Multidrug resistance and reserve antibiotics

Jan Tkadlec

BACK TO THE FUTURE

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Superbug crisis could get worse, killing nearly 40 million people by 2050, study estimates

By Jacqueline Howard, CNN

'It is a pandemic': UK's envoy on superbugs says scale of threat underestimated

Dame Sally Davies says action on deadly antibiotic-resistant infections must be prioritised

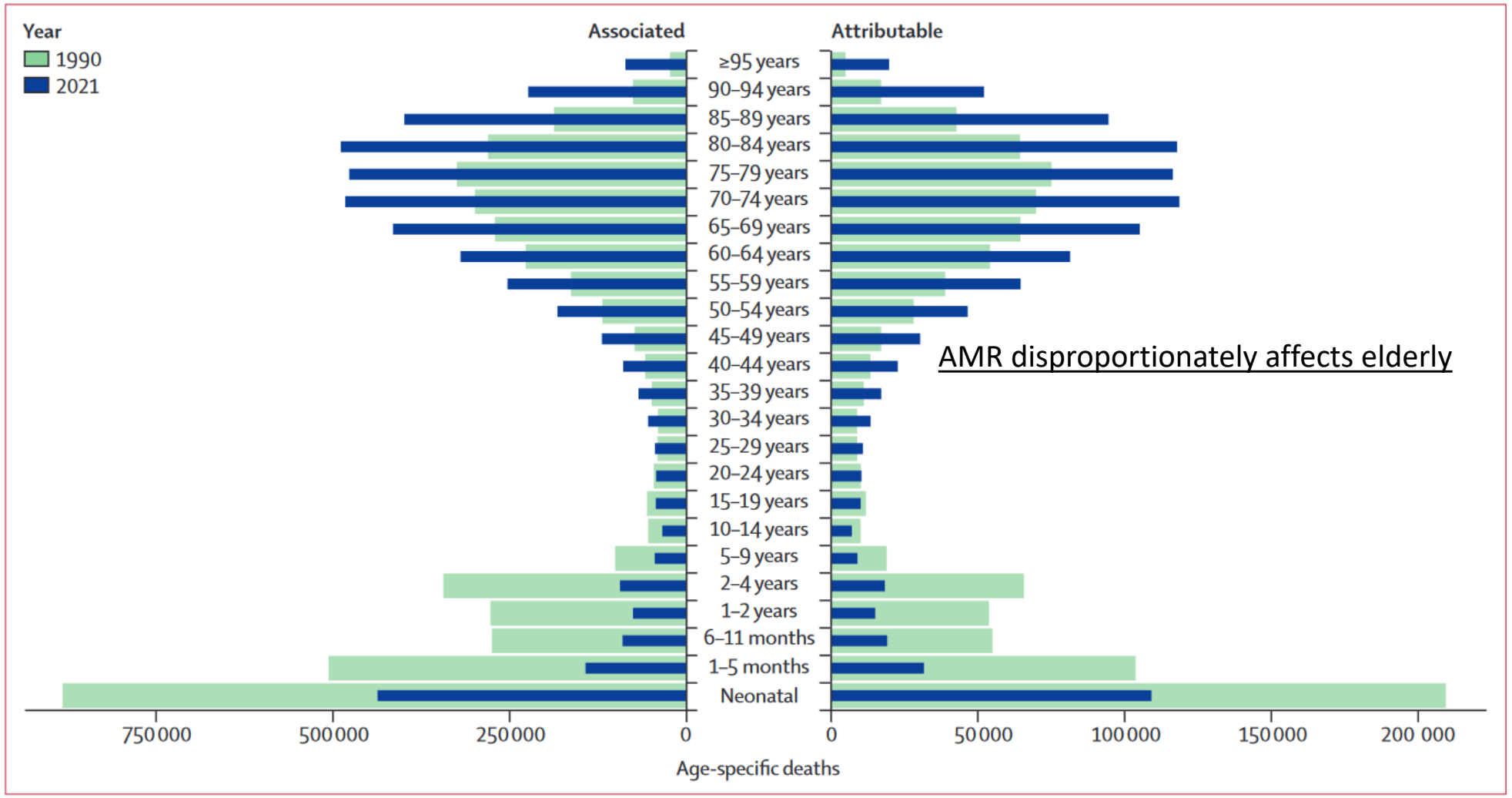
The Guardian Eur

Rise of drug-resistant superbugs could make Covid pandemic look 'minor', expert warns

Common infections will kill millions if drug resistance through misuse of antibiotics is not curbed, says England's ex-chief medical officer

Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050

*GBD 2021 Antimicrobial Resistance Collaborators**



AMR disproportionately affects elderly

Figure 2: **Deaths attributable and associated with antimicrobial resistance, by detailed age group, for 1990 and 2021**
Counterfactuals have distinct x-axes.

Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050

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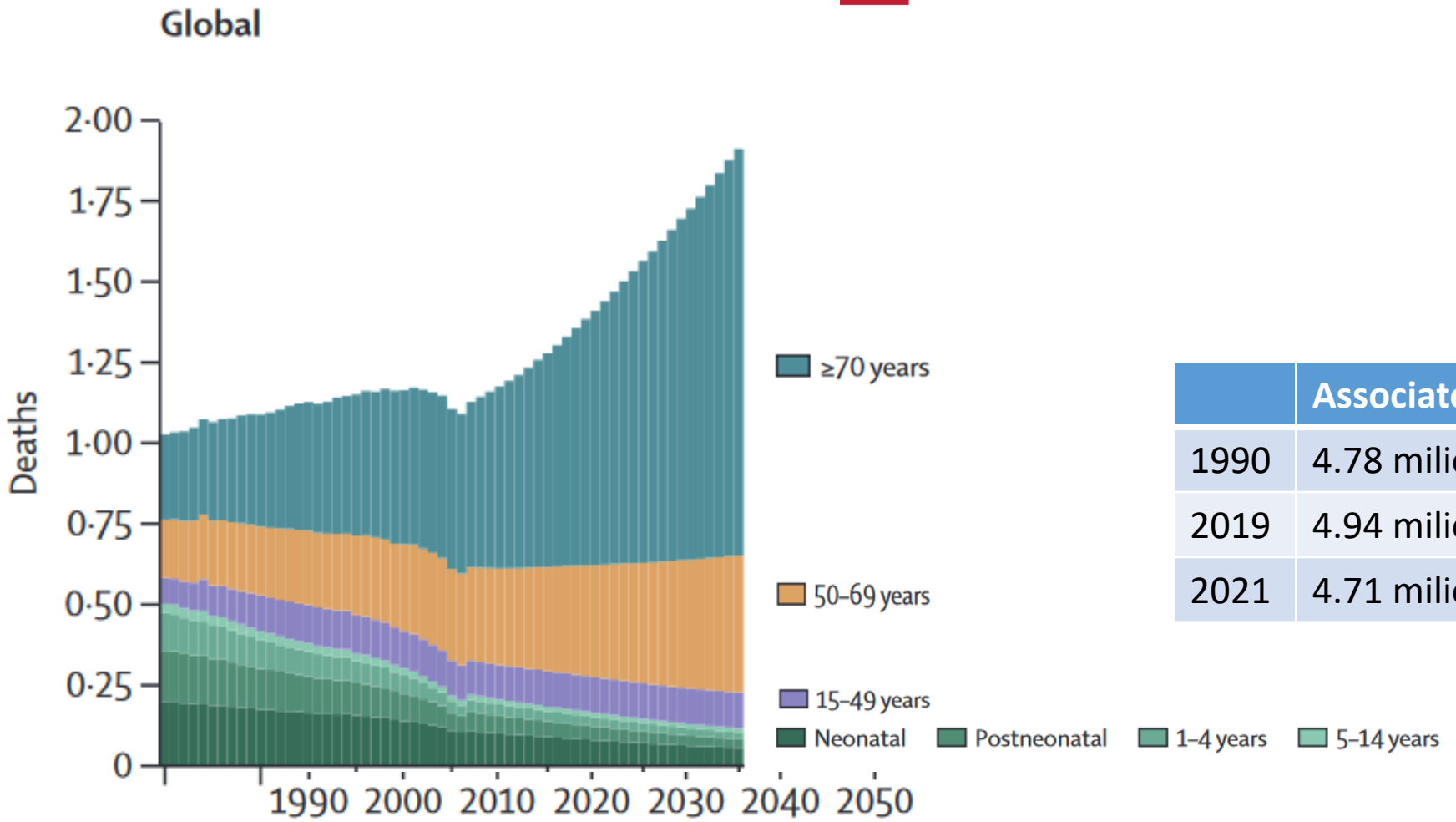


	Associated	Attributable
1990	4.78 milion	1.06 milion
2019	4.94 milion	1.20 milion
2021	4.71 milion	1.14 milion

Figure 7: Deaths attributable to AMR by age group and location in the reference scenario, 2022–2050 Units are in millions.

Superbug definitions

Bacterium	MDR	XDR	PDR
Staphylococcus aureus	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 1[a]	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1.	Non-susceptibility to all agents in all antimicrobial categorie for each bacterium in Tables 1–5
Enterococcus spp.	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 2	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 2.	

MDR - Multidrug resistant= resistence to 3 or more ATB classes
XDR - Extensive drug resistant
PDR - Pandrug resistant

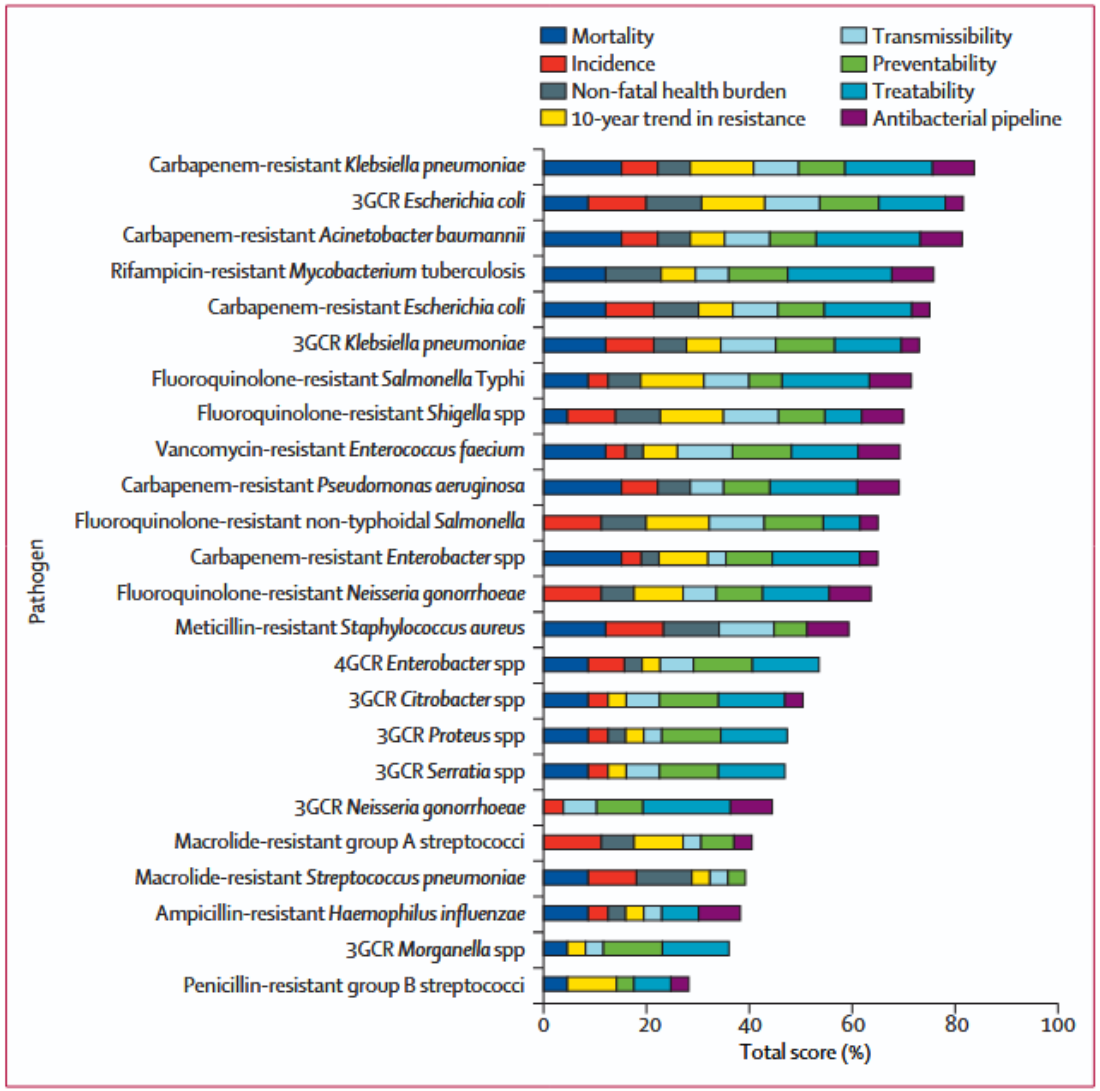
Antimicrobial category	Antimicrobial agent	Results of antimicrobial susceptibility testing (S or NS)
Aminoglycosides	Gentamicin	
Ansamycins	Rifampin/rifampicin	
Anti-MRSA cephalosporins	Ceftaroline	
Anti-staphylococcal β-lactams (or cephamycins)	Oxacillin (or cefoxitin)[a]	
Fluoroquinolones	Ciprofloxacin	
	Moxifloxacin	
Folate pathway inhibitors	Trimethoprim-sulphamethoxazole	
Fucidanes	Fusidic acid	
Glycopeptides	Vancomycin	
	Teicoplanin	
	Telavancin	
Glycylcyclines	Tigecycline	
Lincosamides	Clindamycin	
Lipopeptides	Daptomycin	
Macrolides	Erythromycin	
Oxazolidinones	Linezolid	
Phenicols	Chloramphenicol	
Phosphonic acids	Fosfomycin	
Streptogramins	Quinupristin-dalfopristin	
Tetracyclines	Tetracycline	
	Doxycycline	
	Minocycline	

Source: Magiorakos et al 2012

The WHO Bacterial Priority Pathogens List 2024:

World Health Organization

Final ranking of antibiotic-resistant bacteria in the 2024 WHO BPPL



	2024
Critical priority	*A baumannii*, carbapenem-resistant; Enterobacterales, third-generation cephalosporin-resistant; Enterobacterales, carbapenem-resistant; *Mycobacterium tuberculosis*, rifampicin-resistant*
High priority	*Salmonella enterica* serotype Typhi, fluoroquinolone-resistant; *Shigella* spp, fluoroquinolone-resistant; *E faecium*, vancomycin-resistant; *P aeruginosa*, carbapenem-resistant; non-typhoidal *Salmonella*, fluoroquinolone-resistant; *N gonorrhoeae*, third-generation cephalosporin-resistant, fluoroquinolone-resistant; *S aureus*, meticillin-resistant
Medium priority	Group A streptococci, macrolide-resistant; *S pneumoniae*, macrolide-resistant; *H influenzae*, ampicillin-resistant; group B streptococci, penicillin-resistant

3GCR = 3rd gen cephalosporins Resistance(ESBL, AmpC)

World Health Organization

The WHO Bacterial Priority Pathogens List 2024:

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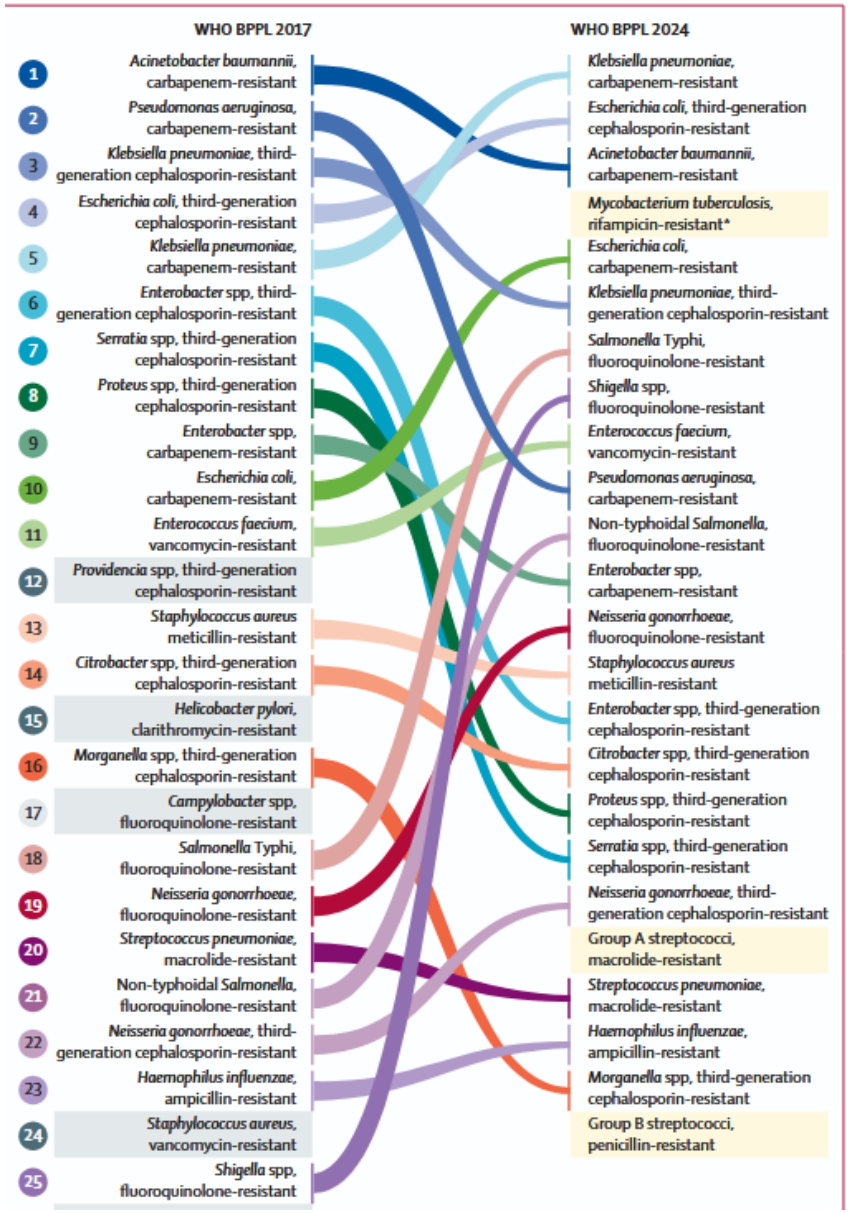


What is a bigger threat?

CENTERS FOR DISEASE CONTROL AND PREVENTION

Urgent Threats

- Carbapenem-resistant *Acinetobacter*
- *Candida auris (C. auris)*
- *Clostridioides difficile (C. difficile)*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae (N. gonorrhoeae)*

Serious Threats

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae
- Vancomycin-resistant *Enterococci* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa (P. aeruginosa)*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae (S. pneumoniae)*
- Drug-resistant Tuberculosis (TB)

Concerning Threats

- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

Watch List

- Azole-resistant *Aspergillus fumigatus (A. fumigatus)*
- Drug-resistant *Mycoplasma genitalium (M. genitalium)*
- Drug-resistant *Bordetella pertussis (B. pertussis)*

Priority groups (critical, high, medium) based on:

1. **Clinical Outcomes and Severity**: infection severity, treatment outcomes, infection site, and patient population risk (e.g., immunocompromised).
2. **Availability of Effective Treatment Options**: Treatment guidelines prioritize antibiotics that are likely to be effective, weighing resistance patterns and new drug availability.
3. **Local and Global Resistance Trends**: resistance in different regions to.
4. **Potential for Prevention and Control**: how easily infections can be prevented or controlled through hygiene or vaccination.

Source: CDC. Antibiotic Resistance Threats in the United States, 2019.

Surveillance of antimicrobial resistance

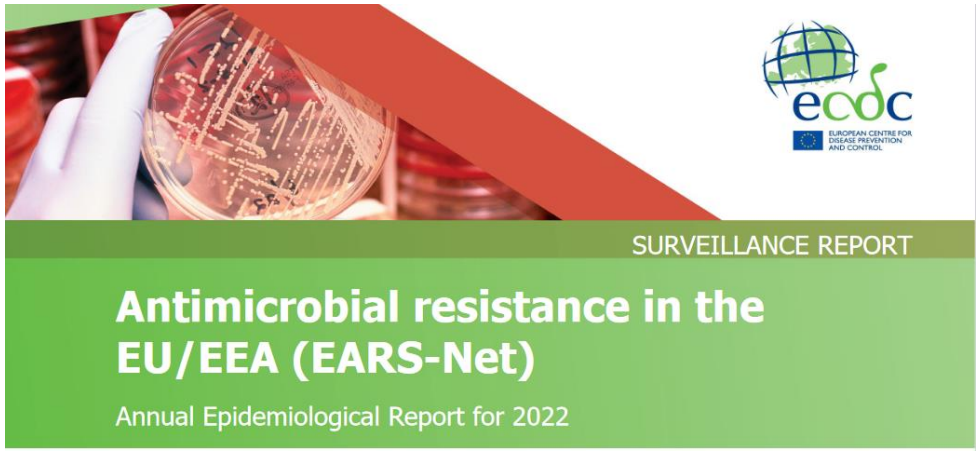
WHO

World Health Organization

Since 2015
132 participating countries

European Antimicrobial Resistance Surveillance Network (EARS-Net)

- Since 1998
- 30 participating countries in Europe
- Hospital laboratories reporting
  - invasive isolates
    - blood or cerebrospinal fluid samples
- Annual reports



EARS-Net

Bacterial species	Assessed antimicrobial group/agent resistance or specific resistance mechanism	Indicative antimicrobial agent(s)
Escherichia coli	Aminopenicillins	Ampicillin or amoxicillin
	Third-generation cephalosporins	Cefotaxime, ceftriaxone or ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin
	Aminoglycosides	Gentamicin or tobramycin
	(Novel antibiotics and combinations)[a]	Aztreonam-avibactam, cefiderocol, ceftazidime-avibactam, imipenem-relebactam, or meropenem-vaborbactam
Klebsiella pneumoniae	Third-generation cephalosporins	Cefotaxime, ceftriaxone or ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin
	Aminoglycosides	Gentamicin or tobramycin
	(Novel antibiotics and combinations) [a]	Aztreonam-avibactam, cefiderocol, ceftazidime-avibactam, imipenem-relebactam, or meropenem-vaborbactam
Pseudomonas aeruginosa	Piperacillin-tazobactam	Piperacillin-tazobactam
	Ceftazidime	Ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Aminoglycosides	Tobramycin
	(Novel antibiotics and combinations) [a]	Cefiderocol, ceftazidime-avibactam, ceftolozane-tazobactam, imipenem-relebactam, or meropenem-vaborbactam
Acinetobacter species	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Aminoglycosides	Gentamicin or tobramycin
	(Novel antibiotics and combinations) [a]	Cefiderocol
Staphylococcus aureus	MRSA	Cefoxitin or oxacillin[b]
	Fluoroquinolones	Ciprofloxacin, levofloxacin or norfloxacin[c]
	Rifampicin	Rifampin
Streptococcus pneumoniae	Penicillins	Penicillin or oxacillin[d]
	Third-generation cephalosporins	Cefotaxime or ceftriaxone
	Fluoroquinolones	Levofloxacin, norfloxacin or moxifloxacin[e]
	Macrolides	Azithromycin, clarithromycin or erythromycin
Enterococcus faecalis	High-level aminoglycoside resistance	Gentamicin
Enterococcus faecium	Aminopenicillins	Ampicillin or amoxicillin
	High-level aminoglycoside resistance	Gentamicin
	Vancomycin	Vancomycin

SURVEILLANCE REPORT

Antimicrobial resistance in the EU/EEA (EARS-Net)

Annual Epidemiological Report for 2024

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

EU targets on antimicrobial resistance

- In 2024, the estimated total EU incidence of meticillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections was 4.48 per 100 000 population (EU country range 0.55–13.63). This was 20.4% lower than in 2019 (baseline year) and 0.31 per 100 000 population lower than the 2030 target of 4.79 per 100 000 population. For the EU overall, a statistically significant decreasing trend was detected between 2019 (baseline year) and 2024.
- The estimated total EU incidence of third-generation cephalosporin-resistant *Escherichia coli* bloodstream infections was 11.03 per 100 000 population (EU country range 3.75–22.79) in 2024. This was 5.9% higher than in 2019 (baseline year) and 1.65 per 100 000 population higher than the 2030 target of 9.38 per 100 000 population. For the EU overall, there was no statistically significant trend detected between 2019 (baseline year) and 2024.
- The estimated total EU incidence of carbapenem-resistant *Klebsiella pneumoniae* bloodstream infections was 3.51 per 100 000 population (EU country range 0.02–20.31) in 2024. This was 61.0% higher than in 2019 (baseline year) and 1.44 per 100 000 population higher than the 2030 target of 2.07 per 100 000 population. For the EU overall, a statistically significant increasing trend was detected between 2019 (baseline year) and 2024.
- In summary, while the EU target for the incidence of MRSA bloodstream infections had already been reached by 2024, the results for the other two EU targets were not on track. The estimated EU incidence of third-generation cephalosporin-resistant *E. coli* bloodstream infections with a 10% reduction target increased by more than 5% compared to 2019 (baseline year). Moreover, the estimated EU incidence of carbapenem-resistant *K. pneumoniae* bloodstream infections increased by over 60% compared to 2019, which differs substantially from the target of a 5% reduction by 2030.

SURVEILLANCE REPORT

Antimicrobial resistance in the EU/EEA (EARS-Net)

Annual Epidemiological Report for 2024

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

- **Surveillance is mainly hospital based and focussing on most severe infection i.e. sepsis**
- **Data are heterogenous**
- **Differences between countries**

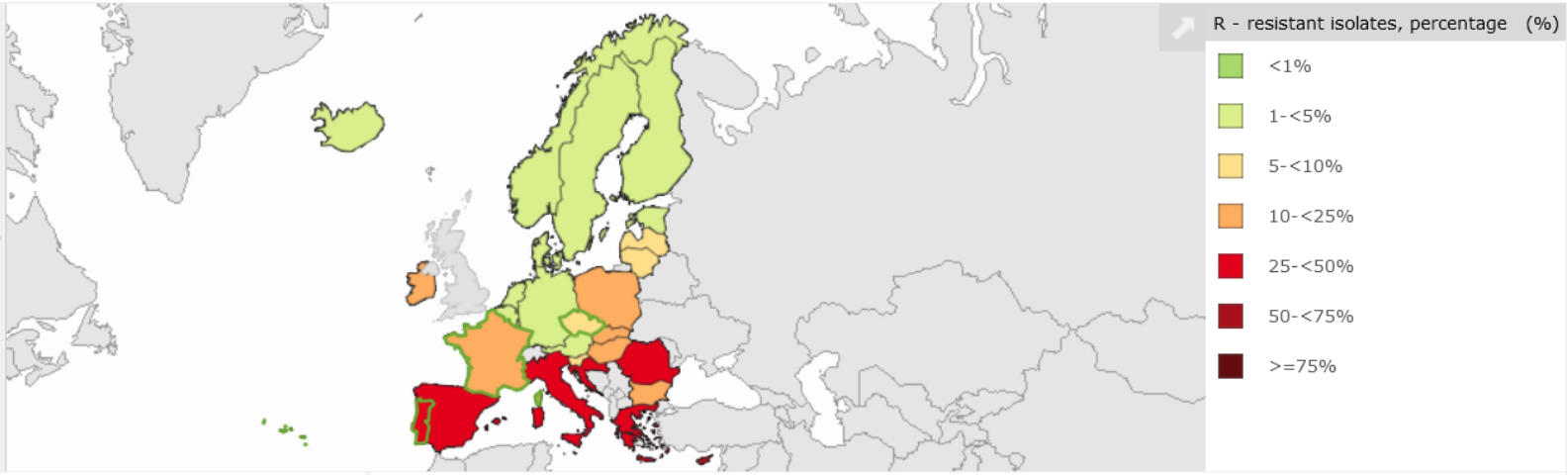
Table 1. Population and hospitals contributing data: coverage, representativeness and blood culture rate, EU/EEA, 2024

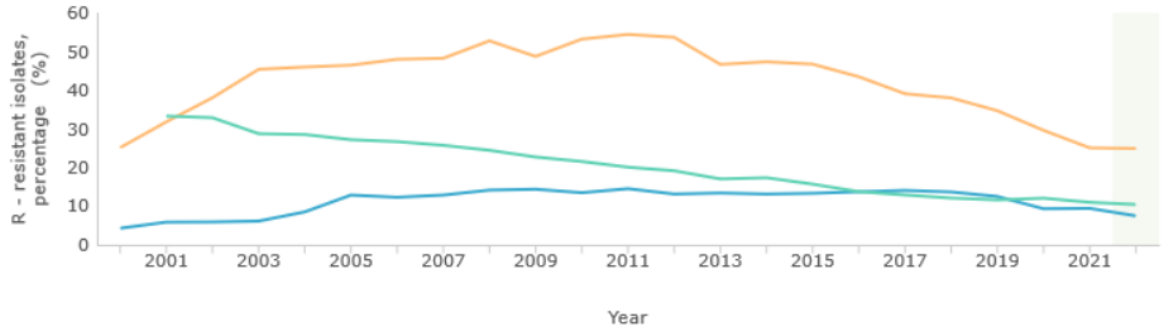
Country	Estimated population coverage[a] (%)	Geographical representativeness[b]	Hospital representativeness[c]	Isolate representativeness[d]	Blood culture rate (blood culture sets/ 1 000 patient-days)[e]
Austria	90	High	High	High	ND
Belgium	40[f]	Medium	Medium	High	145.0[f]
Bulgaria	45	Medium	Medium	Medium	12.2
Croatia	90	High	High	High	39.1
Cyprus	82	High	High	High	70.6
Czechia	70	High	High	High	23.4
Denmark	100	High	High	High	265.8
Estonia	100	High	High	High	38.4

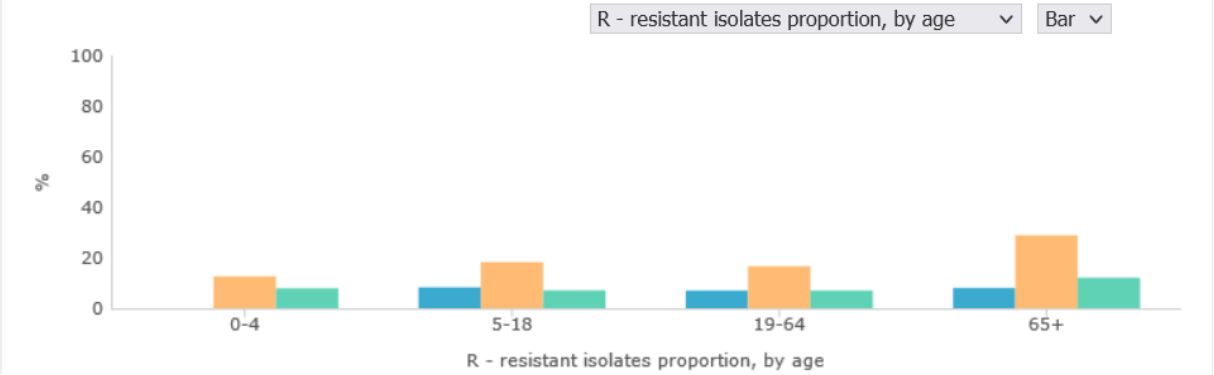
Surveillance Atlas of Infectious Diseases

Antimicrobial resistance | Staphylococcus aureus | Meticillin (MRSA) | R - resistant isolates, percentage | 2022

Region	R - resistant isolates, percentage (%)
Austria	3.9
Belgium	4.2
Bulgaria	12.0
Croatia	31.1
Cyprus	50.8
Czechia	7.5
Denmark	1.9
Estonia	2.2
Finland	2.3
France	10.4
Germany	3.9







Czechia Portugal France

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Freely available information on AMR surveillance in Europe from 2000

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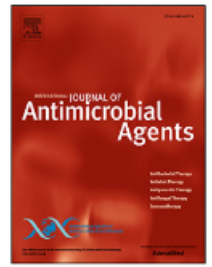


MRSA surveillance programmes worldwide: moving towards a harmonised international approach

Valérie O. Baede[1], Michael Z. David[2], A
Michael Borg[6], Grainne Brennan[7], Bouc
Hege Enger[12], Marie Hallin[13], Marina Iv
Kuntaman Kuntaman[16,17], Anders Rhod
Bruno Pichon[20], Dewi Santosaningsih[21
Guido Werner[25], Dorota Żabicka[11], Hele
Margreet C. Vos[1,*], for the MRSA Surve
Study Group for Nosocomial Infections
Staphylococci and Staphylococcal Disea

survey on MRSA surveillance programmes and organised a webinar to discuss the programmes' strengths and challenges as well as guidelines for harmonisation. Completed surveys represented 24 MRSA surveillance programmes in 16 countries. Several countries reported separate epidemiological and microbiological surveillance. Informing clinicians and national policy-makers were the most common purposes of surveillance. Surveillance of bloodstream infections (BSIs) was present in all programmes. Other invasive infections were often included. Three countries reported active surveillance of MRSA carriage. Methodology and reporting of antimicrobial susceptibility, virulence factors, molecular genotyping and epidemiological metadata varied greatly. Current MRSA surveillance programmes rely upon heterogeneous data collection systems, which hampers international epidemiological monitoring and research. To harmonise MRSA surveillance, we suggest improving the integration of microbiological and epidemiological data, implementation of central biobanks for MRSA isolate collection, and inclusion of a representative sample of skin and soft-tissue infection cases in addition to all BSI cases.

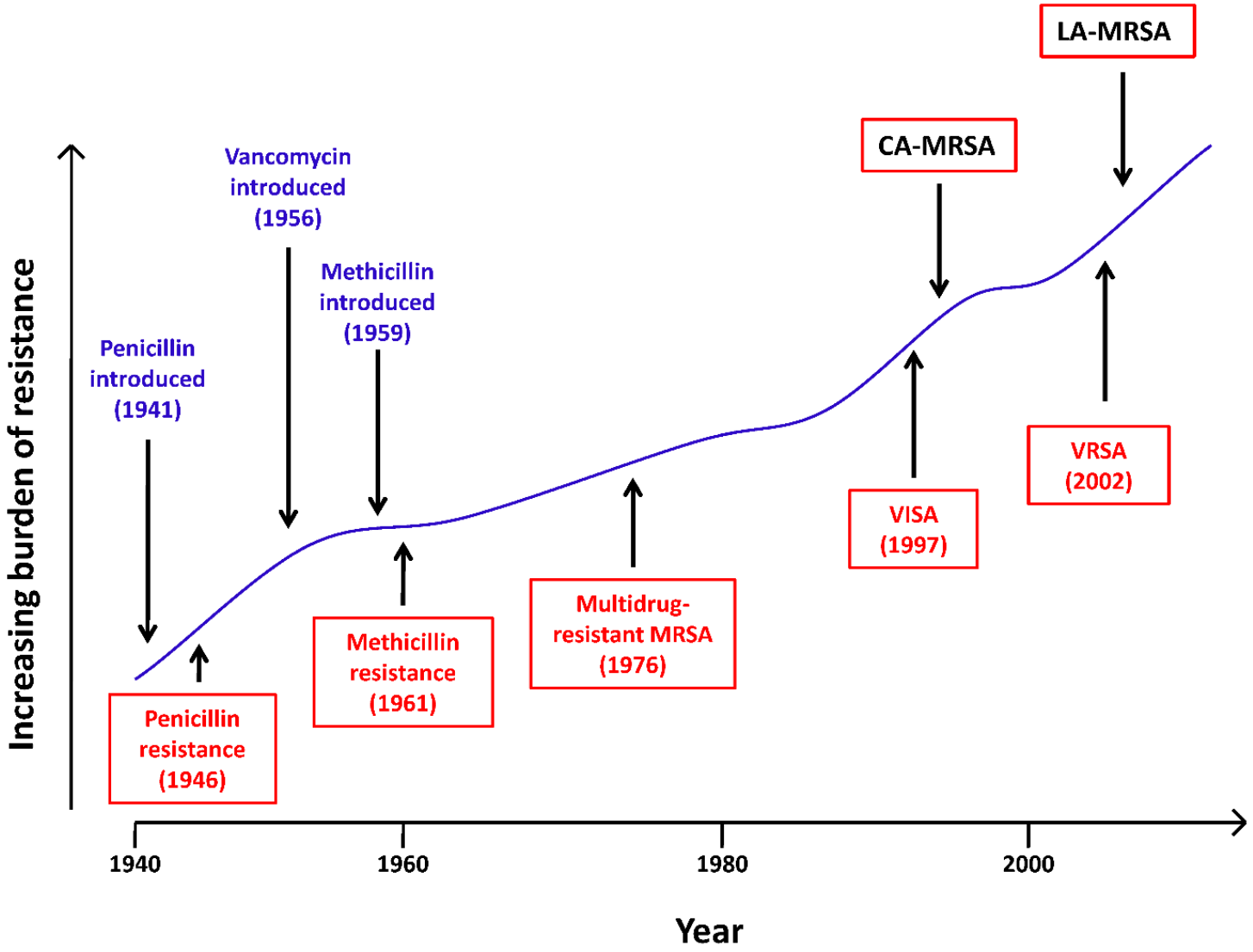
Community spread of resistence is much less studied

Staphylococcus aureus

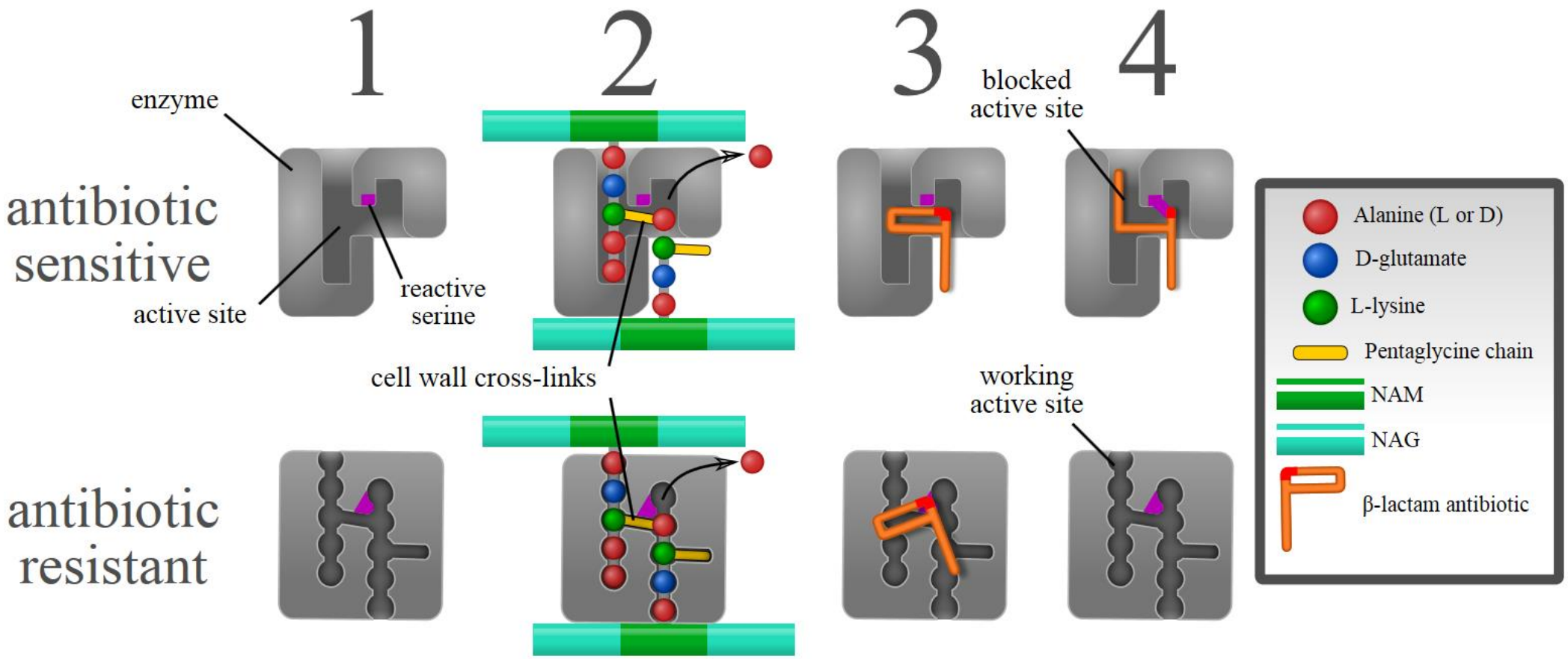
S. aureus – the first superbug

- 1940s – pandemic penicilin resistant-*S. aureus* – enzym penicillinase
- Introduction of methicillin (1959)
  - Semisynthetic derivate of penicillin
  - Resistant to penicillinase
- MRSA (methicillin-resistant *S. aureus*) 1961
  - Resistance to penicillin, methicillin (oxacillin) and cefalosporins
  - MDR: often resistant to fluoroquinolones, tetracyclines, macrolides and aminoglycosides
  - Susceptible to vancomycin, linezolid, daptomycin
  - Higher mortality and morbidity compare to MSSA

Gradual increase of resistence in *S. aureus*

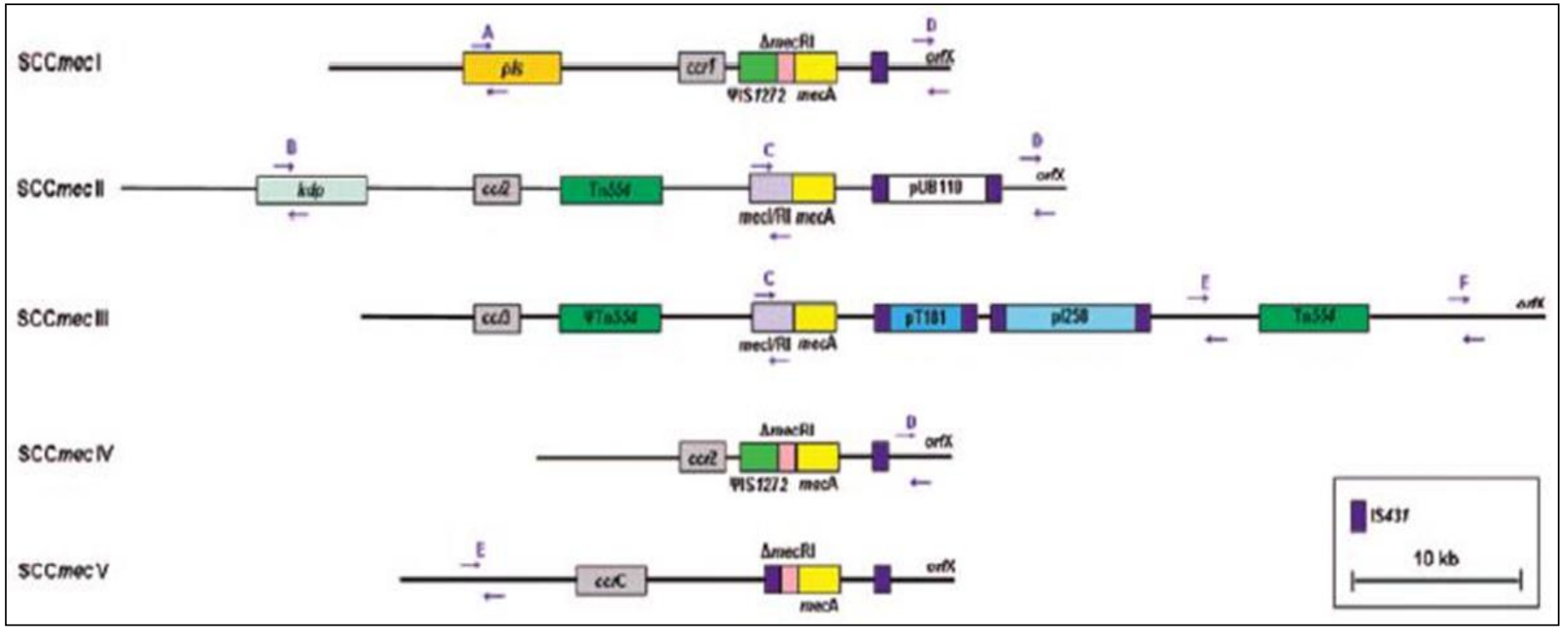


Mechanism of MRSA resistance

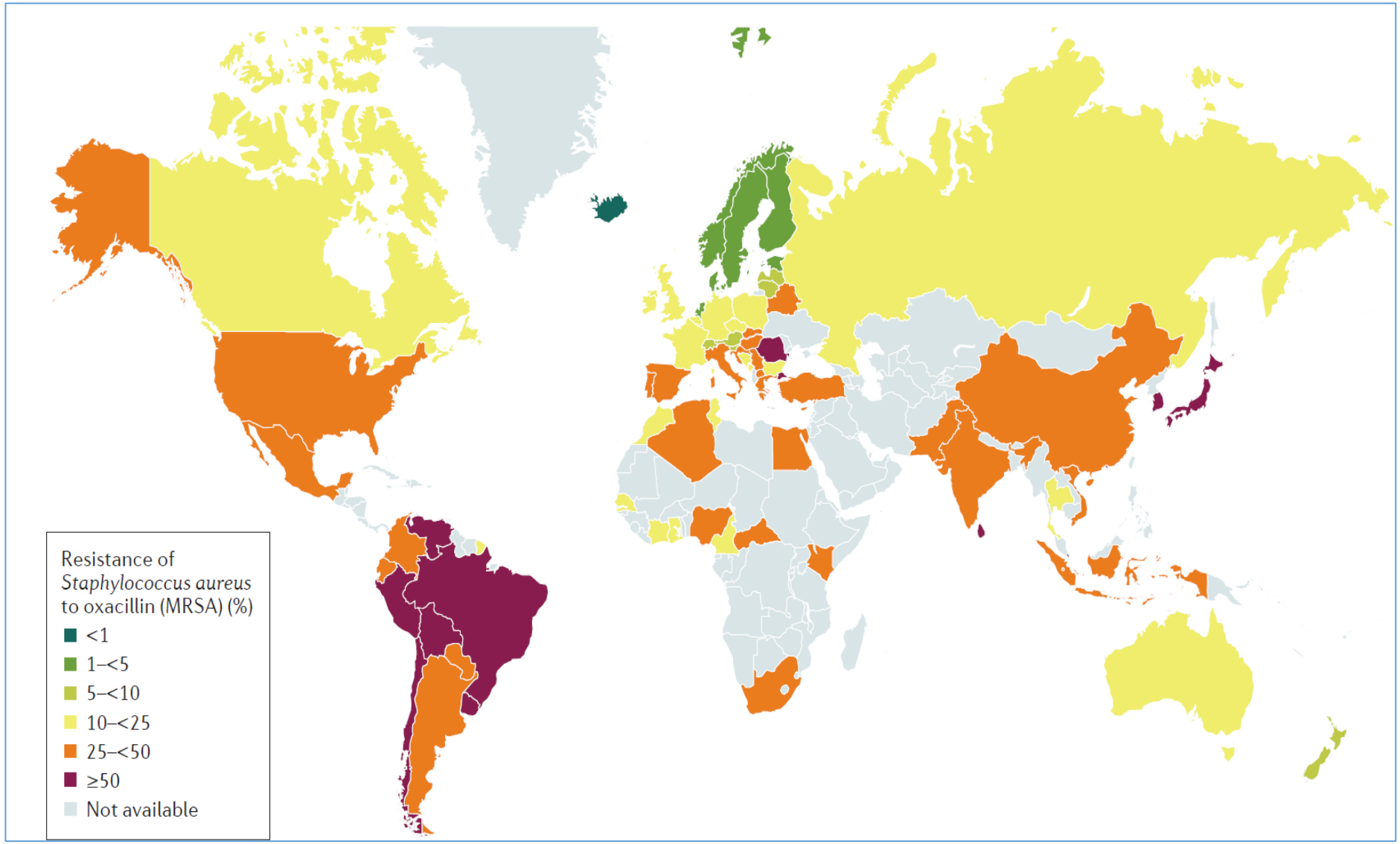


Genetic background for MRSA

- SCC*mec* cassette
  - Gene cassette (mobile genetic element)
  - Codes for PBP2a on the *mecA* gene (plus several other genes).
  - 7 types of varying size and composition (and sub-types)

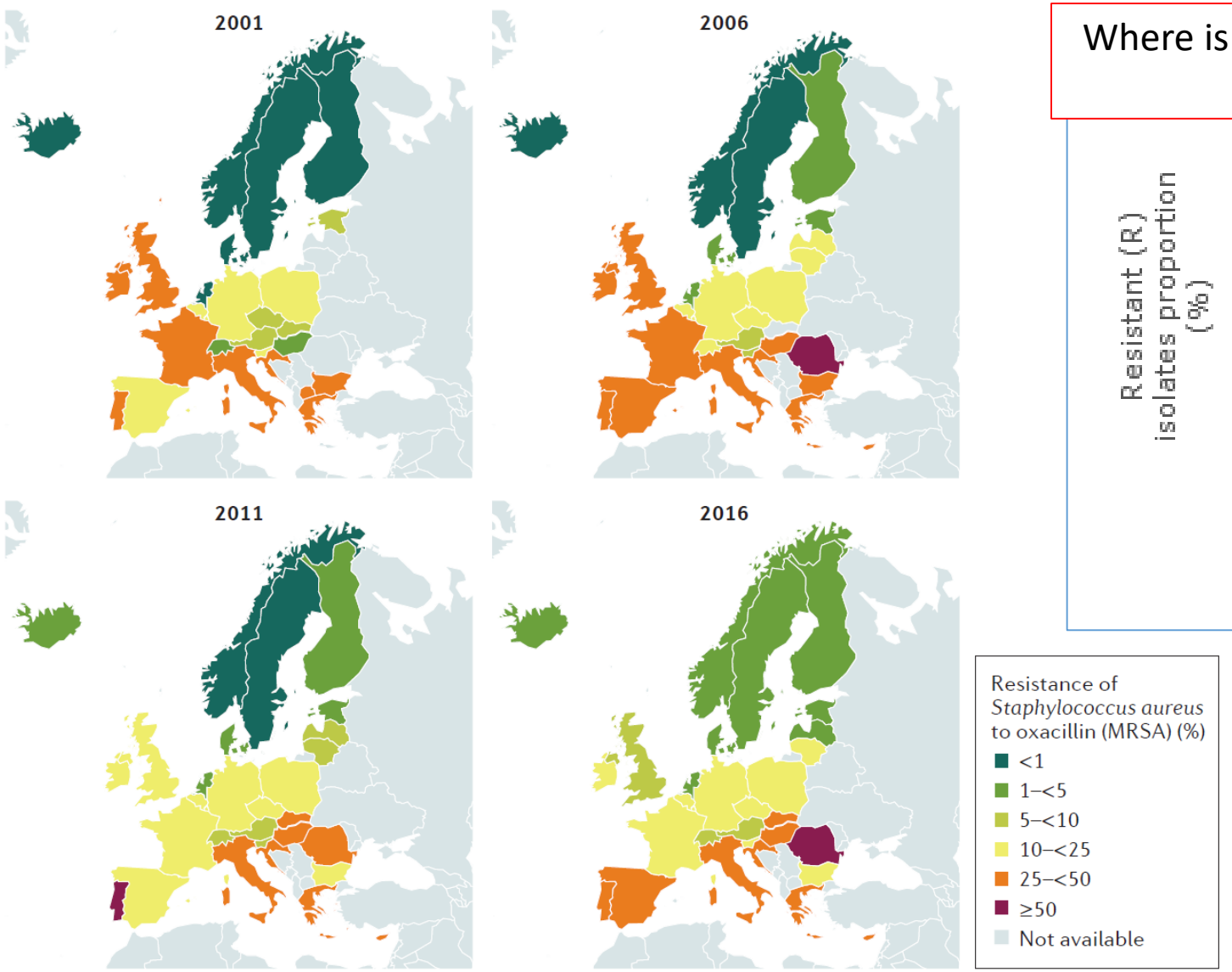


Global MRSA prevalence (%)

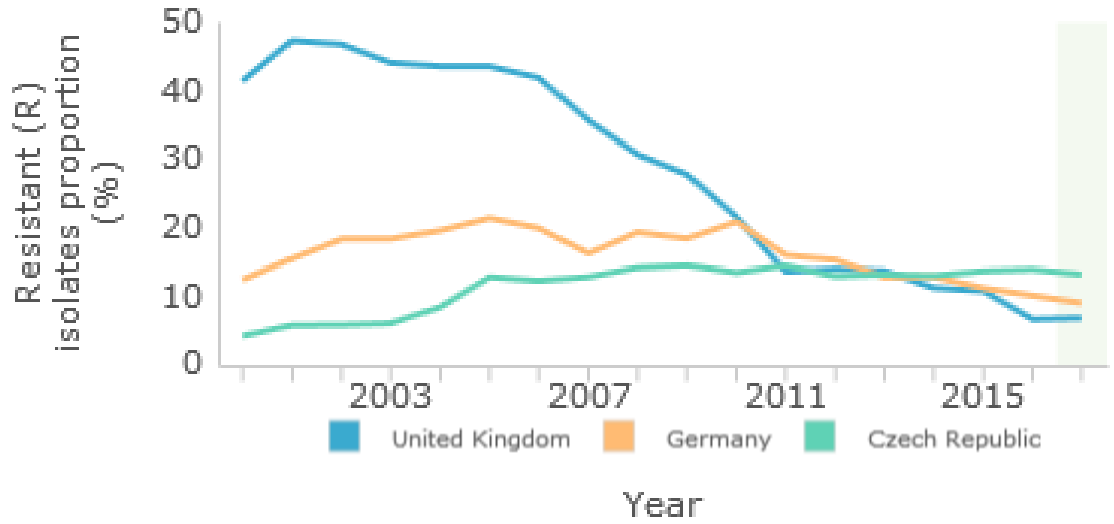


Lee et al 2018

Europe (invasive isolates)



Where is will there is way: Active measures decreased MRSA prevalence in UK



Lee et al, 2018

ECDC, Atlas of antimicrobial resistance

Therapeutic options for MRSA (existing or near future)

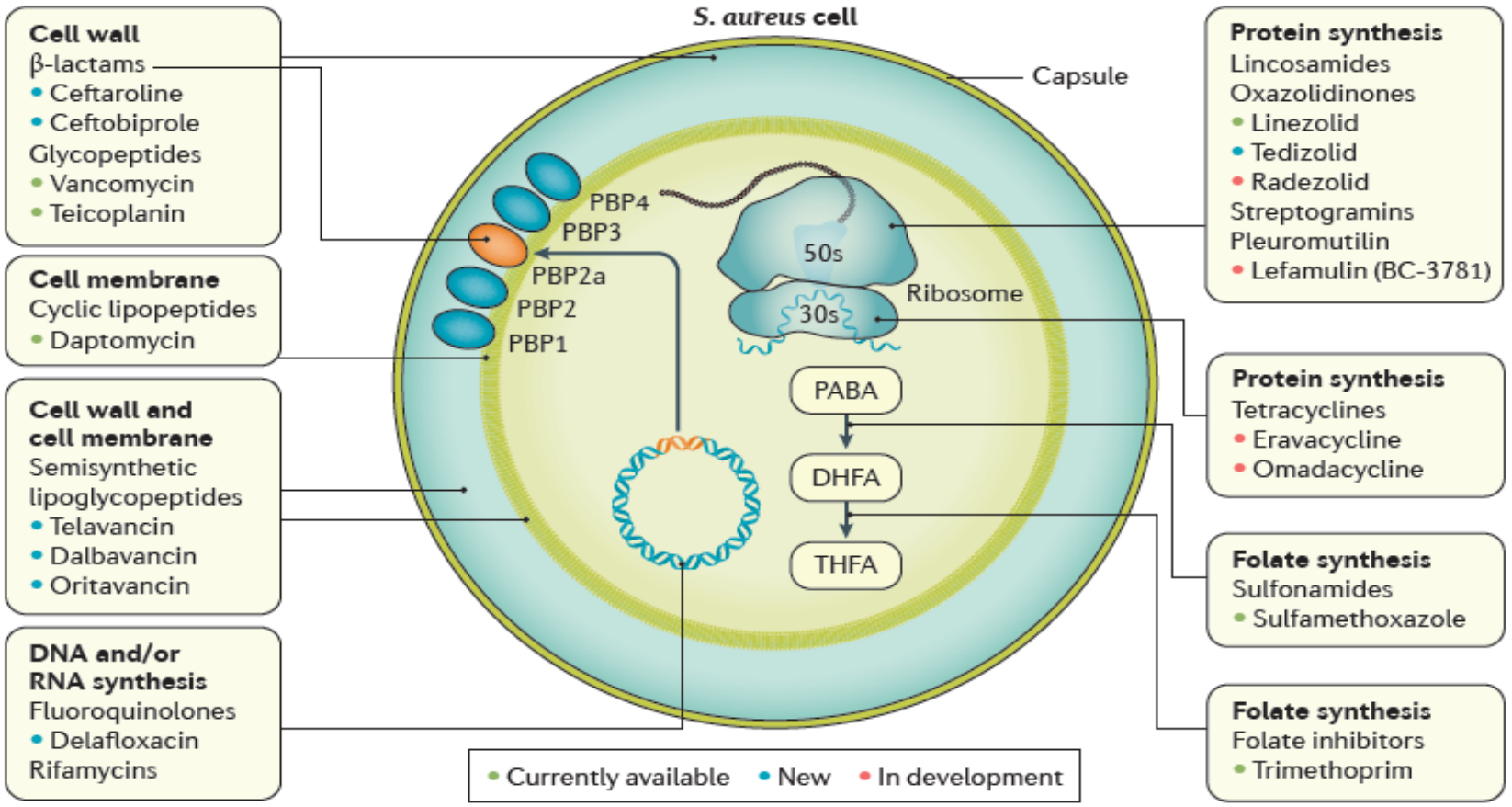
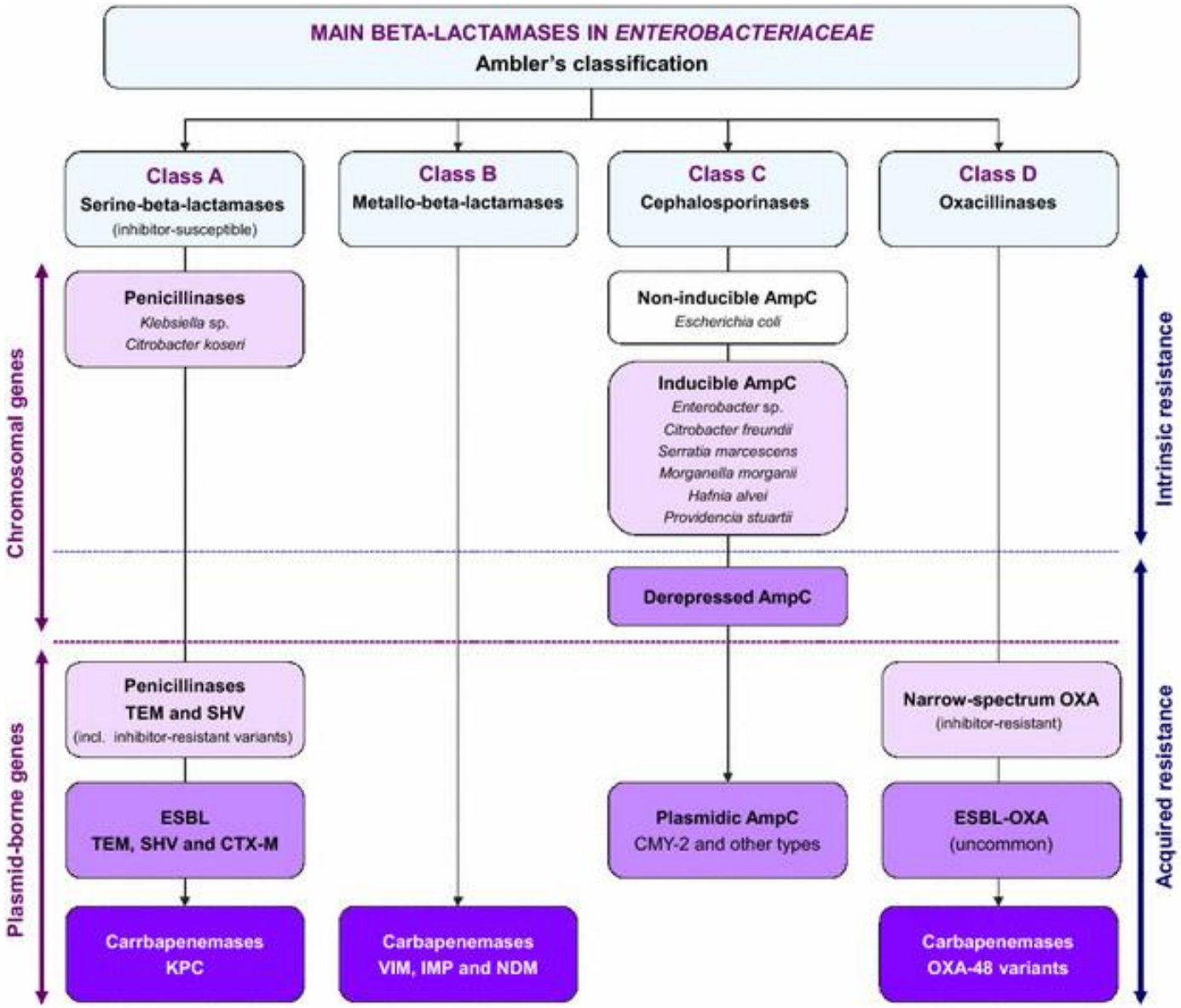


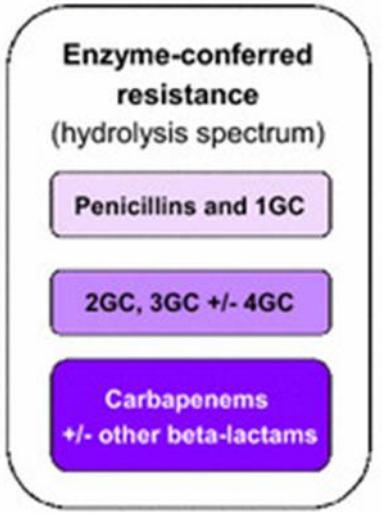
Figure 5 | **Bacterial targets of antibiotics active against MRSA.** Antibiotics have diverse mechanisms of action and target different bacterial structures or metabolic pathways. Existing antibiotic options are in green, new antibiotics approved and on the market are in blue and antibiotics in the pipeline are in orange. DHFA, dihydrofolic acid; PABA, para-aminobenzoic acid; PBP, penicillin-binding protein; *S. aureus*, *Staphylococcus aureus*; THFA, tetrahydrofolic acid. Figure adapted from REF.[229], Macmillan Publishers Limited.

Lee et al, 2018

Enterobacteriaceae

Betalactamases in gramnegative bacteria

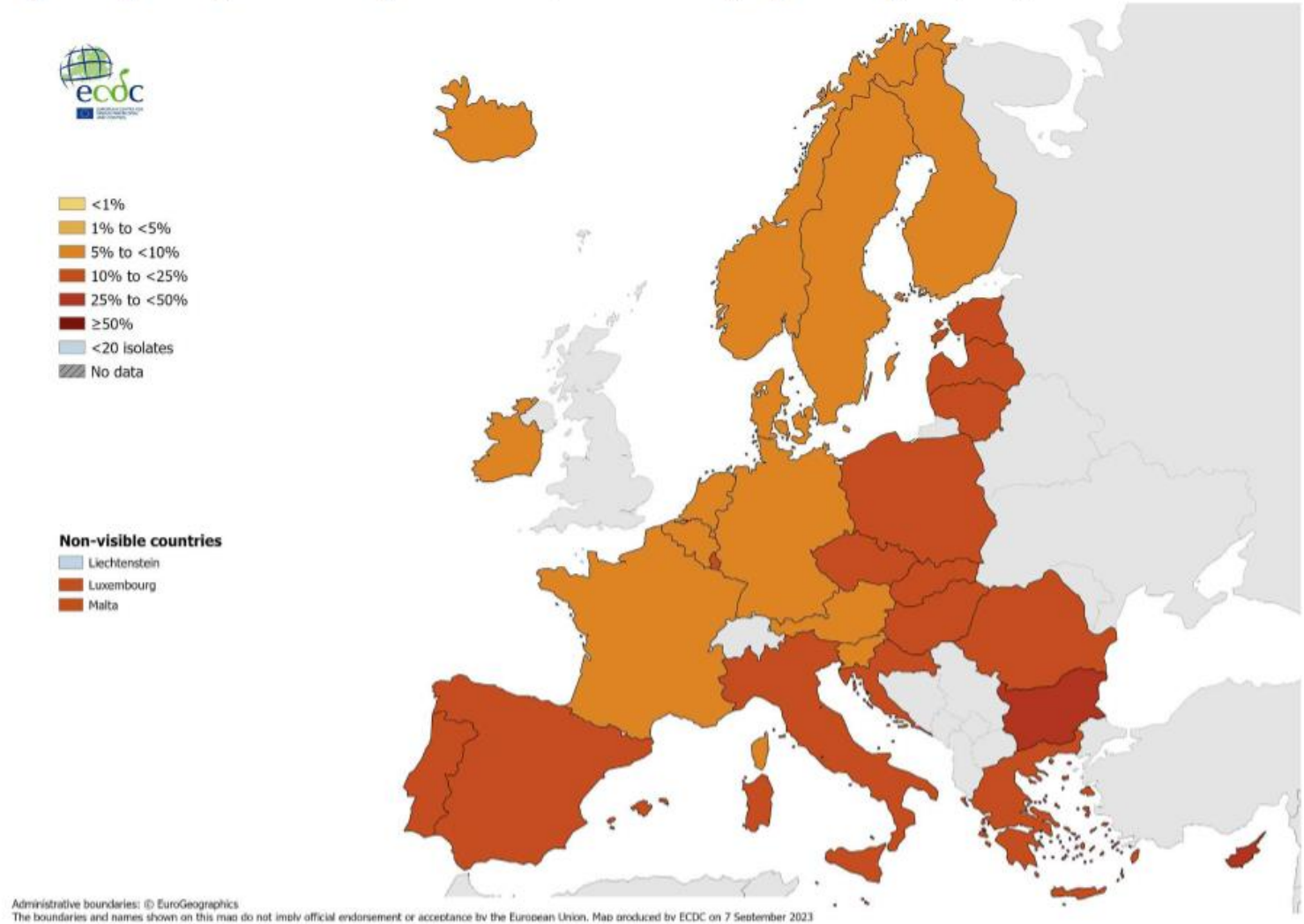




Extended spectrum betalactamase producing bacteria (ESBL)

- *E. coli, K. pneumoniae*
- TEM, SHV, CTX, OXA enzymes
- These enzymes are sensitive to betalactamase inhibitors
- Resistance to penicillins and first to third generation cefalosporins
- Plasmid mediated
- Often resistant to quinolones, trimetoprim, azteonam
- Sensitive to amikacin, carbapenems, colistin

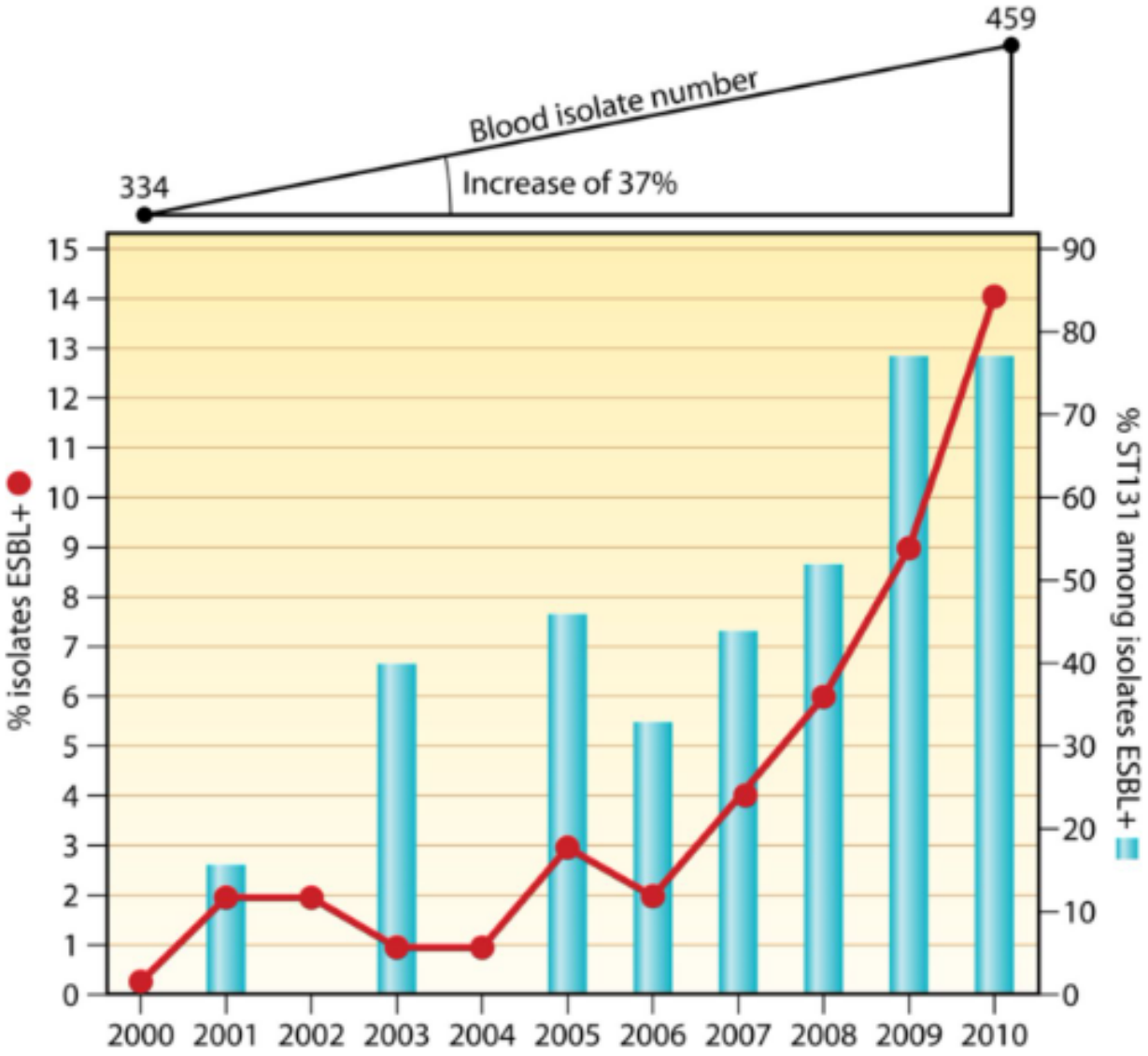
Figure 2. ***Escherichia coli*****. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2022**



Most common MDR in Europe

ECDC: EARSNET report 2022

Steap rise of epidemic clones – *E. coli* ST131 (ESBL+)



ST131: both high patogenic potential and resistance potential

such clones are treat by itself

but also as donors to others G-

Canada, but similar dynamics in USA, and Israel

Nicolas-Chanoine MBertrand X, Madec J. 2014. Escherichia coli ST131, an Intriguing Clonal Group. Clin Microbiol Rev 27

Carbapenem-resistant Enterobacteriaceae (CPE)

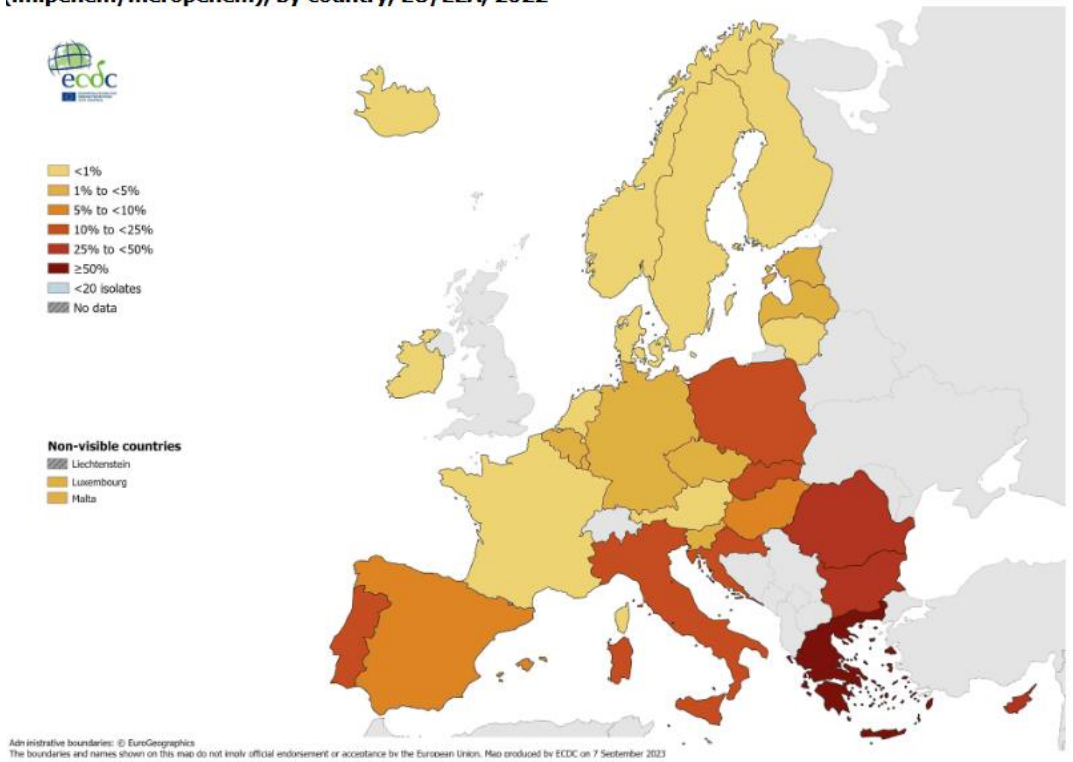
- ***Enterobacteriaceae*** – *Klebsiella pneumoniae, E. coli, Serratia marcescens, Enterobacter, Citrobacter…*
- But also *Pseudomonas aeruginosa* and *Acinetobacter*
- Carbapenems (ertapenem, imipenem, meropenem)
  - For bacteria resistant to other beta-lactams (ESBLs) - the drugs for multidrug-resistant Enterobacteriaceae
- 2008 India: NDM-1 gene - bacteria resistant to everything except colistin and tigecycline
- Spread in hospitals
- Most serious problem today
- Treatment : cefalosporin/inhibitor, aztreonam, colistin, tigecyclin, cefiderocol

Carbapenemases

- Class A
  - KPC, GES, SME, IMI, NMC
  - Sensitive to inhbitors (clavulanic acid, tazobactam, relebactam, avibactam)
  - *Enterobacteriaceae, P. aeruginosa, Acinetobacter* sp
- Class B - metalobetalactamases
  - VIM, IMP, GIM, SIM, NDM,…
  - Resistant to inhibitors
  - *Enterobacteriaceae, P. aeruginosa, Acinetobacter* sp
- Class D - oxacillinases
  - OXA-48 - *K. pneumoniae, E. cloacae, E. coli*
  - OXA-23, OXA-58, OXA-40 - *Acinetobacter* sp
  - Resistant to inhibitors except avibactam/ (OXA-23,48)

Organism Group	Common Examples of Carbapenemases	Clinical Significance
Enterobacterales (CRE)	KPC (*Klebsiella pneumoniae* Carbapenemase), NDM (New Delhi Metallo-β-lactamase), OXA-48	Cause urinary tract, bloodstream, and pneumonia infections. KPC is the most common in the US and Europe.
Pseudomonas aeruginosa (CRPA)	VIM, IMP, KPC	Common cause of hospital-acquired pneumonia and wound infections.
Acinetobacter baumannii (CRAB)	OXA-23, OXA-40, OXA-58	Highly resilient and often found in intensive care units (ICUs). Causes pneumonia and meningitis.

Figure 5. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, EU/EEA, 2022



CPE:
High mortality, over 50% in sepsis
Klebsiella pneumoniae – main threat
Increasing trend
High potential for hospital spread

ECDC: EARSNET report 2022

Risk factors for CPE infection

Recent gastroenterology procedure

Recent intensive care admission

Recent prolonged hospitalisation

Overseas medical treatment

Inapropriate use of antimicrobials

Weakened immunity

Indwelling medical device

Vancomycin resistant enterococci (VRE)

E. faecium
E. faecalis
GIT comensals

vanA or *vanB*
Plasmid mediated

Nosocomial infections in the urinary tract, bloodstream (bacteremia), endocarditis, and surgical wounds.

Intensive Care Units (ICUs) and other units where patients have prolonged hospital stays

Treatment: linezolid, daptomycin, tigecycline, chloramphenycol

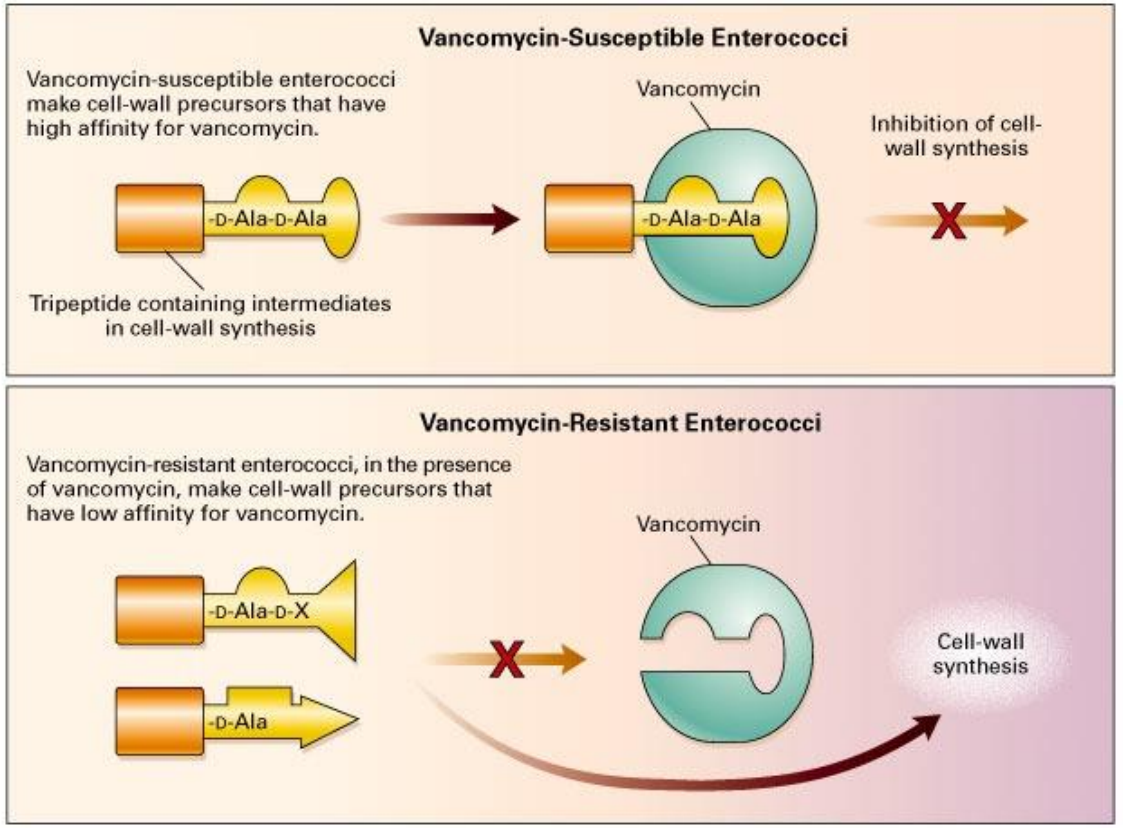
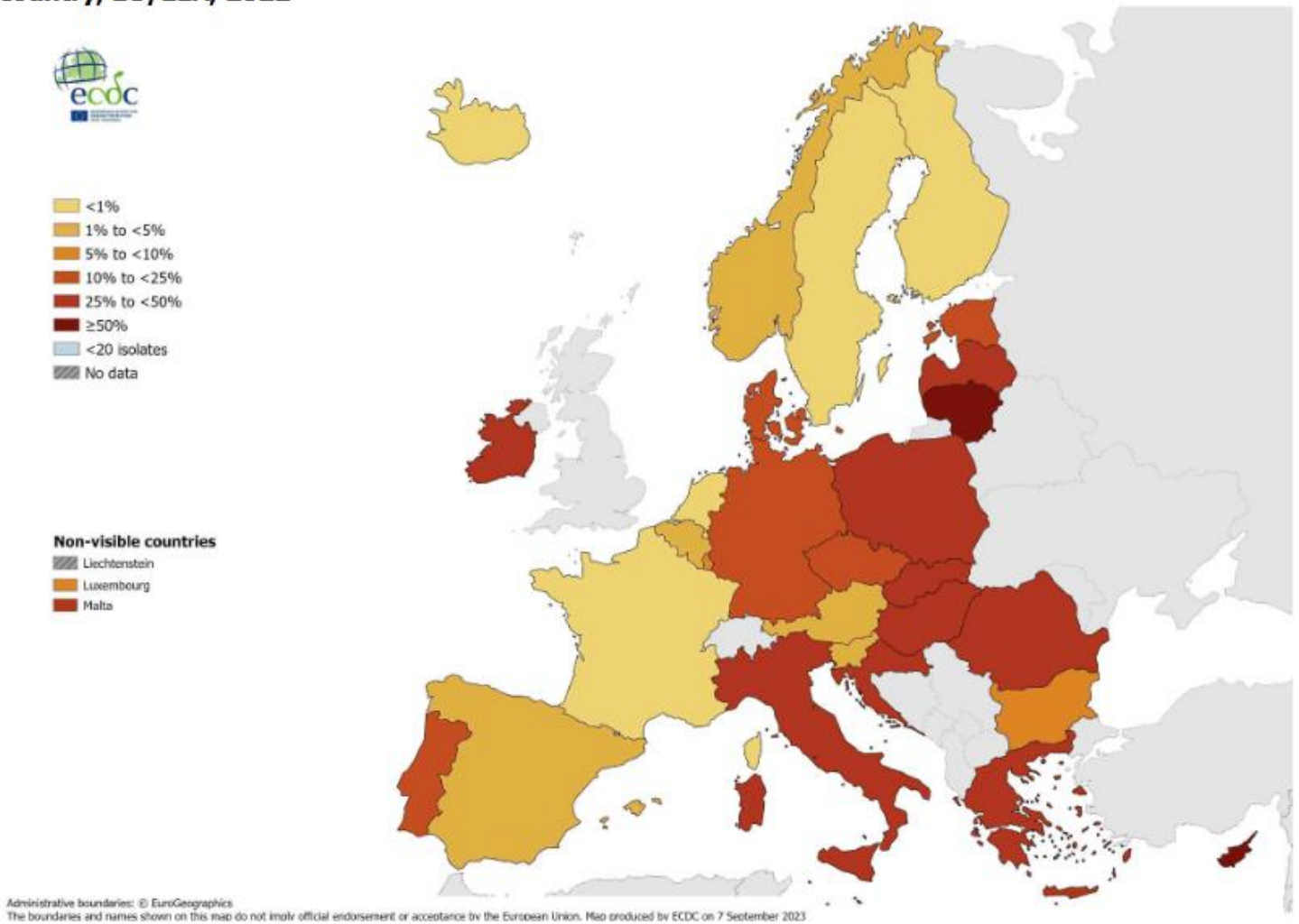


Figure 10. ***Enterococcus faecium*****. Percentage of invasive isolates resistant to vancomycin, by country, EU/EEA, 2022**



Increasing trend

ECDC: EARSNET report 2022

Reserve antibiotics

Classification of antibiotics – different types of therapy

Initial - therapy is started before pathogen identification, broad spectrum to cover all posible causes. E.g. Patient hospitalised with bacterial meningitidis or sepsis

Empirical – treatment without microbiological diagnostics, e.g. Streptococal tonsilitis

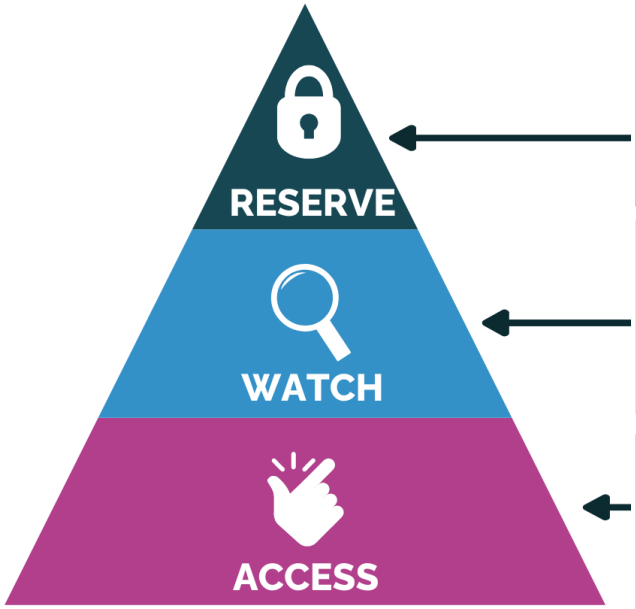
Targetted – known cause end its susceptibility

Deescalation – switch to targetted therapy after identification of cause

Prophylaxis – to prevent infection,e.g. surgical prophylaxis, imunokompromised patients

AWARE classification

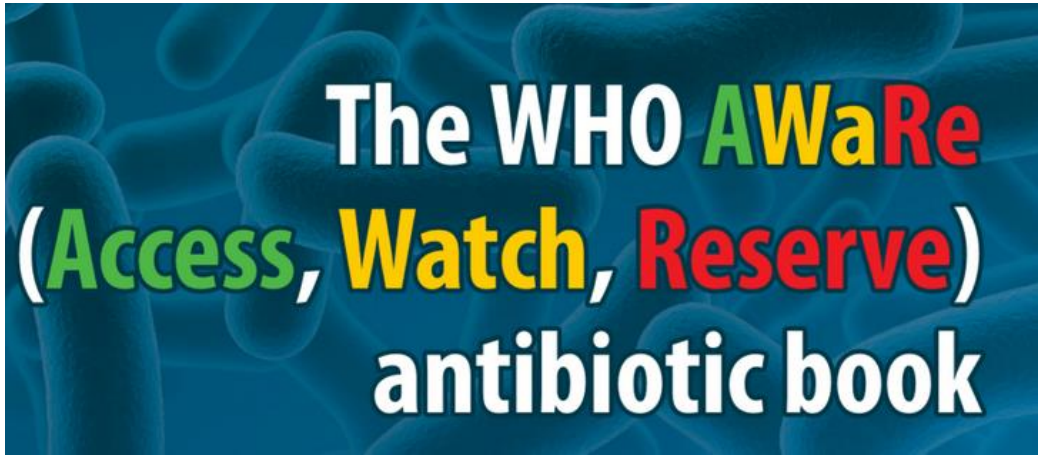
The AWaRe classification is intended as a tool for monitoring antibiotic consumption, defining targets and monitoring the effects of stewardship policies that aim to optimize antibiotic use and curb antimicrobial resistance.



Last line antibiotics to treat MDR bacteria
To be used after other options failed
For serious/complicated infections
New antibiotics

Critically important
High resistence potential,
Limited specific indication

First choice (empiric) for common infection by susceptible bacteria
Save, cheap, low resistence potential
Should be always awailable



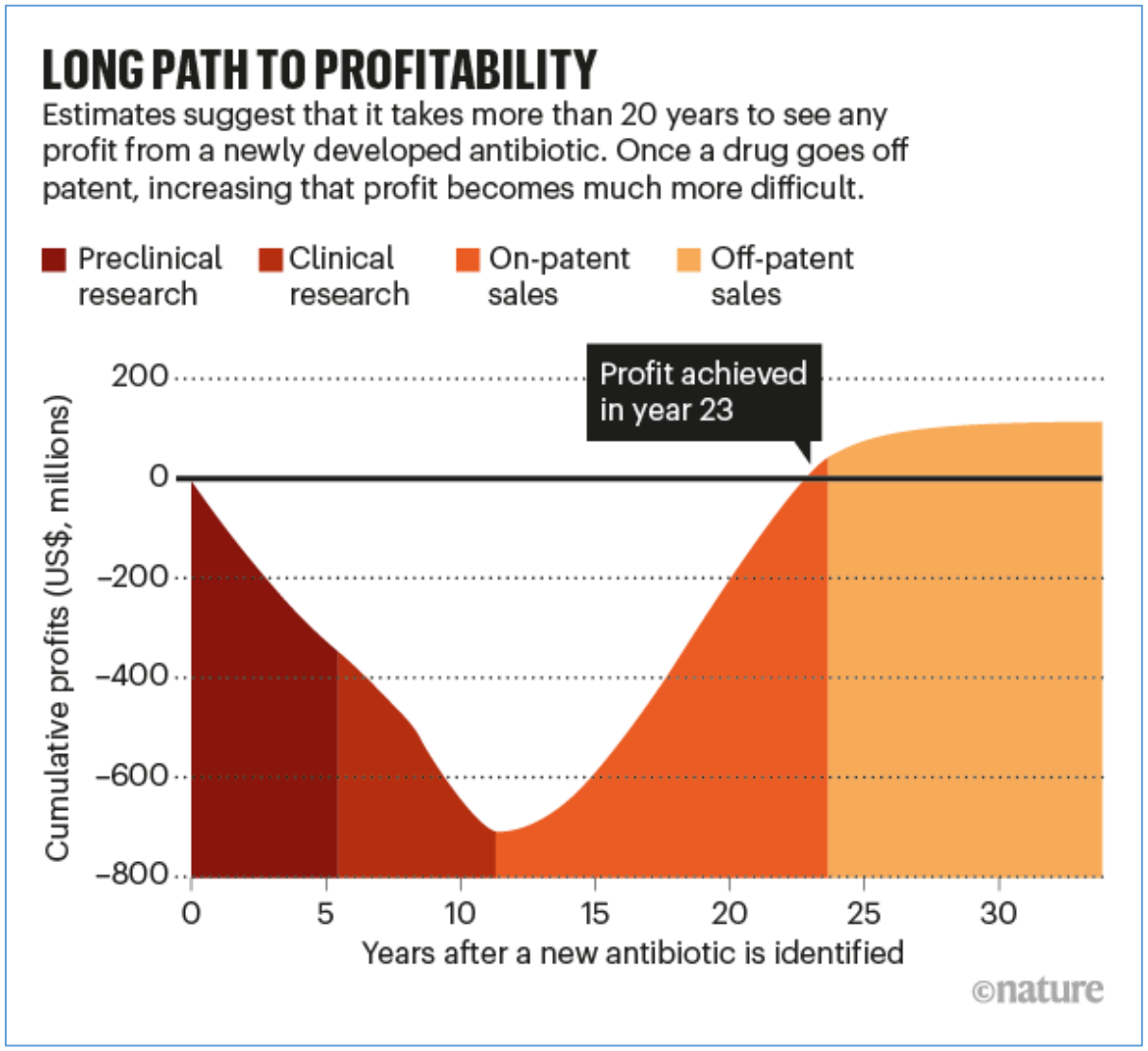
Examples

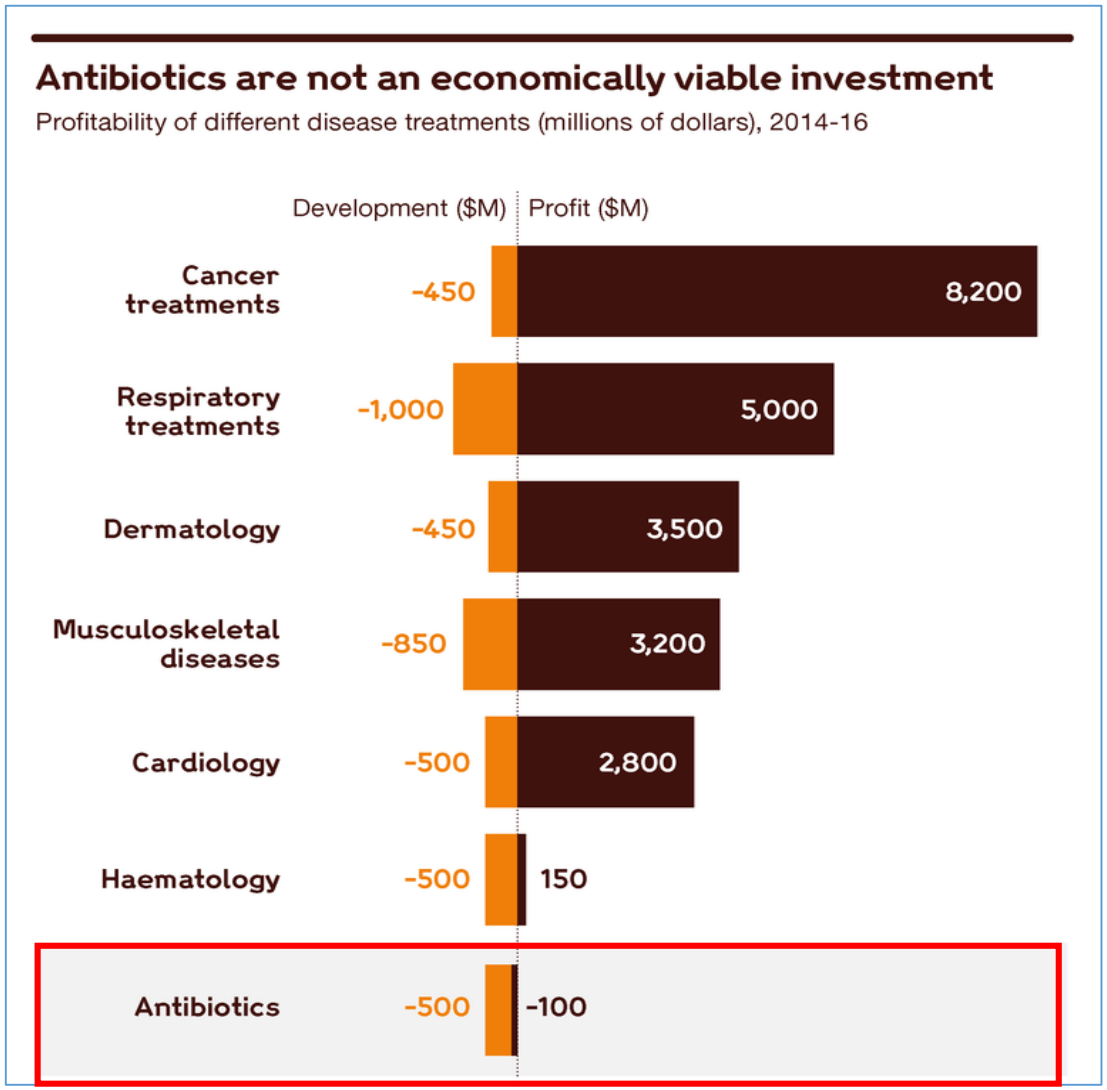
Colistin, tigecycline, linezolid, Meropenem/vaborbactam, Daptomycin, Aztreonam, ceftarolin, cefiderocol

Azithromycin, Ciprofloxacin, 2nd to 4th gen cefalosporins, Erythromycin, fidaxomicin, Meropenem, rifampicin, vancomycin

Ampicillin, clindamycin, doxycyklin, oxacillin, nitrofurantoin, benzylpenicillin, first generation cefalosporins

Antibiotics – high risk business adventure





Price of therapy

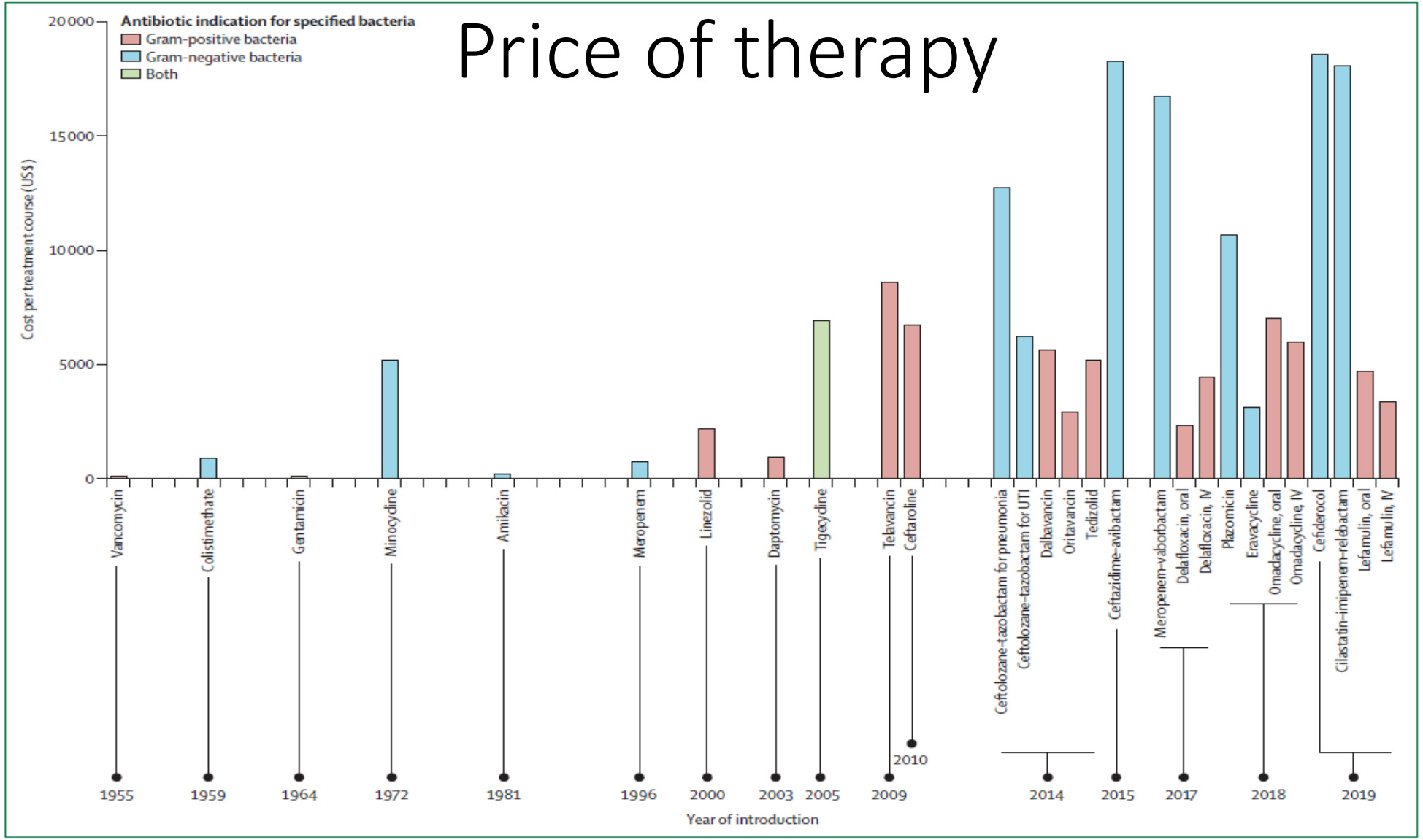
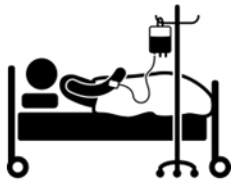


Figure 3: **US price of selected antibiotics introduced between 1955 and 2019**
Prices are shown for a 14-day treatment course in US$ in the USA as of 2021. Selected antibiotics target the following ESKAPE pathogens: vancomycin-resistant *Enterococcus faecium*, methicillin-resistant *Staphylococcus aureus*, carbapenem-resistant *Enterobacterales*, carbapenem-resistant *Acinetobacter baumannii*, and multidrug-resistant *Pseudomonas aeruginosa*. The different colours represent antibiotic indications against specified resistant ESKAPE pathogens. Price data were compiled by Yahav et al (2021).[64] Dates of antibiotic introduction were sourced from Shi et al (2023),[65] Chahine et al (2022),[66] Christensen (2021),[67] Serio et al (2018),[68] Dhariwal and Tullu (2013),[69] Plotkin et al (2011),[70] and Laxminarayan et al (2010).[71] ESKAPE=*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp. IV=intravenous. UTI=urinary tract infection.

What drives antibiotic resistance?





- Consumption of antibiotics
- Spread of resistant bacteria
- Shortage of new ATBs

- Increasing population density
- <u>Ageing population</u>
- Diseases of civilisation
- Poor population health
- Ecological factors
- Globalisation

Hospitals and healthcare facilities are the primary place where the problem of AMR manifests itself

Baquero 2021, International Microbiology: Threats of antibiotic resistance: an obliged reappraisal

Consumption of antimicrobial drives resistance but…

BECOME AN ANTIBIOTIC GUARDIAN

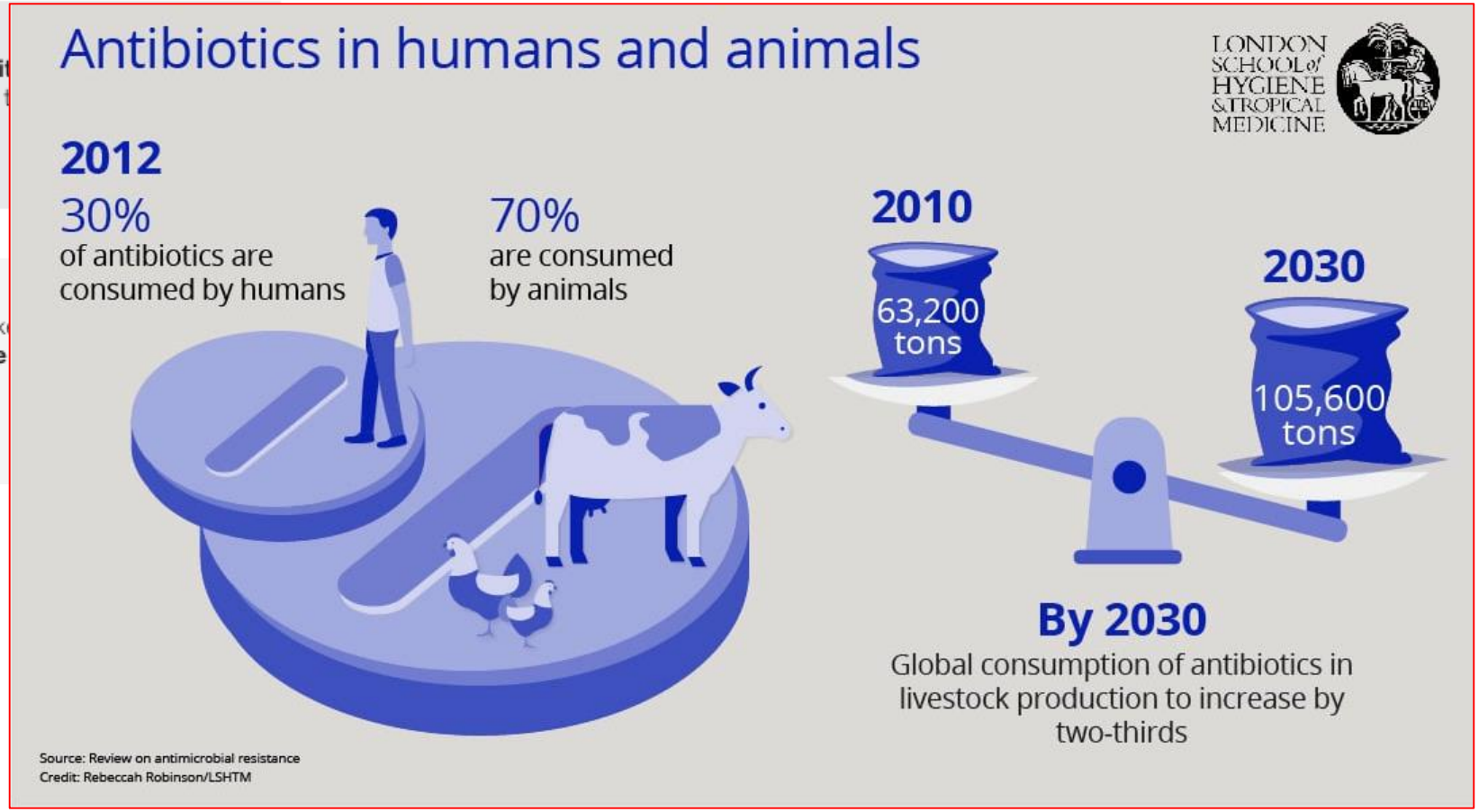
Protect yourself, your family, friends, colleagues and patients against the spread of antibiotic resistance.

10% of the sore throats and 20% of acute sinusitis benefit from antibiotic treatment but t
prescription rates are much higher than this

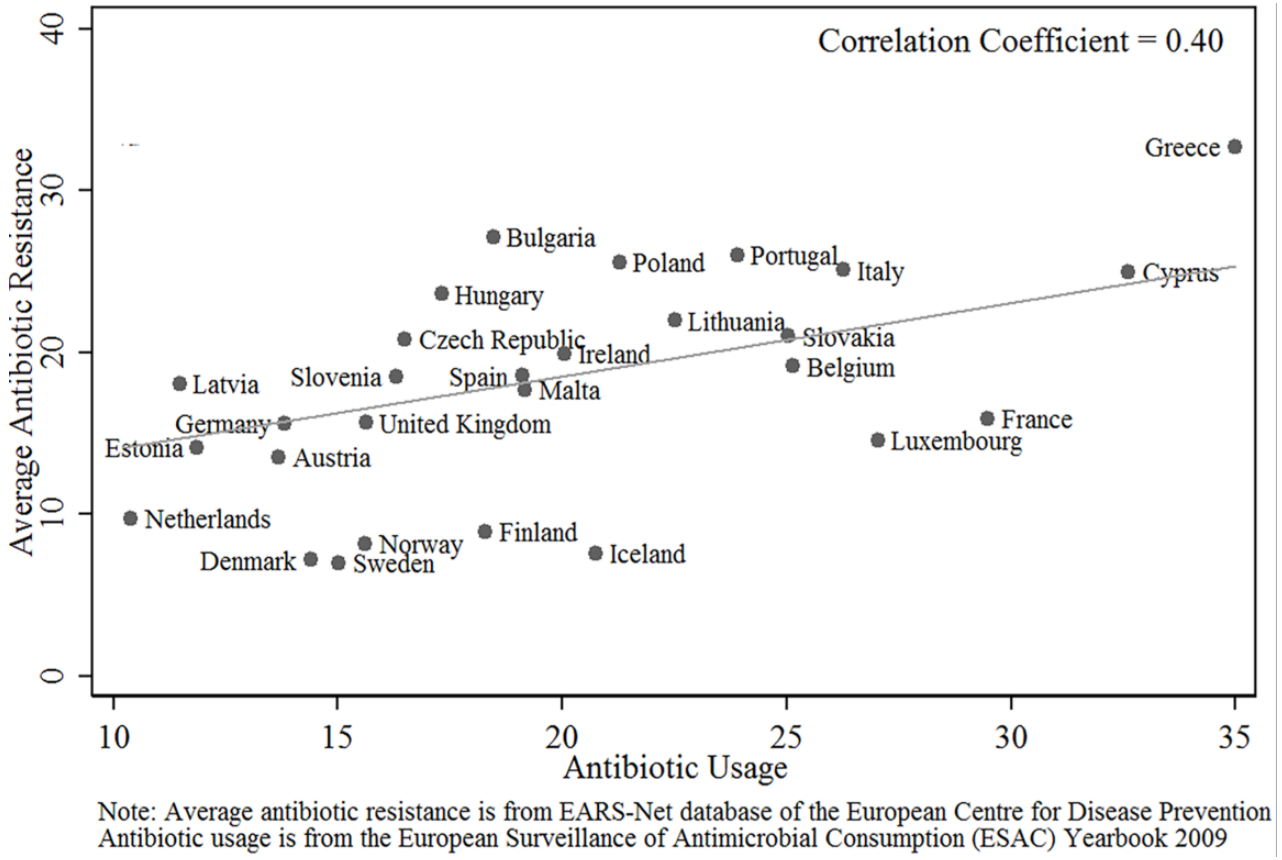
1 IN 3 People in England tak
at least **one course of antibiotics each year**

Advise patients and the public to take these simple actions to keep antibiotics working:

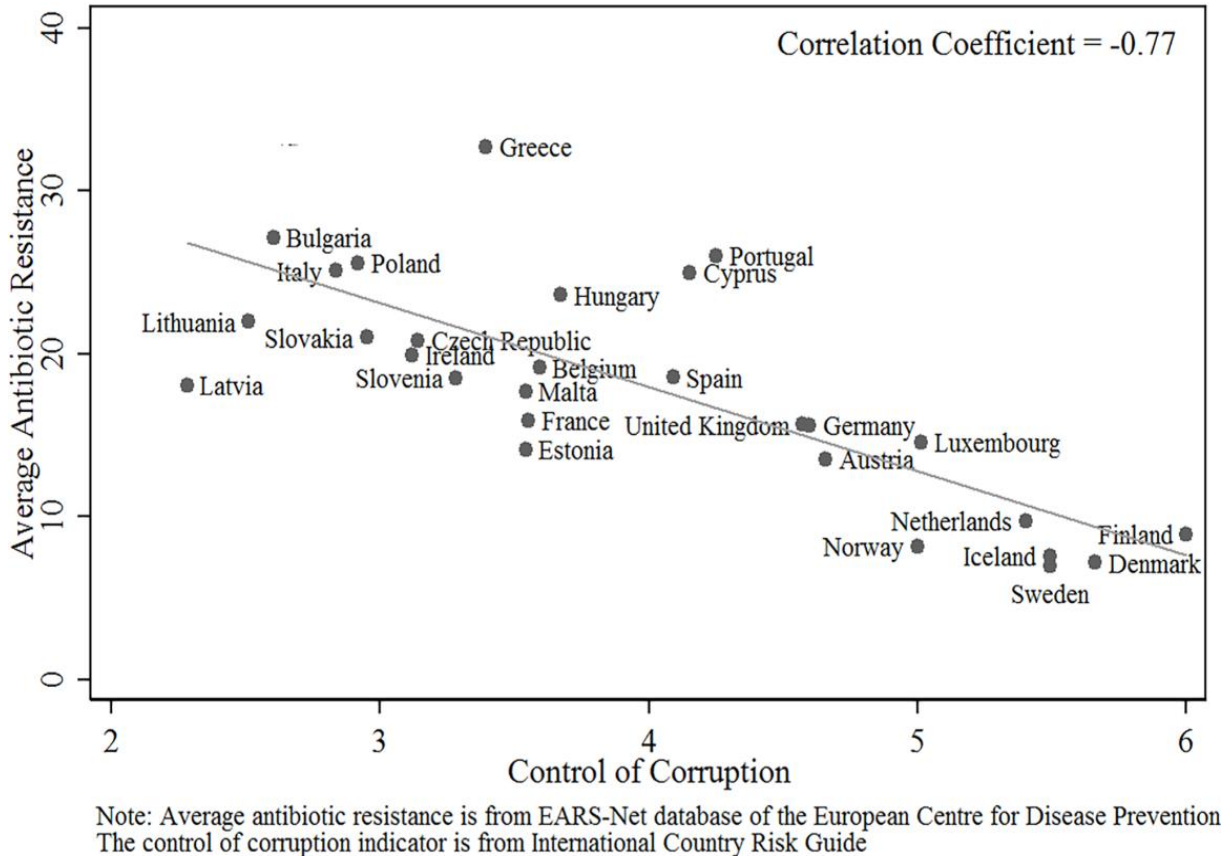
- Ask their pharmacist to recommend medicines to help treat cold or flu symptoms or pain
- Take antibiotics exactly as prescribed, never save them for later, never share them with others
- To spread the word, tell their friends and family about antibiotic resistance



AMR problem is about disfunctional healthcare and society



Note: Average antibiotic resistance is from EARS-Net database of the European Centre for Disease Prevention
Antibiotic usage is from the European Surveillance of Antimicrobial Consumption (ESAC) Yearbook 2009



Note: Average antibiotic resistance is from EARS-Net database of the European Centre for Disease Prevention
The control of corruption indicator is from International Country Risk Guide

Collignon P, Athukorala PC, Senanayake S, Khan F. Antimicrobial resistance: the major contribution of poor governance and corruption to this growing problem. PLoS One 2015;10:e0116746.

Meyer E, Gastmeier P, Schwab F. National MRSA rates run along with fair play of national football teams: a cross-national data analysis of the European Football Championship, 2008. Infection. 2013 Feb;41(1):215-8.

Thank you for your attention!