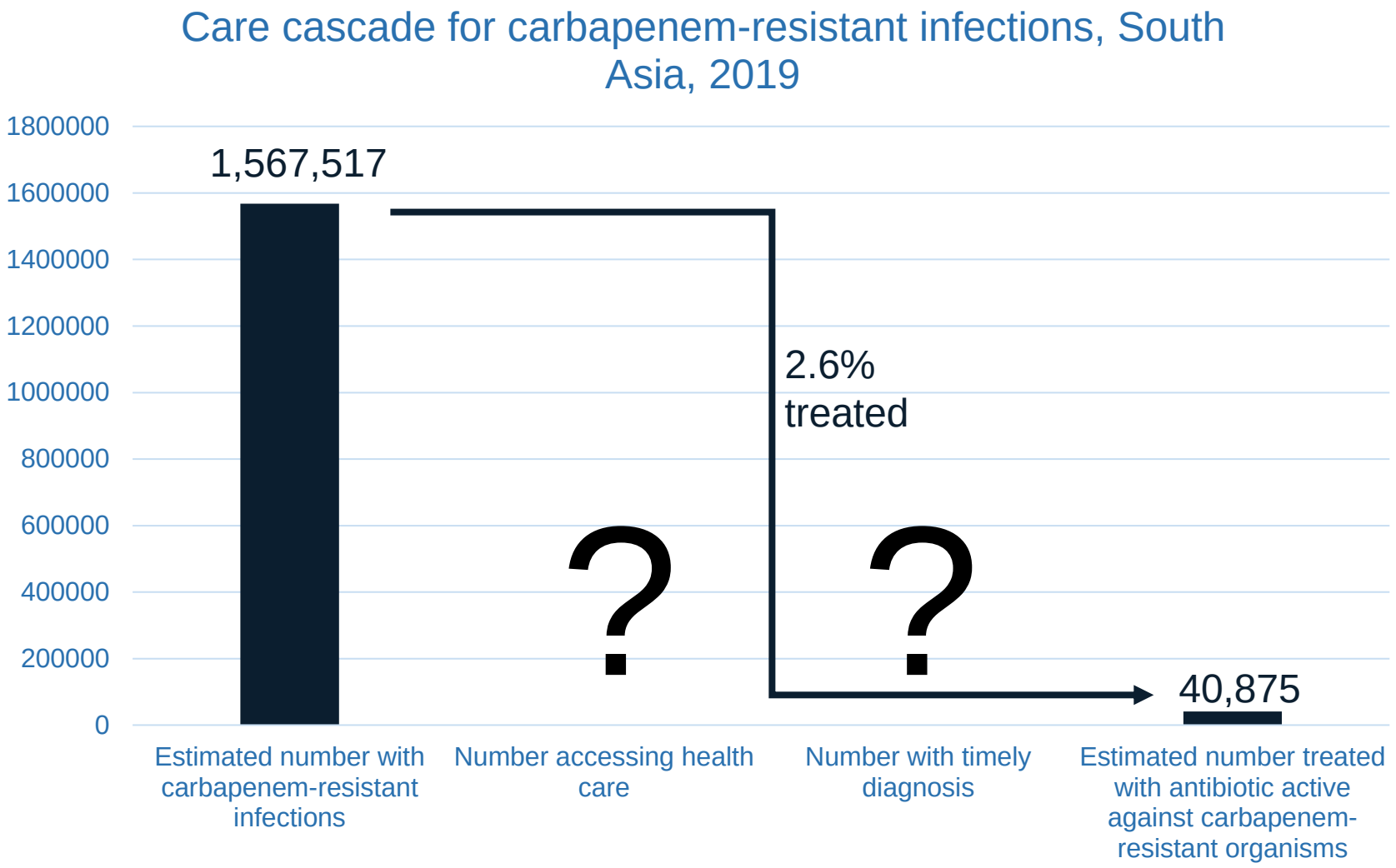
Global Antibiotic Research and Development Partnership (GARDP)

Equitable Access for Antibiotics:
A Summary of Barriers

GARDP
Global Antibiotic Research & Development Partnership

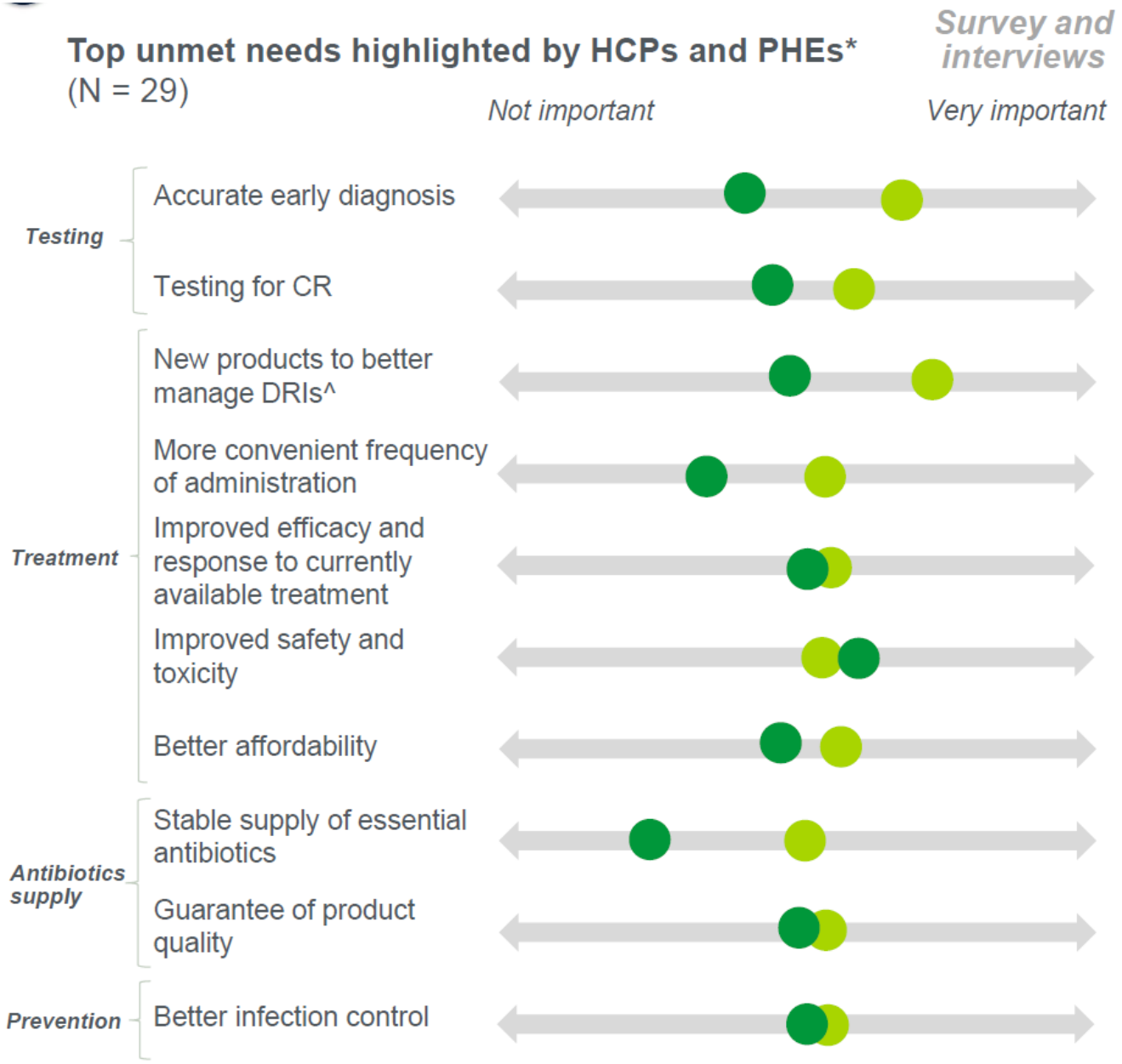
Care Cascade: Carbapenem-resistant infections, South Asia 2019



- Estimated number with carbapenem resistant infections from GRAM CR-associated mortality and indication-weighted case fatality rate
- Estimated number treated from IQVIA data on procurement of CR-active antibiotics, corrected for channel coverage
- Calculated estimates for two ends of the care cascade

Top unmet AMR needs in South Africa

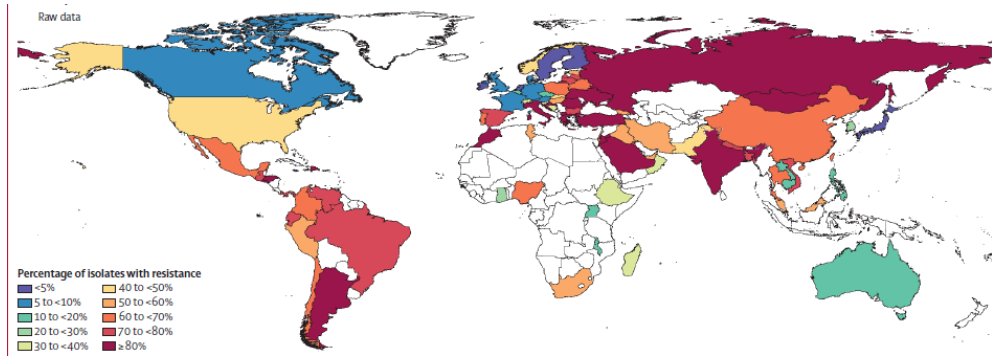
*The survey responses are drawn from qualitative interviews that were conducted in South Africa in 2022 with 16 physicians and public health experts, as well as quantitative research with 20 physicians who deal with AMR.



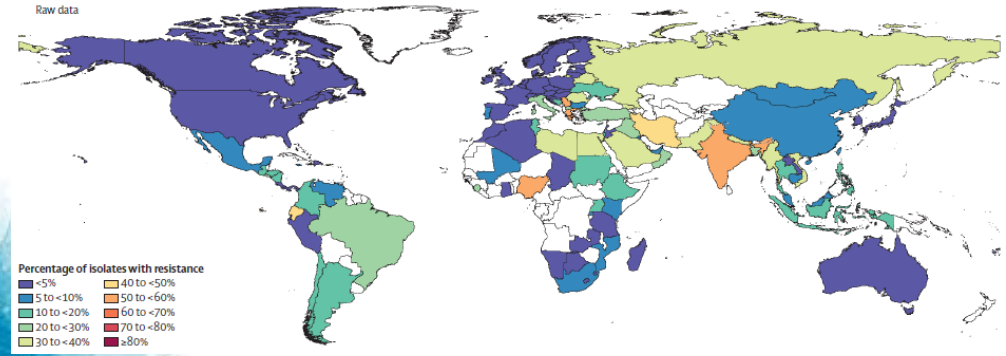
Two trends in antibiotic access

1. Growing antibiotic resistance

Carbapenem-resistant *Acinetobacter baumannii*

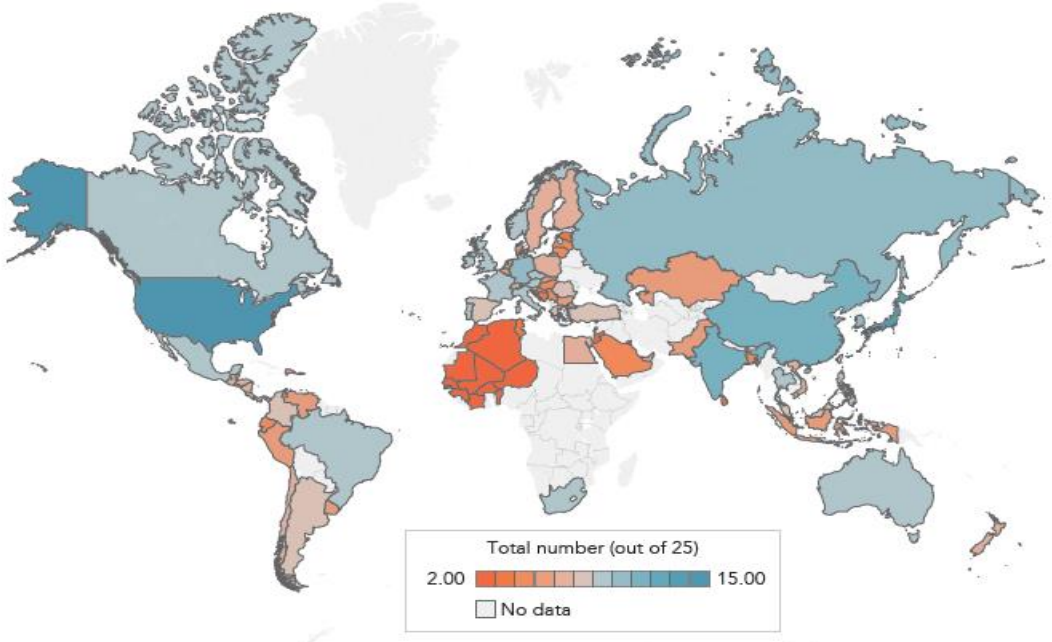


Carbapenem-resistant *Klebsiella pneumoniae*



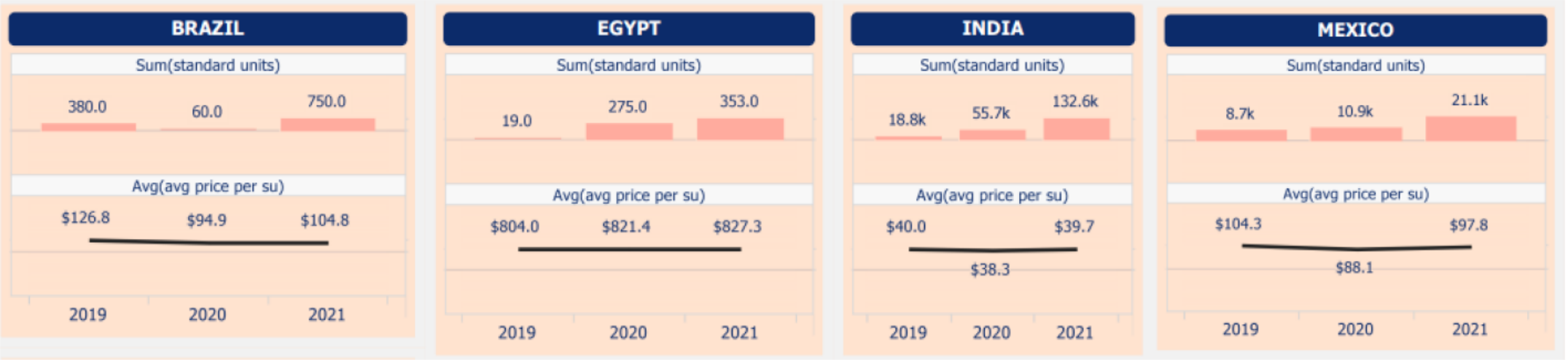
2. Not widely registered

Number of antibiotics registered 1999-2014



AMR collaborators, Lancet 2021; Kallberg et al, PLoS One 2018

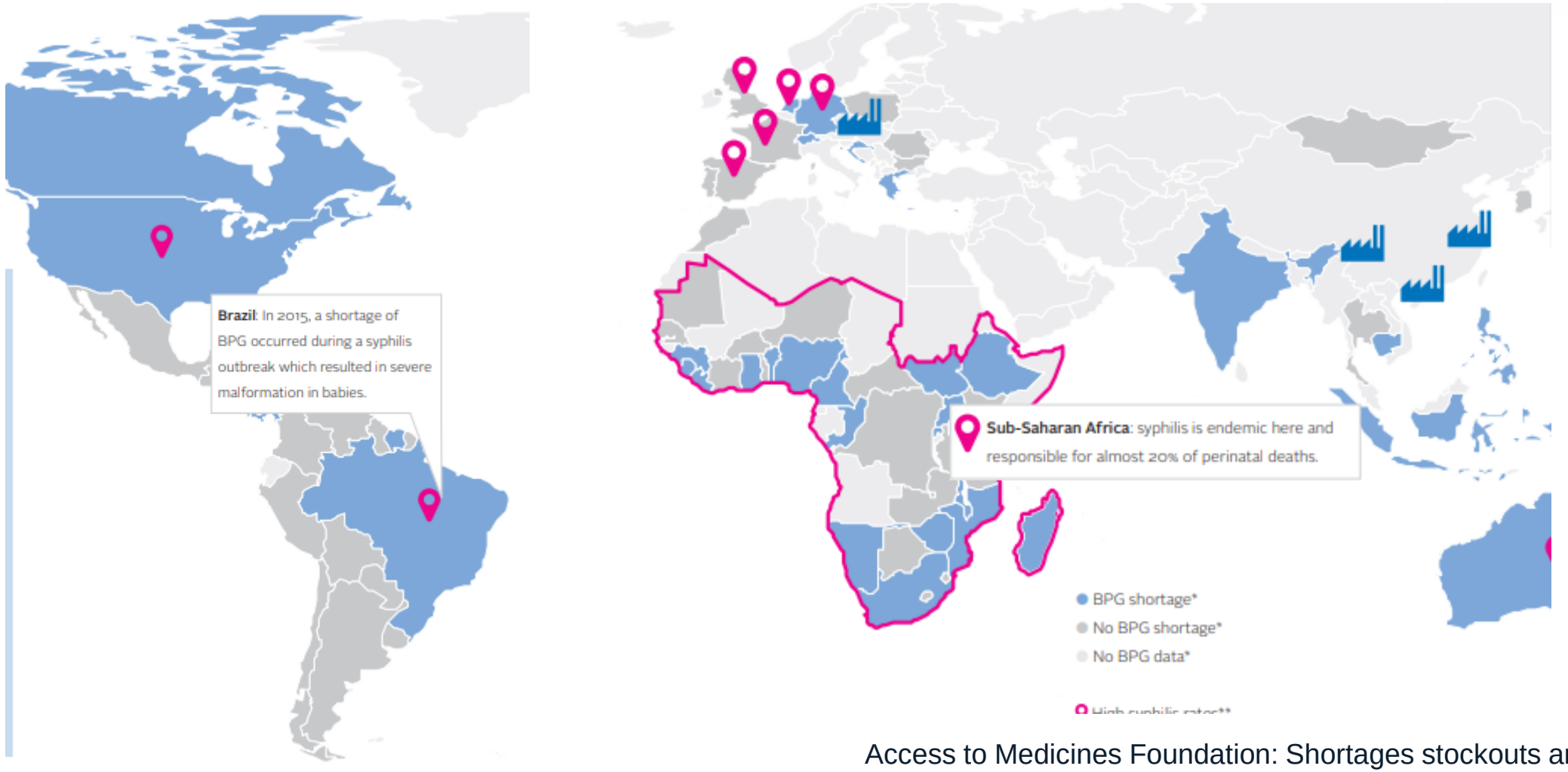
High and variable prices for on-patent Reserve antibiotics (price in USD per vial)



Ceftazadime-avibactam

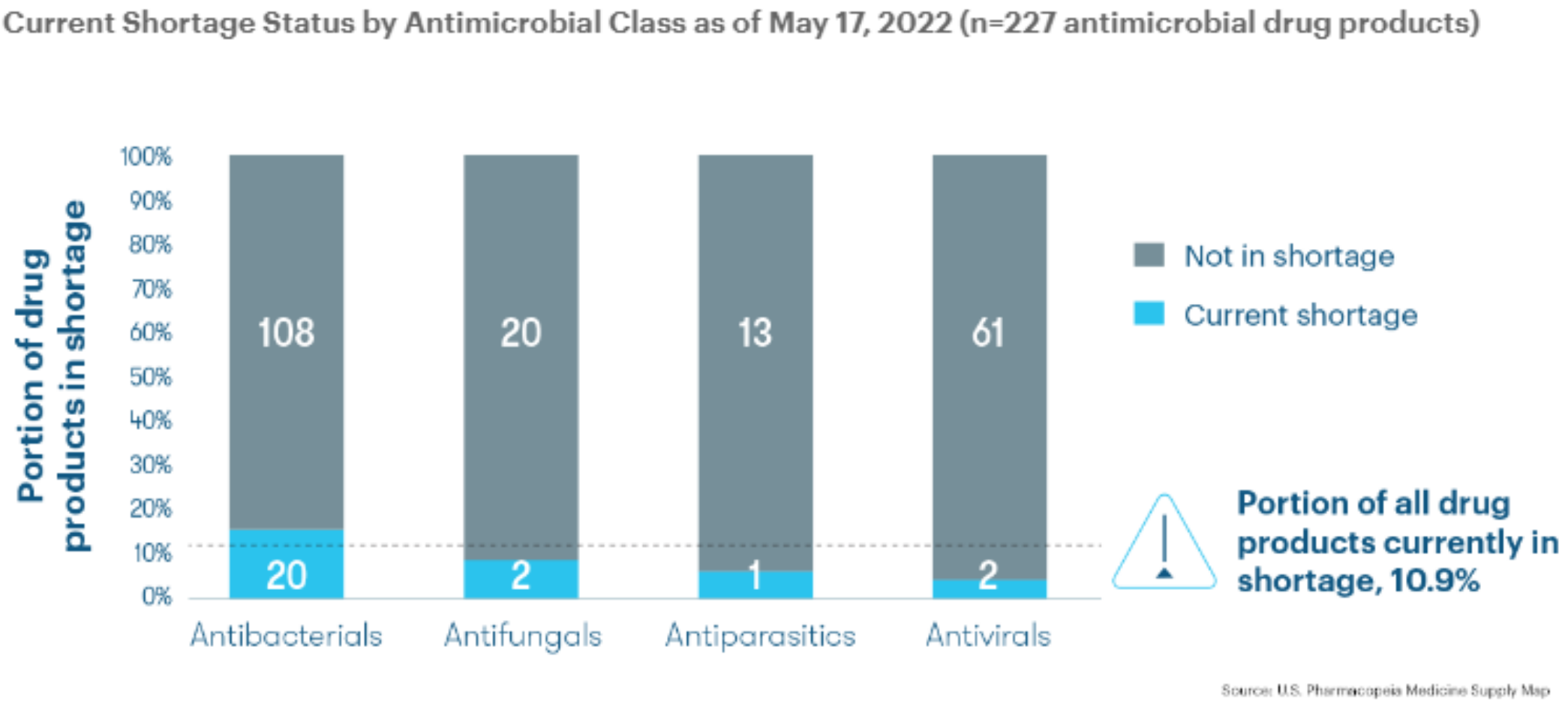
Ceftolozane-tazobactam

Not just new drugs: Drug shortages also have global impact on antibiotic access

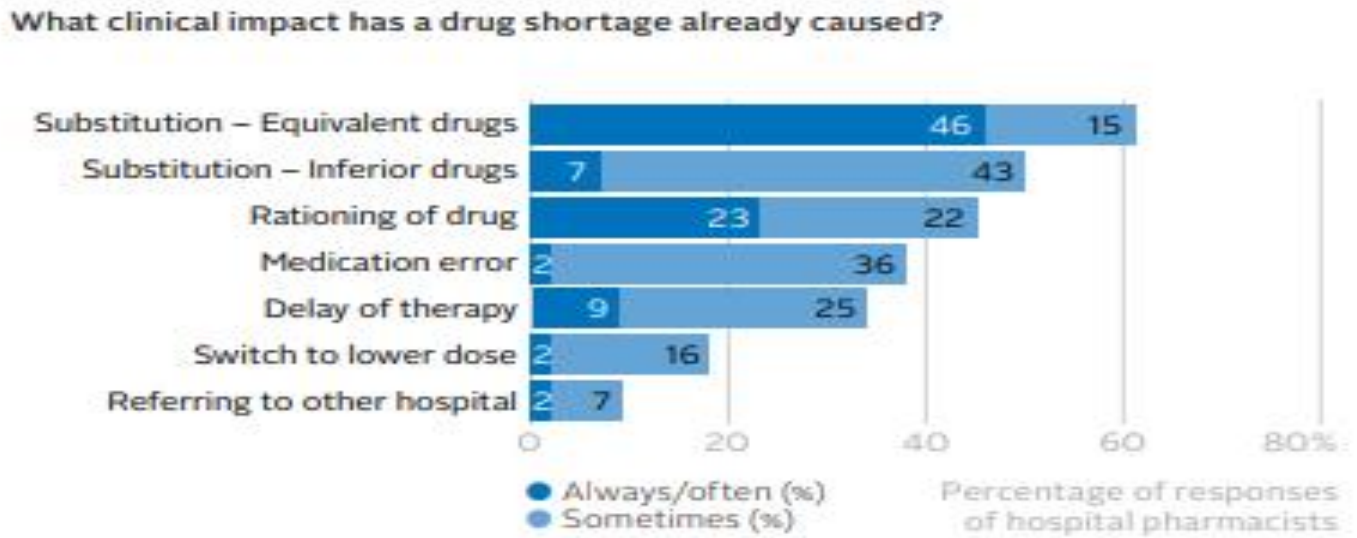


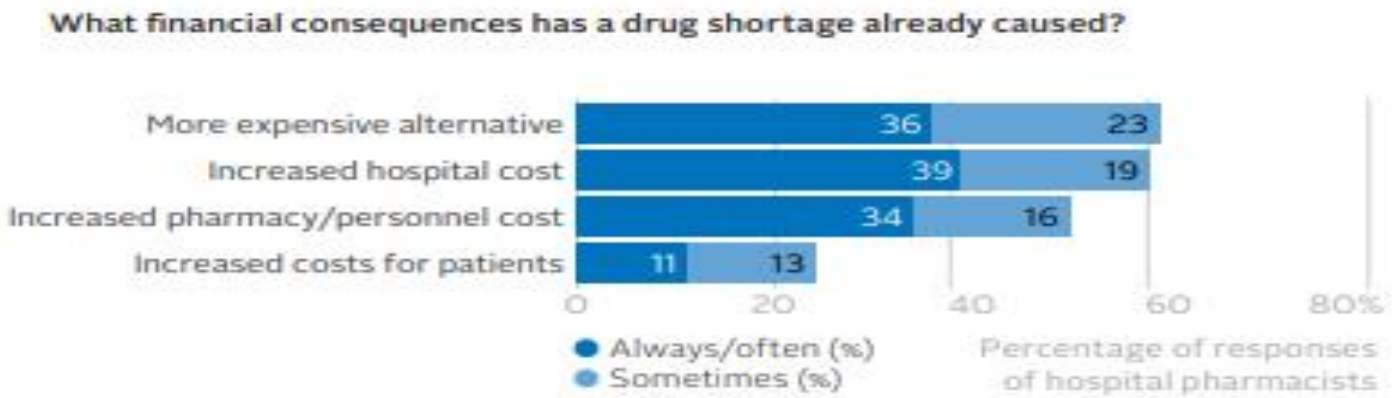
Access to Medicines Foundation: Shortages stockouts and scarcity report, 2018

Antibacterials are at disproportionate risk of shortage



Clinical and financial impacts





Source: Insights into European Drug Shortages: A survey of hospital pharmacists. PLoS ONE, 2015

Shortages are worldwide
Information on shortages isn't

- Shortages with global impact
  - Benzathine penicillin G
  - Pipericillin-tazobactam
  - Cotrimoxazole IV
- Shortages with differential regional impact
  - Chloramphenicol
  - Amoxicillin pediatric formulations
- National shortages
  - Ticarcillin-clavulanate

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

A living systematic review of antibiotic drug shortages and the strategies employed for managing these shortages

Citation

Nusrat Shafiq, Avaneesh Kumar Pandey, Samir Malhotra, Asish Kakkar, Alison Holmes, Marc Mendelson, Rohit Malpani, Manica Balasegaram, Esmita Charani. A living systematic review of antibiotic drug shortages and the strategies employed for managing these shortages. PROSPERO 2021 CRD42021296472 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021296472

Only 20 of 132 papers included specific information from LMICs

Preliminary data, Shafiq et al Review

Proximal Causes

Manufacturing

- Quality failure
- Disaster (fire)
- Inability to rapidly increase production

Supplier availability

- MAH exit

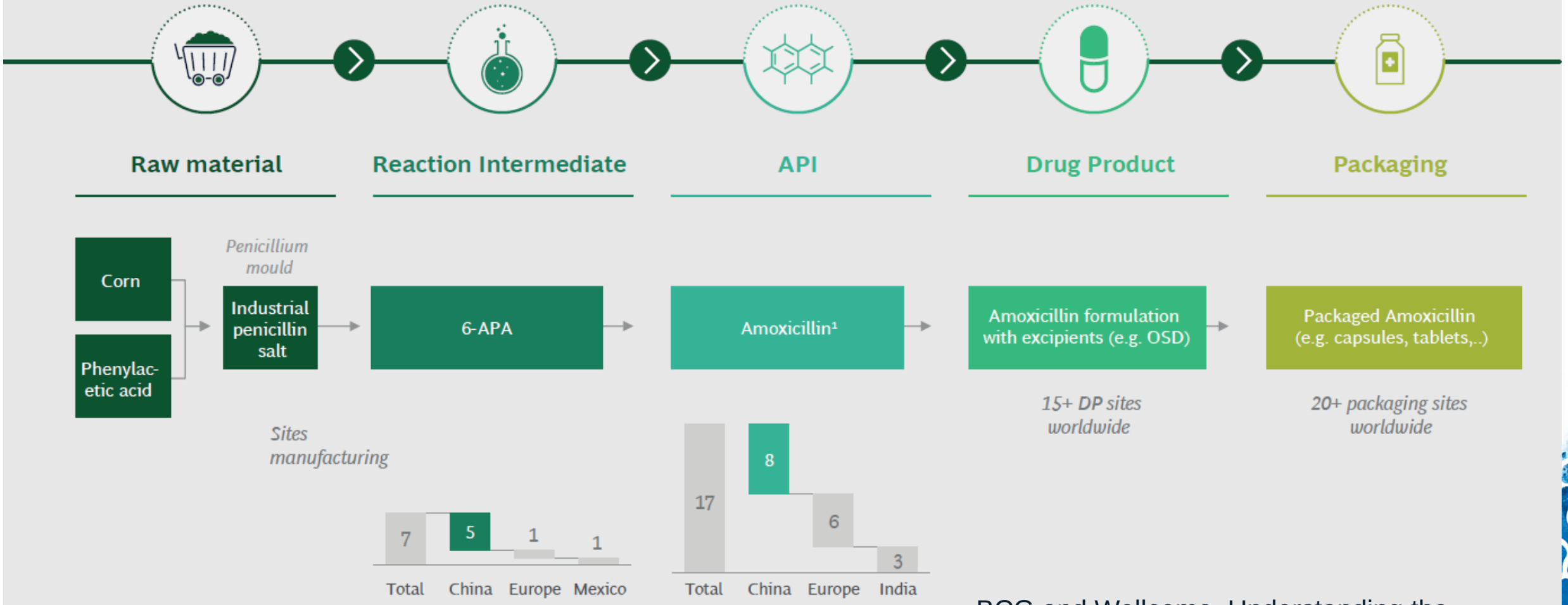
Forecasting, procurement and ordering systems

- Long budgeting and procurement planning cycles
- Unexpected increased demand
- Guideline-procurement mismatch
- Inability to rapidly import from alternative sources

Preliminary data, Shafiq et al Review

Risk: Bottlenecks in supply

FIGURE 5 | End-to-end supply chain of amoxicillin

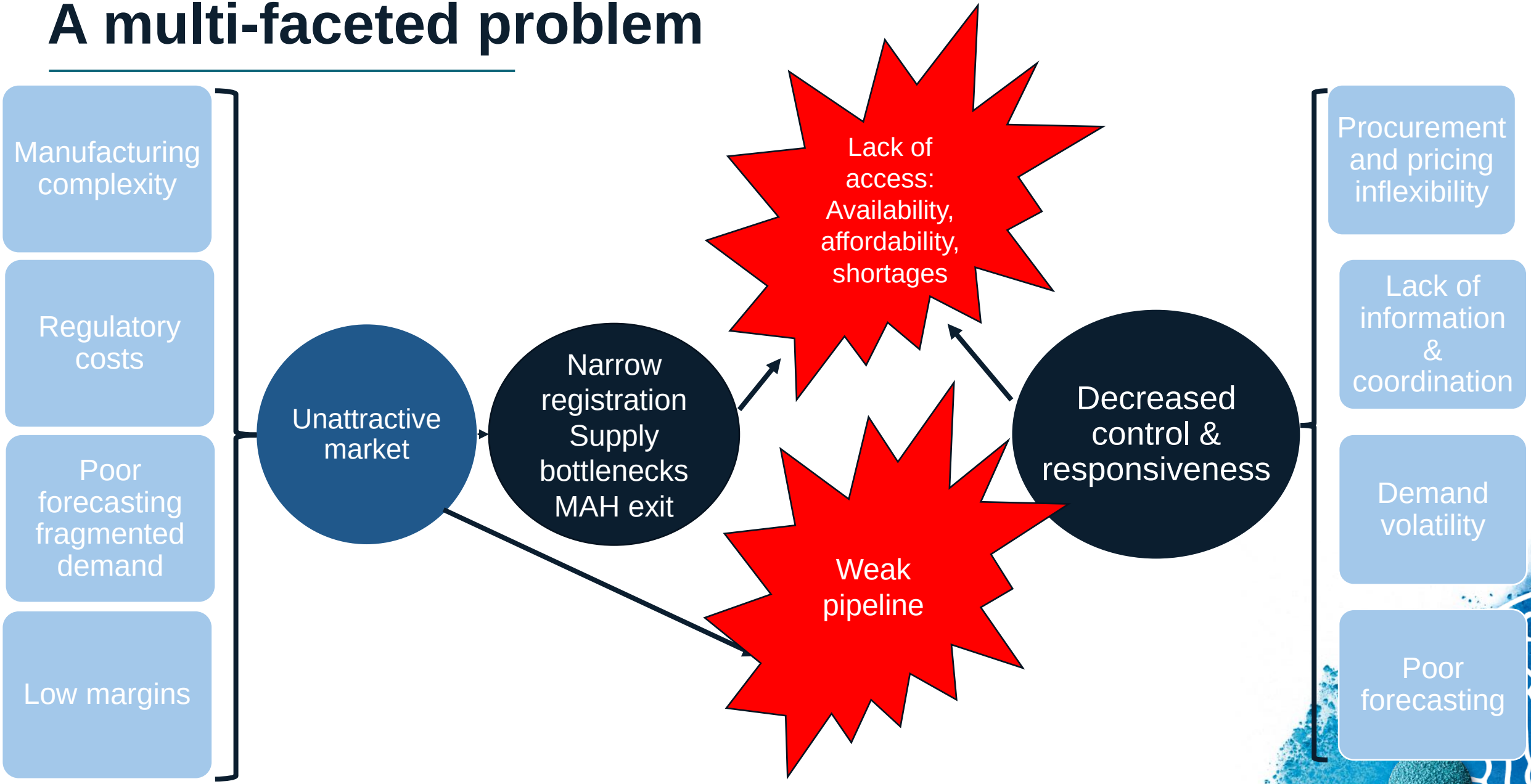


BCG and Wellcome, Understanding the antibiotic manufacturing ecosystem, 2022

Demand-side problems

- Poor forecasting
  - Lack of reliable data
  - Unpredictable demand spikes
- Procurement systems
  - Long procurement cycles
  - Single lowest-price tendering
- Lack of supply visibility leads to inability to plan in case of supply shortfalls
- Poor coordination between buyers/suppliers and among in-country actors
- No buffer for unexpected increases in demand (outbreaks)

A multi-faceted problem



Antibiotics approved without optimal data to inform clinical use

Lack of data across populations (e.g. Pediatrics)

Understanding of data to inform HTAs (and HTAs fit to antibiotics)

Poor market intelligence

Unattractive ROI

Low-volume/high-price traps

API bottlenecks

Unpredictable and fragmented demand

Affordability for on-patent products

Long regulatory approval timelines

Regulatory financial and technical costs

MAH exit

Distributor markups

Lack of strong introduction and use pathways

Inflexible budgeting and tendering

Lack of coordination among in-country actors

Fragmented planning

Develop evidence for optimal treatment and use across populations

Strengthen and harmonize guidelines regionally

Develop and pool forecasting or procurement

Develop and share market intelligence

Improve diagnostic access and local antibiograms

Guaranteed revenue or advance purchase commitment

Voluntary licensing and sub-licensing, including access, environmental and stewardship provisions

Rotating stockpile

Quality standards for inclusion in financial instruments or pooled procurement

Regulatory harmonization

Import waivers as a bridge

Financial or non-financial incentives for stewardship (e.g. Rebates for meeting stewardship targets)

Improve diagnostic access and local antibiograms

Implementation demonstration to scale projects, including stewardship

Improve legal and policy environment for antibiotic access and stewardship

LUXEMBOURG AID & DEVELOPMENT

NIHR | National Institute for Health Research

Ministry of Health, Welfare and Sport

UKaid from the British people

Gouvernement Princier PRINCIPAUTÉ DE MONACO

saMRC advancing life

LE GOUVERNEMENT DU GRAND-DUCHÉ DE LUXEMBOURG

MEDECINS SANS FRONTIERES

BILL & MELINDA GATES foundation

Swiss Confederation
Federal Department of Home Affairs FDHA
Federal Office of Public Health FOPH

wellcome

Federal Ministry of Health

GAMRIF

Federal Ministry of Education and Research

REPUBLIQUE ET CANTON DE GENEVE

Leo Model Foundation

Thank you

World Health Organization

GARDP

DNDi Drugs for Neglected Diseases *initiative*

www.gardp.org