The way forward: Capacity Building

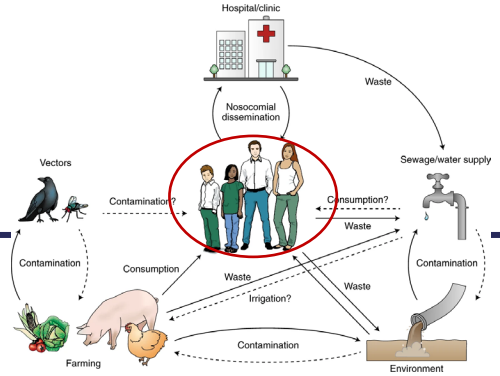
Dr Catrin Moore
St George's University London

CAPTURA Regional Workshop
30th June 2022

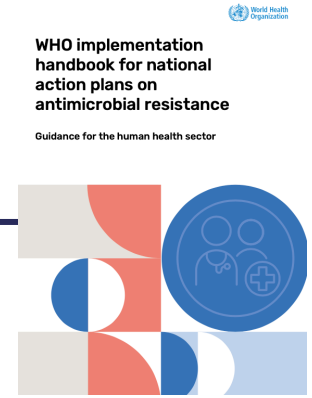
How can we reduce antibiotic resistance (ABR)?

- What is antibiotic resistance?
- What are the drivers that are increasing antibiotic resistance?
- **How many people does ABR kill and where?**
- Does antibiotic use alone drive antibiotic resistance?
- Does human behaviour drive antibiotic resistance?
- What about vaccines to reduce bacterial infections? What do we have and what is in the pipeline?
- We have more political will now, but we need action …
- Limited public awareness of ABR:
    - **Food:** safety controls & regulations, supply chain issues, eating raw/undercooked food, lack of training for farmers, increased demand for meat, intensive farming
    - **Poverty:** overcrowding, sharing habitat with animals, poor sanitation and hygiene, no vaccination (animals/humans), misuse (overuse/lack of access to antibiotics), political drivers, environmental contamination with antibiotics/resistant bacteria, untreated wastewater, animal waste discarded/used as fertilizer
    - **Lack of:** surveillance programmes, laboratory/diagnostic capacity, data on burden/economics, behaviour and use of antibiotics

Background: AMR is a global concern – Political will has increased



Walsh, T.R. A one-health approach to antimicrobial resistance. *Nat Microbiol* **3,** 854–855 (2018). https://doi.org/10.1038/s41564-018-0208-5



2014
UK government commissioned the **O'Neill Review**
Aim: define the economic impact of AMR, raise the profile of AMR and establish global support

2015
- Global Action Plan (**GAP**) Adopted by World Health Assembly for AMR (FAO, OIE, WHO endorsed
- WHO launched the Global Antimicrobial Resistance and Use Surveillance System (**GLASS**) at the World Health Assembly

2016
•AMR resolution at the UN General Assembly – Interagency Coordination Group (IACG) on AMR
•Call for countries to develop and implement national action plans (**NAPs**)
•**Review** on AMR **published**
•Fleming Fund established

2017
IACG was convened

2020
One Health Global Leaders Group is launched

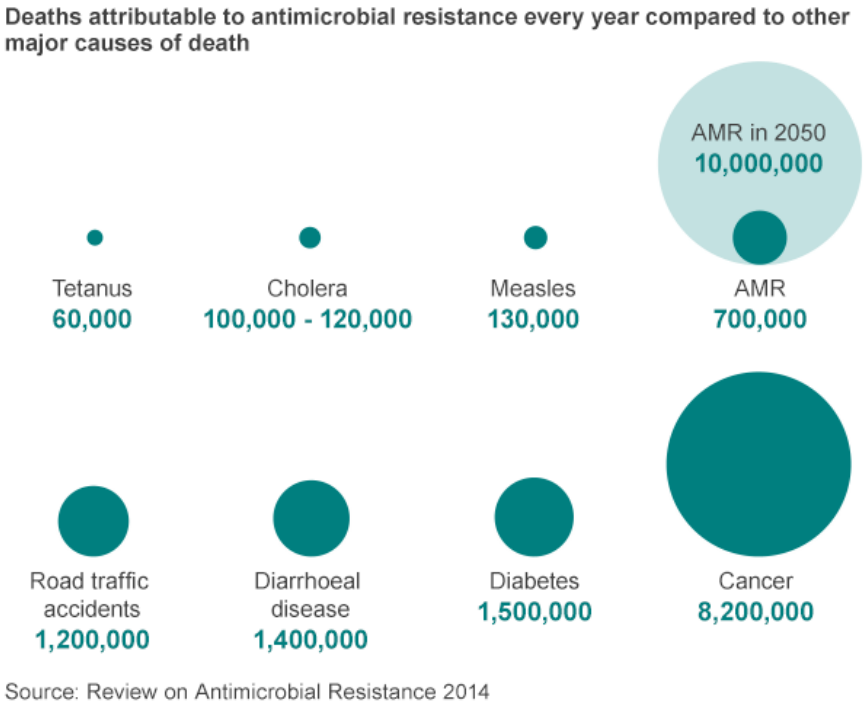
2021
G7/G20 Meetings with AMR on the agenda

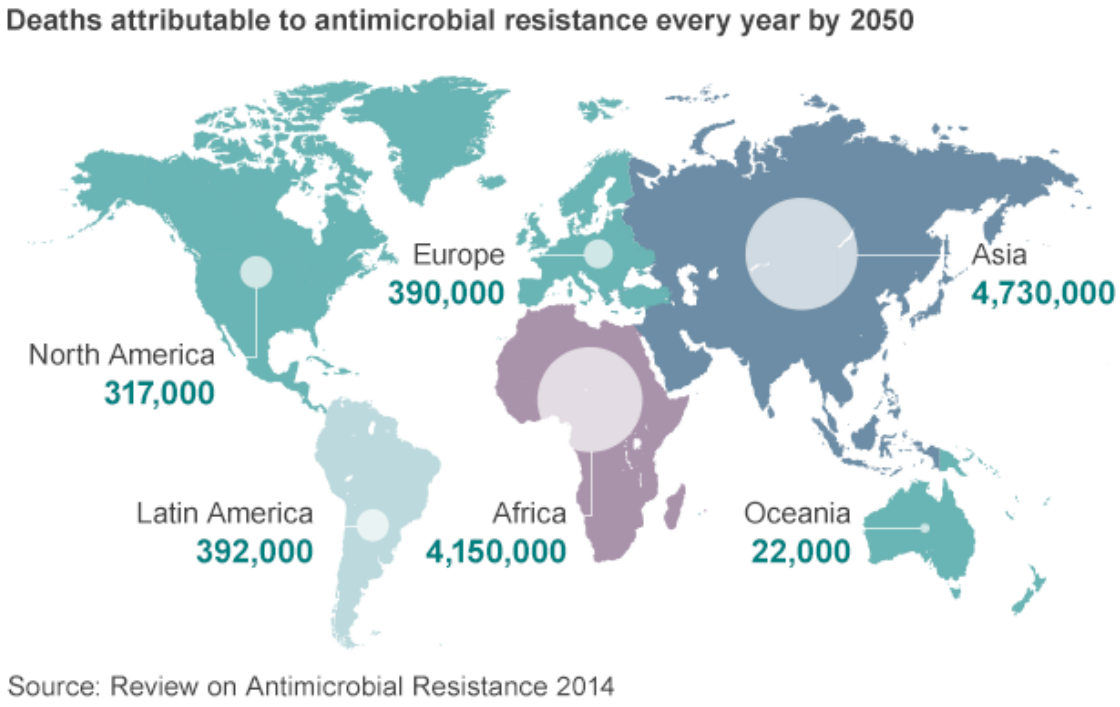
2022
•G7 Health Ministers Communiqué
•UN High Level Meeting on AMR in 2024

3.d.2 = new indicator:
Percentage of bloodstream infections due to selected AMR organisms:
- Methicillin resistant *S. aureus* (MRSA)
- *E. coli* resistant to 3rd generation cephalosporins

What is the **global** burden of AMR?

Were the O'Neill estimates correct?

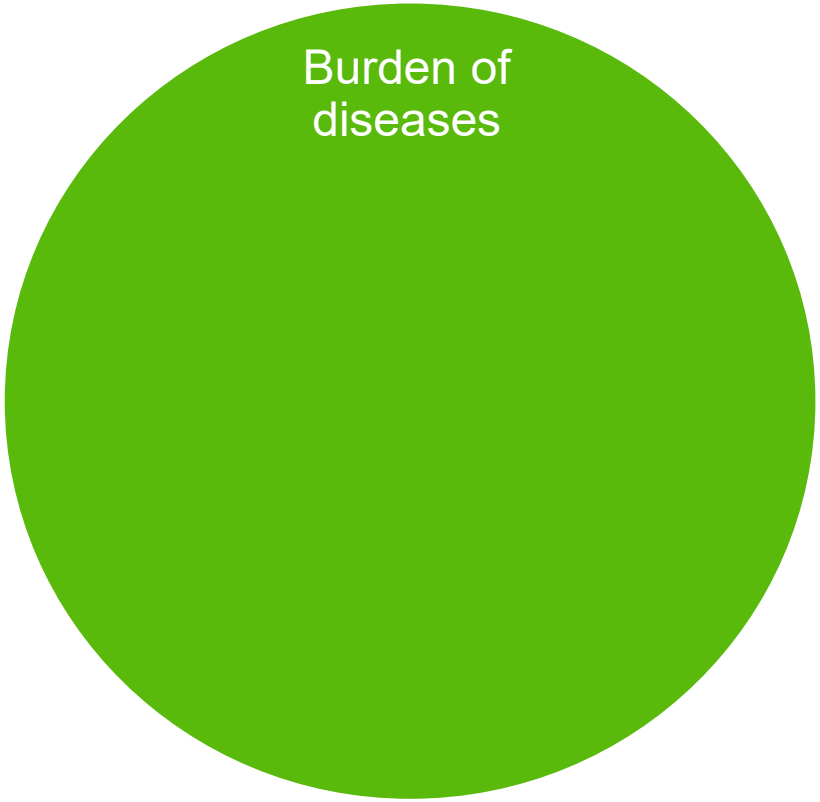




https://www.antibioticresearch.org.uk/superbugs-kill-cancer-2050/

Estimating the burden of AMR

Data input:



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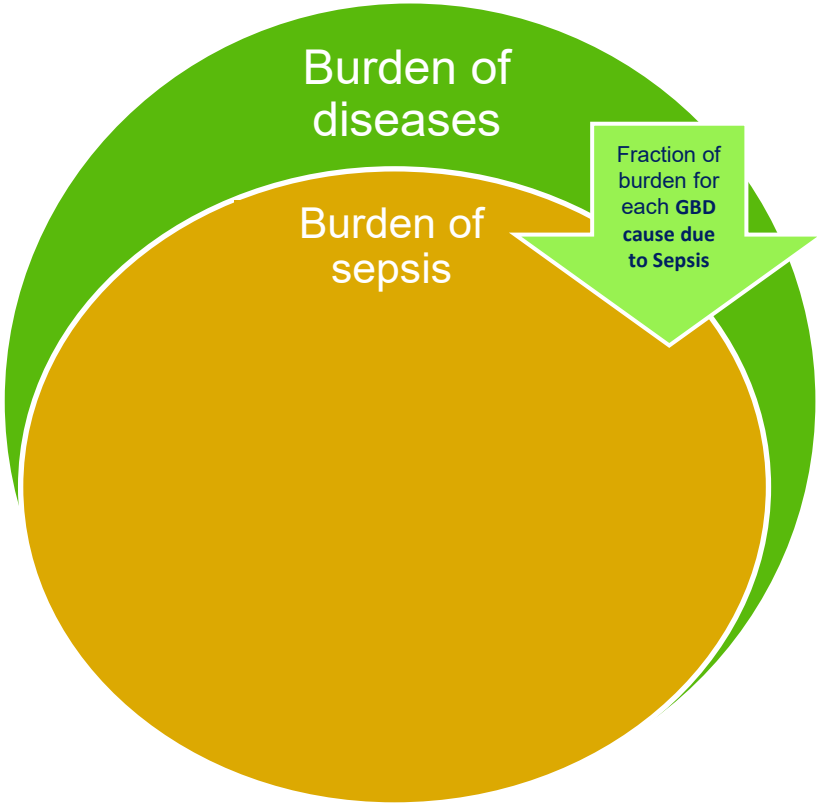
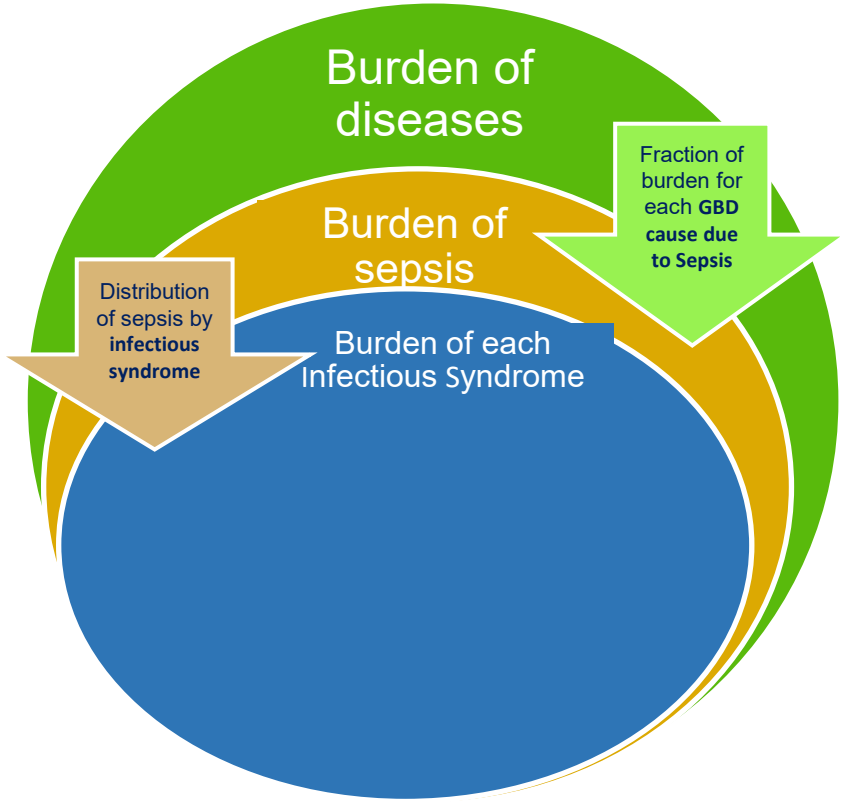


BSI - blood stream infection; CNS – central nervous system; LRI – lower respiratory infection; UTI – urinary tract infection

Estimating the burden of AMR

Data input:

Infectious syndrome	Number of data points
BSI	122,499
CNS (neonatal)	21,717
CNS (post neonatal)	21,672
LRI+	109,967
Intra-abdominal	7,143
Skin	1,065
UTI	24,528
Bone+	1,623



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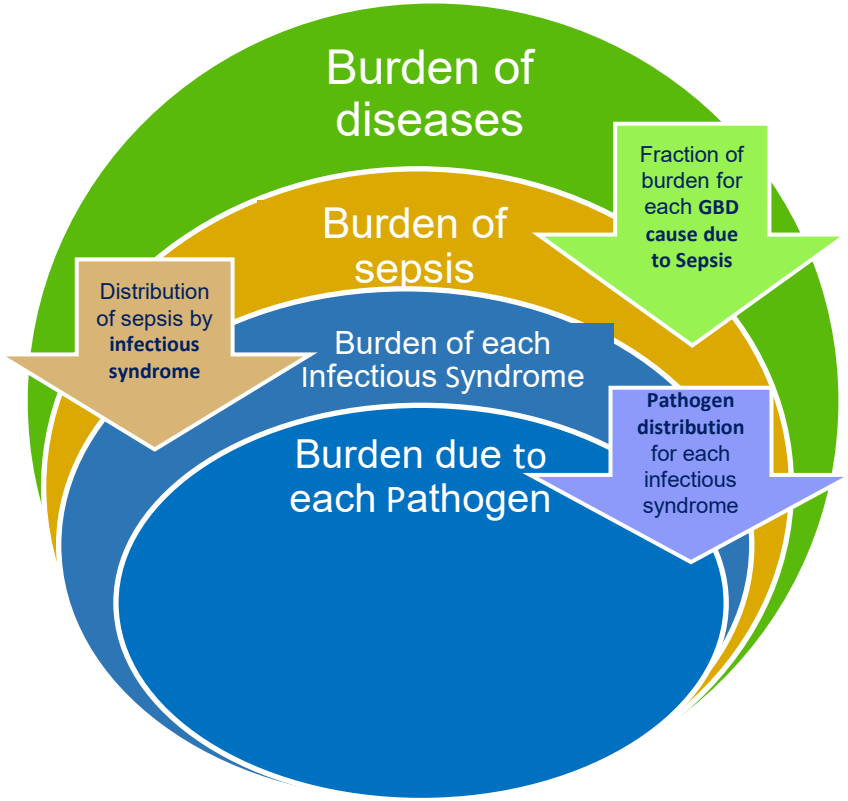
Pathogen	Total	CHAMPS	Hospital	Linkage	Literature	MCOD	Microbiology
E. coli	5.62 million	79	430,064	482	228,102	4,628	4.96 million
S. aureus	4.29 million	57	932,990	1,936	20,746	227,064	3.10 million
K. pneumoniae	1.47 million	259	52,983	144	25,499	19,126	1.37 million
S. pneumoniae	977,898	100	214,761	909	13,110	130,684	618,334
P. aeruginosa	890,089	26	21,773	541	20,178	25,725	812,846
MTB	768,306	6	102402	126	915	661806	3051
A. baumannii	99,254	162			2444		96,648



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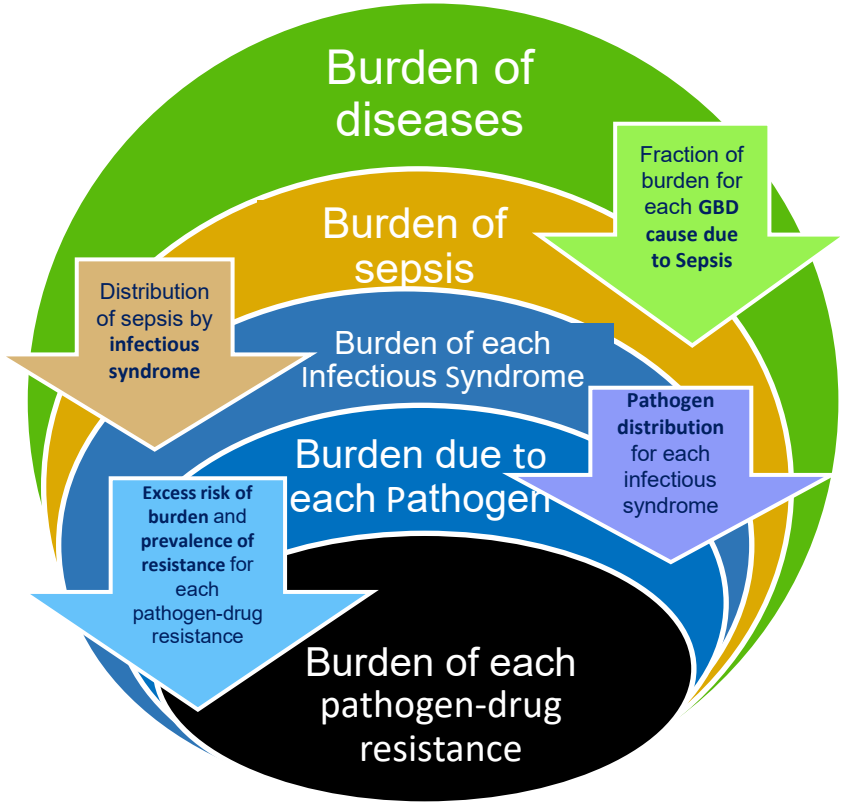

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The GRAM project:

How many people died due to AMR in 2019?

1.27 million deaths

(95% UI 0.91 – 1.71 million) **attributable** to bacterial AMR worldwide in 2019

4.95 million deaths

(95% UI 3.62-6.57 million) **associated** with bacterial AMR worldwide in 2019

AMR is a leading global health issue which disproportionately affects people living in low- and middle- income countries

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

Antimicrobial Resistance Collaborators*

Lancet 2022; 399: 629–55
Published Online January 20, 2022 https://doi.org/10.1016/S0140-6736(21)02724-0
See Comment page 606

*Collaborators are listed at the end of the paper
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Summary

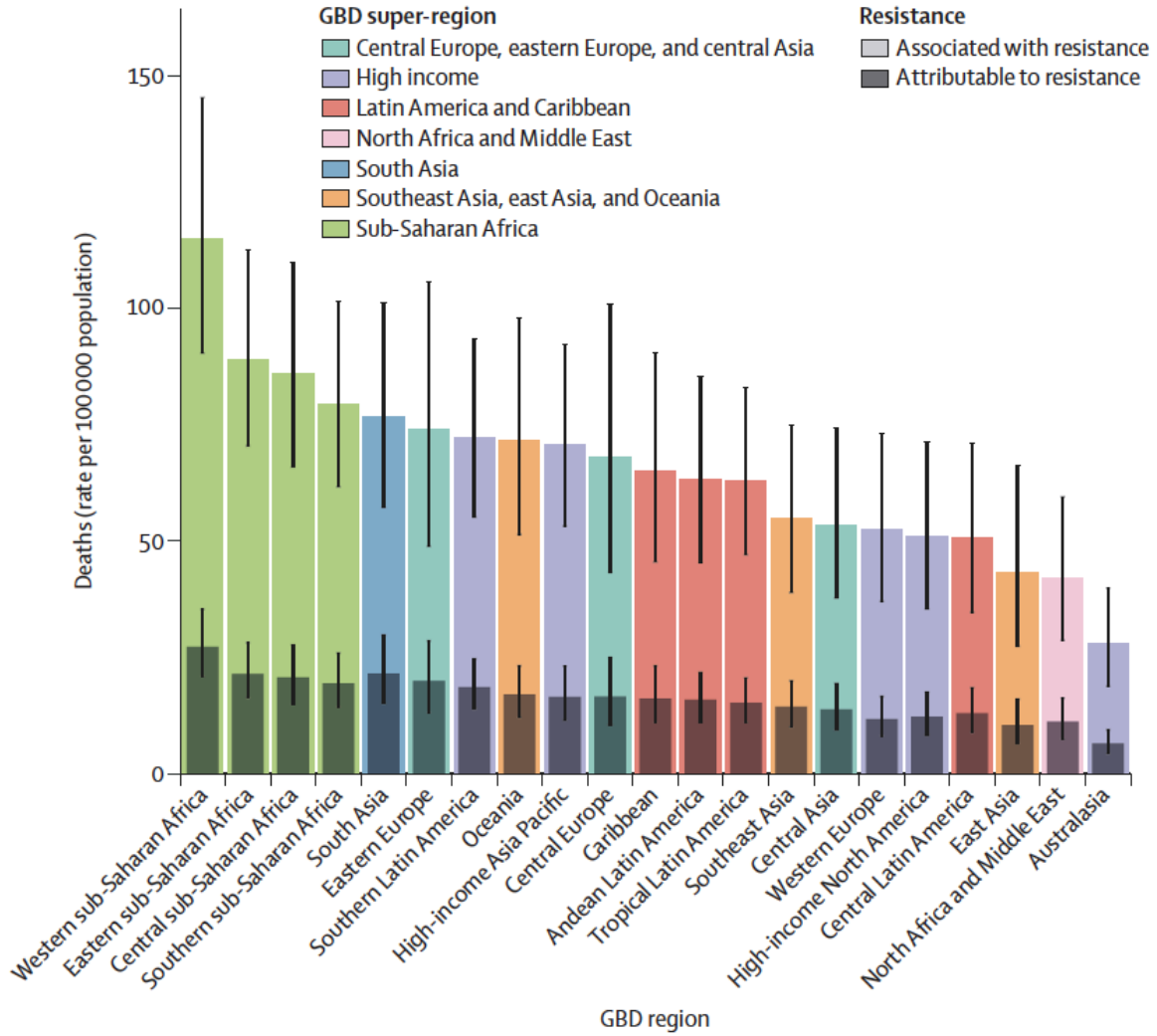
Background Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

Methods We estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for 23 pathogens and 88 pathogen–drug combinations in 204 countries and territories in 2019. We obtained data from systematic literature reviews, hospital systems, surveillance systems, and other sources, covering 471 million individual records or isolates and 7585 study-location-years. We used predictive statistical modelling to produce estimates of AMR burden for all locations, including for locations with no data. Our approach can be divided into five broad components: number of deaths where infection played a role, proportion of infectious deaths attributable to a given infectious syndrome, proportion of infectious syndrome deaths attributable to a given pathogen, the percentage of a given pathogen resistant to an antibiotic of interest, and the excess risk of death or duration of an infection associated with this resistance. Using these components, we estimated disease burden based on two counterfactuals: deaths attributable to AMR (based on an alternative scenario in which all drug-resistant infections were replaced by drug-susceptible infections), and deaths associated with AMR (based on an alternative scenario in which all drug-resistant infections were replaced by no infection). We generated 95% uncertainty intervals (UIs) for final estimates as the 25th and 975th ordered values across 1000 posterior draws, and models were cross-validated for out-of-sample predictive validity. We present final estimates aggregated to the global and regional level.

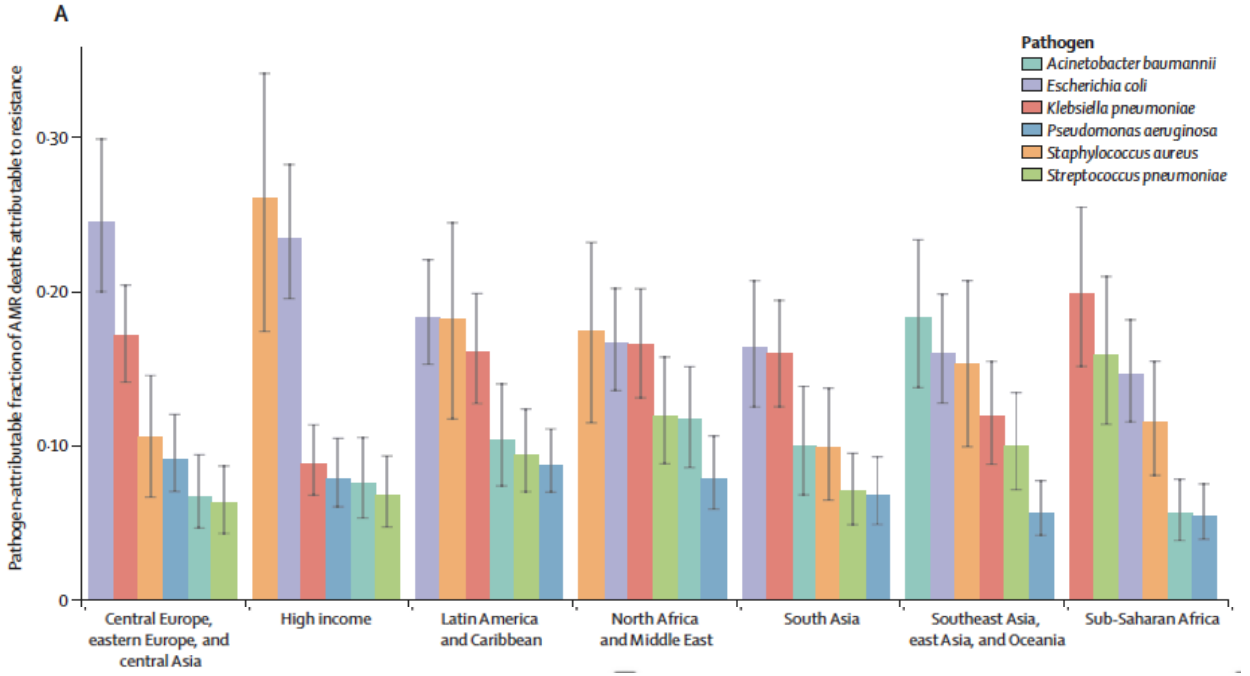
Findings On the basis of our predictive statistical models, there were an estimated 4·95 million (3·62–6·57) deaths associated with bacterial AMR in 2019, including 1·27 million (95% UI 0·911–1·71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at 27·3 deaths per 100 000 (20·9–35·3), and lowest in Australasia, at 6·5 deaths (4·3–9·4) per 100 000. Lower respiratory infections accounted for more than 1·5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome. The six leading pathogens for deaths associated with resistance (*Escherichia coli*, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) were responsible for 929 000 (660 000–1 270 000) deaths attributable to AMR and 3·57 million (2·62–4·78) deaths associated with AMR in 2019. One pathogen–drug combination, meticillin-resistant *S aureus*, caused more than 100 000 deaths attributable to AMR in 2019, while six more each caused 50 000–100 000 deaths: multidrug-resistant excluding extensively drug-resistant tuberculosis, third-generation cephalosporin-resistant *E coli*, carbapenem-resistant *A baumannii*, fluoroquinolone-resistant *E coli*, carbapenem-resistant *K pneumoniae*, and third-generation cephalosporin-resistant *K pneumoniae*.

Interpretation To our knowledge, this study provides the first comprehensive assessment of the global burden of AMR, as well as an evaluation of the availability of data. AMR is a leading cause of death around the world, with the highest burdens in low-resource settings. Understanding the burden of AMR and the leading pathogen–drug combinations contributing to it is crucial to making informed and location-specific policy decisions, particularly about infection prevention and control programmes, access to essential antibiotics, and research and development of new vaccines and antibiotics. There are serious data gaps in many low-income settings, emphasising the need to expand microbiology laboratory capacity and data collection systems to improve our understanding of this important human health threat.

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

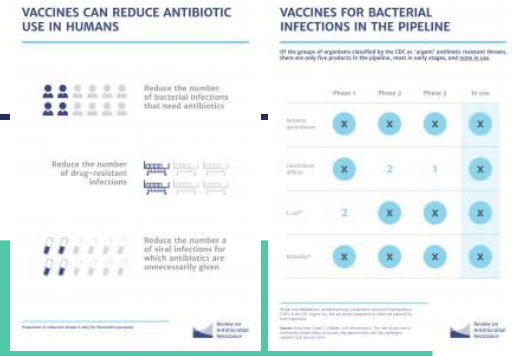


All-age rate of deaths attributable to and associated with bacterial AMR by GBD region, 2019



Pathogen-attributable fraction of deaths attributable to bacterial AMR for the six leading pathogens by GBD super-region, 2019

Outcomes: burden of mortality due to AMR



AMR is the leading cause of death globally – it's higher than HIV/AIDs or malaria

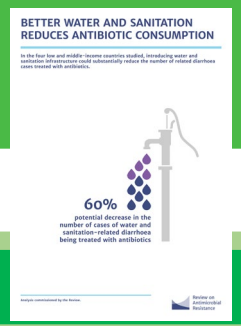
In 2019, 1 in 5 deaths caused by AMR were in children <5 years

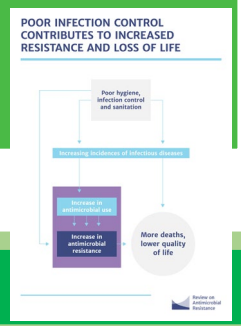
>80,000 deaths were attributable to seven bacteria

(only 2 of these have vaccines and intervention programmes)

The highest burden of AMR was observed in sub-Saharan Africa

Simple WASH improvements and IPC could decrease the AMR burden





The work should be a catalyst for action:

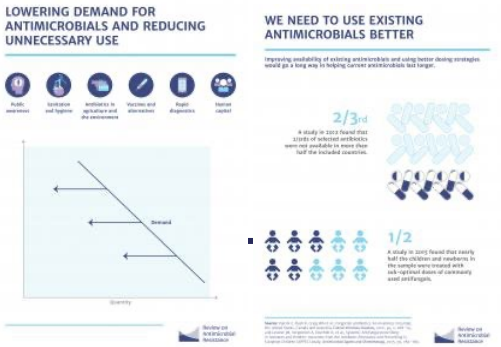
- In 2019–2020 - 88% of 136 responding countries had a NAP on AMR (TrACSS 4.0)
- Only 20% of those countries have fully financed their NAPs
- This reflects a major gap in implementation

Capacity building

We need to translate evidence into action

- Advocacy and awareness for the delivery of health services
  - need trained health providers who understand AMR
- Improve diagnostic capacity to inform clinical care
  - reduce inappropriate antibiotic use
- Improve capacity for:
  - data management, analysis, interpretation and sharingbrings an understanding of local data, issues, analysis and use of the data

What about antibiotics?



Fear of AMR drives irrational prescribing by clinicians

Lack of use of investigations drives irrational prescribing

(eg CSF, urine, radiology)

Where microbiology is done outside the research settings it is often of poor quality

Rapid selection/acquisition of carriage of resistant pathogens occurs in crowded wards

Guidelines are not contextual:

- community vs hospital acquired infection

- prior exposure to antibiotics

PLOS | MEDICINE

RESEARCH ARTICLE

Government policy interventions to reduce human antimicrobial use: A systematic review and evidence map

Susan Rogers Van Katwyk[1,2*], Jeremy M. Grimshaw[3,4], Miriam Nkangu[1], Ranjana Nagi[2], Marc Mendelson[5], Monica Taljaard[1,3], Steven J. Hoffman[2,6,7]

1 School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada, **2** Global Strategy Lab, Dahdaleh Institute for Global Health Research, Faculty of Health and Osgoode Hall Law School, York University, Toronto, Ontario, Canada, **3** Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, **4** Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada, **5** Division of Infectious Diseases and HIV Medicine, Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa, **6** Department of Health Research Methods, Evidence, and Impact, and McMaster Health Forum, McMaster University, Hamilton, Ontario, Canada, **7** Department of Global Health & Population, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts, United States of America

Author summary

Why was this study done?

- Despite global commitments to reduce antimicrobial resistance and protect the effectiveness of antimicrobials, most countries have not yet started implementing government policies to reduce their overuse and misuse of antimicrobials.
- To the best of our knowledge, no evidence syntheses have attempted to identify the policy options available to government policy makers to tackle antimicrobial resistance by reducing antimicrobial use in humans.

What did the researchers do and find?

- We searched 7 academic databases to identify impact evaluations of government policy interventions aiming to reduce human antimicrobial use that were published in any language before January 28, 2019.
- We found 69 studies that evaluated government policy interventions to reduce antimicrobial use around the world. From these, we were able to describe 17 different types of policies that governments have used to tackle this major driver of antimicrobial resistance in humans.
- Commonly used policy strategies included public awareness campaigns and antimicrobial guidelines; however, other policy strategies focused on vaccination, stewardship, and changing regulations around prescribing and reimbursement.
- We found 4 randomized controlled trials and 35 studies using rigorous quasi-experimental designs. The remaining 30 studies used uncontrolled and descriptive study designs.

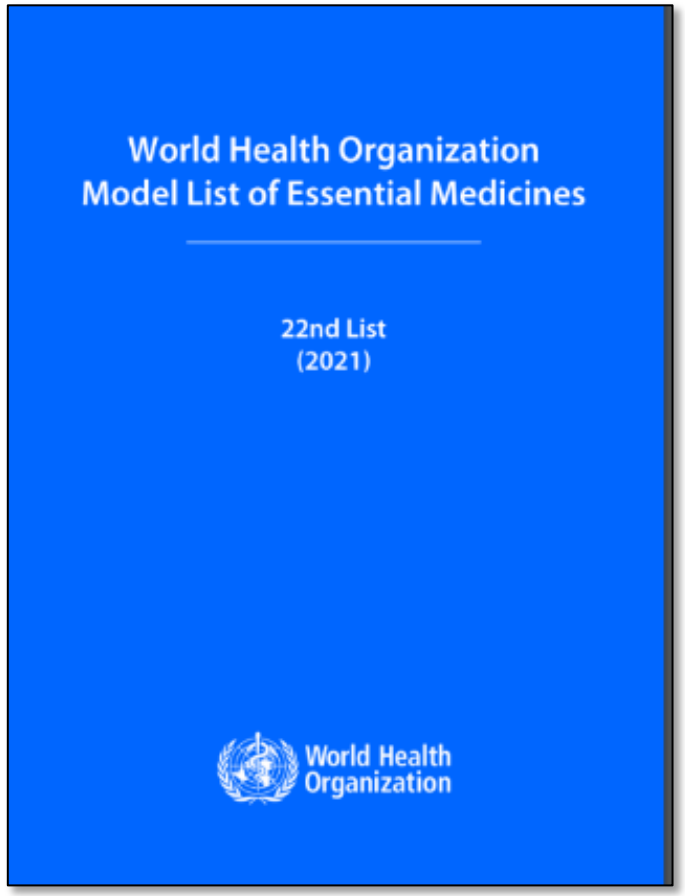
What do these findings mean?

- Our systematic evidence map suggests that governments have a variety of policy options at their disposal to respond to the growing threat of antimicrobial resistance.
- Unfortunately, most existing policy options have not been rigorously evaluated, which limits their usefulness in planning future policy interventions.
- To avoid wasting public resources, governments should ensure that future antimicrobial resistance policy interventions are evaluated using rigorous study designs, and that study results are published.

No Clarity on WHO AMR Policy Goals..

Current focus is on development of policy on Optimal Antibiotic Prescribing in the primary care setting using the AWaRe system

Rogers Van Katwyk, Plos Med, 2019



ACCESS GROUP

- first or second choice antibiotics
- offer the best therapeutic value, while minimizing the potential for resistance

WATCH GROUP

- first or second choice antibiotics
- only indicated for specific, limited number of infective syndromes
- more prone to be a target of antibiotic resistance and thus prioritized as targets of stewardship programs and monitoring

RESERVE GROUP

- "last resort"
- highly selected patients (life-threatening infections due to multi-drug resistant bacteria)
- closely monitored and prioritized as targets of stewardship programs to ensure their continued effectiveness

WHO General Programme of Work (GPW) now includes a Target indicator that the proportion of Access antibiotics should be more than **60%** of total antibiotic use at country level

Trends in AWaRe use - marked increase in LMIC use of oral Watch antibiotics

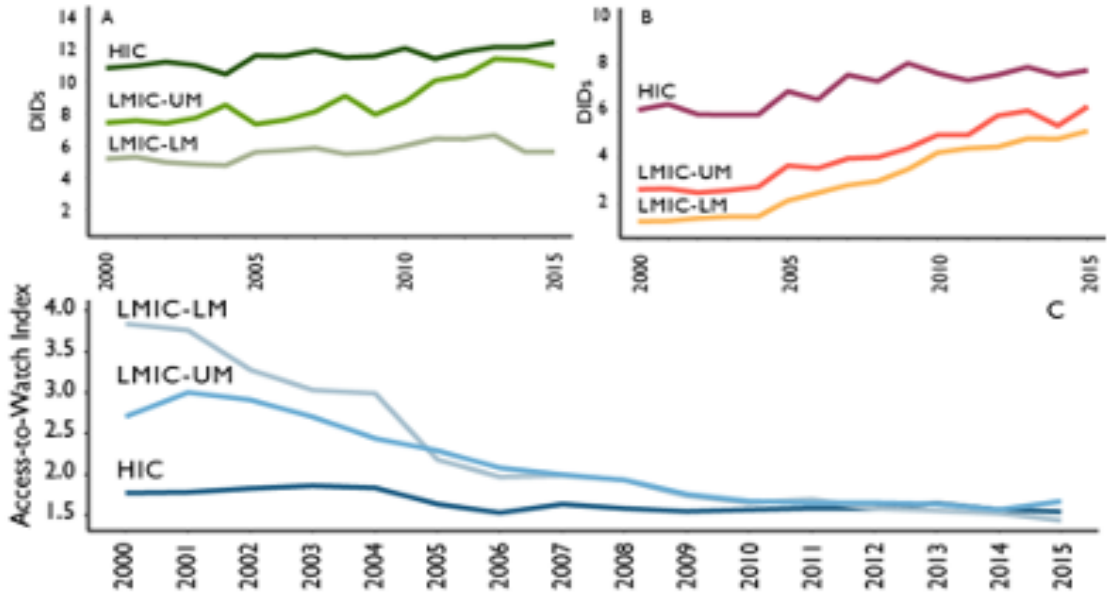
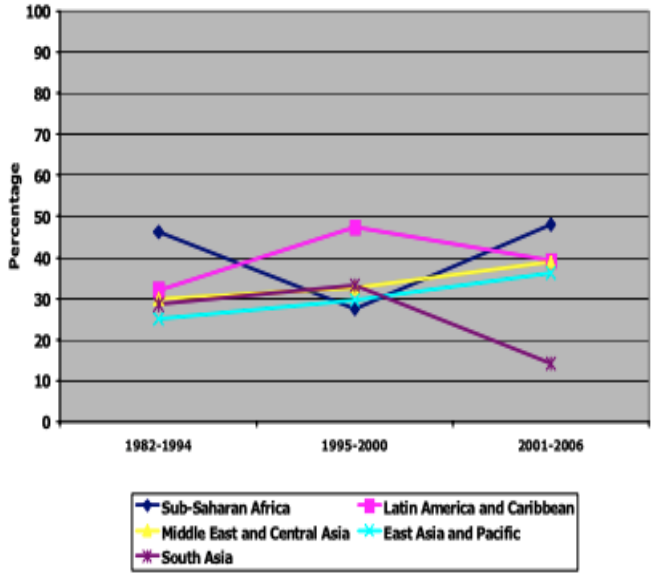


Figure 2. Relative and absolute consumption of Access and Watch antibiotics, 2000-2015
Median consumption in high-income countries (HICs), upper-middle low- and middle-income countries (LMIC-UM), and lower-middle low- and middle-income countries (LMIC-LM) expressed in defined daily doses (DDDs) per 1,000 inhabitants per day (DIDs) for (A) Access and (B) Watch antibiotics. The Access-to-Watch Index (C), which measures the ratio of DIDs of Access to Watch antibiotics, saw large declines in both LMIC-UM and LMIC-LM, which reflects the relatively larger increase in use of Watch antibiotics compared to Access antibiotics. Source: IQVIA MIDAS, 2000–2015, IQVIA Inc. All rights reserved.

Klein EY LID 2020

Figure 4.4: Rates of adherence to clinical guidelines over time, by World Bank region



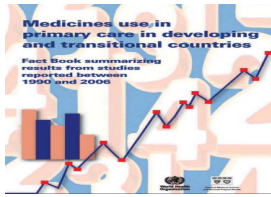
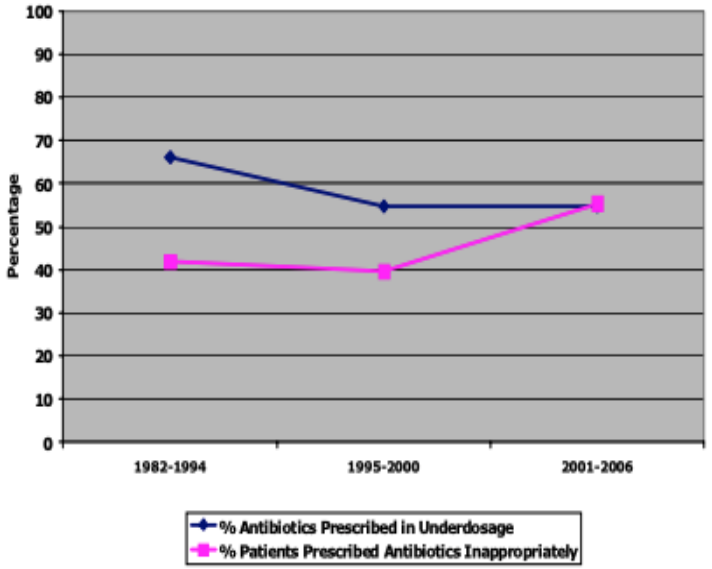


Figure 9.1: Inappropriate prescribing of antibiotics over time



2022 - WHO EML Antibiotic AWaRe Book

- To provide simple guidance on "HOW TO USE the antibiotics on the EML to manage common infections
- Guidance for 36 infections; **primary care** and **facility/hospital setting**, children and adults.
    - acute bacterial infections (Not TB/viral/fungal/parasitic infections)
  - **Recommendations on empiric antibiotic treatment** (i.e. presumptive diagnosis not requiring any laboratory diagnostic)
  - Includes guidance on making the clinical Diagnosis, the Decision if antibiotic needed, the choice of Drug, Dose, Duration
  - Short summaries of key features of microbiology, epidemiology, clinical presentation, diagnostics (in collaboration with EDL), prevention
  - **Target audience: all health professionals giving antibiotics**

Potential Primary Care Goals for optimising use of Access antibiotics

- **Up to 90% of Antibiotic Prescribing in Primary Care** could be **Access** antibiotics

Potential Primary Care Goals for safely reducing inappropriate prescribing (reducing total AB use)

- **60 % of 10 most common infections in primary care can be treated symptomatically/no AB for mild cases**

- **In many settings around half of patients attending a Primary Health Care facility receive an antibiotic (WHO goal of 30%..).**

- **Critical importance of maintaining/enhancing "Access to Access" antibiotics in most vulnerable populations**

Common Primary Care Infections	Recommended AWaRe antibiotic
Bronchitis	None
Pharyngitis	Access
Otitis Media	Access
Sinusitis	Access
CAP (mild)	Access
COPD exacerbations	Access
UTI Lower	Access
Dental	Access
SSTI	Access
Acute Bloody Diarrhoea	Watch

Potential use of AWaRe in developing policy goals

Variation of antibiotic use by countries/regions

The proportion of countries where 60% of total oral antibiotic use was of Access antibiotics was 59/75 (78.7%), but only 14/75 (18.7%) reached 80% of oral Access antibiotic use (Table 1, Figure 5).

Table 1. Number of countries/regions that reached potential goals of oral Access antibiotic use

Access antibiotics accounted for	60% of total oral antibiotic use	70% of total oral antibiotic use	80% of total oral antibiotic use	90% of total oral antibiotic use
HICs, n/39 (%)	31 (79.5)	21 (53.8)	7 (17.9)	0 (0.0)
LMICs, n/36 (%)	28 (77.8)	23 (63.9)	7 (19.4)	0 (0.0)
Total, n/75 (%)	59 (78.7)	44 (58.7)	14 (18.7)	0 (0.0)

HICs, high-income countries/regions; LMICs, low-middle-income countries/regions

The proportion of oral Watch antibiotics for each country varied between 12.1% to 81.5% of total use (median 34.9% in HICs and 38.2% in LMICs) (Figure 5). The use of Not-Recommended antibiotics was higher in LMICs (6.2% of total) compared to HICs (0.7%). The use of oral Reserve antibiotics was very low with the highest proportions in Japan, Egypt, and India (1.2%, 0.7%, and 0.4%, respectively).

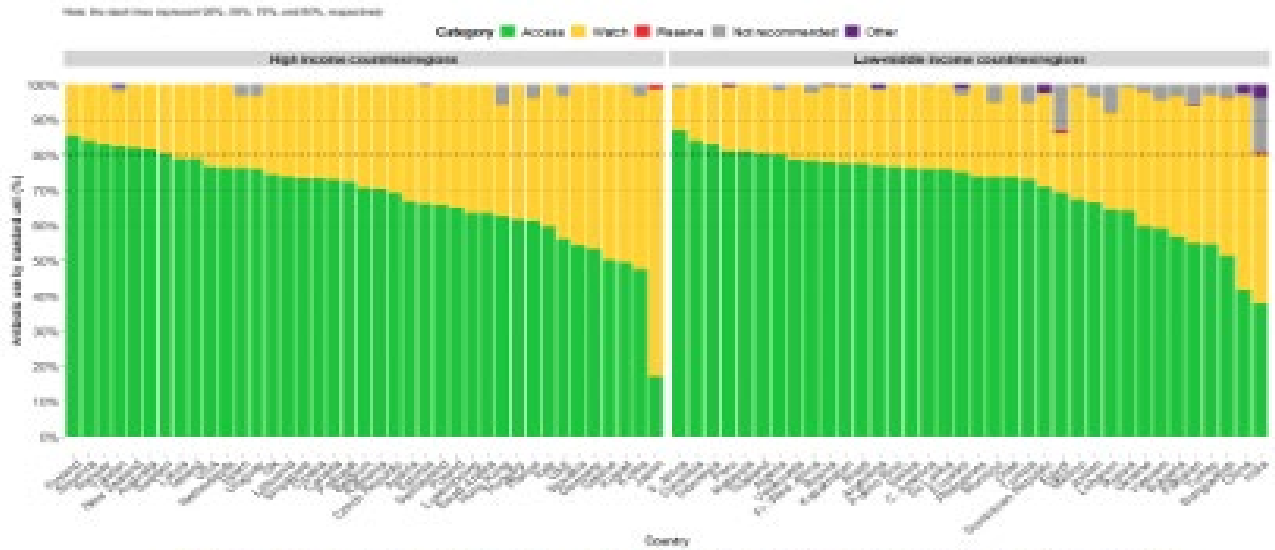
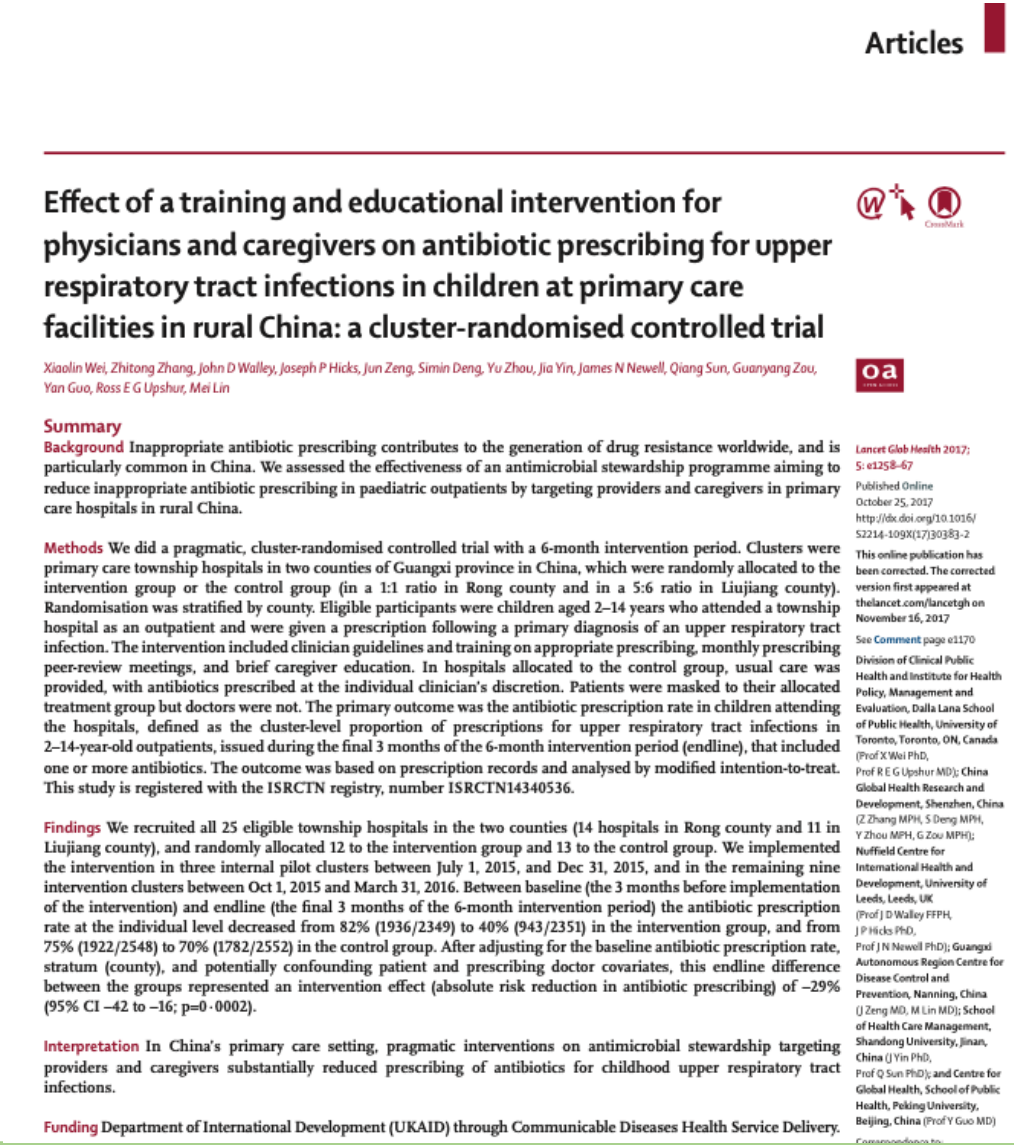


Figure 5. Oral antibiotic use by AWaRe system in 75 countries/regions in 2015

Very limited evidence base to inform policy

- ~5 billion courses of antibiotics given in PHC
- Virtually no RCTs on optimal use of antibiotics in LMIC Primary Care
- Almost no data on efficacy and safety of risk-based approach to prescribing or ASP interventions
- What is the safety of reducing total prescribing in high disease burden countries?



Effect of a training and educational intervention for physicians and caregivers on antibiotic prescribing for upper respiratory tract infections in children at primary care facilities in rural China: a cluster-randomised controlled trial

Xiaolin Wei, Zhitong Zhang, John D Walley, Joseph P Hicks, Jun Zeng, Simin Deng, Yu Zhou, Jia Yin, James N Newell, Qiang Sun, Guanyang Zou, Yan Guo, Ross E G Upshur, Mei Lin

Summary

Background Inappropriate antibiotic prescribing contributes to the generation of drug resistance worldwide, and is particularly common in China. We assessed the effectiveness of an antimicrobial stewardship programme aiming to reduce inappropriate antibiotic prescribing in paediatric outpatients by targeting providers and caregivers in primary care hospitals in rural China.

Methods We did a pragmatic, cluster-randomised controlled trial with a 6-month intervention period. Clusters were primary care township hospitals in two counties of Guangxi province in China, which were randomly allocated to the intervention group or the control group (in a 1:1 ratio in Rong county and in a 5:6 ratio in Liujiang county). Randomisation was stratified by county. Eligible participants were children aged 2–14 years who attended a township hospital as an outpatient and were given a prescription following a primary diagnosis of an upper respiratory tract infection. The intervention included clinician guidelines and training on appropriate prescribing, monthly prescribing peer-review meetings, and brief caregiver education. In hospitals allocated to the control group, usual care was provided, with antibiotics prescribed at the individual clinician's discretion. Patients were masked to their allocated treatment group but doctors were not. The primary outcome was the antibiotic prescription rate in children attending the hospitals, defined as the cluster-level proportion of prescriptions for upper respiratory tract infections in 2–14-year-old outpatients, issued during the final 3 months of the 6-month intervention period (endline), that included one or more antibiotics. The outcome was based on prescription records and analysed by modified intention-to-treat. This study is registered with the ISRCTN registry, number ISRCTN14340536.

Findings We recruited all 25 eligible township hospitals in the two counties (14 hospitals in Rong county and 11 in Liujiang county), and randomly allocated 12 to the intervention group and 13 to the control group. We implemented the intervention in three internal pilot clusters between July 1, 2015, and Dec 31, 2015, and in the remaining nine intervention clusters between Oct 1, 2015 and March 31, 2016. Between baseline (the 3 months before implementation of the intervention) and endline (the final 3 months of the 6-month intervention period) the antibiotic prescription rate at the individual level decreased from 82% (1936/2349) to 40% (943/2351) in the intervention group, and from 75% (1922/2548) to 70% (1782/2552) in the control group. After adjusting for the baseline antibiotic prescription rate, stratum (county), and potentially confounding patient and prescribing doctor covariates, this endline difference between the groups represented an intervention effect (absolute risk reduction in antibiotic prescribing) of –29% (95% CI –42 to –16; p=0·0002).

Interpretation In China's primary care setting, pragmatic interventions on antimicrobial stewardship targeting providers and caregivers substantially reduced prescribing of antibiotics for childhood upper respiratory tract infections.

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Can we have policy goals and indicators for oral antibiotic consumption in the primary healthcare setting?

Over 90% of LMIC antibiotic use is oral in the primary healthcare setting … (similar for HICs)

The great majority of primary care prescribing should be Access antibiotics

Further work needed on AWaRe: relative safety, efficacy, cost and resistance

AWaRe system has potential to develop and implement more formal **policy goals and indicators**

(focus on safely, reducing Total and oral Watch antibiotic use)

We could model:

"observed vs expected " patterns of community & hospital use (…risk adjusted for disease burden & varying levels of resistance)

We need to develop and pilot:

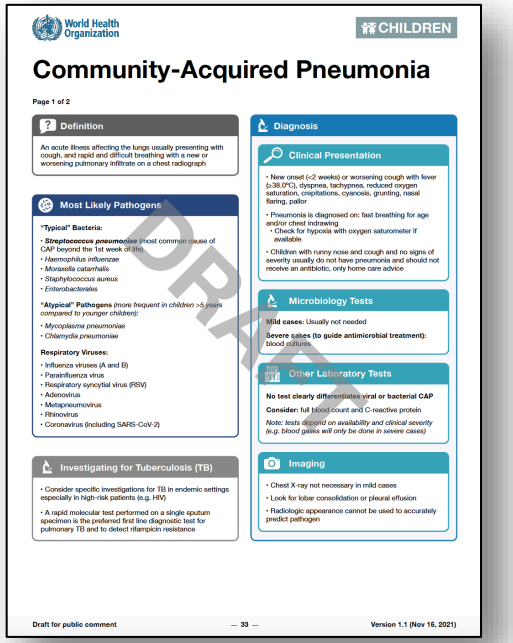
range of AWaRe based tools for optimal implementation of policy goals & monitoring outcomes

We need to conduct LMIC focused trials:

inform policy strategies, safety and impact on resistance = evidence base for global policy leadership

Action:

How can we influence local use of antibiotics?



World Health Organization

CHILDREN

Community-Acquired Pneumonia

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Definition

An acute illness affecting the lungs usually presenting with cough, and rapid and difficult breathing with a new or worsening pulmonary infiltrate on a chest radiograph

Most Likely Pathogens

"Typical" Bacteria:

- ***Streptococcus pneumoniae*** (most common cause of CAP beyond the 1st week of life)
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Staphylococcus aureus*
- *Enterobacteriales*

"Atypical" Pathogens *(more frequent in children >5 years compared to younger children)*:

- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*

Respiratory Viruses:

- Influenza viruses (A and B)
- Parainfluenza virus
- Respiratory syncytial virus (RSV)
- Adenovirus
- Metapneumovirus
- Rhinovirus
- Coronavirus (including SARS-CoV-2)

Investigating for Tuberculosis (TB)

- Consider specific investigations for TB in endemic settings especially in high-risk patients (e.g. HIV)
- A rapid molecular test performed on a single sputum specimen is the preferred first line diagnostic test for pulmonary TB and to detect rifampicin resistance

Diagnosis

Clinical Presentation

- New onset (<2 weeks) or worsening cough with fever (≥38.0°C), dyspnea, tachypnea, reduced oxygen saturation, crepitations, cyanosis, grunting, nasal flaring, pallor
- Pneumonia is diagnosed on: fast breathing for age and/or chest indrawing
  - Check for hypoxia with oxygen saturometer if available
- Children with runny nose and cough and no signs of severity usually do not have pneumonia and should not receive an antibiotic, only home care advice

Microbiology Tests

Mild cases: Usually not needed

Severe cases (to guide antimicrobial treatment): blood culture

Other Laboratory Tests

No test clearly differentiates viral or bacterial CAP

Consider: full blood count and C-reactive protein

Note: tests depend on availability and clinical severity (e.g. blood gases will only be done in severe cases)

Imaging

- Chest X-ray not necessary in mild cases
- Look for lobar consolidation or pleural effusion
- Radiologic appearance cannot be used to accurately predict pathogen

DRAFT

Draft for public comment — 33 — Version 1.1 (Nov 16, 2021)

WHO EML Antibiotic AWaRe Book (2022) - empiric antibiotic guidance, 36 infections (**primary care** and **facility/hospital setting)**.

<u>The ADILA project</u> (AMR Data to Inform Local Action)

- **Local** data and policy action based on the AWaRe categorization and the WHO Essential Medicines List (EML)
- Inform local prescribers to treat patients based on local AMR data, EML guidelines (access antibiotics) and antibiotic availability

The ADILA project

Antimicrobial Resistance Data to Inform Local Action (ADILA)

Goal: Optimise use of AMR surveillance data - develop tools for implementation nationally to inform and support individual countries policies on improving quality of antibiotic use

- **Hospital data**
  - Assess feasibility of developing a **hospital facility** "clinical antibiotic resistance management tool" - inform development of facility level empiric prescribing guidelines and targets of appropriate antibiotic use.
- **Primary Health care data**
  - Assess feasibility of integrating **primary health care (PHC)** antibiotic prescribing with estimates of distribution of clinical infections to inform targets for appropriate levels of antibiotic consumption.
- **Clinical impact**
  - Explore the clinical impact of alternative antibiotic prescribing reductions at a population level
- **Implementation**
  - **Pilot implementation:** integrating the tools and piloting at a country level, focusing on capacity building

- Modelling themes:
  - Hospital data analysis for concordant/discordant treatment
  - Hospital - modelling a hypothetical clinical trial based on data
  - Primary healthcare (PHC) data for observed vs expected prescribing
  - Surveys (PHC) – to ultimately have quality indicators
  - Determine appropriate antibiotic targets (by clinical burden)
  - Outline the data needed for prospective collection
- **Country engagement, capacity building, sharing tools and code**

Capacity building locally

- Retrospective data: we will model data from high income countries to understand which variables are crucial for the models in low-income countries
  - When we exclude variables what does that do to the data
  - Which variables need to be collected going forward
  - This is the data we will prioritise in prospective studies

- Local researchers need to produce and analyse their own data
  - To be able to analyse the prevalence of resistance locally together with antibiotic access and use
  - All of our tools will be openly available on our website (http://cnpi-amr.org/)

- Improve diagnostic capacity to inform clinical care
  - Fleming Fund are building the capacity in this area, this will ultimately provide robust data for analysis

- Improve capacity for data management, analysis, interpretation and sharing
  - Support is needed for this from all funders

Introducing: Monthly webinars and discussion, please join us for our first webinar in September where the WHO EML will be presented by Prof Mike Sharland

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