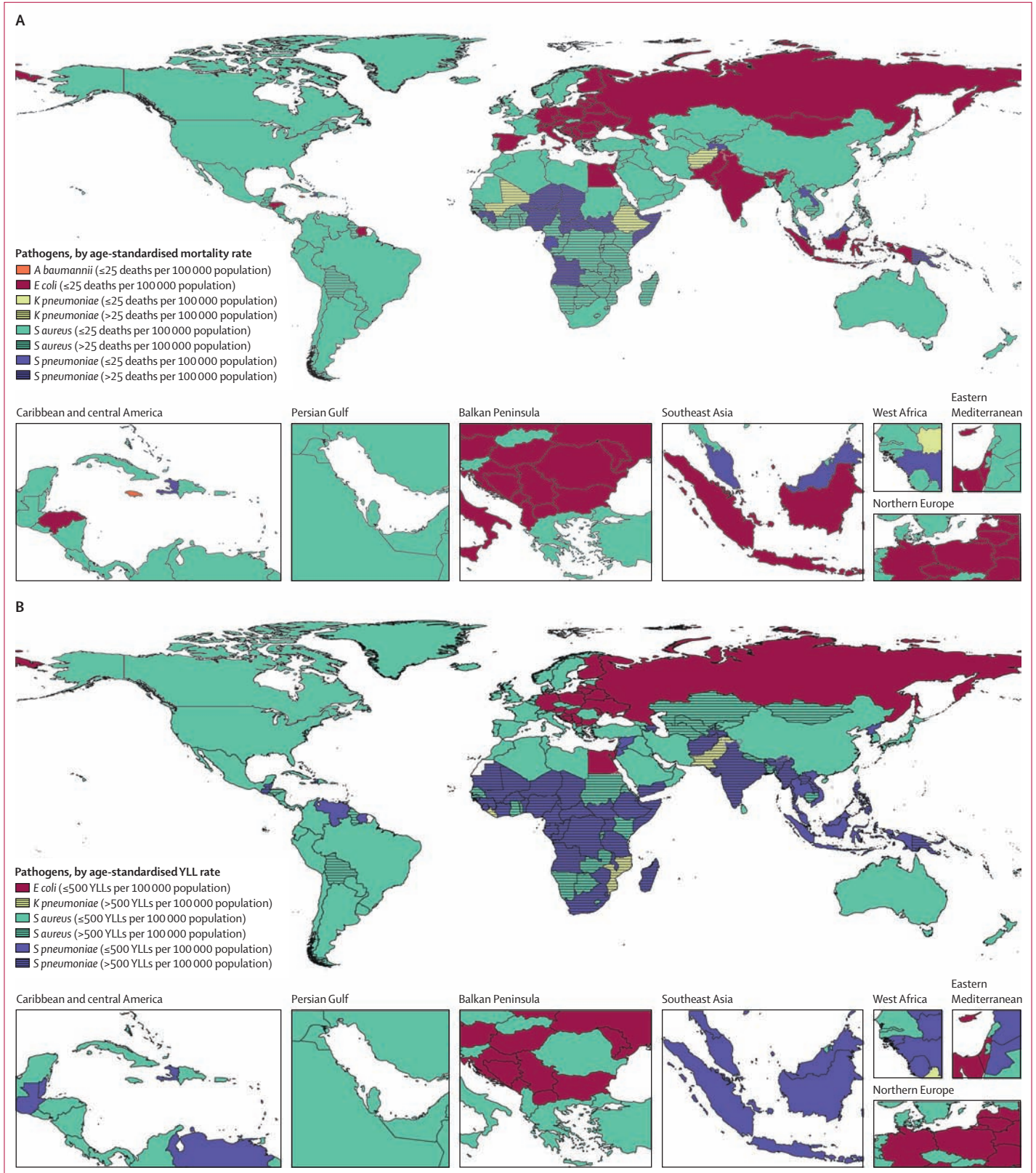
Figure 2: Overall age-standardised mortality rate per 100 000 population for 33 pathogens investigated, 2019

in 2019 but was highest in sub-Saharan Africa, at 230 deaths (95% UI 185–285) per 100 000 population, and lowest in the high-income super-region, at 52·2 deaths (37·4–71·5) per 100 000 population. Central African Republic was the country with the highest age-standardised mortality rate associated with these 33 bacterial pathogens, with 394 deaths (297–518) per 100 000 population, while Iceland had the lowest rate, with 35·7 deaths (25·1–49·3) per 100 000 population in 2019 (figure 2; appendix 1 [section 10]). The pathogens linked to the most deaths varied across locations. *S aureus* was the leading bacterial cause of death in 135 countries, followed by *E coli* (leading cause in 37 countries), *S pneumoniae* (leading cause in 24 countries), and *K pneumoniae* and *Acinetobacter baumannii* (leading causes in four countries each; figure 3A; appendix 2). *S aureus*, *E coli*, *K pneumoniae*, and *S pneumoniae* were among the five leading pathogens associated with the greatest death count and the greatest YLL burden in every super-region (figure 4). *S aureus* was also the pathogen with the highest age-standardised mortality rate in 16 of 21 GBD regions, *S pneumoniae* had the highest rate in three regions (Oceania, South Asia, and western sub-Saharan Africa), and *E coli* had the highest rate in South Asia and central and eastern Europe (appendix 1 [section 10]). The pathogens associated with the greatest age-standardised YLL burden varied across locations (figure 3B). *S aureus* was the leading pathogen in

111 countries, followed by *S pneumoniae* in 69 countries, and *E coli* in 20 countries (appendix 2).

The pathogen associated with the most deaths differed by age. Globally, *S aureus* was the pathogen associated with the most deaths in individuals older than 15 years, with 940 000 deaths (95% UI 682 000–1 276 000) in that age group. *Salmonella enterica* serovar Typhi was associated with the most deaths in children aged 5–14 years (49 000 deaths [23 000–86 000]). *S pneumoniae* was associated with the most deaths among young children post-neonatal to age 4 years (225 000 [180 000–281 000]), whereas *K pneumoniae* was the pathogen associated with the most neonatal deaths (124 000 [89 000–167 000]). We found no differences between males and females in the ranking of deaths associated with the leading six bacteria (*S aureus*, *E coli*, *S pneumoniae*, *K pneumoniae*, *P aeruginosa*, and *A baumannii*). The absolute number of deaths associated with these pathogens was always smaller for females than for males, except among those aged 80 years and older, for whom the number of deaths in females exceeded those in males (figure 5; appendix 1 [section 10]). *S aureus* was estimated to have the largest number of deaths for both males (601 000 deaths [442 000–807 000]) and females (504 000 deaths [371 000–669 000]), and was closely followed by *E coli*, for which the difference in the number of deaths between females (450 000 deaths [329 000–602 000]) and males (500 000 deaths

See Online for appendix 2



[355 000–684 000]) was smaller (figure 5; appendix 1 [section 10]).

Two infectious syndromes were responsible for more than 2 million deaths each in 2019: lower respiratory infections with 4.00 million (95% UI 3.33–4.89) deaths, and bloodstream infections with 2.91 million (1.74–4.53) deaths. Peritoneal and intra-abdominal infections were responsible for 1.28 million (0.826–1.86) deaths. The syndrome responsible for the most deaths due to bacterial infection varied across locations, while the three leading syndromes were consistently lower respiratory infections, bloodstream infections, and peritoneal and intra-abdominal infections. There was variation in terms of which of these three syndromes caused the most deaths across GBD super-regions, with lower respiratory infections being the leading syndrome in five super-regions and bloodstream infections being the leading syndrome in two super-regions (appendix 1 [section 10]).

There was substantial variation in which pathogen was the most dominant across different infectious syndromes, with *S pneumoniae* being the leading cause of fatal lower respiratory infections with 653 000 deaths (95% CI 553 000–777 000), *S aureus* being the leading cause of fatal bloodstream infections with 299 000 deaths (166 000–485 000), and *E coli* being the leading cause of fatal peritoneal and intra-abdominal infections with 290 000 deaths (188 000–423 000; table). Similarly, the most prevalent infectious syndrome varied across pathogens, with 78.9% (73.3–83.3) of deaths due to *S pneumoniae* occurring by way of lower respiratory infections, whereas *E coli* caused a wider range of syndromes, with 30.4% (26.1–35.5) of all *E coli*-associated deaths occurring via peritoneal and intra-abdominal infections, followed by 25.1% (18.7–32.1) occurring via bloodstream infection (figure 1). For each of these three infectious syndromes, the distribution of the responsible pathogen varied across locations (appendix 1 pp 67–68). The greatest differences by location were seen in the role of *S aureus* in bloodstream infection, with the pathogen being associated with 23% of deaths due to bloodstream infections caused by any bacteria in the high-income super-region in 2019 (appendix 1 p 72), but only 5% of deaths due to bloodstream infections caused by any bacteria in sub-Saharan Africa, where *K pneumoniae* caused the most deaths due to bloodstream infections, followed by *N meningitidis*.

## Discussion

To our knowledge, this is the first study to provide global estimates on mortality and YLLs for a wide range of

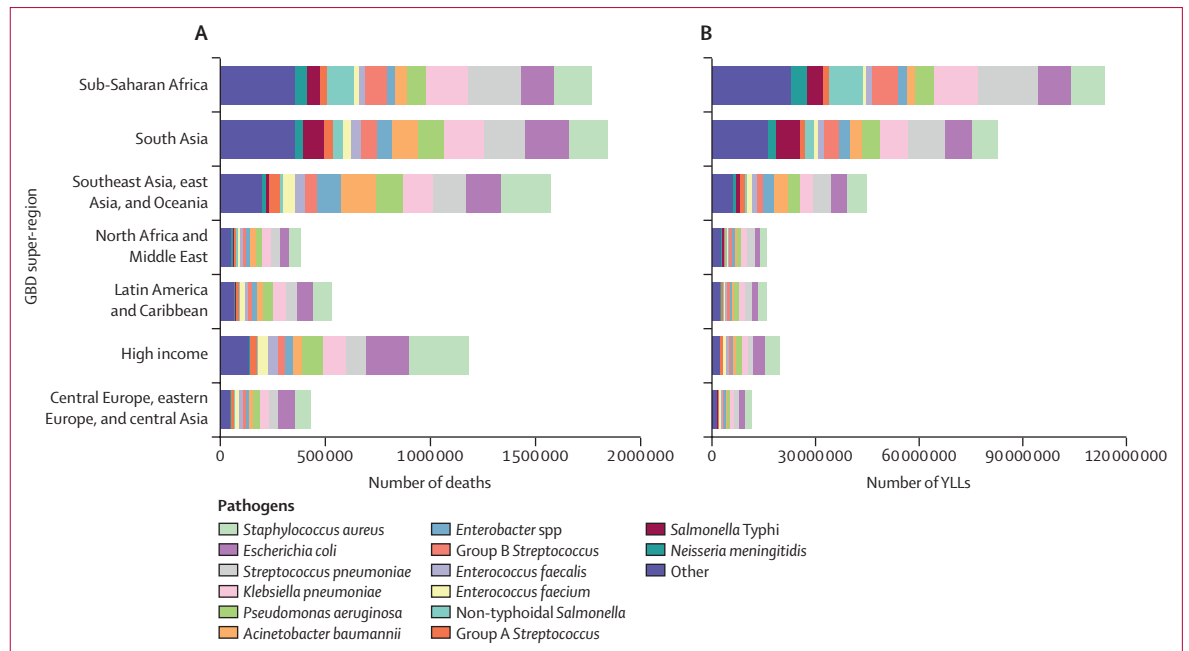
bacterial genera and species across 11 major infectious syndromes. We found that, collectively, the 33 analysed bacteria were associated with 7.7 million (95% UI 5.7–10.2) deaths in 2019, with an all-age mortality rate of 99.6 deaths (74.2–132) per 100 000 population. These bacteria were involved in 13.6% (10.1–18.1) of global deaths in 2019 and, compared with Level 3 GBD underlying causes of death, would rank as the second leading cause of death globally, behind ischaemic heart disease.<sup>3</sup> Individually, four pathogens were associated with more than 750 000 deaths and 30 million YLLs globally in 2019, and their ranks as leading Level 3 causes of death in 2019 would be as follows: *S aureus* would rank as the 15th, *E coli* as the 18th, *S pneumoniae* as the 20th, and *K pneumoniae* as the 21st leading Level 3 cause of death. There was considerable variation in the burden of bacterial infections, with the greatest number of deaths occurring in the sub-Saharan Africa super-region, where we clearly saw the effect of both Gram-positive and Gram-negative pathogens. The disparate burden in sub-Saharan Africa is magnified by the substantial YLL burden associated with these bacteria in this super-region compared with other super-regions.

By estimating mortality and YLLs for a broad range of pathogens and infectious syndromes, we have produced a global account of bacteria for which the burden was previously unknown and, perhaps, underappreciated. More than half of bacterial deaths in our study were caused by one of five pathogens: *S aureus*, *E coli*, *S pneumoniae*, *K pneumoniae*, and *P aeruginosa*. Of these pathogens, only *S pneumoniae* has been the focus of global surveillance and public health initiatives.<sup>19,24</sup> Although infectious diseases like HIV/AIDS, tuberculosis, and neglected tropical diseases each have their own SDG indicators (eg, SDG 3.3) and have substantial global public health investment (eg, The Global Fund to Fight AIDS, Tuberculosis and Malaria), the bacterial pathogens we found to be associated with a greater fatal burden are not a major focus of any global public health initiatives. Only recently have there been calls to expand the scope of The Global Fund to include more common bacteria, although in the context of antimicrobial resistance.<sup>25</sup> *S aureus* was the leading bacterial pathogen in most countries and was the only pathogen associated with more than 1 million deaths and 34 million YLLs globally, yet there is no global public health investment directed at *S aureus*. Instead, *S aureus* is included in surgical site infection prevention<sup>26</sup> and antimicrobial resistance initiatives,<sup>27</sup> which focus on methicillin-resistant *S aureus* (known as MRSA), despite the fact that strains with such resistance comprise only a subset of the *S aureus* burden. Although WHO prioritised *S aureus* in 2014 as one of the seven bacteria of international concern, this was in the context of antimicrobial resistance and little has been done regarding the susceptible *S aureus* burden.<sup>28</sup> Similarly, *E coli* and *K pneumoniae* are collectively associated with more

For more on The Global Fund see <https://www.theglobalfund.org/en/>

**Figure 3:** Pathogen responsible for the highest age-standardised mortality rate per 100 000 population (A) and for the highest age-standardised YLL rate per 100 000 population (B), for each country or territory, 2019

A *baumannii*=*Acinetobacter baumannii*. E *coli*=*Escherichia coli*.  
K *pneumoniae*=*Klebsiella pneumoniae*. S *aureus*=*Staphylococcus aureus*.  
S *pneumoniae*=*Streptococcus pneumoniae*. YLLs=years of life lost.



**Figure 4: Global number of deaths (A) and YLLs (B), by pathogen and GBD super-region, 2019**

Data are presented for the 14 pathogens with the largest number of global deaths; the Other group comprises the additional 19 bacteria estimated in this study. GBD=Global Burden of Diseases, Injuries, and Risk Factors. *Salmonella Typhi*=*Salmonella enterica* serotype Typhi. YLLs=years of life lost.

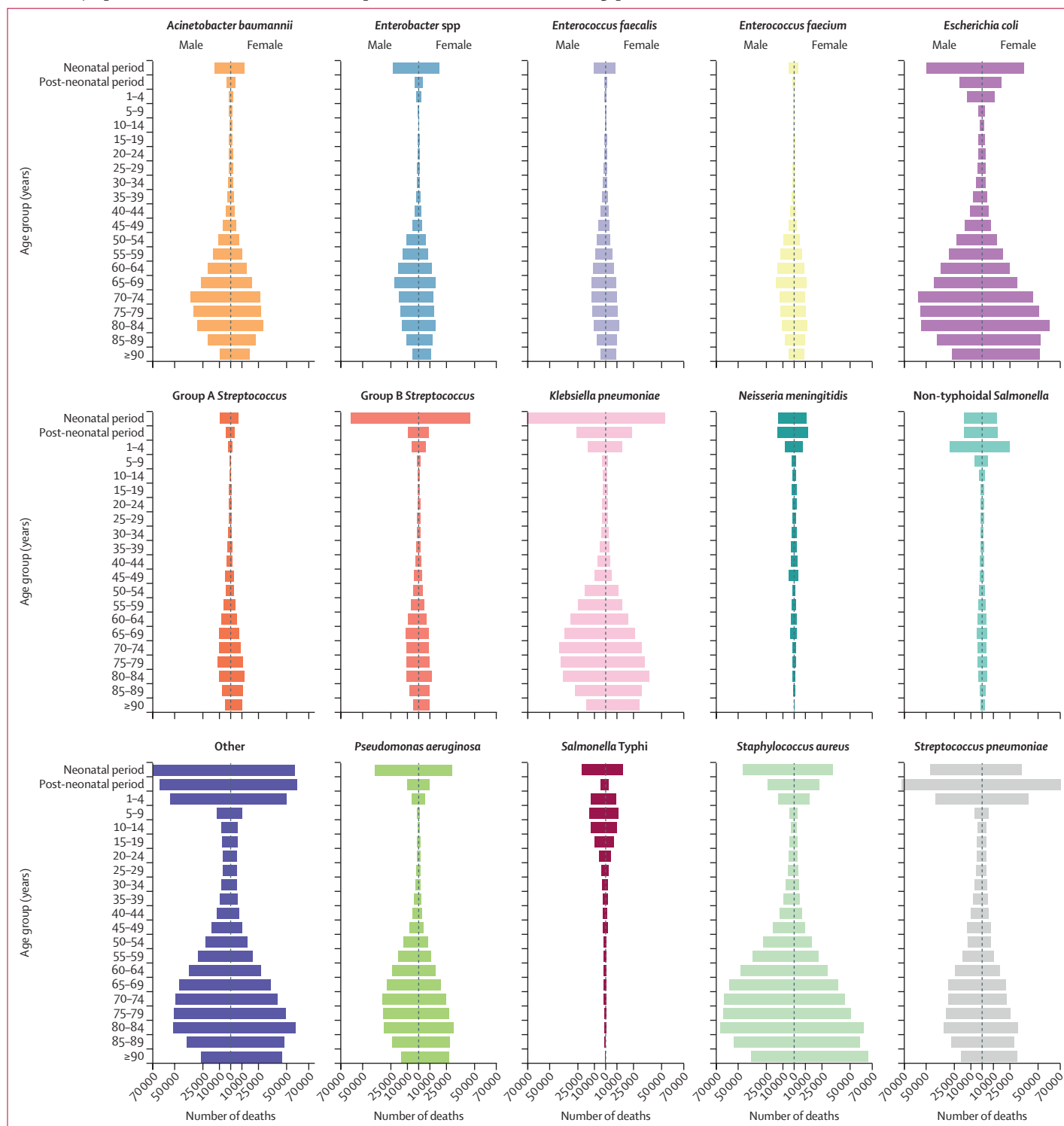
deaths and YLLs than *S pneumoniae* or tuberculosis,<sup>29</sup> yet they receive comparatively little public health attention relative to their burden, and minimal research funding relative to other diseases with a comparable, or lower, burden. A 2020 analysis of global funding for infectious disease research found that HIV research was awarded US\$42 billion in funding compared with \$1.4 billion for research on *Staphylococcus* spp and \$800 million for *E coli* research over the same period (between 2000 and 2017).<sup>30</sup> The investments in HIV research are certainly warranted and, although bacterial infections could be tackled with different overlapping strategies, this disparity in funding might have been driven, in part, by the shortage of global burden numbers for these bacterial pathogens.

The 33 bacterial agents investigated as part of this study comprise a significant cause of health loss globally, and strategies to address this substantial burden cover a wide range of interventions. First, infection prevention is the foundation to reducing the burden of infections. Infection prevention broadly includes in-hospital programmes aimed at reducing hospital-acquired infection,<sup>31</sup> and community programmes that focus on health education, management of malnutrition in LMICs, and the core principles of access to clean water, sanitation, and hygiene.<sup>32,33</sup> Second, vaccination can have a substantial effect on the burden of bacterial infections through a number of routes. Implementation and uptake of vaccines for bacteria like *S pneumoniae* can directly reduce the burden of bacterial infections, and new generations of vaccines will target older age groups that we have found are significantly affected by this bacterial agent.<sup>16</sup> Beyond

this, uptake of vaccination for non-bacterial infections like influenza, where bacterial superinfection is a common complication, can also reduce the burden of bacterial infections.<sup>34</sup> Additionally, vaccine development is crucial for bacteria for which no vaccine exists, and these estimates could help set vaccine development priorities.<sup>9</sup> However, issues on how to tackle the bacteria that can be present as commensal microbiota have to be considered. For example, the alteration of commensal bacteria can influence susceptibility to gastrointestinal diseases, which might be an issue when developing a vaccine against *E coli*; different biology and vaccinology approaches hold the promise of resolving this conundrum.<sup>35</sup> Third, availability of basic acute care services can reduce the number of deaths associated with these bacterial infections. Such services include timely access to appropriate antibiotics, microbiological capacity to identify the responsible pathogen of an infection, and provision of supportive care.<sup>36,37</sup> Finally, a strategic approach and ample investment in the development of new and effective antibiotics are essential to face the increasing threat posed by bacterial antimicrobial resistance and bacterial infections in general.<sup>38</sup>

Effective antimicrobials exist for all 33 of the investigated bacteria, yet much of the disproportionately high burden in LMICs might be attributable to inadequate access to effective antimicrobials, weak health systems, and insufficient prevention programmes.<sup>39,40</sup> Many barriers to accessing these effective antimicrobials have been described. First, health-care-seeking behaviours are impeded by high out-of-pocket costs, driven by deficiencies

in government funding for health and unaffordable drug regulatory issues, self-medication, and restricted prices in LMICs.<sup>41</sup> Second, unwarranted antibiotic use availability of antibiotics can lead to the wrong caused by poor education of health-care providers, antimicrobial being prescribed, which, if too broad, can



**Figure 5: Global number of deaths, by pathogen, age, and sex groups, 2019**

Data are presented for the 14 pathogens with the largest number of global deaths; the Other group comprises the additional 19 bacteria estimated in this study. Neonatal=0 days to 27 days old. Post-neonatal=28 days to <1 year old. *Salmonella Typhi*=*Salmonella enterica* serotype Typhi.



promote resistance and, if ineffective, risks progression of infection.<sup>41</sup> Third, unstable supply chains and poor quality control can result in the desired antibiotic being unavailable or the dissemination of substandard or counterfeit antimicrobials to the consumer.<sup>42</sup> Improving access to antibiotics requires a nuanced and location-specific response because ease of access must be weighed against risk of antibiotic overuse (a problem compounded by the issue of self-medication in LMICs),<sup>43</sup> which contributes to the increase in antimicrobial resistance.<sup>44</sup> Furthermore, the use of antibiotics in animal husbandry must be taken into account.<sup>44</sup> In this study, we addressed the overall burden of infections both susceptible and resistant to antimicrobials, but our previous study<sup>19</sup> highlighted the issue of resistance and its compounding effect on mortality rates. We argue that robust surveillance mechanisms in conjunction with these types of studies will be indispensable to understand the true burden of bacterial infections.

Three syndromes are responsible for more than 75% of the estimated 7·7 million bacteria-related deaths that occurred in 2019. Lower respiratory infections, bloodstream infections, and peritoneal and intra-abdominal infections would rank as the third, seventh, and 13th leading causes of death globally for 2019, respectively, all ahead of other causes such as HIV, colorectal cancer, or self-harm. Lower respiratory infections have long been a global health priority,<sup>45</sup> and bloodstream infections have arguably been included in the umbrella of more recent global sepsis initiatives,<sup>46,47</sup> however, intra-abdominal infections and peritonitis do not receive the same attention as other diseases with similar or lower fatal burden. Although overlap exists in the management of peritoneal and intra-abdominal infections with other bacterial infections (eg, antibiotics and identification of the infection's source), management of peritoneal and intra-abdominal infections poses unique challenges in that radiological imaging is often required to establish a source and surgical intervention might be needed to achieve source control.<sup>48</sup> There is a substantial shortage of medical capacity and trained personnel in many LMICs to address peritoneal and intra-abdominal infections and other infections that require surgical intervention.<sup>49</sup> Recent estimates suggest 4·8 billion people do not have access to timely surgical services, with low-income countries estimated to have fewer than one provider per 100 000 population.<sup>50</sup> Compounding inadequate access to surgical services is the restricted availability of diagnostic radiology, with a recent analysis of ten LMICs across the Caribbean, South Asia, and sub-Saharan Africa finding that CT was available in only 6% of hospitals and ultrasound was available in only 50% of hospitals.<sup>51</sup>

The remarkable geographical variation of responsible pathogens for a given infectious syndrome is highlighted by *S aureus* as the causative pathogen of bloodstream infection. In the high-income super-region, *S aureus*

caused 23% of deaths due to bloodstream infections that involved one of the 33 bacteria investigated, compared with only 5% of deaths due to bloodstream infections in the sub-Saharan Africa super-region. This variation has profound implications on the empirical management of infections when a responsible pathogen has not yet been identified and breadth of coverage must be balanced against risk of antibiotic resistance. The WHO essential medicines list provides global empirical antibiotic recommendations for various infectious syndromes;<sup>52</sup> however, our findings suggest that a move towards region-specific empirical antibiotic recommendations might be more appropriate from an antibiotic stewardship and antimicrobial efficacy standpoint.<sup>53</sup> Region-specific guidance will also help in addressing inappropriate antibiotic use in LMICs, which is one of the key drivers of antimicrobial resistance.<sup>43</sup> We hope that these estimates might be used to guide empirical antibiotic use, yet data sparsity remains a major limitation in creating more granular estimates with sufficient confidence to inform individual clinicians in accordance with clinical needs and the aim to uphold antimicrobial stewardship.<sup>54</sup>

We should also acknowledge *M tuberculosis*, which was not included in our analysis. One reason we did not do additional estimations for this important pathogen is because the global burden estimates provided by GBD 2019 and WHO are quite concordant and well established.<sup>29,55</sup> A GBD study has shown that, in 2019, there were 9·65 million incident cases and 1·21 million deaths due to tuberculosis in both HIV-negative and HIV-positive individuals.<sup>29</sup> There was also a greater incidence and an excess burden in males, which is comparable with the burden of bacterial agents estimated in this study. Geographically, most cases of tuberculosis in 2019 were found in the WHO regions of South-East Asia, Africa, and the Western Pacific,<sup>29,55</sup> which is comparable with the geographical spread of the burden of the 33 bacteria we investigated in this study.

Insufficient microbiological capacity has substantial effects on both population health estimates and the clinical care of individual patients. Correspondingly, an urgent need exists to build microbiology laboratory networks and develop innovative surveillance strategies.<sup>56</sup> Identification of a responsible pathogen in sepsis and other severe infections can help inform optimal antibiotic choice and duration, and lead clinicians to probable sources of infection. Without microbiological data, patients might remain on inappropriate or ineffective antibiotics that contribute to worse health outcomes and fuel the spread of antimicrobial resistance. Practical antibiotic prescribing is also affected because the distribution of pathogens and local patterns of antimicrobial susceptibility are unknown, which hamper the development of dependable treatment protocols. In a recent study,<sup>51</sup> investigators found that fewer than half of hospitals in ten LMICs had the capacity to do Gram staining, and we

speculate that even fewer hospitals in this context could perform cultures and susceptibility testing.<sup>31</sup> Many locations have little or no microbiology data to inform local burden estimates, and so they must rely on modelled estimates to approximate the burden, resulting in wide uncertainty intervals. The barriers to building microbiology capacity in LMICs have been well described,<sup>37</sup> and overcoming these challenges requires greater investment and prioritisation of bacteriology capacity, and the development of national antimicrobial resistance surveillance networks.

Our study has several limitations, many of which are the result of data sparsity. Input data for each modelling step has incomplete geographical coverage and is of varying quality for many LMICs, and we did not have data for 61 countries or territories for all three of our modelling steps. Hence, the locations where the burden is estimated to be the greatest are where the data are most scarce, which is an issue exacerbated by age-targeted surveillance protocols; this data scarcity should underscore the urgency of improving capacity and surveillance systems in LMICs. The identification of deaths in which infection had a role relied on International Classification of Diseases (ICD) coded deaths, which does not perfectly correlate with expert chart review. Our estimates of lower respiratory infections and urinary tract infections split infections into community-acquired versus hospital-acquired infections on the basis of whether ICD coding indicated the infection was an underlying or intermediate cause of death. However, this approach has not previously been validated and has the risk of misclassification. We assumed the same pathogen distribution among culture-negative as among culture-positive infections. This assumption could overestimate pathogens that are easier to detect and underestimate pathogens that are difficult to culture with the use of standard microbiological techniques (eg, culture-negative endocarditis might be caused by *Bordetella* spp or *Coxiella* spp, bacteria that are notoriously difficult to culture, although we expect the effect of this particular example on overall bacteria aetiologies to be quite small). We have a residual polybacterial category in which multiple possible causative pathogens were identified for a single infection; however, because many of these infections involved one or more of the 33 bacteria we investigated, this approach leads to an underestimation of the specified bacteria. Additionally, passive microbial surveillance data could have had some selection bias, particularly if cultures were not routinely drawn. In some locations, cultures might be drawn only if someone is critically ill or has not responded to treatment, which might overestimate more virulent or more resistant pathogens. Finally, this study is supported by the framework of and estimates from the GBD study, which has its own limitations that have been discussed elsewhere.<sup>3</sup>

The 7·7 million deaths associated with the 33 pathogens we investigated are deaths that occurred in people with infections caused by one of these bacteria; however, we cannot conclusively state that if all infections due to these 33 pathogens were eliminated, then 7·7 million deaths would have been prevented. Many of these deaths were identified as deaths due to sepsis, when the underlying cause was non-infectious. In a subset of these deaths, the underlying cause of death might have been so severe that a death would have occurred whether or not the infection took place. For example, someone with terminal pancreatic cancer who dies from *E coli* peritonitis is counted the same as a neonate who dies of neonatal sepsis due to *E coli*. However, most of the estimated 7·7 million deaths occurred when the infection with one of the 33 bacteria was the underlying cause of death, and in those cases, we could reasonably assume that those deaths would have been prevented if the infection had not occurred. Placing infections into discrete categories of clinical syndromes opens up the discussion of how to address bloodstream infections, a syndrome that is not always distinct from other clinical syndromes and is often an intermediary between a precipitating infection and sepsis. Our approach to infectious syndromes used a hierarchy process in which bloodstream infections were ranked the lowest—ie, if bloodstream infection was reported alongside any other infectious syndrome, the other infectious syndrome was used. In other words, bloodstream infections as reported here were primary bloodstream infections for which the point of entry or other associated infectious syndromes could not be identified.

In summary, our analyses show that bacterial infections are a clinically significant cause of health loss globally. Five pathogens were each involved in more than 500 000 deaths in 2019: *S aureus*, *E coli*, *S pneumoniae*, *K pneumoniae*, and *P aeruginosa*. Three infectious syndromes, each responsible for more than 1 million deaths in 2019, comprised more than 75% of deaths due to bacterial infections. A sobering reality is that a high burden of treatable infections occurred in very young age groups. Building stronger health systems with more robust diagnostic infrastructure, improved diagnostic imaging and microbiological capacity, and standardised workflows are crucial steps to address this substantial burden, together with implementing appropriate infection control and antimicrobial stewardship measures. Essential prevention strategies include improved access to safe drinking water and sanitation facilities, increased rates of vaccination, new vaccine development, and improving access to the appropriate antibiotic for an infection. There is a need to reconcile the right to antimicrobial access with non-judicious use, particularly with regard to expensive and newer generation antimicrobials. Predictive mathematical modelling and further advancements in genomic epidemiology of infections will increase insights at the global level to understand pathogens' evolution,

epidemiology, and pathogenesis, and will better inform future approaches.

#### GBD 2019 Antimicrobial Resistance Collaborators

Kevin S Ikuta, Lucien R Swetschinski, Gisela Robles Aguilar, Fablina Sharara, Tomislav Mestrovic, Authia P Gray, Nicole Davis Weaver, Eve E Wool, Chieh Han, Anna Gershberg Hayoon, Amirali Aali, Semagn Mekonnen Abate, Mohsen Abbasi-Kangevari, Zeinab Abbasi-Kangevari, Sherief Abd-Elsalam, Getachew Abebe, Aidin Abedi, Amir Parsa Abhari, Hassan Abidi, Richard Gyan Aboagye, Abdorrahim Absalan, Hiwa Abubaker Ali, Juan Manuel Acuna, Tigist Demsew Adane, Isaac Yeboah Addo, Oyelola A Adegboye, Mohammad Adnan, Qorinah Estiningtyas Sakilah Adnani, Muhammad Sohail Afzal, Saira Afzal, Zahra Babaei Aghdam, Bright Opoku Ahinkorah, Aqeel Ahmad, Araz Ramadan Ahmad, Rizwan Ahmad, Sajjad Ahmad, Sohail Ahmad, Sepideh Ahmadi, Ali Ahmed, Haroon Ahmed, Jivan Qasim Ahmed, Tarik Ahmed Rashid, Marjan Ajami, Budi Aji, Mostafa Akbarzadeh-Khiavi, Chisom Joyqueenet Akunna, Hanadi Al Hamad, Fares Alahdab, Ziyad Al-Aly, Mamoon A Aldeyab, Alicia V Aleman, Fadwa Alhalaïqa Naji Alhalaïqa, Robert Kaba Alhassan, Beriwan Abdulqadir Ali, Liaqat Ali, Syed Shujait Ali, Yousef Alimohamadi, Vahid Alipour, Atiyeh Alizadeh, Syed Mohamed Aljunid, Kasim Allel, Sami Almstanyir, Edward Kwabena Ameyaw, Arianna Maever L Amit, Nivedita Anandavelane, Robert Ancuceanu, Catalina Liliana Andrei, Tudorel Andrei, Dewi Anggraini, Adnan Ansar, Anayochukwu Edward Anyasodor, Jalal Arabloo, Aleksandr Y Aravkin, Demelash Areda, Timur Aripov, Anton A Artamonov, Judie Arulappan, Raphael Taiwo Aruleba, Muhammad Asaduzzaman, Tahira Ashraf, Seyyed Shamsadin Athari, Daniel Atlaw, Sameh Attia, Marcel Ausloos, Tewachew Awoke, Beatriz Paulina Ayala Quintanilla, Tegegn Mulatu Ayana, Sina Azadnajafabad, Amirhossein Azari Jafari, Darshan B B, Muhammad Badar, Ashish D Badiye, Nayereh Baghcheghi, Sara Bagherieh, Atif Amin Baig, Indrajit Banerjee, Aleksandra Barac, Mainak Bardhan, Francesco Barone-Adesi, Hiba Jawdat Barqawi, Amadou Barrow, Pritish Baskaran, Saurav Basu, Abdul-Monim Mohammad Batiha, Neeraj Bedi, Melaku Ashagrie Belete, Uzma Iqbal Belgaumi, Rose G Bender, Bharti Bhandari, Dinesh Bhandari, Pankaj Bhardwaj, Sonu Bhaskar, Kritika Bhattacharyya, Suraj Bhattarai, Saeid Bitaraf, Danilo Buonsenso, Zahid A Butt, Florentino Luciano Caetano dos Santos, Jiao Cai, Daniela Calina, Paulo Camargos, Luis Alberto Cámera, Rosario Cárdenas, Muge Cevik, Joshua Chadwick, Jaykaran Charan, Akhilanand Chaurasia, Patrick R Ching, Sonali Gajanan Choudhari, Enayet Karim Chowdhury, Fazle Rabbi Chowdhury, Dinh-Toi Chu, Isaac Sunday Chukwu, Omid Dadras, Fentaw Teshome Dagnaw, Xiaochen Dai, Saswati Das, Anna Dastiridou, Sisay Abebe Debelo, Fitsum Wolde Demisse, Solomon Demissie, Diriba Dereje, Mrganaw Derese, Hardik Dineshbhai Desai, Fikadu Nugusu Dessalegn, Samuel Abebe A Dessalegn, Belay Desye, Kartik Dhaduk, Meghnath Dhimel, Sameer Dhingra, Nancy Diaó, Daniel Diaz, Shirin Djalalinia, Milad Dodangeh, Deepa Dongarwar, Bezabih Terefe Dora, Fariba Dorostkar, Haneil Larson Dsouza, Eleonora Dubljanin, Susanna J Dunachie, Oyewole Christopher Durojaiye, Hisham Atan Edinur, Habtamu Bekele Ejigu, Michael Ekholuonetale, Temitope Cyrus Ekundayo, Hassan El-Abid, Muhammed Elhadi, Mohamed A Elmonem, Amir Emami, Luchuo Engelbert Bain, Daniel Berhanie Enyew, Rychindorj Erkhembayar, Babak Eshtrati, Farshid Etaee, Adeniyi Francis Fagbamigbe, Shahab Falahi, Aida Fallahzadeh, Emerito Jose A Faraon, Ali Fatehizadeh, Ginenus Fekadu, João C Fernandes, Allegra Ferrari, Getahun Fetensa, Irina Filip, Florian Fischer, Masoud Foroutan, Peter Andras Gaal, Muktar A Gadanya, Abhay Motiramji Gaidhane, Balasankar Ganesan, Mesfin Gebrehiwot, Reza Ghanbari, Mohammad Ghasemi Nour, Ahmad Ghashghae, Ali Gholamrezanezhad, Abdolmajid Gholizadeh, Mahaveer Golechha, Pouya Goleij, Davide Golinelli, Amador Goodridge, Damitha Asanga Gunawardane, Yuming Guo, Rajat Das Gupta, Sapna Gupta, Veer Bala Gupta, Vivek Kumar Gupta, Alemu Guta, Parham Habibzadeh, Atlas Haddadi Awal, Rabih Halwani, Asif Hanif, Md Abdul Hannan, Harapan Harapan, Shoib Hassan,

Hadi Hassankhani, Khezar Hayat, Behzad Heibati, Golnaz Heidari, Mohammad Heidari, Reza Heidari-Soureshjani, Claudiu Herteliu, Demisu Zembaba Heyi, Kamal Hezam, Praveen Hoogar, Nobuyuki Horita, Md Mahbub Hossain, Mehdi Hosseinzadeh, Mihaela Hostiuc, Sorin Hostiuc, Soodabeh Hoveidamanesh, Junjie Huang, Salman Hussain, Nawfal R Hussein, Segun Emmanuel Ibitoye, Olayinka Stephen Ilesanmi, Irena M Ilic, Milena D Ilic, Mohammad Tarique Imam, Mustapha Immurana, Leeberk Raja Inbaraj, Arnaud Iradukunda, Nahlah Elkudssiah Ismail, Chidozie C D Iwu, Chinwe Juliana Iwu, Linda Merin J, Mihajlo Jakovljevic, Elham Jamshidi, Tahereh Javaheri, Fatemeh Javanmardi, Javad Javidnia, Sathish Kumar Jayapal, Umesh Jayarajah, Rime Jebai, Ravi Prakash Jha, Tamas Joo, Nitin Joseph, Farahnaz Joukar, Jacek Jerzy Jozwiak, Salah Eddine Oussama Kacimi, Vidya Kadashetti, Laleh R Kalankesh, Rohollah Kalhor, Vineet Kumar Kamal, Himal Kandel, Neeti Kapoor, Samad Karkhah, Bekalu Getnet Kassa, Nicholas J Kassebaum, Patrick DMC Katoto, Mohammad Keykhaei, Himanshu Khajuria, Abbas Khan, Imteyaz A Khan, Maseer Khan, Md Nuruzzaman Khan, Moien AB Khan, Moawiah Mohammad Khatatbeh, Mona M Khater, Hamid Reza Khayat Kashani, Jagdish Khubchandani, Hanna Kim, Min Seo Kim, Ruth W Kimokoti, Niranjan Kissoon, Sonali Kochhar, Farzad Kompani, Soewarta Kosen, Parvaiz A Koul, Sindhura Lakshmi Koulmane Laxminarayana, Fiorella Krapp Lopez, Kewal Krishan, Vijay Krishnamoorthy, Vishnuthethertha Kulkarni, Naveen Kumar, Om P Kurmi, Ambily Kuttikkattu, Hmwe Hmwe Kyu, Dharmesh Kumar Lal, Judit Lám, Iván Landires, Savita Lasrado, Sang-woong Lee, Jacopo Lenzi, Sonia Lewycka, Shanshan Li, Stephen S Lim, Wei Liu, Rakesh Lodha, Michael J Loftus, Ayush Lohiya, László Lorenzovici, Mojgan Lotfi, Ata Mahmoodpoor, Mansour Adam Mahmoud, Razzagh Mahmoudi, Azeem Majeed, Jamal Majidpoor, Alaa Makki, Galana Ayana Mamo, Yosef Manla, Miquel Martorell, Clara N Matei, Barney McManigal, Entezar Mehrabi Nasab, Ravi Mehrotra, Addisu Melese, Oliver Mendoza-Cano, Ritesh G Menezes, Alexios-Fotios A Mentis, Georgia Micha, Irmira Maria Michalek, Ana Carolina Micheletti Gomide Nogueira de Sá, Neda Milevska Kostova, Shabir Ahmad Mir, Mojgan Mirghafourvand, Seyyedmohammadsadeq Mirmoenei, Erkin M Mirrakhimov, Mohammad Mirza-Aghazadeh-Attari, Abay Sisay Misganaw, Awoke Misganaw, Sanjeev Mitra, Esmaeil Mohammadi, Mokhtar Mohammadi, Abdollah Mohammadian-Hafshejani, Shafiu Mohammed, Syam Mohan, Mohammad Mohseni, Ali H Mokdad, Sara Momtazmanesh, Lorenzo Monasta, Catrin E Moore, Maryam Moradi, Mostafa Moradi Sarabi, Shane Douglas Morrison, Majid Motaghinejad, Haleh Mousavi Isfahani, Amin Mousavi Khaneghah, Seyed Ali Mousavi-Aghdas, Sumaira Mubarak, Francesk Mulita, Getaneh Baye B Mulu, Sandra B Munro, Saravanan Muthupandian, Tapas Sadasivan Nair, Atta Abbas Naqvi, Himanshi Narang, Zuhair S Natto, Muhammad Naveed, Biswa Prakash Nayak, Shumaila Naz, Ionut Negoii, Seyed Aria Nejadghaderi, Sandhya Neupane Kandel, Che Henry Ngwa, Robina Khan Niazi, Antonio Tolentino Nogueira de Sá, Nafise Noroozi, Hasti Nouraei, Ali Nowroozi, Virginia Nuñez-Samudio, Jerry John Nutor, Chimezie Igwegbe Nzopotam, Ogochukwu Janet Nzopotam, Bogdan Oancea, Rahman Md Obaidur, Vivek Anand Ojha, Akinkunmi Paul Okeunle, Osaretin Christabel Okonji, Andrew T Olagunju, Bolajoko Olubukunola Olusanya, Ahmed Omar Bali, Emad Omer, Nikita Ostavnov, Bilcha Oumer, Mahesh P A, Jagadish Rao Padubidri, Keyvan Pakshir, Tamás Palicz, Adrian Pana, Shahina Pardhan, Jose L Paredes, Utsav Parekh, Eun-Cheol Park, Seoyeon Park, Ashish Pathak, Rajan Paudel, Uttam Paudel, Shrikant Pawar, Hamidreza Pazoki Toroudi, Minjin Peng, Umberto Pensato, Veincent Christian Filipino Pepito, Marcos Pereira, Mario F P Peres, Norberto Perico, Ionela-Roxana Petcu, Zahra Zahid Piracha, Indrashis Podder, Nayanum Pokhrel, Ramesh Poluru, Maarten J Postma, Naeimeh Pourtaheri, Akila Prashant, Ibrahim Qattea, Mohammad Rabiee, Navid Rabiee, Amir Radfar, Saber Raeghi, Sima Rafiei, Pankaja Raghav Raghav, Leila Rahbarnia, Vafa Rahimi-Movaghar, Mosiur Rahman, Muhammad Aziz Rahman, Amir Masoud Rahmani, Vahid Rahmanian, Pradhun Ram,

Muhammad Modassar Ali Nawaz Ranjha, Sowmya J Rao, Mohammad-Mahdi Rashidi, Azad Rasul, Zubair Ahmed Ratan, Salman Rawaf, Reza Rawassizadeh, Mohammad Sadegh Razeghinia, Elrashdy Moustafa Mohamed Redwan, Misganu Teshoma Regasa, Giuseppe Remuzzi, Melese Abate Reta, Nazila Rezaei, Aziz Rezapour, Abanoub Riad, Rezaul Karim Ripon, Kristina E Rudd, Basema Saddik, Saeid Sadeghian, Umar Saeed, Mohsen Safaei, Azam Safary, Sher Zaman Safi, Maryam Sahebazzamani, Amirhossein Sahebkar, Harihar Sahoo, Saina Salahi, Sarvenaz Salahi, Hedayat Salari, Sana Salehi, Hossein Samadi Kafil, Abdallah M Samy, Nima Sanadgol, Senthilkumar Sankararaman, Francesco Sanmarchi, Brijesh Sathian, Monika Sawhney, Ganesh Kumar Saya, Subramanian Senthilkumar, Allen Seylani, Pritik A Shah, Masood Ali Shaikh, Elaheh Shaker, Murad Ziyaudinovich Shakhmardanov, Mequanment Melaku Sharew, Athena Sharifi-Razavi, Purva Sharma, Rahim Ali Sheikh, Ali Sheikh, Pavanchand H Shetty, Mika Shigematsu, Jae Il Shin, Hesamaddin Shirzad-Aski, K M Shivakumar, Parnian Shobeiri, Seyed Afshin Shorofi, Sunil Shrestha, Migbar Mekonnen Sibhat, Negussie Boti Sidemo, Mustafa Kamal Sikder, Luis Manuel Lopes Rodrigues Silva, Jasvinder A Singh, Paramdeep Singh, Surjit Singh, Md Shahjahan Siraj, Samarjeet Singh Siwal, Valentin Yurievich Skryabin, Anna Aleksandrovna Skryabina, Bogdan Socea, Damtew Solomom, Yimeng Song, Chandrashekar T Sreeramareddy, Muhammad Suleman, Rizwan Suliankatchi Abdulkader, Saima Sultana, Miklós Szócska, Seyed-Amir Tabatabaeizadeh, Mohammad Tabish, Majid Taheri, Elahe Taki, Ker-Kan Tan, Sarmila Tandukar, Nathan Y Tat, Vivian Y Tat, Belay Negash Tefera, Yibekal Manaye Tefera, Gebremaryam Temesgen, Mohamad-Hani Temsah, Samar Tharwat, Arulmani Thiagarajan, Imad I Tleyjeh, Christopher E Troeger, Krishna Kishore Umaphathi, Era Upadhyay, Sahel Valadan Tahbaz, Pascual R Valdez, Jef Van den Eynde, H Rogier van Doorn, Siavash Vaziri, Georgios-Ioannis Verras, Harimadhav Viswanathan, Bay Vo, Abdul Waris, Gizachew Tadesse Wassie, Nuwan Darshana Wickramasinghe, Sajad Yaghoubi, Gahin Abdurraheem Tayib Yahya Yahya, Seyed Hossein Yahyazadeh Jabbari, Arzu Yigit, Vahit Yiğit, Dong Keon Yon, Naohiro Yonemoto, Mazyar Zahir, Burhan Abdullah Zaman, Sojib Bin Zaman, Moein Zangiabadian, Iman Zare, Mikhail Sergeevich Zastrozhin, Zhi-Jiang Zhang, Peng Zheng, Chenwen Zhong, Mohammad Zoladl, Alimuddin Zumla, Simon I Hay, Christiane Dolecek, Benn Sartorius, Christopher J L Murray, and Mohsen Naghavi.

#### Affiliations

Division of Infectious Diseases (K S Ikuta MD), Veterans Affairs Greater Los Angeles, Los Angeles, CA, USA; Institute for Health Metrics and Evaluation (K S Ikuta MD, L R Swetschinski MSc, T Mestrovic PhD, A P Gray BSc, N Davis Weaver MPH, E E Wool MPH, C Han BA, A Gershberg Hayoon MSc, A Y Aravkin PhD, R G Bender BS, X Dai PhD, N J Kassebaum MD, H H Kyu PhD, Prof S S Lim PhD, A H Mokdad PhD, C E Troeger MPH, P Zheng PhD, Prof S I Hay FMedSci, Prof C J L Murray DPhil, Prof M Naghavi PhD), Department of Applied Mathematics (A Y Aravkin PhD), Department of Health Metrics Sciences, School of Medicine (A Y Aravkin PhD, X Dai PhD, N J Kassebaum MD, H H Kyu PhD, Prof S S Lim PhD, A Misganaw PhD, A H Mokdad PhD, P Zheng PhD, Prof S I Hay FMedSci, B Sartorius PhD, Prof C J L Murray DPhil, Prof M Naghavi PhD), Department of Anesthesiology & Pain Medicine (N J Kassebaum MD, V Krishnamoorthy MD), Department of Global Health (S Kochhar MD), Division of Plastic and Reconstructive Surgery (S D Morrison MD), University of Washington, Seattle, WA, USA; Nuffield Department of Medicine (G Robles Aguilar DPhil, H van Doorn PhD, B Sartorius PhD), Centre for Tropical Medicine and Global Health (S J Dunachie PhD, S Lewycka PhD, B McManigal PhD, B Sartorius PhD), Oxford Centre for Global Health Research (C Dolecek PhD), University of Oxford, Oxford, UK; Independent Consultant, Seattle, WA, USA (F Sharara MS); University Centre Varazdin (T Mestrovic PhD), University North, Varazdin, Croatia; Faculty of Medicine (A Aali MD), E-Learning Center (M Ghasemi Nour MD), School of Medicine (A Haddadi Awal Dipl), Applied Biomedical

Research Center (A Sahebkar PhD), Biotechnology Research Center (A Sahebkar PhD), Mashhad University of Medical Sciences, Mashhad, Iran; Department of Anesthesiology (S M Abate MSc), Dilla University, Addis Ababa, Ethiopia; Non-Communicable Diseases Research Center (NCDR) (M Abbasi-Kangevari MD, S Azadnajafabad MD, M Keykhaei MD, M Rashidi MD, N Rezaei MD, Z Abbasi-Kangevari BSc, S Momtazmanesh MD), Department of Epidemiology and Biostatistics (Y Alimohamadi PhD), School of Medicine (A Fallahzadeh MD, S Momtazmanesh MD, A Nowroozi BMedSc), Students' Scientific Research Center (SSRC) (M Keykhaei MD), Children's Medical Center (F Kompani MD), Tehran Heart Center (E Mehrabi Nasab MD), Faculty of Medicine (E Mohammadi MD, E Shaker MD, P Shobeiri MD), Department of Pharmacology (N Noroozi DVM), Sina Trauma and Surgery Research Center (Prof V Rahimi-Movaghar MD), Medical School (A Sheikh MD), Department of Microbiology (E Taki PhD), Department of Pharmacognosy (A Alizadeh MSc), Tehran University of Medical Sciences, Tehran, Iran (R Heidari-Soureshjani MSc); Social Determinants of Health Research Center (Z Abbasi-Kangevari BSc, M Rashidi MD), School of Advanced Technologies in Medicine (S Ahmadi PhD), Functional Neurosurgery Research Center (E Jamshidi PharmD), Department of Neurosurgery (H Khayat Kashani MD), Chronic Respiratory Disease Research Center (M Motaghinejad PhD), School of Medicine (S Nejadghaderi MD, M Zangiabadian MD), Medical Ethics and Law Research Center (M Taheri PhD), Urology and Nephrology Research Center (M Zahir MD), Shahid Beheshti University of Medical Sciences, Tehran, Iran; Tropical Medicine Department (S Abd-Elsalam PhD), Tanta University, Tanta, Egypt; Department of Medical Anatomy (G Abebe MSc), School of Nursing (T M Ayana MSc), Department of Midwifery (F W Demisse MSc, S A A Dessalegn MSc, B T Dora MSc, B Oumer MPH, G Temesgen MSc), Department of Anatomy (S Demissie MSc), School of Public Health (N B Sidemo MPH), Arba Minch University, Arba Minch, Ethiopia; Department of Neurosurgery (A Abedi MD), Keck School of Medicine (A Abedi MD), Department of Radiology (A Gholamrezanezhad MD), Mark and Mary Stevens Neuroimaging and Informatics Institute (S Salehi MD), University of Southern California, Los Angeles, CA, USA; School of Medicine (A Abhari MD, S Bagherieh BSc), Department of Environmental Health Engineering (A Fatehizadeh PhD), Health Services Management (M Mohseni PhD), Isfahan University of Medical Sciences, Isfahan, Iran; Laboratory Technology Sciences Department (H Abidi PhD), Department of Nursing (M Zoladl PhD), Yasuj University of Medical Sciences, Yasuj, Iran; Department of Family and Community Health (R G Aboagye MPH), University of Health and Allied Sciences, Hohoe, Ghana; Department of Medical Laboratory Sciences (A Absalan PhD), Khomein University of Medical Sciences, Khomein, Iran; Department of Research and Development (A Absalan PhD), Satras Biotechnology Company, Tehran, Iran; Department of Banking and Finance (Prof H Abubaker Ali PhD), Diplomacy and Public Relations Department (A Omar Bali PhD), University of Human Development, Sulaymaniyah, Iraq; Department of Epidemiology and Population Health (Prof J M Acuna MD), Khalifa University, Abu Dhabi, United Arab Emirates; FIU Robert Stempel College of Public Health & Social Work (Prof J M Acuna MD), Department of Epidemiology (R Jebai MPH), Florida International University, Miami, FL, USA; Department of Clinical and Psychosocial Epidemiology (T D Adane MSc, T D Adane MSc), University Medical Center Groningen (Prof M J Postma PhD), School of Economics and Business (Prof M J Postma PhD), University of Groningen, Groningen, Netherlands; Centre for Social Research in Health (I Y Addo PhD), UNSW, Sydney, NSW, Australia; Quality and Systems Performance Unit (I Y Addo PhD), Cancer Institute NSW, Sydney, NSW, Australia; Public Health and Tropical Medicine (O A Adegboye PhD), James Cook University, Townsville, QL, Australia; Department of Neonatology (M Adnan MD), Indiana University Health Ball Memorial Hospital, Muncie, IN, USA; Faculty of Medicine (Q E S Adnani PhD), Universitas Padjadjaran (Padjadjaran University), Bandung, Indonesia; Department of Life Sciences (M S Afzal PhD), University of Management and Technology, Lahore, Pakistan; Department of Community Medicine (Prof S Afzal PhD), King Edward Memorial Hospital, Lahore, Pakistan; Department of Public Health (Prof S Afzal PhD), Public Health

Institute, Lahore, Pakistan; Medical Imaging Sciences Research Team (Z B Aghdam MD), Liver and Gastrointestinal Diseases Research Center (M Akbarzadeh-Khiavi DPhil), School of Nursing and Midwifery (H Hassankhani PhD), Department of Medical Surgical Nursing (M Lotfi PhD), Medical Education Research Center (M Lotfi PhD), Department of Anesthesiology and Critical Care (Prof A Mahmoodpoor MD), Midwifery Department (Prof M Mirghafourvand PhD), Department of Radiology (M Mirza-Aghazadeh-Attari MD), Tuberculosis and Lung Diseases Research Center (S Mousavi-Aghdas MD), Connective Tissue Diseases Research Center (A Safary PhD), Drug Applied Research Center (H Samadi Kafil PhD), Tabriz University of Medical Sciences, Tabriz, Iran; School of Public Health (B O Ahinkorah MPhil), University of Technology Sydney, Sydney, NSW, Australia; Department of Medical Biochemistry (A Ahmad MPhil), Department of Pharmacology (M Tabish MPharm), Shaqra University, Shaqra, Saudi Arabia; College of Nursing (A R Ahmad MPhil), International Relations & Diplomacy, Ranya, Iraq; Department of Administration (A R Ahmad MPhil), University of Raparin, Ranya, Iraq; Department of Natural Products and Alternative Medicine (R Ahmad PhD), Forensic Medicine Division (Prof R G Menezes MD), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; Department of Health and Biological Sciences (S Ahmad MPhil), Abasyn University, Peshawar, Pakistan; Faculty of Pharmacy (S Ahmad FMCPH), MAHSA University, Kuala Langat, Malaysia; School of Pharmacy (A Ahmed FMedSci), Monash University, Bandar Sunway, Malaysia; Department of Pharmacy (A Ahmed FMedSci), Quaid I Azam University Islamabad, Islamabad, Pakistan; Department of Biosciences (H Ahmed MBBS), COMSATS Institute of Information Technology, Islamabad, Pakistan; Department of Pathology and Microbiology (J Q Ahmed MDS, G A Y Yahya MSc), Department of Pharmacology (B A Zaman MSc), University of Duhok, Duhok, Iraq; Department of Computer Science and Engineering (T Ahmed Rashid MBBS), University of Kurdistan Hewler, Erbil, Iraq; Department of Food and Nutrition Policy and Planning Research (M Ajami DPhil), National Institute of Nutrition, Tehran, Iran; National Nutrition and Food Technology Research Institute (M Ajami DPhil), Shahid Beheshti University of Medical Sciences, Tehran, Iran; Faculty of Medicine and Public Health (B Aji DrPH), Jenderal Soedirman University, Purwokerto, Indonesia; Department of Public Health (C J Akunna MBBS), The Intercountry Centre for Oral Health (ICOH) for Africa, Jos, Nigeria; Department of Public Health (C J Akunna MBBS), Federal Ministry of Health, Garki, Nigeria; Geriatric and Long Term Care Department (H Al Hamad DNB, B Sathian PhD), Rumailah Hospital (H Al Hamad DNB), Hamad Medical Corporation, Doha, Qatar; Mayo Evidence-based Practice Center (F Alahdab MDS), Mayo Clinic Foundation for Medical Education and Research, Rochester, MN, USA; John T Milliken Department of Internal Medicine (Z Al-Aly MSPH), Division of Infectious Diseases (P R Ching MD), Washington University in St Louis, St Louis, MO, USA; Clinical Epidemiology Center (Z Al-Aly MSPH), US Department of Veterans Affairs, St Louis, MO, USA; Department of Pharmacy (M A Aldeyab DPhil), University of Huddersfield, Huddersfield, UK; Department of Preventive Medicine (A V Aleman MBBS), University of the Republic, Montevideo, Uruguay; Faculty of Nursing (F A N Alhalaq DM, Prof A M Batiha PhD), Philadelphia University, Amman, Jordan; Psychological Sciences Association, Amman, Jordan (F A N Alhalaq DM); Institute of Health Research (R K Alhassan MPharm, M Immurana PhD), University of Health and Allied Sciences, Ho, Ghana; Erbil Technical Health College (B A Ali MBBS), Erbil Polytechnic University, Erbil, Iraq; School of Pharmacy (B A Ali MBBS), Tishk International University, Erbil, Iraq; Department of Biological Sciences (L Ali PhD, S Naz PhD), National University of Medical Sciences (NUMS), Rawalpindi, Pakistan; Centre for Biotechnology and Microbiology (S S Ali PhD, M Suleman PhD), University of Swat, Pakistan, Swat, Pakistan; Pars Advanced and Minimally Invasive Medical Manners Research Center (Y Alimohamadi PhD), Health Management and Economics Research Center (V Alipour PhD, J Arabloo PhD, A Rezapour PhD), Department of Health Economics (V Alipour PhD), School of Medicine (M Dodangh MD), Department of Medical Laboratory Sciences (F Dorostkar PhD), Preventive Medicine and Public Health Research Center (B Eshtrati PhD), Department of Health Services Management (H Mousavi Isfahani PhD), Department of Physiology (H Pazoki Toroudi PhD), Physiology Research Center (H Pazoki Toroudi PhD), Minimally Invasive Surgery Research Center (S Salahi MD), Trauma and Injury Research Center (M Taheri PhD), Iran University of Medical Sciences, Tehran, Iran (M Moradi MD); Department of Health Policy and Management (Prof S M Aljunid PhD), Kuwait University, Kuwait City, Kuwait; International Centre for Casemix and Clinical Coding (Prof S M Aljunid PhD), National University of Malaysia, Bandar Tun Razak, Malaysia; Department of Disease Control (K Allel MSc), Department of Clinical Research (S Bhattarai MD), London School of Hygiene & Tropical Medicine, London, UK; Institute for Global Health (K Allel MSc), Department of Infection (Prof A Zumla PhD), University College London, London, UK; College of Medicine (S Almustanyir MD), Alfaisal University, Riyadh, Saudi Arabia; Ministry of Health, Riyadh, Saudi Arabia (S Almustanyir MD); School of Graduate Studies (E K Ameyaw MPhil), Lingnan University, Hong Kong Special Administrative Region, China; School of Medicine and Public Health (A L Amit BS), Center for Research and Innovation (V F Pepito MSc), Ateneo De Manila University, Pasig City, Philippines; Department of Pathology and Lab Medicine (N Anandavelane MD), Department of Community Medicine and Family Medicine (P Baskaran MD, P Bhardwaj MD, Prof P R Raghav MD, H Viswanathan MBBS), School of Public Health (P Bhardwaj MD), Department of Pharmacology (J Charan MD, S Singh DM), Department of Surgical Oncology (Prof S Misra MCh), All India Institute of Medical Sciences, Jodhpur, India; Faculty of Pharmacy (Prof R Ancuceanu PhD), Cardiology Department (C Andrei PhD), Internal Medicine Department (M Hostiu PhD), Department of Legal Medicine and Bioethics (S Hostiu PhD), Department of Dermatology (C N Matei PhD), Department of General Surgery (I Negoi PhD, B Socea PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; Department of Statistics and Econometrics (Prof T Andrei PhD, Prof M Ausloos PhD, Prof C Herteliu PhD, I Petcu PhD), Bucharest University of Economic Studies, Bucharest, Romania; Department of Clinical Microbiology (D Anggraini MD), Universitas Riau, Pekanbaru, Indonesia; Microbiology Laboratory (D Anggraini MD), Arifin Achmad Hospital, Pekanbaru, Indonesia; School of Nursing and Midwifery (A Ansar PhD, M Rahman PhD), The Judith Lumley Centre (B Ayala Quintanilla PhD), La Trobe University, Melbourne, VIC, Australia; Special Interest Group International Health (A Ansar PhD), Public Health Association of Australia, Canberra, ACT, Australia; School of Dentistry and Medical Sciences (A E Anyasodor PhD), Charles Sturt University, Orange, NSW, Australia; College of Art and Science (D Areda PhD), Ottawa University, Surprise, AZ, USA; College of Liberal Arts and Sciences (D Areda PhD), Arizona State University, Tempe, AZ, USA; Public Health and Healthcare Management (T Aripov PhD), Tashkent Institute of Postgraduate Medical Education, Tashkent, Uzbekistan; Boston Children's Hospital, Boston, MA, USA (T Aripov PhD); Department of Biophysics (A A Artamonov PhD), Russian Academy of Sciences, Moscow, Russia; Department of Maternal and Child Health (J Arulappan DSc), Sultan Qaboos University, Muscat, Oman; Molecular and Cell Biology (R T Aruleba MSc), University of Cape Town, Cape Town, South Africa; Department of Community Medicine and Global Health (M Asaduzzaman MPH), University of Oslo, Oslo, Norway; University Institute of Radiological Sciences and Medical Imaging Technology (T Ashraf MS), University Institute of Public Health (A Hanif PhD), The University of Lahore, Lahore, Pakistan; Department of Immunology (S Athari PhD), Zanjan University of Medical Sciences, Zanjan, Iran; Department of Biomedical Science (D Atlaw MSc), Department of Anatomy (D D Solomon MSc), Madda Walabu University, Bale Robe, Ethiopia; Department of Oral and Maxillofacial Surgery (S Attia MSc), Justus Liebig University of Giessen, Giessen, Germany; School of Business (Prof M Ausloos PhD), University of Leicester, Leicester, UK; Department of Medical Laboratory Sciences (T Awoke MSc, A Melese MSc), Department of Epidemiology and Biostatistics (G T Wassie MPH), Bahir Dar University, Bahir Dar, Ethiopia; San Martin de Porres University, Lima, Peru (B Ayala Quintanilla PhD); School of Medicine (A Azari Jafari MD, S Mirmoenei MD), Shahroud University of Medical Sciences, Shahroud, Iran; Department of Forensic Medicine and Toxicology (H L Dsouza MD,

J Padubidri MD), Kasturba Medical College of Mangalore (D B B MD), Centre for Bio Cultural Studies (CBiCS) (P Hoogar PhD), Manipal Academy of Higher Education, Manipal, India (J Padubidri MD); Gomal Center of Biochemistry and Biotechnology (M Badar PhD), Gomal University, Dera Ismail Khan, Pakistan; Department of Forensic Science (A D Badiye PhD, N Kapoor PhD), Government Institute of Forensic Science, Nagpur, India; Department of Nursing (N Baghcheghi PhD), Saveh University of Medical Sciences, Saveh, Iran; Unit of Biochemistry (A A Baig PhD), Universiti Sultan Zainal Abidin (Sultan Zainal Abidin University), Kuala Terengganu, Malaysia; Department of Pharmacology (I Banerjee MD), Sir Seewoosagur Ramgoolam Medical College, Belle Rive, Mauritius; Clinic for Infectious and Tropical Diseases (A Barac PhD), Clinical Center of Serbia, Belgrade, Serbia; Faculty of Medicine (A Barac PhD, I M Ilic PhD), Institute of Microbiology and Immunology (E Dubljanin PhD), University of Belgrade, Belgrade, Serbia; Molecular Microbiology and Bacteriology (M Bardhan MD), National Institute of Cholera and Enteric Diseases, Kolkata, India; Department of Molecular Microbiology (M Bardhan MD), Department of Biostatistics (V K Kamal PhD), India Cancer Research Consortium (Prof R Mehrotra DPhil), Indian Council of Medical Research, New Delhi, India; Department of Translational Medicine (F Barone-Adesi PhD), University of Eastern Piedmont, Novara, Italy; Clinical Sciences Department (H J Barqawi MPhil, Prof R Halwani PhD), College of Medicine (Prof R Halwani PhD), Mass Communication Department (A Makki PhD), Sharjah Institute for Medical Research (B Sadiq PhD), University of Sharjah, Sharjah, United Arab Emirates; Department of Public & Environmental Health (A Barrow MPH), University of The Gambia, Brikama, The Gambia; Epidemiology and Disease Control Unit (A Barrow MPH), Ministry of Health, Kotu, The Gambia; Department of Academics (S Basu MD), Indian Institute of Public Health, Gurgaon, India; School of Public Health (Prof N Bedi MD), Dr D Y Patil University, Mumbai, India; Epidemiology Department (M Khan MD), Substance Abuse and Toxicology Research Center (S Mohan PhD), Jazan University, Jazan, Saudi Arabia (Prof N Bedi MD); Medical Laboratory Science (M A Belete MSc), Department of Environmental Health (M Gebrehiwot DSc), Wollo University, Dessie, Ethiopia; Department of Oral Pathology and Microbiology (U I Belgauami MD, V Kadashetti MDS), Public Health Dentistry Department (Prof K M Shivakumar PhD), Krishna Institute of Medical Sciences Deemed To Be University, Karad, India; Department of Physiology (B Bhandari MD), Government Institute of Medical Sciences, Greater Noida, India; School of Public Health (D Bhandari PhD), University of Adelaide, Adelaide, SA, Australia; Public Health Research Laboratory (D Bhandari PhD), Central Department of Public Health (R Paudel MPH), Faculty of Humanities and Social Sciences (U Paudel PhD), Tribhuvan University, Kathmandu, Nepal; Global Health Neurology Lab (S Bhaskar PhD), NSW Brain Clot Bank, Sydney, NSW, Australia; Department of Neurology and Neurophysiology (S Bhaskar PhD), South West Sydney Local Health District and Liverpool Hospital, Sydney, NSW, Australia; Department of Statistical and Computational Genomics (K Bhattacharyya MSc), National Institute of Biomedical Genomics, Kalyani, India; Department of Statistics (K Bhattacharyya MSc), University of Calcutta, Kolkata, India; School of Tropical Medicine and Global Health (S Bhattarai MD), Nagasaki University, Nagasaki, Japan; Department of Biostatistics and Epidemiology (Prof S Bitaraf PhD), Department of Pediatric Neurology (S Sadeghian MD), Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; Department of Woman and Child Health and Public Health (D Buonsenso MD), Fondazione Policlinico Universitario Agostino Gemelli IRCCS (Agostino Gemelli University Polyclinic IRCCS), Roma, Italy; Global Health Research Institute (D Buonsenso MD), Università Cattolica del Sacro Cuore (Catholic University of Sacred Heart), Roma, Italy; School of Public Health and Health Systems (Z A Butt PhD), University of Waterloo, Waterloo, ON, Canada; Al Shifa School of Public Health (Z A Butt PhD), Al Shifa Trust Eye Hospital, Rawalpindi, Pakistan; Institute of Microengineering (F Caetano dos Santos PhD), Federal Polytechnic School of Lausanne, Lausanne, Switzerland; Institute for Health and Environment (J Cai MSc, W Liu PhD), Chongqing University, Chongqing, China; Department of Clinical Pharmacy (Prof D Calina PhD), University of Medicine and Pharmacy of Craiova, Romania, Craiova, Romania; Department of Pediatrics (Prof P Camargos PhD), Department of Maternal and Child Nursing and Public Health (Prof A C Micheletti Gomide Nogueira de Sá MSc), Departamento de Clínica Médica (A T Nogueira de Sá MSc), Federal University of Minas Gerais, Belo Horizonte, Brazil; Internal Medicine Department (Prof L A Cámara MD), Hospital Italiano de Buenos Aires (Italian Hospital of Buenos Aires), Buenos Aires, Argentina; Argentine Society of Medicine, Buenos Aires, Argentina (Prof L A Cámara MD, Prof P R Valdez MEd); Department of Health Care (Prof R Cárdenas DSc), Metropolitan Autonomous University, Mexico City, Mexico; Infection and Global Health Research (M Cevik MD), Population and Behavioural Sciences Division (A F Fagbamigbe PhD), University of St Andrews, St Andrews, UK; Regional Infectious Diseases Unit (M Cevik MD), NHS National Services Scotland, Edinburgh, UK; ICMR School of Public Health (J Chadwick MD), Division of Epidemiology and Biostatistics (V K Kamal PhD), National Institute of Epidemiology, Chennai, India; Department of Oral Medicine and Radiology (A Chaurasia MD), King George's Medical University, Lucknow, India; Department of Community Medicine (Prof S G Choudhary MD, Prof A M Gaidhane MD), Datta Meghe Institute of Medical Sciences, Wardha, India; School of Public Health (E K Chowdhury PhD), Curtin University, Perth, WA, Australia; Department of Epidemiology and Preventive Medicine (E K Chowdhury PhD, Prof Y Guo PhD), School of Public Health and Preventive Medicine (S Li PhD), Department of Infectious Diseases (M J Loftus MBBS), Department of Medicine (S Zaman MSc), Monash University, Melbourne, VIC, Australia; Department of Internal Medicine (F R Chowdhury PhD), Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; Center for Biomedicine and Community Health (D Chu PhD), VNU-International School, Hanoi, Viet Nam; Department of Surgery (I S Chukwu BMedSc), Federal Medical Centre, Umuahia, Nigeria; Section Global Health and Rehabilitation (O Dadrás DrPH), Western Norway University of Applied Sciences, Bergen, Norway; Department of Global Public Health and Primary Care (O Dadrás DrPH), Center for International Health (CIH) (S Hassan Mphil), Bergen Center for Ethics and Priority Setting (BCEPS) (S Hassan Mphil), University of Bergen, Bergen, Norway; Department of Public Health (F T Dagnaw MPH), Department of Midwifery (B G Kassa MSc), Debre Tabor University, Debre Tabor, Ethiopia; Department of Biochemistry (S Das MD), Ministry of Health and Welfare, New Delhi, India; 2nd University Ophthalmology Department (A Dastiridou MD), Aristotle University of Thessaloniki, Thessaloniki, Greece; Ophthalmology Department (A Dastiridou MD), Medical School (F Multa PhD), University of Thessaly, Larissa, Greece; School of Public Health (S Debelá MPH), Salale University, Fiche, Ethiopia; Department of Biomedical Sciences (D Dereje MSc), Jimma University, Jimma, Ethiopia; Department of Nursing (M Derese MSc), Mizan-Tepi University, Mizan-Aman, Ethiopia; Graduate Medical Education (H D Desai MD), Gujarat Adani Institute of Medical Sciences, Bhuj, India; Department of Public Health (F N Dessalegn MPH), Madda Walabu University, Bale Goba, Ethiopia; Department of Public Health (B Desye MSc), Adigrat University, Adigrat, Ethiopia; Department of Internal Medicine (K Dhaduk MD), Geisinger Health System, Wilkes Barre, PA, USA; Health Research Section (M Dhimal PhD), Research Section (U Paudel PhD), Research Department – Infectious Diseases (N Pokhrel MD), Nepal Health Research Council, Kathmandu, Nepal; Department of Pharmacy Practice (S Dhingra PhD), National Institute of Pharmaceutical Education and Research, Hajipur, India; Department of Environmental Health (N Diao DSc), Department of Health Policy and Oral Epidemiology (Z S Natto DrPH), Harvard University, Boston, MA, USA; Center of Complexity Sciences (Prof D Diaz PhD), National Autonomous University of Mexico, Mexico City, Mexico; Faculty of Veterinary Medicine and Zootechnics (Prof D Diaz PhD), Autonomous University of Sinaloa, Culiacán Rosales, Mexico; Development of Research and Technology Center (S Djalalinia PhD), Ministry of Health and Medical Education, Tehran, Iran; Health Science Center (D Dongarwar MS), University of Texas, Houston, TX, USA; Department of Forensic Medicine and Toxicology (H L Dsouza MD, P H Shetty MD), Department of Community Medicine (N Joseph MD), Manipal Academy of Higher Education, Mangalore, India; Mahidol-Oxford Tropical Medicine Research Unit, Bangkok, Thailand (S J Dunachie PhD);

Department of Infection and Tropical Medicine (O C Durojaiye MPH), University of Sheffield, Sheffield, UK; School of Health Sciences (H A Edinur PhD), Universiti Sains Malaysia (University of Science Malaysia), Kubang Kerian, Malaysia; Department of Maternal and Neonatal Nursing (H B Ejigu MSc), Department of Health Informatics (D B Enyew MSc), Department of Epidemiology and Biostatistics (G A Mamo MPH), Department of Public Health and Health Policy (B N Tefera MPH), Haramaya University, Harar, Ethiopia; Department of Epidemiology and Medical Statistics (M Ekholuenetale MSc, A F Fagbamigbe PhD), Faculty of Public Health (M Ekholuenetale MSc), Department of Health Promotion and Education (S E Ibitoye MPH), Department of Community Medicine (O S Ilesanmi PhD), College of Medicine (A P Okeunle PhD), University of Ibadan, Ibadan, Nigeria; Department of Biological Sciences (T C Ekundayo PhD), University of Medical Sciences, Ondo, Nigeria; Direction de L'épidémiologie et la Lutte Contre les Maladies (Directorate of Epidemiology and Diseases Control) (H El-Abid PhD), Ministry of Health, Rabat, Morocco; Faculty of Medicine (M Elhadi MD), University of Tripoli, Tripoli, Libya; Egypt Center for Research and Regenerative Medicine (ECRRM), Cairo, Egypt (M A Elmonem PhD); Burn and Wound Healing Research Center (A Emami PhD, F Javanmardi MSc), Research Center for Health Sciences, Institute of Health (P Habibzadeh MD), Department of Medical Mycology and Parasitology (H Nouraei MSc, Prof K Pakshir PhD), Shiraz University of Medical Sciences, Shiraz, Iran; Lincoln International Institute for Rural Health (L Engelbert Bain PhD), University of Lincoln, Lincoln, UK; Department of International Cyber Education (R Erkhembayar MD), Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; Internal Medicine Department (F Etaee MD), Department of Genetics (S Pawar PhD), School of the Environment (Y Song PhD), Yale University, New Haven, CT, USA; Zoonotic Disease Research Center (S Falahi PhD), Ilam University of Medical Sciences, Ilam, Iran; Endocrinology and Metabolism Population Sciences Institute (A Fallahzadeh MD, A Sheikhy MD), Department of Epidemiology (S Nejadghaderi MD, E Shaker MD), Department of International Studies (P Shobeiri MD), Non-Communicable Diseases Research Center (NCDRC), Tehran, Iran (E Mohammadi MD); Department of Health Policy and Administration (E A Faraon MD), University of the Philippines Manila, Manila, Philippines; School of Pharmacy (G Fekadu MSc), Jockey Club School of Public Health and Primary Care (J Huang MD, C Zhong MD), The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China; Department of Pharmacy (G Fekadu MSc), Department of Nursing (G Fetensa MSc), Institute of Health Science, Department of Midwifery (M Regasa MSc), Wollega University, Nekemte, Ethiopia; Center for Biotechnology and Fine Chemistry (J C Fernandes PhD), Catholic University of Portugal, Porto, Portugal; Department of Health Sciences (DISSAL) (A Ferrari MD), University of Genoa, Genoa, Italy; Psychiatry Department (I Filip MD), Kaiser Permanente, Fontana, CA, USA; School of Health Sciences (I Filip MD), A T Still University, Mesa, AZ, USA; Institute of Public Health (F Fischer PhD), Charité Universitätsmedizin Berlin (Charité Medical University Berlin), Berlin, Germany; Department of Medical Parasitology (M Foroutan PhD), Faculty of Medicine (M Foroutan PhD), Abadan University of Medical Sciences, Abadan, Iran; Health Services Management Training Centre (P A Gaal PhD, T Joo PhD, J Lám PhD, T Palicz MD), Faculty of Health and Public Administration (M Szócska PhD), Semmelweis University, Budapest, Hungary; Department of Applied Social Sciences (P A Gaal PhD), Sapientia Hungarian University of Transylvania, Târgu-Mureş, Romania; Community Medicine Department (M A Gadanya FMCPH), Bayero University, Kano, Kano, Nigeria; Department of Community Medicine (M A Gadanya FMCPH), Aminu Kano Teaching Hospital, Kano, Nigeria; School of Global Health (B Ganesan PhD), Institute of Health & Management, Melbourne, VIC, Australia; Department of Occupational Therapy (B Ganesan PhD), Mahatma Gandhi Occupational Therapy College, Jaipur, India; Department of Environmental Health Engineering (R Ghanbari PhD), School of Public Health (A Ghashghaee BSc), Institute for Prevention of Non-communicable Diseases (R Kalhor PhD), Health Services Management Department (R Kalhor PhD), Department of Food Hygiene and Safety (Prof R Mahmoudi PhD), Social Determinants of Health Research Center (S Rafiei PhD), Qazvin University of Medical Sciences, Qazvin, Iran; Torbat Heydariyeh University of Medical Sciences, Torbat, Iran (A Gholizadeh PhD); Department of Health Systems and Policy Research (M Golechha PhD), Indian Institute of Public Health, Gandhinagar, India; Department of Genetics (P Goleij MSc), Sana Institute of Higher Education, Sari, Iran; Department of Biomedical and Neuromotor Sciences (D Golinelli MD, J Lenzi PhD, F Sanmarchi MD), University of Bologna, Bologna, Italy; Tuberculosis Biomarker Research Unit (A Goodridge PhD), Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (Institute for Scientific Research and High Technology Services), City of Knowledge, Panama; Department of Community Medicine (D A Gunawardane MD), University of Peradeniya, Kandy, Sri Lanka; Department of Epidemiology (Prof Y Guo PhD), Binzhou Medical University, Yantai City, China; Department of Epidemiology and Biostatistics (R Gupta MPH), University of South Carolina, Columbia, SC, USA; Centre for Noncommunicable Diseases and Nutrition (R Gupta MPH), BRAC University, Dhaka, Bangladesh; Toxicology Department (S Gupta MSc), Shriram Institute for Industrial Research, Delhi, Delhi, India; School of Medicine (V Gupta PhD), Deakin University, Geelong, VIC, Australia; Faculty of Medicine Health and Human Sciences (Prof V K Gupta PhD), School of Engineering (N Rabiee PhD), Macquarie University, Sydney, NSW, Australia; Department of Midwifery (A Guta MSc), Dire Dawa University, Dire Dawa, Ethiopia; Department of Biochemistry and Molecular Biology (Prof M Hannan PhD), Bangladesh Agricultural University, Mymensingh, Bangladesh; Department of Anatomy (Prof M Hannan PhD), Dongguk University, Gyeongju, South Korea; Medical Research Unit (H Harapan PhD), Universitas Syiah Kuala (Syiah Kuala University), Banda Aceh, Indonesia; Independent Consultant, Tabriz, Iran (H Hassankhani PhD); Institute of Pharmaceutical Sciences (K Hayat MS), University of Veterinary and Animal Sciences, Lahore, Pakistan; Department of Pharmacy Administration and Clinical Pharmacy (K Hayat MS), Xian Jiaotong University, Xian, China; Research Unit of Population Health (B Heibati PhD), University of Oulu, Oulu, Finland; Independent Consultant, Santa Clara, CA, USA (G Heidari MD); Community-Oriented Nursing Midwifery Research Center (M Heidari PhD), Department of Epidemiology and Biostatistics (A Mohammadian-Hafshejani PhD), Department of Health in Disasters and Emergencies (R Sheikh BHLthSci), Shahrekord University of Medical Sciences, Shahrekord, Iran; School of Business (Prof C Herteliu PhD), London South Bank University, London, UK; Department of Public Health (D Z Heyi MPH), Madda Walabu University, Robe, Ethiopia; Department of Applied Microbiology (K Hezam PhD), Taiz University, Taiz, Yemen; Department of Microbiology (K Hezam PhD), Nankai University, Tianjin, China; Department of Pulmonology (N Horita PhD), Yokohama City University, Yokohama, Japan; National Human Genome Research Institute (NHGRI) (N Horita PhD), National Institutes of Health, Bethesda, MD, USA; Department of Social and Environmental Health Research (M Hossain MPH), Nature Study Society of Bangladesh, Khulna, Bangladesh; Department of Health Promotion and Community Health Sciences (M Hossain MPH), Texas A&M University, College Station, TX, USA; Pattern Recognition and Machine Learning Lab (M Hosseinzadeh PhD, Prof S Lee PhD), Gachon University, Seongnam, South Korea; Clinical Legal Medicine Department (S Hostiuic PhD), National Institute of Legal Medicine Mina Minovici, Bucharest, Romania; Burn Research Center (S Hoveidamanesh MD), Shahid Motahari Hospital, Tehran, Iran; Czech National Centre for Evidence-Based Healthcare and Knowledge Translation (S Hussain PhD), Institute of Biostatistics and Analyses (S Hussain PhD), Department of Public Health (A Riad DDS), Czech National Centre for Evidence-based Healthcare and Knowledge Translation (A Riad DDS), Masaryk University, Brno, Czech Republic; Department of Biomolecular Sciences (N R Hussein PhD), University of Zakho, Zakho, Iraq; Department of Community Medicine (O S Ilesanmi PhD), University College Hospital, Ibadan, Ibadan, Nigeria; Department of Epidemiology (Prof M D Ilic PhD), University of Kragujevac, Kragujevac, Serbia; College of Pharmacy (M Imam PhD), Prince Sattam Bin Abdulaziz University, Al Kharj, Saudi Arabia; Division of Community Health and Family Medicine (L R Inbaraj MD), Bangalore Baptist Hospital,

Bangalore, India; Department of Medicine (A Iradukunda MD), University of Burundi, Burundi; ARNECH Research and Consulting Office, Bujumbura, Burundi (A Iradukunda MD); Department of Clinical Pharmacy (Prof N Ismail PhD), MAHSA University, Bandar Saujana Putra, Malaysia; School of Health Systems and Public Health (C C D Iwu MPH), Department of Medical Microbiology (M A Reta MSc), University of Pretoria, Pretoria, South Africa; South African Medical Research Council, Cape Town, South Africa (C J Iwu PhD); Department of Global Health (C J Iwu PhD, P D Katoto PhD), Stellenbosch University, Cape Town, South Africa; Department of Orthodontics & Dentofacial Orthopedics (L J BDS), Dr D Y Patil University, Pune, India; Institute of Advanced Manufacturing Technologies (Prof M Jakovljevic PhD), Peter the Great St Petersburg Polytechnic University, St Petersburg, Russia; Institute of Comparative Economic Studies (Prof M Jakovljevic PhD), Hosei University, Tokyo, Japan; Division of Pulmonary Medicine (E Jamshidi PharmD), Lausanne University Hospital (CHUV), Lausanne, Switzerland; Health Informatics Lab (T Javaheri PhD), Department of Computer Science (R Rawassizadeh PhD), Boston University, Boston, MA, USA; Department of Medical Mycology (J Javidnia PhD), Department of Neurology (A Sharifi-Razavi MD), Medical-Surgical Nursing (S Shorofi PhD), Mazandaran University of Medical Sciences, Sari, Iran; Centre of Studies and Research (S Jayapal PhD), Ministry of Health, Muscat, Oman; Postgraduate Institute of Medicine (U Jayarajah MD), University of Colombo, Colombo, Sri Lanka; Department of Surgery (U Jayarajah MD), National Hospital, Colombo, Sri Lanka; Department of Community Medicine (R P Jha MSc), Dr Baba Saheb Ambedkar Medical College & Hospital, Delhi, India; Department of Community Medicine (R P Jha MSc), Banaras Hindu University, Varanasi, India; Hungarian Health Management Association, Budapest, Hungary (T Joo PhD, T Palicz MD); Gastrointestinal and Liver Diseases Research Center (F Joukar PhD), Caspian Digestive Disease Research Center (F Joukar PhD), Department of Medical-Surgical Nursing (S Karkhah MSc), Guilan University of Medical Sciences, Rasht, Iran; Department of Family Medicine and Public Health (J J Jozwiak PhD), University of Opole, Opole, Poland; Department of Medicine (S Kacimi MD), Faculty of Medicine, University of Tlemcen, Tlemcen, Algeria; Social Determinants of Health Research Center (L R Kalankesh PhD), Department of Anatomy (J Majidpoor PhD), Gonabad University of Medical Sciences, Gonabad, Iran; Save Sight Institute (H Kandel PhD), University of Sydney, Sydney, NSW, Australia; Sydney Eye Hospital (H Kandel PhD), South Eastern Sydney Local Health District, Sydney, NSW, Australia; Centre for Tropical Diseases and Global Health (P D Katoto PhD), Catholic University of Bukavu, Bukavu, Democratic Republic of the Congo; Amity Institute of Forensic Sciences (H Khajuria PhD, B P Nayak PhD), Amity University, Noida, India; Department of Bioinformatics and Biostatistics (A Khan PhD), Shanghai Jiao Tong University, Shanghai, China; Department of Pediatrics (I A Khan MD), Rutgers University, New Brunswick, NJ, USA; Department of Population Science (M Khan PhD), Jatiya Kabi Kazi Nazrul Islam University, Mymensingh, Bangladesh; Family Medicine Department (M A Khan MSc), United Arab Emirates University, Al Ain, United Arab Emirates; Primary Care Department (M A Khan MSc), NHS North West London, London, UK; Department of Basic Medical Sciences (M M Khatatbeh PhD), Yarmouk University, Irbid, Jordan; Department of Medical Parasitology (M M Khatatbeh PhD), Cairo University, Cairo, Egypt; Department of Public Health (Prof J Khubchandani PhD), New Mexico State University, Las Cruces, NM, USA; College of Medicine (H Kim BN), Ewha Womans University, Seoul, South Korea; Department of Genomics and Digital Health (M Kim MD), Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Seoul, South Korea; Public Health Center (M Kim MD), Ministry of Health and Welfare, Wando, South Korea; Department of Nutrition (R W Kimokoti MD), Simmons University, Boston, MA, USA; Department of Pediatrics (Prof N Kissoon MD), University of British Columbia, Vancouver, BC, Canada; Global Healthcare Consulting, New Delhi, India (S Kochhar MD); 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; Kasturba Medical College, Udupi, India (S Koulmane Laxminarayana MD); Instituto de Medicina Tropical Alexander von Humboldt (F Krapp Lopez MD), Alexander von Humboldt Institute of Tropical Medicine (J L Paredes MD), Cayetano Heredia University, Lima, Peru; Doctoral School of Biomedical Sciences (F Krapp Lopez MD), Katholieke Universiteit Leuven, Leuven, Belgium; Department of Anthropology (Prof K Krishan PhD), Panjab University, Chandigarh, India; Department of Anesthesiology (V Krishnamoorthy MD), Duke University, Durham, NC, USA; Department of Medicine (V Kulkarni MS), Queensland Health, Brisbane, QL, Australia; Amity Institute of Biotechnology (N Kumar PhD, E Upadhyay PhD), Amity University Rajasthan, Jaipur, India; Faculty of Health and Life Sciences (O P Kurmi PhD), Coventry University, Coventry, UK; Department of Medicine (O P Kurmi PhD), Department of Psychiatry and Behavioural Neurosciences (A T Olagunju MD), McMaster University, Hamilton, ON, Canada; Department of Nephrology (A Kuttikkattu MD), Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, India; Public Health Foundation of India, Gurugram, India (D K Lal MD); NEVES Society for Patient Safety, Budapest, Hungary (J Lám PhD); Unit of Genetics and Public Health (Prof I Landires MD), Unit of Microbiology and Public Health (V Nuñez-Samudio PhD), Institute of Medical Sciences, Las Tablas, Panama; Department of Public Health (V Nuñez-Samudio PhD), Ministry of Health, Herrera, Panama (Prof I Landires MD); Department of Otorhinolaryngology (S Lasrado MS), Father Muller Medical College, Mangalore, India; Oxford University Clinical Research Unit (S Lewycka PhD), Wellcome Trust Asia Programme, Hanoi, Viet Nam; Department of Paediatrics (Prof R Lodha MD), All India Institute of Medical Sciences, New Delhi, India; Department of Infectious Diseases (M J Loftus MBBS), Alfred Health, Melbourne, VIC, Australia; Department of Public Health (A Lohiya MD), Kalyan Singh Super Specialty Cancer Institute, Lucknow, India; Department of Health Economics (L Lorenzovici MSc), Syreon Research Romania, Targu Mures, Romania; Department of Doctoral Studies (L Lorenzovici MSc), George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Tirgu Mures, Romania; Department of Clinical and Hospital Pharmacy (M A Mahmoud PhD), Taibah University, Al-Madinah Al-Munawwarah, Saudi Arabia; Department of Primary Care and Public Health (Prof A Majeed MD, Prof S Rawaf MD), Imperial College London, London, UK; Heart and Vascular Institute (Y Manla MD), Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates; Department of Nutrition and Dietetics (M Martorell PhD), Centre for Healthy Living (M Martorell PhD), University of Concepción, Concepción, Chile; Association of Resident Physicians, Bucharest, Romania (C N Matei PhD); Civil Engineering Faculty (Prof O Mendoza-Cano PhD), University of Colima, Coquimatlán City, Mexico; Department of International Dx (A A Mentis MD), BGI Genomics, Shenzhen, China; Anaesthesiology Department (G Micha PhD), "Helena Venizelou" General and Maternity Hospital, Athens, Greece; Polish National Cancer Registry (I Michalek PhD), Department of Pathology (I Michalek PhD), Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; Institute for Social Innovation, Skopje, Macedonia (N Milevska Kostova PhD); Department of Health Policy and Management (N Milevska Kostova PhD), Centre for Regional Policy Research and Cooperation 'Studiorum', Skopje, Macedonia; College of Applied Medical Sciences (S A Mir PhD), Majmaah University, Riyadh, Saudi Arabia; Internal Medicine Programme (Prof E M Mirrakhimov PhD), Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan; Department of Atherosclerosis and Coronary Heart Disease (Prof E M Mirrakhimov PhD), National Center of Cardiology and Internal Disease, Bishkek, Kyrgyzstan; Social Determinants of Health Center (M Mirza-Aghazadeh-Attari MD), Urmia University of Medical Science, Urmia, Iran; Medical Laboratory Sciences (A S Misganaw MSc), Department of Microbial Cellular and Molecular Biology (A S Misganaw MSc), Addis Ababa University, Addis Ababa, Ethiopia; National Data Management Center for Health (A Misganaw PhD), Ethiopian Public Health Institute, Addis Ababa, Ethiopia; Department of Information Technology (M Mohammadi PhD), Lebanese French University, Erbil, Iraq; Health Systems and Policy Research Unit (S Mohammed PhD), Ahmadu Bello University, Zaria, Nigeria; Department of Health Care Management (S Mohammed PhD),



Technical University of Berlin, Berlin, Germany; Center for Transdisciplinary Research (S Mohan PhD), Saveetha Institute of Medical and Technical Science, Chennai, India; Health Services Management (M Mohseni PhD), Iran University of Medical Sciences, Tehran, Iran; Clinical Epidemiology and Public Health Research Unit (L Monasta DSc), Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy; Centre for Neonatal and Paediatric Infection (C E Moore PhD), St George's University of London, London, UK; Department of Clinical Biochemistry (M Moradi Sarabi PhD), Department of Allied Medical Sciences (M Moradi Sarabi PhD), Lorestan University of Medical Sciences, Khorramabad, Iran; Department of Fruit and Vegetable Product Technology (Prof A Mousavi Khaneghah PhD), Prof Waclaw Dąbrowski Institute of Agricultural and Food Biotechnology State Research Institute, Warsaw, Poland; Department of Epidemiology and Biostatistics (S Mubarak MS), School of Medicine (Z Zhang PhD), Wuhan University, Wuhan, China; Department of Surgery (F Mulita PhD, G Verras MD), General University Hospital of Patras, Patras, Greece; Department of Pediatrics and Child Health (G B B Mulu MSc), Debre Berhan University, Debre Berhan, Ethiopia; Scientific Communications Department (S B Munro PhD), Invitae, Boulder, CO, USA; Department of Medical Microbiology and Immunology (S Muthupandian PhD), Mekelle University, Mekelle, Ethiopia; Saveetha Dental College (S Muthupandian PhD), Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, India; Health Workforce Department (T S Nair MD), World Health Organisation, Geneva, Switzerland; School of Pharmacy (A Naqvi PhD), University of Reading, Reading, UK; Department of Forensic Medicine & Toxicology (H Narang MBBS), Muzaffarnagar Medical College, Muzaffarnagar, India; Department of Forensic Medicine & Toxicology (H Narang MBBS), All India Institute of Medical Sciences, Patna, India; Department of Dental Public Health (Z S Natto DrPH), King Abdulaziz University, Jeddah, Saudi Arabia; Department of Biotechnology (M Naveed PhD), University of Central Punjab, Lahore, Pakistan; Department of General Surgery (I Negoi PhD), Emergency Hospital of Bucharest, Bucharest, Romania; Estia Health Blakehurst (S Neupane Kandel BSN), Estia Health, Sydney, NSW, Australia; Department of Public Health and Community Medicine (C Ngwa MSc), University of Gothenburg, Gothenburg, Sweden; International Islamic University Islamabad, Islamabad, Pakistan (R K Niazi PhD); School of Nursing (J Nutor PhD), Department of Bioengineering and Therapeutic Sciences (Prof M S Zastrozhin PhD), University of California San Francisco, San Francisco, CA, USA; Center of Excellence in Reproductive Health Innovation (CERHI) (C I Nzopotam MPH), University of Benin, Benin City, Nigeria; Department of Physiology (O J Nzopotam PhD), University of Benin, Edo, Nigeria; Department of Physiology (O J Nzopotam PhD), Benson Idahosa University, Benin City, Nigeria; Administrative and Economic Sciences Department (Prof B Oancea PhD), University of Bucharest, Bucharest, Romania; Center for Surveillance, Immunization, and Epidemiologic Research (R M Obaidur PhD), National Institute of Infectious Diseases, Tokyo, Japan (M Shigematsu PhD); Global Health Nursing (R M Obaidur PhD), St Luke's International University, Tokyo, Japan; Department of Biochemistry (V A Ojha MD), ESIC Medical College and Hospital, Bihta, Patna, India; Department of Biochemistry (V A Ojha MD, Prof A Prashant PhD), Jagadguru Sri Shivarathreeswara University, Mysuru, India; Department of Food and Nutrition (A P Okekunle PhD), Seoul National University, Seoul, South Korea; School of Pharmacy (O C Okonji MSc), University of the Western Cape, Cape Town, South Africa; Department of Psychiatry (A T Olagunju MD), University of Lagos, Lagos, Nigeria; Centre for Healthy Start Initiative, Lagos, Nigeria (B O Olusanya PhD); Mass Communication Department (E Omer PhD), Ajman University, Dubai, United Arab Emirates; Laboratory of Public Health Indicators Analysis and Health Digitalization (N Otsavnov BA), Moscow Institute of Physics and Technology, Dolgoprudny, Russia; Department of Respiratory Medicine (Prof M P A DNB), Jagadguru Sri Shivarathreeswara Academy of Health Education and Research, Mysore, India; Department of Public Health (A Pana PhD), Babes Bolyai University, Cluj Napoca, Romania; Department of Health Metrics (A Pana PhD), Center for Health Outcomes & Evaluation, Bucharest, Romania; Vision and Eye Research Institute (Prof S Pardhan PhD), Anglia Ruskin University, Cambridge, UK; Department of Forensic Medicine and Toxicology (U Parekh MD), All India Institute of Medical Sciences, Rajkot, India; Department of Preventive Medicine (Prof E Park PhD), Institute of Health Services Research (Prof E Park PhD), Yonsei University College of Medicine (S Park BEng), College of Medicine (Prof J Shin MD), Yonsei University, Seoul, South Korea; Department of Pediatrics (Prof A Pathak PhD), RD Gardi Medical College, Ujjain, India; Department of Global Public Health (Prof A Pathak PhD), Karolinska Institute, Stockholm, Sweden; Department of Infection Control (M Peng MPH), Taihe Hospital, Shiyuan, China; The First Clinical College (M Peng MPH), Hubei University of Medicine, Shiyuan, China; Department of Neurology (U Pensato MD), IRCCS Humanitas Research Hospital, Milan, Italy; Institute of Collective Health (Prof M Pereira PhD), Federal University of Bahia, Salvador, Brazil; Department of Psychiatry (Prof M F P Peres MD), University of São Paulo, Sao Paulo, Brazil; International Institute for Educational Planning (IIEP) (Prof M F P Peres MD), Albert Einstein Hospital, Sao Paulo, Brazil; Mario Negri Institute for Pharmacological Research, Bergamo, Italy (N Perico MD, Prof G Remuzzi MD); International Center of Medical Sciences Research, Islamabad, Pakistan (Z Z Piracha PhD, Prof U Saeed PhD); Department of Dermatology (I Podder MD), College of Medicine and Sagore Dutta Hospital, Kolkata, India; Data Management and Analysis (R Poluru PhD), The INCLIN Trust International, New Delhi, India; Non Communicable Diseases Research Center (N Pourtaheri PhD), Bam University of Medical Sciences, Bam, Iran; Department of Neonatology (I Qattee MD), Department of Pediatrics (S Sankararaman MD), Case Western Reserve University, Cleveland, OH, USA; Biomedical Engineering Department (Prof M Rabiee PhD), Amirkabir University of Technology, Tehran, Iran; Pohang University of Science and Technology, Pohang, South Korea (N Rabiee PhD); College of Medicine (A Radfar MD), University of Central Florida, Orlando, FL, USA; Department of Laboratory Sciences (S Raeghi PhD), Maragheh University of Medical Sciences, Maragheh, Iran; Infectious and Tropical Diseases Research Center (L Rahbarnia PhD), Tabriz University of Medical Sciences, Tabriz, Iran; Department of Population Science and Human Resource Development (M Rahman DrPH), University of Rajshahi, Rajshahi, Bangladesh; School of Nursing and Healthcare Professions (M Rahman PhD), Federation University Australia, Berwick, VIC, Australia; Future Technology Research Center (A Rahmani PhD), National Yunlin University of Science and Technology, Yunlin, Taiwan; Department of Community Medicine (V Rahmanian PhD), Jahrom University of Medical Sciences, Jahrom, Iran; Department of Cardiology (P Ram MD), Emory University, Atlanta, GA, USA; Institute of Food Science and Nutrition (M A Ranjha BSc), University of Sargodha, Sargodha, Pakistan; Department of Oral Pathology (S Rao MDS), Sharavathi Dental College and Hospital, Shimogga, India; Department of Geography (A Rasul PhD), Soran University, Soran, Iraq; Department of Biomedical Engineering (Z Ratan MSc), Khulna University of Engineering and Technology, Khulna, Bangladesh; School of Health and Society (Z Ratan MSc), University of Wollongong, Wollongong, NSW, Australia; Academic Public Health England (Prof S Rawaf MD), Public Health England, London, UK; Department of Immunology and Laboratory Sciences (M Razeghinia MSc), Medical Laboratory Sciences (M Sahebazzamani MSc), Sirjan School of Medical Sciences, Sirjan, Iran; Department of Immunology (M Razeghinia MSc), Kerman University of Medical Sciences, Kerman, Iran; Department of Biological Sciences (Prof E M M Redwan PhD), King Abdulaziz University, Jeddah, Egypt; Department of Protein Research (Prof E M M Redwan PhD), Research and Academic Institution, Alexandria, Egypt; Department of Medical Laboratory Science (M A Reta MSc), Woldia University, Woldia, Ethiopia; Department of Public Health and Informatics (R K Ripon MSPH), Jahangirnagar University, Dhaka, Bangladesh; Department of Critical Care Medicine (K E Rudd MD), University of Pittsburgh, Pittsburgh, PA, USA; Department of Pathology and Microbiology (Prof U Saeed PhD), Jinnah Medical College, Peshawar, Pakistan; Advanced Dental Sciences Research Center (M Safaei PhD), Department of Infectious Disease (Prof S Vaziri MD), Kermanshah University of Medical Sciences, Kermanshah, Iran; Faculty of Medicine, Bioscience and Nursing (S Z Safi PhD), MAHSA University, Selangor, Malaysia; Interdisciplinary Research Centre in Biomedical Materials

(IRCBM) (S Z Safi PhD), COMSATS Institute of Information Technology, Lahore, Pakistan; Department of Medical Biochemistry (M Sahebazzamani MSc), Rafsanjan University of Medical Sciences, Rafsanjan, Iran; Department of Development Studies (H Sahoo PhD), International Institute for Population Sciences, Mumbai, India; Medical Laboratory (S Salahi BMedSc), Azad University of Medical Sciences, Tehran, Iran; Advanced Therapy Medicinal Products Department (S Salahi MD), Royan Institution, Tehran, Iran; Health Policy and Management (H Salari PhD), Bushehr University of Medical Sciences, Bushehr, Iran; Department of Entomology (A M Samy PhD), Ain Shams University, Cairo, Egypt; Department of Biology (N Sanadgol PhD), Zabol University of Medical Sciences, Zabol, Iran; Department of Pediatrics (S Sankararaman MD), University Hospitals Rainbow Babies & Children's Hospital, Cleveland, OH, USA; Faculty of Health & Social Sciences (B Sathian PhD), Bournemouth University, Bournemouth, UK; Department of Public Health Sciences (M Sawhney PhD), University of North Carolina at Charlotte, Charlotte, NC, USA; Department of Preventive and Social Medicine (G Saya MD), Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India; Emergency Department (S Senthilkumaran MD), Manian Medical Centre, Erode, India; National Heart, Lung, and Blood Institute (A Seylani BS), National Institute of Health, Rockville, MD, USA; Department of Infectious Diseases and Microbiology (P A Shah MBBS), Bangalore Medical College and Research Institute, Bangalore, India; HepatoPancreatoBiliary Surgery and Liver Transplant (P A Shah MBBS), HealthCare Global Limited Cancer Care Hospital, Bangalore, India; Independent Consultant, Karachi, Pakistan (M A Shaikh MD); Department of Infectious Diseases and Epidemiology (Prof M Z Shakhmardanov PhD, A A Skryabina MD), Pirogov Russian National Research Medical University, Moscow, Russia; Institute of Public Health (M M Sharew MPH), University of Gondar, Gondar, Ethiopia; Department of Medical Oncology (P Sharma MD), Kent Hospital, Warwick, RI, USA; Infectious Diseases Research Center (H Shirzad-Aski PhD), Golestan University of Medical Sciences, Gorgan, Iran; Department of Nursing and Health Sciences (S Shorofi PhD), Flinders University, Adelaide, SA, Australia; School of Pharmacy (S Shrestha PharmD), Monash University, Selangor Darul Ehsan, Malaysia; Department of Pediatrics and Child Health Nursing (M M Sibhat MSc), Dilla University, Dilla, Ethiopia; Department of International Health (M K Sikder PhD), Johns Hopkins University, Baltimore, MD, USA; Center of Potential and Innovation of Natural Resources (Prof L M R Silva PhD), Polytechnic Institute of Guarda, Guarda, Portugal; Health Sciences Research Centre (Prof L M R Silva PhD), University of Beira Interior, Covilhã, Portugal; School of Medicine (Prof J A Singh MD), University of Alabama at Birmingham, Birmingham, AL, USA; Department of Medicine Service (Prof J A Singh MD), US Department of Veterans Affairs, Birmingham, AL, USA; Department of Radiodiagnosis (P Singh MD), All India Institute of Medical Sciences, Bathinda, India; Maternal and Child Health Division (M Siraj MSc, S Zaman MSc), International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; Department of Chemistry (S S Siwal PhD), Maharishi Markandeshwar (Deemed to be University), Mullana, India; Clinical Branch (V Y Skryabin MD), Moscow Research and Practical Centre on Addictions, Moscow, Russia; Addiction Psychiatry Department (V Y Skryabin MD), Addictology Department (Prof M S Zastrozhin PhD), Russian Medical Academy of Continuous Professional Education, Moscow, Russia; Department of Surgery (B Socea PhD), "Sf. Pantelimon" Emergency Clinical Hospital Bucharest, Bucharest, Romania; Department of Biomedical Science (D D Solomon MSc), Mada Walabu University, Goba, Ethiopia; Division of Community Medicine (C T Sreeramareddy MD), International Medical University, Kuala Lumpur, Malaysia; School of Life Sciences (M Suleman PhD), Xiamen University, Xiamen, China; National Institute of Epidemiology (R Suliankatchi Abdulkader MD), Indian Council of Medical Research, Chennai, India; Department of Maternal and Child Health (S Sultana MPH), Projahnmo Research Foundation, Dhaka, Bangladesh; Department of Nutrition Sciences (S Tabatabaeizadeh PhD), Varastegan Institute for Medical Sciences, Mashhad, Iran; Department of Surgery (K Tan PhD), National University of Singapore, Singapore; Department of Science, Technology and

Natural Resources (S Tandukar PhD), Policy Research Institute, Kathmandu, Nepal; Department of Economics (N Y Tat MS), Rice University, Houston, TX, USA; Department of Research and Innovation (N Y Tat MS), Enventure Medical Innovation, Houston, TX, USA; Department of Pathology (V Y Tat BS), University of Texas, Galveston, TX, USA; Department of Public Health (Y M Tefera MPH), Dire Dawa University, Dire Dawa, Ethiopia; Pediatric Intensive Care Unit (M Temsah MD), King Saud University, Riyadh, Saudi Arabia; Rheumatology and Immunology Unit (S Tharwat MD), Mansoura University, Mansoura, Egypt; Department of Clinical Epidemiology (A Thiyagarajan MPH), Leibniz Institute for Prevention Research and Epidemiology, Bremen, Germany; Infectious Diseases Department (Prof I I Tleyjeh MD), King Fahad Medical City, Riyadh, Saudi Arabia; Division of Infectious Diseases (Prof I I Tleyjeh MD), Mayo Clinic, Rochester, MN, USA; Department of Pediatric Cardiology (K Umaphathi MD), Rush University, Chicago, IL, USA; Clinical Cancer Research Center (S Valadan Tahbaz PhD, S Yahyazadeh Jabbari MD), Milad General Hospital, Tehran, Iran; Department of Microbiology (S Valadan Tahbaz PhD), Islamic Azad University, Tehran, Iran; Velez Sarsfield Hospital, Buenos Aires, Argentina (Prof P R Valdez MED); Department of Cardiovascular Sciences (J Van den Eynde BSc), Katholieke Universiteit Leuven (University of Leuven), Leuven, Belgium; Oxford University Clinical Research Unit - Hanoi, Hanoi, Viet Nam (H van Doorn PhD); College of Medicine and Veterinary Medicine (G Verras MD), University of Edinburgh, Edinburgh, UK; Faculty of Information Technology (B Vo PhD), HUTECH University, Ho Chi Minh City, Viet Nam; Department of Biomedical Sciences (A Waris MS), City University of Hong Kong, Hong Kong Special Administrative Region, China; Department of Community Medicine (N D Wickramasinghe MD), Rajarata University of Sri Lanka, Anuradhapura, Sri Lanka; Department of Clinical Microbiology (S Yaghoubi PhD), Iranshahr University of Medical Sciences, Iranshahr, Iran; Department of Health Management (A Yigit PhD, V Yigit PhD), Süleyman Demirel University, Isparta, Türkiye; Department of Pediatrics (D Yon MD), Kyung Hee University, Seoul, South Korea; Department of Neuropsychopharmacology (N Yonemoto PhD), National Center of Neurology and Psychiatry, Kodaira, Japan; Department of Public Health (N Yonemoto PhD), Juntendo University, Tokyo, Japan; Research and Development Department (I Zare BSc), Sina Medical Biochemistry Technologies, Shiraz, Iran; NIHR-Biomedical Research Centre (NIHR-BRC) (Prof A Zumla PhD), University College London Hospitals, London, UK; Mahidol Oxford Tropical Medicine Research Unit (C Dolecek PhD), Mahidol University, Bangkok, Thailand

#### Contributors

See appendix 1 (section 11) for more detailed information about individual author contributions to the research, divided into the following categories: managing the overall research enterprise; writing the first draft of the manuscript; primary responsibility for applying analytical methods to produce estimates; primary responsibility for seeking, cataloguing, extracting, or cleaning data; designing or coding figures and tables; providing data or critical feedback on data sources; developing methods or computational machinery; providing critical feedback on methods or results; drafting the work or revising it critically for important intellectual content; and managing the estimation or publications process. K S Ikuta and M Naghavi verified and had access to underlying study data in the study and had final responsibility for the decision to submit for publication.

#### Declaration of interests

S Afzal reports support for the present manuscript from Department of Community Medicine and Epidemiology, King Edward Medical University; participation on a data and safety monitoring board or advisory board with Corona Expert Advisory Group and Dengue Expert Advisory Group; leadership or fiduciary roles in board, society, committee, or advocacy groups, unpaid with Pakistan Society of Community Medicine & Public Health, Pakistan Association of Medical Editors, and Pakistan Society of Medical Infectious Diseases. S Bhaskar reports support for the present manuscript from leadership or fiduciary roles in board, society, committee or advocacy groups, paid or unpaid with the Rotary Club of Sydney and Global Health and Migration Hub Community, Global Health Hub Germany as a Board Director and

Co-Manager. X Dai reports support for the present manuscript from the Institute for Health Metrics and Evaluation (IHME) and University of Washington. S Das reports grants or contracts from The Department of Science & Technology (DST) Grant of 16 Lakh INR by the Government of India for COVID-19 Research; leadership or fiduciary roles in board, society, committee or advocacy groups, paid or unpaid with Program Chair The American Association for Clinical Chemistry (AACC) India Section as an executive member in Ambi, India. S J Dunachie reports support for the present manuscript from UK National Institute of Health and Care Research (NIHR), funded by an NIHR Global Research Professorship (NIHR300791); grants or contracts from UK Research and Innovation (UKRI; MR/W02067X/1 and MR/W020653/1), Wellcome Drug Resistant Infections Discretionary Award, UK Department of Health and Social Care, and US Defense Threat Reduction Agency; and consulting fees from the Scottish Parliament and funding committees for Wellcome. C Herteliu reports grants or contracts from Romanian Ministry of Research Innovation and Digitalization, MCID and Romanian National Authority for Scientific Research and Innovation, and CNDS-UEFISCDI. N E Ismail reports leadership or fiduciary roles in board, society, committee, or advocacy groups, unpaid with Malaysian Academy of Pharmacy as a Council Member. J J Jozwiak reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Teva, Amgen, Synexus, Boehringer Ingelheim, ALAB Laboratories, and Zentiva. N J Kassebaum reports research support for the GBD Study and the present manuscript from The Bill & Melinda Gates Foundation. F Krapp Lopez reports support for the present manuscript from University of Oxford, and financial support provided to Universidad Peruana Cayetano Heredia for data extraction and preparation for the present manuscript. K Krishan reports other non-financial support from UGC Centre of Advanced Study, CAS II, Department of Anthropology, Panjab University, Chandigarh, India. A-F A Mentis reports grants or contracts from MilkSafe (A novel pipeline to enrich formula milk using omics technologies), a research co-financed by the European Regional Development Fund of the EU and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH - CREATE - INNOVATE (project code: T2EDK-02222), as well as from ELIDEK (Hellenic Foundation for Research and Innovation, MIMS-860); stocks in a family winery; other financial or non-financial support from the BGI group as a scientific officer. N Milevska Kostova reports grants or contracts from BD Europe and Pfizer (institutional grant for patient education); payment or honoraria for lectures or educational events from Pfizer; and support for attending meetings or travel from Pfizer. S Mohammed reports support for the present manuscript from The Bill & Melinda Gates Foundation and grants or contracts from Alexander von Humboldt Foundation. L Monasta reports support for the present manuscript from the Italian Ministry of Health on project Ricerca Corrente (34/2017) and payments made to the Institute for Maternal and Child Health IRCCS Burlo Garofolo. C E Moore reports support for the present manuscript from the UK Department of Health and Social Care, Wellcome Trust, and The Bill & Melinda Gates Foundation. S B Munro reports stock or stock options in Invitae as an employee. V C F Pepito reports grants from Sanofi Consumer Healthcare and International Initiative for Impact Evaluation. M J Postma reports leadership or fiduciary roles in board, society, committee, or advocacy groups, paid or unpaid, with the Joint Committee of Vaccination and Immunization as a member and stock or stock options in PAG BV (Groningen, Netherlands) and HealthEcore (Zeist, Netherlands). A Radfar reports other support from Avicenna Medical and Clinical Research Institute. K E Rudd reports support for the present manuscript from the National Institutes of Health, National Institute of General Medical Sciences (grant K23GM141463), and consulting fees from Janssen Pharmaceuticals. B Sartorius reports grants or contracts from the Fleming Fund; leadership or fiduciary roles in board, society, committee, or advocacy groups, paid or unpaid, with WHO Reference Group on Health Statistics and GBD Scientific Council. S Shrestha reports other financial or non-financial support from the Graduate Research Merit Scholarship from the School of Pharmacy, Monash University Malaysia. L M L R Silva reports grants or contracts from project code CENTRO-04-3559-FSE-000162, Fundo Social Europeu (FSE). J A Singh reports consulting fees from Crealta/Horizon, Medisys,

Fidia, PK Med, Two Labs, Adept Field Solutions, Clinical Care options, Clearview healthcare partners, Putnam associates, Focus forward, Navigant consulting, Spherix, MediQ, Jupiter Life Science, UBM, Trio Health, Medscape, WebMD, Practice Point communications, the National Institutes of Health, and the American College of Rheumatology; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Simply Speaking; support for attending meetings or travel from the steering committee of OMERACT; participation on a data safety monitoring board or advisory board with the US Food and Drug Administration Arthritis Advisory Committee; leadership or fiduciary role in board, society, committee or advocacy group, paid or unpaid, with OMERACT as a steering committee member, as Chair of the Veterans Affairs Rheumatology Field Advisory Committee, and as Editor and Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis; stock or stock options in TPT Global Tech, Vaxart Pharmaceuticals, Atyu Biopharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, EnzoLytics, Seres Therapeutics, Tonix Pharmaceuticals, and Charlotte's Web Holdings; and previously owning stock options in Amarin, Viking, and Moderna pharmaceuticals. E Upadhyay reports patents published: "A system and method of reusable filters for anti-pollution mask" (patent application number 202011003559), and "A system and method for electricity generation through crop stubble by using microbial fuel cells" (patent application number 202011008531), patents filed: "A system for disposed personal protection equipment (PPE) into biofuel through pyrolysis and method" (patent application number 202111005659) and "A novel herbal pharmaceutical aid for formulation of gel and method thereof" (patent application number 202111023335); and leadership or fiduciary roles in board, society, committee, or advocacy groups, paid or unpaid, with the Indian Meteorological Society, Jaipur Chapter (India) as a joint secretary and life member. H R van Doorn reports participation on a data and safety monitoring board or advisory board with Wellcome SEDRIC (Surveillance and Epidemiology of Drug Resistant Infections).

#### Data sharing

Citations for the data used in the study can be accessed from the Global Health Data Exchange website. Access to the data can also be provided as data use agreements permit.

#### Acknowledgments

Funding for this study was provided by the Bill & Melinda Gates Foundation (OPP1176062), the Wellcome Trust (A126042), and the UK Department of Health and Social Care using UK aid funding managed by the Fleming Fund (R52354 CN001). J M Acuna acknowledges academic support from the Universidad Espiritu Santo. S Afzal acknowledges institutional support from the Department of Community Medicine and Epidemiology for timely revising and completing the modifications and corrections in the manuscript. A Ahmad acknowledges support from the Scientific Research Unit at Shaqra University. S M Aljumid acknowledges support from the Department of Health Policy and Management, College of Public Health, Kuwait University for the support and approval to participate in this research project. M Ausloos acknowledges support from the Romanian National Authority for Scientific Research and Innovation (under CNDS-UEFISCDI: PN-III-P4-ID-PCCF-2016-0084 research grant; Understanding and modelling time-space patterns of psychology-related inequalities and polarization). I Banerjee acknowledges support from Sir Seewoosagar Ramgoolam Medical College (SSRMC), Belle Rive, Mauritius. S J Dunachie acknowledges funding support from an NIHR Global Research Professorship (NIHR300791). T C Ekundayo acknowledges support from the African-German Network of Excellence in Science (AGNES), the Federal Ministry of Education and Research (BMBF), and the Alexander von Humboldt Foundation (AvH) for financial support. A Fatehizadeh acknowledges support from the Department of Environmental Health Engineering of Isfahan University of Medical Sciences, Isfahan, Iran. J C Fernandes acknowledges support from UID/Multi/50016/2019 with funding from Fundação para a Ciência e a Tecnologia; support with funding from Fundação para a Ciência e a Tecnologia (FCT)/Ministro da Ciência, Tecnologia e Ensino Superior (MCTES) through national funds. A Goodridge, I Landires, and V Nuñez-Samudio are supported by the Sistema Nacional de

For the **Global Health Data Exchange website** see <https://ghdx.healthdata.org/record/ihme-data/gbd-2019-bacterial-pathogen-attributable-mortality-2019>

Investigación (SNI) de Panamá, which is supported by Panamá's Secretaría Nacional de Ciencia, Tecnología e Innovación (SENACYT). V B Gupta and V K Gupta acknowledge funding support from National Health and Medical Research Council (NHMRC) Australia. C Herteliu acknowledges support from a grant of the Romanian National Authority for Scientific Research and Innovation (CNDS-UEFISCDI, project number PN-III-P4-ID-PCCF-2016-0084), and from a grant of the Romanian Ministry of Research Innovation and Digitalization (MCID, project number ID-585-CTR-42-PFE-2021). P Hoogar acknowledges support from the Centre for Bio Cultural Studies, Directorate of Research, Manipal Academy of Higher Education (Manipal, India), and Centre for Holistic Development and Research (Kalaghatgi, India). S Hussain acknowledges support from the Operational Programme Research, Development and Education- Project, Postdoc2MUNI (No.CZ.02.2.69/0.0/0.0/18\_053/0016952). M Jakovljevic acknowledges partial financial support through the grant OI 175 014 of the Ministry of Education Science and Technological Development of Serbia. T Joo acknowledges support from the National Research, Development and Innovation Office of Hungary grants and RRF-2.3.1-21-2022-00006 Data-driven Health Division of Health Security National Laboratory. S L Koulmane Laxminarayana acknowledges institutional support from Manipal Academy of Higher Education (Manipal, India). F Krapp Lopez acknowledges support from the Framework Agreement Belgian Directorate of Development Cooperation, the Institute of Tropical Medicine in Antwerp, and the Fogarty International Center, and National Institute of Child Health & Human Development of the National Institutes of Health (D43 TW009763). K Krishan acknowledges support from the UGC Centre of Advanced Study (Phase II), awarded to the Department of Anthropology, Panjab University (Chandigarh, India). A Majeed acknowledges support from the NIHR Research Applied Research Collaboration (ARC) Northwest London; the views expressed in this publication are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care. L Monasta acknowledges support related to the present study received from the Italian Ministry of Health on project Ricerca Corrente 34/2017 at the Institute for Maternal and Child Health IRCCS Burlo Garofolo. JR Padubidri acknowledges support from Kasturba Medical College (Mangalore) and Manipal Academy of Higher Education (Manipal) for their continual support for Research. Z Z Piracha acknowledges support from the International Center of Medical Sciences (ICMSR), Islamabad (44000), Pakistan. A Riad acknowledges support from Masaryk University (grant number MUNI/IGA/1104/2021), and the NPO Systemic Risk Institute LX22NPO5101. U Saeed acknowledges support from the International Center of Medical Sciences (ICMSR), Islamabad (44000), Pakistan. A M Samy acknowledges the support from The Egyptian Fulbright Mission program and Ain Shams University. B Sartorius acknowledges grant support from the UK Department of Health and Social Care using UK aid funding managed by the Fleming Fund (R52354 CN001). P A Shah acknowledges academic support from Bangalore Medical College and Research Institute. P H Shetty acknowledges support from Kasturba Medical College, Mangalore and Manipal Academy of Higher Education, Manipal, India. S S Siwal acknowledges support from Department of Chemistry and Research & Development Cell of Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, Haryana, India. S B Zaman acknowledges scholarship support from the Australian Government Research Training Program (RTP) to support his academic career. R Suliankatchi Abdulkader acknowledges support from the ICMR-National Institute of Epidemiology. A Zumla acknowledges support as co-principal investigator of The Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET, CANTAM-3, and EACCR-3) funded by the European and Developing Countries Clinical Trials Partnership, supported by the EU Horizon 2020 Framework Programme, UK-NIHR Senior Investigator award, and is a Mahathir Science Award and EU-EDCTP Pascoal Mocumbi Prize Laureate.

Editorial note: The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

## References

- UN. Sustainable Development Goals. <https://www.un.org/sustainabledevelopment/sustainable-development-goals/> (accessed Jan 27, 2022).
- UN. Millennium Development Goals. <https://www.un.org/millenniumgoals/> (accessed Jan 27, 2022).
- GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396**: 1204–22.
- Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. *Lancet* 2020; **395**: 200–11.
- Valentine N, Solar O, Irwin A, Nolen L, Prasad A. Health equity at the country level: building capacities and momentum for action. A report on the country stream of work in the commission on social determinants of health. Geneva: World Health Organization, 2008. [https://cdn.who.int/media/docs/default-source/documents/social-determinants-of-health/sdhe\\_csw\\_final\\_report.pdf?sfvrsn=d1752088\\_5&download=true](https://cdn.who.int/media/docs/default-source/documents/social-determinants-of-health/sdhe_csw_final_report.pdf?sfvrsn=d1752088_5&download=true) (accessed Dec 8, 2021).
- GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; **390**: 1151–210.
- UN. Department of Economic and Social Affairs. The 17 goals. <https://sdgs.un.org/goals> (accessed Dec 8, 2021).
- Luby SP, Agboatwalla M, Feikin DR, et al. Effect of handwashing on child health: a randomised controlled trial. *Lancet* 2005; **366**: 225–33.
- Poolman JT. Expanding the role of bacterial vaccines into life-course vaccination strategies and prevention of antimicrobial-resistant infections. *NPJ Vaccines* 2020; **5**: 84.
- Lynch JP 3rd, Zhanel GG. *Streptococcus pneumoniae*: epidemiology, risk factors, and strategies for prevention. *Semin Respir Crit Care Med* 2009; **30**: 189–209.
- Evans L, Rhodes A, Alhazzani W, et al. Executive summary: surviving sepsis campaign: international guidelines for the management of sepsis and septic shock 2021. *Crit Care Med* 2021; **49**: 1974–82.
- Seymour CW, Gesten F, Prescott HC, et al. Time to treatment and mortality during mandated emergency care for sepsis. *N Engl J Med* 2017; **376**: 2235–44.
- O'Brien KL, Wolfson LJ, Watt JP, et al. Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years: global estimates. *Lancet* 2009; **374**: 893–902.
- Thigpen MC, Whitney CG, Messonnier NE, et al. Bacterial meningitis in the United States, 1998–2007. *N Engl J Med* 2011; **364**: 2016–25.
- US Centers for Disease Control and Prevention. GBS Surveillance Report 2019. Centers for Disease Control and Prevention, 2019. [https://www.cdc.gov/abcs/downloads/GBS\\_Surveillance\\_Report\\_2019.pdf](https://www.cdc.gov/abcs/downloads/GBS_Surveillance_Report_2019.pdf) (accessed Dec 8, 2021).
- Wahl B, O'Brien KL, Greenbaum A, et al. Burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease in children in the era of conjugate vaccines: global, regional, and national estimates for 2000–15. *Lancet Glob Health* 2018; **6**: e744–57.
- Centers for Disease Control and Prevention. Active Bacterial Core surveillance (ABCs). July 19, 2021. <https://www.cdc.gov/abcs/index.html> (accessed Dec 8, 2021).
- European Centre for Disease Prevention and Control. European Antimicrobial Resistance Surveillance Network (EARS-Net). <https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/ears-net> (accessed Dec 8, 2021).
- Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* 2022; **399**: 629–55.
- Institute for Health Metrics and Evaluation. Protocol for the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), version 4.0. March, 2020. [https://www.healthdata.org/sites/default/files/files/Projects/GBD/March2020\\_GBD%20Protocol\\_v4.pdf](https://www.healthdata.org/sites/default/files/files/Projects/GBD/March2020_GBD%20Protocol_v4.pdf) (accessed Nov 17, 2021).
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; **372**: n71.
- Stevens GA, Alkema L, Black RE, et al. Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement. *PLoS Med* 2016; **13**: e1002056.
- Nocedal J, Wright SJ. Numerical optimization, second edition. New York, NY: Springer-Verlag, 2006.

- 24 WHO. Immunization agenda 2030: a global strategy to leave no one behind. Geneva: World Health Organization, April, 2020. <https://www.who.int/publications/m/item/immunization-agenda-2030-a-global-strategy-to-leave-no-one-behind> (accessed May 23, 2022).
- 25 The Lancet. Antimicrobial resistance: time to repurpose the Global Fund. *Lancet* 2022; **399**: 335.
- 26 Allegranzi B, Bischoff P, de Jonge S, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis* 2016; **16**: e276–87.
- 27 Tacconelli E. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. World Health Organization, 2017. <https://policycommons.net/artifacts/1818147/global-priority-list-of-antibiotic-resistant-bacteria-to-guide-research-discovery-and-development/2555608/> (accessed Nov 11, 2022).
- 28 WHO. Antimicrobial resistance: global report on surveillance. Geneva: World Health Organization, 2014. <https://apps.who.int/iris/handle/10665/112642> (accessed Dec 8, 2021).
- 29 Ledesma JR, Ma J, Vongpradith A, et al. Global, regional, and national sex differences in the global burden of tuberculosis by HIV status, 1990–2019: results from the Global Burden of Disease Study 2019. *Lancet Infect Dis* 2022; **22**: 222–41.
- 30 Head MG, Brown RJ, Newell M-L, Scott JAG, Batchelor J, Atun R. The allocation of US\$105 billion in global funding from G20 countries for infectious disease research between 2000 and 2017: a content analysis of investments. *Lancet Glob Health* 2020; **8**: e1295–304.
- 31 Burke JP. Infection control - a problem for patient safety. *N Engl J Med* 2003; **348**: 651–56.
- 32 Freeman MC, Stocks ME, Cumming O, et al. Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Trop Med Int Health* 2014; **19**: 906–16.
- 33 Wolf J, Prüss-Ustün A, Cumming O, et al. Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression. *Trop Med Int Health* 2014; **19**: 928–42.
- 34 Smith AM, Huber VC. The unexpected impact of vaccines on secondary bacterial infections following influenza. *Viral Immunol* 2018; **31**: 159–73.
- 35 Nakaya HI, Bruna-Romero O. Is the gut microbiome key to modulating vaccine efficacy? *Expert Rev Vaccines* 2015; **14**: 777–79.
- 36 Society of Critical Care Medicine (SCCM). Surviving sepsis campaign 2021 adult guidelines. <https://sccm.org/SurvivingSepsisCampaign/Guidelines/Adult-Patients> (accessed Dec 8, 2021).
- 37 Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA* 2016; **315**: 801–10.
- 38 Miethke M, Pieroni M, Weber T, et al. Towards the sustainable discovery and development of new antibiotics. *Nat Rev Chem* 2021; **5**: 726–49.
- 39 World Bank. World development indicators. 2021. <https://data.worldbank.org/indicator> (accessed Dec 8, 2021).
- 40 Araya P, Hug J, Joy G, Oschmann F, Rubinstein S. The impact of water and sanitation on diarrhoeal disease burden and over-consumption of antibiotics. London School of Economics and Political Science, March, 2016. <https://amr-review.org/sites/default/files/LSE%20AMR%20Capstone.pdf> (accessed Dec 8, 2021).
- 41 Frost I, Craig J, Joshi J, Faure K, Laxminarayan R. Access barriers to antibiotics. Washington, DC: Center for Disease Dynamics, Economics & Policy, 2019.
- 42 Kelesidis T, Falagas ME. Substandard/counterfeit antimicrobial drugs. *Clin Microbiol Rev* 2015; **28**: 443–64.
- 43 Do NTT, Vu HTL, Nguyen CTK, et al. Community-based antibiotic access and use in six low-income and middle-income countries: a mixed-method approach. *Lancet Glob Health* 2021; **9**: e610–19.
- 44 Laxminarayan R, Van Boeckel T, Frost I, et al. The Lancet Infectious Diseases Commission on antimicrobial resistance: 6 years later. *Lancet Infect Dis* 2020; **20**: e51–60.
- 45 WHO, UNICEF. Ending preventable child deaths from pneumonia and diarrhoea by 2025: the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). 2013. [https://apps.who.int/iris/bitstream/handle/10665/79207/WHO\\_FWC\\_MCA\\_13\\_01\\_eng.pdf?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/79207/WHO_FWC_MCA_13_01_eng.pdf?sequence=1) (accessed Dec 8, 2021).
- 46 WHO. Sepsis. Geneva: World Health Organization, Aug 26, 2020. <https://www.who.int/news-room/fact-sheets/detail/sepsis> (accessed Dec 8, 2021).
- 47 WHO. Global report on the epidemiology and burden of sepsis: current evidence, identifying gaps and future directions. Geneva: World Health Organization, 2020. <https://apps.who.int/iris/handle/10665/334216> (accessed Dec 8, 2021).
- 48 Sartelli M, Chichom-Mefire A, Labricciosa FM, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg* 2017; **12**: 29.
- 49 Alkire BC, Raykar NP, Shrimel MG, et al. Global access to surgical care: a modelling study. *Lancet Glob Health* 2015; **3**: e316–23.
- 50 Holmer H, Lantz A, Kunjumen T, et al. Global distribution of surgeons, anaesthesiologists, and obstetricians. *Lancet Glob Health* 2015; **3** (suppl 2): S9–11.
- 51 Yadav H, Shah D, Sayed S, Horton S, Schroeder LF. Availability of essential diagnostics in ten low-income and middle-income countries: results from national health facility surveys. *Lancet Glob Health* 2021; **9**: e1553–60.
- 52 WHO. WHO model list of essential medicines - 22nd list, 2021. Geneva: World Health Organization, Sept 30, 2021. <https://www.who.int/publications-detail-redirect/WHO-MHP-HPS-EML-2021.02> (accessed Jan 18, 2022).
- 53 Wen SCH, Ezure Y, Rolley L, et al. Gram-negative neonatal sepsis in low- and lower-middle-income countries and WHO empirical antibiotic recommendations: a systematic review and meta-analysis. *PLoS Med* 2021; **18**: e1003787.
- 54 WHO. WHO antibiotic categorization. Geneva: World Health Organization. <https://aware.essentialmeds.org/groups> (accessed Dec 8, 2021).
- 55 WHO. Global tuberculosis report 2020. Geneva: World Health Organization, Oct 15, 2020. <https://www.who.int/publications/i/item/9789240013131> (accessed May 6, 2022).
- 56 Lim C, Ashley EA, Hamers RL, et al. Surveillance strategies using routine microbiology for antimicrobial resistance in low- and middle-income countries. *Clin Microbiol Infect* 2021; **27**: 1391–99.
- 57 Jacobs J, Hardy L, Semret M, et al. Diagnostic bacteriology in district hospitals in sub-Saharan Africa: at the forefront of the containment of antimicrobial resistance. *Front Med (Lausanne)* 2019; **6**: 205.