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AMR
Är kampen forlorad?

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ESCMID President

Är Kampen forlorad?

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- Where?
  - Locally
  - In the Nordic countries
  - Worldwide

- When?
  - Now
  - In a year
  - In 20 years

Worldwide Burden of AMR (2019-2021)

- Infections are associated with 7.75 million deaths per year
  - 1.14 M deaths directly attributed to resistant bacterial infections (ABR / AMR)
  - 20% of deaths are in children < 5 years

- Infections are not only causing deaths but also severe morbidity!
  - 704 million DALYS were lost due to infection in 2019 = 27% of the total DALYs!!
    - 40% in children < 5 years = 65% of the total DALYs in <5 years!!

DALYs = the loss of the equivalent of one year of full health

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, The Lancet, January 2022
Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050 - The Lancet, September 2024
Global burden associated with 85 pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019 - The Lancet Infectious Diseases

Worldwide Burden of AMR (ABR), 2019-2050

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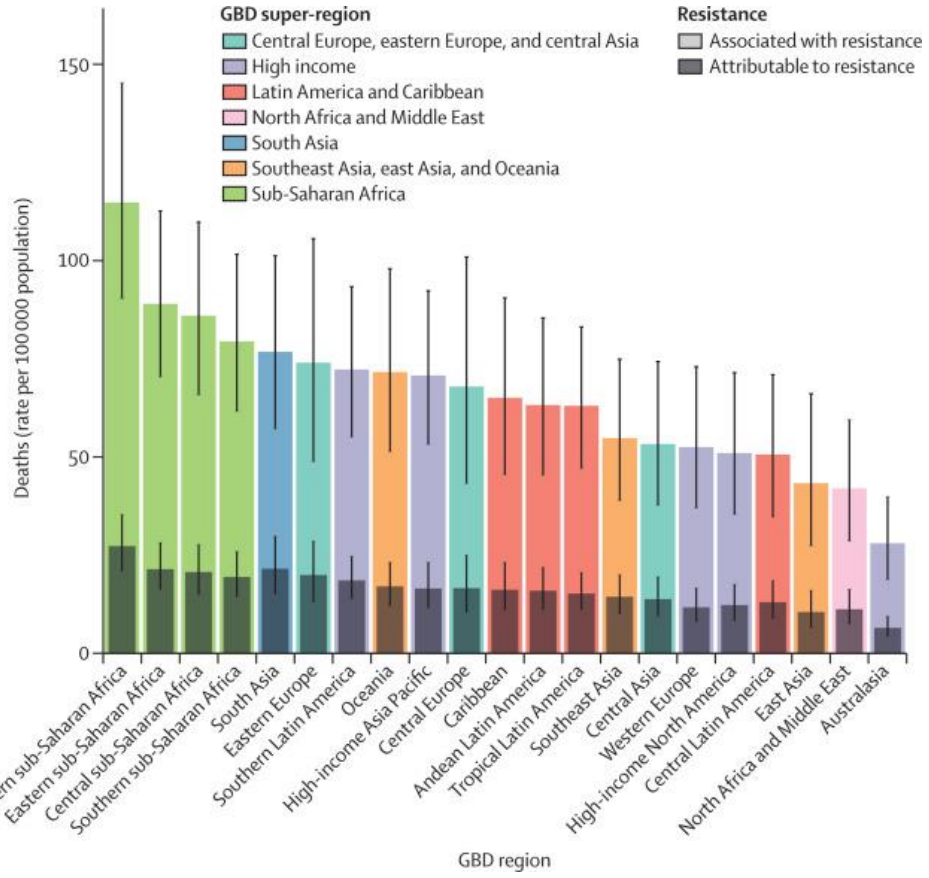
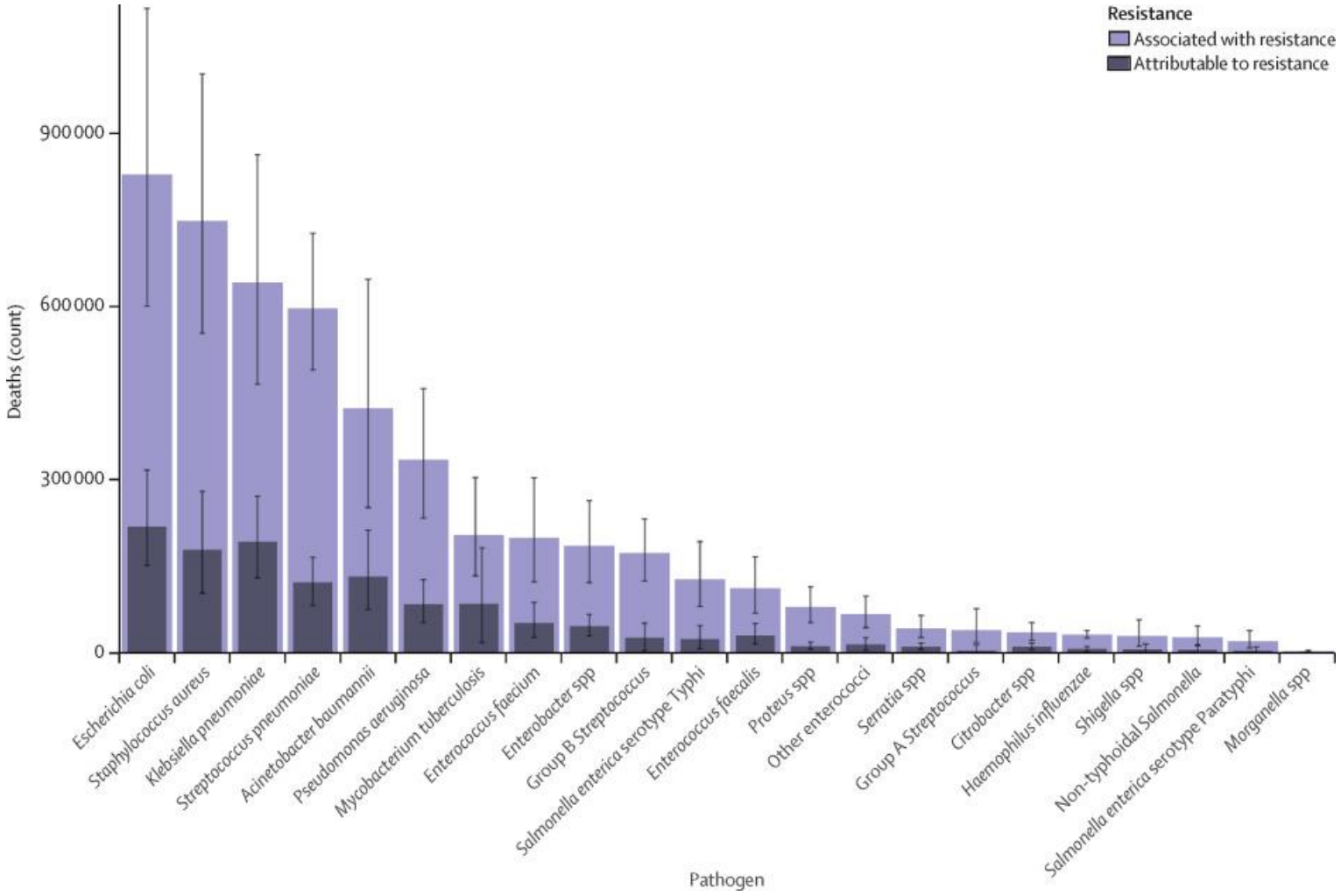
- If left unchecked AMR mortality will increase to 1.9 million/year in 2050
  - 39 million AMR deaths from 2025-2050

- The largest burden is seen in Sub-Saharan Africa and Southeast Asia



Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, The Lancet, January 2022
Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050 - The Lancet, September 2024

Global deaths attributable/associated to AMR

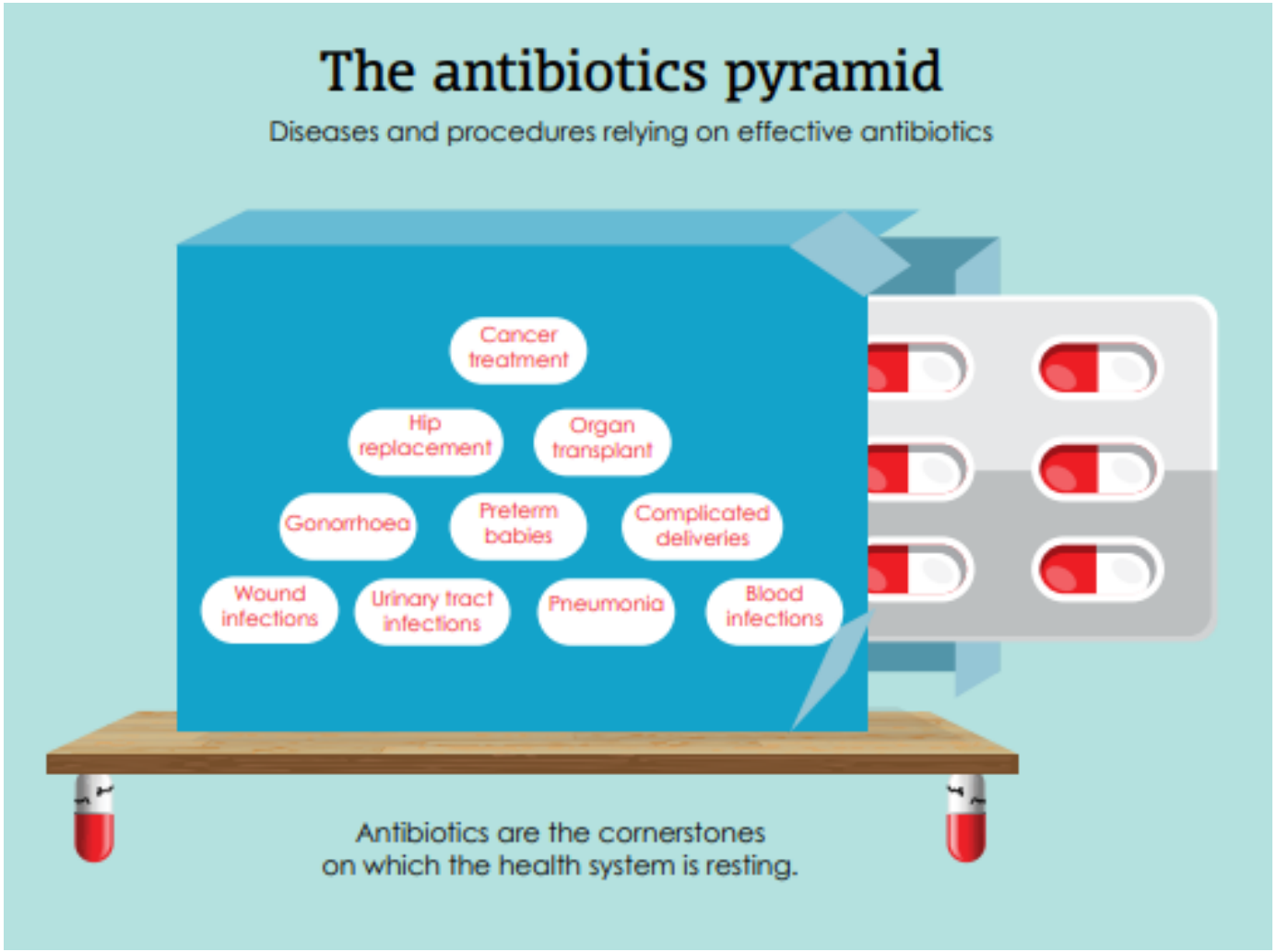


6 bacteria: >70 of the deaths!

- *E.coli*
- *S. aureus (MRSA >100.000)*
- *K. pneumonia*
- *S. pneumonia*
- *A. baumanii*
- *P.aeruginosa*

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis - The Lancet

Loss of antibiotics = loss of modern health care!



ReAct (2019) p. 19 When the Drugs Don't Work

Drug resistant-infections: not only a major threat to global health – but also to economy!

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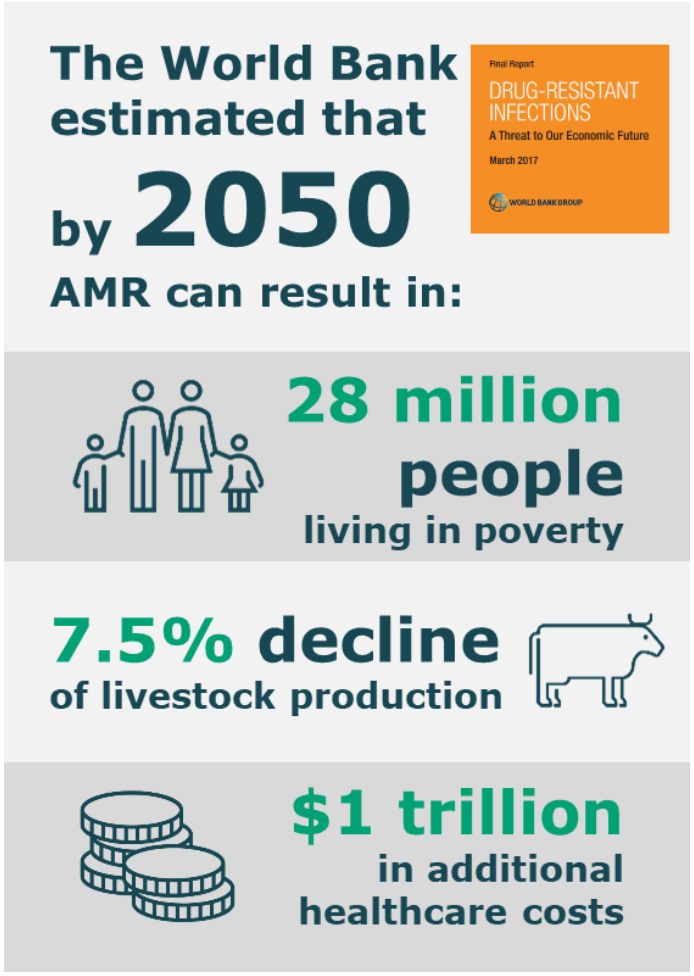

New figures from GLG-AMR / OECD (April2024)

- Extra cost in health care and loss of productivity of US$ **900 mill per year!!!**

Resistance is a natural - but complex phenomenon

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- AMR is a **natural mechanism** that allows microorganisms to survive
- AMR is present **in ALL bacterial communities** (human, agricultural, environment) both in pathogenic and non-pathogenic/commensal bacteria
  - Intrinsic – (the bacteria is born with the Resistance)
  - Acquired
    - De novo “creation” i.e. mutations
    - Uptake of antimicrobial resistance genes (ARG) – also called horizontal gene transfer (HGT)
  - ARG can be part of mobile genetic elements harboring other genes favoring its spread also between different bacterial species
  - Exchange of resistance genes and antibiotic resistant bacteria do not respect borders or sectors!

Resistance is a natural - but complex phenomenon

- AMR is a natural mechanism that allows microorganisms to survive
- AMR
- both

Spread of and level of resistance is determined by

- Use of antimicrobials (AMU)
- Transmission of ARB/ARGs

- ARG can be part of mobile genetic elements harboring other genes favoring its spread also between different bacterial species
- Exchange of resistance genes and antibiotic resistant bacteria do not respect borders or sectors!

Resistance is a natural - but complex phenomenon

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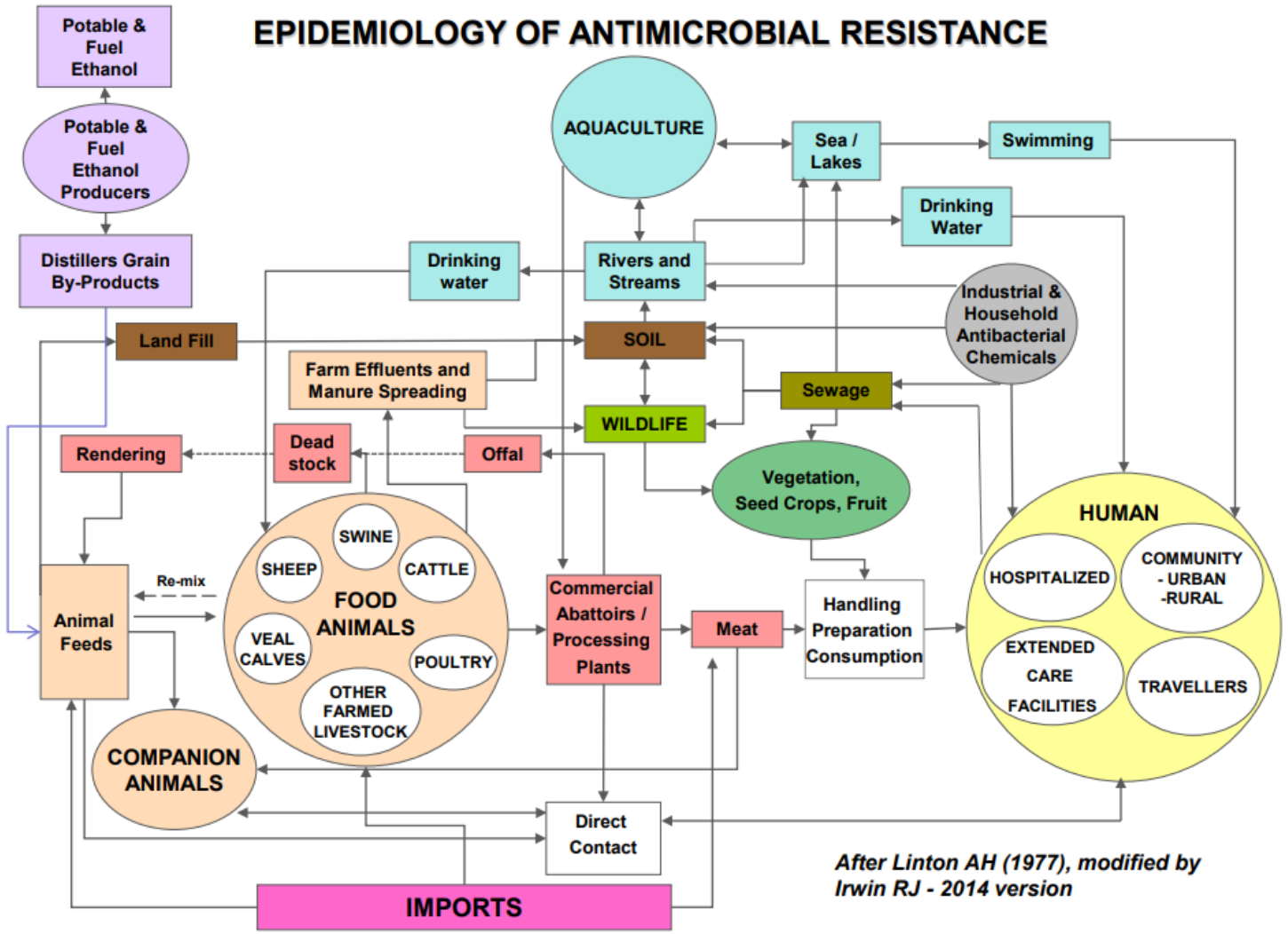
- AMR is a natural mechanism that allows microorganisms to survive
- AMR is pr…environment) both in pa…
  - Intrins…
  - Acquir…
    - De…
    - Up… …ontal gene tra…
  - ARG c… …nes favoring its spread also between different bacterial species
  - Exchange of resistance genes and antibiotic resistant bacteria do not respect borders or sectors!

Spread of and level of resistance influenced by by

- Use of antimicrobials (AMU)
  - **Stewardship**
- Transmission of ARB/ARGs
  - **Infection Prevention and Control/Biosecurity**

ECOLOGY OF RESISTANCE – ONE HEALTH



<u>Biggest drivers for AMR:</u>
Antibiotic misuse / overuse in humans and animals

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Antibiotic use in humans and animals

AMU – healthcare and community - 2023

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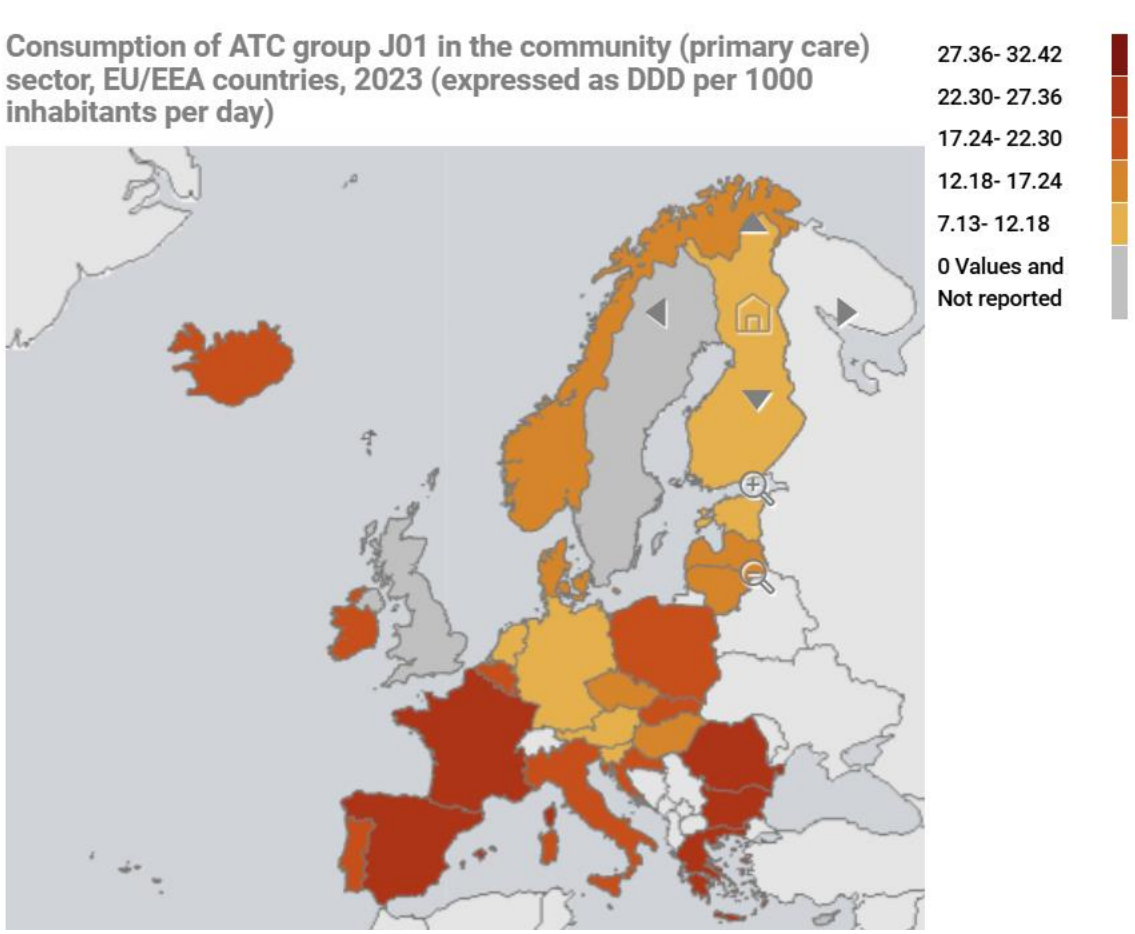
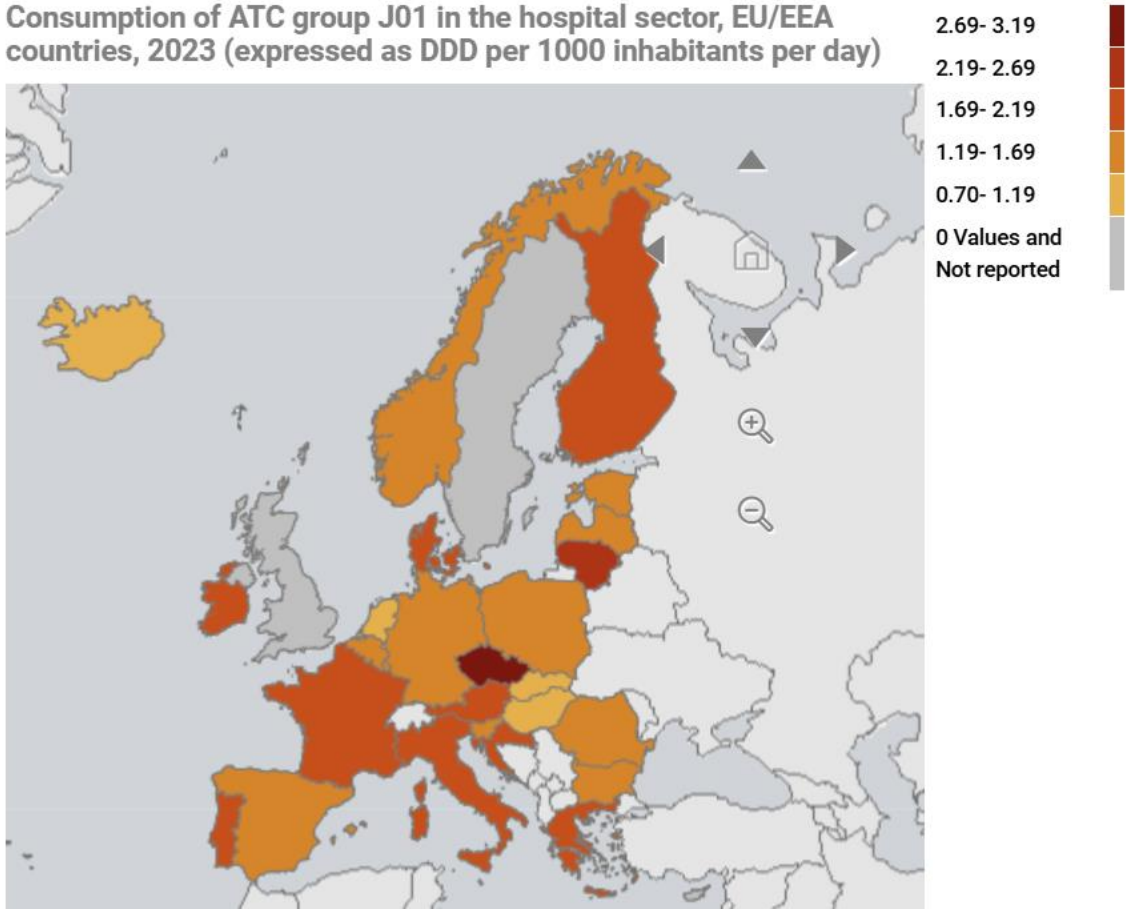


Sweden 9.9 DDD/1000/Day



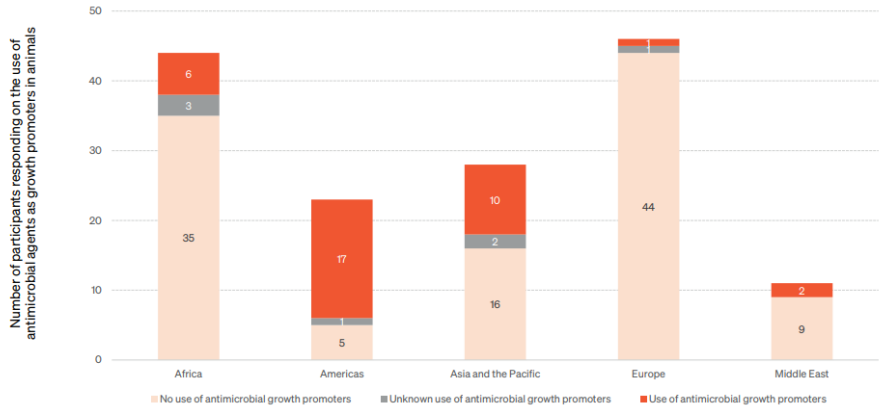
Sweden 1.0 DDD/1000/Day

Global AMU - animals

It is estimated that **>70%** of total consumption of antibiotics globally is for food producing animals!

- In EU countries **average of 45 mg/kg biomass** of food producing animals (ESUAvet)
  - Norway 1.8 mg/kg
  - Sweden 6 mg/kg
  - Finland 9 mg/kg
  - Denmark 20 mg/kg
  - Cyprus 112 mg/Kg

- 24% of 152 countries still allow use of antimicrobials for growth promotion in 2024!



CDDEP (2021), The State of The World's Antibiotics 2021, ESUAvet 2025
OIE (2024). OIE Annual Report on Antimicrobial Agents Intended for Use in Animals

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AMR in humans

AMU AND AMR (EARS- 2022)

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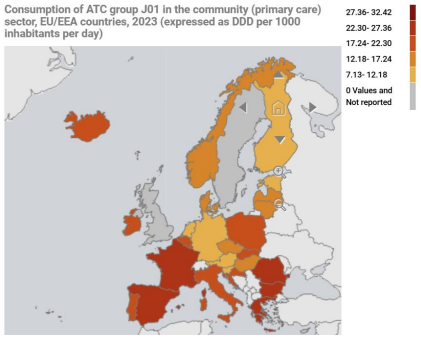


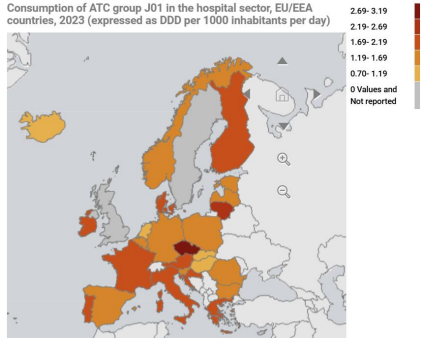


Figure 2. *Escherichia coli*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2022

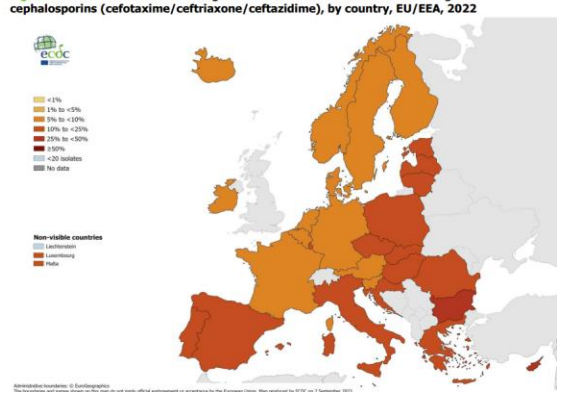


Figure 4. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2022

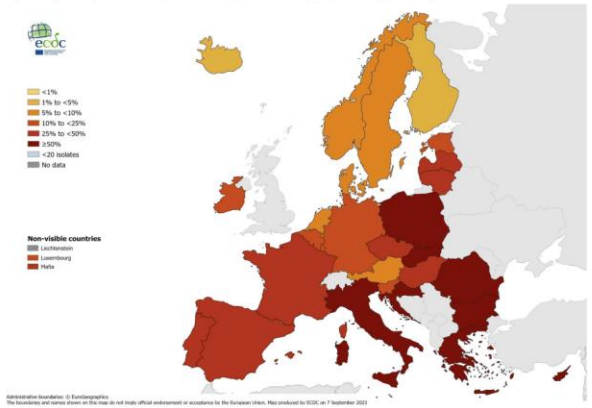


Figure 5. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, EU/EEA, 2022

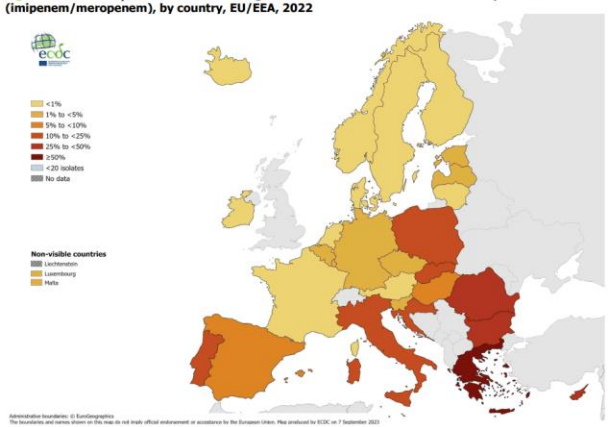


Figure 7. *Acinetobacter* species. Percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country, EU/EEA, 2022

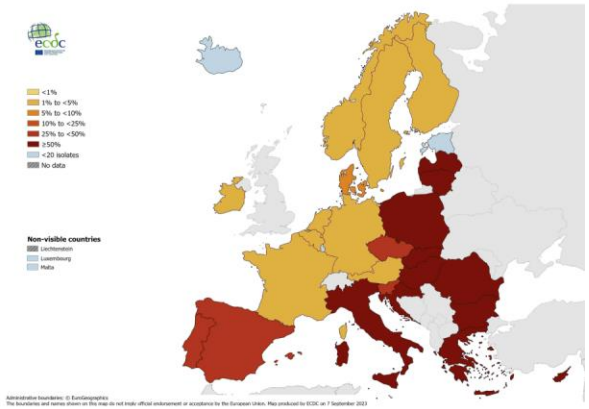


Figure 8. *Staphylococcus aureus*. Percentage of invasive isolates resistant to meticillin (MRSA),[a] by country, EU/EEA, 2022

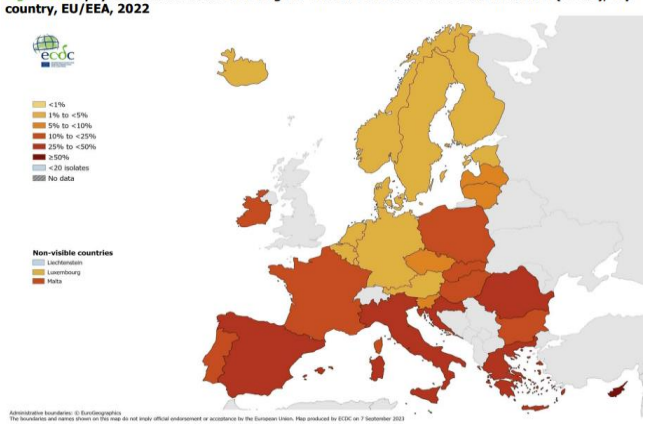
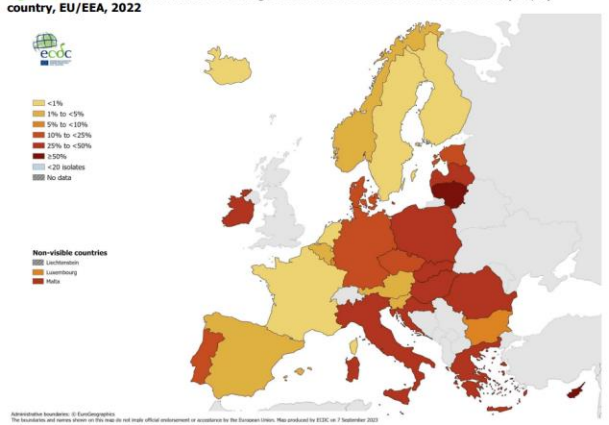
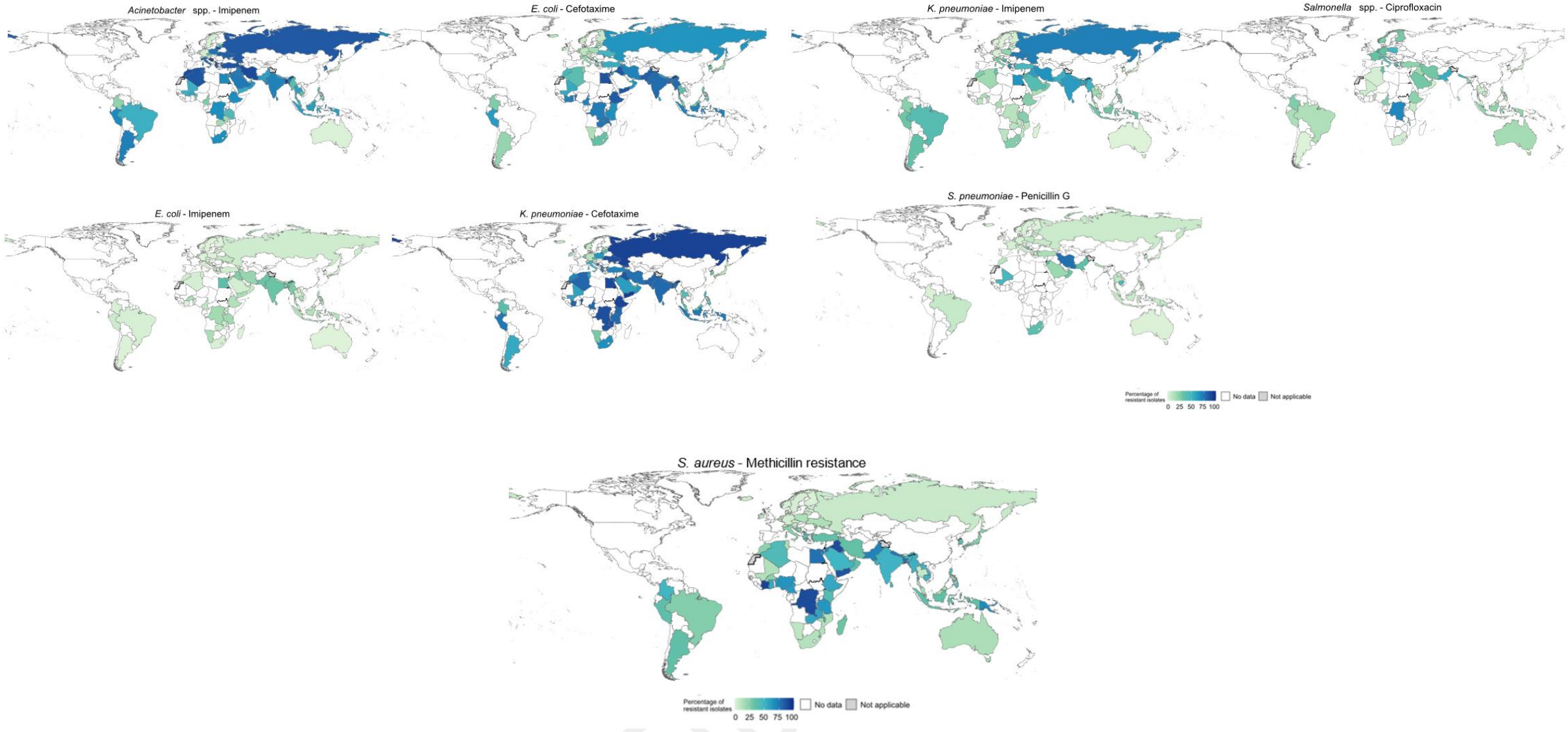


Figure 10. *Enterococcus faecium*. Percentage of invasive isolates resistant to vancomycin, by country, EU/EEA, 2022

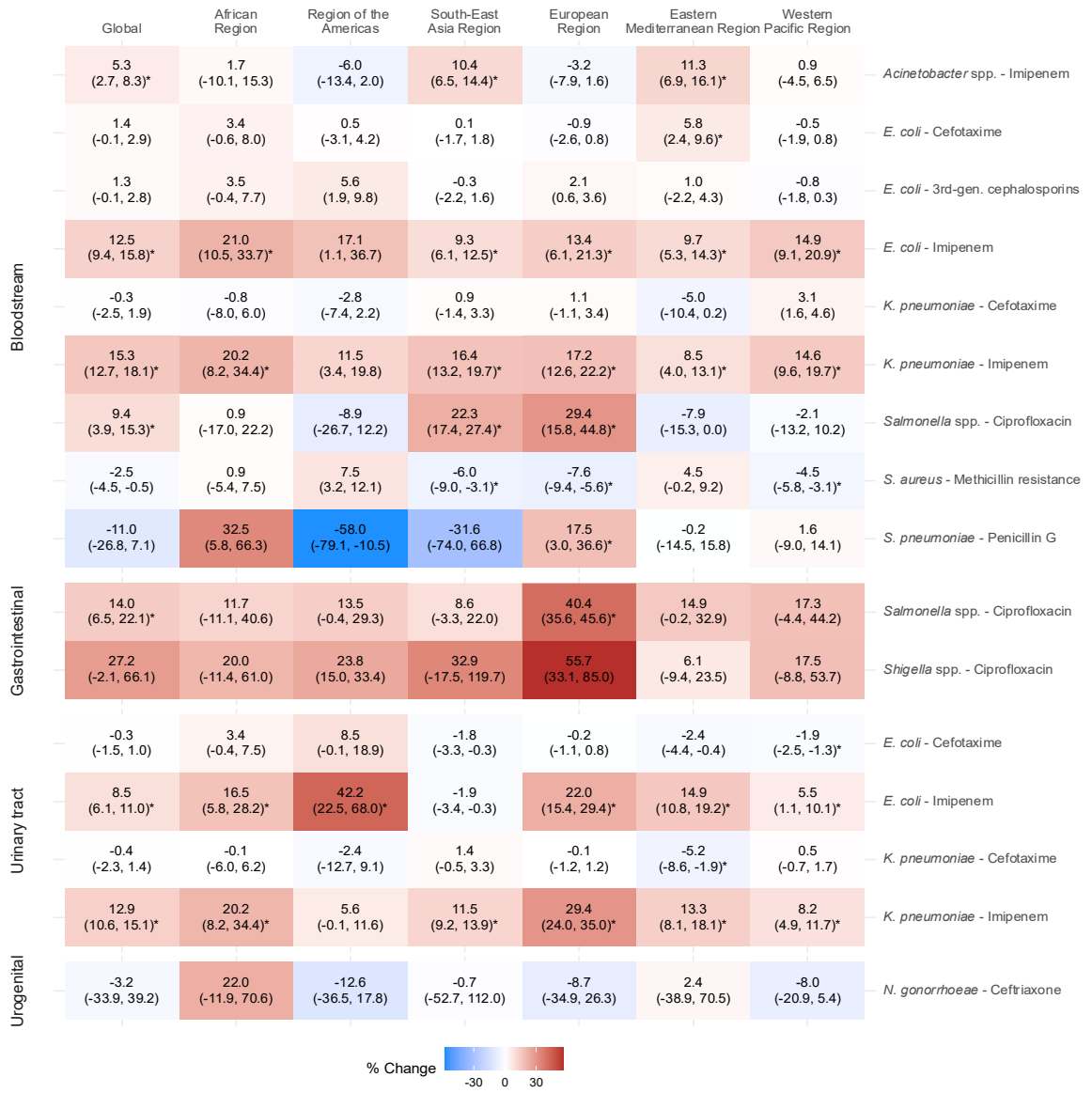


Resistance to selected antibiotics in bloodstream infections, 2023



WHO Global Antibiotic Resistance Report, 2025

Trends in AMR by WHO region and infection type: 2018–2023



WHO Global Antibiotic Resistance Report, 2025

AMR vs Sample intensity

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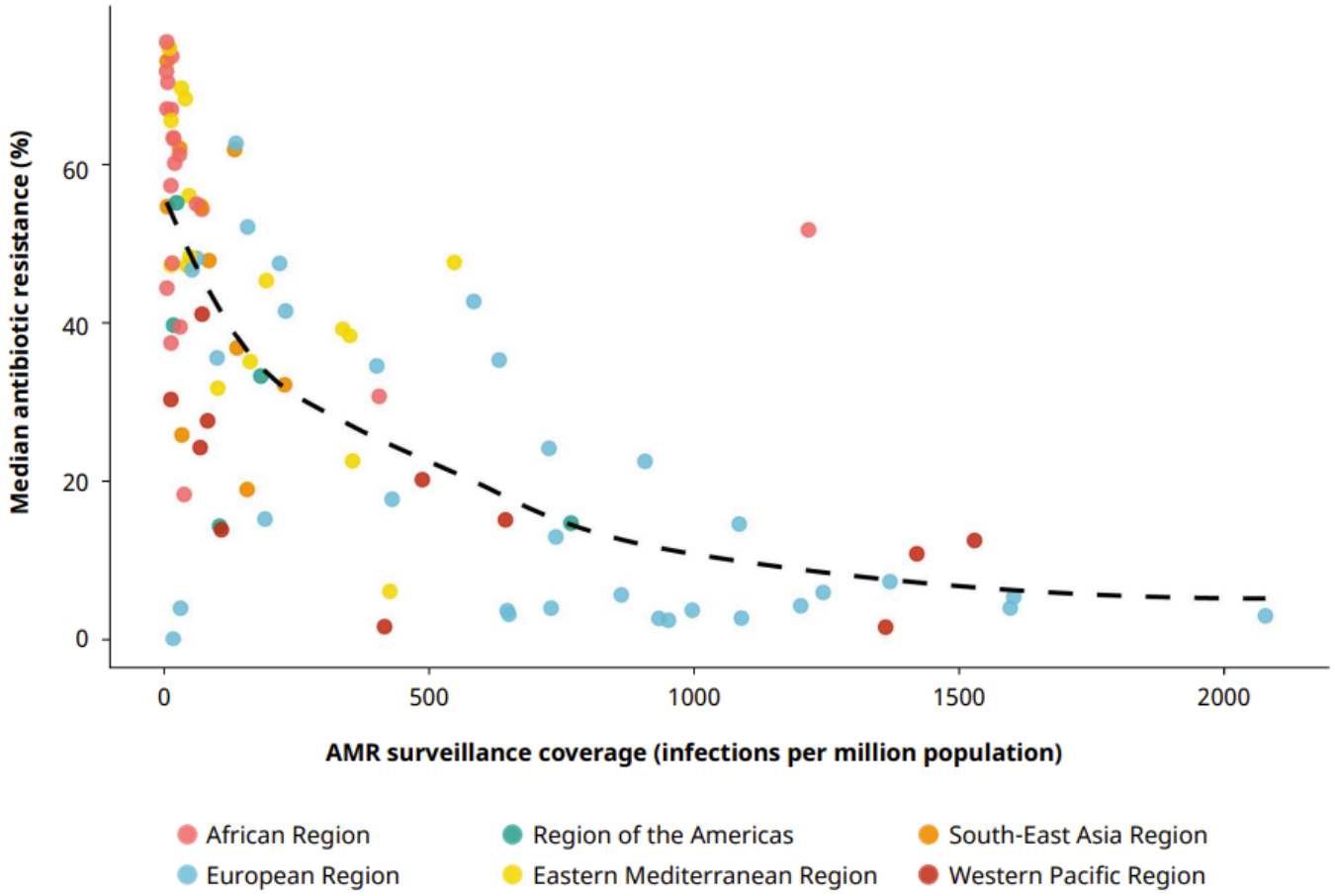
Figure 4. Median national percentage of AMR in bloodstream infections by AMR surveillance coverage, 2023



WHO Global Antibiotic Resistance Report, 2025

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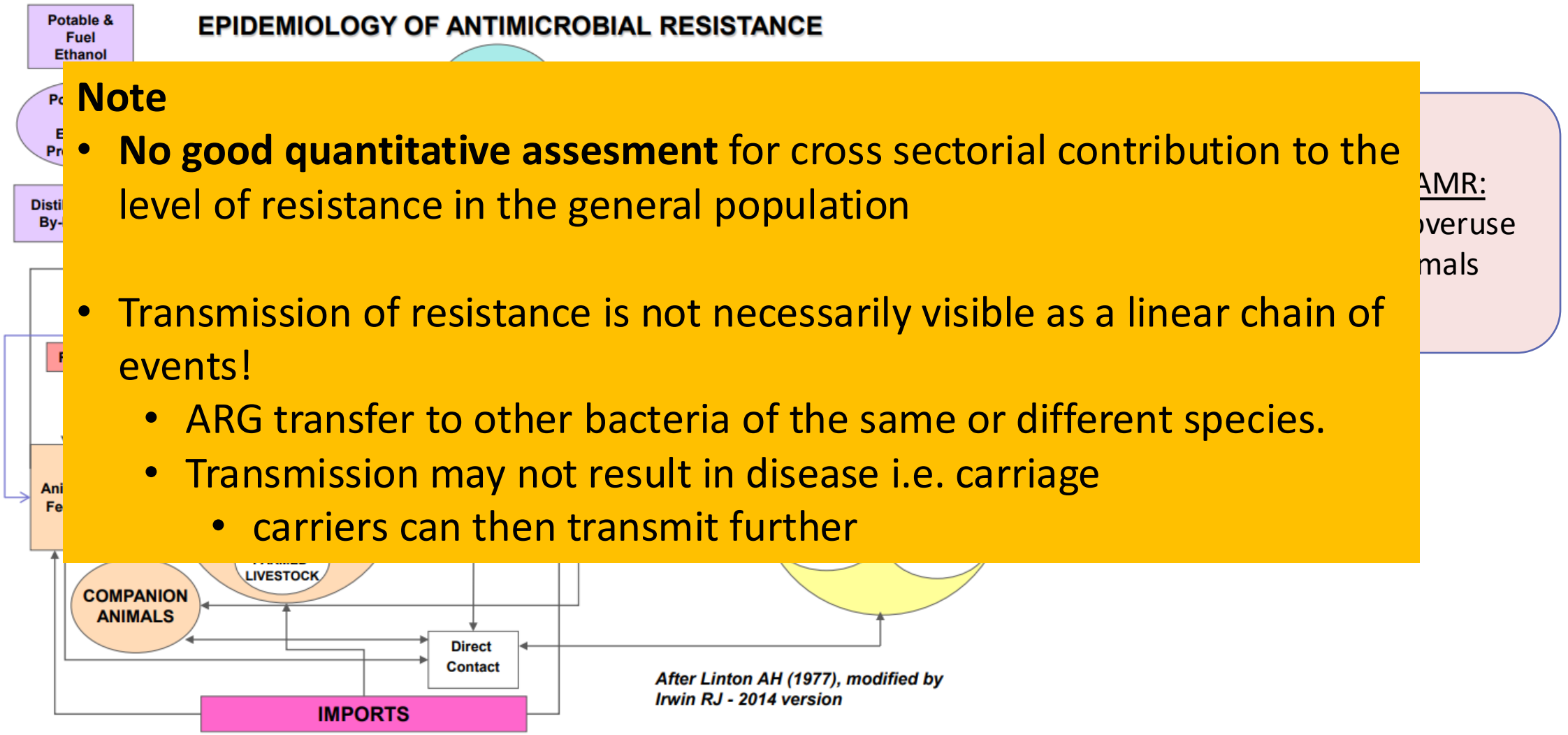
Cross sector transmission of resistance

ECOLOGY OF RESISTANCE – ONE HEALTH



Note

- **No good quantitative assesment** for cross sectorial contribution to the level of resistance in the general population

- Transmission of resistance is not necessarily visible as a linear chain of events!
  - ARG transfer to other bacteria of the same or different species.
  - Transmission may not result in disease i.e. carriage
    - carriers can then transmit further

Zoonotic transmission

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- Zoonotic transmission present as long as humans and animals have interacted
- Classical bacterial zoonoses (examples)
  - salmonellosis, campylobacteriosis, Q fever, brucellosis, listeriosis, psittacosis, tularemia, leptospirosis
- A large number of other bacteria have a zoonotic component
  - *S. aureus, E. coli, C. difficile*
- Resistant zoonotic agents = cross sector transmission of resistance genes
  - Salmonella DT104, monophasic salmonella, FQ resistant campylobacter,
  - AmpC / ESBL / CPE *E. coli,* LA-MRSA

FROM HUMAN MSSA – TO LA-MRSA

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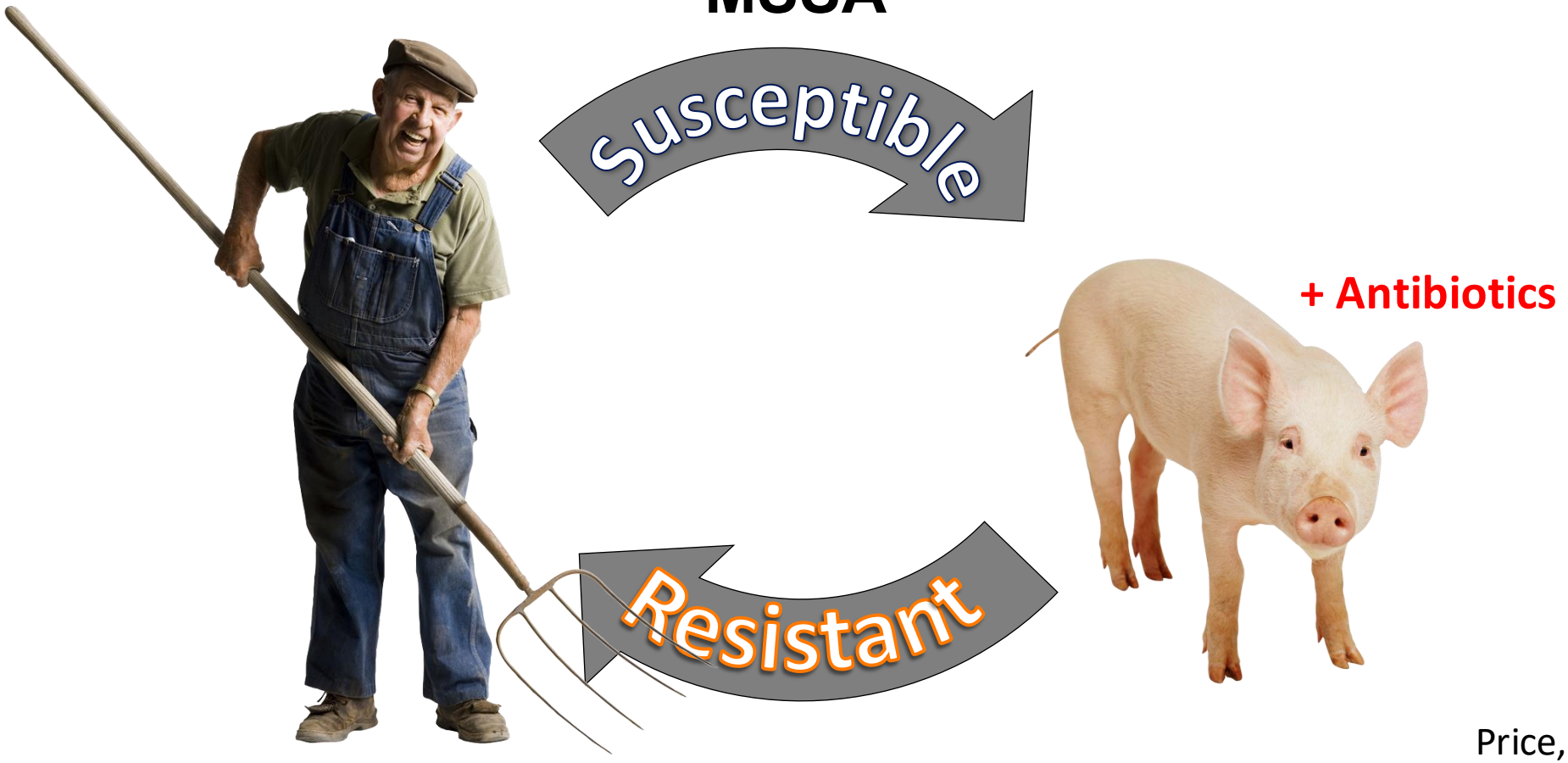
MSSA



Tetracycline R MRSA

Price, mbio 2012

AMR and the environment

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- The environment is very important in the evolution of AMR both for de novo mutations and as a vehicle for transmission!
  - i.e. wastewater containing high levels of antibiotics
    - hospital / intensive farming / pharmaceutical industries
- Antibiotics are a threat to the health of the environment!
  - Change of ecology/adaptation – and thereby select for resistance
- AMR/ARG is in contrary not a threat to the environment itself
  - if no infections then it does not matter if a microorganism is resistant

Larsson; Nature Microbiology, 2023

- **Potential** indicator of the regional resistance levels

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Challenges ahead

Increasing population

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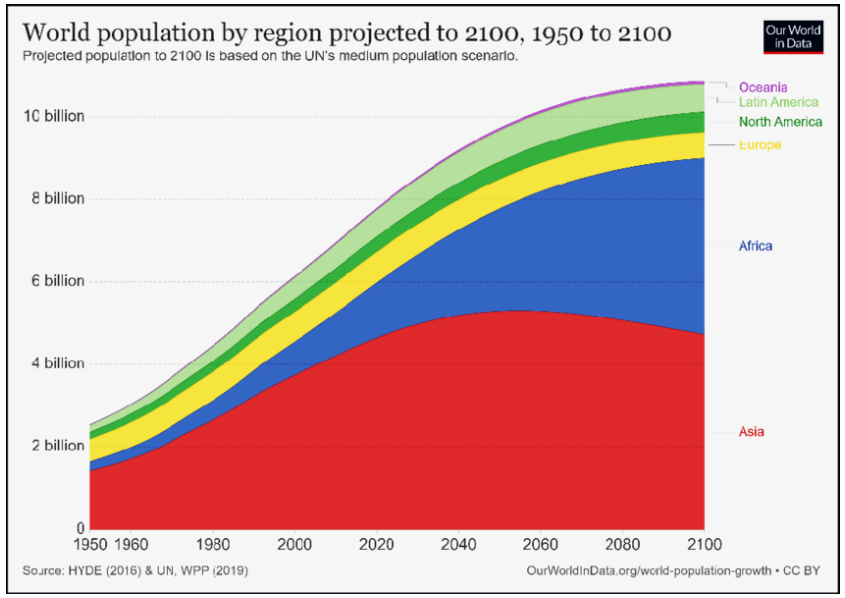

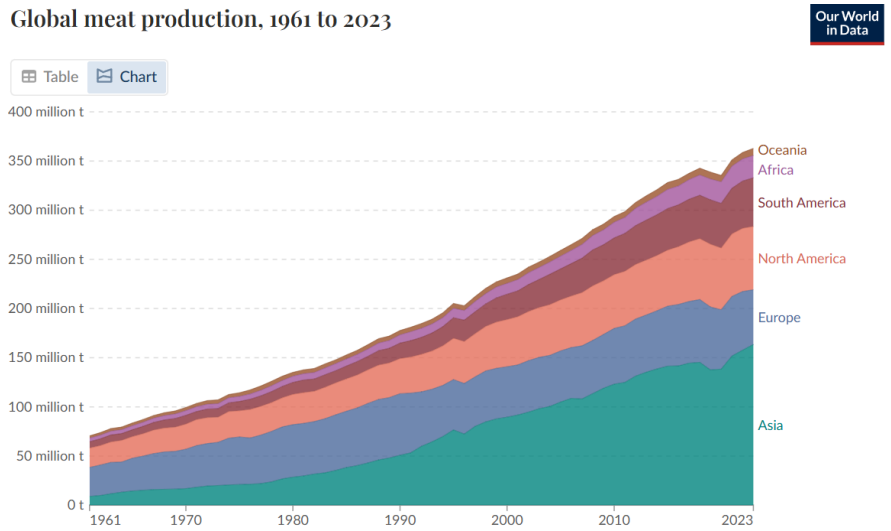

Climate change – new challenges

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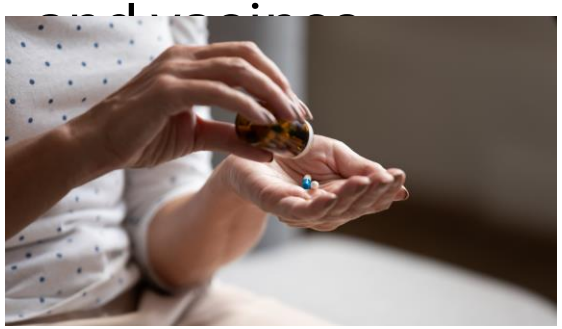
- Altering the distribution, seasonality, and intensity of diseases spread by vectors like mosquitoes, ticks, and fleas
- Deforestation, habitat loss, and changing ecosystems increase human-animal interactions, leading to new infectious disease outbreaks
- Higher temperatures, flooding, and changes in water sources contribute to the spread of bacteria, viruses, and parasites
- Wildfires, pollution, and shifting weather patterns affect respiratory infections

- Exacerbation of AMR through environmental contamination, temperature-related bacterial evolution, and changes in disease patterns

What needs to be done

New antimicrobials and vaccines

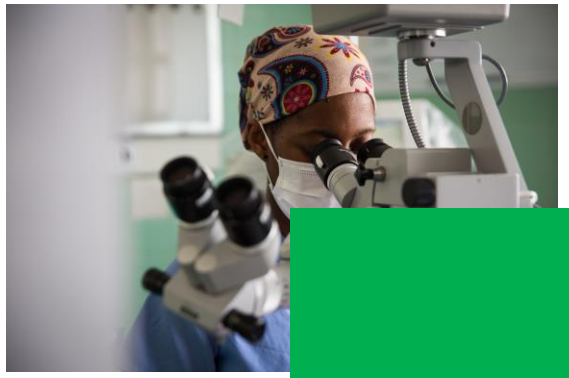
IPC / biosecurity



Rational use of antimicrobials/Diagnostics

Equal access to antimicrobials

What needs to be done



New
antimicrc

osecurity

Local and Global commitment

Rational use of antimicrobials/Diagnostics

Equal access to antimicrobials

Global Action Plan 2015: Strategic Objectives
New GAP is in its making!

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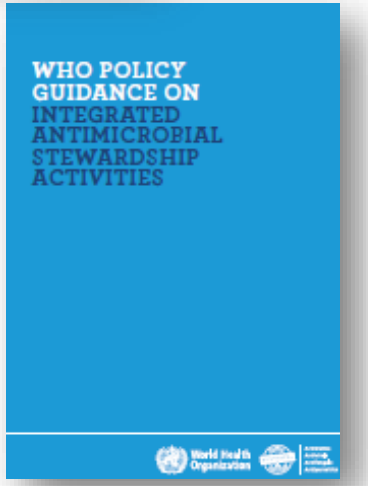

1. Improve awareness and understanding of antimicrobial resistance through effective communication, education and training
2. Strengthen the knowledge and evidence base through surveillance and research
3. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
4. Optimise the use of antimicrobial medicines in human and animal health
5. Develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions

NAP implementation

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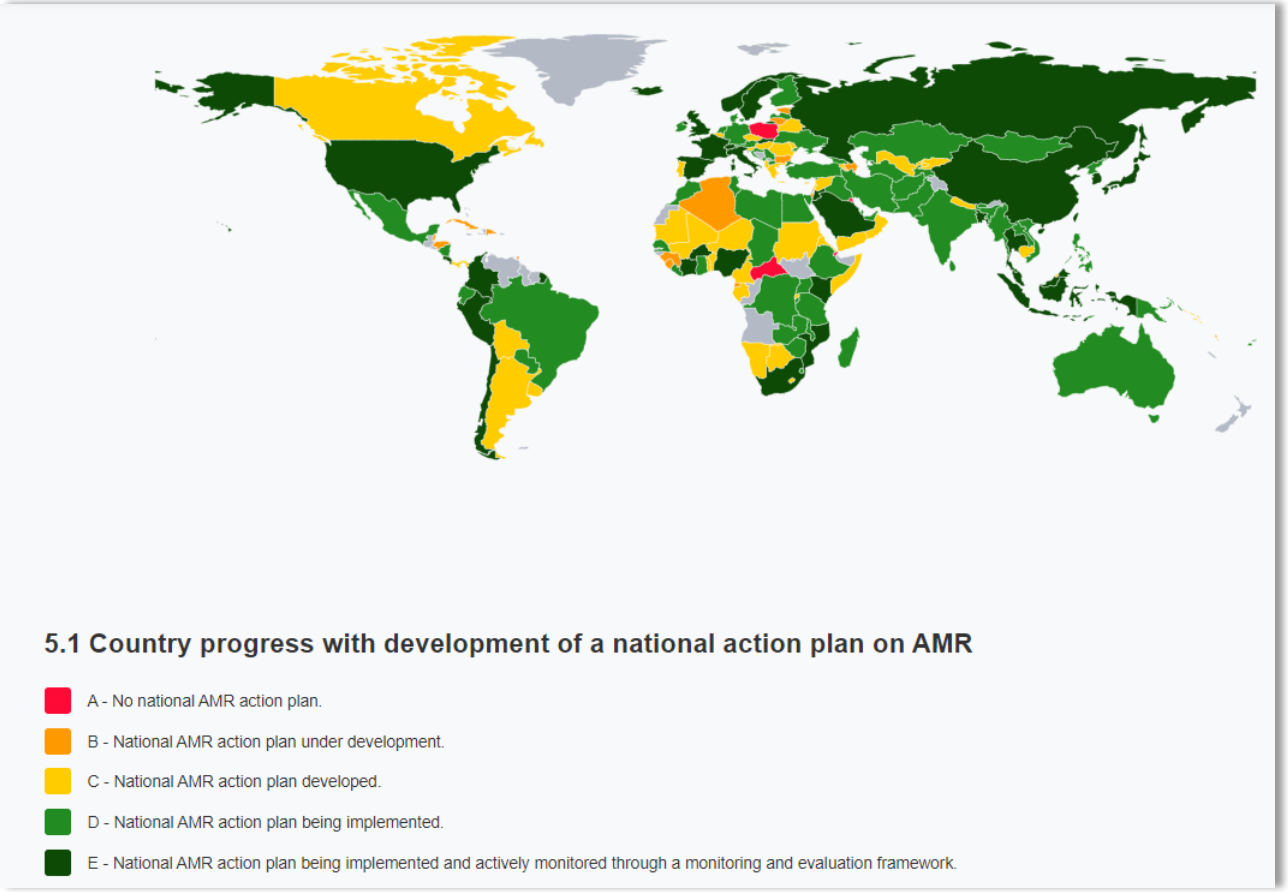
170 countries* has a National Action Plan (NAP) for AMR or is developing a NAP

< 90 countries*
Is implementing their plans

<10% has costed their plans

**per May 2023*



Global Database for the Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS) (amrcountryprogress.org)

Discovery of antibiotic classes for clinical use

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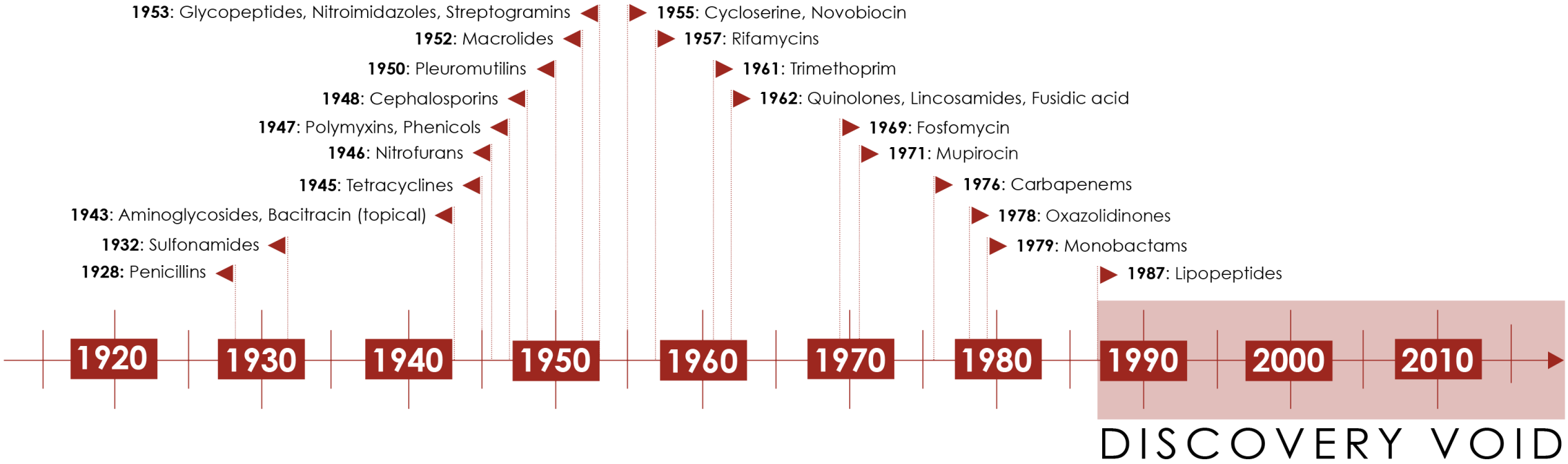

www.reactgroup.org

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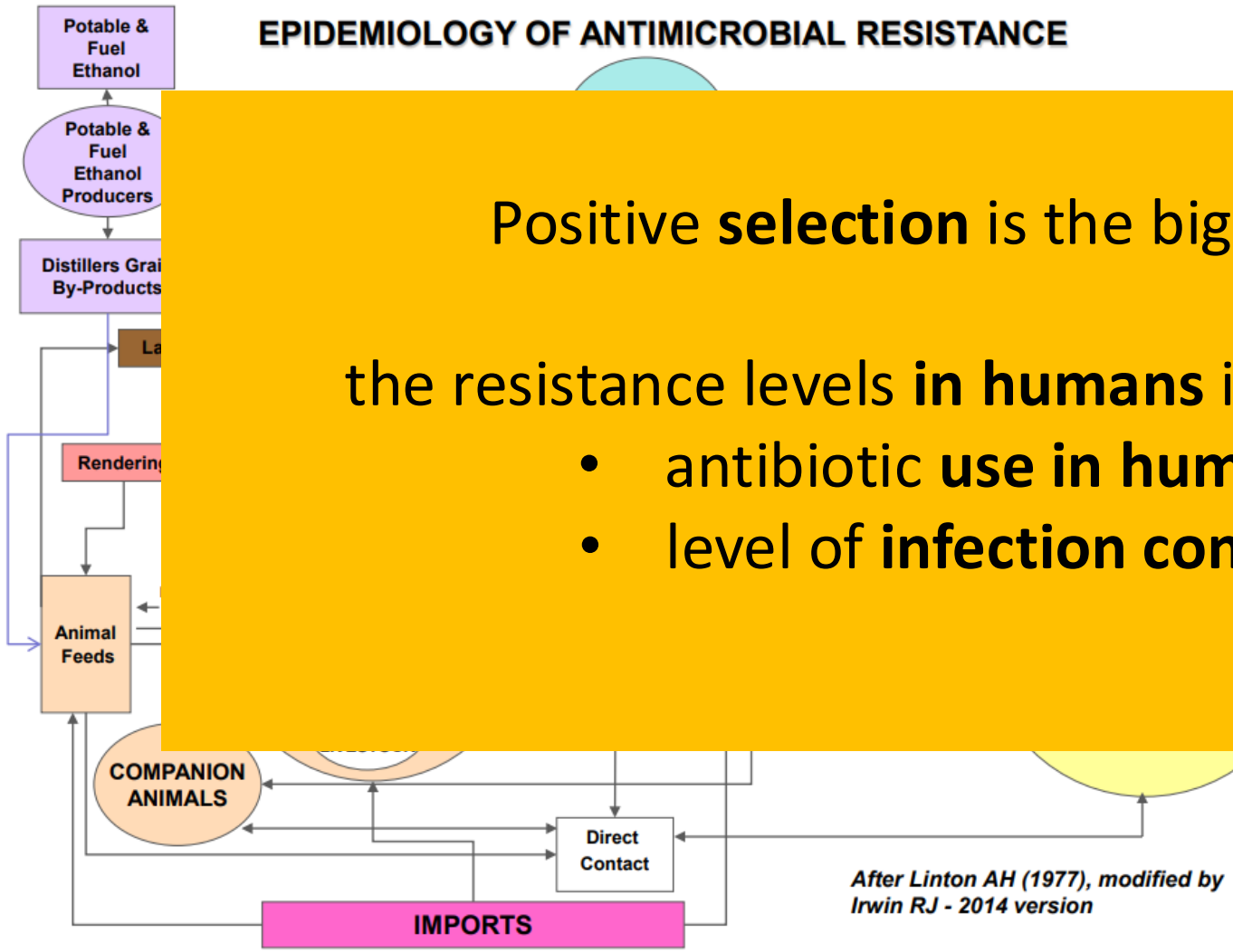
Can resistance /MRB be controlled?

ECOLOGY OF RESISTANCE – ONE HEALTH



Positive **selection** is the big driver!

the resistance levels **in humans** is decided by

- antibiotic **use in humans**
- level of **infection control**

for AMR:
se / overuse
d animals

Can resistance /MRB be controlled?

- The short answer for the health care sector **is yes**
- We know what to do and it works!
  - Hand hygeine
  - Glows and gowns
  - Cleaning and desinfection
  - Isolation
  - Regional coordination!
  - And not the least **leadership**!!!

  - Outbreaks can be controlled
  - National incidence can be lowered

MRSA in Denmark

Figure 8.22 Number of MRSA infections according to epidemiological classification, Denmark, 2015-2024 DANMAP 2024

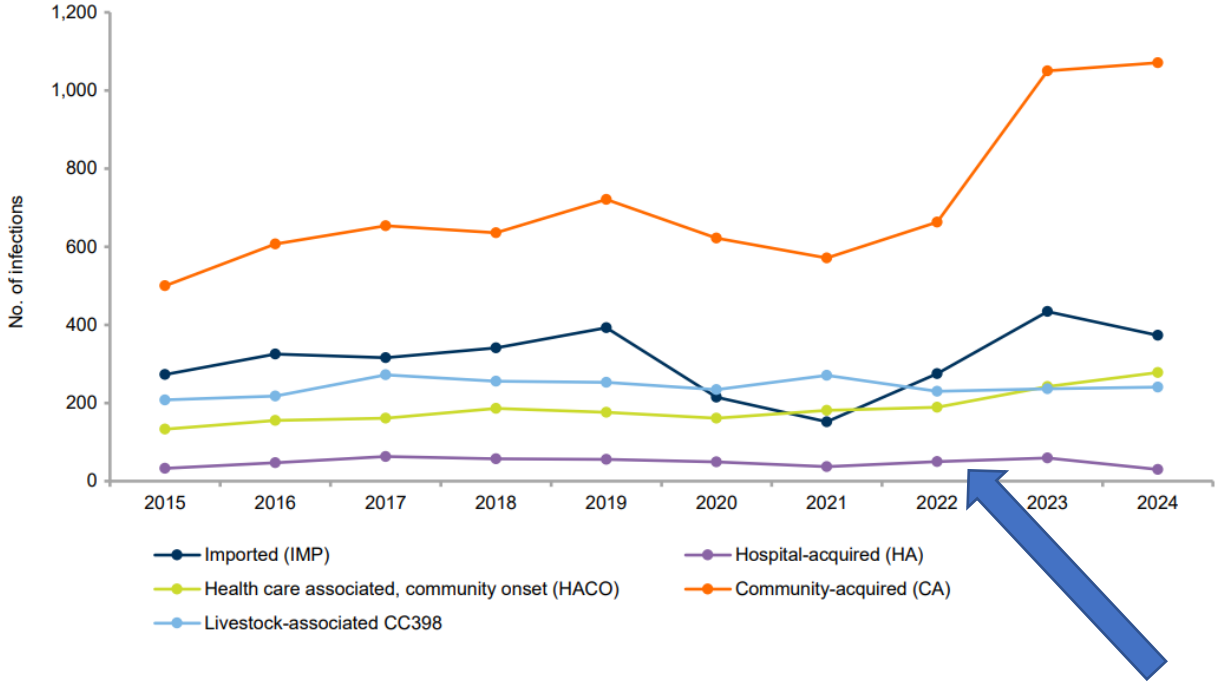
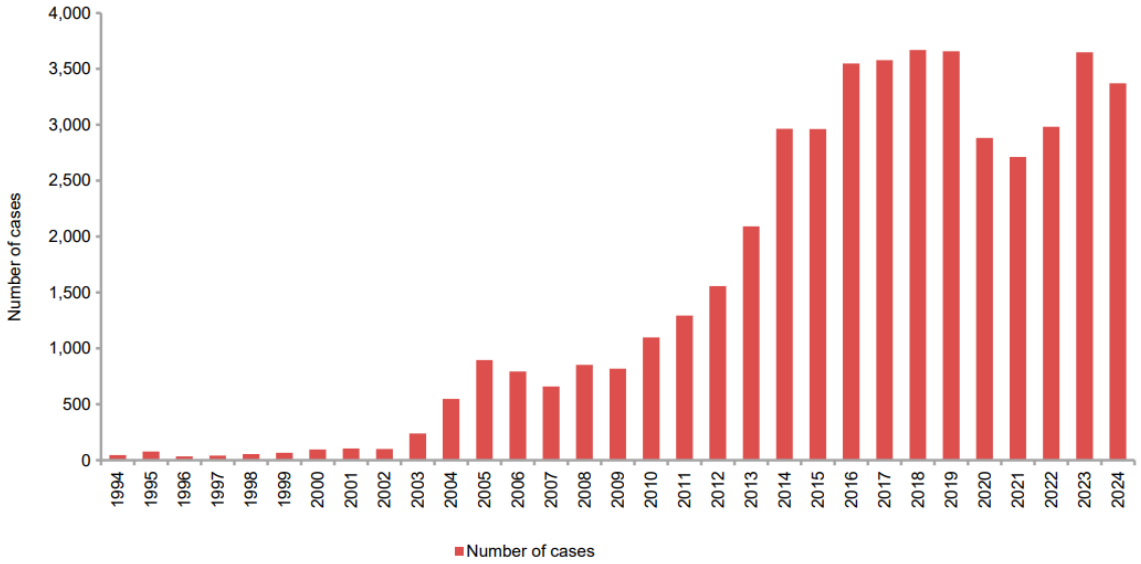
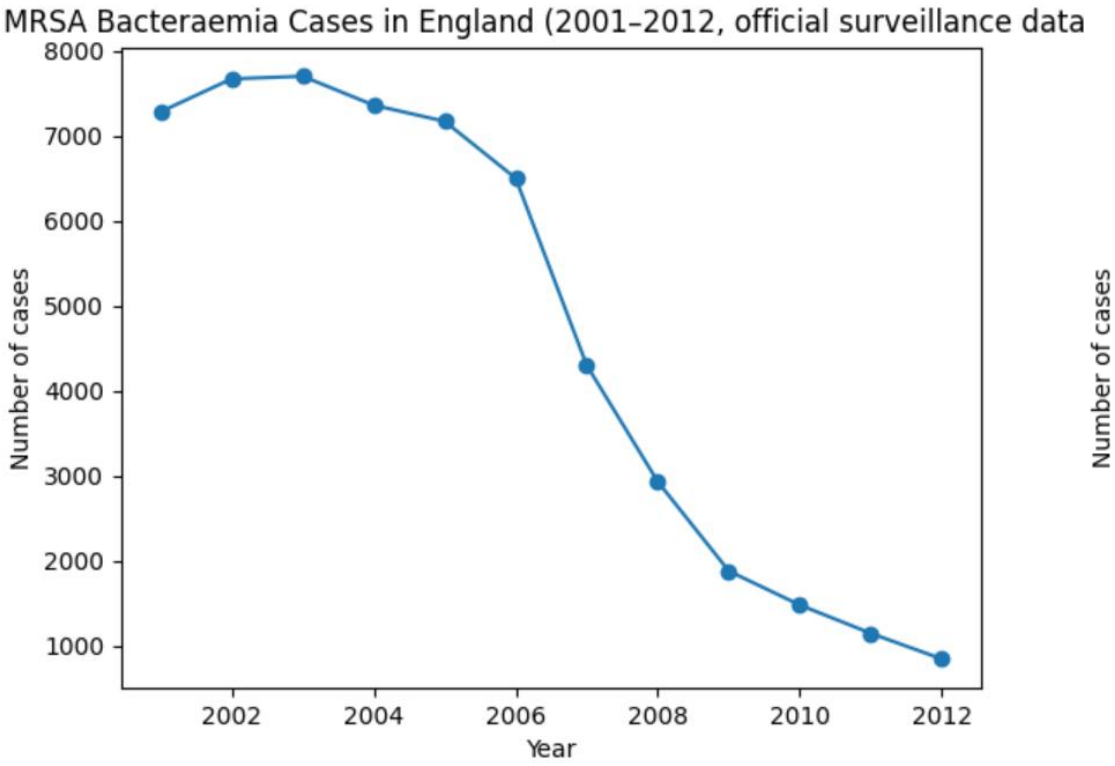
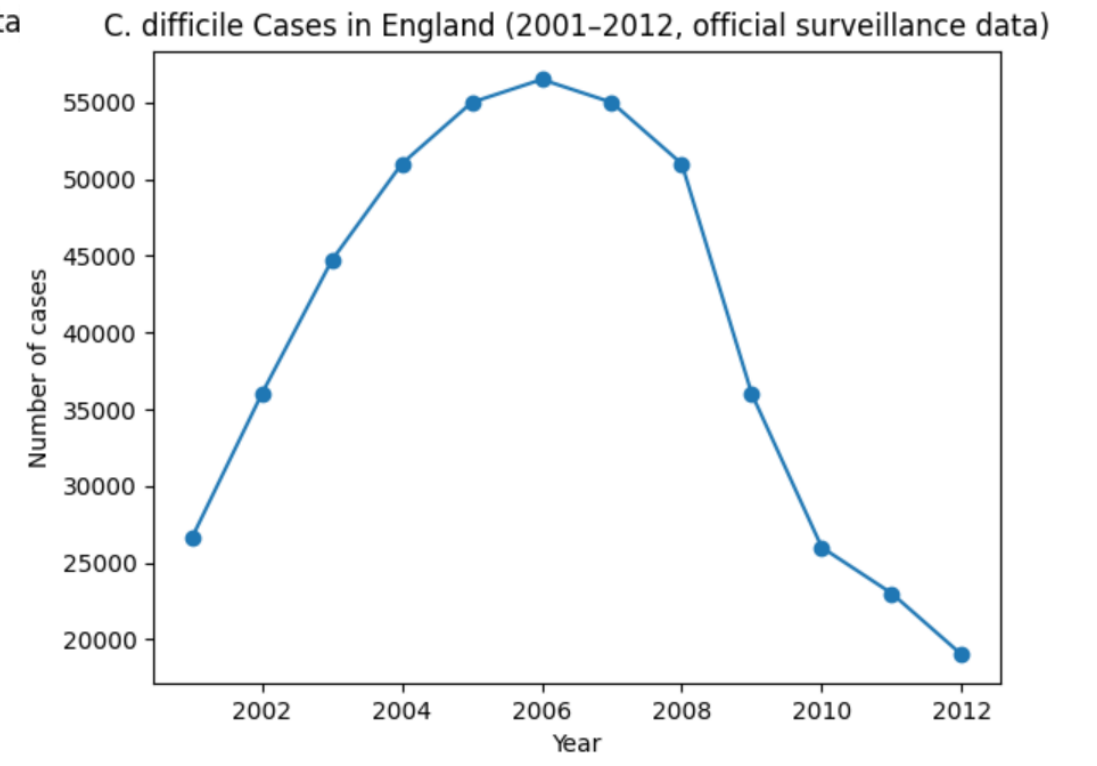


Figure 8.21a Number of new MRSA cases in Denmark 1994-2024 DANMAP 2024

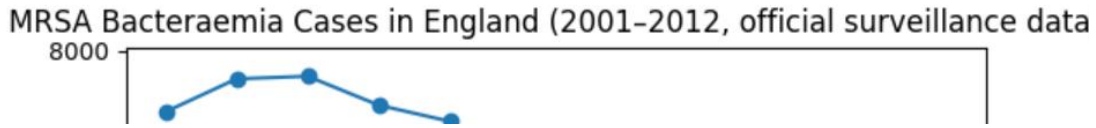


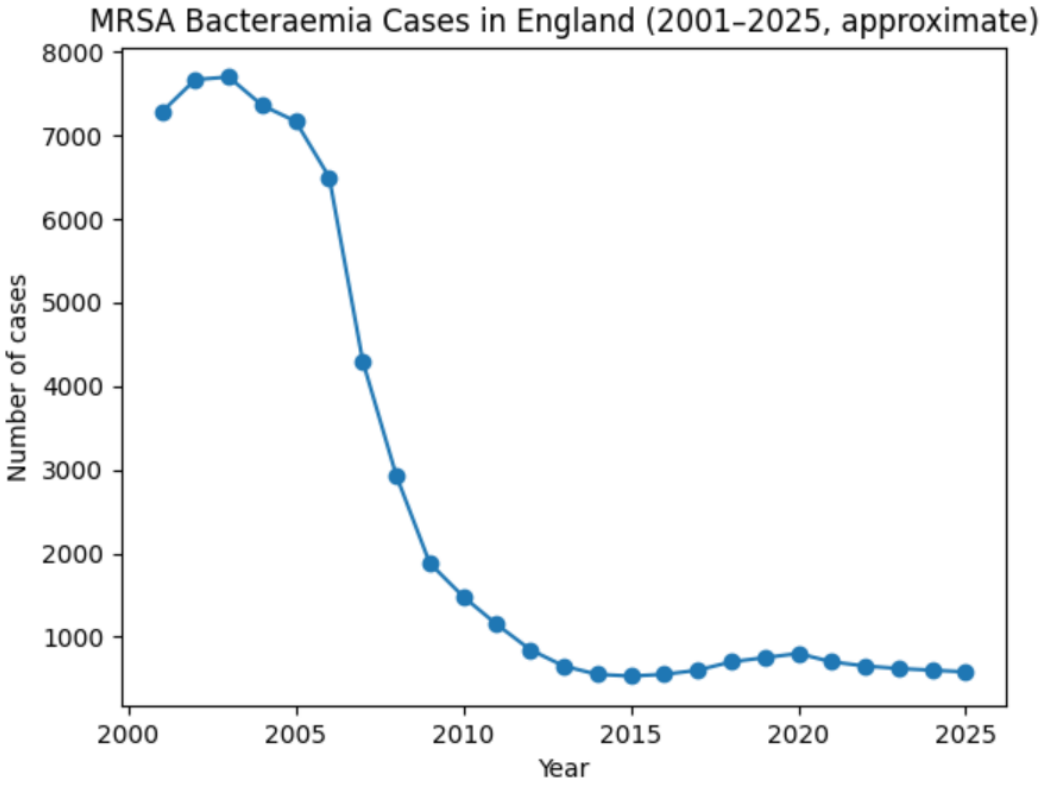
MRSA and C. difficile development in UK

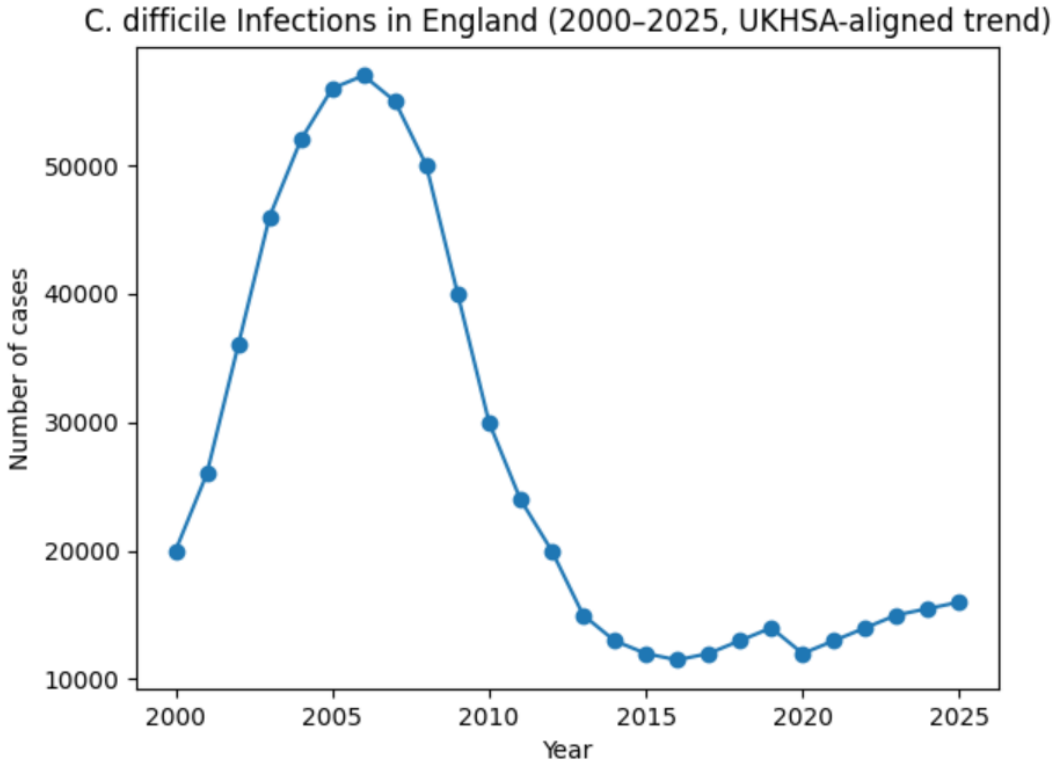




MRSA and C. difficile development in UK







Can resistance /MRB be controlled?

- The short answer is yes
- But – in each community the questions are
  - Is it feasible?
  - Is it acceptible?
  - Is it ”worth it”?
    - On a societal level
    - On a individual level
      - Are you directly affected yourself or not…….
- What about in other sectors and over time?

ARGs in soils over time

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- Use of antimicrobials in agriculture especially from 1950s and onwards; Denmark introduced af ban of growth promotion in the 1990s

- Soils collected in the Netherlands from 1940-2008 and Denmark from 1923-2010
  - qPCR to quantify the presence of selected ARGs.

- Findings
  - Levels of resistance genes rose over time from the pre-antibiotic era (1940) to the present
  - From the 1970s to the present dramatic increase for tetracycline and β-lactam resistance elements!
  - blaCTX-M levels declined in manure spread soils after the ban of growth promotors

Knapp, Environ Sci Technol. 2010
Graham, Sci Reports, 2016

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Conclusions

- AMR is a **silently evolving pandemic** and to a large extent **unrecognized** by civil society, policy makers and politicians
- Urgent need for action in all sectors using **a One health approach**
- Need for getting **policy and infrastructure** in place that ensure **cross-sector mitigation** of AMR
- Locally, regionally and globally
- Är Kampen forlorad?
  - Nej – ikke nødvendigvis!!!

Conclusions

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- **But it requires**
  - **Leadership**
  - **Prudent use** of antimicrobials (AMU) and co-selecting agents **in all sectors**
    - Antimicrobial AND Diagnostic stewardship
      - Rapid, user-near, affordable - innovation highly needed
    - Innovation of
- **Mitigation of transmission** of ARB/ARGs
    - Good hygiene practices / biosecurity
    - Good management practices in food producing animals

- **Innovation** including **sustainable economical models** for development of antimicrobials, non antimicrobial treatment modalities and **diagnostics**

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Thank you