

LE INFEZIONI DEL BASSO TRATTO UROGENITALE FEMMINILE

FERRARA, 22 MAGGIO 2015

**Urinocoltura, antibiogramma,
antibioticoterapia,
antibiotico resistenza:
riflessioni**

Fabio Tumietto

Programma Aziendale

Epidemiologia e Controllo del Rischio Infettivo Correlato alle Organizzazioni Sanitarie

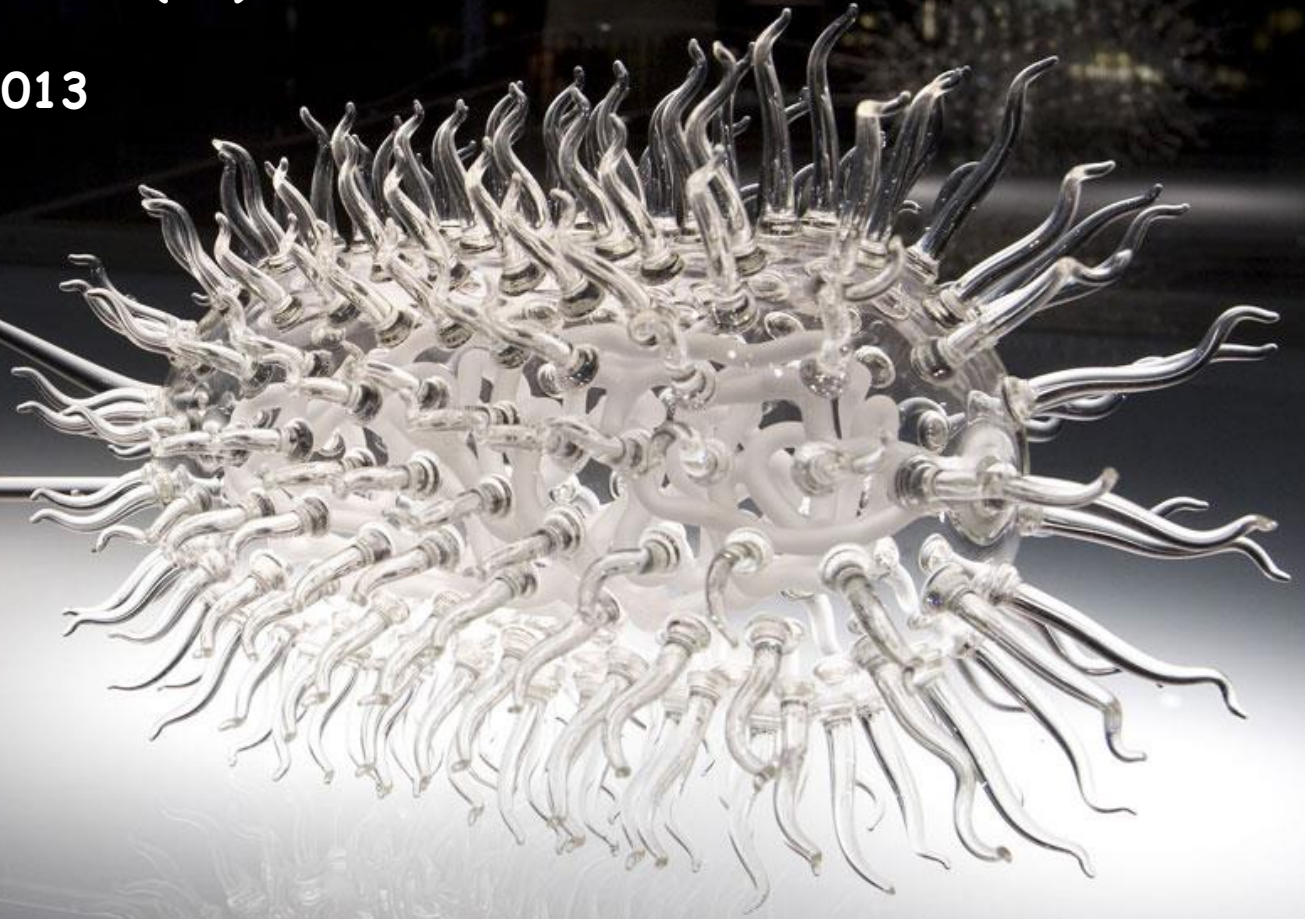
Clinica Malattie Infettive - Bologna



E.coli

Sculpture of glass - Luke Jerram (UK)

Biennale di Venezia 2013



Perhaps the only fascinating aspect of E. coli currently

Levofloxacin resistant *Escherichia coli* sepsis following an ultrasound-guided transrectal prostate biopsy: report of four cases and review of the literature. *Miura T et al. Int J Urol. 2008;15:457-9.*

A near-fatal case of sepsis with an antibiotic-resistant organism complicating a routine transrectal prostate biopsy in a health care worker. *Weber B et al. Can Urol Assoc J. 2008;2:543-5.*

Catastrophic sepsis and hemorrhage following transrectal ultrasound guided prostate biopsies. *Toren P et al. Can Urol Assoc J. 2010;4:E12-4.*

[Septic shock due to fluoroquinolone-resistant *Escherichia coli* after trans-rectal prostate needle biopsy].
Kato R et al. Hinyokika Kyo. 2010;56:453-6.

Bacterial sepsis following prostatic biopsy. *Carmignani L et al. Int Urol Nephrol. 2012; 44:1055-63.*

Prevalence of ciprofloxacin-resistant Enterobacteriaceae in the intestinal flora of patients undergoing trans-rectal prostate biopsy in Norwich, UK *Yazbek Hanna M et al BJU Int. 2014 Jul 31*

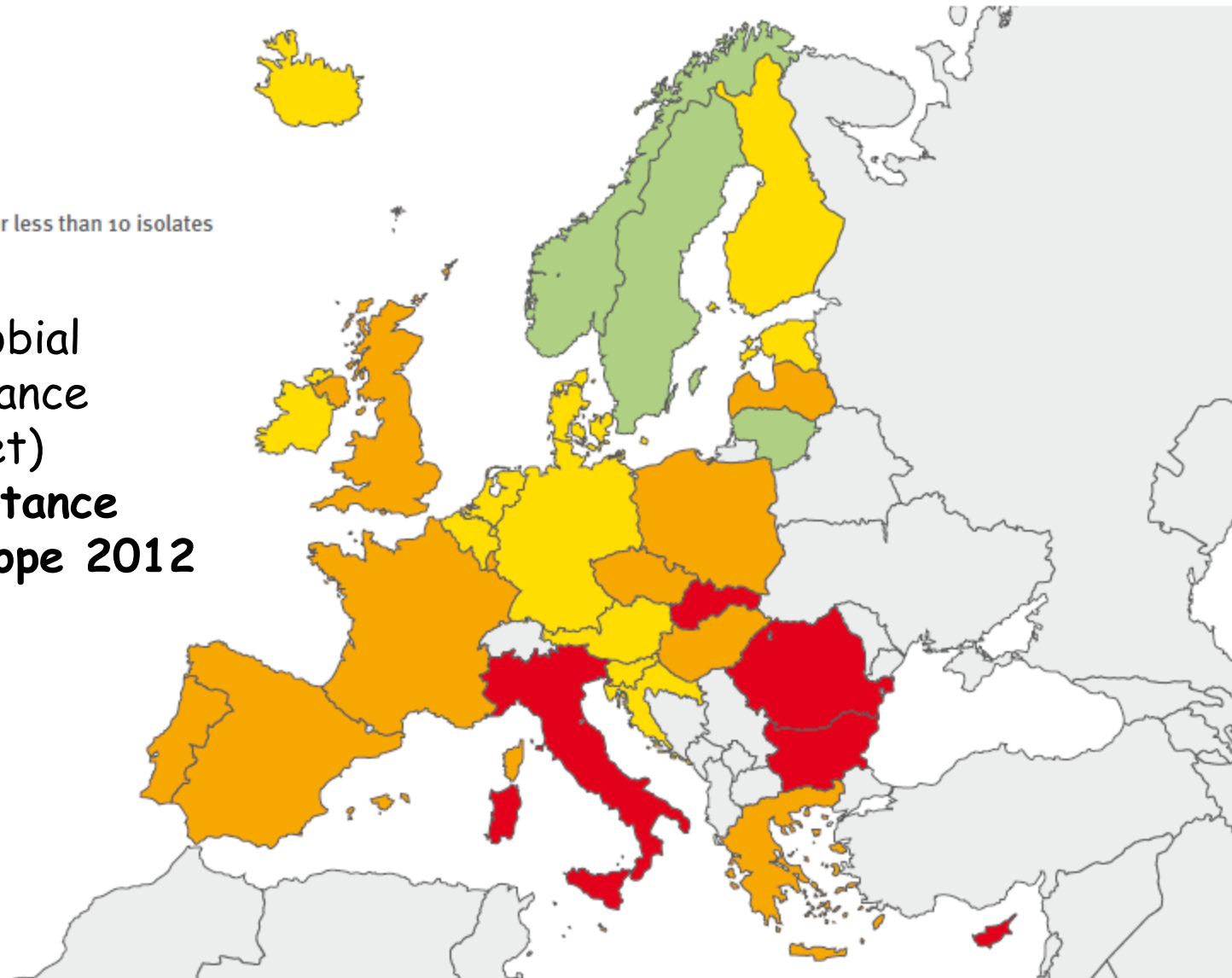
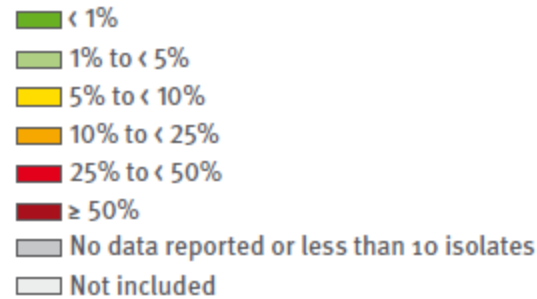
Incidence of infectious complications following transrectal ultrasound-guided prostate biopsy in Calgary, Alberta, Canada: A retrospective population-based analysis. *Rudzinski JK et al Can Urol Assoc J. 2014*

Infectious complications following transrectal ultrasound-guided prostate biopsy: new challenges in the era of multidrug-resistant *Escherichia coli*.

Williamson DA et al. CID 2013;57:267-74.

Transrectal ultrasound (TRUS)-guided prostate biopsy is currently considered the standard technique for obtaining tissue to make a histological diagnosis of prostatic carcinoma. Infectious complications following TRUS-guided prostate biopsy are well described, and are reportedly increasing in incidence. The role of antibiotic prophylaxis in reducing post-TRUS biopsy infections is now established, and **many guidelines suggest that fluoroquinolone antimicrobials are the prophylactic agents of choice**. Of note, however, recent reports suggest an emerging association between TRUS biopsy and subsequent infection with fluoroquinolone-resistant *Escherichia coli*. Against this background, we provide an overview of the epidemiology, prevention, and treatment of infectious complications following TRUS biopsy, in the wider context of increasing global antimicrobial resistance.

Figure 3.1. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins by country, EU/EEA countries, 2012

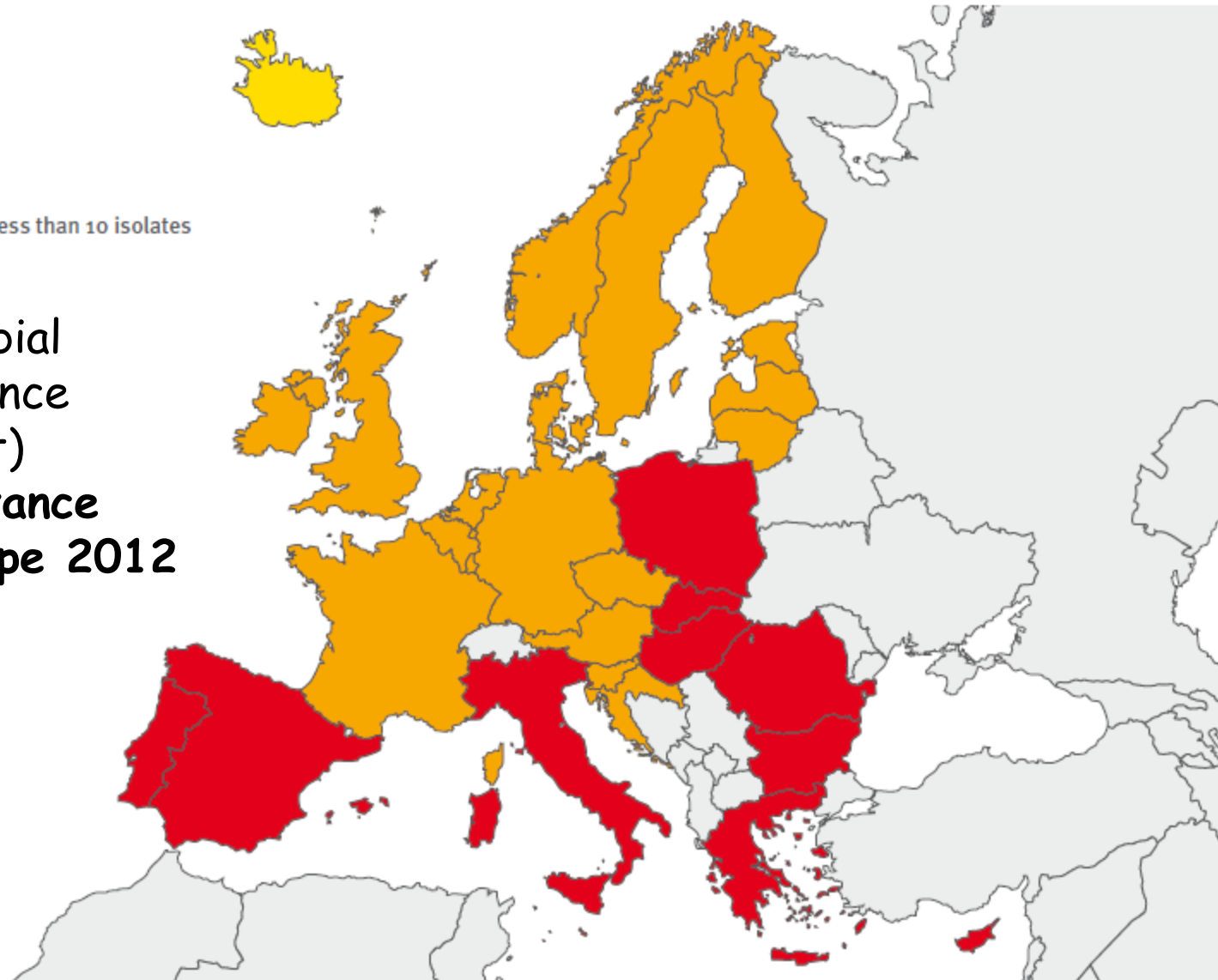
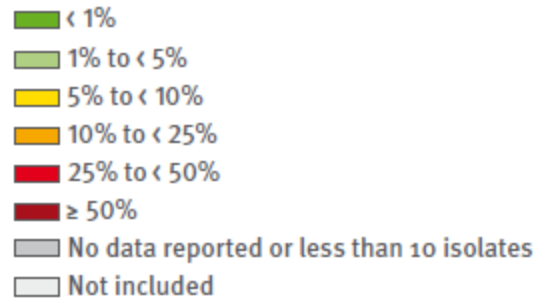


Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

Figure 3.2. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2012

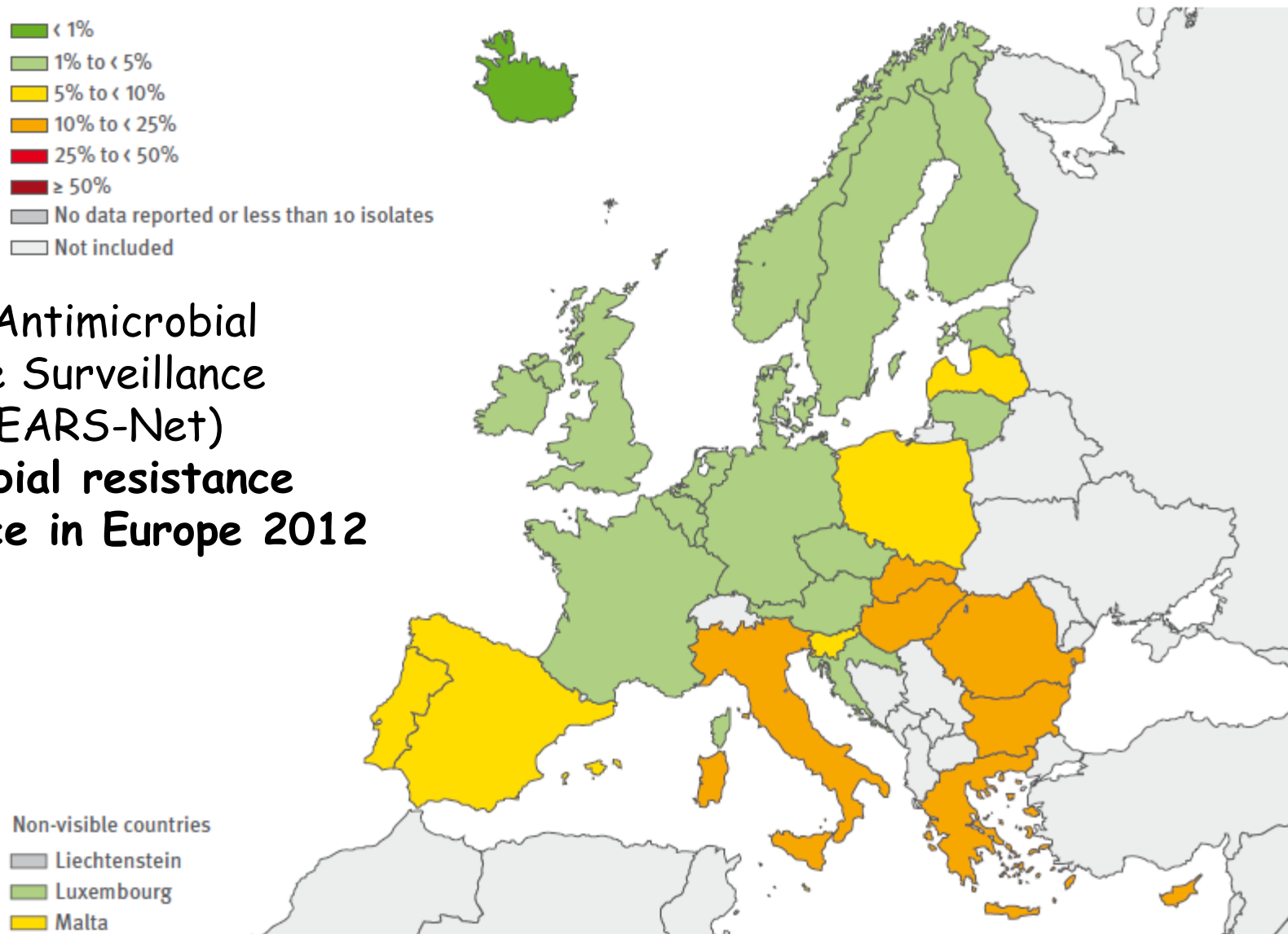


Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

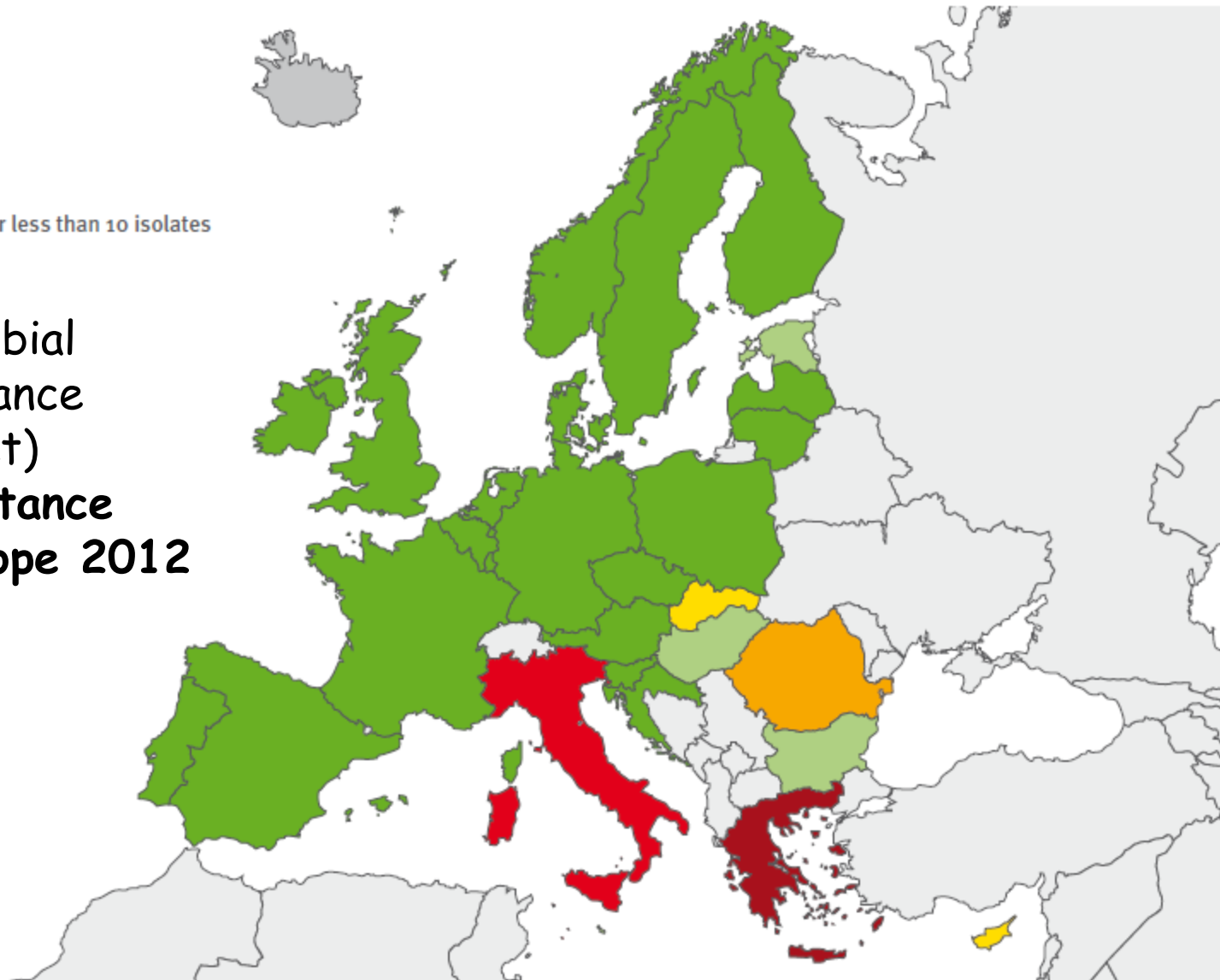
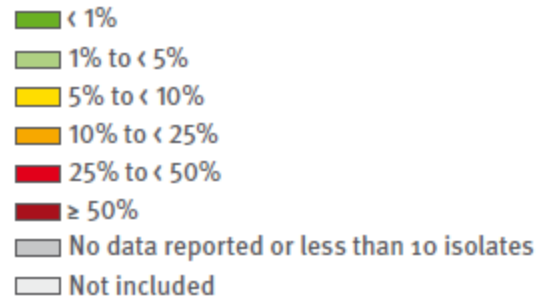
European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

Figure 3.4. *Escherichia coli*. Percentage (%) of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, by country, EU/ EEA countries, 2012



European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

Figure 3.13. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2012

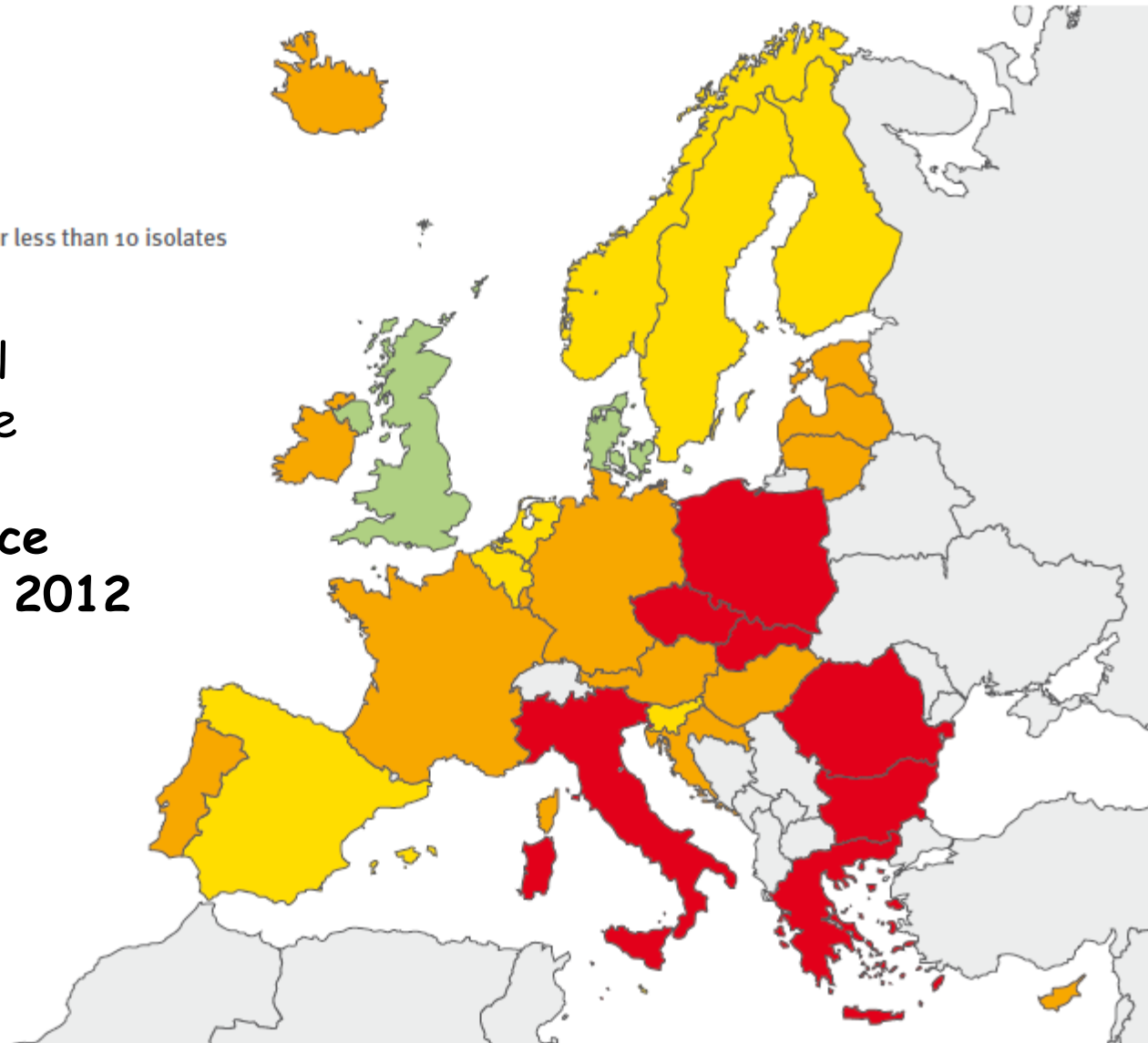


Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

Figure 3.20. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to piperacillin (± tazobactam), by country, EU/EEA countries, 2012

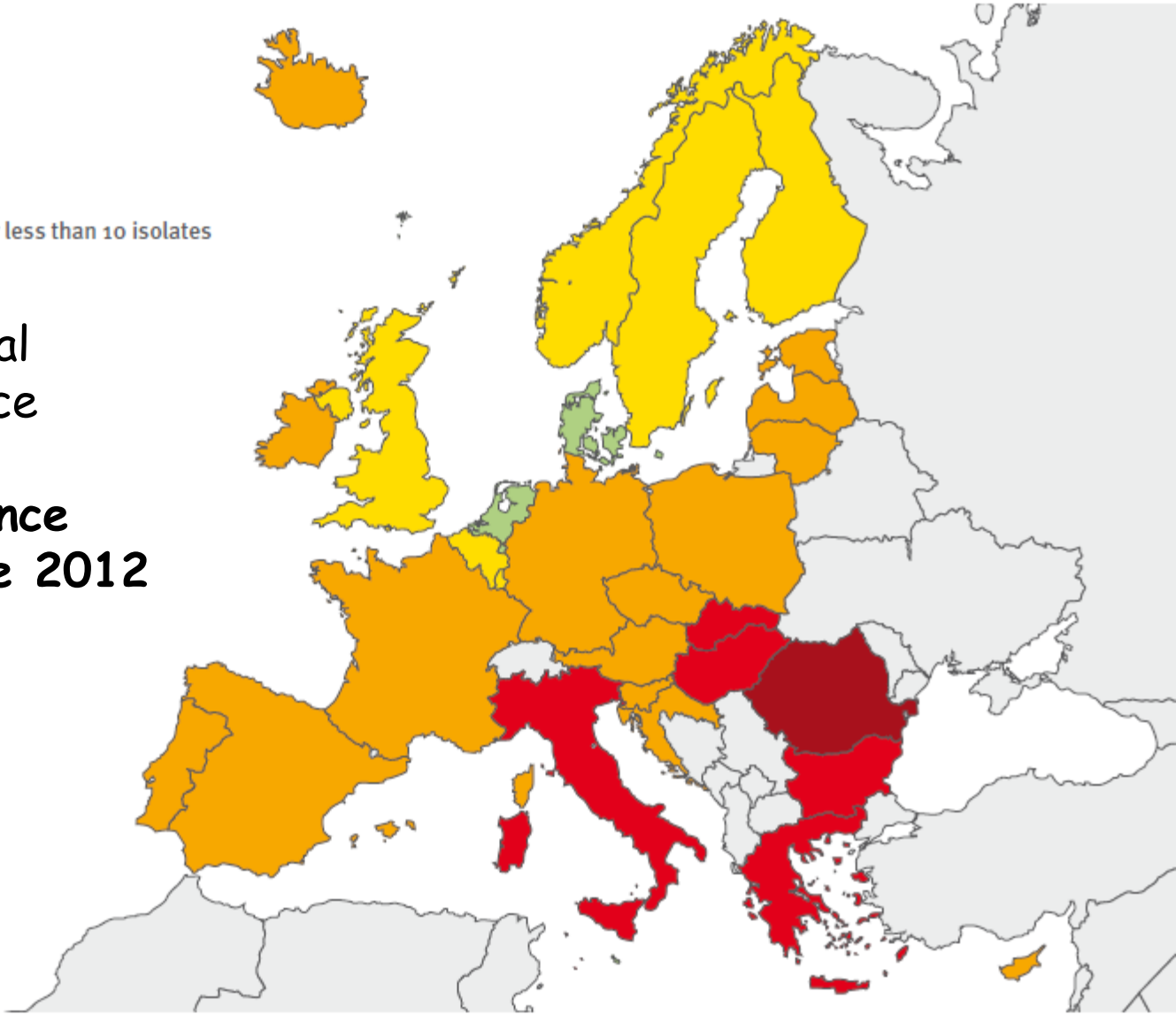
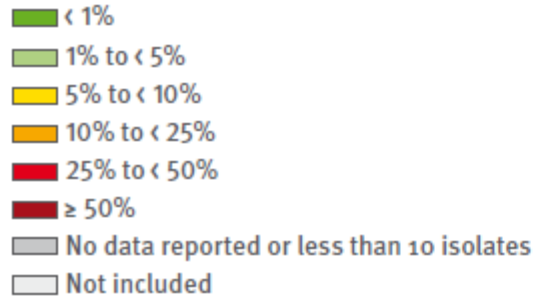


Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

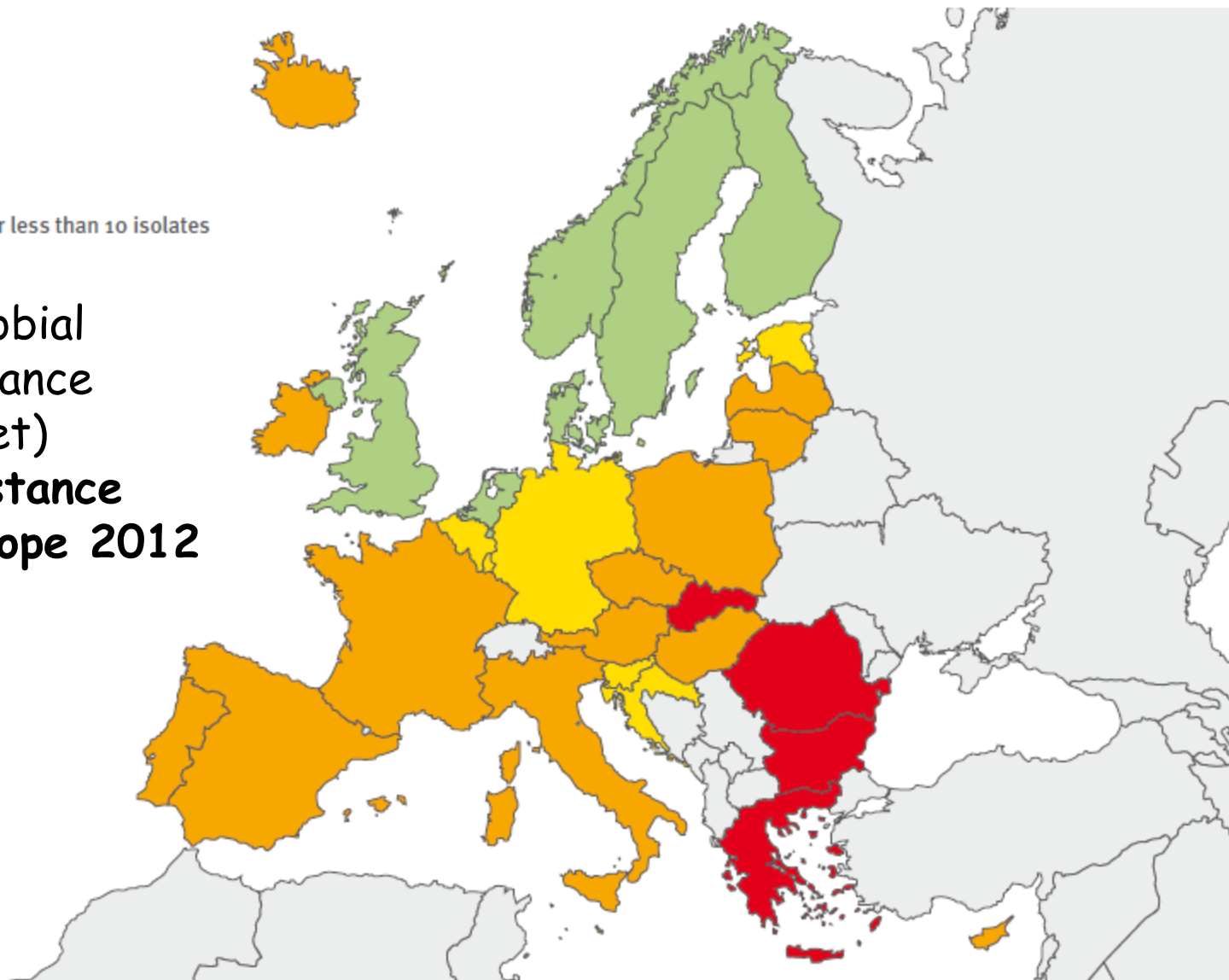
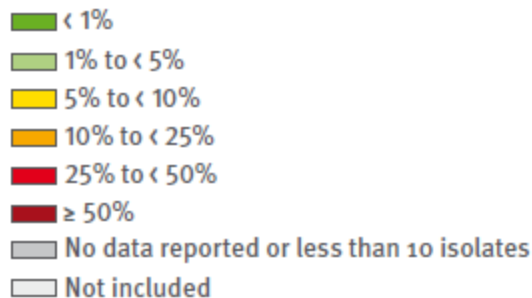
European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

Figure 3.24. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2012



European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

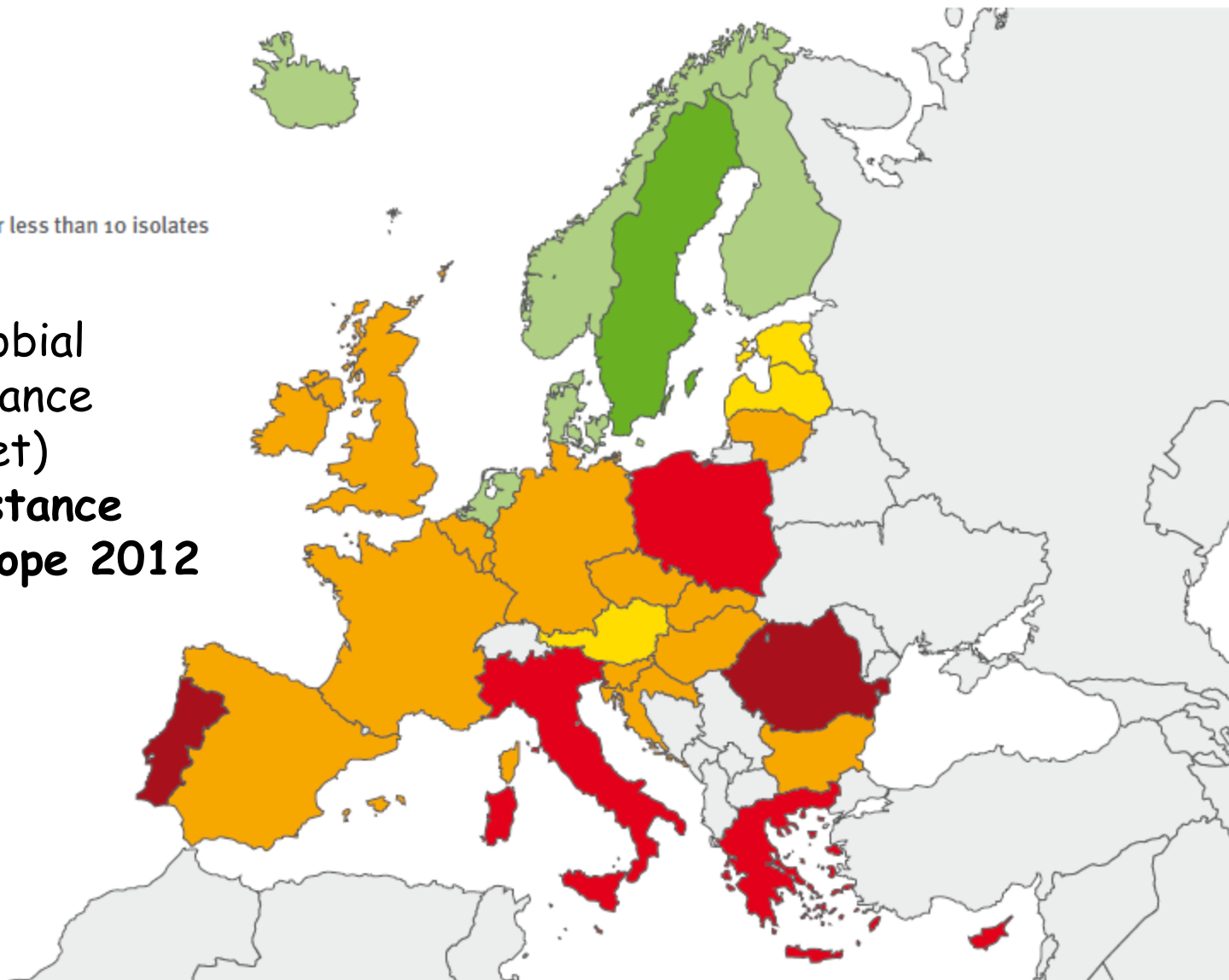
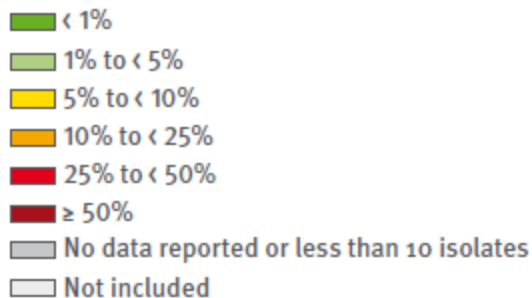
Figure 3.25. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with combined resistance (resistance to three or more antimicrobial classes among piperacillin (± tazobactam), ceftazidime, fluoroquinolones, aminoglycosides and carbapenems), by country, EU/EEA countries, 2012



Non-visible countries
■ Liechtenstein
■ Luxembourg
■ Malta

European Antimicrobial
 Resistance Surveillance
 Network (EARS-Net)
 Antimicrobial resistance
 surveillance in Europe 2012

Figure 3.43. *Staphylococcus aureus*. Percentage (%) of invasive isolates resistant to meticillin (MRSA), by country, EU/EEA countries, 2012

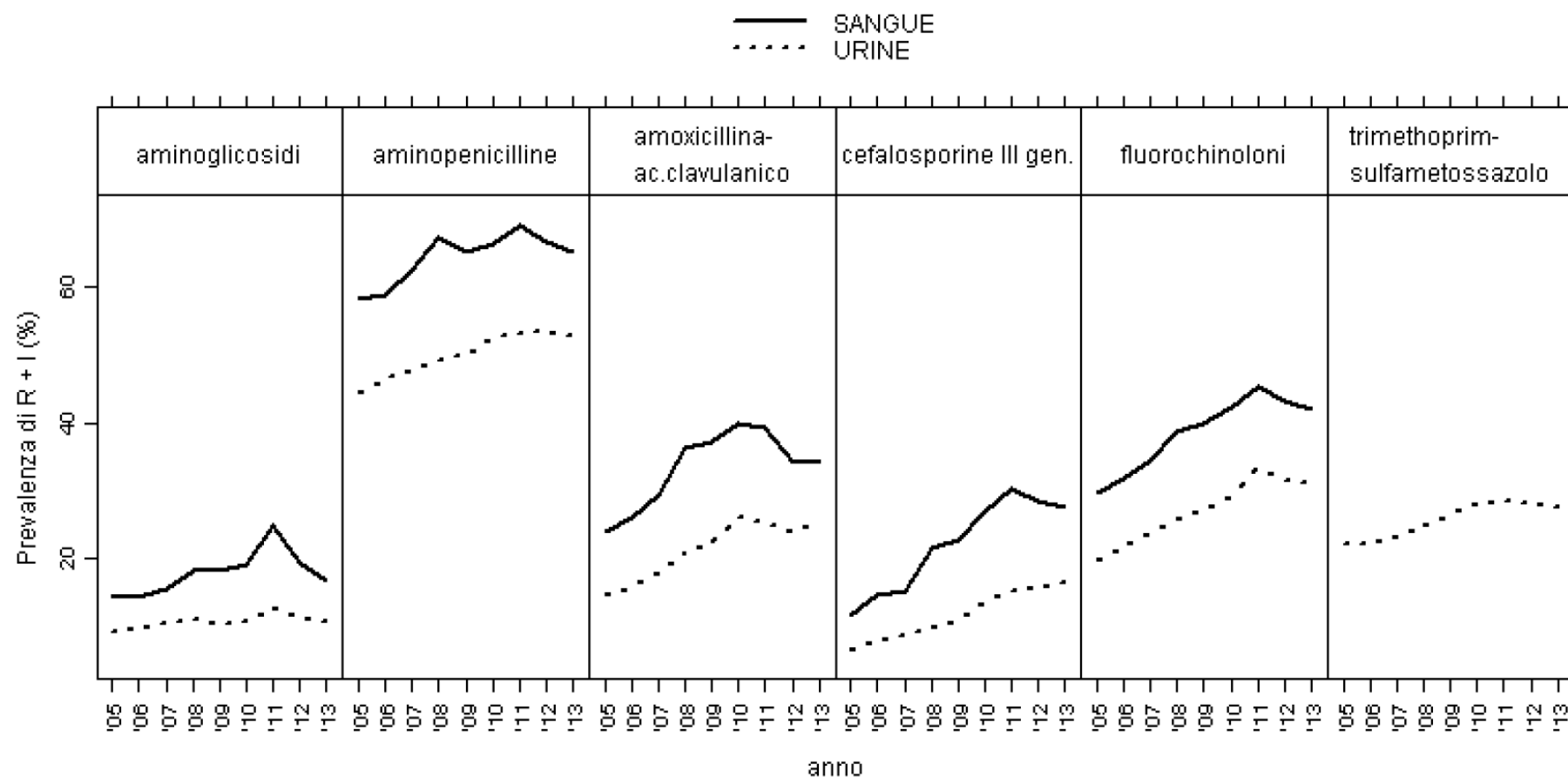


Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

European Antimicrobial
Resistance Surveillance
Network (EARS-Net)
Antimicrobial resistance
surveillance in Europe 2012

Antibioticoresistenza di *Escherichia coli*: emocolture/liquorcolture e urinocolture



Totale microrganismi isolati da esami culturali di campioni patologici di pazienti ricoverati presso il Policlinico

AZIENDA USL OSPEDALE S.Orsola - Malpighi

OSSERVATORIO EPIDEMIOLOGICO

SORVEGLIANZA BATTERICA E MONITORAGGIO DELLA ATTIVITA' DEGLI ANTIBIOTICI

Numero esami positivi (Totale) suddivisi per: Microrganismo / Ospedale

Microrganismo	2010 - Anno		2011 - Anno		2012 - Anno		2013 - Anno	
Ospedale: - Ospedale S.Orsola	Totale		Totale		Totale		Totale	
Escherichia coli	2 270	27.11%	2 224	24.39%	2 078	25.12%	2 232	25.77%
Klebsiella pneumoniae ssp pneumonia	647	7.73%	912	10.00%	738	8.92%	663	7.65%
Pseudomonas aeruginosa	716	8.55%	700	7.68%	636	7.69%	629	7.26%
Enterococcus faecalis	733	8.75%	704	7.72%	583	7.05%	624	7.20%
Staphylococcus aureus	535	6.39%	600	6.58%	490	5.92%	548	6.33%
Staphylococcus epidermidis	380	4.54%	522	5.73%	512	6.19%	502	5.80%
Candida albicans	387	4.62%	445	4.88%	405	4.90%	429	4.95%
Proteus mirabilis	325	3.88%	362	3.97%	316	3.82%	323	3.73%
Coagulase negative Staphylococcus	320	3.82%	342	3.75%	303	3.66%	228	2.63%
Enterococcus faecium	175	2.09%	212	2.33%	210	2.54%	204	2.36%
Enterobacter cloacae	170	2.03%	163	1.79%	172	2.08%	171	1.97%
Acinetobacter baumannii	128	1.53%	163	1.79%	129	1.56%	98	1.13%
Candida glabrata	89	1.06%	120	1.32%	116	1.40%	137	1.58%
Stenotrophomonas maltophilia	111	1.33%	130	1.43%	106	1.28%	99	1.14%
Klebsiella oxytoca	96	1.15%	95	1.04%	90	1.09%	117	1.35%
Staphylococcus haemolyticus	73	0.87%	70	0.77%	90	1.09%	98	1.13%
Morganella morganii ssp morganii	55	0.66%	87	0.95%	74	0.89%	94	1.09%
Serratia marcescens	64	0.76%	65	0.71%	69	0.83%	91	1.05%
Candida tropicalis	57	0.68%	67	0.73%	65	0.79%	61	0.70%
Enterobacter aerogenes	52	0.62%	56	0.61%	69	0.83%	47	0.54%
TOTALE Ospedale: - Ospedale S.Or	8 374		9 117		8 272		8 662	

Microrganismi isolati da emocolture da sangue periferico

Raggruppamento Materiali

Microrganismo

2010 - Anno

2011 - Anno

2012 - Anno

2013 - Anno

Ospedale: - Ospedale S.Orsola

* = probabile contaminazione

	Num.pazienti coinvolti		Num.pazienti coinvolti		Num.pazienti coinvolti		Num.pazienti coinvolti	
Sangue	1 559		1 780		1 688		1 684	
Escherichia coli	260	16.68%	314	17.64%	326	19.31%	319	18.94%
Coagulase negative Staphylococcus*	269	17.25%	302	16.97%	280	16.59%	214	12.71%
Staphylococcus epidermidis	140	8.98%	206	11.57%	204	12.09%	199	11.82%
Staphylococcus aureus	111	7.12%	126	7.08%	101	5.98%	104	6.18%
Klebsiella pneumoniae ssp pneumonia	84	5.39%	126	7.08%	107	6.34%	87	5.17%
Enterococcus faecalis	71	4.55%	79	4.44%	60	3.55%	62	3.68%
Pseudomonas aeruginosa	54	3.46%	58	3.26%	52	3.08%	40	2.38%
Candida albicans	40	2.57%	45	2.53%	43	2.55%	41	2.43%
Enterococcus faecium	37	2.37%	46	2.58%	35	2.07%	44	2.61%
Staphylococcus haemolyticus	29	1.86%	27	1.52%	44	2.61%	48	2.85%
Enterobacter cloacae	32	2.05%	27	1.52%	31	1.84%	26	1.54%
Propionibacterium acnes*	34	2.18%	29	1.63%	28	1.66%	24	1.43%
Staphylococcus hominis ssp hominis			32	1.80%	37	2.19%	37	2.20%
Proteus mirabilis	20	1.28%	23	1.29%	28	1.66%	24	1.43%
Staphylococcus epidermidis group*	92	5.90%						
Corynebacterium species*	19	1.22%	14	0.79%	20	1.18%	7	0.42%
Klebsiella oxytoca	16	1.03%	14	0.79%	13	0.77%	17	1.01%
Streptococcus pneumoniae	12	0.77%	20	1.12%	11	0.65%	13	0.77%
Candida parapsilosis	9	0.58%	21	1.18%	9	0.53%	15	0.89%
Serratia marcescens	12	0.77%	13	0.73%	15	0.89%	12	0.71%
TOTALE Ospedale: - Ospedale S.Or	1 559		1 780		1 688		1 684	

Microrganismi isolati dall'apparato urinario

Raggruppamento Materiali

Microrganismo

2010 - Anno

2011 - Anno

2012 - Anno

2013 - Anno

Ospedale: - Ospedale S.Orsola

Num.pazienti
coinvolti

Num.pazienti
coinvolti

Num.pazienti
coinvolti

Num.pazienti
coinvolti

Apparato urinario

2 880

3 068

2 905

3 064

Escherichia coli

1 261 43.78%

1 308 42.63%

1 221 42.03%

1 311 42.79%

Enterococcus faecalis

462 16.04%

426 13.89%

395 13.60%

422 13.77%

Klebsiella pneumoniae ssp pneumonia

272 9.44%

313 10.20%

278 9.57%

252 8.22%

Proteus mirabilis

169 5.87%

185 6.03%

177 6.09%

203 6.63%

Pseudomonas aeruginosa

159 5.52%

160 5.22%

175 6.02%

161 5.25%

Candida albicans

114 3.96%

142 4.63%

125 4.30%

139 4.54%

Enterococcus faecium

56 1.94%

77 2.51%

85 2.93%

73 2.38%

Enterobacter cloacae

37 1.28%

54 1.76%

49 1.69%

55 1.80%

Klebsiella oxytoca

31 1.08%

47 1.53%

47 1.62%

63 2.06%

Morganella morganii ssp morganii

32 1.11%

52 1.69%

49 1.69%

43 1.40%

Candida glabrata

22 0.76%

44 1.43%

37 1.27%

37 1.21%

Staphylococcus aureus

37 1.28%

28 0.91%

30 1.03%

40 1.31%

Streptococcus agalactiae

20 0.69%

27 0.88%

35 1.20%

22 0.72%

Candida tropicalis

16 0.56%

25 0.81%

23 0.79%

22 0.72%

Enterobacter aerogenes

12 0.42%

21 0.68%

26 0.90%

16 0.52%

Citrobacter freundii

18 0.63%

13 0.42%

20 0.69%

22 0.72%

Providencia stuartii

14 0.49%

23 0.75%

19 0.65%

15 0.49%

Citrobacter koseri

16 0.56%

21 0.68%

16 0.55%

17 0.55%

Acinetobacter baumannii

16 0.56%

15 0.49%

18 0.62%

13 0.42%

Candida pelliculosa

47 1.53%

TOTALE Ospedale: - Ospedale S.Or

2 880

3 068

2 905

3 064

Sensibilità agli antibiotici di *Escherichia coli*

AZIENDA USL OSPEDALE S.Orsola - Malpighi

OSSERVATORIO EPIDEMIOLOGICO

SORVEGLIANZA BATTERICA E MONITORAGGIO DELLA ATTIVITA' DEGLI ANTIBIOTICI

Antibiotici saggiati (Totale) suddivisi per: Antibiotico / Microrganismo

FILTRO APPLICATO: Filtraggio microrganismi ATTIVO Antibiotico: (Nome = Amoxicillin/Clavulanic Acid OR Nome = Ampicillin OR Nome = Cefotaxime OR Nome = Ceftazidime OR Nome = Meropenem OR Nome = Ertapenem OR Nome...[omissis])

Microrganismo Antibiotico	2010 - Anno				2011 - Anno				2012 - Anno				2013 - Anno			
	N.sagg.	%R	%I	%S	N.sagg.	%R	%I	%S	N.sagg.	%R	%I	%S	N.sagg.	%R	%I	%S

Escherichia coli																
Amikacina	2.254	1.7	0.9	97.4	2.209	2.4	6.6	91.0	2.065	1.9	10.4	87.7	2.218	1.4	10.9	87.8
Amoxicillina/Clavulanico	2.256	31.9	17.5	50.6	2.211	40.3	0.2	59.5	2.066	37.5	0.0	62.5	2.217	40.1		59.9
Ampicillina	2.254	70.5	0.8	28.8	2.200	70.8		29.2	2.060	72.5		27.5	2.216	70.1		29.9
Cefotaxima	2.251	31.0	0.0	68.9	2.201	30.2	0.7	69.1	2.058	29.3	0.2	70.6	2.210	31.3	0.5	68.2
Ceftazidima	2.255	31.1		68.9	2.211	22.1	5.9	72.0	2.065	20.5	6.2	73.3	2.218	21.3	7.2	71.5
Ciprofloxacina	2.254	48.1	0.3	51.6	2.212	50.6	1.9	47.5	2.066	48.1	1.5	50.5	2.218	45.6	1.7	52.7
Colistina	15			100.0	91			100.0	140			100.0	268	0.7		99.3
Cotrimoxazolo	2.255	44.3	0.3	55.5	2.212	40.9	0.1	59.0	2.064	41.2		58.8	2.218	40.4	0.1	59.4
Ertapenem	0				151	3.3	1.3	95.4	256	3.1	0.4	96.5	329	0.9		99.1
Fosfomicina	0				323	3.1		96.9	1.345	3.4		96.6	1.463	3.6		96.4
Gentamicina	2.255	17.2	0.4	82.4	1.886	16.8	1.8	81.4	1.931	16.7	0.5	82.8	2.218	18.8	0.5	80.7
Meropenem	348			100.0	303			100.0	255	1.6		98.4	328			100.0
Nitrofurantoina	1.466	2.1	8.6	89.3	1.484	2.4	0.1	97.5	1.347	2.2		97.8	1.205	1.7		98.3
Piperacillina/Tazobactam	2.254	18.5	5.4	76.1	2.194	10.7	3.6	85.7	2.051	11.7	2.5	85.8	2.180	11.6	2.2	86.1
Tigeciclina	4			100.0	90			100.0	140	1.4	2.9	95.7	268	0.7	2.2	97.0

Sensibilità agli antibiotici di *Enterococcus faecalis e faecium*

AZIENDA USL OSPEDALE S.Orsola - Malpighi

OSSERVATORIO EPIDEMIOLOGICO

SORVEGLIANZA BATTERICA E MONITORAGGIO DELLA ATTIVITA' DEGLI ANTIBIOTICI

Antibiotici saggiati (Totale) suddivisi per: Antibiotico / Microrganismo

FILTRO APPLICATO: Filtraggio microrganismi ATTIVO Antibiotico: (Nome = Ampicillin OR Nome = Teicoplanin OR Nome = Vancomycin OR Nome = Synercid OR Nome = Linezolid OR Nome = Gentamicin-high OR Nome = Streptomyc... [omissis])

Microrganismo Antibiotico	2010 - Anno				2011 - Anno				2012 - Anno				2013 - Anno			
	N.sagg.	%R	%I	%S	N.sagg.	%R	%I	%S	N.sagg.	%R	%I	%S	N.sagg.	%R	%I	%S
Enterococcus faecalis																
Ampicillina	732	4.4		95.6	699	4.0	0.6	95.4	580	3.1	0.5	96.4	615	1.6	0.3	98.0
Gentamicina 500	103	46.6		53.4	110	55.5		44.5	77	40.3		59.7	71	52.1		47.9
Linezolid	6			100.0	8			100.0	2			100.0	3			100.0
Nitrofurantoina	501	0.4	0.8	98.8	446	0.2		99.8	416			100.0	439	0.2		99.8
Quinupristina/Dalfopristina	0				0				1	100.0			6	100.0		
Streptomicina 1000	104	44.2		55.8	109	47.7		52.3	77	36.4		63.6	73	39.7		60.3
Teicoplanina	732	0.5		99.5	697	1.1		98.9	580	0.5		99.5	614	0.3		99.7
Vancomicina	19	21.1		78.9	524	1.7		98.3	507	0.8		99.2	553	0.4		99.6
Enterococcus faecium																
Ampicillina	171	88.9		11.1	209	90.0	1.0	9.1	209	94.3		5.7	196	93.9		6.1
Gentamicina 500	57	57.9		42.1	56	66.1		33.9	48	70.8		29.2	64	71.9		28.1
Linezolid	37			100.0	30			100.0	12			100.0	20			100.0
Nitrofurantoina	59	1.7	23.7	74.6	84			100.0	92	1.1		98.9	76	1.3		98.7
Quinupristina/Dalfopristina	16			100.0	61	8.2	27.9	63.9	48		14.6	85.4	62	1.6	14.5	83.9
Streptomicina 1000	56	80.4		19.6	56	78.6		21.4	47	87.2		12.8	66	90.9		9.1
Teicoplanina	171	15.2	1.8	83.0	209	13.9		86.1	210	8.1		91.9	197	13.2		86.8
Vancomicina	78	41.0	1.3	57.7	201	14.4		85.6	205	8.3		91.7	195	15.4		84.6

MIC Breakpoint

Antibiotici	MIC	S/I/R	S≤	R>	Note
Amikacina	≥64	R	8	16	
Amoxicillina + Ac.Clavulanic	≥32	R	8	8	
Ampicillina	≥32	R	8	8	
Cefotaxime	≥64	R	1	2	
Ceftazidime	≥64	R	1	4	
Ciprofloxacina	≥4	R	0.5	1	
Colistina	≤0,5	S	2	2	
Ertapenem	≥8	R	0.5	1	
Gentamicina	4	I	2	4	
Meropenem	≥16	R	2	8	<i>Ceppo con ridotta sensibilità ai carbapenemi, potenzialmente produttore di carbapenemasi: la terapia con carbapenemi potrebbe avere efficacia ridotta anche se in vitro il ceppo appare sensibile ai farmaci. Nel caso in cui si intendano utilizzare tali farmaci si raccomanda preventiva consulenza con un esperto di terapia antibiotica.</i>
Piperacillina+Tazobactam	≥128	R	8	16	
Tigeciclina	4	R	1	2	
Sulfa/Trimeth	≥320	R	40	80	

MIC= Concentrazione Minima Inibente (ug/ml)

S/I/R= Categorie di Interpretazione: S=Sensibile I=Intermedio R=Resistente

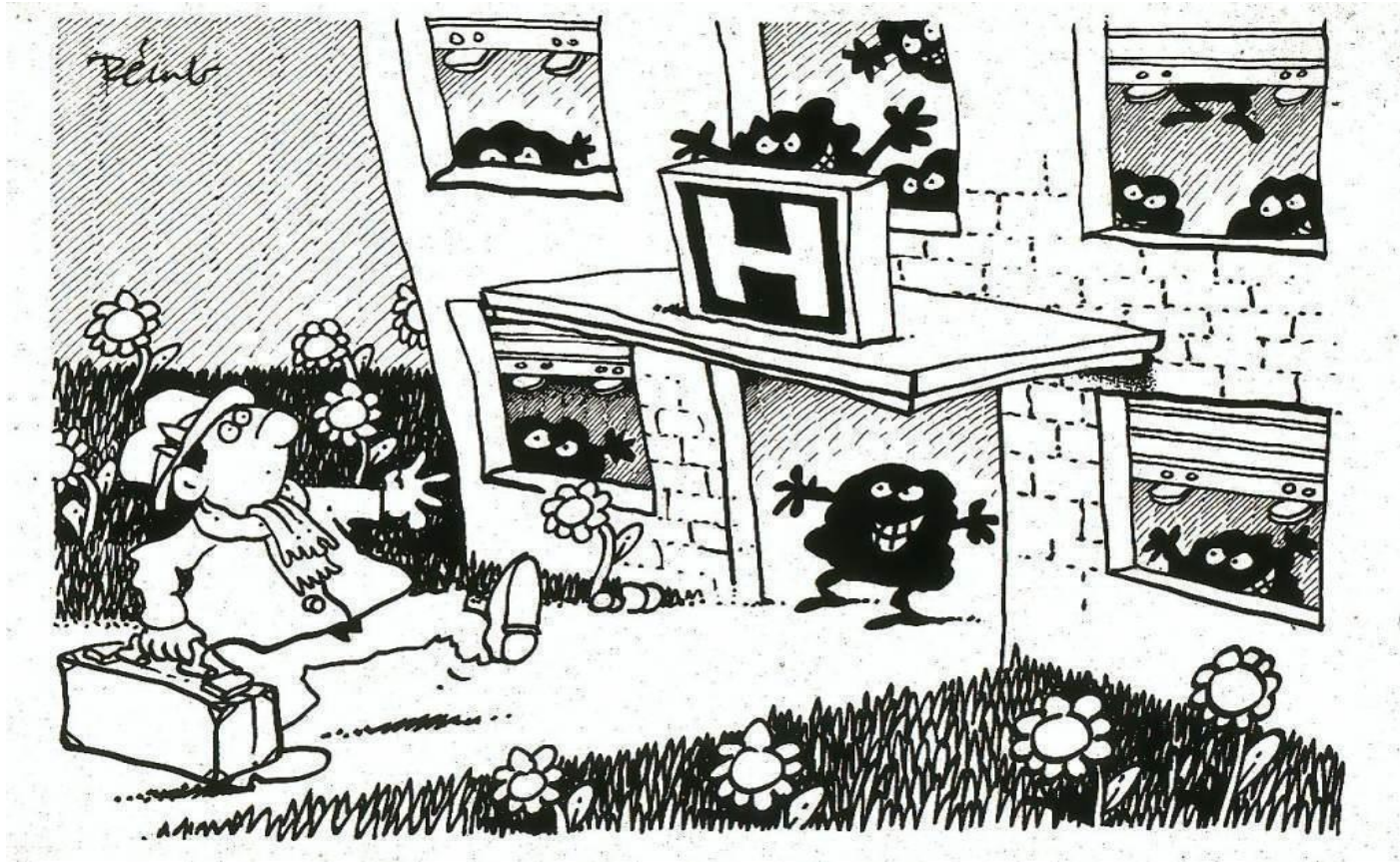
Dal 01/01/2011 l'antibiogramma è interpretato secondo i criteri EUCAST (European Committee on Antimicrobial Susceptibility Testing -

¹ [6] Esame/Ricerca

Produzione di Carbapenemasi: Test di Conferma

Risultato

Positivo



And now...
we move to the post antibiotic era.....

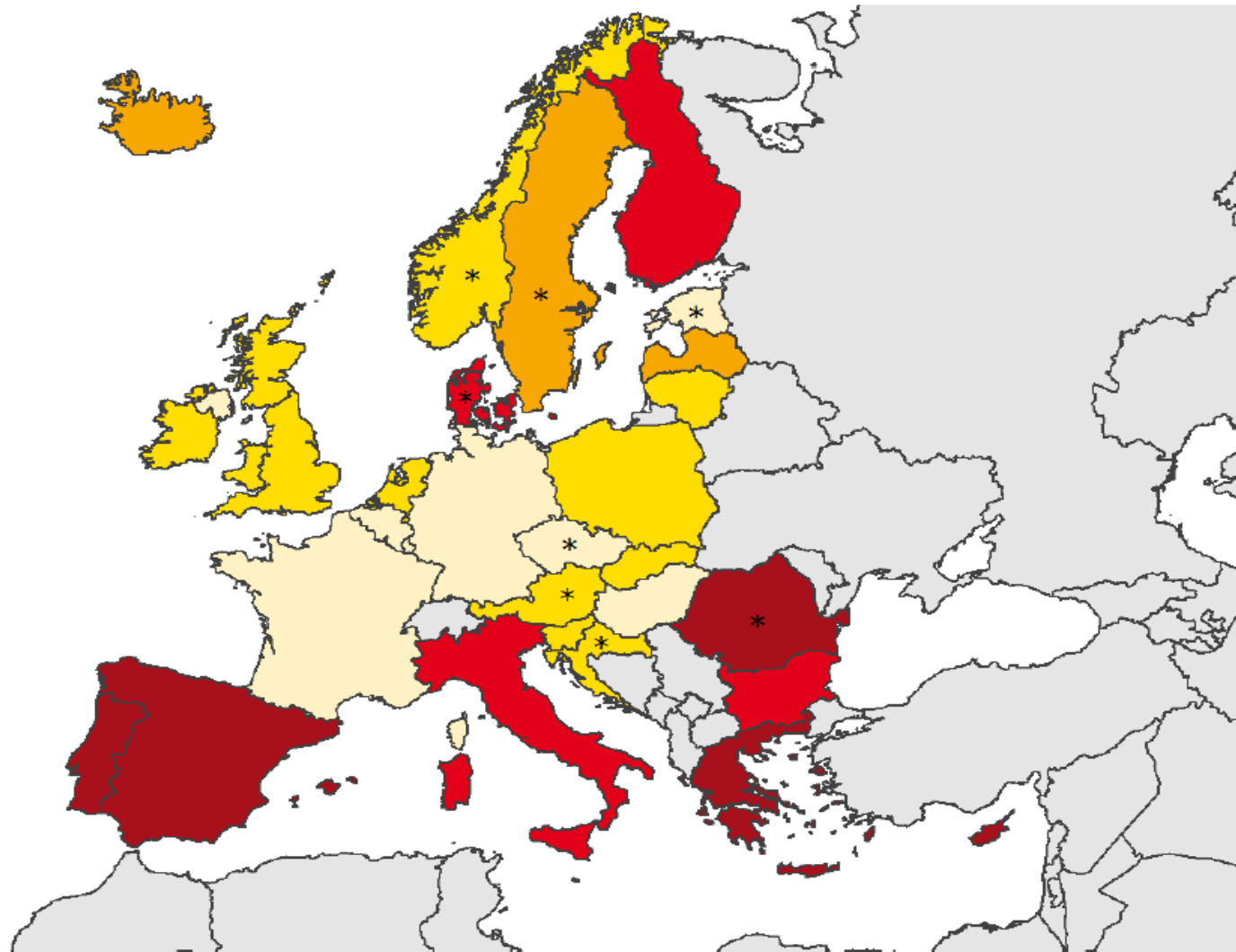
Prevalence of antimicrobial use (percentage of patients receiving at least one antimicrobial agent) in European hospitals, by country, ECDC PPS 2011-2012

Patients on antimicrobials (%)

- <30
- 30 to <35
- 35 to <40
- 40 to <45
- ≥ 45
- Not included

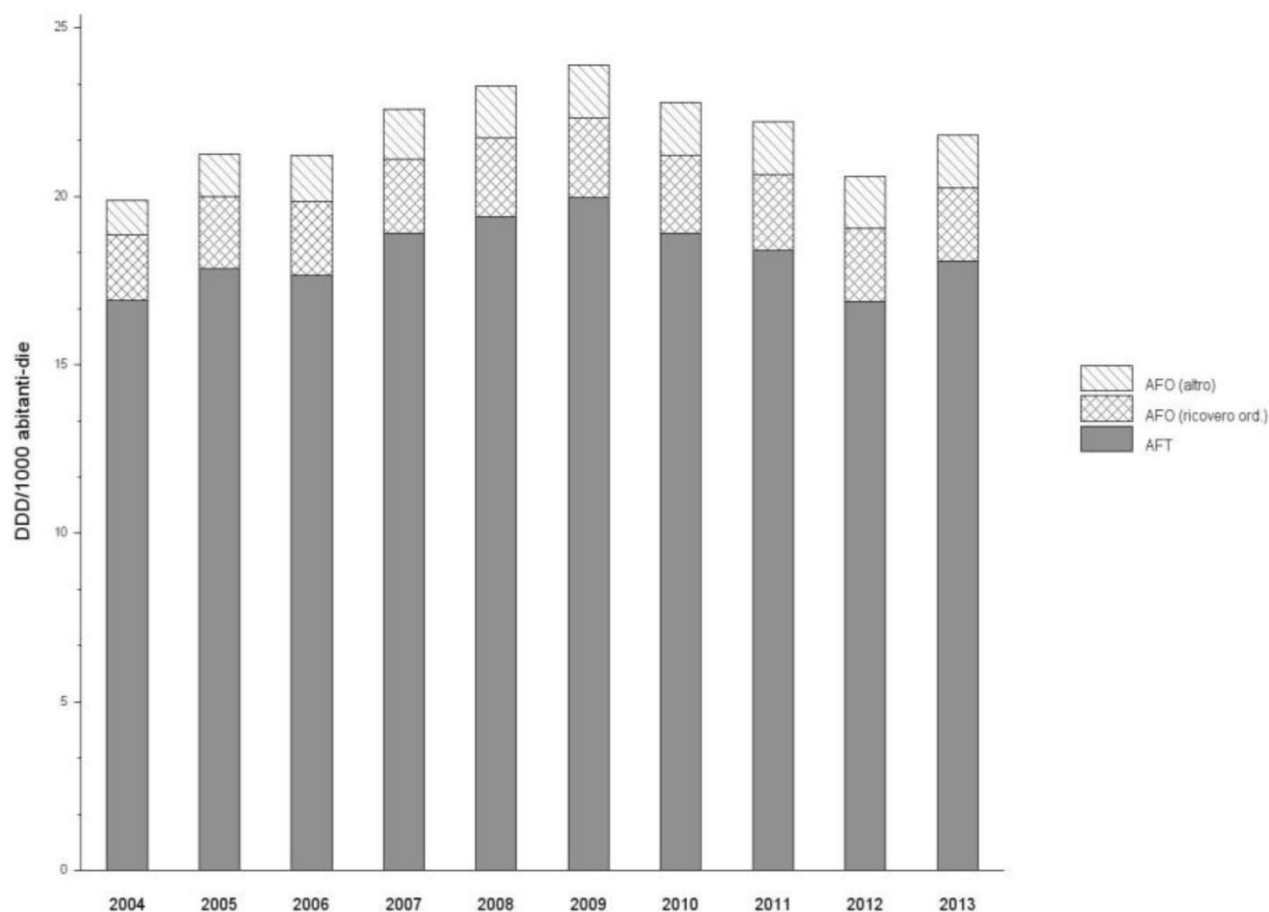
Non-visible countries

- Liechtenstein
- Luxembourg
- Malta



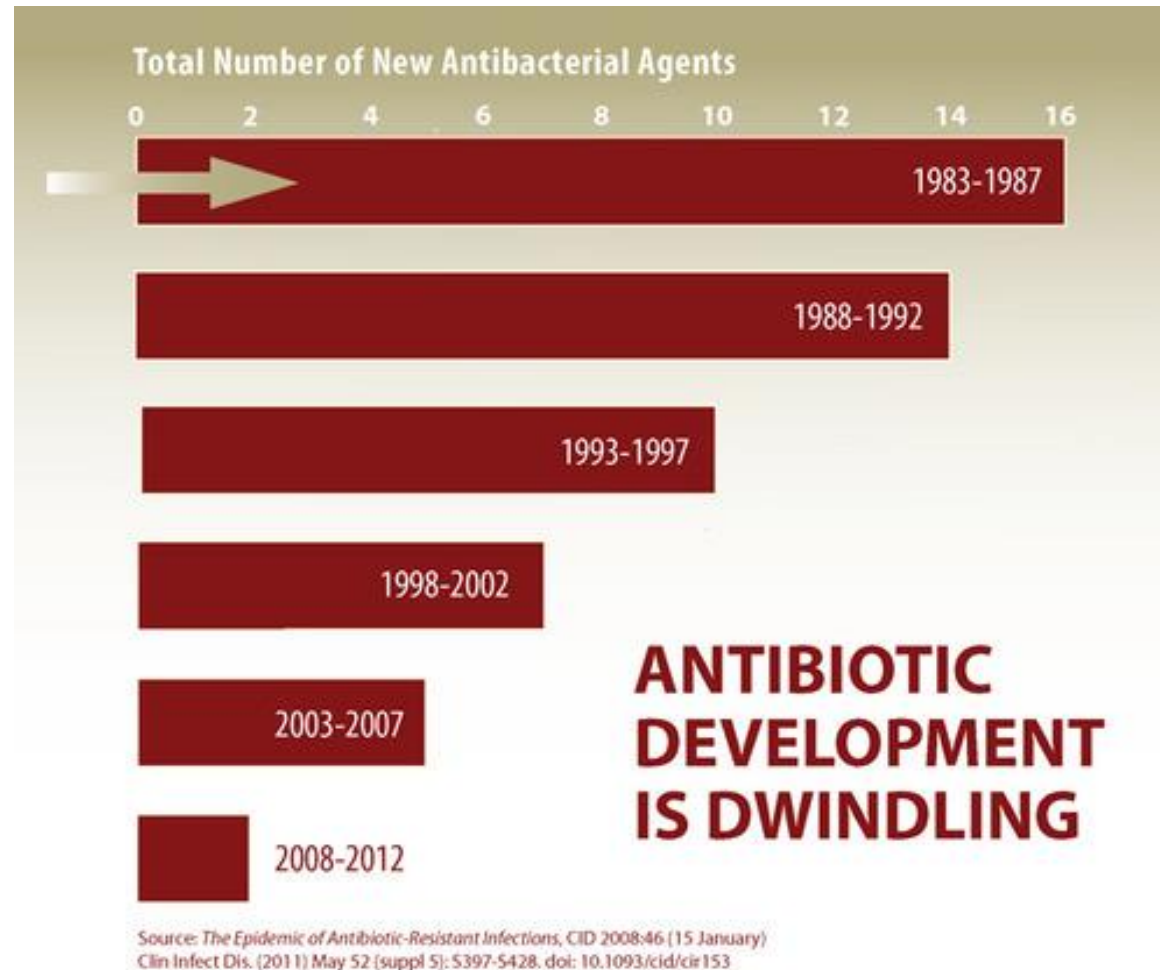
An asterisk indicates that reported PPS data did not provide a proper representation of the situation in a given country. Representativeness of PPS data was poor in Austria, Croatia, the Czech Republic, Estonia, Norway and Romania, and very poor in Denmark and Sweden.

Tasso di consumo di antibiotici in Emilia-Romagna, espresso in DDD/1.000 abitanti-*die* (AFT e AFO 2004-2013)



CDC director warns *antibiotics pipeline 'nearly empty'*

September 16, 2013



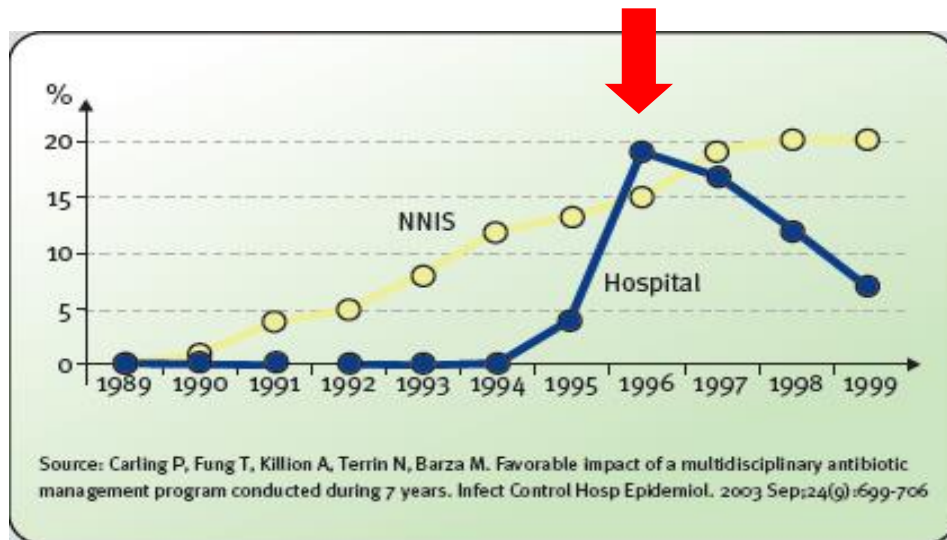


Stoking the antibiotic pipeline

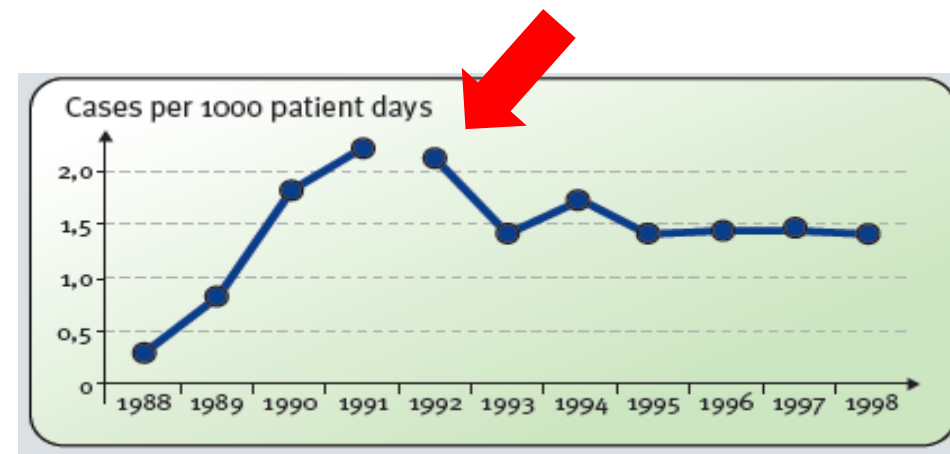
New antibiotics to tackle multidrug resistant bacteria are much needed. Chantal Morel and Elias Mossialos show how financial incentives might be used to persuade drug companies to develop them

Benefici di un uso prudente degli antibiotici

- L'uso prudente degli antibiotici può impedire la comparsa e la selezione di batteri antibiotico-resistenti.¹⁹⁻²³
- Si è dimostrato che diminuendo l'uso di antibiotici si riduce l'incidenza di infezioni da *Clostridium difficile*.²⁴⁻²⁶



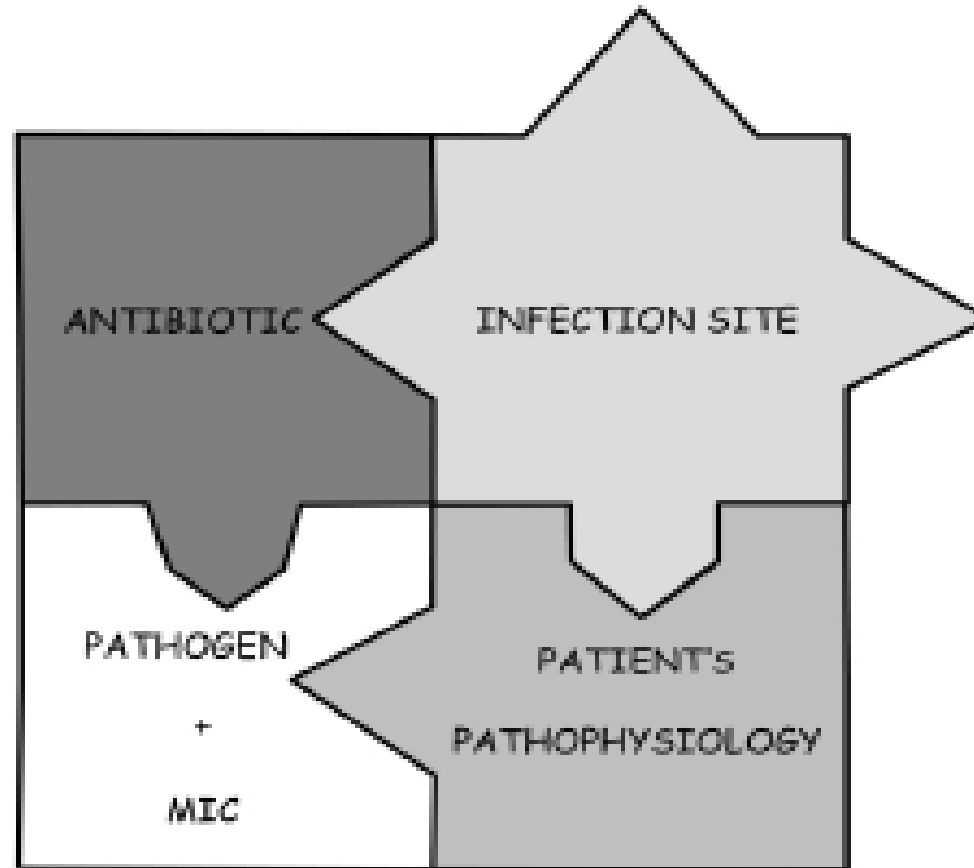
Rates of Vancomycin-resistant *Enterococci* in hospital before and after implementation of the antibiotic management program compared with rates in National Nosocomial Infections Surveillance (NNIS) System* hospitals of similar size.²⁷



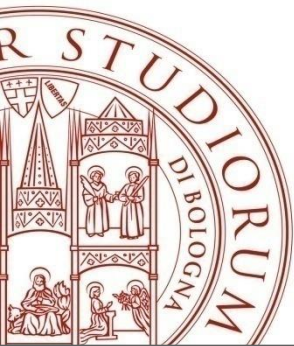
Rates of nosocomial *Clostridium difficile*, expressed per 1,000 patient-days, before and after implementation of the antibiotic management program.²⁸

The Antimicrobial Therapy Puzzle: Could Pharmacokinetic-Pharmacodynamic Relationships Be Helpful in Addressing the Issue of Appropriate Pneumonia Treatment in Critically Ill Patients?

F Pea, P Viale CID 2006;42:1764-71



The antimicrobial therapy puzzle



LE INFEZIONI DEL BASSO TRATTO UROGENITALE FEMMINILE

FERRARA, 22 MAGGIO 2015

**Urinocoltura, antibiogramma,
antibioticoterapia,
antibiotico resistenza:
riflessioni**

Fabio Tumietto

Programma Aziendale

Epidemiologia e Controllo del Rischio Infettivo Correlato alle Organizzazioni Sanitarie

Clinica Malattie Infettive - Bologna

