Need to conserve the use of critically important antimicrobials for managing severe infections in children

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Back ground

AMR : the hidden threat lurking behind COVID-19: Need of one health approach

- Based on current trends, global deaths related to AMR will rise from the current figure of 700,000 to 20 million per year by 2050

- 70% to 80% of antibiotics manufactured in USA & Europe are used for veterinary practice. In India, exact data not known but on higher side.

- Among 75000 hospitals in India less than 1% is running an effective AMR Program ; in USA - 80% hospitals running Antibiotic stewardship program

One Health & AMR

- Zoonotic diseases represent more than 60% of emerging and re-emerging infectious disease worldwide.
- The destruction of natural environment, globalised trade and travel have created numerous pathways for new pathogens to jump between animals and humans .
- Critical intersection between human health, domestic and wild animal health and the environment requires a new integrated framework — **a paradigm called 'One Health'**
- The integral components of AMR Program are infection prevention control, antibiotic stewardship program, rational antibiotic therapy and AMR surveillance

ANTIMICROBIAL RESISTANCE – A BIG PUBLIC HEALTH ISSUE

GLOBAL

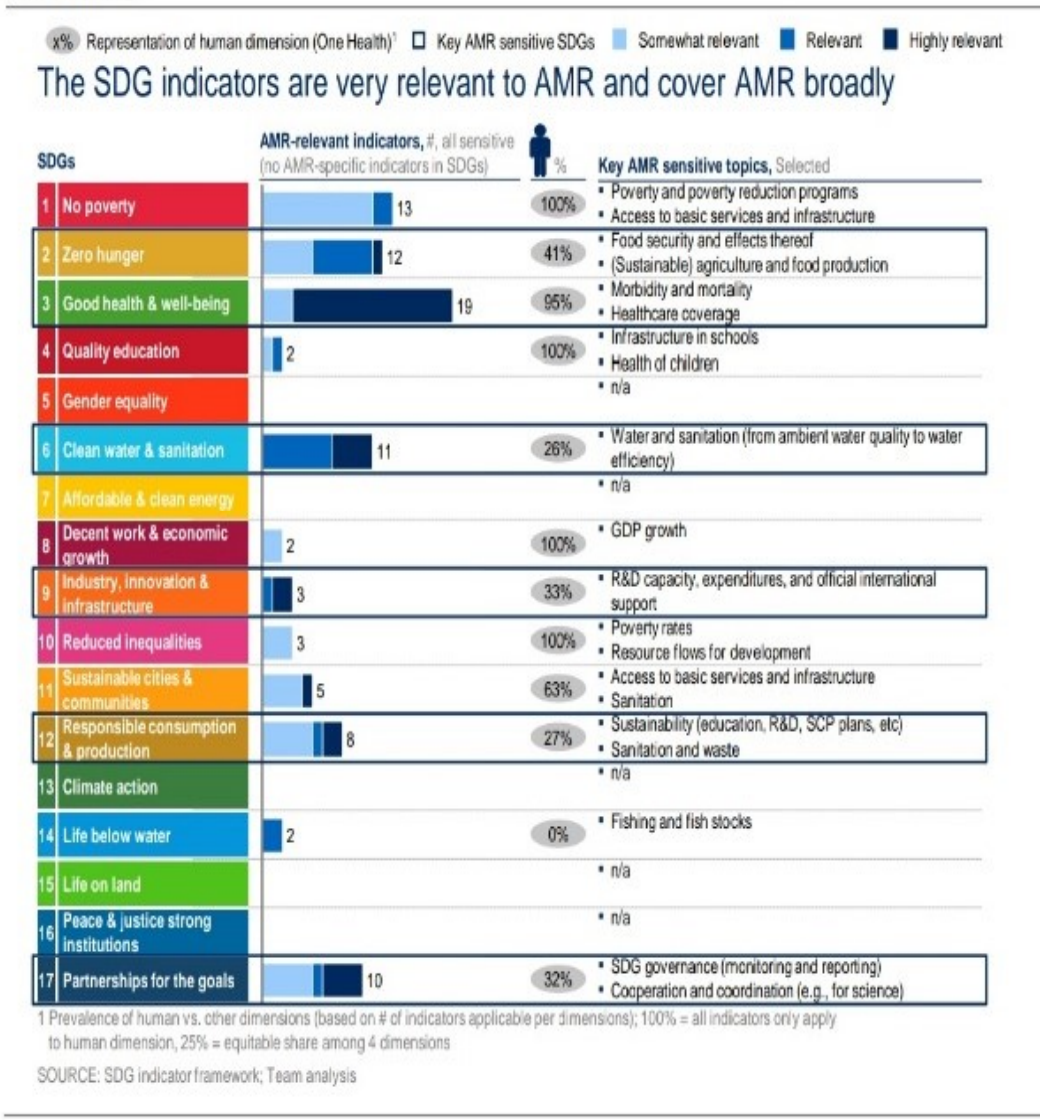
A failure to address the problem of antibiotic resistance could result in:

10m deaths by 2050

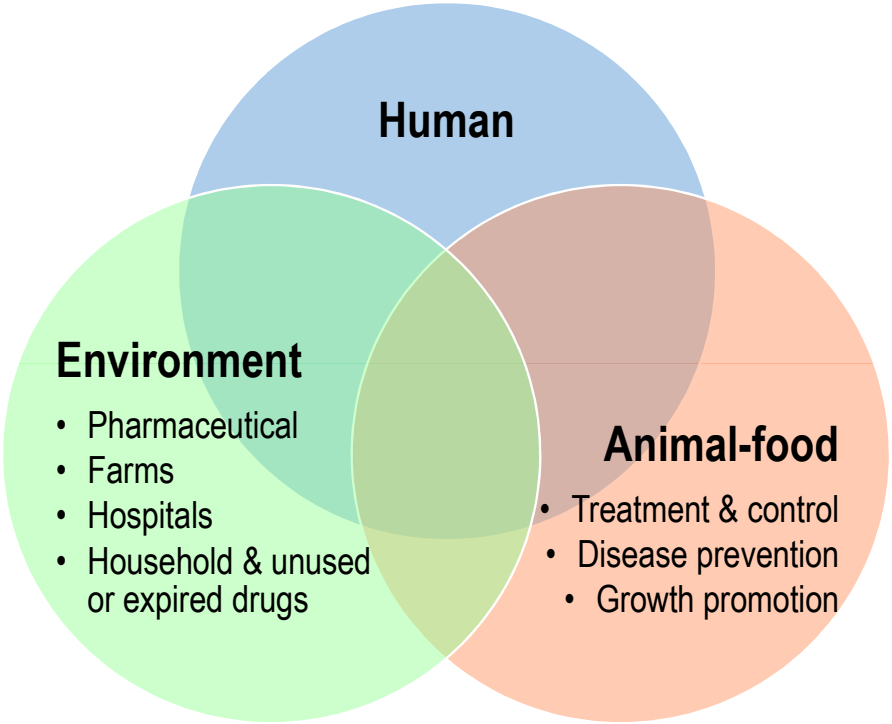
Costing £66 trillion

5 ways AMR disrupts SDG

Five ways antimicrobial resistance disrupts the Sustainable Development Goals.



Antimicrobial resistance is a complex issue



Major health, food security, environment & economic threat

Table 1: Critically important antimicrobials as per the 2018 WHO list

Antimicrobial class	Antimicrobials (examples)#
Highest priority critically important antimicrobials	
Cephalosporins (third-, fourth- and fifth-generation)	Cefixime, cefodizime, cefoperazone, cefotaxime, cefpodoxime, cefquinome, ceftazidime, ceftiofur, ceftizoxime, ceftriaxone
Glycopeptides*	Avoparcin, teicoplanin, vancomycin
Macrolides and ketolides	Azithromycin, clarithromycin, erythromycin, flurithromycin, roxithromycin, spiramycin, tulathromycin, tylosin, tylvalosin
Polymyxins	Colistin, polymyxin B
Quinolones**	Ciprofloxacin, danofloxacin, enrofloxacin, flumequine, gatifloxacin, levofloxacin, lomefloxacin, moxifloxacin, nalidixic acid, norfloxacin, ofloxacin, oxolinic acid
Critically important antimicrobials^	
Aminoglycosides	Amikacin, apramycin, dihydrostreptomycin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin
Ansamycins	Rifampicin, rifamycin
Carbapenems and other penems	Ertapenem, imipenem, meropenem
Glycylcyclines	Tigecycline
Lipopeptides	Daptomycin
Monobactams	Aztreonam
Oxazolidinones	Linezolid
Penicillins (antipseudomonal)	Piperacillin, ticarcillin
Penicillins (aminopenicillins)	Amoxicillin, ampicillin
Penicillins (aminopenicillins with beta-lactamase inhibitors)	Amoxicillin-clavulanic acid, ampicillin-sulbactam
Phosphonic acid derivatives	Fosfomycin
Drugs used solely to treat tuberculosis/ mycobacterial diseases	Bedaquiline, ethambutol, isoniazid, pyrazinamide

Specific examples wherein critically important antimicrobials are recommended for human health in India

- **Cefoperazone** for treatment of obstetric sepsis during pregnancy, microbiologically infected burn wounds, infection of vascular catheters, ventilator-associated or hospital-acquired pneumonia, catheter-associated urinary tract infection in adults.
- **Ceftriaxone** for use in adults but is also in children for septicaemia, neonatal meningitis, severe pneumonia, complicated or severe UTI, antimicrobial coverage for paediatric surgical procedures.
- **Azithromycin** for use in acute pharyngitis, enteric fever, bacterial dysentery, community-acquired pneumonia, acute rheumatic fever, chemoprophylaxis in children.
- **Ciprofloxacin** for treatment of cornea infections, multi-drug resistant bacterial infections, acute inflammatory infective diarrhoeas, serious infected diabetic ulcers, infected burn wounds, severe acute pelvic inflammatory disease, acute prostatitis.
- **Amikacin** for pyelonephritis, pneumonia and in children for urinary tract infection, septicaemia or pneumonia in infants with severe sepsis.
- **Gentamicin** for endocarditis, obstetric sepsis during pregnancy, corneal infections, osteomyelitis, septic arthritis and in children for the treatment of neonatal meningitis, septicaemia, pneumonia.
- **Ampicillin** for infective endocarditis, group B streptococcal disease, septic abortion, peritonitis, vancomycin resistant enterococcus and neonatal meningitis, severe pneumonia, neonatal septicaemia.
- **Amoxicillin** is advised for the treatment of cellulitis, acute pharyngitis, rhinosinusitis, acute bacterial exacerbation of chronic obstructive pulmonary disease, asymptomatic bacteriuria (an obstetrics and gynaecology infection), obstetric sepsis during pregnancy, acute otitis media, acute rheumatic fever and other acute ear infection.

Indian Priority Pathogens List

Critical priority

Enterobacteriaceae (*Klebsiella pneumoniae* and *Escherichia coli*): Carbapenem, tigecycline and colistin-R

Non-fermenting bacteria (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*): Carbapenem and colistin-R

High priority

Staphylococcus aureus: methicillin-resistant *S. aureus*, heterogenous vancomycin-intermediate *S. aureus*, daptomycin-NS, linezolid-R

Enterococcus species: Vancomycin and linezolid-R, daptomycin-NS

Salmonella species (typhoidal and non-typhoidal): Azithromycin, third-generation cephalosporins and carbapenem-NS

Medium priority

Streptococcus pneumoniae: Cephalosporin, fluoroquinolones and linezolid-R

Staphylococcus, coagulase-negative: Vancomycin and linezolid-R

Shigella species: Third-generation cephalosporins and azithromycin-R

Haemophilus influenza: Third-generation cephalosporin and carbapenem-NS

Neisseria meningitides: Fluoroquinolones and third-generation cephalosporins-NS

Note: R: resistant; NS: non-susceptible; Mycobacteria, including *Mycobacterium tuberculosis*, were not included in this prioritization exercise as it is a well-established global and national priority for which innovative new treatments are urgently needed and being developed.

Resistance and susceptibility trends in bacteria against critically important antimicrobials

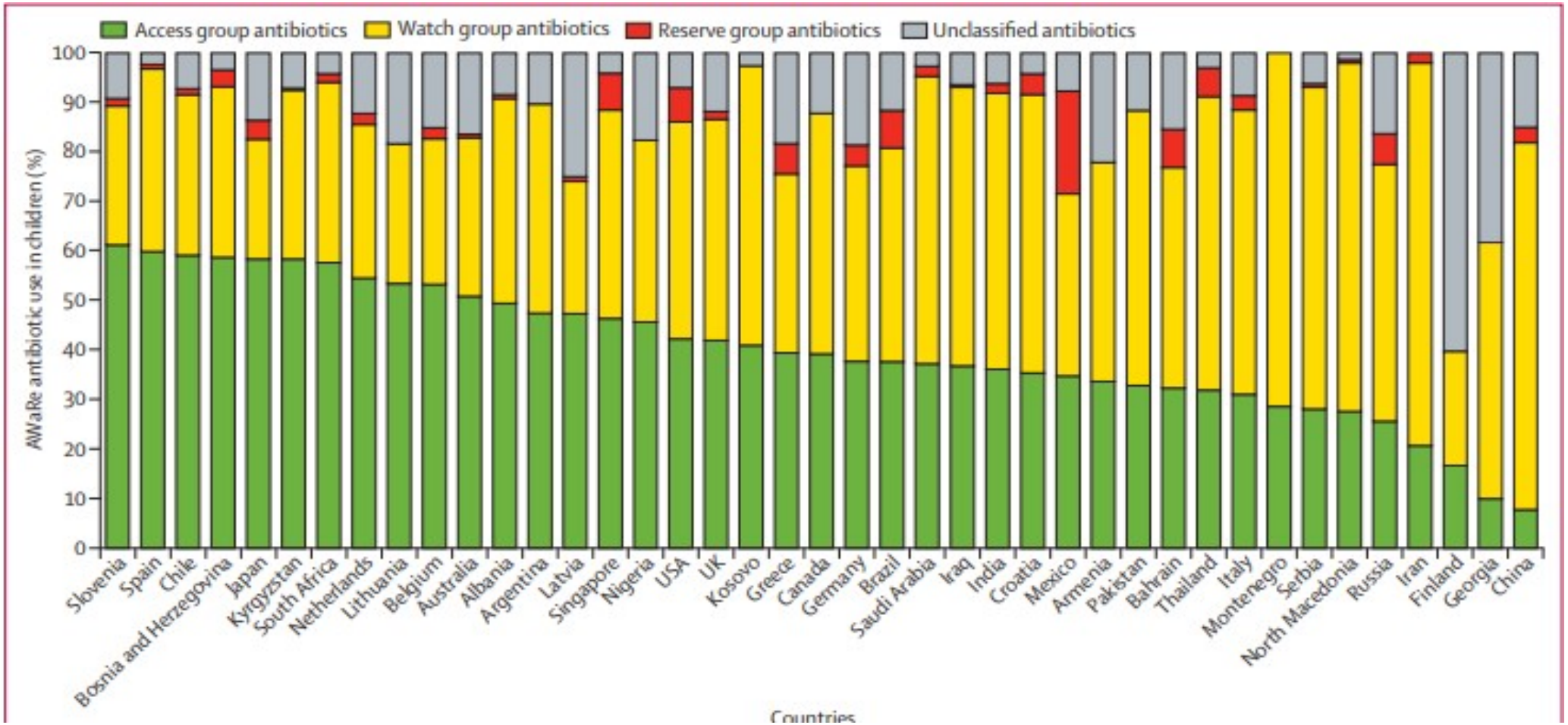
Antibiotic (class)	*S. aureus*	*Enterococcus* sp.	*E. coli*	*Klebsiella* sp.	*Pseudomonas* sp.	*Acinetobacter* sp.	*S. aureus*	*E. faecalis*	*E. faecium*	*E. coli*	*K. pneumoniae*	*P. aeruginosa*	*A. baumannii*
	Per cent resistance (NCDC, 2019)						Per cent susceptibility (ICMR, 2019)						
Cefotaxime (third-, fourth- and fifth-generation cephalosporins)*	–	–	78.0	79.0	–	–	–	–	–	14.5	21.3	–	–
Ceftazidime (third-, fourth- and fifth-generation cephalosporins)*	–	–	–	–	53.0	78.0	–	–	–	20.0	25.3	63.1	12.2
Ciprofloxacin (quinolones and fluoroquinolones)*	66.0	77.0	79.0	71.0	54.0	65.0	17.8	16.4	8.0	20.8	36.0	57.7	–
Levofloxacin (quinolones and fluoroquinolones)*	–	–	–	–	–	–	–	–	–	19.0	35.0	56.5	19.1
Erythromycin (macrolides and ketolides)*	60.0	80.0	–	–	–	–	40.2	–	–	–	–	–	–
Gentamicin (aminoglycosides)	23.0	48.0	–	–	49.0	55.0	–	57.5	35.0	–	–	62.2	–
Amikacin (aminoglycosides)	–	–	–	47.0	45.0	60.0	–	–	–	79.2	50.1	67.9	20.4
Ampicillin (penicillins)	–	61.0	87.0	–	–	–	–	80.8	18.1	–	–	–	–

WHO AWaRe classification .. 2017

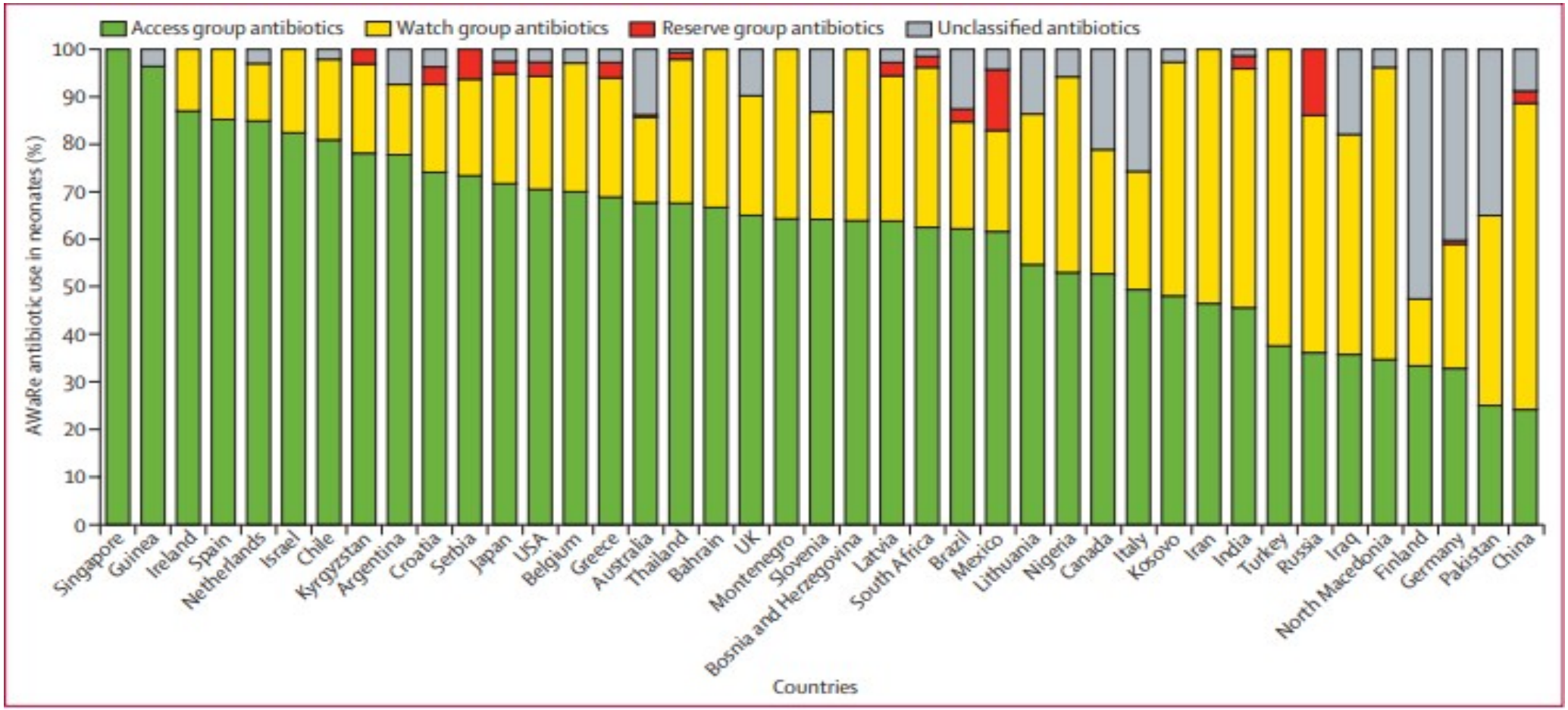
A	**Amikacin, amoxicillin, chloramphenicol, Amoxicillin – clavulanic acid, Ampicillin, Cefazolin, Cephalexin, cloxacillin, Procaine benzyl penicillin, clindamycin, doxycycline, gentamicin, metronidazole, nitrofurantoin, sulphadoxine-trimethoprim**	ACCESS
WA	**Quinolones, 3rd generation cephalosporins with or without beta lactamase inhibitors, macrolides, glycopeptides, antipseudomonal, penicillins + beta lactamase inhibitors, carbapenems, penems**	WATCH
RE	**Aztreomycin, Fosfomycin (IV), 4th generation cephalosporins, LINEZOLID , 5th generation cephalosporins, tigecycline, polymixin, daptomycin**	RESERVE

Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): an analysis of paediatric survey data from 56 countries

Yingfen Hsia, Brian R Lee, Ann Versporten, Yonghong Yang, Julia Bielicki, Charlotte Jackson, Jason Newland, Herman Goossens, Nicola Magrini,

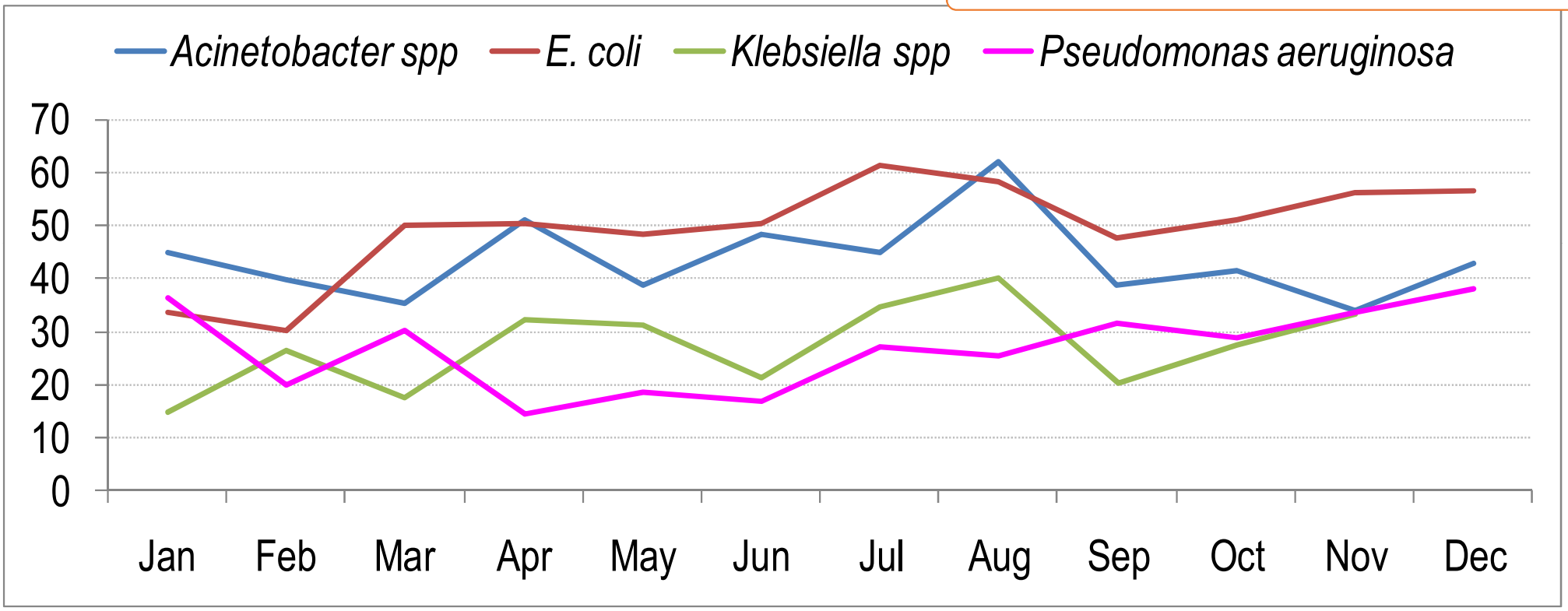


AWaRe Use In Neonates



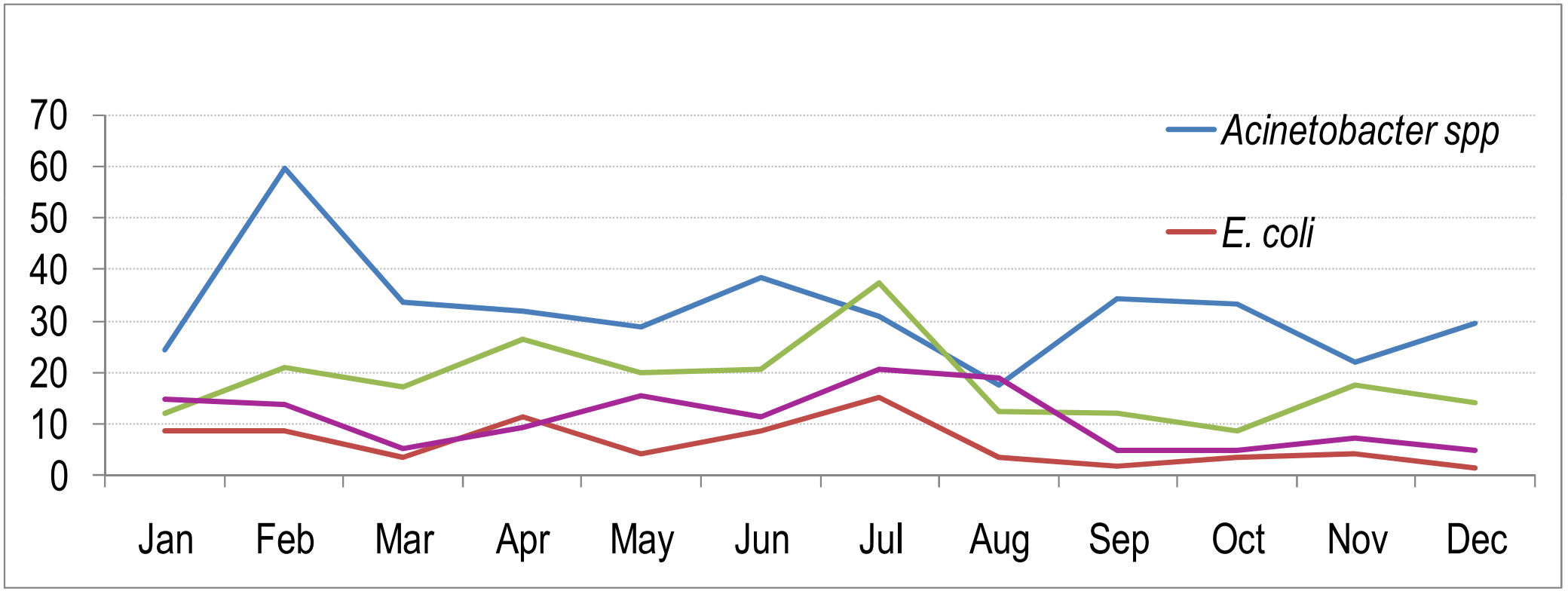
% of ESBL producers

% of ESBL producers (India)	
Acinetobacter spp	65
E. coli	61
Klebsiella spp	62
Pseud. aeruginosa	65



Carbapenem resistance

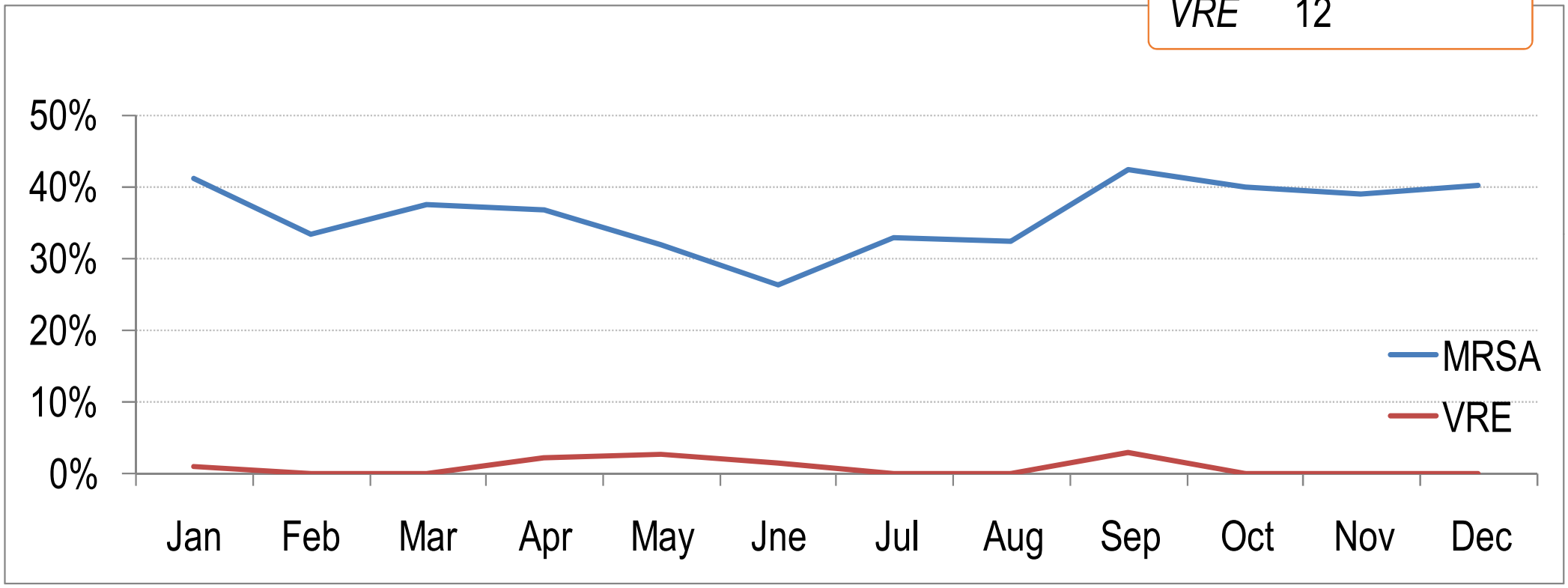
Carbepenem resistance (India)	
Acinetobacter spp	70
E. coli	12
Klebsiella spp	51
Pseud. aeruginosa	42



Gram positives

Resistance (India)

MRSA	47
VRE	12



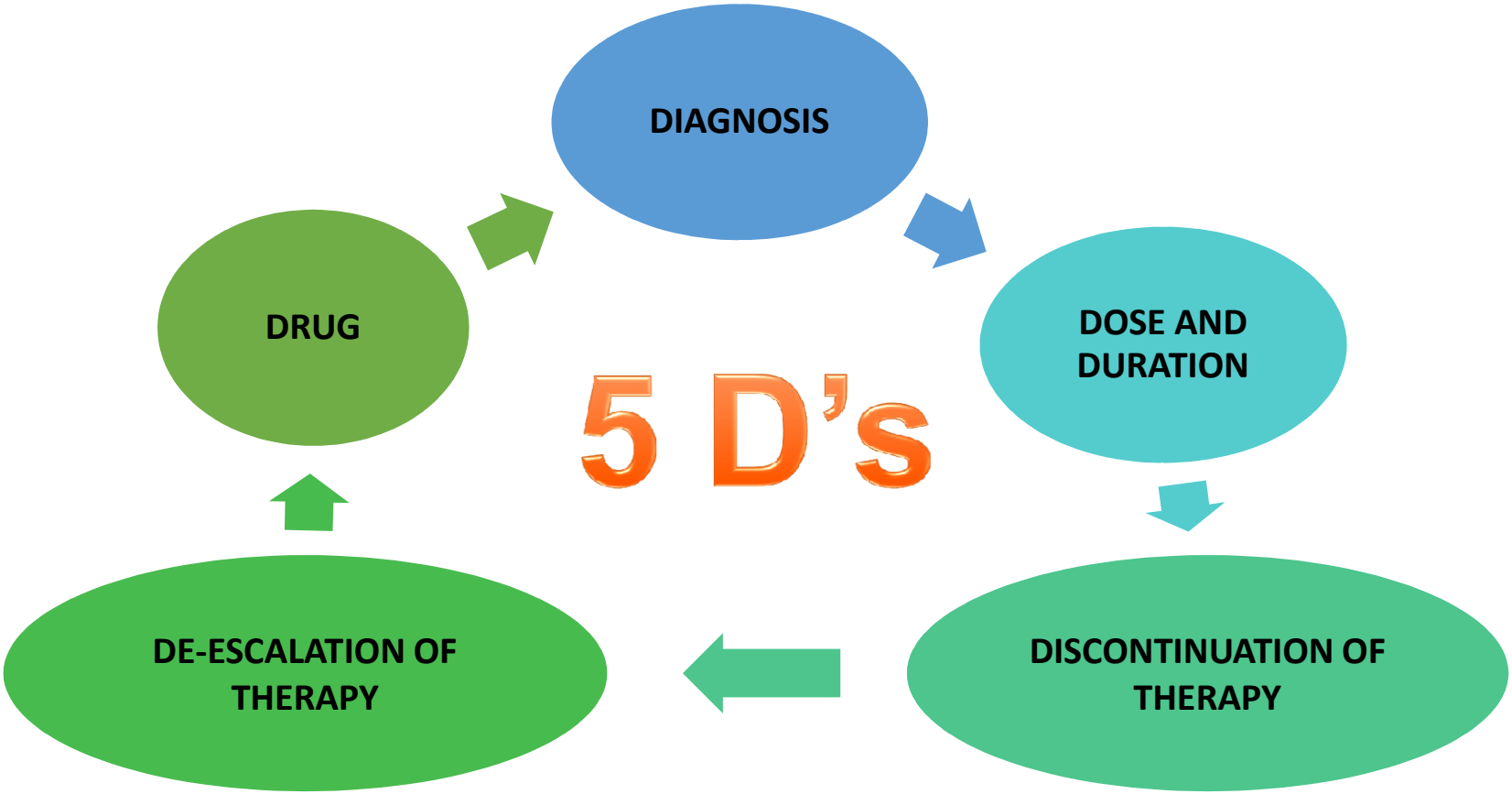
What is Antimicrobial Stewardship?

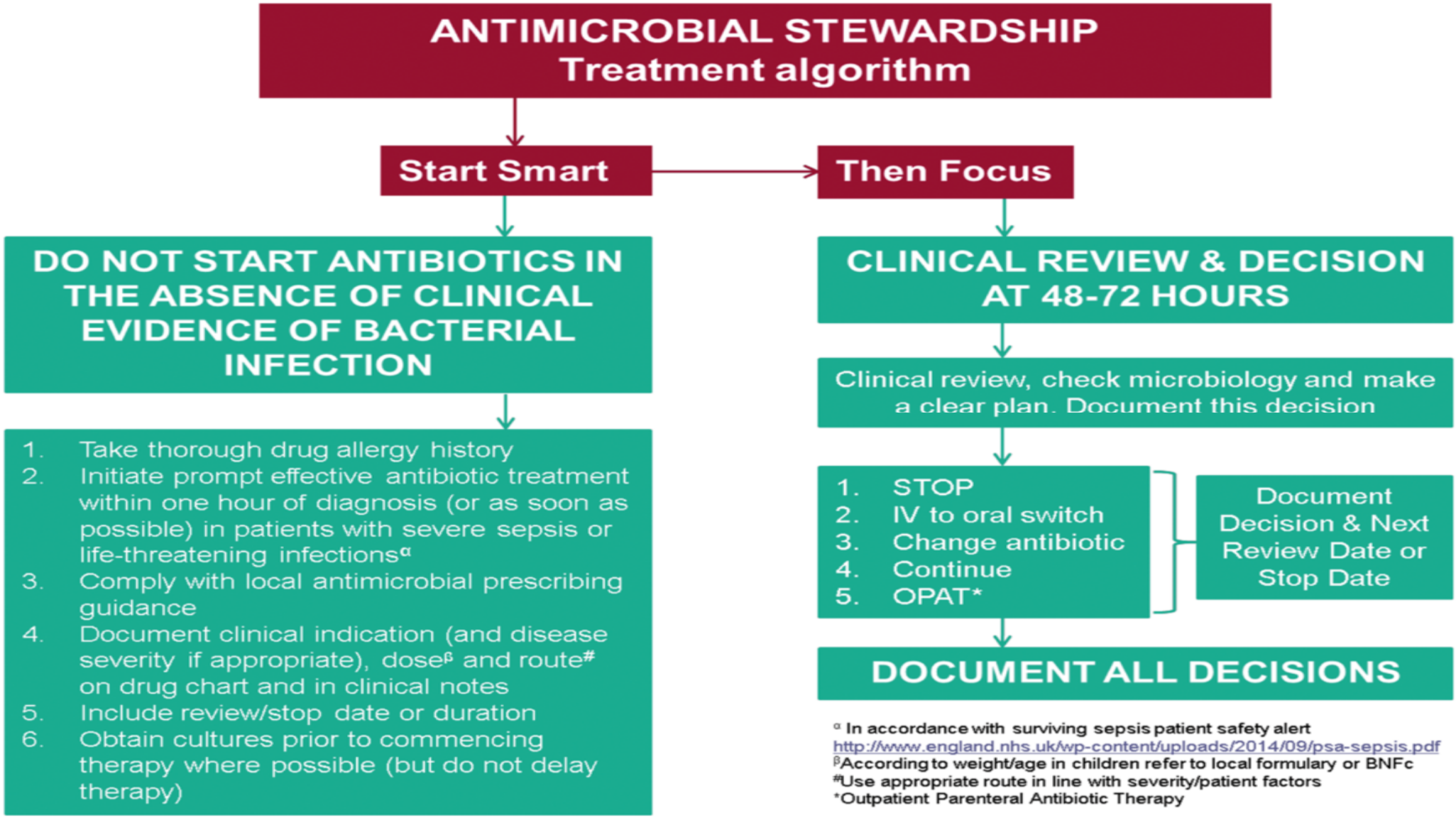
- The commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

- **RIGHT** ANTIBIOTIC, AT **RIGHT** TIME, AT **RIGHT** DOSE, FOR **RIGHT** DURATION FOR **RIGHT** PATIENT.

- Objectives:
  - Maximum antimicrobial benefit
  - Avoid harm from adverse reactions and drug allergies
  - Improve patient outcomes
  - Decrease antimicrobial resistance
  - Decrease healthcare costs

Antibiotic Resistance Threats in the United States. CDC. 2013.


DIAGNOSIS
DOSE AND DURATION
DISCONTINUATION OF THERAPY
DE-ESCALATION OF THERAPY
DRUG
5 D's



From: Antibiotic stewardship in critical care BJA Educ. 2016;17(4):111-116. doi:10.1093/bjaed/mkw059

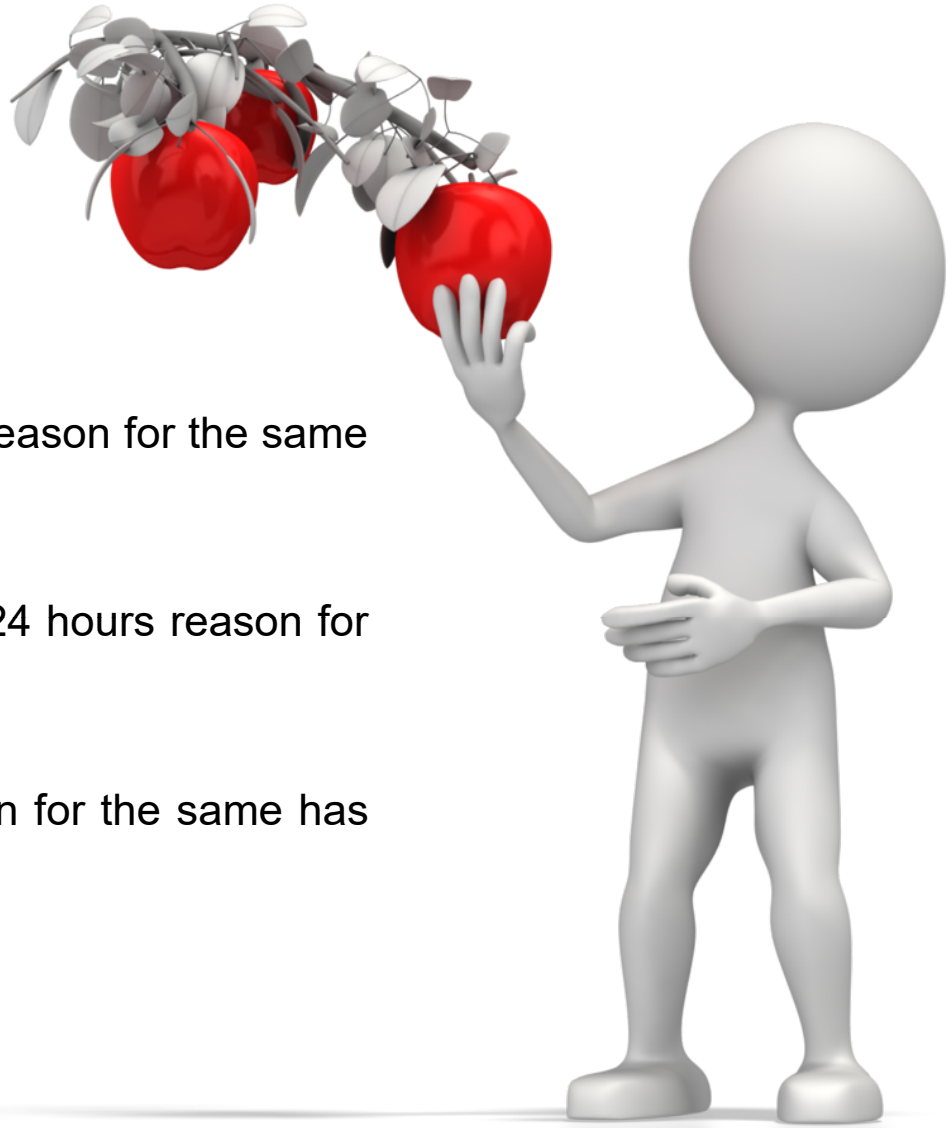
- **Low hanging fruit model for Antibiotic stewardship**

a. Antibiotic prescription for inpatients have to be put under a bracket.

b. If WHO RESERVE antibiotics are prescribed, need for the same has to be documented In the case sheet.

c. If de-escalation is not practiced based on susceptibility report, the reason for the same has to be documented in the case sheet.

d. Double anaerobic coverage is redundant. If double anaerobic coverage is given, reason for the same has to be documented In the case sheet.



e. If antibiotics are continued for more than 7 days, reason for the same has to be documented in the case sheet.

f. If surgical prophylaxis is continued for more than 24 hours reason for the same has to be documented in the case sheet.

g. If more than two antibiotics are prescribed, reason for the same has to be documented in the case sheet.

Antibiotic resistance is a slow-motion pandemic — whose speed will increase because of COVID-19. A concentrated global effort is now needed to ensure it is addressed with the same urgency that's likely to bring us a COVID-19 vaccine in the months ahead...


THANK YOU