Introducing the GRAM Project: Estimating the Global Burden of Antimicrobial Resistance

To address the growing threat of antimicrobial resistance (AMR), leaders in global health research came together to create the Global Research on Antimicrobial Resistance (GRAM) Project, a partnership between IHME and the University of Oxford.

GRAM aims to provide robust, comprehensive, and timely evidence on the global burden of AMR, to help drive awareness, support better surveillance efforts, and prompt policy action to control AMR, including facilitating antimicrobial stewardship.

Our aims and objectives

- Consolidate, review, and analyse all available data and scientific information on AMR worldwide, to generate comparable AMR burden estimates for pathogen-drug combinations and clinical syndromes, from 1990 to the present, for all 195 countries and territories included in the Global Burden of Disease (GBD) study.
- Produce geospatial maps of AMR burden as detailed as the data will allow, to enable policymakers and researchers to tailor interventions based on the local burden of disease.
- Promote the widespread dissemination of the results to the public, the development community, academics, and policymakers via the use of tools and interactive data visualisations.

The global burden of drug-resistant infections

Our project focuses initially on AMR in the following bacterial pathogens, but we aim to extend our work to all relevant pathogen-drug-clinical syndrome combinations globally.

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Antibiotic</th>
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<tbody>
<tr>
<td>Salmonella enterica serovars Typhi and Paratyphi</td>
<td>Fluoroquinolones, chloramphenicol</td>
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<tr>
<td>Non-typhoidal Salmonellae</td>
<td>Fluoroquinolones</td>
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<tr>
<td>Shigella species</td>
<td>Fluoroquinolones</td>
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<tr>
<td>Staphylococcus aureus</td>
<td>Methicillin</td>
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<td>Streptococcus pneumoniae</td>
<td>Penicillin</td>
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<tr>
<td>Escherichia coli</td>
<td>Third-generation cephalosporins, fluoroquinolones</td>
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<tr>
<td>Klebsiella pneumoniae complex</td>
<td>Third-generation cephalosporins, carbapenems</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis complex</td>
<td>First-line: isoniazid, rifampicin</td>
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<tr>
<td></td>
<td>Second-line: fluoroquinolones, amikacin, capreomycin, kanamycin</td>
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<tr>
<td>Neisseria gonorrhoeae</td>
<td>Third-generation cephalosporins</td>
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The GRAM Project emerged in response to major gaps in data on the geographical prevalence of AMR and its risk factors globally; the absence of a formal framework for combining worldwide surveillance findings; and, lack of consensus on diagnostic methodology, data collection, and the global standards and definitions needed to facilitate comparison and evaluation of programmes to tackle AMR.

Reports by the World Health Organisation, European Centre for Disease Prevention and Control, and UK Government have raised concerns about increasing rates of AMR globally – e.g., with one study by the UK’s O’Neill Review (2016) estimating that drug-resistant infections claim 700,000 lives each year, and that without proactive mitigation the number could rise to 10 million per year by 2050.

To address concerns about this potentially serious health risk, the GBD study can provide a scientifically rigorous and comprehensive framework for estimating the burden of AMR, as well as the epidemiological granularity needed by policymakers to address it.

Typhoid and Paratyphoid: a case study

- The GBD currently estimates global health loss due to typhoid and paratyphoid.
- The addition of AMR to the GBD will show how much typhoid- and paratyphoid-related health loss is due to disease-resistant infections versus other causes, strengthening knowledge of the disease burden both for AMR and overall.

Typhoid and paratyphoid killed approximately 23,500 male and female children under 5 globally in 2017.*

More accurate measures of drug-resistant infections could tell us:
- The variation in the burden of drug resistance by geographic location
- Which interventions might improve public health at the local, national, or international levels

*Uncertainty interval: 10,644 – 44,294; SOURCE: GBD Compare

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