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Purpose

*Shigella* is the second leading cause of diarrhoeal mortality, with an estimated 220,000 deaths annually. It is estimated that each year 264 million episodes of shigellosis occur (1). Antimicrobial resistance of Gram-negative bacteria is increasingly reported worldwide, rendering multiple antibiotics ineffective.

Identifying the spatial and temporal trends in the distribution of drug resistant *Shigella* is important to identify hotspots of disease, close gaps in knowledge and inform policy regarding the use of antibiotics.

Research objectives:

1. To collect, review and analyse all available data on antimicrobial resistant *Shigella* species worldwide.
2. Produce maps of the prevalence of antimicrobial resistant *Shigella* sp. using geospatial modelling techniques to predict the prevalence at a fine spatial resolution from 1990-2018.
Methods and Materials

A global dataset was compiled through a systematic review to obtain the proportion of *Shigella* isolates (including all four *Shigella* species) with nalidixic acid resistance, linked to time and geographic location. Data were extracted from the published literature, from 1990 to 2018. The median prevalence of nalidixic acid resistance was calculated and presented by region and 5-year time periods. The proportion of *Shigella* isolates with nalidixic acid resistance will be modelled at a high spatial resolution. Results will be incorporated into the Global Burden of Disease study (GBD).

- Data were extracted from the published literature 1990 to 2018.
- Data were collected on all four *Shigella* species; *S. dysenteriae*, *S. flexneri*, *S. boydii* and *S. sonnei*, with all isolates from stool culture.
Fig. 1: Prisma flowchart of the Shigella systematic review

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**Fig. 2:** Data availability by year and country: All included data are plotted by country (y-axis) and year (x-axis), grouped by Global Burden of Disease (GBD) region (2). The number of studies for each country-year is depicted by the size of the point.

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Results

Our systematic search identified 3,633 articles. We extracted data from 521 articles into our database.

- Most studies were from India, Iran and China, were conducted in a hospital and included both children and adults.
- Multidrug resistance (MDR) was reported in 30% of studies. However, the definition of MDR varied between studies. Many reported patterns of resistance to different antibiotics or defined MDR as resistant to "3 or more antibiotics."
- Method sections seldom stated the susceptibility testing methods, which guidelines were followed and control strain used, meaning we were unable to give an objective assessment of data quality.

Figures 3 and 4 show:

- High prevalence of nalidixic acid resistance is seen in North Africa and the Middle East, Southeast Asia, and Southern Sub-Saharan Africa.
- Resistance in South Asia is consistently low, whereas in Southeast Asia and North Africa and the Middle East, resistance has persisted over time.
- Resistance remains mostly high in Central Latin America between 2005-14. Only sparse data was available from Latin America and Oceania.
Fig. 3: Crude estimates of the median prevalence (percent) of nalidixic acid resistant shigella isolates at regional level. Dark grey areas show where no data was available. The white areas depict 0% resistance and the red area is 100% resistance.

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Fig. 4: Crude estimates of the median prevalence (percentage) of nalidixic acid resistant Shigella isolates, group by GBD region and 5-year time period and GBD region. Number of studies and isolates are displayed.

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Conclusion

- A comprehensive review of the published literature is provided, revealing widespread resistance to nalidixic acid.
- This systematic review is limited by lack of published data from many countries, especially Sub-Saharan Africa, and often the quality of microbiology culture and susceptibility testing could not be formally evaluated.
- Next steps will be to develop a geospatial modelling framework to address the data’s inherent heterogeneity, to produce estimates of antimicrobial resistant *Shigella* sp. globally and address the data’s inherent heterogeneity. This systematic review data will be supplemented with data from additional sources, such as surveillance systems and unpublished data through collaborative efforts.

Bahar joined the Oxford GBD Group as a Data Analyst in February 2018 before commencing her doctorate in tropical medicine and global health later in the year. Her DPhil work focuses on building geospatial models to predict the level of antibiotic resistance in *Shigella, E.coli* and *K. pneumoniae* infections at a high spatial and temporal resolution.