Antimicrobial resistance
Did we lose the magic bullet?

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Conflict of interest

Nothing to disclose

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Self-assessment questions

Please answer YES or NO

1. Are Gram-positive bacteria the most common pathogens in ICU-acquired pneumonia?

2. Does E. coli or Klebsiella pneumoniae have comparable rates of resistance in all European countries?

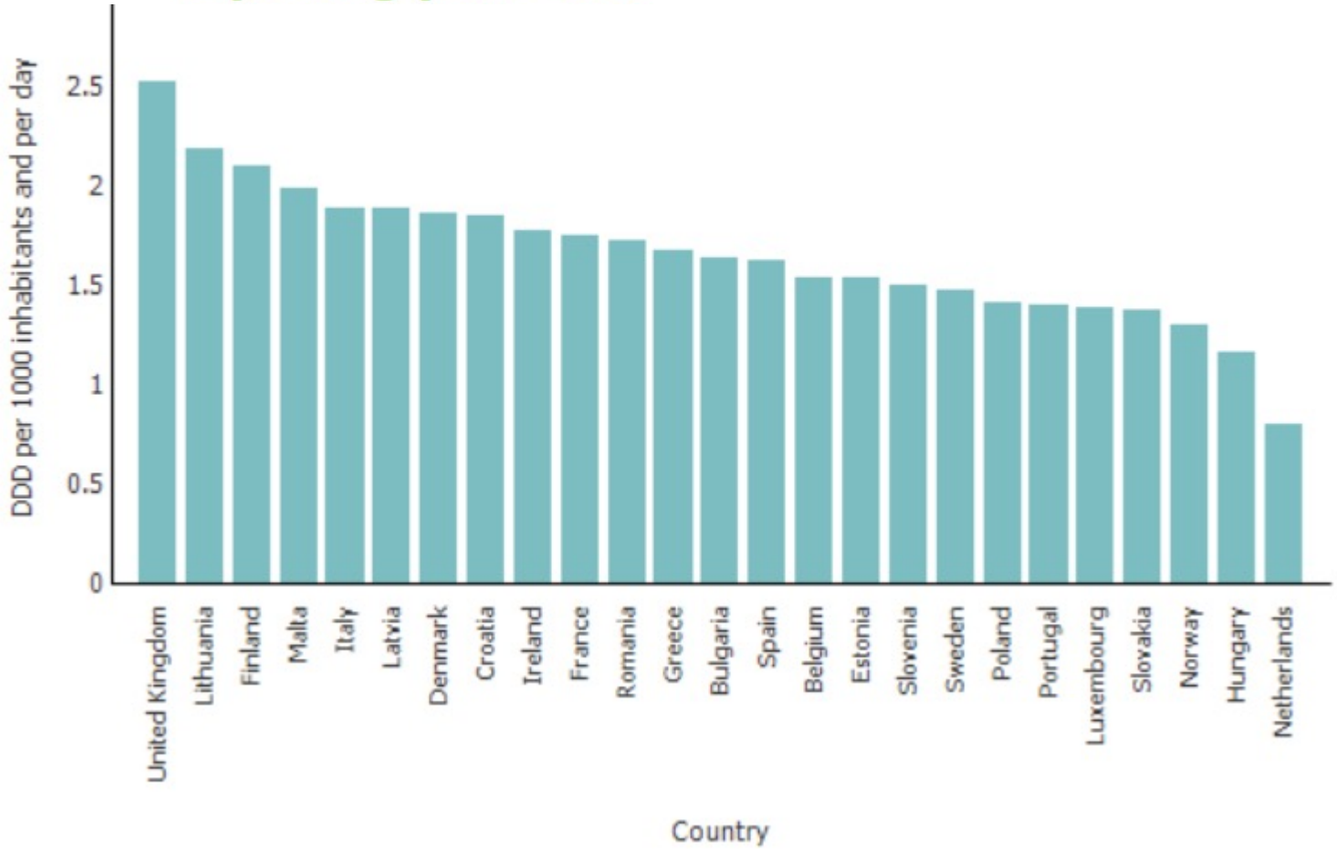
3. Can reduced consumption of antibiotics influence resistance rates?

Agenda

- Antibiotic consumption
- Antibiotic resistance in most relevant bacteria
- Therapeutic options
- What should be done?

Consumption of antibiotics in Europe

Consumption of Antibacterials for systemic use (ATC group J01) in the hospital sector in Europe, reporting year 2019



Average consumption in hospital sector:
1.8 DDD per 1 000 inhabitants per day
(country range: 0.8–2.5)

DDD: Daily defined dose per 1,000 inhabitants per day

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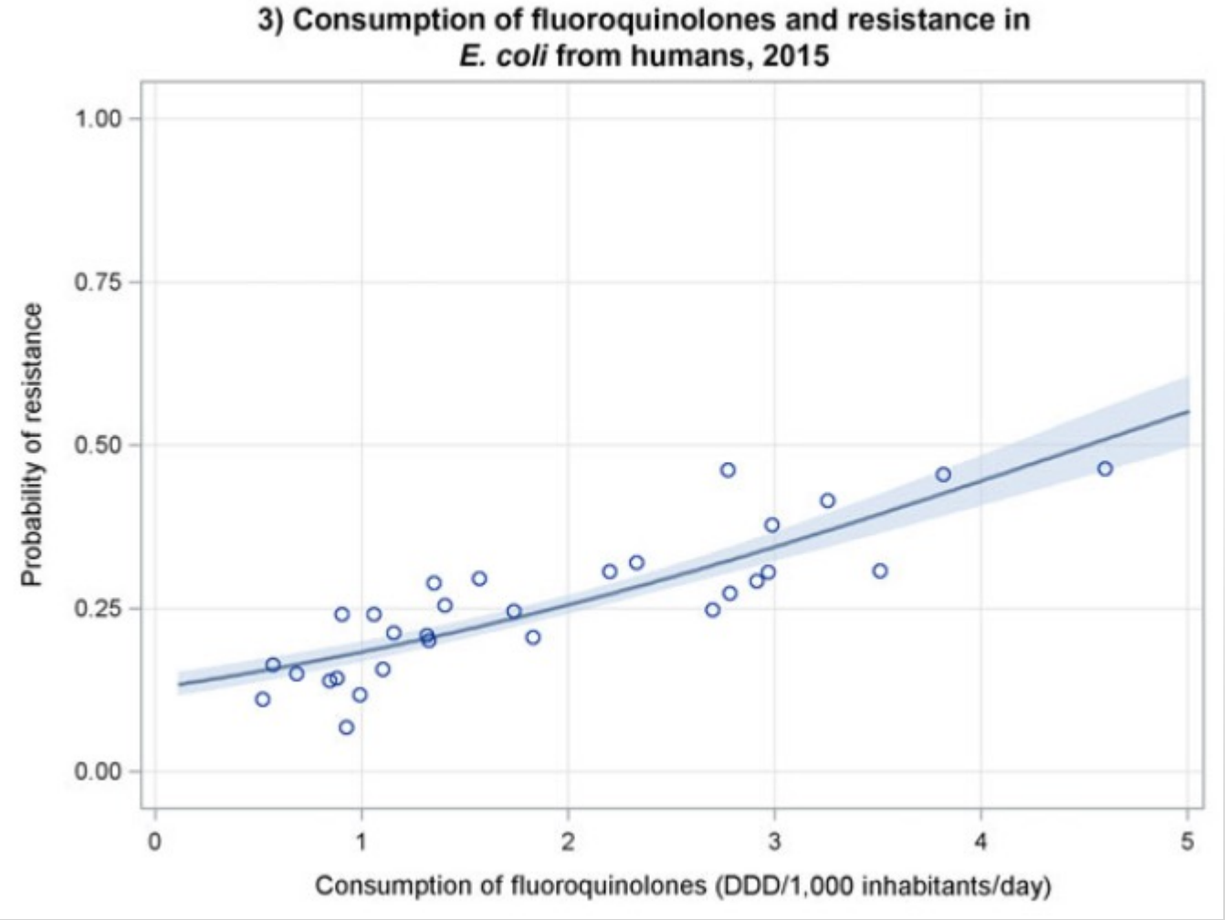
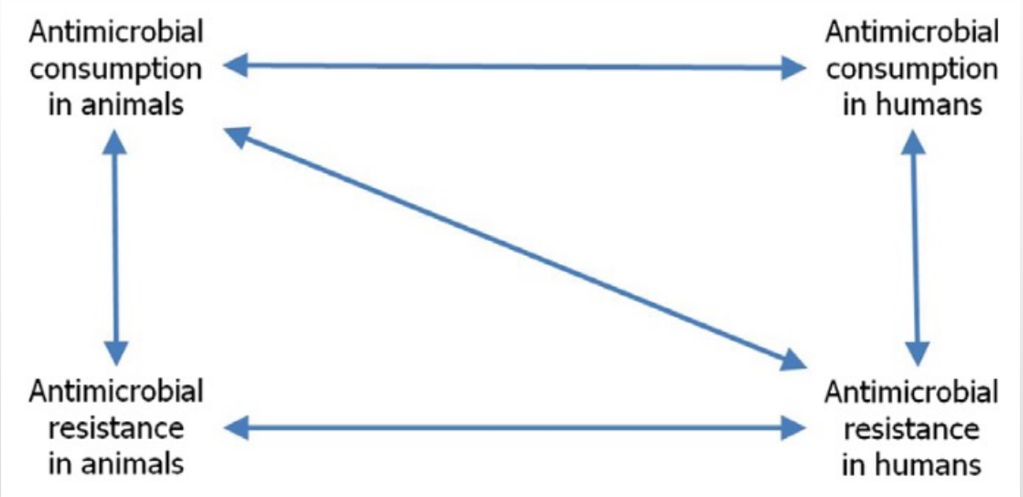
Antibiotic consumption - resistance

SCIENTIFIC REPORT



Logistic regression analysis of the total (community and hospital) consumption of fluoroquinolones in humans, (DDD per 1,000 inhabitants per day) and the probability of resistance to fluoroquinolones in invasive E. coli from humans

‘One-health’ perspective



EFSA Journal 2017;15(7):4872

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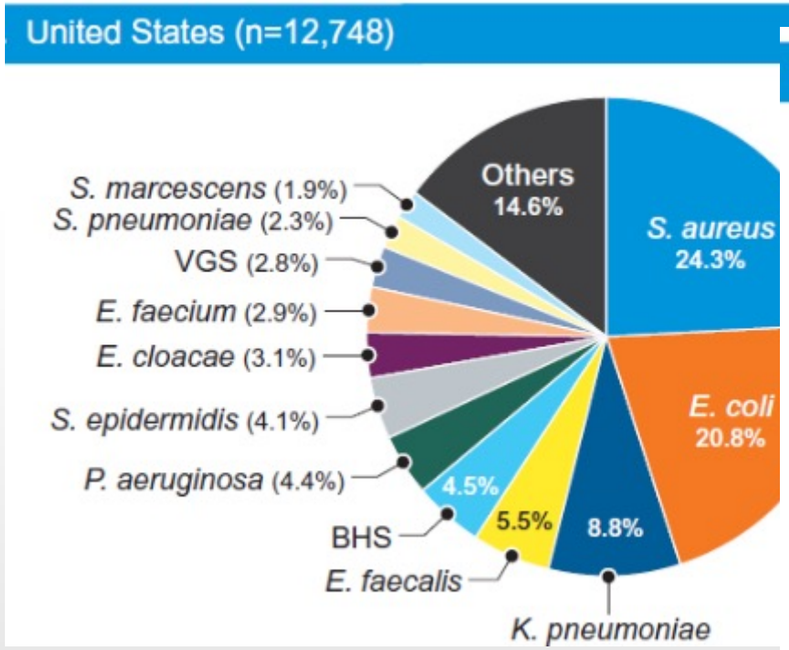
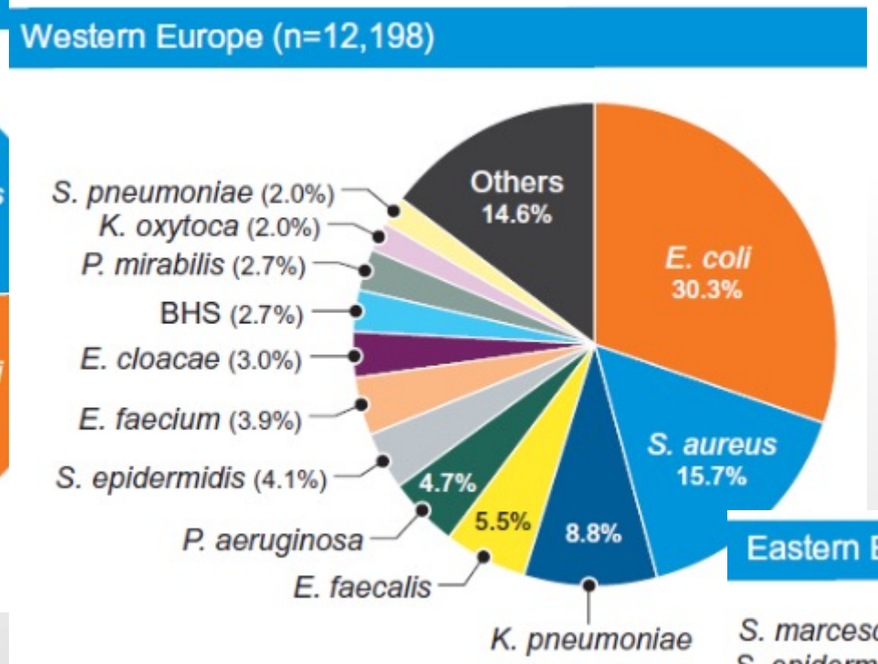
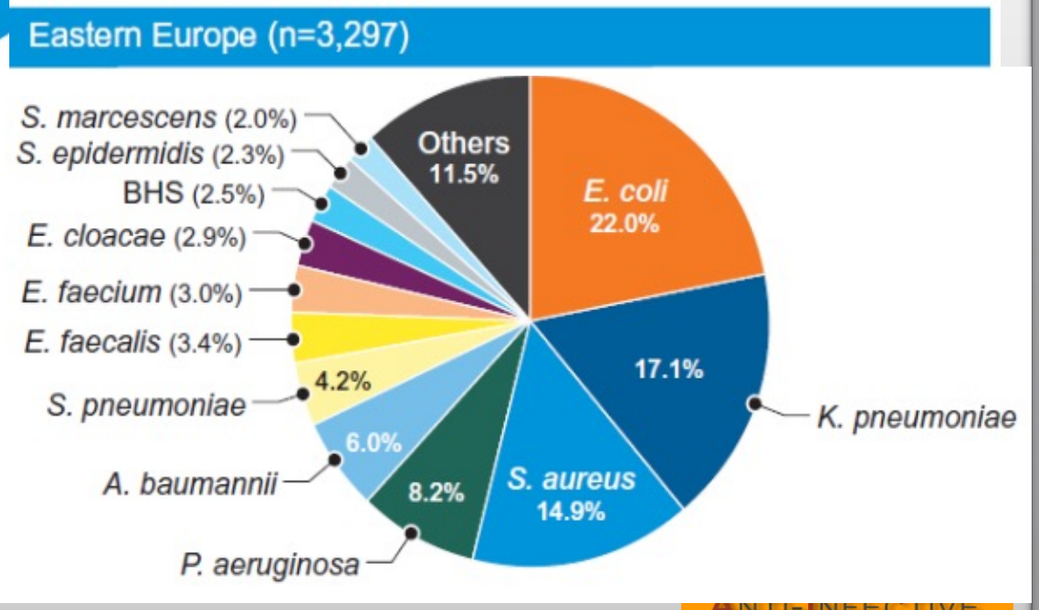
Bloodstream Infections

Bloodstream Infections in the US and Europe (SENTRY, 2016-2019)







- **Gram-negative bacteria** (main resistance problems)
  - **E. coli** (Ceph. 3 Gen, often fluoroquinolones,….)
  - **K. pneumoniae** (almost all β-lactams incl. carbapenems, fluoroquinolones, aminoglycosides,….)
  - **P. aeruginosa** (almost all β-lactams incl. carbapenems, fluoroquinolones, aminoglycosides,….)
  - **A. baumannii** (almost all β-lactams incl. carbapenems, fluoroquinolones, aminoglycosides,….)

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Healthcare-associated infections acquired in European ICUs (2017)

- ICU-acquired pneumonia
  - P. aeruginosa (20%, 7-33%),
    S. aureus (19%, 0-31%),
    Klebsiella spp.(15%, 9-37%),
    E.coli (14%, 3-21%)
- Bloodstream infections (incl. microbiologically confirmed catheter-related BSIs)
  - Coagulase-negative staphylococci (24%, 0-45%),
    Enterococcus spp. (6-53%, 15%),
    Klebsiella spp. (12%, 5-44%),
    S. aureus (12%, 5-18%)
- Urinary tract infection
  - E. coli (32%, 14-44%)
    Enterococcus spp. (21%, 9-32%),
    Klebsiella spp. (15%, 0-38%),
    P. aeruginosa (14%, 7-33%)

Gram-positive
Gram-negative

ECDC 2019: Healthcare-associated infections acquired in intensive care units. Annual epidemiological report for 2017.

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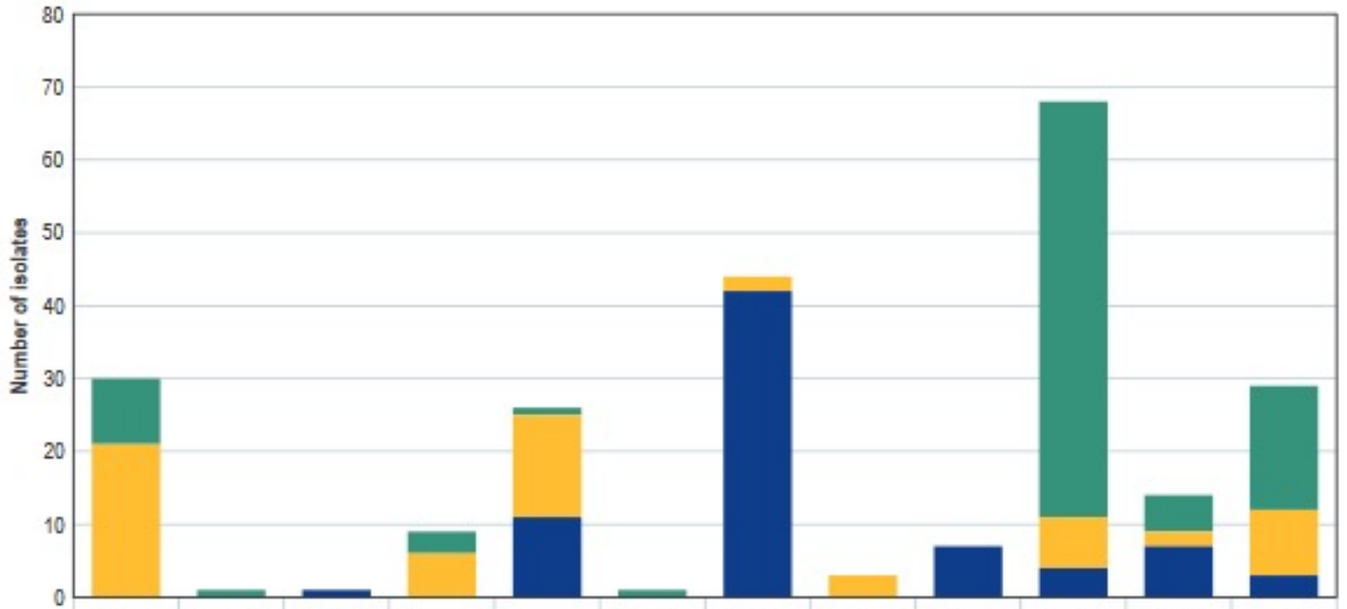
Enterobacterales from European patients with HAP/VAP (2014–2019)

Rate of carbapenem-resistance in enterobacterales (**CRE**) in European countries 5,3%.
Type of carbapenemase: KPC, metallo-β-lactamases (MBL) or OXA-48-like carbapenemases

High variation of types of carbapenemases → Variable activity of new antibiotics depending on type of resistance!



	Belarus	Belgium	Czech Republic	Germany	Greece	Ireland	Italy	Poland	Portugal	Russia	Spain	Turkey
OXA-48-like	9	1	0	3	1	1	0	0	0	57	5	17
MBL	21	0	0	6	14	0	2	3	0	7	2	9
KPC	0	0	1	0	11	0	42	0	7	4	7	3

OXA-48-like carbapenemases
MBL- NDM (n=50) or VIM (n=14) metallo-β-lactamases;
KPC- *Klebsiella pneumoniae* carbapenemase, KPC 2, 3 and 12.

D Shortridge et al. DWEEK 2020, Poster #1590

New antibiotics:
- Ceftazidime/avibactam
- Meropenem/vaborbactam (carbapenem/BLI)
- Imipenem/relebactam (carbapenem/BLI)
- Cefiderocol (Cephalosporine conjugate)

Need for rapid diagnostics and surveillance data!

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What should be done to reduce resistance?

- Antimicrobial Stewardship
  - Reduce overall antibiotic consumption
  - Choice of antibiotic, de-escalate empiric broad antibiotic therapy, treatment duration, re-evaluate early and stop therapy if possible, one-dose surgical prophylaxis whenever possible, switch early from iv to oral application to reduce risks, use a variety of antibiotic classes according to individual situations
- Adhere to evidence-based guidelines
  - International, national, regional, local
- Minimize transmission: Hygiene, infection control
- Support the ONE HEALTH approach
  - Use of antibiotics in animals and agriculture
  - Environment

https://www.ecdc.europa.eu/en/publications-data/directory-guidance-prevention-and-control/prudent-use-antibiotics/antimicrobial
S.Doron, LE Davidson. Antimicrobial stewardship. *Mayo Clinic proceedings* vol. 86,11 (2011): 1113-23

Take-home messages

- Resistance is still increasing in many countries, especially in many Gram-negative bacteria (E. coli, Klebsiella, Pseudomonas, Acinetobacter)
- New antibiotics will not solve the problem of the most resistant bacteria
- Reducing consumption of antibiotics and selection pressure are important activities to control resistance