Sustainable use of available medicines
Session 5: Access NASEM Meeting
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Research Landscape

Inequities abound:

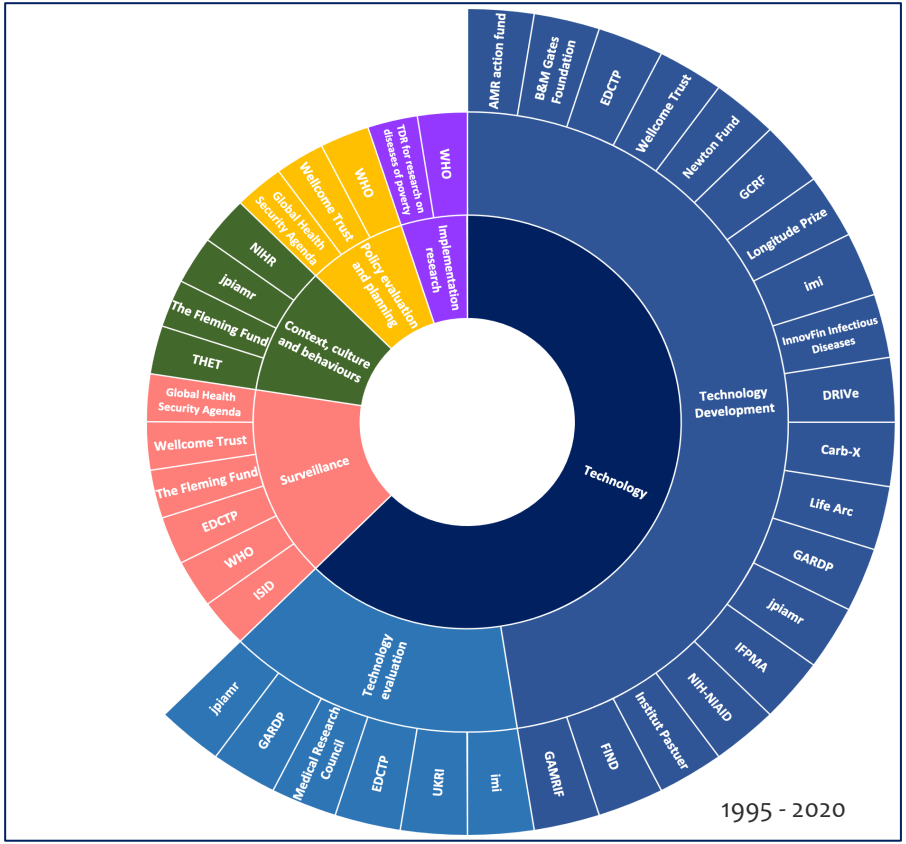
LMIC vs HIC funding

R&D for new drugs vs optimising existing ones

Tech development vs implementation

Policy and strategy – gaps in operationalisation

Contextual and culture under investigated

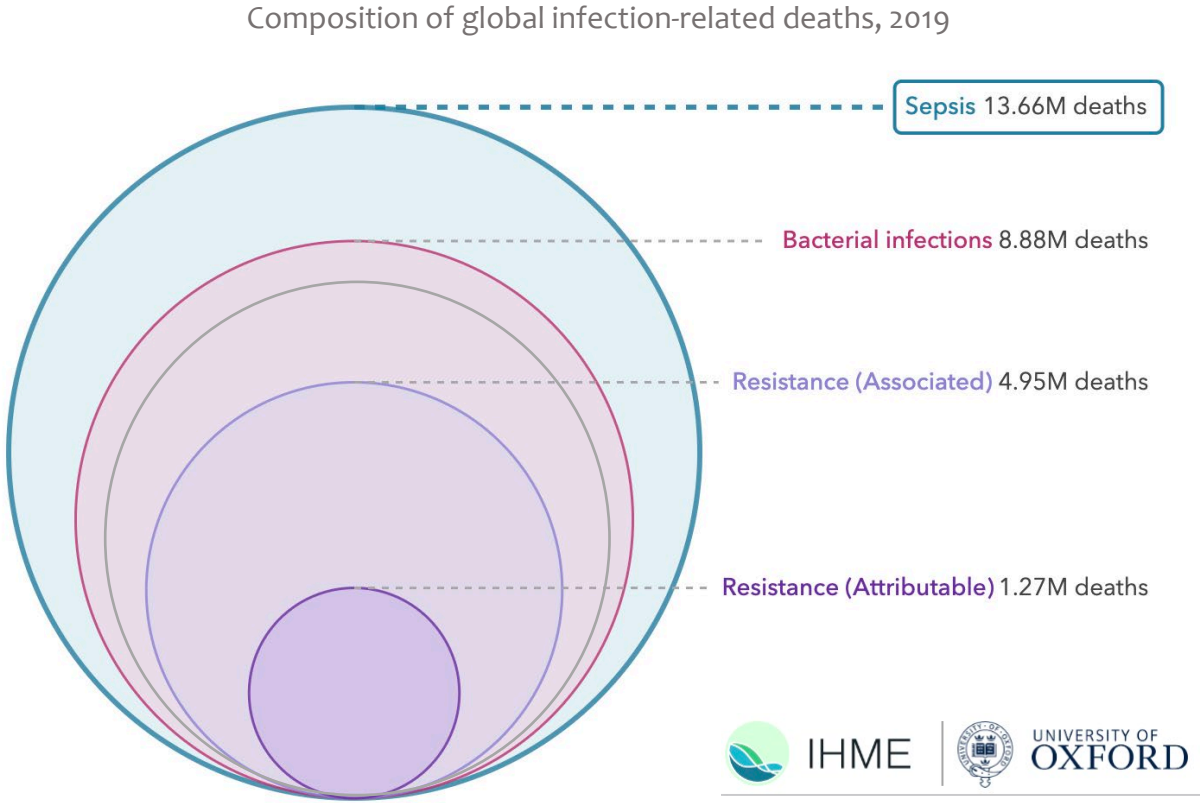


The Lancet Regional Health - Europe (2021)

Slide courtesy of Marc Mendelson

Why Access?

Non-resistant bacterial infections 3.93 million deaths



https://vizhub.healthdata.org/microbe/

Access to antibiotics

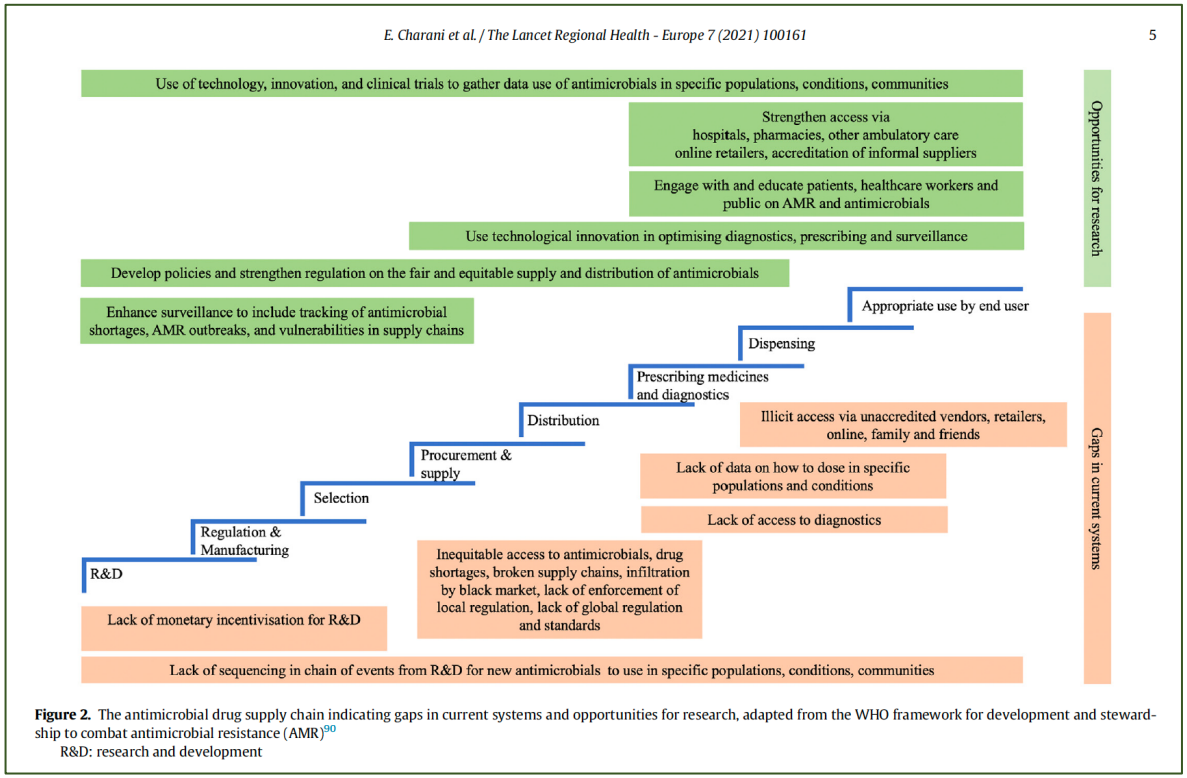


Figure 2. The antimicrobial drug supply chain indicating gaps in current systems and opportunities for research, adapted from the WHO framework for development and stewardship to combat antimicrobial resistance (AMR)[90]
R&D: research and development

Lancet Regional Health Europe (2021)

Existing NAPs

Health Policy

An analysis of existing national action plans for antimicrobial resistance—gaps and opportunities in strategies optimising antibiotic use in human populations

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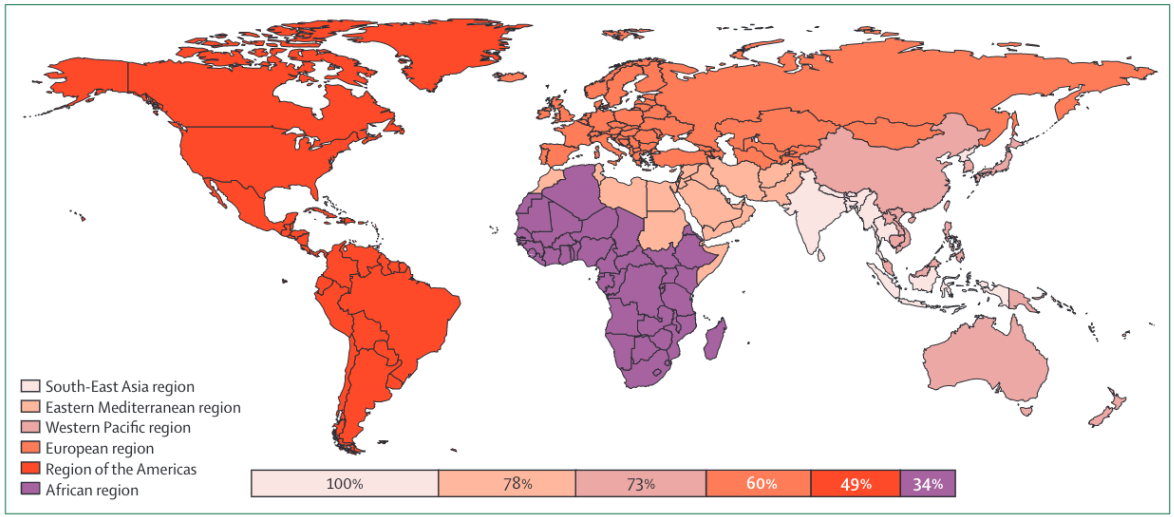


Figure 2: **Availability of national action plans by WHO region as of February, 2022**

Lancet Global Health, 2023

Key recommendations

Policy and strategic planning

Economic impact assessment of the strategies implemented to tackle AMR and the resource and infrastructure requirements as a tool for gaining **political and financial commitment**

Medicines management

Assess existing prescribing tools for optimum prescribing and surveillance
Identify mechanisms for data sharing on supply chain issues (local, national, and international)
Develop and evaluate strategies to enforce antibiotic prescribing, purchase, and access-related legislation

Technology and diagnostics

Investigate the whole-health-system integration of technologies – **Fit for context, affordable**

Patient and public engagement

Interventions across socioeconomically diverse populations – intersectional research

Fragile and fractured systems

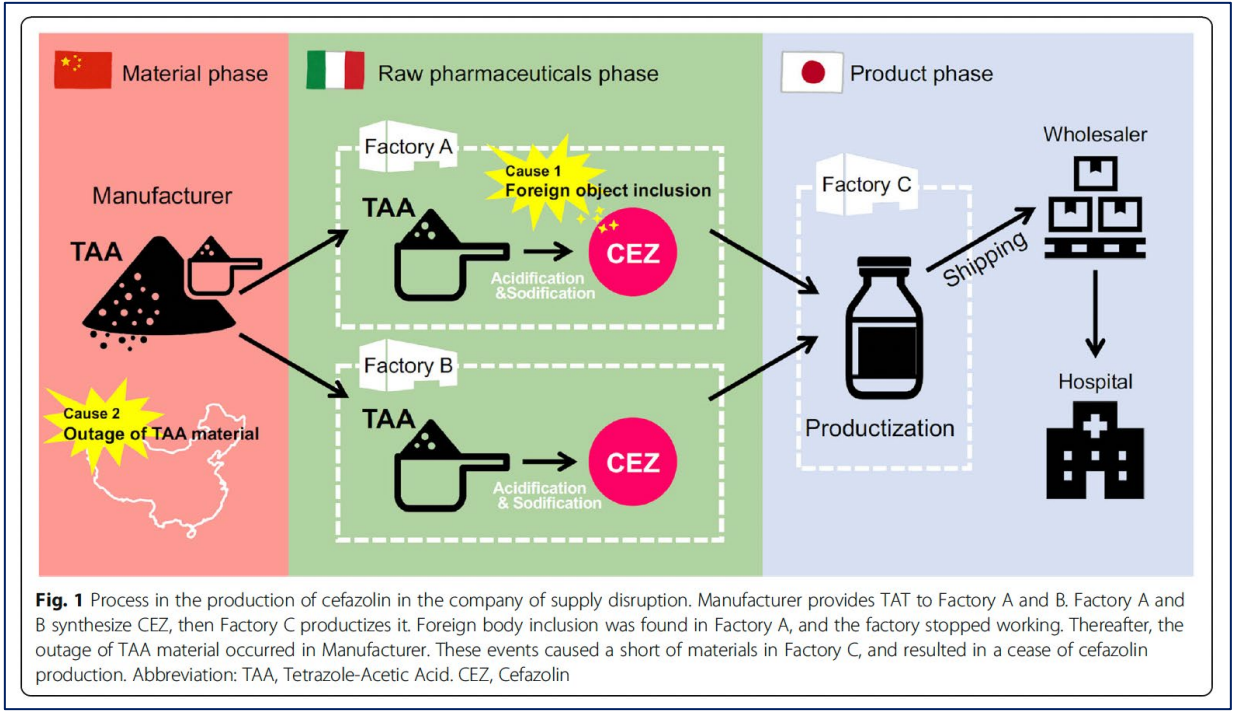


Fig. 1 Process in the production of cefazolin in the company of supply disruption. Manufacturer provides TAT to Factory A and B. Factory A and B synthesize CEZ, then Factory C productizes it. Foreign body inclusion was found in Factory A, and the factory stopped working. Thereafter, the outage of TAA material occurred in Manufacturer. These events caused a short of materials in Factory C, and resulted in a cease of cefazolin production. Abbreviation: TAA, Tetrazole-Acetic Acid. CEZ, Cefazolin

Koizumi et al., 2021

Collateral damage

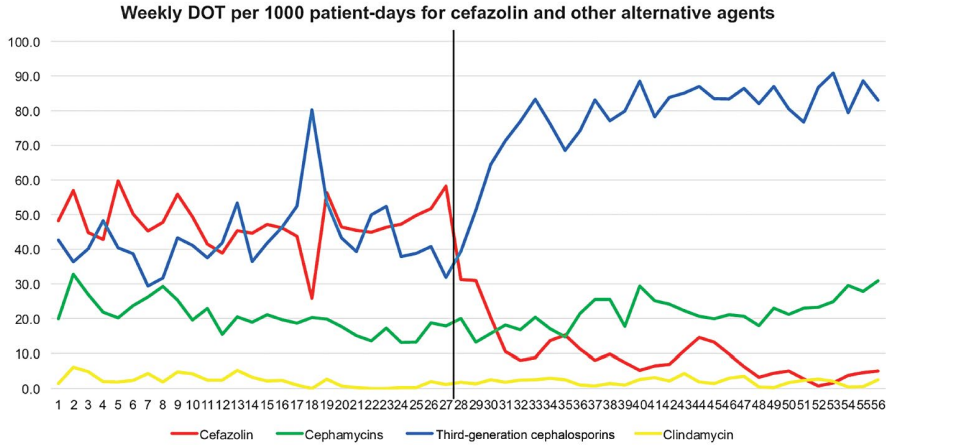


Figure 1. Changes in the use of cefazolin and alternative antimicrobial agents during a cefazolin shortage. Data were tracked from September 2018 to September 2019. The x-axis represents a weekly time period (periods 1–56), and the y-axis represents days of therapy per 1000 patient-days (PD). The vertical line represents the shortage started at the study institution (period 27: from 11 March 2019). The time-series model revealed an increase of third-generation cephalosporins (+18.88 days of therapy [DOT] per 1000 PD [$P < .01$ for intercept] and +0.65 DOT per 1000 PD/week [$P = .04$ for trend]), cefamycins (+0.78 DOT per 1000 PD/week [$P < .001$ for trend]), and clindamycin (+1.78 DOT per 1000 PD [$P = .008$ for intercept] and +0.12 DOT per 1000 PD/week [$P = .003$ for trend]), and significantly decreased use of cefazolin (–27.6 DOT per 1000 PD [$P < .001$ for intercept] and –0.59 DOT per 1000 PD/week [$P = .005$ for trend]).

Undermining stewardship efforts

Treatment failure, e.g. vancomycin for MSSA

Increased consumption of other agents

Shortage of substitute antibiotics

Honda et al., 2020

Reported causes

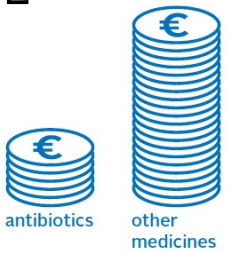
Manufacturers not legally required to provide reason for shortages

Active pharmaceutical ingredient – 60 to 80% of raw material produced outside of Europe

Dwindling interest in manufacturing due to increased regulatory requirement and quality control

Price competition of off patent agents - includes many on EML

Procurement mismanagement



Pandey et al, in draft 2024

Reported consequences

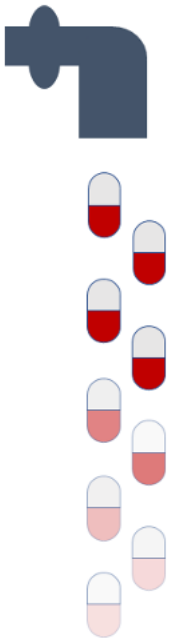
Cefazolin - Japan (Nakaraj et al., 2021)
Surgical prophylaxis – **increased reoperation and surgical site infection rates**

Piperacillin-Tazobactam - USA (Gross et al., 2017)
Increased *C. difficile* rates reported

Penicillin G – Brazil, (Araoju et al., 2020) Global (Findlay et al., 2017)
Increased congenital syphilis and still births, poorer outcomes associated with socioeconomic deprivation index

Increased out of pocket costs for patients, increased medication errors (Phoung et al., 2019)

Reported consequences



Antibiotic use – broad-spectrum use

Clinical outcomes – varied evidence

Economic – no robust evaluations, indirect evidence of cost to systems

Mitigation strategies – AMS key feature of successful mitigation strategies

Pandey et al, in draft 2024

What do the experts say?

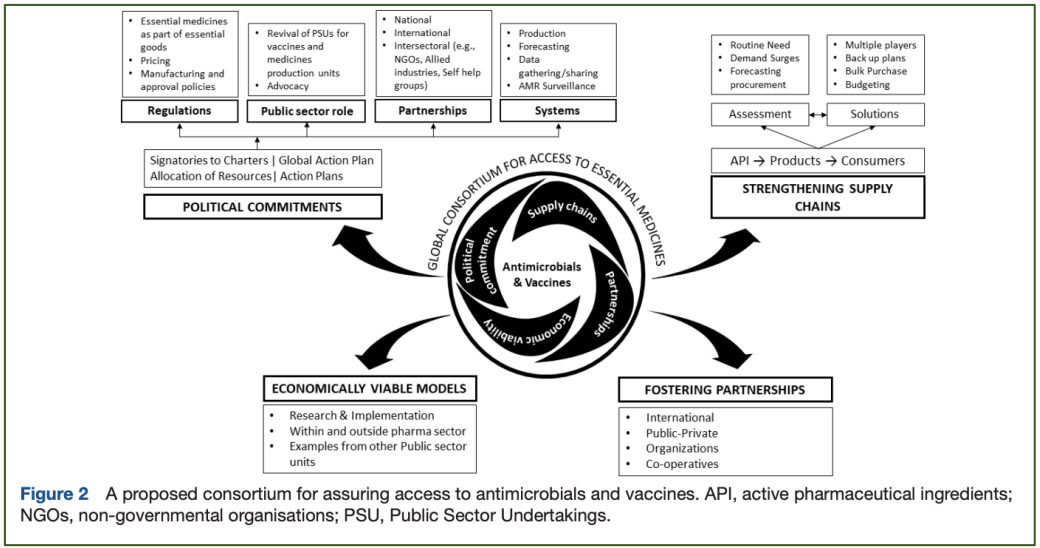


Figure 2 A proposed consortium for assuring access to antimicrobials and vaccines. API, active pharmaceutical ingredients; NGOs, non-governmental organisations; PSU, Public Sector Undertakings.

Shafiq et al., 2020

GARD P

Global Antibiotic Research & Development Partnership

A GARDP funded research project at the University of Cape Town, with collaborating sites in India and UK

Provided platform for follow on Wellcome Trust Funding

wellcome

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Thank you

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