

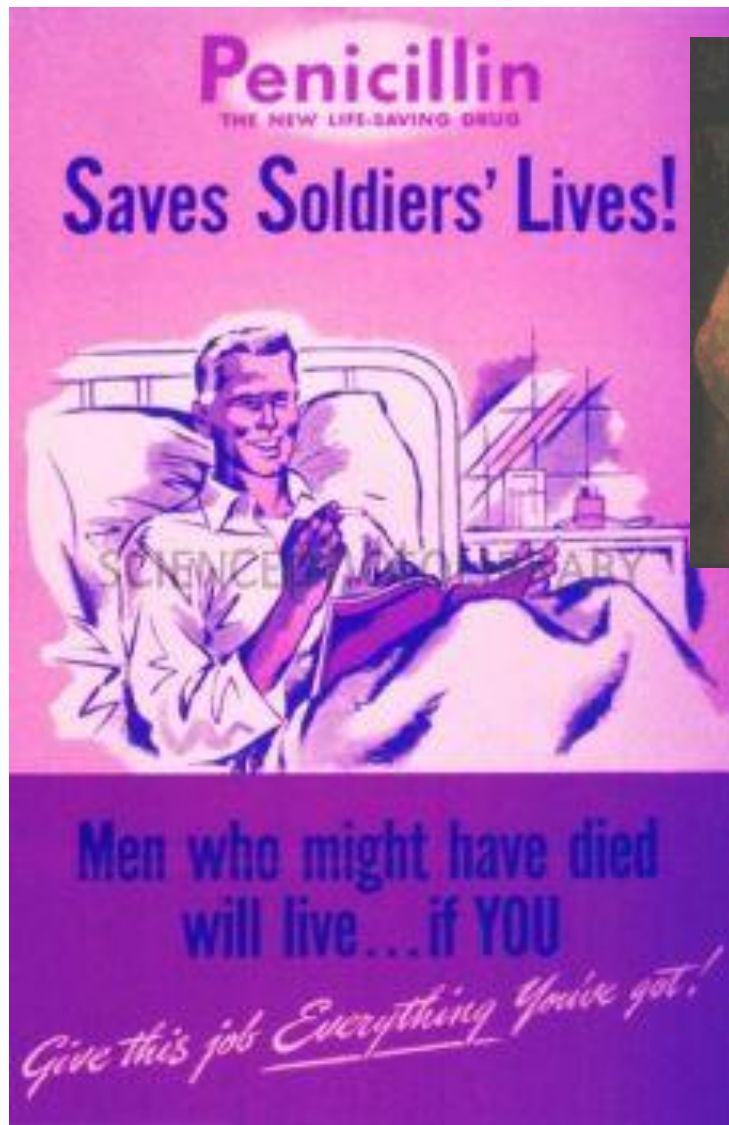
# **Pomen protimikrobnih zdravil in skrbi za njihovo ustrezno predpisovanje**

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# Pomen antibiotičnega zdravljenja

- **Smrtnost pljučnice po gripi zmanjšana s 30 na 10%** (predvidena resnost gripe leta 1918 flu v današnjih razmerah, Chen YW, et al. PlosOne 2012; 7: e29219.)
- **Zmanjšanje smrtnosti bakterijskega meningitisa z 80% na 20%** (1935 - 1957, Wilson FM, Lerner AM, NEJM 1964; 271: 1235-8.)
- **Zmanjšanje pogostnosti okužb kirurške rane pri kolorektalni kirurgiji z 20 na 10%**

Talbot TR, Kaiser AB. Postoperative infections and antimicrobial prophylaxis. V: Mandell GL, Bennett JE, Dolin R. Mandel, Douglas, and Bennett's principles and practice of infectious diseases. Philadelphia: Elsevier Churchill Livingstone; 2005. p 3533-47.



- 
- Veliki kirurški posegi
  - Transplantacije organov
  - Obravnava na oddelkih za intenzivno zdravljenje
  - Nevtropenični bolniki
  - Drugi imunsko oslabeledi bolniki
  - Okužbe pri kroničnih bolnikih
  - Okužbe pri starostnikih

**SMRTNO  
NEVARNO**

# Razvoj odpornosti proti antibiotikom

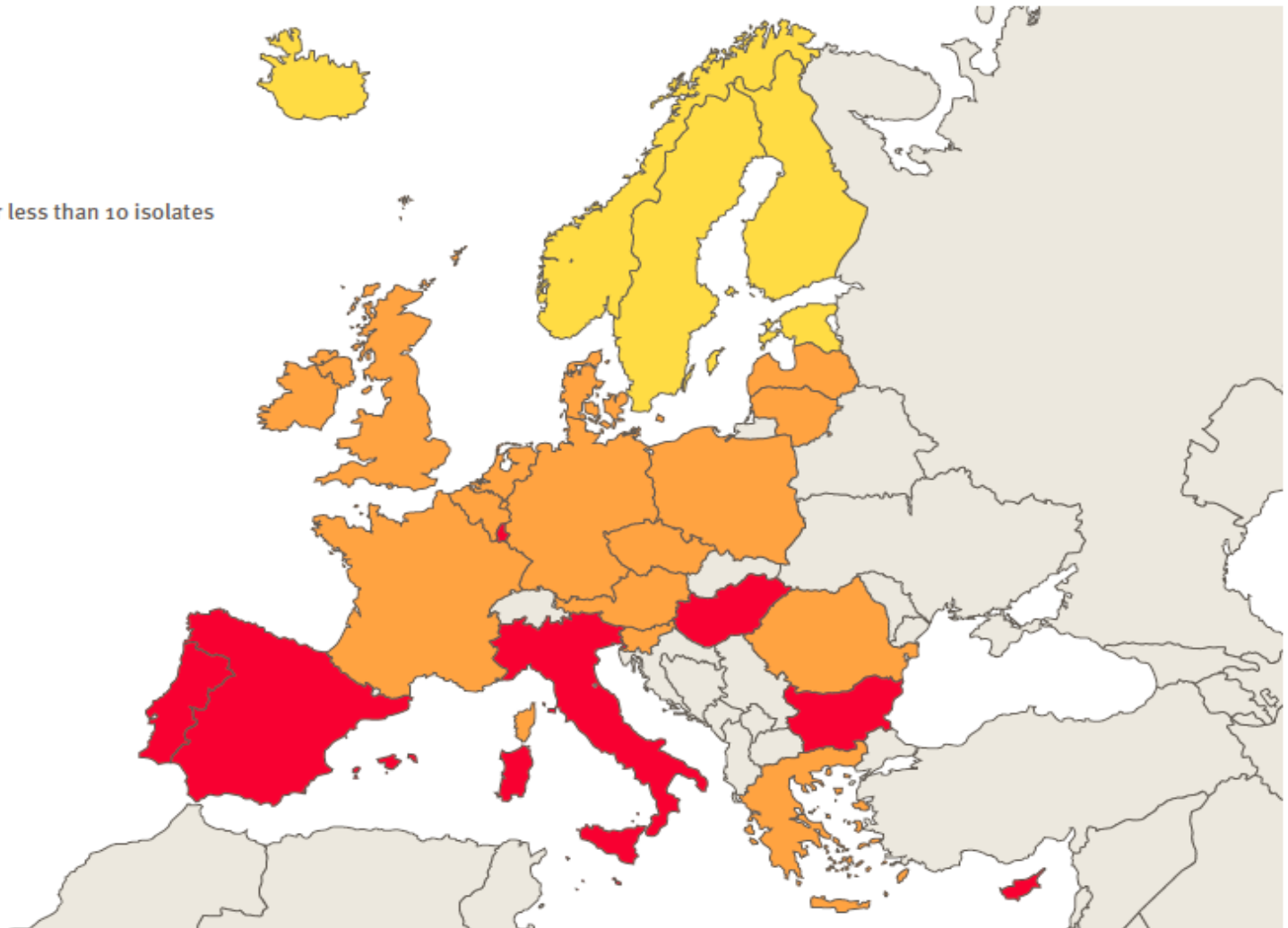
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<u>First Report Of Resistance</u>	<u>Agent</u>	<u>Date of FDA Approval</u>
1940	Penicillin	1943
1947	Streptomycin	1947
1956	Tetracycline	1952
1970	Gentamicin	1967
1983 (1981)	Cefotaxime	1981
1999	Linezolid	2000

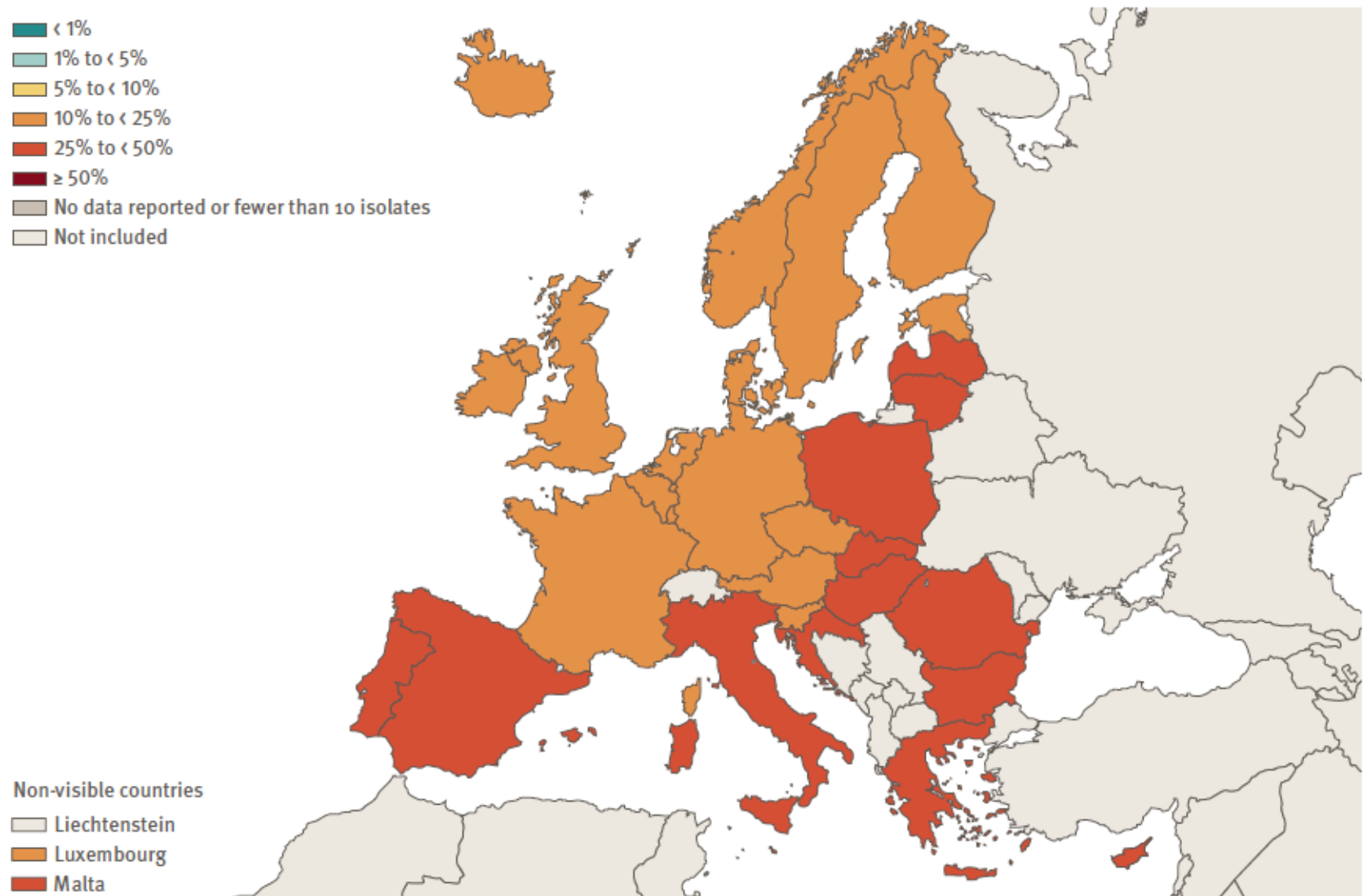
**Figure 5.15:** *Escherichia coli*: proportion of invasive isolates with resistance to fluoroquinolones in 2009

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

- Non-visible countries
- Luxembourg
  - Malta



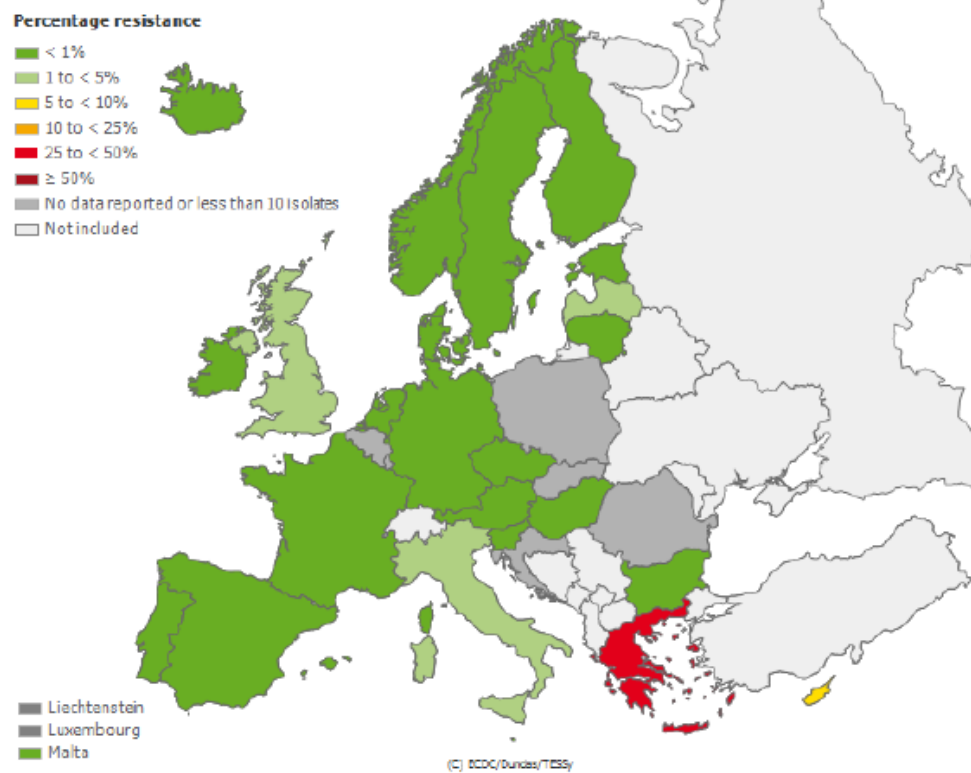
**Figure 3.2. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2017**





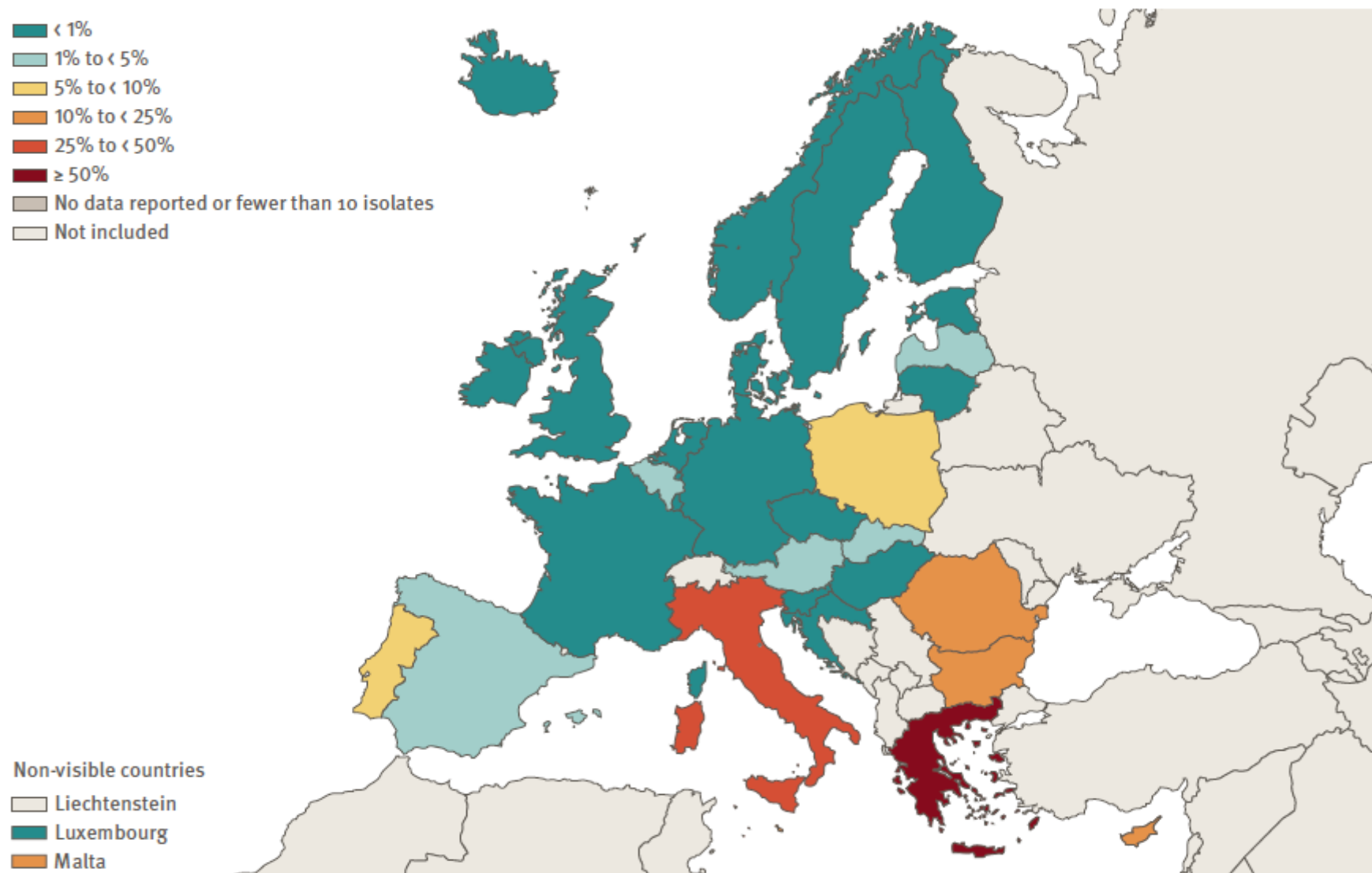


## Proportion of Carbapenems Resistant (R) *Klebsiella pneumoniae* Isolates in Participating Countries in 2008

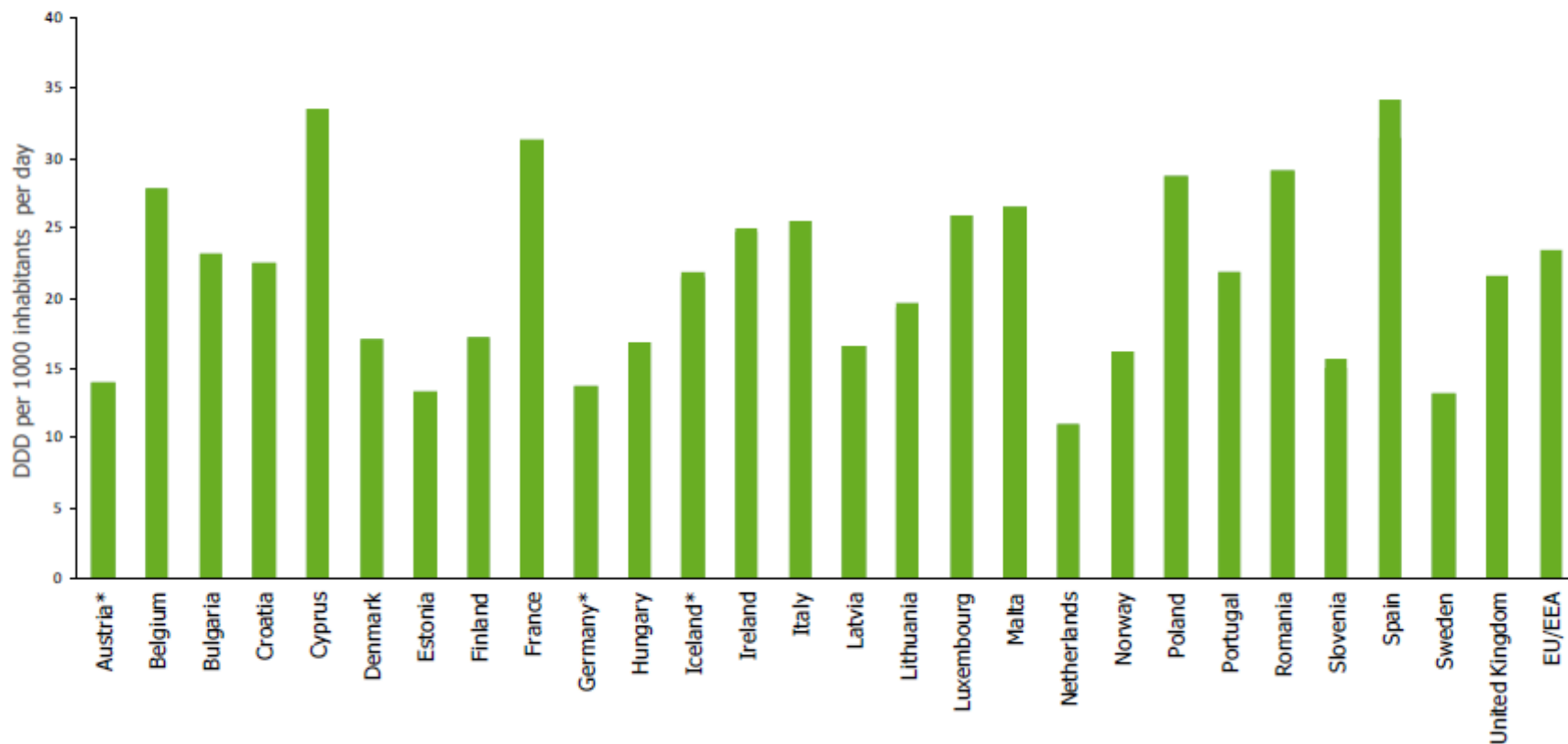


This report has been generated from data submitted to TESSy, The European Surveillance System on 2015-04-17. Page: 1 of 1. The report reflects the state of submissions in TESSy as of 2015-04-17 at 16:00

**Figure 3.11.** *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2017



**Figure 1. Total consumption of antibacterials for systemic use (ATC group J01), EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**



European Centre for Disease Control and Prevention. Antimicrobial Consumption. In: ECDC. Annual Epidemiological report for 2017. Stockholm: ECDC; 2018.

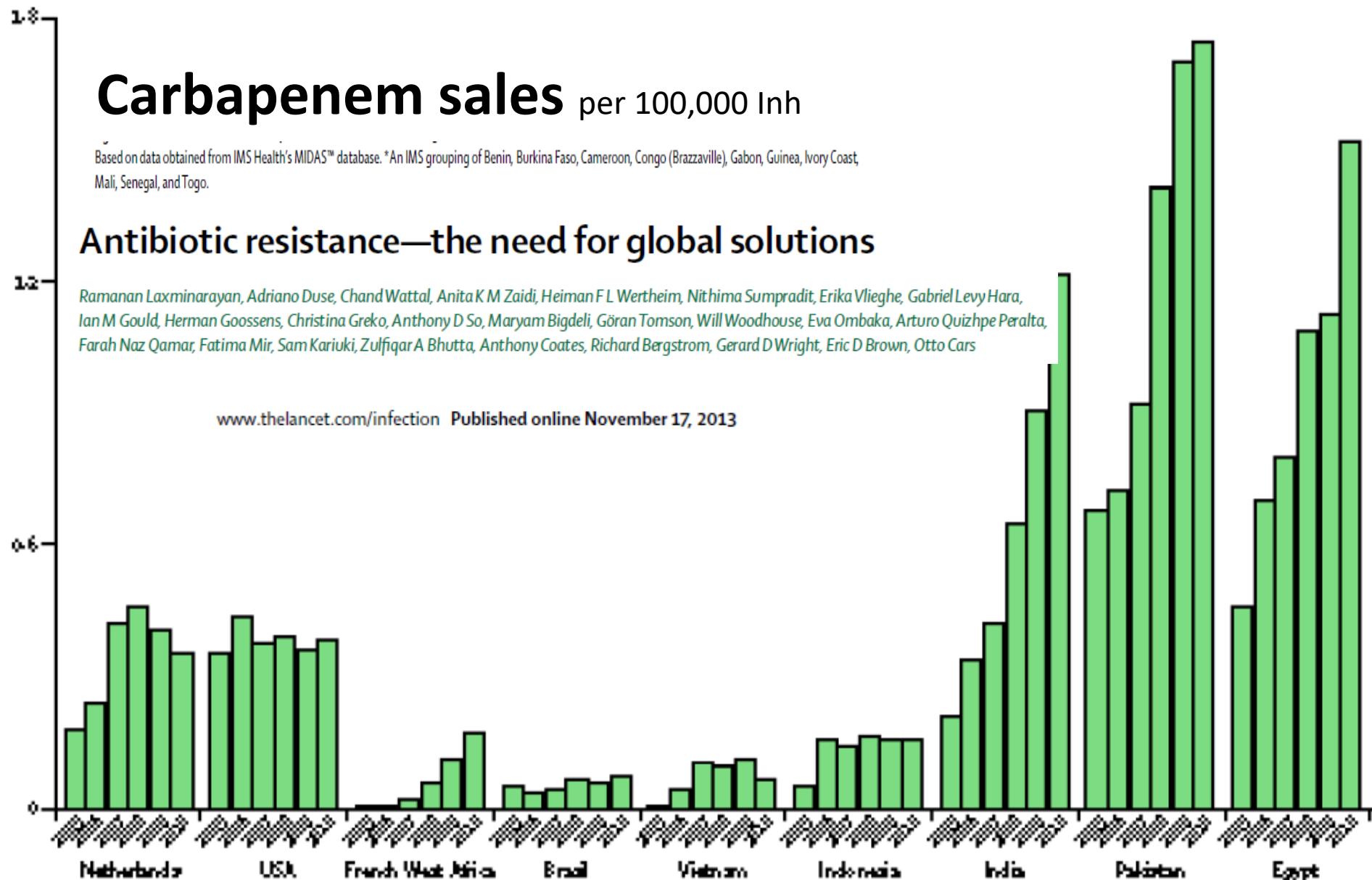
# Carbapenem sales per 100,000 Inh

Based on data obtained from IMS Health's MIDAS™ database. \*An IMS grouping of Benin, Burkina Faso, Cameroon, Congo (Brazzaville), Gabon, Guinea, Ivory Coast, Mali, Senegal, and Togo.

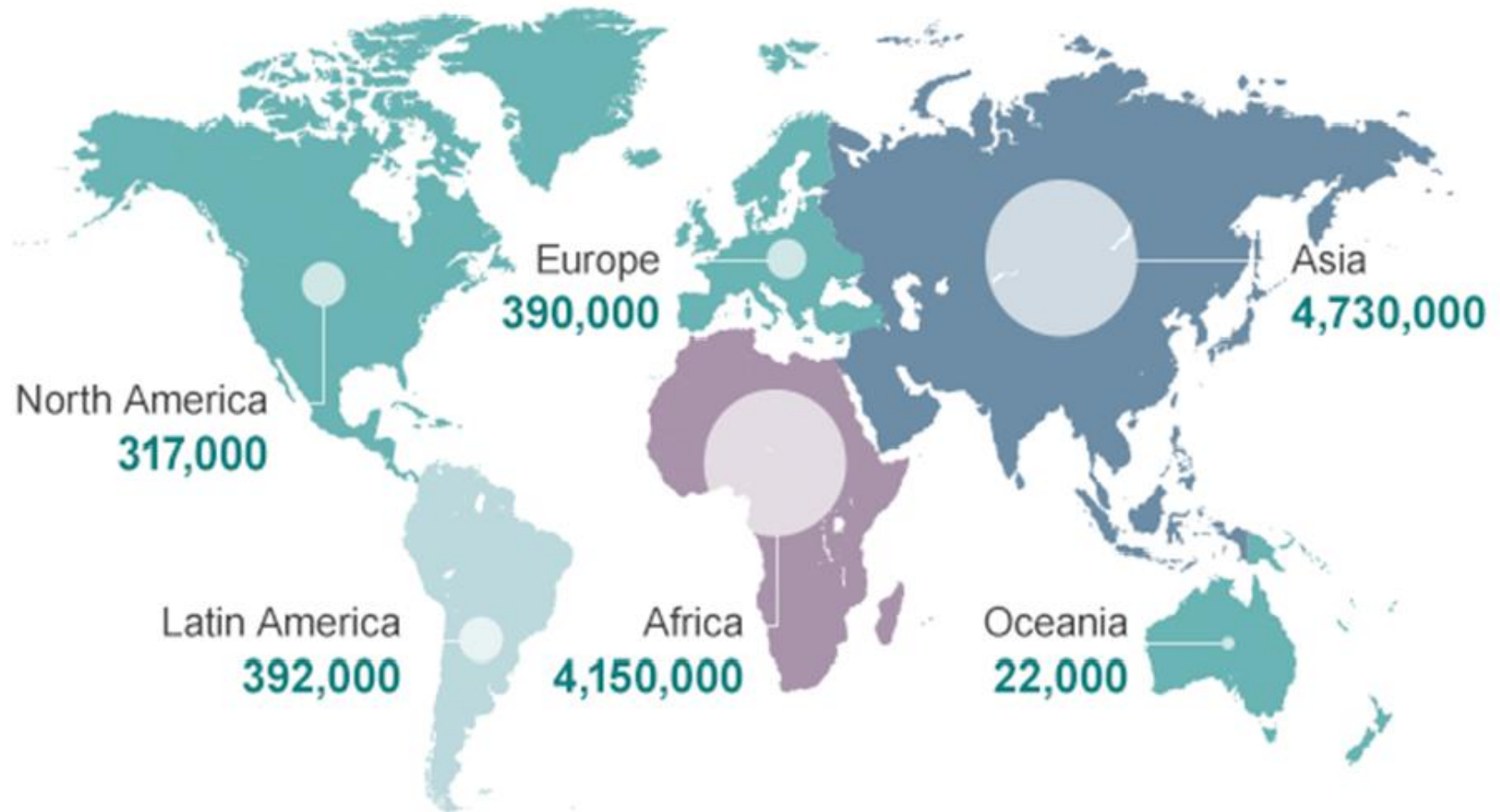
## Antibiotic resistance—the need for global solutions

Ramanan Laxminarayan, Adriano Duse, Chand Wattal, Anita KM Zaidi, Heiman FL Wertheim, Nithima Sumpradit, Erika Vlieghe, Gabriel Levy Hara, Ian M Gould, Herman Goossens, Christina Greko, Anthony D So, Maryam Bigdeli, Göran Tomson, Will Woodhouse, Eva Ombaka, Arturo Quizhpe Peralta, Farah Naz Qamar, Fatima Mir, Sam Kariuki, Zulfiqar A Bhutta, Anthony Coates, Richard Bergstrom, Gerard D Wright, Eric D Brown, Otto Cars

[www.thelancet.com/infection](http://www.thelancet.com/infection) Published online November 17, 2013



# Letno število smrti zaradi protimikrobne odpornosti leta 2050





# Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis

Alessandro Cassini, Liselotte Diaz Högberg, Diamantis Plachouras, Annalisa Quattrocchi, Ana Hoxha, Gunnar Skov Simonsen, Mélanie Colomb-Cotinat, Mirjam E Kretzschmar, Brecht Devleeschauwer, Michele Cecchini, Driss Ait Ouakrim, Tiago Cravo Oliveira, Marc J Struelens, Carl Suetens, Dominique L Monnet, and the Burden of AMR Collaborative Group\*

Lancet Infect Dis 2018

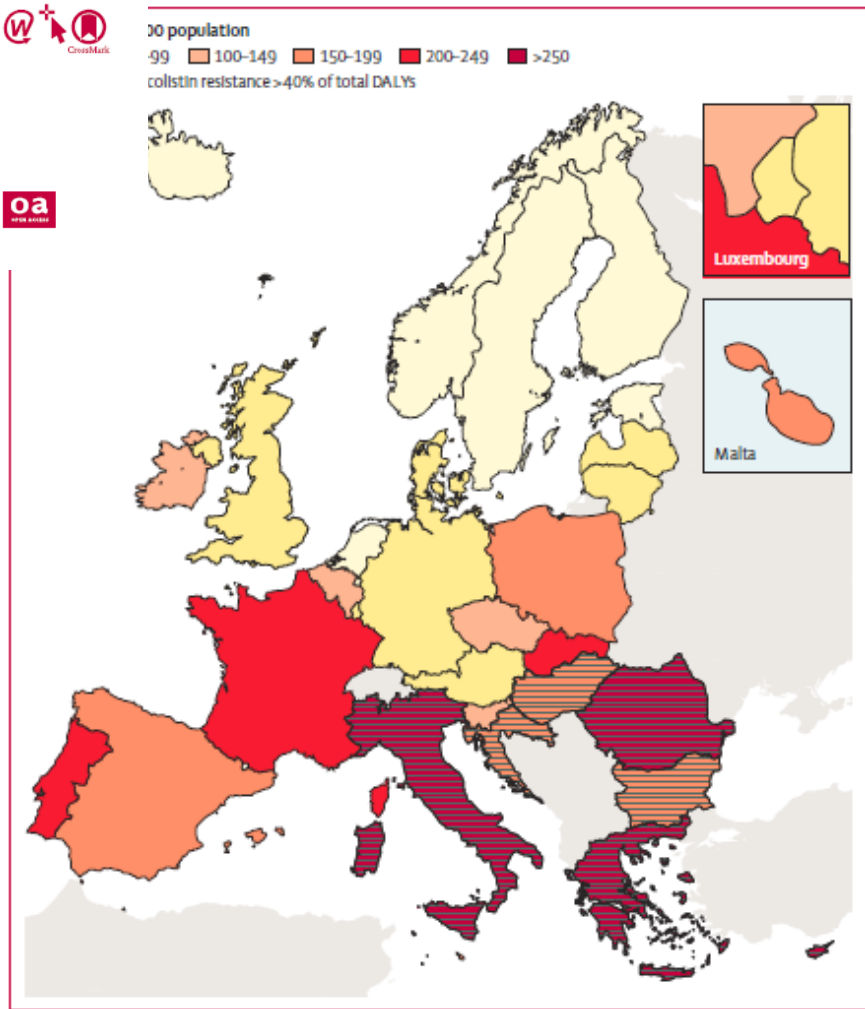


Figure 4: Model estimates of the burden of infections with selected antibiotic-resistant bacteria of public health importance in DALYs per 100 000 population, EU and European Economic Area, 2015

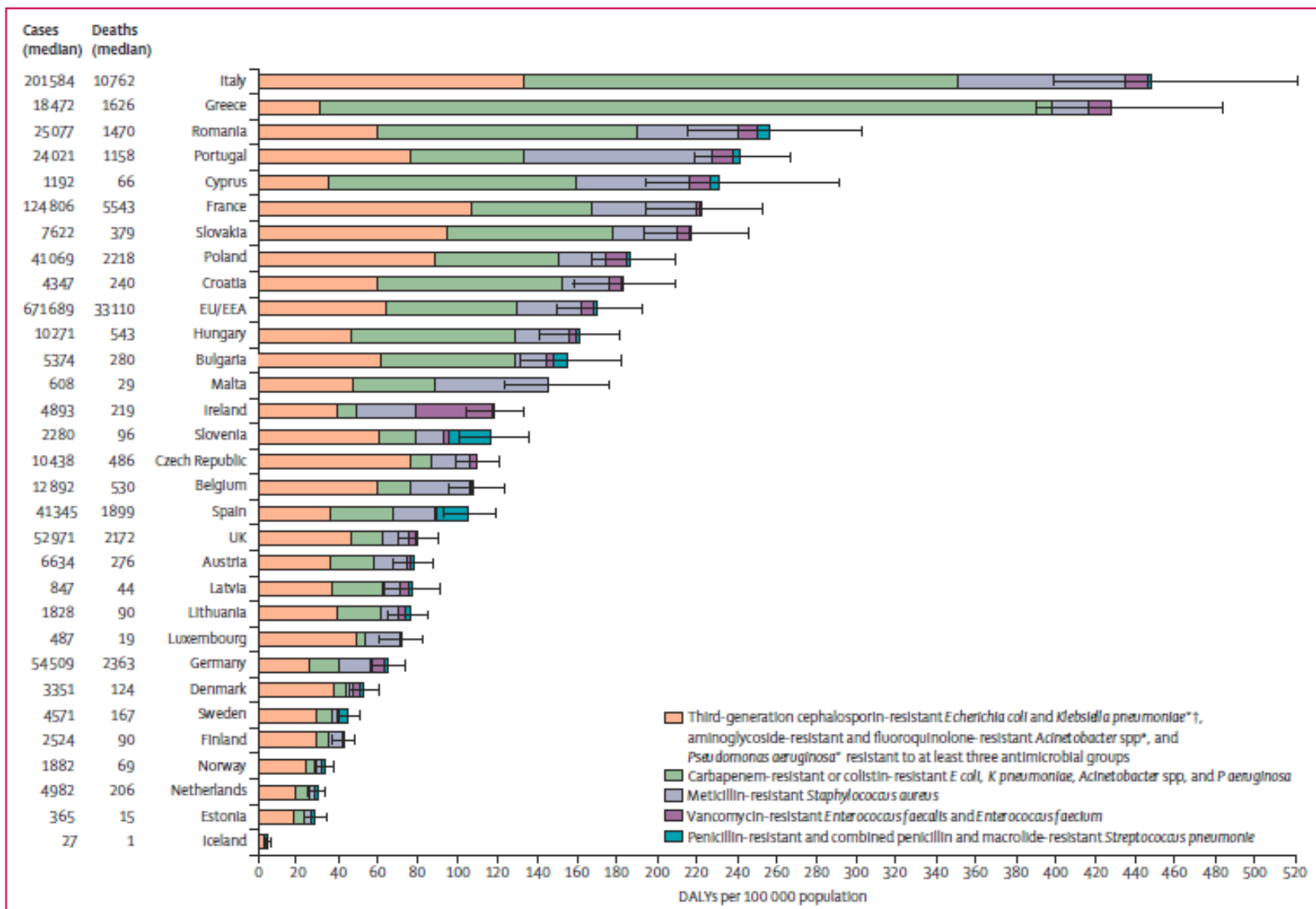
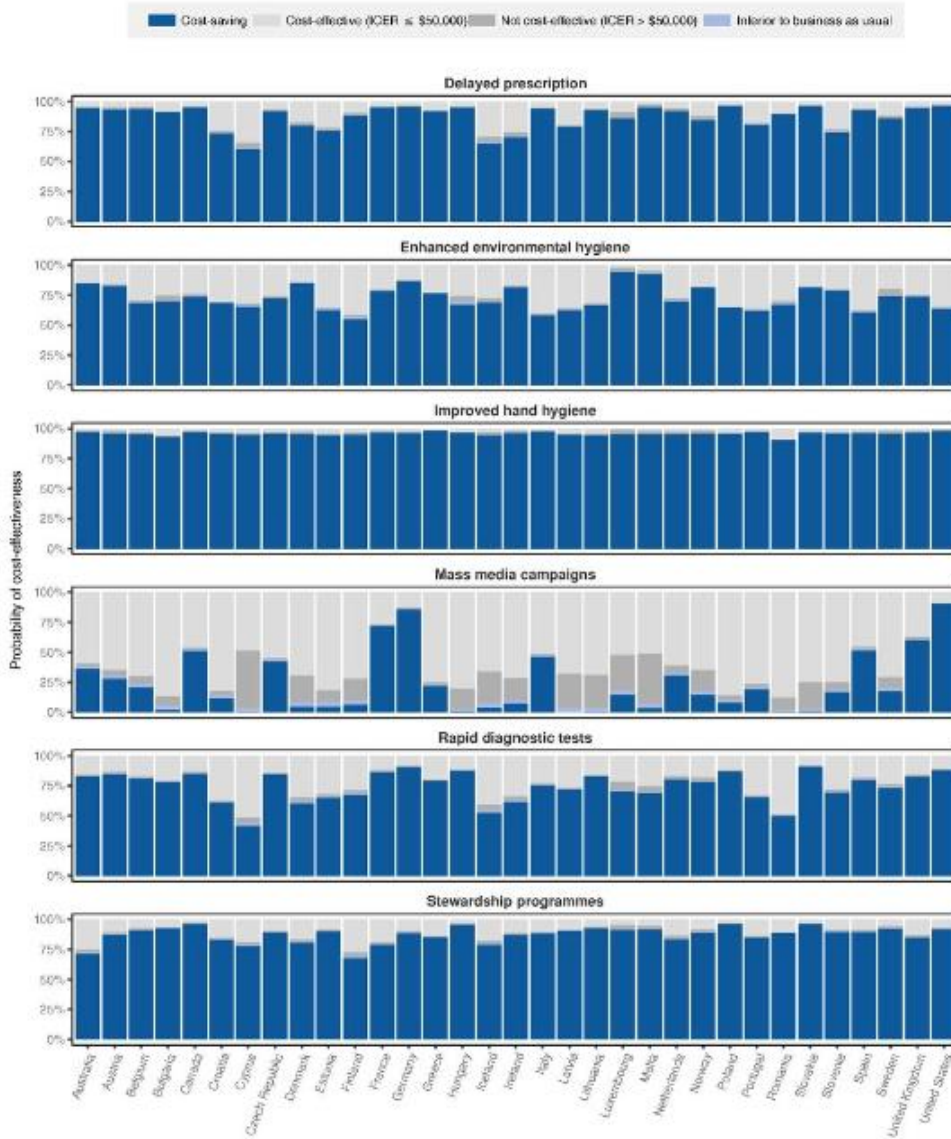


Figure 3: Burden of infections with antibiotic-resistant bacteria in DALYs, EU and European Economic Area, 2015



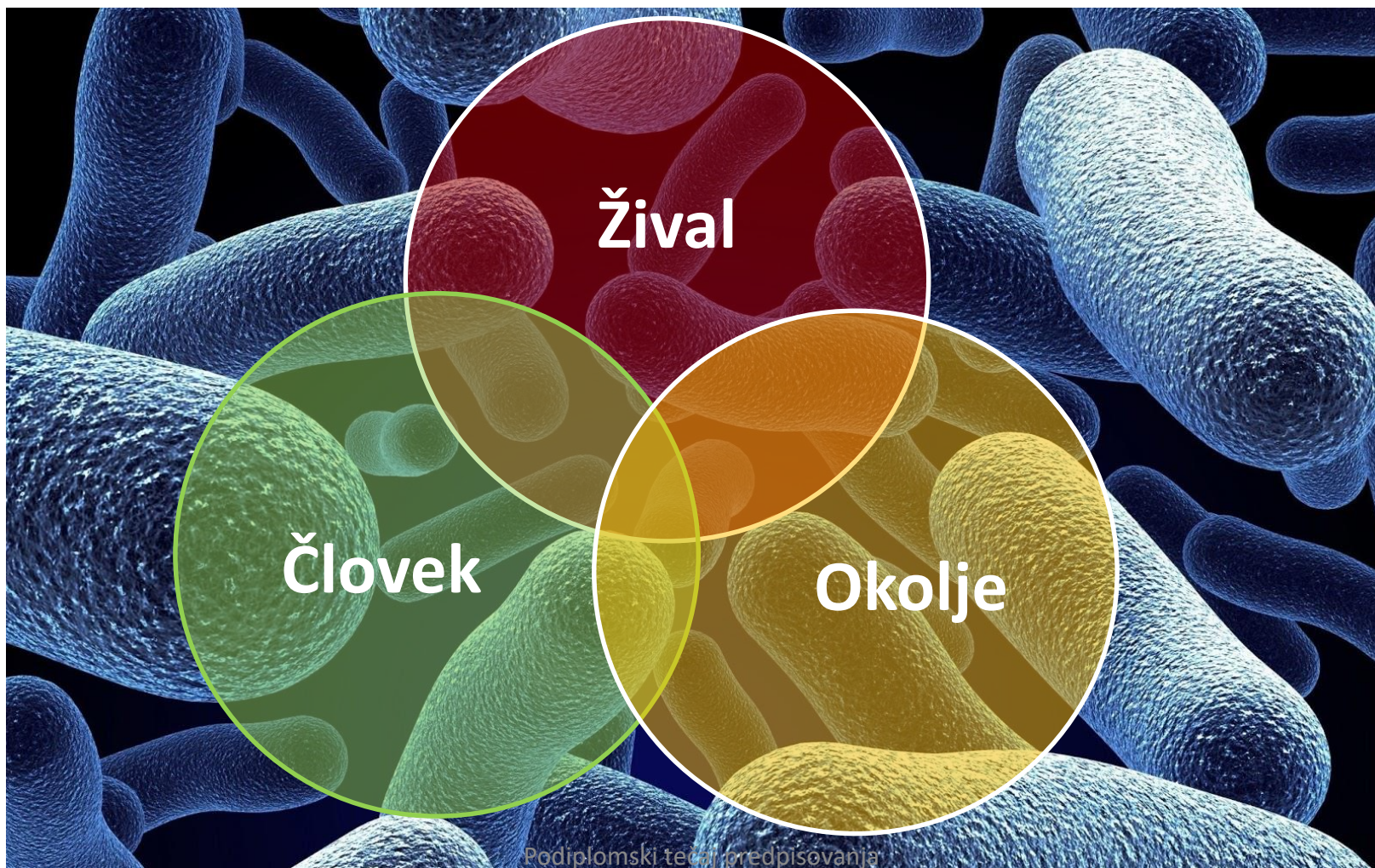
**NRA zmanjšuje stroške zdravljenja skoraj tako učinkovito kot higiena rok!**

# Bakterije so naše najbližje okolje





# Načelo „Enega zdravja“ (One Health)



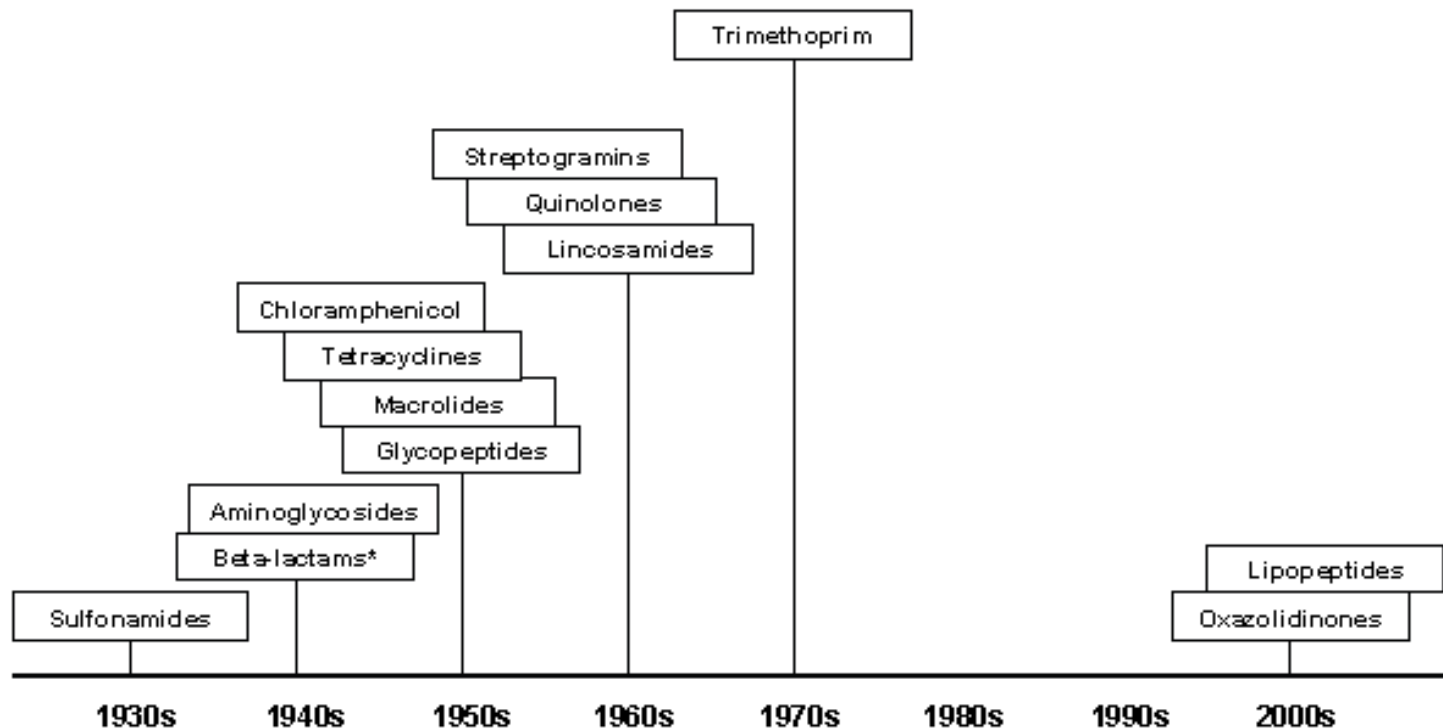


# Protimikrobna odpornost je ena od ekoloških katastrof, ki jih je povzročil človek!



Antibiotic resistance: another man-made environmental catastrophe that our politicians refuse to talk about. Available at: <http://www.conservativehome.com/the-deep-end/2015/05/antibiotic-resistance-another-man-made-environmental-catastrophe-that-our-politicians-refuse-talk-about.html>. [Accessed September 2016]., <http://www.telesurtv.net/english/multimedia/Biggest-Ecological-Disaster-in-Brazils-History-20151124-0012.html>, <http://www.telesurtv.net/english/multimedia/Biggest-Ecological-Disaster-in-Brazils-History-20151124-0012.html>, [http://www.stormchaser.ca/Environmental\\_Disasters/Aral%20Sea/Aral\\_Sea.html](http://www.stormchaser.ca/Environmental_Disasters/Aral%20Sea/Aral_Sea.html), <http://www.thehindu.com/todays-paper/tp-national/bhopal-toxic-waste-to-be-sent-to-germany/article3507271.ece>

# New Classes of Antibiotics on the Market



EMA & ECDC. The Bacterial Challenge: Time to React. [www.ecdc.europa.eu](http://www.ecdc.europa.eu)

Podiplomski tečaj predpisovanja  
protimikrobnih zdravil za bolnišnične  
zdravnike 2019



# Kakšen je razvoj novih antibiotikov?

Antibiotiki, ki delujejo proti po Gramu negativnim odpornim bakterijam v zadnjih fazah razvoja ali so bili odobreni nedavno:

16 novih molekul

2 z novim mehanizmom delovanja:  
murepavadin  
cefiderokol

- Talbot GH, et al. Clin Infect Dis. 2019 Feb 1. doi: 10.1093/cid/ciz089.

# Kaj še lahko storimo?

- **cepiva, monoklonska ali poliklonska protitelesa**
- **bakteriofagi**
- **hemoperfuzijska sredstva**
- **zaviralci „quorum sensing“**
- **zaviralci citotoksinov**
- **neimunska toleranca za bolezni**
- **vpliv na mikrobiom (probiotiki)**
- **.....**





## Več energije ali njena smotrna raba?



# Kaj lahko storimo?

**Primer: 53 letna pacientka s plazmocitomom, ugotovljenim pred 2,5 leti**  
**Področje velike protimikrobne odpornosti JV Evropa, Azija**

- Uspešna avtologna PKMC pred 8 meseci
- Pljučnica, pnevmokoki v sputumu, pnevmokokni antigen poz v urinu, zdravnik se vseeno odloči za TMP-SMX, meropenem, moksifloksacin, ganciklovir, liposomalni amphotericin.
- **Dan 3:** boljša, na oralnem moksifloksacin plus TMP-SMX.
- **Dan 10,** bolnica afebrilna, a postane tahipnoična
- Kontrolni HRCT, eden narejen že ob sprejemu, pokaže isto sliko in še dodatno konsolidacijo v desnem srednjem režnju
- Radiolog je mnenja, da gre za pričakovano evolucijo pnevmokokne pljučnice

Primer: 53 letna pacientka s plazmocitomom, ugotovljenim pred 2,5 leti  
**Področje velike protimikrobne odpornosti JV Evropa, Azija**

## Kateri antibiotik boste izbrali?

**1. Nadaljujete moksifloksacin**

Slovenija: *Pseudomonas aeruginosa*: 17,4% R proti karbapenemom, R proti pip/tazo 13,0%

**2. HAP: piperacilin-tazobaktam**

*K. pneumoniae*: 23,7% ESBL, 0,0 CRE

**3. HAP: meropenem**

Grčija: *P. aeruginosa* 49,3% R proti karbapenemom, R proti pip/tazo 29,6%

**4. HAP: meropenem + kolistin**

*K. pneumoniae* ESBL 69,2%, CRE 64,7% (EARS-NET)

**5. HAP: meropenem + kolistin + vankomicin**

European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2018.

Primer: 53 letna pacientka s plazmocitomom, ugotovljenim pred 2,5 leti  
**Področje velike protimikrobne odpornosti JV Evropa, Azija**

- **Dan 13:** ponovno vročina (39C) bolnica postane hipoksična, še vedno na moksifloksacinu.
- Odvzete hemokulture, BAL, zamenjan CVK

*S prijaznostjo prof Hakana Hanbergerja, Univerza Linkoping, Švedska*

**Dan 13:** Pip-tazo dodan.

**Dan 14 in 15;** BAL in hemokulture: *P. aeruginosa*, občutljiv samo za kolistin, dodan kolistin

MIC( $\mu\text{g/ml}$ )	IMIP	P/T	CAZ	AMK	CIP	COL
<i>Ps.aeruginosa</i> MBL pharyngeal culture one day before intubation	>8	>64/4	>16	>32	>2	0.75
<i>Ps. aeruginosa</i> MBL(+) in BAL	>8	>64/4	>16	>32	>2	0.75
<i>Ps. aeruginosa</i> MBL(+) in blood	>8	>64/4	>16	>32	>2	0.75

**Dan 16:** bolnica umre v septičnem šoku



**Primer: 53 letna pacientka s plazmocitomom, ugotovljenim pred 2,5 leti**  
**Področje majhne protimikrobne odpornosti: Skandinavija**

- Uspešna avtologna PKMC pred 8 meseci
- Pljučnica, pnevmokoki v sputumu, pnevmokokni antigen poz v urinu
- Stabilna, saturacija 95%, RR 120/80, FP 84/min, T 38,6, FD 22/min

*S prijaznostjo prof Hakana Hanbergerja, Univerza Linkoping, Švedska*

**Primer: 53 letna pacientka s plazmocitomom, ugotovljenim pred 2,5 leti**  
**Področje majhne protimikrobne odpornosti: Skandinavija**

- **Dan 3**; izboljšanje, preklop pa amoksicilin p.o.
- **Dan 10**, bolnica afebrilna, a postane tahipnoična
- Kontrolni HRCT, eden narejen že ob sprejemu, pokaže isto sliko in še dodatno konsolidacijo v desnem srednjem režnju
- Radiolog je mnenja, da gre za pričakovano evolucijo pnevmokokne pljučnice

Primer: 53 letna pacientka s plazmocitomom, ugotovljenim pred 2,5 leti  
**Področje majhne protimikrobne odpornosti: Skandinavija**

## Kateri antibiotik izberejo?

1. HAP: Piperacilin-tazobaktam
2. HAP: meropenem
3. HAP: meropenem + kolistin
4. HAP: meropenem + kolistin + vancomycin
5. HAP: Pip-tazo + kolistin
6. HAP: Pip-tazo + kolistin + vankomicin

Švedska: *P.aeruginosa*, odporen proti karbapenemom: 9,0%, pip/tazo 6,3%  
*K. pneumoniae* ESBL 5,6% (EARS-net)

European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2018.

# **Kje bi želeli imeti hospitalizirano svojo mamo?**