Antimicrobial resistance. Antibiotic use. Antibiotic access.
AMR GAP strategic objectives and key areas in GAP and NAPs

<table>
<thead>
<tr>
<th>Objective</th>
<th>Key Areas</th>
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<tr>
<td>1. Improve awareness and understanding of AMR</td>
<td>Risk communication, Education, Research and development</td>
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<td>2. Strengthen knowledge through surveillance and research</td>
<td>National AMR surveillance, Laboratory capacities, Research and development</td>
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<td>3. Reduce the incidence of infection through effective hygiene &amp; IPC</td>
<td>IPC in health care, Community level prevention, Animal health: prevention and control</td>
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<td>4. Optimize the use of antimicrobial medicines in human &amp; animal health</td>
<td>Access to qualified antimicrobial medicines, regulation, AMS, Use in veterinary and agriculture</td>
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<tr>
<td>5. Ensure sustainable investment through research &amp; development</td>
<td>Measuring the burden of AMR, Assessing investment needs, Establishing procedures for participation</td>
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Global activities

- Infection Prevention and Control core components (2016)
- Global Priority Pathogens List of Antibiotic-Resistant Bacteria (2017)
- Updated Essential Medicines List update (2017)
- Global Framework for Development & Stewardship
9.1 Optimizing antimicrobial use in human health

- A - No/weak national policy & regulations for appropriate use.
- B - National policy for antimicrobial governance and regulation developed for the community and health care settings.
- C - Practices to assure appropriate antimicrobial use being implemented in some healthcare facilities and guidelines for appropriate use of antimicrobials available.
- D - Guidelines and other practices to enable appropriate use are implemented in most health facilities nationwide. Monitoring and surveillance results are used to inform action and to update treatment guidelines and essential medicines lists.
- E - Guidelines on optimizing antibiotic use are implemented for all major syndromes and data on use is systematically fed back to prescribers.
WHO Model Lists of Essential Medicines and AWaRe categorization

- **Aim to ensure that**
  - antibiotics are available when needed
  - the right antibiotics are prescribed for the right infections.

- **This in turn should enhance**
  - treatment outcomes, reduce the development of drug-resistant bacteria and preserve
  - the effectiveness of last-resort antibiotics that are needed when all others lose their efficacy.
**AWaRe Categorisation**

**ACCESS GROUP** (29 antibiotics)

First and second choice antibiotics for the empiric treatment of most common/relevant infectious syndromes (21 syndromes).

First choices are usually narrow spectrum agents with positive benefit-to-risk ratios, and low resistance potential, whereas second choices are generally broader spectrum antibiotics with higher resistance potential, or less favorable benefit-to-risk ratios.

**WATCH GROUP** (7 antibiotic classes)

Antibiotics with higher resistance potential whose use as first and second choice treatment should be limited to a small number of syndromes or patient groups.

These medicines should be prioritized as key targets of stewardship programs and monitoring.

**RESERVE GROUP** (8 antibiotics or classes)

Antibiotics to be used mainly as ‘last resort’ treatment options that could be protected and prioritized as key targets of high-intensity stewardship programs.
List of antibiotics, classified into Access, Watch, and Reserve groups

**Access**
- Amoxicillin
- Amoxicillin and clavulanic acid
- Ampicillin
- Benzathine benzylpenicillin
- Benzylpenicillin
- Cefalexin or cefazolin
- Chloramphenicol
- Clindamycin
- Cloxacillin
- Doxycycline
- Gentamicin or amikacin
- Metronidazole
- Nitrofurantoin
- Phenoxymethylpenicillin
- Procaine benzylpenicillin
- Spectinomycin
- Sulfamethoxazole and trimethoprim

**Watch**
- Azithromycin
- Cefixime
- Cefotaxime
- Ceftriaxone
- Ciprofloxacin
- Clarithromycin
- Piperacillin and tazobactam
- Meropenem
- Vancomycin

* Antibiotics that are also in the Watch group

**Reserve**
- Aztreonam
- Cephalosporins, fourth generation (eg, cefepime)
- Cephalosporins, fifth generation (eg, ceftaroline)
- Daptomycin
- Fosfomycin (intravenous)
- Oxazolidinones (eg, linezolid)
- Polymyxins (eg, colistin, polymyxin B)
- Tigecycline
Monitoring of the consumption of antimicrobials at national level

Methodology for monitoring national antimicrobial consumption (AMC):

- Based on sales of antimicrobial medicines
- Concerns hospital and community sectors
- Information on the level of use and types of antimicrobials at country level
- Targets: policy makers and prescribers
- Data reported at substance level in Defined Daily Doses, with option for kg.
- Similar to OIE methodology

Support to countries for implementing national program on monitoring antimicrobial consumption

- In collaboration with regional offices, more than 70 countries trained

GLASS AMC Module

- To be released in 2019
- Option to report product level and substance level data
- Official data call to WHO MS to collect AMC data and report to WHO in 2019

https://www.who.int/medicines/areas/rational_use/AMU_Surveillance/en/
Table 4.6 Oral and parenteral antibiotic substances that made up 75% of all antibiotic consumption in the African Region, number of countries in which they were part of the country-specific DU75 list and the median proportional consumption (% of total DDD) in these countries

| Oral | | | |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Antibiotic | Appears in country’s DU75 | Median proportion (IQR) | | |
| Amoxicillin | 3/4 | 25.1 (22.3–29.3) | | |
| Ciprofloxacin | 3/4 | 14.4 (14.2–22.9) | | |
| Sulfamethoxazole and trimethoprim | 3/4 | 24.2 (15.1–27.9) | | |
| Metronidazole | 2/4 | 18.6 (12.8–24.4) | | |
| Amoxicillin and beta-lactamase inhibitor | 1/4 | 9 | | |
| Cefalexin | 1/4 | 8.2 | | |
| Doxycycline | 1/4 | 9.6 | | |
| Tetracycline | 1/4 | 9.4 | | |
| Tinidazole | 1/4 | 4.7 | | |

| Parenteral | | | |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Antibiotic | Appears in country’s DU75 | Median proportion (IQR) | | |
| Ceftriaxone | 2/4 | 40.7 (34.9–46.5) | | |
| Amoxicillin | 1/4 | 11.8 | | |
| Ampicillin | 1/4 | 18.6 | | |
| Benzathine benzylpenicillin | 1/4 | 23.2 | | |
| Benzylpenicillin | 1/4 | 50.8 | | |
| Gentamicin | 1/4 | 67.8 | | |
| Metronidazole | 1/4 | 9.4 | | |
| - | - | - | | |

*Median of the total proportional consumption of the countries in which the respective substance is part of the DU75 list.

Fig. 4.3 Proportional consumption of antibiotics (%) by AWaRe categorization in four countries of the African Region (2015)

- Other
- Reserve
- Watch
- Access

* Only public sector reported.

* Data from 2016.
Antimicrobial use surveys

Protocols for surveys on use of antibiotics (prescription/purchase) in different health settings (not focus on other antimicrobial classes)

To understand how antibiotics are used

In hospitals

• Using the ECDC HAI-Net PPS protocol with some adaption for LMIC’s contexts
• Only survey on use, no HAI data collected
• Published in February 2019
• Goals:
  • Based on patient level data, prescriptions
  • Provides information on the level of use, types of antibiotics and how these medicines are used at hospital level
  • Targets: policy makers (National), prescribers, stewardship team, IPC team (Hospital)
• Ongoing WHO surveys in Africa, Americas, Middle East, Asia
• Should provide data similar to ECDC HAI-Net PPS data on AMU

In community settings (to be developed)

• Already existing methodologies for surveys on use of medicines
• Needs to be reviewed and adapted to antibiotics

Global report on AMR surveillance

- 17% (22/129) countries provided info on all 9 drug-pathogen combinations
- Widespread high levels of AMR

*National data means data obtained from official sources, but not that data necessarily are representative for the population or country as a whole
Antimicrobial resistance among children in sub-Saharan Africa

Phoebe C M Williams, David Isaacs, James A Berkley

- Systematic review of studies of AMR among children in sub-Saharan Africa since 2005. 18 of 1075 articles reviewed met inclusion criteria with 67 451 invasive bacterial isolates.

- Among neonates, Gram-negative organisms were the predominant cause of early-onset neonatal sepsis, with a high prevalence of extended-spectrum β-lactamase-producing organisms.

- Gram-positive bacteria were responsible for a high proportion of infections among children beyond the neonatal period, with high reported prevalence of non-susceptibility to treatment advocated by the WHO therapeutic guidelines.

BUT

- Data mostly from inconsistently defined populations in predominantly urban tertiary settings. There are few up-to-date or representative studies given the magnitude of the problem of antimicrobial resistance, especially regarding community-acquired infections.
Global Antimicrobial Surveillance System (GLASS)

- The first global system to collect **official national data** on AMR in selected bacterial pathogens that cause common infections in humans.

  - requested by the WHO Member States (Resolution WHA68.7) ➔ launched in October 2015
  - provides a standardized approach to the collection, analysis, and sharing of AMR data
  - includes epidemiological, clinical, and microbiological data
  - Progressive inclusion of other types of AMR-related surveillance (e.g. food chain, antimicrobial consumption and use, environment)
  - Early implementation phase: 2015-2019
Countries enrolled in GLASS
As of 9 April 2019*

* Call for country enrolment issued on 21 March 2016
2018 data call and 2nd GLASS report

- **64%** increase in country enrolment and more than **twice** the number of countries submitting AMR data
- **13** of the countries that last year only provided information on the status of their national AMR surveillance system reported AMR data
- **11** LIC and LMC reported AMR data
- **11** countries (5 in the preceding year) submitted data on the total sampled population
URINE - Klebsiella pneumoniae

Frequency of Meropenem resistance (per 100,000 tested patients)
Access to medicines

VISION
A world where every child, man and woman has access to the quality essential medicines, vaccines and other health products they need to lead a healthy and productive life.

Access to medicines: “having medicines continuously available and affordable at public or private health facilities or medicine outlets that are an hour’s walking distance from the home”

Main factors that determine access to essential medicines:
• Rational selection of medicines,
• Affordable prices,
• Sustainable financing,
• And reliable healthcare and supply systems
Draft road map for access to medicines, vaccines and other health products, 2019–2023*

Ensuring quality, safety and efficacy of health products

- Regulatory system strengthening
- Assessment of the quality, safety and efficacy/performance of health products through prequalification
- Market surveillance of quality, safety and performance

Improving equitable access

- Research and development that meets public health needs and improves access to health products
- Application and management of intellectual property to contribute to innovation and promote public health
- Evidence-based selection and fair and affordable pricing
- Procurement and supply chain management
- Appropriate prescribing, dispensing and rational use

* to be presented at the WHA 72