

BACTERIAL RESISTANCE AND ANTIBIOTIC THERAPY

Milan Kolar

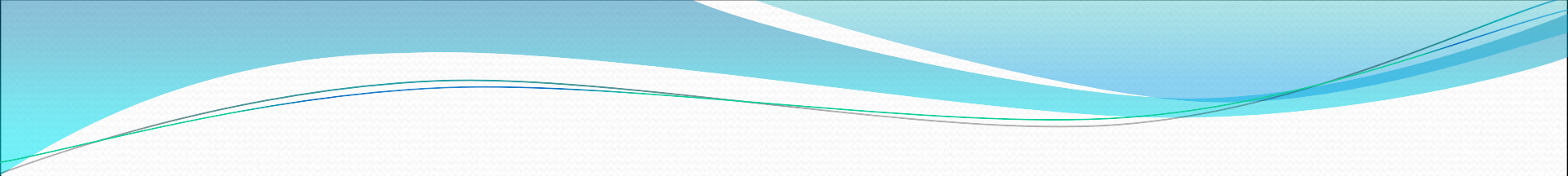
Department of Microbiology

Faculty of Medicine and Dentistry

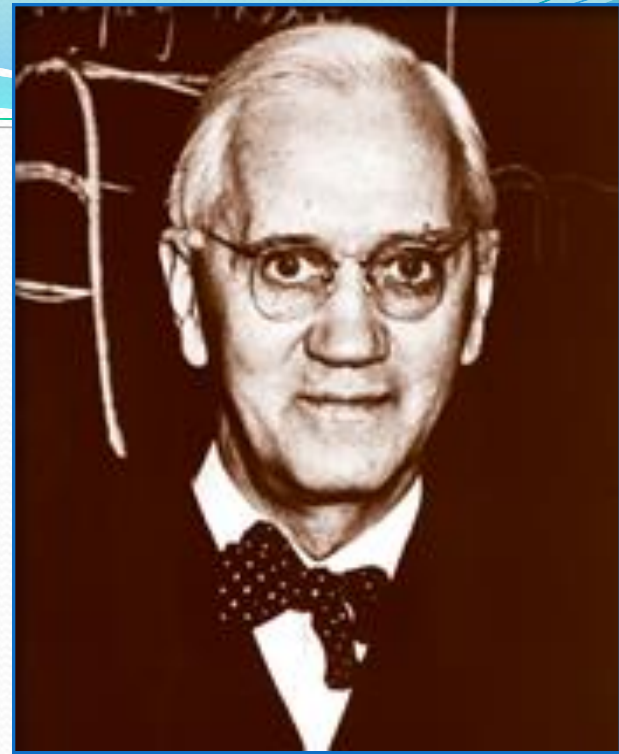
Palacky University Olomouc, Czech Republic



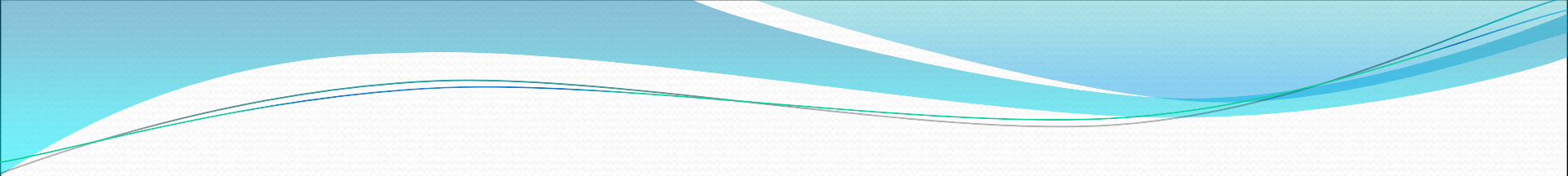
Faculty of Medicine
and Dentistry
Palacky University Olomouc

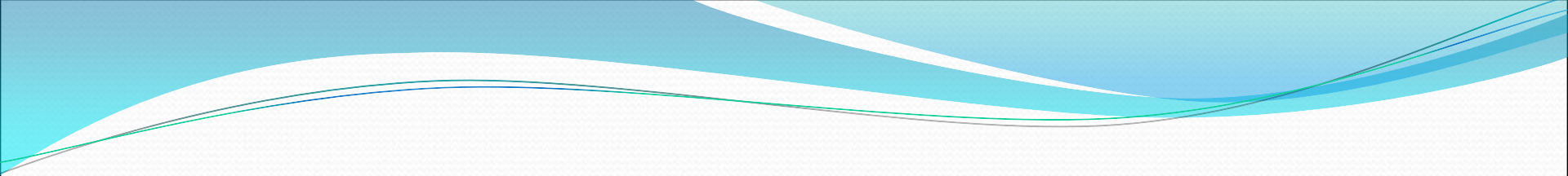
- 
- An integral part of treatment of patients with bacterial infections is application of antibiotics, the effectiveness of which is increasingly limited by rising bacterial resistance.

- In 1928, Sir Alexander Fleming described antibacterial effects of a fungus from the genus *Penicillium* on a strain of *Staphylococcus aureus*. This description started the antibiotic era, one of the most important phases in the development of medicine.



- The beginning of the use of penicillin in medical practice in 1942 and subsequent development of other antibiotic agents brought the hope that bacterial diseases would no longer be a problem.

- 
- Unfortunately, the hope has not been fulfilled and it is clear now that bacterial infections will continue to be one of the most serious problems in medicine.
 - Among the main reasons are the ability of bacteria to adapt to external conditions and the related development and spread of bacterial resistance.

- 
- Increasing bacterial resistance to antibiotics is one of the most serious problems in current medicine.
 - An important factor contributing to the growing prevalence of multiresistant bacteria is application of antibiotics.

- In the last three decades, several studies have been carried out on the relationship between consumption of antimicrobial agents and development of bacterial resistance, **suggesting a positive correlation.**

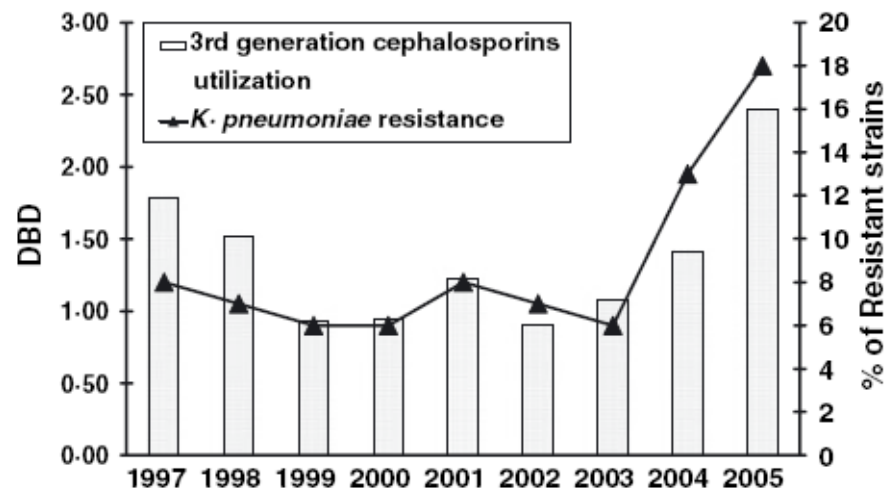


Fig. 4. Association of rate of *Klebsiella pneumoniae* resistance with third-generation cephalosporin utilization.

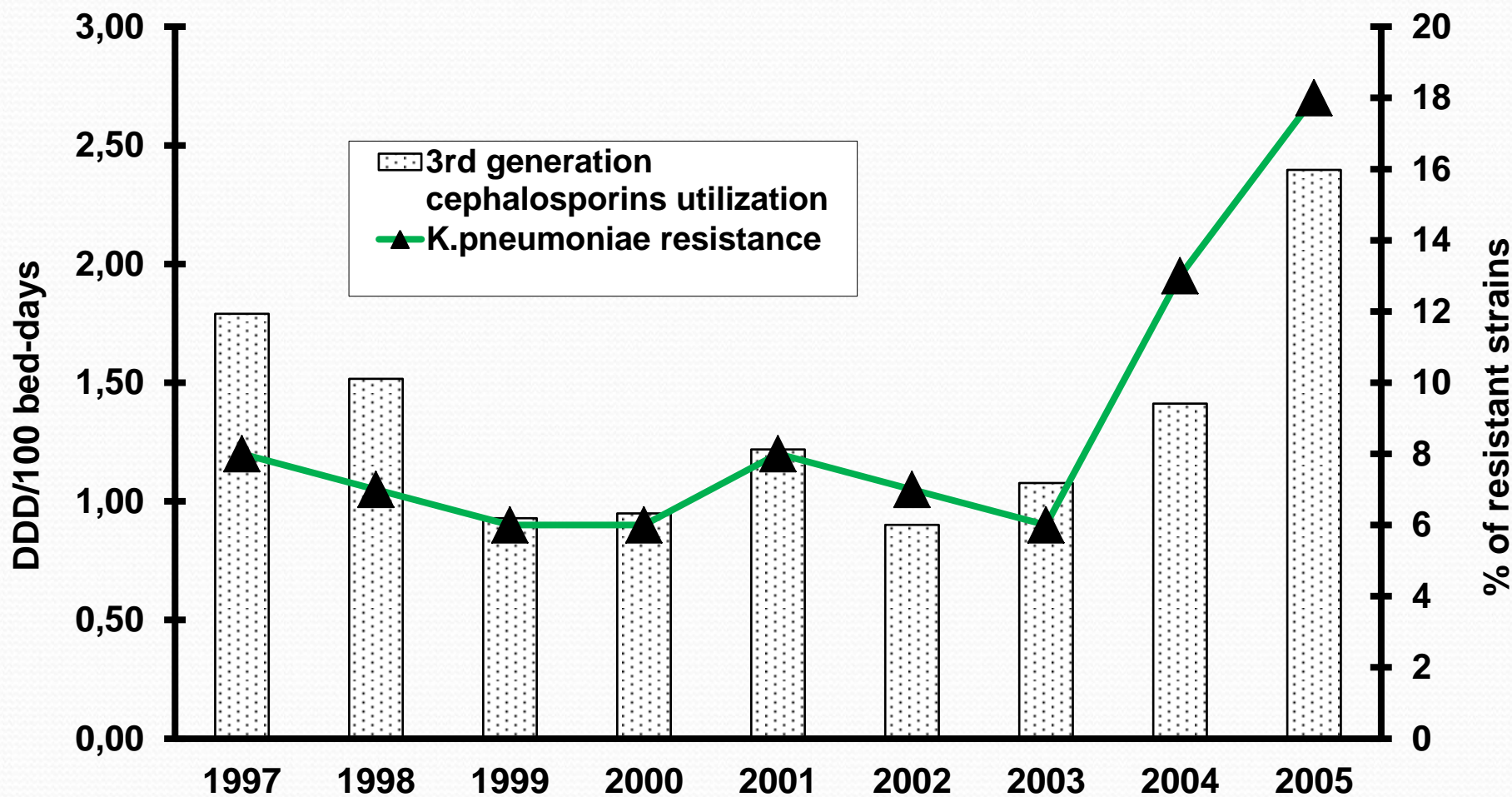
ORIGINAL ARTICLE

Influence of third-generation cephalosporin utilization on the occurrence of ESBL-positive *Klebsiella pneumoniae* strains

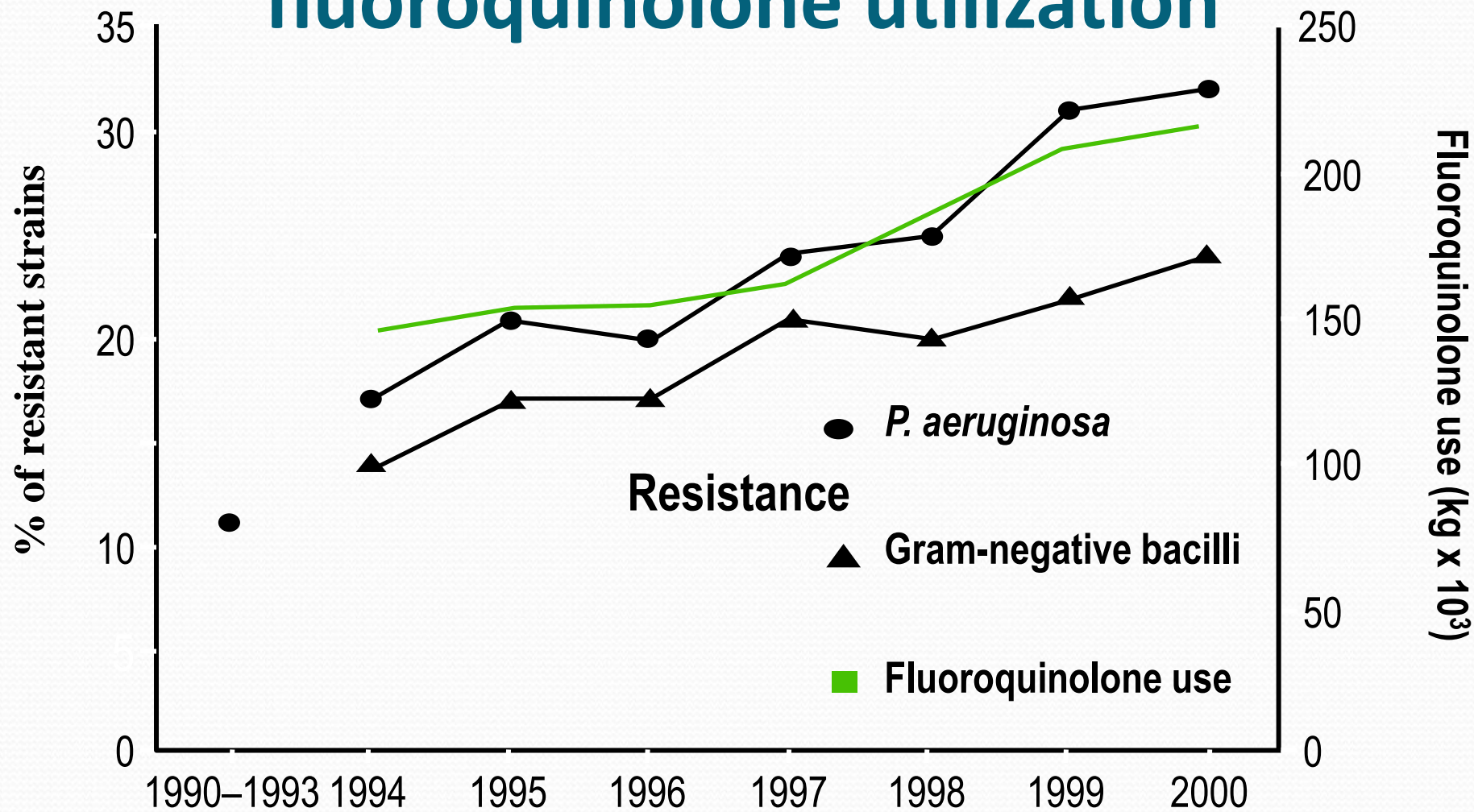
K. Urbánek* MD PhD, M. Kolář† MD PhD, Y. Lovečková† MD, J. Strojil* MD and L. Šantavá* PharmD

Departments of *Pharmacology and †Microbiology, Faculty of Medicine and University Hospital, Olomouc, Czech Republic

Dependence of *K. pneumoniae* resistance on 3rd generation cephalosporins utilization



Dependence of bacterial resistance on fluoroquinolone utilization



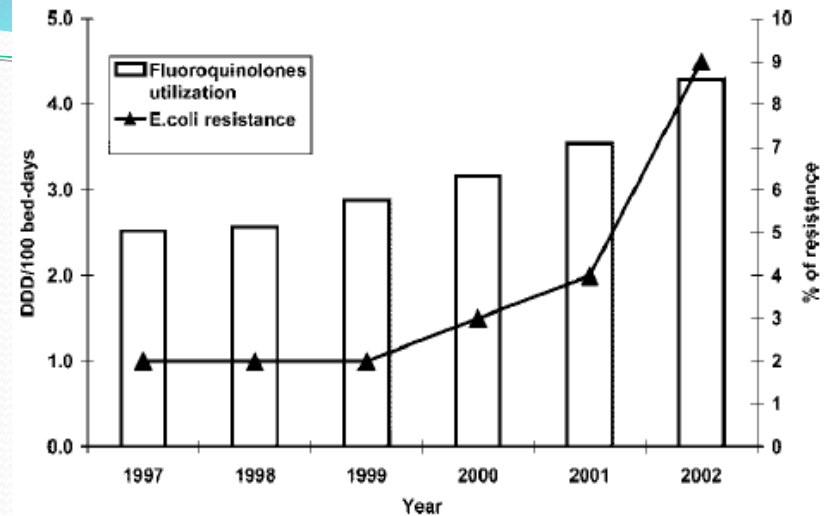


Figure 1. Utilization of fluoroquinolones and *E. coli* resistance to fluoroquinolones in inpatients of the Teaching Hospital Olomouc.

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2005; 14: 1–5

Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/pds.1110

ORIGINAL REPORT

Utilization of fluoroquinolones and *Escherichia coli* resistance in urinary tract infection: inpatients and outpatients

Karel Urbánek MD, PhD^{1*}, Milan Kolář², Jan Strojil¹, Dagmar Koukalová², Luboslava Čekanová² and Petr Hejnar²

¹Department of Pharmacology, Faculty of Medicine, Palacký University, Olomouc, Czech Republic

²Department of Microbiology, Faculty of Medicine, Palacký University, Olomouc, Czech Republic

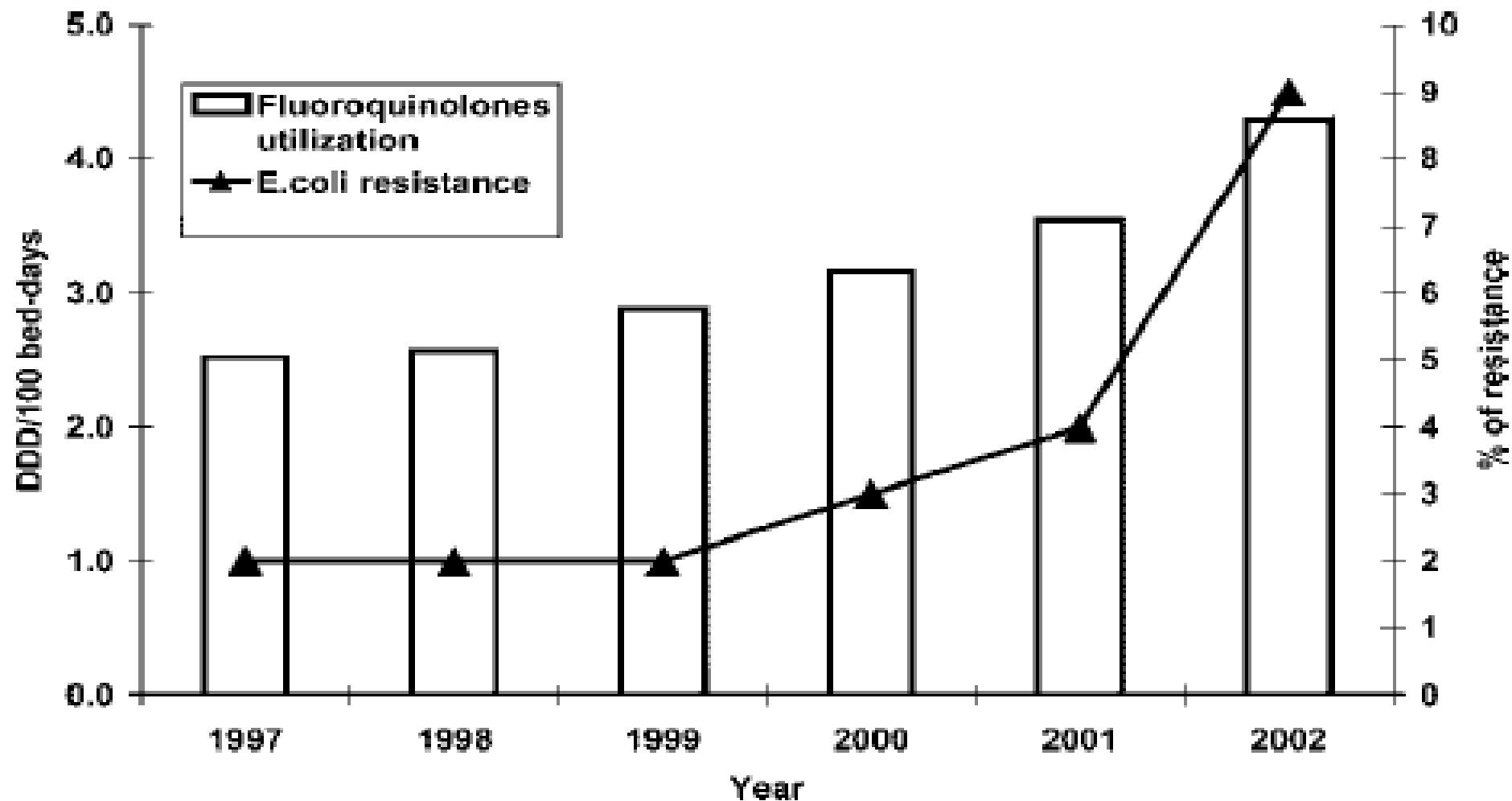
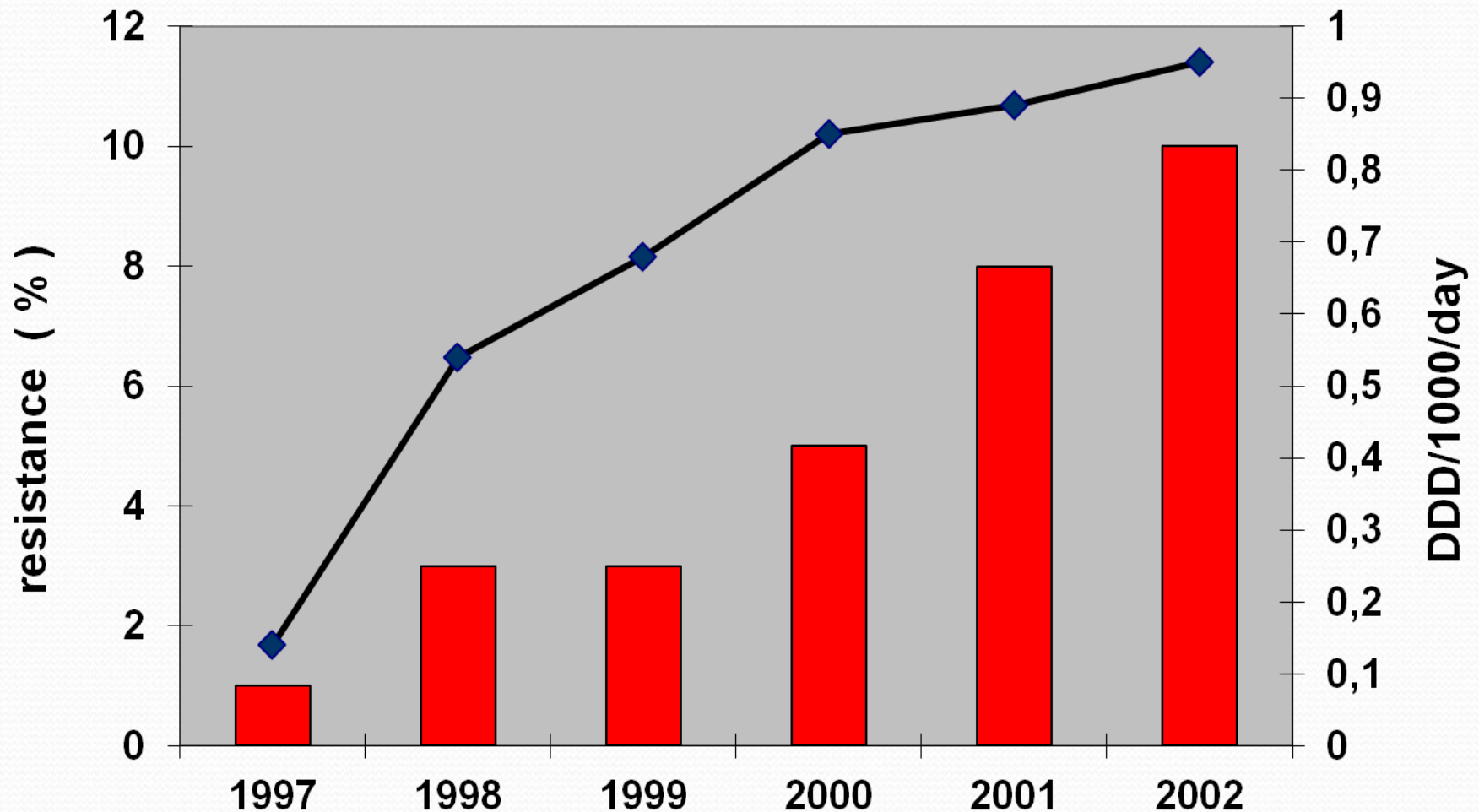


Figure 1. Utilization of fluoroquinolones and *E. coli* resistance to fluoroquinolones in inpatients of the Teaching Hospital Olomouc.

Dependence of *Escherichia coli* resistance on fluoroquinolone utilization in community UTI



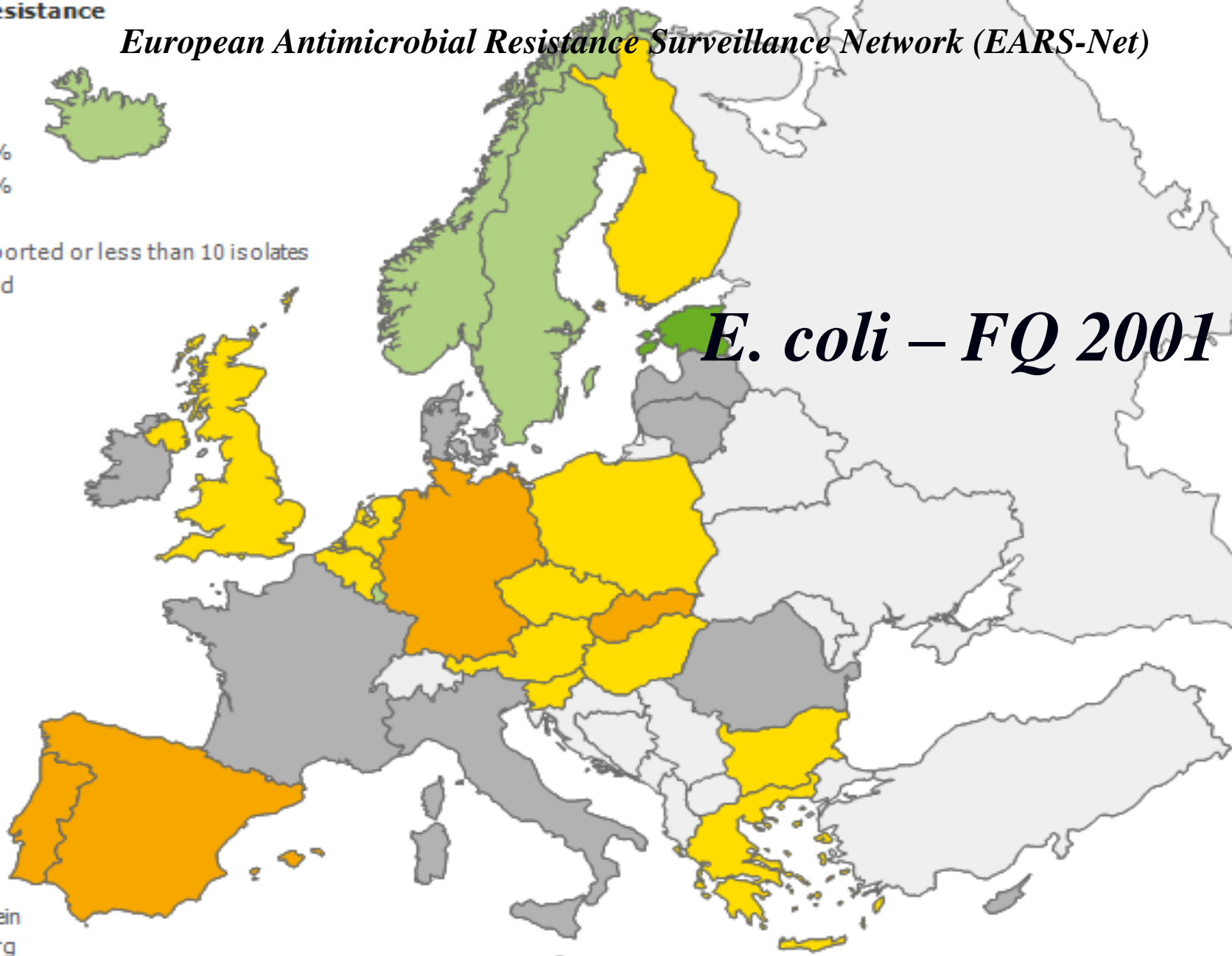
Percentage resistance

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

European Antimicrobial Resistance Surveillance Network (EARS-Net)

E. coli – FQ 2001

- Liechtenstein
- Luxembourg
- Malta



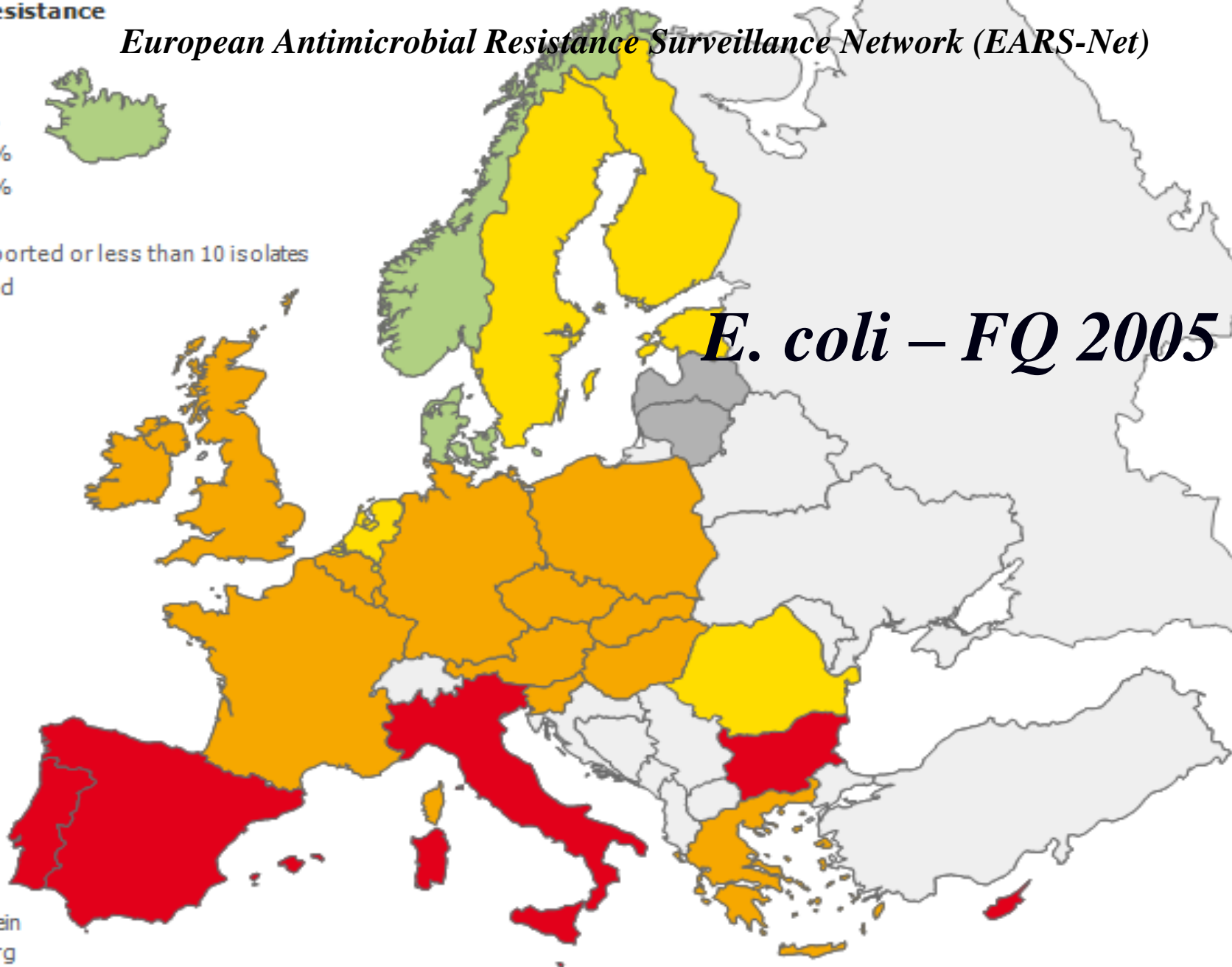
Percentage resistance

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

European Antimicrobial Resistance Surveillance Network (EARS-Net)

E. coli – FQ 2005

- Liechtenstein
- Luxembourg
- Malta



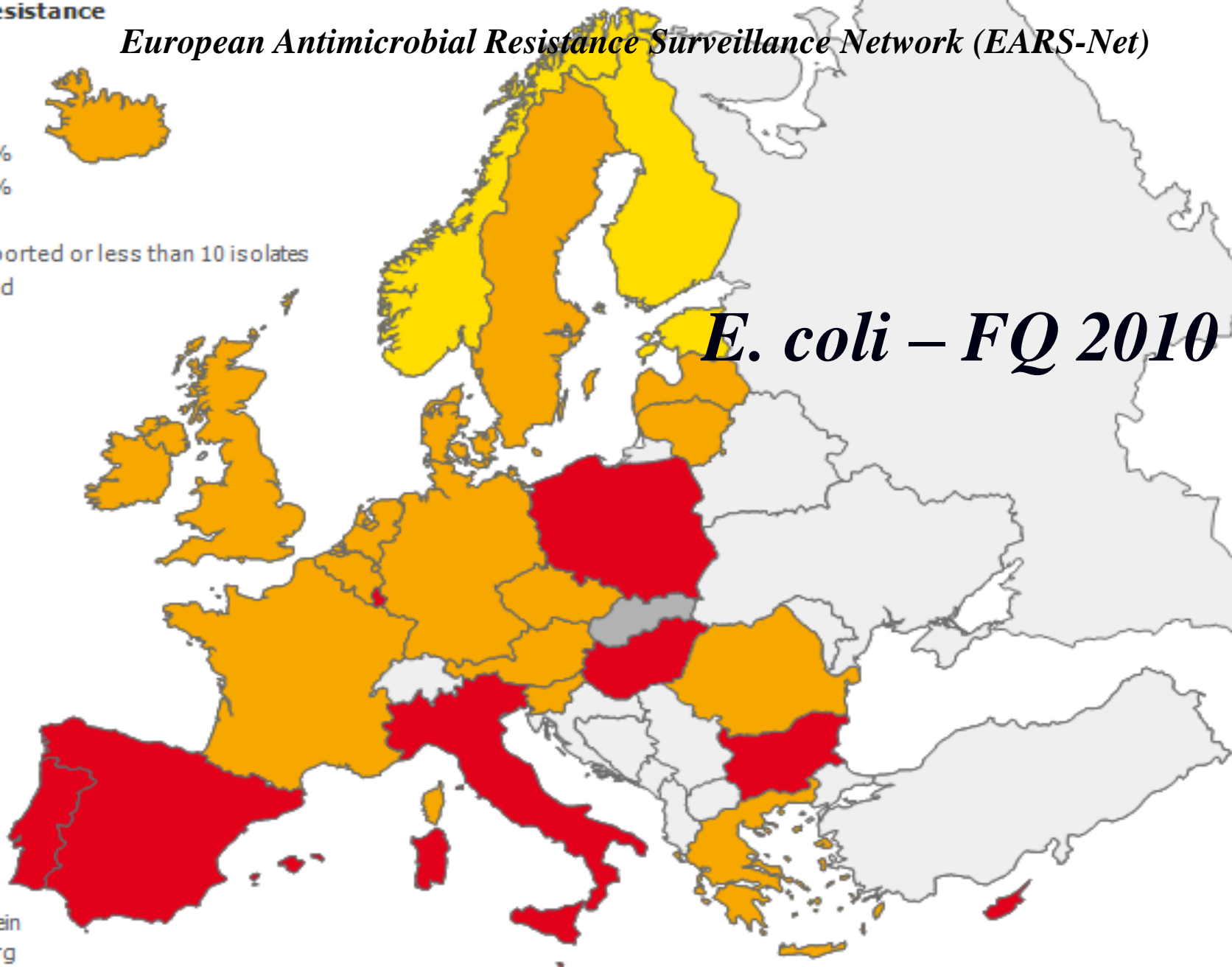
Percentage resistance

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

European Antimicrobial Resistance Surveillance Network (EARS-Net)

E. coli – FQ 2010

- Liechtenstein
- Luxembourg
- Malta



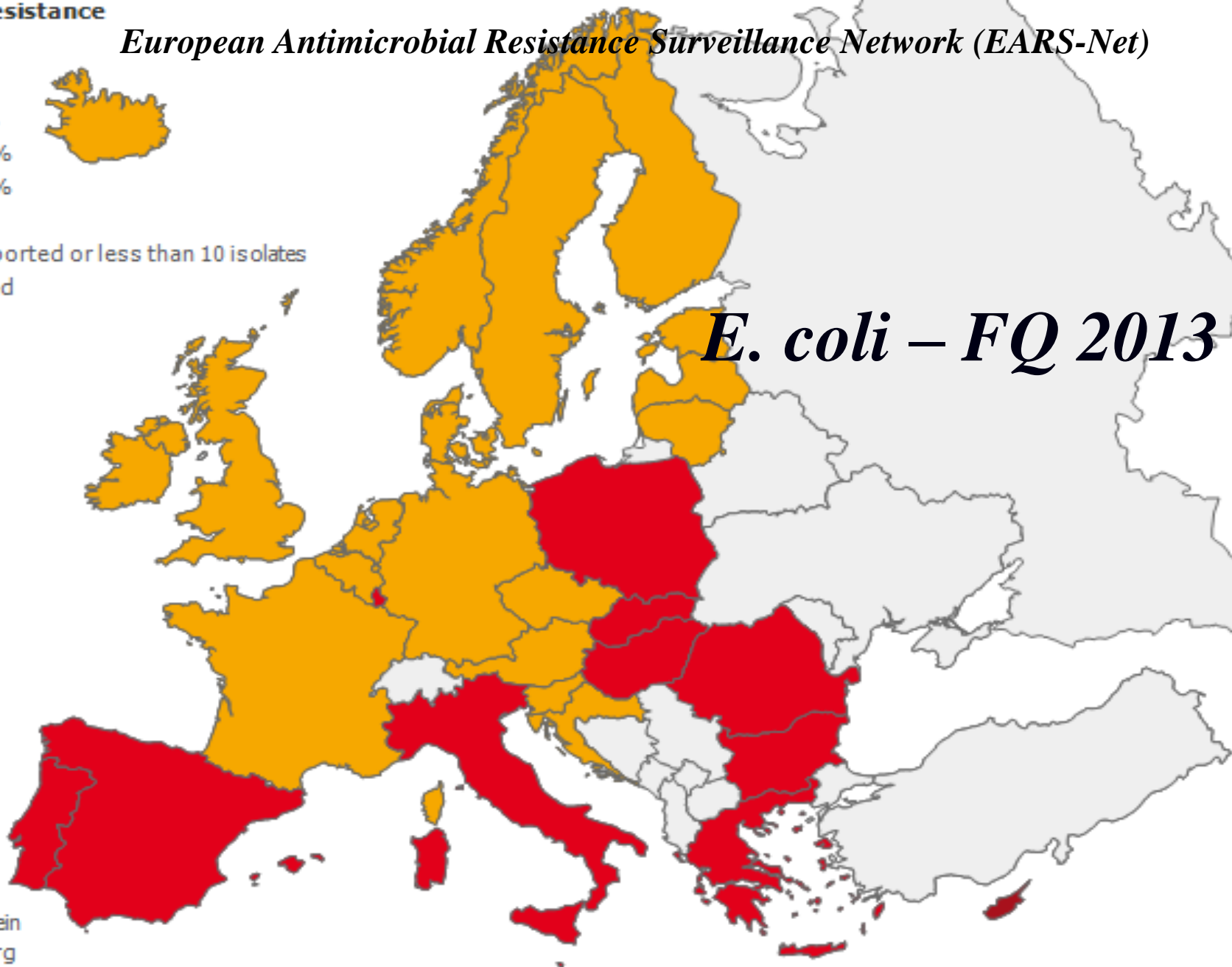
Percentage resistance

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

European Antimicrobial Resistance Surveillance Network (EARS-Net)

E. coli – FQ 2013

- Liechtenstein
- Luxembourg
- Malta



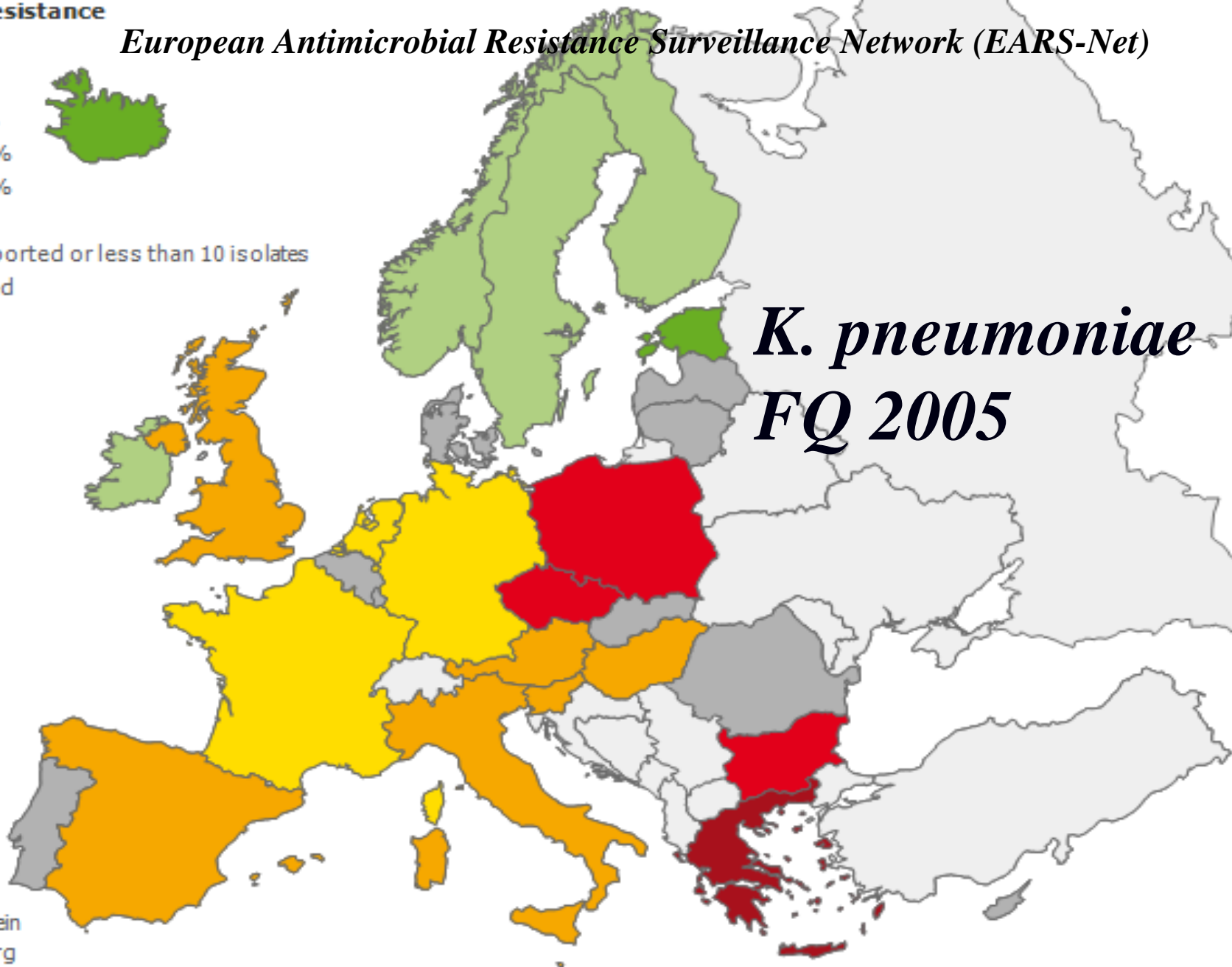
Percentage resistance

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

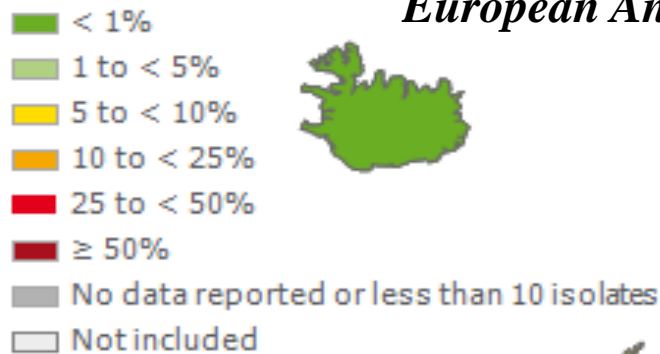
European Antimicrobial Resistance Surveillance Network (EARS-Net)

K. pneumoniae
FQ 2005

- Liechtenstein
- Luxembourg
- Malta



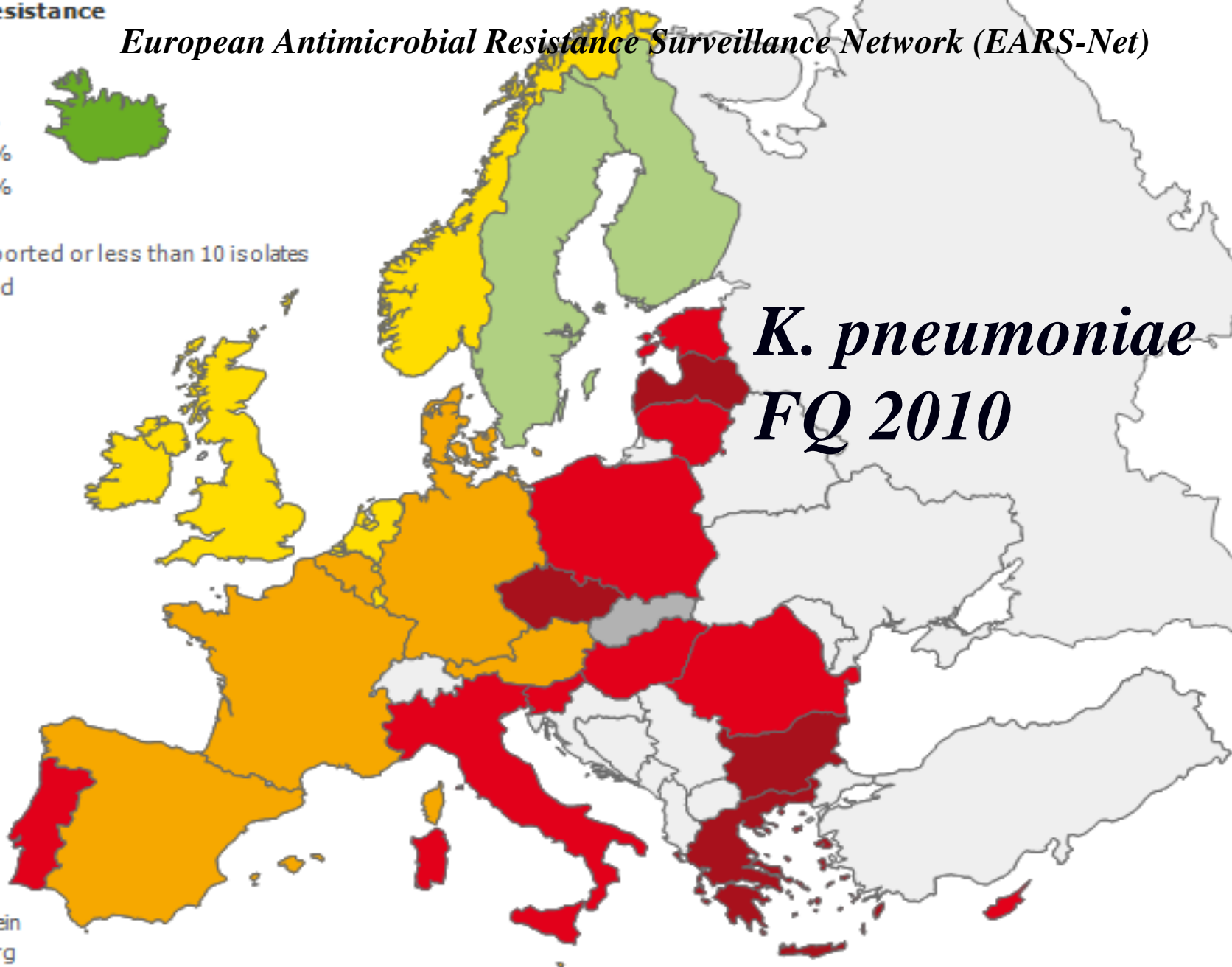
Percentage resistance



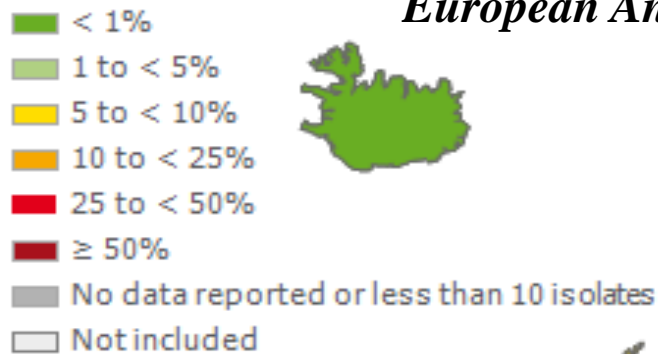
European Antimicrobial Resistance Surveillance Network (EARS-Net)

K. pneumoniae
FQ 2010

■ Liechtenstein
■ Luxembourg
■ Malta

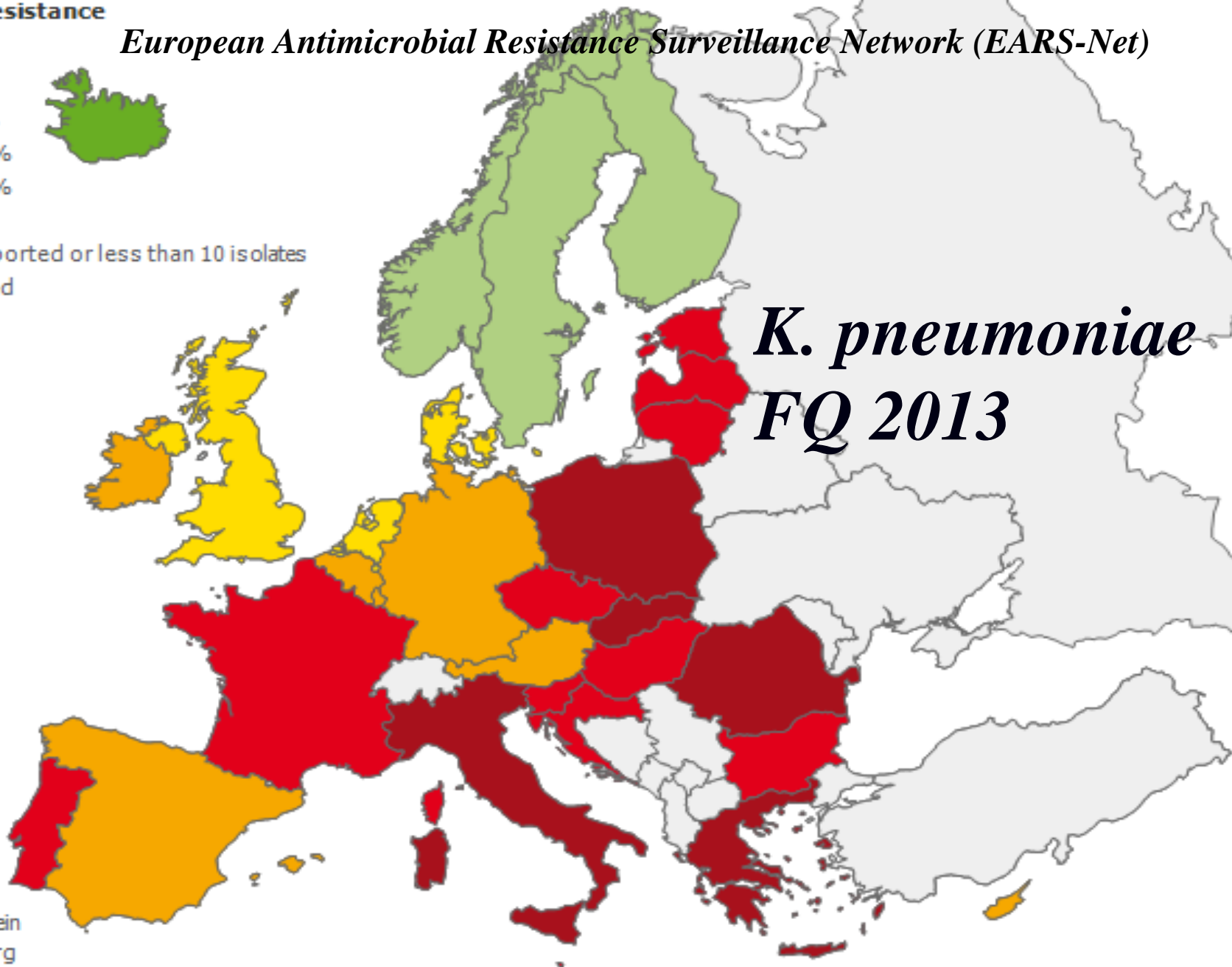
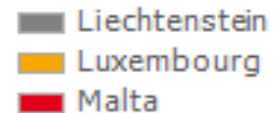


Percentage resistance

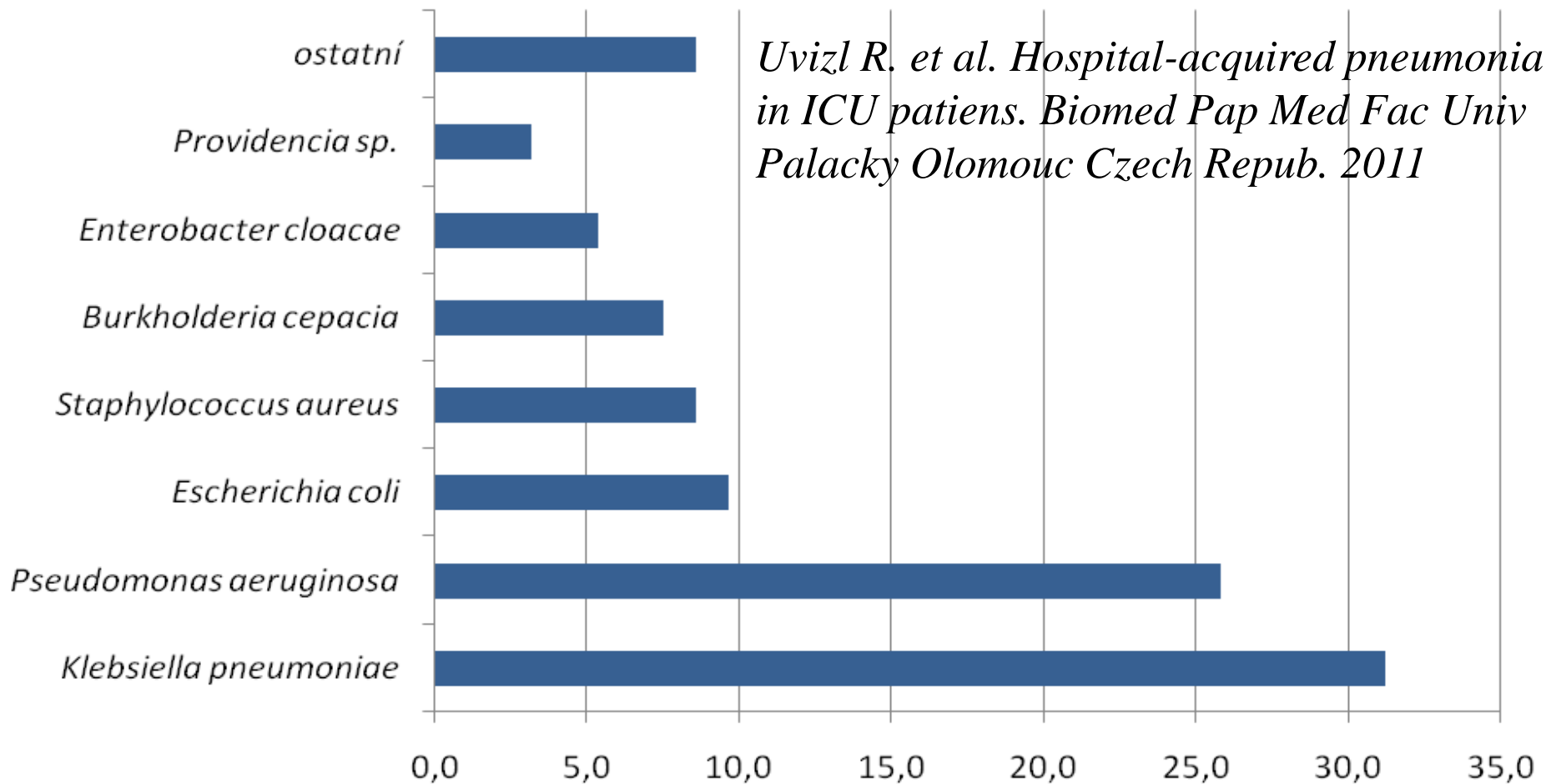


European Antimicrobial Resistance Surveillance Network (EARS-Net)

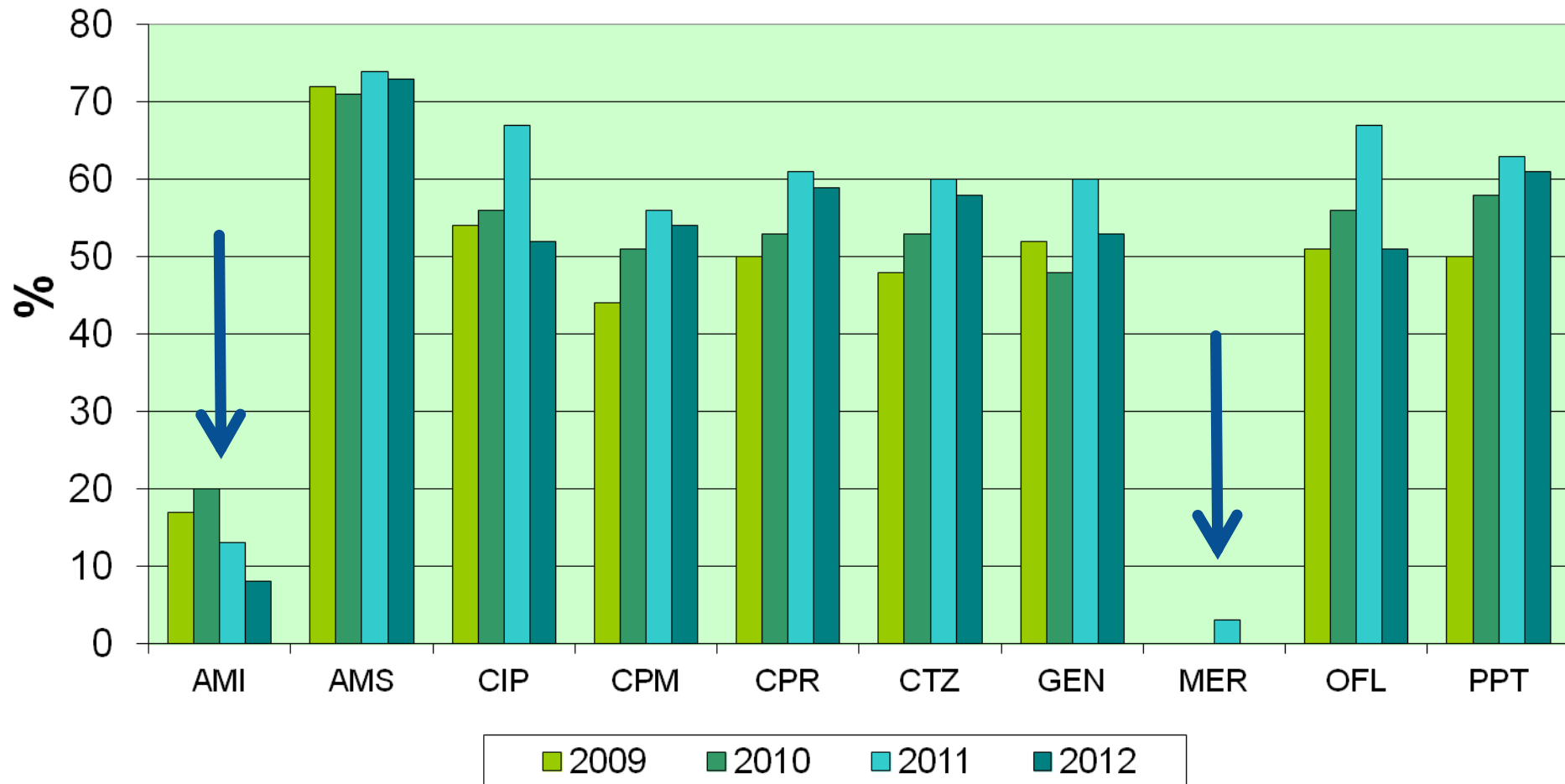
K. pneumoniae
FQ 2013



Bacterial etiological agents of nosocomial pneumonias



Resistance of *K. pneumoniae* to antibiotics in ICU patients of University hospital Olomouc



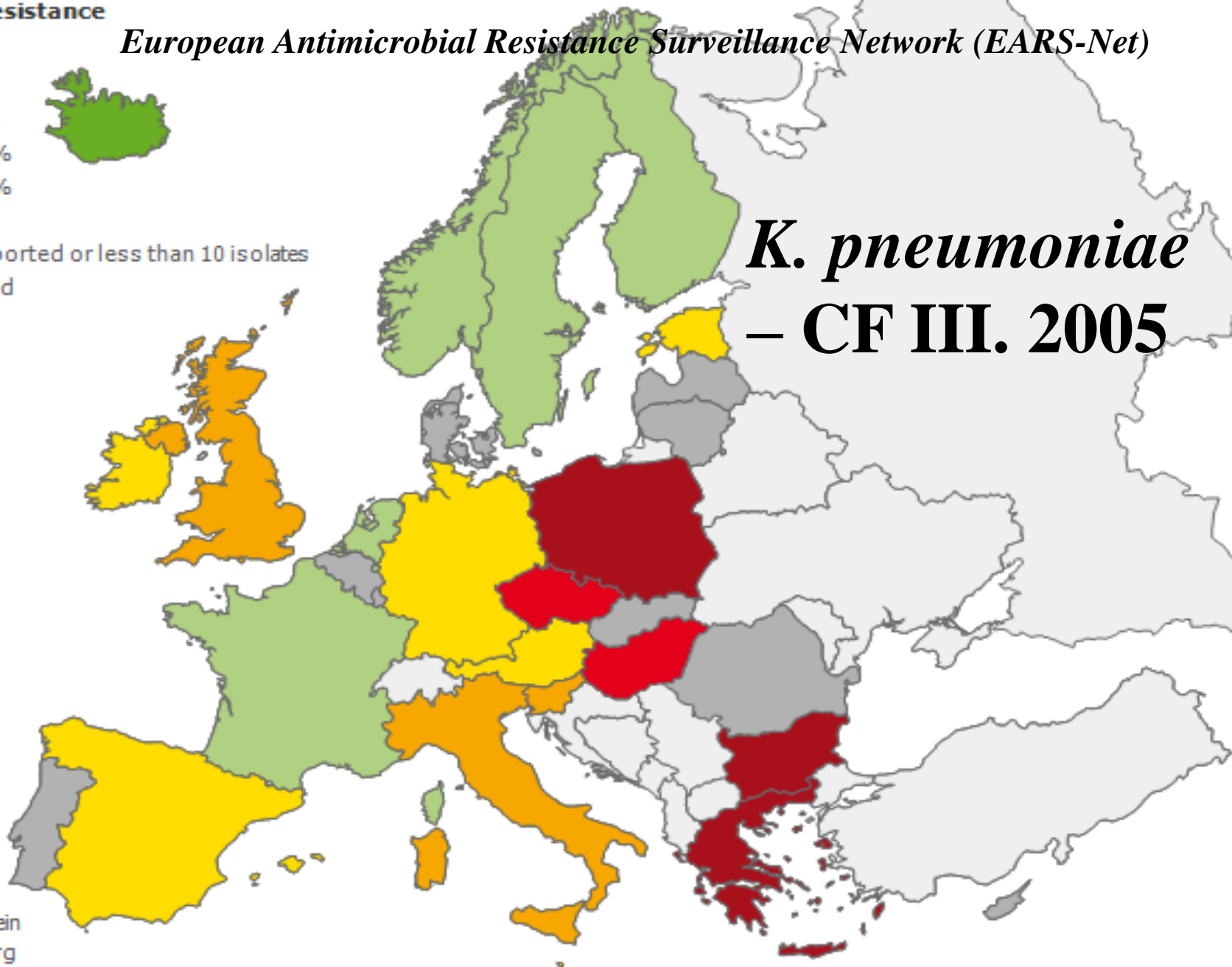
Percentage resistance

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

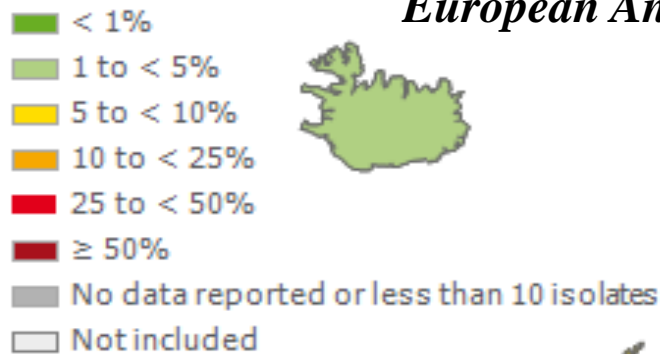
European Antimicrobial Resistance Surveillance Network (EARS-Net)

K. pneumoniae
– CF III. 2005

- Liechtenstein
- Luxembourg
- Malta



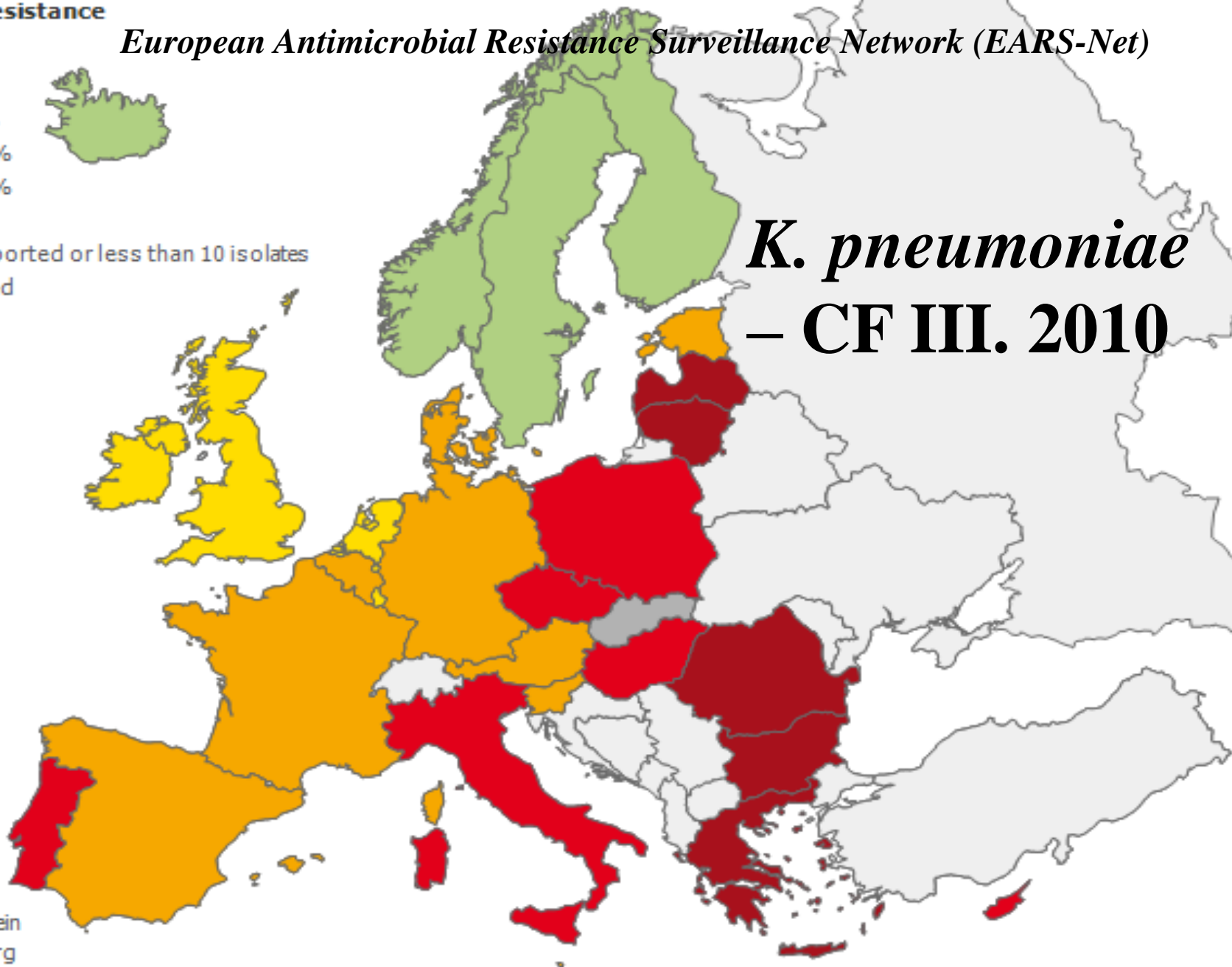
Percentage resistance



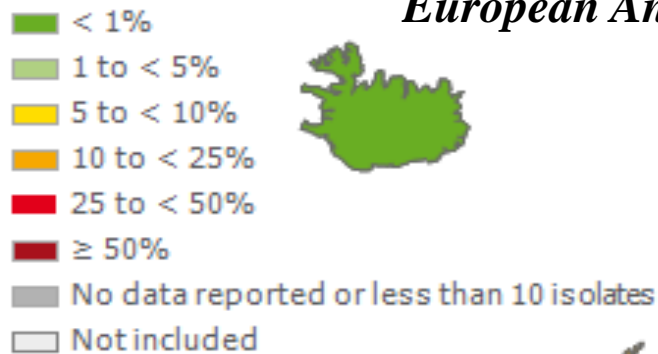
European Antimicrobial Resistance Surveillance Network (EARS-Net)

K. pneumoniae
– CF III. 2010

■ Liechtenstein
■ Luxembourg
■ Malta



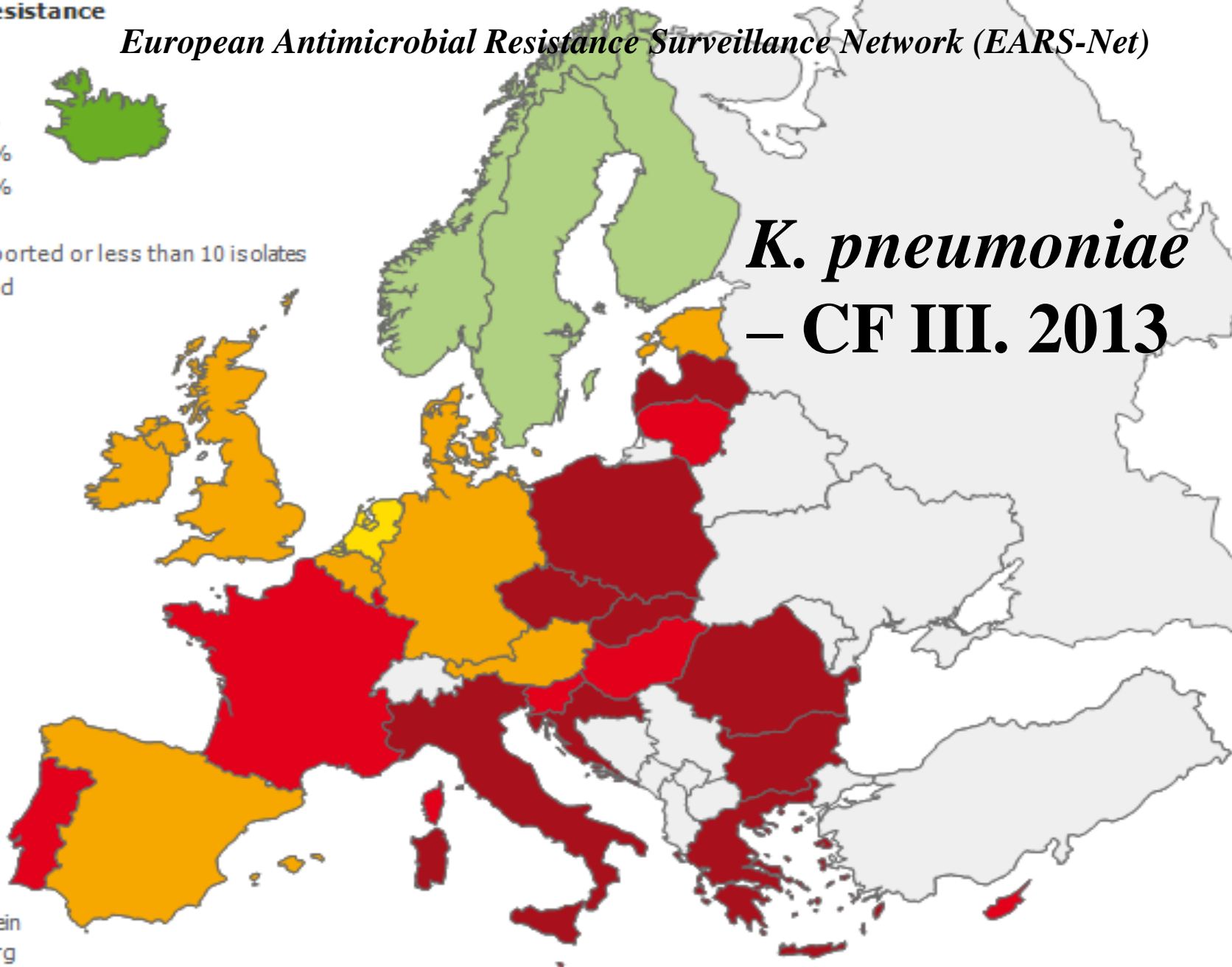
Percentage resistance



European Antimicrobial Resistance Surveillance Network (EARS-Net)

K. pneumoniae
– CF III. 2013

■ Liechtenstein
■ Luxembourg
■ Malta

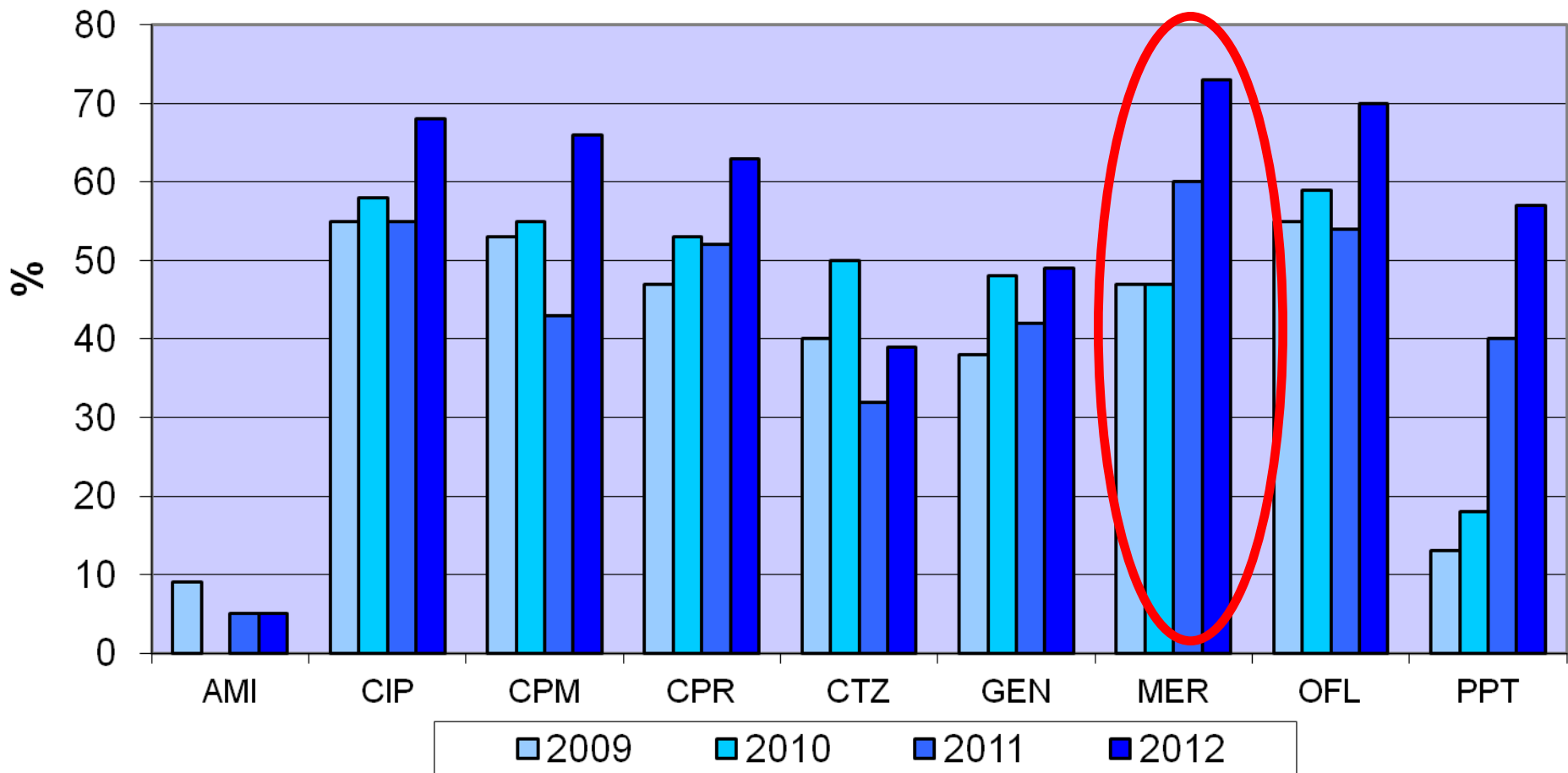


- The increasing frequency of *Enterobacteriaceae* producing broad-spectrum beta-lactamases leads to a rise in carbapenem consumption.
- A negative consequence of this fact is increasing frequency of meropenem-resistant strains of *P. aeruginosa*.

Utilisation of ATBs in University hospital Olomouc (in % according DDDatb)

ATB group	2007	2008	2009	2010	2011	2012
combined penicillins	43,9	44,5	44,6	47,0	45,5	43,6
fluoroquinolones	8,2	9,1	7,0	5,9	5,7	6,0
carbapenems	1,3	1,9	2,6	2,4	3,0	3,5
cephalosporins I. gen.		2,2	2,3	2,3	2,3	2,5
cephalosporins II. gen.	8,2	8,5	7,4	8,2	8,9	7,9
cephalosporins III. and IV gen.	3,4	3,1	2,3	2,4	2,4	2,2
aminoglycosides	5,3	5,2	5,7	4,5	6,0	6,0
lincosamides	1,9	1,3	1,9	2,0	2,3	2,8
glycopeptides	2,1	1,9	1,7	1,5	1,4	1,7
other	23,3	22,3	24,5	23,8	22,5	23,8

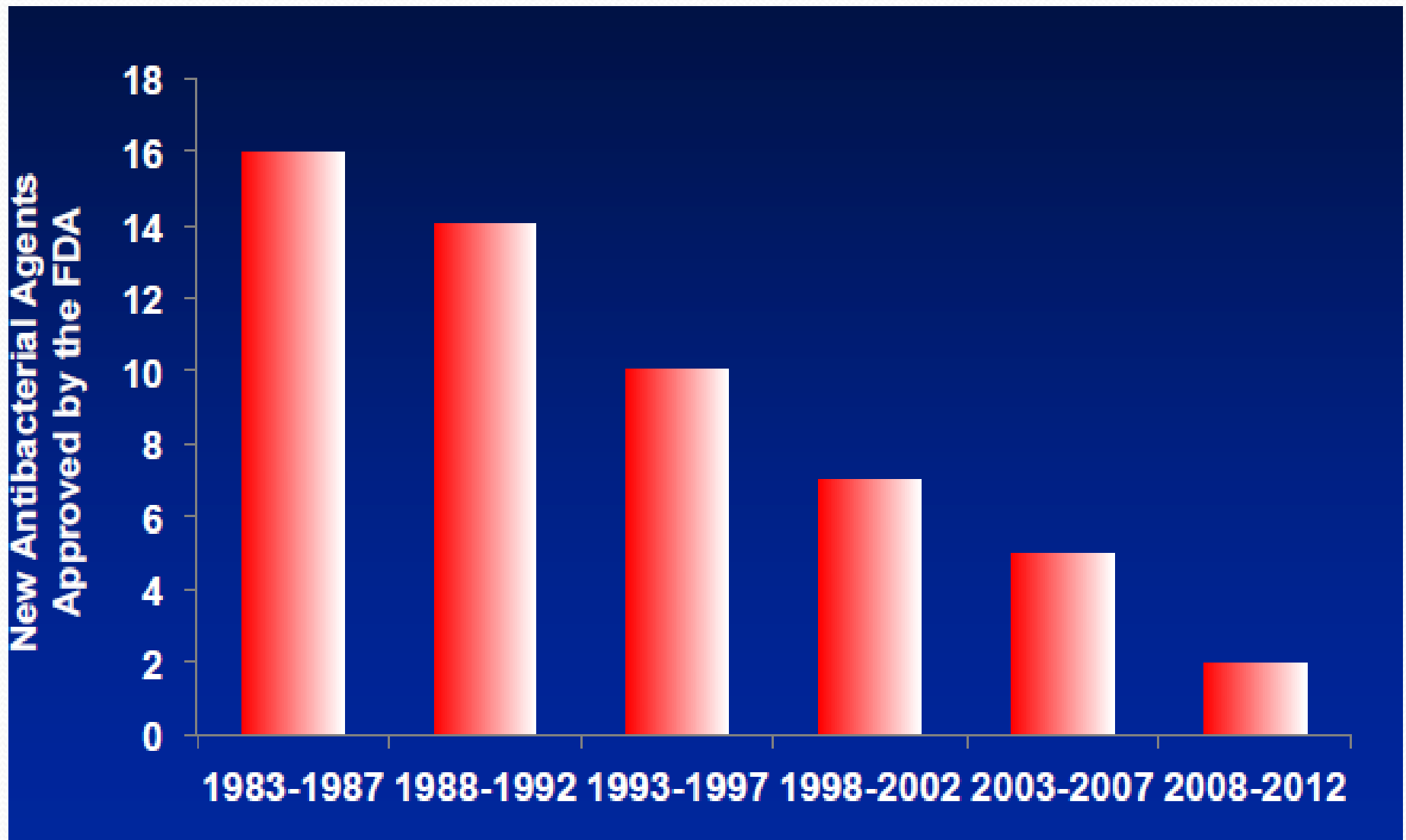
Resistance of *P. aeruginosa* to antibiotics in ICU patients of University hospital Olomouc



Controlling resistance

- Less antibiotic use
- Better tailored use
- Development of new antibiotics

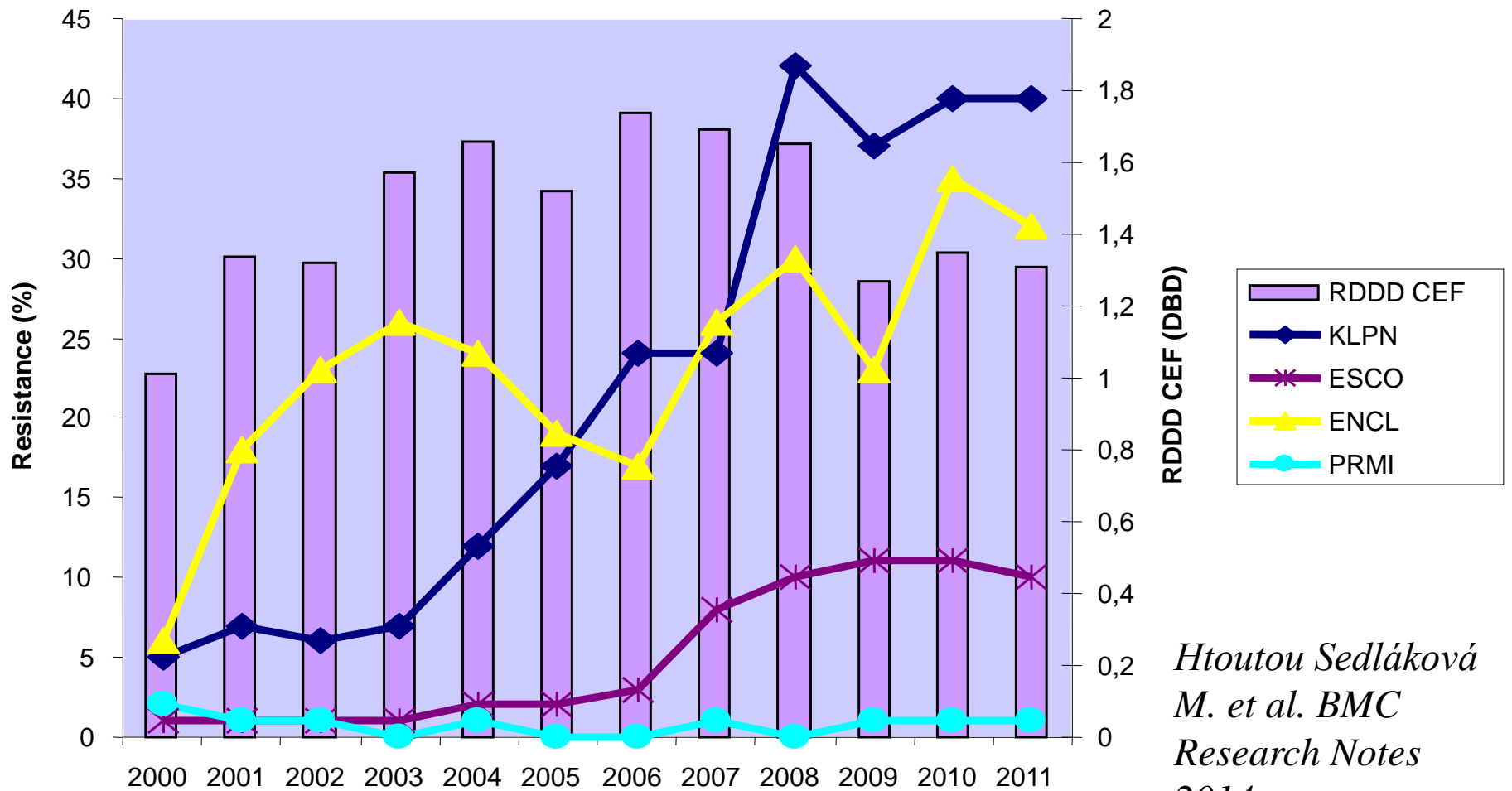
Development of new antibiotics





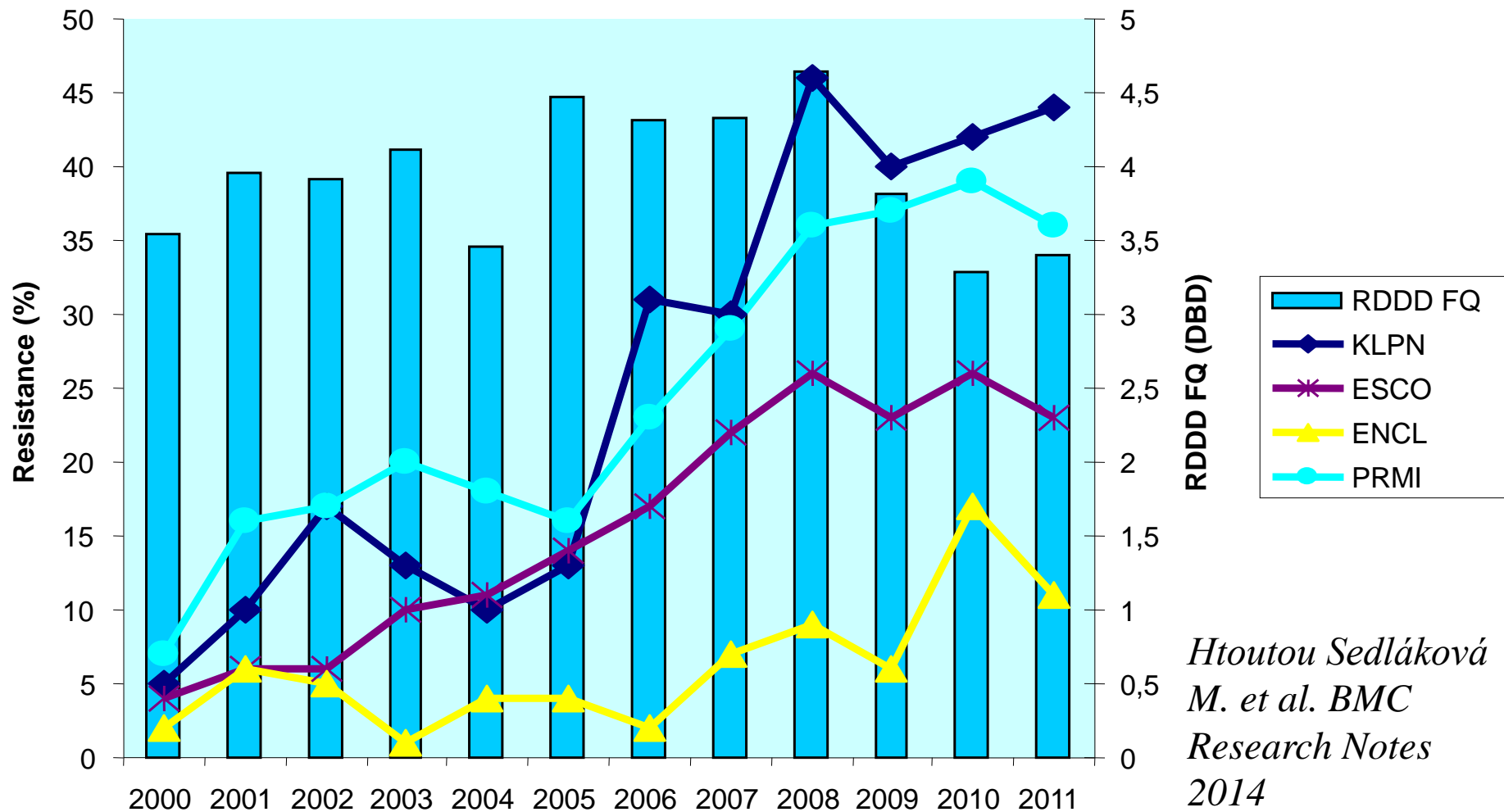
- It may be theoretically assumed that the increasing bacterial resistance may potentially be solved by reducing consumption of antibiotics.
- Recently, however, it has been repeatedly reported that application of selected antibiotics and bacterial resistance may not be directly related.

Development of resistance of enterobacteria to ceftazidime with respect to consumption of third- and fourth-generation cephalosporins



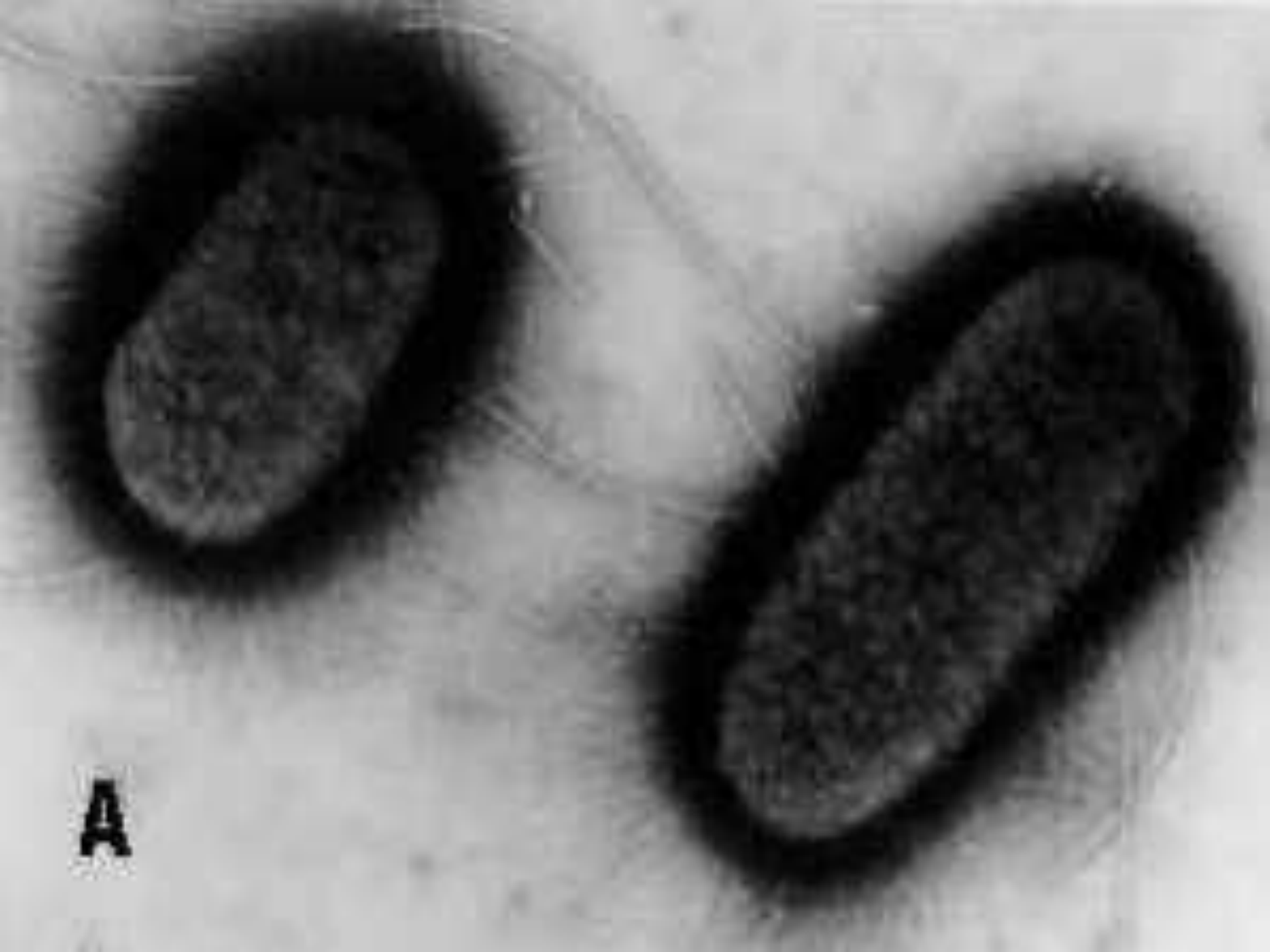
*Htoutou Sedláková
M. et al. BMC
Research Notes
2014*

Development of resistance of enterobacteria to ciprofloxacin with respect to consumption of fluoroquinolones



*Htoutou Sedláková
M. et al. BMC
Research Notes
2014*

- It can be supposed that the relationship between resistance and antibiotic administration is probably determined by additional factors and it cannot be influenced by a mere decrease in consumption.
- There are two other mechanisms of bacterial resistance spread besides the selective pressure:
 - horizontal clonal spread of the identical multiresistant isolates
 - **recombination processes such as conjugation of bacterial plasmids**



A

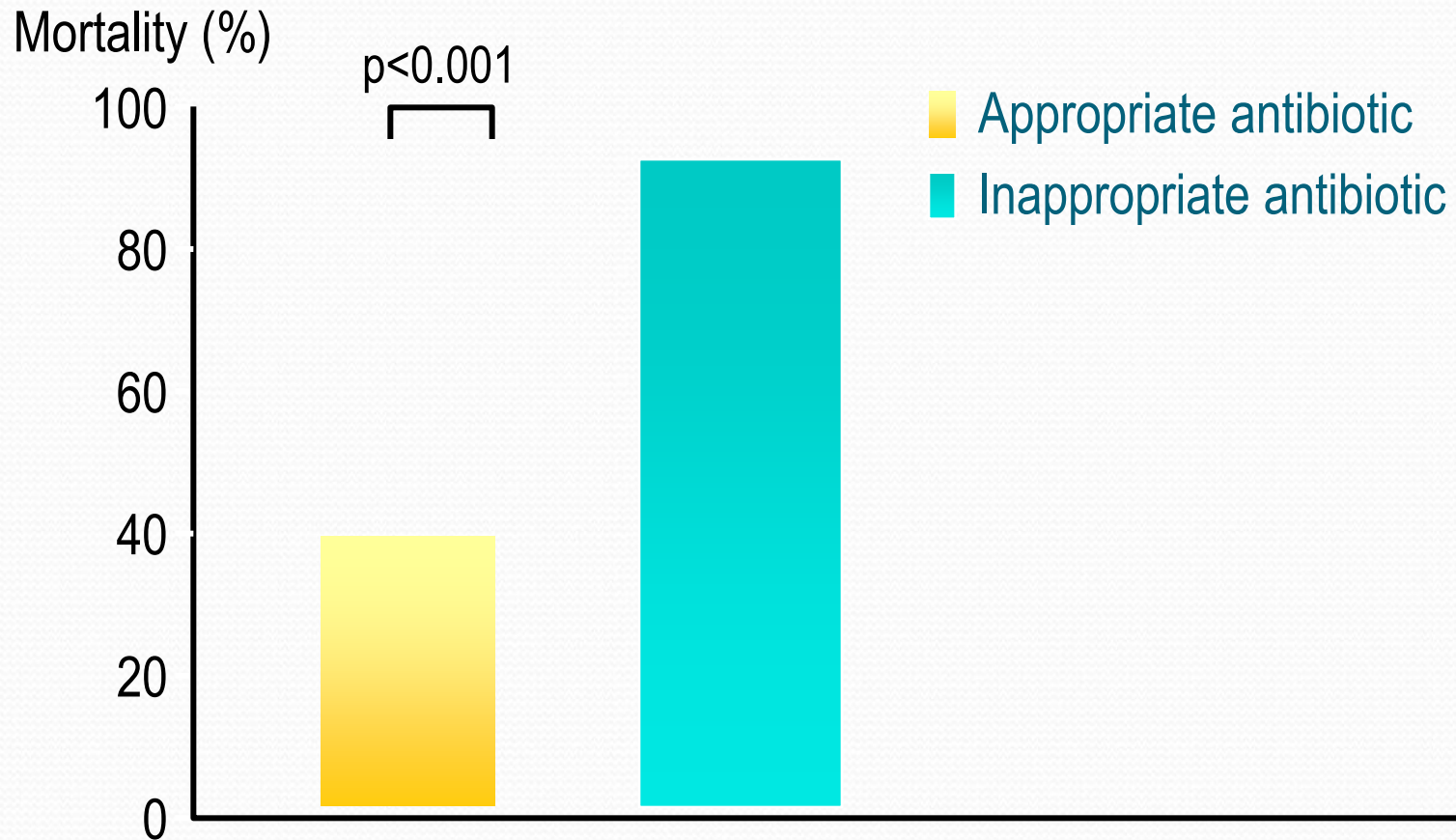
- An imaginary threshold has been crossed and the bacterial resistance is maintained through transfer of mobile genetic elements encoding resistance.
- That threshold is a certain level of resistance genes circulating in the bacterial population that are horizontally transmitted by recombination processes, causing the unstoppable spread of antibiotic resistance independent on their consumption.
- This hypothesis could be an explanation for the implication of our results that selection pressure does not play the main role in the increasing resistance to fluoroquinolones and third- and fourth-generation cephalosporins in *Enterobacteriaceae*.

- It is likely that in antibiotic groups where the reasonable level of resistance has been exceeded, the increasing trend will be impossible to reverse.
- This leads to a heretical notion that rational antibiotic policy will neither reverse nor inhibit the increase of resistance and that this may actually be the end of the antibiotic era.



- Bacterial resistance is not a term used by microbiologists to scare other health professionals and to remind them of the importance of microbiology.
- It is a term with practical negative consequences in the form of antibiotic treatment failure and the related higher morbidity and mortality rates.

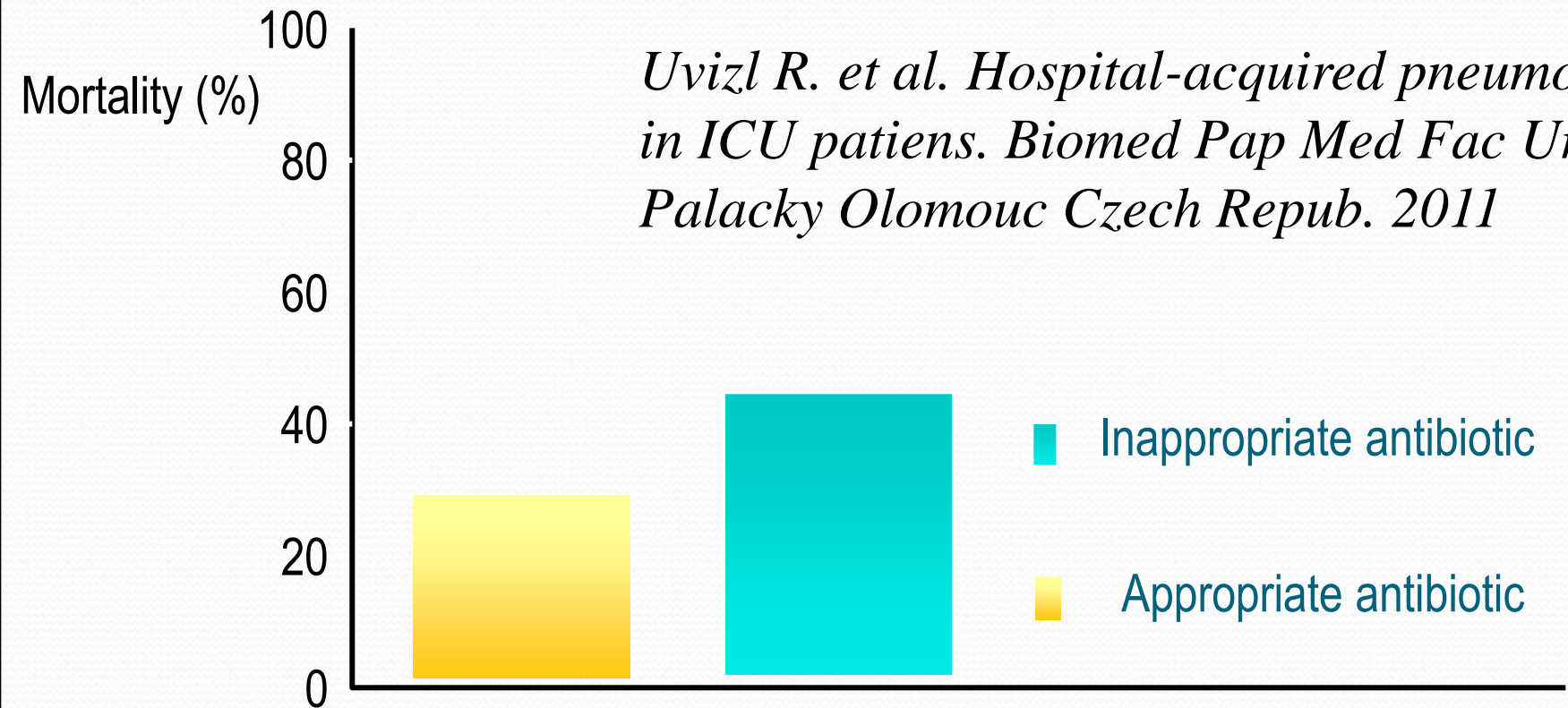
Mortality in patients with VAP



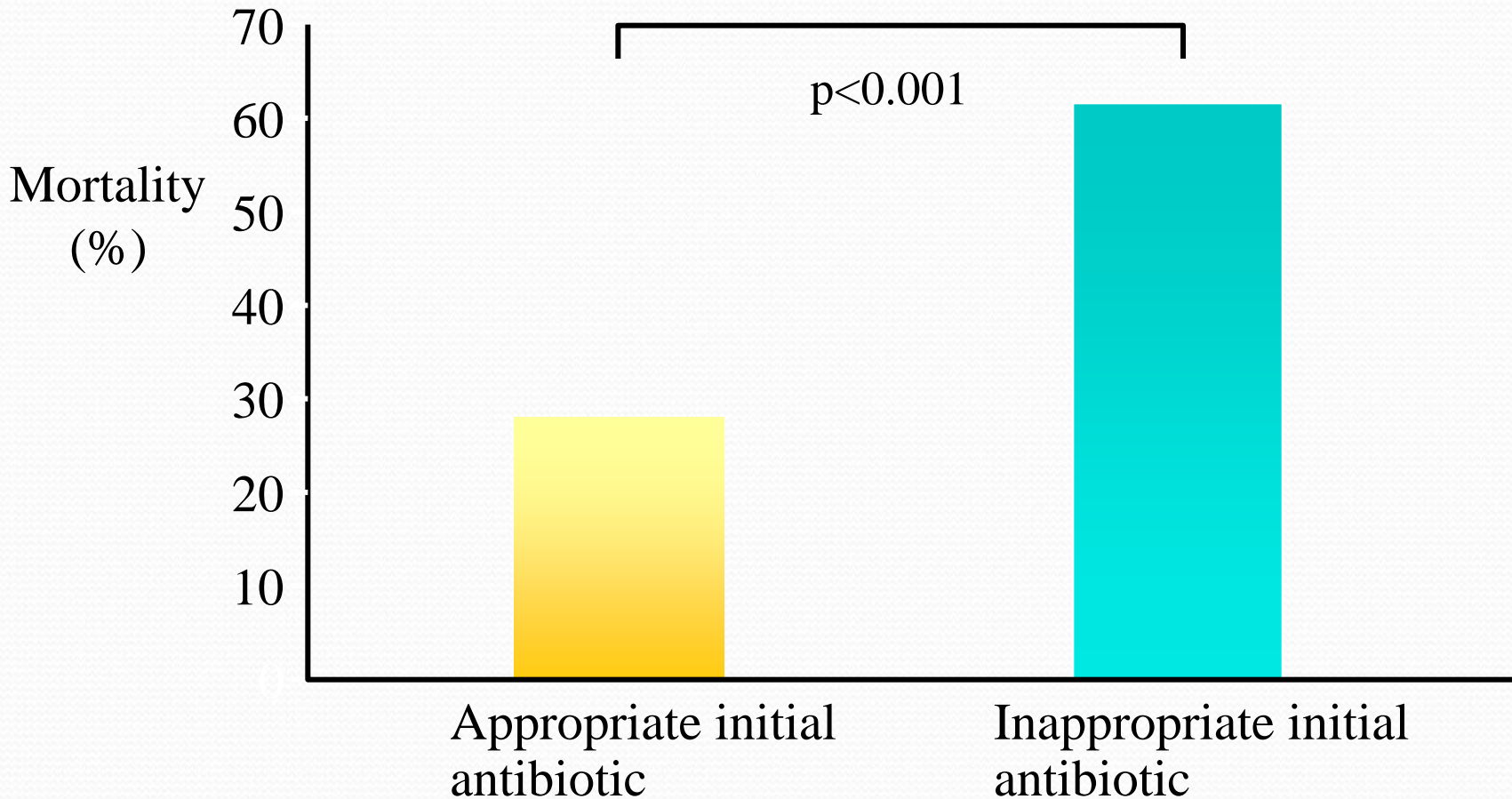
Luna et al. Chest 1997;111:676–685

Mortality in patients with VAP

Uvizl R. et al. Hospital-acquired pneumonia in ICU patients. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2011



Mortality rates in patients with bloodstream infection



Summary

- Antibiotic resistance is increasing at an alarming rate and is likely to have an important impact on antibiotic therapy.
- Steps must be taken now to control the increase in antibiotic resistance.

Motto:

Bacteria appeared on this planet much earlier than humans and there is no doubt they would also be here much longer. Nevertheless, everything must be done to ensure that humans and bacteria live together for as long as possible.

Milan Kolář



Faculty of Medicine
and Dentistry
Palacky University Olomouc