Modelling the Global Prevalence of Antimicrobial Resistant Invasive Non-Typhoidal Salmonella Infections, 2000 to 2019.

Frederick Fell

Contents

- Aims of the study.

- Where is our data from?

- What is our data availability?

- Modelling Methods.

- Results.

- Discussion.

Our work on invasive NTS is part of the GRAM project, which is a collaboration between the University of Oxford and the Institute of Health Metrics and Evaluation in Seattle, the authors of the Global Burden of Disease study.
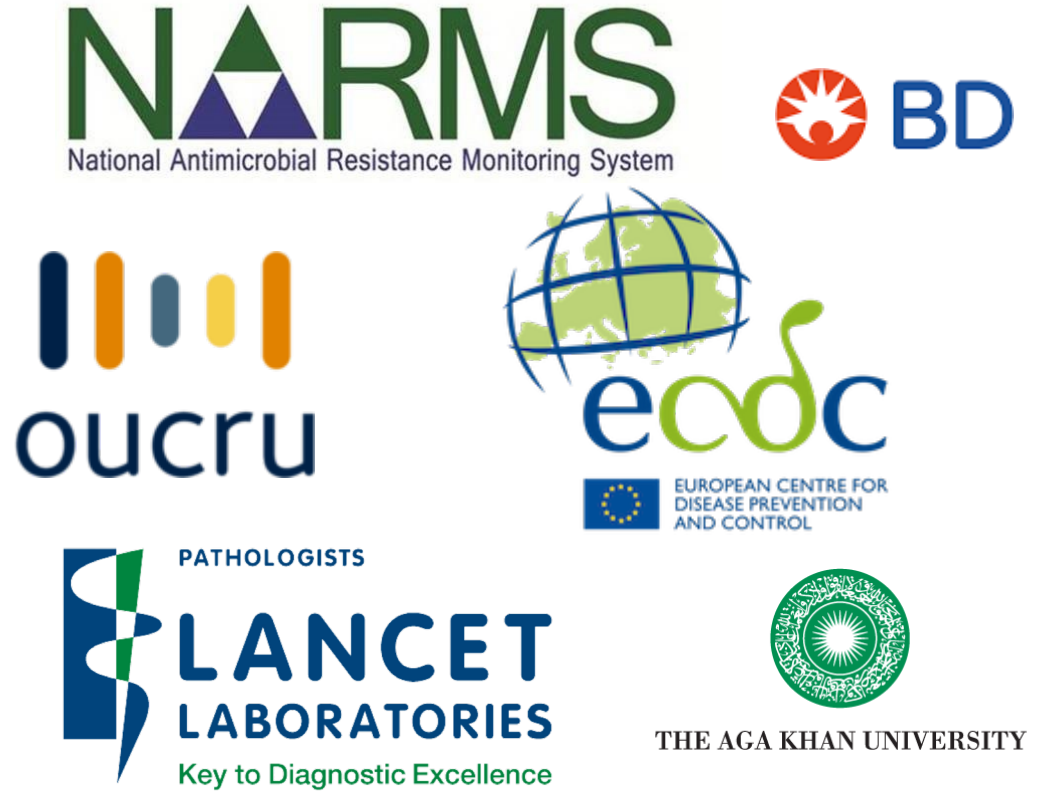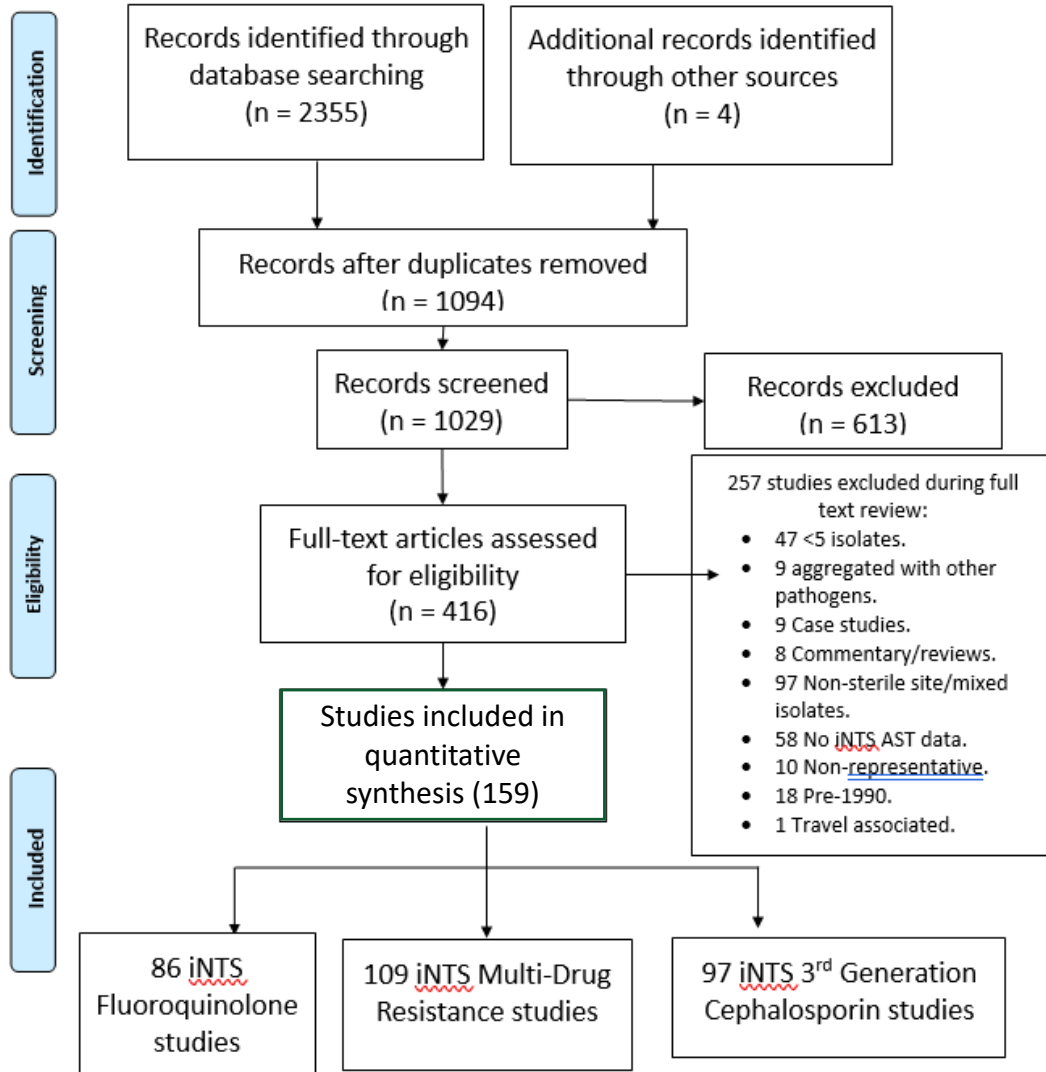
The GRAM project measures and maps the global burden of AMR. It was estimated that:

- 4.95 million deaths in 2019 associated with drug resistance.

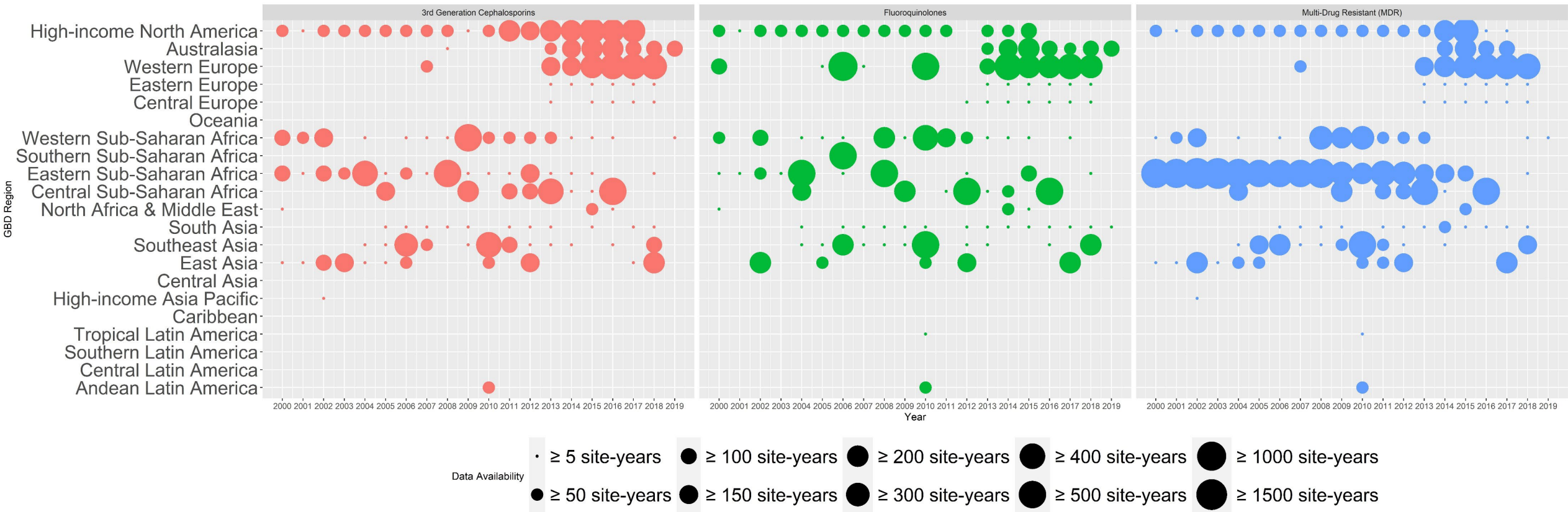- 1.27 million deaths in 2019 were attributable to AMR.

Background

- Often where the most attention is needed, we have the least information. What is the situation globally?

- AIM: To make use of a network of data providers.

- AIM: Use spatial-temporal modelling to help lend information from neighbouring countries in time and space.

- For invasive Non-typhoidal Salmonella, we want to determine the prevalence of fluoroquinolone non-susceptibility (FQNS), multi drug resistance (MDR) and 3rd generation cephalosporin resistance (3GCR).
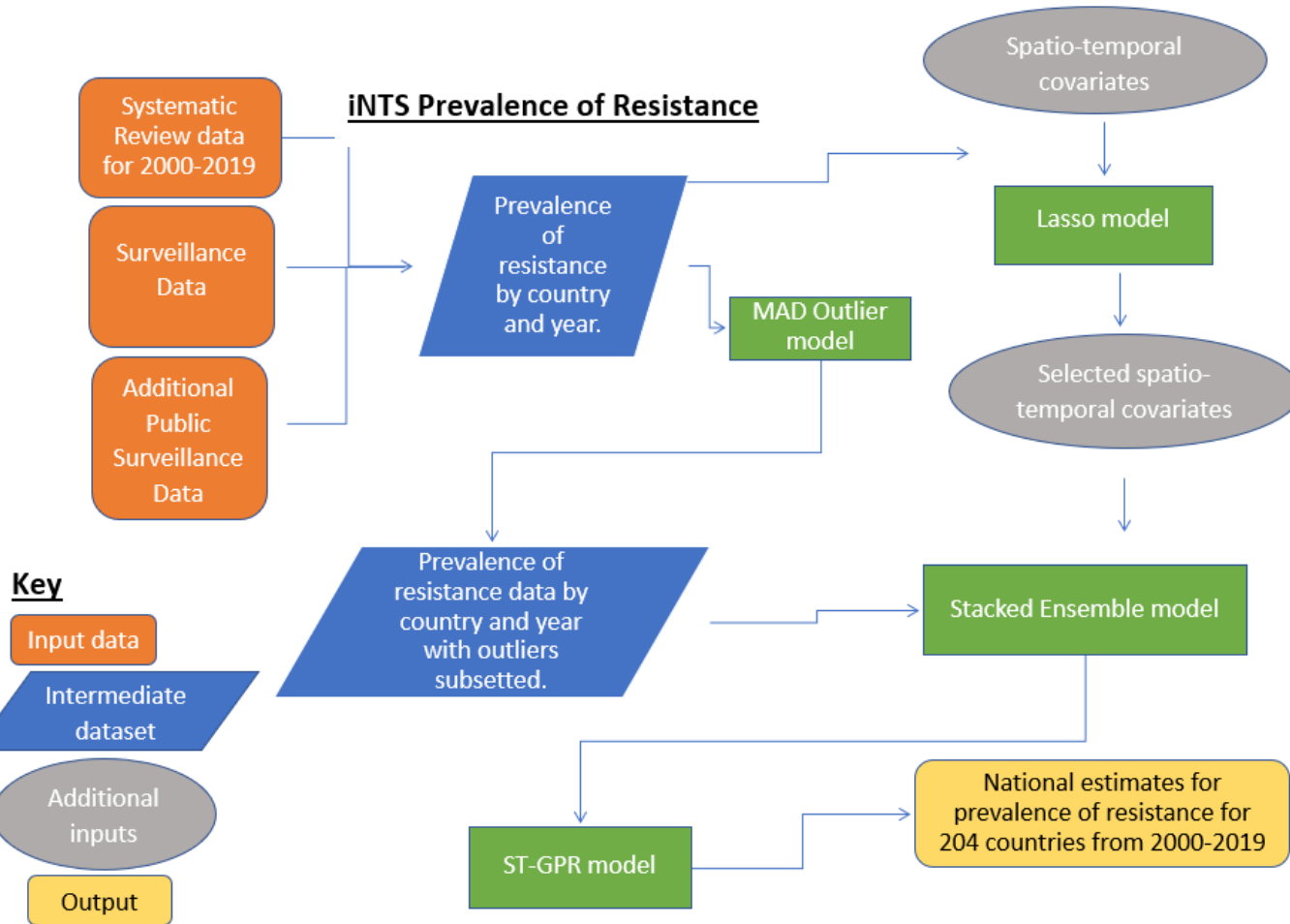
Data

PRISMA flow diagram:

- Identification
  - Records identified through database searching (n = 2355)
  - Additional records identified through other sources (n = 4)
- Screening
  - Records after duplicates removed (n = 1094)
  - Records screened (n = 1029)
  - Records excluded (n = 613)
- Eligibility
  - Full-text articles assessed for eligibility (n = 416)
  - 257 studies excluded during full text review:
    - 47 <5 isolates.
    - 9 aggregated with other pathogens.
    - 9 Case studies.
    - 8 Commentary/reviews.
    - 97 Non-sterile site/mixed isolates.
    - 58 No iNTS AST data.
    - 10 Non-representative.
    - 18 Pre-1990.
    - 1 Travel associated.
- Included
  - Studies included in quantitative synthesis (159)
    - 86 iNTS Fluoroquinolone studies
    - 109 iNTS Multi-Drug Resistance studies
    - 97 iNTS 3rd Generation Cephalosporin studies
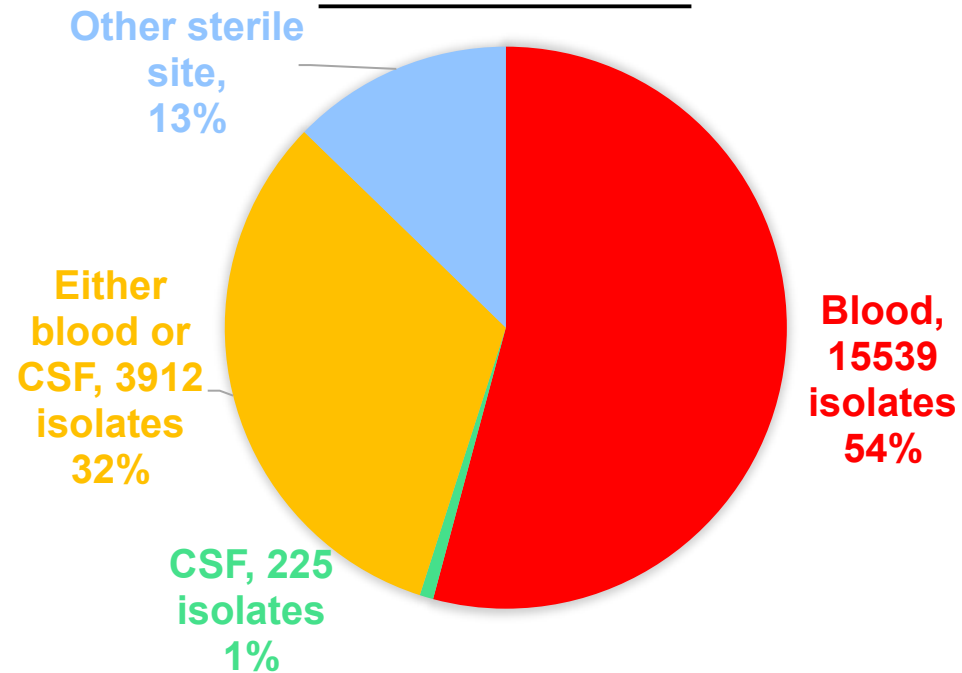
Data Availability

Methods

1. Outlier the most extreme values using a Mean absolute deviation model.

2. Identify important covariates using a Lasso Model.

3. Use a Stacked-ensemble model with the covariates, stacking different machine learning algorithms together.

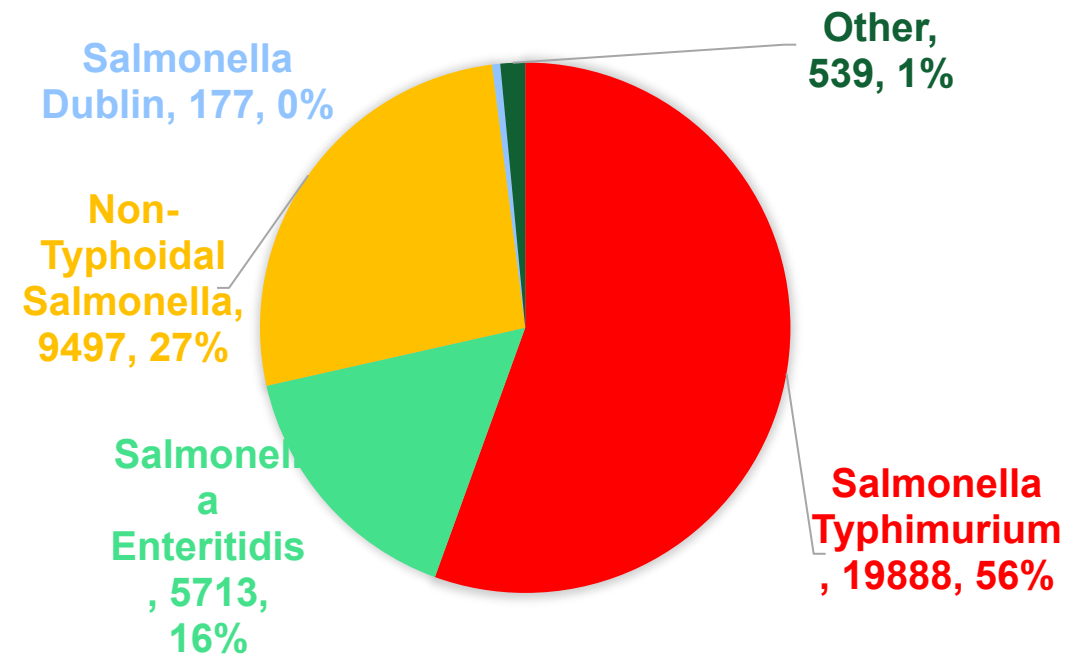4. Run a Spatial-Temporal Gaussian Process Regression model.

Results

- Data were included from 149 sources with 54,593 iNTS isolates covering 60 countries within 16 global regions over 20 years. 31 countries from LMICs.
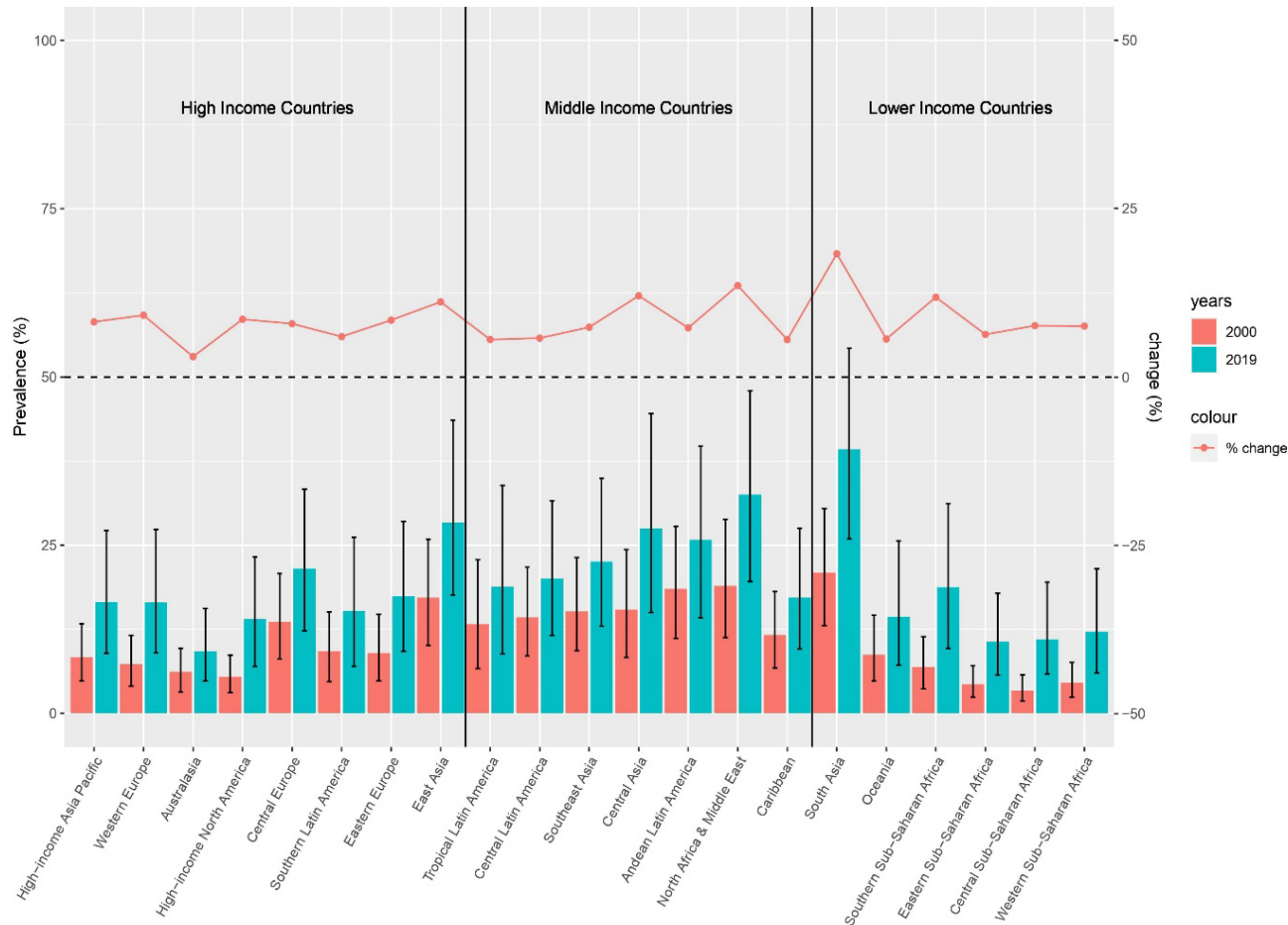

Sample Sites from Africa data

Other sterile site, 13%
Either blood or CSF, 3912 isolates 32%
CSF, 225 isolates 1%
Blood, 15539 isolates 54%

Distribution of Serovars from Africa data

Salmonella Dublin, 177, 0%
Non-Typhoidal Salmonella, 9497, 27%
Salmonella Enteritidis, 5713, 16%
Other, 539, 1%
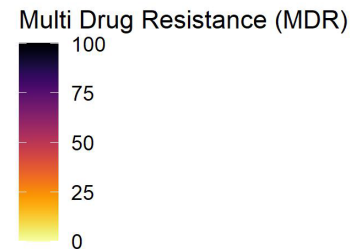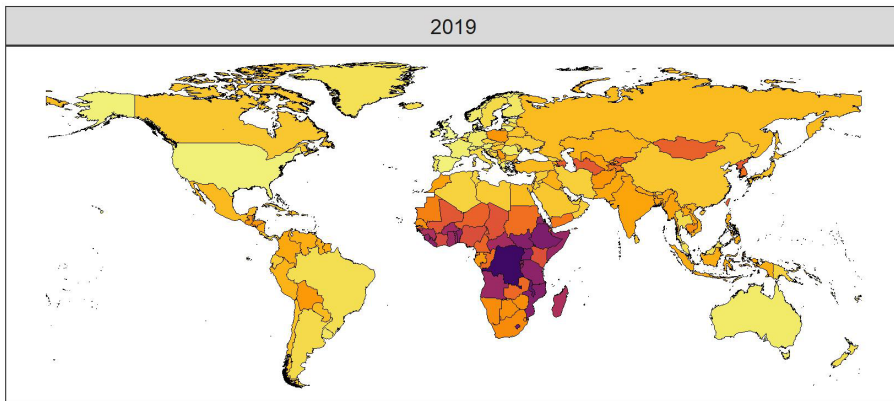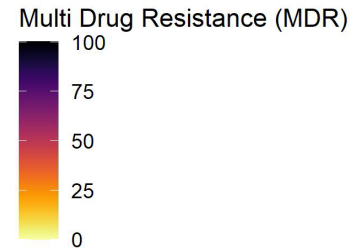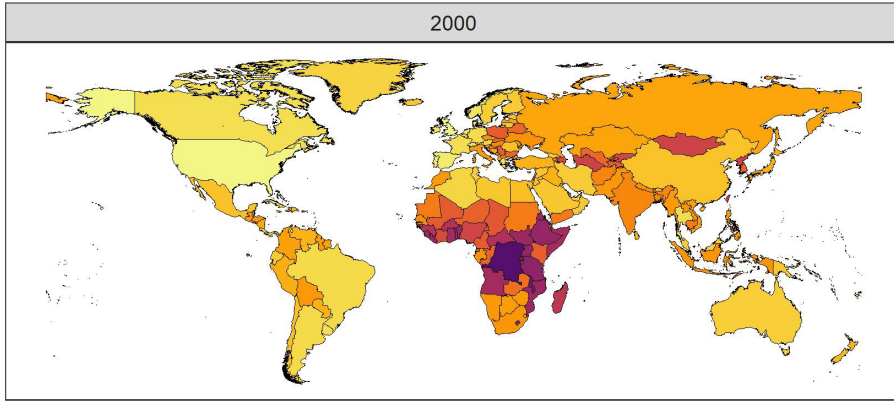Salmonella Typhimurium, 19888, 56%

Results - Fluoroquinolones

- FQNS in iNTS increased globally by 8.5%.

- We estimate that the prevalence of iNTS FQNS in South Asia increased by 18.3% in the period 2000-2019.

- Of isolates tested for FQNS, 3587 (23%) were Salmonella Typhimurium and 2325 (15%) were Salmonella Enteritidis.

Results – Multi-Drug Resistance.

2000

2019

- MDR started at a high level in 2019 and remained high.

- This was especially true for Sub-Saharan Africa. We estimate that, for 2019, iNTS MDR to be at 55% in east, 47% central, 44% west and 32% south.

- There were small increases in 3GCR.

Discussion

- AMR is increasing in Africa which follows the global trend for iNTS and also other pathogens.

- For iNTS this is especially true for fluoroquinolones and multi-drug resistance.

- It is estimated that Sub-Saharan Africa accounted for 79% of all iNTS cases globally in 2017 - The global burden of non-typhoidal salmonella invasive disease: a systematic analysis for the Global Burden of Disease Study.

Limitations

- There were data gaps and sparsity.

- One potential limitation is that AMR might be overestimated, because sensitive isolates might have been treated successfully in the community without any diagnostics.

What Next?

- This work highlights increasing resistance globally. The Institute for Health Metrics and Evaluation (IHME) estimates of the global burden of disease from iNTS in 2019 are 594,000 cases, 79,000 deaths and 6.11 million global DALYs.

- More needs to be done in terms of prevention of iNTS including vaccination. This modelling work could potentially help to estimate the impact of a future vaccine.

- This work will feed into the Global Burden of Disease study and regular updates will be made available.

Thank you!

- Prof Christiane Dolecek,
- Dr Benn Sartorius,
- Prof Ben Cooper.