Antimicrobial use and stewardship: a global perspective

Uso e gestione degli antimicrobici in una visione globale

17.06.2025
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Disclaimer 1

I am full-time staff member of WHO

Disclaimer 2

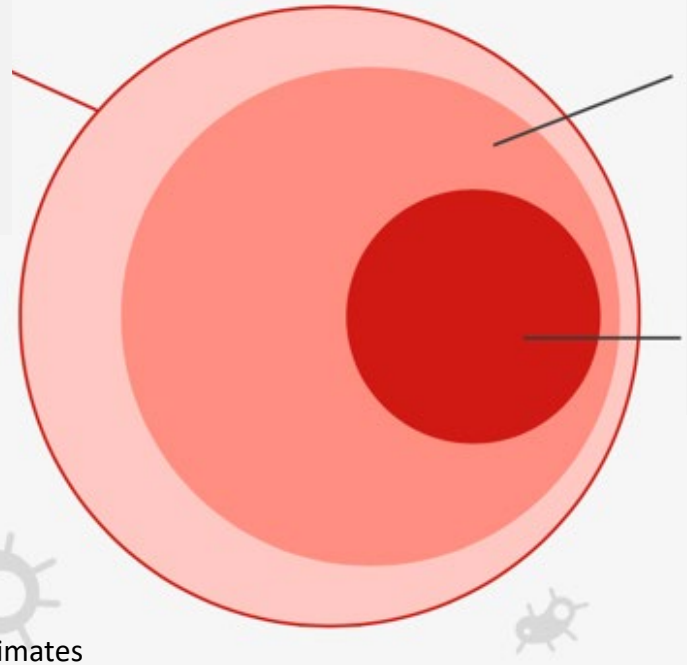
Il mio italiano è un po’ «arrugginito»...

Burden of Antimicrobial Resistance

Increase in deaths from sepsis (>5 years) from
8.81 million (8.30–9.32) in 1990, to **11.0 million (10.2–11.7) in 2019**

- **8.51% (8.00–8.95) sepsis deaths attributable to AMR**

7.7 m
annual deaths due to bacterial infections



4.71 m
annual deaths associated with AMR

1.14 m
annual deaths attributable to AMR

2021 estimates

Counterfactuals:

- **associated with AMR: no infection**
- **attributable to AMR: drug-sensitive infection**

US$ 855
billion/year
for treating resistant infections and productivity losses by 2050

Up to
11%
decline in livestock by 2050

GBD, Lancet, 2024; GLG group. 2024; World Bank Group. 2017.

WHO strategic and operational priorities to address drug-resistant bacterial infections in the human health sector, 2025-2035

World Health Organization

Resolution WHA77.6 welcomed WHO priorities for addressing drug-resistant bacterial infections, 2025-2035. Priorities align with **WHO's Fourteenth General Programme of Work.**

Priority 1: Prevention of infections through IPC components, WASH guidelines, and vaccine research.

Priority 2:

Universal **access** to affordable, quality diagnosis and **appropriate treatment of infections**.

Priority 3: Strategic information, science and innovation

Priority 4:

Effective governance and financing, mainstreaming AMR interventions in primary health care.

Antibiotics are among the most commonly prescribed medicines

- Globally: 34.3 billion billion DDD in 2023 for a population of 8.1 billion
  - = about **4.2 DDD for every person in the world per year**

- In some LMICs children **receive up to 25 antibiotic prescriptions** for respiratory tract infection or fever **during their first 5 years of life**
  - Most of them inappropriate

et al. Proc Natl Acad Sci U S A. 2024 Dec 3;121(49):e2411919121.
Fink et al. Lancet Infect Dis. 2020 Feb;20(2):179-187.

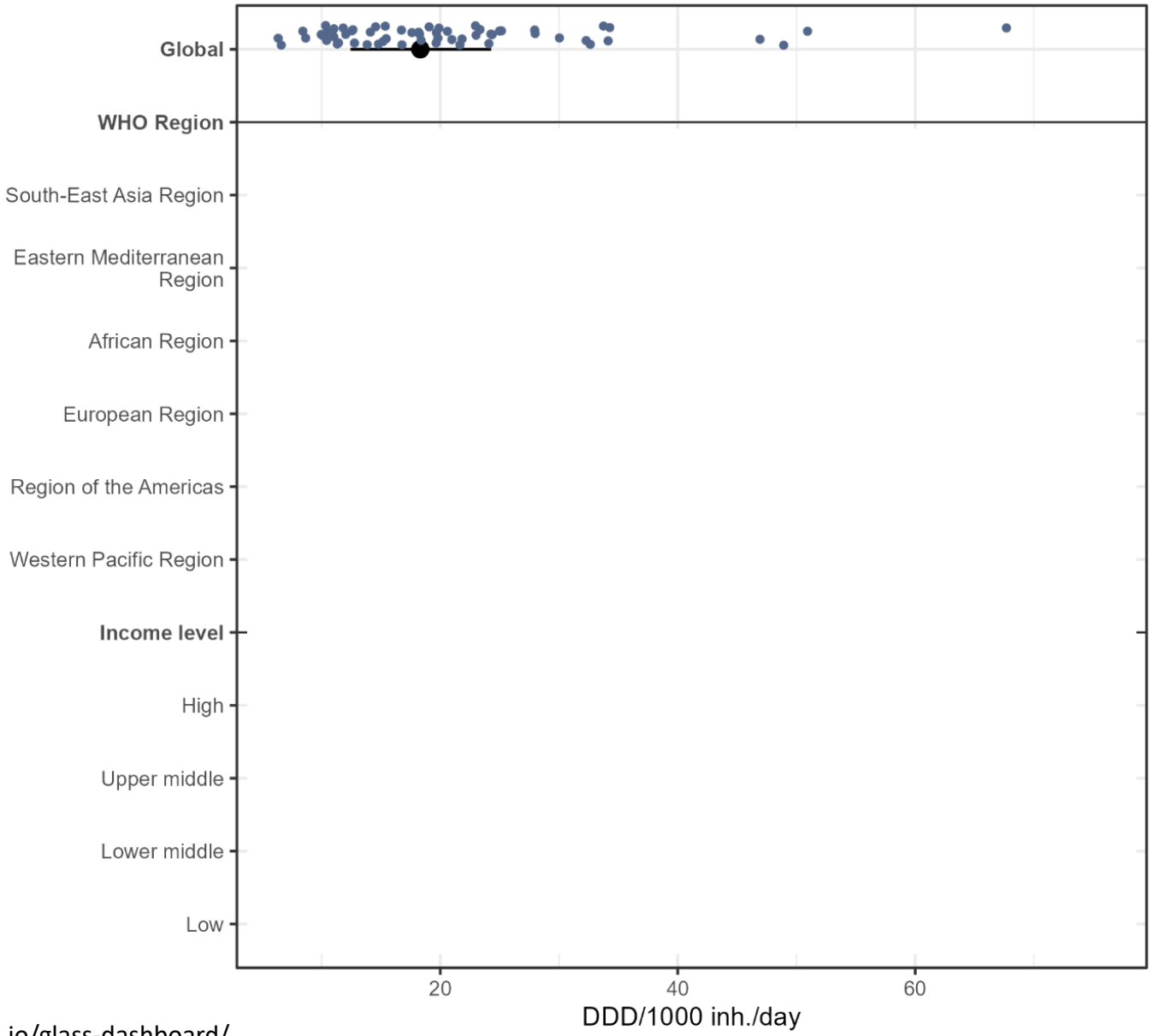
Inappropriate use of antibiotics is common everywhere

- Two recent stories from my family

- 55-year-old female, COVID (PCR +), sore throat
  - Physician performs rapid streptococcal antigen test => positive
  - Amoxicillin / calvulanate at pediatric dose for 10 days
  - **Wrong indication, wrong antibiotic, wrong dose, wrong duration**

- 30-year-old otherwise healthy female, fever, mild sore throat, headache
  - Prescription of amoxicillin / clavulanate by telephone
  - Duration not specified
  - **Wrong indication, wrong antibiotic, wrong dose, wrong duration**

Total antibiotic use expressed as DDD per 1000 inhabitants per day in 60 CTAs in 2022, globally and by WHO Regions and World Bank income group classification



https://worldhealthorg.shinyapps.io/glass-dashboard/_

World Health Organization

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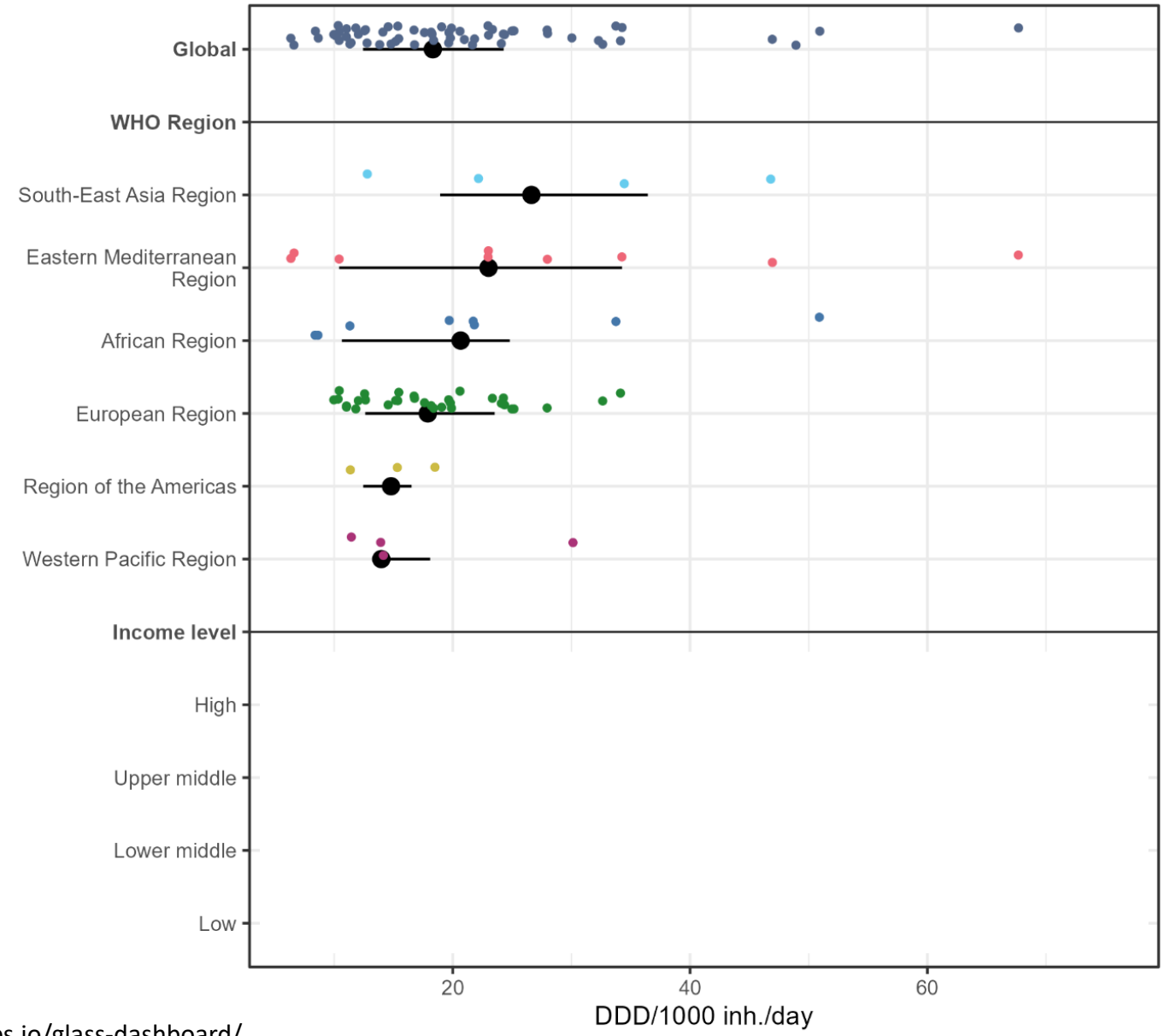

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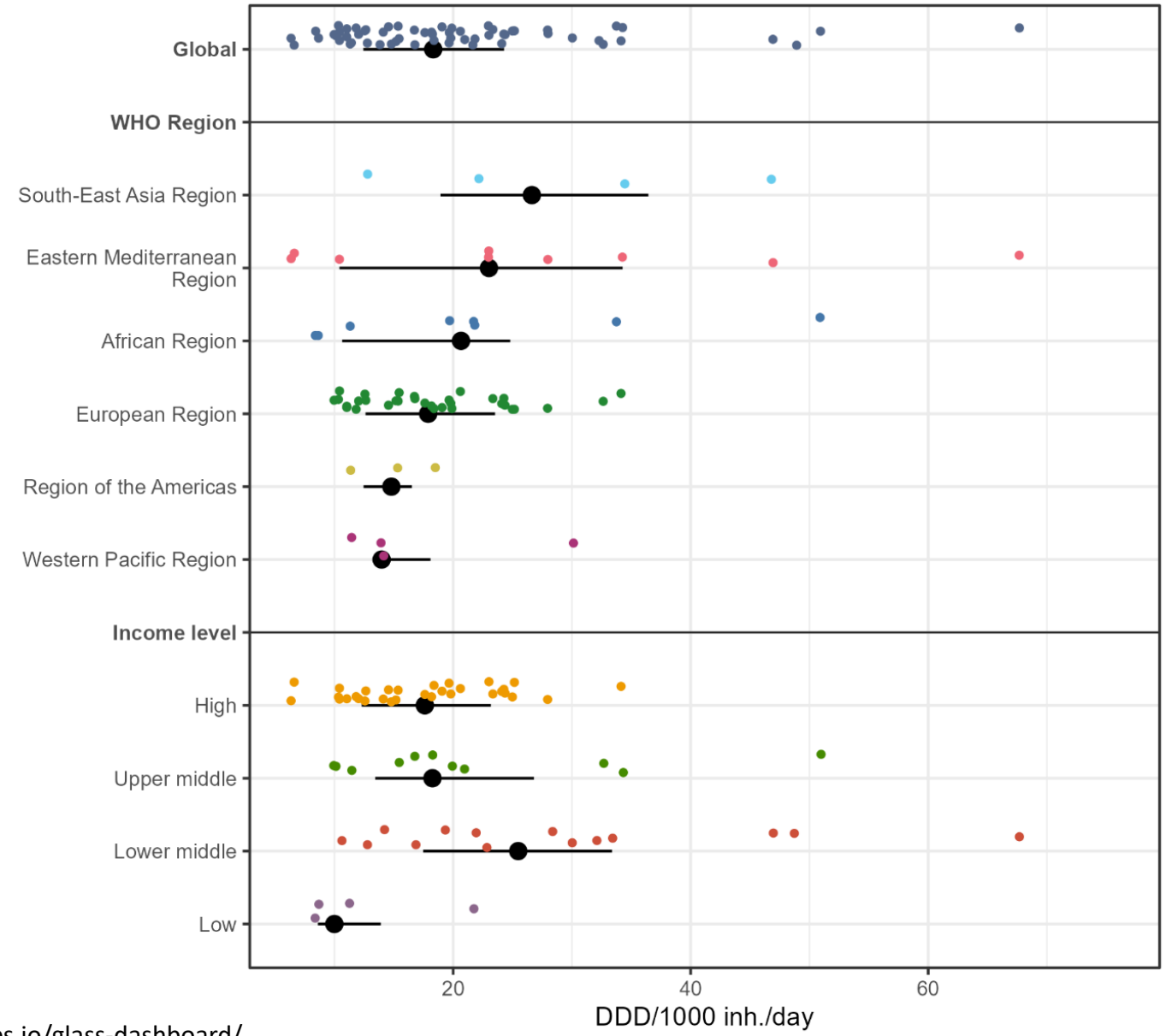

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World Health Organization

Italy

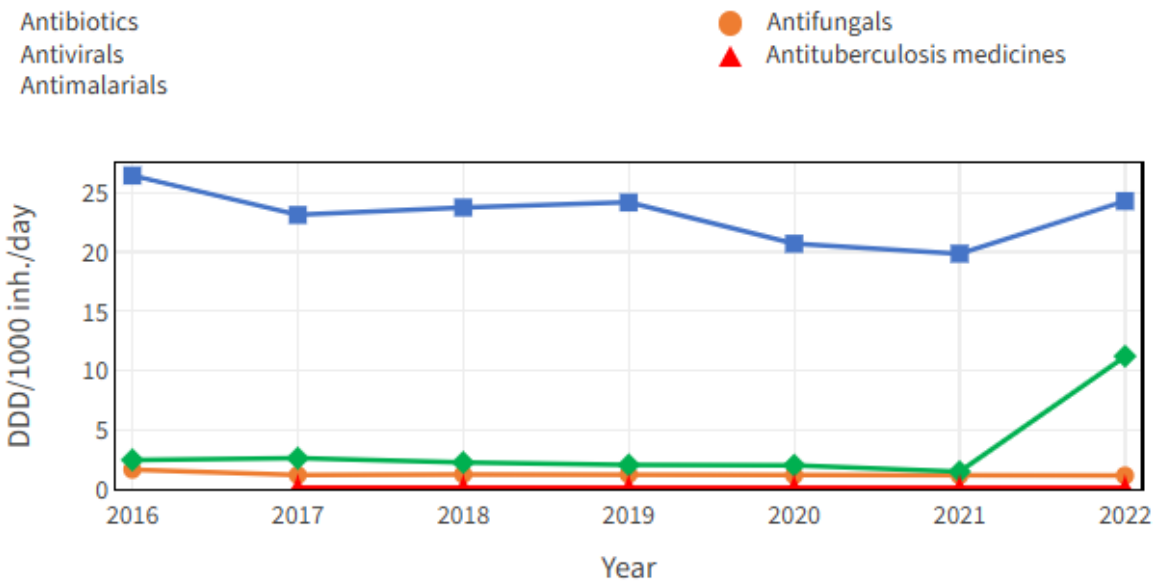
GLASS-AMU Country, territory or area profiles

Antimicrobial use, for the period 2016 to 2022

Use by antimicrobial classes in 2022

Antimicrobial classes	DDD/1000 inh./day
Antibiotics (ATC J01, A07AA, P01AB)	24.27
Antimycotics and antifungals for systemic use (ATC J02, D01B)	1.13
Antivirals for systemic use (ATC J05)	11.18
Drugs for the treatment of tuberculosis (ATC J04A)	0.10
Antimalarials (ATC P01B)	Not reported

Use by antimicrobial classes, 2016-2022

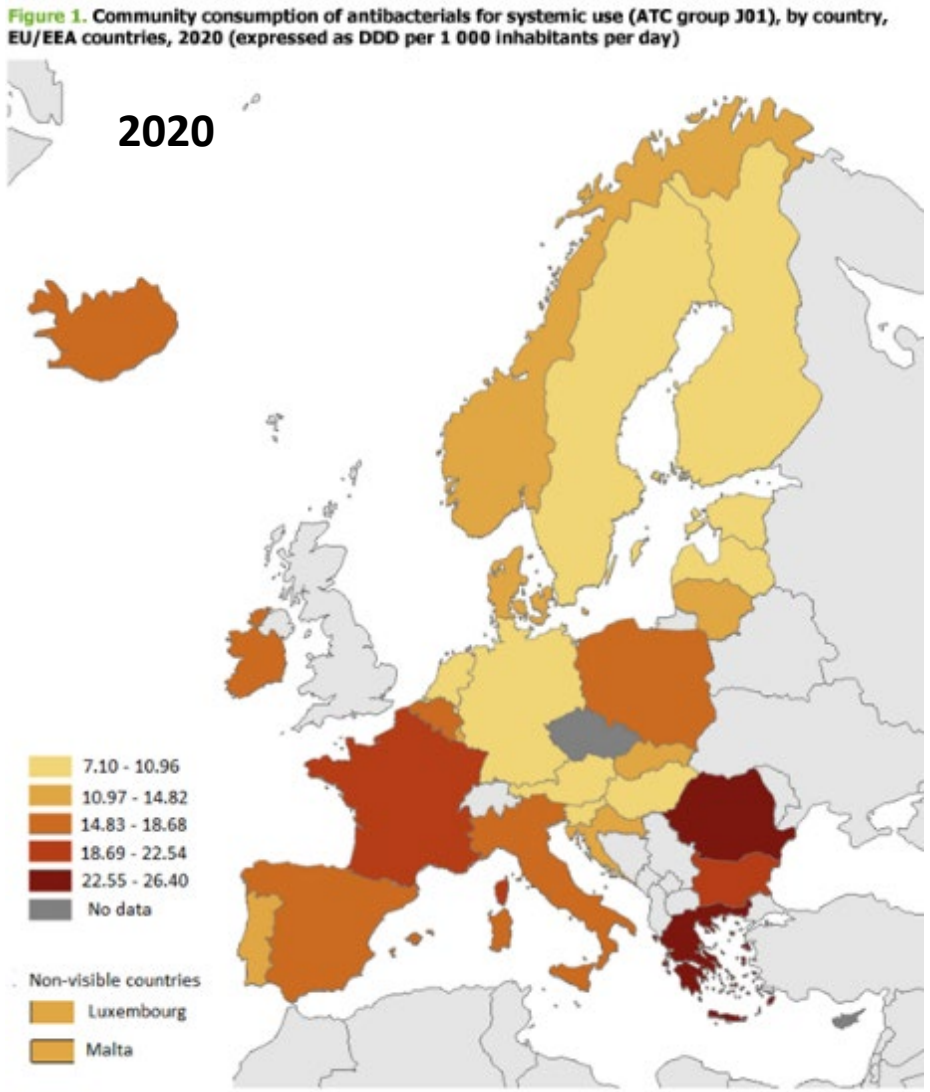


Median total AMU in 60 CTAs in 2022 was 18.3 DID (GLASS-AMU)

GLASS Global Antimicrobial Resistance and Use Surveillance System

World Health Organization

Antimicrobial consumption in the EU/EEA (ESAC-Net)



- Mean consumption of antibacterials for systemic use in 2023*:20.0 DDD per 1000 inhabitants per day


- Country range: 9.6–28.5
- Italy: 23.1 DID

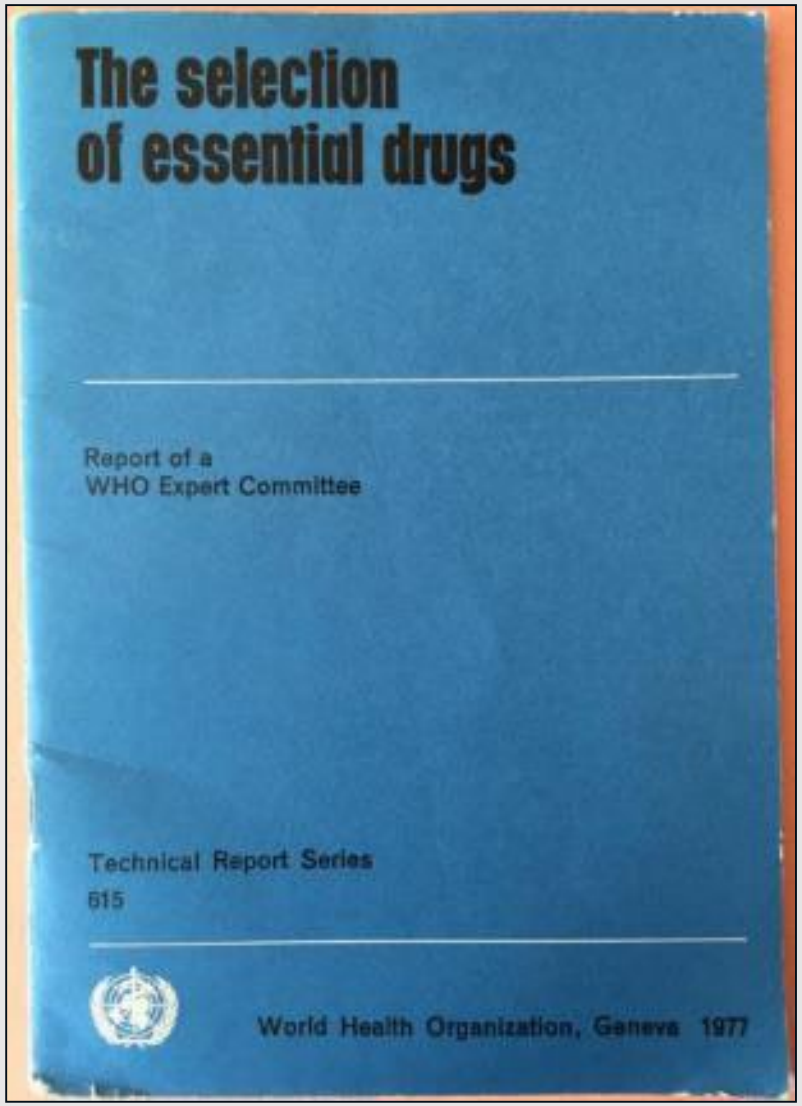
https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-consumption-europe-2020
https://www.ecdc.europa.eu/sites/default/files/documents/ESAC-Net_report-2023.pdf

*community and hospital sector combined

But what about quality of use ?

The WHO Model List of Essential Medicines (EML)

- Updated every two years by the Expert Committee on Selection and Use of Essential Medicines
- First EML published in 1977
  - First EML for children published in 2007
- Since 2017 extensive update / review of antibiotics on the EML
  - In the context of WHO's global action plan on antimicrobial resistance



1977

First EML

- 16 antibiotics

(of 240 medicines ≈ 7%)

In a report [1] to the Twenty-eighth World Health Assembly in 1975, the Director-General reviewed the main drug problems facing the developing countries and outlined possible new drug policies. The Director-General also referred to the experience gained in some countries where schemes of basic or essential drugs had been implemented. Such schemes were intended to extend the accessibility of the most necessary drugs to those populations whose basic health needs could not be met by the existing supply system. The Director-General pointed out that the selection of these essential drugs would depend on the health needs and on the structure and development of health services of each country, and that lists of essential drugs should be drawn up locally, and periodically updated, with the advice of experts in public health, medicine, pharmacology, pharmacy and drug management. He also considered that adequate information on the properties, indications and use of the drugs listed should be provided. By resolution WHA28.66, the Health Assembly requested the Director-General to implement the proposals contained in his report and, in particular, to advise Member States on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs.

Antibacterial drugs

ampicillin (1) *
benzathine benzylpenicillin (5) *
benzylpenicillin *

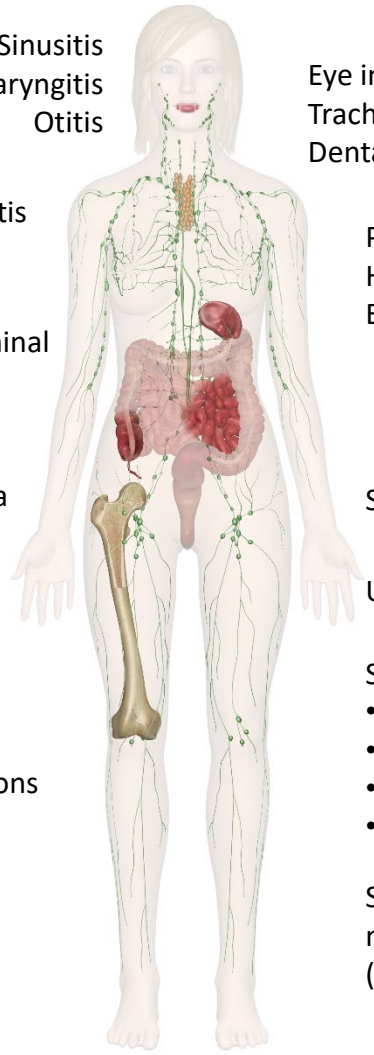
chloramphenicol (7) * *
cloxacillin (penicillinase-resistant, 1)
erythromycin *
gentamicin (4) *
phenoxymethylpenicillin *
salazosulfapyridine
sulfadimidine (1)
sulfamethoxazole + trimethoprim *
tetracycline (1, 4) *

Complementary

amikacin (1, 4, 10) *
doxycycline (6, 5) *
procaine benzyl-penicillin (7) *
sulfadiazine (7, 8) *

* On 2023 EML/c

EML updates
2017 / 2019 / 2021



Meningitis

Sinusitis
Pharyngitis
Otitis

Eye infections
Trachoma
Dental infections

Lymphadenitis

Pneumonia (CAP)
HCAP
Exacerbation of COPD

Complicated intraabdominal Infections
Enteric fever

Acute infectious diarrhea
- Cholera
- Shigellosis
- *Clostridoides difficile*

Sepsis

UTI

STD
- *Chlamydia*
- Gonorrhea
- Syphilis
- Trichomoniasis

Bone infections
Septic arthritis
Skin & soft tissue infections

Febrile neutropenia

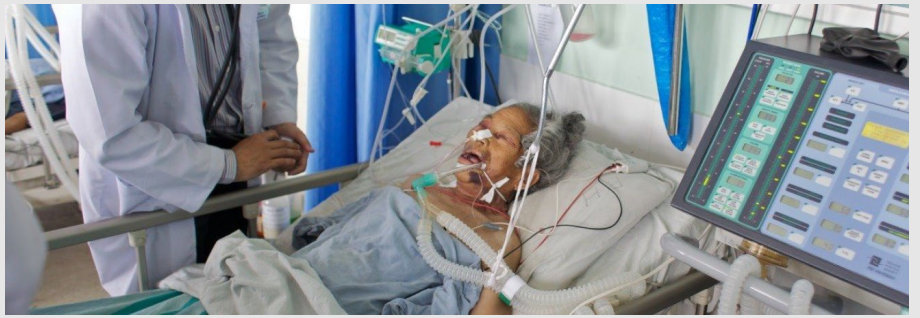
Severe malnutrition (children)

Surgical prophylaxis

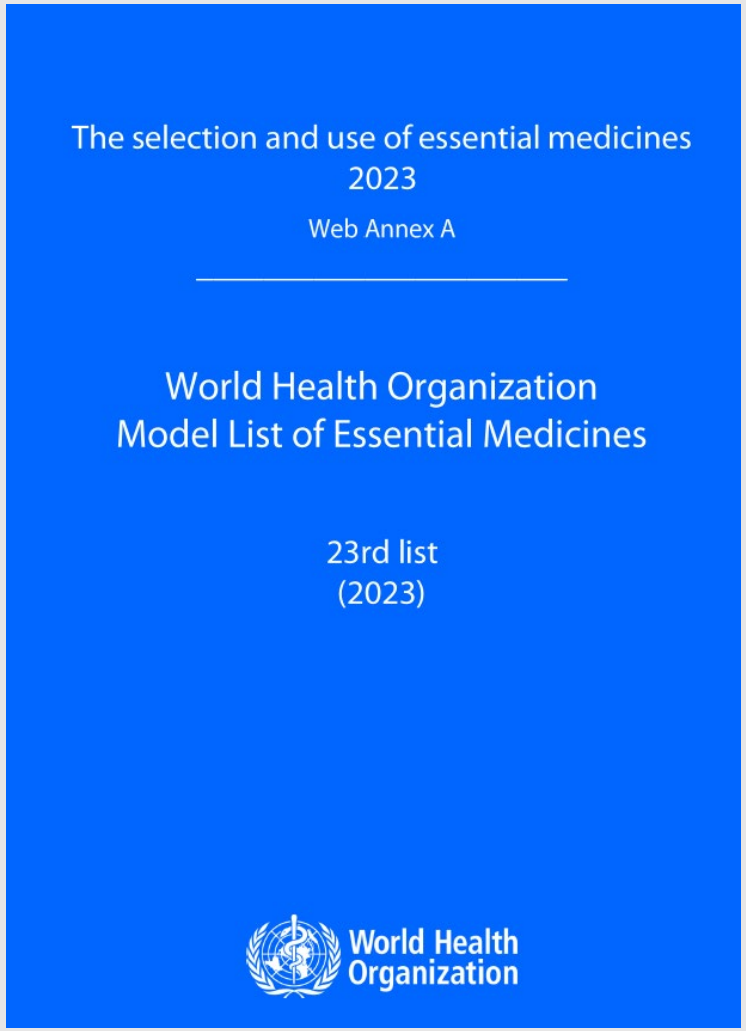
Antibiotics on the EML

Review of infections

- Frequent infections
  - Mostly community-acquired infections
  - Mostly empiric use
- Certain infections by specific pathogens
  - Syphilis, cholera, gonorrhea, shigellosis,…
- Review of systematic reviews and guidelines
- Selection of 1st and 2nd choice antibiotics
  - Efficacy, safety, impact on antibiotic resistance



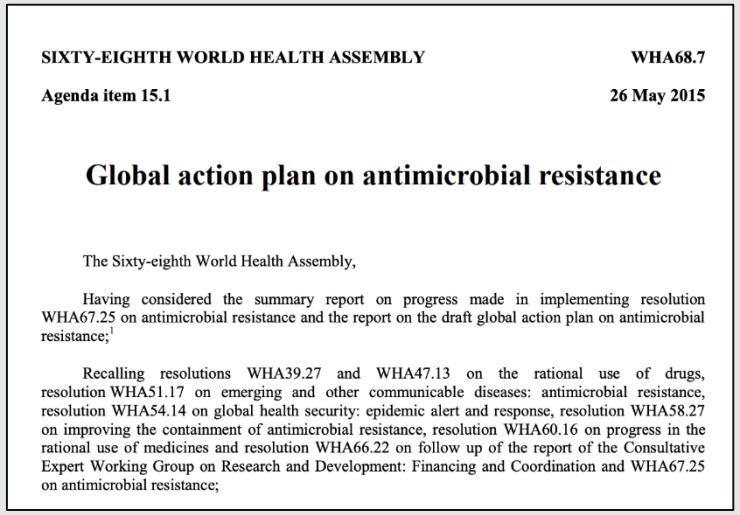
2023



24th EML

- 41 antibiotics (EMLc 37)

(of 502 medicines ≈ 8%)



SIXTY-EIGHTH WORLD HEALTH ASSEMBLY — WHA68.7

Agenda item 15.1 — 26 May 2015

Global action plan on antimicrobial resistance

The Sixty-eighth World Health Assembly,

Having considered the summary report on progress made in implementing resolution WHA67.25 on antimicrobial resistance and the report on the draft global action plan on antimicrobial resistance;[1]

Recalling resolutions WHA39.27 and WHA47.13 on the rational use of drugs, resolution WHA51.17 on emerging and other communicable diseases: antimicrobial resistance, resolution WHA54.14 on global health security: epidemic alert and response, resolution WHA58.27 on improving the containment of antimicrobial resistance, resolution WHA60.16 on progress in the rational use of medicines and resolution WHA66.22 on follow up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination and WHA67.25 on antimicrobial resistance;

ACCESS GROUP	WATCH GROUP	RESERVE GROUP
Amikacin	Azithromycin	Cefiderocol
Amoxicillin	Cefixime	Ceftolozane/tazobactam
Amoxicillin/clavulanic-acid	Cefotaxime	Ceftazidime/avibactam
Ampicillin	Ceftazidime	Colistin (IV)
Benzathine-benzylpenicillin	Ceftriaxone	Fosfomycin (IV)
Benzylpenicillin	Cefuroxime	Linezolid
Cefalexin	Ciprofloxacin	Meropenem/vaborbactam
Cefazolin	Clarithromycin	Plazomicin
Chloramphenicol	Meropenem	Polymyxin B (IV)
Clindamycin	Piperacillin/tazobactam	Tedizolid
Cloxacillin	Vancomycin (IV and oral)	
Doxycycline		
Gentamicin		
Metronidazole		
Nitrofurantoin		
Phenoxymethylpenicillin		
Procaine-benzylpenicillin		
Spectinomycin		
Sulfamethoxazole/TMP		
Trimethoprim		

AWaRe : Antibiotics are categorized into three groups

Essential Access, Watch and Reserve antibiotics need to be accessible and affordable for those who need them!

"Last-resort" options against MDRO

Higher "resistance potential"

Often 1st or 2nd choice for common infectious syndromes

Lower "resistance potential"

Not-recommended antibiotics (Fixed-dose combinations)

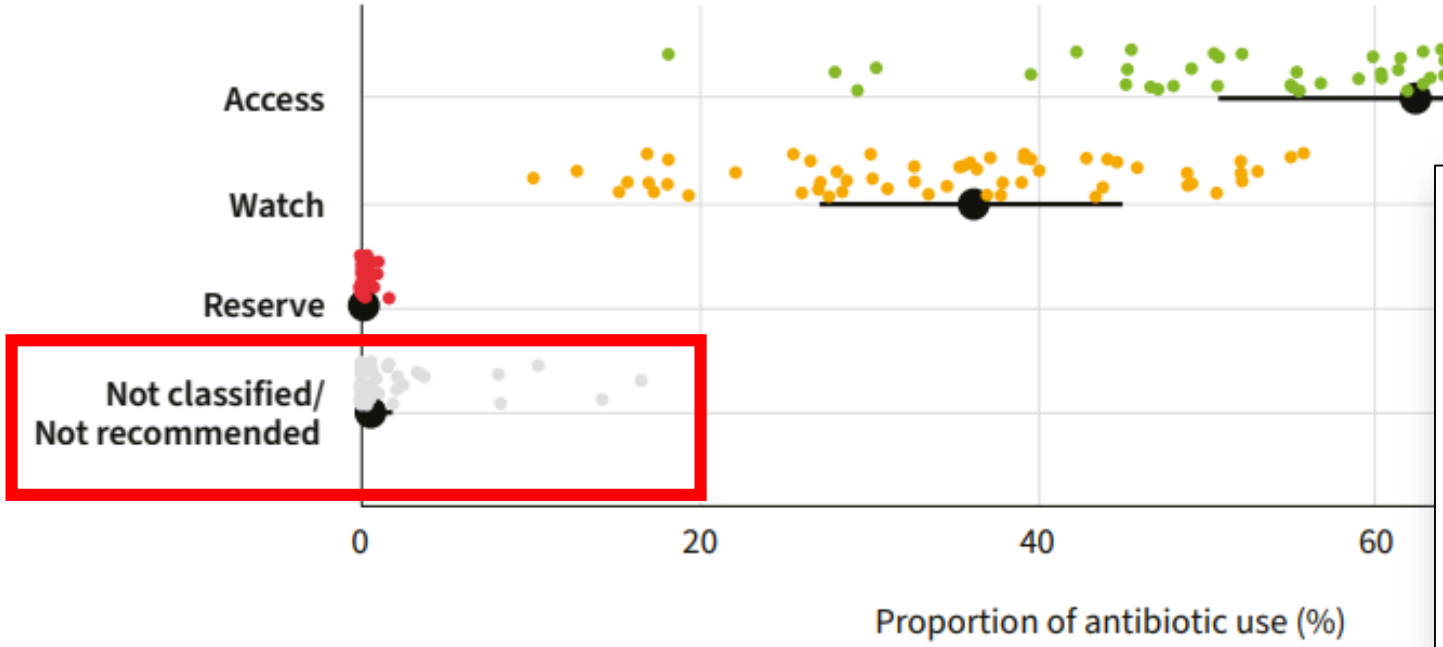
Table 1. Categories of antibiotic Fixed Dose Combinations (FDCs).

FDC types	Standard Unite sold	Number of FDCs
Aminopenicillin /β-lactamase inhibitor //- other agents	8.60×10^9	8
Sulphonamides/trimethoprim+/- other agents	3.62×10^9	9
Aminopenicillin / β-lactamase resistant penicillin +/- other agents	1.54×10^9	21
Antipseudomonal penicillin /β-lactamase inhibitor	0.95×10^9	4
3^{rd}-4^{th}-5^{th} gen. cephalosporins /β-lactamase inhibitor +/- other agents	0.55×10^9	15
Cephalosporins / fluoroquinolones	0.40×10^9	6
1^{st}-2^{nd} gen. cephalosporins / β-lactamase inhibitor +/- other agents	0.26×10^9	8
Macrolide/ 5-nitroimidazole	0.24×10^9	3
Macrolide/cephalosporin+/-other agents	0.21×10^9	3
Cephalosporin/ β-lactamase resistant penicillin +/- other agents	0.10×10^9	7
Cephalosporin/trimethoprim	0.09×10^9	2
Cephalosporin/oxazolidinone	0.04×10^9	2
Fluoroquinolone/ 5-nitroimidazole	0.04×10^9	8
Macrolide / fluoroquinolone +/- other agents	0.04×10^9	2
Cephalosporin/5-nitroimidazole	0.03×10^9	1
Other combinations	0.01×10^9	20

- Analysis of IQVIA-MIDAS® data for antibiotic FDCs from 75 countries in 2015
- 22% of total antibiotic consumption in 2015
- 92% (110/119) were not approved by the US FDA
- >80% not compatible with EML

Bortone et al. PLoS One. 2021; 16(1): e0241899.

Fig. 6. Distribution of proportional antibiotic use by AWaRe classification in 60 CTAs in 2022



Each coloured dot represents one CTA. The large black dot represents the median, and lines

HEALTH

Nepal drugs regulator bans 103 antibiotic combinations

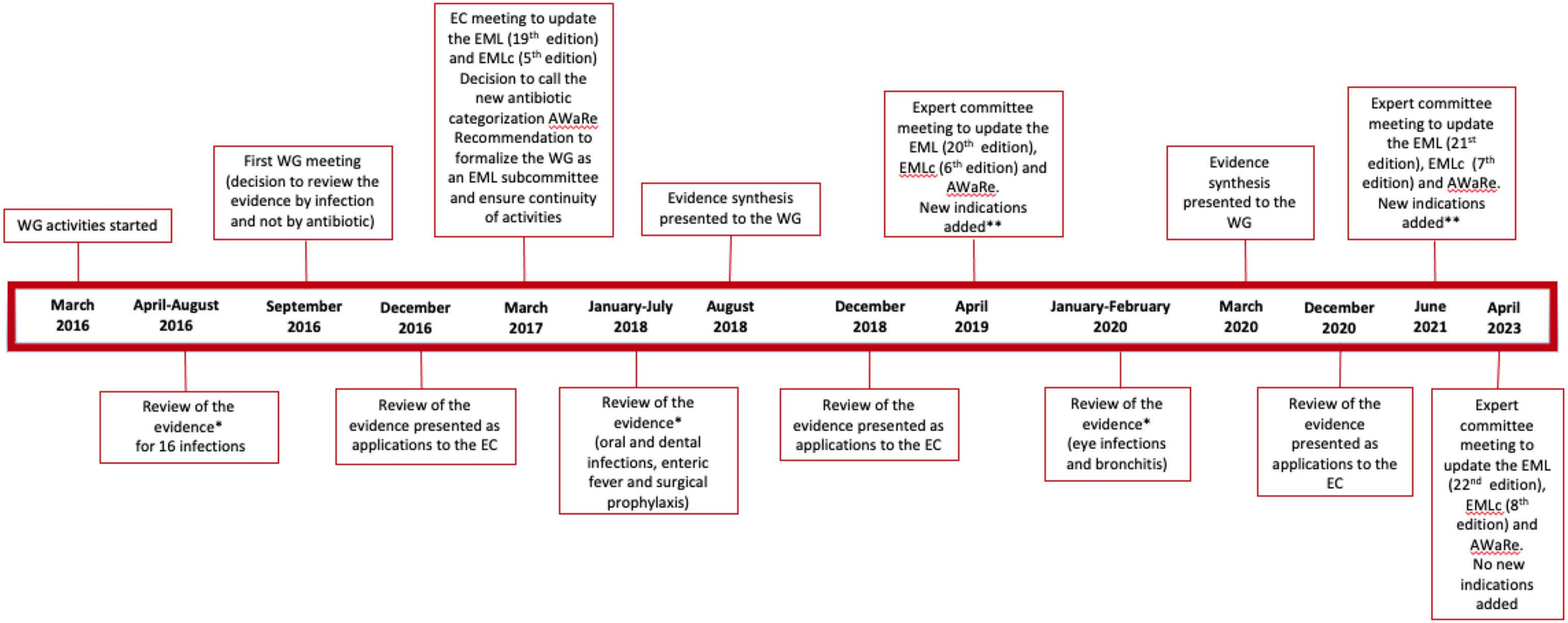
Of the 103 combos, 14 are being used in Nepal. Irrational use of combinations is fuelling antibiotic resistance.

Shutterstock

https://kathmandupost.com/health/2023/09/19/nepal-drugs-regulator-bans-103-antibiotic-combinations

WHO's essential medicines and AWaRe: recommendations on first- and second-choice antibiotics for empiric treatment of clinical infections

Clinical Microbiology and Infection
Volume 30, Supplement 2, April 2024, Pages S1-S51



*The review of the evidence was performed at the WHO collaborating centre at McMaster University (Hamilton, Canada) for all infections except enteric fever (Centre for Tropical Medicine and Global Health, University of Oxford) and surgical prophylaxis (WHO department of Service Delivery and Safety)
**New indications added (2019: oral and dental infections, enteric fever and surgical prophylaxis; 2021: eye infections and bronchitis)
WG: Working Group; EC: Expert Committee

WHO AWaRe classification Evolution

In **2019** major revision

- AWaRe extended beyond the EML
- Listing of specific molecules (not classes)
- Classification of most antibiotics classified as “Other” before

In **2021 and 2023**

- Addition of further **Reserve** antibiotics

Plans for **2027**

- Better definition of the different classes (notably **Reserve** and **Watch**)

Antibiotics on the 2023 EML by AWaRe category

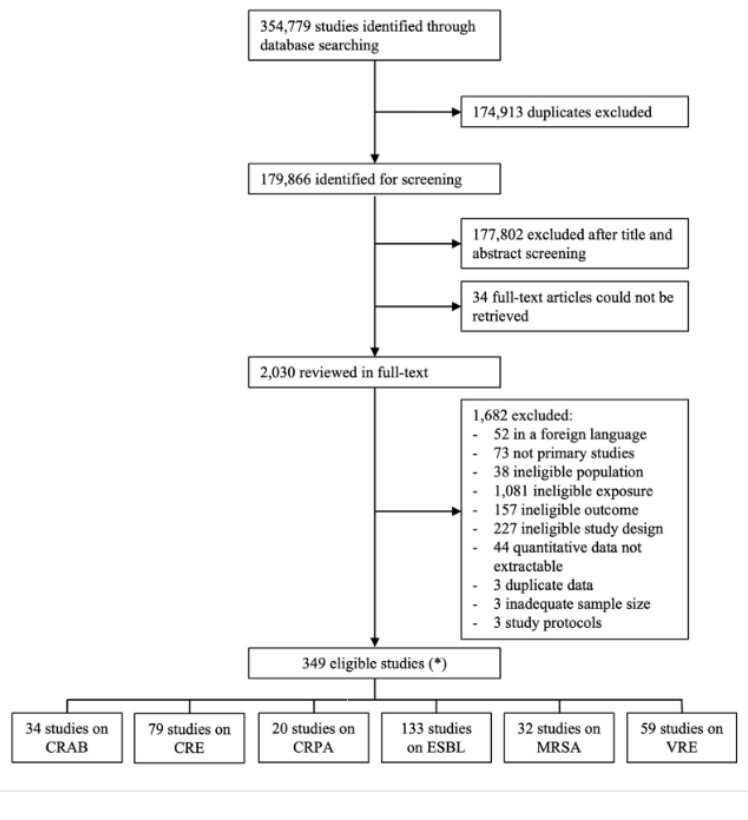
Amikacin	Azithromycin
Amoxicillin	Cefixime
Amoxicillin/clavulanic-acid	Cefotaxime
Ampicillin	Ceftazidime
Benzathine-benzylpenicillin	Ceftriaxone
Benzylpenicillin	Cefuroxime
Cefalexin	Ciprofloxacin
Cefazolin	Clarithromycin
Chloramphenicol	Meropenem
Clindamycin	Piperacillin/tazobactam
Cloxacillin	Vancomycin (IV and oral)
Doxycycline	Cefiderocol
Gentamicin	Ceftolozane/tazobactam
Metronidazole	Ceftazidime/avibactam
Nitrofurantoin	Colistin (IV)
Phenoxymethylpenicillin	Fosfomycin (IV)
Procaine-benzylpenicillin	Linezolid
Spectinomycin	Meropenem/vaborbactam
Sulfamethoxazole/TMP	Plazomicin
Trimethoprim	Polymyxin B (IV)
	Tedizolid

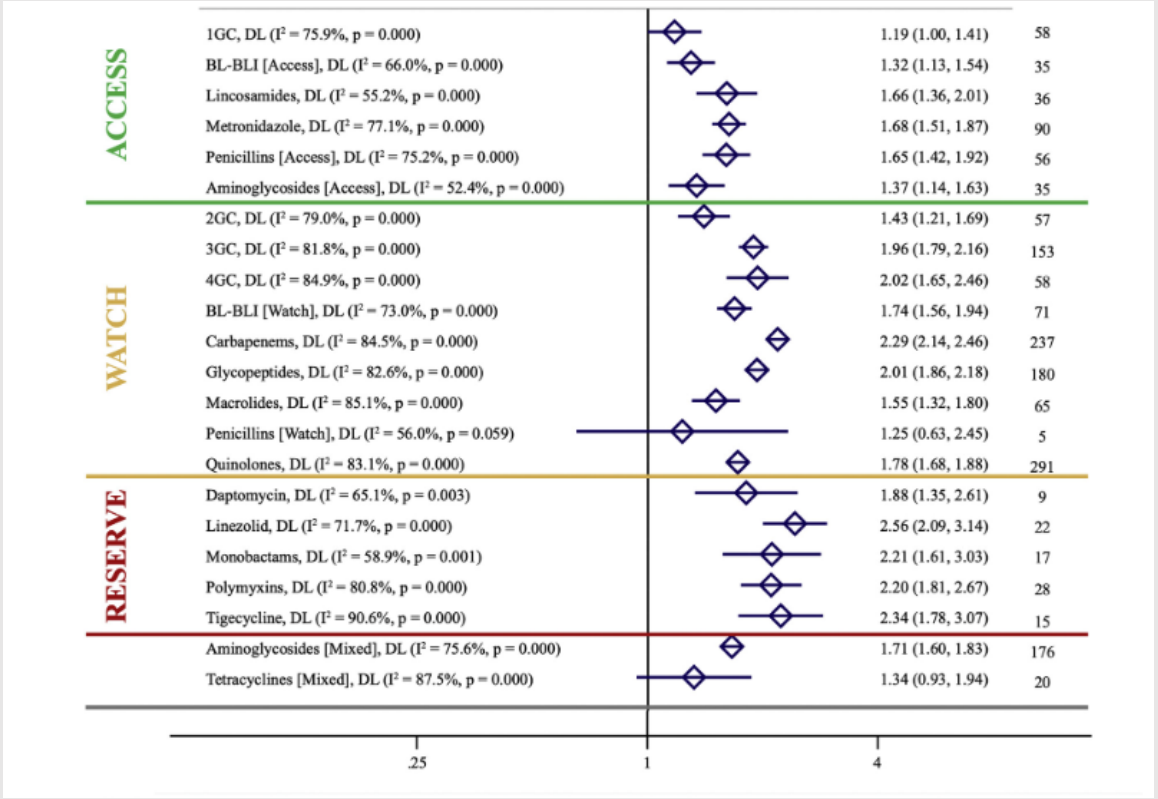
https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.04


What is the evidence base for AWaRe ?

Risk of resistance by AWaRe category: results from a systematic review

Sulis et al. Clin Microbiol Infect. 2022 Mar 23;S1198-743X(22)00153-7.





Any antibiotic treatment is associated with an increased risk of being colonized or infected with antibiotic-resistant bacteria

This risk is higher for Reserve and Watch antibiotics than for Access antibiotics

Overlap with medically important antibiotics

Fig. 1. Prioritization of antimicrobial classes in the WHO MIA List

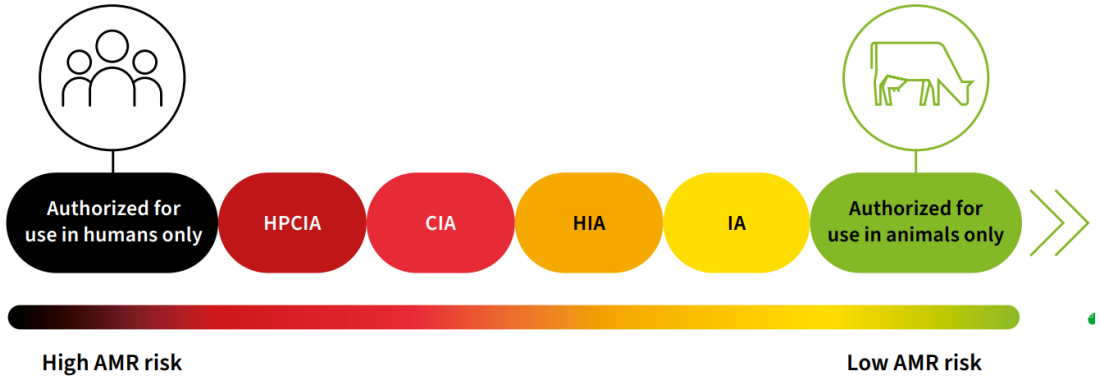
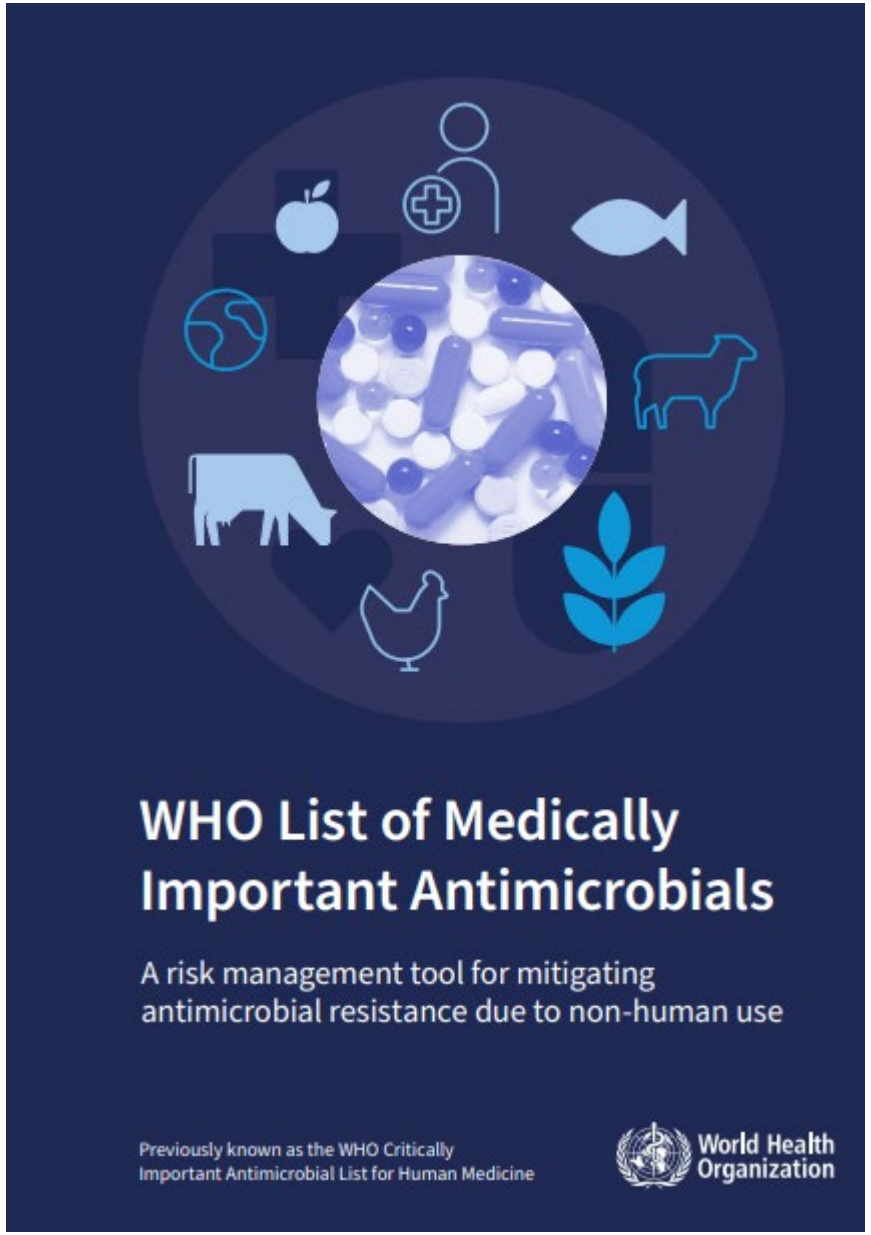
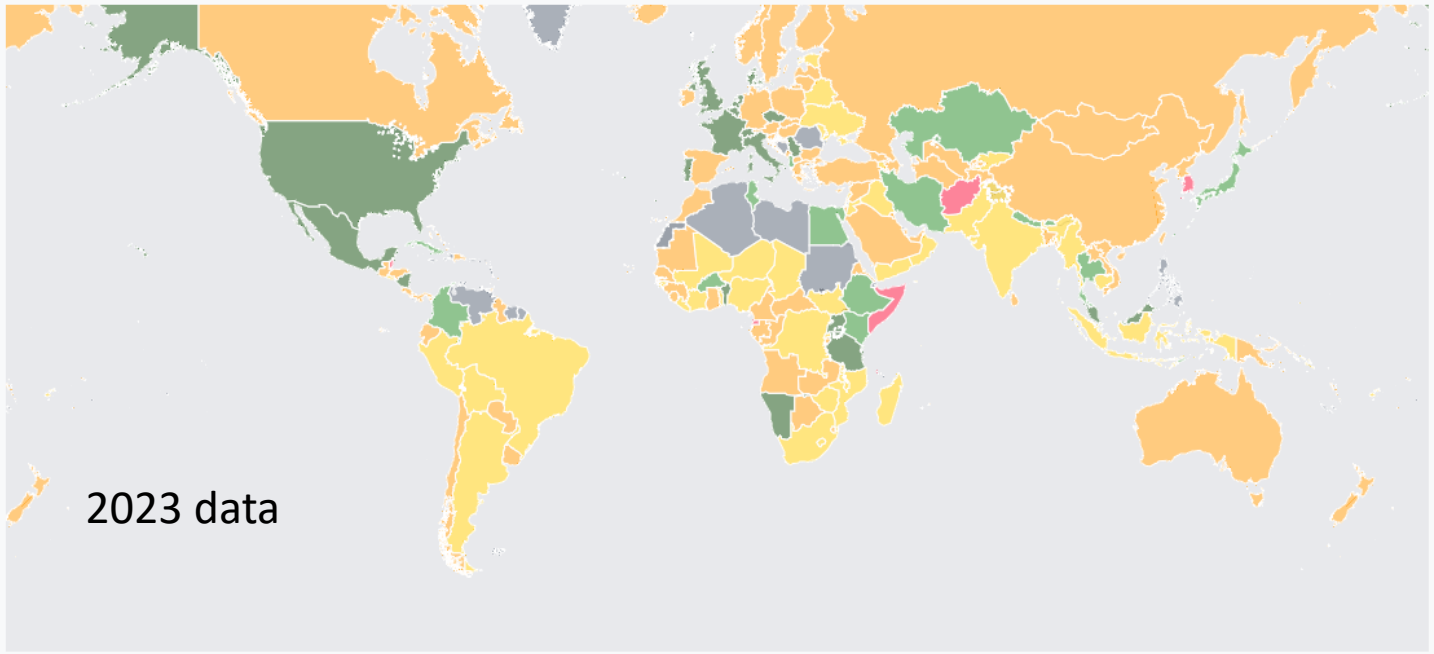


Table 1. Antimicrobials grouped according to authorized use

Medically important antimicrobials						Not medically important
Authorized for use in humans only		Authorized for both humans and animals				Not authorized in humans
Class	Class	Categorization of categorization of antimicrobials antimicrobials				
		HPCIA	CIA	HIA	IA	
Aminoglycosides (plazomicin)	Lipopeptides	Cephalosporins (3rd, 4th generation)	Aminoglycosides	Amphenicols	Aminocyclitols	Aminocoumarins
Aminomethycyclines	Macrolides 18-membered ring (fidaxomicin)	Quinolones	Ansamycins	Cephalosporins (1st- and 2nd-generation) and cephamycins	Cyclic polypeptides	Arsenicals
Anti-pseudomonal penicillins (carboxypenicillin and ureidopenicillin)	Monobactams	Polymyxins	Macrolides (14-, 15-, 16-membered ring)	Lincosamides	Heterocyclic compounds	Bicyclomycins
Anti-pseudomonal penicillins with β-lactamase inhibitors	Oxazolidinones	Phosphonic acid derivatives		Nitroimidazoles	Hydroxyquinoline	Orthosomycins
				Tetracyclines		
Carbapenems with or without β-lactamase inhibitors	Riminofenazines			Penicillins (amidinopenicillins and aminopenicillins)	Pleuromutilins	Phosphoglycolipids
Cephalosporins (3rd-, 4th- and 5th-generation with β-lactamase inhibitors)	Sulfones			Penicillins (aminopenicillins with β-lactamase inhibitors)	Nitrofuran derivatives	Ionophores (including polyethers)
Cephalosporins (5th-generation)	Glycopeptides and lipoglycopeptides			Penicillins (anti-staphylococcal)		Quinoxalines



Country Self- Assessment Survey (TrACSS)



3.7 Adoption of "AWaRe" classification of antibiotics in the National Essential Medicines List

- A - Country has no knowledge or information about the AWaRe classification of antibiotics.
- B - Country has knowledge about the AWaRe classification of antibiotics but has not yet adopted it.
- C - Country has adopted the AWaRe classification of antibiotics in their National Essential Medicines List.
- D - Country has adopted the AWaRe classification of antibiotics in their National Essential Medicines List and is monitoring its antibiotic consumption and reporting it according to the AWaRe classification.
- E - Country has adopted the AWaRe classification of antibiotics in their National Essential Medicines List, is monitoring its antibiotic consumption and reporting it according to the AWaRe classification and has incorporated AWaRe into its antimicrobial stewardship strategies (e.g. treatment guidelines).

The country membership amongst the Quadripartite organizations can differ. Based on the administration of the TrACSS questionnaire, and for consistency, WHO Member States (n=194) and map are used on this website.

https://amrcountryprogress.org/#/map-view

JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlaf031

JAC-Antimicrobial Resistance

Increasing the use of the WHO AWaRe system in antibiotic surveillance and stewardship programmes in low- and middle-income countries

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Introduction: Antimicrobial resistance (AMR) presents a major global health threat, driven in part by the inappropriate use of antibiotics including in low- and middle-income countries (LMICs). Improving the quality of antibiotic use is a key rationale for the development of the WHO's AWaRe (Access, Watch and Reserve) system. There is a need to review the uptake of the AWaRe system since its launch to guide future practice.

Methods: A literature search was conducted between 2017, the launch of AWaRe, and 2024. Inclusion criteria were studies that reported on antibiotic use in LMICs using the AWaRe system.

Results: Eighty-five studies were included in the review, of which 56.4% focused on antibiotic use trends, with 28.2% reporting on prescribing patterns; 51.7% of the studies included inpatients. Only 14.1% of studies reported meeting the 2024 United Nations General Assembly (UNGA) AMR recommended target of at least 70% of human antibiotic use being Access antibiotics, with a concerning trend of overuse of Watch antibiotics (68.2% of studies). Dispensing practices revealed significant dispensing of antibiotics without prescriptions especially in Pakistan and Bangladesh. Watch antibiotics were more available but also more expensive than Access antibiotics.

Conclusions: Encouragingly, many LMICs are now reporting antibiotic use via the AWaRe system, including in antimicrobial stewardship programmes (ASPs). Wide variation exists in the proportion of AWaRe antibiotics used across LMICs, with overuse of Watch antibiotics. There is an urgent need for targeted AWaRe-based ASPs in LMICs to meet recent UNGA recommendations. Improving the use, availability and affordability of Access antibiotics is essential to combat AMR.

World Health Organization

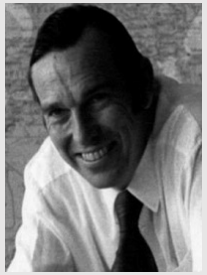
Appropriate use of essential medicines

It is not enough that essential medicines are available and affordable

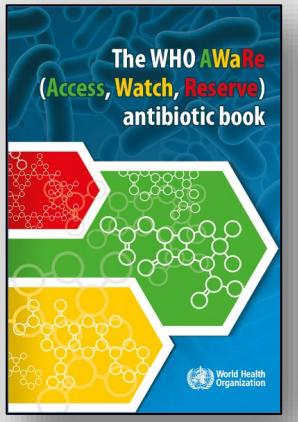
- They must be used appropriately

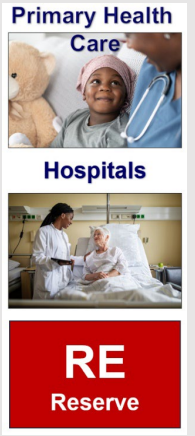
In a report [1] to the Twenty-eighth World Health Assembly in 1975, the Director-General reviewed the main drug problems facing the developing countries and outlined possible new drug policies. The Director-General also referred to the experience gained in some countries where schemes of basic or essential drugs had been implemented. Such schemes were intended to extend the accessibility of the most necessary drugs to those populations whose basic health needs could not be met by the existing supply system. The Director-General pointed out that the selection of these essential drugs would depend on the health needs and on the structure and development of health services of each country, and that lists of essential drugs should be drawn up locally, and periodically updated, with the advice of experts in public health, medicine, pharmacology, pharmacy and drug management. He also considered that adequate information on the properties, indications and use of the drugs listed should be provided. By resolution WHA28.66, the Health Assembly requested the Director-General to implement the proposals contained in his report and, in particular, to advise Member States on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs.

"He also considered that adequate information on the properties, Indications and use of the drugs listed should be provided"



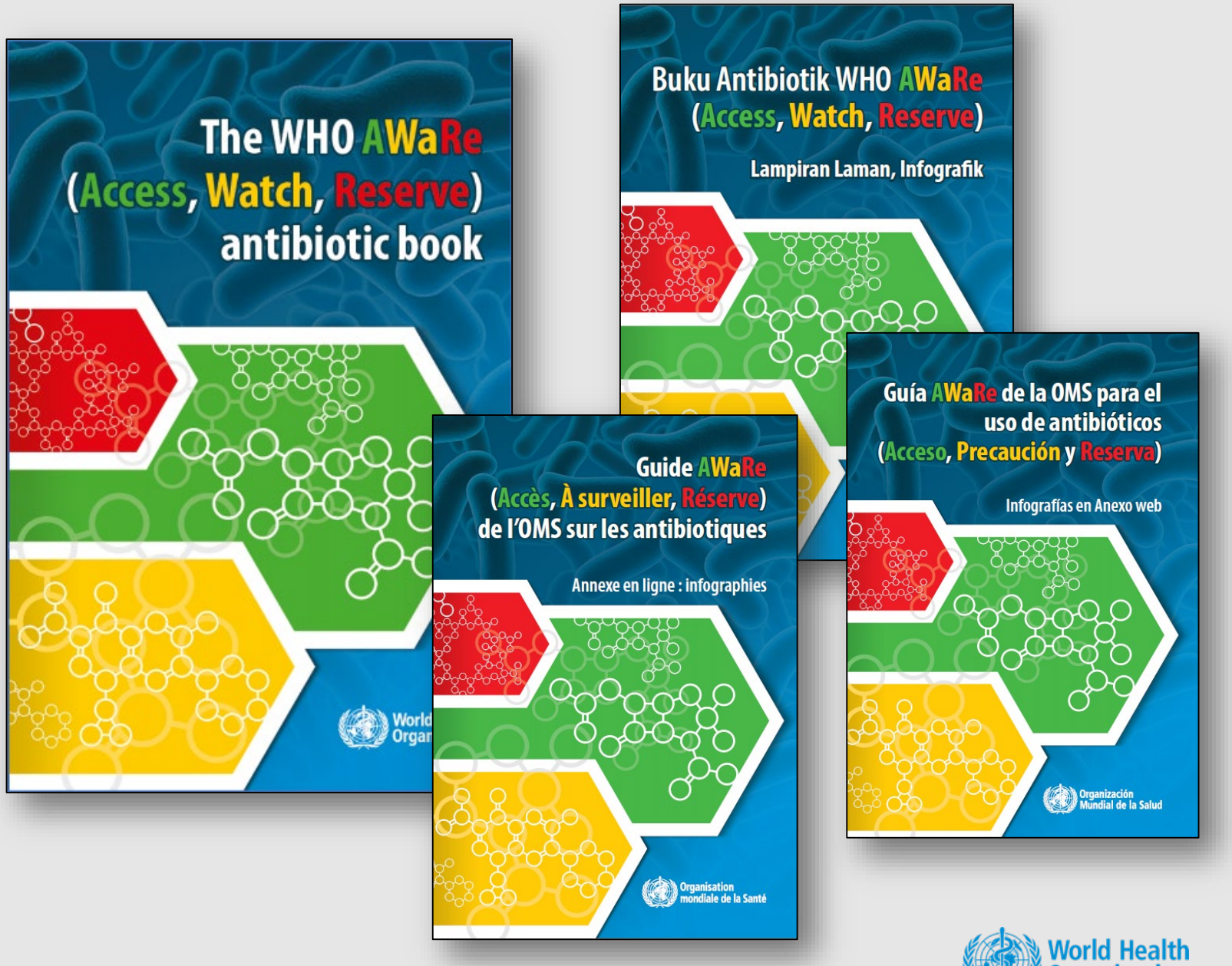
Dr Halfdan Mahler (WHO DG 1973-1988)





World Health Organization

The WHO AWaRe Antibiotic Book

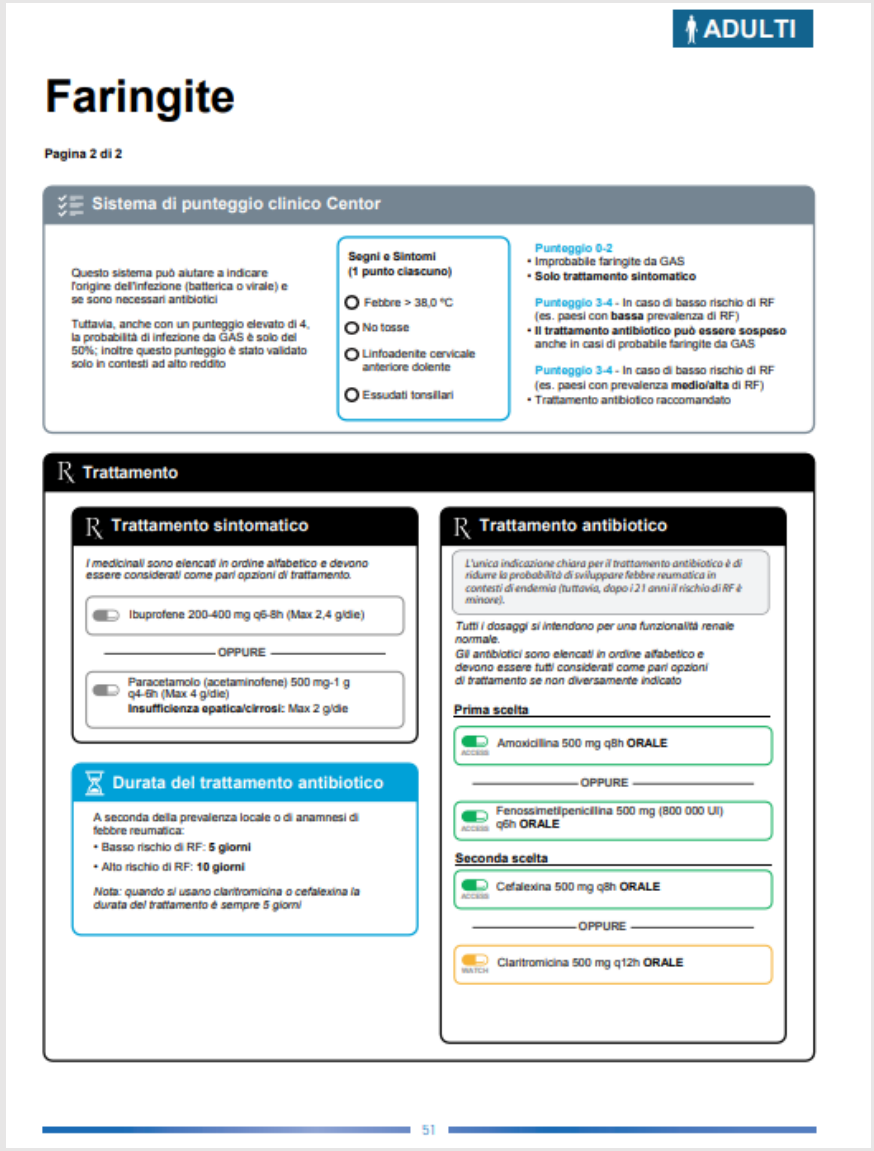


World Health Organization

Manuale antibiotici AWaRe (Access, Watch, Reserve)

Edizione italiana del "The WHO AWaRe Antibiotic Book"

AIFA AGENZIA ITALIANA DEL FARMACO



ADULTI

Faringite

Pagina 2 di 2

Sistema di punteggio clinico Centor

Questo sistema può aiutare a indicare l'origine dell'infezione (batterica o virale) e se sono necessari antibiotici

Tuttavia, anche con un punteggio elevato di 4, la probabilità di infezione da GAS è solo del 50%; inoltre questo punteggio è stato validato solo in contesti ad alto reddito

Segni e Sintomi (1 punto ciascuno)

- Febbre > 38,0 °C
- No tosse
- Linfoadenite cervicale anteriore dolente
- Essudati tonsillari

Punteggio 0-2
- Improbabile faringite da GAS
- **Solo trattamento sintomatico**

Punteggio 3-4 - In caso di basso rischio di RF (es. paesi con **bassa** prevalenza di RF)
- **Il trattamento antibiotico può essere sospeso** anche in casi di probabile faringite da GAS

Punteggio 3-4 - In caso di basso rischio di RF (es. paesi con prevalenza **medio/alta** di RF)
- Trattamento antibiotico raccomandato

℞ Trattamento

℞ Trattamento sintomatico

I medicinali sono elencati in ordine alfabetico e devono essere considerati come pari opzioni di trattamento.

Ibuprofene 200-400 mg q6-8h (Max 2,4 g/die)

— OPPURE —

Paracetamolo (acetaminofene) 500 mg-1 g q4-6h (Max 4 g/die)
Insufficienza epatica/cirrosi: Max 2 g/die

Durata del trattamento antibiotico

A seconda della prevalenza locale o di anamnesi di febbre reumatica:
- Basso rischio di RF: **5 giorni**
- Alto rischio di RF: **10 giorni**

Nota: quando si usano claritromicina o cefalexina la durata del trattamento è sempre 5 giorni

℞ Trattamento antibiotico

L'unica indicazione chiara per il trattamento antibiotico è di ridurre la probabilità di sviluppare febbre reumatica in contesti di endemia (tuttavia, dopo i 21 anni il rischio di RF è minore).

Tutti i dosaggi si intendono per una funzionalità renale normale.
Gli antibiotici sono elencati in ordine alfabetico e devono essere tutti considerati come pari opzioni di trattamento se non diversamente indicato

Prima scelta

Amoxicillina 500 mg q8h **ORALE**

— OPPURE —

Fenossimetilpenicillina 500 mg (800 000 UI) q6h **ORALE**

Seconda scelta

Cefalexina 500 mg q8h **ORALE**

— OPPURE —

Claritromicina 500 mg q12h **ORALE**

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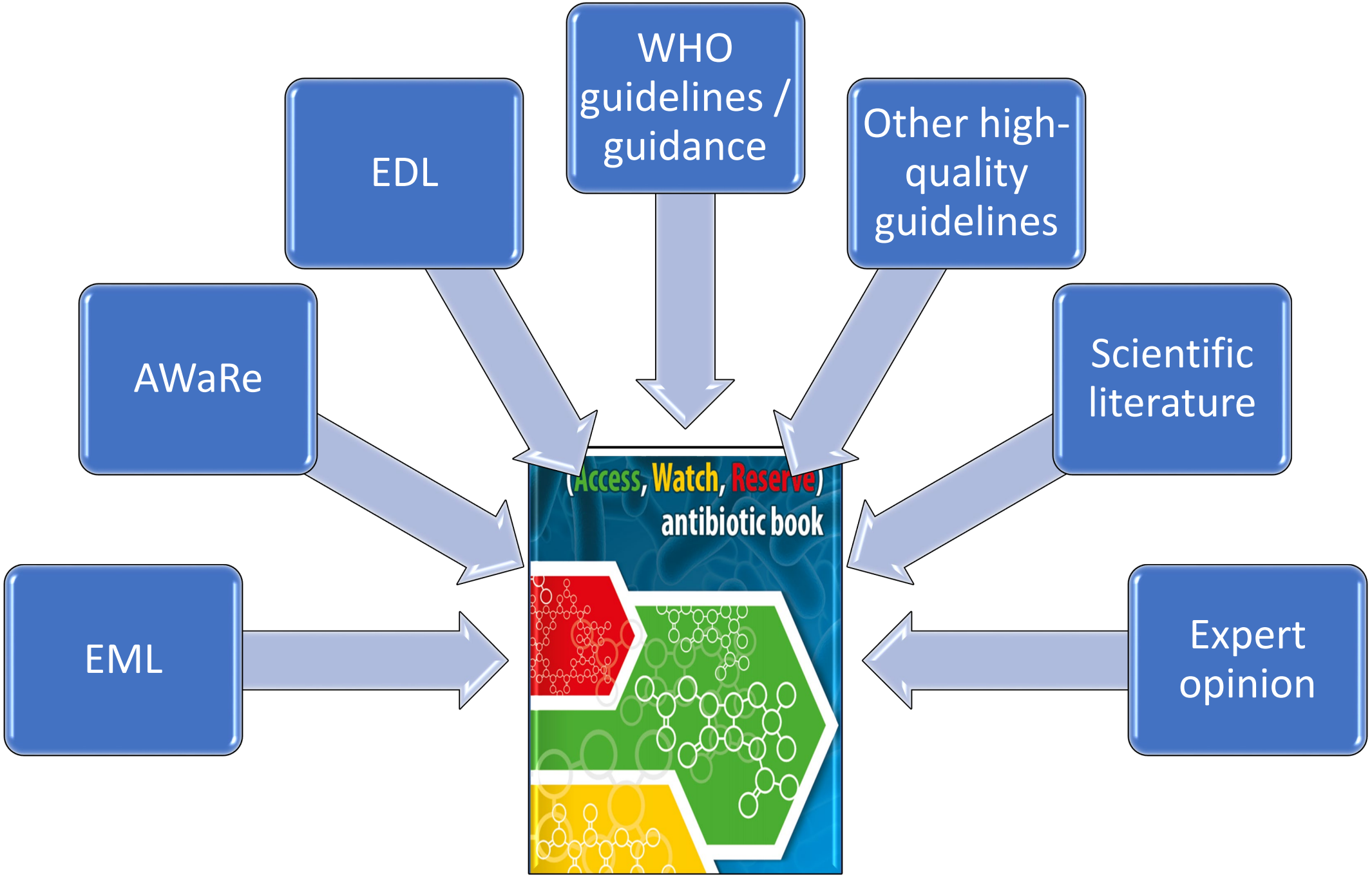
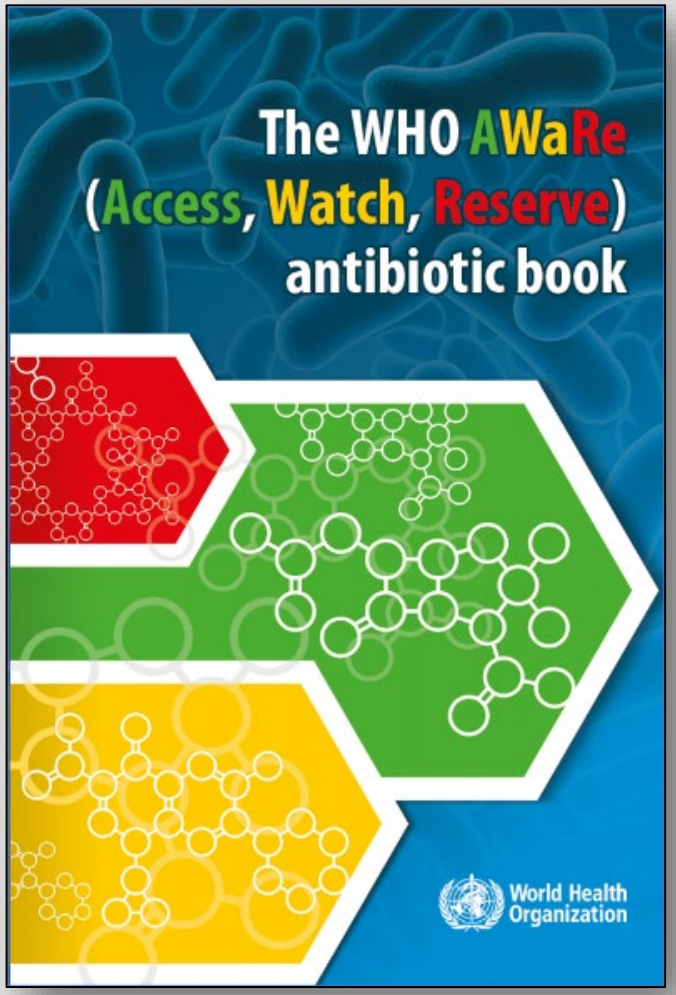
https://www.aifa.gov.it/documents/20142/1811463/Manuale_antibiotici_AWaRe.pdf

World Health Organization


WHO guidelines / guidance
EDL
Other high-quality guidelines
AWaRe
Scientific literature
(Access, Watch, Reserve) antibiotic book
EML
Expert opinion

WHO AWaRe antibiotic book



To provide simple guidance on **"HOW TO USE"** the antibiotics on the EML to manage common infections

Guidance for 34 common infections, surgical prophylaxis and use of Reserve antibiotics; **primary care** and **facility / hospital setting**, in **children and adults**.

Recommendations on empiric antibiotic treatment

(i.e., presumptive diagnosis not requiring any laboratory diagnostic)

Includes guidance on making the clinical **Diagnosis**, the **Decision** if antibiotic needed, the choice of **Drug, Dose, Duration**

Short summaries of key features of microbiology, epidemiology, clinical presentation, diagnostics (in collaboration with EDL) and prevention

Target audience: **all health professionals giving antibiotics**

Contents

Primary Health Care

Hospitals

RE

Reserve

The WHO AWaRe (Access, Watch, Reserve) antibiotic book

INFOGRAPHICS

CHILDREN

Community-acquired pneumonia

Page 1 of 2

Definition

An acute illness affecting the lungs usually presenting with cough, and rapid and difficult breathing with a new or worsening pulmonary infiltrate on a chest radiograph

Most Likely Pathogens

"Typical" bacteria:

- ***Streptococcus pneumoniae*** (most common cause of CAP beyond the 1st week of life)
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Staphylococcus aureus*
- *Enterobacterales*

"Atypical" pathogens (more frequent in children >5 years compared to younger children):

- *Mycoplasma pneumoniae*
- *Chlamydophila pneumoniae*

Respiratory viruses:

- Respiratory syncytial virus (RSV)
- Influenza viruses (A and B)
- Metapneumovirus
- Parainfluenza virus
- Coronavirus (including SARS-CoV-2)
- Adenovirus
- Rhinovirus
- Other respiratory viruses

Investigating for Tuberculosis (TB)

- Consider specific investigations for TB in endemic settings especially in high-risk patients (e.g. HIV)
- A rapid molecular test performed on a single sputum specimen is the preferred first line diagnostic test for pulmonary TB and to detect rifampicin resistance

Diagnosis

Clinical Presentation

- New onset (<2 weeks) or worsening cough with fever (≥38.0° C), dyspnea, tachypnea, reduced oxygen saturation, crepitations, cyanosis, grunting, nasal flaring, pallor
- Pneumonia is diagnosed on: fast breathing for age and/or chest indrawing
  - Check for hypoxia with oxygen saturometer if available
- Children with runny nose and cough and no signs of severity usually do not have pneumonia and should not receive an antibiotic, only home care advice

Microbiology Tests

Mild cases: usually not needed

Severe cases (to guide antimicrobial treatment): blood cultures

Tests for COVID-19 and influenza can be considered if clinically indicated and available

Other Laboratory Tests

No test clearly differentiates viral or bacterial CAP

Consider: full blood count and C-reactive protein

Note: tests depend on availability and clinical severity (e.g. blood gases will only be done in severe cases)

Imaging

- Chest X-ray not necessary in mild cases
- Look for lobar consolidation or pleural effusion
- Radiologic appearance cannot be used to accurately predict pathogen

PRIMARY HEALTH CARE
12. Community-acquired pneumonia – mild

CHILDREN

Community-acquired pneumonia

Page 2 of 2

Severity Assessment and Considerations

Children with **pneumonia**:

- Should be treated with oral amoxicillin at home with home care advice
- Pneumonia is diagnosed on either:
  1. Fast breathing (respiratory rate > 50 breaths/minute in children aged 2-11 months; resp rate > 40 breaths/min in children aged 1-5 years)
  2. Chest indrawing

Children with **severe pneumonia** (or a child with pneumonia who cannot tolerate oral antibiotics):

- **Should be admitted to hospital and treated with intravenous antibiotics**
- Severe pneumonia is characterized by signs of pneumonia:
  - Fast breathing (+/- chest indrawing)

  PLUS
  - A general danger sign:
    - Inability to breastfeed or drink
    - Convulsions
    - Lethargy or reduced level of consciousness
    - Severe respiratory distress

Antibiotic Treatment Duration

3 days: in areas of low HIV prevalence and no chest indrawing

5 days: in areas of high HIV prevalence and the child has chest indrawing

If severe disease, consider longer treatment and look for complications such as empyema, if patient not clinically stable at day 5

Mild to Moderate Cases

All dosages are for normal renal function

Amoxicillin 80-90 mg/kg/day **ORAL**

- **Oral weight bands**:

3-<6 kg	250 mg q12h
6-<10 kg	375 mg q12h
10-<15 kg	500 mg q12h
15-<20 kg	750 mg q12h
≥20 kg	500 mg q8h or 1 g q12h

Treatment

Severe Cases

Please see Severity Assessment and Considerations for diagnosis of severe cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

Amoxicillin 50 mg/kg/dose **IV/IM**
- ≤1wk of life: q12h
- >1wk of life: q8h

OR

Ampicillin 50 mg/kg/dose **IV/IM**
- ≤1wk of life: q12h
- >1wk of life: q8h

OR

Benzylpenicillin 30 mg/kg/dose (50000 IU/kg/dose) q8h IV

COMBINED WITH

Gentamicin **IV/IM**
- Neonates: 5 mg/kg/dose q24h
- Children: 7.5 mg/kg/dose q24h

IF HIV POSITIVE AND <1 YR OLD
To treat potential Pneumocystis jirovecii pneumonia, **ADD**

Sulfamethoxazole+trimethoprim 40 mg/kg SMX+8 mg/kg TMP q8h **IV/ORAL** for 3 weeks

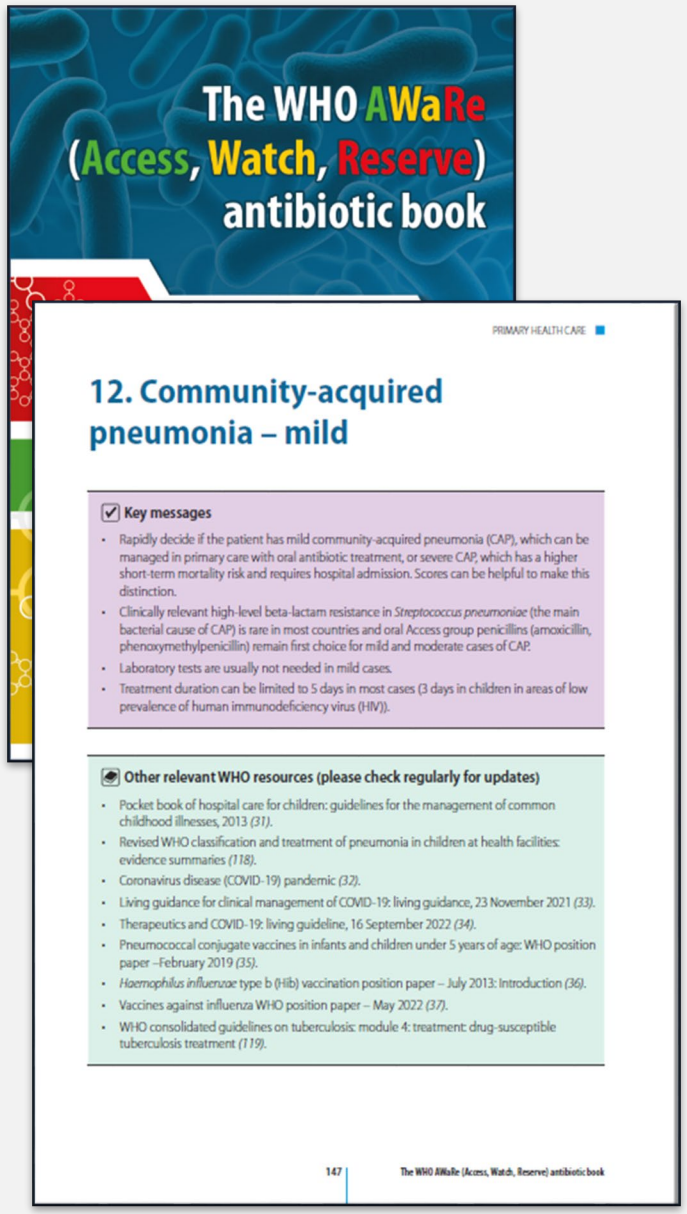
Second Choice
If NO Clinical Response to First Choice after 48-72 hours

Cefotaxime 50 mg/kg/dose q8h **IV/IM**

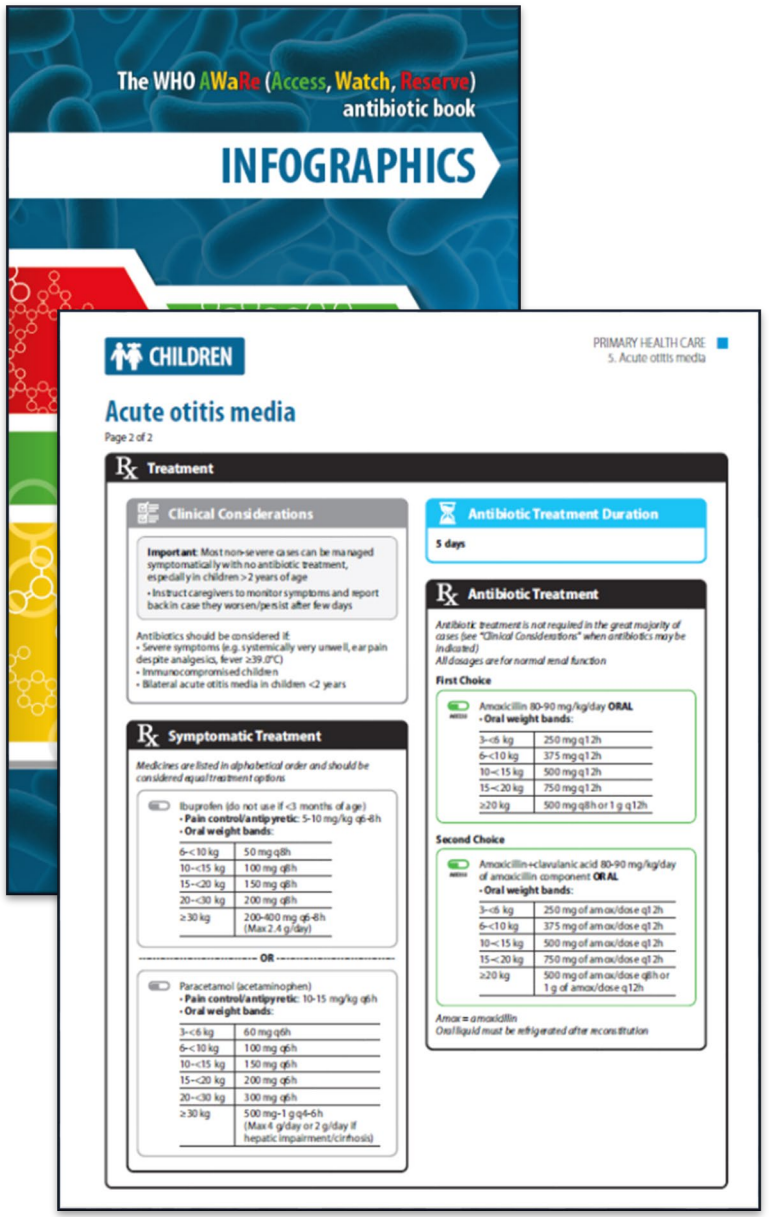
OR

Ceftriaxone 80 mg/kg/dose q24h **IV/IM**

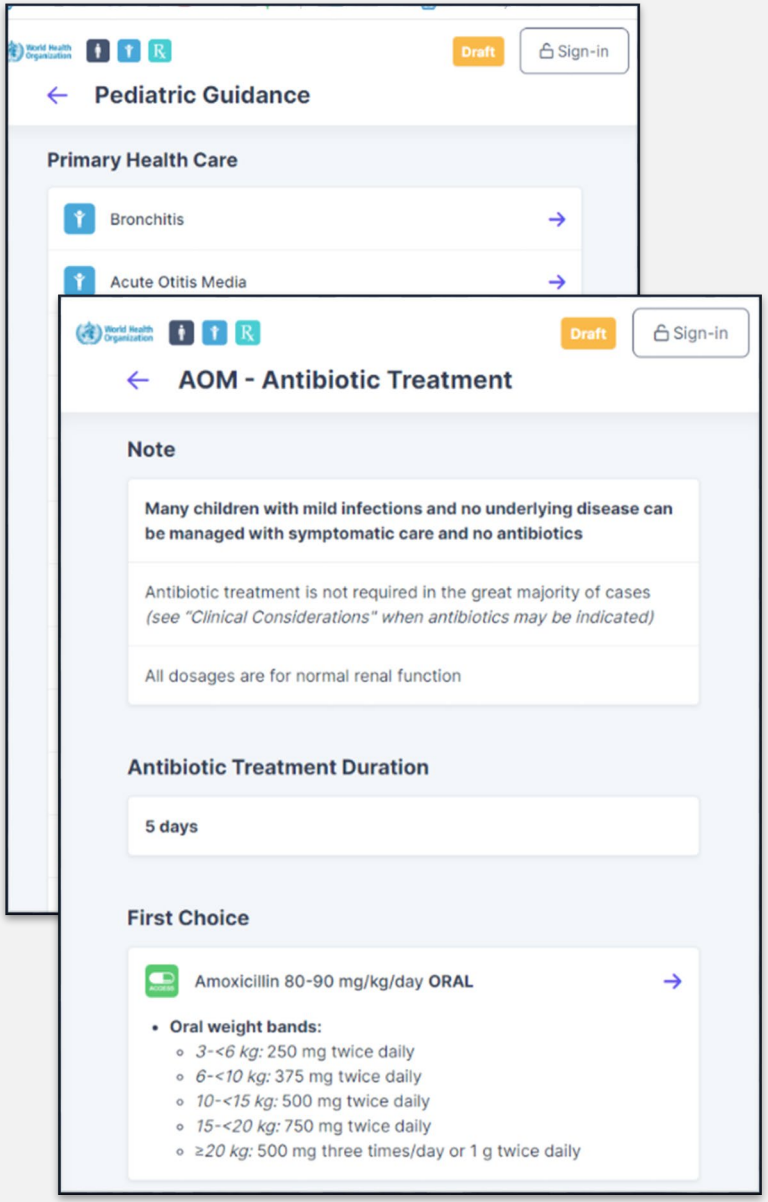
(1) Book



(2) Infographics



(3) App



Local adaptation

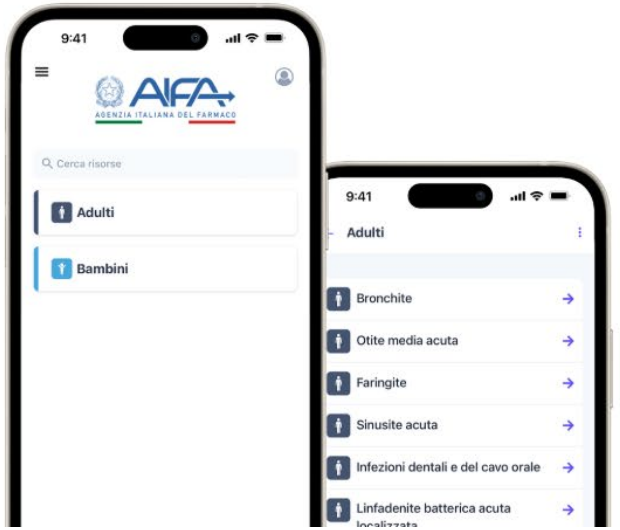
https://firstline.org/aifa

AIFA AGENZIA ITALIANA DEL FARMACO

Firstline

Insieme per un uso responsabile degli antibiotici

Firstline è gratuito ed è rivolto principalmente agli operatori sanitari



Puoi iniziare adesso:

1. Scarica Firstline sul cellulare o accedi alla versione per il web
2. Fai clic su "Seleziona posizione" e scegli **"Agenzia Italiana del Farmaco"**
3. Accedi alle raccomandazioni dell'OMS adattate al contesto epidemiologico e alla disponibilità di farmaci in Italia.

Ricorda che gli antibiotici sono farmaci soggetti a prescrizione

Limited availability of local antibiotic treatment guidelines

Review of official websites for published standardized treatment guidelines in the 55 African Union countries

Complemented by contact with focal points from African CDC and WHO

31 standardized treatment guidelines from 20 countries identified (2001-2018)

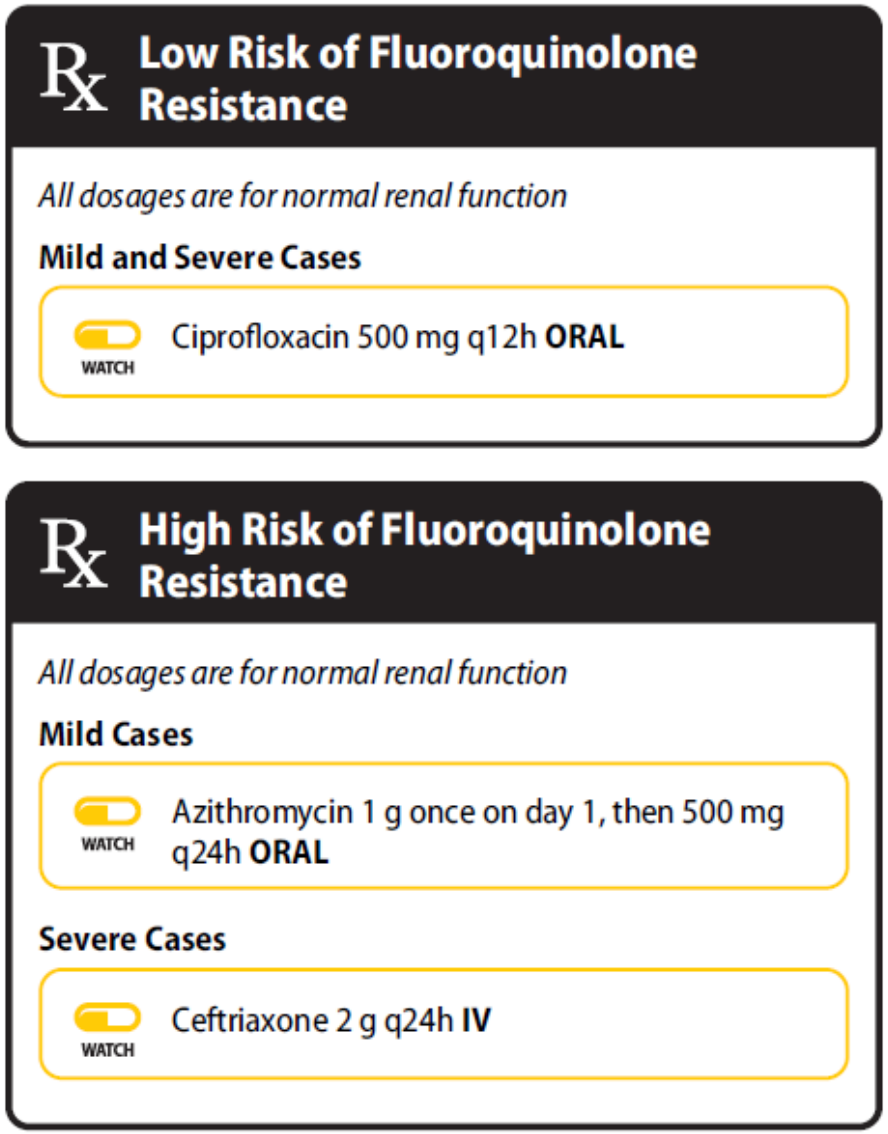
35 countries no guidelines identified	None developed according to GRADE methodology	Important variation in antimicrobial selection and dosage and duration of recommended therapies	None stated that antibiotic selection was based on local epidemiology of antibiotic resistance

Craig et al. Bull World Health Organ. 2022 Jan 1;100(1):50-59.

World Health Organization

AWaRe antibiotic book - enteric fever

- ***"In settings where ceftriaxone-resistance is increasing, azithromycin should be prioritized.*** *Outbreaks of enteric fever caused by extensively antibiotic-resistant Salmonella Typhi have been reported, for example, in Pakistan since 2016 and in travel-related cases across the world."*

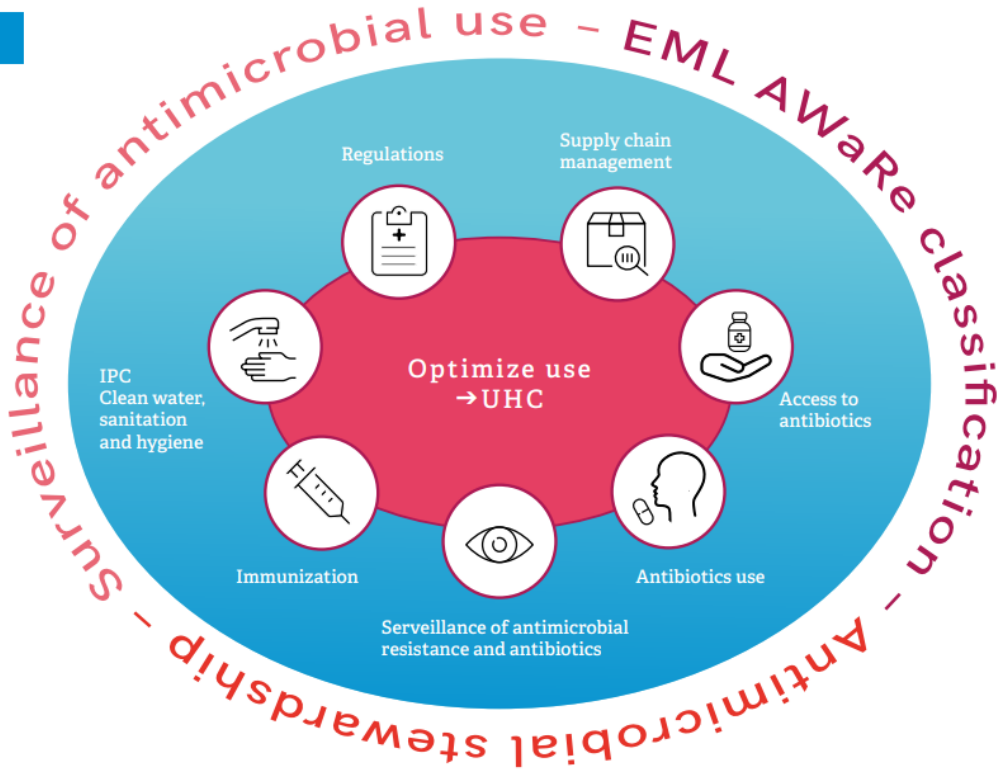


Local adaptation of the AWaRe antibiotic book

- Align with / update the national list of essential medicines and existing guidelines
- Involve and engage key national stakeholders from all relevant areas
- Use the book for education of healthcare professionals
- Avoid the temptation to prolong duration
- Try to keep other antimicrobial stewardship principles (Access, parsimony)
- Develop a strategy on how to implement the guidance

FIGURE 1

Integrated approach to optimizing use of antimicrobials towards universal health coverage



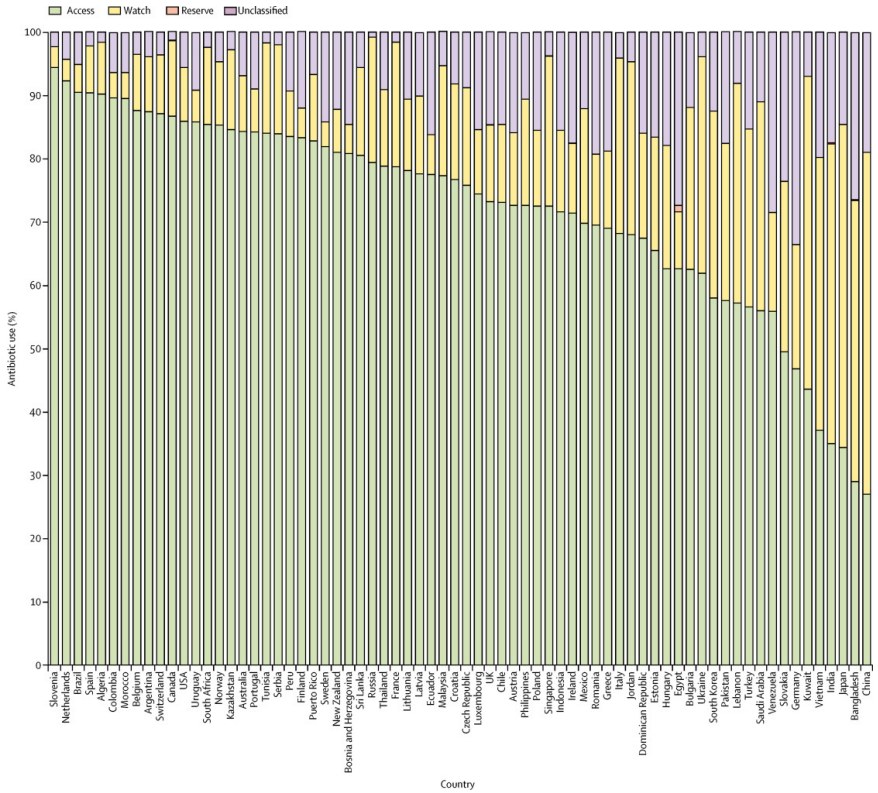
AWaRe indicators and targets

Target **≥60%** of total antibiotic consumption* being **Access** group antibiotics (GPW13 target 4b)

WHO's 13th General Program of Work antibiotic use indicator

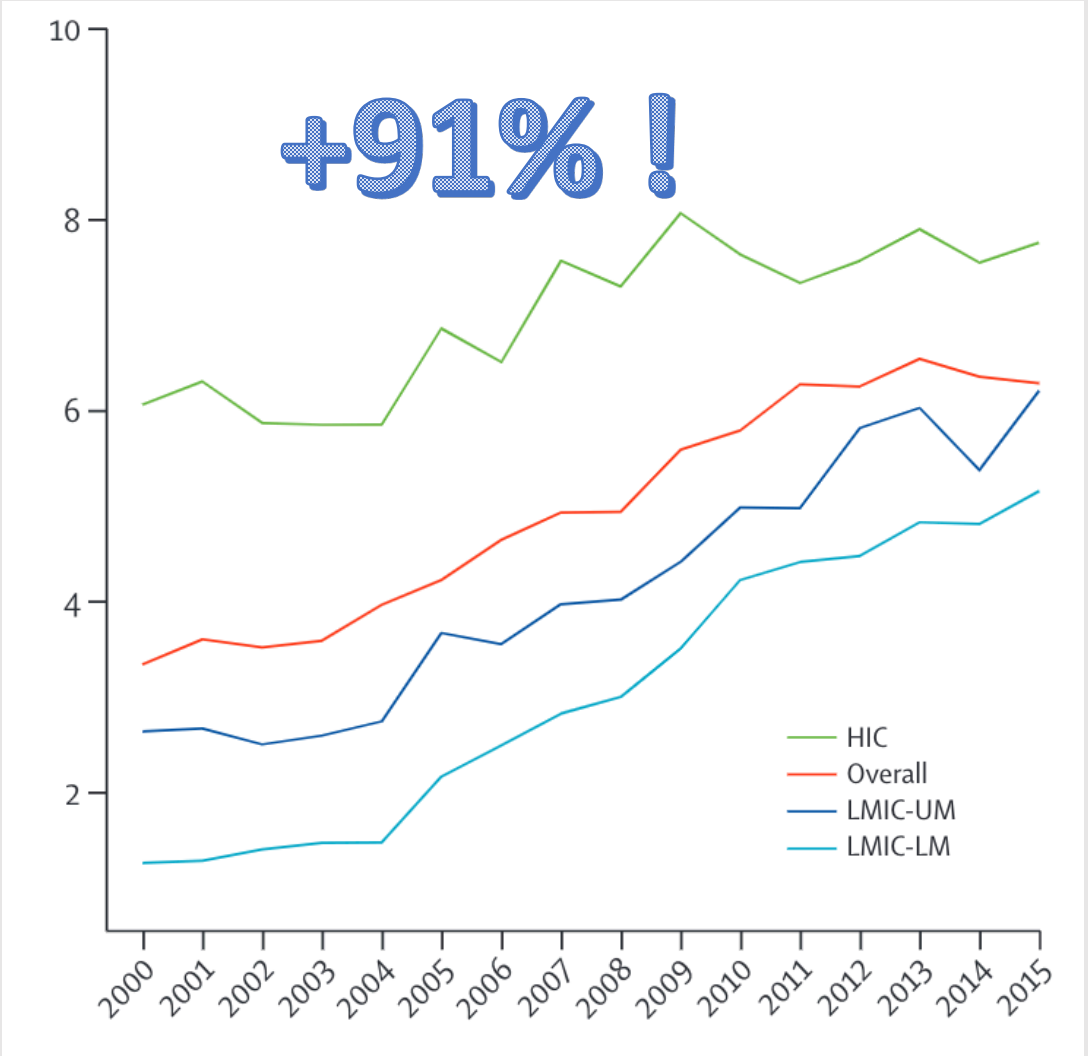
*ATC/DDD methodology; ATC classes: A07AA, J01, and P01AB

Why 60% ?

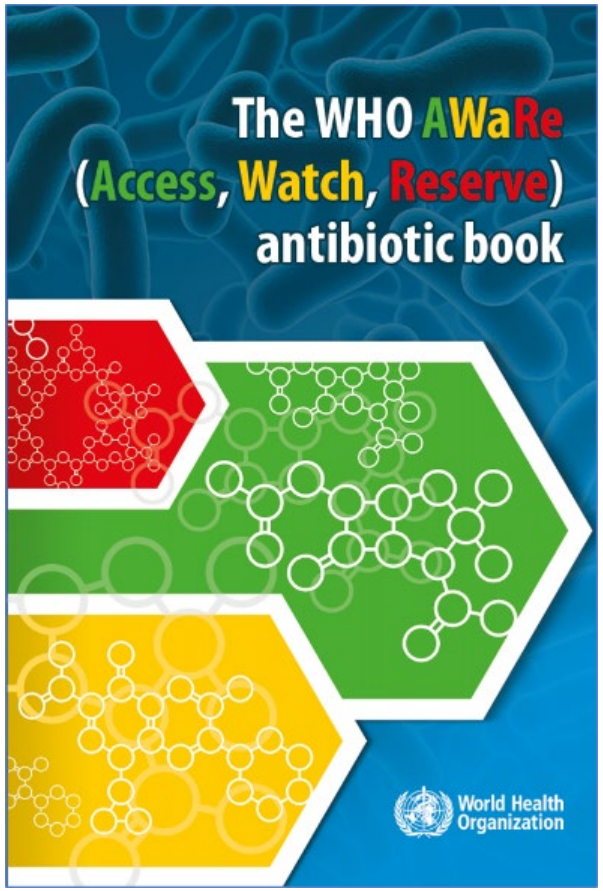


Percentage antibiotic use of child-appropriate oral formulations according to WHO AWaRe grouping

Absolute consumption of **Watch** antibiotics 2000–2015



Klein et al. Lancet Infect Dis. 2021 Jan;21(1):107-115.



Infection	Can it be safely treated without antibiotics?	Type of antibiotic (if indicated)
Bronchitis	Yes	
COPD exacerbations	Yes, in most mild cases	Access
Dental infections	Yes, in most mild cases	Access
Otitis media	Yes, in most mild cases	Access
Pharyngitis	Yes, in most mild cases	Access
Sinusitis	Yes, in most mild cases	Access
Skin and soft tissue infections (mild)	Only for certain conditions and in certain patients	Access
Urinary tract infection (lower)	Only in a few patients with no risk factors for complicated infections	Access
Acute Bloody Diarrhoea	Antibiotics are usually indicated if significant bloody diarrhea	Watch
Community acquired pneumonia (mild to moderate)	No	Access

Could the target be even higher than 60% Access ?

Recommended treatment for common primary care infections in the AWaRe antibiotic book

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1 Focosi D, Maggi F, Casadevall A. Mucosal vaccines, sterilizing immunity, and the future of SARS-CoV-2 virulence. *Viruses* 2022; **14**: 187.
2 Havervall S, Marking U, Svensson J, et al. Anti-spike mucosal IgA protection against SARS-CoV-2 omicron infection. *N Engl J Med* 2022; **387**: 1333–36.
3 Gilboa M, Regev-Yochay G, Mandelboim M, et al. Durability of immune response after COVID-19 booster vaccination and association with COVID-19 omicron infection. *JAMA Netw Open* 2022; **5**: e2231778–78.
4 Blom K, Marking U, Havervall S, et al. Immune responses after omicron infection in triple-vaccinated health-care workers with and without previous SARS-CoV-2 infection. *Lancet Infect Dis* 2022; **22**: 943–45.
5 Reynolds CJ, Pade C, Gibbons JM, et al. Immune boosting by B.1.1.529 (omicron) depends on previous SARS-CoV-2 exposure. *Science* 2022; **377**: eabq1841.
6 Malato J, Ribeiro RM, Leite PP, et al. Risk of BA.5 infection among persons exposed to previous SARS-CoV-2 variants. *N Engl J Med* 2022; **387**: 953–54.
7 Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Protective effect of previous SARS-CoV-2 infection against omicron BA.4 and BA.5 subvariants. *N Engl J Med* 2022; **387**: 1620–22.

See Online for appendix

Setting a realistic AWaRe target for primary care antibiotic use in LMICs

Published Online January 6, 2023 https://doi.org/10.1016/S1473-3099(23)00002-6

We welcome the WHO AWaRe (Access/Watch/Reserve) Antibiotic Book, released on Dec 9, 2022. Sharland and colleagues[1] proposed two antibiotic use targets that could support its introduction and the evaluation of its effectiveness, as follows: 90% of infections requiring an antibiotic in primary health care can be treated with oral Access antibiotics rather than broad spectrum Watch antibiotics and more than 50% of minor infections can be treated without antibiotics. In low-income and middle-income countries, use of Watch antibiotics has been rapidly increasing,[2] yet after careful clinical evaluation, three-quarters of Watch antibiotics could be discontinued or replaced by Access antibiotics.[3] A complication is that self-medication with antibiotics is frequent; more than 50% of populations in African countries reported self-medication with antibiotics,[4] limiting the impact of guidance targeting health centres. To evaluate whether the (Watch) antibiotic use targets are realistic, we analysed data from patient surveys after visits to (private and public) health centres and over-the-counter dispensing in (private and public) medicine stores in November and December, 2021, in Nanoro health district, Burkina Faso, and November, 2019, in Kisantu healthzone, DR Congo,[5] and estimated the proportion of Watch antibiotic use that could be averted by applying the treatment guidelines in the WHO AWaRe Antibiotic Book (appendix p 1).

In primary health centres, 638 (60%) of 1062 patients in Burkina Faso and 297 (80%) of 371 patients in DR Congo used antibiotics, whereas 87 (8%) and 113 (30%) used Watch antibiotics, respectively. Malaria, which is not in the WHO AWaRe Antibiotic Book, accounted for the use of 79 (40%) of 200 Watch antibiotic courses in health centres. Patients' clinical evolution after antimalarial treatment is generally not reassessed, so potential co-infections are treated simultaneously during a single visit, perhaps with consideration that severe malaria is a known risk factor for invasive non-Typhi salmonella infection, which underlies most bloodstream infections in both countries.[6] For gastrointestinal complaints without diarrhoea (15 [8%] of 200 courses), skin infection (15 [8%] of 200 courses), and bronchitis (12 [6%] of 200 courses), Watch antibiotics were used but not indicated. The prevalence of Watch antibiotic use as self-medication (55 [7%] of 757 courses in Burkina Faso and 63 [14%] of 440 courses in DR Congo) was lower than reported in health centres but still significant (appendix p 3).

Adhering to the AWaRe Antibiotic Book, 69% of Watch antibiotic use in Burkina Faso and 75% of Watch antibiotic use in DR Congo could be replaced by Access antibiotics or no antibiotic use, which implies that the 90% Access target is theoretically attainable in both countries. Similarly, the proportion of Access antibiotics from self-medication (80% in Burkina Faso and 69% in DR Congo) could increase when 66% and 60% of Watch antibiotic use, respectively, is avoided.

The WHO AWaRe Antibiotic Book has great potential to optimise antibiotic use in primary care, foremost when at once regulating or guiding over-the-counter dispensing of Watch antibiotics, and facilitating follow-up of patients' clinical evolution.

We declare no competing interests.

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1 Sharland M, Cappello B, Ombajo LA, et al. The WHO AWaRe Antibiotic Book: providing guidance on optimal use and informing policy. *Lancet Infect Dis* 2022; **22**: 1528–30.
2 Klein EY, Milkowska-Shibata M, Tseng KK, et al. Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: an analysis of pharmaceutical sales data. *Lancet Infect Dis* 2021; **21**: 107–15.
3 Ingelbeen B, Koirala KD, Verdonck K, et al. Antibiotic use prior to seeking medical care in patients with persistent fever: a cross-sectional study in four low- and middle-income countries. *Clin Microbiol Infect* 2021; **27**: 1293–300.

Ingelbeen et al. Lancet Infect Dis. 2023 Feb;23(2):152-153.

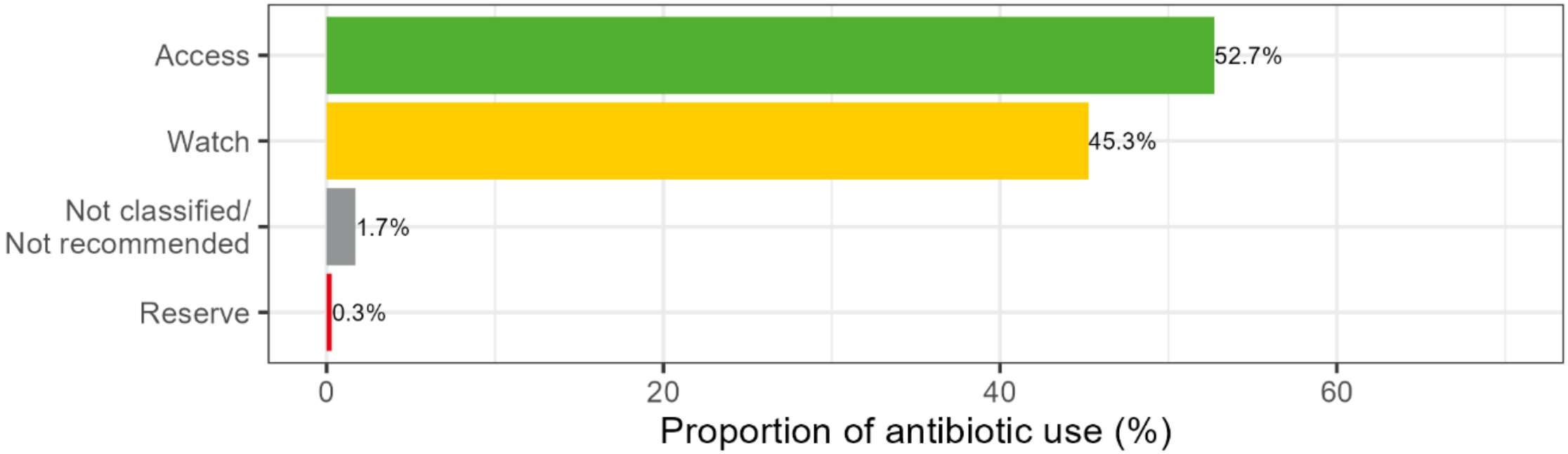
"To evaluate whether the (Watch) antibiotic use targets are realistic, we analysed data from patient surveys after visits
to (private and public) health centres and over-the-counter dispensing
in (private and public) medicine stores
… in Nanoro health district, **Burkina Faso**, and … in Kisantu healthzone, **DR Congo**, and estimated the **proportion of Watch antibiotic use that could be averted by applying the treatment guidelines in the WHO AWaRe Antibiotic Book**"

"Adhering to the AWaRe Antibiotic Book, 69% of Watch antibiotic use in Burkina Faso and 75% of Watch antibiotic use in DR Congo could be replaced by Access antibiotics or no antibiotic use, which **implies that the 90% Access target is theoretically attainable in both countries**."

"Ensure, by 2030, that the use of WHO Access group antibiotics is expanded from the 2023 global target, and in that regard, taking into account national contexts, aim to achieve at least 70 per cent overall human antibiotic use globally, through investing in and strengthening stewardship programmes"

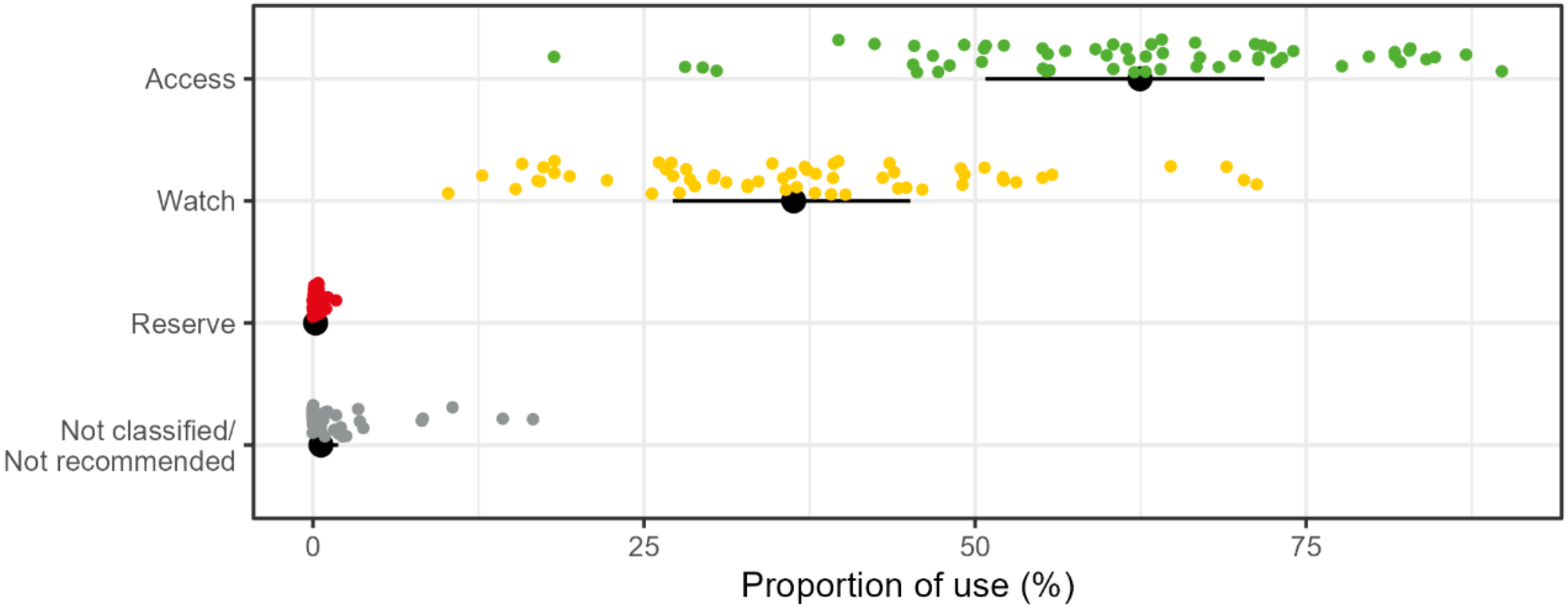
Political Declaration of the High-level Meeting on Antimicrobial Resistance (September 2024)

Proportion of the global volume of antibiotics reported by 60 countries, territories and areas in 2022 by WHO AWaRe classification



World Health Organization

Distribution of the proportional antibiotic use by AWaRe classification in 60 countries, territories and areas in 2022



Countries, territories and areas **meeting the GP 2023 60% Access target and the UNGA 2030 70% Access target by WHO Regions, World Bank income group classification and level of antibiotic use in 60 CTAs in 2022**

	CTAs	60% antibiotic use being Access	70% antibiotic use being Access
	n	n (%)	n (%)
Global	60	35 (58.3)	19 (31.7)
WHO Regions			
African	8	5 (62.5)	5 (62.5)
Eastern Mediterranean	9	4 (44.4)	1 (11.1)
European	32	18 (56.2)	9 (28.1)
Americas	3	3 (100)	1 (33.3)
South-East Asia	4	1 (25)	1 (25)
Western Pacific	4	4 (100)	2 (50)
Income level			
High	31	22 (71)	11 (35.5)
Upper middle	11	5 (45.5)	2 (18.2)
Lower middle	14	6 (42.9)	4 (28.6)
Low	4	2 (50)	2 (50)
Level of total antibiotic use			
Below 25th percentile	15	11 (66.7)	6 (40.0)
Between 25th - 75th percentile	30	20 (73.3)	11 (36.7)
Above 75th percentile	15	4 (26.7)	2 (13.3)

World Health Organization

Italy

GLASS-AMU Country, territory or area profiles

Antimicrobial use, for the period 2016 to 2022

Use of antibiotics by AWaRe classification, 2016-2022

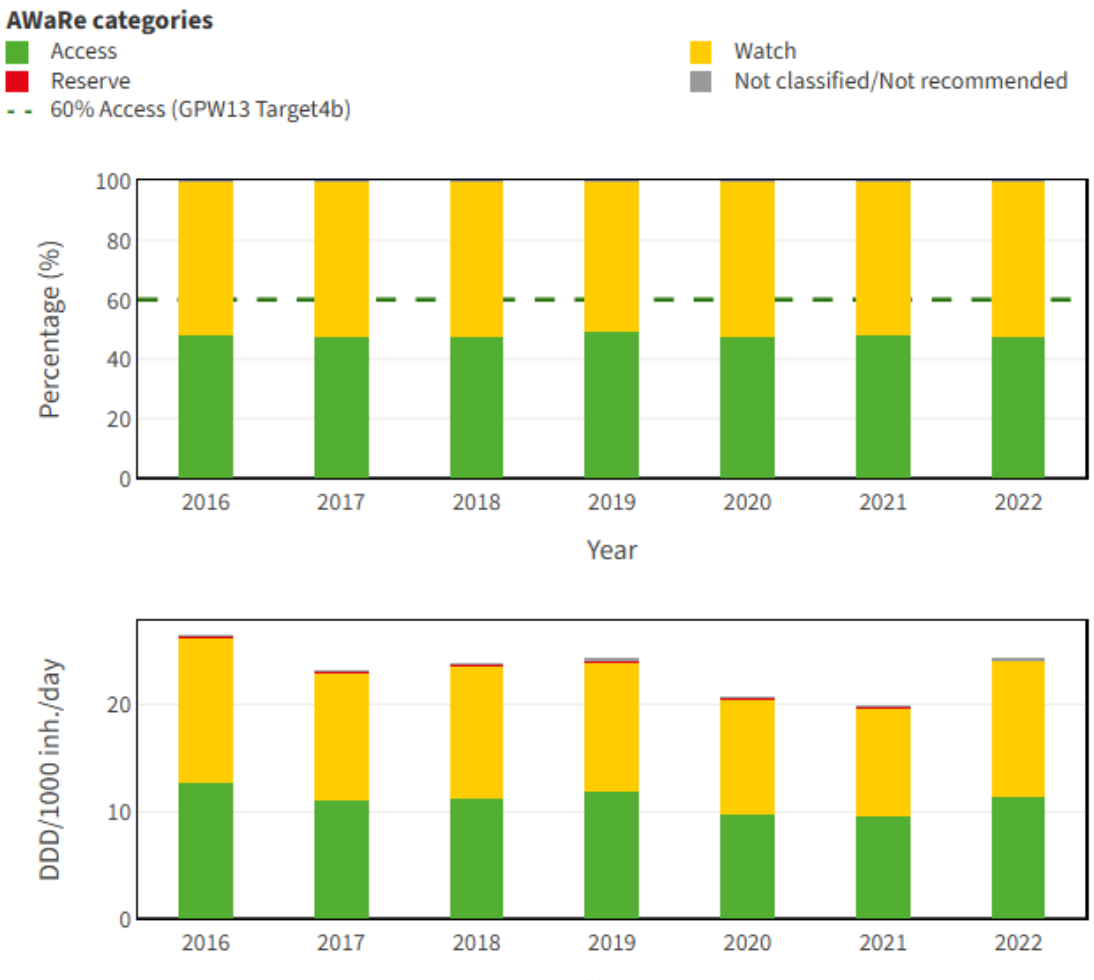
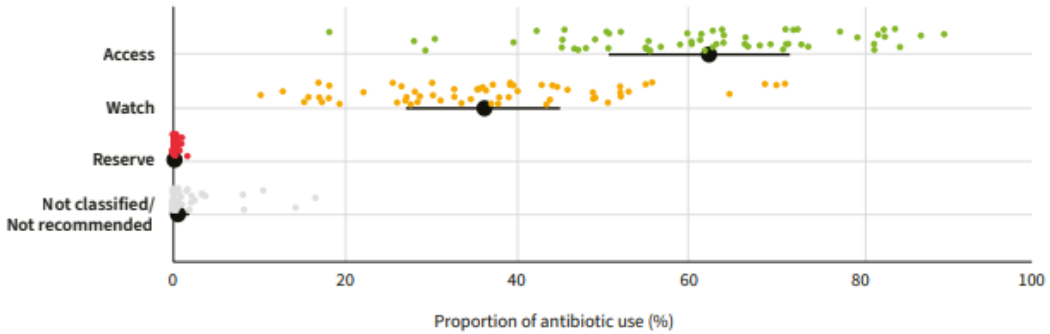
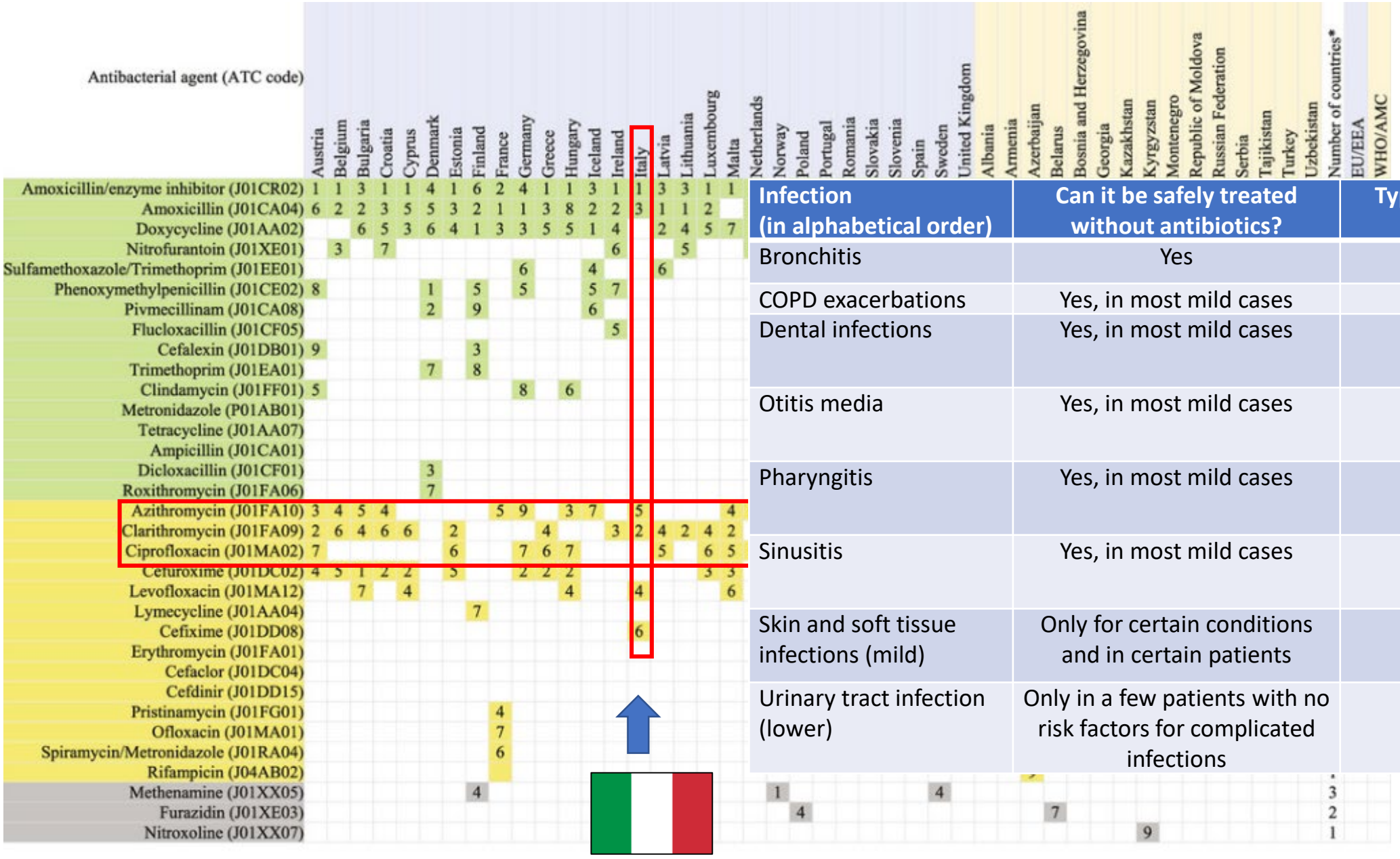


Fig. 6. Distribution of proportional antibiotic use by AWaRe classification in 60 CTAs in 2022

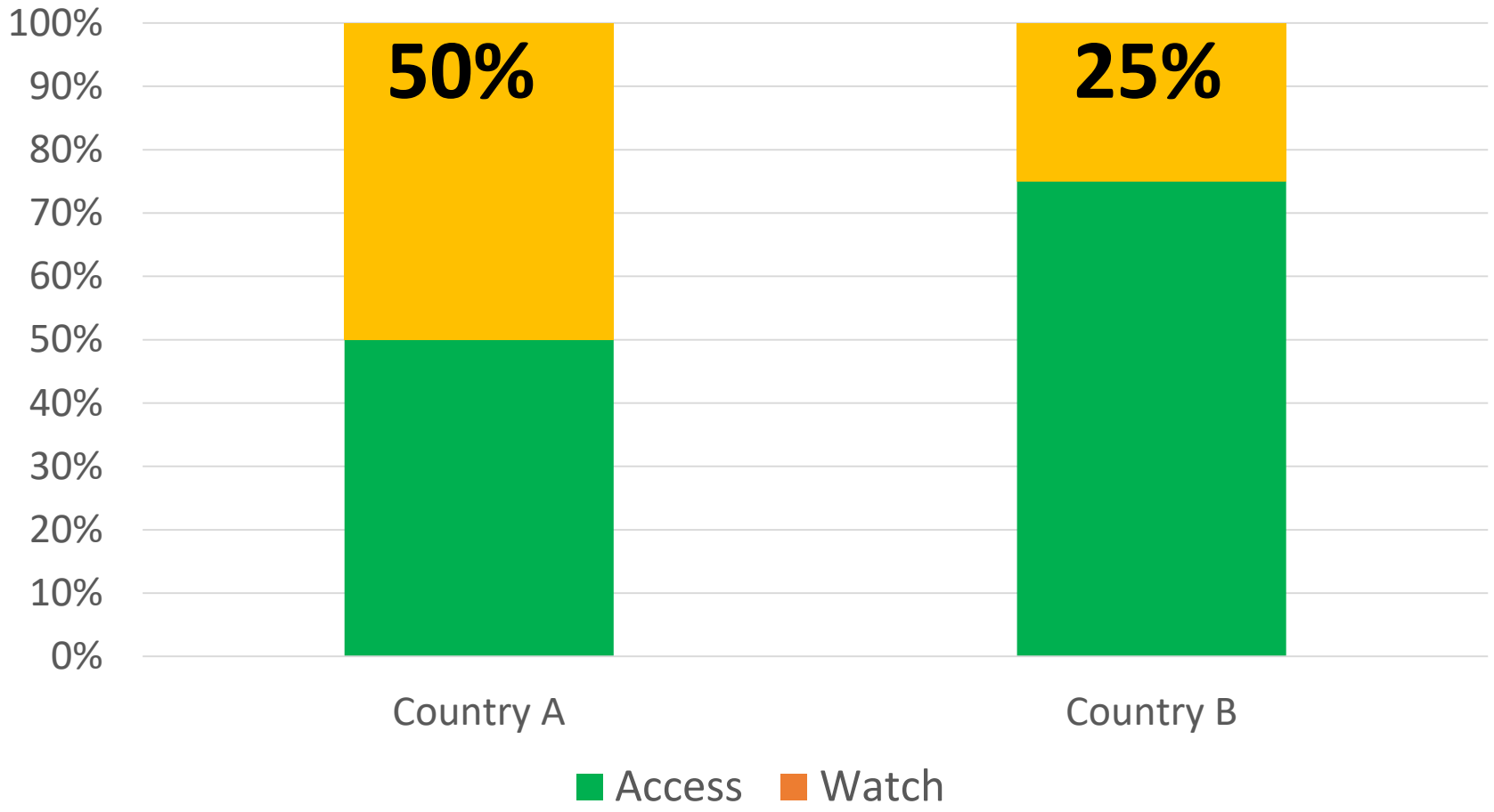




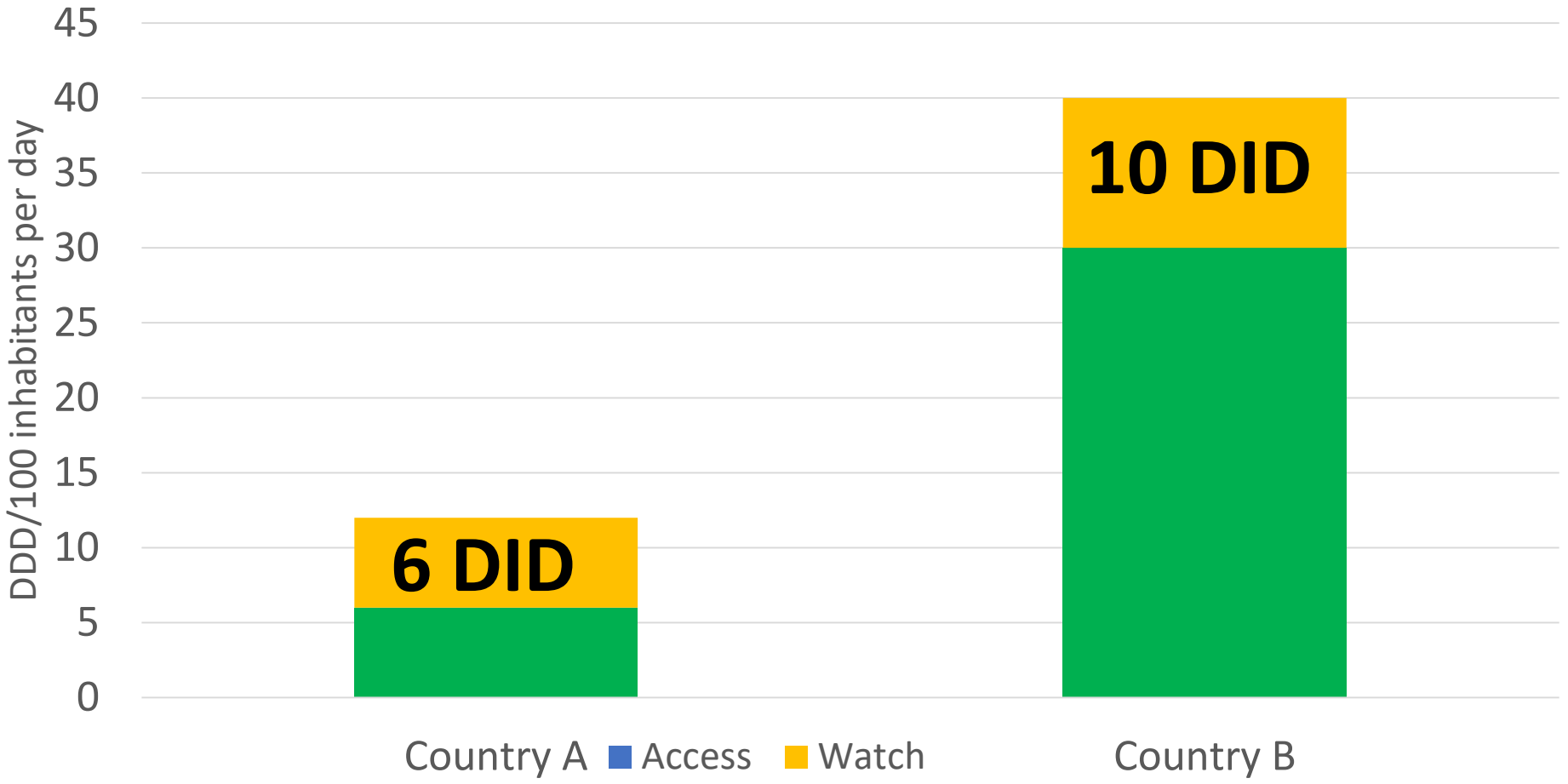
Infection (in alphabetical order)	Can it be safely treated without antibiotics?	Type of antibiotic (if indicated)
Bronchitis	Yes	
COPD exacerbations	Yes, in most mild cases	Access
Dental infections	Yes, in most mild cases	Access
Otitis media	Yes, in most mild cases	Access
Pharyngitis	Yes, in most mild cases	Access
Sinusitis	Yes, in most mild cases	Access
Skin and soft tissue infections (mild)	Only for certain conditions and in certain patients	Access
Urinary tract infection (lower)	Only in a few patients with no risk factors for complicated infections	Access

Robertson et al. Front Pharmacol. 2021 Jun 17;12:639207.

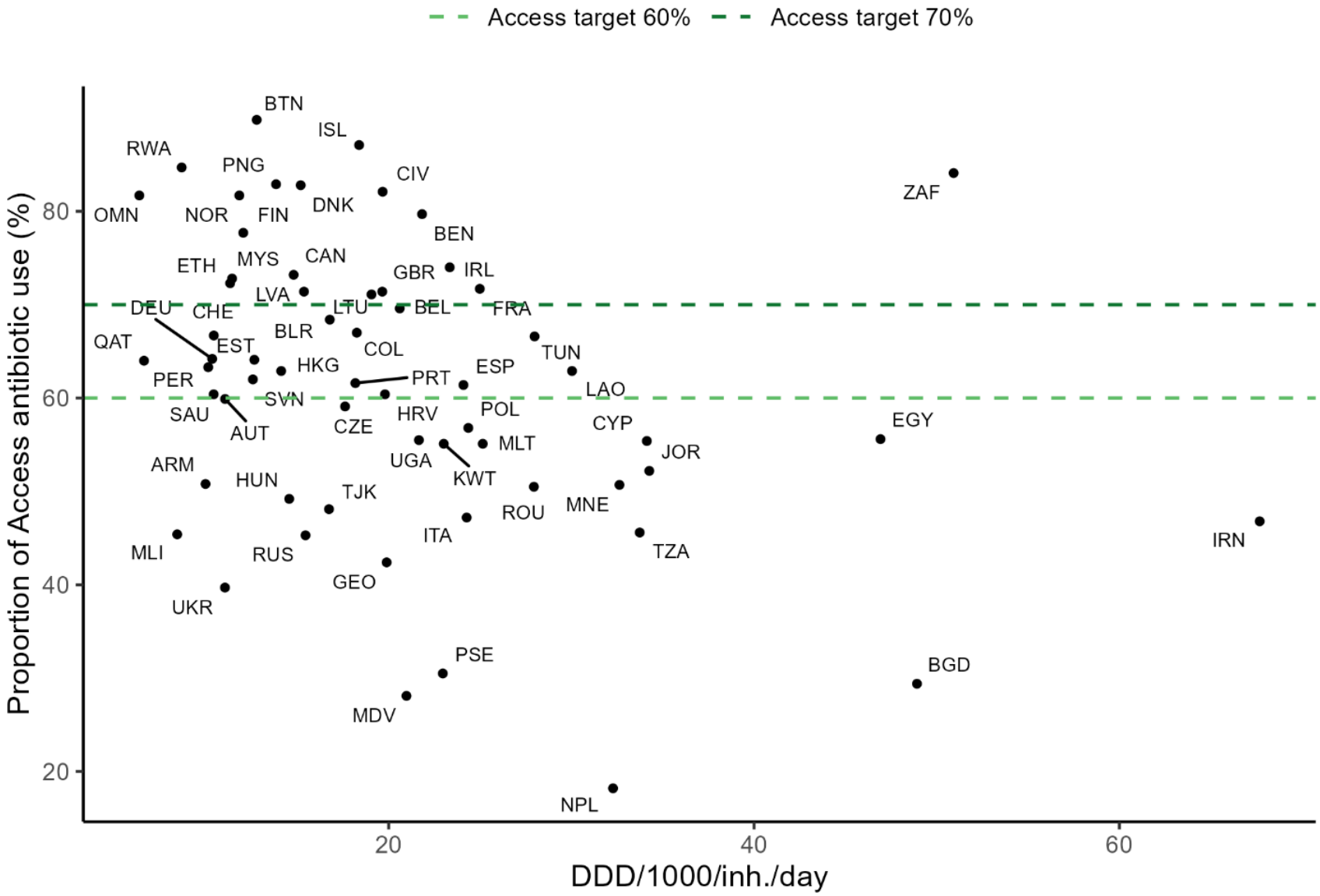
Which country uses antibiotics more appropriately ?



Overall use also needs to be considered



Relative use of Access antibiotic use compared to total use level expressed in DDD per 1000 inhabitants per day in 60 countries, territories and areas in 2022



AWaRe system

- The variation in antibiotic use among countries and the drivers of inappropriate use need to be better understood
- The AWaRe system provides evidence-based guidance on how to best use essential antibiotics
- The AWaRe antibiotic book can be used to develop or adapt national / local guidelines that are based on the AWaRe system
- The 70% Access target will need to be complemented by further indicators / targets to improve antibiotic use globally and control AMR

World Health Organization

Grazie mille!

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