Be AWaRe – using the new WHO antibiotic groupings for hospital antibiotic stewardship

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Project StAR-2, StAR National Antimicrobial Stewardship Programmes

SwissASP workshop & networking event Fri, 5th November 2021:

Antimicrobial stewardship in practice: Making the most of what you have.

What do you know about AWaRe

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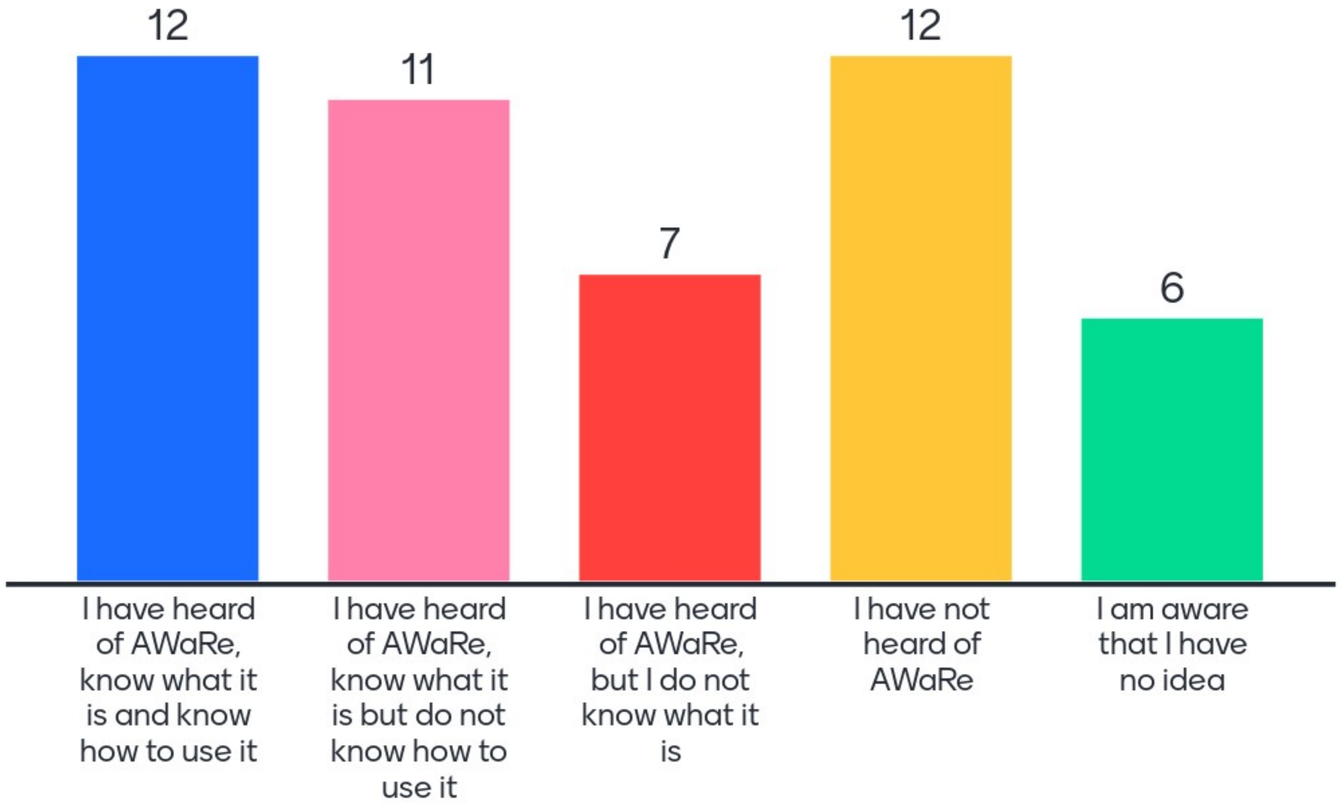

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This report contains the collective views of an International group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization

The selection of essential drugs

Report of a
WHO Expert Committee

World Health Organization
Technical Report Series
615

World Health Organization Geneva 1977

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.

1977

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

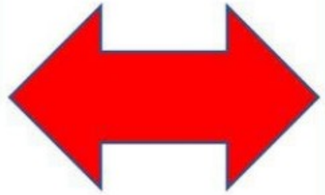
amikacin (1, 4, 10)
doxycycline (6, 5)
procaine benzylpenicillin (7)
sulfadiazine (7, 8)

Not all antibiotics are equal

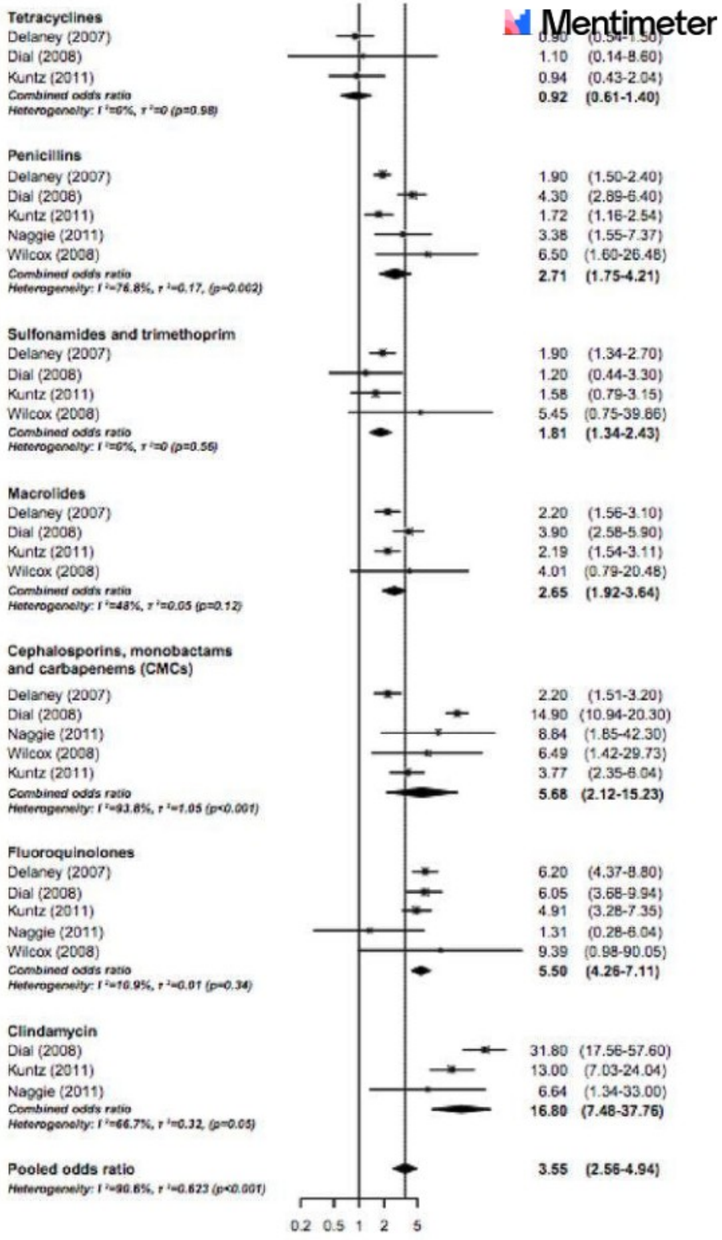
But how can this be communicated to effectively to the different stakeholders?

- Some antibiotics select more easily for antimicrobial resistance
  - E.g. fluoroquinolones, cephalosporins

1. Short-term benefits for the patient

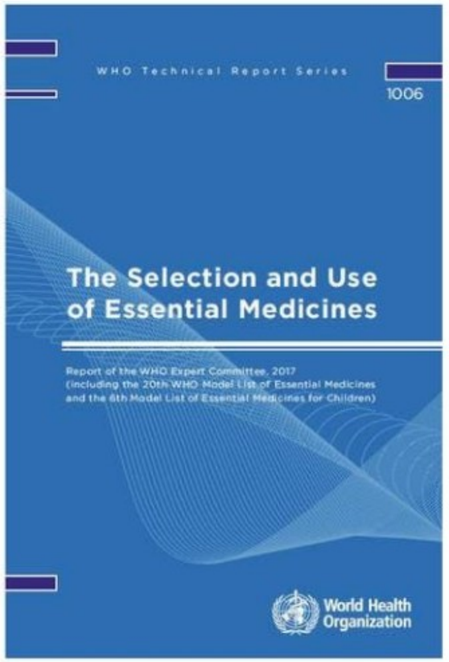


2. Adverse effects on the patient's commensal microbiota
3. Adverse effects on bacterial ecology through the selection of multi-resistant bacteria



Incidence of *C. difficile* infections according to antibiotic class

Brown et al. Antimicrob Agents Chemother. 2013 May;57(5):2326-32.



AWaRe: A new way of looking at antibiotic consumption

- 2017 revision of the WHO EML/c antibiotic list
  - reviews of antibiotic use for priority infection syndromes in adults and children
  - conducted by McMaster University, Canada, and groups within WHO

- **Goal:** defining **1st and 2nd choice antibiotics** for the priority infection syndromes prioritize these over and above other antibiotics
  - Narrower “spectrum”
  - Lesser chance of “driving resistance”

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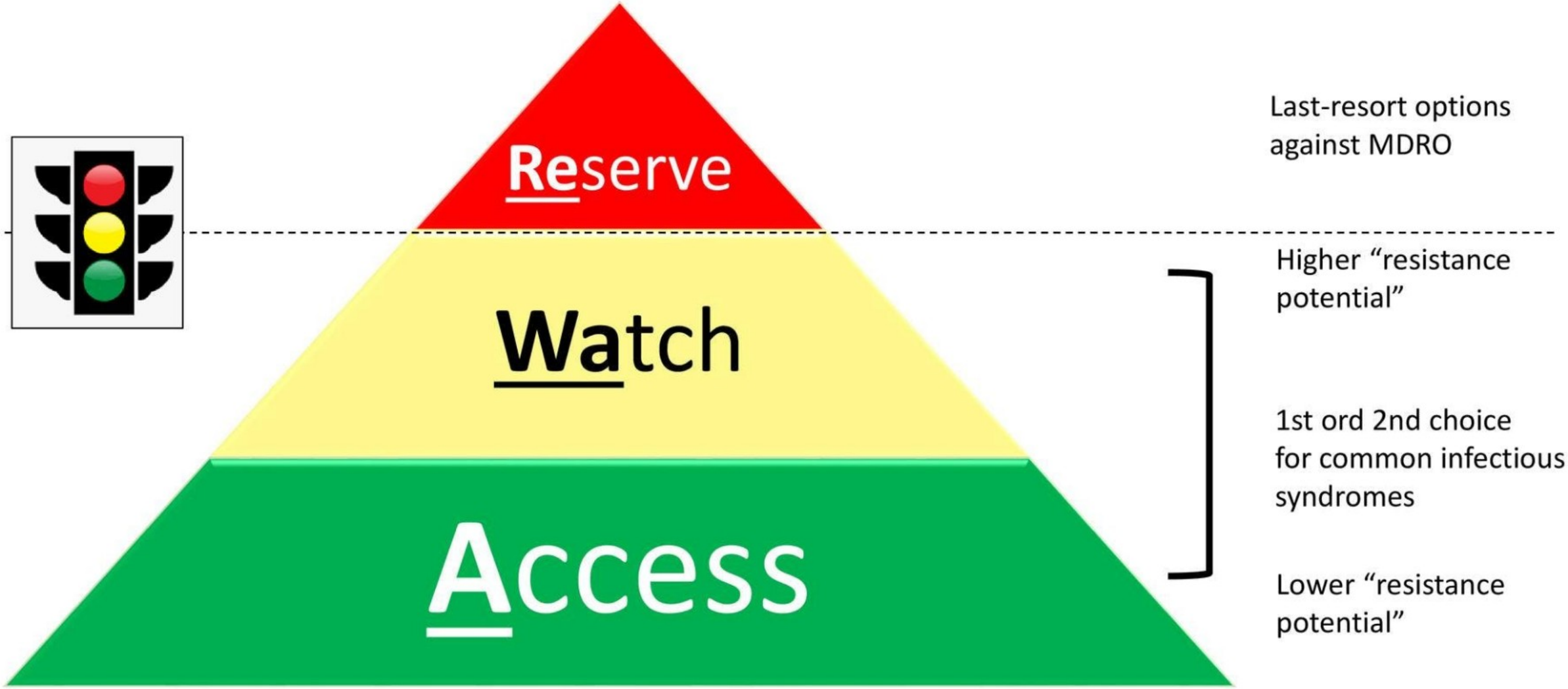
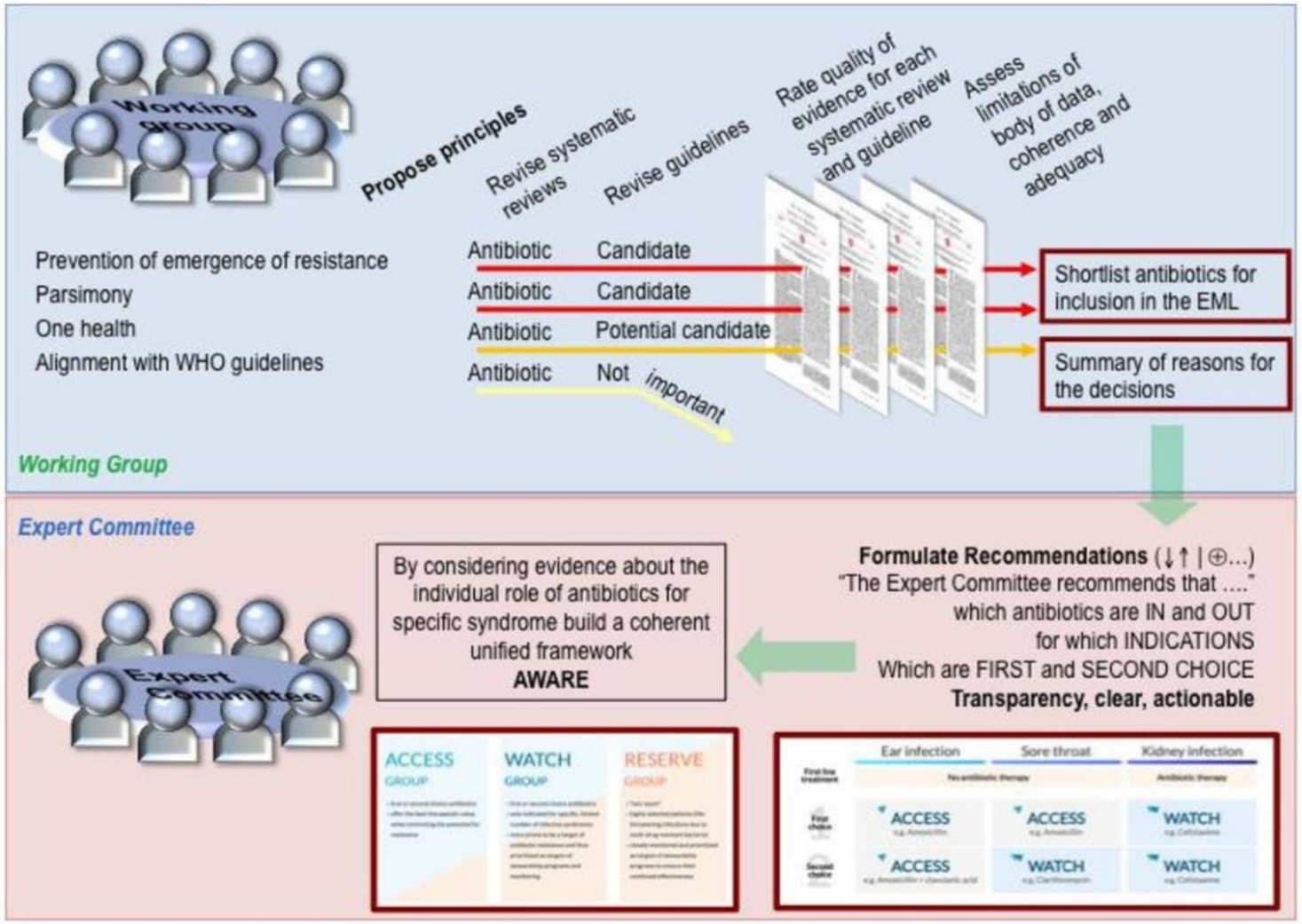
Antibiotics are categorized into three groups



EML: interactions working group and expert committee



List of participants 2021

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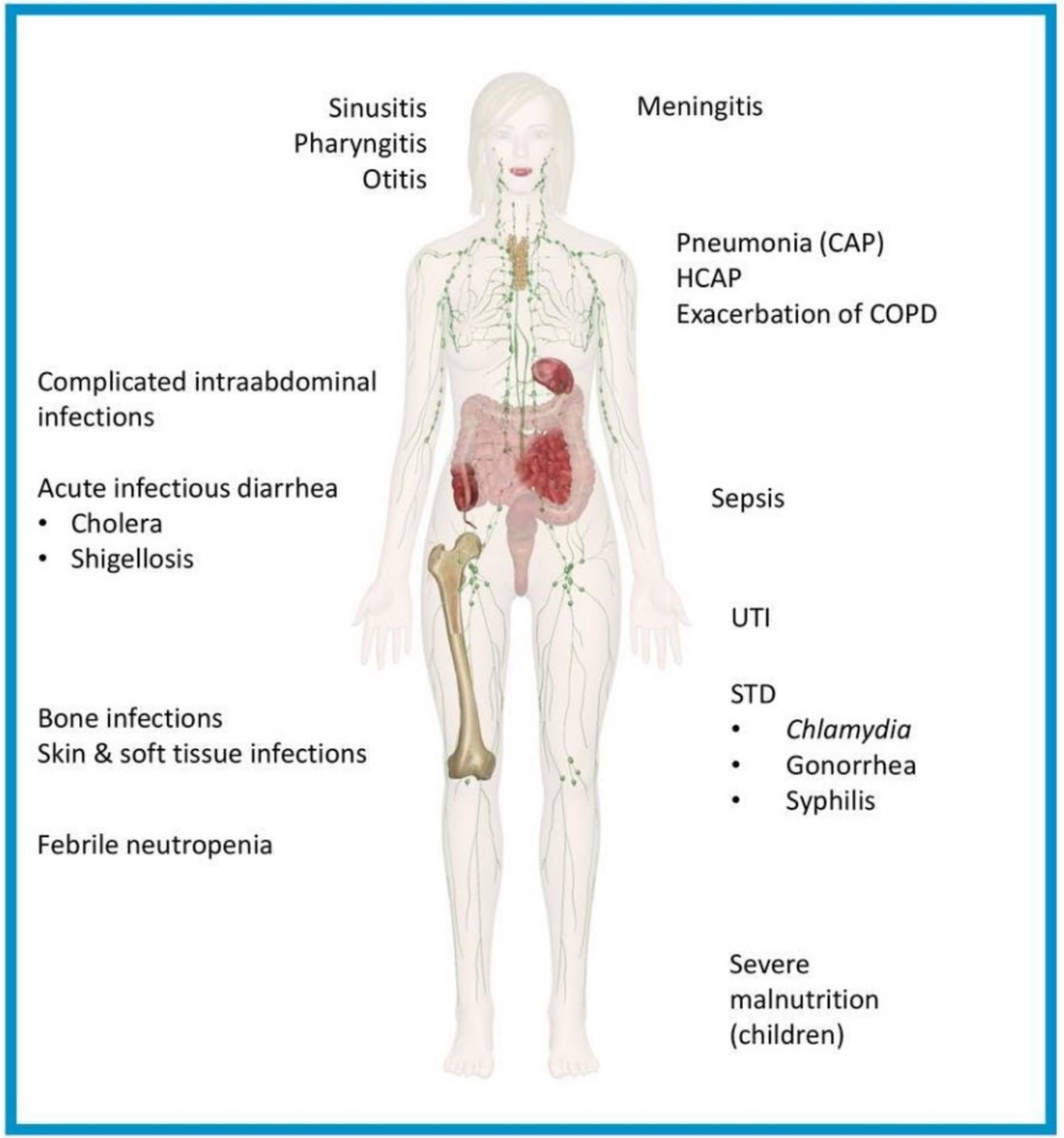

Review of syndromes

EML 2017 / 2019

- Frequent syndromes
- Certain infections by specific pathogens (syphilis, cholera, gonorrhea, shigellosis,…)
- «syndromes» / indications reviewed 2019
  - Antibiotic prophylaxis
  - Dental infections
  - Typhoid fever
- Review of systematic reviews

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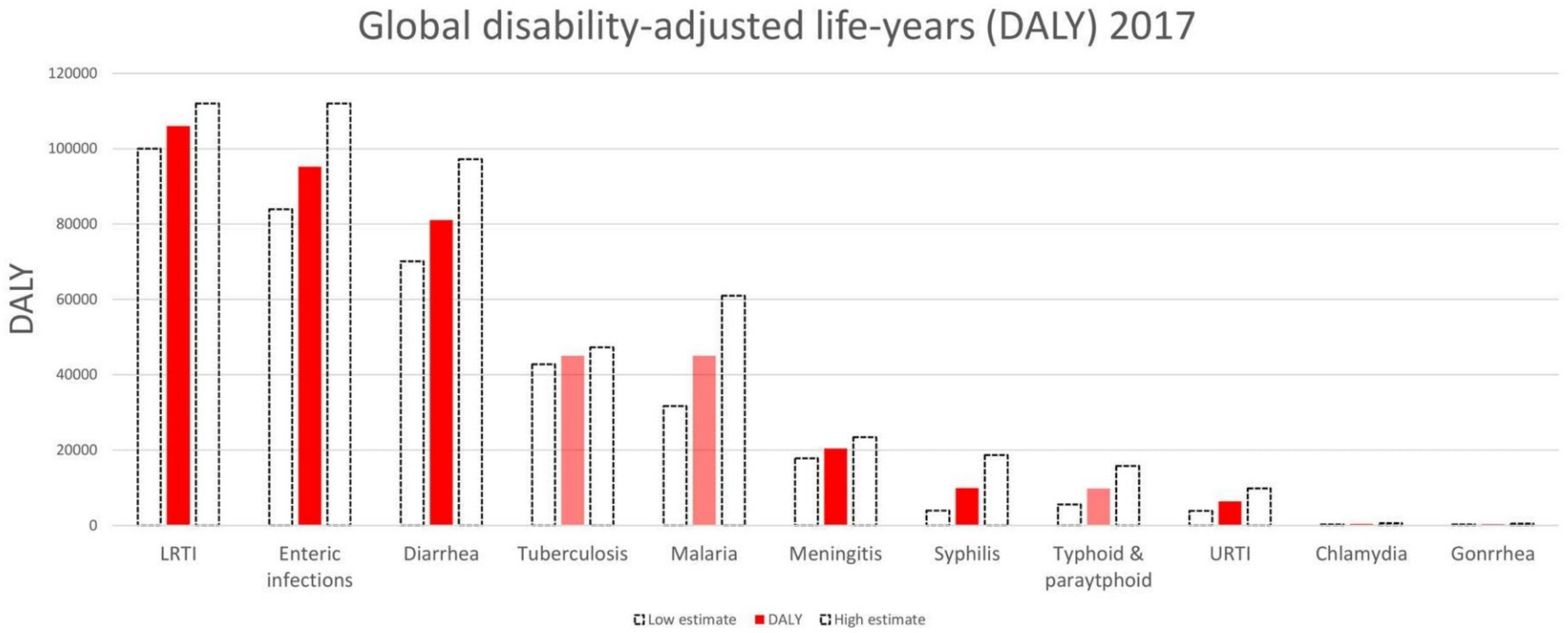
Global burden of infectious diseases



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First and second choice antibiotics (EML 2017)

1st criterion: efficacy

1st choice antibiotics

- Narrower spectrum
- Low potential to induce / select antimicrobial resistance
- Positive risk-benefit ratio

2nd choice antibiotics

- Broader spectrum
- Greater potential to induce / select antimicrobial resistance
- Less positive risk-benefit ratio

Example community-acquired pneumonia

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Example community-acquired pneumonia

- 21 systematic reviews and 8 clinical practice recommendations reviewed
  - 9 systematic reviews and 2 guidelines met the eligibility criteria

- Results of the review of systematic reviews and clinical practice recommendations
  - No significant advantage of one class of antibiotics over another (wide confidence intervals)
  - Fewer adverse events with clarithromycin compared to erythromycin
  - More adverse events with azithromycin compared to levofloxacin (OR 1.78, 95% CI: 1.04 to 3.03) => azithromycin not included
  - No additional benefit from atypical coverage in patients with mild to moderate CAP

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Example community-acquired pneumonia

Working group considerations

- Amoxicillin (or phenoxymethylpenicillin) first choice for mild to moderate CAP
- Non-inferiority of beta-lactams in a RCT
- Lack of evidence for better efficacy of one class compared to another in systematic reviews
- Relatively low resistance potential of narrow-spectrum beta-lactams compared to macrolides and fluoroquinolones
- Selection of amoxicillin as the first choice in some guidelines
- Amoxicillin / clavulanic acid and 2nd choice doxycycline

Expert committee decisions

Community acquired pneumonia	
First choice	**Second choice**
Mild to moderate CAP	
Amoxicillin	Amoxicillin+clavulanic acid
Phenoxymethylpenicillin	Doxycycline
Severe CAP	
Ceftriaxone or Cefotaxime + Clarithromycin	Amoxicillin+clavulanic + Clarithromycin
Antibiotics initially proposed by the Working Group but rejected	
Piperacillin-tazobactam[1] Ceftazidime[2] Levofloxacin[3] Gentamicin (children)[4]	Vancomycin[5]

Initial WHO AWaRe Classification (2017)

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

Core access antibiotics

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

* Antibiotics that are also in the Watch group

Watch
Anti-pseudomonal penicillins with beta-lactamase inhibitor (eg, piperacillin and tazobactam)
Carbapenems or penems (eg, faropenem, imipenem and cilastatin, meropenem)
Cephalosporins, third generation (with or without beta-lactamase inhibitor; eg, cefixime, cefotaxime, ceftazidime, ceftriaxone)
Glycopeptides (eg, teicoplanin, vancomycin)
Macrolides (eg, azithromycin, clarithromycin, erythromycin)
Quinolones and fluoroquinolones (eg, ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin)

Reserve
Aztreonam
Cephalosporins, fourth generation (eg, cefepime)
Cephalosporins, fifth generation (eg, ceftaroline)
Daptomycin
Fosfomycin (intravenous)
Oxazolidinones (eg, linezolid)
Polymyxins (eg, colistin, polymyxin B)
Tigecycline

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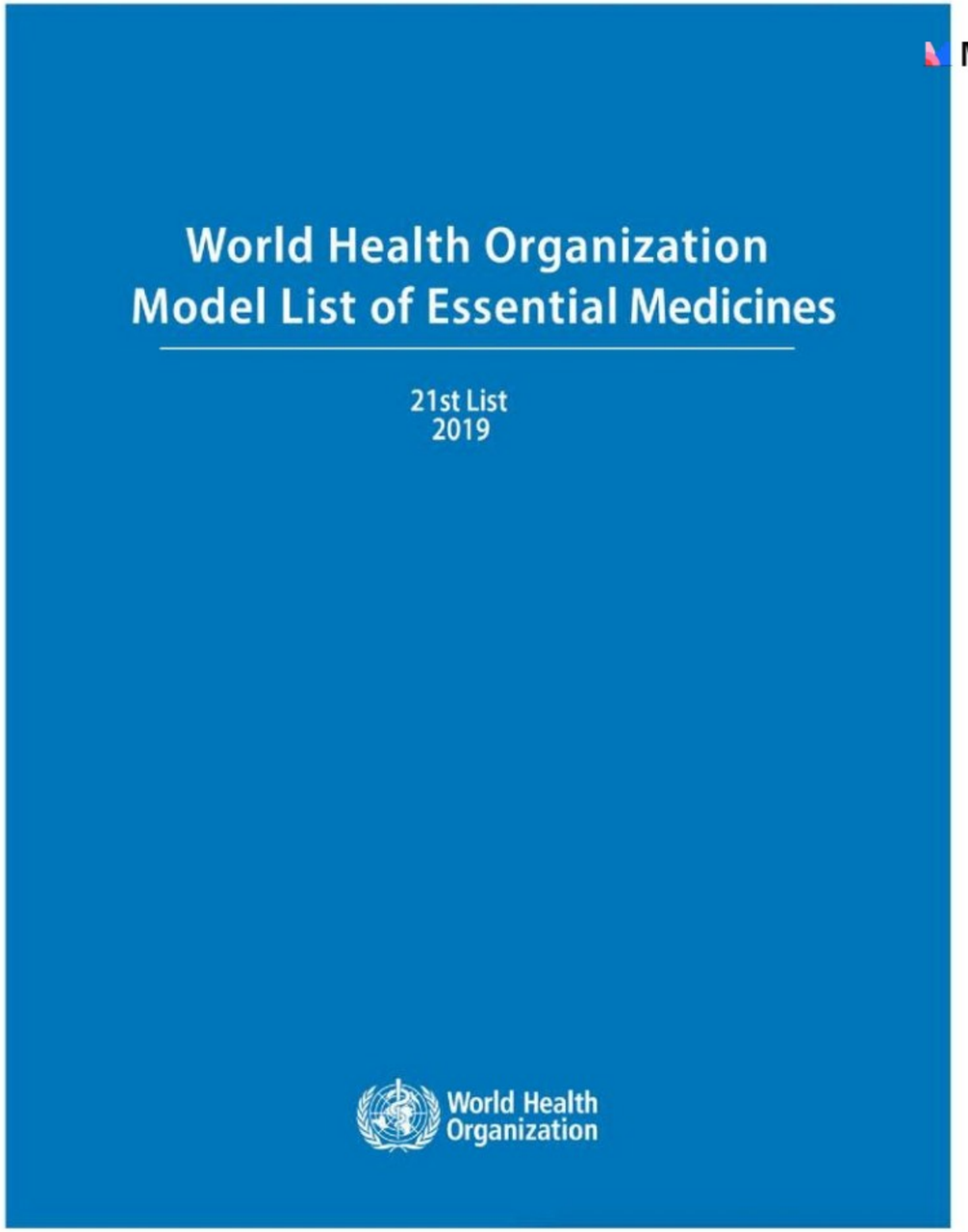
A 2nd revision took place in 2019, further refining (and simplifying) the list and groupings of antibiotics



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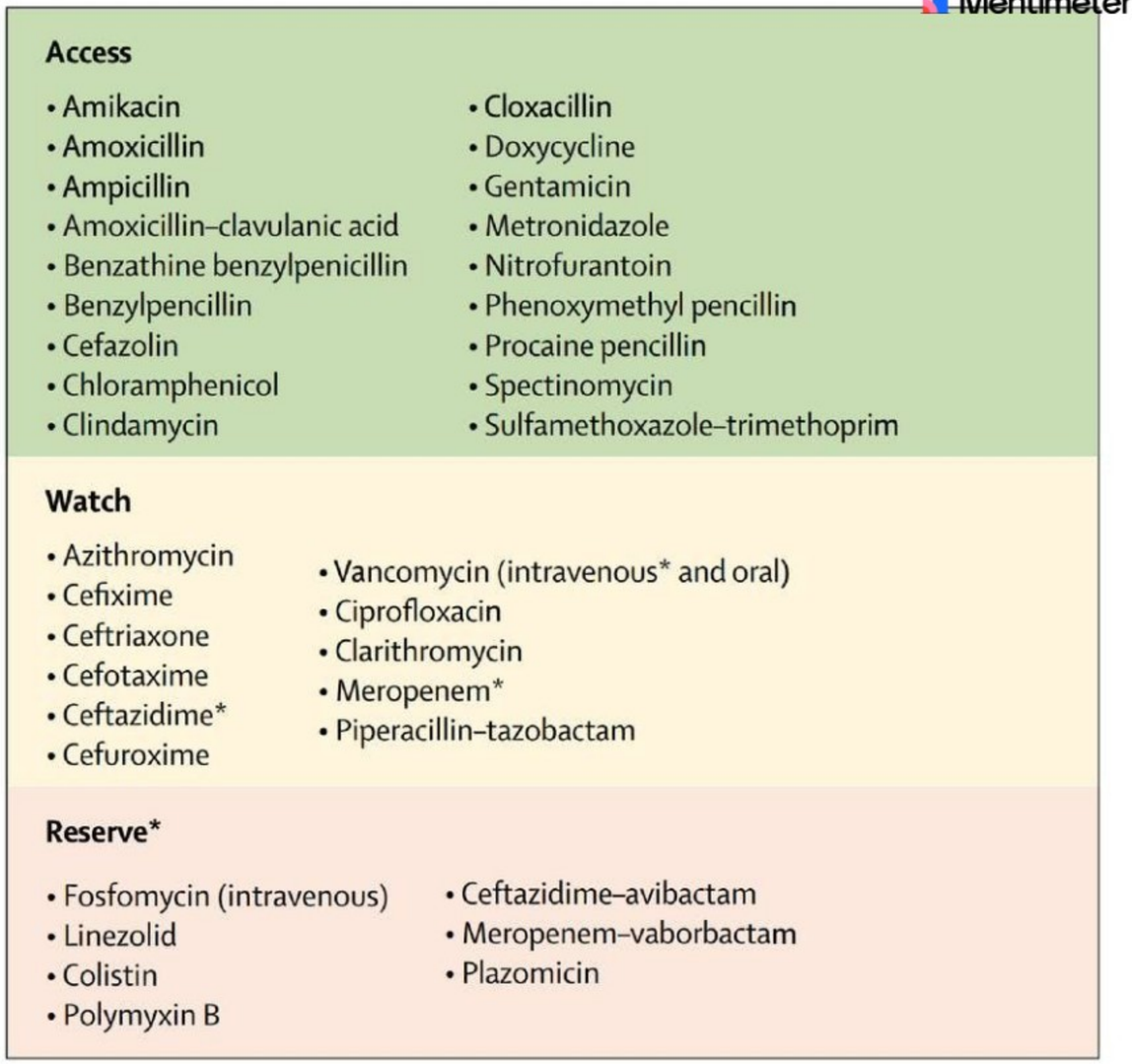
WHO AWaRe Classification (2019)

- Separation of AWaRe from the EML
- Listing of specific molecules (not classes)
- Classification of most antibiotics classified as “Other” before
- Introduction of a “not recommended” group (e.g. antibiotic combinations without clear indication)
- A further few minor changes in 2021
  - Cefiderocol added as Reserve antibiotic on EML



Access

- Amikacin
- Amoxicillin
- Ampicillin
- Amoxicillin–clavulanic acid
- Benzathine benzylpenicillin
- Benzylpencillin
- Cefazolin
- Chloramphenicol
- Clindamycin
- Cloxacillin
- Doxycycline
- Gentamicin
- Metronidazole
- Nitrofurantoin
- Phenoxymethyl pencillin
- Procaine pencillin
- Spectinomycin
- Sulfamethoxazole–trimethoprim

Watch

- Azithromycin
- Cefixime
- Ceftriaxone
- Cefotaxime
- Ceftazidime*
- Cefuroxime
- Vancomycin (intravenous* and oral)
- Ciprofloxacin
- Clarithromycin
- Meropenem*
- Piperacillin–tazobactam

Reserve*

- Fosfomycin (intravenous)
- Linezolid
- Colistin
- Polymyxin B
- Ceftazidime–avibactam
- Meropenem–vaborbactam
- Plazomicin

***Figure:* Antibiotics included in 2019 WHO Essential Medicines List by AWaRe group**

*Antibiotics listed in the complementary list of the 2019 WHO Essential Medicines List, indicating the need for specialist supervision.

Sharland et al. Lancet Infect Dis 2019 (accepted for publication)

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WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2021

To assist in the development of tools for antibiotic stewardship at local, national and global levels and to reduce antimicrobial resistance, the Access, Watch, Reserve (AWaRe) classification of antibiotics was developed – where antibiotics are classified into different groups to emphasize the importance of their appropriate use.
This classification is intended to be used as a tool for countries to better support antibiotic monitoring and stewardship activities. It is not intended as model for the inclusion of antibiotics on national essential medicine lists. Antibiotics classified under AWaRe and also included on the WHO Model Lists of Essential Medicines are indicated in the worksheets.

Antibiotic	Class	ATC code	Category	Listed on EML/EMLc 2021
Amikacin	Aminoglycosides	J01GB06	Access	Yes
Amoxicillin	Penicillins	J01CA04	Access	Yes
Amoxicillin/clavulanic-acid	Beta-lactam/beta-lactamase-inhibitor	J01CR02	Access	Yes
Ampicillin	Penicillins	J01CA01	Access	Yes
Ampicillin/sulbactam	Beta-lactam/beta-lactamase-inhibitor	J01CR01	Access	No
Arbekacin	Aminoglycosides	J01GB12	Watch	No
Aspoxicillin	Penicillins	J01CA19	Watch	No
Azidocillin	Penicillins	J01CE04	Access	No
Azithromycin	Macrolides	J01FA10	Watch	Yes
Azlocillin	Penicillins	J01CA09	Watch	No
Aztreonam	Monobactams	J01DF01	Reserve	No
Bacampicillin	Penicillins	J01CA06	Access	No
Bekanamycin	Aminoglycosides	J01GB13	Watch	No
Benzathine-benzylpenicillin	Penicillins	J01CE08	Access	Yes
Benzylpenicillin	Penicillins	J01CE01	Access	Yes
Biapenem	Carbapenems	J01DH05	Watch	No
Brodimoprim	Trimethoprim-derivatives	J01EA02	Access	No
Carbenicillin	Penicillins	J01CA03	Watch	No
Carindacillin	Penicillins	J01CA05	Watch	No
Carumonam	Monobactams	J01DF02	Reserve	No
Cefacetrile	First-generation-cephalosporins	J01DB10	Access	No
Cefaclor	Second-generation-cephalosporins	J01DC04	Watch	No
Cefadroxil	First-generation-cephalosporins	J01DB05	Access	No
Cefalexin	First-generation-cephalosporins	J01DB01	Access	Yes
Cefaloridine	First-generation-cephalosporins	J01DB02	Access	No
Cefalotin	First-generation-cephalosporins	J01DB03	Access	No
Cefamandole	Second-generation-cephalosporins	J01DC03	Watch	No
Cefapirin	First-generation-cephalosporins	J01DB08	Access	No

Copyright & Disclaimers | AWaRe classification 2021 | Access | Watch | Reserve | Not recommended | 22nd EML 2021 | 8th EMLc 2021

https://www.who.int/publications/i/item/2021-aware-classification

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ACCESS GROUP

- first or second choice antibiotics
- offer the best therapeutic value, while minimizing the potential for resistance

WATCH GROUP

- first or second choice antibiotics
- only indicated for specific, limited number of infective syndromes
- more prone to be a target of antibiotic resistance and thus prioritized as targets of stewardship programs and monitoring

RESERVE GROUP

- "last resort"
- highly selected patients (life-threatening infections due to multi-drug resistant bacteria)
- closely monitored and prioritized as targets of stewardship programs to ensure their continued effectiveness

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EML Access group antibiotics

- Core set of **20 antibiotics**
  - 1st or 2nd line choice for ***empirical*** treatment of the priority clinical infection syndromes
- Generally characterized by **narrow-spectrum** (with limited risk of resistance) and/or low toxicity
- Prioritized for use over Watch and Reserve antibiotics
- Should be available everywhere
  - at an appropriate quantity, dose, and formulation

ACCESS on the 2021 EML

Amikacin
Amoxicillin
Amoxicillin/clavulanic-acid
Ampicillin
Benzathine-benzylpenicillin
Benzylpenicillin
Cefalexin
Cefazolin
Chloramphenicol
Clindamycin
Cloxacillin
Doxycycline
Gentamicin
Metronidazole
Nitrofurantoin
Phenoxymethylpenicillin
Procaine-benzylpenicillin
Spectinomycin
Sulfamethoxazole/trimethoprim
Trimethoprim

Slide courtesy of Nicola Magrini

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EML Watch group antibiotics

- Recommended only for a limited number of specific syndromes – 11 antibiotics
- AB classes that have a **higher potential to drive bacterial resistance**
  - e.g. fluoroquinolones and macrolides
- These antibiotics are also highest priority agents of CIA List
  - (critically important antimicrobials for human medicine)
- Active stewardship important for optimal (specific) uses
- Active monitoring of Watch antibiotics is encouraged
  - e.g., through point-prevalence surveys as a stewardship tool

WATCH on the 2021 EML

Azithromycin

Cefixime

Cefotaxime

Ceftazidime

Ceftriaxone

Cefuroxime

Ciprofloxacin

Clarithromycin (or Erythromycin)

Meropenem (or Imipenem)

Piperacillin + tazobactam

Vancomycin (IV & PO)

Slide courtesy of Nicola Magrini

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EML Reserve group antibiotics

- **Currently 8 "last-resort" antibiotics on EML**
  - proven activity against critical and high priority pathogens (according to WHO PPL)
- Restricted to use in specific patients and clinical settings
  - such as life-threatening infections with MDR- or XDR-resistant bacteria
  - when all Access or Watch group alternatives have failed or not suitable
- Key targets of high intensity national and international stewardship programs
- New antibiotics are likely (but not automatically) to be placed in this group

RESERVE on the 2021 EML

Cefiderocol
Ceftazidime/avibactam
Colistin (IV)
Fosfomycin (IV)
Linezolid
Meropenem/vaborbactam
Plazomicin
Polymyxin-B (IV)

Slide courtesy of Nicola Magrini

RESERVE group antibiotics (2021)

Listed on EML
Ceftazidime-avibactam
Colistin
Fosfomycin (IV)
Linezolid
Meropenem-vaborbactam
Plazomicin
Polymyxin B
Ceftazidime-avibactam
Cefiderocol

Not listed on EML
Aztreonam
Carumonam
Ceftaroline-fosamil
Ceftobiprole-medocaril
Ceftolozane/tazobactam
Colistin_oral
Dalbavancin
Dalfopristin/quinupristin
Daptomycin
Eravacycline
Faropenem
Iclaprim
Imipenem/cilastatin/relebactam
Lefamulin
Minocycline_IV
Omadacycline
Oritavancin
Polymyxin-B_oral
Tedizolid
Telavancin
Tigecycline

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RESERVE group antibiotics

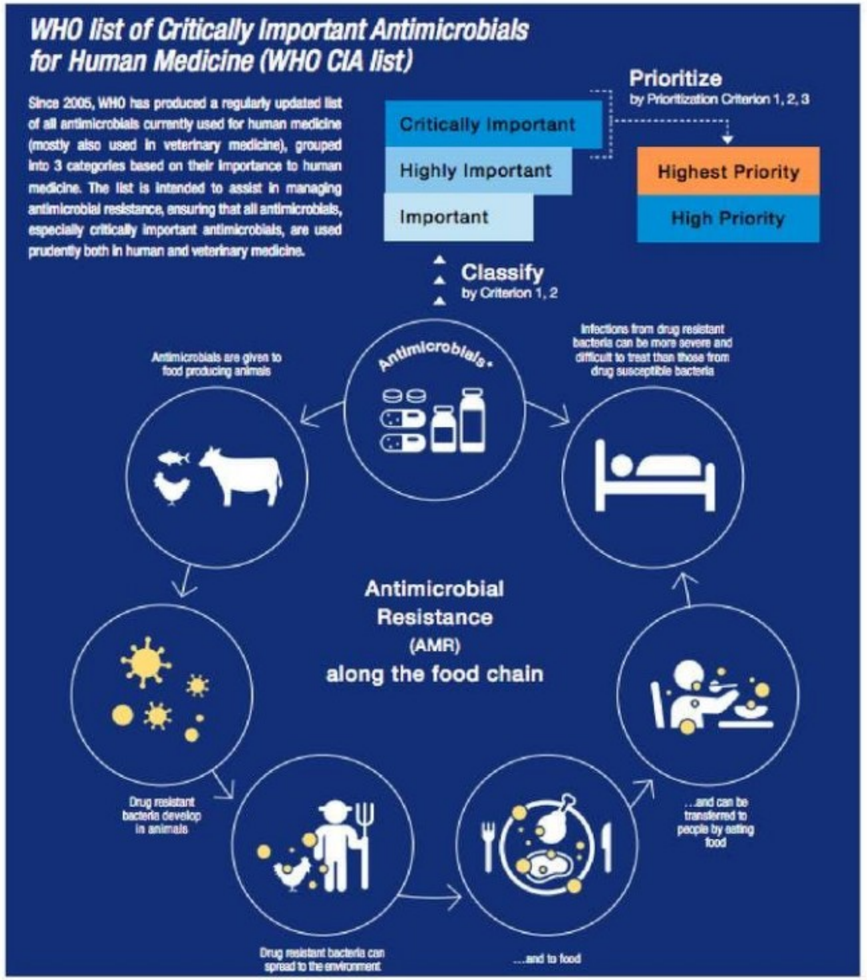
- **Never** listed as first or second-line antibiotic options for any of the 21 infectious syndromes reviewed during the update of the EML

- **BUT:**
  - only empirical treatment was considered for the choice of first or second-line options
  - some important nosocomial infections (such as ventilator associated pneumonia) were excluded from the review.
  - **Use of a RESERVE antibiotic (even empirically) may be appropriate in specific settings**

Overlap with critically important antibiotics

Critically Important

Antimicrobial class	Criterion (Yes = ●)				
CRITICALLY IMPORTANT ANTIMICROBIALS	C1	C2	P1	P2	P3
HIGHEST PRIORITY					
Highest Priority — *Cephalosporins (3rd, 4th and 5th generation)*	●	●	●	●	●
Highest Priority — *Glycopeptides*	●	●	●	●	●
Highest Priority — *Macrolides and ketolides*	●	●	●	●	●
Highest Priority — *Polymyxins*	●	●	●	●	●
Highest Priority — *Quinolones*	●	●	●	●	●
HIGH PRIORITY					
Aminoglycosides	●	●		●	●
Ansamycins	●	●	●	●	
Carbapenems and other penems	●	●	●	●	
Glycylcyclines	●	●	●		
Lipopeptides	●	●	●		
Monobactams	●	●	●		
Oxazolidinones	●	●	●		
Penicillins (natural, aminopenicillins, and antipseudomonal)	●	●		●	●
Phosphonic acid derivatives	●	●	●	●	
Drugs used solely to treat tuberculosis or other mycobacterial diseases	●	●	●	●	



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How to adopt AWaRE

AWaRe for monitoring antibiotic use

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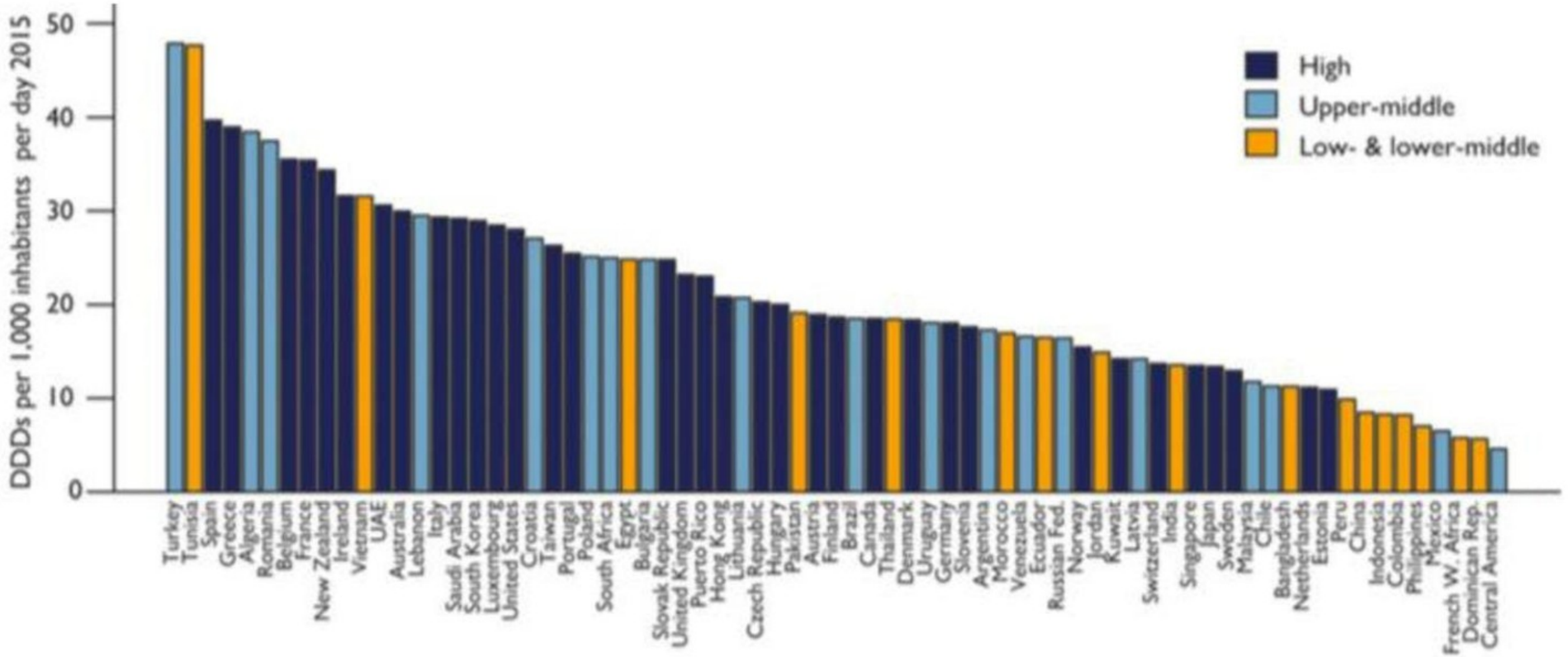
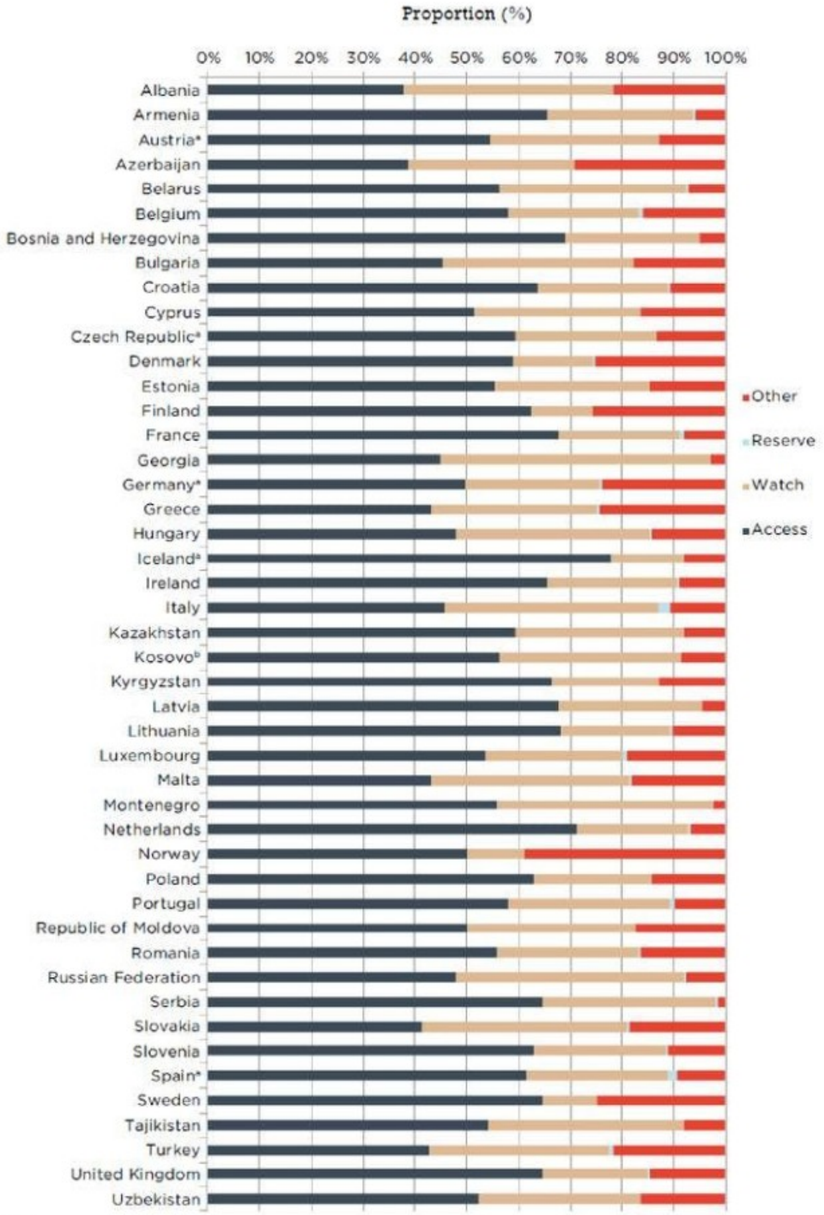
- AWaRe is a relatively “easy” tool that offers more than overall antibiotic use or more conventional classifications (such as broad- vs. narrow-spectrum antibiotics)



Klein et al. Proc Natl Acad Sci U S A. 2018 Mar 26. pii: 201717295.

Fig. 4.7 Proportional consumption (%) of antibiotics by AWaRe categorization in 45 countries and Kosovo[b] of the European Region (2015)



[a] Only community consumption reported.

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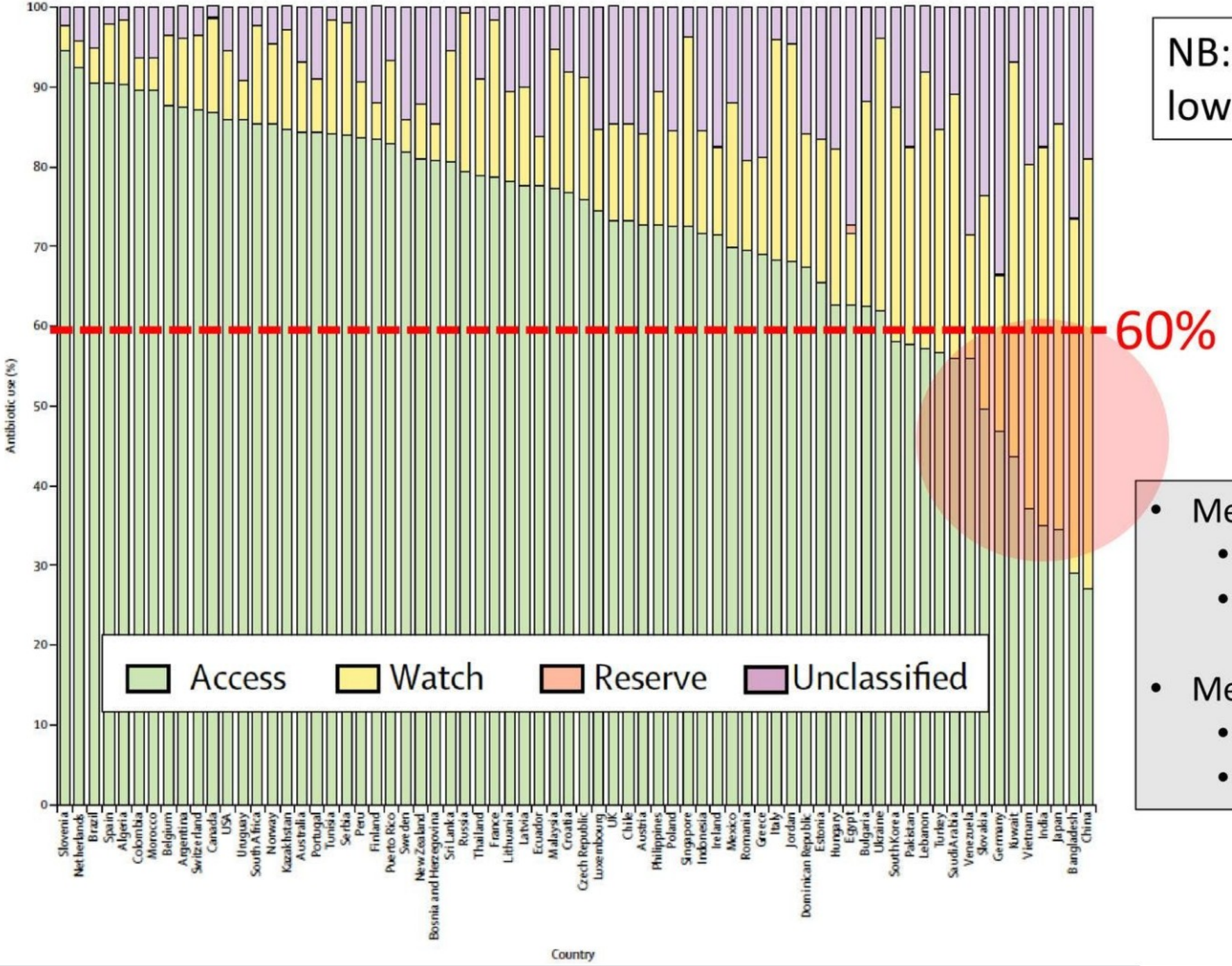
Measuring antibiotic use

Consumption of oral antibiotic formulations for young children according to the WHO Access, Watch, Reserve (AWaRe) antibiotic groups: an analysis of sales data from 70 middle-income and high-income countries

Yingfen Hsia, Mike Sharland, Charlotte Jackson, Ian C K Wong, Nicola Magrini, Julia A Bielicki

Analysis of 2015 wholesale antibiotic sales data from 70 middle-income and high-income countries (IQVIA-MIDAS database)



NB: No country-level data for low-income countries !

- Median **Access** group use 76·3%
  - Max 94·4% Slovenia
  - Min 27·0% China
- Median **Watch** group use 12·3%
  - Max China 54·0%
  - Min Slovenia 3·3%

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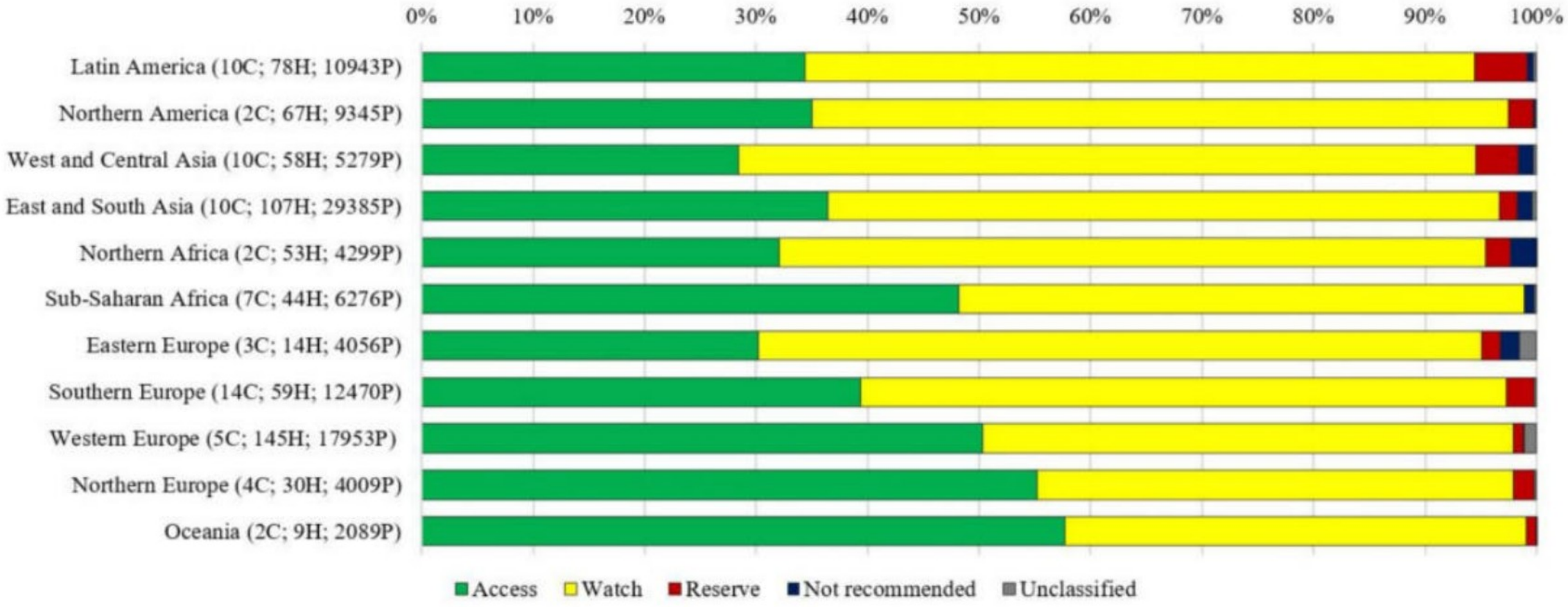

Hospital antibiotic prescribing patterns - PPS (Pauwels et al. JAC 2021)

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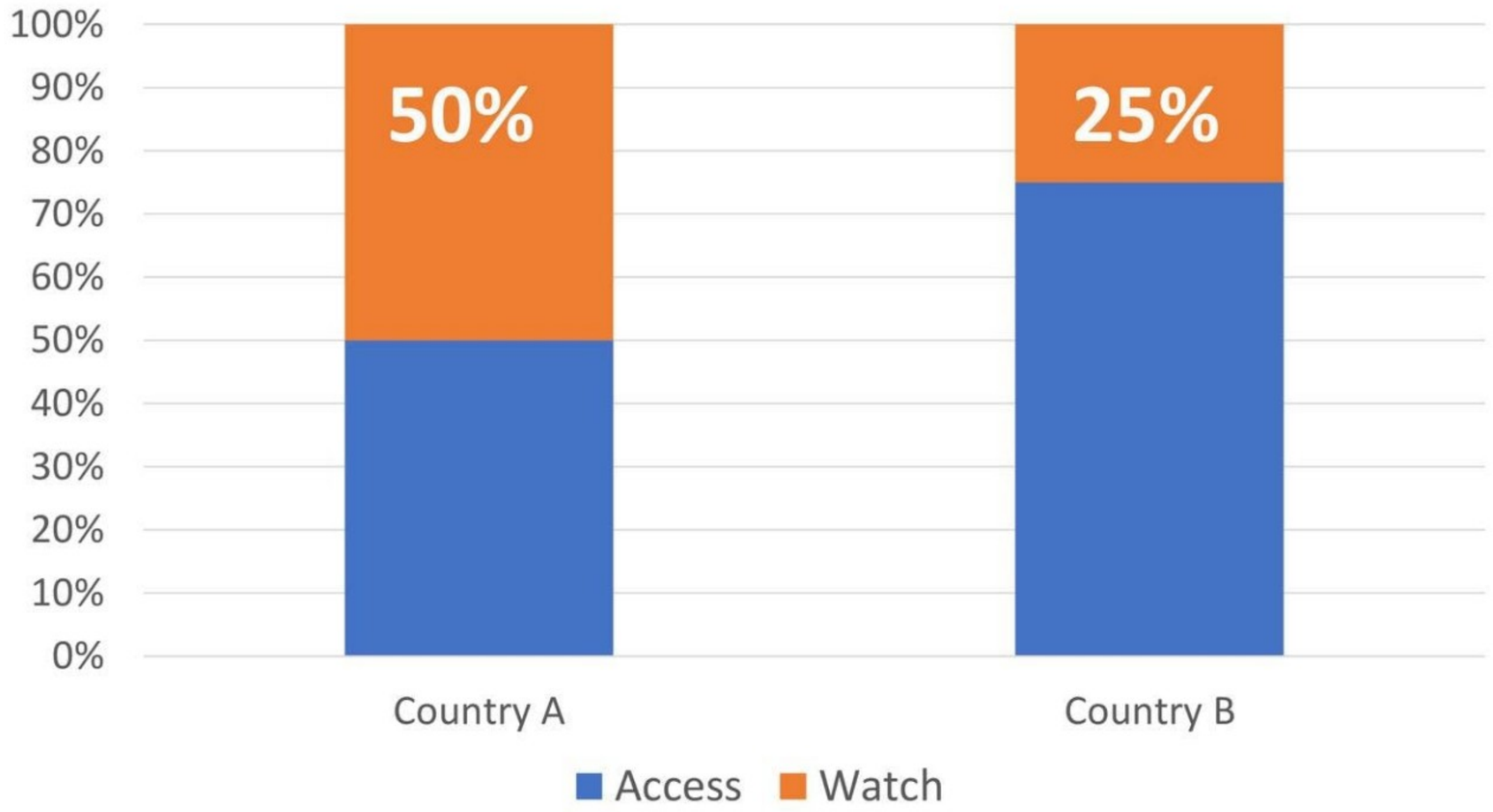
Relative use



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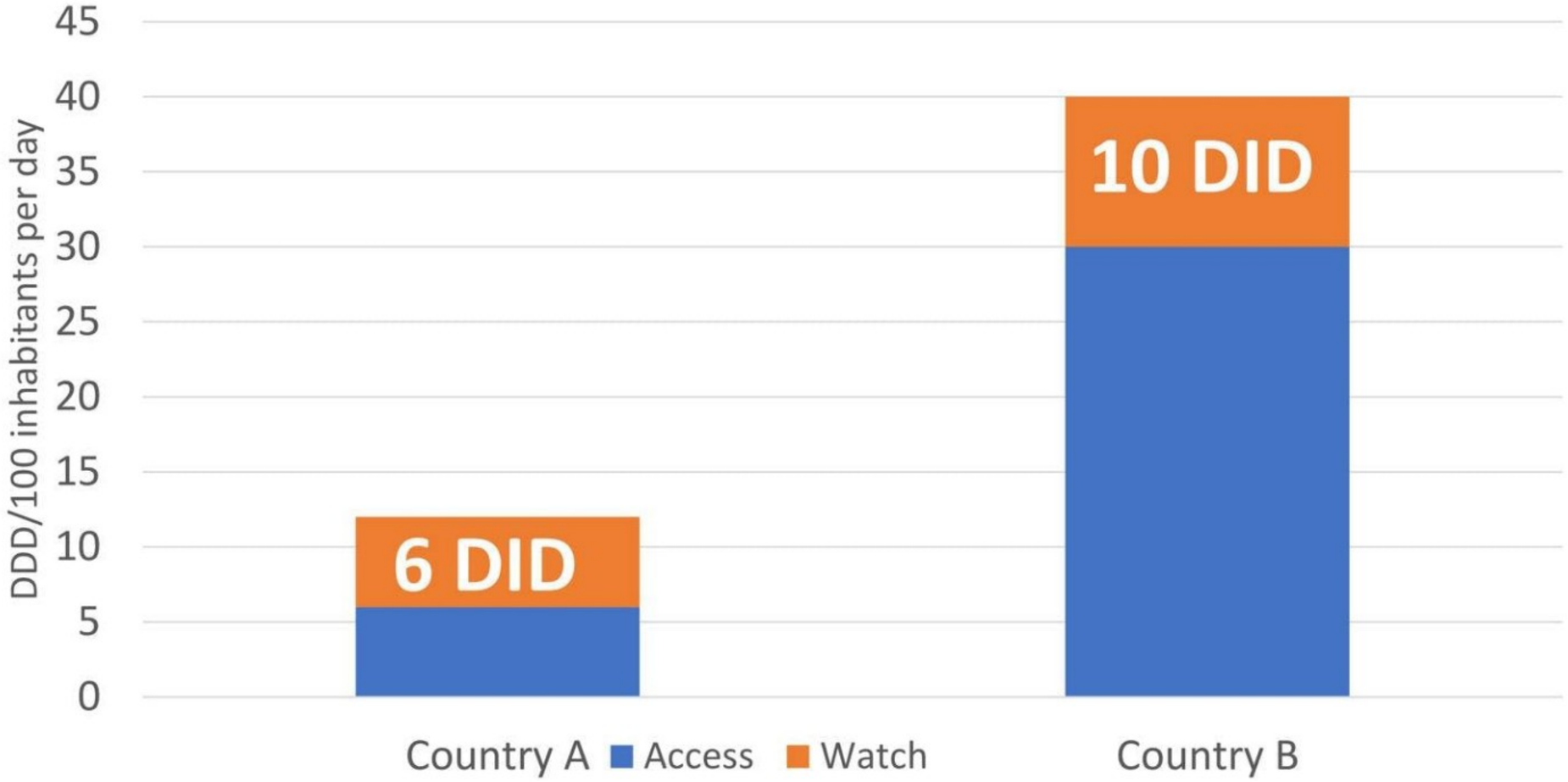
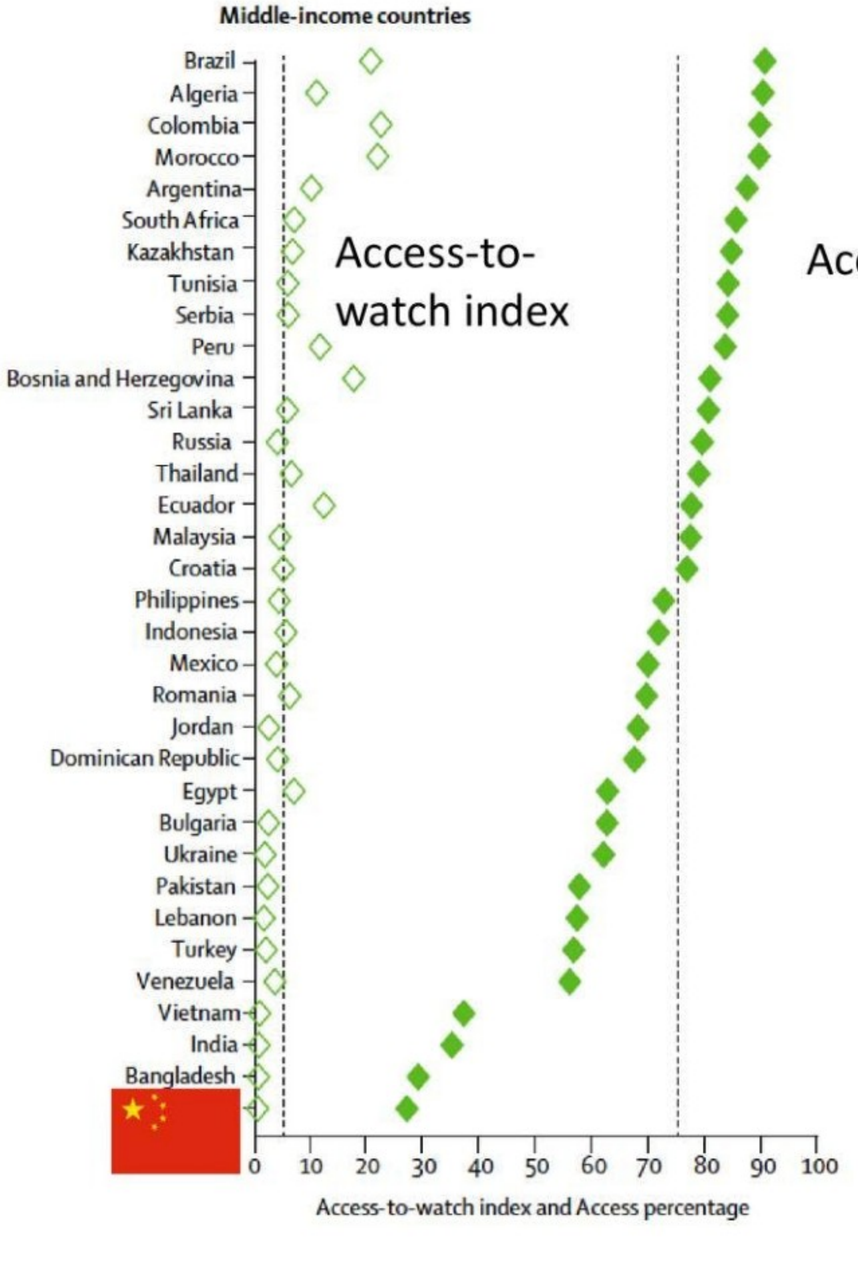
Overall use also needs to be considered





Access-to-watch index

Access %

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- Median **Access** group use 76·3%
  - Max 94·4% Slovenia
  - Min 27·0% China
- Median **Watch** group use 12·3%
  - Max China 54·0%
  - Min Slovenia 3·3%

Table 1. Recategorization of antibiotics within the AWaRe index for use in English national stewardship policy

ATC name	ATC code	AWaRe WHO	AWaRe England	Rationale for movement
Amikacin	J01GB06	Access	Watch	antibiotic used for resistant Gram-negative infections
Amoxicillin and enzyme inhibitor	J01CR02	Access	Watch	to avoid overuse as resistance increasing and associated with increased risk of *C. difficile* infections
Ampicillin combinations	J01CA51	Other	Access	similar category as amoxicillin; rare use
Cefaclor	J01DC04	Other	Watch	associated with increased risk of *C. difficile* infections
Cefadroxil	J01DB05	Other	Watch	associated with increased risk of *C. difficile* infections
Cefalexin	J01DB01	Access	Watch	associated with increased risk of *C. difficile* infections
Cefamandole	J01DC03	Other	Watch	associated with increased risk of *C. difficile* infections
Cefazolin	J01DB04	Access	Watch	associated with increased risk of *C. difficile* infections
Cefoxitin	J01DC01	Other	Watch	associated with increased risk of *C. difficile* infections
Cefprozil	J01DC10	Other	Watch	associated with increased risk of *C. difficile* infections
Cefradine	J01DB09	Other	Watch	associated with increased risk of *C. difficile* infections
Cefuroxime	J01DC02	Other	Watch	associated with increased risk of *C. difficile* infections
Ceftazidime and enzyme inhibitor	J01DD52	Watch	Reserve	novel combination reserved for treatment failures
Chloramphenicol	J01BA01	Access	Watch	second-line antibiotic, use in penicillin allergy
Clindamycin	J01FF01	Access	Watch	associated with increased risk of *C. difficile* infections
Dalbavancin	J01XA04	Watch	Reserve	novel antibiotic reserved for treatment failures and OPAT
Doripenem	J01DH04	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Ertapenem	J01DH03	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Fosfomycin (oral)	J01XX01	Other	Access	narrow spectrum, recommended for uncomplicated UTI
Fusidic acid	J01XC01	Other	Access	narrow spectrum
Imipenem	J01DH51	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Lymecycline	J01AA04	Other	Watch	used for acne, alternative non-antimicrobial drugs available
Meropenem	J01DH02	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Minocycline	J01AA08	Other	Watch	used for acne, alternative non-antimicrobial drugs available
Neomycin	J01GB05	Other	Access	not routinely used in England, monitor carefully for change in use
Oxytetracycline	J01AA06	Other	Watch	used for acne, alternative non-antimicrobial drugs available
Piperacillin	J01CA12	Other	Watch	avoid overuse as resistance increasing
Pivmecillinam	J01CA08	Other	Access	narrow spectrum, recommended for uncomplicated UTI
Pristinamycin	J01FG01	Other	Watch	not routinely used in England, monitor carefully for change in use
Quinupristin	J01FG02	Other	Watch	not routinely used in England, monitor carefully for change in use
Telavancin	J01XA03	Watch	Reserve	not routinely used in England, monitor carefully for change in use
Temocillin	J01CA17	Other	Watch	antibiotic used for resistant Gram-negative infections
Tetracycline	J01AA07	Other	Access	narrow spectrum, recommended in treatment guidelines
Ticarcillin	J01CA13	Other	Watch	not routinely used in England, monitor carefully for change in use
Tobramycin	J01GB01	Other	Watch	antibiotic used for resistant Gram-negative infections
Tetracycline combinations	J01AA20	Other	Watch	used for acne, alternative non-antimicrobial drugs available

Any antibiotics categorized as both Access and Watch within the WHO AWaRe index were automatically classified as Watch antibiotics for UK stewardship purposes. The rationale for all other reclassifications is presented in this table. OPAT, outpatient parenteral antimicrobial therapy.

Some countries adapted AWaRe

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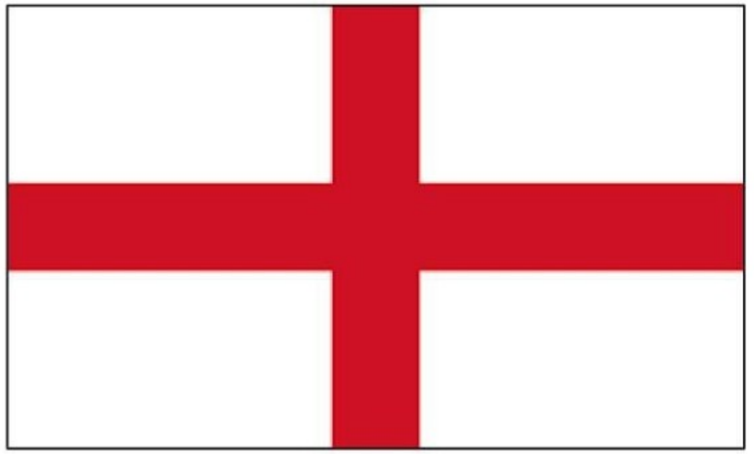
International comparison goodbye?



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WATCH and RESERVE group antibiotics

What to do?

- Monitor use
- Provide feedback on use
- Consider restrictions if overuse
- Develop guidelines when their uses is justified and how they should be used

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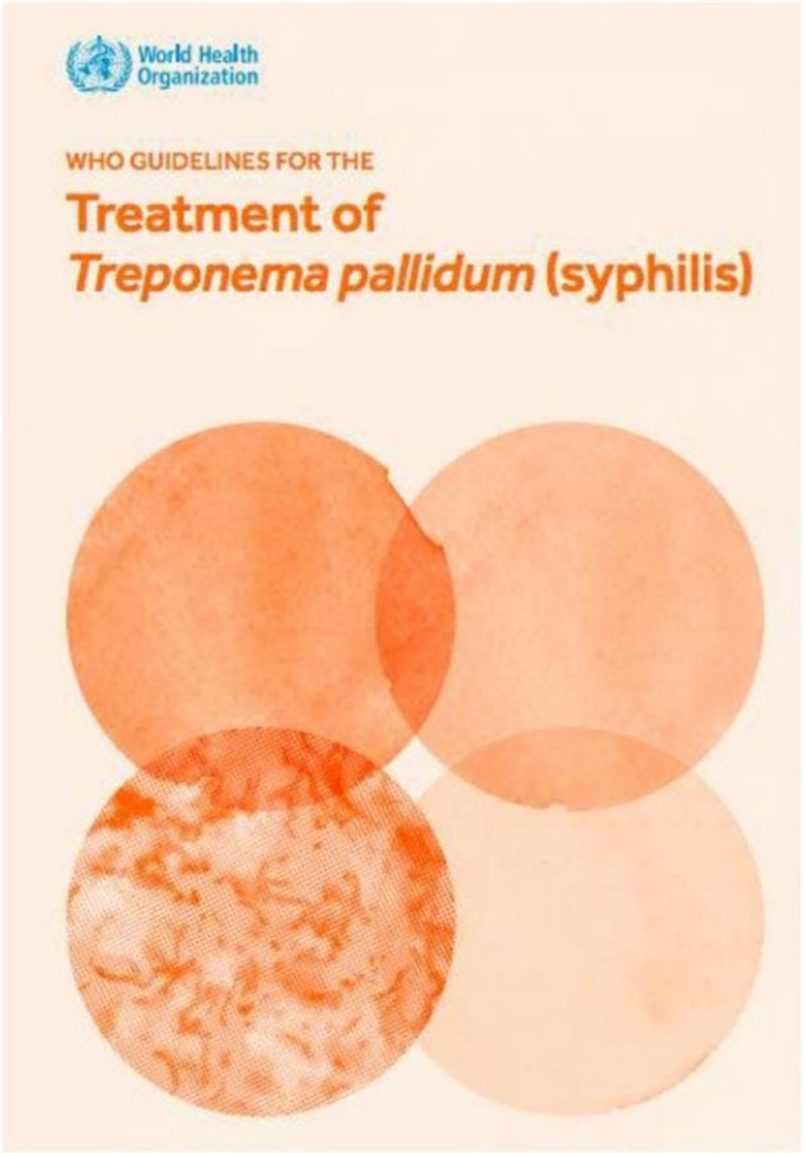

AWaRe and medical guidelines

GUIDELINES

- May not always be available
- May not be syndrome-based (“when not to prescribe”)
- May also not be used
  - A different but important issue
- Should incorporate AWARE

	VOIE	eGFR ≥90	eGFR 60-89	eGFR 30-59	eGFR 15-29	eGFR <15	HEMODIAFLI-TRATION EERC	HEMODIALYSE	COMMENTAIRES
Ceftazidime / Avibactam (PP sur 2h) (TDM – ceftazidime) (cf. pages 128-129) RESERVE	IV	2.5g/8h	2.5g/8h	1.25g/8h	0.94g/12h	0.94g/24h	1.25g/8h (peu de données)	0.94g/48 (PD)	Antibiotique de dernier recours. Utilisation uniquement en accord avec le SMI. En 02/2018 pas encore dispponible en CH.
Ceftaroline RESERVE	IV	600mg/12h	600mg/12h	400mg/12h	300mg/12h	200mg/12h	Pas de données	200mg/12h	Antibiotique de dernier recours. Utilisation uniquement après accord SMI.
Ceftobriprole (PP sur 2h) RESERVE	IV	500mg/8h	500mg/8h	500mg/12h	250mg/12h	250mg/24h	Pas de données	250mg/24h	Antibiotique de dernier recours. Utilisation uniquement après accord SMI.
Ceftolozane / tazobactam RESERVE	IV	1.5g/8h	1.5g/8h	0.75g/8h	0.375g/8h	Pas de données	Pas de données	charge 0.75mg PUIS 0.15mg/8h PD	CAVE la posologie de 1.5/8h n'est probablement pas suffisante pour le traitement d'une pneumonie
Ciprofloxacine WATCH	PO	500mg 2x/j 750mg 2x/j*	500mg 2x/j 750mg 2x/j	500mg 2x/j 750mg 2x/j	250mg 2x/j 500mg 2x/j	250mg 2x/j 250mg 2x/j	-	250mg 2x/j (PD)	CAVE: QT, tendinopathie (FR: âge, stéroïdes) *Posologie élevée pour infections sévères
Ciprofloxacine WATCH	(IV)	400mg/12h 400mg/8h*	400mg/12h 400mg/8h	300mg/12h 300mg/8h	200mg/12h 200mg/8h	200mg/12h 200mg/12h	200mg/12h	200mg/12h (PD)	Favoriser traitement PO si possible (excellente biodisponibilité) *Posologie élevée pour infections sévères
Clarithromycine WATCH	PO	500mg 2x/j	500mg 2x/j	500mg 2x/j	500mg 2x/j	250mg 2x/j	-	250mg 2x/j	CAVE interactions médicamenteuses, QT
Clarithromycine WATCH	(IV)	500mg/12h	500mg/12h	500mg/12h	250mg/8h	250mg/12h	250mg/12h	250 mg/12h	CAVE interactions médicamenteuses, QT Favoriser traitement PO si possible (excellente biodisponibilité)
Clindamycine	PO (IV)	600mg/8h 900mg/8h	Pas d'adaptation	Pas d'adaptation	Pas d'adaptation	Pas d'adaptation	Pas d'adaptation	Pas d'adaptation	Favoriser traitement PO si possible (excellente biodisponibilité)
Colistine RESERVE	IV	Selon algorithme SMI	Selon algorithme SMI	Selon algorithme SMI	Selon algorithme SMI	Selon algorithme SMI	Selon algorithme SMI	Selon algorithme SMI	Antibiotique de dernier recours. Utilisation uniquement après accord SMI selon algorithme SMI (basé sur Clin Infect Dis. 2017 Mar 1;64(5):565-571.) CAVE: néphrotoxicité

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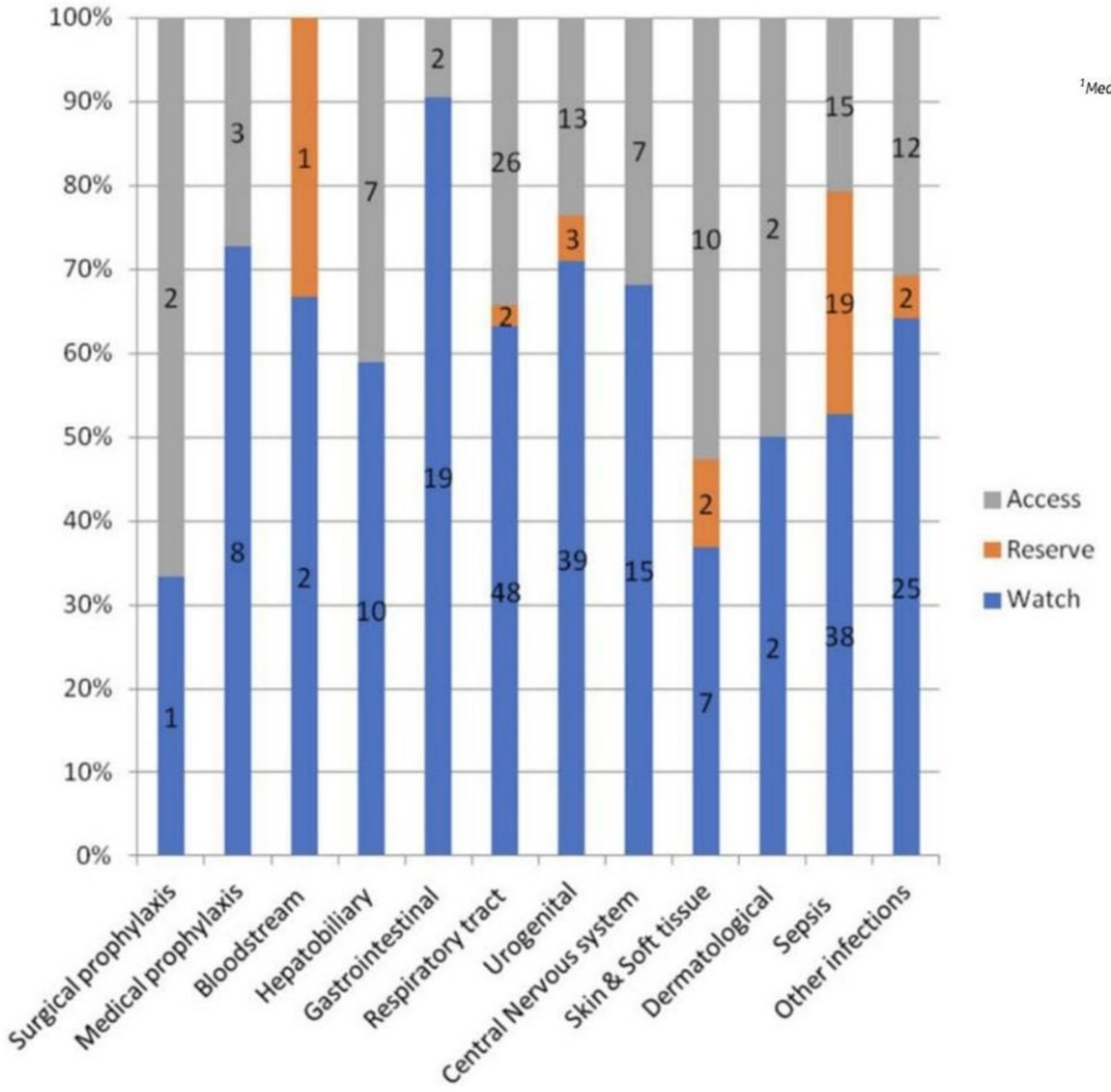
Antibiotic consumption according to the AWaRe categorization of the WHO in the inpatient setting, Switzerland (2017–2019)

AWaRe groups**	Consumption*			Relative consumption		
	2017	2018	2019	2017	2018	2019
Access group	27.9	27.8	26.5	51%	52%	51%
Watch group	25.7	25.3	24.7	47%	47%	48%
Reserve group	0.8	0.7	0.7	2%	1%	1%

* Consumption expressed in DDDs per 100 bed-days

** See Annex I for the list of antibiotics and their corresponding AWaRe group

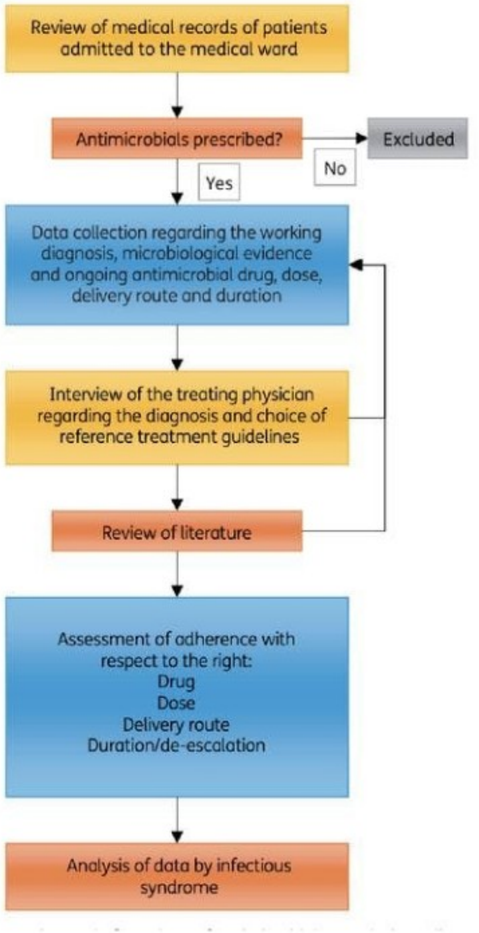
https://www.star.admin.ch/star/en/home/star/Newsletter-Beitraege/swiss-antibiotic-resistance-report-2020.html



Compliance with the 4Ds of antimicrobial stewardship practice in a tertiary care centre

Diksha Dixit[1], Rajat Ranka[2] and Prasan Kumar Panda[2*]

[1]Medical School, All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand, India; [2]Department of Internal Medicine, All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand, India



Dixit et al. JAC Antimicrob Resist. 2021 Sep 15;3(3):dlab135.

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Potential issues with AWaRe

- Ecologic impact of antibiotics ?
  - Microbiome ?
  - Resistance selection ?
  - Transmission ?
- May differ by setting
- More studies examining these issues

TABLE 3. Consensual ranking of β-lactams according to both their spectrum and their resistance-promoting potential

Rank	Molecule(s)	Similar response rate (%)[a]	Consensus reaching round number[b]
1	Amoxicillin	100	2
2	Amoxicillin + Clavulanic Acid	88	3
3	Third-generation cephalosporin Ureido/carboxy-penicillin	81	3
4	Piperacilin + Tazobactam Ticarcilin + Clavulanic Acid Fourth-generation cephalosporin, Antipseudomonal third-generation cephalosporin	71	4
5	Ertapenem	81	3
6	Imipenem Meropenem Doripenem	85	2

[a]Indicates the proportion of the Expert Panel members that agreed with the molecules included in each rank of the classification.
[b]Indicates how many rounds of the Delphi process were necessary to reach a consensus.

Weiss et al. Clin Microbiol Infect. 2015 Jul;21(7):649.e1-10.

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EML/AWaRe 2021 Next steps

World Health Organization

ADULTS

Community-Acquired Pneumonia

Page 1 of 2

Definition

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

Most Likely Pathogens

"Typical" Bacteria:

- ***Streptococcus pneumoniae*** (most cases)
- *Staphylococcus aureus* (often associated with influenza)
- *Haemophilus influenzae* (chronic lung diseases, smoking)
- *Moraxella catarrhalis* (chronic lung diseases, smoking)
- *Enterobacterales* (severe comorbidities, e.g. chronic lung diseases, dementia, stroke)

"Atypical" Bacteria:

- *Mycoplasma pneumoniae* (more frequent in young adults)
- *Chlamydia pneumoniae* and *psittaci* (more frequent in young adults)
- *Legionella* spp. (chronic lung diseases or other underlying illness, travel, exposure to hot tubs
- *Coxiella burnetii* (rural areas, exposure to livestock)

Respiratory Viruses:

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

Bacteria to consider in Specific Settings:

- *Burkholderia pseudomallei* (SE Asia, Australia)

Investigating for 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 rifampicin resistance

Diagnosis

Clinical Presentation

- New onset (<2 weeks) or worsening cough with fever (≥38.0°C), sputum production, dyspnea, tachypnea, reduced oxygen saturation, crepitations on lung auscultation, chest pain/discomfort without alternative explanation
- Extrapulmonary features (i.e. confusion, disorientation) may predominate in elderly, and immunosuppressed patients and fever may be absent

Microbiology Tests

Mild cases: usually not needed

Severe cases (to guide antimicrobial treatment): blood cultures, urinary antigens for *L. pneumophila* and *S. pneumoniae*

Selected cases (depending on epidemiology and risk factors): sputum rapid molecular test for *M. tuberculosis*, nasopharyngeal swab for influenza viruses and SARS-CoV-2, HIV testing in settings with high HIV prevalence and in case of recurrent and/or severe pneumonia

Other Laboratory Tests

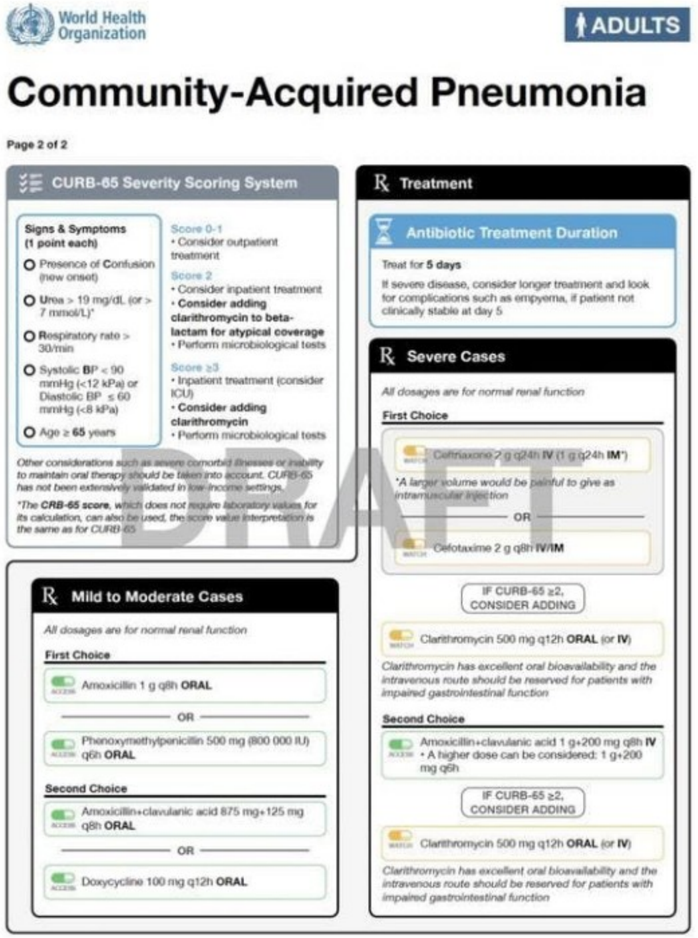
Determine disease severity: blood urea nitrogen (see CURB-65 Scoring System box), blood pH and gases, white blood cell count

Differentiate bacterial and viral (taking into account pre-test probability): C-reactive protein and/or procalcitonin

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
- Infiltrate may not always be evident (e.g. dehydration) and non-infectious etiologies may mimic infiltrates (e.g. lung edema, pulmonary embolism)
- Radiologic appearance cannot be used to accurately predict pathogen



World Health Organization

ADULTS

Community-Acquired Pneumonia

Page 2 of 2

CURB-65 Severity Scoring System

Signs & Symptoms (1 point each)

- Presence of **C**onfusion (new onset)
- **U**rea > 19 mg/dL (or > 7 mmol/L)*
- **R**espiratory rate > 30/min
- Systolic **B**P < 90 mmHg (<12 kPa) or Diastolic BP ≤ 60 mmHg (<8 kPa)
- Age ≥ **65** years

Score 0-1
- Consider outpatient treatment

Score 2
- Consider inpatient treatment
- **Consider adding clarithromycin to beta-lactam for atypical coverage**
- Perform microbiological tests

Score ≥3
- Inpatient treatment (consider ICU)
- **Consider adding clarithromycin**
- Perform microbiological tests

Other considerations such as severe comorbid illnesses or inability to maintain oral therapy should be taken into account. CURB-65 has not been extensively validated in low-income settings.

**The CRB-65 score*, which does not require laboratory values for its calculation, can also be used, the score value interpretation is the same as for CURB-65*

Mild to Moderate Cases

All dosages are for normal renal function

First Choice

- Amoxicillin 1 g q8h **ORAL**

OR

- Phenoxymethylpenicillin 500 mg (800 000 IU) q6h **ORAL**

Second Choice

- Amoxicillin+clavulanic acid 875 mg+125 mg q8h **ORAL**

OR

- Doxycycline 100 mg q12h **ORAL**

Treatment

Antibiotic Treatment Duration

Treat for **5 days**

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

Severe Cases

All dosages are for normal renal function

First Choice

- Ceftriaxone 2 g q24h **IV** (1 g q24h **IM***)

**A larger volume would be painful to give as intramuscular injection*

OR

- Cefotaxime 2 g q8h **IV/IM**

IF CURB-65 ≥2, CONSIDER ADDING

- Clarithromycin 500 mg q12h **ORAL** (or **IV**)

Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function

Second Choice

- Amoxicillin+clavulanic acid 1 g+200 mg q8h **IV**
- A higher dose can be considered: 1 g+200 mg q8h

IF CURB-65 ≥2, CONSIDER ADDING

- Clarithromycin 500 mg q12h **ORAL** (or **IV**)

Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function

DRAFT

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Summary

- AWaRe offers a new way to monitor antibiotic use in a more “meaningful” way
  - But: a single indicator is insufficient and assessing “quality” will ultimately need patient-level data
  - For hospitals: Watch and Reserve antibiotics as target for antibiotic stewardship
- Medical guideline should privilege Access (and if indicated Watch) antibiotics according to the EML
  - Development of a WHO handbook for common infectious syndromes
- The AWaRe classification is not static and will be adapted based on comments, availability of new antibiotics etc.
  - Harmonization with critically important antibiotics for veterinary use

After the presentation, ho do you feel about AWaRe?

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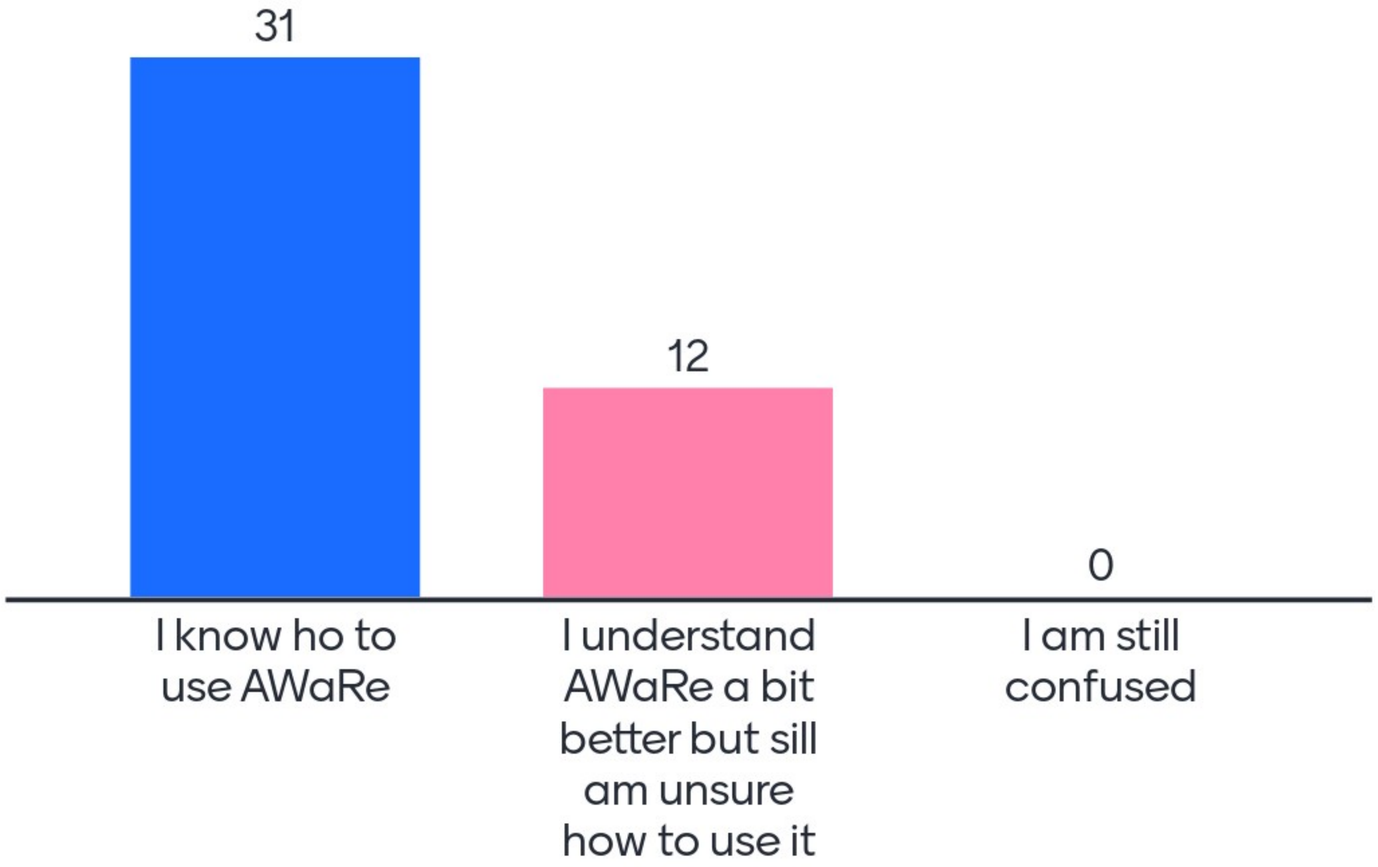

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Thank you for your attention!

Questions / Comments

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Excellent

Thank you - much appreciated

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