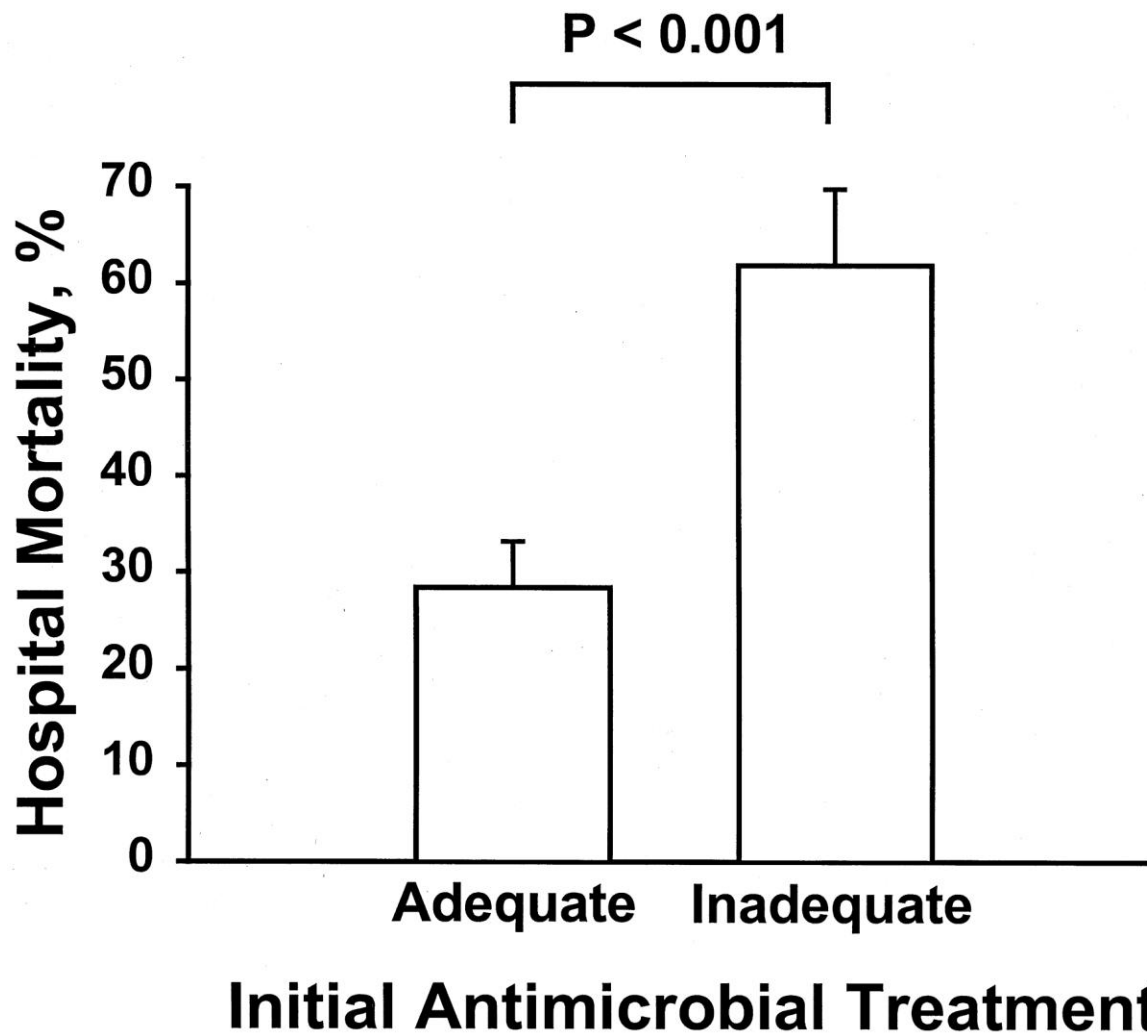


Antibiootikumiresistentsus Eesti meditsiinisüsteemi vaatepunktist

Irja Lutsar

Tallinn, 28.aprill 2014

Initial adequate AB therapy & mortality of sepsis



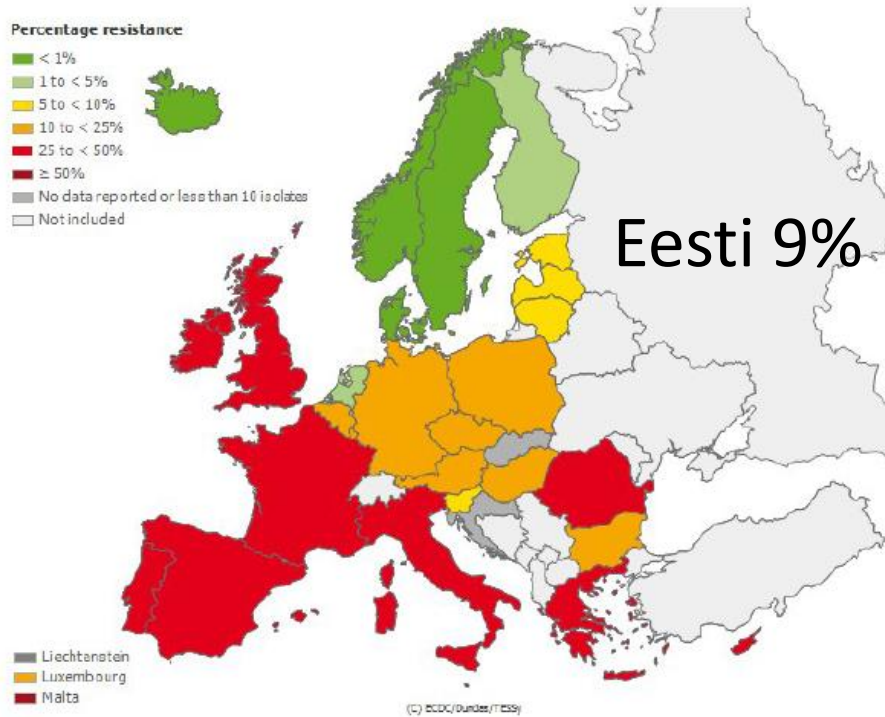
Antibiootikum-resistentsus on globaalne probleem

Relevant hospital acquired microbes

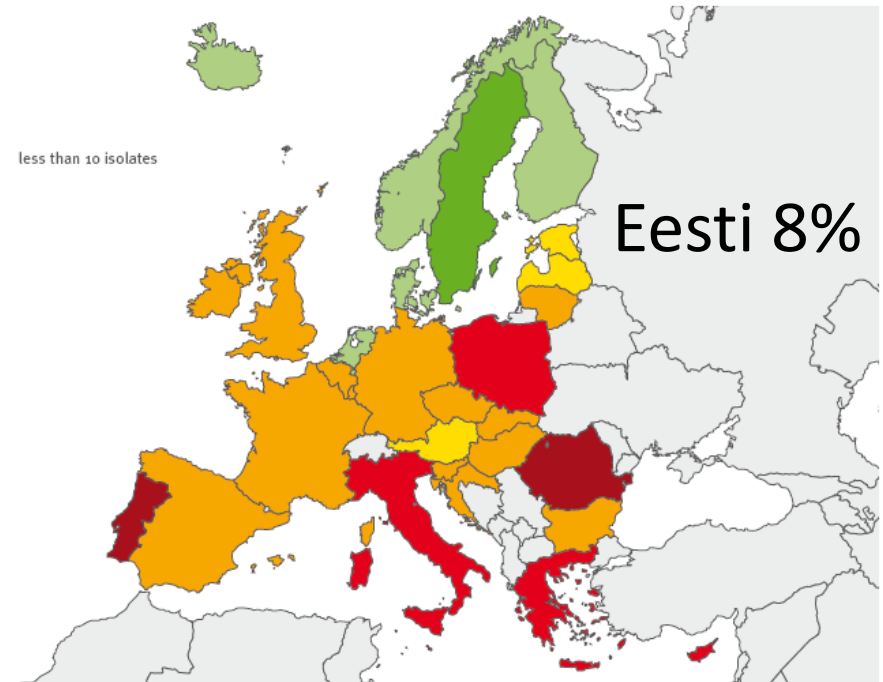
G-positive	Resistance in Estonia	G-negative	Resistance in Estonia
MRSA	8-9%	<i>Klebsiella</i> spp.	10% MDR 13% AG-R 18% 3rd gen Ceph-R
MRSA → VRSA	None	<i>Enterobacter</i> spp.	
VRE	Extremely rare	<i>P.aeruginosa</i>	25% AG-R 13% Carb-R 16% FQ-R 16% Pip/tazo-R
		<i>Acinetobacter baumannii</i>	2% of bloodstream isolates

Metitsilliin-resistentne *Staphylococcus aureus* (MRSA)

2007



2012



MRSA püsib Euroopas stabiilsel tasemel

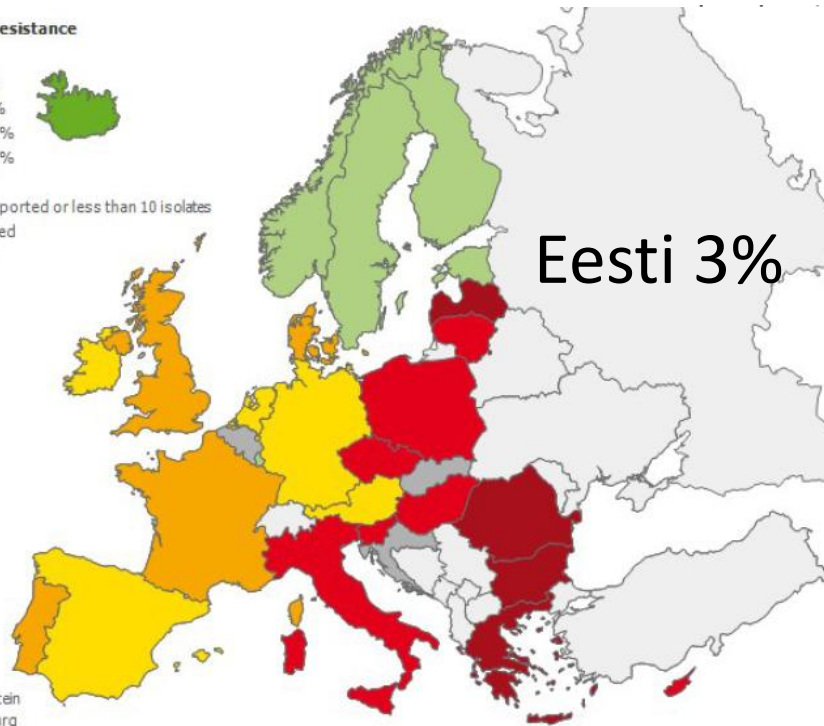
3. põlvkonna tsefalosporiinidele resistentne (ESBL) *Klebsiella pneumoniae*

2007

Percentage resistance

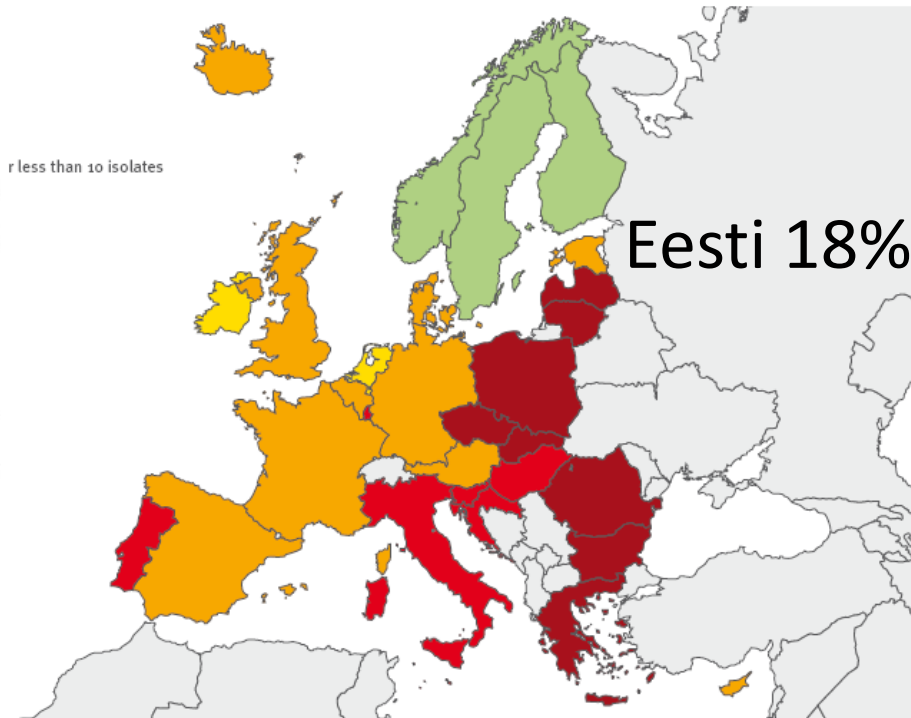
- < 1%
- 1 to < 5%
- 5 to < 10%
- 10 to < 25%
- 25 to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

- Liechtenstein
- Luxembourg
- Malta



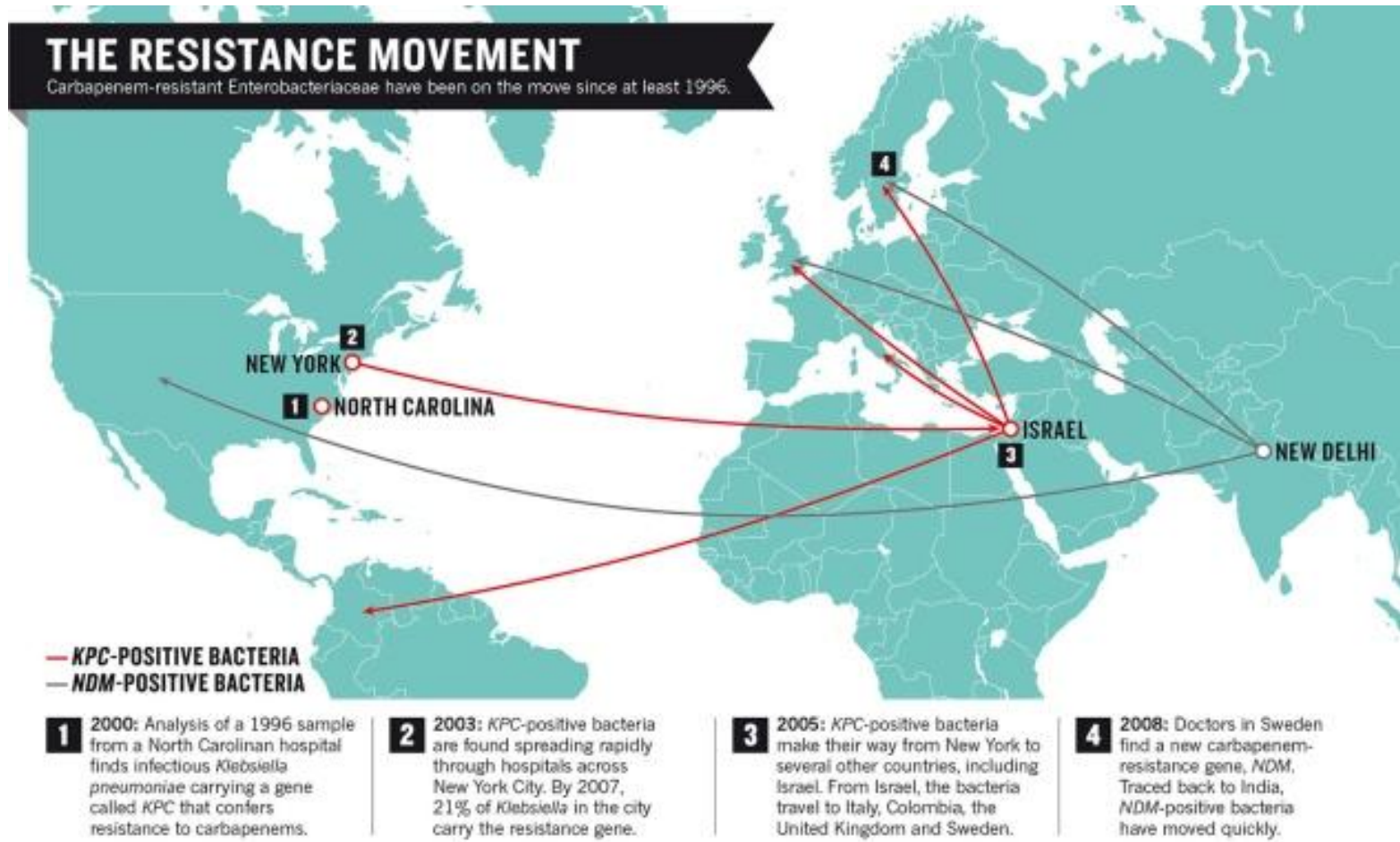
2012

less than 10 isolates



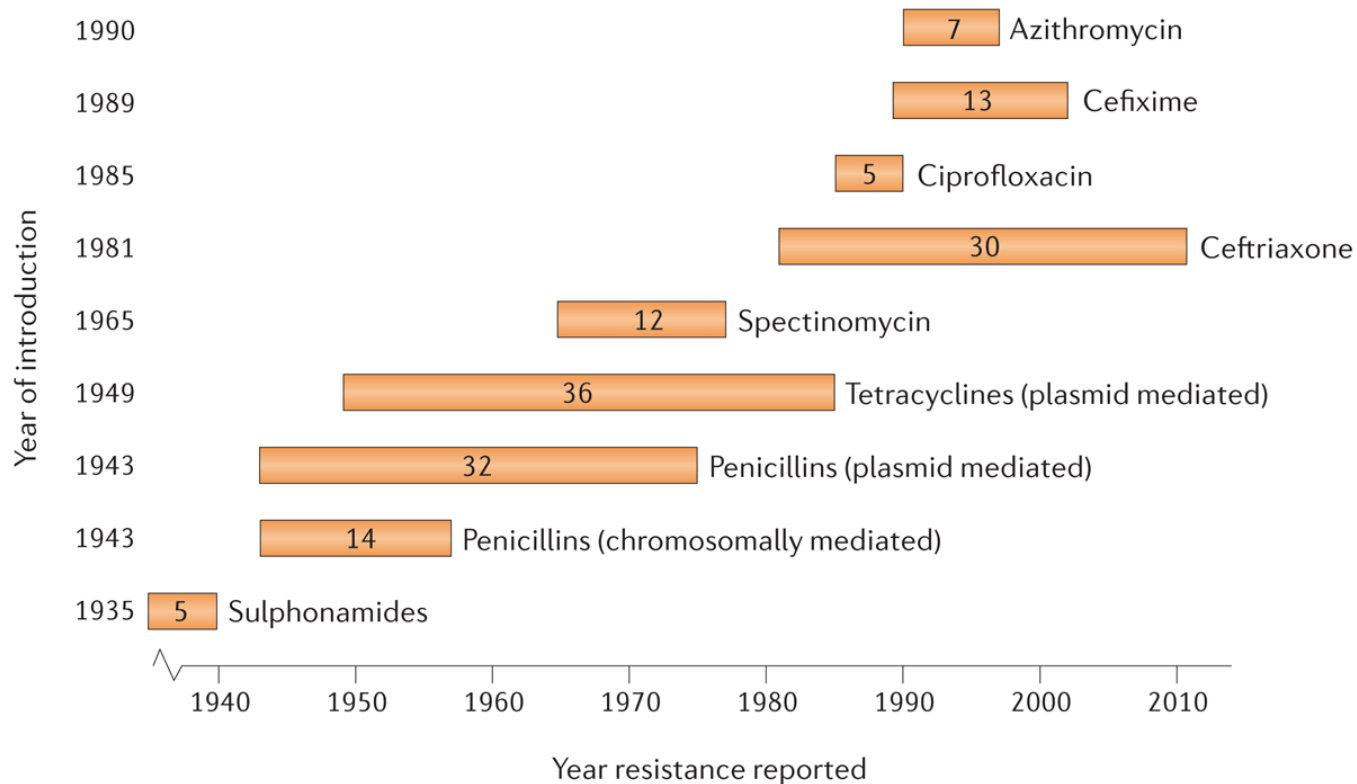
Gram negatiivsete mikroobide resistentsus suureneb

Antibiootikum-resistentsuse migratsioon



**Antibiootikumide kasutamine on
seotud antibiootikumresistentsuse
tekkega**

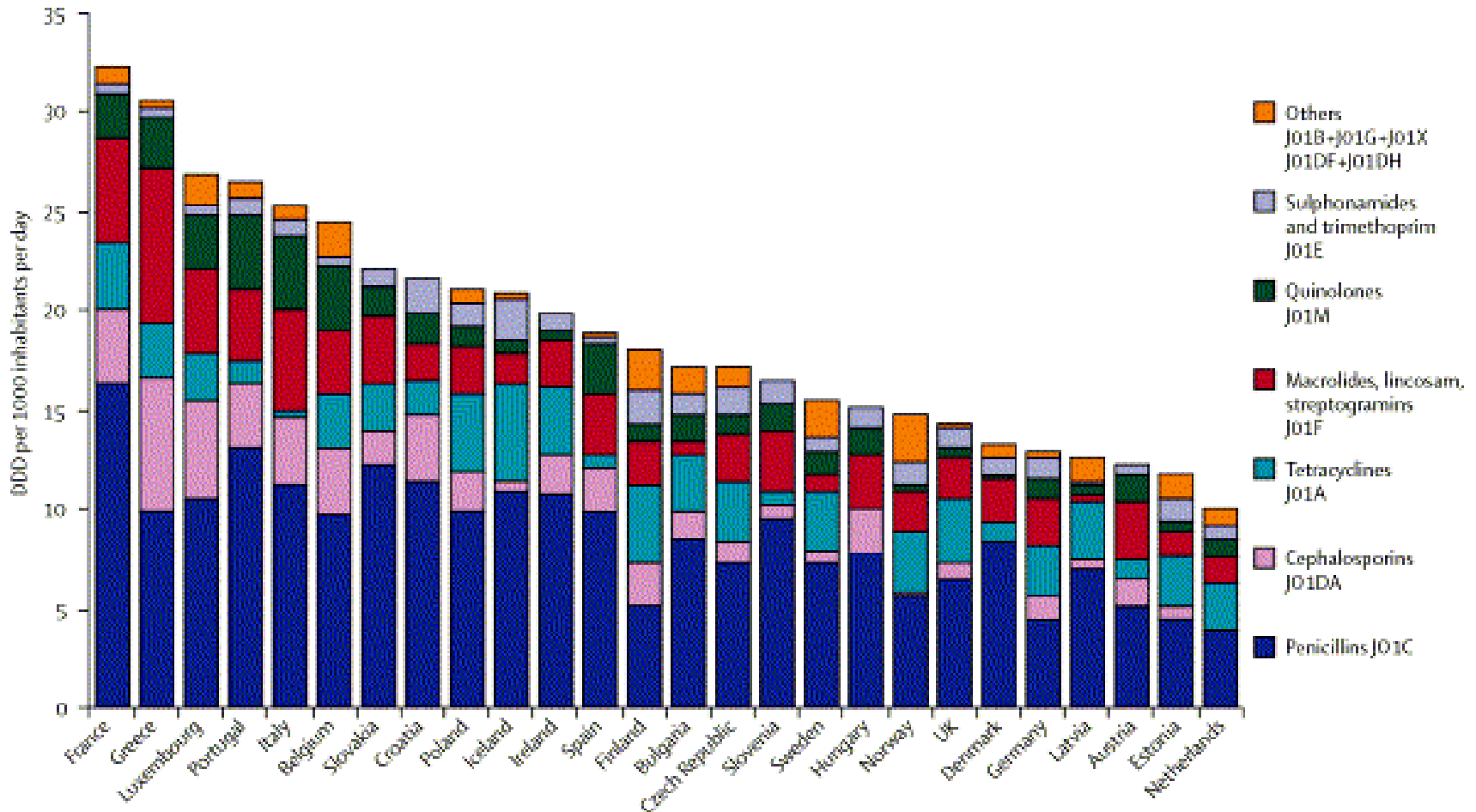
The history of *N. gonorrhoea* antimicrobial resistance



Nature Reviews | Microbiology

Nature Reviews Microbiology 12, 223–229 (2014)

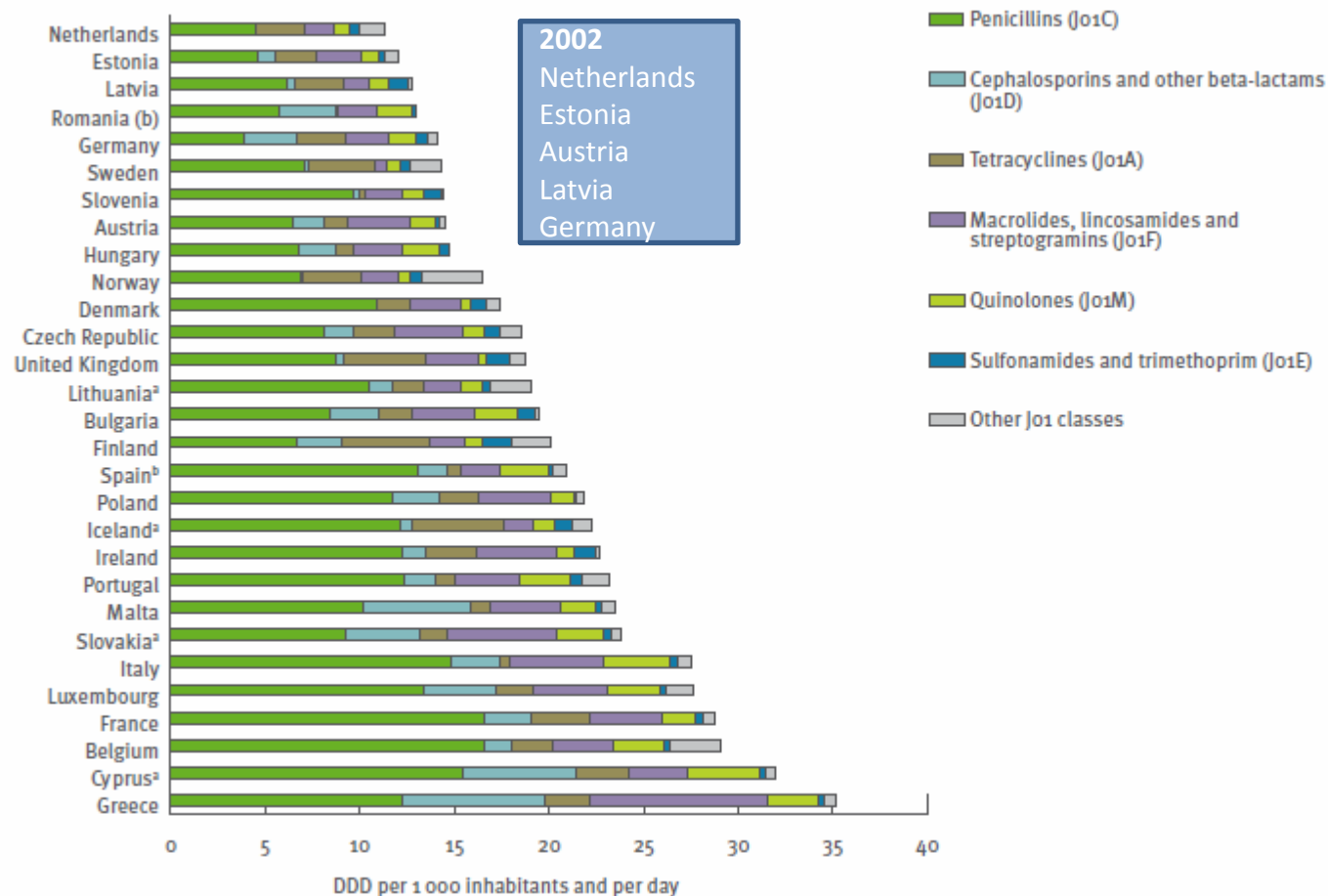
Total outpatient antibiotic use in 26 European countries in 2002



Lancet 2005; 365: 579-587

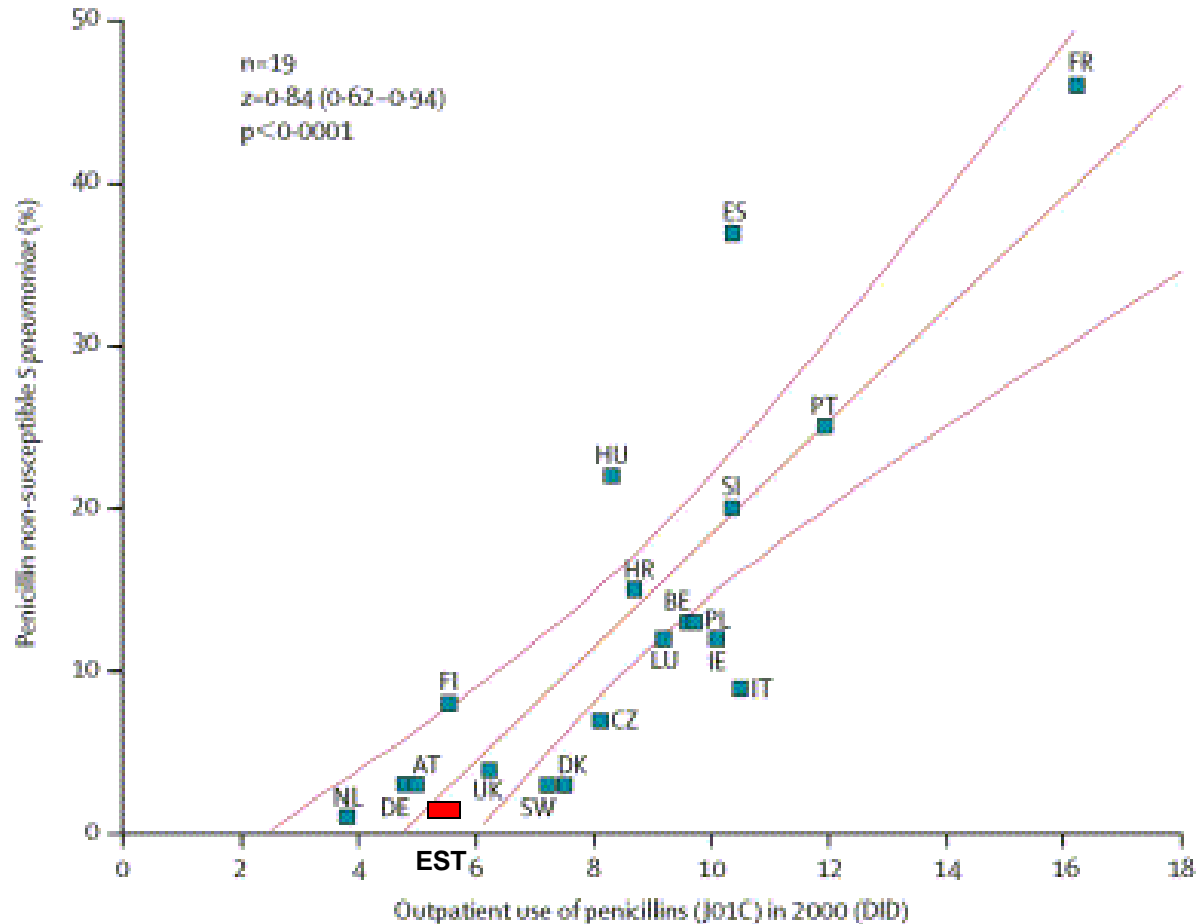
Antibiotic consumption in the community in Europe in 2011

Figure 2.6.6. Distribution of consumption of antibacterials for systemic use (ATC group J01) in the community (outside of hospitals) at ATC group level 3, EU/EEA, 2011, expressed as DDD per 1000 inhabitants and per day



(a) Cyprus, Iceland, Lithuania and Slovakia provided total care data, i.e. including the hospital sector. On average, 90% of total care data correspond to consumption in the community.
 (b) Romania and Spain provided reimbursement data, i.e. not including consumption of antibiotics obtained without a prescription and other non-reimbursed courses.

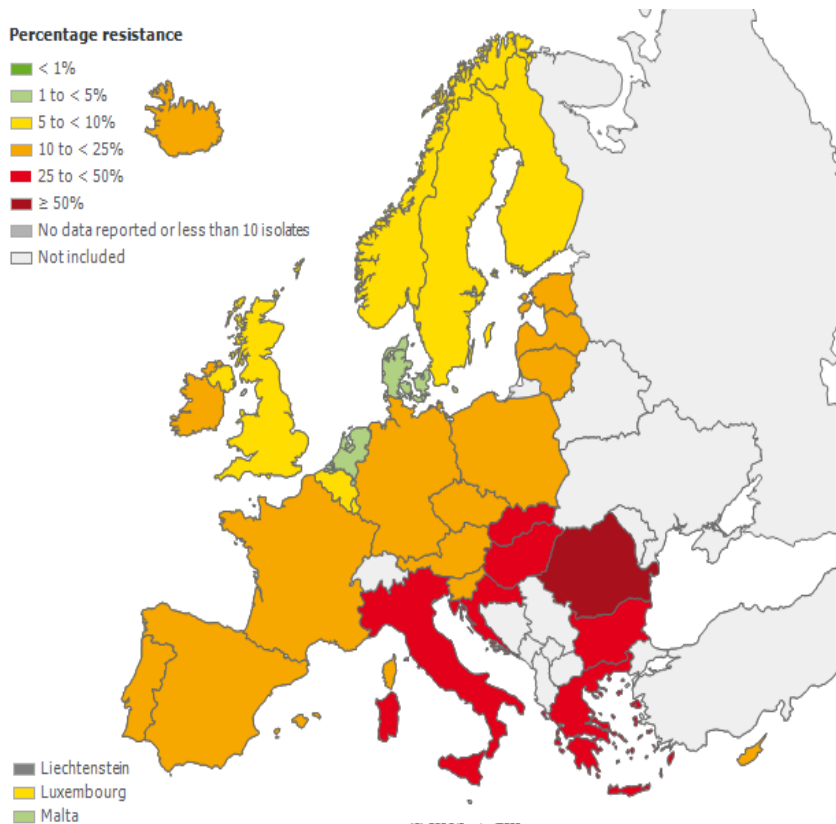
Penicillins use and prevalence of PNS - *S. pneumoniae*



**Antibiootikumide kasutamine
ei ole ainuke põhjus
resistentsuse tekkeks**

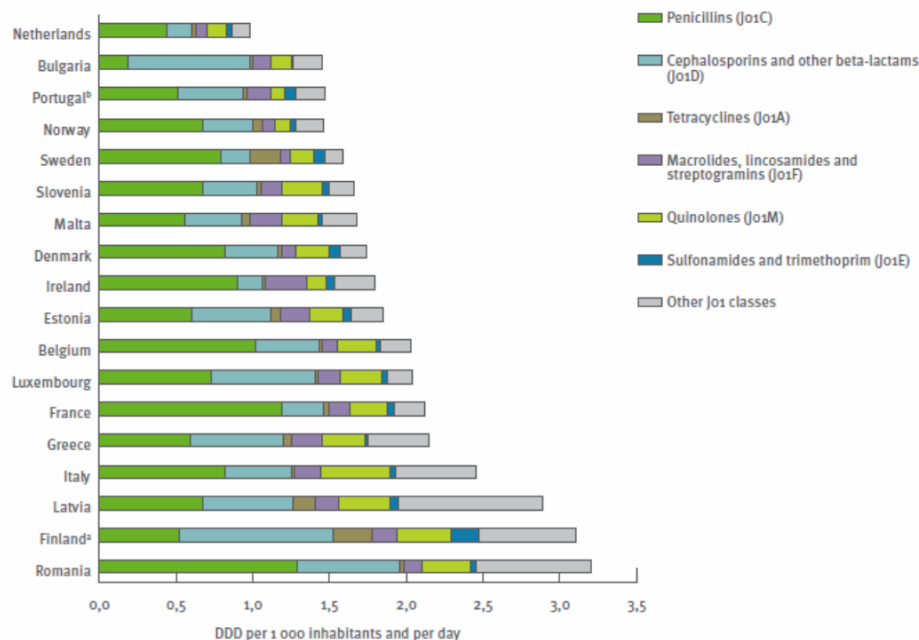
P.aeruginosa carbapenem resistance and antibiotic consumption in hospitals

P.aeruginosa resistance



Antibiotic consumption in hospitals in 2011

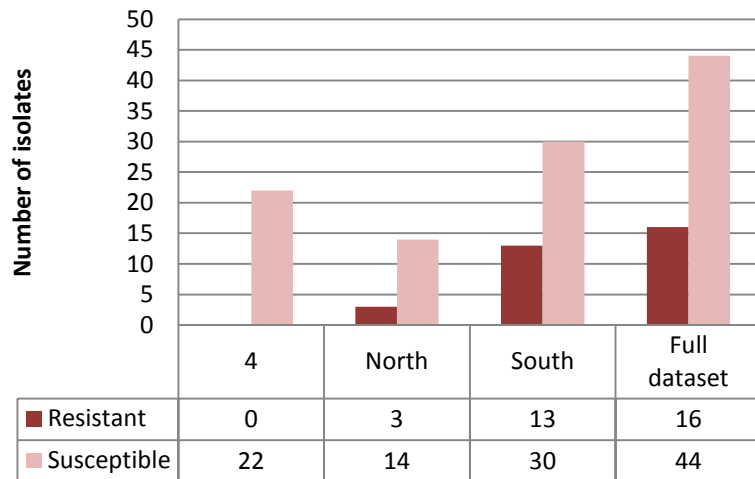
Figure 2.6.8. Distribution of consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the hospital sector, EU/EEA, 2011, expressed as DDD per 1000 inhabitants and per day



(a) Finland: data include consumption in remote primary healthcare centres and nursing homes
 (b) Portugal: data only correspond to public hospitals

Resistance patterns – *P. aeruginosa*

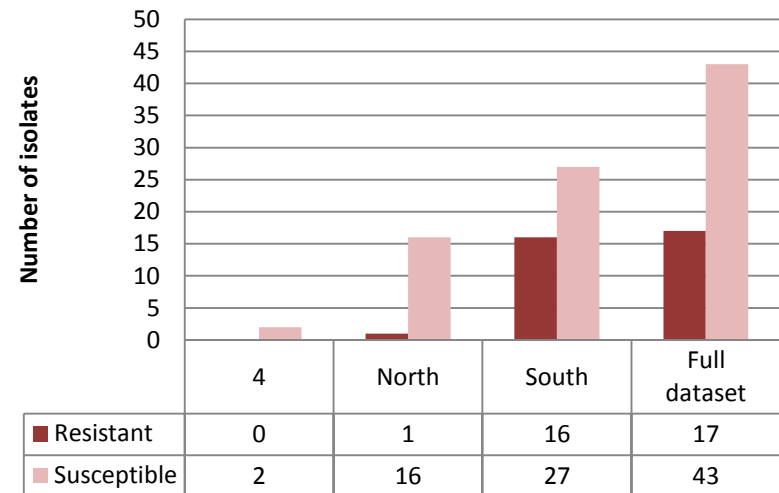
Aminoglycoside resistance



Prevalence of aminoglycoside resistance:
26.7%, 95%CI: 16.1-39.7%

Prevalence of aminoglycoside resistance in
EARS-Net: 17.7%

Fluoroquinolone resistance



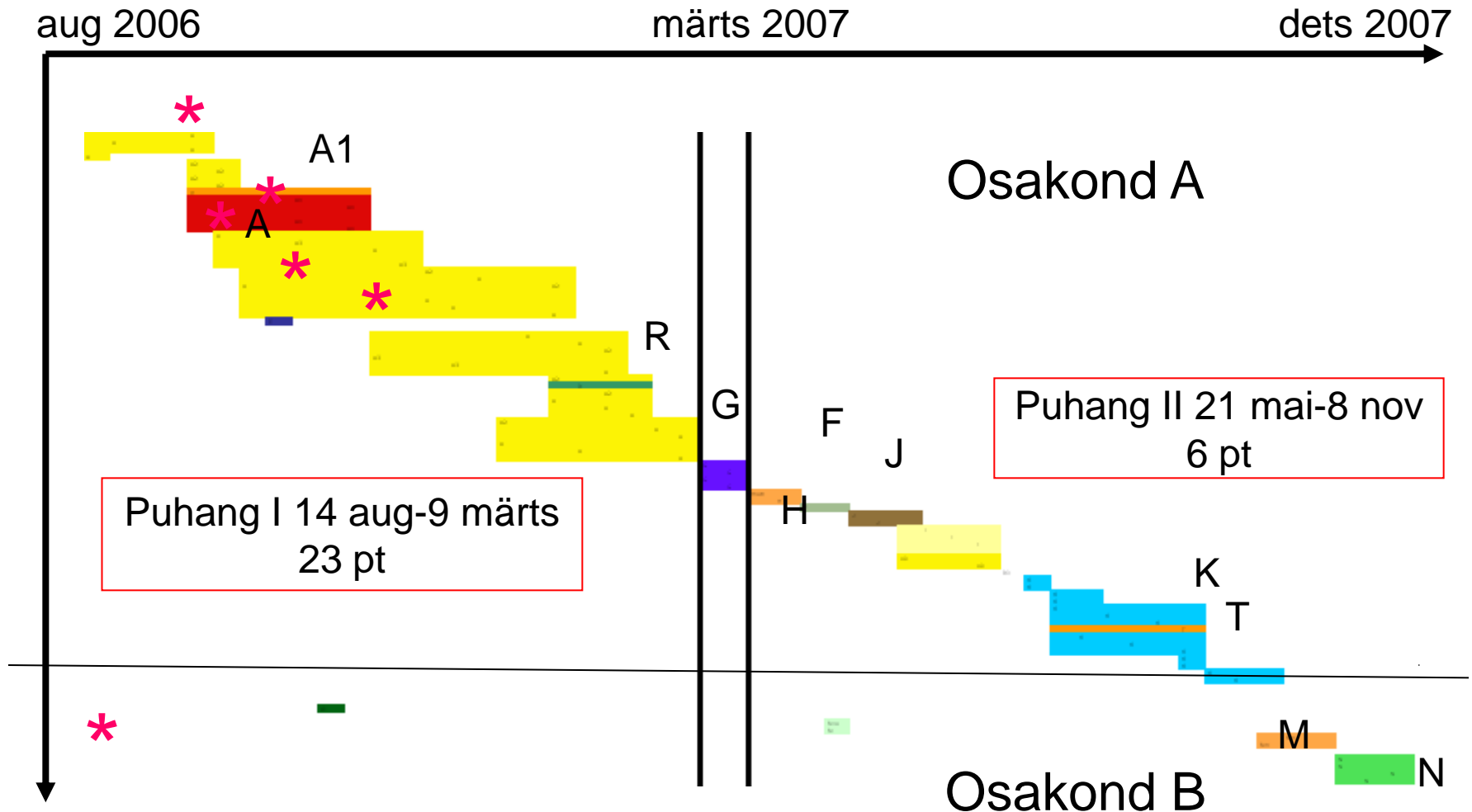
Prevalence of fluoroquinolone resistance :
28.3%, 95%CI 17.5-41.4%

Prevalence of fluoroquinolone resistance in
EARS-Net: 22.5%



K. pneumoniae kolonisatsioon: ALFP

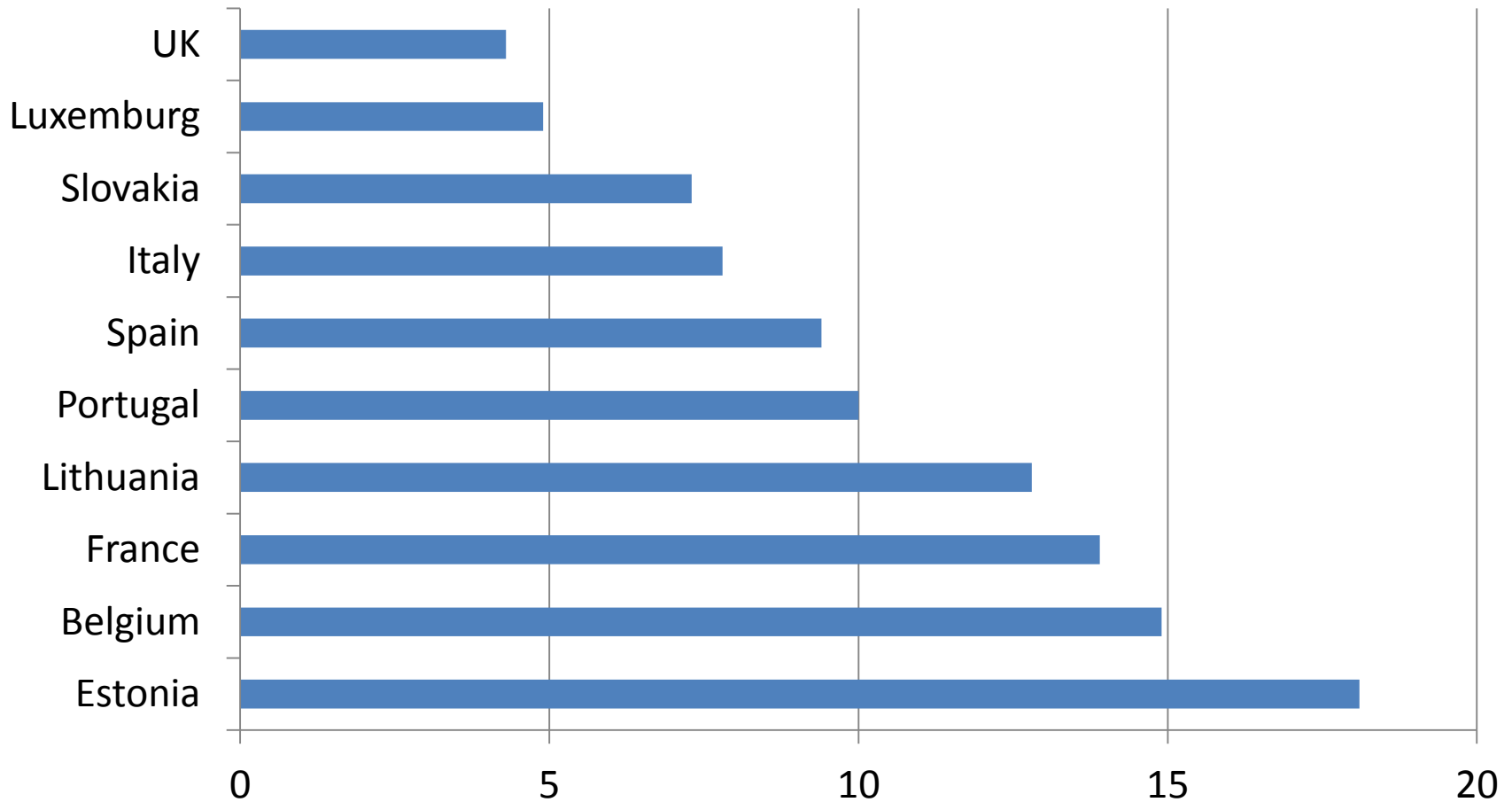
143 isolaati 48 haigelt



ALFP – amplified fragment length polymorphism

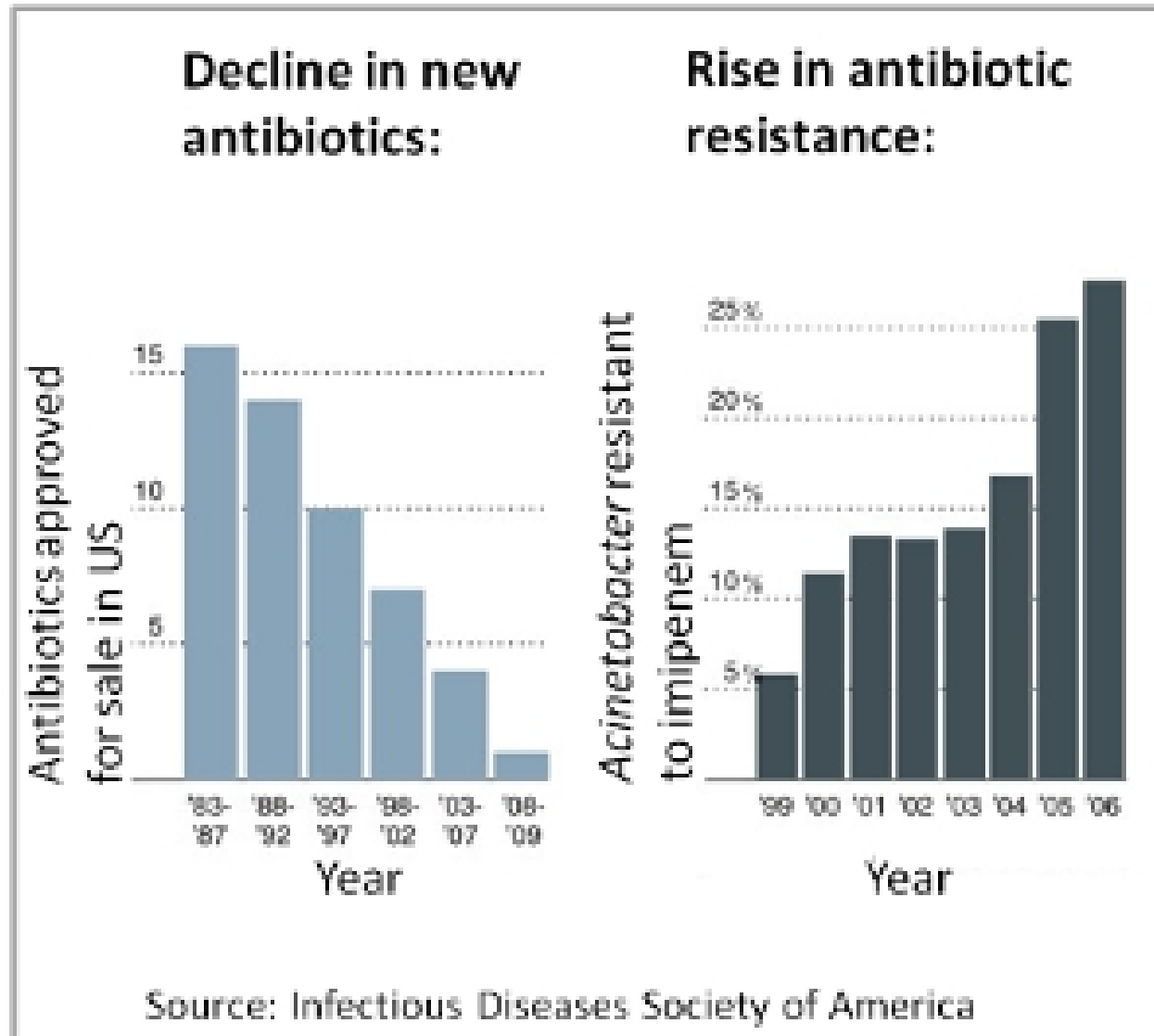
Parm *et al.* 2012

Rate of VAP in ICU in 2011 per 1000 intubation days

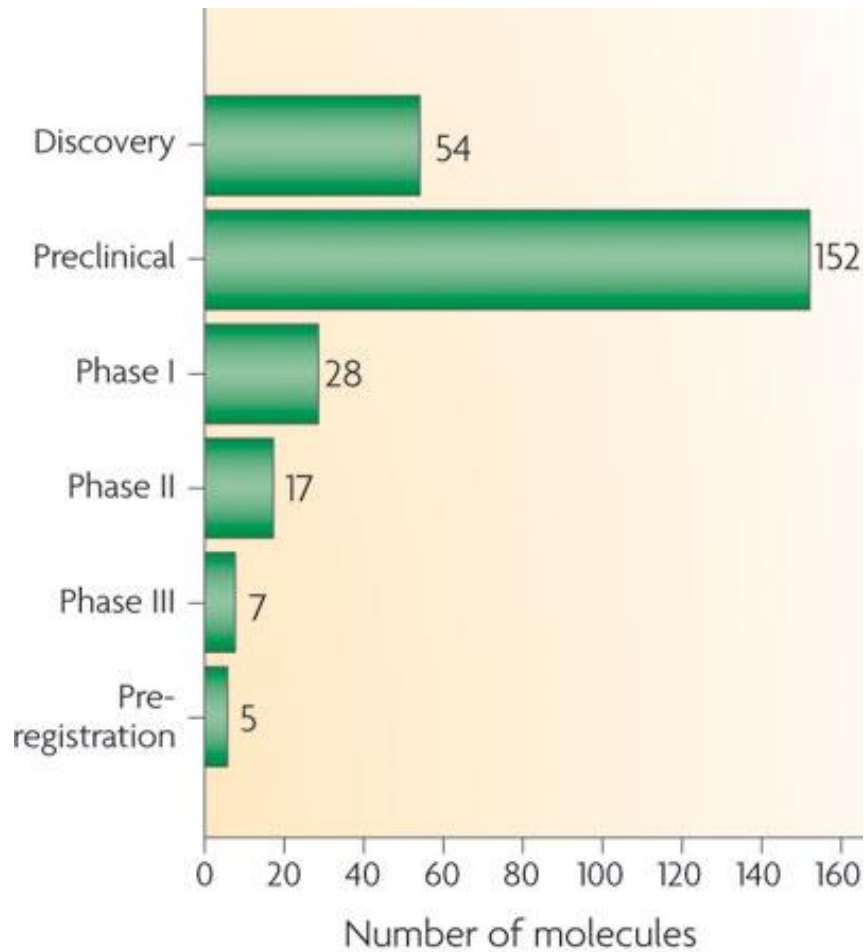


Uued antibiootikumid

Antibiotikum-resistentsus vs uued antibiotikumid

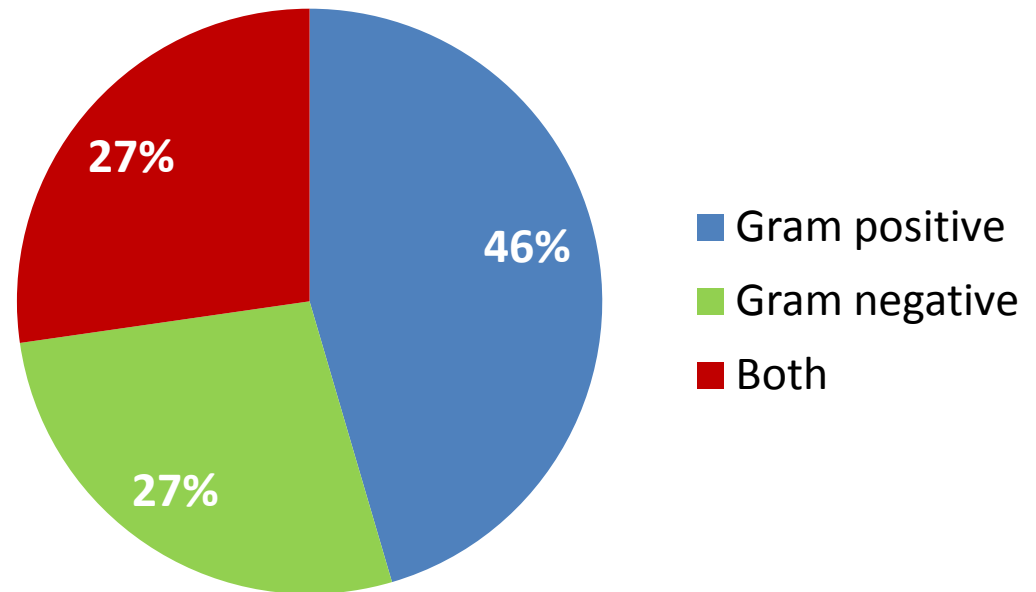


Antibiotic pipeline 2009



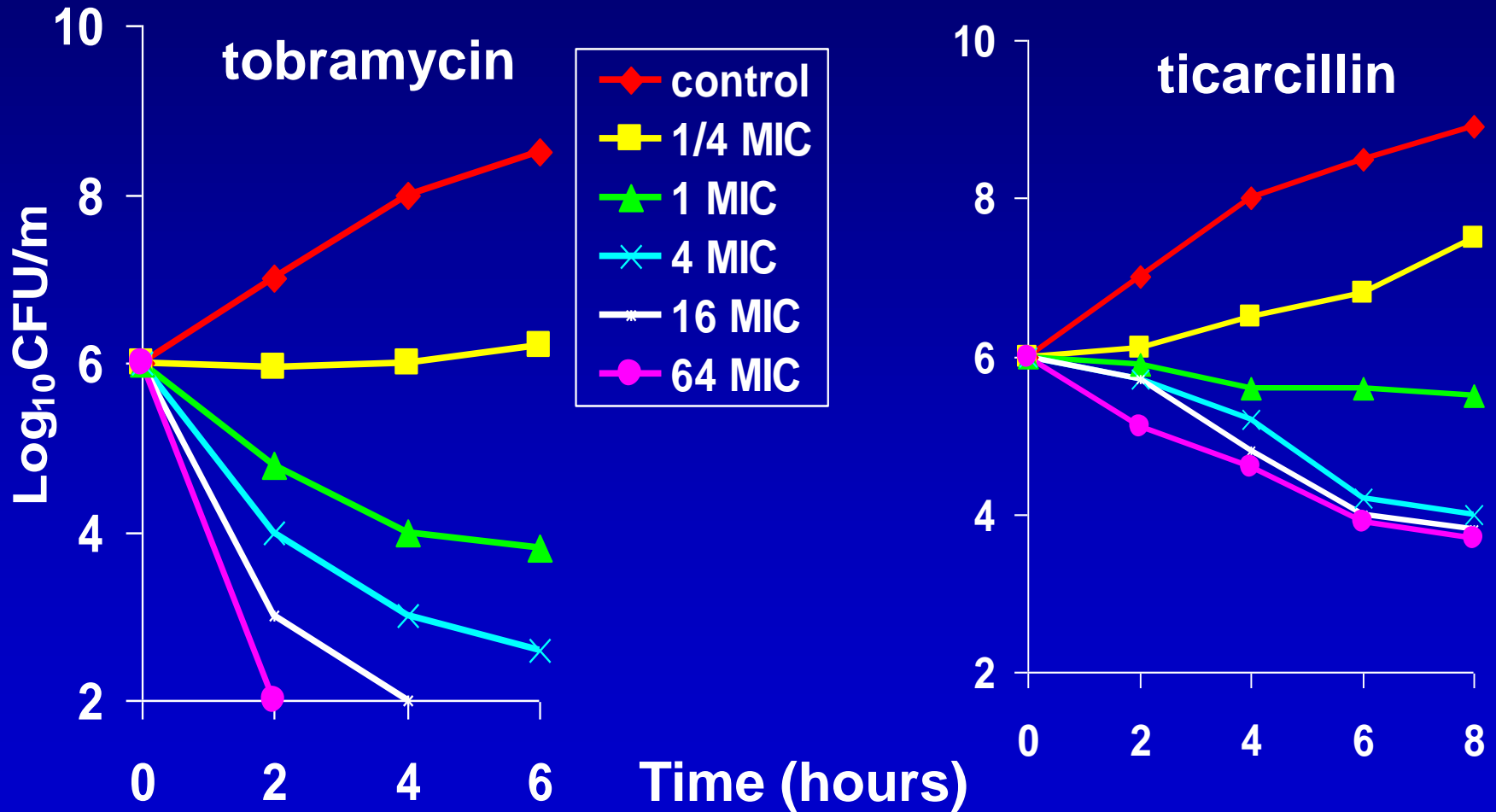
Antibiotics approved in EU in 21 century

Aztreonam lysin
Ceftaroline fosamil
Daptomycin
Doripenem
monohydrate
Ertapenem sodium
Fidaxomicin
Linezolid
Moxifloxacin
Retapumilin
Telithromycin
Tigecyclin

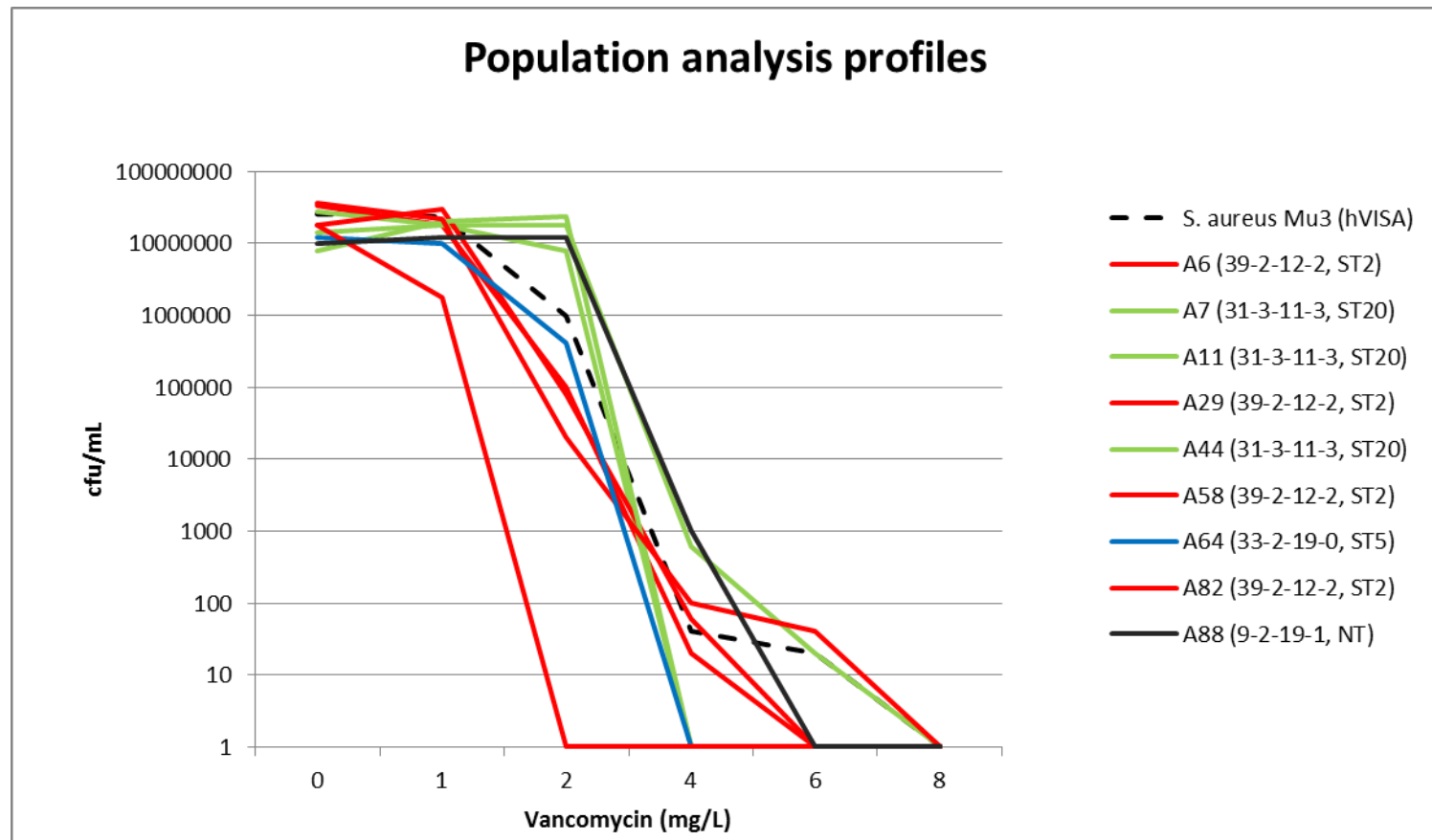


Farmakodünaamilne printsiip antibiootikum-resistentsete infektsioonide ravis

Time-Kill Curves of *P.aeruginosa* with Tobramycin and Ticarcillin



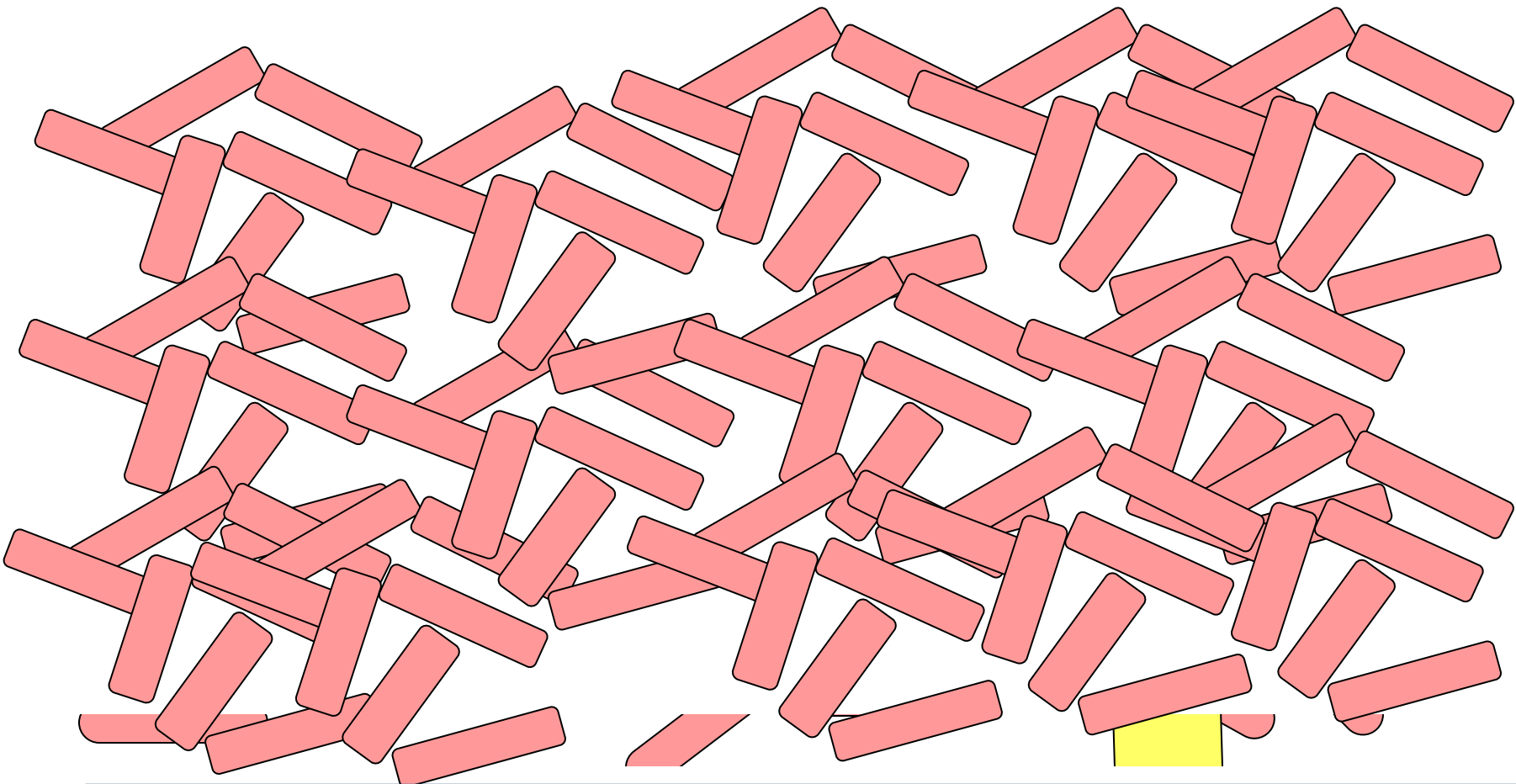
Heteroresistance of *S. epidermidis* blood isolates



Clinical MIC 2 $\mu\text{g/ml}$

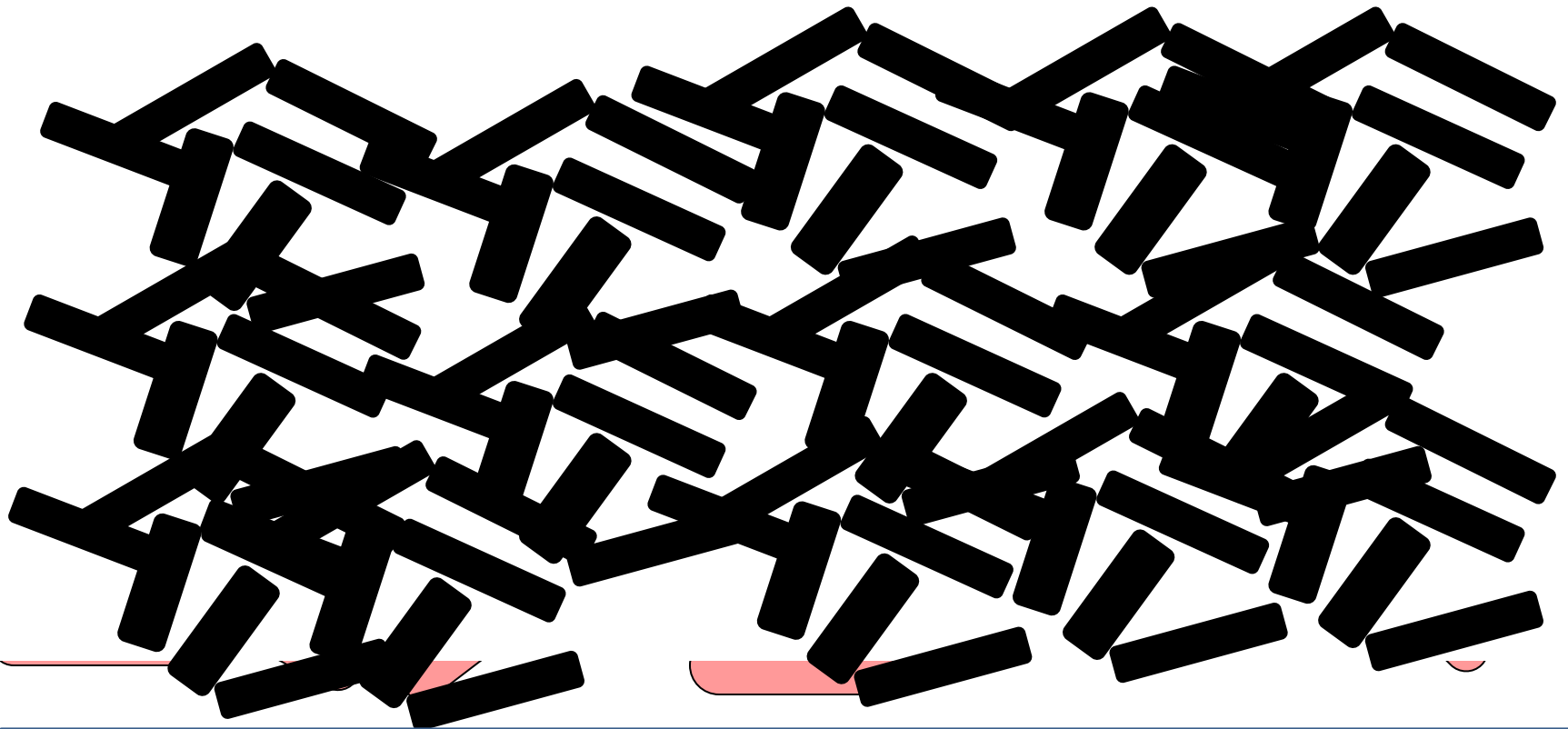
Soeorg *et al.* unpublished

Resistentsed bakterid ilma antibiootikumita



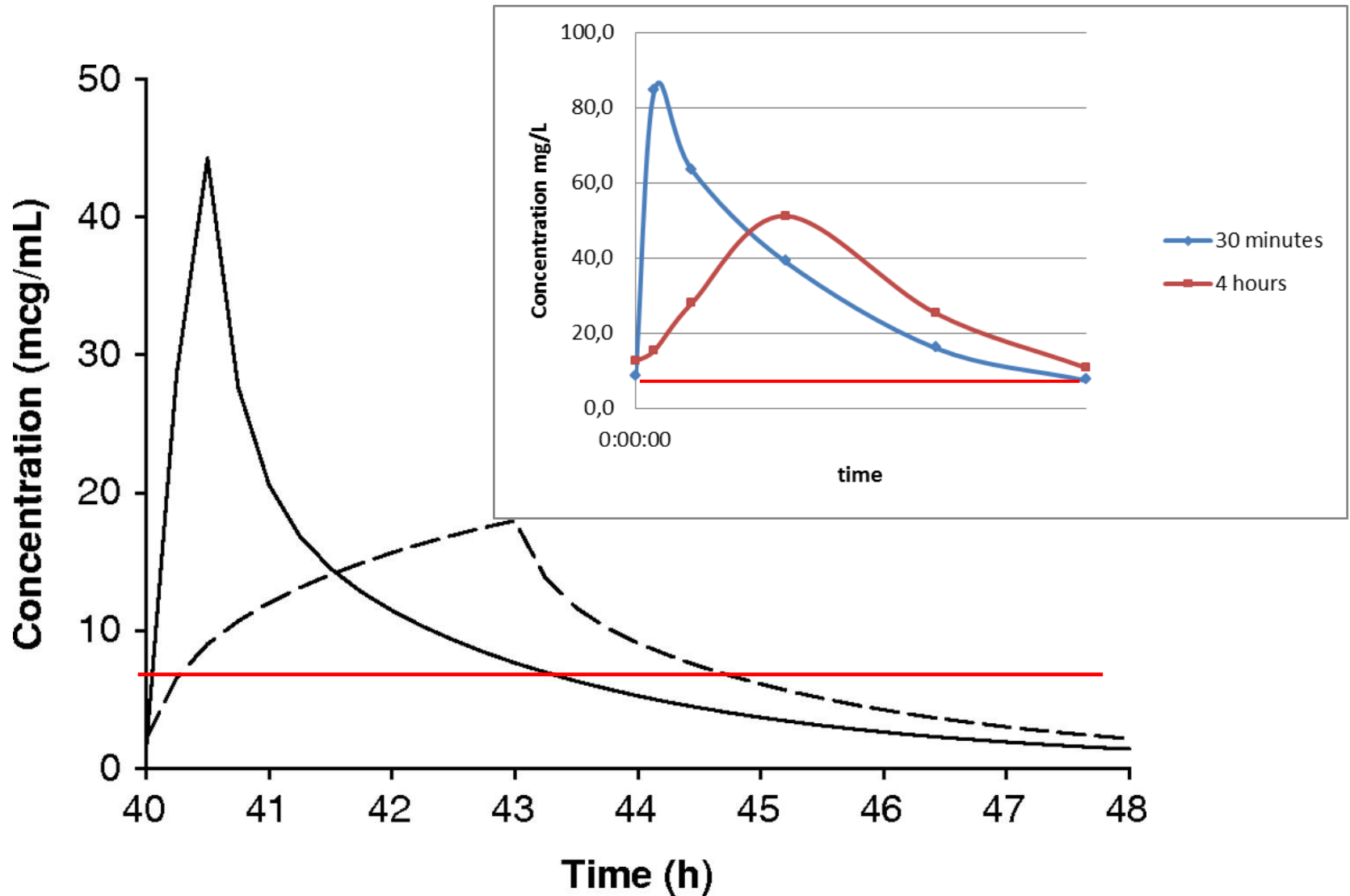
Resistentsetel bakteritel pole paljunemises eelist ning nad surutakse maha tundlike bakterite poolt

Resistentsed mikroobid ja ebaefektiivne antibiootikumravi



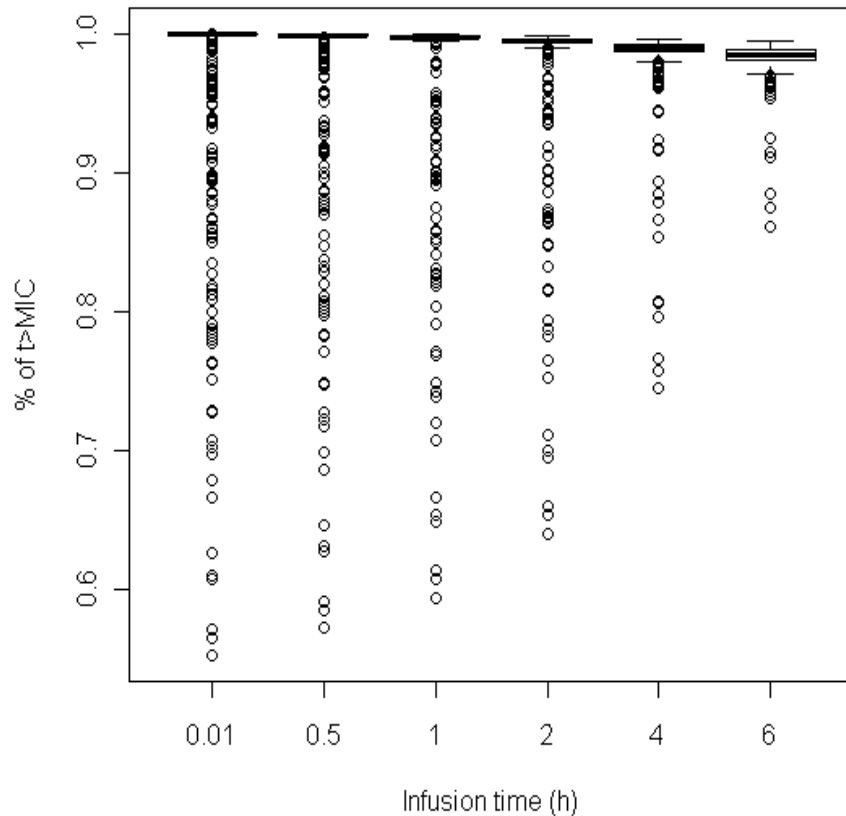
Ebapiisava antibiootikumi kontsentratsiooni korral resistentsel mikroobidel tekib kasvueelis kuna tundlikud bakterid hävitatakse

Meropeneemi kontsentratsioon lastel ja täiskasvanutel

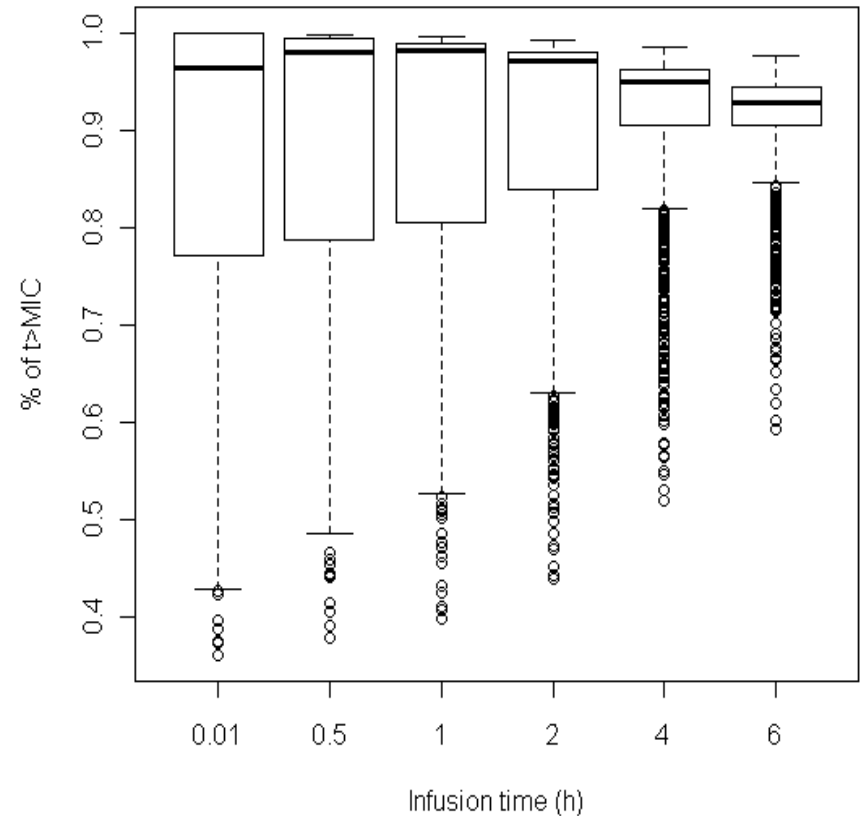


fT>MIC versus infusion duration for meropenem EUCAST *Enterobacteriaceae* breakpoints of 2 and 8mg/L

FTAU vs. Infusion time (MIC=2)

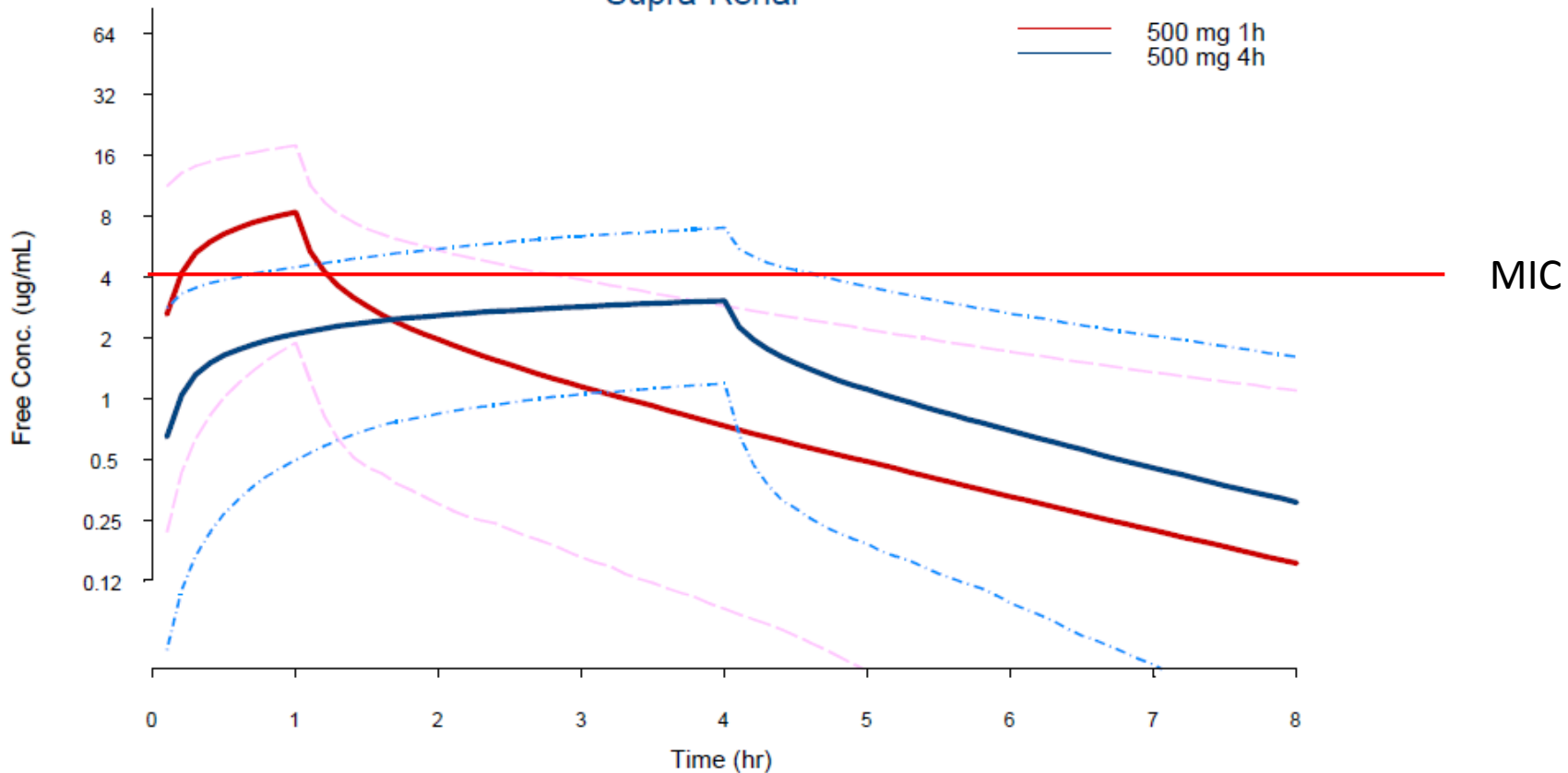


FTAU vs. Infusion time (MIC=8)



Patients with augmented renal clearance 1h vs 4h infusion of a beta-lactam

Figure 8: 500 mg 1-hour Infusion versus 4-hour Infusion
50th % Quantile & 95 Percentile Band for IIV in PK
Supra-Renal



Kokkuvõtteks

- Antibiootikum-resistentsusest on saanud 21. sajandi pandeemia
- Antibiootikum-resistentsust soodustavad
 - Antibiootikumide ebaõige kasutamine
 - Haiglahügieeni reeglite ignoreerimine
 - Resistentsusgeenide liikidevaheline levik
- Lahendused
 - Uued antibiootikumid
 - Vanade antibiootikumide ratsionaalne ja farmakodünaamilal põhinev kasutamine