ANTIBIOTICI: PER FARNE BUON USO

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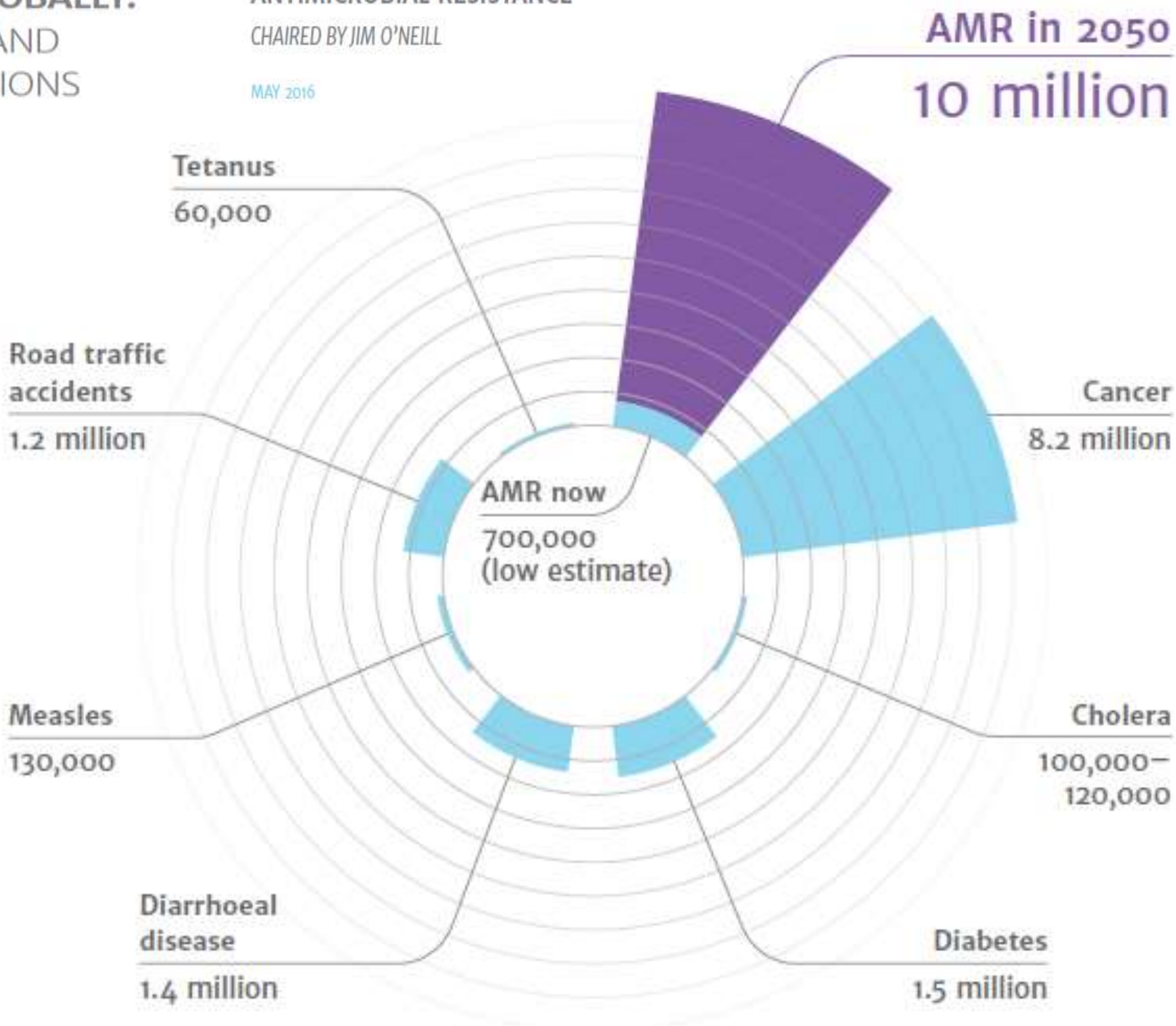
TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY:
FINAL REPORT AND RECOMMENDATIONS

THE REVIEW ON ANTIMICROBIAL RESISTANCE

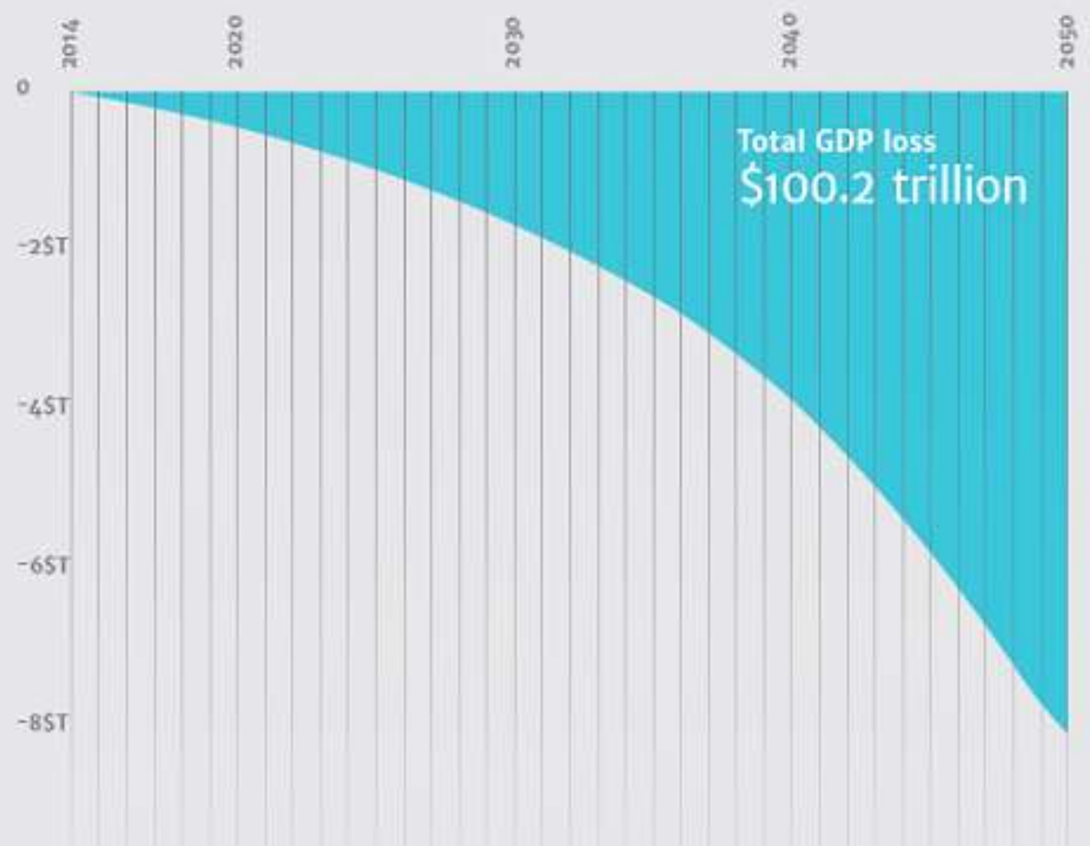
CHAIRED BY JIM O'NEILL

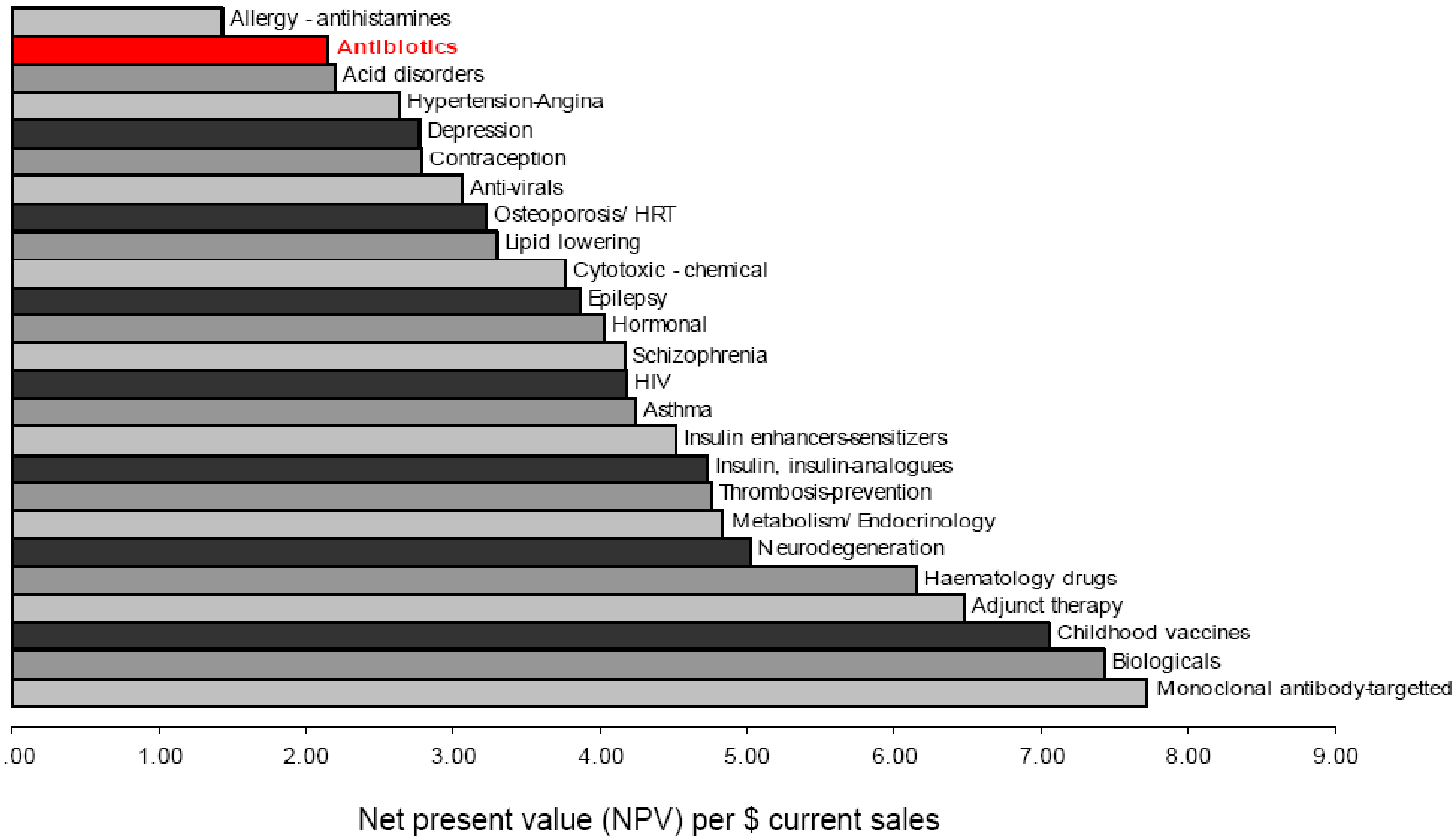
MAY 2016



Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations

AMR's impact on World GDP
in trillions of USD

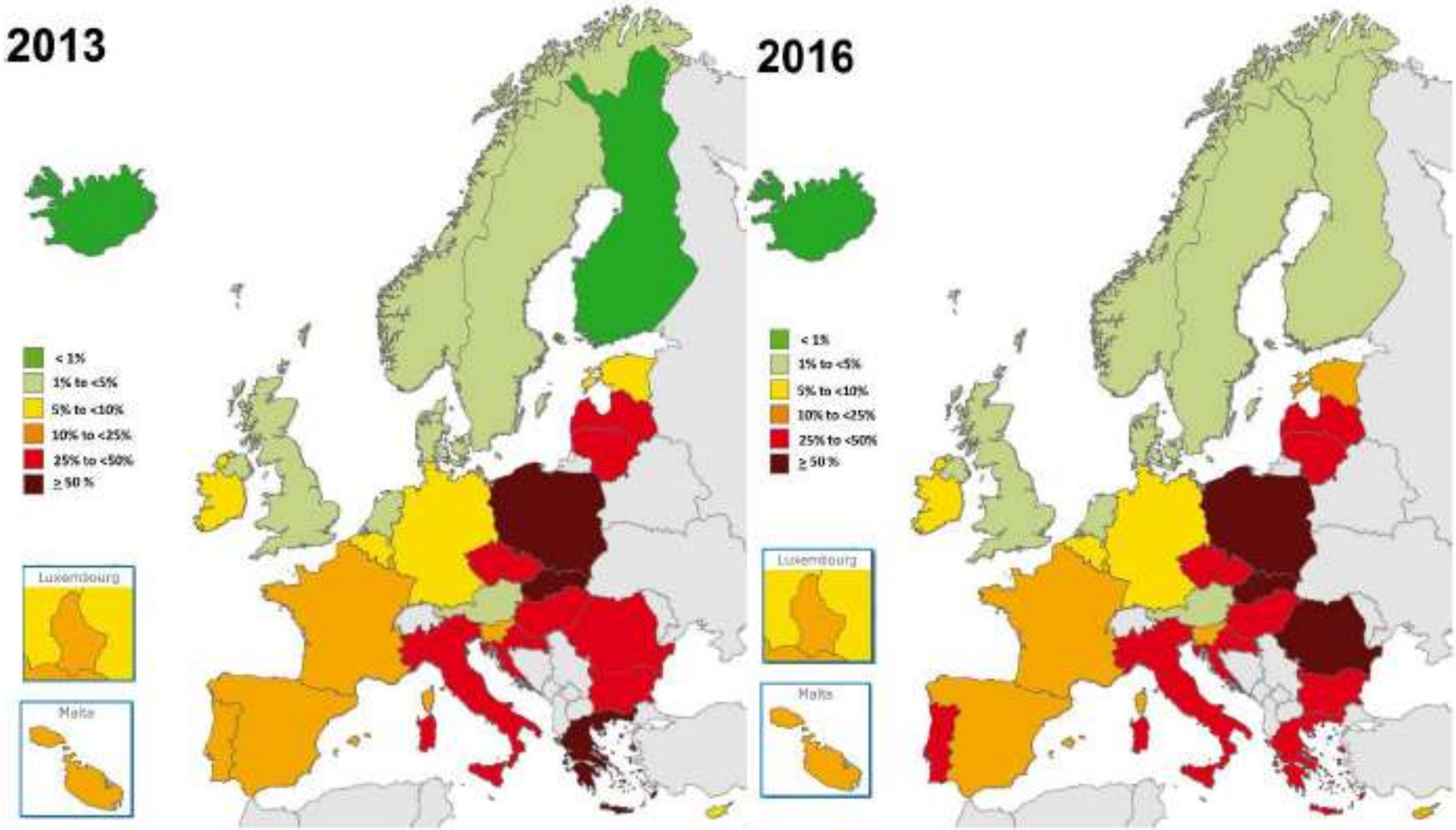




Source: Lehman Brothers PharmaPipelines

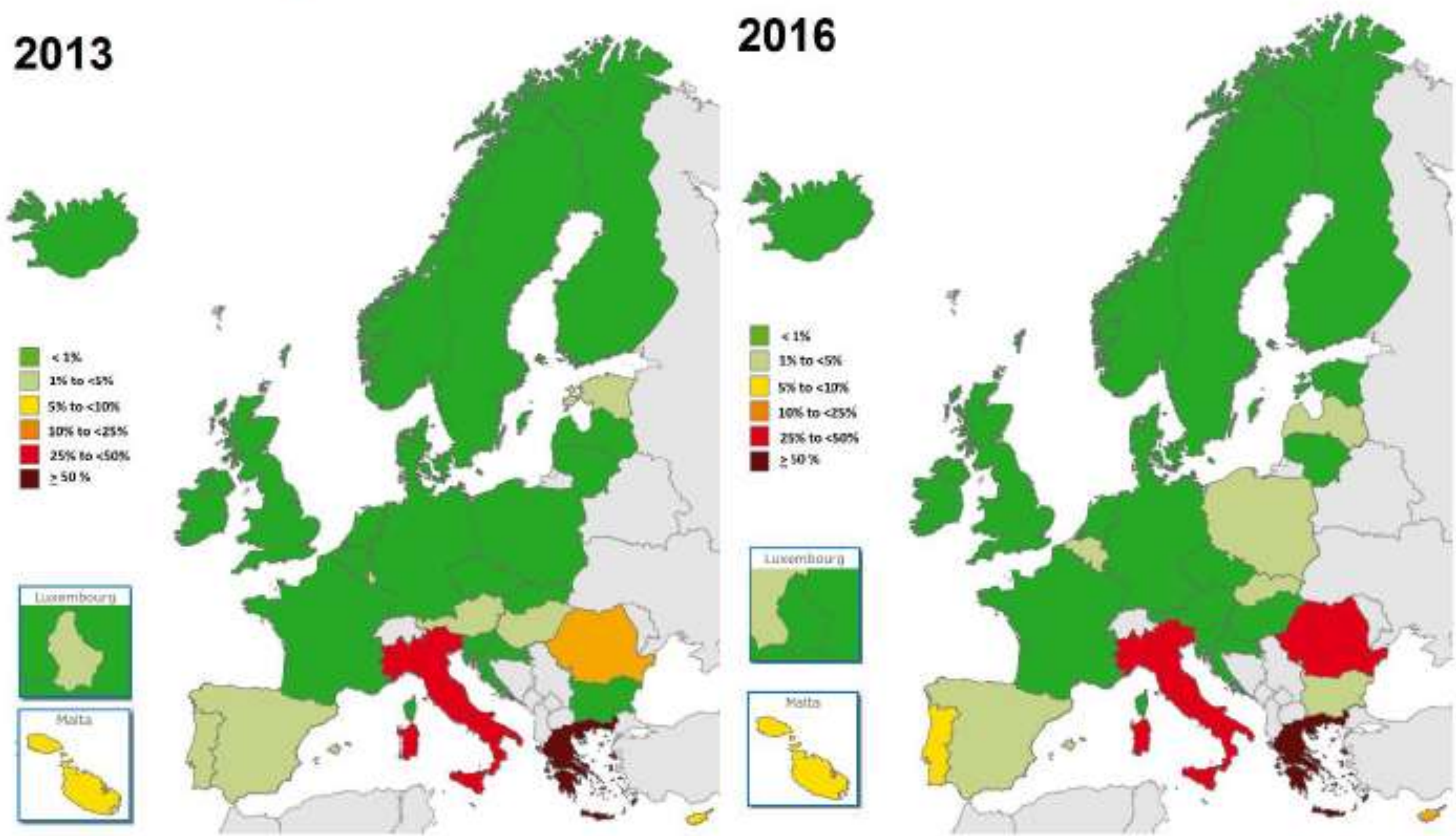
EARS-Net surveillance data
November 2017

Figure 1. *Klebsiella pneumoniae*: percentage of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, EU/EEA, 2013 (left), 2016 (right)



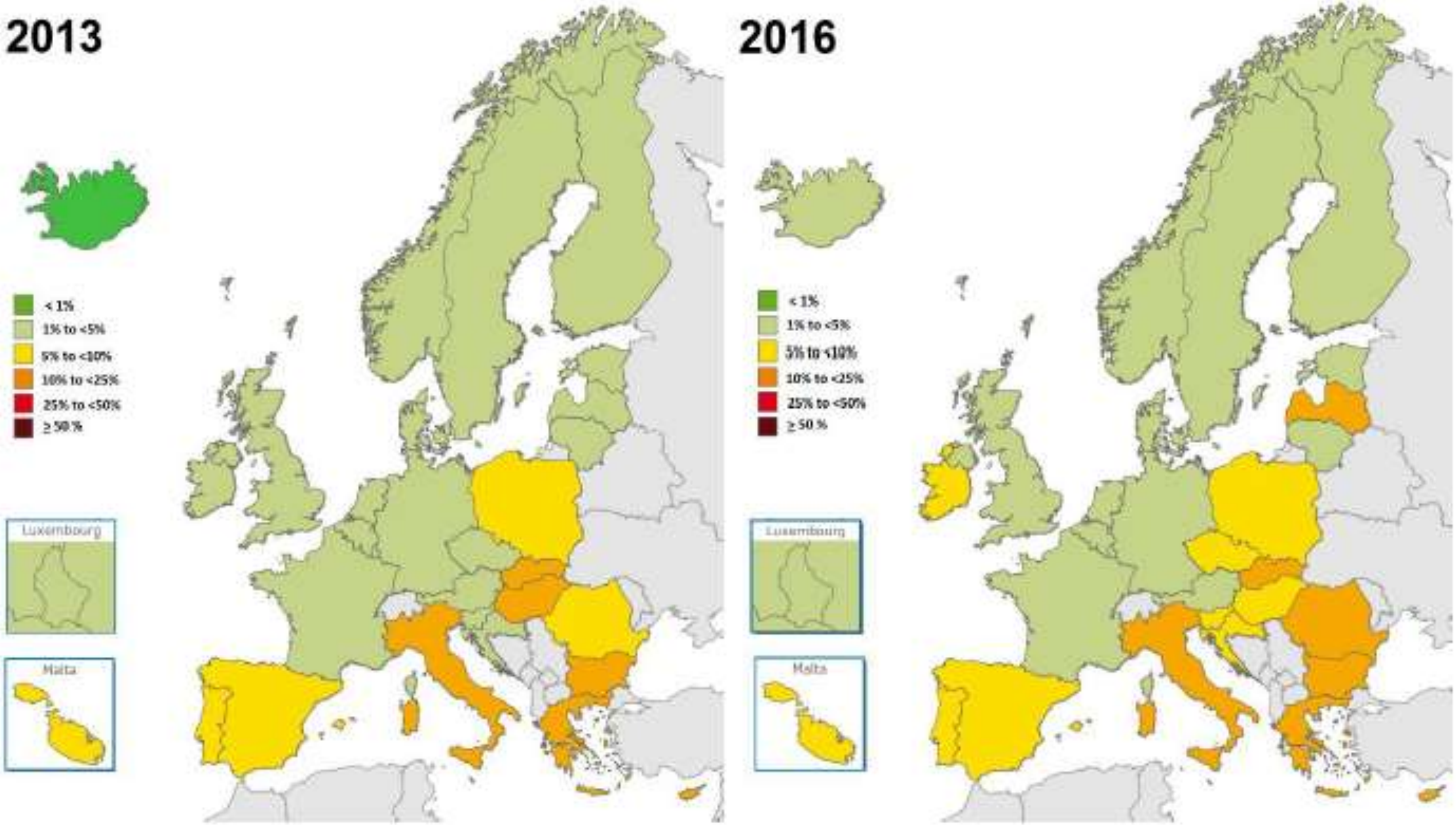
EARS-Net surveillance data
November 2017

Figure 2. ***Klebsiella pneumoniae*: percentage of invasive isolates with resistance to carbapenems, EU/EEA, 2013 (left), 2016 (right)**



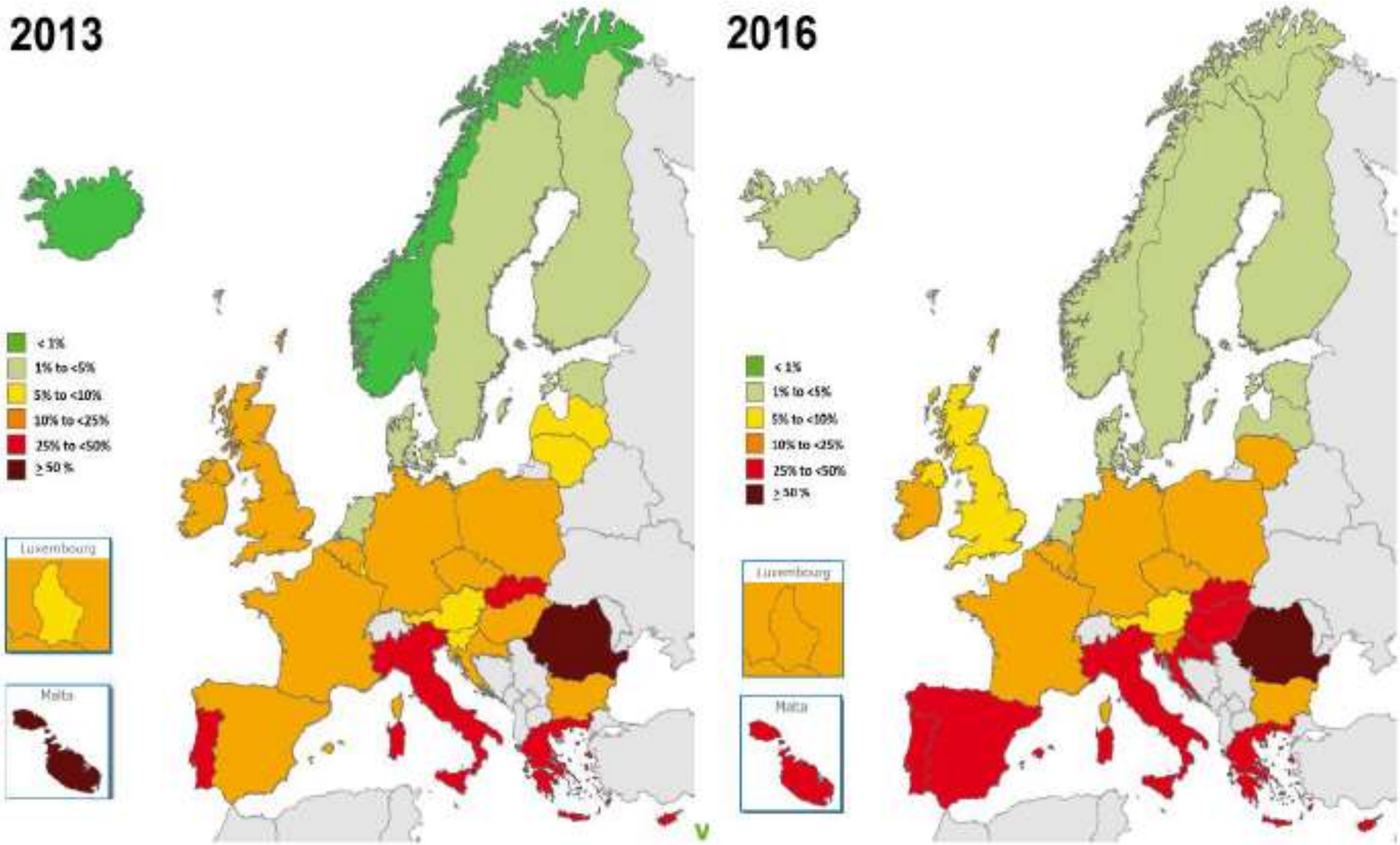
EARS-Net surveillance data
November 2017

Figure 5. *Escherichia coli*: percentage of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, EU/EEA, 2013 (left), 2016 (right)



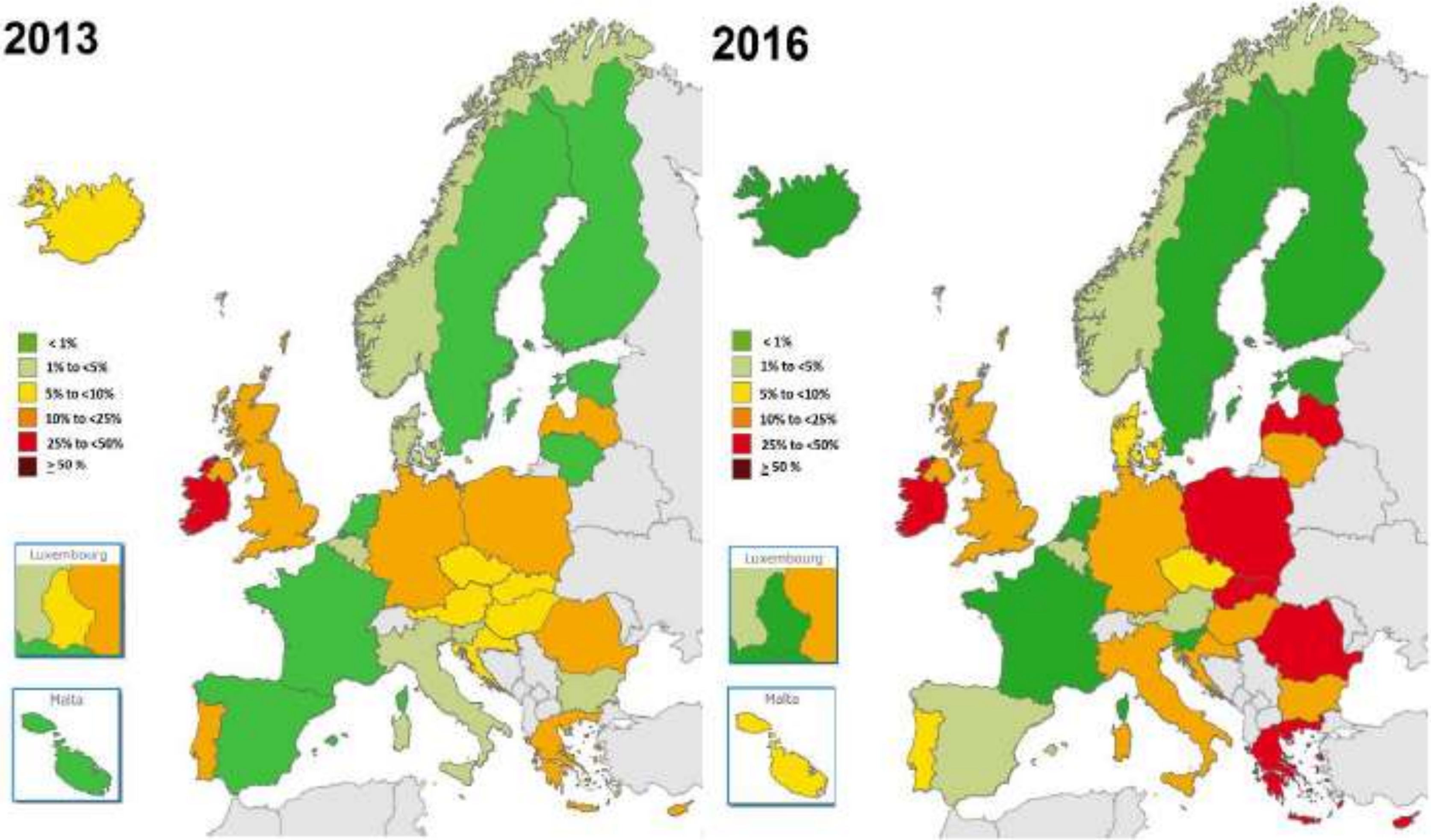
EARS-Net surveillance data
November 2017

Figure 7. *Staphylococcus aureus*: percentage of invasive isolates with resistance to meticillin (MRSA), EU/EEA, 2013 (left), 2016 (right)



EARS-Net surveillance data
November 2017

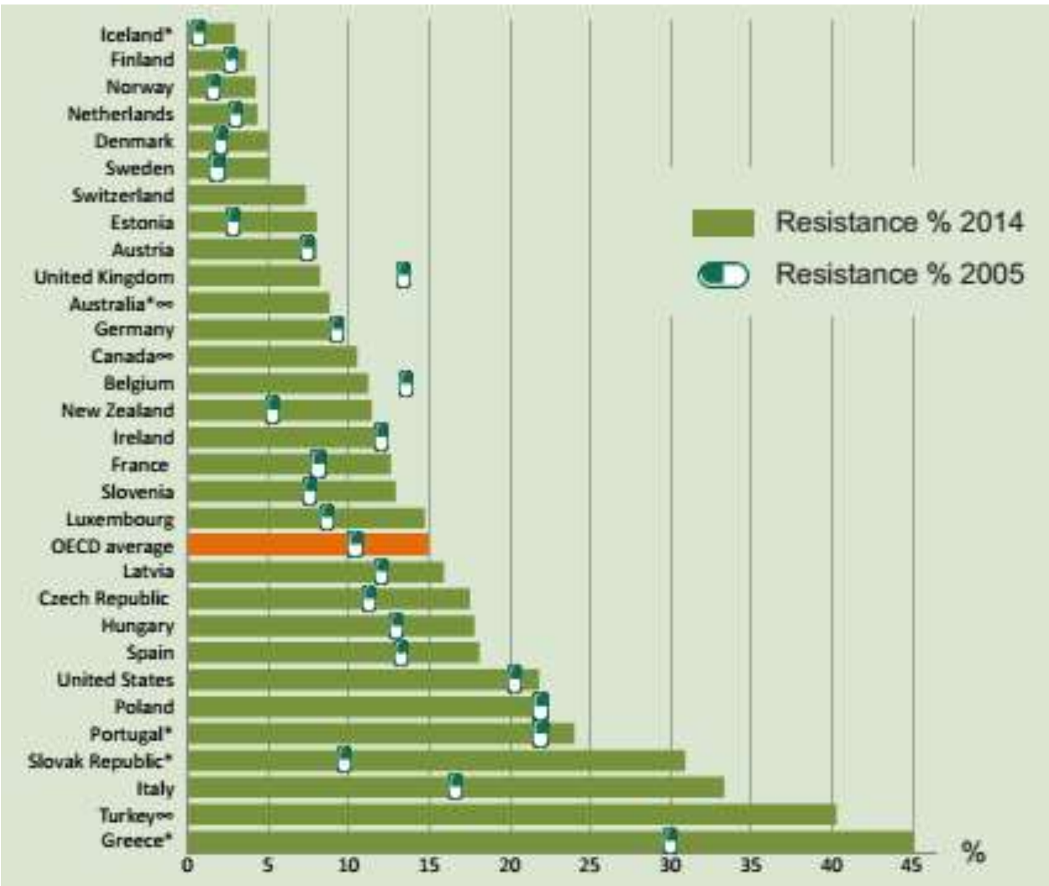
Figure 8. ***Enterococcus faecium*****: percentage of invasive isolates with resistance to vancomycin, EU/EEA, 2013 (left), 2016 (right)**



Antimicrobial resistance

Policy insights

OECD



Trends across OECD countries

Antibiotic resistance is growing

- 700000 decessi/anno attribuiti a antibioticoresistenza; se aumenta del 40% ci saranno 9,5 milioni decessi/anno
- Incremento di 10-40000 dollari per trattare un paziente con infezione da batteri MDR
- Agli attuali livelli di resistenza incremento di 29 miliardi di dollari di spesa sanitaria al 2050

TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY:
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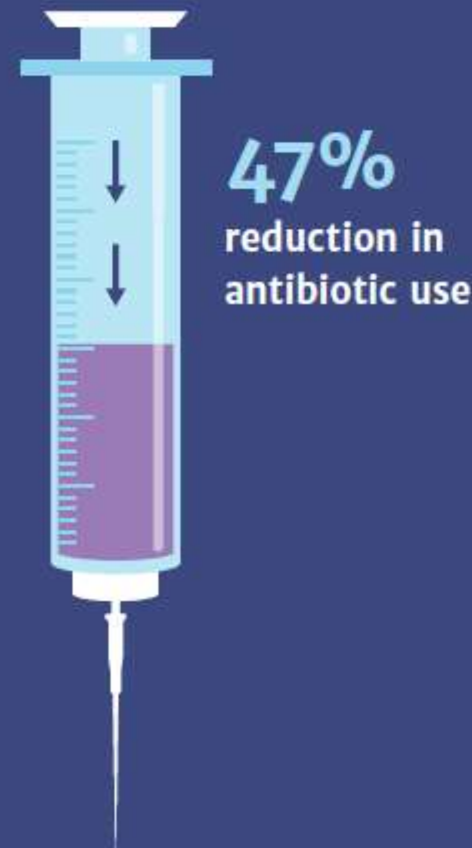
MAY 2016

INCREASING COVERAGE OF VACCINES CAN REDUCE ANTIBIOTIC USE

Universal coverage by a pneumococcal conjugate vaccine could potentially avert 11.4 million days of antibiotic use per year in children younger than five, roughly a 47% reduction in the amount of antibiotics used for pneumonia cases caused by *S. pneumoniae*.



Use of mathematical modelling to assess the impact of vaccines on antibiotic resistance

Katherine E Atkins, Erin I Lafferty, Sarah R Deeny, Nicholas G Davies, Julie V Robotham, Mark Jit

Lancet Infect Dis 2018; 18: e204–13

Direct level

1 Effectiveness against carriage of drug-resistant or drug-sensitive bacteria
2 Effectiveness against infection by drug-resistant or drug-sensitive bacteria
3 Effectiveness against other pathogens

Population level

4 Onward transmission of drug-resistant or drug-sensitive bacteria in community and hospital
5 Transmission of other pathogens in community and hospital

Pathogen level

6 Population size for emergence of resistance
7 Rate of de-novo mutation and horizontal gene transfer per cell replication
8 Treatment-dependent selection for resistance

Health level

9 Progression to disease (via carriage reduction, infection prevention, or a decrease in co-infection)

Care level

10 Antibiotic use against drug-resistant or drug-sensitive infection
11 Collateral antibiotic use (inappropriate use on viral infections or bystander effect, or both)

OECD

Health at a Glance 2017: OECD Indicators

Italy – Relative performance compared to the OECD average

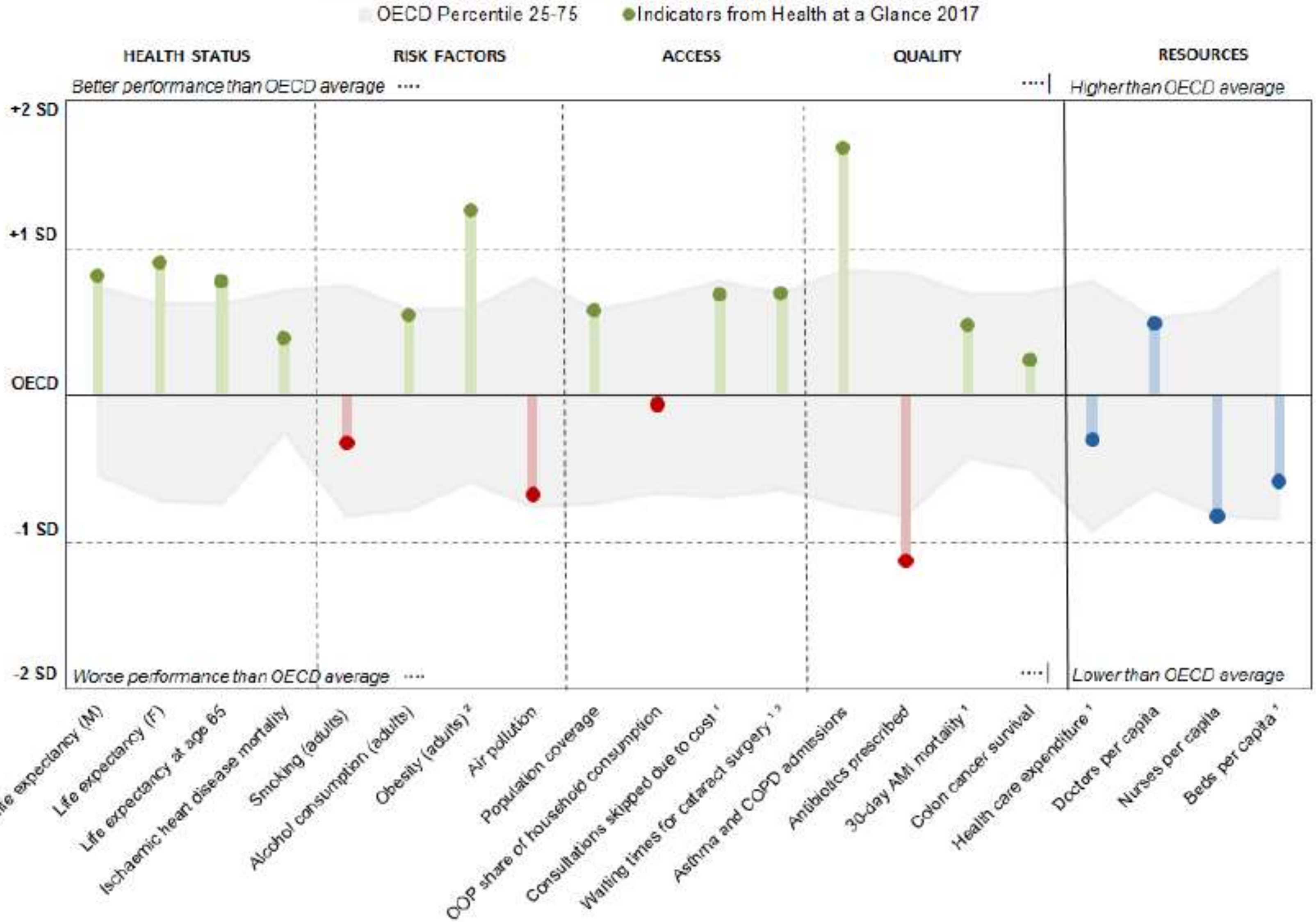
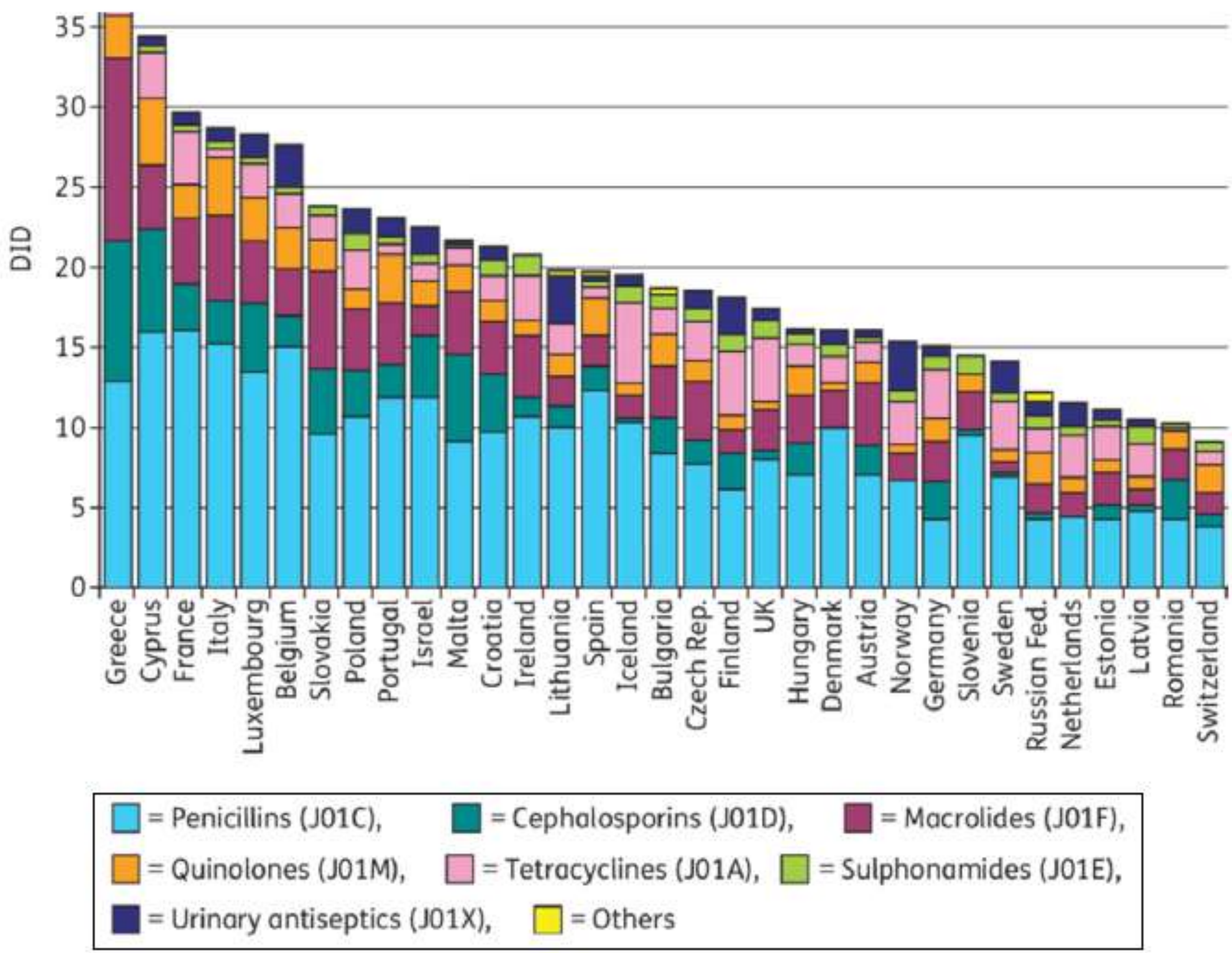
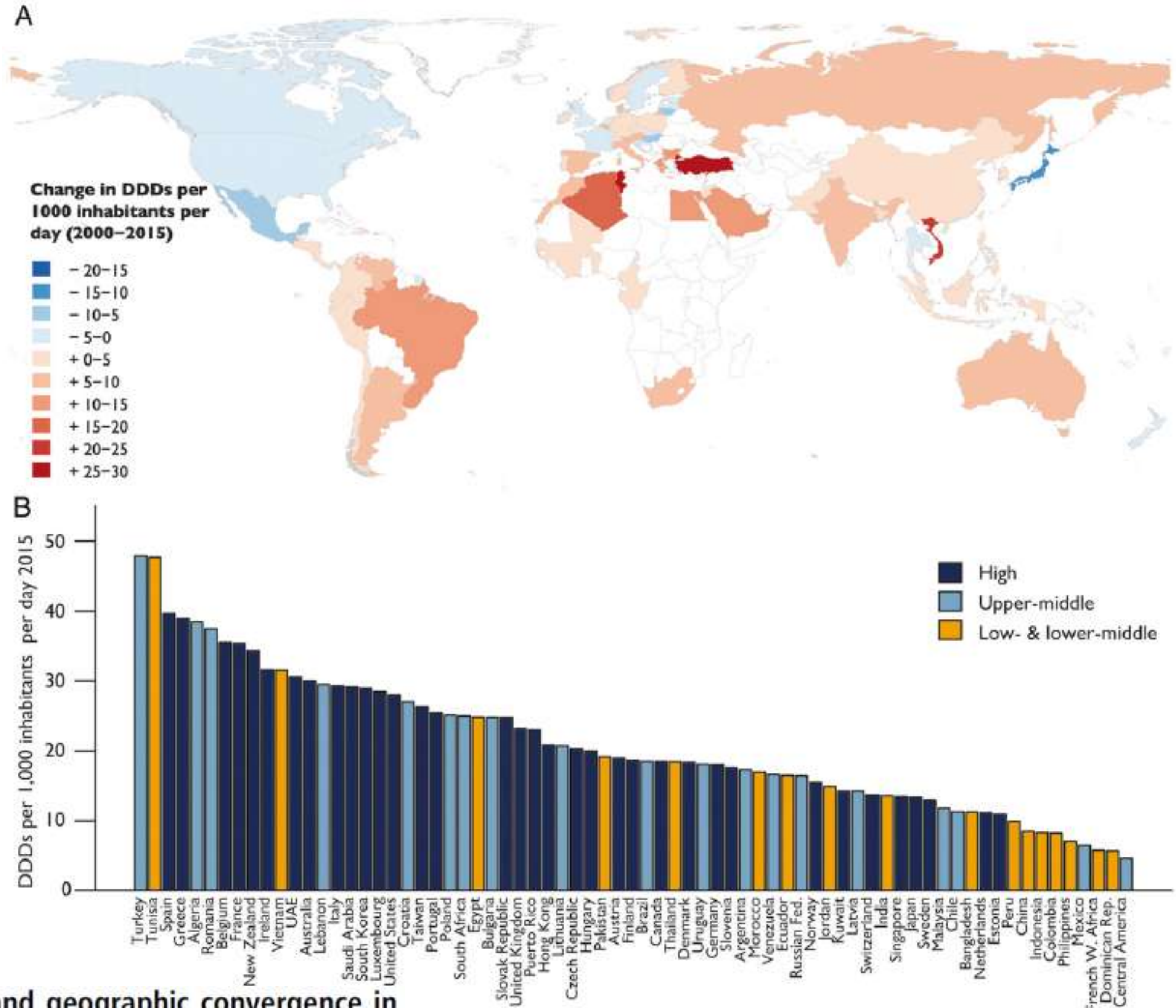


Fig.2.1 Consumption of antimicrobials for systemic use (ATC group J01) at ATC level 3 in the community, EU/EAA countries, 2012, expressed in DDD per 1000 inhabitant per day





Global increase and geographic convergence in antibiotic consumption between 2000 and 2015

www.pnas.org/cgi/doi/10.1073/pnas.1717295115

Consumo di antibiotici (indicatori nazionali)
Indicatore: Riduzione >10% del consumo di antibiotici sistemici in ambito territoriale nel 2020 rispetto al 2016 **Modalità di calcolo**: I consumi vengono calcolati in DDD/1000 abitanti-die. **Formula per calcolare l'indicatore**: [(Consumi 2020/Consumi 2016)-1]*100.
Indicatore: Riduzione >10% del consumo territoriale di fluorochinoloni nel 2020 rispetto al 2016. **Modalità di calcolo**: I consumi vengono calcolati in DDD/1000 abitanti-die. **Formula per calcolare l'indicatore**: [(Consumi 2020/Consumi 2016)-1]*100.

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

World Health Organization

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

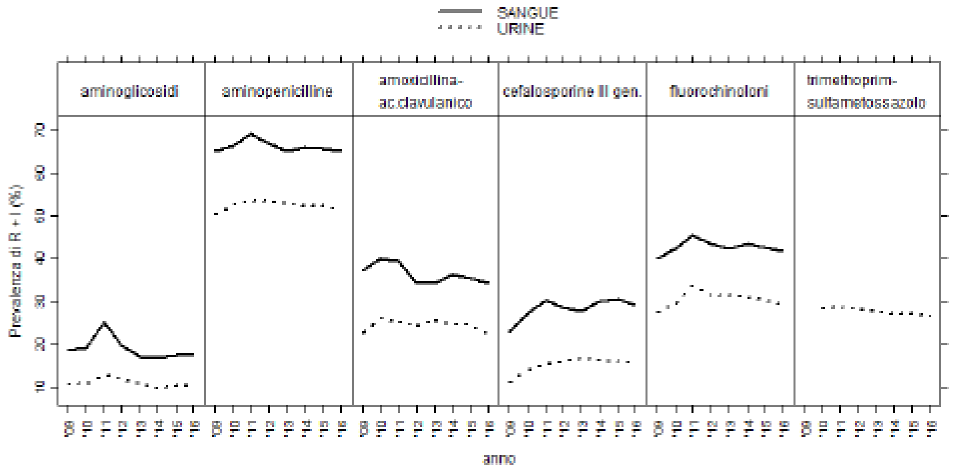
Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

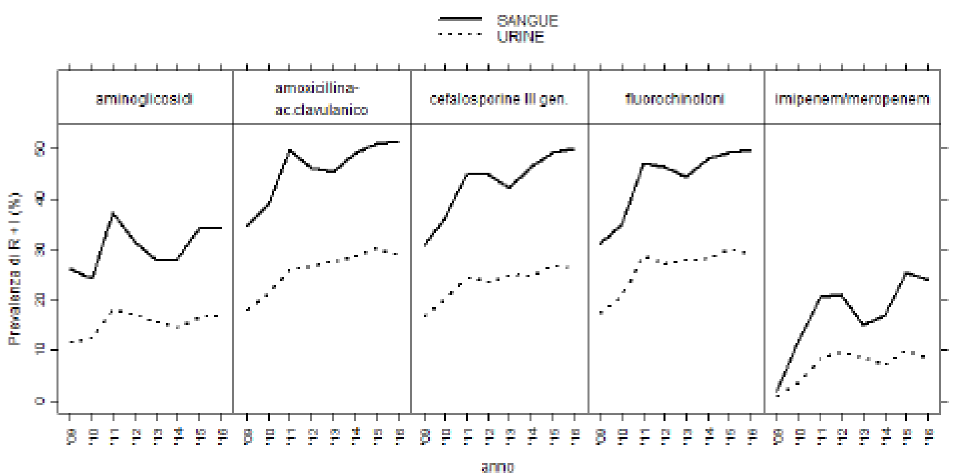
4.1. *Escherichia coli*

Figura 2. Antibioticoresistenza di *Escherichia coli*: emocolture/liquorcolture e urinocolture



4.2. *Klebsiella pneumoniae*

Figura 3. Resistenze di *Klebsiella pneumoniae*: emocolture e urinocolture

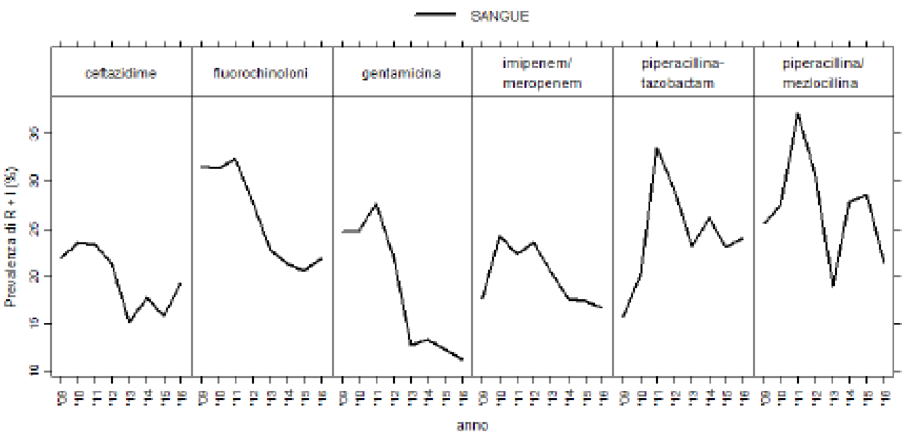


Sorveglianza dell'antibioticoresistenza e uso di antibiotici sistemici in Emilia-Romagna

Rapporto 2016

5.1. *Pseudomonas aeruginosa* e *Acinetobacter baumannii*

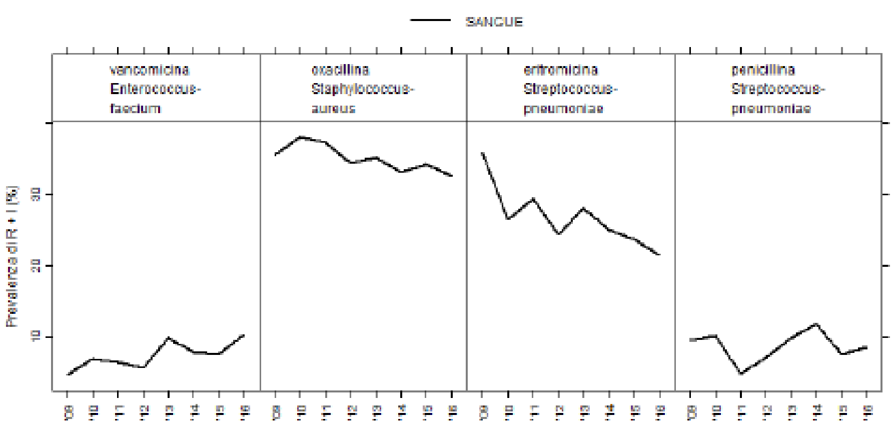
Figura 6. Resistenze di *Pseudomonas aeruginosa*: emocolture*



* La variazione della resistenza di *P. aeruginosa* a fluorochinoloni, gentamicina, piperacillina e piperacillina-tazobactam tra 2010 e 2011 è verosimilmente dovuta all'introduzione delle linee guida EUCAST.

6.1. *Staphylococcus aureus, Streptococcus pneumoniae* ed *Enterococcus faecium*

Figura 7. Resistenze nelle infezioni invasive da *Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus faecium*



RegioneEmilia-Romagna

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

Agenzia sanitaria e sociale regionale

Sorveglianza dell'antibioticoresistenza e uso di antibiotici sistemici in Emilia-Romagna

Rapporto 2016

	2015	2016
MRSA %	20,5	27,7
numero assoluto	122	119,0
VRE %	0,0	14,0
n assoluto	32	43
E. coli ESBL	32,0	33,5
n assoluto	222	182
K pneumoniae ESBL	51,6	45,5
n assoluto	91	88
K oxytoca ESBL	14,3	14,3
n assoluto	13,0	14,0
TOT ESBL %	36,8	36,3
n assoluto	326,0	284,0
E. coli CR	0,0	1,1
K pneumoniae CR	34,1	25,0
K oxytoca CR	7,1	0,0
TOT CRE %	9,8	8,5

Saggi di sensibilità:

M.I.C. e breakpoint

Il cardine di tutti i saggi è la

M.I.C.

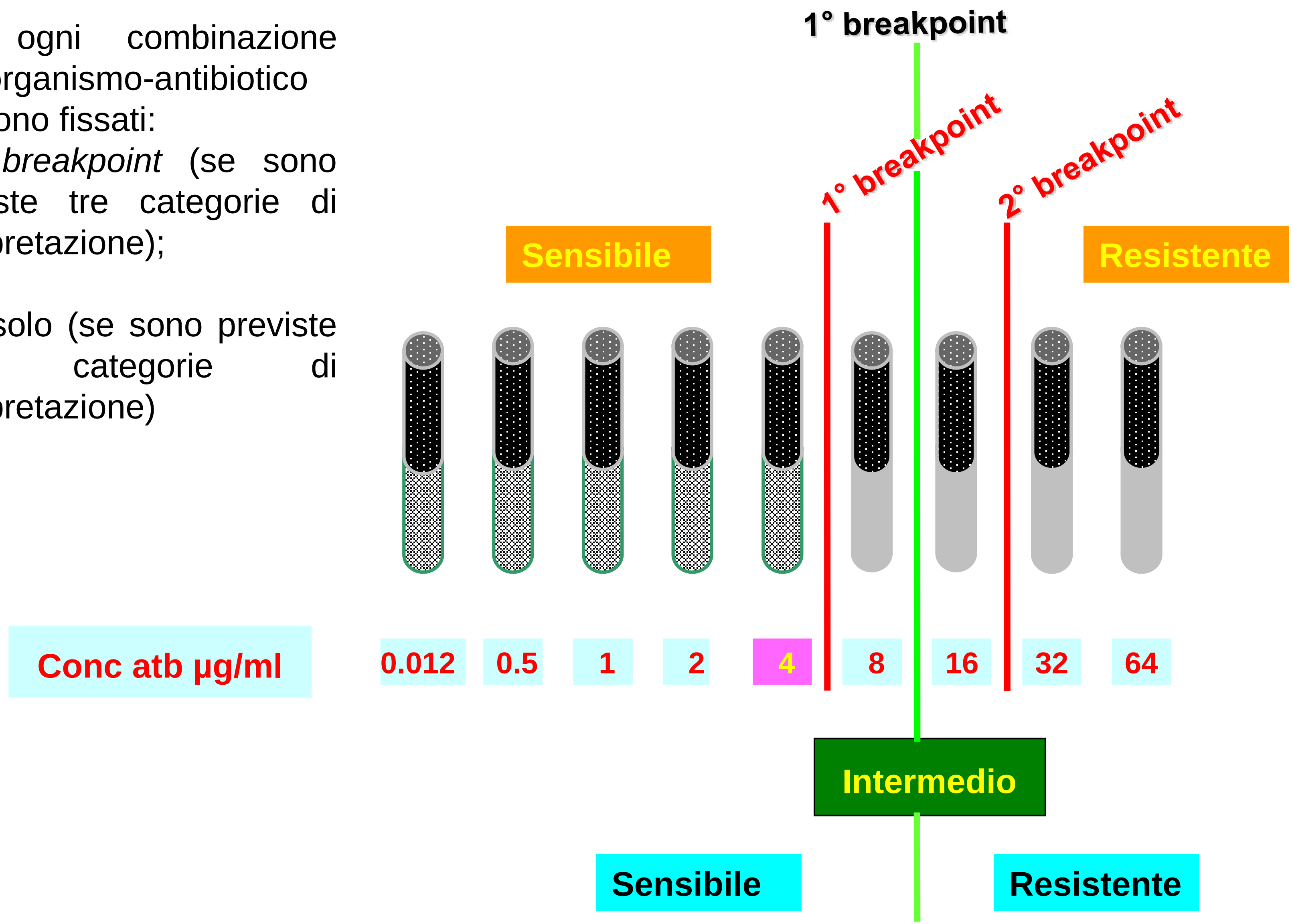
La M.I.C. è alla base della determinazione dei breakpoint

breakpoint servono per interpretare i saggi di sensibilità

Breakpoint e categorie di interpretazione

Per ogni combinazione microrganismo-antibiotico vengono fissati:
due *breakpoint* (se sono previste tre categorie di interpretazione);

uno solo (se sono previste due categorie di interpretazione)



Impossibile visualizzare l'immagine.

Per interpretarla in modo corretto va considerato che:

- Valori preceduti dal segno $\leq$ indicano che la crescita del microrganismo è stata inibita dalla più bassa concentrazione dell'antibiotico usata nel saggio (Sensibilità indipendentemente dal valore numerico):

Es A:

MIC antibiotico X $\leq$ 8

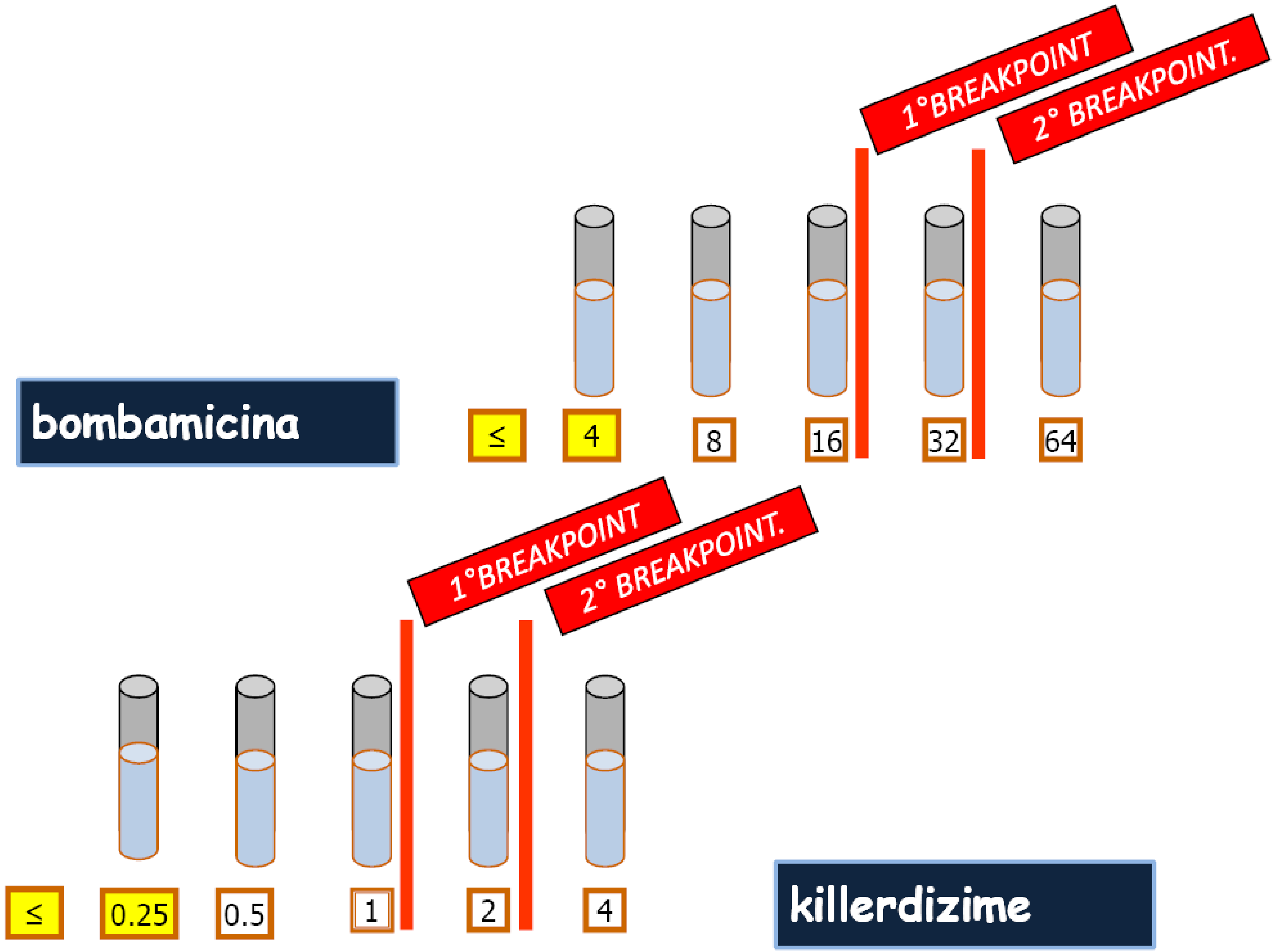
MIC antibiotico Y $\leq$ 0.5

Il microrganismo è sensibile tanto ad X quanto ad Y

Es. colturale URINA DA CATETERE

E. coli 10^6 ufc/ml

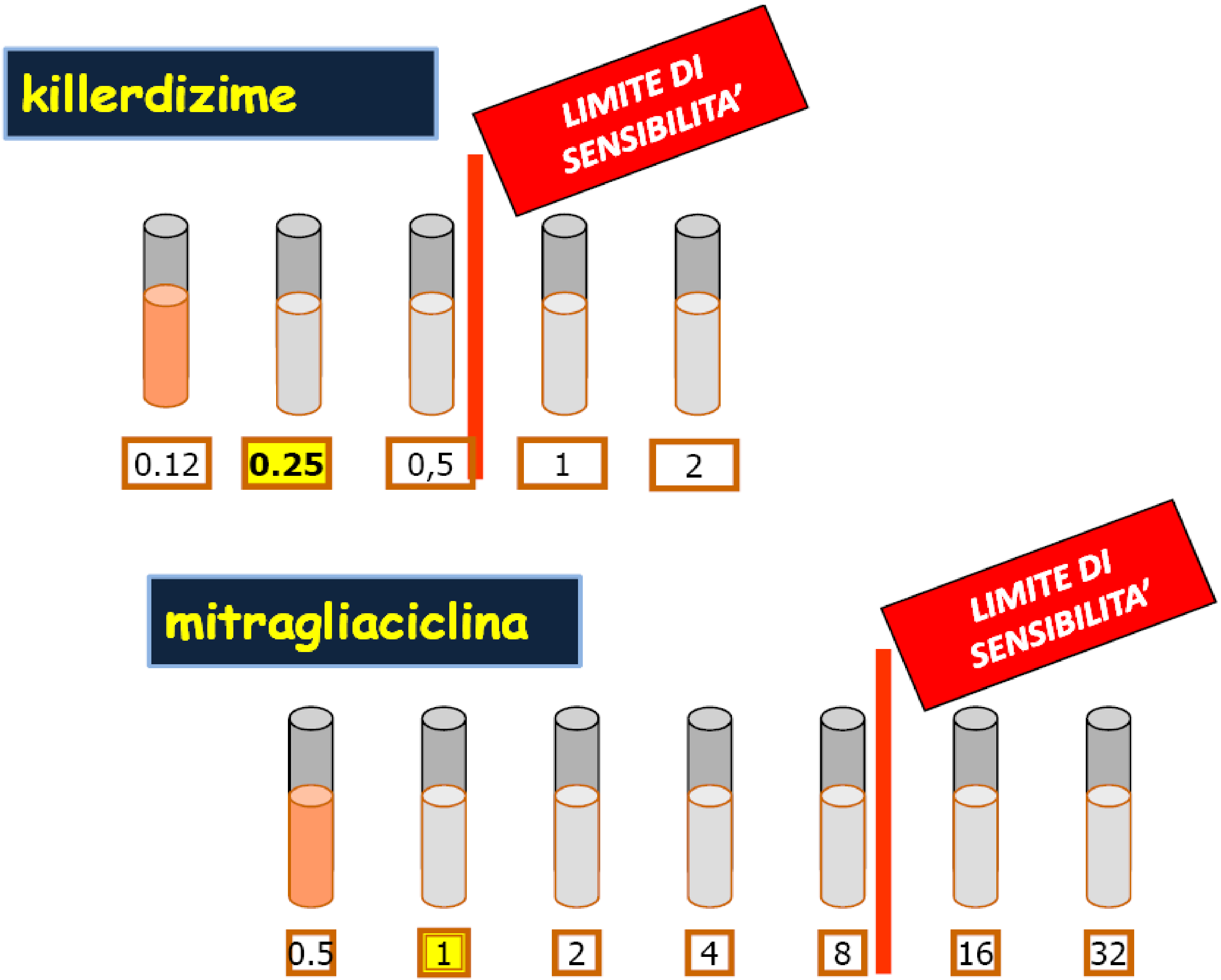
		MIC
bombamicina	S	≤ 4
supercillina	S	≤ 1
killerdizime	S	≤ 0,25
stupendaciclina	S	≤ 2
mitragliaciclina	S	≤ 1
terripenem	S	≤ 1


1°BREAKPOINT
2° BREAKPOINT.
bombamicina
≤
4
8
16
32
64
1°BREAKPOINT
2° BREAKPOINT.
≤
0.25
0.5
1
2
4
killerdizime

Es. colturale URINA DA CATETERE

E. coli 10^6 ufc/ml

		MIC	Limite di sensibilità
bombamicina	S	4	32
supercillina	S	1	4
killerdizime	**S**	**0,25**	**0,5**
stupendaciclina	S	2	8
mitragliaciclina	**S**	**1**	**8**
terripenem	S	1	2


killerdizime
LIMITE DI SENSIBILITA'
0.12
0.25
0,5
1
2
mitragliaciclina
LIMITE DI SENSIBILITA'
0.5
1
2
4
8
16
32