Global Antibiotic Research and Development Partnership (GARDP)

Equitable Access for Antibiotics:
A Summary of Barriers
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

<table>
<thead>
<tr>
<th>Estimated number with carbapenem-resistant infections</th>
<th>Number accessing health care</th>
<th>Number with timely diagnosis</th>
<th>Estimated number treated with antibiotic active against carbapenem-resistant organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,567,517</td>
<td>40,875</td>
<td>2.6% treated</td>
<td>40,875</td>
</tr>
</tbody>
</table>

Care cascade for carbapenem-resistant infections, South Asia, 2019

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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*

2. Not widely registered
   Number of antibiotics registered 1999-2014

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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

Current Shortage Status by Antimicrobial Class as of May 17, 2022 (n=227 antimicrobial drug products)

- Antibacterials: 108 products, 20 in shortage (18.2%)
- Antifungals: 20 products, 2 in shortage (10.0%)
- Antiparasitics: 13 products, 1 in shortage (7.7%)
- Antivirals: 61 products, 2 in shortage (3.3%)

Portion of all drug products currently in shortage, 10.9%

Source: U.S. Pharmacopeia Medicine Supply Map
Clinical and financial impacts

What clinical impact has a drug shortage already caused?

- Substitution – Equivalent drugs: 46% always/often, 15% sometimes
- Substitution – Inferior drugs: 7% always/often, 43% sometimes
- Rationing of drug: 23% always/often, 22% sometimes
- Medication error: 2% always/often, 36% sometimes
- Delay of therapy: 9% always/often, 25% sometimes
- Switch to lower dose: 2% always/often, 16% sometimes
- Referring to other hospital: 2% always/often, 7% sometimes

What financial consequences has a drug shortage already caused?

- More expensive alternative: 36% always/often, 23% sometimes
- Increased hospital cost: 39% always/often, 19% sometimes
- Increased pharmacy/personnel cost: 34% always/often, 16% sometimes
- Increased costs for patients: 11% always/often, 13% sometimes

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

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

- Manufacturing complexity
- Regulatory costs
- Poor forecasting fragmented demand
- Low margins

- Unattractive market
- Narrow registration
- Supply bottlenecks
- MAH exit

- Lack of access: Availability, affordability, shortages

- Decreased control & responsiveness
- Weak pipeline

- Lack of information & coordination
- Demand volatility
- Poor forecasting

Procurement and pricing inflexibility
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
Thank you

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