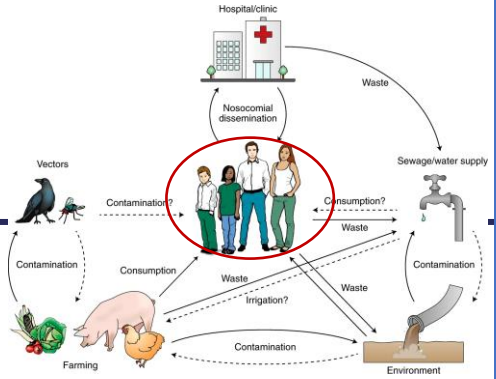
Policy recommendations from the GRAM project

The Global Research on Antimicrobial Resistance (GRAM) project

Dr Catrin Moore

13th April 2022

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**

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

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

2017
IACG convened

2020
One Health Global Leaders Group launched

2021
G7/G20 Meetings: AMR on the agenda

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

Results: 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

Articles

Joanna V

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

*Antimicrobial Resistance Collaborators**

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.

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*Collaborators are listed at the end of the paper

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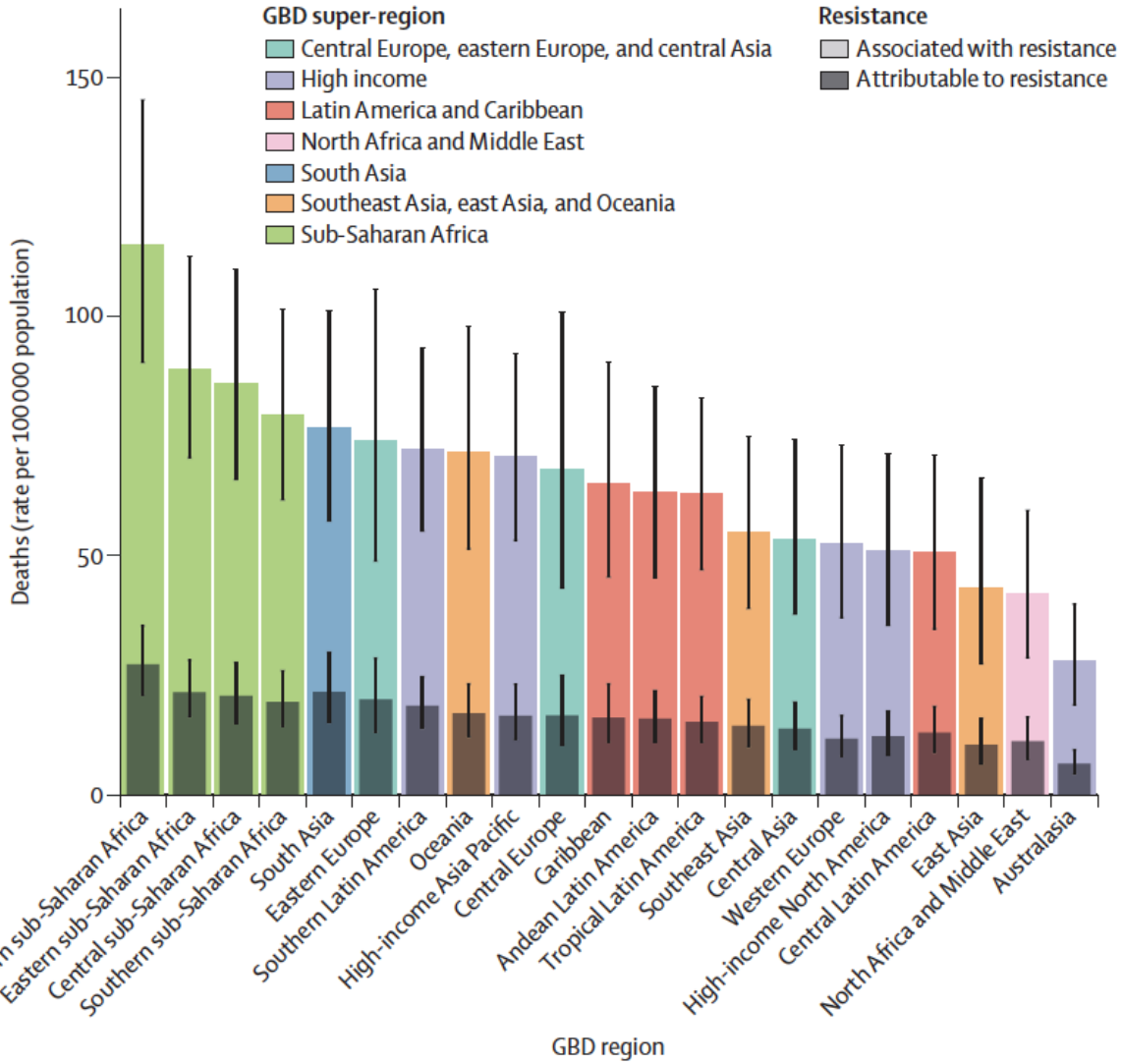
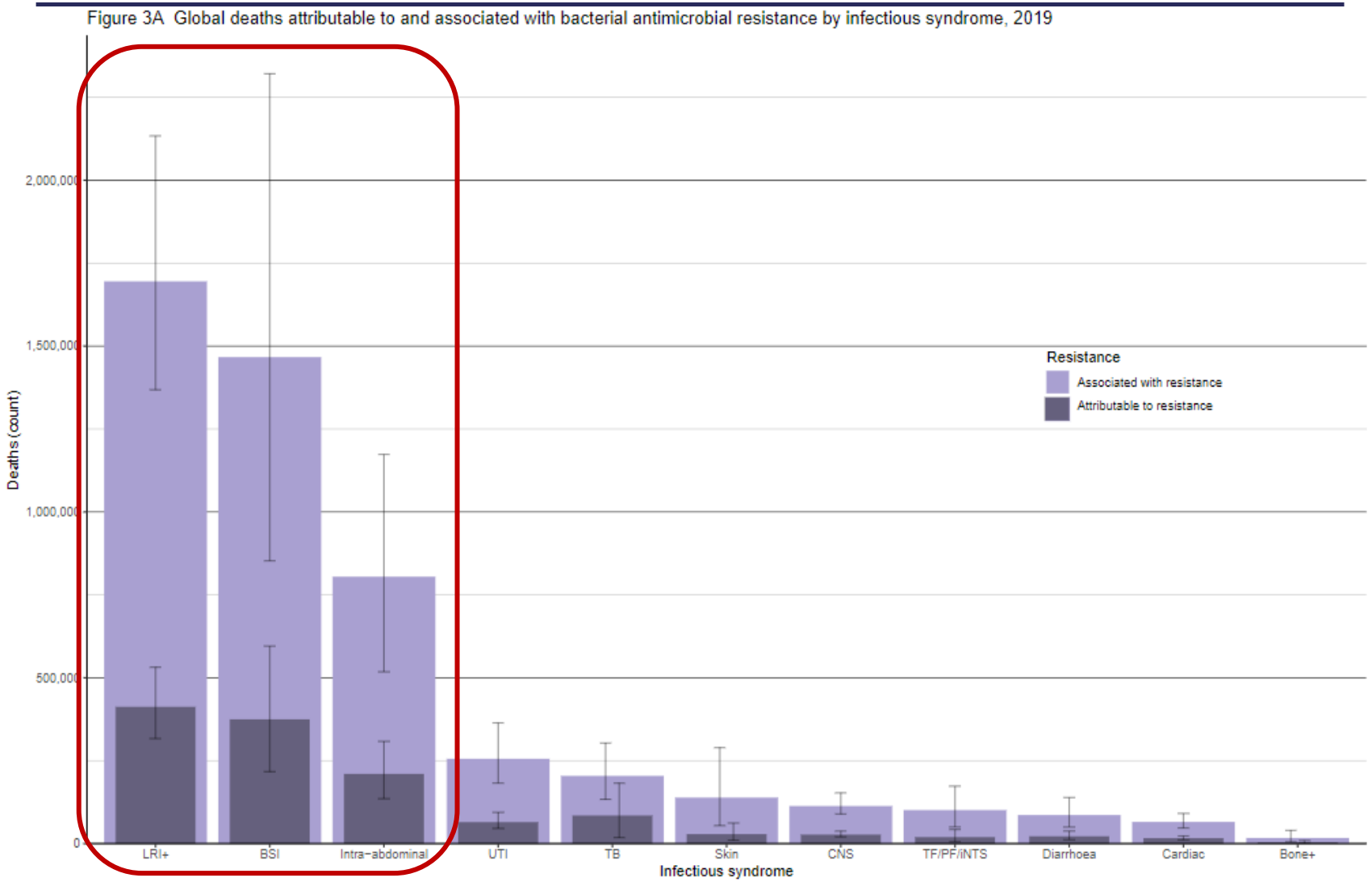
The take home messages from the GRAM paper

1. AMR is a leading cause of death globally, it kills more than HIV/AIDs or Malaria.
2. Our action plans need to be more ambitious and faster to control the threat.
3. AMR puts extra pressure on frontline healthcare workers by making common infections harder to treat, people die because of AMR.
4. Through this work we can identify immediate actions that can help countries around the world protect their health systems against the threat of AMR.

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

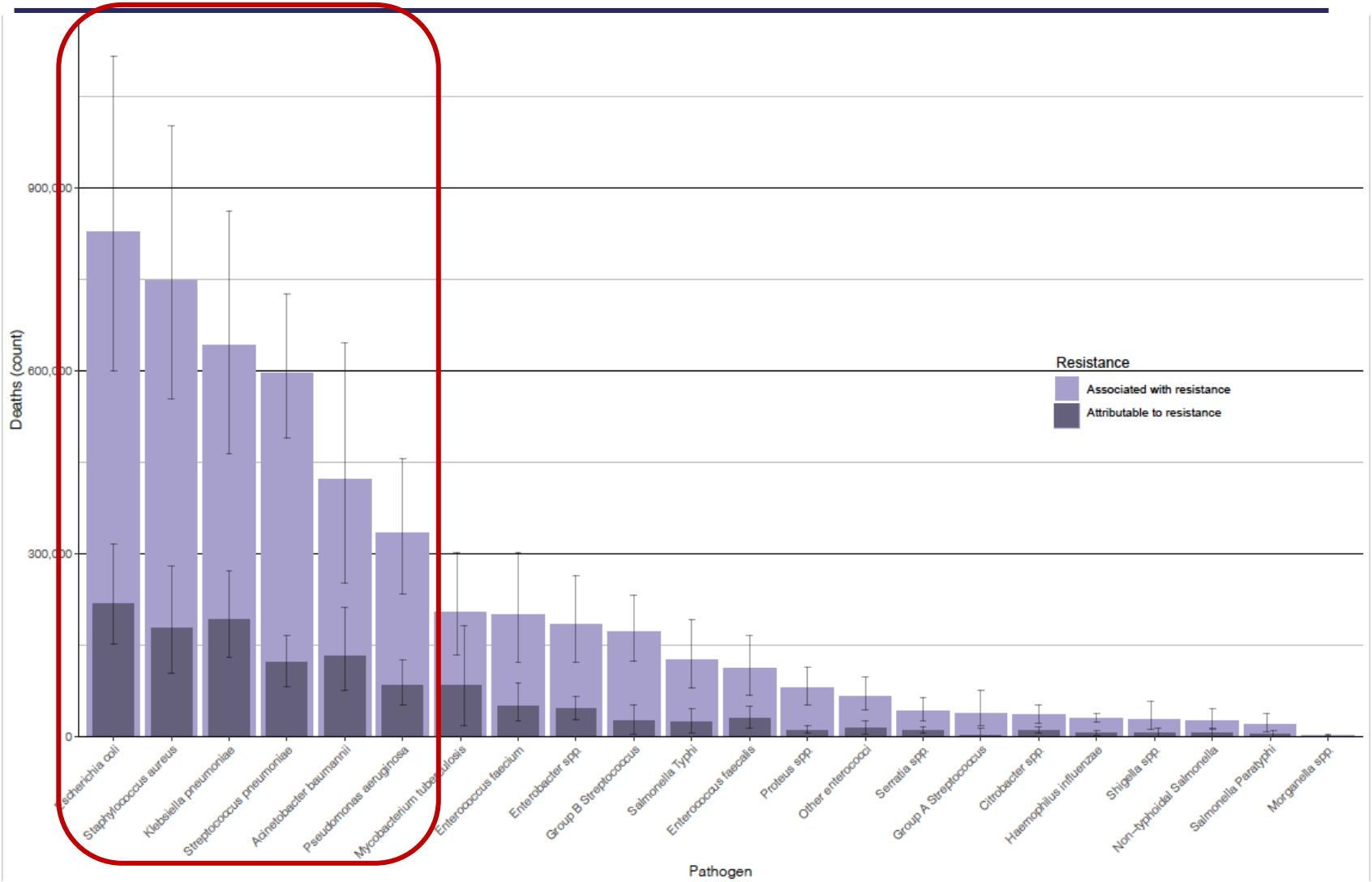


Results



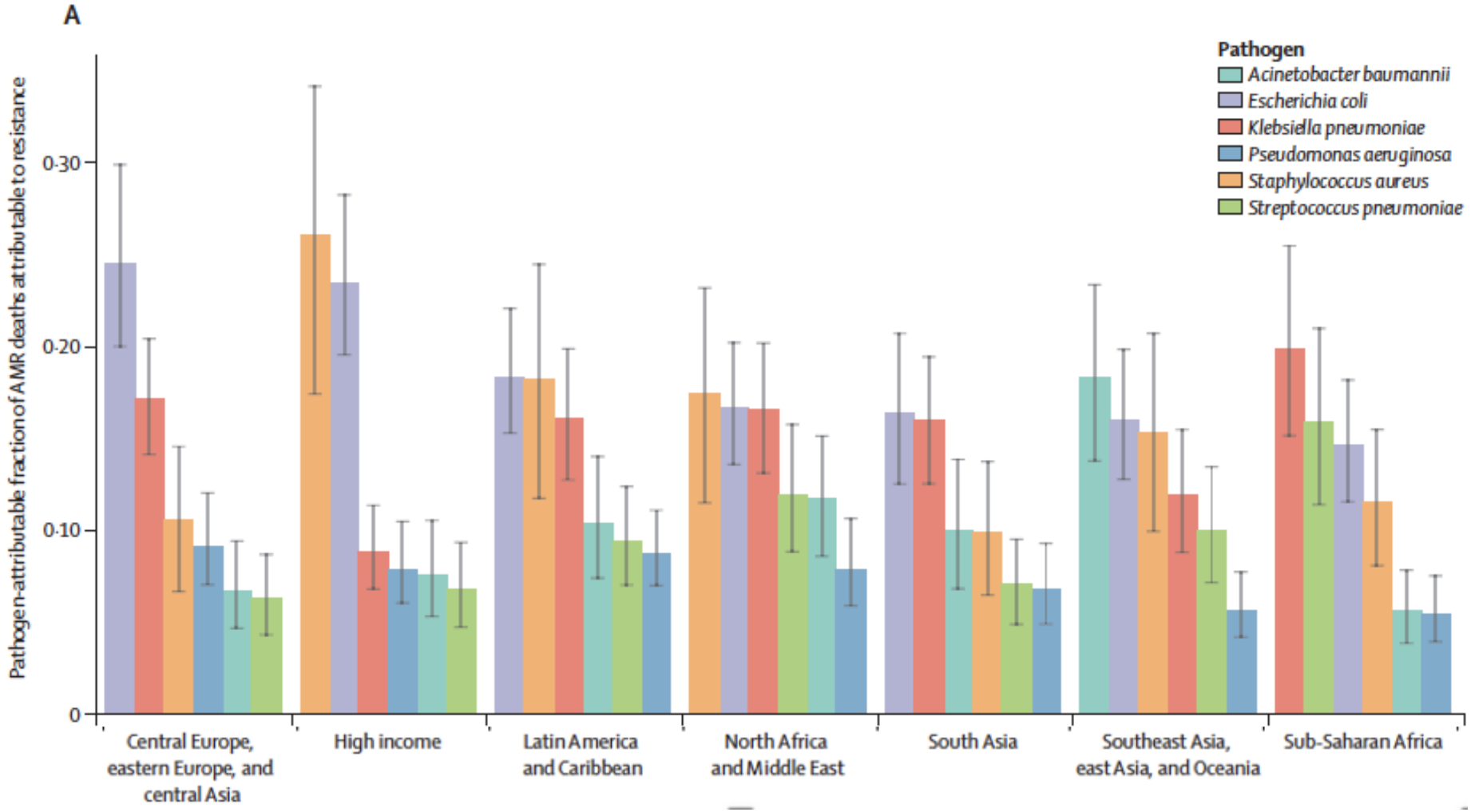
AMR deaths by infectious syndrome, 2019

Results



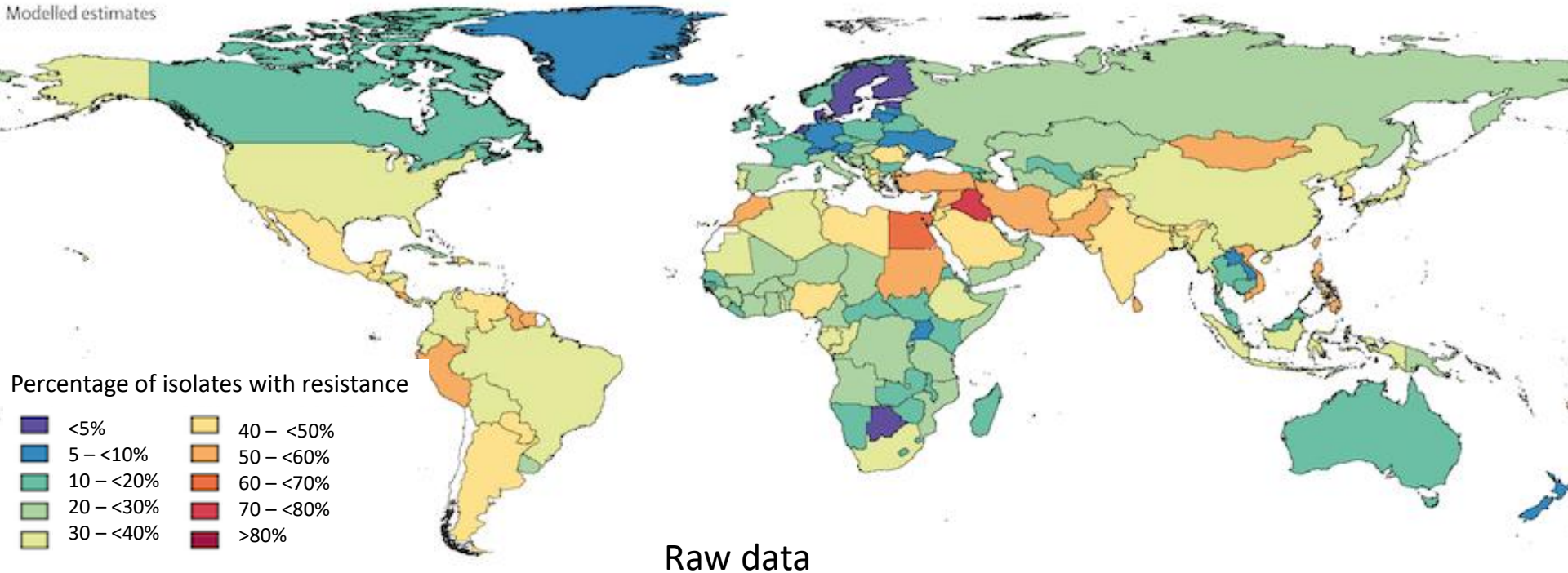
Global deaths attributable to and associated with AMR by pathogen, 2019

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

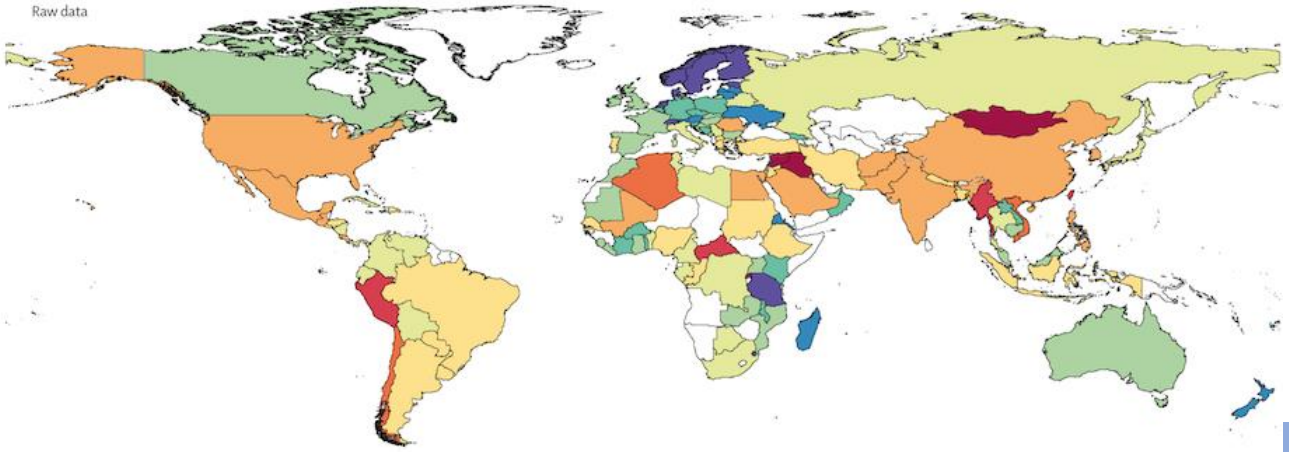


Methicillin resistant *S. aureus* (MRSA), 2019

Modelled estimates



Raw data



Outcomes from the study:

- 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

"AMR is already one of the greatest challenges facing humanity. Behind these new numbers are families and communities who are tragically bearing the brunt of the silent AMR pandemic. We must use this data as a warning signal to spur on action at every level."

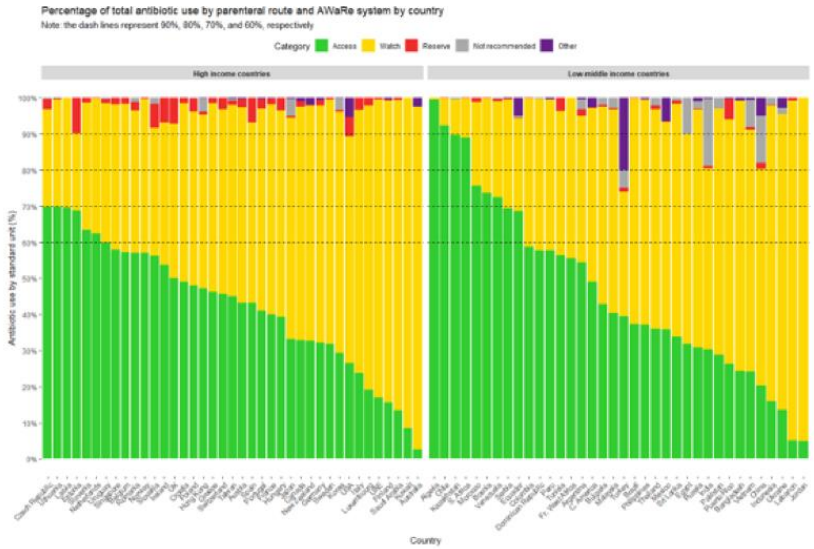
Professor Dame Sally Davies, 2022

The ADILA project

2017 WHO EML Expert Committee developed the AWaRe classification of Essential Antibiotics on the EML/c as Access/ Watch/Reserve

ACCESS group: narrow spectrum affordable antibiotics widely available
WaTCH group: broader spectrum antibiotics - specific and limited indications (higher resistance and toxicity potential)
ReSERVE group: last resort antibiotics - used only when other antibiotics have failed or for treatment of multi-resistant bacteria.

Antimicrobial Resistance, Prescribing, and Consumption Data to Inform Country Antibiotic Guidance and Local Action (ADILA)



Total parental antibiotic use by AWaRe categories in 75 countries/regions in 2015

Funded by the Wellcome Trust, began 1st April 2022

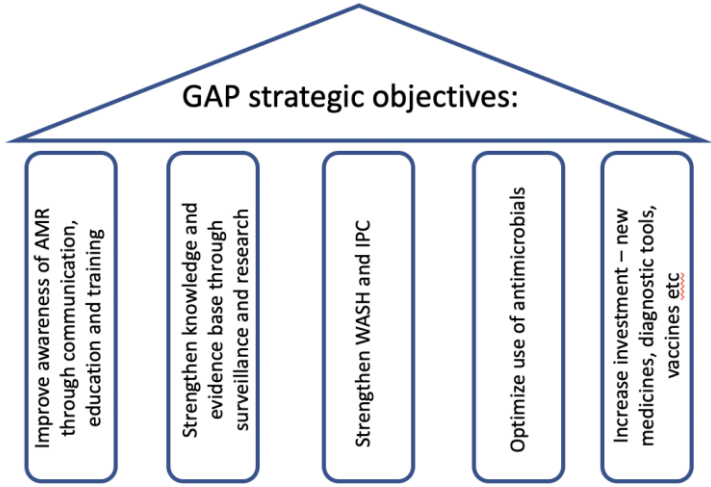
The objectives

Goal: Optimise the use of AMR surveillance data by developing tools that can be implemented nationally to inform and support individual countries policies on improving the quality of antibiotic use.

We are:

- Assessing the feasibility of developing a **hospital facility** based “clinical antibiotic resistance management tool”
- Assessing the feasibility of integrating (sub)national estimates of **primary health care** (PHC) antibiotic prescribing with estimates of distribution of clinical infections
- Exploratory the clinical impact of alternative antibiotic prescribing reductions at a population level through models
- Working closely with a small number of countries to integrate the tools and pilot their implementation at a country level, focusing on capacity building.

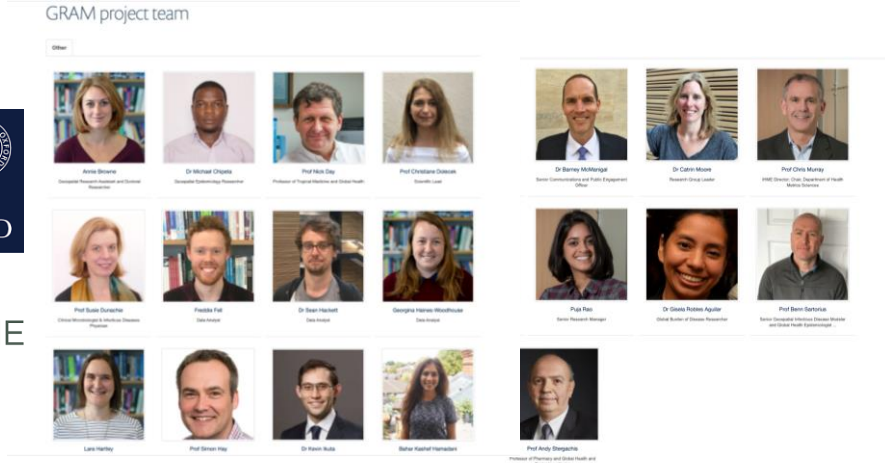
Thoughts for future policy action

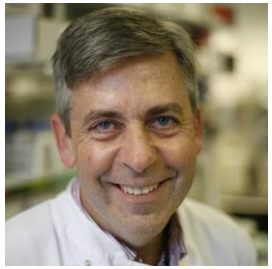


- We need to translate evidence into action
  - there needs to be a continuous quality improvement through …
    - advocacy and awareness for the delivery of health services
    - Improved diagnostic capacity and informed clinical care
    - Improved capacity for data management, analysis, interpretation and sharing

- We need to learn from COVID-19 and other pandemics: **prevention is key**
  - Awareness
  - Prevention
  - Improved use of antibiotics (reduced misuse)
  - Create the knowledge outside of academia
  - Provide sufficient funding to all sectors

Thank you …





Collaborators

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Global

- Global Tuberculosis Programme (**GTB**) of the World Health Organization (**WHO**), Geneva, Switzerland.
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