

# THE LANCET

## Supplementary appendix

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## Appendix 1: supplementary methods and results to “Global burden of bacterial antimicrobial resistance in 2019”

This appendix provides further methodological details and supplementary results for “Global burden of bacterial antimicrobial resistance in 2019”.

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## Section 1: List of abbreviations

Abbreviation	Full phrase
AGAR	Australian Group on Antimicrobial Resistance
AHC	Angkor Hospital for Children
AMASS	AutoMated tool for Antimicrobial resistance Surveillance System
AMR	antimicrobial resistance
APUA	Alliance for the Prudent Use of Antibiotics
ARSP	Antimicrobial Resistance Surveillance Program
ATLAS	Antimicrobial Testing Leadership and Surveillance
AURA	Antimicrobial Use and Resistance in Australia
AWARE	Assessing Worldwide Antimicrobial Resistance Evaluation
BARNARDS	Burden of Antibiotic Resistance in Neonates from Developing Societies
BD	Becton, Dickinson, and Company
BSI	bloodstream infections
CAESAR	Central Asian and European Surveillance of Antimicrobial Resistance
CAI	community-acquired infection
CDC	Centers for Disease Control and Prevention
CFR	case fatality ratio
CHAIN	Childhood Acute Illness and Nutrition
CHAMPS	Child Health and Mortality Prevention Surveillance
cIAI	complicated intra-abdominal infection
COMRU	Cambodia Oxford Medical Research Unit
CTMRF	CHILDS Trust Medical Research Foundation
cUTI	complicated urinary tract infection
DALYs	Disability-adjusted life-years
DHS	Demographic Health Surveys
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
GAM	generalised additive models
GBD	Global Burden of Diseases, Injuries, and Risk Factors Study
GBS	group B <i>Streptococcus</i>
GLASS	Global Antimicrobial Resistance Surveillance System

GLM	generalised linear model
GPR	Gaussian process regression
HAI	hospital-acquired infection
HAQ Index	Healthcare Access and Quality Index
HHS	U.S. Department of Health and Human Services
ICD	International Classification of Diseases
ICU	intensive care unit
INFORM	International Network for Optimal Resistance Monitoring
INICC	International Nosocomial Infection Control Consortium
iNTS	invasive non-typhoidal Salmonella
IOD	Infections in Oxfordshire Research Database
IQVIA	IMS Health and Quintiles
JANIS	Japan Nosocomial Infections Surveillance
KEMRI	Kenya Medical Research Institute
LRI	lower respiratory infection
MCoD	multiple causes of death data
MEPCO	multinomial estimation of partial and composite observations
MICS	Multiple Indicators Cluster Surveys
MITS	minimally invasive tissue sampling
MR-BRT	meta-regression—Bayesian, regularised, trimmed
MRC	Medical Research Council
NARMS	National Antimicrobial Resistance Monitoring System for Enteric Bacteria
NICD	National Institute for Communicable Diseases
OUCRU	Oxford University Clinical Research Unit
PPS HAI	Point Prevalence Survey on Nosocomial Infections and Antibiotic Use
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SDI	Socio-demographic Index
SEV	summary exposure value
SGUL-GARPEC	St. George's Hospital, University of London - Global Antimicrobial Resistance, Prescribing and Efficacy Among Neonates and Children
SOAR	Survey on Antibiotic Resistance
ST-GPR	spatiotemporal Gaussian process regression

TB	tuberculosis
TESSy	The European Surveillance System
TEST	Tigecycline Evaluation Surveillance Trial
TSAP	Typhoid Fever Surveillance in Africa Program
UI	uncertainty interval
UPCH	Cayetano Heredia University
USDA	U.S. Department of Agriculture
UTI	urinary tract infection
VR	vital registration
WHO	World Health Organization
WRP	Walter Reed Project
YLDs	years lived with disability
YLLs	years of life lost

## Section 2: Data sources

The data used for this study can be categorised into the following types: multiple causes of death (MCoD), hospital discharge, linkage, mortality surveillance, literature reviews, , microbial, single drug-resistance profiles, pharmaceutical sales, and antibiotic use data; as well as estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019.<sup>1</sup> More detailed information on data inputs are available at <http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019>.

### Section 2.1: Multiple causes of death and vital registration (MCoD-VR)

Multiple cause of death (MCoD) data is a type of vital registration obtained from death certificates that contain the underlying cause of death, intermediate and immediate causes of death, and contributing conditions. MCoD data differ from other vital registration (VR) sources, because many countries have VR systems that only document the underlying cause of death. MCoD data were used in the sepsis, infectious syndrome, and pathogen distribution component models and data processing, and modelling methods can be found in sections 4 and 6. MCoD-VR data came from the following sources.

- United States National Vital Statistics System
- Brazil Mortality Information System
- National Institute of Statistics (Italy)
- Statistics South Africa
- National Institute of Statistics and Geography (Mexico)
- National Administrative Department of Statistics (Colombia)
- Taiwan Ministry of Health and Welfare

### Section 2.2: Hospital discharge

Hospital admissions and discharge data are data sources collected from inpatient hospital and other clinical settings. These data include information on the primary and secondary diagnosis for each patient, as applicable, and were obtained from the sources listed below. Hospital data were used in the sepsis, infectious syndrome, pathogen

distribution, and case fatality ratio component models and data processing, and modelling methods can be found in sections 4–6.

- USA National Hospital Discharge Survey
- USA State Inpatient Databases
- Brazil Hospital Information System
- Italy Hospital Inpatient Discharges
- Sistema Automatizado de Egresos Hospitalarios (Mexico)
- Austria Hospital Inpatient Discharges
- New Zealand National Minimum Dataset
- Canada Discharge Abstract Database

### Section 2.3: Microbial data with outcome

Microbial data are data sources from hospital and lab networks that collect pathogen cultures from patients. The cultures are tested for both pathogen and the pathogen’s resistance to antibiotics. The culture results are linked to patient outcome, diagnoses, or both. Microbial data without these outcomes or diagnoses are listed in section 2.4. These data also include the specimen from which the pathogen was isolated and whether the infection was community- or hospital-acquired, if available. When hospital versus community acquisition was not specified, we used the difference between admission or diagnosis date and the specimen collection date, and if 48 hours or fewer had passed between those two dates, then the infection was assumed to be community-acquired. We assumed the infection was hospital-acquired when more than 48 hours had passed, consistent with CDC/National Healthcare Safety Network guidelines.<sup>2</sup> Microbial data with outcome were used in the case fatality ratio, pathogen distribution, prevalence of resistance, and relative risk component models and data processing, and modelling methods can be found in sections 5–8. Microbiology data types, with outcome and diagnoses were obtained from the sources below.

- **USA Becton, Dickinson, and Co. (BD) Insights, Research and Analytics Database microbiology test and in-patient hospital data:** data procured by BD via MedMined. Covers a range of regions in the United States from 2011 to 2017.
- **UK Infections in Oxfordshire Research Database (IORD):** patient microbiology and episodes data from Oxford University Hospitals NHS Foundation Trust.
- **International Nosocomial Infection Control Consortium (INICC) surveillance online system:** data from the INICC data collection software. ICU patient microbiology and hospital data from 50 countries across Latin America, Asia, the Middle East, eastern Europe, and Africa from 2009 to 2020.
- **Bulgaria antimicrobial resistance data:** Medical University of Varna in Varna, Bulgaria. Covers 2014–2020.
- **St. George's Hospital, University of London - Global Antimicrobial Resistance, Prescribing and Efficacy Among Neonates and Children (SGUL-GARPEC) Project bloodstream infection data:** Penta-sponsored global surveillance network focusing on neonatal and paediatric antimicrobial resistance and the organisms causing blood stream infections.
- **Burden of Antibiotic Resistance in Neonates from Developing Societies (BARNARDS):** BARNARDS includes locations in Nigeria, South Africa, Pakistan, Rwanda, Bangladesh, Ethiopia and India from 2015 to 2018.
- **Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU). Children and adults with fever, inpatient admissions:** information from children and adults with fever who were admitted as inpatients between 1996 and 2019 to Mahosot Hospital, Vientiane, Laos. Microbial analysis was carried out by the Microbiology Laboratory at Mahosot Hospital.
- **Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), Kumasi, Ghana together with the Bernhard Nocht Institute for Tropical Medicine. Data on children and adults admitted in hospital with fever:** information from children and adults with fever admitted as inpatients at the Bernhard Nocht Institute for Tropical Medicine in Ghana between 2007 and 2015.
- **Vietnam Hospital for Tropical Diseases, Ho Chi Minh City. Hospital-acquired infections in ICU patients:** prospective observational study at the Oxford University Clinical Research Unit (OUCRU) in the

Ho Chi Minh City Hospital for Tropical Diseases, Vietnam from November 2014 to January 2016 to assess the ICU-acquired colonisation and infections among adult patients with more than 48 hours of ICU stay.

- **Medical Research Council (MRC) Unit The Gambia. Diagnostic antimicrobial susceptibility testing:** information on hospital admission and discharge, pathogens cultured, resistance susceptibility test and antibiotics prescribed between 2005 and 2015 from the MCR Unit The Gambia, now part of the London School of Hygiene and Tropical Medicine.
- **Cambodia Oxford Medical Research Unit (COMRU) and Angkor Hospital for Children (AHC). Suspected invasive bacterial infection hospitalisations:** reports children aged 0–21 years who were hospitalised with suspected invasive bacterial infection between 2015 and 2018.
- **Taiwan hospital-acquired infections and outcomes:** infectious disease surveillance linked to vital registration from Taiwan (province of China).
- **Childhood Acute Illness and Nutrition (CHAIN) Network antimicrobial resistance data:** CHAIN Network study informs on hospitalised children under 2 years old with acute illness in Bangladesh, Burkina Faso, Pakistan, Kenya, Malawi, and Uganda.
- **Lima, Peru Cayetano Heredia University (UPCH) antimicrobial resistance data:** data from UPCH hospital sites across Lima, Peru with discharge disposition for infectious pulmonary disease
- **Jordan King Abdulla University Hospital culture and sensitivity tests:** information on inpatients at the King Abdulla University Hospital in 2020 part of the Jordan University of Science and Technology.
- **Iran antimicrobial resistance in burn patients and identified in blood, cerebrospinal fluid, and urine cultures:** data from inpatients across different hospital sites in Iran between 2016 and 2020.
- **Dhaka, Bangladesh Bangabandhu Sheikh Mujib Medical University hospital inpatient data:** data from 201 inpatients in 2017 at the Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
- **Chiangrai Prachanukroh Hospital, Chiangrai Clinical Research Unit and Mahidol Oxford Tropical Medicine Research Unit:** data from inpatients with positive cultures at the Chiangrai Prachanukroh Hospital from 2017 to 2019.
- **KEMRI/US Army Medical Research Directorate**
- **Chennai, India Kanchi Kamakoti CHILDS Trust Medical Research Foundation (CTMRF) hospital inpatient data**

#### Section 2.4: Microbial data without outcome

Microbial data were also obtained from laboratories, which do not necessarily link to patients' hospital records nor information on their discharge disposition. These sources report specimen or site of infection, pathogens isolated, antimicrobial susceptibility tests, age and gender and other demographic characteristics. This information proved useful to inform pathogen distribution and prevalence of resistance component models and data processing, and modelling methods can be found in sections 6 and 7. Microbial data without outcome and diagnoses were obtained from the sources below.

- **SENTRY:** SENTRY Antimicrobial Surveillance Program established by JMI Labs in 1997. Sites are in the USA, Europe, Latin America, parts of Asia, and the Western Pacific
- **Germany National Point Prevalence Survey on Nosocomial Infections and Antibiotic Use (PPS HAI):** Point Prevalence Survey for 2016 data reporting the pathogen distribution for hospital-acquired infections.
- **Madagascar – Fondation Merieux:** data collected from inpatients with positive culture admitted in three hospital sites in Madagascar, funded by Fondation Merieux.
- **AMASS:** data collected in an automated tool by Oxford Tropical Network Research Units.
- **The European Surveillance System (TESSy):** managed by the European Centre for Disease Prevention and Control (ECDC), provided data from the following surveillance systems:
  - European Antimicrobial Resistance Surveillance Network (EARS-Net)
  - Food-and Waterborne Diseases and Zoonoses Surveillance Network.
  - Invasive Pneumococcal Disease Surveillance Network, including discharge disposition.
  - Gonococcal Antimicrobial Surveillance Programme.

- Healthcare Associated Infections Surveillance Network (ICU protocol), including discharge disposition.
- European Tuberculosis Surveillance Network
- European Surveillance of Antimicrobial Consumption Network

For the European Union/European Economic Area (EU/EEA), data were obtained from the European Surveillance System (TESSy) as provided by Austria, Belgium, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom, and released by the European Centre for Disease Prevention and Control (ECDC).

- **Pfizer ATLAS Programme:** the Antimicrobial Testing Leadership and Surveillance (ATLAS) database includes the Tigecycline Evaluation Surveillance Trial (TEST), the Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) and the International Network for Optimal Resistance Monitoring (INFORM) programs. The study spans in coverage across more than 70 countries between 2004 and 2017.
- **Malawi Queen Elizabeth Hospital microbiology tests of blood specimens:** microbiology tests of blood specimens from inpatients at the Queen Elizabeth Hospital in Malawi from 1998 to 2016, part of the Institute of Infection and Global Health, University of Liverpool in collaboration with the Malawi-Liverpool-Wellcome Trust and the Wellcome Trust Sanger Institute.
- **Central African Republic National Laboratory of Clinical Biology and Public Health:** data collected by the Laboratoire National de Biologie Clinique et de Sante Publique in Central African Republic between 2017 and 2020.
- **The Ethiopian AMR surveillance:** conducted from July 2018 to July 2020 across sentinel surveillance sites and the National AMR Surveillance Coordinating Centre for the Ethiopian Public Health Institute.
- **Lancet Labs:** data obtained from Lancet Laboratories, a network of private laboratories across different sites in Africa.
- **The Typhoid Fever Surveillance in Africa Program (TSAP):** was established by the International Vaccine Institute to obtain comparable incidence data on typhoid fever and invasive non-typhoidal *Salmonella* disease in Ghana, Burkina Faso, Ethiopia, Guinea Bissau, Kenya, Madagascar, Senegal, South Africa, Sudan, and Tanzania.
- **Invasive *Salmonella* infections at multiple surveillance sites in the Democratic Republic of the Congo study:** data published as part of the study on invasive *Salmonella* infections at multiple surveillance sites in the Democratic Republic of the Congo between 2011 and 2014.
- **Suva, Fiji Colonial War Memorial Hospital:** Information on sequential *S. aureus* and Enterobacterial bloodstream infections at the Colonial War Memorial Hospital (analysis by Monash University) in Suva, Fiji, between 21 July 2020 and 29 October 2020.
- **World Health Organization (WHO) Global Tuberculosis Programme**
- **Germany EARS-Net surveillance data 2017–2018**
- **WHO Meningitis surveillance:** sentinel hospital surveillance of suspected meningitis cases among children under 5 years old and positive cultures, provided by the World Health Organization (WHO) Global Rotavirus, Invasive Bacterial Vaccine Preventable Diseases Surveillance Network Collaboration from 2008 to 2020.
- **United States Active Bacterial Core Surveillance (ABCs) Reports:** case reports on healthcare-associated Infections and community interface infections from the Emerging Infections Program Network coordinated by the Center for Disease Control and Prevention (CDC).

### Section 2.5: Literature studies

We conducted literature searches to obtain input data for the following components in the analysis: maternal and neonatal sepsis aetiology, lower respiratory infections (LRIs) aetiology, urinary tract infections (UTIs) aetiology, skin infections aetiology, meningitis aetiology and case fatality, intra-abdominal infection aetiology, bone and joint infections aetiology, prevalence of resistance, relative risk and length of stay. Literature searches were performed on



PubMed using the following search strings, and extracted studies covered the time range 1980–2020. The search string for these searches can be found below. Literature was used in the case fatality ratio, pathogen distribution, prevalence of resistance and relative risk component models and data processing, and modelling methods can be found in sections 5–8. Literature studies were also used as input into the modelling of the antibiotic usage covariate.<sup>3</sup>

### *Section 2.5.1: Maternal sepsis, neonatal sepsis, and LRI aetiology*

Aetiology terms, combined with OR:

- Infection (Infect\*)
- Microbiology (Microbiolog\*)
- Aetiology (Aetiolog\*)
- Etiology (Etiolog\*)
- Virology (Virolog\*)
- Bacteriology (Bacteriolog\*)
- Fungus (fung\*)

AND

Syndrome terms, combined with OR:

Maternal Sepsis

- puerperal sepsis (puerper\* sepsis)
- maternal sepsis (matern\* sepsis)
- puerperal septicaemia (puerper\* septicaemia, American spelling too - septicemia)
- maternal septicaemia (matern\* septicaemia, American spelling too - septicemia)
- puerperal infection (puerper\* infection)
- maternal infection (matern\* infection)
- puerperal bacteraemia (puerper\* bacteraemia, American spelling too - bacteremia)
- maternal bacteraemia (matern\* bacteraemia, American spelling too - bacteremia)

Neonatal Sepsis

- Neonatal sepsis (Neonat\* sepsis within 3 or 5 words of each other)
- Neonatal septicaemia (Neonat\* septicaemia within 3 or 5 words of each other, American spelling too - septicemia)
- Infant sepsis (Infant\* sepsis)
- Infant septicaemia (Infant\* septicaemia, American spelling too - septicemia)
- Neonatal bacteraemia (Neonat\* bacteraemia, American spelling too - bacteremia)
- Infant bacteraemia (Infant\* bacteraemia, American spelling too - bacteremia)

Lower respiratory infections

- LRI
- Lower respiratory infection
- LRTI
- Lower respiratory tract infection
- Pneumonia

### *Section 2.5.2: Urinary tract infections aetiology*

("complicated"[Title/Abstract] OR "uncomplicated"[Title/Abstract]) AND (("Cystitis/etiology"[majr:noexp] OR "Cystitis/microbiology"[majr:noexp]) OR ("Pyelonephritis/etiology"[majr:noexp] OR "Pyelonephritis/microbiology"[majr:noexp]) OR ("Urinary Tract Infections/etiology"[majr:noexp] OR "Urinary Tract Infections/microbiology"[majr:noexp])) OR ("Urinary tract infections"[tiab] AND ("etiology"[tiab] OR "microbiology"[tiab]))

### *Section 2.5.3: Skin infections aetiology*

(( "Cellulitis/epidemiology"[majr:noexp] OR "Cellulitis/etiology"[majr:noexp] OR "Cellulitis/microbiology"[majr:noexp]) OR ("Pyoderma/epidemiology"[majr:noexp] OR "Pyoderma/etiology"[majr:noexp] OR "Pyoderma/microbiology"[majr:noexp]) OR

"Pressure Ulcer/microbiology"[majr:noexp])

*Section 2.5.4: Intra-abdominal infection aetiology*

(( "Peritonitis/epidemiology"[majr:noexp] OR "Peritonitis /etiology"[majr:noexp] OR "Peritonitis /microbiology"[majr:noexp] ) OR ( "Intraabdominal infections/epidemiology"[majr:noexp] OR "Intraabdominal infections /etiology"[majr:noexp] OR "Intraabdominal infections /microbiology"[majr:noexp]) OR ( "abdominal abscess/epidemiology"[majr:noexp] OR " abdominal abscess /etiology"[majr:noexp] OR "abdominal abscess/microbiology"[majr:noexp]))

*Section 2.5.5: Bone and joint infections aetiology*

("Osteomyelitis/etiology"[majr:noexp] OR "Osteomyelitis/microbiology"[majr:noexp] NOT 'chronic') OR ("Arthritis, infectious/etiology"[majr:noexp] OR "Arthritis, infectious/microbiology"[majr:noexp] NOT 'lyme')

*Section 2.5.6: Meningitis infection aetiology*

((meningitis[title]) AND (1990/05/01[PDat] : 2018/12/31[PDat]) AND ((etiolog\*[title/abstract]) AND Humans[MeSH Terms])

*Section 2.5.7: Relative risk studies for specific drug-bug combinations*

("Acinetobacter baumannii"[MeSH Terms] AND "carbapenem resistance"[All Fields]) OR ("Acinetobacter baumannii"[ MeSH Terms] AND "carbapenem resistant"[All Fields])

('Escherichia coli'[MeSH Terms] AND 'carbapenem resistance'[All Fields]) OR ('Escherichia coli'[MeSH Terms] AND 'carbapenem resistant'[All Fields])

('Escherichia coli'[MeSH Terms] AND 'fluoroquinolone resistance'[All Fields]) OR ('Escherichia coli'[MeSH Terms] AND 'fluoroquinolone resistant'[All Fields])

('Escherichia coli'[MeSH Terms] AND 'third generation cephalosporin'[All Fields]) OR ('Escherichia coli'[MeSH Terms] AND ESBL OR extended-spectrum beta lactamase'[All Fields])

('Klebsiella pneumoniae'[MeSH Terms] AND 'third generation cephalosporin'[All Fields]) OR ('Klebsiella pneumoniae'[MeSH Terms] AND 'ESBL OR extended-spectrum beta lactamase'[All Fields])

('Klebsiella pneumoniae'[MeSH Terms] AND 'carbapenem resistance'[All Fields]) OR ('Klebsiella pneumoniae'[MeSH Terms] AND 'carbapenem resistant'[All Fields])

('Streptococcus pneumoniae'[MeSH Terms] AND 'penicillin resistance'[All Fields]) OR ('Streptococcus pneumoniae'[MeSH Terms] AND 'penicillin resistant'[All Fields])

('Pseudomonas aeruginosa'[MeSH Terms] AND 'carbapenem resistant'[All Fields] AND 'mortality' [MeSH Terms]) OR ('Pseudomonas aeruginosa'[MeSH Terms] AND 'carbapenem resistant' AND 'mortality' [All Fields])

('Enterococcus faec\*[MeSH Terms] AND 'vancomycin-resistant'[All Fields])

("haemophilus influenzae"[MeSH Terms] AND ("penicillin resistance"[MeSH Terms] OR ("penicillin"[All Fields] AND "resistance"[All Fields]) OR "penicillin resistance"[All Fields])) AND ("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms])

("streptococcus agalactiae"[MeSH Terms] AND ("azithromycin resistance"[MeSH Terms] OR ("azithromycin "[All Fields] AND "resistance"[All Fields]) OR " azithromycin resistance"[All Fields] OR "penicillin resistance"[MeSH Terms] OR ("penicillin"[All Fields] AND "resistance"[All Fields]) OR "penicillin resistance"[All Fields] OR "clindamycin resistance"[MeSH Terms] OR ("clindamycin "[All Fields] AND "resistance"[All Fields]) OR "erythromycin resistance"[All Fields] OR "erythromycin resistance"[MeSH Terms] OR ("erythromycin"[All Fields] AND "resistance"[All Fields]) OR "clindamycin resistance"[All Fields]) AND ("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms])

### *Section 2.5.8: Prevalence of resistance for specific organisms*

Medical Subject Heading (MeSH) terms with free text terms in the title and abstract fields for *Escherichia coli*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae* and *Staphylococcus aureus* with the terms for antimicrobial drug resistance (resistan\*, suscept\*, surveil\*, etc), limited from 1990 up to the search date. The search was undertaken on MEDLINE, Ovid Embase, Global Health, Cochrane Library.

Medical Subject Headings (MeSH) and free text terms for the pathogens of interest (e.g. *S. Typhi*, *S. Paratyphi A*, enteric fever) with terms for antimicrobial resistance (e.g. resistan\*, suscept\*, surveil\*). The search was undertaken on MEDLINE, Ovid Embase, Global Health, Cochrane Library, Scopus, Web of Science-Core Collection and LILACS regional WHO database.

Medical Subject Heading (MeSH) terms with free text terms in the title and abstract fields for non-typhoidal *Salmonella* or *Salmonellosis* (non-typhi or nontyph or non-typh *Salmonel*...) with the terms for antimicrobial drug resistance (resistan\*, suscept\*, surveil\*, etc) and invasive (blood stream infection, septicaemia etc), limited from 1990 up to the search date. The search was undertaken on MEDLINE, Ovid Embase, Global Health, Cochrane Library, Scopus, Web of Science-Core Collection and LILACS regional WHO.

Medical Subject Heading (MeSH) terms with free text terms in the title and abstract fields for *Shigella* or *Shigellosis* with the terms for antimicrobial drug resistance (resistan\*, suscept\*, surveil\*, etc), limited from 1990 up to the search date. The search was undertaken on MEDLINE, Ovid Embase, Global Health, Cochrane Library, Scopus, Web of Science-Core Collection and LILACS regional WHO database.

Medical Subject Heading (MeSH) terms with free text terms in the title and abstract fields for *Neisseria gonorrhoeae*, with the terms for antimicrobial drug resistance (resistan\*, suscept\*, surveil\*, etc), MDR, XDR, limited from 1990 up to the search date. The search was undertaken on MEDLINE, Ovid Embase, Global Health, Cochrane Library, Scopus, Web of Science-Core Collection and LILACS regional WHO database.

### **Section 2.6: Single drug-resistance profiles**

Data sources used to inform single drug resistance profiles were obtained from surveillance networks and aggregated reports where the full antibiogram of a pathogen for all drugs tested is not reported. Data from these sources generally do not include any individual records linked to a patient outcome. They are used to inform current and past resistance trends for specific pathogen–drug combinations. Single drug resistance data were used in the prevalence of resistance component model and data processing, and modelling methods can be found in section 7. The data sources for single drug resistance profiles were obtained from the sources below.

- **GLASS:** Global Antimicrobial Resistance Surveillance System by WHO
- **CAESAR:** Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) is a network of national AMR surveillance systems and includes 19 countries in the WHO European Region that are not part of EARS-Net.
- **Japan Nosocomial Infections Surveillance (JANIS):** is a national surveillance program designed to provide basic information on the incidence and prevalence of nosocomial infections and antimicrobial-resistant bacteria in Japanese medical settings. Data available from 2013.
- **NARMS:** The National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) is a collaboration of agencies within The U.S. Department of Health and Human Services (HHS) (FDA and CDC) and the U.S. Department of Agriculture (USDA). It tracks enteric bacteria and selected animal pathogens and their resistance to antimicrobials, and data is available from 1997 onwards.
- **SOAR:** Survey on Antibiotic Resistance (SOAR) sponsored by GSK.
- **ReLAVRA and SIREVA:** The Latin American Network for Antimicrobial Resistance Surveillance (ReLAVRA by its Spanish acronym) and the Serotype and Antimicrobial Resistance Surveillance Program (SIREVA by its English acronym) which are coordinated by the Pan-American Health Organization (WHO/PAHO)
- **SMART:** Study for Monitoring Antimicrobial Resistance Trends which monitors complicated intra-abdominal infections (cIAIs), complicated urinary tract infections (cUTIs) and respiratory infections worldwide, funded by Merck & Co.

- **South Africa National Institute for Communicable Diseases (NICD):** Aggregated data from South Africa's AMR surveillance in public healthcare centres which is submitted to the GLASS.
- **Surveillance on Invasive Pulmonary Disease by the New Zealand Public Health Action.**
- **Surveillance of Antimicrobial Resistance in Hospital Acquired Infection by Kendokteran Laboratorium, Indonesia**
- **Alliance for the Prudent Use of Antibiotics (APUA), Nepal**
- **Hospital Civil de Guadalajara Fray Antonio Alcalde, Mexico**
- **Australian Group on Antimicrobial Resistance (AGAR)**
- **Antimicrobial Resistance Surveillance Program (ARSP)**
- **Antimicrobial Use and Resistance in Australia (AURA)**
- **Australian Government Department of Health**
- **Canadian Antimicrobial Resistance Surveillance System**
- **The China Antimicrobial Surveillance Network**
- **National Surveillance of Antimicrobial Resistance, Malaysia**
- **Pakistan Antimicrobial Resistant Network**

### Section 2.7: Pharmaceutical sales and antibiotic use

These data were used to model the antibiotic use covariate, which was used as an input in the prevalence of resistance models; full details on this model can be found in section 7. Pharmaceutical sales and antibiotic use data were obtained from the following sources.

- **IMS Health and Quintiles (IQVIA):** antibiotic sales data for 77 countries between 2000 and 2018..
- **Demographic Health Surveys (DH):** households health surveys carried out across more than 90 countries, they include questions on antibiotic usage among those who had cough or diarrhoea in a period of two weeks before the survey.
- **Multiple Indicators Cluster Surveys (MICS):** households health surveys carried out across more than 90 countries, they include questions on antibiotic usage among those who had cough or diarrhoea in a period of two weeks before the survey.
- **European Surveillance of Antimicrobial Consumption Network (ESAC-NET):** antibiotic consumption data for 5 countries over 101 country-years
- **WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation:** report on antibiotic consumption for 21 countries over 21 country-years

### Section 2.8: Mortality surveillance

Mortality surveillance data were used in the sepsis, syndrome, and pathogen distribution models; full details on these models can be found in sections 4 and 6. Mortality surveillance data came from the source listed below.

- **Child Health and Mortality Prevention Surveillance (CHAMPS):** Under-5 mortality surveillance sites in South Africa, Mali, Bangladesh, Kenya, Ethiopia, and Mozambique. Researchers use minimally invasive tissue sampling (MITS) to gather information about pathogens involved and are able to discern a more accurate cause of death.

### Section 2.9: Linkage (mortality only)

Linkage data were used in sepsis and infectious syndrome models; full details on these models can be found in section 4. Mortality-only linkage data include:

- **Italy Friuli-Venezia Giulia MCoD data**
- **New Zealand linked national minimum dataset to mortality collection data**

### **Section 3: Summary of GBD 2019 estimation process**

A comprehensive description of data sources, data quality, statistical modelling and analyses for GBD 2019 have been reported elsewhere.<sup>1</sup> A brief summary of the fatal and non-fatal estimation processes are briefly summarised below.

#### **Section 3.1: GBD 2019 cause of death estimation process**

The overarching steps for the fatal estimation process for each age, sex, location, and year are to first estimate all-cause mortality rates, then calculate cause-specific mortality rates, and finally scale the cause-specific mortality rates to the all-cause mortality rates for internal consistency. First, all-cause mortality is estimated using 7417 sources as data inputs for under-5 mortality estimation and 7355 sources as data inputs for adult mortality estimation. ST-GPR was used to produce estimates of HIV-free mortality rate for every location-year after adjusting for completeness and other known biases in the input data. Added to this HIV-free mortality rate are the HIV-specific mortality rate and deaths from fatal discontinuities, or shocks, which are events that are stochastic in nature and cannot be modelled, such as natural disasters and conflicts. GBD then estimated the cause-specific mortality rates of 301 diseases and injuries. This cause of death analysis utilizes 19 354 sources covering 2525 country years in the cause of death (CoD) database. There are eight types of data sources in the CoD database: vital registration, verbal autopsy,<sup>4</sup> cancer registry, police records, sibling history, surveillance, survey/census, and minimally invasive tissue sampling (MITS) diagnoses. VR is considered the most comprehensive source of cause of death data, but less than half the world's population has deaths captured in a VR system (appendix figure S6), so causes of death statistics are supplemented with other data types. These various data sources are largely ICD coded causes of death and use heterogeneous ICD versions so are standardised to GBD causes of death. Once standardised and adjusted for known biases due to ICD classification changes,<sup>5</sup> garbage coding,<sup>5-7</sup> HIV correction,<sup>8</sup> stochastic noise,<sup>1</sup> and completeness,<sup>9</sup> causes of death are modelled using CODEm<sup>10</sup> to determine the cause fraction for each underlying cause of death by age, sex, year, and location. CODEm provides an ensemble prediction based on a combination of candidate models that vary across outcome and covariate combinations chosen for out-of-sample predictive performance. Because each cause is modelled independently, it is possible the sum of these models will not equal the all-cause mortality estimates, so cause-specific results are run through the CoDCorrect process to make cause-specific and all-cause mortality estimates internally consistent. This process rescales cause-specific estimates to the all-cause mortality envelope.

#### **Section 3.2: GBD 2019 non-fatal estimation process**

Non-fatal health outcomes are estimated using DisMod-MR 2.1, a Bayesian-regression analytical tool that synthesises various data inputs to produce estimates of disease incidence and prevalence. The data used for this analysis include systematic reviews done at the Institute of Health Metrics and Evaluation (IHME), data from household surveys including the demographic and health surveys, multiple indicator cluster surveys, living standards measurement surveys, reproductive health surveys, administrative claims data, inpatient hospital discharge records, outpatient hospital data, disease registries, programme-level data on disease burden from government agencies, surveillance system data on disease burden, and sources suggested to us by in-country collaborators and surveys identified in major multinational survey data catalogues such as the WHO Central data catalog. 51 272 sources were used for this analysis, 31 499 reporting incidence and 19 773 reporting prevalence. Data from these sources are extracted. Pre-modelling bias adjustments are made using crosswalking to account for various sources of bias, such as heterogeneous case definitions and methods of measurement. The pre-modelling bias adjustments are made using the MR-BRT environment, a meta-regression tool that allows for Bayesian priors, regularization, and trimming and has been described in greater detail previously.<sup>11</sup> Using these bias-adjusted data an estimate of prevalence and incidence for each cause is produced using the DisMod-MR 2.1 modelling framework. DisMod-MR 2.1 accepts all available data on mortality, incidence, prevalence, and remission and uses a compartmental model to enforce consistency between all quantities.

## Section 4: Deaths where infection plays a role and infectious syndrome estimation

### Section 4.1: Input data

#### Section 4.1.1: Multiple causes of death

MCoD data are individual-based records that provide underlying causes of death and two or more intermediate causes in the chain of death. Additionally, each record includes age, sex, residence, and the date of death.

#### Section 4.1.2: Hospital record with multiple diagnoses and discharge status of death

This type of data is an individual-based hospital record of a patient that provides the main diagnosis and two or more additional diagnoses. Additionally, each record includes age, sex, residence, date of admission, date of discharge, and outcome (dead or alive). Only hospital discharges with discharge status of death were used in this component model, since we aimed to estimate the fraction of deaths that involve infection and the infectious syndrome distribution of those deaths.

#### Section 4.1.3: Linkage data

Linkage data are generated using probabilistic methods in a defined population that link individual-based hospital data to individual-based MCoD data. Linkage data offer a wider dataset that includes main diagnosis, other diagnoses, underlying cause of death, and intermediate causes of death in the chain.

#### Section 4.1.4: Mortality surveillance (Child Health and Mortality Prevention Surveillance [CHAMPS])

The CHAMPS network tracks the causes of under-5 mortality and stillbirths at sites in sub-Saharan Africa and south Asia through epidemiological surveillance of under-5 deaths and stillbirths utilising minimally invasive tissue sampling (MITS), laboratory diagnostics including conventional and advanced histopathology and molecular screening of various pathogens, verbal autopsy, and available clinical and demographic data.

Table 4.1.5: Input different data point for calculation of fraction of death by sepsis in different underlying causes

Location	Data type	Years	Year range	Deaths
United States	MCoD	38	1980–2017	82,453,798
	Hospital data with fatal outcome	31	1980–2010	2,028,371
	Linkage data			
Brazil	MCoD	19	1999–2017	16,930,050
	Hospital data with fatal outcome	2	2015–2016	294,461
	Linkage data			
Italy	MCoD	13	2003–2015	7,640,383
	Hospital data with fatal outcome	12	2005–2016	2,385,430
	Linkage data	16	2003–2018	112,555
South Africa	MCoD	20	1997–2016	4,696,348
	Hospital data with fatal outcome			
	Linkage data			
Mexico	MCoD	8	2009–2016	4,336,713
	Hospital data with fatal outcome	7	2003–2009	168,582
	Linkage data			
Colombia	MCoD	20	1998–2017	3,624,771
	Hospital data with fatal outcome			
	Linkage data			
Taiwan (province of China)	MCoD	10	2007–2016	1,189,309
	Hospital data with fatal outcome			
	Linkage data			
Austria	MCoD			



	Hospital data with fatal outcome	14	2001–2014	461,538
	Linkage data			
New Zealand	MCoD			
	Hospital data with fatal outcome	18	2000–2017	169,454
	Linkage data	11	2000–2010	151,455
Canada	MCoD			
	Hospital data with fatal outcome	16	1994–2009	38,405
	Linkage data			
CHAMPS Surveillance Sites	MITs	3	2017–2019	870
Total	MCoD	128	1980–2017	120,871,372
	Hospital data with fatal outcome	100	1980–2017	5,546,241
	Linkage data	27	2000–2018	264,010
	MITs	3	2017–2019	870

## Section 4.2: Data processing

Data for the USA, Brazil, Italy, South Africa, and Mexico were extracted at the subnational level by GBD 2019 age groups, sex, year, and causes of death and/or diagnoses, while data for the remaining countries and territories were analysed at the national level. This allowed us to expand the location-years of data that we had for each Socio-demographic Index (SDI)<sup>12</sup> value.

## Section 4.3: Mapping the data

Prepared data were mapped to GBD causes. The GBD cause list is a mutually exclusive and collectively exhaustive list of diseases and injuries. The GBD cause list is organised hierarchically to accommodate different purposes and needs of various users. The first two levels aggregate causes into general groupings. At Level 1, there are three cause groups: communicable, maternal, neonatal, and nutritional diseases (Group 1 diseases); non-communicable diseases (Group 2); and injuries (Group 3). These Level 1 aggregates are subdivided at Level 2 of the hierarchy into 22 cause groupings (eg, neonatal disorders, neurological disorders, and transport injuries). The disaggregation into Levels 3 and 4 contains the finest level of detail for causes captured in GBD 2019. See section 14, table S1 for the full GBD cause hierarchy by level.

The underlying cause of death or main diagnosis for each record in the data was mapped to a GBD cause. After the mapping of underlying cause, we used the GBD 2019 garbage code redistribution algorithm (see appendix 1, section 2.4 in Vos et al.<sup>1</sup>) to ensure that all deaths had a plausible and specific underlying cause of death. The redistribution of garbage codes for underlying causes of death followed the same age and sex restrictions as GBD 2019. We did not redistribute garbage codes in the chain causes because the concept of a garbage code applies only to plausible underlying cause of death (see Rudd et al.<sup>13</sup> and appendix 1, section 2.5 in Vos et al.<sup>1</sup>).

## Section 4.4: Intermediate cause and infectious syndrome mapping hierarchy

### Section 4.4.1: Intermediate cause mapping

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. Infectious syndromes can be both underlying causes of death and intermediate causes of death.

For mapping underlying and intermediate causes of death and hospital diagnoses to sepsis and infectious syndromes, we designed a new map, called “AMR, sepsis, and infectious syndrome map”. This map is a list of mutually exclusive and collectively exhaustive infectious syndromes that we divided into four levels to form the infectious syndrome hierarchy.

Each level of infectious syndrome is mutually exclusive and collectively exhaustive. Furthermore, the infectious syndrome hierarchy is internally consistent across any metric (eg, number, cause fraction)—aggregating across

Level 3 syndromes gives us Level 2 syndromes, aggregating the Level 2 syndromes gives us Level 1 syndromes, and the total of Level 1 syndromes is equal to the value of sepsis (figure 4.4.2.1).

Level 0: All International Classification of Diseases 9<sup>th</sup> (ICD-9) or 10<sup>th</sup> revision (ICD-10) coded deaths divided into three groups:

- Explicit sepsis (A40, R65.2 in ICD-10 and 039 in ICD-9): Any death has specific ICD code for sepsis in the MCoD chain or hospital diagnoses was considered explicit sepsis<sup>13</sup>
- Implicit sepsis: Any death that has an infectious disease code in the underlying cause or cause chain and a specific organ dysfunction code was considered implicit sepsis
- Non-sepsis: Any death that does not meet either of the two above criteria (section 14, tables S2, S3)

Of the estimated infection-related deaths with explicit sepsis or implicit sepsis and infectious diseases, 59.4% occur with communicable, maternal, neonatal, and nutritional underlying causes of death. 38.9% infection related deaths occur with non-communicable disease as the underlying cause of death, and 1.7% occur with injuries as the underlying cause of death.

Level 1: All implicit and explicit sepsis deaths were divided into 12 Level 1 infectious syndromes and an “other” category (table 4.4.1.1).

Table 4.4.1.1: Level 1 of infectious syndromes

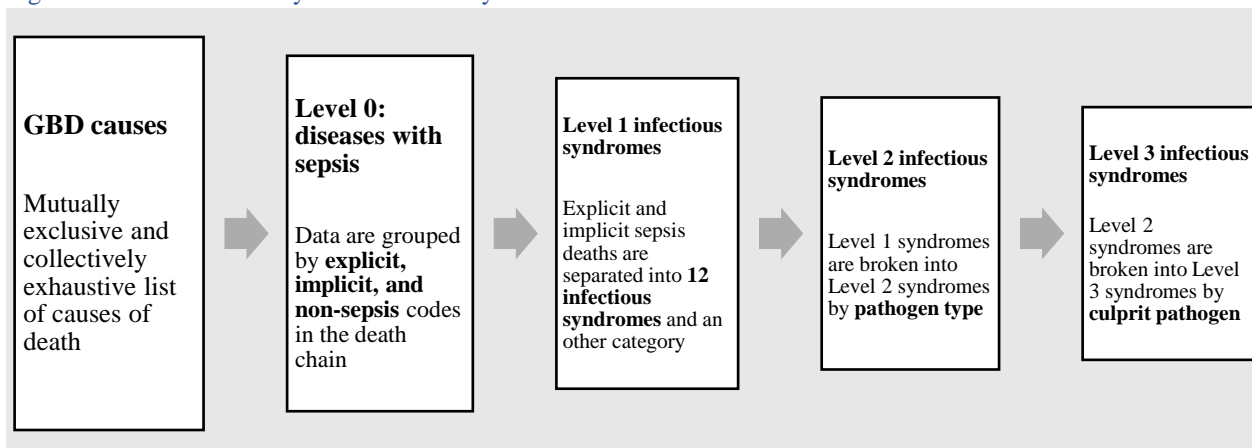
	<b>Infectious syndrome</b>
1	Bacterial infections of the skin and subcutaneous systems
2	Bloodstream infections
3	Gonorrhoea and chlamydia
4	Diarrhoea
5	Endocarditis and other cardiac infections
6	Infections of bones, joints, and related organs
7	Lower respiratory infections and all related infections in the thorax
8	Meningitis and other bacterial central nervous system infections
9	Peritoneal and intra-abdominal infections
10	Tuberculosis
11	Typhoid, paratyphoid, and invasive non-typhoidal Salmonella
12	Urinary tract infections and pyelonephritis
13	Other infections

Level 2: Each Level 1 infectious syndrome was divided into Level 2 infectious syndromes based on the pathogen type (eg, bacterial, fungal, viral) causing the infection. Examples include specified bacterial, unspecified bacterial, fungal, viral, and unspecified pathogen.

Level 3: Each specified bacterial infectious syndrome in Level 2 was divided to Level 3 infectious syndromes by the bacterium causing infection. Table S3 (section 14) shows this list and bacterial hierarchy.



Figure 4.4.2.1. Infectious syndrome hierarchy



### Section 4.4.3: Informative ranking

Due to our data often having multiple diagnoses associated with each record, a single case of sepsis could potentially map to multiple candidate infectious syndromes. Because multiple infectious syndrome assignments pose a risk of double counting, we employed an informative ranking hierarchy. The informative ranking allowed us to determine the infectious syndrome that provided the most information on the culprit pathogen. The goal of this hierarchy was to produce the most accurate pathogen burden estimate such that when there were multiple infectious syndromes, we prioritised the syndrome with the most distinctive distribution. For example, bloodstream infections (BSIs) are common infections in sepsis but there is often an earlier source of the infection such as a UTI, cellulitis, or LRI, and each has a unique pathogen distribution that provides more information than the distribution of BSI. In the event that a patient record reflected both BSI and LRI, we would assign the infectious syndrome based on the pathogen distribution that would be the most proximal aetiologic syndrome, LRI (see table 4.4.3.1).

Table 4.4.3.1. Level 1 Infectious syndrome informative ranking hierarchy

Organised from most informative (top) to least (bottom).

Level 1 infectious syndrome informative ranking hierarchy
Meningitis and other bacterial central nervous system infections
Endocarditis and other 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 bone, joints, and related organs
Diarrhoea
Urinary tract infections and pyelonephritis
Other infections
Bloodstream infections

### Section 4.4.4: Two modelling pathways

After mapping the underlying and chain causes of death, our database went through two separate modelling pathways. The first model estimated the fraction of deaths that are sepsis-related in each GBD cause; these sepsis-related deaths for non-infectious GBD causes were combined with GBD deaths for infectious causes to create the total envelope of all deaths where infection plays a role. The second pathway estimated each infectious syndrome as a fraction of sepsis-related mortality in each GBD cause. In the last step of infectious syndrome estimation, the fractions of sepsis by Level 1 infectious syndromes were squeezed to sum to one so as to not exceed the sepsis mortality envelope and multiplied by the sepsis estimate in each GBD cause by country and territory, age, and sex in

2019.

## Section 4.5: First pathway: deaths where infection plays a role

### Section 4.5.1: Sepsis model

We used a mixed-effects binomial logistic regression to model the logit of the fraction of sepsis-related deaths by GBD cause-age-sex-location, consistent with the modelling approach used by Rudd et al.<sup>13</sup> Sex and Healthcare Access and Quality Index (HAQ Index)<sup>14</sup> were included as covariates and a nested random effect on underlying cause of death was included. A separate model was run for each GBD 2019 age group (0–6, 7–27, 28–364 [days], 1–4, 5–9, 10–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, 95+ [years]):

$$\text{sepsis related deaths} \sim B(\text{total deaths}, \text{sepsis fraction}) \quad (4.5.1.1)$$

$$\text{logit}(\text{sepsis fraction}) = \beta_0 + \beta_1 * \text{HAQ Index} + \beta_2 * \text{sex} + \pi_{\text{level } 1, \text{level } 2}$$

Where  $\pi_{\text{level } 1, \text{level } 2}$  is a nested random effect on underlying cause of death. The nested random-effect's structure in the model on underlying cause of death allowed the prediction of sepsis fractions where data were limited by borrowing information from diseases within the same group. There were 22 groups of underlying causes of death, each categorised by physiological relatedness. We produced our predictions and uncertainty intervals (UIs) by generating 1000 draws from the normal distribution of the fixed coefficients, separately for each GBD location, age group, sex, and cause in 2019. The means of our results were used for the point estimates and the 95% UIs were delineated using the 2.5<sup>th</sup> and 97.5<sup>th</sup> percentiles of the draws. Uncertainty is attributable to sample size variability between data sources, data availability, and model specifications.

All underlying causes of death that are infectious diseases were included in the model; however, for these causes we used the GBD death estimates rather than the modelled sepsis estimate, since infection inherently plays a role in these deaths even if the pathway doesn't include sepsis. These causes and their associated infectious syndromes are listed in table 4.5.1.1.

Table 4.5.1.1. Underlying causes that are infectious diseases and their corresponding syndromes

Cause name	Infectious syndrome
Appendicitis	Peritoneal and intra-abdominal infections
Bacterial skin diseases	Bacterial infections of the skin and subcutaneous systems
Chlamydial infection	Gonorrhoea and chlamydia
Diarrhoeal diseases	Diarrhoea
Endocarditis	Endocarditis and other cardiac infections
Gonococcal infection	Gonorrhoea and chlamydia
Invasive non-typhoidal Salmonella	Typhoid, paratyphoid, and invasive non-typhoidal Salmonella
Lower respiratory infections	Lower respiratory infections and all related infections in the thorax
Maternal sepsis and other maternal infections	Bloodstream infections
Meningitis	Meningitis and other bacterial central nervous system infections
Neonatal sepsis and other neonatal infections	Bloodstream infections
Paratyphoid fever	Typhoid, paratyphoid, and invasive non-typhoidal Salmonella
Tuberculosis	Tuberculosis
Typhoid fever	Typhoid, paratyphoid, and invasive non-typhoidal Salmonella
Upper respiratory infections	Lower respiratory infections and all related infections in the thorax
Urinary tract infections and interstitial nephritis	Urinary tract infections and pyelonephritis

For all other causes, we calculated the number of sepsis-related deaths in 2019 by multiplying our predictions of cause-, age group-, sex-, year-, and location-specific sepsis fractions by GBD 2019 death estimates. Finally, we aggregated our results to arrive at regional and global sepsis-related mortality in non-infectious underlying causes of death, which we combined with the GBD infectious disease deaths estimates to create the mortality envelope of all deaths related to infection.

For transparency, histograms of the available input data by HAQ Index are shown below. MCoD input data is used to estimate the proportion of non-infectious disease that involves sepsis, while the GBD mortality data for Group 1

causes (communicable, maternal, neonatal, and nutritional diseases) is inclusive and representative of the input data used to estimate mortality associated with primary infection underlying cause.

Figure 4.5.1.1. MCoD input data by HAQ Index

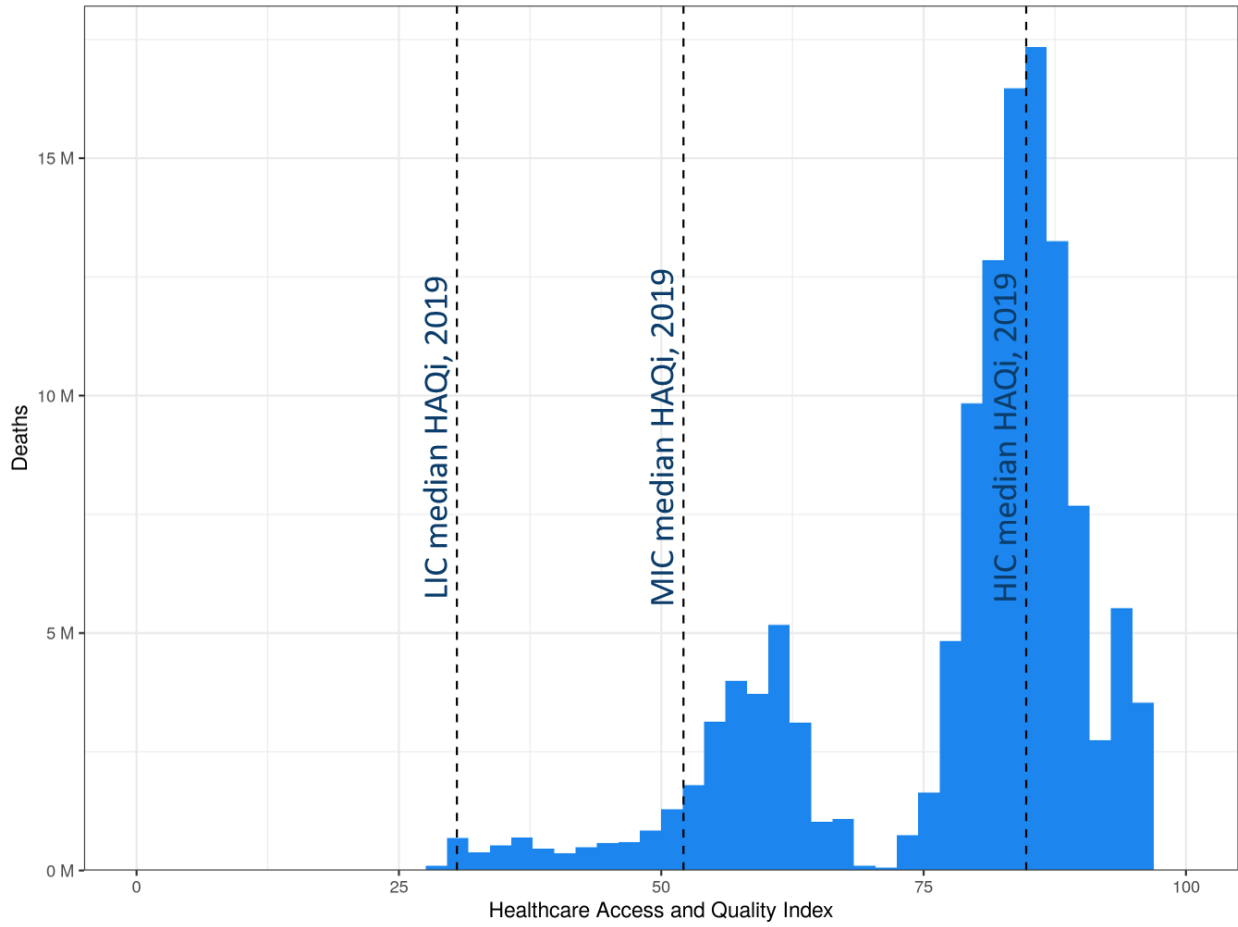
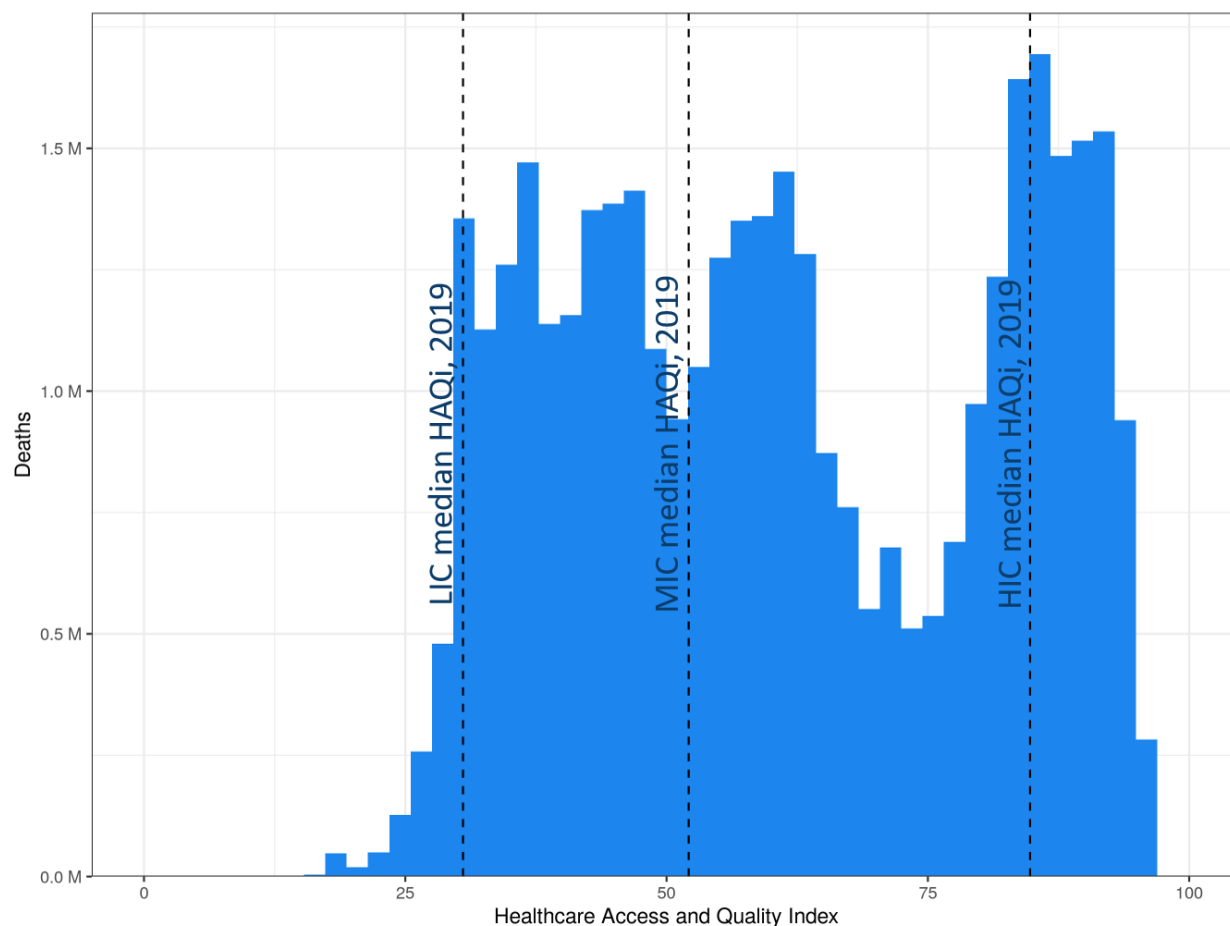


Figure 4.5.1.2. GBD mortality input data for Group 1 (communicable, maternal, neonatal, and nutritional diseases) by HAQ Index



HIC = high-income country, LIC = low-income country, MIC = middle-income country

#### Section 4.6: Second pathway: fraction of deaths where infection plays a role by infectious syndrome in each GBD cause

We used a mixed-effects binomial logistic regression to model the logit of the infectious syndrome fraction of sepsis-related mortality by GBD cause. The model covariates varied by infectious syndrome (table 4.6.1). All models included HAQ Index as a covariate and most included a summary exposure value (SEV) scalar calculated for GBD 2019.

The pathogen distribution for hospital-acquired infections (HAIs) and community-acquired infections (CAIs) differs markedly for some infectious syndromes.<sup>15-20</sup> To more accurately estimate the burden of pathogens responsible for infection, we separated infectious syndromes into hospital-acquired and community-acquired for LRI+ and UTI. For all ICD-coded administrative datasets (hospital discharge, MCoD, and linkage), we assumed that an infection was community-acquired if it was the primary diagnosis or underlying cause of death. Similarly, an infection was considered hospital-acquired if it was not the primary diagnosis or underlying cause of death. We recognise that this is a strong assumption that will not always be correct; however, there is no established method for determining HAI versus CAI in administrative data.<sup>21,22</sup> We considered it to be more important to estimate hospital- and community-acquired separately to account for their distinct pathogen distributions despite the strong assumptions involved. We present the fraction of all infectious syndrome deaths in 2019 that our model predicted to be hospital-acquired for LRI+ and UTI in table 4.6.2 for transparency.

Table 4.6.1: Infectious syndrome model covariates and age groups

Infectious syndrome	Covariates	Age groups modelled
Bloodstream infections	HAQ Index <sup>14</sup> Sex SEV scalar of maternal sepsis <sup>23</sup> SEV scalar of neonatal sepsis <sup>23</sup>	GBD 2019 age groups
Infections of bone, joints, and related organs	HAQ Index Sex	0–9, 10–14, 15–19, 20–24, 25–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, 95+
Endocarditis and other cardiac infections	HAQ Index Sex SEV scalar of age-standardised endocarditis <sup>23</sup>	GBD 2019 age groups
Meningitis and other bacterial central nervous system infections	HAQ Index Sex SEV scalar of age-standardised meningitis <sup>23</sup>	GBD 2019 age groups
Diarrhoea	HAQ Index Sex SEV scalar of age-standardised diarrhoea <sup>23</sup>	GBD 2019 age groups
Other infections	HAQ Index Sex	GBD 2019 age groups
Peritoneal and intra-abdominal infections	HAQ Index Sex	GBD 2019 age groups
CAI lower respiratory infections and all related infections in the thorax	HAQ Index Sex SEV scalar of age-standardised LRIs <sup>23</sup>	Neonatal, Post neonatal–5, 5–69, 70+
HAI lower respiratory infections and all related infections in the thorax	HAQ Index Sex SEV scalar of age-standardised LRIs	Neonatal, Post neonatal–5, 5–69, 70+
Bacterial infections of the skin and subcutaneous systems	HAQ Index Sex SEV scalar of age-standardised no access to handwashing facility <sup>23</sup>	GBD 2019 age groups
CAI urinary tract infections and pyelonephritis	HAQ Index Sex SEV scalar of age-standardised no access to handwashing facility	0–39, 40+
HAI urinary tract infections and pyelonephritis	HAQ Index Sex SEV scalar of age-standardised no access to handwashing facility	0–39, 40+

CAI=community-acquired infection. HAI=hospital-acquired infection. HAQ Index=Healthcare Access and Quality Index. LRI=lower respiratory infection. SEV=summary exposure value. SEVs are a risk-weighted prevalence calculated based on exposure, from 0, where the entire population (among the age groups where exposure is possible) is exposed at the minimum risk level, to 100, where the entire population is exposed at the maximum risk exposure level.

Table 4.6.2: Model predictions for proportion of deaths in 2019 that were hospital-acquired by GBD super-region and infectious syndrome

Infectious syndrome	Super-region	Proportion (95% UI)
Lower respiratory infections and all related infections in the thorax	Global	17.4% (13.1 - 22.4)
	Southeast Asia, east Asia, and Oceania	23.3% (18.0 - 28.9)

	Central Europe, eastern Europe, and central Asia	27.9% (20.5 - 35.8)
	High-income	17.8% (12.5 - 24.8)
	Latin America and Caribbean	24.8% (19.1 - 30.7)
	North Africa and Middle East	22.2% (17.7 - 26.8)
	South Asia	16.4% (13.0 - 20.1)
	Sub-Saharan Africa	9.3% (6.9 - 12.8)
Urinary tract infections and pyelonephritis	Global	39.1% (32.4 - 61.5)
	Southeast Asia, east Asia, and Oceania	64.5% (48.4 - 74.7)
	Central Europe, eastern Europe, and central Asia	48.4% (32.4 - 61.5)
	High-income	27.2% (15.8 - 40.7)
	Latin America and Caribbean	28.5% (20.2 - 40.6)
	North Africa and Middle East	73.0% (58.2 - 80.0)
	South Asia	29.9% (20.2 - 40.7)
	Sub-Saharan Africa	24.9% (18.0 - 31.1)

The infectious syndrome models were specified as mixed-effects binomial logistic regressions, one for each infectious syndrome and age group:

$$\text{syndrome related deaths} \sim B(\text{total sepsis deaths}, \text{syndrome fraction}) \quad (4.6.2.1)$$

$$\text{logit}(\text{syndrome fraction}) = \beta_0 + \beta * X + \pi_{\text{level } 1, \text{level } 2}$$

where  $\beta$  and  $X$  are vectors of length  $n + 1$  for  $n$  covariates and  $\pi_{\text{level } 1, \text{level } 2}$  is a nested random effect on underlying cause of death. The granularity of the age groups estimated for each infectious syndrome was chosen based on the age pattern of the infectious syndrome and the limitations of data sparsity.

As in the first pathway, we derived our predictions and UIs by generating 1000 draws from the normal distribution of the fixed coefficients separately for each GBD location, age group, sex, and cause in 2019. We used the means of our results for the point estimates and the 95% UIs were delineated using the 2.5th and 97.5th percentiles of the draws.

#### *Section 4.6.3: Aggregation to the sepsis mortality envelope*

We calculated the number of deaths attributable to each infectious syndrome in 2019 by multiplying our predictions of cause-, age group-, sex-, year-, and location-specific infectious syndrome fractions by our sepsis-mortality estimates from the first pathway. All infectious syndrome fractions were squeezed to sum to one prior to multiplication in order to ensure that we did not exceed the sepsis mortality envelope.

Finally, we aggregated our results to arrive at regional and global sepsis-related mortality by infectious syndrome.

#### *Section 4.6.4: Infectious syndromes using GBD 2019 results*

Out of the 12 explicit Level 1 infectious syndromes included in our hierarchy, we excluded (i) tuberculosis (TB), (ii) typhoid, paratyphoid, and invasive non-typhoidal Salmonella, and (iii) gonorrhoea and chlamydia from our binomial mixed-effects linear regression model. Instead, we used the published results from GBD 2019<sup>1</sup> for these causes of death, as we believe the GBD 2019 estimates fully represent these infectious syndromes because they are usually not intermediate causes of death.

### **Section 4.7: Model validation**

Infectious syndrome modelling aims to predict which cases of infection belong to a specific infectious syndrome, which is a multi-class classification problem. We therefore use the Area Under the Receiver Operating Characteristics (ROC) Curve (AUC) to evaluate model performance. The ROC Curve is determined by the sensitivity (or true positive rate) and the specificity (or false positive rate) of the model, and a higher AUC score

indicates that the model is capable of discerning between the different categories. Accuracy is a related measure which considers the proportion of true positives and true negatives predicted by the model with respect to the total number of predictions.

The out-of-sample strategy for this validation excluded 20% of the sample on each iteration. Table 4.7.1 reports the Accuracy and AUC score<sup>24</sup> for each of the age groups within the infectious syndrome models and table 4.7.2 reports the same metrics for the sepsis models. 99% of the models have an AUC score between 0.7 and 1, indicating an overall excellent performance of this modelling framework.

*Table 4.7.1: Accuracy and AUC score for out-of-sample validation of infectious syndromes models*

<b>Model</b>	<b>Age group name</b>	<b>Accuracy</b>	<b>AUC score</b>
Bacterial infections of the skin and subcutaneous systems	1 to 4	1.00	0.87
Bacterial infections of the skin and subcutaneous systems	10 to 14	0.99	0.87
Bacterial infections of the skin and subcutaneous systems	15 to 19	0.98	0.90
Bacterial infections of the skin and subcutaneous systems	20 to 24	0.99	0.93
Bacterial infections of the skin and subcutaneous systems	25 to 29	0.99	0.94
Bacterial infections of the skin and subcutaneous systems	30 to 34	0.99	0.95
Bacterial infections of the skin and subcutaneous systems	35 to 39	0.99	0.94
Bacterial infections of the skin and subcutaneous systems	40 to 44	0.98	0.94
Bacterial infections of the skin and subcutaneous systems	45 to 49	0.98	0.93
Bacterial infections of the skin and subcutaneous systems	5 to 9	0.99	0.87
Bacterial infections of the skin and subcutaneous systems	50 to 54	0.98	0.92
Bacterial infections of the skin and subcutaneous systems	55 to 59	0.97	0.92
Bacterial infections of the skin and subcutaneous systems	60 to 64	0.97	0.92
Bacterial infections of the skin and subcutaneous systems	65 to 69	0.97	0.92
Bacterial infections of the skin and subcutaneous systems	70 to 74	0.98	0.92
Bacterial infections of the skin and subcutaneous systems	75 to 79	0.98	0.93
Bacterial infections of the skin and subcutaneous systems	80 to 84	0.98	0.94
Bacterial infections of the skin and subcutaneous systems	85 to 89	0.98	0.95
Bacterial infections of the skin and subcutaneous systems	90 to 94	0.98	0.96
Bacterial infections of the skin and subcutaneous systems	95 plus	0.98	0.97
Bacterial infections of the skin and subcutaneous systems	Early Neonatal	0.99	0.94
Bacterial infections of the skin and subcutaneous systems	Late Neonatal	0.99	0.98
Bacterial infections of the skin and subcutaneous systems	Post Neonatal	1.00	0.89
Bloodstream infections	1 to 4	0.91	0.95
Bloodstream infections	10 to 14	0.85	0.92
Bloodstream infections	15 to 19	0.84	0.91
Bloodstream infections	20 to 24	0.89	0.94
Bloodstream infections	25 to 29	0.92	0.94
Bloodstream infections	30 to 34	0.93	0.94
Bloodstream infections	35 to 39	0.92	0.93
Bloodstream infections	40 to 44	0.90	0.92
Bloodstream infections	45 to 49	0.89	0.90
Bloodstream infections	5 to 9	0.87	0.94

Bloodstream infections	50 to 54	0.88	0.89
Bloodstream infections	55 to 59	0.88	0.87
Bloodstream infections	60 to 64	0.88	0.87
Bloodstream infections	65 to 69	0.89	0.87
Bloodstream infections	70 to 74	0.90	0.88
Bloodstream infections	75 to 79	0.91	0.89
Bloodstream infections	80 to 84	0.92	0.91
Bloodstream infections	85 to 89	0.93	0.92
Bloodstream infections	90 to 94	0.94	0.93
Bloodstream infections	95 plus	0.94	0.95
Bloodstream infections	Early Neonatal	0.94	0.96
Bloodstream infections	Late Neonatal	0.95	0.96
Bloodstream infections	Post Neonatal	0.93	0.96
CAI lower respiratory infections and all related infections in the thorax	5 to 69	0.99	0.99
CAI lower respiratory infections and all related infections in the thorax	70+ years	0.99	1.00
CAI lower respiratory infections and all related infections in the thorax	Neonatal	0.95	0.96
CAI lower respiratory infections and all related infections in the thorax	Post Neonatal to 5	0.99	1.00
CAI urinary tract infections and pyelonephritis	0 to 39	1.00	1.00
CAI urinary tract infections and pyelonephritis	40 plus	1.00	1.00
Diarrhoea	1 to 4	0.99	1.00
Diarrhoea	10 to 14	0.99	0.99
Diarrhoea	15 to 19	0.99	0.99
Diarrhoea	20 to 24	0.99	1.00
Diarrhoea	25 to 29	0.99	1.00
Diarrhoea	30 to 34	0.99	1.00
Diarrhoea	35 to 39	0.99	1.00
Diarrhoea	40 to 44	0.99	0.99
Diarrhoea	45 to 49	0.99	0.99
Diarrhoea	5 to 9	0.99	0.99
Diarrhoea	50 to 54	0.99	0.98
Diarrhoea	55 to 59	0.99	0.97
Diarrhoea	60 to 64	0.99	0.97
Diarrhoea	65 to 69	0.99	0.96
Diarrhoea	70 to 74	0.99	0.96
Diarrhoea	75 to 79	0.99	0.97
Diarrhoea	80 to 84	0.99	0.97
Diarrhoea	85 to 89	0.99	0.98
Diarrhoea	90 to 94	0.99	0.98
Diarrhoea	95 plus	0.99	0.99
Diarrhoea	Early Neonatal	1.00	1.00
Diarrhoea	Late Neonatal	1.00	1.00



Diarrhoea	Post Neonatal	0.98	0.99
Endocarditis and other cardiac infections	1 to 4	0.99	0.94
Endocarditis and other cardiac infections	10 to 14	0.99	0.97
Endocarditis and other cardiac infections	15 to 19	0.99	0.96
Endocarditis and other cardiac infections	20 to 24	0.99	0.96
Endocarditis and other cardiac infections	25 to 29	0.99	0.97
Endocarditis and other cardiac infections	30 to 34	0.99	0.97
Endocarditis and other cardiac infections	35 to 39	0.99	0.97
Endocarditis and other cardiac infections	40 to 44	0.99	0.97
Endocarditis and other cardiac infections	45 to 49	0.99	0.96
Endocarditis and other cardiac infections	5 to 9	0.99	0.95
Endocarditis and other cardiac infections	50 to 54	0.99	0.96
Endocarditis and other cardiac infections	55 to 59	0.99	0.95
Endocarditis and other cardiac infections	60 to 64	0.99	0.95
Endocarditis and other cardiac infections	65 to 69	0.99	0.95
Endocarditis and other cardiac infections	70 to 74	0.99	0.96
Endocarditis and other cardiac infections	75 to 79	0.99	0.96
Endocarditis and other cardiac infections	80 to 84	0.99	0.97
Endocarditis and other cardiac infections	85 to 89	0.99	0.98
Endocarditis and other cardiac infections	90 to 94	0.99	0.98
Endocarditis and other cardiac infections	95 plus	0.99	0.98
Endocarditis and other cardiac infections	Early Neonatal	0.99	0.98
Endocarditis and other cardiac infections	Late Neonatal	0.99	0.98
Endocarditis and other cardiac infections	Post Neonatal	0.99	0.89
HAI lower respiratory infections and all related infections in the thorax	5 to 69	0.96	0.89
HAI lower respiratory infections and all related infections in the thorax	70+ years	0.96	0.89
HAI lower respiratory infections and all related infections in the thorax	Neonatal	0.99	0.50
HAI lower respiratory infections and all related infections in the thorax	Post Neonatal to 5	0.97	0.94
HAI urinary tract infections and pyelonephritis	0 to 39	0.99	0.77
HAI urinary tract infections and pyelonephritis	40 plus	0.99	0.86
Infections of bone, joints, and related organs	0 to 9	0.99	0.94
Infections of bone, joints, and related organs	10 to 14	0.99	0.95
Infections of bone, joints, and related organs	15 to 19	0.99	0.88
Infections of bone, joints, and related organs	20 to 24	0.99	0.82
Infections of bone, joints, and related organs	25 to 29	0.99	0.85
Infections of bone, joints, and related organs	30 to 34	0.99	0.83
Infections of bone, joints, and related organs	35 to 39	0.99	0.85
Infections of bone, joints, and related organs	40 to 44	0.99	0.84
Infections of bone, joints, and related organs	45 to 49	0.99	0.84
Infections of bone, joints, and related organs	50 to 54	0.99	0.88
Infections of bone, joints, and related organs	55 to 59	0.99	0.89

Infections of bone, joints, and related organs	60 to 64	0.99	0.90
Infections of bone, joints, and related organs	65 to 69	0.99	0.90
Infections of bone, joints, and related organs	70 to 74	0.99	0.91
Infections of bone, joints, and related organs	75 to 79	0.99	0.92
Infections of bone, joints, and related organs	80 to 84	0.99	0.93
Infections of bone, joints, and related organs	85 to 89	0.99	0.94
Infections of bone, joints, and related organs	90 to 94	0.99	0.94
Infections of bone, joints, and related organs	95 plus	0.99	0.95
Meningitis and other bacterial central nervous system infections	1 to 4	0.98	0.98
Meningitis and other bacterial central nervous system infections	10 to 14	0.97	0.98
Meningitis and other bacterial central nervous system infections	15 to 19	0.98	0.97
Meningitis and other bacterial central nervous system infections	20 to 24	0.99	0.97
Meningitis and other bacterial central nervous system infections	25 to 29	0.99	0.98
Meningitis and other bacterial central nervous system infections	30 to 34	0.99	0.98
Meningitis and other bacterial central nervous system infections	35 to 39	0.99	0.97
Meningitis and other bacterial central nervous system infections	40 to 44	0.99	0.96
Meningitis and other bacterial central nervous system infections	45 to 49	0.99	0.96
Meningitis and other bacterial central nervous system infections	5 to 9	0.97	0.97
Meningitis and other bacterial central nervous system infections	50 to 54	0.99	0.94
Meningitis and other bacterial central nervous system infections	55 to 59	0.99	0.93
Meningitis and other bacterial central nervous system infections	60 to 64	0.99	0.93
Meningitis and other bacterial central nervous system infections	65 to 69	0.99	0.92
Meningitis and other bacterial central nervous system infections	70 to 74	0.99	0.92
Meningitis and other bacterial central nervous system infections	75 to 79	0.99	0.91
Meningitis and other bacterial central nervous system infections	80 to 84	0.99	0.92
Meningitis and other bacterial central nervous system infections	85 to 89	0.99	0.92
Meningitis and other bacterial central nervous system infections	90 to 94	0.99	0.93
Meningitis and other bacterial central nervous system infections	95 plus	0.99	0.92
Meningitis and other bacterial central nervous system infections	Early Neonatal	0.99	0.99
Meningitis and other bacterial central nervous system infections	Late Neonatal	1.00	0.99
Meningitis and other bacterial central nervous system infections	Post Neonatal	0.99	0.98
Peritoneal and intra-abdominal infections	1 to 4	0.99	0.97
Peritoneal and intra-abdominal infections	10 to 14	0.97	0.96
Peritoneal and intra-abdominal infections	15 to 19	0.96	0.96
Peritoneal and intra-abdominal infections	20 to 24	0.97	0.97
Peritoneal and intra-abdominal infections	25 to 29	0.98	0.98
Peritoneal and intra-abdominal infections	30 to 34	0.98	0.98
Peritoneal and intra-abdominal infections	35 to 39	0.98	0.98
Peritoneal and intra-abdominal infections	40 to 44	0.97	0.97
Peritoneal and intra-abdominal infections	45 to 49	0.97	0.96
Peritoneal and intra-abdominal infections	5 to 9	0.98	0.97

Peritoneal and intra-abdominal infections	50 to 54	0.96	0.95
Peritoneal and intra-abdominal infections	55 to 59	0.96	0.95
Peritoneal and intra-abdominal infections	60 to 64	0.96	0.95
Peritoneal and intra-abdominal infections	65 to 69	0.96	0.95
Peritoneal and intra-abdominal infections	70 to 74	0.97	0.96
Peritoneal and intra-abdominal infections	75 to 79	0.97	0.97
Peritoneal and intra-abdominal infections	80 to 84	0.98	0.98
Peritoneal and intra-abdominal infections	85 to 89	0.98	0.98
Peritoneal and intra-abdominal infections	90 to 94	0.98	0.98
Peritoneal and intra-abdominal infections	95 plus	0.99	0.98
Peritoneal and intra-abdominal infections	Early Neonatal	0.99	0.97
Peritoneal and intra-abdominal infections	Late Neonatal	0.99	0.97
Peritoneal and intra-abdominal infections	Post Neonatal	0.98	0.94

*Table 4.7.2: Accuracy and AUC score for out-of-sample validation of sepsis models*

<b>Model</b>	<b>Age group name</b>	<b>Accuracy</b>	<b>AUC score</b>
Sepsis	1 to 4	0.89	0.93
Sepsis	10 to 14	0.90	0.92
Sepsis	15 to 19	0.95	0.94
Sepsis	20 to 24	0.95	0.94
Sepsis	25 to 29	0.94	0.95
Sepsis	30 to 34	0.93	0.94
Sepsis	35 to 39	0.93	0.93
Sepsis	40 to 44	0.93	0.91
Sepsis	45 to 49	0.93	0.88
Sepsis	5 to 9	0.89	0.92
Sepsis	50 to 54	0.93	0.86
Sepsis	55 to 59	0.94	0.84
Sepsis	60 to 64	0.94	0.83
Sepsis	65 to 69	0.94	0.83
Sepsis	70 to 74	0.95	0.84
Sepsis	75 to 79	0.95	0.85
Sepsis	80 to 84	0.96	0.87
Sepsis	85 to 89	0.96	0.88
Sepsis	90 to 94	0.96	0.90
Sepsis	95 plus	0.96	0.92
Sepsis	Early Neonatal	0.91	0.87
Sepsis	Late Neonatal	0.87	0.88
Sepsis	Post Neonatal	0.88	0.89

## Section 5: Case fatality ratios

### Section 5.1: Input data

Case fatality ratios (CFRs) were modelled for the pathogens and infectious syndromes of interest using all available data detailing the organism responsible for infection, the infectious syndrome, and patient outcome. This included hospital and microbial data, totaling 19.7 million isolates and cases, as shown in table S4 (section 14). We additionally included 52 907 cases from literature sources for CNS infections, which had been previously extracted for a systematic review in GBD.

### Section 5.2: Data processing

All input data sources were processed as described in sections 6.2.1–6.2.4 and section 6.2.7 and pathogens of interest were chosen as described in section 6.2.5. Input data for the CFR models were aggregated based on data source, year, GBD location, and age group (as well as hospital/community acquired status, in the case of the lower respiratory and urogenital infectious models). For lower respiratory and blood stream infections, for which CFRs could be vastly different in neonates, we modelled the following age groups: neonatal, post-neonatal–5 years, 5–50 years, 50–70 years, and 70 years and older. For all other infectious syndromes, we modelled the following age groups: neonatal–5 years, 5–50 years, 50–70 years, and 70 years and older. We excluded from the analysis any source-location-year-age with fewer than five cases and zero deaths.

To allow us to implement linear models, CFRs were logit-transformed. We used the delta method to compute the standard error of CFRs in logit space. To incorporate data with zero deaths, or with an equal number of deaths and cases, we applied a 1% offset, such that the CFRs for data with zero deaths was represented as 1% and the CFR for data with an equal number of deaths and cases was represented as 99%.

### Section 5.3: Modelling overview

Pathogen-specific CFRs were modelled separately by infectious syndrome and were calculated as a function of HAQ Index and age. We used the HAQ Index to extrapolate CFRs determined from the input data, which often had a broad but not comprehensive geographic scope, to all 204 GBD countries and territories. To account for heterogeneity across the sources of input data, we implemented a mixed-effects meta-regression framework, modelling data source as a random effect. We further incorporated a binary fixed-effect denoting whether the data source only included intensive care unit (ICU) patients, for which CFRs were expected to be higher.

The pathogens of interest for each infectious syndrome were determined by prevalence in the data and expert opinion, with the goal of modelling approximately 90% of specified-pathogens associated with each infectious syndrome (see section 6.2.5). Because each data source generally reported only a set of the pathogens we evaluated in our research, the input data for the pathogens varied in geographic coverage; nearly all pathogens were well reported in high-income areas, but some pathogens were not well represented in the smaller subset of data we collected from low- and middle-income locations.

For those pathogens with ‘rich’ data, defined by our method as having at least ten high-quality data points below a moderate HAQ Index (0.7), we modelled a unique effect of HAQ Index, achieved by interacting the HAQ Index fixed-effect with the pathogen-specific fixed-effect. This process, referred to from here on as the ‘interaction model,’ allowed the relative deadliness of pathogens to vary depending on a location’s HAQ Index. For those pathogens with fewer than 10 high quality data points below 0.7 HAQ Index, or those whose results in the interaction models indicated an unrealistically large influence of HAQ Index (eg, 70% CFR in low HAQ Index countries, 1% CFR in high HAQ Index countries), we modelled a pathogen-specific intercept with an HAQ Index fixed-effect shared across the pathogens. As a consequence of the single fixed-effect on HAQ Index, a pathogen that was predicted to be the deadliest in low HAQ Index countries would also be predicted to be the deadliest in high HAQ Index countries in these ‘intercept models.’ To estimate the CFRs for other known bacteria, which either were not selected as a pathogen of interest or lacked sufficient data for inclusion in the intercept models, we pooled all bacterial data together and estimated a single CFR curve from age, HAQ Index, and the data source heterogeneity covariates. Thus, up to three models were run for each infectious syndrome:

- 1) an interaction model including data for all data rich pathogens and ‘other specified bacteria’ (which was included to inform the overall influence of HAQ Index on CFR, predictions were only generated for the data rich pathogens),
- 2) an intercept model including data for data rich and data sparse pathogens, as well as ‘other specified bacteria’ (predictions were only generated for the data sparse pathogens), and
- 3) an ‘other bacteria’ model that included data for all bacterial pathogens (predictions were generated by HAQ Index and age, without any pathogen specific term).

Table S5 (section 14) details which CFR model framework was used to assess the pathogens for each infectious syndrome. Whenever needed, the CFR for any bacterial pathogen “not explicitly modelled” was estimated using the ‘other bacteria’ model for subsequent steps of our modelling processes.

For some infectious syndromes, the relative deadliness of a pathogen may be strongly determined by either the age of the patient or whether the infection was community- or hospital-acquired. For bloodstream infections, we ran two distinct sets of CFR models, one for neonates (0-27 days) and another for post neonates, to capture the differing dynamics of pathogen deadliness in these two populations. As is done for our other modelling processes, we also separate community-acquired and hospital-acquired cases in our CFR models for lower respiratory and urogenital infections. Because some data sources did not provide enough information to infer whether an infection was community- or hospital-acquired, but still included important information on the relative pathogenesis and the difference in CFRs across varying HAQ indices, infections of unknown origin were included in both the community-acquired and hospital-acquired models for these two syndromes. Any bias in these ‘unknown origin’ infections was adjusted for using a binary fixed-effect representing an ‘unknown origin’ infection, and predictions were generated for the community- and hospital-acquired infections only.

#### Section 5.4 Modelling framework

The data were analysed using a meta-analytic mixed effects structure. The main model can be specified as follows:

$$\text{logit}(y_i) = X_i\beta + u_i1 + \epsilon_i, \quad \epsilon_i \sim N(0, \Sigma_i), \quad u_i \sim N(0, \gamma) \quad (5.4.1)$$

where

- $y_i$  contains CFRs for data source  $i$
- Design matrix  $X_i$  contains as columns the following covariates
  - in all models:
    - HAQ Index
    - dummy-coded indicator for age group
    - dummy-coded ICU indicator for data source (1 if data source only compiles information on ICU patients, 0 if a mix between ICU/non-ICU patients)
  - in ‘interaction’ and ‘intercept’ models:
    - dummy-coded indicator for pathogen
  - in ‘interaction’ models only:
    - interaction between pathogen and HAQ Index (product of dummy-coded pathogen columns and HAQ Index)
  - in models evaluating community/hospital acquired infection (LRI+, UTI):
    - dummy-coded variable indicating source of infection (1 if unknown source, 0 if community OR hospital acquired, depending on whether the model is evaluating community or hospital infections)
- $\beta$  are fixed effect multipliers
- $\epsilon_i$  are observation error terms with known variances
- $u_i$  are data source-specific random intercepts with unknown covariance  $\gamma$

The underlying program used to fit the model (meta-regression, Bayesian, regularized, trimmed [MR-BRT]) is described elsewhere.<sup>11</sup> The program allows specification of priors on  $\gamma$  and  $\beta$ .

- Prior on  $\gamma$ , data source random effect: Many input data-sources cover only a single country, leading to low variability in HAQ Index within each data-source. Such collinearity adversely influenced the accuracy of the estimated effect of HAQ Index, which was instrumental in extrapolating trends from the input data to global results. To emphasise the contribution of HAQ Index over data-source in the modelled estimates, we implemented a strong Gaussian prior (mean 0, standard error 0.001) on  $\gamma$ .
- Prior on  $\beta$  for HAQ Index: There were a handful of cases in which the estimated effect of HAQ Index on CFRs given our data was clinically implausible. For skin and neonatal bloodstream infections, we had very limited data from low HAQ Index locations, with available data indicating a very intense influence of HAQ Index. Initial model results for these syndromes indicated more than 10-fold higher CFRs in low HAQ Index countries relative to high HAQ Index countries. To attenuate the effect of HAQ Index in these models we implemented a Gaussian prior on the HAQ Index  $\beta$  with mean 0 and standard error 0.2.

Similarly, the peritoneal and intra-abdominal infection CFR models did not have enough input data from low HAQ Index countries to estimate a sensible HAQ Index-CFR trend; initial models indicated very strong positive associations between CFR and HAQ Index such that the CFR in low HAQ Index countries were nearly zero. To amend this, we implemented a Gaussian prior on the HAQ Index  $\beta$  with mean equal to the coefficient estimate for HAQ Index in the adult BSI models. The standard error for this prior was 0.2.

For the urogenital infection models (which were ran separately for community- and hospital-acquired infections) and those for hospital-acquired lower respiratory infections, there was substantial collinearity between HAQ Index and the indicator variable for infections of unknown origin; data that did not indicate the origin of infection were generally sourced from countries with much lower HAQ Indices and much higher baseline CFRs. To emphasize the attribution of this effect to HAQ Index, rather than 'unknown infection origin,' we implemented a Gaussian prior on the HAQ Index  $\beta$ . The mean of this prior was centered at a value estimated for the coefficient of HAQ Index on CFR from weighted simple linear regression, with the weights equal to the inverse of the standard error of the CFRs. The standard error for this prior was 0.2.

*Table 5.4.1: Number of data points and parameters estimated in each case fatality ratio model*

Infectious syndrome	Sub-model	CFR model type	Data points (source-location-years)	Estimated parameters
CNS	-	Interaction	2094	13
CNS	-	Intercept	2756	15
CNS	-	Other	2756	7
Intra-abdominal	-	Intercept	639	12
Intra-abdominal	-	Other	639	6
LRI+	Community-acquired	Intercept	10485	23
LRI+	Community-acquired	Other	10485	8
LRI+	Hospital-acquired	Intercept	10122	23
LRI+	Hospital-acquired	Other	10122	8
Skin	-	Intercept	1866	15
Skin	-	Other	1897	6
Bone+	-	Intercept	432	12
Bone+	-	Other	432	5
UTI	Community-acquired	Intercept	1596	20
UTI	Community-acquired	Other	1596	7
UTI	Hospital-acquired	Intercept	1844	20
UTI	Hospital-acquired	Other	1844	7
BSI	Neonatal	Intercept	1413	18

BSI	Neonatal	Other	1271	3
BSI	Non-neonatal	Interaction	7468	24
BSI	Non-neonatal	Intercept	10842	25
BSI	Non-neonatal	Other	10842	6
Diarrhoea	-	Intercept	4041	14
Diarrhoea	-	Other	3525	6

BSI = Bloodstream infections. CNS = Meningitis and other bacterial central nervous system infections. LRI+ = Lower respiratory infections and all related infections in the thorax. Intra-abdominal = Peritoneal and intra-abdominal infections. Skin = Bacterial infections of the skin and subcutaneous systems. UTI = Urinary tract infections and pyelonephritis. Bone+ = Infections of bones, joints, and related organs.

### Section 5.5 Predictions and uncertainty

Predictions for 2019 CFRs were generated for each country, age group, and pathogen as a function of each country's HAQ Index, assuming mixed ICU/non-ICU patients and, in the case of models for UTI and LRI+, that the infection was community- or hospital-acquired (in contrast to infections of unknown origin). For pathogens with insufficient data to estimate a syndrome-specific CFR, we predicted out using the 'other bacteria' CFR associated with the infectious syndrome. Importantly, all of the CFRs we calculate by infectious syndrome are independent of that syndrome's underlying cause.

Uncertainty estimates were generated using asymptotic uncertainty intervals. Specifically, for the model, the posterior uncertainty for the coefficients  $\beta$  is Gaussian, with mean and variance given below:

$$\hat{\beta} = (\sum_i X_i^T V_i^{-1} X_i)^{-1} (\sum_i X_i^T V_i^{-1} y_i) \quad (5.5.1)$$

$$Var(\hat{\beta}) = (\sum_i X_i^T V_i^{-1} X_i)^{-1} \quad (5.5.2)$$

where

$$V_i = 11^T + \hat{\gamma}I \quad (5.5.2)$$

The variance-covariance matrix was used to obtain 1000 draws for the coefficients, which are then used to get intervals for the predictions.

## Section 6: Pathogen distribution

### Section 6.1: Input data

With this model, we aimed to estimate the distribution of pathogens causing each infectious syndrome. To get input data for this model, we gathered all available data sources described in section 2 that meet the following criteria:

- Sufficient diagnosis (for patient- or admission-level datasets) or sample specimen type (for isolate- or culture-level datasets) information for us to determine the infectious syndrome
- Information on which pathogen(s) caused the infection or which pathogen(s) were detected in an infectious sample, as determined through culture or genomic-based methods
- Did not have a strongly biased sampling framework across pathogens (for example, did not deliberately sample until 100 cases of every pathogen of interest had been obtained)

The input data source types that met these criteria were:

- Multiple causes of death data
- Hospital discharge
- Linkage data
- Microbial data with and without outcome information
- Literature studies from the aetiology literature reviews
- Mortality surveillance (Child Health and Mortality Prevention Surveillance [CHAMPS])

From these sources combined, there was a total of 30.4 million isolates and cases. Table S6 (section 14) provides a detailed breakdown of this total by pathogen.

## Section 6.2: Data processing

### Section 6.2.1: Extraction and standardisation

We extracted and standardised the location, year, age, sex, diagnoses, specimen type, pathogens, and hospital- and community-acquired (HAI and CAI) status of each record in every dataset. HAI or CAI status in microbial data was determined as described in section 2.3, while in MCoD, hospital discharge, and linkage data, a record was considered CAI if the infectious syndrome was the primary or underlying diagnosis and HAI otherwise, as described in section 4. These datasets report a variety of metrics, including deaths, admissions, cases, cultures, and isolates. While these metrics are not completely comparable (for example, a single patient may often have multiple cultures taken during a single hospital admission), we chose to standardise them into two categories: “deaths,” for any unit associated with an outcome of death, and “cases,” for any unit regardless of outcome. We assigned a unique identifier, sample ID, to track each unique unit of analysis whenever a dataset included enough line-level data to make this possible. We did not track the relationship between sample ID and patient or admission, in many cases because this was not possible; an improvement to future analyses may be to track this information and account for multiple isolates or cultures from a single admission. The majority of the data informing culprit pathogen were from microbiological analysis of various isolates, but we also considered antigen testing, such as the urinary strep antigen, and polymerase chain reaction (PCR)-based testing when assigning the pathogen responsible for infection.

### Section 6.2.2: Assigning infectious syndrome

After standardising the data, we mapped every sample ID or tabulated figure in the data to infectious syndrome based on its diagnoses and specimen type. Infectious syndrome was assigned first based on any diagnosis associated with a given sample ID or tabulated figure. For samples IDs or tabulated figures with multiple diagnoses and/or an underlying diagnosis, we followed the rules laid out in section 4 for assigning infectious syndrome based on multiple causes. If a dataset contained no diagnoses or the diagnoses provided no information on infectious syndrome, we assigned infectious syndrome based on specimen type (table 6.2.2.1). This is an imprecise method because a patient may have a sample taken from an organ system that is not the site of their primary infection, most commonly from the blood. Finally, if neither diagnosis nor specimen information provided information on infectious syndrome, we assigned infectious syndrome based on pathogen for a select number of pathogens (table 6.2.2.2).

Table.6.2.2.1: Syndrome assignment based on standardised specimen types

Standard specimen	Assigned to syndrome
Blood	Bloodstream infections
Bone & joint	Infections of bones, joints, and related organs
Catheter	Bacterial infections of the skin and subcutaneous systems
Cerebrospinal fluid	Meningitis and other bacterial central nervous system infections
Gastrointestinal tract & bowel	Diarrhoea
Urinary tract infection	Urinary tract infections and pyelonephritis
Intra-abdominal	Peritoneal and intra-abdominal infections
Rectal/stool	Diarrhoea
Lower respiratory	Lower respiratory infections and all related infections in the thorax
Skin	Bacterial infections of the skin and subcutaneous systems
Upper respiratory	Other infections
Urogenital	Other infections
Other and unspecified specimens	No infectious syndrome

Table 6.2.2.2: Syndrome assignment based on pathogen for entries lacking diagnostic and specimen information

Pathogen	Assigned to syndrome
<i>Salmonella</i> Typhi	Typhoid, paratyphoid, and invasive non-typhoidal <i>Salmonella</i>
<i>Salmonella</i> Paratyphi	Typhoid, paratyphoid, and invasive non-typhoidal <i>Salmonella</i>
<i>Salmonella</i> Typhi or Paratyphi	Typhoid, paratyphoid, and invasive non-typhoidal <i>Salmonella</i>
Non-typhoidal <i>Salmonella</i> species	Typhoid, paratyphoid, and invasive non-typhoidal <i>Salmonella</i>
<i>Mycobacterium tuberculosis</i>	Tuberculosis
<i>Neisseria meningitidis</i>	Central nervous system infections
<i>Neisseria gonorrhoeae</i>	Gonorrhoea and chlamydia



### *Section 6.2.3: Contaminants and no aetiology detected*

Some pathogens cause disease so rarely or are so commonly contaminants that we considered them to be contaminants, unlikely to be the true cause of disease. Examples include many *Corynebacterium* species and *Staphylococcus epidermidis*. We dropped all such contaminants from the analysis, as well as any record listed by treating clinicians in the data as a contaminant. Contaminants are identified at the most-detailed species or serotype level reported in the data; thus, in the broad pathogen categories that are eventually modelled, like fungi in LRI+, specific contaminant species have already been removed.

We also dropped from the analysis all records where no pathogen was detected, or the patient diagnosis indicated an unspecified bacterium. This assumes that the distribution of pathogens among cases with known aetiology are the same as those with unknown aetiology; in other words, that the probability of detection is the same for every pathogen. This assumption may break down if certain pathogens are more difficult to detect than others, or in cases where a pathogen is irregularly tested for within a laboratory.

### *Section 6.2.4: Polymicrobial infections*

A single infection may be caused by multiple bacteria, and the co-occurrence of several bacteria can have significant effects on the treatment and outcome of disease. Some of our line-level data sources report multiple pathogens per individual record, allowing us to quantify the extent of polymicrobial infection. Other data sources tabulate over pathogen with no linking clinical information, thereby masking this information, or do not report the co-occurrence of additional bacteria.

For data sources where multiple pathogens were listed per sample ID, we classified these cases according to the following criteria. First, if a case contained more than one of “unspecified bacteria,” “virus,” “fungus,” and another pathogen(s), we chose to drop all these pathogens except the one(s) most likely to be responsible for disease, with the following ranking from most to least likely:

1. Another pathogen(s)
2. Unspecified bacteria
3. Virus
4. Fungus

This was to drop co-occurrence profiles that we consider to be uninformative, like a viral infection co-occurring with a fungal infection. For example, for a sample ID with pathogens *Escherichia coli*, *Acinetobacter baumannii*, and a virus, we would drop the virus and retain both the *E. coli* and *A. baumannii*. After applying this drop, we considered any sample ID that contained more than one pathogen to be polymicrobial. Polymicrobial was treated as a distinct pathogen category in all further analysis. We did not estimate the exact composition of the pathogens comprising the polymicrobial category for a given infectious syndrome. Furthermore, it can be difficult to determine the clinical meaning of a polymicrobial result, as it is unclear which pathogen or if any pathogen is ultimately responsible for the infection. For these reasons, we were unable to include any AMR burden from polymicrobial infections in our final results. This possibly underestimates the burden of AMR by hiding infections caused by resistant pathogens of interest in the polymicrobial category.

By standardising all datasets that report polymicrobial infections into distinct mono-pathogen and poly-pathogen categories, we created an inconsistency between these datasets and datasets that do not report the co-occurrence of pathogens. For example, a dataset that reports the co-occurrence of *E. coli* and *A. baumannii* would be standardised into three groups, mono-*E.coli*, mono-*A. baumannii*, and co-occurring *E. coli* and *A. baumannii*, while a dataset that reports *E. coli* and *A. baumannii* separately would have two categories that both have some unknown overlap. In order to allow us to use both data types, we chose to assume that the relative prevalences of pathogens in datasets that do not report co-occurrence would be comparable to their mono-pathogenic counterparts in datasets that do report co-occurrence. This assumes that the co-occurrence of pathogens is random and is not correlated for certain pathogens. We did not have sufficient data to fully test the validity of this assumption, given that few datasets report the full universe of pathogens which may co-occur.

### *Section 6.2.5: Selecting pathogens for estimation*

For each infectious syndrome, we selected roughly 10–20 pathogens to estimate explicitly in the pathogen distribution based on the following criteria:

- The prevalence of each pathogen in the raw data
- Clinical knowledge about the primary etiologies of each infectious syndrome
- The amount of available data, which limits the number of pathogens that can be estimated successfully

In addition to the  $n$  pathogens for a given syndrome that we estimate explicitly, we also included an “other specified pathogens” category for every infectious syndrome, to which we mapped all other aetiologies identified in the data. Thus, the set of estimated pathogens for each infectious syndrome is mutually exclusive and collectively exhaustive of all possible aetiologies. Polymicrobial infections were either estimated explicitly or included in the “other” category, making all explicitly estimated individual pathogens mono-pathogenic. In addition to these criteria, we also considered the following factors:

- Since we were ultimately interested in estimating the burden of AMR in bacteria, we erred on the side of estimating bacteria with strong evidence of AMR, rather than bacteria with low evidence of AMR or non-bacterial aetiologies.
- Clinically relevant aetiologies differ from syndrome to syndrome, and we were unable to estimate all pathogens explicitly in every syndrome due to a lack of data. Therefore, the “other” pathogen category is composed of slightly different pathogens for every infectious syndrome, and can occasionally contain pathogens that are explicitly estimated for another infectious syndrome. We attempted to mitigate this by including bacteria with strong evidence of AMR in the estimation of all infectious syndromes whenever possible.
- We included enough explicitly estimated pathogens to ensure that the “other” category remained below 10% for all infectious syndromes.

For a list of pathogens covered in each infectious syndrome model, please refer to table 6.3.2.

### *Section 6.2.6: Estimating unbiased other and polymicrobial categories*

One of the central challenges of estimating pathogen distributions was that not every data source tested for or reported every possible aetiology of a given infectious syndrome. For example, many literature studies on the aetiologies of meningitis only report on bacterial aetiologies. Some surveillance systems, like the US Centers for Disease Control and Prevention (CDC) Active Bacterial Core surveillance (ABCs), only collect data on certain pathogens of interest. Only certain pathogens are referenced explicitly in the International Classification of Diseases (ICD), limiting which pathogens can be identified from ICD-based data types like MCoD and hospital discharge. Finally, some datasets reported only a subset of the pathogens that we are interested in for a given infectious syndrome, reporting the remaining aetiologies in an aggregate “other” category. These practices have led to inconsistencies in the “other” and “polymicrobial” categories across data sources. Datasets can either over or under-report “other,” and datasets that report fewer specific pathogens will automatically report fewer polymicrobial infections.

To address this problem, we maintained a list of data sources that we believe have sufficient testing and reporting to give unbiased estimates of other and polymicrobial for all syndromes. We dropped any data on polymicrobial or other that did not come from these data sources. These data sources all had a complete sampling framework (eg, they do not limit the scope of aetiologies that they test for) and reported their results without any deliberate aggregation. While we believe this list provided an accurate starting place for the estimation of other and polymicrobial, future work to improve this method would involve a more detailed analysis of sampling framework and reporting categories in each dataset, specific to each infectious syndrome.

There were two major exceptions to this method for handling “other specified pathogens.” First, determining the pathogenic aetiology of LRI with microbiology represents challenges that have been well described previously.<sup>25,26</sup> In order to account for this limitation, we utilised a vaccine probe design to inform the *Streptococcus pneumoniae* cause fraction of LRI, consistent with the approach used in the GBD aetiology estimation process.<sup>27,28</sup> In brief, we

extracted the vaccine efficacy of the pneumococcal vaccine against all pneumonia from 18 vaccine probe studies with randomised-control trial, before-after, and cohort designs among children and adults. We then calculated the PAF of pneumonia due to *S. pneumoniae* in each study (*Strep Base PAF*) based on these vaccine efficacies ( $VE_{all\ pneumonia}$ ), the vaccine efficacy of pneumococcal vaccine against vaccine-type pneumococcal pneumonia as pooled from three studies (two in children and one in adults) ( $VE_{vttp}$ ), the percentage of the population covered by the pneumococcal vaccine as modelled in GBD (100% for RCTs) ( $Cov_{PCV3}$ ),<sup>29</sup> and the percent of serotypes covered by the vaccine<sup>30</sup> ( $Cov_{serotype}$ ) (equation 6.2.6.1). We modelled a global age-specific PAF for *S. pneumoniae* based on these data in the MR-BRT environment and finally adjusted this PAF based on the vaccine coverage in children in every GBD location in 2019 and optimal vaccine efficacy in children (*Strep Final PAF*) (equation 6.2.6.2). In adults (age 5+), we assumed the effects of vaccination on adults would be primarily indirect from vaccination in children, and included an adjustment factor on the vaccine efficacy to account for this, derived from Grijalva et al.<sup>31</sup>

$$Strep\ Base\ PAF = \frac{VE_{all\ pneumonia}}{VE_{vttp}Cov_{PCV3}Cov_{serotype}} \quad (6.2.6.1)$$

$$Strep\ Final\ PAF = \frac{Strep\ Base\ PAF(1 - Cov_{PCV3}Cov_{serotype}VE_{PCV3\ optimal})}{1 - (Strep\ Base\ PAF)Cov_{PCV3}Cov_{serotype}VE_{PCV3\ optimal}} \quad (6.2.6.2)$$

In this vaccine probe analysis,  $(1 - Strep\ Final\ PAF)$  is not consistent with the “other” category in our model, since it includes all non-*S. pneumoniae* aetiologies. We retained all of the data from the vaccine probe analysis as two categories, *S. pneumoniae* and “not *S. pneumoniae*” and addressed the inconsistencies between them and our other data using our modelling framework.

The second major exception involves several literature studies on the proportion of neonatal bacterial meningitis caused by *Streptococcus agalactiae* (Group B *Streptococcus*; GBS). We found that these literature studies were important to our estimation of the pathogen distribution of neonatal meningitis, which is distinct from other age groups because of its high proportion of GBS. However, these studies either only reported or were only extracted with two categories, GBS and “other bacterial, not GBS.” We retained both these categories and addressed the inconsistencies between them and our other data using our modelling framework.

### Section 6.2.7: Age-sex splitting

We standardised age and sex across all datasets to the following most-detailed groups using the GBD causes of death age-sex splitting algorithm for age:<sup>1</sup> 0–6, 7–27, and 28–364 days, and 1–4, 5–9, 10–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, 95+ years; and sex: male and female. This algorithm is based on the assumption that age-sex pattern of the death or case rate for a given infectious syndrome or pathogen is inherent to the pathology of the disease and is therefore constant across location and year.

To apply the algorithm, we first calculated distinct age-sex weights for every infectious syndrome and pathogen, separately for deaths and cases. These weights are the aggregate death and case rates across all datasets that report every detailed age-sex group. If we were to use a dataset that only reported some of the detailed age-sex groups, then the unreported age-sex groups would be biased downwards in the weight distribution. Calculating rates based on raw data counts could lead to extremely low rates, since we are typically comparing the entire population of a given location-year to deaths or cases captured within a single study, hospital, or surveillance system. Since the age-sex splitting algorithm only relies on the relative distribution of the weights, however, rather than their absolute level, this bias ultimately had no effect. For any infectious syndrome or pathogen combination for which we did not have enough data to create plausible age-sex weights, we used a set of all-pathogen weights for that infectious syndrome instead.

Since we split cases and deaths independently, it is possible for a detailed age-sex group produced by the splitting algorithm to contain fewer cases than deaths. When this occurred, we capped the deaths to match the cases. For

future improvement, a possible solution to this problem may be to split deaths, survivors, and cases without indication of outcome separately.

### *Section 6.2.8: Standardising measures*

The input data sources reported a variety of combinations of measures, including some that reported deaths only, some that reported cases only, and some that reported both cases and deaths. In order to standardise these measures to cases, we estimated infectious syndrome- and pathogen-specific CFRs (see section 5) and used these CFRs to convert all deaths-only datasets to cases. For any infectious syndrome or pathogen combination for which we did not have enough data to estimate plausible CFRs, we used a set of all-bacteria CFRs for that infectious syndrome instead. All modelling was done in case space.

Several of our microbial databases came exclusively from ICUs and were therefore heavily biased towards severe illness. In order to mitigate this bias, we dropped all information on cases in ICU-only datasets and recalculated implied cases based on reported deaths and our CFRs. No similar adjustment was made to attempt to account for biases between hospitalised and un-hospitalised populations, although we did account for HAI versus CAI for two infectious syndromes—LRI and thorax infections and UTI—within our modelling framework. The use of hospital-based data to calculate both pathogen-specific case fatality ratios and pathogen distributions biases our estimate of the distribution of pathogens in incident cases towards more severe disease, particularly for less-severe infectious syndromes like lower respiratory infections; adjusting for this bias would improve the accuracy of our non-fatal estimates

### *Section 6.2.9: Year adjustments*

Over the course of this study, we received a total of approximately 57 000 individual records from 2020 from seven microbial and mortality surveillance data sources. Additionally, we found a total of eight literature studies on pathogen distributions from 1975–1979 that were appropriate for inclusion. We included these 2020 and 1975–1979 data as inputs into our case fatality ratio and pathogen distribution models with the nearest year of covariate estimates available (2019 and 1980 respectively) in order to maximise data availability. While the COVID-19 pandemic had a significant impact on LRI disease burden in 2020, we found a total of only seven viral LRI and thorax infections reported in 2020 in our input data, and so we believe that the inclusion of these data did not significantly skew our estimates of the pathogen distribution of LRI in 2019.

## **Section 6.3: Modelling framework**

### *Section 6.3.1: Overview*

To model the distribution of pathogens for each infectious syndrome, we developed a method for the multinomial estimation of partial and compositional observations (MEPCO). We assumed that the aetiologies of a given infectious syndrome followed a multinomial distribution. Due to inconsistencies in which pathogens are tested for and reported by different data sources, each data source contained partial observations of the possible outcomes of the underlying multinomial distribution. Certain data sources like the vaccine probe estimates and the GBS neonatal meningitis studies represent compositional observations, where pathogens like “not *S. pneumoniae*” and “other bacterial, not GBS” represent aggregates of more detailed pathogens.

In order to use both partial and compositional data, we constructed a network model with the dependent variable as the log ratio of cases between different pathogens and estimated over a flexible parameterisation of multinomial parameters using a maximum likelihood approach. Consider a given infectious syndrome with a multinomial distribution of  $n$  mutually exclusive, collectively exhaustive aetiologies with probabilities  $p = (p_1, \dots, p_n)$ , so that each  $p_j \in (0,1)$  and  $\sum_j p_j = 1$ . The likelihood of an observation of  $c = (c_1, \dots, c_n)$ , where  $c_j =$  number of cases of pathogen  $j$  in a total sample of  $N$  infections ( $\sum_j c_j = N$ ), is:

$$P(c|p) = N! \prod_{j=1}^n \frac{p_j^{c_j}}{c_j!} \quad (6.3.1.1)$$

We modelled the probabilities using a composition of a link function with a linear predictor:

$$p_{i,j} = \exp(x_{i,j}^T \beta_j) \quad (6.3.1.2)$$

for observations  $i$ , a vector of covariates  $x_{i,j}$ , and a vector of coefficients  $\beta_j$  for each pathogen  $j$ . Table 6.3.2 shows the covariates used for infectious syndrome model; a typical specification included an intercept term, HAQ Index, a categorical age group dummy for large age bins, and any relevant vaccine coverage proportions by country. However, we did not observe these probabilities directly. Rather, we observed ratios between sums of these probabilities, which reduce to ratios between sums of cases within each study. These observations therefore take the form:

$$y_i = \frac{\text{cases of pathogen A}}{\text{cases of pathogen B}} = \frac{\sum_{j=1}^n w_{i,j}^a \exp(x_{i,j}^T \beta_j)}{\sum_{j=1}^n w_{i,j}^b \exp(x_{i,j}^T \beta_j)} \quad (6.3.1.3)$$

where  $w_{i,j}^a$  is a weight of 0 or 1 that selects the mutually exclusive, collectively exhaustive most-detailed pathogens that make up observed pathogen A, which may be a composite observation. For example, for the ‘‘other bacterial, non-GBS’’ pathogen,  $w_{i,j}$  would be 1 for *Staphylococcus aureus*, *S. pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Listeria monocytogenes*, *K. pneumoniae*, *E. coli*, and other pathogens and 0 for GBS and virus. We dropped all observations where either the numerator or denominator had 0 observed cases in order to make this calculation and a forthcoming log transform possible. This may bias the model towards overestimating less common pathogens.

It is not possible to infer all coefficients  $\beta_j$  from the observations, since they are all relative. However, if we fix all of the coefficients for one pathogen to 0 as a reference group, then we obtain a well-posed inverse problem, as long as there is enough data to estimate the remaining coefficients. Without loss of generality, we assumed  $\beta_1 = 0$  for all elements and obtain estimates of the remaining  $\beta_2, \dots, \beta_n$  by minimising the sum of the residuals between log-transformed observations  $y$  and corresponding log-transformed predictions from equation 6.3.1.3:

$$\min_{\beta_2, \dots, \beta_n} f(\beta) := \sum_i \frac{1}{\sigma_i^2} \left[ \ln(y_i) - \ln \left( \sum_{j=1}^n w_{i,j}^a \exp(x_{i,j}^T \beta_j) \right) + \ln \left( \sum_{j=1}^n w_{i,j}^b \exp(x_{i,j}^T \beta_j) \right) \right]^2 \quad (6.3.1.4)$$

where  $\sigma_i^2$  are variances corresponding to the data points. Equation 6.3.4 is a nonlinear likelihood minimisation problem that that we optimised using a standard implementation of the Gauss-Newton method.<sup>32</sup> We then re-normalised the optimal coefficients to obtain final predictions of the probabilities of each pathogen:

$$p_{i,j} = \frac{\exp(x_{i,j}^T \beta_j)}{\sum_j \exp(x_{i,j}^T \beta_j)} \quad (6.3.1.5)$$

To quantify the uncertainty of this estimate, we used asymptotic statistics to obtain the posterior distribution of  $(\beta_2, \dots, \beta_n)$ . Specifically, using the Gauss-Newton Hessian approximation gave us the asymptotic information matrix for all  $\beta_j$  except for the reference pathogen, allowing us to sample draws of  $\beta = (\beta_1 = 0, \beta_2, \dots, \beta_n)$ . For each  $\beta$  draw and given feature  $x$ , we obtained a corresponding draw of  $p$  using equation 6.3.1.5.

Finally, to convert  $p_{i,j}$  for a given demographic group  $i$  from case space to deaths space, we transformed using our CFR estimate for demographic  $i$ :

$$p_{i,j}^{\text{deaths}} = \frac{p_{i,j} \times CFR_i}{\sum_j p_{i,j} \times CFR_i} \quad (6.3.1.6)$$

This network regression with covariates framework allowed us to use partial and composite data that reported on one or only a few pathogens, or that reported multiple pathogens aggregated together. Networks, however, can be unstable with sparse data and stable estimates have in some cases required the use of Bayesian priors in these models. In particular, we imposed Gaussian priors with mean 0 and non-zero variance on all coefficients except

intercepts, to bias the model away from spurious effects driven by data sparsity. These priors were based on expert opinion and can improved with further empirical validation in the future. Table 6.3.4 provides a list of these priors.

Table 6.3.2: Pathogens assessed, covariates, and age groups for each infectious syndrome

Infectious syndrome	Pathogens assessed	Model covariates	Age groups
Bloodstream infections	<i>Acinetobacter baumannii</i> , <i>Citrobacter</i> spp., <i>Enterobacter</i> spp., <i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , other enterococci, <i>Escherichia coli</i> , fungus, group A <i>Streptococcus</i> , group B <i>Streptococcus</i> , <i>Klebsiella pneumoniae</i> , <i>Neisseria meningitidis</i> , non-typhoidal <i>Salmonella</i> , polymicrobial, <i>Proteus</i> spp., <i>Pseudomonas aeruginosa</i> , <i>Salmonella</i> Typhi, <i>Serratia</i> spp., <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i>	HAQ Index, <sup>14</sup> age group, age-standardised proportion of intravenous drug use, <sup>23</sup> proportion coverage by PCV3 vaccine, <sup>33</sup> indicator variable for Europe	Neonatal, Post-neonatal–5, 5–50, 50–70, 70+
Infections of bones, joints, and related organs	<i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , other enterococci, <i>Escherichia coli</i> , group A <i>Streptococcus</i> , group B <i>Streptococcus</i> , <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	HAQ Index, age group	Under 5, 5–50, 50–70, 70+
Endocarditis and other cardiac infections	See bloodstream infection pathogens	Not explicitly modelled. Pathogen distribution for bloodstream infections is used.	Neonatal, Post-neonatal–5, 5–50, 50–70, 70+
Diarrhoea	Adenovirus, <i>Aeromonas</i> spp., Amebiasis, <i>Campylobacter</i> spp., <i>Clostridium difficile</i> , cryptosporidium, enteropathogenic <i>Escherichia coli</i> , enterotoxigenic <i>Escherichia coli</i> , non-typhoidal <i>Salmonella</i> , norovirus, rotavirus, <i>Shigella</i> spp., <i>Vibrio cholerae</i>	Not modelled here. GBD diarrhoea aetiology estimates are used.	GBD most detailed age groups
Lower respiratory infections and all related infections in the thorax	<i>Acinetobacter baumannii</i> , <i>Chlamydia</i> spp., <i>Enterobacter</i> spp., <i>Escherichia coli</i> , fungus, group B <i>Streptococcus</i> , <i>Haemophilus influenzae</i> , <i>Klebsiella pneumoniae</i> , <i>Legionella</i> spp., <i>Mycoplasma</i> spp., polymicrobial, <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , virus	HAQ Index, proportion coverage by PCV3 vaccine, proportion coverage by Hib3 vaccine, <sup>33</sup> age group, HAI/CAI	Neonatal, Post-neonatal–5, 5–50, 50–70, 70+
Meningitis and other bacterial central nervous system infections	<i>Escherichia coli</i> , group B <i>Streptococcus</i> , <i>Haemophilus influenzae</i> , <i>Klebsiella pneumoniae</i> , <i>Listeria monocytogenes</i> , <i>Neisseria meningitidis</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , virus	HAQ Index, proportion coverage by PCV3 vaccine, proportion coverage by Hib3 vaccine, age group, proportion of population covered by *10-15 MenAfriVac rollout <sup>1,34</sup>	Neonatal, Post-neonatal–5, 5–50, 50–70, 70+
Peritoneal and intra-abdominal infections	<i>Citrobacter</i> spp., <i>Enterobacter</i> spp., <i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , other <i>Klebsiella</i> species, <i>Proteus</i> spp., <i>Pseudomonas aeruginosa</i> , <i>Serratia</i> spp., <i>Staphylococcus aureus</i>	HAQ Index, age group	Under 5, 5–50, 50–70, 70+
Bacterial infections of the skin and subcutaneous systems	<i>Acinetobacter baumannii</i> , <i>Enterobacter</i> spp., <i>Enterococcus faecalis</i> , other enterococci, <i>Escherichia coli</i> , group A <i>Streptococcus</i> , group B <i>Streptococcus</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus</i> spp., <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	HAQ Index, age group	Under 5, 5–50, 50–70, 70+
Urinary tract infections and pyelonephritis	<i>Acinetobacter baumannii</i> , <i>Citrobacter</i> spp., <i>Enterobacter</i> spp., <i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , other enterococci, <i>Escherichia coli</i> , group B <i>Streptococcus</i> , <i>Klebsiella pneumoniae</i> , <i>Morganella</i> spp., <i>Proteus</i> spp., <i>Providencia</i> spp., <i>Pseudomonas aeruginosa</i> , <i>Serratia</i> spp., <i>Staphylococcus aureus</i>	HAQ Index, age group, HAI/CAI	Under 5, 5–50, 50–70, 70+

Group A *Streptococcus* = *Streptococcus pyogenes*. Group B *Streptococcus* = *Streptococcus agalactiae*. HAQ Index = Healthcare Access and Quality Index. HAI/CAI = hospital-acquired infection/community-acquired infection.



Table 6.3.3: Number of data points and parameters in each pathogen distribution model

Infectious syndrome	Subtype	Number of data points	Number of parameters
LRI+		158967	135
BSI		126417	180
Skin		1105	55
CNS	Neonatal	25615	81
CNS	Post neonatal	25579	81
UTI		23662	96
Bone+		1870	45
Intra-abdominal		2458	55

BSI = Bloodstream infections. CNS = Meningitis and other bacterial central nervous system infections. LRI+ = Lower respiratory infections and all related infections in the thorax. Intra-abdominal = Peritoneal and intra-abdominal infections. Skin = Bacterial infections of the skin and subcutaneous systems. UTI = Urinary tract infections and pyelonephritis. Bone+ = Infections of bones, joints, and related organs.

Table 6.3.4. Gaussian prior standard deviations for non-intercept coefficients for each pathogen distribution model

Infectious syndrome	Sub-type	Gaussian prior standard deviation
BSI		0.1
CNS	Neonatal	0.1
CNS	Non-neonatal	0.1
LRI+		0.1
Intra-abdominal		0.3
Skin		0.3
UTI		0.02 for <i>A. baumannii</i> /HAQ Index coefficient 0.1 for all others
Bone+		0.5

BSI = Bloodstream infections. CNS = Meningitis and other bacterial central nervous system infections. LRI+ = Lower respiratory infections and all related infections in the thorax. Intra-abdominal = Peritoneal and intra-abdominal infections. Skin = Bacterial infections of the skin and subcutaneous systems. UTI = Urinary tract infections and pyelonephritis. Bone+ = Infections of bones, joints, and related organs.

## Section 6.4: Exceptions and special handling

There were several notable exceptions and special handling decisions made for each individual pathogen distribution model. We hope to address many of these exceptions with more sustainable methods in our future work.

### Section 6.4.1: Cardiac infections

For cardiac infections, we used the pathogen distribution for bloodstream infections rather than estimating specific distributions for these syndromes, due to a lack of complete literature reviews on the aetiologies and case-fatality rates of these syndromes. We consider this to be a serious limitation of our methodology, but do not anticipate that is seriously impactful on our final estimates, since cardiac infections are the third-lowest syndrome by deaths and years lived with disability (YLDs), comprising just 1.33% (95% UI 1.02–1.67) of all deaths associated with AMR.

### Section 6.4.2: Diarrhoea

In diarrhoea patients, cultures of specimens taken from the gastrointestinal tract, bowels, rectum, or stool are almost always affected by contaminants or pathogens that are not the cause of diarrhoea. For this reason, we believe that our input data and modelling framework are not able to accurately capture the aetiologies of diarrhoea. We chose to use GBD estimates of the aetiologies of diarrhoea in deaths instead of running our own model.<sup>35</sup> These estimates are based on the odds ratio of having diarrhea given the detection of a pathogen, obtained from the Global Enteric Multicenter Study, therefore removing the influence of any pathogen that does not increase the risk of diarrhea.

A major limitation of using this study is that the GBD diarrhoea aetiology estimates are population attributable fractions (PAFs) for each pathogen. These PAFs may add to greater than 1 and the authors made no attempt to quantify the extent of co-occurrence of pathogens. This is inconsistent with the pathogen distribution estimation method used in our study, which quantifies polymicrobial infections and estimates all pathogens as mono-infections. In order to avoid duplication of cases in our framework, we had to make some assumptions about the co-occurrence of pathogens in diarrhoea. We chose to normalise the PAFs to 1 for any demographic where the sum of GBD diarrhoea aetiology PAFs was greater than 1. This assumed that co-occurrence of pathogens was random and that

the “other” pathogens category was negligible in these demographics. We made no adjustment to demographics where the PAFs added to less than 1. To convert the fatal PAFs to a distribution of aetiologies in incidence, we rescaled the distribution according to our estimates of the pathogen-specific case fatality ratios of diarrhea, calculated as described in section 5.

#### *Section 6.4.3: Bacterial infections of the skin and subcutaneous systems*

Certain skin and subcutaneous samples are easily affected by contaminants, colonization, and other pathogens that are not the cause of infection. For this reason, we considered microbial data and mortality surveillance to be too difficult to extract meaningful aetiology information from, and instead used only ICD-coded databases (multiple cause of death, hospital discharge, and linkage data) and literature studies as inputs into our model of the pathogen distribution of skin infections.

#### *Section 6.4.4: Lower respiratory infections and all related infections in the thorax*

We dropped all data on *S. pneumoniae* for community-acquired LRI and thorax infections in non-neonatal age groups except our estimates from the vaccine probe analysis. Our model also predicted a high fraction of polymicrobial in neonates for community-acquired infections for this infectious syndrome based off of only 1 study, CHAMPS. We found this to be implausible and so dropped polymicrobial from the estimates for this age group in community-acquired infections and renormalized the proportions for all other pathogens to 1.

#### *Section 6.4.5: Peritoneal and intra-abdominal infections*

Because dedicated anaerobic cultures were not routinely performed for peritoneal samples, we dropped all anaerobes observed in the data for and excluded anaerobes as an etiology of intra-abdominal infections.

#### *Section 6.4.6: Meningitis and other bacterial central nervous system infections*

Due to the unique pattern of meningitis in neonates, particularly the high prevalence of GBS, we modeled neonatal and adult central nervous system infections separately.

#### *Section 6.4.7: Infectious syndromes not modelled*

For three infectious syndromes, we did not run a pathogen distribution model. These syndromes are all caused by distinct pathogens whose individual burdens are already estimated in GBD as separate causes of death. For these syndromes, we simply used GBD estimates (table 6.4.6.1)

Table 6.4.6.1: Infectious syndromes for which we used GBD estimates to obtain the pathogen distribution

Infectious syndrome	Pathogens	GBD causes
Typhoid, paratyphoid, and invasive non-typhoidal Salmonella	<i>Salmonella</i> Typhi	Typhoid fever
	<i>Salmonella</i> Paratyphi	Paratyphoid fever
	Non-typhoidal <i>Salmonella</i>	Invasive non-typhoidal Salmonella
Tuberculosis	<i>Mycobacterium tuberculosis</i>	Tuberculosis
Gonorrhoea and chlamydia	<i>Neisseria gonorrhoeae</i>	Gonococcal infection
	<i>Chlamydia trachomatis</i>	Chlamydial infection

### Section 6.5: Model validation

To assess model validity, we calculated the root mean square error (RMSE) and coefficient of determination ( $R^2$ ) for each pathogen distribution model in proportion space for both in-sample and out-of-sample predictions (Table 6.5.1). Proportions were predicted for each observation using the specific denominator observed from that study. For example, if a given study reported on only *E. coli* and *S. pneumoniae*, the predictions for model validation for this study were calculated as proportions of the total for *E. coli* and *S. pneumoniae*. In order to calculate out-of-sample fit, we perform non-exhaustive cross-validation, with each round of the validation holding out 1 country of data at a time. This leave-one-country-out approach simulates the prediction task of estimating the pathogen distribution of a country for which we have no data.

$R^2$  ranges from 0.784 to 0.867 in-sample and from 0.755 to 0.837 out of sample, indicating good model fit with only modest losses when data are moved out of sample. RMSE ranges from 0.129 to 0.149 in-sample and from 0.141 to



0.159 out of sample. Given that the data are expected to vary from the model predictions according to the observation-level variance, and the fact that the RMSEs are relatively consistent between in-sample and out-of-sample, these RMSEs are reasonable. Overall, these metrics show that these models have good fit and good out-of-sample predictive ability.

Table 6.5.1 In-sample and out-of-sample validation metrics for pathogen distribution models

Infectious syndrome	Model type	R <sup>2</sup>		RMSE	
		In sample	Out of sample	In sample	Out of sample
Bacterial infections of the skin and subcutaneous systems		0.808	0.771	0.129	0.141
Bloodstream infections		0.822	0.785	0.128	0.141
Infections of bones, joints, and related organs		0.858	0.837	0.141	0.151
Lower respiratory infections and all related infections in the thorax		0.810	0.780	0.142	0.153
Meningitis and other bacterial central nervous system infections	Neonatal	0.858	0.803	0.134	0.158
	Non-neonatal	0.867	0.822	0.129	0.150
Peritoneal and intra-abdominal infections		0.815	0.812	0.147	0.148
Urinary tract infections and pyelonephritis		0.784	0.755	0.149	0.159

Out of sample metrics calculated using leave-one-country-out cross validation

## Section 7: Prevalence of resistance

### Section 7.1: Input data

We identified line level and aggregate data on the prevalence of resistance in bacterial pathogens, which were linked to the country and year in which the infection was acquired, from datasets obtained from pharmaceutical companies, surveillance networks, academic institutions, and individual hospitals (see section 2). In total, we gathered over 52.8 million test results for the 88 pathogen–drug combinations we assessed. Table S7 provides a detailed breakdown of this total by pathogen–drug combination.

We supplemented microbiological data with systematic reviews following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,<sup>36</sup> to collect resistance data published from countries and territories where surveillance systems do not routinely collect data to ensure extensive coverage of the pathogen–drug combinations thought to contribute the greatest burden of drug resistant infections, which we termed core pathogen–drug combinations (table 7.2.1). Data on the prevalence of AMR in these pathogen–drug combinations were extracted from published literature and compiled into comprehensive datasets. The systematic reviews followed similar methodologies; a detailed description can be found either in published literature (*S. Typhi* and *S. Paratyphi*<sup>37</sup>) or in the corresponding PROSPERO records (*E. coli*, *K. pneumoniae*, *S. aureus* and *S. pneumoniae* PROSPERO registration CRD42019145148; *Shigella* species PROSPERO registration CRD42019127603; iNTS PROSPERO registration CRD42020189935; *N. gonorrhoeae* SPF unique identifier osf.io/4vy5n). The *S. Typhi* and *S. Paratyphi* A systematic review was expanded to include non-blood culture isolates for the current analysis.

Forms were created, and screening and data extraction were completed using web-based systematic review software (DistillerSR, Evidence Partners, Ottawa, Canada) for all pathogens except *Salmonella*, for which a smaller number of manuscripts were identified.

To more comprehensively account for the burden of AMR in bacteria, we also estimated the prevalence of resistance for 71 supplementary pathogen–drug combinations for which we did not conduct a systematic literature review. Data for these supplementary combinations were extracted from the datasets obtained from pharmaceutical companies, academic institutes, and individual hospitals using the same processing procedure as was used for the core pathogen–drug combinations. The list of supplementary combinations is presented in table 7.2.2.

For the prevalence of drug resistance in *Mycobacterium tuberculosis* for multi-drug resistance (MDR, characterised by isoniazid and rifampicin co-resistance) excluding extensive drug resistance (XDR, characterised by resistance to isoniazid, rifampicin, and fluoroquinolone, as well as either aminoglycosides or capreomycin) and XDR, we used previously published GBD results.<sup>1</sup> Notably, GBD MDR excluding XDR TB estimates and the MDR/rifampin mono-resistant TB estimate from WHO differ, primarily because HIV/TB cases are included as part of WHO TB estimates. GBD adjusts the miscoding of deaths cause by HIV and TB in locations with high prevalence of both diseases, such as South Africa, assigning more deaths to HIV/TB (which are attributed to HIV) and these methodological differences lead to lower MDR TB mortality across GBD burden estimates. An additional difference in estimates for MDR is that WHO includes rifampicin mono-resistance as part of their MDR TB figures.

## Section 7.2: Data processing

The prevalence of resistance for each pathogen–drug combination was calculated for each data source, by country and year. Whenever possible, we classified resistance using the most recent CLSI guidelines based on the MICs provided in the data. When MICs were unavailable, we deferred to lab interpretation to classify the isolates. All isolates determined to have intermediate resistance were classified as resistant. To determine the prevalence of resistance to a class of antibiotics (eg, fluoroquinolones), resistance to any one of the antibiotics in the class was sufficient to classify an isolate as resistant for line level data (ie, susceptibility data for individual isolates). For aggregate data (ie, the proportion of isolates resistant to various antibiotics), the highest prevalence of resistance to any antibiotic in the class was selected. Multidrug resistance in *Salmonella* species was defined as concurrent resistance to ampicillin/amoxicillin, chloramphenicol, and trimethoprim-sulfamethoxazole; and fluoroquinolone resistance was defined as ciprofloxacin minimum inhibitory concentration of 0.125 µg/ml or higher, or nalidixic acid resistance (CLSI breakpoint for *Salmonella* spp. were updated in 2012 to include 0.125 µg/ml as isolates with ‘decreased ciprofloxacin susceptibility’, and we have considered these as resistant). Nalidixic acid resistance was also used as a proxy for fluoroquinolone non-susceptibility for *Shigella* species.

Table 7.2.1: Core pathogen–drug combinations

Pathogen	Antimicrobial
<i>Escherichia coli</i>	Third-generation cephalosporins Fluoroquinolones
<i>Klebsiella pneumoniae</i>	Third-generation cephalosporins Carbapenems
<i>Staphylococcus aureus</i>	Methicillin
<i>Streptococcus pneumoniae</i>	Penicillin
<i>Salmonella</i> Typhi & Paratyphi A	Multidrug resistance Fluoroquinolones
Invasive non-typhoidal <i>Salmonella</i>	Fluoroquinolones
<i>Shigella</i> species	Fluoroquinolones
<i>Neisseria gonorrhoeae</i>	Third-generation cephalosporins
<i>Mycobacterium tuberculosis</i>	Isoniazid mono-resistance, Rifampicin mono-resistance

Table 7.2.2: Supplementary pathogen–drug combinations

Pathogen	Antimicrobial
<i>Acinetobacter baumannii</i>	Aminoglycosides, Anti-pseudomonal penicillin/Beta-lactamase inhibitors, Beta-lactam/Beta-lactamase inhibitors, Carbapenems, Third-generation cephalosporins, Fourth-generation cephalosporins, Fluoroquinolones
<i>Citrobacter</i> species	Aminoglycosides, Anti-pseudomonal penicillin/Beta-lactamase inhibitors, Carbapenems, Third-generation cephalosporins, Fourth-generation cephalosporins, Fluoroquinolones
<i>Enterobacter</i> species	Aminoglycosides, Anti-pseudomonal penicillin/Beta-lactamase inhibitors, Carbapenems, Fourth-generation cephalosporins, Fluoroquinolones, Trimethoprim-Sulfamethoxazole
<i>Enterococcus faecalis</i>	Fluoroquinolones, Vancomycin
<i>Enterococcus faecium</i>	Fluoroquinolones, Vancomycin
<i>Enterococcus</i> species	Fluoroquinolones, Vancomycin

<i>Escherichia coli</i>	Aminoglycosides, Aminopenicillin, Beta-lactam/Beta-lactamase inhibitors, Carbapenems, Trimethoprim-Sulfamethoxazole
Group A <i>Streptococcus</i>	Macrolide
Group B <i>Streptococcus</i>	Fluoroquinolones, Macrolide, Penicillin
<i>Haemophilus influenzae</i>	Aminopenicillin, Third-generation cephalosporins
<i>Klebsiella pneumoniae</i>	Aminoglycosides, Beta-lactam/Beta-lactamase inhibitors, Fluoroquinolones, Trimethoprim-Sulfamethoxazole
<i>Morganella</i> species	Third-generation cephalosporins, Fourth-generation cephalosporins, Fluoroquinolones
<i>Neisseria gonorrhoeae</i>	Fluoroquinolones
<i>Proteus</i> species	Aminoglycosides, Aminopenicillins, Third-generation cephalosporins, Fluoroquinolones, Trimethoprim-Sulfamethoxazole
<i>Pseudomonas aeruginosa</i>	Aminoglycosides, Anti-pseudomonal penicillin/Beta-lactamase inhibitors, Carbapenems, Third-generation cephalosporins, Fourth-generation cephalosporins, Fluoroquinolones
<i>Serratia</i> species	Aminoglycosides, Anti-pseudomonal penicillin/Beta-lactamase inhibitors, Carbapenems, Third-generation cephalosporins, Fourth-generation cephalosporins, Fluoroquinolones
<i>Staphylococcus aureus</i>	Fluoroquinolones, Macrolide, Trimethoprim-Sulfamethoxazole, Vancomycin
<i>Streptococcus pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors, Carbapenems, Third-generation cephalosporins, Fluoroquinolones, Macrolide, Trimethoprim-Sulfamethoxazole

Group A *Streptococcus* = *Streptococcus pyogenes*. Group B *Streptococcus* = *Streptococcus agalactiae*

To account for biased level of resistance found in tertiary care settings, we reviewed all input data used for the prevalence of resistance estimation and classified each data source as either tertiary, non-tertiary, or unknown/mixed designation, which was a commonly used classification for large resistance surveillance networks which don't report on the hospitals they collect data from. We located datasets that either provided facility information at the line-level or reported samples from exclusively tertiary or non-tertiary facilities. Where possible, we used tertiary/non-tertiary assignments from the data providers. When no assignments were available, we classified sites as tertiary, primary, and secondary by following the definitions provided by Jamison et al.<sup>38</sup> in table 7.2.3. We first considered hospital name when classifying. If the name did not include any of the terms listed in table 7.2.3, we searched the facility website for self-designations of tertiary/non-tertiary (most preferred), number of specialties, and bed-size. We classified facilities with vague names and with no websites or websites with insufficient information as “mixed/unknown”; data from these facilities could contain both tertiary and non-tertiary samples. Finally, we grouped primary and secondary facilities together in the non-tertiary category.

Table 7.2.3: Definitions and terms for different levels of hospital

Disease Control Priorities Project: terminology and definitions	Alternative terms commonly found in the literature
Primary-level hospital: few specialties—mainly internal medicine, obstetrics and gynecology, pediatrics, and general surgery, or just general practice; limited laboratory services available for general but not specialized pathological analysis	District hospital Rural hospital Community hospital General hospital
Secondary-level hospital: highly differentiated by function with 5 to 10 clinical specialties; size ranges from 200 to 800 beds; often referred to as a provincial hospital	Regional hospital Provincial hospital (or equivalent administrative area such as county) General hospital
Tertiary-level hospital: highly specialized staff and technical equipment— for example, cardiology, intensive care unit, and specialized imaging units; clinical services highly differentiated by function; could have teaching activities; size ranges from 300 to 1,500 beds	National hospital Central hospital Academic or teaching or university hospital

For systematic review data collected from sub-Saharan Africa, we referred to Maina et al.<sup>39</sup> who identified and defined health facilities at each service delivery level (primary to tertiary) in sub-Saharan Africa using both information from health sector policies and strategic plans for each country in the region. They also undertook further comparative/validation analyses to cross reference the completeness/robustness of their classifications against the corresponding number of facilities reported at each level in the most current country-level health sector strategic plans and other health sector reports. Using this hierarchy by country (please see online table 2 in Maina et al.) we classified facilities in sub-Saharan Africa from the systematic review data as tertiary versus non-tertiary.

The proportion of data classified as originating from a tertiary facility differed substantially by super region, ranging from 0.3% of cases in the high-income super-region to 25.0% of cases in sub-Saharan Africa; this stark difference reaffirmed the importance of adjusting the data. To create robust inputs for the crosswalk, data were aggregated by source, year, tertiary/non-tertiary status, and super-region. Because there was no reliable way to determine the mix of hospital types in mixed/unknown data, this data was grouped with non-tertiary. We chose to cluster this data with non-tertiary rather than omit it, as, for some super-regions, the proportion of definitively non-tertiary data was very low (e.g., 0.05% for high-income). After aggregating the data in this way, we created a set of matched pairs, matching every tertiary data point to non-tertiary data for the same pathogen–drug combination from the same super-region collected within 5 years from one another.

Because the degree of bias in resistance between tertiary and non-tertiary data could vary across different parts of the world, we ran a separate crosswalk for each super region and pathogen–drug *super group* combination. Certain bacteria and antimicrobials were clustered into super groups to provide the models with more robust input data, though, crucially, while a given model would contain several pathogen–drug combinations in its inputs, every matched pair was made comparing tertiary and non-tertiary values for the same combination. Bacteria were classified as follows:

Table 7.2.4: Pathogens in each pathogen super group

Pathogen super group	Incorporated pathogens
Gram-negatives	<i>Enterococcus faecalis</i> , <i>Enterococcus faecium</i> , <i>Enterococcus</i> spp., Group A <i>Streptococcus</i> , Group B <i>Streptococcus</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i>
Enterobacterales	<i>Citrobacter</i> spp., <i>Enterobacter</i> spp., <i>Escherichia coli</i> , <i>Haemophilus influenzae</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus</i> spp., <i>Serratia</i> spp.
Pseudomonadales	<i>Acinetobacter baumannii</i> , <i>Pseudomonas aeruginosa</i>

Notably, some pathogens were excluded from the tertiary crosswalk procedure because it was believed that infections with such pathogens would be robust to tertiary care bias. These pathogens were: *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, non-typhoidal *Salmonella*, *Salmonella paratyphi*, *Salmonella typhi*, and *Shigella* spp. Data for *Morganella* spp. was not crosswalked as there was no input data for that pathogen from tertiary facilities.

Only one group of antimicrobials was clustered to create an antimicrobial super group, the  $\beta$ -lactam group, which was comprised of: aminopenicillin, anti-pseudomonal penicillin,  $\beta$ -lactamase inhibitors, carbapenems, third and fourth generation cephalosporins, methicillin, and penicillin. All other antibiotic classes (aminoglycosides, fluoroquinolones, macrolides, sulfanoamides, and vancomycin) each individually comprised their own antimicrobial super group.

To allow us to implement linear models, resistance values were logit-transformed. We used the delta method to compute the standard error of the prevalence of resistance in logit space. To incorporate data with zero resistance, or with complete resistance, we applied a 0.1% offset, such that the prevalence of resistance for data with zero resistance was represented as 0.1% and the prevalence of resistance for data with total resistance was represented as 99.9%. We then used the MR-BRT modelling framework to estimate the logit difference of tertiary and non-tertiary data for each super region-pathogen/antimicrobial ‘super combination,’ including a random effect for each pathogen–drug combination within the super combination and employing a positivity prior to enforce the constraint that the tertiary data exceed or be equal to the non-tertiary data. For the super region-pathogen/antimicrobial super combinations with sparse input data (fewer than 250 matched pairs) we instead used global estimated logit

differences between tertiary and non-tertiary data for that pathogen/antimicrobial super combination, employing the same positivity prior.

After modelling the difference between tertiary and non-tertiary data, we implemented the models to adjust all the country-level tertiary input data that was indicated as biased. We then used the adjusted prevalence of resistance estimates from tertiary care facilities and unadjusted prevalence of resistance from non-tertiary/mixed care facilities as data inputs for the prevalence of resistance models. As was done before, resistance values were offset prior to logit-transformation to allow the use of linear models; data with zero resistance or complete resistance was offset by 2%. Exceptions to this offset were made for two combinations, *Staphylococcus aureus*/vancomycin and Group B *Streptococcus*/penicillin, which were anticipated to often have values beneath 2% resistance. For these combinations, we applied a 0.5% offset instead.

### Section 7.3: Modelling framework

The prevalence of AMR in each pathogen–drug combination was modelled separately. For the core combinations, excluding *N. gonorrhoeae*/3GC, we selected a range of spatially- and temporally-explicit health and socio-demographic-related covariates with biologically plausible associations to the prevalence of AMR in each pathogen from the Global Health Data Exchange (<http://ghdx.healthdata.org/>), and from published literature.<sup>3</sup> This list was narrowed down by fitting a lasso penalised regression model between the data and the covariates for each dataset (using the ‘glmnet’ package version 3.0.2 in R version 3.6.1) and selecting the most influential covariates in each of the pathogen–drug models to be taken forward. For the supplementary pathogen–drug combinations and *N. gonorrhoeae*/3GC, we utilised a standard set of covariates for all models: HAQ Index, pigs per capita (as a proxy for antibiotic use in animal husbandry), mean temperature, and antibiotic consumption of the antibiotic class relevant to each pathogen–drug combination. Determining more individualised sets of covariates for each of these supplementary pathogen–drug combinations is an ongoing focus for future extensions of this research.

Due to the high heterogeneity of the input datasets, we outliered data points found to have the most extreme values for the prevalence of resistance. An initial generalised linear model (GLM) was fit to the data and covariates and input data points that lay outside of two times the median absolute deviation from the modelled estimate for each location were determined to be outliers and removed. The GLM was fit with nested random effects based on the GBD super-region, region, and country or territory to capture spatial effects, and was fit using the ‘lme4’ package version 1.1-21 in R version 3.6.1.

After the removal of extreme values, the datasets were used to fit spatiotemporal statistical models of the prevalence of AMR. Firstly, we used a stacked ensemble model to fit the associations between selected covariates and data. For each of the pathogen–drug combinations, we considered the following child models for inclusion: generalised additive models (GAM), penalised regression models (elastic-net, ridge, lasso), random forest, cubist, and neural-networks. Models were fit in R version 3.6.1, using the packages ‘CARET’ version 6.085, ‘mgcv’ version 1.8.31, and ‘glmnet’ version 3.0.2. We fit the child models using five-fold cross validation for each combination and selected the best performing, non-correlated child models based on the out-of-sample predictive performance (final covariates for each pathogen–drug combination are shown in table S8). We then calculated the  $R^2$ -weighted mean of the estimates of the child models, constraining the coefficients to sum to one, and used these ensemble estimates to fit a spatiotemporal Gaussian process regression (ST-GPR) model for each pathogen–drug combination.

ST-GPR is described in detail elsewhere.<sup>1</sup> In brief, spatial and temporal weights were applied to the residuals of the stacked ensemble model; these were then added to the modelled estimates to smooth them in time and space. A Gaussian process regression (GPR) was then fit, and the mean prevalence of AMR was calculated from 1000 draws of the GPR for each location and year with endemic disease. The 1000 draws of the model were taken through to the next stage of calculations to propagate uncertainty throughout.

## Section 7.4: Covariates

Appendix table S8 shows all of the covariates used to model the core pathogen–drug combinations and provides citations detailing the methods used to estimate these covariates. For certain covariates, we provide a brief summary of the estimation method below.

**Mean temperature:** Temperature data are obtained from Climatic Research Unit, University of East Anglia.<sup>40</sup> For each GBD geography, the temperature and population datasets (rasters) are cropped to just cover said geography. The population weighted mean temperature is calculated for each pixel of data in that geography, and then those values are aggregated to produce a single value for the geography. This is repeated for each country-year.

**Pigs per capita:** Data on the global distribution of pigs were obtained from the Food and Agriculture Organization of the United Nations.<sup>41,42</sup> The raw pig count raster is cropped to GBD geography. Total number of pigs is calculated by summing all pixels in that geography, the result is then divided by the total population of that geography to calculate pigs per capita. This is repeated for each country-year.

**Population density:** First, population density per pixel was calculated by dividing the population count per pixel by the land area per pixel. The result raster is then thresholded for those pixels where there are more than 1000 people per sq km. The result is multiplied by population, and then the area summed to get a total population in a geography in that bin. Finally this value is divided by total population in the geography to get the final proportion result.

**Oral rehydration:** Data on oral rehydration, defined as the proportion of children under 5 who had diarrhea in the last 2 weeks who received oral rehydration (ORS) treatment, were collected from multi-country population health surveys such as the Demographic and Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS), Reproductive Health Surveys (RHS), and Living Standards Measure Study (LSMS) survey, as well some country-specific surveys (see <http://ghdx.healthdata.org/gbd-2019/data-input-sources>). Only nationally representative datasets are included, and the most extreme 10% of the data is removed from each quintile of Socio-demographic Index (SDI) or HAQ Index. A forward stepwise method is used to select covariates, resulting in SDI and antenatal care (1 visit) coverage being selected. Finally, ST-GPR is run using a mixed effects stage 1 regression with fixed effects on SDI and antenatal care coverage and random effects for super-regions, regions, and countries. Predictions are made for all GBD geographies.

## Section 7.5: Resistance profiles

To accurately assess the burden associated with resistance to each antibiotic, we needed to first understand the landscape of multidrug-resistant bacteria, for which the burden would be shared across several antibiotics. We therefore estimated, for each bacteria studied, a set of ‘resistance profiles’ characterized as the probabilities for each possible combination of resistance/susceptibility for all of the antibiotics analyzed. For example, for a bacterium for which we assessed three antibiotics, we would estimate eight probabilities: SSS, SSR, SRS, RSS, SRR, RSR, RRS, and RRR (S – susceptible, R – resistant). These probabilities encompass the entire set of possibilities of resistance for the bacterium, and sum to 1.

For a pathogen for which we assessed  $n$  antibiotics, resistance profiles were estimated by optimising over a  $2^n - 1$ -dimensional probability simplex with  $\frac{n(n+1)}{2}$  linear constraints. Every such set of resistance profiles corresponds to a full specification of a multivariate binomial distribution. The target set of constraints were as follows:

- The inferred marginal probability of resistance for each antibiotic (the prevalence of resistance to an antibiotic irrespective of all others analyzed) exactly matches the estimates from our prevalence of resistance models. Since there are  $n$  antibiotics, this set comprises  $n$  constraints.
- The inferred pairwise likelihood of co-resistance for each pair of antibiotics exactly matches the likelihood inferred from the marginal probability of each antibiotic in the pair, and the Pearson correlation of resistance between the two antibiotics observed across all of the laboratory data we compiled. These represent  $\frac{n^2-n}{2}$  additional constraints.



The input format for these constraints for an example case with  $n = 3$  is shown in figure 7.5.1.

Figure 7.5.1: Example input matrix for calculating resistance profiles for a pathogen with 3 antibiotic classes (A,B,C)

Prev(A)	Prev(A&B)	Prev(A&C)	Prev(X): prevalence of resistance of antibiotic X from ST-GPR model, by location and draw  Prev(X&Y): prevalence of resistance in both X and Y, back calculated from Prev(X), Prev(Y) and the Pearson correlation of X&Y in the lab data with multiple resistance screens
-	Prev(B)	Prev(B&C)	
-	-	Prev(C)	

In the  $n=2$  case, the number of constraints in our framework (3) is equal to the number of unknowns in the probability simplex ( $2^n - 1 = 3$ ), and therefore at most one set of resistance profiles is possible. For all larger values of  $n$ , however, the number of unknowns exceeds the number of constraints, and there are infinite potential resistance profiles. Thus, our resistance profiles are generated by solving for a single sample from the probability simplex formed under the established constraints of marginal resistance and co-resistance.

There is no a priori guarantee that the observables generate a feasible solution. To prevent the constraints from delineating an infeasible probability simplex (for example, an input suggesting the individual resistances to antibiotics A and B are both above 90% but the probability of co-resistance to A and B is below 10%), we solved an optimization problem that identified, for each input matrix, the closest feasible set of input constraints and a corresponding set of resistance profiles that fits these constraints. The 1-simplex in any dimension is specified by

$$\Delta := \{p: \quad 0 \leq p_i \leq 1, \sum p_i = 1\} \quad (7.5.1.1)$$

Each marginal observation and each pairwise co-resistance corresponds to a linear constraint, where a sum over a subset of the  $p$  in the simplex should be a given value  $v_i$ :

$$m_i^T p = v_i \quad (7.5.1.2)$$

where  $m_i$  is a ‘mask vector’ of zeros and ones, used to pick out the appropriate summands. Overall, there are  $\frac{n(n+1)}{2}$  such affine constraints. The optimisation problem we solve is to find the nearest feasible simplex given these constraints:

$$\min_{p \in \Delta} f(p) := \sum_{i=1}^{n(n+1)/2} \frac{1}{\sigma_i^2} (m_i^T p - v_i)^2 \quad (7.5.1.3)$$

Where  $\frac{1}{\sigma_i^2}$  can be used to provide importance weights for the data. This is a least squares problem with linear equality and inequality constraints (corresponding to the simplex), and can be solved very efficiently even for relatively large  $n$  (such as 10 co-occurring antibiotic classes). The result is guaranteed to return the probability simplex closest to the specified constraint, even if the original set of constraints is infeasible, and corresponding set of resistance profiles that fits this nearest simplex.

To propagate uncertainty, we repeat this procedure for each of the 1,000 draws we estimate for prevalence of antibiotic resistance. To generate the  $i$ -th draw of our resistance profiles, we input the  $i$ -th draw of the marginal probability of resistance for each antibiotic analyzed for a given pathogen into the probability simplex optimization algorithm. Updating the marginal probabilities of resistance in turn influences the probabilities of co-resistance, and each element of the input we feed the algorithm is unique to the  $i$ -th draw. The optimization is also initialized randomly for every draw. This process is implemented for each GBD country, resulting in 1000 resistance profiles for each country for each pathogen in our analysis.

It is important to note that while we produce resistance profiles unique to each country, the Pearson correlations of co-resistance that we derive from the input data are assumed to be constant across location, sex, and infectious syndrome. Due to data sparsity, we cannot currently identify co-resistance patterns in several locations (particularly LMICs) with insufficient or non-existent line-level data; indeed, the data sources providing multiple resistance tests for a single isolate are among the most detailed of those we collected for this research and require exceptional data quality standards that are not easily achieved throughout the world. Identifying differences in patterns of co-resistance by location or infectious syndrome is of considerable interest in the future.

### **Section 7.6: Model validation**

Validation of prevalence of resistance modelling occurs in two instances. For the ensemble estimates, machine-learning candidate models are validated using five random holdout sets, and we select models correlated below a Pearson correlation coefficient threshold of 0.8 which showed the best performance based on the  $R^2$  predictive validity for the out-of-sample predictions. These intermediary results are not reported in this paper because they do not pertain to the final prevalence of resistance estimate.

We then validate the entire ensemble ST-GPR process by calculating in-sample and out-of-sample accuracy metrics. Accuracy is measured as the proportion of correctly classified resistant/susceptible isolates based on the modelled estimate and the raw data's prevalence of resistance. As a written example, if there were 10 isolates with 50% resistance in the raw data and the model predicted 60% resistance for that location, we would have 5 correctly classified resistant samples (true positives), 1 incorrectly classified resistant sample (false positive), and 4 correctly classified susceptible samples (true negatives), for 90% accuracy. For out-of-sample cross-validation, we withheld, at the outset of the ensemble modelling process, a set of countries with data as a holdout group: for the core-combinations we withheld 20% of countries each iteration, for 5 total holdout sets, while for the supplementary-combinations we withheld 10% of countries each iteration, for 10 holdout sets. By holding out all of the data for a set of countries, our out-of-sample accuracy metrics reflect the potential model fit we have for countries that have no input data in the entire prevalence of resistance process. Table 7.6.1 reports the accuracy metric for each pathogen–drug combination. Our in-sample accuracy values range from 77.2% to 99.8%, while our out-of-sample accuracy values range from 57.1% to 99.7%.



Table 7.6.1: In-sample and out-of-sample accuracy estimates for prevalence of resistance models

Pathogen	Antibiotic class	IS accuracy	OOS accuracy
<i>Acinetobacter baumannii</i>	3GC	0.98	0.892
<i>Acinetobacter baumannii</i>	4GC	0.964	0.88
<i>Acinetobacter baumannii</i>	AG	0.772	0.645
<i>Acinetobacter baumannii</i>	Anti-pseudomonal	0.96	0.816
<i>Acinetobacter baumannii</i>	BL-BLI	0.969	0.636
<i>Acinetobacter baumannii</i>	CP	0.901	0.768
<i>Acinetobacter baumannii</i>	FQ	0.964	0.821
<i>Citrobacter</i> spp.	3GC	0.987	0.922
<i>Citrobacter</i> spp.	4GC	0.991	0.974
<i>Citrobacter</i> spp.	AG	0.993	0.959
<i>Citrobacter</i> spp.	Anti-pseudomonal	0.984	0.912
<i>Citrobacter</i> spp.	CP	0.995	0.973
<i>Citrobacter</i> spp.	FQ	0.989	0.967
<i>Enterobacter</i> spp.	4GC	0.982	0.941
<i>Enterobacter</i> spp.	AG	0.989	0.976
<i>Enterobacter</i> spp.	Anti-pseudomonal	0.984	0.939
<i>Enterobacter</i> spp.	CP	0.988	0.973
<i>Enterobacter</i> spp.	FQ	0.991	0.98
<i>Enterobacter</i> spp.	TMP-SMX	0.996	0.883
<i>Enterococcus faecalis</i>	FQ	0.982	0.856
<i>Enterococcus faecalis</i>	Vanco	0.993	0.987
<i>Enterococcus faecium</i>	FQ	0.992	0.985
<i>Enterococcus faecium</i>	Vanco	0.976	0.703
<i>Escherichia coli</i>	3GC	0.977	0.973
<i>Escherichia coli</i>	AG	0.979	0.96
<i>Escherichia coli</i>	Aminopenicillin	0.959	0.915
<i>Escherichia coli</i>	BL-BLI	0.932	0.909
<i>Escherichia coli</i>	CP	0.988	0.972
<i>Escherichia coli</i>	FQ	0.983	0.98
<i>Escherichia coli</i>	TMP-SMX	0.907	0.903
Group A <i>Streptococcus</i>	Macrolide	0.987	0.863
Group B <i>Streptococcus</i>	FQ	0.993	0.731
Group B <i>Streptococcus</i>	Macrolide	0.986	0.907
Group B <i>Streptococcus</i>	PCN	0.997	0.992
<i>Haemophilus influenzae</i>	3GC	0.995	0.981
<i>Haemophilus influenzae</i>	Aminopenicillin	0.958	0.849
<i>Klebsiella pneumoniae</i>	3GC	0.981	0.985
<i>Klebsiella pneumoniae</i>	AG	0.983	0.901
<i>Klebsiella pneumoniae</i>	BL-BLI	0.979	0.832
<i>Klebsiella pneumoniae</i>	CP	0.987	0.992
<i>Klebsiella pneumoniae</i>	FQ	0.935	0.755
<i>Klebsiella pneumoniae</i>	TMP-SMX	0.973	0.816
<i>Morganella</i> spp.	3GC	0.922	0.834
<i>Morganella</i> spp.	4GC	0.974	0.917
<i>Morganella</i> spp.	FQ	0.928	0.839
<i>Mycobacterium tuberculosis</i> (new)	Mono INH	0.993	0.966
<i>Mycobacterium tuberculosis</i> (new)	Mono RIF	0.996	0.987
<i>Mycobacterium tuberculosis</i> (retreated)	Mono INH	0.982	0.968

<i>Mycobacterium tuberculosis</i> (retreated)	Mono RIF	0.994	0.966
<i>Neisseria gonorrhoeae</i>	3GC	0.987	0.982
<i>Neisseria gonorrhoeae</i>	FQ	0.972	0.841
Non-typhoidal <i>Salmonella</i>	FQ	0.911	0.967
Other enterococci	FQ	0.928	0.829
Other enterococci	Vanco	0.966	0.924
<i>Proteus</i> spp.	3GC	0.993	0.981
<i>Proteus</i> spp.	AG	0.989	0.906
<i>Proteus</i> spp.	Aminopenicillin	0.991	0.571
<i>Proteus</i> spp.	FQ	0.966	0.842
<i>Proteus</i> spp.	TMP-SMX	0.997	0.986
<i>Pseudomonas aeruginosa</i>	3GC	0.949	0.908
<i>Pseudomonas aeruginosa</i>	4GC	0.988	0.96
<i>Pseudomonas aeruginosa</i>	AG	0.977	0.95
<i>Pseudomonas aeruginosa</i>	Anti-pseudomonal	0.975	0.895
<i>Pseudomonas aeruginosa</i>	CP	0.977	0.912
<i>Pseudomonas aeruginosa</i>	FQ	0.986	0.95
<i>Salmonella</i> Paratyphi	FQ	0.839	0.74
<i>Salmonella</i> Paratyphi	MDR	0.962	0.96
<i>Salmonella</i> Typhi	FQ	0.83	0.8
<i>Salmonella</i> Typhi	MDR	0.87	0.77
<i>Serratia</i> spp.	3GC	0.984	0.946
<i>Serratia</i> spp.	4GC	0.992	0.951
<i>Serratia</i> spp.	AG	0.987	0.965
<i>Serratia</i> spp.	Anti-pseudomonal	0.958	0.894
<i>Serratia</i> spp.	CP	0.991	0.986
<i>Serratia</i> spp.	FQ	0.987	0.953
<i>Shigella</i> spp.	FQ	0.934	0.86
<i>Staphylococcus aureus</i>	FQ	0.984	0.924
<i>Staphylococcus aureus</i>	Macrolide	0.945	0.934
<i>Staphylococcus aureus</i>	Methicillin	0.975	0.883
<i>Staphylococcus aureus</i>	TMP-SMX	0.995	0.992
<i>Staphylococcus aureus</i>	Vanco	0.998	0.997
<i>Streptococcus pneumoniae</i>	3GC	0.98	0.953
<i>Streptococcus pneumoniae</i>	BL-BLI	0.982	0.956
<i>Streptococcus pneumoniae</i>	CP	0.981	0.966
<i>Streptococcus pneumoniae</i>	FQ	0.949	0.925
<i>Streptococcus pneumoniae</i>	Macrolide	0.984	0.884
<i>Streptococcus pneumoniae</i>	PCN	0.945	0.901
<i>Streptococcus pneumoniae</i>	TMP-SMX	0.97	0.884

3GC = Third-generation cephalosporins. 4GC = Fourth-generation cephalosporins. AG = Aminoglycosides. Anti-pseudomonal = Anti-pseudomonal penicillin/Beta-Lactamase inhibitors. BL-BLI = Beta Lactam/Beta-lactamase inhibitors. CP = Carbapenems. FQ = Fluoroquinolones. MDR excluding XDR in TB = Multi-drug resistance excluding extensive drug resistance in TB. MDR in *S. Typhi* and Paratyphi = Multi-drug resistance in *Salmonella Typhi* and Paratyphi. Mono INH = Isoniazid mono-resistance. Mono RIF = Rifampicin mono-resistance. PCN = Penicillin. TMP-SMX = Trimethoprim-Sulfamethoxazole. Vanco = Vancomycin. XDR in TB = Extensive drug resistance in TB.

## Section 8: Relative risk

### Section 8.1 Input data

The input data for the relative risk estimation step included literature data that provided relative risk of death for resistant and susceptible organisms and hospital-based microbiology surveillance data linked to outcomes, as well as other clinical parameters (eg, demographics, diagnoses). Published studies were identified from a recent meta-analysis performed by Cassini and colleagues.<sup>43</sup>

The data inputs for the excess duration estimates were literature data that reported on length of stay for resistant and susceptible organisms and hospital-based microbiology surveillance data that were linked to outcomes as well as various other clinical parameters (eg, demographics, diagnoses). The number of days between a positive specimen date and discharge date was used to obtain the mean duration of infection. We considered days elapsed between admission and discharge as mean duration of stay if this was the only piece of information provided in the study. We also considered median duration of infection or median duration of stay if the study only provided this piece of information.

### Section 8.2: Data processing

There were 9.4 million possible samples from 73 countries to inform our relative risk of death estimates. Many of the 9.4 million potential samples were further de-duplicated as part of the modeling process (modelling details in 7.3). A detailed breakdown of this 9.4 million by pathogen–drug is in table S9 (section 14). Relative risk estimates were extracted from primary literature as were study characteristics that described the adjustments made by the study. When no adjustments were made, or an adjusted odds ratio was presented, we extracted the crude relative risk. For hospital data that contained admission diagnoses, diagnoses were mapped to GBD Level 2 causes. Admission diagnoses were mapped to GBD causes using ICD codes when provided; when admission diagnoses were free-text entries, they were mapped using two expert reviews.

### Section 8.3 Modelling overview

The measure of excess risk used to estimate the fatal burden of AMR was the relative risk of death from an infection with a pathogen resistant to the antibiotic of interest as compared to an infection of the same site with the same organism that was susceptible to the antibiotic of interest. The relative risk estimate was produced after adjusting for various potential confounders including age, admission diagnosis (mapped to GBD causes), site of culture, and hospital versus community onset. Because of data sparsity, a single measure of relative risk was estimated for each pathogen–drug combination, representing a global estimate for all sites of infection and all underlying causes.

When data availability allowed it, relative risk from hospital-based microbiology surveillance data was estimated after adjusting for age, admission diagnosis, site of culture, and hospital- versus community-acquired infection, otherwise a crude relative risk was used. The adjusted estimates of relative risks were then included with the crude relative risks in a two-stage nested mixed effects meta-regression model using MR-BRT. The stage one model was a meta-regression for each antibiotic class, which was used to produce a prior for the stage two model. We considered study-specific adjustments such as age of patients, admission diagnosis, site of culture and hospital-versus community acquired infection as potential covariates to be included in the second stage. Covariate selection was based on a set of log-linear models with a range of Lasso penalty parameters, and only statistically significant covariates were selected. The stage two model was run for each antibiotic class with a random effect for pathogen and fixed effects for study level characteristics that described whether the relative risk estimate from a study or dataset adjusted for each parameter using the prior from the stage one model for the antibiotic class.

$$Relative\ Risk_{pathogen_n drug_d} = \beta_0 + \beta_d \cdot x + u_{pathogen_n} + \epsilon_d \quad (8.3.1)$$

Where  $x$  is a bias covariate,  $u_{pathogen_n}$  is a random effect for pathogen  $n$  within an antibiotic class,  $\epsilon_K$  is the measurement error,  $d$  is antibiotic class and  $\beta$  and  $X$  are vectors of length  $i + 1$  for  $i$  covariates. From this stage two model, we produced 1000 draws to estimate the relative risk of death and uncertainty attributable to resistance for each pathogen–drug combination.

For non-fatal burden estimation, we estimated the excess duration attributable to resistance—comparing the length of hospital stay for an infection with a pathogen resistant to the antibiotic of interest to an infection of the same site with the same organism that was susceptible to the antibiotic of interest. For community-acquired infections the entire duration of length of stay was attributed to the infection, for hospital-acquired infections we used the time from first positive culture to time of discharge to estimate length of stay. To address the potential confounding effect of longer admissions resulting in higher probability of acquiring resistant infections, we adjusted the relative length of stay obtained from patient level data for the number of hospital days prior to culture positivity. We observed a generally lower relative length of stay when we applied this adjustment, which was expected. We then used the same two-stage nested mixed effects meta-regression modelling framework described for fatal estimation to produce a relative length of stay attributable to resistance for each pathogen–drug combination. One exception to this estimation process was *Neisseria gonorrhoeae*, which had too little data to produce an estimate on the impact of resistance on duration of illness. As a result, we produced a YLD estimate based on the excess duration of illness for a given antibiotic class. This was a 1.29 fold increase in duration for fluoroquinolones-resistant bacteria and a 1.43 fold increase in duration for third-generation cephalosporin-resistant bacteria.

The analysis of relative risk followed the definitions of the prevalence of resistance step (section 7) as closely as possible. Both analyses identified resistance to a given antibiotics class if the isolate had an intermediate or resistant interpretation to any one of the antibiotics in that given class. But the analysis of relative risk diverged from the analysis of prevalence of resistance in the following circumstances. First, the relative risk step included molecular resistance testing if this was the only data provided by a study, eg,  $\beta$ -lactamase or MecA positive pathogens; this could potentially misclassify some resistant organisms as sensitive if they had an alternate mechanism for resistance, such as a porin alteration leading to carbapenem resistance. Second, the relative risk estimate produced was for sterile sites of infection, as there was limited data from non-sterile sites. Third, it was not possible to assess relative risk of multidrug-resistant pathogens because of limited data availability and because it did not fit in the modelling strategy at the antibiotic class level. Instead, the relative risk of each of the components of multidrug-resistant pathogens was calculated and the antibiotic class with the highest relative risk was used; for *Salmonella* Typhi this was relative risk to Trimethoprim-Suflamethoxazole. Fourth, we had limited availability of data on fatalities attributable to *Salmonella* Paratyphi and *Shigella* species; as a result, we used fatal relative risk estimates from *Salmonella* Typhi as a proxy. Fifth, there were limited data on fatalities attributable to resistant *N. gonorrhoeae*, so we excluded the fatal estimate for this pathogen. Finally, the relative risk of *Mycobacterium tuberculosis* was assessed for multidrug and extensively drug-resistant infections as reported previously in GBD. Estimates of relative risk of death for sterile sources of specimen across 88 pathogen–drug combinations are given in table S10.

#### Section 8.4 Model validation

We report three summary metrics to evaluate the relative risk of death models: the root-mean squared error (RMSE), the Mean Average Error (MAE) and the percent coverage of observed data within the full variance of the model. These three metrics were calculated using the real relative risk ratio in the whole sample of data and also by holding out 25% of the sample within antibiotic class in 4 iterations. Table 8.4.1 provides details for each of the antibiotic class model evaluated. Large MAE and RMSE values indicate that observed data deviates from the mean model estimate. We also see a large proportion of the data (82% and more) falls within the total variance of each model estimates. This indicates that large deviations from the mean estimate coincide with large variances of the data observed.

Table 8.4.1: In-sample and out-of-sample performance metrics for relative risk of death models

Antibiotic class	MAE		RMSE		Coverage	
	in-sample	out-of-sample	in-sample	out-of-sample	in-sample	out-of-sample
Vancomycin	0.71	0.65	1.33	0.94	82%	82%
Fluoroquinolones	0.73	0.75	1.61	1.52	88%	90%
Third-generation cephalosporins	0.75	0.76	1.63	1.49	93%	93%
Macrolide	0.71	0.73	1.25	1.24	95%	94%
Methicillin	0.65	0.67	1.3	1.13	96%	94%
Penicillin	0.48	0.69	0.83	0.97	96%	98%
Carbapenem	0.64	0.64	1.54	1.29	98%	97%
Aminoglycosides	0.37	0.41	0.61	0.58	100%	100%
Aminopenicillin	0.9	0.86	1.82	1.68	100%	100%
Anti-pseudomonal penicillin/Beta-Lactamase inhibitors	0.76	0.8	1.76	1.64	100%	100%
Beta Lactam/Beta-lactamase inhibitors	0.36	0.3	0.61	0.37	100%	100%
Fourth-generation cephalosporins	1.22	1.54	3.21	3.46	100%	100%
Trimethoprim-Sulfamethoxazole	0.64	0.6	1.17	0.97	100%	100%

This approach for relative risk estimation had a number of limitations; most were attributable to data sparsity. First, it is likely that the impact of resistance on mortality is different across locations. In locations where overall health-care access and quality are very poor, the impact of resistance may be smaller because the management of susceptible infections is sub-optimal. On the other hand, in locations where broad, second- and third-line antimicrobials are not available, one would expect the impact of resistance to be greater. Second, it is possible that the relative risk of death attributable to resistance is different across anatomical sites of infection because of variable penetrance of antibiotics to different anatomical locations. As we continue efforts to expand data collection and reporting, we hope to be able to address these limitations in future iterations.

## Section 9: Counterfactuals and AMR estimation

### Section 9.1: Estimating AMR burden with counterfactual of no infection

We computed two counterfactuals to estimate the drug-resistant burden. First, we estimated the burden of AMR using the counterfactual of no infection. We estimated the fatal burden of individual pathogen–drug combinations by taking the product of the deaths for each underlying cause, fraction of deaths related to infection, infectious syndrome fraction, fatal pathogen fraction, and fatal prevalence of resistance and then summed across all infectious syndromes and underlying causes:

$$Deaths\ with\ Resistance_{kd} = \sum_J \sum_L D_J \times S_J \times M_{LJ} \times P_{LK} \times R_{Kd} \quad (9.1.1)$$

where D = deaths, S = fraction related to infection, M = infectious syndrome fraction, P = fatal pathogen fraction, R = fatal prevalence of resistance, J = cause, L = syndrome, K = pathogen, d = drug. To produce an estimate of deaths with resistance to any antibiotic estimated, we employed the same formula but used the fatal prevalence of resistance to any antibiotic using the resistance profiles, described previously. We calculated the fatal prevalence of resistance R for a given drug *d* based on the non-fatal prevalence of resistance *R'* and relative risk of death *RR* for this drug:

$$R_{kd} = \frac{R'_{kd} RR_{kd}}{(1 - R'_{kd}) + R'_{kd} RR_{kd}} \quad (9.1.2)$$

We calculated the fatal prevalence of resistance to any antibiotic estimated based on the non-fatal prevalences of each resistance profile, incorporating all resistance profiles  $\delta$  that are resistant to at least 1 drug with corresponding relative risks  $RR_{Kd^*}$ , determined by the method described below (section 9.2):

$$R_{K,all\ drugs} = \frac{\sum_{\delta} R'_{K\delta} RR_{Kd^*}}{(1 - \sum_{\delta} R'_{K\delta}) + \sum_{\delta} R'_{K\delta} RR_{Kd^*}} \quad (9.1.3)$$

We then estimated YLLs using standard GBD methods to convert age-sex specific deaths into YLLs.<sup>1</sup>

For the non-fatal estimate, we first estimated the incidence of each infectious syndrome in each underlying cause. For infectious underlying causes (table 9.1.1), we simply used the incidence estimated in GBD. For non-infectious underlying causes, we divided the infectious syndrome deaths ( $D_j \times S_j \times M_{Lj}$ ) by the syndrome- and pathogen-specific CFRs calculated in section 5, aggregated across pathogen using the nonfatal pathogen distribution  $P'$  calculated above.

$$Incidence_{jL} = \frac{D_j S_j M_{Lj}}{\sum_K CFR_{LK} P'_{LK}} \quad (9.1.4)$$

*Table 9.1.1: Infectious GBD causes for which we used GBD YLD and incidence estimates*

<b>Infectious syndrome</b>	<b>GBD cause</b>
Meningitis and other bacterial central nervous system infections	Meningitis
Lower respiratory infections and other related infections in the thorax	Lower respiratory infections
Bacterial infections of the skin and subcutaneous systems	Pyoderma Cellulitis Decubitus ulcer
Urinary tract infections and pyelonephritis	Urinary tract infections
Bloodstream infections	Maternal sepsis Neonatal sepsis
Diarrhoea	Diarrhea
Tuberculosis	Tuberculosis
Typhoid, paratyphoid, and invasive non-typhoidal Salmonella	Typhoid fever Paratyphoid fever Invasive non-typhoidal Salmonella
Gonorrhoea and chlamydia	Chlamydia Gonococcal infection

We then took the product of the infectious syndrome incidence, the non-fatal pathogen fraction, and the non-fatal prevalence of resistance and summed across all infectious syndromes and underlying causes to get incidence with resistance for every pathogen and drug. As with the fatal estimate, to produce an estimate of incident infections with resistance to any antibiotic, we used the same formula and used the non-fatal prevalence of resistance to any antibiotic estimated from the resistance profiles.

We then calculated YLDs for each pathogen. For some GBD causes, we simply used the GBD YLD estimates and multiplied them by the corresponding nonfatal pathogen distribution (table 8.1.2) For all other causes, we multiplied together the infectious syndrome incidence, the non-fatal pathogen fraction, and a syndrome-specific YLDs per incident case rate, calculated using a proxy cause from GBD.<sup>1</sup> To estimate the YLDs per incident case rate, we extracted GBD incidence and YLD estimates for the proxy causes and divided the YLDs by the incidence for each age, sex, and location. Three infectious syndromes are not estimated in the GBD, and therefore have no standard sequelae or disability weights: bloodstream infections, intra-abdominal infections, and bone and joint infections. For the proxy causes for these three syndromes, we used the closest approximate disease as determined by a group of experts in infectious diseases and epidemiology (table 9.1.2). This approach is a significant limitation of the study and should be improved in future work.

Table 9.1.2. Proxy causes used to calculate YLDs per incidence case rate for each infectious syndrome

Infectious syndrome	Proxy cause
Meningitis and other bacterial central nervous system infections	Meningitis
Endocarditis and other cardiac infections	Endocarditis
Peritoneal and intra-abdominal infections	Paralytic ileus and intestinal obstruction
Lower respiratory infections and all related infections in the thorax	Lower respiratory infections
Bacterial infections of the skin and subcutaneous systems	Bacterial skin diseases
Infections of bones, joints, and related organs	Bacterial skin diseases
Diarrhoea	Diarrhoea
Bloodstream infections	Maternal sepsis – <i>Extrapolated to males</i>
Urinary tract infections and pyelonephritis	Urinary tract infections

To get the YLDs associated with resistance for each pathogen, we used the non-fatal prevalences of resistance for each drug and resistance profile and relative length of stay (LOS) for each pathogen–drug combination to calculate the fraction of YLDs associated with resistance for each pathogen, using equations analogous to equations 9.1.2 and 9.1.3. We multiplied this fraction by the YLDs for each pathogen to get YLDs associated with resistance to each pathogen–drug combination and YLDs associated with resistance any antibiotics estimated. We then added YLLs and YLDs to produce the DALY estimate for burden associated with resistance.

### Section 9.2: Estimating AMR burden with counterfactual of infection with susceptible organism

For the second counterfactual—comparing resistant to susceptible infections—we calculated mutually exclusive pathogen–drug estimates. To do this, we first estimated the population attributable fraction of deaths (*Mortality PAF*) for each resistance profile with resistance to at least 1 drug,  $\delta$ . The inputs for the PAF were the non-fatal prevalence of the given resistance profile,  $R'_{K\delta}$ , and the relative risk of death for resistant infection compared to susceptible infection for each drug,  $RR_{Kd}$ . Because of data sparsity, we were unable to calculate the relative risk for every possible resistance profile, and so instead used the highest relative risk of all of the drugs in the resistance profile. For example, if for a resistance profile of resistant to penicillin and fluoroquinolones, the relative risk was 1.1 for penicillin and 1.4 for fluoroquinolones, we would use a relative risk of 1.4 for this profile. The mortality PAF is calculated as a multi-category exposure:

$$Mortality\ PAF_{K\delta} = \frac{R'_{K\delta}(RR_{Kd^*} - 1)}{1 + \sum_{\delta} R'_{K\delta}(RR_{Kd^*} - 1)} \quad (9.2.1)$$

where  $d^*$  is the drug in the resistance profile  $\delta$  with the highest relative risk.

We then took the product of the deaths for each underlying cause, fraction of deaths related to infection, infectious syndrome fraction, fatal pathogen fraction, and the mortality PAF for each resistance profile to get the deaths attributable to resistance for every resistance profile:

$$Deaths\ due\ to\ Resistance_{K\delta} = \sum_J \sum_L D_J \times S_J \times M_{LJ} \times P_{LK} \times Mortality\ PAF_{K\delta} \quad (9.2.2)$$

When the resistance profile described resistance to more than one antibiotic, the deaths were then distributed to the component pathogen–drug combinations based on the excess risk of the pathogen–drug combination divided by the sum of the excess risk of all pathogen–drug combinations in the resistance profile. For a resistance profile  $\delta$  with resistance to drugs  $i = 1, \dots, n$ :

$$Redistribution\ Weight_{Kd_i} = \frac{RR_{Kd_i} - 1}{\sum_i (RR_{Kd_i} - 1)} \quad (9.2.3)$$

For co-resistance amongst beta-lactam antibiotics (i.e. carbapenems, 4GC, 3GC, antipseudomonal, BL/BLI, aminopenicillins, and penicillin), we used a different approach to redistributing burden. Similar to Cassini et al., we applied a hierarchy such that the burden was categorically attributed to the broadest beta-lactam antibiotic, rather than split the burden between multiple beta-lactam antibiotics.<sup>43</sup> We used the hierarchy in table 9.2.1 to assign burden in the presence of co-occurring beta-lactam resistance. When a pathogen was resistant to multiple beta-



lactams and a non-beta-lactam antibiotic, we first applied the hierarchy to determine the ‘highest’ beta-lactam resistance and then generated redistribution weights using only the ‘highest’ beta-lactam and the non-beta-lactams. We then used these attributable death estimates to estimate YLLs using standard GBD methods to convert age-sex specific deaths to YLLs.

A similar approach was taken to estimate non-fatal burden for the counterfactual of antibiotic-susceptible infection. We first assumed that antibiotic resistance has no effect on the attack rate of pathogens; therefore, there are 0 incident cases attributable to resistance and all non-fatal burden comes from increased length of illness. To quantify the extent of this increased length of illness, we first produced a length of stay (LOS) PAF for each resistance profile using the non-fatal prevalence of resistance and relative LOS for resistant infections as compared to susceptible infections in a method analogous to equation 9.2.1. Because of data sparsity, we were unable to calculate the relative LOS for every resistance profile, and so instead used the relative LOS for the drug with the highest relative LOS in the profile. We then took the product of the YLDs for each infectious syndrome, the non-fatal pathogen distribution, and the LOS PAF to produce attributable YLD estimates. This assumes that the attributable LOS PAF is equally applicable to all sequelae, which is an assumption made because of a lack of data on the impact of resistance on the likelihood of different sequelae and the duration of specific sequelae. We then added YLLs and YLDs to produce an estimate of DALYs attributable to resistance.

*Table 9.2.1 Beta-lactam hierarchy*

Rank	Antibiotic class
1	Carbapenem
2	Antipseudomonal Penicillin/Beta-lactamase Inhibitor
3	Fourth Generation Cephalosporin
4	Third Generation Cephalosporin
5	Beta-lactam/Beta-lactamase Inhibitor
6	Aminopenicillin
7	Penicillin

Because of the optimisation approach used to derive each resistance profile, the prevalence of resistance to for a given pathogen–drug as modelled using ensemble ST-GPR (section 7.3),  $R'_{kd}$ , will not necessarily be exactly equal to the sum of all resistance profiles  $R'_{k\delta}$  that include resistance to drug  $d$ . Due to this inconsistency, in extremely rare cases, an estimate of AMR burden in the susceptible counterfactual may slightly exceed the corresponding estimate of AMR burden in the no infection counterfactual for a specific pathogen–drug. We consider the ensemble ST-GPR estimate to be more accurate than the resistance profiles, since the latter are based on Pearson correlations of multidrug resistance that are calculated from limited microdata and generalized to all locations. For this reason, we cap all individual pathogen–drug estimates of burden for the susceptible counterfactual, which are based on the resistance profiles, to the burden for the no infection counterfactual, which are based on the ensemble ST-GPR estimates.

### Section 9.3: Excluded combinations

Although our approach attempted to be exhaustive and include all clinically-relevant pathogen–drug combinations, there are two combinations included in the WHO priority list for which we could not produce an estimate. The first is clarithromycin resistance in *Helicobacter pylori* and the second is fluoroquinolone resistance in *Campylobacter* species. These were excluded due to limited data availability as highlighted by a recent study in the European Union that found that, as of 2019, no member countries had implemented publicly accessible, mandatory reporting surveillance programmes for these two pathogen–drug combinations.<sup>44</sup> *H. pylori* and *Campylobacter* spp are commonly diagnosed without culture so resistance profiles are uncommon in passive surveillance systems. The burden of *H. pylori* is not currently estimated in GBD, though some of the consequent diseases are, like peptic ulcer disease and gastric cancer. Producing a burden estimate of *H. pylori* was outside the scope of this work, and without a pathogen burden estimate, we could not produce an estimate of the burden attributable to clarithromycin-resistant



*H. pylori*. In contrast, GBD does produce an estimate on the burden of *Campylobacter* spp. There were, however, too few data to produce an estimate on the excess risk of death or duration associated with fluoroquinolone resistance and limited data to inform a global prevalence of resistance estimate. Given these limitations, we did not produce burden estimates for clarithromycin-resistant *H. pylori* or fluoroquinolone-resistant *Campylobacter* spp. Because of the lack of data on risk of death associated with drug-resistant *Neisseria gonorrhoeae*, we were unable to produce an estimate of the fatal burden of resistance so produce only a non-fatal estimate. Many potential pathogen–drug combinations were excluded due to the spectrum of antimicrobial activity (ie, Vancomycin and *E. coli*), intrinsic resistance (eg, BL/BLI resistance in *Pseudomonas aeruginosa*) or resistance that is exceedingly common (eg, penicillin resistance in *S. aureus*); these combinations were decided by a group of experts in infectious diseases, microbiology, epidemiology, and population health. There was insufficient data to produce a global estimate for many pathogen–drug combinations of interest, such as aminopenicillin resistance in *Enterococcus* spp, fluoroquinolone resistance in *Acinetobacter baumannii*, or colistin resistance in any pathogen estimated. This is largely due to either a lack of regional data to inform the prevalence of resistance component or a lack of microbial data linked to outcomes to inform the measure of excess risk component. A final constraint was the computational burden of estimating more than seven antibiotic classes for a single pathogen. Because of the approach to co-resistance described in section 7.4, each antibiotic class added led to an exponential increase in the computation needs and anything above seven antibiotic classes was not tenable. As additional data are made available, we plan to add clinically relevant combinations and iterate on the computational approach so that we can describe the burden of bacterial AMR more comprehensively.

## Section 10. Analysis of total AMR burden decomposed by infection and resistance

Appendix table S11 shows our estimates of the fatal burden of AMR by GBD region, decomposed into several key components: all-cause mortality, the fraction of all deaths that involve infection (infection fraction), the fraction of deaths involving infection that are associated with resistance (prevalence of resistance), and the fraction of deaths involving infection that are attributable to resistance (PAF). The number of deaths associated with resistance is the product of all-cause deaths, infection fraction, and resistance-associated fraction, while the number of deaths attributable to resistance is the product of all-cause deaths, infection fraction, and resistance-attributable fraction. Decomposing our results into these components shows how the burden of AMR is variously influenced by overall regional death rates, the prevalence of infectious disease, and the prevalence of resistance in different regions of the world.

While the regions of sub-Saharan Africa have among the highest death rates per 100,000 person-years associated with and attributable to AMR in the world, the majority of this burden is driven by the high rates of infectious disease in these regions, rather than the prevalence of resistance itself. The GBD regions of central, eastern, southern, and western sub-Saharan Africa have the four leading infectious fractions, at 48.0% (95% UI 40.2 - 56.1), 50.7% (43.1 – 58.8), 45.6% (38.4 – 52.7), and 53.5% (45.4 – 62.0) respectively, but also have the bottom 4 fraction of infectious deaths that are associated with AMR, 27.0% (24.3 – 30.1), 27.9% (25.6 – 30.1), 18.6% (16.6 – 20.9), and 28.3% (25.4 – 30.8) respectively. In contrast, the three regions with the lowest death rate associated with AMR, Australasia, north Africa and the Middle East, and east Asia, have significantly higher fractions of infectious deaths that are associated with AMR than sub-Saharan Africa (31.0% (29.2 – 32.8), 45.3% (42.6 – 47.7), and 47.1% (44.6 – 49.2)), but relatively low infectious fractions (12.7% (8.9 – 17.6), 18.1% (13.2 – 24.2), and 12.2% (8.2 – 17.5)). The burden of AMR can also be analysed through the lens of death counts, in which case the large populations of east Asia and south Asia combined with relatively high infection fraction in south Asia (31.8% [26.0 – 39.2]) and relatively high fraction of infectious deaths that are associated with AMR (36.4% [30.8 – 41.4] in south Asia, 47.1% [44.6 – 49.2] in east Asia), result in these regions having the most deaths associated with and attributable to AMR in 2019.

Analysing infection and AMR as distinct the drivers of AMR burden has critical consequences for any policy intervention. Investments in infection control and prevention (IPC), water, sanitation, and hygiene, and vaccination can be made in areas with high infection fraction, while efforts in antibiotic stewardship can be enhanced in areas with high prevalence of resistance. Notably, our estimates show that rates of infectious disease are ultimately a

stronger driver of the burden of AMR than the prevalence of resistance itself, and should therefore be addressed first and foremost in any effort to reduce the burden of AMR.

## Section 11. GATHER compliance

This study complies with GATHER recommendations.<sup>45</sup> We have documented the steps in our analytical procedures and detailed the data sources used. See table S12 for the GATHER checklist. The GATHER recommendations can be found on the GATHER website.

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## Section 14: Appendix tables and figures

<b>Table S1. GBD cause hierarchy with levels</b>	
<b>Cause</b>	<b>level</b>
All causes	0
Communicable, maternal, neonatal, and nutritional diseases	1
HIV/AIDS and sexually transmitted infections	2
HIV/AIDS	3
HIV/AIDS–drug-susceptible tuberculosis	4
HIV/AIDS–multidrug-resistant TB without extensive drug resistance	4
HIV/AIDS–extensively drug-resistant tuberculosis	4
HIV/AIDS resulting in other diseases	4
Sexually transmitted infections excluding HIV	3
Syphilis	4
Chlamydial infection	4
Gonococcal infection	4
Trichomoniasis	4
Genital herpes	4
Other sexually transmitted infections	4
Respiratory infections and tuberculosis	2
Tuberculosis	3
Latent tuberculosis infection	4
Drug-susceptible tuberculosis	4
Multidrug-resistant TB without extensive drug resistance	4
Extensively drug-resistant tuberculosis	4
Lower respiratory infections	3
Upper respiratory infections	3
Otitis media	3
Enteric infections	2
Diarrhoeal diseases	3
Typhoid and paratyphoid	3
Typhoid fever	4
Paratyphoid fever	4
Invasive non-typhoidal Salmonella (iNTS)	3
Other intestinal infectious diseases	3
Neglected tropical diseases and malaria	2
Malaria	3
Chagas disease	3
Leishmaniasis	3
Visceral leishmaniasis	4
Cutaneous and mucocutaneous leishmaniasis	4
African trypanosomiasis	3
Schistosomiasis	3
Cysticercosis	3
Cystic echinococcosis	3
Lymphatic filariasis	3
Onchocerciasis	3



Trachoma	3
Dengue	3
Yellow fever	3
Rabies	3
Intestinal nematode infections	3
Ascariasis	4
Trichuriasis	4
Hookworm disease	4
Food-borne trematodiasis	3
Leprosy	3
Ebola virus disease	3
Zika virus disease	3
Guinea worm disease	3
Other neglected tropical diseases	3
Other infectious diseases	2
Meningitis	3
Encephalitis	3
Diphtheria	3
Whooping cough	3
Tetanus	3
Measles	3
Varicella and herpes zoster	3
Acute hepatitis	3
Acute hepatitis A	4
Acute hepatitis B	4
Acute hepatitis C	4
Acute hepatitis E	4
Other unspecified infectious diseases	3
Maternal and neonatal disorders	2
Maternal disorders	3
Maternal haemorrhage	4
Maternal sepsis and other maternal infections	4
Maternal hypertensive disorders	4
Maternal obstructed labor and uterine rupture	4
Maternal abortion and miscarriage	4
Ectopic pregnancy	4
Indirect maternal deaths	4
Late maternal deaths	4
Maternal deaths aggravated by HIV/AIDS	4
Other maternal disorders	4
Neonatal disorders	3
Neonatal preterm birth	4
Neonatal encephalopathy due to birth asphyxia and trauma	4
Neonatal sepsis and other neonatal infections	4
Haemolytic disease and other neonatal jaundice	4

Other neonatal disorders	4
Nutritional deficiencies	2
Protein-energy malnutrition	3
Iodine deficiency	3
Vitamin A deficiency	3
Dietary iron deficiency	3
Other nutritional deficiencies	3
Non-communicable diseases	1
Neoplasms	2
Lip and oral cavity cancer	3
Nasopharynx cancer	3
Other pharynx cancer	3
Oesophageal cancer	3
Stomach cancer	3
Colon and rectum cancer	3
Liver cancer	3
Liver cancer due to hepatitis B	4
Liver cancer due to hepatitis C	4
Liver cancer due to alcohol use	4
Liver cancer due to NASH	4
Liver cancer due to other causes	4
Gallbladder and biliary tract cancer	3
Pancreatic cancer	3
Larynx cancer	3
Tracheal, bronchus, and lung cancer	3
Malignant skin melanoma	3
Non-melanoma skin cancer	3
Non-melanoma skin cancer (squamous-cell carcinoma)	4
Non-melanoma skin cancer (basal-cell carcinoma)	4
Breast cancer	3
Cervical cancer	3
Uterine cancer	3
Ovarian cancer	3
Prostate cancer	3
Testicular cancer	3
Kidney cancer	3
Bladder cancer	3
Brain and central nervous system cancer	3
Thyroid cancer	3
Mesothelioma	3
Hodgkin lymphoma	3
Non-Hodgkin lymphoma	3
Multiple myeloma	3
Leukaemia	3
Acute lymphoid leukaemia	4

Chronic lymphoid leukaemia	4
Acute myeloid leukaemia	4
Chronic myeloid leukaemia	4
Other leukaemia	4
Other malignant neoplasms	3
Other neoplasms	3
Myelodysplastic, myeloproliferative, and other haematopoietic neoplasms	4
Benign and in situ intestinal neoplasms	4
Benign and in situ cervical and uterine neoplasms	4
Other benign and in situ neoplasms	4
Cardiovascular diseases	2
Rheumatic heart disease	3
Ischaemic heart disease	3
Stroke	3
Ischaemic stroke	4
Intracerebral haemorrhage	4
Subarachnoid haemorrhage	4
Hypertensive heart disease	3
Non-rheumatic valvular heart disease	3
Non-rheumatic calcific aortic valve disease	4
Non-rheumatic degenerative mitral valve disease	4
Other non-rheumatic valve diseases	4
Cardiomyopathy and myocarditis	3
Myocarditis	4
Alcoholic cardiomyopathy	4
Other cardiomyopathy	4
Atrial fibrillation and flutter	3
Aortic aneurysm	3
Peripheral artery disease	3
Endocarditis	3
Other cardiovascular and circulatory diseases	3
Chronic respiratory diseases	2
Chronic obstructive pulmonary disease	3
Pneumoconiosis	3
Silicosis	4
Asbestosis	4
Coal workers pneumoconiosis	4
Other pneumoconiosis	4
Asthma	3
Interstitial lung disease and pulmonary sarcoidosis	3
Other chronic respiratory diseases	3
Digestive diseases	2
Cirrhosis and other chronic liver diseases	3
Cirrhosis and other chronic liver diseases due to hepatitis B	4
Cirrhosis and other chronic liver diseases due to hepatitis C	4

Cirrhosis and other chronic liver diseases due to alcohol use	4
Cirrhosis and other chronic liver diseases due to NAFLD	4
Cirrhosis and other chronic liver diseases due to other causes	4
Upper digestive system diseases	3
Peptic ulcer disease	4
Gastritis and duodenitis	4
Gastro-oesophageal reflux disease	4
Appendicitis	3
Paralytic ileus and intestinal obstruction	3
Inguinal, femoral, and abdominal hernia	3
Inflammatory bowel disease	3
Vascular intestinal disorders	3
Gallbladder and biliary diseases	3
Pancreatitis	3
Other digestive diseases	3
Neurological disorders	2
Alzheimer's disease and other dementias	3
Parkinson's disease	3
Idiopathic epilepsy	3
Multiple sclerosis	3
Motor neuron disease	3
Headache disorders	3
Migraine	4
Tension-type headache	4
Other neurological disorders	3
Mental disorders	2
Schizophrenia	3
Depressive disorders	3
Major depressive disorder	4
Dysthymia	4
Bipolar disorder	3
Anxiety disorders	3
Eating disorders	3
Anorexia nervosa	4
Bulimia nervosa	4
Autism spectrum disorders	3
Attention-deficit/hyperactivity disorder	3
Conduct disorder	3
Idiopathic developmental intellectual disability	3
Other mental disorders	3
Substance use disorders	2
Alcohol use disorders	3
Drug use disorders	3
Opioid use disorders	4
Cocaine use disorders	4

Amphetamine use disorders	4
Cannabis use disorders	4
Other drug use disorders	4
Diabetes and kidney diseases	2
Diabetes mellitus	3
Diabetes mellitus type 1	4
Diabetes mellitus type 2	4
Chronic kidney disease	3
Chronic kidney disease due to diabetes mellitus type 1	4
Chronic kidney disease due to diabetes mellitus type 2	4
Chronic kidney disease due to hypertension	4
Chronic kidney disease due to glomerulonephritis	4
Chronic kidney disease due to other and unspecified causes	4
Acute glomerulonephritis	3
Skin and subcutaneous diseases	2
Dermatitis	3
Atopic dermatitis	4
Contact dermatitis	4
Seborrhoeic dermatitis	4
Psoriasis	3
Bacterial skin diseases	3
Cellulitis	4
Pyoderma	4
Scabies	3
Fungal skin diseases	3
Viral skin diseases	3
Acne vulgaris	3
Alopecia areata	3
Pruritus	3
Urticaria	3
Decubitus ulcer	3
Other skin and subcutaneous diseases	3
Sense organ diseases	2
Blindness and vision loss	3
Glaucoma	4
Cataract	4
Age-related macular degeneration	4
Refraction disorders	4
Near vision loss	4
Other vision loss	4
Age-related and other hearing loss	3
Other sense organ diseases	3
Musculoskeletal disorders	2
Rheumatoid arthritis	3
Osteoarthritis	3

Osteoarthritis hip	4
Osteoarthritis knee	4
Osteoarthritis hand	4
Osteoarthritis other	4
Low back pain	3
Neck pain	3
Gout	3
Other musculoskeletal disorders	3
Other non-communicable diseases	2
Congenital birth defects	3
Neural tube defects	4
Congenital heart anomalies	4
Orofacial clefts	4
Down syndrome	4
Turner syndrome	4
Klinefelter syndrome	4
Other chromosomal abnormalities	4
Congenital musculoskeletal and limb anomalies	4
Urogenital congenital anomalies	4
Digestive congenital anomalies	4
Other congenital birth defects	4
Urinary diseases and male infertility	3
Urinary tract infections	4
Urolithiasis	4
Benign prostatic hyperplasia	4
Male infertility	4
Other urinary diseases	4
Gynaecological diseases	3
Uterine fibroids	4
Polycystic ovarian syndrome	4
Female infertility	4
Endometriosis	4
Genital prolapse	4
Premenstrual syndrome	4
Other gynaecological diseases	4
Haemoglobinopathies and haemolytic anaemias	3
Thalassaemias	4
Thalassaemias trait	4
Sickle cell disorders	4
Sickle cell trait	4
G6PD deficiency	4
G6PD trait	4
Other haemoglobinopathies and haemolytic anaemias	4
Endocrine, metabolic, blood, and immune disorders	3
Oral disorders	3

Caries of deciduous teeth	4
Caries of permanent teeth	4
Periodontal diseases	4
Edentulism and severe tooth loss	4
Other oral disorders	4
Sudden infant death syndrome	3
Injuries	1
Transport injuries	2
Road injuries	3
Pedestrian road injuries	4
Cyclist road injuries	4
Motorcyclist road injuries	4
Motor vehicle road injuries	4
Other road injuries	4
Other transport injuries	3
Unintentional injuries	2
Falls	3
Drowning	3
Fire, heat, and hot substances	3
Poisonings	3
Poisoning by carbon monoxide	4
Poisoning by other means	4
Exposure to mechanical forces	3
Unintentional firearm injuries	4
Other exposure to mechanical forces	4
Adverse effects of medical treatment	3
Animal contact	3
Venomous animal contact	4
Non-venomous animal contact	4
Foreign body	3
Pulmonary aspiration and foreign body in airway	4
Foreign body in eyes	4
Foreign body in other body part	4
Environmental heat and cold exposure	3
Exposure to forces of nature	3
Other unintentional injuries	3
Self-harm and interpersonal violence	2
Self-harm	3
Self-harm by firearm	4
Self-harm by other specified means	4
Interpersonal violence	3
Physical violence by firearm	4
Physical violence by sharp object	4
Sexual violence	4
Physical violence by other means	4

Conflict and terrorism	3
Executions and police conflict	3



**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Communicable, maternal, neonatal, and nutritional diseases	A00-A00.9, A01.0-A14, A15-A28.9, A32-A39.9, A48.1-A48.2, A48.4-A48.5, A50-A58, A60-A60.9, A63-A63.8, A65-A65.0, A68-A70, A74, A74.8-A75.9, A77-A96.9, A98-A98.8, B00-B06.9, B10-B10.8, B15-B16.2, B17.0, B17.2, B19.1, B20-B27.9, B29.4, B33-B33.1, B33.3-B33.8, B47-B48.8, B50-B54.0, B55.0, B56-B57.5, B60-B60.8, B63, B65-B67.9, B69-B72.0, B74.3-B75, B77-B77.9, B83-B83.8, B90-B91, B94.1, B95-B95.5, B97.4-B97.6, C58-C58.0, D50.1-D50.8, D51-D52.0, D52.8-D53.9, D70.3, D89.3, E00-E02, E40-E46.9, E51-E61.9, E63-E64.0, E64.2-E64.9, F02.1, F02.4, F07.1, G00.0-G00.8, G03-G03.8, G04-G05.8, G14-G14.6, G21.3, H70-H70.9, I00, I02, I02.9, I98.0-I98.1, J00-J02.8, J03-J03.8, J04-J04.2, J05-J05.1, J06.0-J06.8, J09-J15.8, J16-J16.9, J20-J21.9, J36-J36.0, J91.0, K52.1, K67.0-K67.8, K75.3, K76.3, K77.0, K93.0-K93.1, M03.1, M12.1, M49.0-M49.1, M73.0-M73.1, M89.6, N74.1, N96, N98-N98.9, O00-O07.9, O09-O16.9, O20-O26.9, O28-O36.9, O40-O48.1, O60-O77.9, O80-O92.7, O96-O98.6, O98.8-P04.2, P04.5-P05.9, P07-P15.9, P19-P22.9, P23.0-P23.4, P24-P29.9, P35-P37.2, P37.5-P39.9, P50-P61.9, P70-P70.1, P70.3-P72.9, P74-P78.9, P80-P81.9, P83-P84, P90-P94.9, P96, P96.3-P96.4, P96.8, R19.7, U04-U04.9, U06-U06.9, U82-U89, Z16-Z16.3	001-001.9, 002.0-029, 032-034.9, 036-036.3, 036.5-037.9, 040, 040.1-041.0, 042-066.9, 070.0-070.2, 071-075.9, 078.3-078.7, 079-079.7, 080-083.9, 084.0-084.5, 084.7-084.9, 085.0, 086-088, 088.8-088.9, 090-101.6, 104-104.9, 120-124.9, 125.4-125.9, 127-127.1, 128-129.0, 136-136.2, 137-139.0, 181-181.9, 244.2, 260-263.9, 265-269.9, 281.0-281.9, 320.0-320.8, 321-323.9, 381-383.9, 390-390.9, 392, 392.9, 425.6, 460-464.4, 464.8-464.9, 465.0-465.8, 466-469, 470.0, 475-475.9, 476.9, 480-482.8, 483.0-483.9, 484.0-484.7, 487-489, 630-636.9, 638-638.9, 640-679.1, 716.0, 730.4-730.6, 760-760.6, 760.8-768, 768.2-770, 770.1-775.0, 775.4-779.3, 779.6-779.8, V09-V09.9
HIV/AIDS and sexually transmitted infections	A50-A58, A60-A60.9, A63-A63.8, B20-B24.9, B63, F02.4, I98.0, K67.0-K67.2, M03.1, M73.0-M73.1	042-044.9, 054.1, 090-099.9
HIV/AIDS	B20-B24.9, F02.4	042-044.9
HIV/AIDS–drug-susceptible tuberculosis	B20.0	
HIV/AIDS–multidrug-resistant tuberculosis without extensive drug resistance		
HIV/AIDS–extensively drug-resistant tuberculosis		
HIV/AIDS resulting in other diseases	B20, B20.1-B24.9, F02.4	042-044.9
Sexually transmitted infections excluding HIV	A50-A58, A60-A60.9, A63-A63.8, B63, I98.0, K67.0-K67.2, M03.1, M73.0-M73.1	054.1, 090-099.9
Syphilis	A50-A53.9, I98.0, K67.2, M03.1, M73.1	090-097.9
Chlamydial infection	A55-A56.8, K67.0	
Gonococcal infection	A54-A54.9, K67.1, M73.0	098-098.9
Other sexually transmitted infections	A57-A58, A63-A63.8, B63	099-099.9
Respiratory infections and tuberculosis	A10-A14, A15-A19.9, A48.1, A70, B90-B90.9, B97.4-B97.6, H70-H70.9, J00-J02.8, J03-J03.8, J04-J04.2, J05-J05.1, J06.0-J06.8, J09-J15.8, J16-J16.9, J20-J21.9, J36-J36.0, J91.0, K67.3, K93.0, M49.0, N74.1, P23.0-P23.4, P37.0, U04-U04.9, U84.3	010-019.9, 034.0, 079.6, 137-137.9, 138.0-138.9, 381-383.9, 460-464.4, 464.8-464.9, 465.0-465.8, 466-469, 470.0, 475-475.9, 476.9, 480-482.8, 483.0-483.9, 484.1-484.2, 484.6-484.7, 487-489, 730.4-730.6
Tuberculosis	A10-A14, A15-A19.9, B90-B90.9, K67.3, K93.0, M49.0, N74.1, P37.0, U84.3	010-019.9, 137-137.9, 138.0-138.9, 730.4-730.6
Drug-susceptible tuberculosis	A10-A14, A15-A19.9, B90-B90.9, K67.3, K93.0, M49.0, N74.1, P37.0	010-019.9, 137-137.9, 138.0-138.9, 730.4-730.6
Multidrug-resistant tuberculosis without extensive drug resistance	U84.3	
Extensively drug-resistant tuberculosis		
Lower respiratory infections	A48.1, A70, B97.4-B97.6, J09-J15.8, J16-J16.9, J20-J21.9, J91.0, P23.0-P23.4, U04-U04.9	079.6, 466-469, 470.0, 480-482.8, 483.0-483.9, 484.1-484.2, 484.6-484.7, 487-489
Upper respiratory infections	J00-J02.8, J03-J03.8, J04-J04.2, J05-J05.1, J06.0-J06.8, J36-J36.0	034.0, 460-464.4, 464.8-464.9, 465.0-465.8, 475-475.9, 476.9
Otitis media	H70-H70.9	381-383.9
Enteric infections	A00-A00.9, A01.0-A09.9, A80-A80.9, K52.1, R19.7	001-001.9, 002.0-009.9, 045-045.9, 138
Diarrheal diseases	A00-A00.9, A02-A02.0, A02.8-A07, A07.2-A07.4, A08-A09.9, K52.1, R19.7	001-001.9, 003.8-006.9, 007.4-007.8, 008.2-009.9
Typhoid and paratyphoid	A01.0-A01.4	002.0-002.9
Typhoid fever	A01.0	002.0
Paratyphoid fever	A01.1-A01.4	002.1-002.9
Invasive non-typhoidal Salmonella (iNTS)	A02.1-A02.2	003-003.7
Other intestinal infectious diseases	A07.0-A07.1, A07.8-A07.9, A80-A80.9	007-007.3, 007.9-008.1, 045-045.9, 138
Neglected tropical diseases and malaria	A68-A68.9, A69.2-A69.9, A75-A75.9, A77-A79.9, A82-A82.9, A90-A96.9, A98-A98.8, B33.0-B33.1, B50-B54.0, B55.0, B56-B57.5, B60-B60.8, B65-B67.9, B69-B72.0, B74.3-B75, B77-B77.9, B83-B83.8, K93.1, P37.1, U06-U06.9	060-061.8, 065-066.9, 071-071.9, 080-083.9, 084.0-084.5, 084.7-084.9, 085.0, 086-088, 088.8-088.9, 120-124.9, 125.4-125.9, 127-127.1, 128-129.0, 425.6
Malaria	B50-B54.0	084.0-084.5, 084.7-084.9
Leprosy	A30-A30.9	030-030.9
Chagas disease	B57-B57.5, K93.1	086-086.2, 086.9, 425.6
Leishmaniasis	B55.0	085.0
Visceral leishmaniasis	B55.0	085.0
African trypanosomiasis	B56-B56.9	086.3-086.5
Schistosomiasis	B65-B65.9	120-120.9
Cysticercosis	B69-B69.9	123.1
Cystic echinococcosis	B67-B67.4, B67.8-B67.9	122-122.4, 122.8-122.9
Dengue	A90-A91.9	061-061.8
Yellow fever	A95-A95.9	060-060.9
Rabies	A82-A82.9	071-071.9
Intestinal nematode infections	B77-B77.9	127.0
Ascariasis	B77-B77.9	127.0
Ebola virus disease	A98.4	
Zika virus disease	U06-U06.9	
Other neglected tropical diseases	A68-A68.9, A69.2-A69.9, A75-A75.9, A77-A79.9, A92-A94.0, A96-A96.9, A98-A98.3, A98.5-A98.8, B33.0-B33.1, B60-B60.8, B67.5-B67.7, B70-B71.9, B74.3-B75, B83-B83.8, P37.1	065-066.9, 080-083.9, 087-088, 088.8-088.9, 122.5-122.7, 123-123.0, 123.2-124.9, 125.4-125.6, 125.9, 127, 127.1, 128-129.0

**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Other infectious diseases	A20-A28.9, A32-A39.9, A48.2, A48.4-A48.5, A65-A65.0, A69-A69.1, A74, A74.8-A74.9, A81-A81.9, A83-A89.9, B00-B06.9, B10-B10.8, B15-B16.2, B17.0, B17.2, B19.1, B25-B27.9, B29.4, B33, B33.3-B33.8, B47-B48.8, B91, B94.1, B95-B95.5, D70.3, D89.3, F02.1, F07.1, G00.0-G00.8, G03-G03.8, G04-G05.8, G14-G14.6, G21.3, I00, I02, I02.9, I98.1, K67.8, K75.3, K76.3, K77.0, M49.1, M89.6, P35-P35.9, P37, P37.2, P37.5-P37.9, U82-U84, U85-U89, Z16-Z16.3	020-029, 032-034, 034.1-034.9, 036-036.3, 036.5-037.9, 040, 040.1-041.0, 046-054.0, 054.2-059.9, 062-064.9, 070.0-070.2, 072-075.9, 078.3-078.7, 079-079.5, 079.7, 100-101.6, 104-104.9, 136-136.2, 139-139.0, 320.0-320.8, 321-323.9, 390-390.9, 392, 392.9, 484.0, 484.3-484.5, 771.0-771.3, V09-V09.9
Meningitis	A39-A39.9, A87-A87.9, G00.0-G00.8, G03-G03.8	036-036.3, 036.5-036.9, 047-049.9, 320.0-320.8, 321-322.9
Encephalitis	A83-A86.4, B94.1, F07.1, G04-G05.8, G21.3	062-064.9, 139.0, 323, 323.4-323.9
Diphtheria	A36-A36.9	032-032.9
Whooping cough	A37-A37.9	033-033.9, 484.3
Tetanus	A33-A35.0	037-037.9, 771.3
Measles	B05-B05.9	055-055.9, 484.0
Varicella and herpes zoster	B01-B02.9, P35.8	052-053.9
Acute hepatitis	B15-B16.2, B17.0, B17.2, B19.1, P35.3	070.0-070.2
Acute hepatitis A	B15-B15.9	070.0-070.1
Acute hepatitis B	B16-B16.2, B17.0, B19.1, P35.3	070.2
Acute hepatitis C		
Acute hepatitis E	B17.2	
Other unspecified infectious diseases	A20-A28.9, A32-A32.9, A38-A38.9, A48.2, A48.4-A48.5, A65-A65.0, A69-A69.1, A74, A74.8-A74.9, A81-A81.9, A88-A89.9, B00-B00.9, B03-B04, B06-B06.9, B10-B10.8, B25-B27.9, B29.4, B33, B33.3-B33.8, B47-B48.8, B91, B95-B95.5, D70.3, D89.3, F02.1, G14-G14.6, I00, I02, I02.9, I98.1, K67.8, K75.3, K76.3, K77.0, M49.1, M89.6, P35-P35.2, P35.9, P37, P37.2, P37.5-P37.9, U82-U84, U85-U89, Z16-Z16.3	020-029, 034, 034.1-034.9, 040, 040.1-041.0, 046-046.9, 050-051.9, 054-054.0, 054.2-054.9, 056-059.9, 072-075.9, 078.3-078.7, 079-079.5, 079.7, 100-101.6, 104-104.9, 136-136.2, 139, 323.0-323.3, 390-390.9, 392, 392.9, 484.4-484.5, 771.0-771.2, V09-V09.9
Maternal and neonatal disorders	C58-C58.0, N96, N98-N98.9, O00-O07.9, O09-O16.9, O20-O26.9, O28-O36.9, O40-O48.1, O60-O77.9, O80-O92.7, O96-O98.6, O98.8-P04.2, P04.5-P05.9, P07-P15.9, P19-P22.9, P24-P29.9, P36-P36.9, P38-P39.9, P50-P61.9, P70-P70.1, P70.3-P72.9, P74-P78.9, P80-P81.9, P83-P84, P90-P94.9, P96, P96.3-P96.4, P96.8	181-181.9, 630-636.9, 638-638.9, 640-679.1, 760-760.6, 760.8-768, 768.2-770, 770.1-771, 771.4-775.0, 775.4-779.3, 779.6-779.8
Maternal disorders	C58-C58.0, N96, N98-N98.9, O00-O07.9, O09-O16.9, O20-O26.9, O28-O36.9, O40-O48.1, O60-O77.9, O80-O92.7, O96-O98.6, O98.8-O99.9	181-181.9, 630-636.9, 638-638.9, 640-679.1
Maternal haemorrhage	O20-O20.9, O43.2, O44-O46.9, O62-O62.9, O67-O67.9, O70, O72-O72.3	640-641.9, 661-661.9, 665, 666-666.9
Maternal sepsis and other maternal infections	O23-O23.9, O85-O86.8, O91-O91.2	659.3, 670-670.9
Maternal hypertensive disorders	O10-O16.9	642-642.9
Maternal obstructed labor and uterine rupture	O32-O33.9, O64-O66.9, O71-O71.9	652-653.9, 660-660.9, 665.0-665.3
Maternal abortion and miscarriage	N96, O01-O07.9	630-632.9, 634-636.9, 638-638.9, 646.3
Ectopic pregnancy	O00-O00.9	633-633.9
Indirect maternal deaths	O24-O25.3, O98-O98.6, O98.8-O99.9	646-646.2, 646.4-649.9
Late maternal deaths	O96-O97.9	
Maternal deaths aggravated by HIV/AIDS		
Other maternal disorders	C58-C58.0, N98-N98.9, O09-O09.9, O21-O22.9, O26-O26.9, O28-O31.8, O34-O36.9, O40-O43.1, O43.8-O43.9, O47-O48.1, O60-O61.9, O63-O63.9, O68-O69.9, O70.0-O70.9, O73-O77.9, O80-O84.9, O87-O90.9, O92-O92.7	181-181.9, 643-645.2, 650-651.9, 654-659.2, 659.4-659.9, 662-664.9, 665.4-665.9, 667-669.9, 671-679.1
Neonatal disorders	P00-P04.2, P04.5-P05.9, P07-P15.9, P19-P22.9, P24-P29.9, P36-P36.9, P38-P39.9, P50-P61.9, P70-P70.1, P70.3-P72.9, P74-P78.9, P80-P81.9, P83-P84, P90-P94.9, P96, P96.3-P96.4, P96.8	760-760.6, 760.8-768, 768.2-770, 770.1-771, 771.4-775.0, 775.4-779.3, 779.6-779.8
Neonatal preterm birth	P01.0-P01.1, P07-P07.3, P22-P22.9, P25-P28.9, P61.2, P77-P77.9	761.0-761.1, 765-765.9, 769-769.9, 770.2-770.9, 776.6, 777.5-777.6
Neonatal encephalopathy due to birth asphyxia and trauma	P01.7, P02-P03.9, P10-P15.9, P20-P21.9, P24-P24.9, P90-P91.9	761.7-763.9, 767-768, 768.2-768.9, 770.1, 772.1-772.9, 779.0-779.2
Neonatal sepsis and other neonatal infections	P36-P36.9, P38-P39.9	771.4-771.9
Hemolytic disease and other neonatal jaundice	P55-P59.9	773-774.9
Other neonatal disorders	P00-P01, P01.2-P01.6, P01.8-P01.9, P04-P04.2, P04.5-P05.9, P08-P09, P19-P19.9, P29-P29.9, P50-P54.9, P60-P61.1, P61.3-P61.9, P70-P70.1, P70.3-P72.9, P74-P76.9, P78-P78.9, P80-P81.9, P83-P84, P92-P94.9, P96, P96.3-P96.4, P96.8	760-760.6, 760.8-761, 761.2-761.6, 764-764.9, 766-766.9, 770, 771, 772-772.0, 775-775.0, 775.4-776.5, 776.7-777.4, 777.7-779, 779.3, 779.6-779.8
Nutritional deficiencies	D50.1-D50.8, D51-D52.0, D52.8-D53.9, E00-E02, E40-E46.9, E51-E61.9, E63-E64.0, E64.2-E64.9, M12.1	244.2, 260-263.9, 265-269.9, 281.0-281.9, 716.0
Protein-energy malnutrition	E40-E46.9, E64.0	260-263.9
Other nutritional deficiencies	D51-D52.0, D52.8-D53.9, E00-E02, E51-E61.9, E63-E64, E64.2-E64.9, M12.1	244.2, 265-269.9, 281.0-281.9, 716.0

**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Non-communicable diseases	A46-A46.0, A66-A67.9, B18-B18.9, B33.2, B86, C00-C13.9, C15-C22.8, C23-C25.9, C30-C34.9, C37-C38.8, C40-C41.9, C43-C45.9, C47-C54.9, C56-C57.8, C60-C63.8, C64-C67.9, C68.0-C68.8, C69.0-C69.8, C70-C73.9, C75-C75.8, C81-C86.6, C88-C91.0, C91.2-C91.3, C91.6, C92-C92.6, C93-C93.1, C93.3, C93.8, C94-C96.9, D00.1-D00.2, D01.0-D01.3, D02.0-D02.3, D03-D06.9, D07.0-D07.2, D07.4-D07.5, D09.0, D09.2-D09.3, D09.8, D10.0-D10.7, D11-D12.9, D13.0-D13.7, D14.0-D14.3, D15-D16.9, D22-D27.9, D28.0-D28.7, D29.0-D29.8, D30.0-D30.8, D31-D36, D36.1-D36.7, D37.1-D37.5, D38.0-D38.5, D39.1-D39.2, D39.8, D40.0-D40.8, D41.0-D41.8, D42-D43.9, D44.0-D44.8, D45-D47.9, D48.0-D48.6, D49.2-D49.4, D49.6, D52.1, D55-D58.9, D59.0-D59.3, D59.5-D59.6, D60-D61.9, D63.1, D64.0, D66-D67, D68.0-D69.8, D70-D70.2, D70.4-D75.8, D76-D78.8, D86-D86.9, D89-D89.2, E03-E07.1, E09-E11.9, E15.0, E16.0-E16.9, E20-E34, E34.1-E34.8, E36-E36.8, E65-E68, E70-E85.2, E88-E89.9, F00-F02.0, F02.2-F02.3, F02.8-F03.9, F10-F16.9, F18-F18.9, F24, F50.0-F50.5, G10-G13.8, G20-G20.9, G21.0-G21.1, G23-G26.0, G30-G31.9, G35-G37.9, G40-G41.9, G45-G46.8, G47.3, G61-G61.9, G62.1, G70-G73.7, G90-G90.9, G93.7, G95-G95.9, G97-G97.9, H05.0-H05.1, I01-I01.9, I02.0, I05-I09.9, I11-I13.9, I20-I25.9, I27.0-I27.2, I28-I28.9, I30-I31.1, I31.8-I37.8, I38-I41.9, I42.1-I42.8, I43-I43.9, I47-I48.9, I51.0-I51.4, I60-I63.9, I65-I66.9, I67.0-I67.3, I67.5-I67.7, I68.0-I68.2, I69.0-I69.3, I70.2-I70.8, I71-I73.9, I77-I89.9, I95.2-I95.3, I97-I98, I98.2, I98.9, J30-J35.9, J37-J39.9, J41-J46.9, J60-J63.8, J65-J68.9, J70-J70.9, J82, J84-J84.9, J91, J91.8-J92.9, J95-J95.9, K20-K20.9, K22-K22.6, K22.8-K29.9, K31-K31.8, K35-K38.9, K40-K46.9, K50-K52.0, K52.2-K52.9, K55-K62.9, K63.5, K64-K64.9, K66.8, K67, K68, K70-K70.3, K71.7, K73-K75, K75.1-K75.2, K75.4-K76.2, K76.4-K77, K77.8, K80-K83.9, K85-K86.9, K90-K91.9, K92.8, K93.8-K95.8, L00-L05.9, L08-L08.9, L10-L14.0, L51-L51.9, L88-L89.9, L93-L93.2, L97-L98.4, M00-M03.0, M03.2-M03.6, M05-M09.8, M30-M36.8, M40-M43.1, M65-M65.0, M71.0-M71.1, M72.5-M72.6, M80-M82.8, M86.3-M86.4, M87-M87.1, M88-M89.0, M89.5, M89.7-M89.9, N00-N08.8, N10-N12.9, N13.6, N14-N16.8, N18-N18.9, N20-N23.0, N25-N28.1, N29-N30.3, N30.8-N32.0, N32.3-N32.4, N34-N34.3, N36-N36.9, N39-N39.2, N41-N41.9, N44-N44.0, N45-N45.9, N49-N49.9, N60-N60.9, N65-N65.1, N72-N72.0, N75-N77.8, N80-N81.9, N83-N83.9, N84.0-N84.1, N87-N87.9, N99-N99.9, P04.3-P04.4, P70.2, P96.0-P96.2, P96.5, Q00-Q07.9, Q10.4-Q18.9, Q20-Q28.9, Q30-Q36, Q37-Q45.9, Q50-Q87.8, Q89-Q89.8, Q90-Q93.9, Q95-Q99.8, R50.2, R78.0-R78.5, R95-R95.9, X45-X45.9, X65-X65.9, Y15-Y15.9	035-035.9, 036.4, 102-103.9, 133-133.6, 135-135.9, 140-148.9, 150-155.1, 155.3-158.9, 160-164.9, 170-175.9, 180-180.9, 182-183.8, 184.0-184.4, 184.8, 185-186.9, 187.1-187.8, 188-188.9, 189.0-189.8, 190-190.8, 191-193.9, 194.1-194.8, 200-204.0, 204.2, 205-205.3, 206-206.1, 207-208.9, 209.0-209.1, 209.4-209.5, 210.0-210.9, 211.0-211.8, 212.0-212.8, 213-213.9, 217-220.9, 221.0-221.8, 222.0-222.8, 223.0-223.8, 224-228.9, 229.0, 229.8, 230.1-230.8, 231.0-231.2, 232-232.9, 233.0-233.2, 233.4-233.5, 233.7, 234.0-234.8, 235.0, 235.4, 235.6-235.8, 236.0-236.2, 236.4-236.5, 236.7, 237-237.3, 237.5-237.9, 238.0-238.9, 239.2-239.4, 239.6, 240-243.9, 244.0-244.1, 244.3-244.8, 245-246.9, 251-259.1, 259.3-259.9, 270-273.9, 275-276, 277-277.2, 277.4-277.9, 278.0-278.8, 282-284.9, 286-286.5, 286.7-289.0, 289.4-289.7, 290-292.9, 294.1-294.9, 303-303.9, 304.0-304.8, 305.0, 305.2-305.8, 307.1, 327.2-327.8, 330-331.2, 331.5-332.0, 333-337.9, 340-341.9, 345-345.9, 349, 349.2-349.8, 353.8-353.9, 356-356.9, 357.0-357.1, 357.3-357.7, 358-359.9, 376.0-376.1, 391-391.9, 392.0, 393-398.9, 402-404.9, 410-414.9, 416.0-416.1, 417-417.9, 420-423, 423.1-423.9, 424.0-424.3, 424.8, 425.0-425.3, 425.5, 425.7-425.8, 427.0-427.3, 427.6-427.8, 429.0, 430-435.9, 437.0-437.2, 437.4-437.8, 440.2, 440.4, 441-443.9, 446-457, 457.1-457.9, 459, 459.1-459.3, 470, 470.9-474.9, 476-476.1, 477-479, 491-493.9, 495-504.9, 506-506.9, 508-509, 515, 516-517.8, 518.6-518.7, 518.9, 519.0-519.4, 530-530.0, 530.2-530.6, 531-536.1, 536.4, 537-537.6, 537.8, 538-543.9, 550-553.6, 555-558.9, 560-560.3, 560.8-560.9, 562-562.1, 564-564.7, 565-566.9, 569.0-569.7, 571-571.9, 572.2-573.0, 573.4-577.9, 579-583.9, 585-585.9, 588-590.9, 592-593.8, 594-599.6, 599.8, 601-602.9, 604-604.9, 608.2, 610-610.9, 617-618.9, 620-620.9, 621.4-621.9, 622.1-622.7, 629-629.8, 680-689, 694-695.5, 707-707.9, 710-711.9, 714-714.3, 714.8-714.9, 730.1, 732-732.9, 733.0-733.1, 740-749.0, 749.2-758.9, 759.0-759.8, 760.7, 775.1-775.3, 779.4-779.5, 788.0, 790.3, 798-798.0, E850, E860
Neoplasms	C00-C13.9, C15-C22.8, C23-C25.9, C30-C34.9, C37-C38.8, C40-C41.9, C43-C45.9, C47-C54.9, C56-C57.8, C60-C63.8, C64-C67.9, C68.0-C68.8, C69.0-C69.8, C70-C73.9, C75-C75.8, C81-C86.6, C88-C91.0, C91.2-C91.3, C91.6, C92-C92.6, C93-C93.1, C93.3, C93.8, C94-C96.9, D00.1-D00.2, D01.0-D01.3, D02.0-D02.3, D03-D06.9, D07.0-D07.2, D07.4-D07.5, D09.0, D09.2-D09.3, D09.8, D10.0-D10.7, D11-D12.9, D13.0-D13.7, D14.0-D14.3, D15-D16.9, D22-D24.9, D26.0-D27.9, D28.0-D28.1, D28.7, D29.0-D29.8, D30.0-D30.8, D31-D36, D36.1-D36.7, D37.1-D37.5, D38.0-D38.5, D39.1-D39.2, D39.8, D40.0-D40.8, D41.0-D41.8, D42-D43.9, D44.0-D44.8, D45-D47.9, D48.0-D48.6, D49.2-D49.4, D49.6, K62.0-K62.1, K63.5, N60-N60.9, N84.0-N84.1, N87-N87.9	140-148.9, 150-155.1, 155.3-158.9, 160-164.9, 170-175.9, 180-180.9, 182-183.8, 184.0-184.4, 184.8, 185-186.9, 187.1-187.8, 188-188.9, 189.0-189.8, 190-190.8, 191-193.9, 194.1-194.8, 200-204.0, 204.2, 205-205.3, 206-206.1, 207-208.9, 209.0-209.1, 209.4-209.5, 210.0-210.9, 211.0-211.8, 212.0-212.8, 213-213.9, 217-217.8, 219.0, 220-220.9, 221.0-221.8, 222.0-222.8, 223.0-223.8, 224-228.9, 229.0, 229.8, 230.1-230.8, 231.0-231.2, 232-232.9, 233.0-233.2, 233.4-233.5, 233.7, 234.0-234.8, 235.0, 235.4, 235.6-235.8, 236.1-236.2, 236.4-236.5, 236.7, 237-237.3, 237.5-237.9, 238.0-238.9, 239.2-239.4, 239.6, 569.0, 610-610.9, 622.1-622.2, 622.7
Lip and oral cavity cancer	C00-C08.9, D10.0-D10.5, D11-D11.9	140-145.9, 210.0-210.6, 235.0
Nasopharynx cancer	C11-C11.9, D10.6	147-147.9, 210.7-210.9
Other pharynx cancer	C09-C10.9, C12-C13.9, D10.7	146-146.9, 148-148.9
Oesophageal cancer	C15-C15.9, D00.1, D13.0	150-150.9, 211.0, 230.1
Stomach cancer	C16-C16.9, D00.2, D13.1, D37.1	151-151.9, 211.1, 230.2
Colon and rectum cancer	C18-C21.9, D01.0-D01.3, D12-D12.9, D37.3-D37.5	153-154.9, 209.1, 209.5, 211.3-211.4, 230.3-230.6, 569.0
Liver cancer	C22-C22.8, D13.4	155-155.1, 155.3-155.9, 211.5
Liver cancer due to hepatitis B		
Liver cancer due to hepatitis C		
Liver cancer due to alcohol use		
Liver cancer due to NASH		
Hepatoblastoma	C22.2	
Liver cancer due to other causes (internal)		
Gallbladder and biliary tract cancer	C23-C24.9, D13.5	156-156.9
Pancreatic cancer	C25-C25.9, D13.6-D13.7	157-157.9, 211.6-211.7
Larynx cancer	C32-C32.9, D02.0, D14.1, D38.0	161-161.9, 212.1, 231.0, 235.6
Tracheal, bronchus, and lung cancer	C33-C34.9, D02.1-D02.3, D14.2-D14.3, D38.1	162-162.9, 212.2-212.3, 231.1-231.2, 235.7
Malignant skin melanoma	C43-C43.9, D03-D03.9, D22-D23.9, D48.5	172-172.9
Non-melanoma skin cancer	C44-C44.9, D04-D04.9, D49.2	173-173.9, 222.4, 232-232.9, 238.2
Non-melanoma skin cancer (squamous-cell carcinoma)	C44-C44.9, D04-D04.9, D49.2	173-173.9, 222.4, 232-232.9, 238.2
Soft tissue and other extraosseous sarcomas	C49-C49.9	171-171.9
Malignant neoplasm of bone and articular cartilage	C40-C41.9	170-170.9
Breast cancer	C50-C50.9, D05-D05.9, D24-D24.9, D48.6, D49.3	174-175.9, 217-217.8, 233.0, 238.3, 239.3, 610-610.9
Cervical cancer	C53-C53.9, D06-D06.9, D26.0	180-180.9, 219.0, 233.1, 622.1-622.2, 622.7
Uterine cancer	C54-C54.9, D07.0-D07.2, D26.1-D26.9	182-182.9, 233.2
Ovarian cancer	C56-C56.9, D27-D27.9, D39.1	183-183.0, 220-220.9, 236.2
Prostate cancer	C61-C61.9, D07.5, D29.1, D40.0	185-185.9, 222.2, 236.5
Testicular cancer	C62-C62.9, D29.2-D29.8, D40.1-D40.8	186-186.9, 222.0, 222.3, 236.4
Kidney cancer	C64-C65.9, D30.0-D30.1, D41.0-D41.1	189.0-189.1, 189.5-189.6, 223.0-223.1
Bladder cancer	C67-C67.9, D09.0, D30.3, D41.4-D41.8, D49.4	188-188.9, 223.3, 233.7, 236.7, 239.4
Brain and central nervous system cancer	C70-C72.9	191-192.9
Eye cancer	C69.0-C69.8	190-190.8
Retinoblastoma	C69.2	190.5
Other eye cancers	C69.0-C69.1, C69.3-C69.8	190-190.4, 190.6-190.8

**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Neuroblastoma and other peripheral nervous cell tumors	C47-C47.9	
Thyroid cancer	C73-C73.9, D09.3, D09.8, D34-D34.9, D44.0	193-193.9, 226-226.9
Mesothelioma	C45-C45.9	
Hodgkin lymphoma	C81-C81.9	201-201.9
Non-Hodgkin lymphoma	C82-C86.6, C96-C96.9	200-200.9, 202-202.9
Burkitt lymphoma	C83.7-C83.8	200.2
Other non-Hodgkin lymphoma	C82-C83.6, C83.9-C86.6, C96-C96.9	200-200.1, 200.3-200.9, 202-202.9
Multiple myeloma	C88-C90.9	203-203.9
Leukaemia	C91-C91.0, C91.2-C91.3, C91.6, C92-C92.6, C93-C93.1, C93.3, C93.8, C94-C95.9	204-204.0, 204.2, 205-205.3, 206-206.1, 207-208.9
Acute lymphoid leukaemia	C91.0, C91.2-C91.3, C91.6	204.0, 204.2
Chronic lymphoid leukaemia		
Acute myeloid leukaemia	C92.0, C92.3-C92.6, C93.0, C94.0, C94.2, C94.4-C94.5	205.0, 205.2-205.3, 206.0, 207.0, 207.2-207.8
Chronic myeloid leukaemia	C92.1-C92.2	205.1
Other leukaemia	C93.1, C93.3, C93.8, C94.1, C94.3, C94.6-C95.9	206.1, 207.1, 207.9-208.9
Other malignant neoplasms (internal)	C17-C17.9, C30-C31.9, C37-C38.8, C48-C48.9, C4A, C51-C52.9, C57-C57.8, C60-C60.9, C63-C63.8, C66-C66.9, C68.0-C68.8, C75-C75.8, D07.4, D09.2, D13.2-D13.3, D14.0, D15-D16.9, D28.0-D28.1, D28.7, D29.0, D30.2, D30.4-D30.8, D31-D31.9, D35-D35.2, D35.5-D36, D36.1-D36.7, D37.2, D38.2-D38.5, D39.2, D39.8, D41.2-D41.3, D44.1-D44.8, D48.0-D48.4	152-152.9, 158-158.9, 160-160.9, 163-164.9, 183.2-183.8, 184.0-184.4, 184.8, 187.1-187.8, 189.2-189.4, 189.8, 194.1-194.8, 209.0, 209.4, 211.2, 211.8, 212.0, 212.4-212.8, 213-213.9, 221.0-221.8, 222.1, 222.8, 223.2, 223.8, 224-224.9, 227-228.9, 229.0, 229.8, 230.7-230.8, 233.4-233.5, 234.0-234.8, 235.4, 235.8, 236.1, 238.0-238.1, 239.2
Other neoplasms	D32-D33.9, D35.3-D35.4, D42-D43.9, D45-D47.9, D49.6, K62.0-K62.1, K63.5, N60-N60.9, N84.0-N84.1, N87-N87.9	225-225.9, 237-237.3, 237.5-237.9, 238.4-238.9, 239.6
Myelodysplastic, myeloproliferative, and other haematopoietic neoplasms	D45-D47.9	238.4-238.9
Cardiovascular diseases	B33.2, G45-G46.8, I01-I01.9, I02.0, I05-I09.9, I11-I11.9, I20-I25.9, I27.0, I27.2, I28-I28.9, I30-I31.1, I31.8-I37.8, I38-I41.9, I42.1-I42.8, I43-I43.9, I47-I48.9, I51.0-I51.4, I60-I63.9, I65-I66.9, I67.0-I67.3, I67.5-I67.6, I68.0-I68.2, I69.0-I69.3, I70.2-I70.8, I71-I73.9, I77-I83.9, I86-I89.0, I89.9, I98, K75.1	036.4, 391-391.9, 392.0, 393-398.9, 402-402.9, 410-414.9, 416.0, 417-417.9, 420-423, 423.1-423.9, 424.0-424.3, 424.8, 425.0-425.3, 425.5, 425.7-425.8, 427.0-427.3, 427.6-427.8, 429.0, 430-435.9, 437.0-437.2, 437.5-437.8, 440.2, 440.4, 441-443.9, 447-454.9, 456, 456.3-457, 457.1, 457.8-457.9, 459, 459.1-459.3
Rheumatic heart disease	I01-I01.9, I02.0, I05-I09.9	391-391.9, 392.0, 393-398.9
Ischaemic heart disease	I20-I25.9	410-414.9
Stroke	G45-G46.8, I60-I63.9, I65-I66.9, I67.0-I67.3, I67.5-I67.6, I68.1-I68.2, I69.0-I69.3	430-435.9, 437.0-437.2, 437.5-437.8
Ischaemic stroke	G45-G46.8, I63-I63.9, I65-I66.9, I67.2-I67.3, I67.5-I67.6, I69.3	433-435.9, 437.0-437.1, 437.5-437.8
Intracerebral haemorrhage	I61-I62, I62.1-I62.9, I68.1-I68.2, I69.1-I69.2	431-432.9, 437.2
Subarachnoid hemorrhage	I60-I60.9, I62.0, I67.0-I67.1, I69.0	430-430.9
Hypertensive heart disease	I11-I11.9	402-402.9
Non-rheumatic valvular heart disease	I34-I37.8	424.0-424.3, 424.8
Non-rheumatic calcific aortic valvular heart disease	I35-I35.9	424.1
Non-rheumatic degenerative mitral valvular heart disease	I34-I34.9	424.0
Other non-rheumatic valvular heart diseases	I36-I37.8	424.2-424.3, 424.8
Cardiomyopathy and myocarditis	B33.2, I40-I41.9, I42.1-I42.8, I43-I43.9, I51.4	422-422.9, 425.0-425.3, 425.5, 425.7-425.8, 429.0
Myocarditis	B33.2, I40-I41.9, I51.4	422-422.9
Alcoholic cardiomyopathy	I42.6	425.5
Other cardiomyopathy	I42.1-I42.5, I42.7-I42.8, I43-I43.9	425.0-425.3, 425.7-425.8, 429.0
Pulmonary arterial hypertension	I27.0, I27.2	416.0
Atrial fibrillation and flutter	I48-I48.9	427.3
Aortic aneurysm	I71-I71.9	441-441.9
Peripheral artery disease	I70.2-I70.8, I73-I73.9	440.2, 440.4, 443.0-443.9
Endocarditis	I33-I33.9, I38-I39.9	421-421.9
Other cardiovascular and circulatory diseases (internal)	I28-I28.9, I30-I31.1, I31.8-I32.8, I47-I47.9, I51.0-I51.3, I68.0, I72-I72.9, I77-I83.9, I86-I89.0, I89.9, I98, K75.1	036.4, 417-417.9, 420-420.9, 423, 423.1-423.9, 427.0-427.2, 427.6-427.8, 442-443, 447-454.9, 456, 456.3-457, 457.1, 457.8-457.9, 459, 459.1-459.3
Chronic respiratory diseases	D86-D86.2, D86.9, G47.3, J30-J35.9, J37-J39.9, J41-J46.9, J60-J63.8, J65-J68.9, J70, J70.8-J70.9, J82, J84-J84.9, J91, J91.8-J92.9	135-135.9, 327.2-327.8, 470, 470.9-474.9, 476-476.1, 477-479, 491-493.9, 495-504.9, 506-506.9, 508-509, 515, 516-517.8, 518.6, 518.9, 519.1-519.4
Chronic obstructive pulmonary disease	J41-J44.9	491-492.9, 496-499
Pneumoconiosis	J60-J63.8, J65-J65.0, J92.0	500-504.9
Silicosis	J62-J62.9	502-502.9, 503.0, 503.9
Asbestosis	J61-J61.0, J92.0	501
Coal workers pneumoconiosis	J60-J60.0	500-500.9, 501.0-501.9
Other pneumoconiosis	J63-J63.8, J65-J65.0	503, 503.1, 504-504.9
Asthma	J45-J46.9	493-493.9
Interstitial lung disease and pulmonary sarcoidosis	D86-D86.2, D86.9, J84-J84.9	135-135.9, 515, 516-516.9
Other chronic respiratory diseases	G47.3, J30-J35.9, J37-J39.9, J66-J68.9, J70, J70.8-J70.9, J82, J91, J91.8-J92, J92.9	327.2-327.8, 470, 470.9-474.9, 476-476.1, 477-479, 495-495.9, 506-506.9, 508-509, 517-517.8, 518.6, 518.9, 519.1-519.4
Digestive diseases	B18-B18.9, I84-I85.9, I98.2, K20-K20.9, K22-K22.6, K22.8-K29.9, K31-K31.8, K35-K38.9, K40-K42.9, K44-K46.9, K50-K52, K52.2-K52.9, K55-K62, K62.2-K62.6, K62.8-K62.9, K64-K64.9, K66.8, K67, K68, K70-K70.3, K71.7, K73-K75, K75.2, K75.4-K76.2, K76.4-K77, K77.8, K80-K83.9, K85-K86.9, K90-K90.9, K92.8, K93.8, M09.1	455-455.9, 456.0-456.2, 530-530.0, 530.2-530.6, 531-536.1, 537-537.6, 537.8, 538, 540-543.9, 550-551.1, 551.3-552.1, 552.3-553.6, 555-558.9, 560-560.3, 560.8-560.9, 562-562.1, 564-564.1, 564.5-564.7, 565-566.9, 569.1-569.5, 569.7, 571-571.9, 572.2-573.0, 573.4-577.9, 579-579.2, 579.4-579.9
Cirrhosis and other chronic liver diseases	B18-B18.9, I85-I85.9, I98.2, K70-K70.3, K71.7, K73-K75, K75.2, K75.4-K76.2, K76.4-K76.9, K77.8	456.0-456.2, 571-571.9, 572.2-573.0, 573.4-573.9
Cirrhosis and other chronic liver diseases due to hepatitis B		
Cirrhosis and other chronic liver diseases due to hepatitis C		
Cirrhosis and other chronic liver diseases due to alcohol use		



**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Cirrhosis and other chronic liver diseases due to NAFLD		
Cirrhosis and other chronic liver diseases due to other causes		
Upper digestive system diseases	K25-K29.9	531-535.9
Peptic ulcer disease	K25-K28.9	531-534.9
Gastritis and duodenitis	K29-K29.9	535-535.9
Appendicitis	K35-K37.9, K38.3-K38.9	540-542.9
Paralytic ileus and intestinal obstruction	K56-K56.9	560-560.3, 560.8-560.9
Inguinal, femoral, and abdominal hernia	K40-K42.9, K44-K46.9	550-551.1, 551.3-552.1, 552.3-553.0, 553.6
Inflammatory bowel disease	K50-K52, K52.8-K52.9, M09.1	555-556.9, 558-558.9, 569.5
Vascular intestinal disorders	K55-K55.9	557-557.9
Gallbladder and biliary diseases	K80-K83.9	574-576.9
Pancreatitis	K85-K86.9	577-577.9, 579.4
Other digestive diseases	I84-I84.9, K20-K20.9, K22-K22.6, K22.8-K24, K31-K31.8, K38-K38.2, K52.2-K52.3, K57-K62, K62.2-K62.6, K62.8-K62.9, K64-K64.9, K66.8, K67, K68, K77, K90-K90.9, K92.8, K93.8	455-455.9, 530-530.0, 530.2-530.6, 536-536.1, 537-537.6, 537.8, 538, 543-543.9, 553.1-553.3, 562-562.1, 564-564.1, 564.5-564.7, 565-566.9, 569.1-569.4, 569.7, 579-579.2, 579.8-579.9
Neurological disorders	F00-F02.0, F02.2-F02.3, F02.8-F03.9, G10-G13.8, G20-G20.9, G23-G24, G24.1-G25.0, G25.2-G25.3, G25.5, G25.8-G26.0, G30-G31.1, G31.8-G31.9, G35-G37.9, G40-G41.9, G61-G61.9, G70-G71.1, G71.3-G72, G72.2-G73.7, G90-G90.9, G95-G95.9, M33-M33.9	290-290.9, 294.1-294.9, 330-331.2, 331.5-332.0, 333-337.9, 340-341.9, 345-345.9, 349, 349.2-349.8, 353.8-353.9, 356-356.9, 357.0-357.1, 357.3-357.4, 357.7, 358-359.9, 775.2
Alzheimer's disease and other dementias	F00-F02.0, F02.8-F03.9, G30-G31.1, G31.8-G31.9	290-290.9, 294.1-294.9, 331-331.2
Parkinson's disease	F02.3, G20-G20.9	332-332.0
Idiopathic epilepsy	G40-G41.9	345-345.9
Multiple sclerosis	G35-G35.9	340-340.9
Motor neuron disease	G12.2-G12.9	335-335.2, 335.8-335.9
Other neurological disorders	F02.2, G10-G12.1, G13-G13.8, G23-G24, G24.1-G25.0, G25.2-G25.3, G25.5, G25.8-G26.0, G36-G37.9, G61-G61.9, G70-G71.1, G71.3-G72, G72.2-G73.7, G90-G90.9, G95-G95.9, M33-M33.9	330-330.9, 331.5-331.9, 333-334.9, 335.3, 336-337.9, 341-341.9, 349, 349.2-349.8, 353.8-353.9, 356-356.9, 357.0-357.1, 357.3-357.4, 357.7, 358-359.9, 775.2
Mental disorders	F24, F50.0-F50.5	307.1
Eating disorders	F50.0-F50.5	307.1
Anorexia nervosa	F50.0-F50.1	307.1
Bulimia nervosa	F50.2-F50.5	
Substance use disorders	E24.4, F10-F16.9, F18-F18.9, G31.2, G62.1, G72.1, P04.3-P04.4, P96.1, Q86.0, R78.0-R78.5, X45-X45.9, X65-X65.9, Y15-Y15.9	291-292.9, 303-303.9, 304.0-304.8, 305.0, 305.2-305.8, 357.5, 760.7, 790.3, E850, E860
Alcohol use disorders	E24.4, F10-F10.9, G31.2, G62.1, G72.1, P04.3, Q86.0, R78.0, X45-X45.9, X65-X65.9, Y15-Y15.9	291-291.9, 303-303.9, 305.0, 357.5, 790.3, E860
Drug use disorders	F11-F16.9, F18-F18.9, P04.4, P96.1, R78.1-R78.5	292-292.9, 304.0-304.8, 305.2-305.8, 760.7, E850
Opioid use disorders	F11-F11.9, P96.1, R78.1	304.0, 305.5
Cocaine use disorders	F14-F14.9, R78.2	304.2, 305.6
Amphetamine use disorders	F15-F15.9	304.4, 305.7
Other drug use disorders	F13-F13.9, F16-F16.9, F18-F18.9, P04.4, R78.3-R78.5	292-292.9, 304.1, 304.5-304.8, 305.3-305.4, 305.8, 760.7
Diabetes and kidney diseases	D63.1, E10-E11.9, I12-I13.9, N00-N08.8, N15.0, N18-N18.9, P70.2, Q61-Q62.8	403-404.9, 580-583.9, 585-585.9, 589-589.9, 753-753.3, 775.1
Diabetes mellitus	E10-E10.1, E10.3-E11.1, E11.3-E11.9, P70.2	775.1
Diabetes mellitus type 1	E10-E10.1, E10.3-E10.9, P70.2	775.1
Diabetes mellitus type 2	E11-E11.1, E11.3-E11.9	
Chronic kidney disease	D63.1, E10.2, E11.2, I12-I13.9, N02-N08.8, N15.0, N18-N18.9, Q61-Q62.8	403-404.9, 581-583.9, 585-585.9, 589-589.9, 753-753.3
Chronic kidney disease due to diabetes mellitus type 1	E10.2	
Chronic kidney disease due to diabetes mellitus type 2	E11.2	
Chronic kidney disease due to hypertension	I12-I13.9	403-404.9
Chronic kidney disease due to glomerulonephritis	N03-N06.9	581-583.9
Chronic kidney disease due to other and unspecified causes	N02-N02.9, N07-N08.8, N15.0, Q61-Q62.8	589-589.9, 753-753.3
Acute glomerulonephritis	N00-N01.9	580-580.9
Skin and subcutaneous diseases	A46-A46.0, A66-A67.9, B86, D86.3, I89.1-I89.8, L00-L05.9, L08-L08.9, L10-L14.0, L51-L51.9, L88-L89.9, L97-L98.4, M72.5-M72.6	035-035.9, 102-103.9, 133-133.6, 457.2-457.3, 680-689, 694-695.3, 707-707.9
Bacterial skin diseases	A46-A46.0, A66-A67.9, I89.1-I89.8, L00-L05.9, L08-L08.9, L88, L97-L98.4, M72.5-M72.6	035-035.9, 102-103.9, 457.2-457.3, 680-689
Cellulitis	L03-L03.9, M72.5-M72.6	681-682.9
Pyoderma	A46-A46.0, A66-A67.9, I89.1-I89.8, L00-L02.9, L04-L05.9, L08-L08.9, L88, L97-L98.4	035-035.9, 102-103.9, 457.2-457.3, 680-680.9, 683-689
Decubitus ulcer	L89-L89.9	707-707.9
Other skin and subcutaneous diseases	D86.3, L10-L14.0, L51-L51.9	694-695.3
Musculoskeletal disorders	I27.1, I67.7, L93-L93.2, M00-M03.0, M03.2-M03.6, M05-M09.0, M09.2-M09.8, M30-M32.9, M34-M36.8, M40-M43.1, M65-M65.0, M71.0-M71.1, M80-M82.8, M86.3-M86.4, M87-M87.0, M88-M89.0, M89.5, M89.7-M89.9	416.1, 437.4, 446-446.9, 695.4-695.5, 710-711.9, 714-714.3, 714.8-714.9, 730.1, 732-732.9, 733.0-733.1
Rheumatoid arthritis	M05-M06.9, M08.0-M08.8	714-714.3, 714.8-714.9
Other musculoskeletal disorders	I27.1, I67.7, L93-L93.2, M00-M03.0, M03.2-M03.6, M07-M08, M08.9-M09.0, M09.2-M09.8, M30-M32.9, M34-M36.8, M40-M43.1, M65-M65.0, M71.0-M71.1, M80-M82.8, M86.3-M86.4, M87-M87.0, M88-M89.0, M89.5, M89.7-M89.9	416.1, 437.4, 446-446.9, 695.4-695.5, 710-711.9, 730.1, 732-732.9, 733.0-733.1

**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Other non-communicable diseases	D25-D26, D28.2, D52.1, D55-D58.9, D59.0-D59.3, D59.5-D59.6, D60-D61.9, D64.0, D66-D67, D68.0-D69.8, D70-D70.2, D70.4-D75.8, D76-D78.8, D86.8, D89-D89.2, E03-E07.1, E09-E09.9, E15.0, E16.0-E16.9, E20-E24.3, E24.8-E34, E34.1-E34.8, E36-E36.8, E65-E68, E70-E85.2, E88-E89.9, G21.0-G21.1, G24.0, G25.1, G25.4, G25.6-G25.7, G71.2, G72.0, G93.7, G97-G97.9, I95.2-I95.3, I97-I97.9, I98.9, J70.0-J70.5, J95-J95.9, K43-K43.9, K52.0, K62.7, K91-K91.9, K94-K95.8, M87.1, N10-N12.9, N13.6, N14-N15, N15.1-N16.8, N20-N23.0, N25-N28.1, N29-N30.3, N30.8-N32.0, N32.3-N32.4, N34-N34.3, N36-N36.9, N39-N39.2, N41-N41.9, N44-N44.0, N45-N45.9, N49-N49.9, N65-N65.1, N72-N72.0, N75-N77.8, N80-N81.9, N83-N83.9, N99-N99.9, P96.0, P96.2, P96.5, Q00-Q07.9, Q10.4-Q18.9, Q20-Q28.9, Q30-Q36, Q37-Q45.9, Q50-Q60.6, Q63-Q86, Q86.1-Q87.8, Q89-Q89.8, Q90-Q93.9, Q95-Q99.8, R50.2, R95-R95.9	218-219, 219.1-219.9, 236.0, 240-243.9, 244.0-244.1, 244.3-244.8, 245-246.9, 251-259.1, 259.3-259.9, 270-273.9, 275-276, 277-277.2, 277.4-277.9, 278.0-278.8, 282-284.9, 286-286.5, 286.7-289.0, 289.4-289.7, 357.6, 518.7, 519.0, 536.4, 539-539.9, 551.2, 552.2, 564.2-564.4, 569.6, 579.3, 588-588.9, 590-590.9, 592-593.8, 594-599.6, 599.8, 601-602.9, 604-604.9, 608.2, 617-618.9, 620-620.9, 621.4-621.9, 622.3-622.6, 629-629.8, 740-749.0, 749.2-752.9, 753.4-758.9, 759.0-759.8, 775.3, 779.4-779.5, 788.0, 798-798.0
Congenital birth defects	G71.2, P96.0, Q00-Q07.9, Q10.4-Q18.9, Q20-Q28.9, Q30-Q36, Q37-Q45.9, Q50-Q60.6, Q63-Q86, Q86.1-Q87.8, Q89-Q89.8, Q90-Q93.9, Q95-Q99.8	740-749.0, 749.2-752.9, 753.4-758.9, 759.0-759.8
Neural tube defects	Q00-Q01.9, Q05-Q05.9	740-741.9, 742.0
Congenital heart anomalies	Q20-Q28.9	745-747.9
Orofacial clefts	Q35-Q36, Q37-Q37.9	749-749.0, 749.2-749.9
Down syndrome	Q90-Q90.9	758.0
Other chromosomal abnormalities	Q87-Q87.8, Q91-Q93.9, Q95-Q95.9, Q97-Q97.9, Q99-Q99.8	758, 758.1-758.6, 758.8-758.9
Congenital musculoskeletal and limb anomalies	Q65-Q79, Q79.6-Q79.9	742.5, 754-756.5, 756.8-756.9
Urogenital congenital anomalies	P96.0, Q50-Q60.6, Q63-Q64.9	752-752.9, 753.4-753.9
Digestive congenital anomalies	Q38-Q45.9, Q79.0-Q79.5	750-751.9, 756.6-756.7
Other congenital birth defects	G71.2, Q02-Q04.9, Q06-Q07.9, Q10.4-Q18.9, Q30-Q34.9, Q80-Q86, Q86.1-Q86.8, Q89-Q89.8	742, 742.1-742.4, 742.8-744.9, 748-748.9, 757-757.9, 759.0-759.8
Urinary diseases and male infertility	N10-N12.9, N13.6, N15, N15.1-N16.8, N20-N23.0, N25-N28.1, N29-N30.3, N30.8-N32.0, N32.3-N32.4, N34-N34.3, N36-N36.9, N39-N39.2, N41-N41.9, N44-N44.0, N45-N45.9, N49-N49.9	588-588.9, 590-590.9, 592-593.8, 594-598.1, 598.8-599.6, 599.8, 601-602.9, 604-604.9, 608.2, 788.0
Urinary tract infection and interstitial nephritis	N10-N12.9, N13.6, N15, N15.1-N16.8, N30-N30.3, N30.8-N30.9, N34-N34.3, N39.0-N39.2	590-590.9, 595-595.9, 597-597.9, 599.0
Urolithiasis	N20-N23.0	592-592.9, 594-594.9, 788.0
Other urinary diseases	N25-N28.1, N29-N29.8, N31-N32.0, N32.3-N32.4, N36-N36.9, N39, N41-N41.9, N44-N44.0, N45-N45.9, N49-N49.9	588-588.9, 593-593.8, 596-596.9, 598-598.1, 598.8-599, 599.1-599.6, 599.8, 601-602.9, 604-604.9, 608.2
Gynaecological diseases	D25-D26, D28.2, E28.2, N72-N72.0, N75-N77.8, N80-N81.9, N83-N83.9	218-219, 219.1-219.9, 236.0, 256.4, 617-618.9, 620-620.9, 621.4-621.9, 622.3-622.6, 629-629.8
Uterine fibroids	D25-D26, D28.2	218-219, 219.1-219.9, 236.0
Endometriosis	N80-N80.9	617-617.9
Genital prolapse	N81-N81.9	618-618.9
Other gynaecological diseases	N72-N72.0, N75-N77.8, N83-N83.9	620-620.9, 621.4-621.9, 622.3-622.6, 629-629.8
Haemoglobinopathies and haemolytic anaemias	D55-D58.9, D59.1, D59.3, D59.5, D60-D61.9, D64.0	282-284.9
Thalassaemias	D56-D56.9	282.4-282.5
Sickle cell disorders	D57-D57.8	282.6
G6PD deficiency	D55-D55.2	282.2-282.3
Other haemoglobinopathies and haemolytic anaemias	D55.3-D55.9, D58-D58.9, D59.1, D59.3, D59.5, D60-D61.9, D64.0	282-282.1, 282.7-284.9
Endocrine, metabolic, blood, and immune disorders	D52.1, D59.0, D59.2, D59.6, D66-D67, D68.0-D69.8, D70-D70.2, D70.4-D75.8, D76-D78.8, D86.8, D89-D89.2, E03-E07.1, E09-E09.9, E15.0, E16.0-E16.9, E20-E24.3, E24.8-E28.1, E28.3-E34, E34.1-E34.8, E36-E36.8, E65-E68, E70-E85.2, E88-E89.9, G21.0-G21.1, G24.0, G25.1, G25.4, G25.6-G25.7, G72.0, G93.7, G97-G97.9, I95.2-I95.3, I97-I97.9, I98.9, J70.0-J70.5, J95-J95.9, K43-K43.9, K52.0, K62.7, K91-K91.9, K94-K95.8, M87.1, N14-N14.4, N65-N65.1, N99-N99.9, P96.2, P96.5, R50.2	240-243.9, 244.0-244.1, 244.3-244.8, 245-246.9, 251-256.3, 256.8-259.1, 259.3-259.9, 270-273.9, 275-276, 277-277.2, 277.4-277.9, 278.0-278.8, 286-286.5, 286.7-289.0, 289.4-289.7, 357.6, 518.7, 519.0, 536.4, 539-539.9, 551.2, 552.2, 564.2-564.4, 569.6, 579.3, 598.2, 775.3, 779.4-779.5
Sudden infant death syndrome	R95-R95.9	798-798.0
Injuries	L55-L55.9, L56.3, L56.8-L56.9, L58-L58.9, N30.4, U00-U03, V00-V86.9, V87.2-V87.3, V88.2-V88.3, V90-V98.8, W00-W46.2, W49-W62.9, W64-W70.9, W73-W75.9, W77-W81.9, W83-W94.9, W97.9, W99-X06.9, X08-X39.9, X47-X48.9, X50-X54.9, X57-X58.9, X60-X64.9, X66-X83.9, X85-Y08.9, Y35-Y84.9, Y87.0-Y87.1, Y88-Y88.3, Y89.0-Y89.1	349.0-349.1, 457.0, E800-E807, E830-E838, E840-E849, E856-E857, E861-E865, E867-E869, E870-E876, E878-E879, E880-E886, E888-E928, E930-E979, E990-E999
Transport injuries	V00-V86.9, V87.2-V87.3, V88.2-V88.3, V90-V98.8	E800-E807, E830-E838, E840-E849
Road injuries	V01-V04.9, V06-V80.9, V82-V82.9, V87.2-V87.3	
Pedestrian road injuries	V01-V04.9, V06-V09.9	
Cyclist road injuries	V10-V19.9	
Motorcyclist road injuries	V20-V29.9	
Motor vehicle road injuries	V30-V79.9, V87.2-V87.3	
Other road injuries	V80-V80.9, V82-V82.9	
Other transport injuries	V00-V00.8, V05-V05.9, V81-V81.9, V83-V86.9, V88.2-V88.3, V90-V98.8	E800-E807, E830-E838, E840-E849
Unintentional injuries	L55-L55.9, L56.3, L56.8-L56.9, L58-L58.9, N30.4, W00-W46.2, W49-W62.9, W64-W70.9, W73-W75.9, W77-W81.9, W83-W94.9, W97.9, W99-X06.9, X08-X39.9, X47-X48.9, X50-X54.9, X57-X58.9, Y40-Y84.9, Y88-Y88.3	349.0-349.1, 457.0, E856-E857, E861-E865, E867-E869, E870-E876, E878-E879, E880-E886, E888-E928, E930-E949
Falls	W00-W19.9	E880-E886, E888
Drowning	W65-W70.9, W73-W74.9	E910
Fire, heat, and hot substances	X00-X06.9, X08-X19.9	E890-E899, E924
Poisonings	X47-X48.9	E856-E857, E861-E865, E867-E869
Poisoning by carbon monoxide	X47-X47.9	E862, E868-E869
Poisoning by other means	X48-X48.9	E856-E857, E861, E863-E865, E867
Exposure to mechanical forces	W20-W38.9, W40-W43.9, W45.0-W45.2, W46-W46.2, W49-W52	E916-E922
Unintentional firearm injuries	W32-W34.9	E922

**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Other exposure to mechanical forces	W20-W31.9, W35-W38.9, W40-W43.9, W45.0-W45.2, W46-W46.2, W49-W52	E916-E921
Adverse effects of medical treatment	N30.4, Y40-Y84.9, Y88-Y88.3	349.0-349.1, 457.0, E870-E876, E878-E879, E930-E949
Animal contact	W52.0-W62.9, W64-W64.9, X20-X29.9	E905-E906
Venomous animal contact	X20-X29.9	E905
Non-venomous animal contact	W52.0-W62.9, W64-W64.9	E906
Foreign body	W44-W45, W45.3-W45.9, W75-W75.9, W78-W80.9, W83-W84.9	E911-E915
Pulmonary aspiration and foreign body in airway	W75-W75.9, W78-W80.9, W83-W84.9	E911-E913
Foreign body in other body part	W44-W45, W45.3-W45.9	E914-E915
Environmental heat and cold exposure	L55-L55.9, L56.3, L56.8-L56.9, L58-L58.9, W88-W94.9, W97.9, W99-W99.9, X30-X32.9, X39-X39.9	E900-E902, E926
Exposure to forces of nature	X33-X38.9	E907-E909
Still Born	P95-P95.9	768.0-768.1
Other unintentional injuries	W39-W39.9, W77-W77.9, W81-W81.9, W85-W87.9, X50-X54.9, X57-X58.9	E903-E904, E923, E925, E927-E928
Self-harm and interpersonal violence	U00-U03, X60-X64.9, X66-X83.9, X85-Y08.9, Y35-Y38.9, Y87.0-Y87.1, Y89.0-Y89.1	E950-E979, E990-E999
Self-harm	X60-X64.9, X66-X83.9, Y87.0	E950-E959
Self-harm by firearm	X72-X74.9	E955
Self-harm by other specified means	X60-X64.9, X66-X71.9, X75-X83.9, Y87.0	E950-E954, E956-E959
Interpersonal violence	X85-Y08.9, Y87.1	E960-E969
Physical violence by firearm	X93-X95.9	E965
Physical violence by sharp object	X99-X99.9	E966
Physical violence by other means	X85-X92.9, X96-X98.9, Y00-Y04.9, Y06-Y08.9, Y87.1	E961-E964, E967-E969
Conflict and terrorism	U00-U03, Y36-Y38.9, Y89.1	E979, E990-E999
Police conflict and executions	Y35-Y35.9, Y89.0	E970-E978
Garbage Code (GBD Level 1)	A40-A41.9, A48.0, A48.3, A49.0-A49.1, A59-A59.9, A71-A71.9, A74.0, B07-B07.9, B30-B30.9, B35-B36.9, B85-B85.4, B87-B88.9, B94.0, D50-D50.0, D50.9, D62-D63.0, D63.8-D64, D64.1-D65.9, D68, D69.9, E15, E16, E50-E50.9, E64.1, E85.3-E87.6, E87.8-E87.9, F06.2-F06.4, F07.2, F09-F09.9, F19-F23.9, F25-F49, F51-F99.0, G06-G08.0, G32-G32.8, G43-G44.2, G44.4-G44.8, G47-G47.2, G47.4-G47.9, G50-G60.9, G62-G62.0, G62.2-G65.2, G80-G83.9, G89-G89.4, G91-G91.2, G91.4-G93, G93.1-G93.2, G93.4-G93.6, G94.0-G94.8, G99-H05, H05.2-H69.9, H71-H99, I26-I26.9, I31.2-I31.4, I46-I46.9, I50.0-I50.4, I76, I95-I95.1, I95.8-I95.9, I69-J69.9, J80-J80.9, J81.0, J85-J85.3, J86-J86.9, J93-J93.1, J93.8-J93.9, J94.2, J96-J96.9, J98.1-J98.3, K00-K19, K30, K65-K66.1, K66.9, K68.1-K68.9, K71-K71.6, K71.8-K72.9, K75.0, L20-L30.9, L40-L50.9, L52-L54.8, L56-L56.2, L56.4-L56.5, L57-L57.9, L59-L68.9, L70-L76.8, L80-L87.9, L90-L92.9, L94-L96, L98.5-L99.8, M04, M10-M12.0, M12.2-M29, M37-M39, M43.2-M49, M49.2-M64, M65.1-M71, M71.2-M72.4, M72.8-M73, M73.8-M79.9, M83-M86.2, M86.5-M86.9, M87.2-M87.9, M89.1-M89.4, M90-M99.9, N17-N17.9, N19-N19.9, N32.1-N32.2, N32.8-N33.8, N35-N35.9, N37-N37.8, N39.3-N39.8, N42-N43.4, N44.1-N44.8, N46-N48.9, N50-N53.9, N61-N64.9, N82-N82.9, N91-N91.5, N95, N95.1-N95.9, N97-N97.9, R02-R02.9, R03.1, R07.0, R08-R09, R09.3, R11-R12.0, R14-R19.6, R19.8-R23, R23.1-R30.9, R32-R50.1, R50.8-R57.9, R58.0-R72.9, R74-R78, R78.6-R94.8, R96-R99.9, U05, U07-U81, U89.9-U99, X40-X44.9, X46-X46.9, X49-X49.9, Y10-Y14.9, Y16-Y19.9, Z00-Z15.8, Z17-unspl.	038-038.9, 040.0, 041.1, 076-078.2, 110-111.9, 125-125.3, 126-126.9, 127.2-127.9, 131-132.9, 133.8-134.9, 136.6, 139.1, 139.9, 247-248, 264-264.9, 274-274.9, 276.0-276.5, 276.7-276.9, 277.3, 280-281, 285-285.9, 286.6, 289.1-289.3, 293, 294-294.0, 295-302.9, 305, 305.9-307.0, 307.2-307.4, 307.6-319.9, 324-327.1, 328-329, 338-339.1, 339.3-339.8, 342-344.9, 346-346.9, 350-353.6, 354-355.9, 360-362, 362.1-376, 376.2-380.9, 384-389.9, 415-415.9, 423.0, 424, 424.4-424.5, 424.9, 427.5, 427.9, 428.9, 437.3, 458-458.9, 459.0, 507-507.9, 510-510.9, 512-513.9, 518.1-518.2, 520-529.9, 536.3, 536.8-536.9, 537.7, 537.9, 564.8-564.9, 567-568.9, 570-570.9, 572-572.1, 573.1-573.3, 584-584.9, 586-587.9, 603-603.9, 605-608.1, 608.3-609, 611-612.1, 615-616.9, 619-619.9, 621-621.3, 622-622.0, 622.8-623.6, 623.8-624.5, 624.8-628.9, 629.9, 690-693.9, 695.8-706.9, 708-709.9, 712-713.8, 715-716, 716.2-721.6, 721.8-730.0, 730.2-730.3, 730.7-731.9, 733, 733.2-734.2, 737-738, 738.2-739.9, 780-782.4, 782.6-784.6, 784.9, 785.4-786, 786.6, 786.8, 787, 787.3-788, 788.3-789, 789.1-789.2, 789.5, 790-790.1, 790.4-796.1, 796.3-797.9, 798.1-799, 799.2-799.9, 999.0-999.9, E851-E855, E858, E866, E980-E982, V01-V08, V10-uns
Garbage Code (GBD Level 2)	A14.9, A29-A30.9, A45-A45.9, A47-A48, A48.8-A49, A49.3-A49.9, A61-A62, A72-A73, A76, A97, B08-B09, B11-B14, B28-B29, B31-B32.4, B34-B34.9, B61-B62, B68-B68.9, B73-B74.2, B76-B76.9, B78-B81.8, B84, B92-B94, B94.8-B94.9, B95.6-B97.3, B97.7-B99.9, D59, D59.4, D59.8-D59.9, F17-F17.9, G44.3, G91.3, G93.0, G93.3, I10-I10.9, I15-I15.9, I27, I27.8-I27.9, I50, I50.8-I50.9, I67.4, I70-I70.1, I70.9, I74-I75.8, J81, J81.1, J90-J90.0, J94-J94.1, J94.8-J94.9, K92.0-K92.2, N70-N71.9, N73-N74.0, N74.2-N74.8, R03-R03.0, R04-R06.9, R09.0-R09.2, R09.8-R10.9, R13-R13.9, R23.0, R58, S00-T98.3, W47-W48, W63, W71-W72, W76-W76.9, W82, W95-W97, W98, X07, X55-X56, X59-X59.9, Y20-Y34.9, Y86-Y87, Y87.2, Y89, Y89.9-Y99.9	000-000.9, 030-030.9, 041.2-041.9, 067-069, 078.8-078.9, 079.8-079.9, 089-089.9, 105-109.9, 119, 136.8-136.9, 139.8, 304, 304.9, 305.1, 339.2, 401-401.9, 405-405.9, 416, 416.2-416.9, 440-440.1, 440.3, 440.8-440.9, 444-445.8, 490-490.9, 494-494.9, 511-511.9, 514-514.9, 515.0-515.9, 518-518.0, 518.3-518.5, 518.8, 536.2, 578-578.9, 599.7, 613-614.9, 714.4, 716.1, 721.7, 735-736.9, 738.0-738.1, 784.7-784.8, 786.3, 787.0-787.2, 789.0, 789.3-789.4, 789.6-789.9, 796.2, 799.0-799.1, 800-999, E000-E80, E83, E839, E85, E859, E87, E877, E88, E887, E929, E983-E985, E988-E989

**Table S2: List of International Classification of Diseases (ICD) codes mapped to the Global Burden of Disease cause list for causes of death**

Cause	ICD10	ICD9
Garbage Code (GBD Level 3)	A01, A31-A31.9, A42-A44.9, A49.2, A64-A64.0, A99-A99.0, B17, B17.1, B17.8-B17.9, B19-B19.0, B19.2-B19.9, B37-B46.9, B49-B49.9, B55, B55.1-B55.9, B58-B59.9, B89, B94.2, C14-C14.9, C22.9, C26-C29, C35-C36, C39-C39.9, C42, C46-C46.9, C55-C55.9, C57.9, C59, C63.9, C68, C68.9, C74-C74.9, C75.9-C80.9, C87, C97-D00.0, D01, D01.4-D02, D02.4-D02.9, D07, D07.3, D07.6-D09, D09.1, D09.7, D09.9-D10, D10.9, D13, D13.9-D14, D14.4, D17-D21.9, D28, D28.9-D29, D29.9-D30, D30.9, D36.0, D36.9-D37.0, D37.6-D38, D38.6-D39.0, D39.7, D39.9-D40, D40.9-D41, D41.9, D44, D44.9, D48, D48.7-D49.1, D49.5, D49.7-D49.9, D54, D75.9, D79-D85, D87-D88, D89.8-D99, E07.8-E08.9, E17-E19, E34.0, E34.9-E35.8, E37-E39, E47-E49., E62, E69, E87.7, E90-E998, F04-F06.1, F06.5-F07.0, F07.8-F08, F50, F50.8-F50.9, G09-G09.9, G15-G19, G21, G21.2, G21.4-G22.0, G27-G29, G33-G34, G38-G39., G42, G48-G49, G66-G69, G74-G79, G84-G88, G93.8-G94, G96-G96.9, G98-G98.9, I00.0, I03-I04., I14-I14., I16-I19, I29-I29.9, I44-I45.9, I49-I49.9, I51, I51.6-I59, I90-I94, I96-I96.9, I98.4-I98.8, I99-ID5.9, J02.9, J03.9, J04.3, J06, J06.9, J40-J40.9, J47-J59, J71-J79, J81.9, J83, J85.9, J87-J89, J90.9, J93.6, J97-J98.0, J98.4-J99.8, K21-K21.9, K22.7, K31.9-K34, K39, K47-K49, K53-K54, K63-K63.4, K63.8-K63.9, K69, K70.4-K70.9, K78-K79, K84, K87-K89, K92, K92.9-K93, K96-K99, L06-L07, L09, L15-L19, L31-L39, L69, L77-L79, N09, N13-N13.5, N13.7-N13.9, N24, N28.8-N28.9, N38, N39.9-N40.9, N54-N59, N66-N69, N78-N79, N84, N84.2-N86, N88-N90.9, N92-N94.9, N95.0, O08-O08.9, O17-O19, O27, O37-O39, O49-O59, O78-O79, O93-O95.9, P06, P16-P18, P30-P34.2, P40-P49, P62-P69, P73, P79, P82, P85-P89, P96.9-P99.9, Q08-Q10.3, Q19, Q29-Q29., Q36.0-Q36.9, Q46-Q49, Q88, Q89.9, Q94, Q99.9-R01.2, R07, R07.1-R07.9, R31-R31.9	002, 031-031.9, 039-039.9, 070, 070.4-070.9, 085, 085.1-085.9, 088.0-088.7, 112-118.9, 130-130.9, 136.3-136.5, 149-149.9, 155.2, 159-159.9, 165-169, 176-179.9, 183.9-184, 184.5, 184.9, 187, 187.9, 189, 189.9, 190.9, 195-199.9, 209, 209.2-209.3, 209.6-210, 211, 211.9-212, 212.9, 214-216.9, 221, 221.9-222, 222.9-223, 223.9, 229, 229.1, 229.9-230.0, 230.9-231, 231.8-231.9, 233, 233.3, 233.6, 233.9-234, 234.9-235, 235.1-235.3, 235.5, 235.9-236, 236.3, 236.6, 236.9, 237.4, 239-239.1, 239.5, 239.7-239.9, 249-249.9, 259.2, 276.6, 278, 279-279.9, 293.0-293.9, 331.3-331.4, 332.1-332.9, 347-348.9, 349.9, 357, 357.8-357.9, 399-400.0, 406-409.4, 418-419.9, 426-427, 427.4, 429, 429.2-429.9, 459.5-459.9, 464.5, 465, 465.9, 505-505.9, 519, 519.8-519.9, 530.1, 530.7-530.9, 544-549, 553.8-553.9, 559-559.0, 560.4-560.7, 561, 562.2-563, 569, 569.8-569.9, 591-591.9, 593.9, 599.9-600.9, 623.7, 624.6, 637-637.9, 639-639.9, 749.1, 759, 759.9, 779.9, 782.5, 785-785.3, 786.0-786.2, 786.4-786.5, 786.7, 786.9, 788.1-788.2, E986-E987
Garbage Code (GBD Level 4)	B16.9, B64, B82-B82.9, B83.9, C69, C69.9, C91.1, C91.4-C91.5, C91.7-C91.9, C92.7-C92.9, C93.2, C93.5-C93.7, C93.9, E12-E14.9, G00, G00.9-G02.8, G03.9, I37.9, I42-I42.0, I42.9, I51.5, I64-I64.9, I67, I67.8-I68, I68.8-I69, I69.4-I69.9, J07-J08, J15.9, J17-J19.6, J22-J29, J64-J64.9, P23, P23.5-P23.9, P37.3-P37.4, R73-R73.9, V87-V87.1, V87.4-V88.1, V88.4-V89.9, V99-V99.0, X84-X84.9, Y09-Y09.9, Y85-Y85.9	070.3, 084, 084.6, 194-194.0, 194.9, 204.1, 204.5-204.9, 205.8-205.9, 206.2-206.9, 238, 244, 244.9, 250-250.9, 289.8-289.9, 307.5, 320, 320.9, 357.2, 362.0, 425, 425.4, 425.9, 429.1, 436-437, 437.9-439.6, 482.9-483, 484, 484.8-486.9, 770.0, 790.2, E808-E829







Table S3. List of infectious syndromes mapped to International Classification of Diseases (ICD) codes

Infectious syndrome name and level				Infectious syndrome name and ICD code	Infectious syndrome name and level				Infectious syndrome name and ICD code	
Level	L0	L1	L2	L3	ICD Codes for all level	L0	L1	L2	L3	ICD Codes for all level
101	3		Neonatal bloodstream infections due to anaerobes		P36.5					
102	3		Neonatal bloodstream infections due to listeria		P37.2					
103	3		Neonatal bloodstream infections due to unspecified bacteria		P36			Neonatal bloodstream infections due to unspecified bacteria		771-771.2, 771.4-771.9
104	1	Other and non bacterial infectious			A29, A36-A36.9, A42-A42.2, A42.8-A43.9, A42.7, B37.7, P37, A54.3, A54.5-A54.6, A59-A63.8, A71-A71.9, A80-A86.4, A88-B20.0, B20.2-B34.1, B34.3-B37.6, B37.8-B94.8, B97-B97.1, B97.3, B97.7-B97.8, F07.1, G04-G05.8, G14-G14.6, G21.3, H05.1, H60.2, H62-H62.3, H65-H68.0, H70-H70.9, H73.0, H75-H75.0, I02.9, I00-I06.9, I31-I32.5, I35-I37.1, I39.0-I39.1, I85-I85.3, I86-I86.9, J91.0, K05.1, M89.6, K72-K72.9, N75-N77.8, O98.4-O98.7, P35-P35.9, P37.1, P37.3-P37.5, T81.4, T82.6-T82.7, T84.5-T84.7, U06-U06.9, Z21-Z21.0, Z22.5-Z22.6	Upper respiratory infections and otitis due to corynebacterium diphtheriae		032-032.9, 034.0, 042-046.9, 050-072.9, 074-076, 077-078.2, 078.4-079.5, 079.8-079.9, 084-086.9, 088.9-089.9, 098.4, 098.6-098.7, 099, 099.4-099.9, 110-134.9, 136-139.9, 323-323.9, 381-383.9, 425.6, 460-465.9, 472-476.9, 522-523.9, 616-616.9, 647.4-647.6		
105	2	Non bacterial protozoal infections			A59-A59.9, B50-B64, P37.1, P37.3-P37.4	Non bacterial protozoal infections				084-086.9, 089-089.9, 647.4
106	2	Non bacterial protozoal infections			P37	Non bacterial protozoal infections				
107	2	Non bacterial fungal infections			B65-B94, B94.2-B94.8, H05.1, K93.1, U06-U06.9	Non bacterial fungal infections				088.9, 120-134.9, 136-137.9, 138.0-139, 139.1-139.9, 425.6
108	2	non bacterial fungal infections			B35-B36.9, P37.5	non bacterial fungal infections				110-119
109	2	non bacterial viral infections			A60-A63.8, B01-B20.0, B20.2-B34.1, B34.3-B34.9, B94.1, B97-B97.1, B97.3, B97.7-B97.8, J91.0, M89.6, O98.4-O98.7, P35-P35.9, Z21-Z21.0, Z22.5-Z22.6	non bacterial viral infections			042-046.9, 050-061.8, 070-072.9, 138, 647.5-647.6	
110	2	Other opportunistic infatious			A29, A42-A42.2, A42.8-A43.9, B37-B37.6, B37.8-B49.9, T81.4, T82.6-T82.7, T84.5-T84.7, A42.7, B37.7	Other opportunistic infatious				
112	2	Viral encephalitis			A80-A86.4, A88-B00.9, F07.1, G04-G05.8, G14-G14.6, G21.3	Viral encephalitis				062-069, 139.0, 323-323.9
113	2	Other locl infectious			A54.3, A54.5-A54.6, A71-A71.9, B94.0, N72-N72.0, N75-N77.8	Other locl infectious				076, 098.4, 098.6-098.7, 099, 099.4-099.9, 522-523.9, 616-616.9
114	2	Upper respiratory infections and otitis due to specified bacteria			A36-A36.9, I02.9, I02.0, I03.0	Upper respiratory infections and otitis due to specified bacteria				034.0
115	3	Upper respiratory infections and otitis due to corynebacterium diphtheriae			A36-A36.9	Upper respiratory infections and otitis due to corynebacterium diphtheriae				032-032.9
116	3	Upper respiratory infections and otitis due to group a strep			I02.9, I02.0, I03.0	Upper respiratory infections and otitis due to group a strep				
117	2	Upper respiratory infections and otitis due to unspecified bacteria			H60.2, H62-H62.3, H65-H68.0, H70-H70.9, H73.0, H75-H75.0	Upper respiratory infections and otitis due to unspecified bacteria				381-383.9
118	2	Upper respiratory infections and otitis due to unspecified bacteria			J36-J36.0, J39.0-J39.1, J85-J85.3, J86-J86.9	Upper respiratory infections and otitis due to unspecified bacteria				464.5, 465, 465.9, 472-474.9, 476-476.1
119	2					Upper respiratory infections and otitis due to Virus				074-075.9, 077-077.9, 078.8, 079.8-079.9
120	2	Upper respiratory infections and otitis due to unspecified pathogen			J00-J02, J02.8-J03, J03.8-J06.9, J31-J32.9, J35-J35.9, J37-J37.1	Upper respiratory infections and otitis due to unspecified pathogen				460-464.4, 464.8-464.9, 465.0-465.8, 475-475.9, 476.9
121	2					Urogenital infections due to virus				078-078.2, 078.4-078.7, 078.9-079.5
122	1	Meningitis and other bacterial central nervous system abases			A32.1, A39-A39.0, A87-A87.9, G00-G03.9, G06-G08.0, R83.5	Meningitis and other bacterial central nervous system abases				036-036.1, 047-049.9, 320-320.3, 320.5-322.9, 324-326.9
123	2	Meningitis due to specific bacteria			A32.1, A39-A39.0, G00.0-G00.3	Meningitis due to specific bacteria				036-036.1, 320.0-320.3, 320.5-320.8
124	3	Meningitis due to listeria			A32.1	Meningitis due to listeria				
125	3	Meningitis due to neisseria meningitidis			A39-A39.0	Meningitis due to neisseria meningitidis				036-036.1, 320.5-320.8
126	3	Meningitis due to haemophilus			G00.0	Meningitis due to haemophilus				320.0
127	3	Meningitis due to streptococcus pneumoniae			G00.1	Meningitis due to streptococcus pneumoniae				320.1
128	3	Meningitis due to group b strep			G00.2	Meningitis due to group b strep				320.2
129	3	Meningitis due to staphylococcus aureus			G00.3	Meningitis due to staphylococcus aureus				320.3
130	2	Meningitis due to virus			A87-A87.9, G03.0	Meningitis due to virus				047-049.9
131	2	Meningitis due to unspecified pathogen			G00, G00.8, G01-G02.8, G03.1-G03.9, G06-G08.0, R83.5	Meningitis due to unspecified pathogen				320, 320.9-321.8, 322.0-322.9, 324-326.9
132	2	Meningitis due to unspecified bacteria			G00.0, G03	Meningitis due to unspecified bacteria				322
133	1	Respiratory infectious			A37-A37.9, A48.1-A48.2, A70, B34.2, B97.2, B97.4-B97.6, J09-J22.9, J40-J42.6, P00.2, P22-P23.9, R84.5, U04.9, U07-U07.2	Respiratory infectious				033-033.9, 039.1, 073-073.9, 079.6-079.7, 466-469, 470.0, 480-491.9, 510-511.9, 513-513.9, 519.2, 519.8-519.9, 770.0
134	2	Lower respiratory infections due to specific bacteria			A37-A37.9, A48.1-A48.2, A70, J13-J14.0, J15.0-J15.7, J16.0, J20.0-J20.2, P23.1-P23.5	Lower respiratory infections due to specific bacteria				033-033.9, 039.1, 073-073.9, 466-469, 470.0, 481-481.9, 482.0-482.4, 483.0-483.1, 484.2-484.5
135	3	Lower respiratory infections due to bordetella pertussis			A37-A37.9	Lower respiratory infections due to bordetella pertussis				033-033.9, 484.3
136	3	Lower respiratory infections due to legionella spp			A48.1-A48.2	Lower respiratory infections due to legionella spp				
137	3					Lower respiratory infections due to actinomyces				039.1
138	3	Lower respiratory infections due to chlamydia spp			A70, J16.0, P23.1	Lower respiratory infections due to chlamydia spp				073-073.9, 483.1, 484.2
139	3	Lower respiratory infections due to streptococcus pneumoniae			J13-J13.9, J15.4, J20.2	Lower respiratory infections due to streptococcus pneumoniae				481-481.9, 482.3
140	3	Lower respiratory infections due to haemophilus influenzae			J14-J14.0, J20.1	Lower respiratory infections due to haemophilus influenzae				482.2
141	3	Lower respiratory infections due to klebsiella pneumoniae			J15.0	Lower respiratory infections due to klebsiella pneumoniae				482.0
142	3					Lower respiratory infections due to pseudomonas spp				482.1
143	3	Lower respiratory infections due to Pseudomonas aeruginosa			J15.1, P23.5	Lower respiratory infections due to Pseudomonas aeruginosa				
144	3	Lower respiratory infections due to staphylococcus aureus			J15.2, P23.2	Lower respiratory infections due to staphylococcus aureus				482.4
145	3	Lower respiratory infections due to group b strep			J15.3, P23.3	Lower respiratory infections due to group b strep				
146	3	Lower respiratory infections due to escherichia coli			J15.5, P23.4	Lower respiratory infections due to escherichia coli				
147	3	Lower respiratory infections due to mycoplasma			J15.7, J20.0	Lower respiratory infections due to mycoplasma				483.0
148	3					Lower respiratory infections due to francisella-tularensis				484.4
149	3					Lower respiratory infections due to bacillus-anthraxis				484.5
150	2	Lower respiratory infections due to unspecified Bacteria			J15, J15.8-J16, J16.8-J17, J17.1, J18, J20, J20.9-J21, J21.8, J22.9, J40-J42.6, P23.6-P23.9, R84.5	Lower respiratory infections due to unspecified Bacteria				482, 482.8-483, 483.8-484, 484.8-486.9, 490-491.9
151	3	Lower respiratory infections due to other gram negative bacteria			J15.6	Lower respiratory infections due to other gram negative bacteria				
152	2	Lower respiratory infections due to virus			B34.2, B97.2, B97.4-B97.6, J09-J12.9, J17.0, J17.2-J17.8, J20.3-J20.8, J21.0-J21.1, P23.0, U04.9, U07-U07.2	Lower respiratory infections due to virus				079.6-079.7, 480-480.9, 484.0-484.1, 487-489
153	3	Lower respiratory infections due to coronaviruses			B34.2, B97.2, J12.8	Lower respiratory infections due to coronaviruses				
154	3	Lower respiratory infections due to syncytial virus (rsv)			B97.4, J12.1, J20.5, J21.0	Lower respiratory infections due to syncytial virus (rsv)				
155	3	Lower respiratory infections due to influenza viruses			J09-J11.8	Lower respiratory infections due to influenza viruses				
156	3	Lower respiratory infections due to other virus			J12, J12.3, J12.9, J17.0, J17.2-J17.8, J20.3, J20.7-J20.8, J21.1	Lower respiratory infections due to other virus				
157	3	Lower respiratory infections due to adenoviruses			J12.0	Lower respiratory infections due to adenoviruses				
158	3	Lower respiratory infections due to parainfluenza viruses			J12.2, J20.4	Lower respiratory infections due to parainfluenza viruses				
159	3	Lower respiratory infections due to rhinoviruses			J20.6	Lower respiratory infections due to rhinoviruses				
160	3					Lower respiratory infections due to fungi				484.6-484.7
161	3					Lung abscess and pyothorax due to unspecified pathogen				510-511.9, 513-513.9
162	2	Lower respiratory infections due to unspecified pathogen			P00.2, P22-P23	Lower respiratory infections due to unspecified pathogen				519.2, 519.8-519.9, 770.0
163	1	Skin Bacterial Infectious			A46-A46.0, A48.0, A66-A67.9, H05.0, H09.1, I96-I96.9, K61-K61.4, L00-L08.9, L20.3, L88-L89.9, L97-L98.1, L98.4, M72.5-M72.6, R02-R02.9	Skin Bacterial Infectious				035-035.9, 039-039.0, 039.3-039.9, 102-104.9, 376.0-376.1, 457.1-457.9, 680-689, 707-707.9, 785.4
164	2	Bacterial infections of skin and subcutaneous system due to specific bacteria			A46-A46.0, A48.0, A66-A67.9, L00	Bacterial infections of skin and subcutaneous system due to specific bacteria				035-035.9, 039-039.0, 039.3-039.9, 102-104.9
165	3	Bacterial infections of skin and subcutaneous system due to group a strep			A46-A46.0	Bacterial infections of skin and subcutaneous system due to group a strep				035-035.9
166	3	Bacterial infections of skin and subcutaneous system due to clostridium perfringens			A48.0	Bacterial infections of skin and subcutaneous system due to clostridium perfringens				
167	3	Bacterial infections of skin and subcutaneous system due to treponema pallidum			A66-A66.9	Bacterial infections of skin and subcutaneous system due to treponema pallidum				102-102.9, 104-104.9
168	3	Bacterial infections of skin and subcutaneous system due to treponema carateum			A67-A67.9	Bacterial infections of skin and subcutaneous system due to treponema carateum				
169	3	Bacterial infections of skin and subcutaneous system due to staphylococcus aureus			L00	Bacterial infections of skin and subcutaneous system due to staphylococcus aureus				
170	3					Bacterial infections of skin and subcutaneous system due to yersinia pestis				103-103.9
171	3					Bacterial infections of skin and subcutaneous system due to other specific bacteria				039.0
172	2	Bacterial infections of skin and subcutaneous system due to unspecified bacteria			H05.0, H89.1, I96-I96.9, K61-K61.4, L01-L08.9, L30.3, L88-L89.9, L97-L98.1, L98.4, M72.5-M72.6, R02-R02.9	Bacterial infections of skin and subcutaneous system due to unspecified bacteria				376.0-376.1, 457.1-457.9, 680-689, 707-707.9, 785.4
173	1	chlamydia and gonorrhoea			A54-A54.2, A54.8-A56.8	chlamydia and gonorrhoea				098-098.3, 098.8-098.9, 099.1, 099.3
174	1	infections of bone, joints and related part			A54.4, M00-M01.8, M46.2-M46.5, M65.0-M65.1, M71.0-M71.1, M73.0-M73.8, M86-M86.9	infections of bone, joints and related part				098.5, 711-711.9, 730-730.3, 730.7-730.9
175	2	infections of bone, joints and related part due to specific bacteria			A54.4, M00-M00.2	infections of bone, joints and related part due to specific bacteria				098.5
176	3	infections of bone, joints and related part due to neisseria gonorrhoea			A54.4	infections of bone, joints and related part due to neisseria gonorrhoea				098.5
177	3	infections of bone, joints and related part due to staphylococcus aureus			M00-M00.0	infections of bone, joints and related part due to staphylococcus aureus				
178	3	infections of bone, joints and related part due to streptococcus pneumoniae			M00.1	infections of bone, joints and related part due to streptococcus pneumoniae				
179	3	infections of bone, joints and related part due to group a strep			M00.2	infections of bone, joints and related part due to group a strep				
180	2	infections of bone, joints and related part due to unspecified bacteria			M00.8-M01.8, M46.2-M46.5, M65.0-M65.1, M71.0-M71.1, M73.0-M73.8, M86-M86.9	infections of bone, joints and related part due to unspecified bacteria				711-711.9, 730-730.3, 730.7-730.9
181	1	Urinary tract infections and nephritis			A57-A58, A64-A64.0, N10-N12.9, N13.4, N15, N15.1-N16.8, N30-N30.9, N34-N34.3, N39.0-N39.2, N41-N41.9, N45-N45.9, N49-N49.9, O23.0-O23.5	Urinary tract infections and nephritis				099.0, 099.2, 590-590.9, 595-595.9, 597-597.9, 599.0, 601-601.9, 604-604.9, 647.2
182	2	Urinary tract infections and nephritis due to specific bacteria			A57-A58	Urinary tract infections and nephritis due to specific bacteria				099.0, 099.2
183	3	Urinary tract infections and nephritis due to haemophilus ducreyi			A57-A57.0	Urinary tract infections and nephritis due to haemophilus ducreyi				099.0
184	3	Urinary tract infections and nephritis due to klebsiella granulomatis			A58	Urinary tract infections and nephritis due to klebsiella granulomatis				099.2
185	2	Urinary tract infections and nephritis due to unspecified bacteria			A64-A64.0, N10-N12.9, N13.4, N15, N15.1-N16.8, N30-N30.9, N34-N34.3, N39.0-N39.2, N41-N41.9, N45-N45.9, N49-N49.9, O23.0-O23.5	Urinary tract infections and nephritis due to unspecified bacteria				590-590.9, 595-595.9, 597-597.9, 599.0, 601-601.9, 604-604.9, 647.2
186	1	Endocarditis and other cardiac infections			I00, I01-I02.0, I00, I01, I33-I33.9, I38-I41.9	Endocarditis and other cardiac infections				390-392.9, 420-424.9, 457
187	2	Endocarditis due to specific bacteria			I00, I01-I02.0	Endocarditis due to specific bacteria				390-392.9, 421-421.9
188	3	Endocarditis due to group a strep			I00, I01-I02.0	Endocarditis due to group a strep				390-392.9
189	2	Endocarditis due to unspecified bacteria			I30, I30.1, I33-I33.9, I38-I41.9	Endocarditis due to unspecified bacteria				420-420.9, 422-424.9, 457
190	1	Peritoneal and intra abdomen infections			K35-K37.9, K38.3-K38.9, K40-K42.0, K44-K46.9, K50-K52, K52.8-K52.9, K55-K57.9, K63.0-K63.1, K65-K65.9, K67-K67.2, K67.8-K69, K75.0-K75.1, K75.3, K76.3, K77.0, K80-K83.9, M09.1, N70-N71.9, N73-N74.0, N74.3-N74.8, N98.0, O98.2-O98.3, O98.8-O98.9, R65.0, R85.5, R86.5, R87.5, O03.0, O41.1, O75.3, O98	Peritoneal and intra abdomen infections			039.2, 540-542.9, 550-551.1, 551.3-552.1, 552.3-553.1, 553.3-558.0, 560-560.3, 560.8-560.9, 562-562.1, 567-567.9, 569.5, 572.0-572.1, 574-576.9, 614-615.9, 647.0-647.1	
191	2	Peritoneal and intra abdomen infections due to specific bacteria			K67.0-K67.2	Peritoneal and intra abdomen infections due to specific bacteria				039.2
192	3	Peritoneal and intra abdomen infections due to chlamydia spp			K67.0	Peritoneal and intra abdomen infections due to chlamydia spp				
193	3	Peritoneal and intra abdomen infections due to neisseria gonorrhoea			K67.1	Peritoneal and intra abdomen infections due to neisseria gonorrhoea				647.1
194	3					Peritoneal and intra abdomen infections due to actinomyces				039.2
195	3	Peritoneal and intra abdomen infections due to treponema pallidum			K67.2	Peritoneal and intra abdomen infections due to treponema pallidum				
196	2	Peritoneal and intra abdomen infections due to due to specific bacteria			N74.3-N74.4, O98.2	Peritoneal and intra abdomen infections due to due to specific bacteria				647.1

Table S3. List of infectious syndromes mapped to International Classification of Diseases (ICD) codes

Infectious syndrome name and level				Infectious syndrome name and ICD code	Infectious syndrome name and level				Infectious syndrome name and ICD code			
Level	L0	L1	L2	L3	ICD Codes for all level	L0	L1	L2	L3	ICD Codes for all level		
197	2				<p>K35-K37.9, K38.3-K38.9, K40-K42.9, K44-K46.9, K50-K52, K52.8-K52.9, K55-K57.9, K61.0-K63.1, K65-K65.9, K67, K67.8-K69, K75.0-K75.1, K75.3, K76.3, K77.0, K80-K83.9, M89.1, N70-N71.9, N73-N74.0, N74.8, N98.0, O98.3, O98.8-O98.9, R05.0, R85.5, R86.5, R87.5, R87.5, O03.0, O41.1, O75.3, O98</p> <p>C00-D64.9, D66-D69.4, D69.6-D70.2, D70.4-D89.2, D89.8-E87.1, E88-F02.0, F02.2-F02.3, F02.8-F07.0, F07.2-F99.0, G09-G13.8, G15-G21.2, G21.4-G93.3, G93.5-H05, H05.2-H60.1, H60.3-H61.9, H62.4-H62.8, H68.1-H69.9, H71-H73, H73.1-H74.9, H75.8-H99, I00.0, I05-I29.9, I30.0, I30.8-I32.8, I34-I37.9, I42-I45.9, I47-I75.8, I77-I79.8, K83-K87, K87.1, K89.4, K93.8-K95.0, P7, P98, P98.2-H95.9, R07, R08, T23-T30.9, U33-U34.9, U38, U39, U39.2, U39.9, U42.9-U79, J81-J84.9, J85.9, J87-J91, J91.8-J95.1, J95.4-J95.9, J97-K03.9, K05.6-K34, K38-K38.2, K39, K43-K43.9, K47-K49, K52.0, K53-K54, K58-K60.5, K62-K63, K63.2-K64.9, K66-K66.9, K70-K71.9, K75-K75.7, K75.2, K75.4-K76.2, K76.4-K77, K77.8-K79, K84-K93, K93.8-K99, L09-L20.2, L20.4-L27.9, L90-L96, L98.5-L99.8, M02-M09.0, M09.2-M46.1, M46.8-M49, M49.2-M65, M65.2-M71, M71.2-M72.4, M72.8-M73, M74-M85.9, M87-M89.5, M89.7-M99.9, N02-N09, N13-N13.5, N13.7-N14.4, N15.0, N18-N29.8, N31-N33.8, N35-N39, K93.3-N60.9, N62-N41.8, N66-N83.9, N85-N99, N79-N98, N98.1-O05, O01.1-O01.4, O01.6-O04, O41.1-O44, O54.6-O05, O05.1-O05.4, O05.6-O06, O06.1-O06.4, O06.6-O07, O07.1-O07.4, O07.6-O08, O08.1-O22.9, O24-O41.0, O41.8-O75.2, O75.4-O84.9, O87-O88.2, O88.8-O90.9, O92-O97.9, O99-P00.1, P00.3-P21.9, P24-P34.2, P40-P01.2, R03-R09.1, R09.3-R19.9, R19.8-R40, R41-R54.9, R56-R56.9, R58-R05, R65.1, R66-R83.4, R83.6-R84.4, R84.6-R85.4, R85.6-R86.4, R86.6-R87.4, R87.6-T80.1, T80.3-T81.3, T81.5-T82.5, T82.8-T83.4, T83.7-T84.4, T84.8-T85.6, T85.8-T87.3, T87.5-T88, T88.1-U03, U05, U08-U81, U90-Y61.9, Y63-Y94, Y96-Z03, Z01.1-Z11.0, Z11.2-Z15.8, Z17-Z20.9, Z23-Z80, D85-D85.9, D89.3, D90.3, E87.2-E87.9, F02.1, F02.4, G93.4, I46-I46.9, I80-I82.9, I87.0, I95.1-I95.9, I90-I90.9, J95.2-J95.3, J96-J96.9, K72-K72.9, L98.2-L98.3, N00-N01.9, N17-N17.9, R09.2, R40.0-R40.4, R55-R55.0, R57-R57.9, T78-T80.1, T80.3-T81.3, T81.5-T82.5, T82.8-T83.4, T83.7-T84.4, T84.8-T85.6, T85.8-T87.3, T87.5-T88, T88.1-T89.3, Y40-Y61.9, Y63-Y84.9, Y88-Y88.3, S00-T69.9</p>					<p>Peritoneal and intra abdomen infections due to unspecified Bacteria</p>	<p>Peritoneal and intra abdomen infections due to unspecified Bacteria</p>	<p>540-542.9, 550-551.1, 551.3-552.1, 552.3-553.1, 553.3-558.0, 560-560.3, 560.8-560.9, 562-562.1, 567-567.9, 569.5, 572.0-572.1, 574-576.9, 614-615.9, 647.0</p>
199	0				<p>No Sepsis, No infectious diseases and unspecified</p>					<p>No Sepsis, No infectious diseases and unspecified</p>	<p>000-000.9, 019-019.9, 105-109.9, 140-275.5, 277-286.5, 286.7-292.9, 294.0-319.9, 327-346.9, 348-379, 379.2-380.9, 384-389.9, 391-419.9, 425-425.5, 425.7-427.4, 427.6-450, 454-456.9, 459-459.9, 470, 470.9-471.9, 477-479, 492-509, 512-512.9, 514-519.0, 520-521.9, 524-539.9, 543-549, 551.2, 552.2, 553.2, 558.1, 559-559.0, 560.4-560.7, 561, 562.2-566.9, 568-569.4, 569.6-572, 572.2-573.9, 577-583.9, 585-589.9, 591-594.9, 596-596.9, 598-599, 599.1-600.9, 602-603.9, 605-613, 617-634, 634.1-634.9, 635.1-635.4, 635.6-636, 636.1-636.4, 636.6-636.9, 637.1-637.4, 637.6-638, 638.1-639, 639.1-646.9, 648-658.3, 658.8-659.2, 659.4-660.0, 669.2-669.9, 671-671.1, 671.8-671.9, 673-674.9, 676-679.1, 680-706.9, 708-710.9, 712-729.9, 731, 768.7, 769.0-770, 770.1-770.9, 772-779.9, 780.4-785.3, 785.6-790.6, 790.8-797.9, 799.3-999.8, 996-996.8, 996.7-E871.9, E873-E999.1, 800-999.8, E000-E871.9, E873-E930, E950-E999.1, 996-996.5, 996.7-999.9, E930.0-E949.9, I35-I35.9, 275.8-276.9, 286.6, 293-294, 347-347.9, 427.5, 451-453.9, 457.0, 458-458.9, 519.1, 519.3-519.4, 584-584.9, 635.5, 636.5, 637.5, 669.1, 768.9-769, 780-780.3, 785.5, 798-799.2, 135-135.9, 275.8-276.9, 286.6, 293-294, 347-347.9, 427.5, 451, 453.9, 457.0, 458-458.9, 519.1, 519.3-519.4, 584-584.9, 635.5, 636.5, 637.5, 669.1, 768.9-769, 780-780.3, 785.5, 798-799.2</p>	

**Table S4. Summary of case fatality ratio data**

Pathogen	Hospital	Literature	Microbiology	Total
<i>Acinetobacter baumannii</i>			287390	287390
Adenovirus	3904			3904
<i>Aeromonas</i> spp.			280	280
<i>Campylobacter</i> spp.	24330		62	24392
<i>Chlamydia</i> spp.	14362			14362
<i>Citrobacter</i> spp.			156376	156376
<i>Clostridium difficile</i>	415011		7171	422182
<i>Cryptosporidium</i>	2010			2010
<i>Entamoeba histolytica</i>	9438			9438
<i>Enterobacter</i> spp.			730786	730786
<i>Enterococcus faecalis</i>			177234	177234
<i>Enterococcus faecium</i>			242584	242584
Other enterococci	6771		15062	21833
<i>Escherichia coli</i>	430064		2393259	2823323
Fungi	702794		6052	708846
Group A <i>Streptococcus</i>	280314		80761	361075
Group B <i>Streptococcus</i>	165579	2726	172333	340638
<i>Haemophilus influenzae</i>	56781	2134	197294	256209
<i>Klebsiella pneumoniae</i>	52983		1212459	1265442
Other <i>Klebsiella</i> species	39855		140357	180212
<i>Legionella</i> spp.	1396		54	1450
<i>Listeria monocytogenes</i>	5502		41	5543
<i>Morganella</i> spp.			87403	87403
<i>Mycobacterium tuberculosis</i>	102402		3032	105434
<i>Mycoplasma</i> spp.	53762			53762
<i>Neisseria gonorrhoeae</i>	11483		5540	17023
<i>Neisseria meningitidis</i>	9505	20952	110	30567
Non-typhoidal <i>Salmonella</i>	6194		172130	178324
Norovirus	8266			8266
Other pathogens	920212		357838	1278050
Polybacterial			92	92
<i>Proteus</i> spp.	41032		405684	446716
<i>Providencia</i> spp.			47268	47268
<i>Pseudomonas aeruginosa</i>	21773		1010873	1032646
Rotavirus	22818			22818
<i>Salmonella</i> Paratyphi	818		364	1182
<i>Salmonella</i> Typhi	5010		5088	10098
<i>Serratia</i> spp.	6497		260684	267181
<i>Shigella</i> spp.	4273		11361	15634
<i>Staphylococcus aureus</i>	932990		2545845	3478835
<i>Streptococcus pneumoniae</i>	214761	27095	441302	683158
<i>Vibrio cholerae</i>	740		6	746
Viruses	3903630		2	3903632
<b>TOTAL</b>	<b>8477260</b>	<b>52907</b>	<b>11174177</b>	<b>19704344</b>



Table S5. Case fatality ratio modelling framework by pathogen and syndrome

BSI = bloodstream infections, CNS = meningitis and other bacterial central nervous system infections, LRI+ = lower respiratory infections and all related infections in the thorax. Intra-abdominal = peritoneal and intra-abdominal infections, Skin = bacterial infections of the skin and subcutaneous systems, UTI = urinary tract infections and pyelonephritis.

	BSI (neonatal)	BSI (post-neonatal and older)	CNS	Diarrhoea	LRI+ (community-acquired)	LRI+ (hospital-acquired)	Intra-abdominal	Skin	UTI (community-acquired)	UTI (hospital-acquired)
<i>Acinetobacter baumannii</i>	intercept	interaction	not explicitly modelled	not explicitly modelled	intercept	intercept	not explicitly modelled	intercept	intercept	intercept
<i>Campylobacter</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Chlamydia</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Citrobacter</i> spp.	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept
<i>Clostridium difficile</i>	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Cryptosporidium</i>	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Entamoeba histolytica</i>	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Enterobacter</i> spp.	intercept	interaction	not explicitly modelled	not explicitly modelled	intercept	intercept	intercept	intercept	intercept	intercept
<i>Enterococcus faecalis</i>	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Enterococcus faecium</i>	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept	intercept	intercept
Other Enterococci	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled
<i>Escherichia coli</i>	intercept	interaction	intercept	intercept	intercept	intercept	intercept	intercept	intercept	intercept
Fungus	intercept	interaction	not explicitly modelled	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
Group A <i>Streptococcus</i>	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled
Group B <i>Streptococcus</i>	intercept	interaction	intercept	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Haemophilus influenzae</i>	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Klebsiella pneumoniae</i>	intercept	interaction	intercept	not explicitly modelled	intercept	intercept	intercept	intercept	intercept	intercept
<i>Legionella</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Listeria monocytogenes</i>	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Moraxella</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Morganella</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept
<i>Mycoplasma</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Neisseria meningitidis</i>	intercept	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
Polybacterial	intercept	interaction	not explicitly modelled	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Proteus</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept	intercept
<i>Providencia</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept
<i>Pseudomonas aeruginosa</i>	not explicitly modelled	interaction	not explicitly modelled	not explicitly modelled	intercept	intercept	intercept	intercept	intercept	intercept
<i>Salmonella</i> Typhi	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
Non-typhoidal <i>Salmonella</i>	not explicitly modelled	intercept	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Serratia</i> spp.	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	intercept
<i>Shigella</i> spp.	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Staphylococcus aureus</i>	intercept	interaction	intercept	intercept	intercept	intercept	intercept	intercept	intercept	intercept
<i>Streptococcus pneumoniae</i>	intercept	intercept	interaction	not explicitly modelled	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
<i>Vibrio cholerae</i>	not explicitly modelled	not explicitly modelled	not explicitly modelled	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled
Virus	not explicitly modelled	not explicitly modelled	interaction	intercept	intercept	intercept	not explicitly modelled	not explicitly modelled	not explicitly modelled	not explicitly modelled

<b>Table S6. Summary of pathogen distribution data</b>							
<b>Pathogen</b>	<b>CHAMPS</b>	<b>Hospital</b>	<b>Linkage</b>	<b>Literature</b>	<b>MCOD</b>	<b>Microbiology</b>	<b>Total</b>
<i>Acinetobacter baumannii</i>	162			2449		95614	98225
<i>Chlamydia</i> spp.		14362	7	481	730	1	15581
<i>Citrobacter</i> spp.				3330		64006	67336
<i>Enterobacter</i> spp.	9			9357		263748	273114
<i>Enterococcus faecalis</i>	13			13858		338708	352579
<i>Enterococcus faecium</i>	11			1464		411508	412983
Other enterococci	2	6771	44	12749	1	7351	26918
<i>Escherichia coli</i>	79	430064	482	205847	4628	4964020	5605120
Fungi	41	702794	334	8276	92562	6405	810412
Group A <i>Streptococcus</i>	9	280314	258	1947	48148	34637	365313
Group B <i>Streptococcus</i>	16	165579	203	8656	31183	8898	214535
<i>Haemophilus influenzae</i>	42	56781	310	5900	7831	25840	96704
<i>Klebsiella pneumoniae</i>	259	52983	144	22780	19126	1369389	1464681
Other <i>Klebsiella</i> species		39855	116	17240	28	13800	71039
<i>Legionella</i> spp.		1396	35	112	3726	54	5323
<i>Listeria monocytogenes</i>	5	5502	38	221	10416	41	16223
<i>Morganella</i> spp.				1480		63705	65185
<i>Mycobacterium tuberculosis</i>	6	102402	126	945	661806	3063	768348
<i>Mycoplasma</i> spp.		53762	56	1061	2722		57601
<i>Neisseria gonorrhoeae</i>		11483	1	115	220	5162	16981
<i>Neisseria meningitidis</i>	3	9505	107	10921	14304	5719	40559
Non-typhoidal <i>Salmonella</i>	9	6194	17	472	2002	34478	43172
Other bacteria	130	920212	1202	49723	299761	143107	1414135
Polybacterial	1			4565		115	4681
<i>Proteus</i> spp.	2	41032	52	19493	180	328345	389104
<i>Providencia</i> spp.				592		35144	35736
<i>Pseudomonas aeruginosa</i>	26	21773	541	17358	25725	819446	884869
<i>Salmonella</i> Paratyphi	1	818			29	365	1213
<i>Salmonella</i> Typhi		5010	1	4	573	10892	16480
<i>Serratia</i> spp.		6497	3	1360		96314	104174
<i>Staphylococcus aureus</i>	57	932990	1936	19521	227064	3109956	4291524
<i>Streptococcus pneumoniae</i>	100	214761	909	11044	130684	623928	981426
Viruses	164	3903630	2779	46049	2064708	4	6017334
<b>TOTAL</b>	<b>1147</b>	<b>7986470</b>	<b>9701</b>	<b>499370</b>	<b>3648157</b>	<b>12883763</b>	<b>25028608</b>

**Table S7. Summary of prevalence of resistance data**

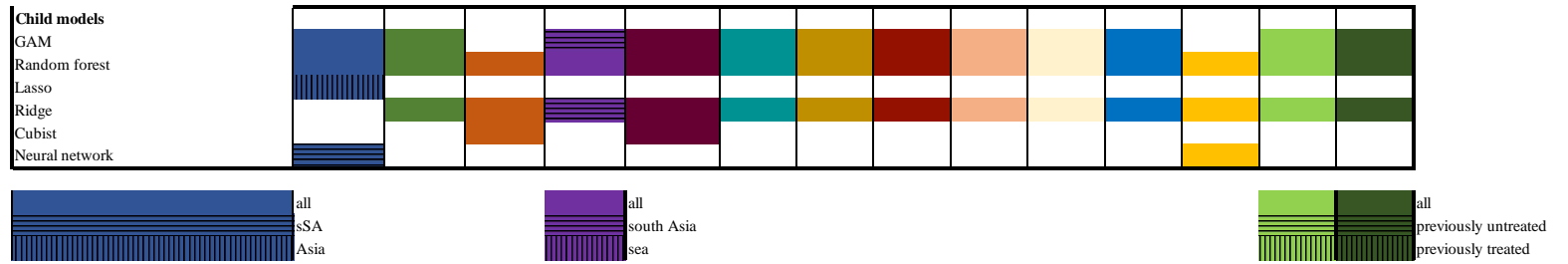
Pathogen	Antibiotic Class	Literature	Microbiology	Surveillance report	Total
<i>Acinetobacter baumannii</i>	Aminoglycosides		52393		52393
<i>Acinetobacter baumannii</i>	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		15723		15723
<i>Acinetobacter baumannii</i>	Beta-lactam/Beta-lactamase inhibitors		20205		20205
<i>Acinetobacter baumannii</i>	Carbapenem		43437		43437
<i>Acinetobacter baumannii</i>	Fluoroquinolones		38766		38766
<i>Acinetobacter baumannii</i>	Fourth-generation cephalosporins		26953		26953
<i>Acinetobacter baumannii</i>	Third-generation cephalosporins		49034		49034
<i>Citrobacter</i> spp.	Aminoglycosides		194936	4996	199932
<i>Citrobacter</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		229701	2931	232632
<i>Citrobacter</i> spp.	Carbapenem		273016	6907	279923
<i>Citrobacter</i> spp.	Fluoroquinolones		240317	5862	246179
<i>Citrobacter</i> spp.	Fourth-generation cephalosporins		126201	2931	129132
<i>Citrobacter</i> spp.	Third-generation cephalosporins		353349	8793	362142
<i>Enterobacter</i> spp.	Aminoglycosides		1050287	6737	1057024
<i>Enterobacter</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		766210	6072	772282
<i>Enterobacter</i> spp.	Carbapenem		891579	14916	906495
<i>Enterobacter</i> spp.	Fluoroquinolones		785309	12809	798118
<i>Enterobacter</i> spp.	Fourth-generation cephalosporins		417357		417357
<i>Enterobacter</i> spp.	Trimethoprim-Sulfamethoxazole		437597		437597
<i>Enterococcus faecalis</i>	Fluoroquinolones		637781		637781
<i>Enterococcus faecalis</i>	Vancomycin		846045		846045
<i>Enterococcus faecium</i>	Fluoroquinolones		193447		193447
<i>Enterococcus faecium</i>	Vancomycin		353515		353515
Other Enterococci	Fluoroquinolones		801		801
Other Enterococci	Vancomycin		3287		3287
<i>Escherichia coli</i>	Aminoglycosides		10524486	13012	10537498
<i>Escherichia coli</i>	Aminopenicillin		5162728	3582	5166310
<i>Escherichia coli</i>	Beta-lactam/Beta-lactamase inhibitors		4547346	3582	4550928
<i>Escherichia coli</i>	Carbapenem		8443688	224	8443912
<i>Escherichia coli</i>	Fluoroquinolones	946267	6505222	2398783	9850272
<i>Escherichia coli</i>	Third-generation cephalosporins	433884	2043110	2900403	5377397
<i>Escherichia coli</i>	Trimethoprim-Sulfamethoxazole		3459423	7164	3466587
Group A <i>Streptococcus</i>	Macrolide		10915	7933	18848
Group B <i>Streptococcus</i>	Fluoroquinolones		20050		20050
Group B <i>Streptococcus</i>	Macrolide		34507		34507
Group B <i>Streptococcus</i>	Penicillin		20424		20424
<i>Haemophilus influenzae</i>	Aminopenicillin		297932	3128	301060
<i>Haemophilus influenzae</i>	Third-generation cephalosporins		476427	2900	479327
<i>Klebsiella pneumoniae</i>	Aminoglycosides		3453036		3453036
<i>Klebsiella pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors		1556408		1556408
<i>Klebsiella pneumoniae</i>	Carbapenem	268169	873691	1182391	2324251
<i>Klebsiella pneumoniae</i>	Fluoroquinolones		2551051		2551051
<i>Klebsiella pneumoniae</i>	Third-generation cephalosporins	245676	851217	1059474	2156367
<i>Klebsiella pneumoniae</i>	Trimethoprim-Sulfamethoxazole		1225771		1225771
<i>Morganella</i> spp.	Fluoroquinolones		48697	3054	51751
<i>Morganella</i> spp.	Fourth-generation cephalosporins		23231	1527	24758
<i>Morganella</i> spp.	Third-generation cephalosporins		49780	4581	54361
<i>Mycobacterium tuberculosis</i>	Extensive drug resistance		15210		15210
<i>Mycobacterium tuberculosis</i>	Isoniazid mono-resistance		1980958	81360	2062318
<i>Mycobacterium tuberculosis</i>	Multi-drug resistance		14028		14028
<i>Mycobacterium tuberculosis</i>	Rifampicin mono-resistance		2846360	54169	2900529
<i>Neisseria gonorrhoeae</i>	Fluoroquinolones		27356		27356
<i>Neisseria gonorrhoeae</i>	Third-generation cephalosporins		49779		49779
Non-typhoidal <i>Salmonella</i>	Fluoroquinolones	6660	14		6674
<i>Proteus</i> spp.	Aminoglycosides		553876	3816	557692
<i>Proteus</i> spp.	Aminopenicillin		334346		334346
<i>Proteus</i> spp.	Fluoroquinolones		538122	7632	545754
<i>Proteus</i> spp.	Third-generation cephalosporins		656754	11448	668202
<i>Proteus</i> spp.	Trimethoprim-Sulfamethoxazole		171233		171233
<i>Pseudomonas aeruginosa</i>	Aminoglycosides		2801891		2801891
<i>Pseudomonas aeruginosa</i>	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		2029407		2029407
<i>Pseudomonas aeruginosa</i>	Carbapenem		2311724		2311724
<i>Pseudomonas aeruginosa</i>	Fluoroquinolones		2331732		2331732
<i>Pseudomonas aeruginosa</i>	Fourth-generation cephalosporins		1138828		1138828
<i>Pseudomonas aeruginosa</i>	Third-generation cephalosporins		1315517		1315517
<i>Salmonella</i> Paratyphi	Fluoroquinolones	11123	6		11129
<i>Salmonella</i> Paratyphi	Multi-drug resistance	31383	12	237	31632
<i>Salmonella</i> Typhi	Fluoroquinolones	41718	162	1528	43408
<i>Salmonella</i> Typhi	Multi-drug resistance	113258	3608	6593	123459
<i>Serratia</i> spp.	Aminoglycosides		261873	1652	263525
<i>Serratia</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		302571	1652	304223
<i>Serratia</i> spp.	Carbapenem		355742	3986	359728

<i>Serratia</i> spp.	Fluoroquinolones		322402	3304	325706
<i>Serratia</i> spp.	Fourth-generation cephalosporins		167538	1652	169190
<i>Serratia</i> spp.	Third-generation cephalosporins		419093	4956	424049
<i>Shigella</i> spp.	Fluoroquinolones	72148	13911	53514	139573
<i>Staphylococcus aureus</i>	Fluoroquinolones		4009367		4009367
<i>Staphylococcus aureus</i>	Macrolide		5963254		5963254
<i>Staphylococcus aureus</i>	Methicillin	178620	1893838	2471297	4543755
<i>Staphylococcus aureus</i>	Trimethoprim-Sulfamethoxazole		2645319		2645319
<i>Staphylococcus aureus</i>	Vancomycin		2859122		2859122
<i>Streptococcus pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors		5968		5968
<i>Streptococcus pneumoniae</i>	Carbapenem		298257		298257
<i>Streptococcus pneumoniae</i>	Fluoroquinolones		527610		527610
<i>Streptococcus pneumoniae</i>	Macrolide		760157	2687	762844
<i>Streptococcus pneumoniae</i>	Penicillin	60129	259584	314432	634145
<i>Streptococcus pneumoniae</i>	Third-generation cephalosporins		787948	2669	790617
<i>Streptococcus pneumoniae</i>	Trimethoprim-Sulfamethoxazole		31189	2684	33873
TOTAL		2409035	101202814	10695960	114307809



Table S8. Covariates for each core pathogen–drug combination (excluding 3GC-resistant *N. gonorrhoeae*)

Covariate name	MDR <i>S. Typhi</i>	FQ <i>S. Typhi</i>	MDR <i>S. Paratyphi A</i>	FQ <i>S. Paratyphi A</i>	FQ INTS	FQ <i>Shigella spp.</i>	FQ <i>E. coli</i>	3GC <i>E. coli</i>	3GC <i>K. pneumoniae</i>	Carbapenems <i>K. pneumoniae</i>	Penicillin <i>S. pneumoniae</i>	Methicillin <i>S. pneumoniae</i>	Mono-Isoniazid TB	Mono-Rifampicin TB
Alcohol use <sup>23</sup>														
Antenatal care <sup>1</sup>														
Antibiotic usage proportion <sup>3</sup>														
Antimalarial effectiveness <sup>46</sup>														
BCG coverage <sup>33</sup>														
Childhood stunting <sup>47</sup>														
Corruption Index <sup>48</sup>														
Diabetes <sup>1</sup>														
DPT coverage <sup>33</sup>														
DDD per 1000 <sup>3</sup>														
Fraction of OOP health expenditure <sup>49</sup>														
Handwashing <sup>23</sup>														
Healthcare Access and Quality Index <sup>50</sup>														
HIB coverage <sup>33</sup>														
HIV death rate (adults) <sup>1</sup>														
HIV incidence <sup>1</sup>														
HIV prevalence per capita <sup>1</sup>														
Hospital beds per 1000 population <sup>1</sup>														
Improved sanitation <sup>23</sup>														
Improved water <sup>23</sup>														
J01C antibiotic consumption <sup>3</sup>														
J01D antibiotic consumption <sup>3</sup>														
J01G antibiotic consumption <sup>3</sup>														
J01M antibiotic consumption <sup>3</sup>														
Lag-distributed income <sup>12</sup>														
Latitude														
Mean temperature <sup>1*</sup>														
Maternal education <sup>51</sup>														
Oral rehydration therapy <sup>1*</sup>														
Outdoor air pollution <sup>52</sup>														
Paratyphoid incidence <sup>1</sup>														
PCV3 coverage <sup>33</sup>														
Physicians per capita <sup>1</sup>														
Pharmacists per capita <sup>53</sup>														
Pigs per capita <sup>1*</sup>														
Population density <sup>1*</sup>														
Proportion of underweight adults <sup>1</sup>														
Prop of pop in agricultural activities <sup>23</sup>														
Quality assessment (typhoid)														
Skilled birth attendant coverage <sup>54</sup>														
Smoking prevalence <sup>23</sup>														
Socio-demographic Index <sup>12</sup>														
Total antibiotic consumption <sup>3</sup>														
Total fertility rate <sup>12</sup>														
TB prevalence <sup>1</sup>														
TB strain transmission risk <sup>1</sup>														
Typhoid incidence <sup>1</sup>														



\*See Appendix Section 7.4 for more details

**Table S9. Summary of relative risk data**

Pathogen	Antibiotic class	Literature	Microbiology	Total
<i>Acinetobacter baumannii</i>	Aminoglycosides		26547	26547
<i>Acinetobacter baumannii</i>	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		8594	8594
<i>Acinetobacter baumannii</i>	Beta-lactam/Beta-lactamase inhibitors		10107	10107
<i>Acinetobacter baumannii</i>	Carbapenem		33071	33071
<i>Acinetobacter baumannii</i>	Fluoroquinolones		21091	21091
<i>Acinetobacter baumannii</i>	Fourth-generation cephalosporins		17670	17670
<i>Acinetobacter baumannii</i>	Third-generation cephalosporins		31653	31653
<i>Citrobacter</i> spp.	Aminoglycosides		27196	27196
<i>Citrobacter</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		9695	9695
<i>Citrobacter</i> spp.	Carbapenem		18268	18268
<i>Citrobacter</i> spp.	Fluoroquinolones		21393	21393
<i>Citrobacter</i> spp.	Fourth-generation cephalosporins		9533	9533
<i>Citrobacter</i> spp.	Third-generation cephalosporins		22418	22418
<i>Enterobacter</i> spp.	Aminoglycosides		99118	99118
<i>Enterobacter</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		40914	40914
<i>Enterobacter</i> spp.	Carbapenem		69258	69258
<i>Enterobacter</i> spp.	Fluoroquinolones		76075	76075
<i>Enterobacter</i> spp.	Fourth-generation cephalosporins		38593	38593
<i>Enterobacter</i> spp.	Trimethoprim-Sulfamethoxazole		44611	44611
<i>Enterococcus faecalis</i>	Fluoroquinolones		1948	1948
<i>Enterococcus faecalis</i>	Vancomycin		2832	2832
<i>Enterococcus faecium</i>	Fluoroquinolones		20642	20642
<i>Enterococcus faecium</i>	Vancomycin		37044	37044
Other Enterococci	Fluoroquinolones		670	670
Other Enterococci	Vancomycin	5948	8827	14775
<i>Escherichia coli</i>	Aminoglycosides		843033	843033
<i>Escherichia coli</i>	Aminopenicillin		372390	372390
<i>Escherichia coli</i>	Beta-lactam/Beta-lactamase inhibitors		439472	439472
<i>Escherichia coli</i>	Carbapenem	220	545090	545310
<i>Escherichia coli</i>	Fluoroquinolones	5734	646667	652401
<i>Escherichia coli</i>	Third-generation cephalosporins	15176	634823	649999
<i>Escherichia coli</i>	Trimethoprim-Sulfamethoxazole		394397	394397
Group A <i>Streptococcus</i>	Macrolide		413	413
Group B <i>Streptococcus</i>	Fluoroquinolones		135	135
Group B <i>Streptococcus</i>	Macrolide	432	208	640
Group B <i>Streptococcus</i>	Penicillin		128	128
<i>Haemophilus influenzae</i>	Aminopenicillin	1403	1577	2980
<i>Haemophilus influenzae</i>	Third-generation cephalosporins		553	553
<i>Klebsiella pneumoniae</i>	Aminoglycosides		293876	293876
<i>Klebsiella pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors		157604	157604
<i>Klebsiella pneumoniae</i>	Carbapenem	5019	204322	209341
<i>Klebsiella pneumoniae</i>	Fluoroquinolones		222853	222853
<i>Klebsiella pneumoniae</i>	Third-generation cephalosporins	1507	226729	228236
<i>Klebsiella pneumoniae</i>	Trimethoprim-Sulfamethoxazole		135376	135376
<i>Morganella</i> spp.	Fluoroquinolones		22376	22376
<i>Morganella</i> spp.	Fourth-generation cephalosporins		10417	10417
<i>Morganella</i> spp.	Third-generation cephalosporins		23186	23186
<i>Mycobacterium tuberculosis</i>	Extensive drug resistance		15210	15210
<i>Mycobacterium tuberculosis</i>	Multi-drug resistance		14028	14028
<i>Neisseria gonorrhoeae</i>	Fluoroquinolones		6	6
<i>Neisseria gonorrhoeae</i>	Third-generation cephalosporins		10	10
Non-typhoidal <i>Salmonella</i>	Fluoroquinolones		3059	3059
<i>Proteus</i> spp.	Aminoglycosides		171236	171236
<i>Proteus</i> spp.	Aminopenicillin		74260	74260
<i>Proteus</i> spp.	Fluoroquinolones		127450	127450
<i>Proteus</i> spp.	Third-generation cephalosporins		118679	118679
<i>Proteus</i> spp.	Trimethoprim-Sulfamethoxazole		77075	77075
<i>Pseudomonas aeruginosa</i>	Aminoglycosides		332015	332015
<i>Pseudomonas aeruginosa</i>	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		138518	138518
<i>Pseudomonas aeruginosa</i>	Carbapenem	6141	180048	186189
<i>Pseudomonas aeruginosa</i>	Fluoroquinolones		218513	218513
<i>Pseudomonas aeruginosa</i>	Fourth-generation cephalosporins		129631	129631
<i>Pseudomonas aeruginosa</i>	Third-generation cephalosporins		132327	132327
<i>Salmonella</i> Paratyphi	Fluoroquinolones		66	66
<i>Salmonella</i> Typhi	Fluoroquinolones		795	795
<i>Serratia</i> spp.	Aminoglycosides		37402	37402
<i>Serratia</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors		11760	11760
<i>Serratia</i> spp.	Carbapenem		25054	25054
<i>Serratia</i> spp.	Fluoroquinolones		29148	29148

<i>Serratia</i> spp.	Fourth-generation cephalosporins		14622	14622
<i>Serratia</i> spp.	Third-generation cephalosporins		32521	32521
<i>Shigella</i> spp.	Fluoroquinolones		471	471
<i>Staphylococcus aureus</i>	Fluoroquinolones		292371	292371
<i>Staphylococcus aureus</i>	Macrolide		504053	504053
<i>Staphylococcus aureus</i>	Methicillin	25051	385688	410739
<i>Staphylococcus aureus</i>	Trimethoprim-Sulfamethoxazole		278366	278366
<i>Staphylococcus aureus</i>	Vancomycin		277781	277781
<i>Streptococcus pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors		2318	2318
<i>Streptococcus pneumoniae</i>	Carbapenem		4600	4600
<i>Streptococcus pneumoniae</i>	Fluoroquinolones	233	12940	13173
<i>Streptococcus pneumoniae</i>	Macrolide	871	20166	21037
<i>Streptococcus pneumoniae</i>	Penicillin	9172	44986	54158
<i>Streptococcus pneumoniae</i>	Third-generation cephalosporins	5100	37484	42584
<i>Streptococcus pneumoniae</i>	Trimethoprim-Sulfamethoxazole		9386	9386
TOTAL		82007	9627436	9709443

**Table S10. Relative risk estimates for sterile sources of specimen across 88 pathogen–drug combinations**

Pathogen	Drug	Sample size	Mean relative risk	Lower bound	Upper bound
<i>Acinetobacter baumannii</i>	Anti-pseudomonal penicillin/Beta-lactamase inhibitors	948	1.31	1.12	1.52
<i>Acinetobacter baumannii</i>	Beta-lactam/Beta-lactamase inhibitors	1555	1.27	1.11	1.44
<i>Acinetobacter baumannii</i>	Carbapenem	3232	1.42	1.27	1.58
<i>Acinetobacter baumannii</i>	Fourth-generation cephalosporins	1439	1.31	1.14	1.51
<i>Acinetobacter baumannii</i>	Third-generation cephalosporins	2055	1.35	1.13	1.62
<i>Acinetobacter baumannii</i>	Aminoglycosides	2066	1.1	0.97	1.25
<i>Acinetobacter baumannii</i>	Fluoroquinolones	3020	1.38	1.21	1.56
<i>Citrobacter</i> spp.	Aminoglycosides	4069	1.09	0.94	1.28
<i>Citrobacter</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors	3127	1.32	1.14	1.53
<i>Citrobacter</i> spp.	Carbapenem	3097	1.48	1.25	1.76
<i>Citrobacter</i> spp.	Fluoroquinolones	4387	1.36	1.18	1.57
<i>Citrobacter</i> spp.	Fourth-generation cephalosporins	2718	1.31	1.1	1.56
<i>Citrobacter</i> spp.	Third-generation cephalosporins	3984	1.38	1.16	1.64
<i>Enterobacter</i> spp.	Aminoglycosides	15211	1.19	1.06	1.34
<i>Enterobacter</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors	11857	1.23	1.13	1.34
<i>Enterobacter</i> spp.	Carbapenem	13299	1.53	1.4	1.67
<i>Enterobacter</i> spp.	Fluoroquinolones	17552	1.28	1.17	1.4
<i>Enterobacter</i> spp.	Fourth-generation cephalosporins	11482	1.31	1.18	1.45
<i>Enterobacter</i> spp.	Trimethoprim-Sulfamethoxazole	14798	1.09	0.98	1.21
<i>Enterococcus faecalis</i>	Fluoroquinolones	1126	1.43	1.24	1.64
<i>Enterococcus faecalis</i>	Vancomycin	36	1.7	1.39	2.07
<i>Enterococcus faecium</i>	Fluoroquinolones	4082	1.37	1.14	1.64
<i>Enterococcus faecium</i>	Vancomycin	9242	1.54	1.39	1.7
Other Enterococci	Fluoroquinolones	107	1.28	1.07	1.55
Other Enterococci	Vancomycin	7730	1.37	1.29	1.46
<i>Escherichia coli</i>	Aminoglycosides	164196	1.2	1.16	1.25
<i>Escherichia coli</i>	Aminopenicillin	157276	1.21	1.17	1.25
<i>Escherichia coli</i>	Beta-lactam/Beta-lactamase inhibitors	143458	1.15	1.11	1.18
<i>Escherichia coli</i>	Carbapenem	131382	1.7	1.5	1.93
<i>Escherichia coli</i>	Trimethoprim-Sulfamethoxazole	164240	1.14	1.11	1.18
Group A <i>Streptococcus</i>	Macrolide	130	1.07	0.89	1.29
Group B <i>Streptococcus</i>	Fluoroquinolones	44	1.26	1.04	1.53
Group B <i>Streptococcus</i>	Macrolide	465	1.18	0.99	1.41
Group B <i>Streptococcus</i>	Penicillin	15	1.29	1.06	1.57
<i>Haemophilus influenzae</i>	Aminopenicillin	1438	1.27	1.06	1.51
<i>Haemophilus influenzae</i>	Third-generation cephalosporins	308	1.48	1.23	1.79
<i>Klebsiella pneumoniae</i>	Aminoglycosides	51811	1.24	1.17	1.32
<i>Klebsiella pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors	46753	1.19	1.13	1.25
<i>Klebsiella pneumoniae</i>	Fluoroquinolones	53414	1.19	1.12	1.26
<i>Klebsiella pneumoniae</i>	Trimethoprim-Sulfamethoxazole	51737	1.12	1.06	1.19
<i>Morganella</i> spp.	Fluoroquinolones	3290	1.26	1.1	1.44
<i>Morganella</i> spp.	Fourth-generation cephalosporins	2352	1.23	1.02	1.49
<i>Morganella</i> spp.	Third-generation cephalosporins	3407	1.33	1.12	1.58
<i>Proteus</i> spp.	Aminoglycosides	21844	1.1	1.01	1.2
<i>Proteus</i> spp.	Aminopenicillin	20638	1.01	0.94	1.09
<i>Proteus</i> spp.	Fluoroquinolones	22141	1.13	1.05	1.21
<i>Proteus</i> spp.	Trimethoprim-Sulfamethoxazole	21838	1.06	0.98	1.14
<i>Proteus</i> spp.	Third-generation cephalosporins	18775	1.27	1.08	1.5
<i>Pseudomonas aeruginosa</i>	Aminoglycosides	39341	1.03	0.98	1.09
<i>Pseudomonas aeruginosa</i>	Anti-pseudomonal penicillin/Beta-lactamase inhibitors	36016	1.3	1.22	1.37
<i>Pseudomonas aeruginosa</i>	Carbapenem	41777	1.27	1.22	1.32
<i>Pseudomonas aeruginosa</i>	Fluoroquinolones	47417	1.19	1.15	1.23
<i>Pseudomonas aeruginosa</i>	Fourth-generation cephalosporins	34020	1.24	1.17	1.31
<i>Pseudomonas aeruginosa</i>	Third-generation cephalosporins	31041	1.35	1.15	1.59
<i>Serratia</i> spp.	Aminoglycosides	5250	1.05	0.93	1.19
<i>Serratia</i> spp.	Anti-pseudomonal penicillin/Beta-lactamase inhibitors	3003	1.17	1.01	1.35
<i>Serratia</i> spp.	Carbapenem	3639	1.39	1.2	1.63
<i>Serratia</i> spp.	Fluoroquinolones	5252	1.09	0.94	1.26
<i>Serratia</i> spp.	Fourth-generation cephalosporins	3928	1.17	0.99	1.38
<i>Serratia</i> spp.	Third-generation cephalosporins	5960	1.29	1.09	1.52
<i>Staphylococcus aureus</i>	Fluoroquinolones	37963	1.07	1.02	1.11
<i>Staphylococcus aureus</i>	Macrolide	53005	1.06	1.02	1.09
<i>Staphylococcus aureus</i>	Trimethoprim-Sulfamethoxazole	59632	1.17	1.09	1.25
<i>Streptococcus pneumoniae</i>	Beta-lactam/Beta-lactamase inhibitors	1419	1.14	0.95	1.37
<i>Streptococcus pneumoniae</i>	Carbapenem	1947	1.37	1.16	1.61
<i>Streptococcus pneumoniae</i>	Fluoroquinolones	6499	1.23	1.05	1.45
<i>Streptococcus pneumoniae</i>	Macrolide	7348	1.05	0.94	1.17
<i>Streptococcus pneumoniae</i>	Trimethoprim-Sulfamethoxazole	5413	1.14	1.01	1.28
<i>Streptococcus pneumoniae</i>	Third-generation cephalosporins	10457	1.33	1.13	1.57
<i>Escherichia coli</i>	Fluoroquinolones	171311	1.31	1.27	1.35
<i>Escherichia coli</i>	Third-generation cephalosporins	163801	1.37	1.17	1.61
<i>Klebsiella pneumoniae</i>	Carbapenem	41943	1.68	1.56	1.82
<i>Klebsiella pneumoniae</i>	Third-generation cephalosporins	52090	1.36	1.16	1.6
<i>Mycobacterium tuberculosis</i>	Extensive drug resistance	428524	2.59	2.46	2.72
<i>Mycobacterium tuberculosis</i>	Isoniazid mono-resistance	14537	1.19	0.84	1.67
<i>Mycobacterium tuberculosis</i>	Multidrug resistance	427342	2.5	1.17	4.74
<i>Mycobacterium tuberculosis</i>	Rifampicin mono-resistance	7161	1.39	1.06	1.77
Non-typhoidal <i>Salmonella</i>	Fluoroquinolones	42	1.23	1.01	1.5
<i>Salmonella</i> Paratyphi	Fluoroquinolones	24	1.24	1.02	1.52
<i>Salmonella</i> Paratyphi	Multidrug resistance	25	1.24	1.03	1.5
<i>Salmonella</i> Typhi	Fluoroquinolones	24	1.24	1.02	1.52
<i>Salmonella</i> Typhi	Multidrug resistance	25	1.24	1.03	1.5
<i>Shigella</i> spp.	Fluoroquinolones	24	1.24	1.02	1.52
<i>Staphylococcus aureus</i>	Methicillin	95696	1.43	1.2	1.7
<i>Streptococcus pneumoniae</i>	Penicillin	30849	1.27	1.18	1.36
<i>Staphylococcus aureus</i>	Vancomycin	53623	1.52	1.28	1.81

Sample size are the admission reported with known discharge disposition and antimicrobial susceptibility test.

**Table S11: Decomposition of fatal antimicrobial resistance burden by GBD region, 2019**

GBD region	All-cause death counts	All-cause death rate per 100 000	Fraction of all deaths that involve infection	Death counts involving infection	Death rate per 100 000 involving infection	Fraction of deaths involving infection that are associated with resistance	Death counts associated with resistance	Death rate per 100 000 associated with resistance	Fraction of deaths involving infection that are attributable to resistance	Death counts attributable to resistance	Death rate per 100 000 attributable to resistance
Central Asia	637,000 (587,000–697,000)	681.5 (628.0–744.7)	16.1% (11.9%–21.5%)	102,000 (74,200–140,000)	109.5 (79.3–150.1)	48.6% (46.7%–50.2%)	49,800 (35,300–69,500)	53.3 (37.7–74.3)	12.6% (11.1%–14.3%)	12,900 (8,870–18,200)	13.8 (9.5–19.5)
Central Europe	1,370,000 (1,230,000–1,520,000)	1201.3 (1074.6–1329.3)	11.5% (7.9%–16.1%)	157,000 (106,000–227,000)	137.8 (92.5–198.7)	49.1% (46.6%–51.5%)	77,600 (49,400–115,000)	68.0 (43.2–100.9)	12.0% (10.7%–13.4%)	19,000 (12,000–28,500)	16.6 (10.5–25.0)
Eastern Europe	2,730,000 (2,520,000–2,970,000)	1300.9 (1202.0–1415.4)	11.5% (8.1%–16.0%)	315,000 (217,000–434,000)	150.0 (103.5–206.6)	49.2% (46.7%–51.6%)	155,000 (103,000–222,000)	74.0 (48.8–105.6)	13.3% (11.7%–15.0%)	41,800 (27,600–59,900)	19.9 (13.1–28.5)
Australasia	205,000 (202,000–209,000)	706.6 (695.7–717.7)	12.7% (8.9%–17.6%)	26,200 (18,400–36,100)	90.0 (63.2–124.4)	31.0% (29.2%–32.8%)	8,140 (5,460–11,600)	28.0 (18.8–39.9)	7.2% (6.2%–8.2%)	1,880 (1,250–2,730)	6.5 (4.3–9.4)
High-income Asia Pacific	1,740,000 (1,730,000–1,760,000)	931.0 (921.9–940.3)	18.3% (14.2%–23.1%)	319,000 (248,000–405,000)	170.2 (132.5–216.0)	41.5% (39.6%–43.4%)	132,000 (99,700–173,000)	70.7 (53.2–92.3)	9.7% (7.9%–11.5%)	30,900 (21,700–43,300)	16.5 (11.6–23.1)
High-income North America	3,240,000 (3,210,000–3,260,000)	887.4 (881.1–893.8)	13.8% (10.0%–18.9%)	448,000 (323,000–612,000)	122.8 (88.7–167.9)	41.4% (39.5%–43.2%)	186,000 (129,000–261,000)	51.0 (35.4–71.5)	10.0% (8.6%–11.5%)	44,800 (30,300–63,900)	12.5 (8.3–17.5)
Southern Latin America	496,000 (485,000–507,000)	742.7 (726.9–760.0)	22.7% (18.1%–28.4%)	112,000 (89,800–141,000)	168.3 (134.5–210.8)	42.8% (40.9%–44.9%)	48,200 (36,800–62,300)	72.3 (55.1–93.4)	11.0% (9.5%–12.6%)	12,400 (9,280–16,500)	18.6 (13.9–24.7)
Western Europe	4,280,000 (4,240,000–4,320,000)	979.9 (970.7–989.4)	14.3% (10.7%–19.1%)	613,000 (457,000–816,000)	140.5 (104.7–186.9)	37.2% (34.9%–39.6%)	229,000 (162,000–318,000)	52.5 (37.0–73.0)	8.3% (7.3%–9.4%)	51,100 (35,100–72,400)	11.7 (8.0–16.6)
Andean Latin America	321,000 (270,000–381,000)	504.6 (423.9–599.2)	27.3% (22.0%–33.7%)	87,500 (64,700–116,000)	137.6 (101.7–182.1)	45.9% (43.3%–48.0%)	40,200 (28,900–54,300)	63.2 (45.4–85.4)	11.5% (10.1%–13.2%)	10,100 (7,050–13,900)	15.9 (11.1–21.9)
Caribbean	379,000 (335,000–427,000)	804.0 (709.5–905.2)	22.5% (17.5%–28.6%)	85,200 (63,900–112,000)	180.6 (135.5–237.8)	35.9% (32.9%–38.8%)	30,700 (21,500–42,700)	65.1 (45.5–90.5)	8.9% (7.7%–10.2%)	7,630 (5,200–10,900)	16.2 (11.0–23.2)
Central Latin America	1,430,000 (1,260,000–1,630,000)	573.2 (503.8–651.2)	19.9% (14.7%–26.5%)	285,000 (204,000–391,000)	113.9 (81.4–156.2)	44.3% (42.0%–46.3%)	127,000 (86,700–177,000)	50.6 (34.7–70.9)	11.4% (10.0%–13.0%)	32,600 (22,000–46,200)	13.0 (8.8–18.5)
Tropical Latin America	1,450,000 (1,410,000–1,490,000)	646.3 (629.1–664.3)	22.0% (17.2%–27.9%)	318,000 (249,000–404,000)	142.2 (111.5–180.6)	44.2% (42.3%–46.1%)	141,000 (105,000–186,000)	63.0 (47.1–83.1)	10.7% (9.6%–11.9%)	34,000 (24,800–46,000)	15.2 (11.1–20.6)
North Africa and Middle East	3,100,000 (2,820,000–3,420,000)	509.7 (462.6–561.1)	18.1% (13.2%–24.2%)	563,000 (402,000–774,000)	92.5 (66.0–127.1)	45.3% (42.6%–47.7%)	256,000 (174,000–362,000)	42.0 (28.7–59.5)	12.1% (10.7%–13.5%)	68,300 (45,600–99,000)	11.2 (7.5–16.3)
South Asia	11,900,000 (10,900,000–13,000,000)	661.3 (604.0–721.0)	31.8% (26.0%–39.2%)	3,800,000 (3,040,000–4,730,000)	210.6 (168.3–262.2)	36.4% (30.8%–41.4%)	1,390,000 (1,030,000–1,830,000)	76.8 (57.2–101.2)	10.2% (8.1%–12.7%)	389,000 (273,000–538,000)	21.5 (15.1–29.8)
East Asia	11,100,000 (9,730,000–12,500,000)	752.3 (661.0–848.3)	12.2% (8.2%–17.5%)	1,350,000 (900,000–2,000,000)	91.6 (61.2–135.8)	47.1% (44.6%–49.2%)	638,000 (404,000–973,000)	43.3 (27.4–66.1)	11.4% (9.9%–13.0%)	154,000 (96,000–235,000)	10.5 (6.5–16.0)
Oceania	97,200 (80,000–118,000)	732.4 (602.3–891.7)	33.1% (27.0%–40.4%)	32,200 (23,300–42,900)	242.6 (175.7–323.3)	29.5% (24.9%–33.0%)	9,500 (6,820–13,000)	71.6 (51.4–98.0)	7.0% (5.7%–8.3%)	2,260 (1,610–3,080)	17.0 (12.1–23.2)
Southeast Asia	4,390,000 (4,010,000–4,750,000)	651.3 (595.7–704.9)	25.8% (20.8%–32.0%)	1,130,000 (899,000–1,440,000)	168.2 (133.4–213.7)	32.4% (28.8%–35.7%)	369,000 (262,000–505,000)	54.8 (38.9–74.9)	8.5% (7.3%–9.9%)	97,000 (67,500–135,000)	14.4 (10.0–20.0)
Central Sub-Saharan Africa	872,000 (748,000–1,010,000)	662.8 (568.6–769.2)	48.0% (40.2%–56.1%)	418,000 (335,000–520,000)	317.7 (254.9–395.6)	27.0% (24.3%–30.1%)	113,000 (86,600–144,000)	86.0 (65.9–109.8)	6.5% (5.3%–8.1%)	27,200 (19,600–36,400)	20.7 (14.9–27.7)
Eastern Sub-Saharan Africa	2,590,000 (2,340,000–2,900,000)	628.3 (568.1–703.1)	50.7% (43.1%–58.8%)	1,310,000 (1,080,000–1,610,000)	318.9 (261.3–390.1)	27.9% (25.6%–30.1%)	366,000 (290,000–464,000)	89.0 (70.5–112.6)	6.7% (5.7%–7.9%)	88,200 (67,000–116,000)	21.4 (16.3–28.1)
Southern Sub-Saharan Africa	732,000 (688,000–787,000)	932.2 (875.3–1002.1)	45.6% (38.4%–52.7%)	334,000 (276,000–399,000)	425.4 (351.5–507.4)	18.6% (16.6%–20.9%)	62,400 (48,400–79,800)	79.4 (61.7–101.6)	4.6% (3.7%–5.7%)	15,300 (11,300–20,400)	19.4 (14.3–25.9)
Western Sub-Saharan Africa	3,460,000 (3,070,000–3,940,000)	757.8 (672.5–864.4)	53.5% (45.4%–62.0%)	1,850,000 (1,510,000–2,270,000)	405.5 (331.6–497.6)	28.3% (25.4%–30.8%)	524,000 (412,000–663,000)	114.8 (90.4–145.3)	6.7% (5.7%–7.7%)	125,000 (95,400–161,000)	27.3 (20.9–35.3)

**Table S12. GATHER checklist**

Item #	Checklist item	Reporting location:
<b>Objectives and funding</b>		
1	Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made.	Main text methods section (overview)
2	List the funding sources for the work.	Main text funding statement and acknowledgements
<b>Data Inputs</b>		
<i>For all data inputs from multiple sources that are synthesized as part of the study:</i>		
3	Describe how the data were identified and how the data were accessed.	Main text methods section + supplementary appendix (sections 2, 4.1, 5.1, 6.1, 7.1, 8.1)
4	Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions.	Supplementary appendix (section 2)
5	Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.	Some data source information in supplementary appendix (section 2); main characteristics of data, metadata, and/or NIDs available at <a href="http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019">http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019</a>
6	Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5).	Main text limitations section + supplementary appendix (biases for input data in each modelling step identified in each section)
<i>For data inputs that contribute to the analysis but were not synthesized as part of the study:</i>		
7	Describe and give sources for any other data inputs.	GBD 2019 estimates ( <a href="http://ghdx.healthdata.org/gbd-results-tool">http://ghdx.healthdata.org/gbd-results-tool</a> )
<i>For all data inputs:</i>		
8	Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.	Data inputs and/or contact information available at <a href="http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019">http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019</a>
<b>Data analysis</b>		
9	Provide a conceptual overview of the data analysis method. A diagram may be helpful.	Main text methods section + main text figure 1 (flowchart of methods)
10	Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).	Supplementary appendix (sections 4–9)

<b>11</b>	Describe how candidate models were evaluated and how the final model(s) were selected.	Supplementary appendix (sections 4–8)
<b>12</b>	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis.	Supplementary appendix (sections 4.7, 6.5, 7.6, 8.4)
<b>13</b>	Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.	Main text methods section (uncertainty analysis) + limitations section (scarcity of data) + supplementary appendix (sections 4–8)
<b>14</b>	State how analytic or statistical source code used to generate estimates can be accessed.	GitHub code found at: <a href="http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019">http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019</a>
<b>Results and Discussion</b>		
<b>15</b>	Provide published estimates in a file format from which data can be efficiently extracted.	CSVs of tabulated estimates are available at: <a href="http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019">http://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistance-burden-estimates-2019</a>
<b>16</b>	Report a quantitative measure of the uncertainty of the estimates (e.g. uncertainty intervals).	UIs provided for all estimates throughout the main text (summary, results, and discussion sections)
<b>17</b>	Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates.	Main text introduction and discussion sections
<b>18</b>	Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates.	Main text limitations section + supplementary appendix (sections 4–8; table S21)



**Table S13. GBD location hierarchy with levels**

Location	level
<b>Global</b>	<b>0</b>
<b>Central Europe, eastern Europe, and central Asia</b>	<b>1</b>
<b>Central Asia</b>	<b>2</b>
Armenia	3
Azerbaijan	3
Georgia	3
Kazakhstan	3
Kyrgyzstan	3
Mongolia	3
Tajikistan	3
Turkmenistan	3
Uzbekistan	3
<b>Central Europe</b>	<b>2</b>
Albania	3
Bosnia and Herzegovina	3
Bulgaria	3
Croatia	3
Czechia	3
Hungary	3
Montenegro	3
North Macedonia	3
Poland	3
Romania	3
Serbia	3
Slovakia	3
Slovenia	3
<b>Eastern Europe</b>	<b>2</b>
Belarus	3
Estonia	3
Latvia	3
Lithuania	3
Moldova	3
Russia	3
Ukraine	3
<b>High income</b>	<b>1</b>
<b>Australasia</b>	<b>2</b>
Australia	3
New Zealand	3

<b>High-income Asia Pacific</b>	<b>2</b>
Brunei	3
Japan	3
Singapore	3
South Korea	3
<b>High-income North America</b>	<b>2</b>
Canada	3
Greenland	3
USA	3
<b>Southern Latin America</b>	<b>2</b>
Argentina	3
Chile	3
Uruguay	3
<b>Western Europe</b>	<b>2</b>
Andorra	3
Austria	3
Belgium	3
Cyprus	3
Denmark	3
Finland	3
France	3
Germany	3
Greece	3
Iceland	3
Ireland	3
Israel	3
Italy	3
Luxembourg	3
Malta	3
Monaco	3
Netherlands	3
Norway	3
Portugal	3
San Marino	3
Spain	3
Sweden	3
Switzerland	3
UK	3
<b>Latin America and Caribbean</b>	<b>1</b>
<b>Andean Latin America</b>	<b>2</b>
Bolivia	3
Ecuador	3
Peru	3
<b>Caribbean</b>	<b>2</b>
Antigua and Barbuda	3
The Bahamas	3
Barbados	3

Belize	3
Bermuda	3
Cuba	3
Dominica	3
Dominican Republic	3
Grenada	3
Guyana	3
Haiti	3
Jamaica	3
Puerto Rico	3
Saint Kitts and Nevis	3
Saint Lucia	3
Saint Vincent and the Grenadines	3
Suriname	3
Trinidad and Tobago	3
Virgin Islands	3
<b>Central Latin America</b>	<b>2</b>
Colombia	3
Costa Rica	3
El Salvador	3
Guatemala	3
Honduras	3
Mexico	3
Nicaragua	3
Panama	3
Venezuela	3
<b>Tropical Latin America</b>	<b>2</b>
Brazil	3
Paraguay	3
<b>North Africa and Middle East</b>	<b>1</b>
<b>North Africa and Middle East</b>	<b>2</b>
Afghanistan	3
Algeria	3
Bahrain	3
Egypt	3
Iran	3
Iraq	3
Jordan	3
Kuwait	3
Lebanon	3
Libya	3
Morocco	3
Oman	3
Palestine	3
Qatar	3
Saudi Arabia	3
Sudan	3
Syria	3

Tunisia	3
Turkey	3
United Arab Emirates	3
Yemen	3
<b>South Asia</b>	<b>1</b>
<b>South Asia</b>	<b>2</b>
Bangladesh	3
Bhutan	3
India	3
Nepal	3
Pakistan	3
<b>Southeast Asia, east Asia, and Oceania</b>	<b>1</b>
<b>East Asia</b>	<b>2</b>
China	3
North Korea	3
Taiwan (province of China)	3
<b>Oceania</b>	<b>2</b>
American Samoa	3
Cook Islands	3
Fiji	3
Guam	3
Kiribati	3
Marshall Islands	3
Federated States of Micronesia	3
Nauru	3
Niue	3
Northern Mariana Islands	3
Palau	3
Papua New Guinea	3
Samoa	3
Solomon Islands	3
Tokelau	3
Tonga	3
Tuvalu	3
Vanuatu	3
<b>Southeast Asia</b>	<b>2</b>
Cambodia	3
Indonesia	3
Laos	3
Malaysia	3
Maldives	3
Mauritius	3
Myanmar	3
Philippines	3
Seychelles	3
Sri Lanka	3
Thailand	3
Timor-Leste	3

Vietnam	3
<b>Sub-Saharan Africa</b>	<b>1</b>
<b>Central sub-Saharan Africa</b>	<b>2</b>
Angola	3
Central African Republic	3
Congo (Brazzaville)	3
DR Congo	3
Equatorial Guinea	3
Gabon	3
Burundi	3
Comoros	3
Djibouti	3
Eritrea	3
Ethiopia	3
Kenya	3
Madagascar	3
Malawi	3
Mozambique	3
Rwanda	3
Somalia	3
South Sudan	3
Uganda	3
Tanzania	3
Zambia	3
<b>Southern sub-Saharan Africa</b>	<b>2</b>
Botswana	3
Eswatini	3
Lesotho	3
Namibia	3
South Africa	3
Zimbabwe	3
<b>Western sub-Saharan Africa</b>	<b>2</b>
Benin	3
Burkina Faso	3
Cape Verde	3
Cameroon	3
Chad	3
Côte d'Ivoire	3
The Gambia	3
Ghana	3
Guinea	3
Guinea-Bissau	3
Liberia	3
Mali	3
Mauritania	3
Niger	3
Nigeria	3
São Tomé and Príncipe	3

Senegal  
Sierra Leone  
Togo

3  
3  
3

**Table S4.1. Deaths and DALYs (in counts and age-specific rates) associated with and attributable to bacterial antimicrobial resistance by pathogen-drug combination, by age group, 2019; central Europe, eastern Europe, and central Asia sub-region**

Pathogen	Antibiotic Class	Central Europe												Eastern Europe												Central Asia																				
		Associated with resistance						Attributable to resistance						Associated with resistance						Attributable to resistance						Associated with resistance						Attributable to resistance														
		Deaths	DALYs	Counts	Rate per 100 000	Counts	Rate per 100 000	Deaths	DALYs	Counts	Rate per 100 000	Counts	Rate per 100 000	Deaths	DALYs	Counts	Rate per 100 000	Counts	Rate per 100 000	Deaths	DALYs	Counts	Rate per 100 000	Counts	Rate per 100 000	Deaths	DALYs	Counts	Rate per 100 000	Counts	Rate per 100 000	Deaths	DALYs	Counts	Rate per 100 000											
Aerobacterium	Resistance to one or more antibiotics	640(130-623)	142(31-85)	4060(17000)	107(17-2589)	19700(7000)	2460(11726)	1000(1730)	200(107)	1800(7210)	227(194-262)	597(0-284)	149(3-3212)	7(0-67)	17(0-42)	597(0-284)	149(3-3212)	7(0-67)	17(0-42)	640(130-623)	142(31-85)	4060(17000)	107(17-2589)	19700(7000)	2460(11726)	1000(1730)	200(107)	1800(7210)	227(194-262)	597(0-284)	149(3-3212)	7(0-67)	17(0-42)	597(0-284)	149(3-3212)	7(0-67)	17(0-42)									
		1980(1300-2000)	51(6-59)	14200(13700-14300)	2861(2007-3905)	1000(13000)	111(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)		
Aerobacterium	Antimicrobial resistance	396(127-391)	81(12-131)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	396(127-391)	81(12-131)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	1800(11000)	46(24-79)	
		1980(1300-2000)	51(6-59)	14200(13700-14300)	2861(2007-3905)	1000(13000)	111(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)	107(1230)	1100(10000)







**Table 3.15: State and local tax revenue and growth rates by type of tax and revenue by jurisdiction, 2013-2015**

Jurisdiction	State	Local	2013		2014		2015		2013-2015	2013-2015		2013-2015		2013-2015		2013-2015		2013-2015	
			Revenue (\$)	% of GDP	Revenue (\$)	% of GDP	Revenue (\$)	% of GDP		% Change	% Change	% Change	% Change	% Change	% Change	% Change	% Change	% Change	% Change
Alabama	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Alaska	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Arizona	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Arkansas	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
California	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Colorado	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Connecticut	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Delaware	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
District of Columbia	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Florida	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Georgia	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Hawaii	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Idaho	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Illinois	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Indiana	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Iowa	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Kansas	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Kentucky	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Louisiana	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Maine	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Maryland	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Massachusetts	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Michigan	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Minnesota	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Mississippi	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Missouri	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Montana	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Nebraska	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Nevada	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
New Hampshire	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
New Jersey	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
New Mexico	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
New York	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
North Carolina	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
North Dakota	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Ohio	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Oklahoma	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Oregon	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Pennsylvania	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Rhode Island	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
South Carolina	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
South Dakota	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Tennessee	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Texas	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Utah	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Vermont	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Virginia	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Washington	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
West Virginia	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Wisconsin	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Wyoming	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...







Table 100: Risk and Return by type, asset group, asset class and sub-class in financial markets (return by category data available by asset group, asset class and asset type)

Table with 10 columns: Category, Sub-category, Asset Type, Risk, Return, and 8 columns of Return and Risk data for various asset groups (Equity, Fixed Income, Real Estate, Commodities, Alternative, Multi-Asset, Cash, and Other). Each cell contains numerical values representing risk and return metrics.



**Table 3.1: Study and BAC-Via rates and age-specific rates associated with and attributable to licensed/unlicensed children by purchase drug combination by age group 2015, combined AEs and AEs and Opioids**

Purchase	Active Child	Age Group 1 (0-4)										Age Group 2 (5-9)										Age Group 3 (10-14)										Age Group 4 (15-19)									
		Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI	Rate per 1000	95% CI								
Morphine	Residence in a new address	1751 (201.70)	157.12-187.66	1985 (229.12)	178.51-219.14	2269 (258.42)	231.28-265.56	2518 (282.78)	271.13-306.43	2811 (312.12)	321.12-363.12	3121 (342.12)	351.12-393.12	3431 (372.12)	381.12-413.12	3741 (402.12)	413.12-453.12	4051 (432.12)	453.12-493.12	4361 (462.12)	513.12-553.12	4671 (492.12)	553.12-593.12	4981 (522.12)	613.12-653.12	5291 (552.12)	653.12-693.12	5601 (582.12)	693.12-733.12	5911 (612.12)	733.12-773.12	6221 (642.12)	773.12-813.12								
		1751 (201.70)	157.12-187.66	1985 (229.12)	178.51-219.14	2269 (258.42)	231.28-265.56	2518 (282.78)	271.13-306.43	2811 (312.12)	321.12-363.12	3121 (342.12)	351.12-393.12	3431 (372.12)	381.12-413.12	3741 (402.12)	413.12-453.12	4051 (432.12)	453.12-493.12	4361 (462.12)	513.12-553.12	4671 (492.12)	553.12-593.12	4981 (522.12)	613.12-653.12	5291 (552.12)	653.12-693.12	5601 (582.12)	693.12-733.12	5911 (612.12)	733.12-773.12	6221 (642.12)	773.12-813.12								
Morphine	Residence in a new address	1751 (201.70)	157.12-187.66	1985 (229.12)	178.51-219.14	2269 (258.42)	231.28-265.56	2518 (282.78)	271.13-306.43	2811 (312.12)	321.12-363.12	3121 (342.12)	351.12-393.12	3431 (372.12)	381.12-413.12	3741 (402.12)	413.12-453.12	4051 (432.12)	453.12-493.12	4361 (462.12)	513.12-553.12	4671 (492.12)	553.12-593.12	4981 (522.12)	613.12-653.12	5291 (552.12)	653.12-693.12	5601 (582.12)	693.12-733.12	5911 (612.12)	733.12-773.12	6221 (642.12)	773.12-813.12								
		1751 (201.70)	157.12-187.66	1985 (229.12)	178.51-219.14	2269 (258.42)	231.28-265.56	2518 (282.78)	271.13-306.43	2811 (312.12)	321.12-363.12	3121 (342.12)	351.12-393.12	3431 (372.12)	381.12-413.12	3741 (402.12)	413.12-453.12	4051 (432.12)	453.12-493.12	4361 (462.12)	513.12-553.12	4671 (492.12)	553.12-593.12	4981 (522.12)	613.12-653.12	5291 (552.12)	653.12-693.12	5601 (582.12)	693.12-733.12	5911 (612.12)	733.12-773.12	6221 (642.12)	773.12-813.12								
Morphine	Residence in a new address	1751 (201.70)	157.12-187.66	1985 (229.12)	178.51-219.14	2269 (258.42)	231.28-265.56	2518 (282.78)	271.13-306.43	2811 (312.12)	321.12-363.12	3121 (342.12)	351.12-393.12	3431 (372.12)	381.12-413.12	3741 (402.12)	413.12-453.12	4051 (432.12)	453.12-493.12	4361 (462.12)	513.12-553.12	4671 (492.12)	553.12-593.12	4981 (522.12)	613.12-653.12	5291 (552.12)	653.12-693.12	5601 (582.12)	693.12-733.12	5911 (612.12)	733.12-773.12	6221 (642.12)	773.12-813.12								
		1751 (201.70)	157.12-187.66	1985 (229.12)	178.51-219.14	2269 (258.42)	231.28-265.56	2518 (282.78)	271.13-306.43	2811 (312.12)	321.12-363.12	3121 (342.12)	351.12-393.12	3431 (372.12)	381.12-413.12	3741 (402.12)	413.12-453.12	4051 (432.12)	453.12-493.12	4361 (462.12)	513.12-553.12	4671 (492.12)	553.12-593.12	4981 (522.12)	613.12-653.12	5291 (552.12)	653.12-693.12	5601 (582.12)	693.12-733.12	5911 (612.12)	733.12-773.12	6221 (642.12)	773.12-813.12								



Table with columns for 'Country', 'Region', 'Year', 'Value', 'Unit', and 'Source'. The table contains multiple rows of data organized by country and region, with values ranging from small percentages to large absolute numbers. The table is partially obscured by a large watermark.

Table 300: Number of DMEPOS codes and average rates associated with each procedure in historical administrative data by payor type. 300-00-0000-0000

Payor Type	Procedure Code	Description	2018		2019		2020		2021		2022		2023		2024		
			Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	
Medicare	90.00	EKG	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000
			1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000
Medicaid	90.00	EKG	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000
			1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000
Private	90.00	EKG	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000
			1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000	100.00	1000000



**Table S21. Limitations of each primary modelling component**

Type of limitation	1. Fraction of sepsis and infectious syndromes	2. Case fatality ratio	3. Pathogen distribution	4. Fraction of resistance	5. Relative risk
Input data	Limited geographic coverage in the data. Analysis of the fraction of sepsis included multiple cause of death (MCoD), hospital discharge, linkage, and CHAMPS surveillance data which represented 16 countries	Almost all of the input data relies on hospital-based sampling, excluding all community infections and deaths from the analysis.	Many data sources like microbial databases and hospital discharges rely on hospital-based sampling, excluding community-based infections.	There is heterogeneity in the interpretation guidelines used for antimicrobial susceptibility test and in most cases it was not possible to harmonise this interpretation to the most recent CLSI guidelines.	There was limited data on the fatalities due to resistant <i>Neisseria gonorrhoeae</i> so we did not produce a fatal estimate for this pathogen.
		Literature review of case fatality ratios available for central nervous system infections only.	We excluded from analysis all records of infection where no pathogen was detected. This assumes that all pathogens are equally like to be detected, which may be untrue due to issues like variable diagnostic methods (PCR, culture, etc) and irregular testing.	There is heterogeneity in the breadth of data gathered for the 17 core pathogen-drug combinations, for which we implemented a systematic review, and the remaining 69 combinations for which no systematic review was implemented.	There was limited data on fatalities due to resistant <i>Shigella</i> and <i>Salmonella Paratyphi</i> , for which we based our results on estimates for <i>Salmonella Typhi</i> .
		Because each data source generally reported only a set of the pathogens we evaluated in our research, the input data for the pathogens varied in geographic coverage; nearly all pathogens were well reported in high-income areas, but some pathogens were not well represented in the smaller subset of data we collected from low- and middle-income locations.	Lack of diagnostic data linked with microbiology lab results for some data sources forces us to rely only on specimen type to assign infectious syndrome, obscuring the primary site of infection for samples such as blood.	Were unable to collect data on resistance prevalence more recently than 2018; we estimated resistance for 2018 and assumed no change in prevalence of resistance for 2019.	There was limited availability of outcomes disaggregated by age and gender groups and different anatomical sites of infection.
		For some pathogen-syndrome combinations, we had no data available with outcomes that could be used to model CFRs; for these, we defaulted to a general bacteria model of CFR.		Some facilities could not be classified as tertiary/non-tertiary due to vague facilities names and/or lack of sufficient website information (see appendix section 7.2).	
				When data providers did not describe a facility as tertiary or non-tertiary and the name of the facility was not descriptive, we used self-assignments of tertiary/non-tertiary from facility websites. This form of classification is vulnerable to differences in tertiary/non-tertiary definitions (such as describing a facility as tertiary when only a select ward offers tertiary care).	

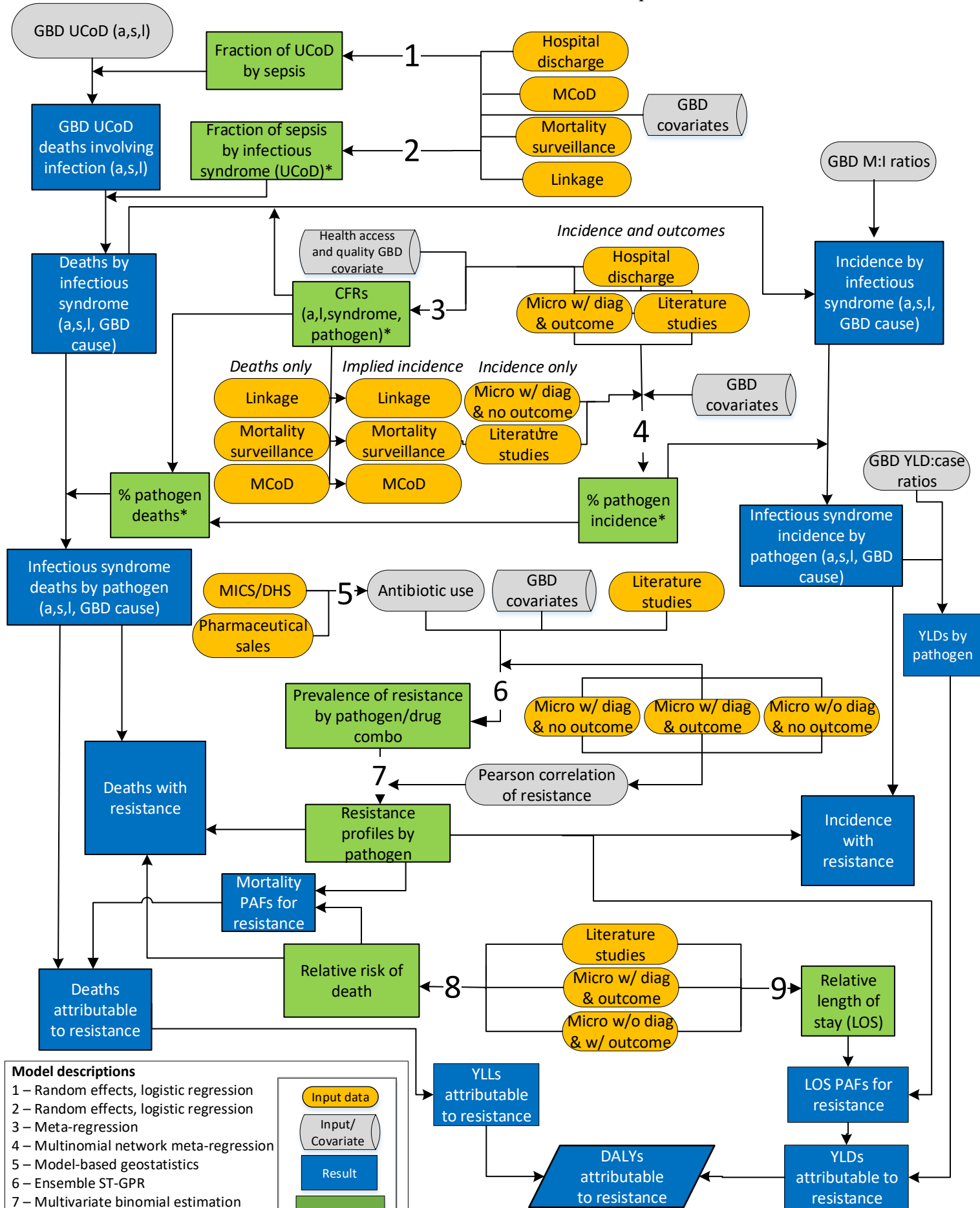
	<p>Tuberculosis, Gonorrhoea and chlamydia, and Typhoid, paratyphoid, and invasive nontyphoidal Salmonella were not included as infectious syndrome models. We used GBD 2019 results by setting the fraction of sepsis to 100% for all deaths in these causes prior to multiplying onto the sepsis-related mortality envelope</p>	<p>Pathogen-syndrome-specific case fatality ratios assumed to be constant across underlying cause of illness.</p>	<p>The distribution of pathogens causing a given infectious syndrome is assumed to be constant across the underlying cause of illness.</p>	<p>We assumed the same fraction of resistance for different age and gender groups, for different sites of infection and hospital or community acquired settings.</p>	<p>We assumed the same relative risk for different age and gender groups, different anatomical sites of infection, and different locations.</p>
<b>Modelling</b>	<p>We assumed that infections were community acquired if they were listed as primary diagnoses or underlying causes of death. Otherwise, the infection was assumed to be hospital acquired.</p>	<p>Geographic distribution of CFR based solely on Healthcare Access and Quality Index.</p>	<p>Co-infection of pathogens is assumed to be random and not correlated for certain pathogens.</p>	<p>We assumed that the correlation structure of co-resistance of multiple drugs for the same pathogen was the same as the average across regions</p>	<p>We assumed that the relative risk of a co-resistant infection is the same as the highest mono-resistant relative risk among the antibiotics considered, which is likely an underestimation of the true co-resistant relative risk.</p>
	<p>Data stochasticity. At the most granular age-, sex-, location-, year-, cause-specific level, the dataset for each individual model is stochastic and there are few clusters to guide the model fit.</p>		<p>Use of expert-opinion Gaussian priors with mean 0 and non-zero variance on model coefficients to bias the models away from spurious effects driven by data sparsity.</p>	<p>We included designations of "mixed/unknown" in the crosswalk to attenuate the effect of tertiary samples in our results. This was due to the low proportion of definitively non-tertiary samples in several super regions for which we produce estimates.</p>	<p>We assumed that the relative length of stay has the same impact duration for all sequelae, which impacts specifically bloodstream infections and intraabdominal infections</p>
			<p>Pathogen distribution of cardiac infections is assumed to the same as bloodstream infections.</p>		

**Table S22. Global deaths and DALYs (in counts and all-age rates) associated with and attributable to bacterial antimicrobial resistance by pathogen-drug combination, 2019**

Pathogen	Antibiotic Class	Associated with resistance				Attributable to resistance			
		Deaths		DALYs		Deaths		DALYs	
		Counts (thousands)	Rate per 100 000	Counts (thousands)	Rate per 100 000	Counts (thousands)	Rate per 100 000	Counts (thousands)	Rate per 100 000
All pathogens	Resistance to one or more antibiotics	4,950 (3,620-6,570)	64.0 (46.8-84.9)	192,000 (146,000-248,000)	2,477.7 (1,889.9-3,199.1)	1,270 (911-1,710)	16.4 (11.8-22.0)	47,900 (35,300-63,700)	618.7 (455.7-823.2)
<i>Acinetobacter baumannii</i>	Aminoglycosides	239 (140-374)	3.1 (1.8-4.8)	6,730 (4,120-10,300)	86.9 (53.3-133.5)	10.4 (0-26.7)	0.1 (0.0-0.3)	296 (1.84-737)	3.8 (0.0-9.5)
<i>Acinetobacter baumannii</i>	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors	359 (213-551)	4.6 (2.8-7.1)	10,300 (6,400-15,600)	132.7 (82.7-202.2)	13.3 (6.88-22.6)	0.2 (0.1-0.3)	463 (243-753)	6.0 (3.1-9.7)
<i>Acinetobacter baumannii</i>	Beta Lactam/Beta-lactamase inhibitors	306 (182-469)	3.9 (2.4-6.1)	8,490 (5,260-13,000)	109.8 (68.0-167.5)	0.811 (0.219-1.65)	0.0 (0.0-0.0)	17.3 (4.64-35.1)	0.2 (0.1-0.5)
<i>Acinetobacter baumannii</i>	Carbapenem	326 (192-504)	4.2 (2.5-6.5)	8,790 (5,380-13,400)	113.6 (69.5-173.5)	57.7 (30.3-102)	0.7 (0.4-1.3)	1,540 (817-2,630)	19.9 (10.6-34.0)
<i>Acinetobacter baumannii</i>	Fluoroquinolones	316 (186-488)	4.1 (2.4-6.3)	8,800 (5,390-13,300)	113.7 (69.7-172.0)	40 (19.8-66.6)	0.5 (0.3-0.9)	1,120 (557-1,880)	14.4 (7.2-24.3)
<i>Acinetobacter baumannii</i>	Fourth-generation cephalosporins	360 (212-554)	4.7 (2.7-7.2)	9,880 (6,090-15,000)	127.7 (78.7-194.4)	3.28 (1.36-6.27)	0.0 (0.0-0.1)	79.1 (33.7-150)	1.0 (0.4-1.9)
<i>Acinetobacter baumannii</i>	Third-generation cephalosporins	377 (222-575)	4.9 (2.9-7.4)	10,400 (6,430-15,800)	134.3 (83.1-204.6)	6.86 (2.66-12.9)	0.1 (0.0-0.2)	163 (64.7-306)	2.1 (0.8-4.0)
<i>Acinetobacter baumannii</i>	Resistance to one or more antibiotics	423 (252-647)	5.5 (3.3-8.4)	11,800 (7,290-17,800)	152.3 (94.2-229.8)	132 (75.7-213)	1.7 (1.0-2.8)	3,670 (2,150-5,760)	47.5 (27.8-74.5)
<i>Citrobacter</i> spp.	Aminoglycosides	8.48 (5.23-12.8)	0.1 (0.1-0.2)	384 (234-584)	5.0 (3.0-7.5)	0.411 (0-1)	0.0 (0.0-0.0)	18.6 (0-45.2)	0.2 (0.0-0.6)
<i>Citrobacter</i> spp.	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors	14.1 (8.65-21.7)	0.2 (0.1-0.3)	568 (348-867)	7.3 (4.5-11.2)	2.17 (1-3.78)	0.0 (0.0-0.0)	83.9 (41.8-147)	1.1 (0.5-1.9)
<i>Citrobacter</i> spp.	Carbapenem	10.4 (6.18-16.1)	0.1 (0.1-0.2)	404 (242-621)	5.2 (3.1-8.0)	2.3 (1.15-4)	0.0 (0.0-0.1)	87.5 (44.1-151)	1.1 (0.6-1.9)
<i>Citrobacter</i> spp.	Fluoroquinolones	17.9 (10.9-27.3)	0.2 (0.1-0.4)	734 (451-1,110)	9.5 (5.8-14.4)	2.51 (1.12-4.58)	0.0 (0.0-0.1)	102 (46.4-191)	1.3 (0.6-2.5)
<i>Citrobacter</i> spp.	Fourth-generation cephalosporins	18.7 (11.4-28.4)	0.2 (0.1-0.4)	821 (498-1,260)	10.6 (6.4-16.2)	1.34 (0.577-2.53)	0.0 (0.0-0.0)	60.7 (27-109)	0.8 (0.3-1.4)
<i>Citrobacter</i> spp.	Third-generation cephalosporins	28.1 (17.3-43)	0.4 (0.2-0.6)	1,120 (689-1,700)	14.5 (8.9-21.9)	1.84 (0.762-3.38)	0.0 (0.0-0.0)	63.4 (26-115)	0.8 (0.3-1.5)
<i>Citrobacter</i> spp.	Resistance to one or more antibiotics	35.5 (21.7-52.9)	0.5 (0.3-0.7)	1,400 (861-2,110)	18.1 (11.1-27.2)	10.6 (5.93-17.3)	0.1 (0.1-0.2)	416 (237-668)	5.4 (3.1-8.6)
<i>Enterobacter</i> spp.	Aminoglycosides	51.6 (34.9-73.6)	0.7 (0.5-1.0)	2,310 (1,600-3,280)	29.9 (20.7-42.3)	3 (0.879-5.87)	0.0 (0.0-0.1)	135 (40.2-253)	1.7 (0.5-3.3)
<i>Enterobacter</i> spp.	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors	99.2 (65.3-142)	1.3 (0.8-1.8)	3,640 (2,460-5,230)	47.0 (31.8-67.6)	9.95 (5.61-15.9)	0.1 (0.1-0.2)	337 (190-532)	4.4 (2.5-6.9)
<i>Enterobacter</i> spp.	Carbapenem	61.6 (40-90.1)	0.8 (0.5-1.2)	2,340 (1,550-3,350)	30.2 (20.1-43.3)	15.3 (8.87-24.2)	0.2 (0.1-0.3)	568 (334-884)	7.3 (4.3-11.4)
<i>Enterobacter</i> spp.	Fluoroquinolones	74.7 (49.2-107)	1.0 (0.6-1.4)	3,150 (2,160-4,560)	40.6 (27.9-59.0)	7.8 (4.15-13.2)	0.1 (0.1-0.2)	319 (176-544)	4.1 (2.3-7.0)
<i>Enterobacter</i> spp.	Fourth-generation cephalosporins	112 (74.5-159)	1.4 (1.0-2.1)	4,730 (3,270-6,720)	61.1 (42.2-86.9)	5.32 (2.66-9.29)	0.1 (0.0-0.1)	238 (119-412)	3.1 (1.5-5.3)
<i>Enterobacter</i> spp.	Trimethoprim-Sulfamethoxazole	87.5 (57.6-125)	1.1 (0.7-1.6)	3,580 (2,470-4,960)	46.3 (31.9-64.1)	4.65 (0-9.8)	0.1 (0.0-0.1)	180 (0-377)	2.3 (0.0-4.9)
<i>Enterobacter</i> spp.	Resistance to one or more antibiotics	185 (122-264)	2.4 (1.6-3.4)	7,070 (4,830-10,000)	91.4 (62.4-129.8)	46.1 (29.6-67.1)	0.6 (0.4-0.9)	1,780 (1,160-2,580)	23.0 (15.1-33.4)
<i>Enterococcus faecalis</i>	Fluoroquinolones	109 (66.6-162)	1.4 (0.9-2.1)	3,780 (2,460-5,450)	48.9 (31.8-70.5)	26.8 (12.4-47.3)	0.3 (0.2-0.6)	930 (455-1,560)	12.0 (5.9-20.2)
<i>Enterococcus faecalis</i>	Vancomycin	12.1 (7.25-19.6)	0.2 (0.1-0.3)	403 (253-611)	5.2 (3.3-7.9)	3.42 (1.46-6.48)	0.0 (0.0-0.1)	111 (48.2-209)	1.4 (0.6-2.7)
<i>Enterococcus faecalis</i>	Resistance to one or more antibiotics	112 (69.2-167)	1.4 (0.9-2.2)	3,880 (2,540-5,610)	50.2 (32.8-72.5)	30.2 (15.5-51.2)	0.4 (0.2-0.7)	1,040 (545-1,700)	13.4 (7.0-22.0)
<i>Enterococcus faecium</i>	Fluoroquinolones	198 (122-300)	2.6 (1.6-3.9)	5,390 (3,290-8,340)	69.6 (42.5-107.8)	37.2 (11-70.7)	0.5 (0.1-0.9)	1,020 (303-1,930)	13.1 (3.9-25.0)
<i>Enterococcus faecium</i>	Vancomycin	59.9 (37.3-92.1)	0.8 (0.5-1.2)	1,610 (990-2,490)	20.8 (12.8-32.2)	14.3 (7.19-24.7)	0.2 (0.1-0.3)	384 (192-667)	5.0 (2.5-8.6)
<i>Enterococcus faecium</i>	Resistance to one or more antibiotics	200 (123-303)	2.6 (1.6-3.9)	5,440 (3,320-8,420)	70.3 (42.9-108.8)	51.5 (27.1-87.7)	0.7 (0.4-1.1)	1,400 (734-2,400)	18.1 (9.5-31.1)
Other enterococci	Fluoroquinolones	65.2 (42.8-96)	0.8 (0.6-1.2)	2,110 (1,380-3,120)	27.2 (17.9-40.3)	12.2 (1.87-24)	0.2 (0.0-0.3)	398 (63.9-782)	5.1 (0.8-10.1)
Other enterococci	Vancomycin	11.8 (7.62-17.1)	0.2 (0.1-0.2)	301 (196-444)	3.9 (2.5-5.7)	2.22 (1.19-3.94)	0.0 (0.0-0.1)	56.5 (30.3-100)	0.7 (0.4-1.3)
Other enterococci	Resistance to one or more antibiotics	67.1 (44-98.4)	0.9 (0.6-1.3)	2,150 (1,410-3,170)	27.7 (18.3-41.0)	14.5 (4.9-26.5)	0.2 (0.1-0.3)	454 (144-841)	5.9 (1.9-10.9)
<i>Escherichia coli</i>	Aminoglycosides	200 (146-266)	2.6 (1.9-3.4)	7,560 (5,700-9,860)	97.7 (73.7-127.4)	11.7 (7.65-16.5)	0.2 (0.1-0.2)	437 (291-612)	5.6 (3.8-7.9)
<i>Escherichia coli</i>	Aminopenicillin	764 (554-1,030)	9.9 (7.2-13.3)	26,000 (19,600-34,200)	336.6 (253.3-442.0)	10.5 (6.94-15.1)	0.1 (0.1-0.2)	298 (201-416)	3.9 (2.6-5.4)
<i>Escherichia coli</i>	Beta Lactam/Beta-lactamase inhibitors	586 (425-788)	7.6 (5.5-10.2)	20,400 (15,400-26,800)	263.2 (198.6-346.1)	21.3 (14.7-30)	0.3 (0.2-0.4)	634 (452-873)	8.2 (5.8-11.3)
<i>Escherichia coli</i>	Carbapenem	140 (102-188)	1.8 (1.3-2.4)	5,270 (3,930-6,980)	68.1 (50.8-90.1)	29.5 (17.1-45)	0.4 (0.2-0.6)	1,090 (640-1,670)	14.1 (8.3-21.5)
<i>Escherichia coli</i>	Fluoroquinolones	532 (384-708)	6.9 (5.0-9.1)	18,400 (13,900-24,100)	238.0 (179.1-311.4)	56 (38.5-78.7)	0.7 (0.5-1.0)	1,890 (1,310-2,580)	24.4 (16.9-33.3)
<i>Escherichia coli</i>	Third-generation cephalosporins	499 (362-673)	6.5 (4.7-8.7)	17,900 (13,400-23,800)	231.2 (173.4-307.2)	59.9 (26.3-109)	0.8 (0.3-1.4)	2,080 (947-3,660)	26.9 (12.2-47.2)
<i>Escherichia coli</i>	Trimethoprim-Sulfamethoxazole	536 (390-713)	6.9 (5.0-9.2)	19,500 (14,700-25,500)	251.8 (190.2-329.9)	30.2 (20.2-42.8)	0.4 (0.3-0.6)	1,080 (718-1,520)	14.0 (9.3-19.6)
<i>Escherichia coli</i>	Resistance to one or more antibiotics	829 (601-1,120)	10.7 (7.8-14.4)	28,000 (21,000-36,900)	362.2 (272.0-476.8)	219 (152-316)	2.8 (2.0-4.1)	7,520 (5,270-10,500)	97.1 (68.2-136.2)
Group A <i>Streptococcus</i>	Macrolide	39 (18.3-77.1)	0.5 (0.2-1.0)	1,170 (653-2,090)	15.1 (8.4-27.0)	3.63 (0-13.9)	0.0 (0.0-0.2)	108 (0-376)	1.4 (0.0-4.9)
Group A <i>Streptococcus</i>	Resistance to one or more antibiotics	39 (18.3-77.1)	0.5 (0.2-1.0)	1,170 (653-2,090)	15.1 (8.4-27.0)	3.63 (0-13.9)	0.0 (0.0-0.2)	108 (0-376)	1.4 (0.0-4.9)
Group B <i>Streptococcus</i>	Fluoroquinolones	67.5 (49-91)	0.9 (0.6-1.2)	4,240 (3,070-5,750)	54.8 (39.6-74.4)	11.5 (1.92-24.9)	0.1 (0.0-0.3)	723 (125-1,580)	9.3 (1.6-20.9)
Group B <i>Streptococcus</i>	Macrolide	142 (102-193)	1.8 (1.3-2.5)	7,230 (5,230-9,740)	93.4 (67.6-125.9)	13.5 (0-36.3)	0.2 (0.0-0.5)	672 (0-1,780)	8.7 (0.0-23.0)
Group B <i>Streptococcus</i>	Penicillin	3.74 (2.59-5.25)	0.0 (0.0-0.1)	203 (141-281)	2.6 (1.8-3.6)	0.799 (0.165-1.7)	0.0 (0.0-0.0)	42.9 (8.52-91.5)	0.6 (0.1-1.2)
Group B <i>Streptococcus</i>	Resistance to one or more antibiotics	173 (125-232)	2.2 (1.6-3.0)	9,190 (6,770-12,300)	118.8 (87.5-158.4)	25.8 (3.92-51.8)	0.3 (0.1-0.7)	1,440 (281-2,780)	18.2 (3.6-36.0)
<i>Haemophilus influenzae</i>	Aminopenicillin	27.4 (21.8-34.2)	0.4 (0.3-0.4)	1,450 (1,120-1,840)	18.7 (14.4-23.8)	4.29 (0.393-8.3)	0.1 (0.0-0.1)	218 (21.5-431)	2.8 (0.3-5.6)
<i>Haemophilus influenzae</i>	Third-generation cephalosporins	8.57 (6.41-11.1)	0.1 (0.1-0.1)	560 (413-738)	7.2 (5.3-9.5)	2.47 (1.14-4.16)	0.0 (0.0-0.1)	161 (71.7-272)	2.1 (0.9-3.5)
<i>Haemophilus influenzae</i>	Resistance to one or more antibiotics	31.5 (25.5-39)	0.4 (0.3-0.5)	1,720 (1,340-2,180)	22.3 (17.4-28.2)	6.76 (2.63-11.3)	0.1 (0.0-0.1)	379 (156-619)	4.9 (2.0-8.0)
<i>Klebsiella pneumoniae</i>	Aminoglycosides	345 (254-463)	4.5 (3.3-6.0)	16,500 (12,400-21,600)	213.5 (160.2-279.4)	26.3 (16.2-38.9)	0.3 (0.2-0.5)	1,230 (773-1,780)	16.0 (10.0-23.0)
<i>Klebsiella pneumoniae</i>	Beta Lactam/Beta-lactamase inhibitors	545 (396-725)	7.0 (5.1-9.4)	24,100 (17,900-31,700)	311.4 (232.0-409.8)	7.93 (4.59-12.1)	0.1 (0.1-0.2)	316 (182-478)	4.1 (2.3-6.2)
<i>Klebsiella pneumoniae</i>	Carbapenem	234 (164-332)	3.0 (2.1-4.3)	9,280 (6,640-12,800)	119.9 (85.9-165.6)	55.7 (36.3-81.3)	0.7 (0.5-1.1)	2,170 (1,430-3,120)	28.0 (18.5-40.3)
<i>Klebsiella pneumoniae</i>	Fluoroquinolones	426 (312-576)	5.5 (4.0-7.4)	18,900 (14,100-24,900)	244.3 (181.8-322.1)	29 (17.4-44.1)	0.4 (0.2-0.6)	1,260 (761-1,880)	16.2 (9.8-24.3)
<i>Klebsiella pneumoniae</i>	Third-generation cephalosporins	526 (384-717)	6.8 (5.0-9.3)	22,900 (17,100-30,100)	296.4 (221.4-388.9)	50.1 (19-94.4)	0.6 (0.2-1.2)	2,210 (836-4,070)	28.6 (10.8-52.6)
<i>Klebsiella pneumoniae</i>	Trimethoprim-Sulfamethoxazole	488 (356-653)	6.3 (4.6-8.4)	21,900 (16,300-28,800)	282.4 (211.3-372.3)	23.5 (11.5-39.7)	0.3 (0.1-0.5)	1,010 (494-1,660)	13.1 (6.4-21.5)
<i>Klebsiella pneumoniae</i>	Resistance to one or more antibiotics	642 (465-863)	8.3 (6.0-11.2)	27,400 (20,300-36,100)	354.5 (261.8-466.0)	193 (130-272)	2.5 (1.7-3.5)	8,200 (5,550-11,400)	106.0 (71.8-147.5)
<i>Morganella</i> spp.	Fluoroquinolones	2.59 (1.64-3.94)	0.0 (0.0-0.1)	56.7 (36.4-85.8)	0.7 (0.5-1.1)	0.427 (0.174-0.78)	0.0 (0.0-0.0)	9.21 (3.76-16.8)	0.1 (0.0-0.2)
<i>Morganella</i> spp.	Fourth-generation cephalosporins	1 (0.621-1.55)	0.0 (0.0-0.0)	23.7 (14.7-36.2)	0.3 (0.2-0.5)	0.154 (0-0.321)	0.0 (0.0-0.0)	3.5 (1.14-7.23)	0.0 (0.0-0.1)
<i>Morganella</i> spp.	Third-generation cephalosporins	1.45 (0.907-2.19)	0.0 (0.0-0.0)	30.2 (19-45.6)	0.4 (0.2-0.6)	0.168 (0-0.342)	0.0 (0.0-0.0)	3.2 (1.28-6.52)	0.0 (0.0-0.1)
<i>Morganella</i> spp.	Resistance to one or more antibiotics	3 (1.93-4.59)	0.0 (0.0-0.1)	64.7 (41.5-98)	0.8 (0.5-1.3)	0.749 (0.394-1.27)	0.0 (0.0-0.0)	15.9 (8.56-27)	0.2 (0.1-0.3)
<i>Mycobacterium tuberculosis</i>	Extensive drug resistance in TB	8.5 (4-15.2)	0.1 (0.1-0.2)	311 (151-553)	4.0 (1.9-7.1)	5.21 (2.48-9.31)	0.1 (0.0-0.1)	181 (88.4-319)	2.3 (1.1-4.1)
<i>Mycobacterium tuberculosis</i>	Isoniazid mono-resistance	73.8 (50.7-103)	1.0 (0.7-1.3)	2,880 (2,040-3,930)	37.2 (26.4-50.7)	11.6 (0-40.2)	0.2 (0.0-0.5)	419 (0-1,410)	5.4 (0.0-18.3)
<i>Mycobacterium tuberculosis</i>	Multi-drug resistance excluding extensive drug resistance in TB	110 (43.6-210)	1.4 (0.6-2.7)	4,210 (1,740-7,990)	54.5 (22.5-103.3)	64.6 (6.6-160)	0.8 (0.1-2.1)	2,320 (225-5,660)	30.0 (2.9-73.2)
<i>Mycobacterium tuberculosis</i>	Rifampicin mono-resistance	12 (8.85-15.6)	0.2 (0.1-0.2)	494 (368-644)	6.4 (4.8-8.3)	3.35 (0.569-6.54)	0.0 (0.0-0.1)	130 (26.6-249)	1.7 (0.3-3.2)
<i>Mycobacterium tuberculosis</i>	Resistance to one or more antibiotics	204 (134-303)	2.6 (1.7-3.9)	7,900 (5,260-11,600)	102.0 (68.0-149.9)	84.8 (18			

<i>Salmonella Paratyphi</i>	Resistance to one or more antibiotics	20.2 (8.54-39.1)	0.3 (0.1-0.5)	1,420 (588-2,760)	18.3 (7.6-35.7)	4.11 (0.677-10.3)	0.1 (0.0-0.1)	287 (47.2-718)	3.7 (0.6-9.3)
<i>Salmonella Typhi</i>	Fluoroquinolones	90.6 (54.1-143)	1.2 (0.7-1.9)	6,570 (3,880-10,600)	84.9 (50.2-136.7)	17.2 (2.96-39.1)	0.2 (0.0-0.5)	1,240 (213-2,810)	16.0 (2.8-36.3)
<i>Salmonella Typhi</i>	Multi-drug resistance in <i>Salmonella Typhi</i> and <i>Paratyphi</i>	58.3 (38.2-84.2)	0.8 (0.5-1.1)	4,400 (2,860-6,410)	56.9 (37.0-82.8)	6.46 (0-16.5)	0.1 (0.0-0.2)	488 (0-1,240)	6.3 (0.0-16.0)
<i>Salmonella Typhi</i>	Resistance to one or more antibiotics	127 (80.9-193)	1.6 (1.0-2.5)	9,350 (5,890-14,200)	120.8 (76.1-183.9)	23.7 (7.55-47.2)	0.3 (0.1-0.6)	1,720 (536-3,400)	22.3 (6.9-43.9)
Non-typhoidal <i>Salmonella</i>	Fluoroquinolones	27.1 (14-46.8)	0.4 (0.2-0.6)	1,390 (717-2,450)	18.0 (9.3-31.7)	5.62 (0.809-13.1)	0.1 (0.0-0.2)	264 (46.3-597)	3.4 (0.6-7.7)
Non-typhoidal <i>Salmonella</i>	Resistance to one or more antibiotics	27.1 (14-46.8)	0.4 (0.2-0.6)	1,390 (717-2,450)	18.0 (9.3-31.7)	5.62 (0.809-13.1)	0.1 (0.0-0.2)	264 (46.3-597)	3.4 (0.6-7.7)
<i>Serratia</i> spp.	Aminoglycosides	16.5 (10.4-25)	0.2 (0.1-0.3)	830 (531-1,260)	10.7 (6.9-16.2)	0.953 (0-2.52)	0.0 (0.0-0.0)	48.1 (0-128)	0.6 (0.0-1.6)
<i>Serratia</i> spp.	Anti-pseudomonal penicillin/Beta-Lactamase inhibitors	13.7 (8.41-21.3)	0.2 (0.1-0.3)	567 (357-871)	7.3 (4.6-11.3)	2.48 (1.21-4.34)	0.0 (0.0-0.1)	103 (51.3-181)	1.3 (0.7-2.3)
<i>Serratia</i> spp.	Carbapenem	8.99 (5.35-14.3)	0.1 (0.1-0.2)	342 (211-524)	4.4 (2.7-6.8)	2.45 (1.23-4.35)	0.0 (0.0-0.1)	93.1 (47.9-164)	1.2 (0.6-2.1)
<i>Serratia</i> spp.	Fluoroquinolones	10.4 (6.55-16.1)	0.1 (0.1-0.2)	477 (308-736)	6.2 (4.0-9.5)	1 (0.224-2.31)	0.0 (0.0-0.0)	49.1 (9.48-109)	0.6 (0.1-1.4)
<i>Serratia</i> spp.	Fourth-generation cephalosporins	23.8 (14.9-36.6)	0.3 (0.2-0.5)	1,180 (764-1,820)	15.3 (9.9-23.5)	2.61 (1.12-4.9)	0.0 (0.0-0.1)	140 (59.8-254)	1.8 (0.8-3.3)
<i>Serratia</i> spp.	Third-generation cephalosporins	25.1 (16-38.1)	0.3 (0.2-0.5)	1,150 (736-1,710)	14.8 (9.5-22.1)	1.1 (0.403-2.13)	0.0 (0.0-0.0)	44.6 (16.9-85)	0.6 (0.2-1.1)
<i>Serratia</i> spp.	Resistance to one or more antibiotics	42.7 (27-65.3)	0.6 (0.3-0.8)	1,930 (1,260-2,900)	24.9 (16.3-37.5)	10.7 (6.11-17.5)	0.1 (0.1-0.2)	478 (274-760)	6.2 (3.5-9.8)
<i>Shigella</i> spp.	Fluoroquinolones	29.1 (11.8-57.7)	0.4 (0.2-0.7)	1,650 (705-3,070)	21.3 (9.1-39.7)	5.99 (0.689-15.4)	0.1 (0.0-0.2)	330 (48-803)	4.3 (0.6-10.4)
<i>Shigella</i> spp.	Resistance to one or more antibiotics	29.1 (11.8-57.7)	0.4 (0.2-0.7)	1,650 (705-3,070)	21.3 (9.1-39.7)	5.99 (0.689-15.4)	0.1 (0.0-0.2)	330 (48-803)	4.3 (0.6-10.4)
<i>Staphylococcus aureus</i>	Fluoroquinolones	366 (266-494)	4.7 (3.4-6.4)	11,800 (8,680-15,800)	152.8 (112.2-203.6)	15.9 (7-27.5)	0.2 (0.1-0.4)	501 (226-853)	6.5 (2.9-11.0)
<i>Staphylococcus aureus</i>	Macrolide	522 (380-704)	6.7 (4.9-9.1)	16,600 (12,300-22,000)	214.5 (158.9-284.3)	19.6 (7.78-35)	0.3 (0.1-0.5)	603 (245-1,050)	7.8 (3.2-13.5)
<i>Staphylococcus aureus</i>	Methicillin	473 (344-642)	6.1 (4.5-8.3)	15,200 (11,100-20,500)	195.9 (143.8-264.6)	121 (53.2-207)	1.6 (0.7-2.7)	3,790 (1,650-6,390)	48.9 (21.3-82.5)
<i>Staphylococcus aureus</i>	Trimethoprim-Sulfamethoxazole	201 (154-262)	2.6 (2.0-3.4)	9,310 (7,190-11,900)	120.3 (92.9-154.1)	18.7 (9.75-28.7)	0.2 (0.1-0.4)	878 (463-1,340)	11.3 (6.0-17.3)
<i>Staphylococcus aureus</i>	Vancomycin	10.3 (7.35-14.6)	0.1 (0.1-0.2)	358 (258-500)	4.6 (3.3-6.5)	3.12 (1.61-5.65)	0.0 (0.0-0.1)	103 (53.9-181)	1.3 (0.7-2.3)
<i>Staphylococcus aureus</i>	Resistance to one or more antibiotics	748 (554-1,000)	9.7 (7.2-13.0)	24,900 (18,600-32,700)	321.3 (240.4-423.2)	178 (104-280)	2.3 (1.3-3.6)	5,870 (3,550-9,220)	75.9 (45.9-119.2)
<i>Streptococcus pneumoniae</i>	Beta Lactam/Beta-lactamase inhibitors	107 (82-138)	1.4 (1.1-1.8)	5,430 (4,150-6,960)	70.2 (53.6-89.9)	2.65 (0.054-6.62)	0.0 (0.0-0.1)	114 (1.44-284)	1.5 (0.0-3.7)
<i>Streptococcus pneumoniae</i>	Carbapenem	191 (148-242)	2.5 (1.9-3.1)	9,100 (7,070-11,500)	117.6 (91.3-148.7)	41.9 (20.5-70)	0.5 (0.3-0.9)	1,990 (957-3,310)	25.7 (12.4-42.8)
<i>Streptococcus pneumoniae</i>	Fluoroquinolones	89.8 (70.8-113)	1.2 (0.9-1.5)	5,240 (4,100-6,680)	67.7 (53.0-86.3)	11.2 (2.64-22.3)	0.1 (0.0-0.3)	643 (153-1,280)	8.3 (2.0-16.5)
<i>Streptococcus pneumoniae</i>	Macrolide	313 (252-391)	4.0 (3.3-5.1)	13,300 (10,700-16,700)	172.2 (138.6-216.0)	12.5 (0-32.6)	0.2 (0.0-0.4)	517 (0-1,330)	6.7 (0.0-17.2)
<i>Streptococcus pneumoniae</i>	Penicillin	230 (184-290)	3.0 (2.4-3.8)	11,200 (8,910-14,000)	144.4 (115.1-181.2)	12.4 (6.69-20.3)	0.2 (0.1-0.3)	597 (327-980)	7.7 (4.2-12.7)
<i>Streptococcus pneumoniae</i>	Third-generation cephalosporins	94.2 (72.5-123)	1.2 (0.9-1.6)	4,720 (3,690-6,140)	61.0 (47.6-79.3)	3.33 (1.39-6.21)	0.0 (0.0-0.1)	177 (73.2-336)	2.3 (0.9-4.3)
<i>Streptococcus pneumoniae</i>	Trimethoprim-Sulfamethoxazole	446 (364-548)	5.8 (4.7-7.1)	23,600 (19,100-29,300)	305.3 (247.3-379.2)	38.7 (5.73-77.2)	0.5 (0.1-1.0)	2,070 (298-4,160)	26.8 (3.9-53.8)
<i>Streptococcus pneumoniae</i>	Resistance to one or more antibiotics	596 (490-727)	7.7 (6.3-9.4)	29,800 (24,400-36,700)	385.8 (314.7-473.8)	122 (82.4-166)	1.6 (1.1-2.1)	6,110 (4,050-8,330)	78.9 (52.4-107.7)

Figure S1 Flowchart of antimicrobial resistance fatal and non-fatal estimation steps



Micro w/ diag & outcome = Microbial data with diagnosis and outcome.  
 Micro w/o diag & w/ outcome = Microbial data without diagnosis and with outcome.  
 Micro w/ diag & no outcome = Microbial data with diagnosis and without outcome.  
 Micro w/o diag & no outcome = Microbial data without diagnosis and without outcome. 123  
 Full descriptions of each data type are provided in the appendix section 2.



Figure S2 All-age rate of DALYs attributable to and associated with bacterial antimicrobial resistance by GBD region, 2019

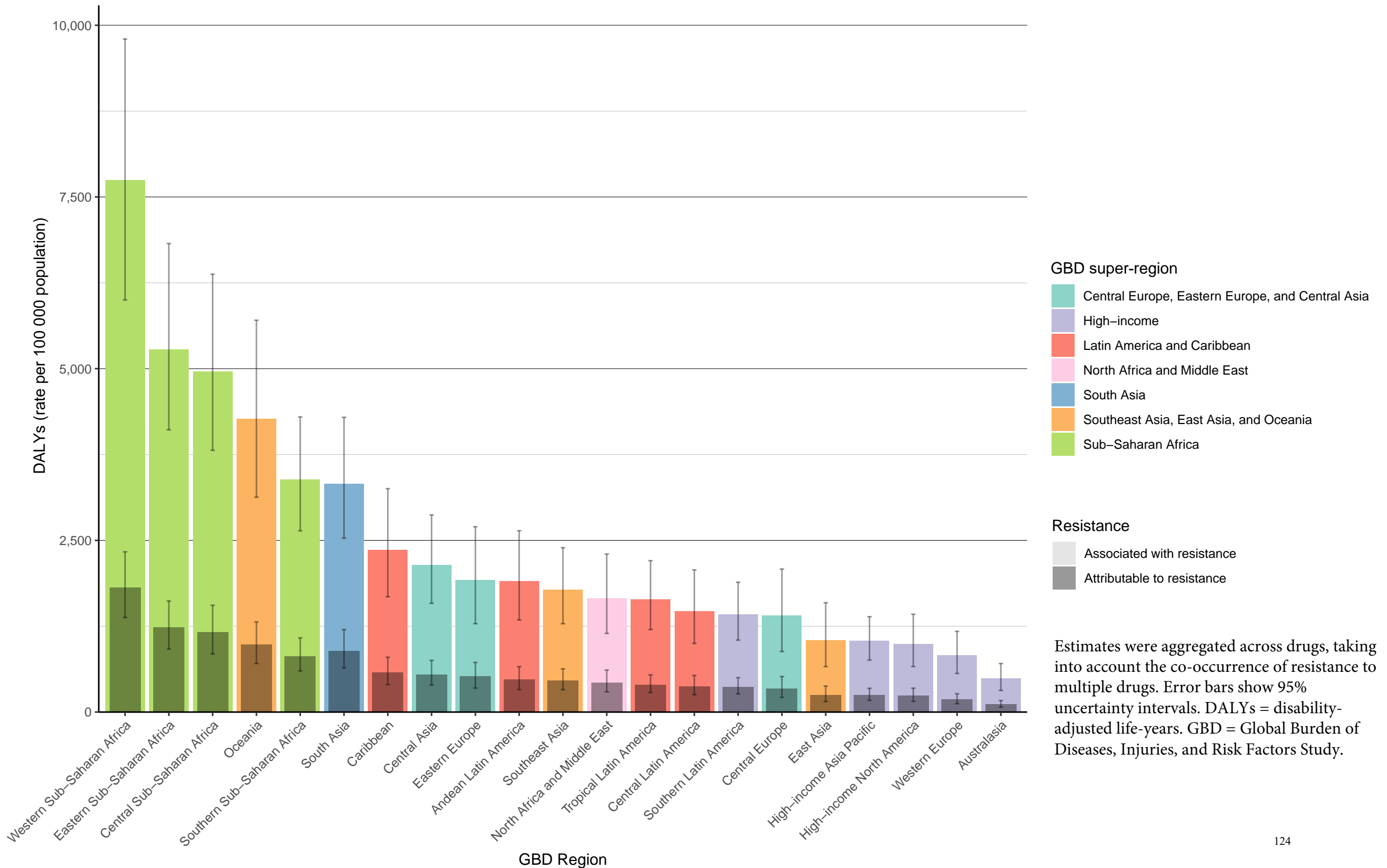


Figure S3 Global DALYs (in counts) attributable to and associated with bacterial antimicrobial resistance by infectious syndrome, 2019

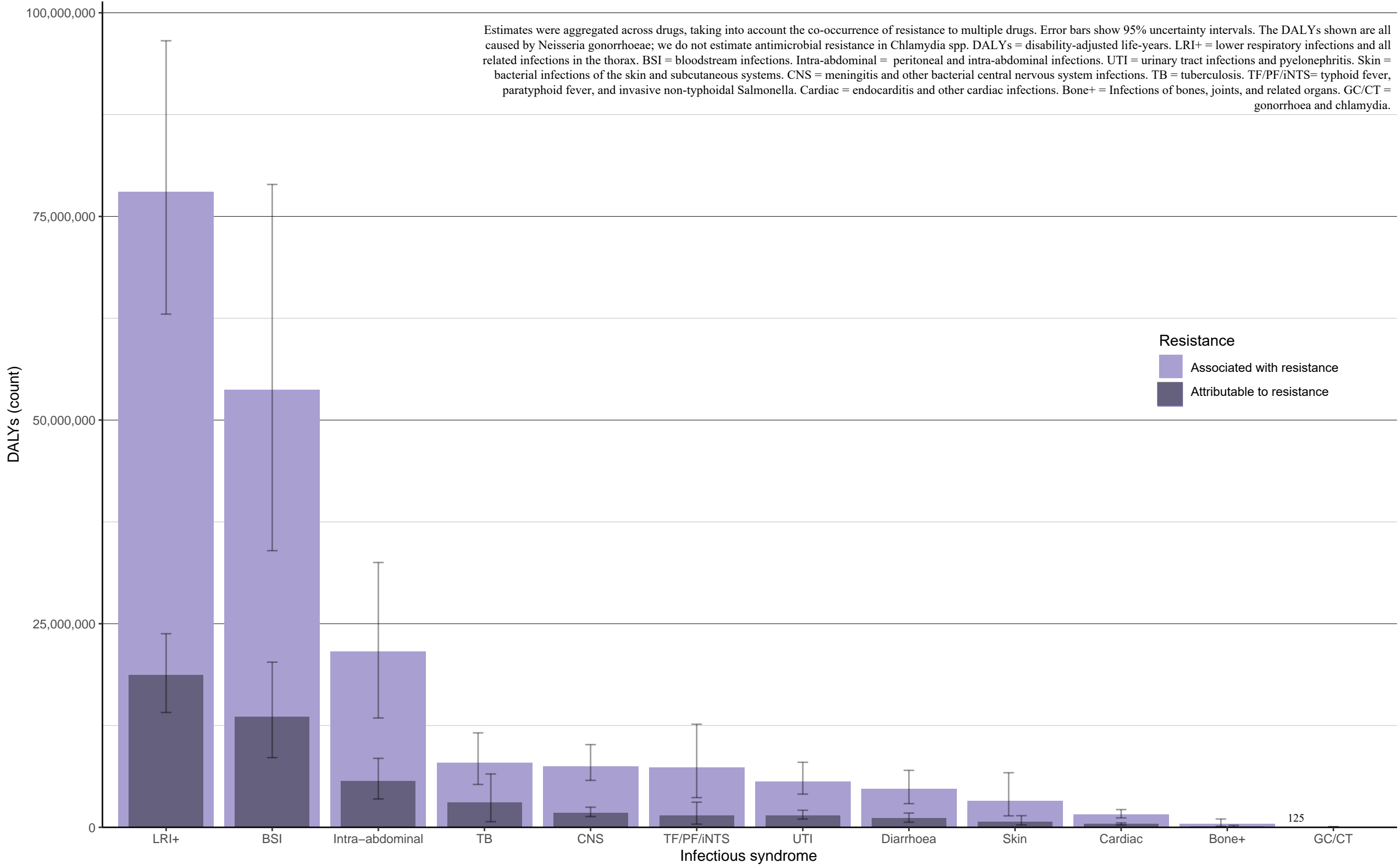


Figure S4 Global DALYs (in counts) attributable to and associated with bacterial antimicrobial resistance by pathogen, 2019

Estimates were aggregated across drugs, taking into account the co-occurrence of resistance to multiple drugs. Error bars show 95% uncertainty intervals. AMR = antimicrobial resistance. DALYs = disability-adjusted life-years.

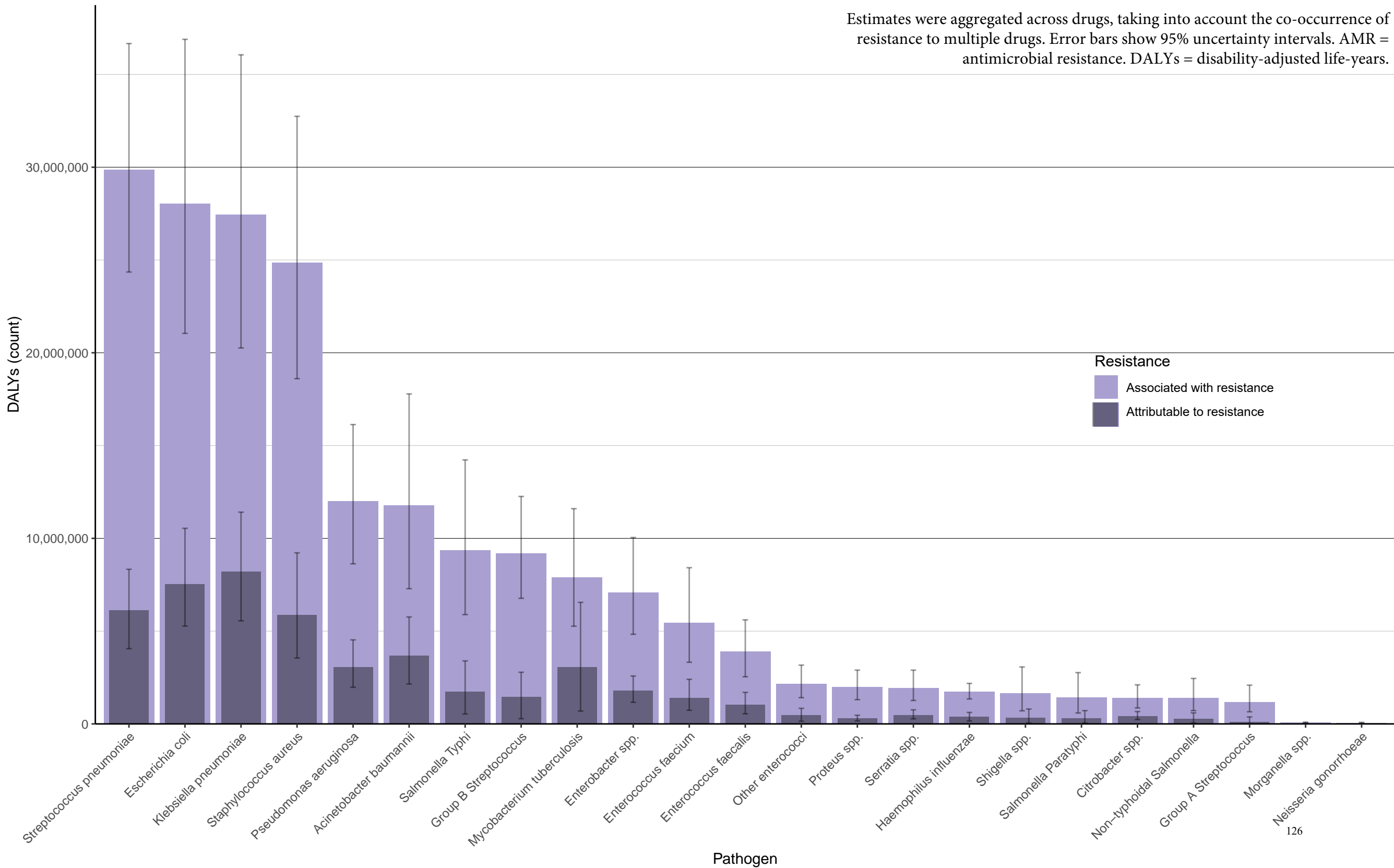


Figure S5A Pathogen-attributable fraction of DALYs attributable to bacterial antimicrobial resistance for the six leading pathogens by GBD super-region, 2019

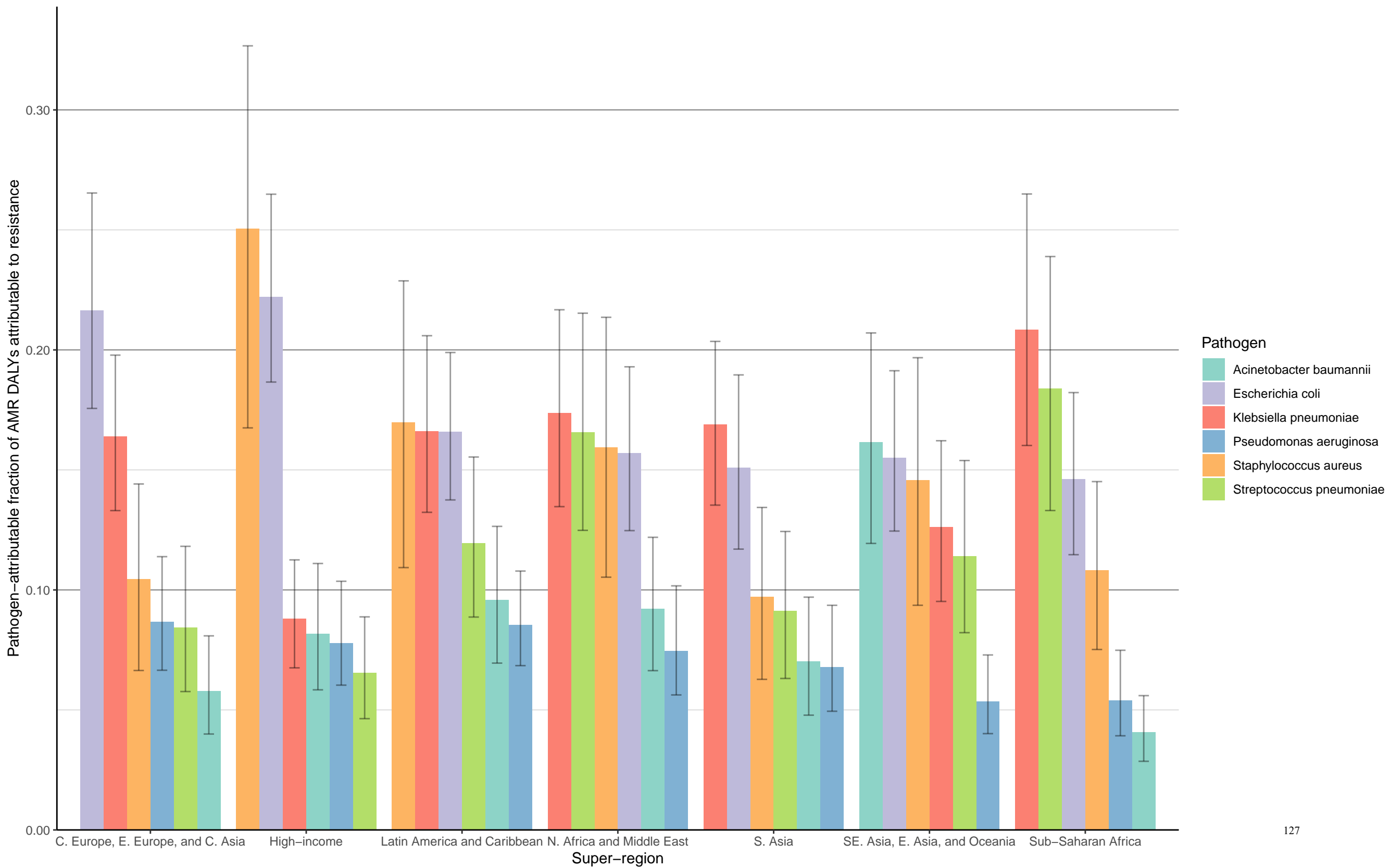
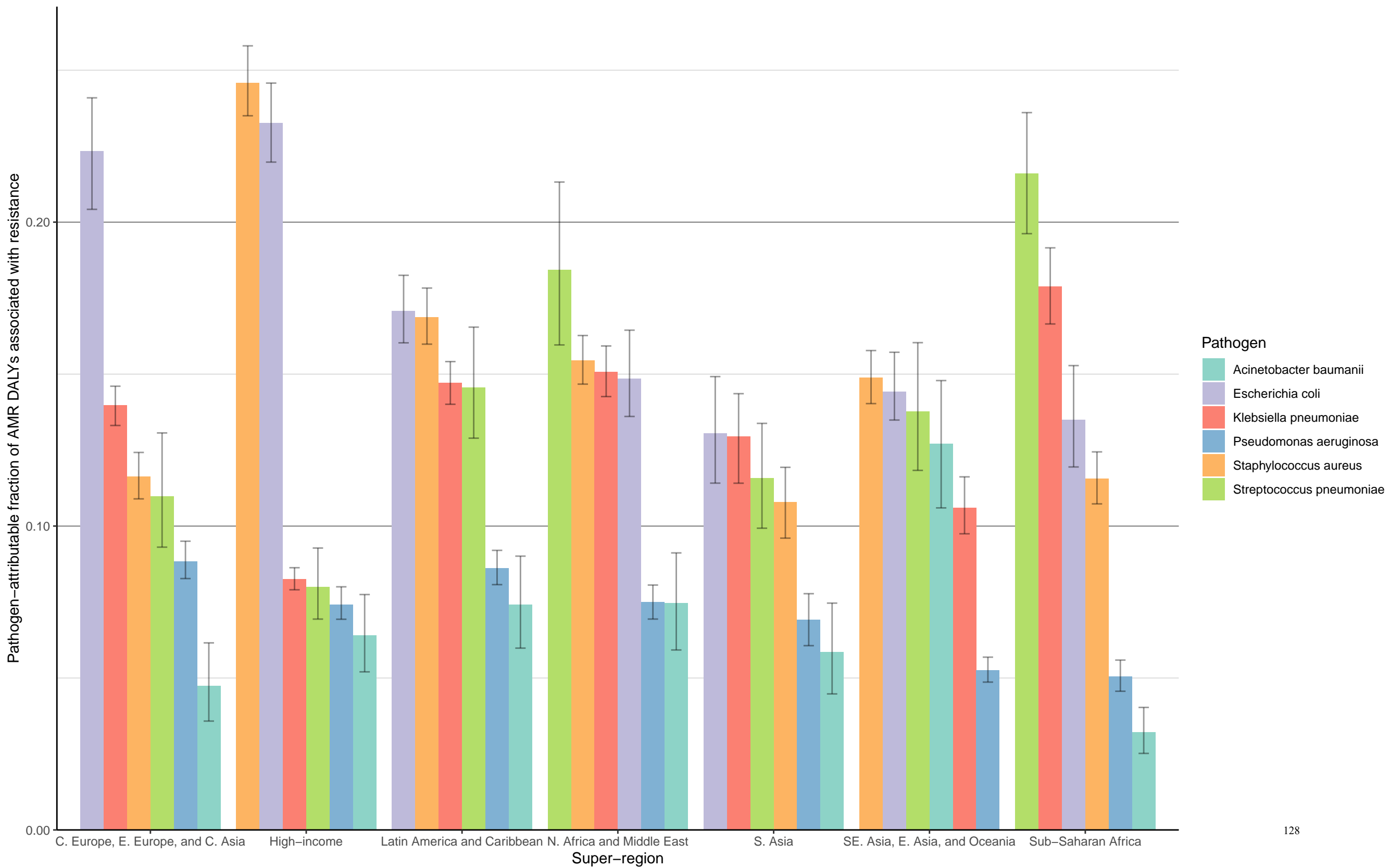
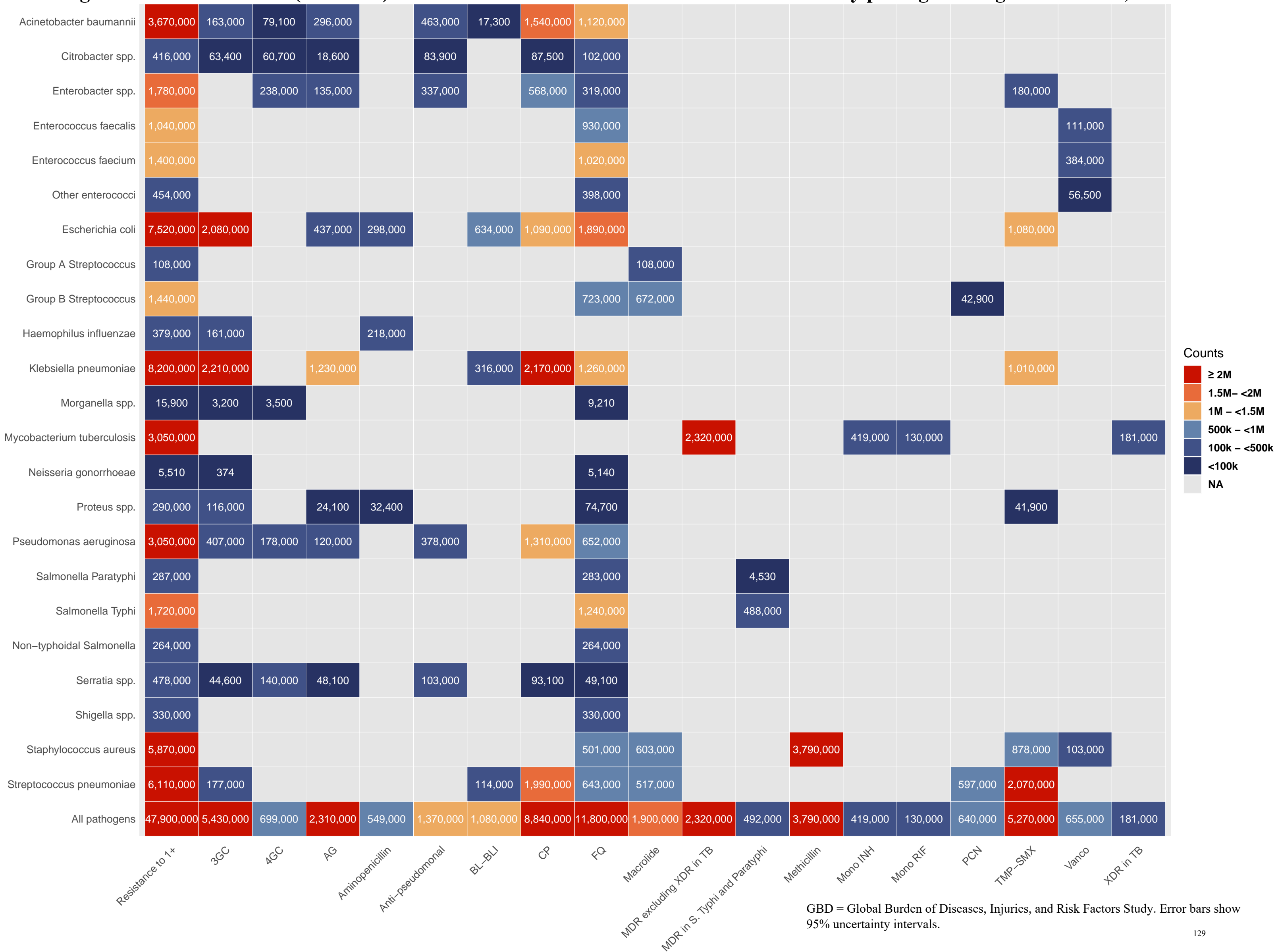


Figure S5B Pathogen-attributable fraction of DALYs associated with bacterial antimicrobial resistance for the six leading pathogens by GBD super-region, 2019



**Figure S6 Global DALYs (in counts) attributable to bacterial antimicrobial resistance by pathogen–drug combination, 2019**



GBD = Global Burden of Diseases, Injuries, and Risk Factors Study. Error bars show 95% uncertainty intervals.

