Odpornost bakterij v svetu in pri nas

doc. dr. Mateja Pirš, dr.med.

Inštitut za mikrobiologijo in imunologijo, UL MF

Laboratoriji:

- Inštitut za mikrobiologijo in imunologijo, Medicinska fakulteta v Ljubljani
- Nacionalni laboratorij za zdravje, okolje in hrano:
  - Maribor
  - Celje
  - Murska Sobota
  - Kranj
  - Koper
  - Nova Gorica
  - Novo Mesto
- Splošna bolnišnica:
  - Franca Derganca Nova Gorica
  - Slovenj Gradec
- Univerzitetna klinika za pljučne bolezni in alergijo Golnik

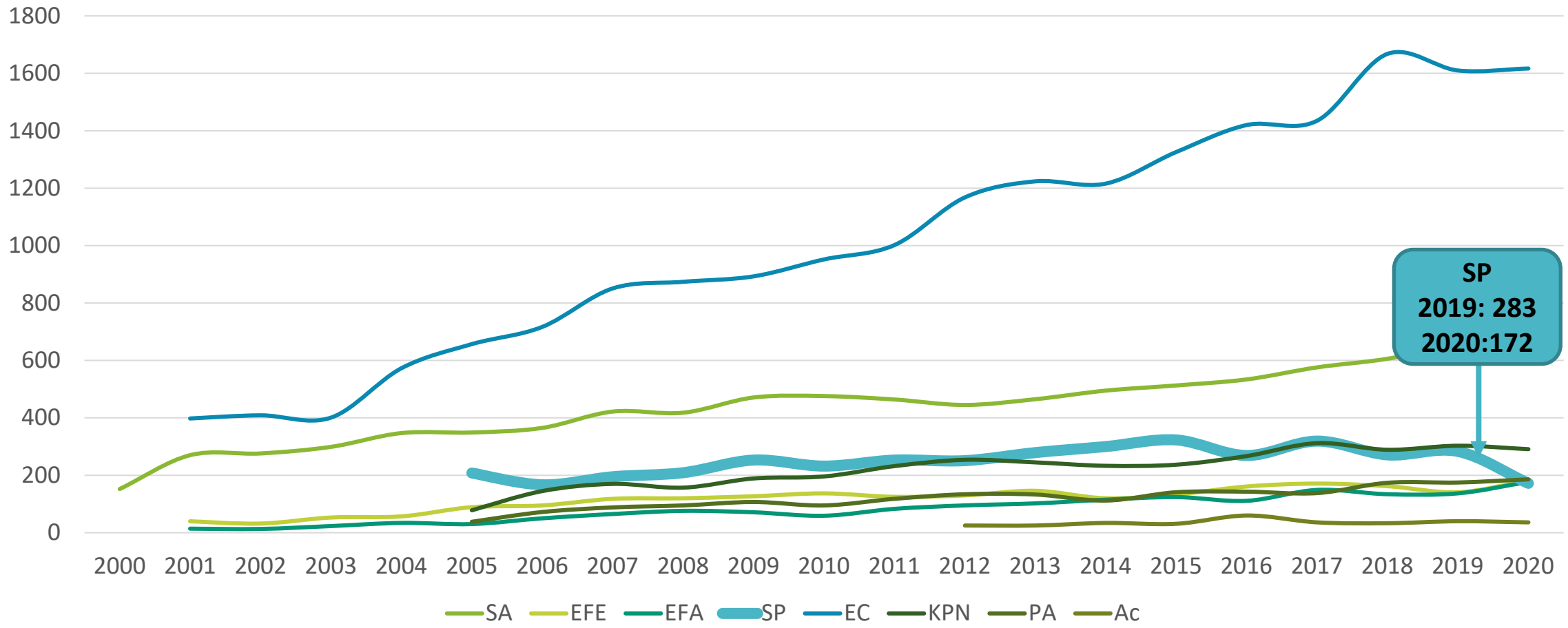
- EARS–Net ECDC 2020:
  - države EU
  - 8 vrst, invazivni izolati
- SKUOPZ poročila 2017
  - Slovenija,
  - 19 bakterijskih vrst, vse klinične kužnine

EUROPEAN ANTIBIOTIC AWARENESS DAY
A EUROPEAN HEALTH INITIATIVE

- CEASAR - Central Asian and Eastern European Surveillance of Antimicrobial Resistance

  Antimicrobial Resistance Global Report on Surveillance, WHO 2020

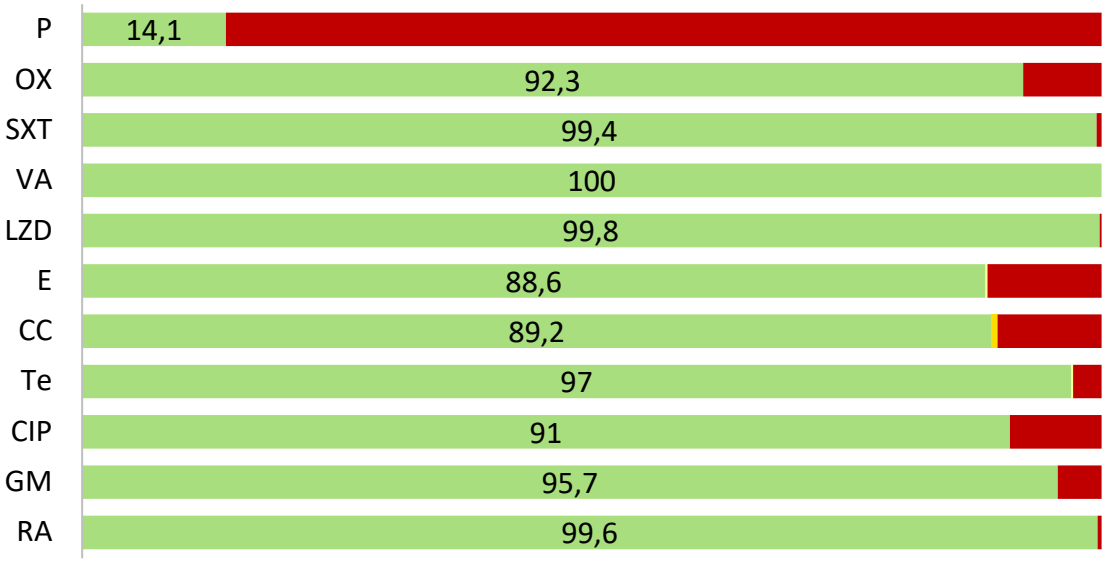
EARS-Net Slovenija



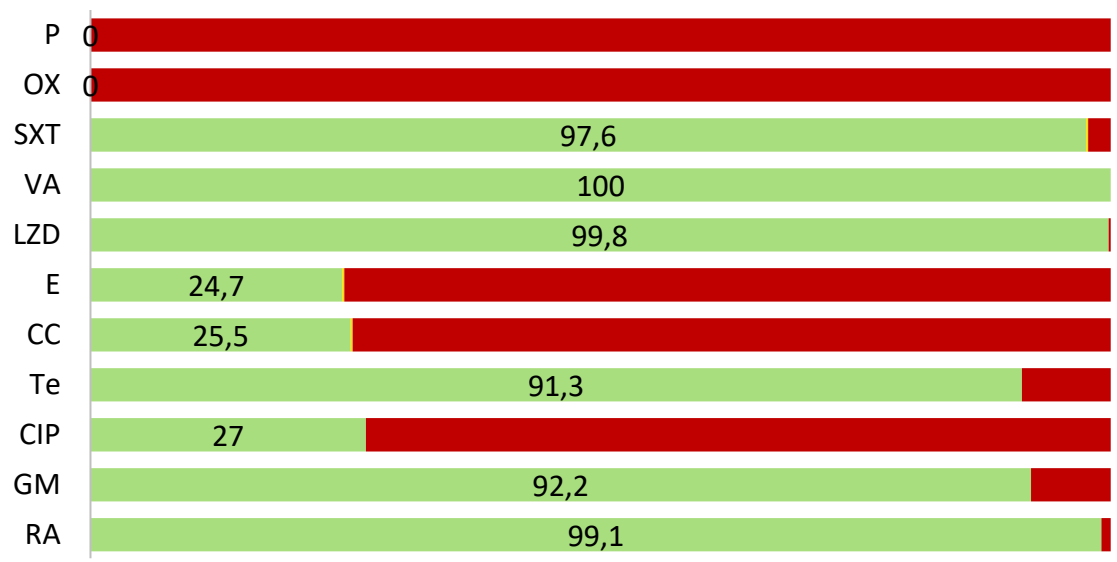
Blood-culture sets/1000 patient days	2015	2016	2017	2018	2019	2020
	35,1	35,0	41,2	36,8	40,4	47,1

Staphylococcus aureus

S.aureus



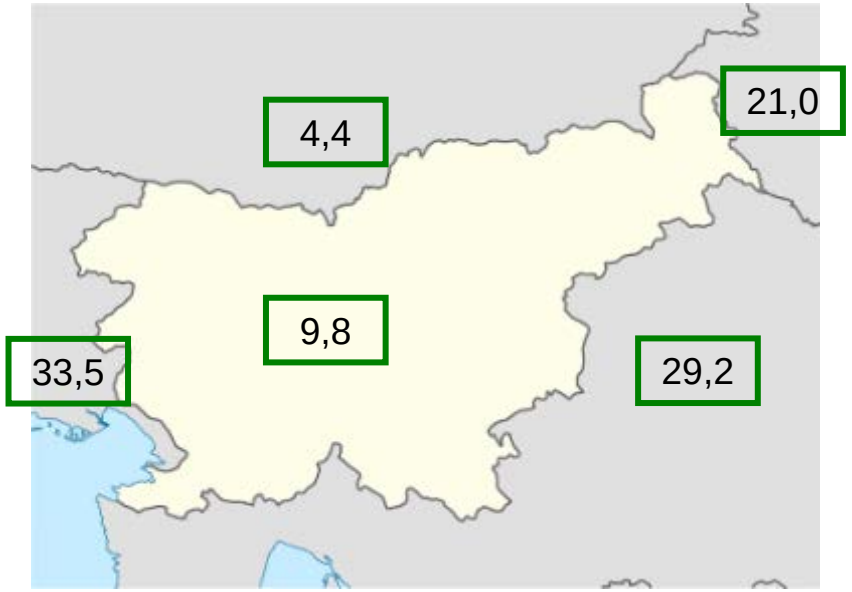
MRSA



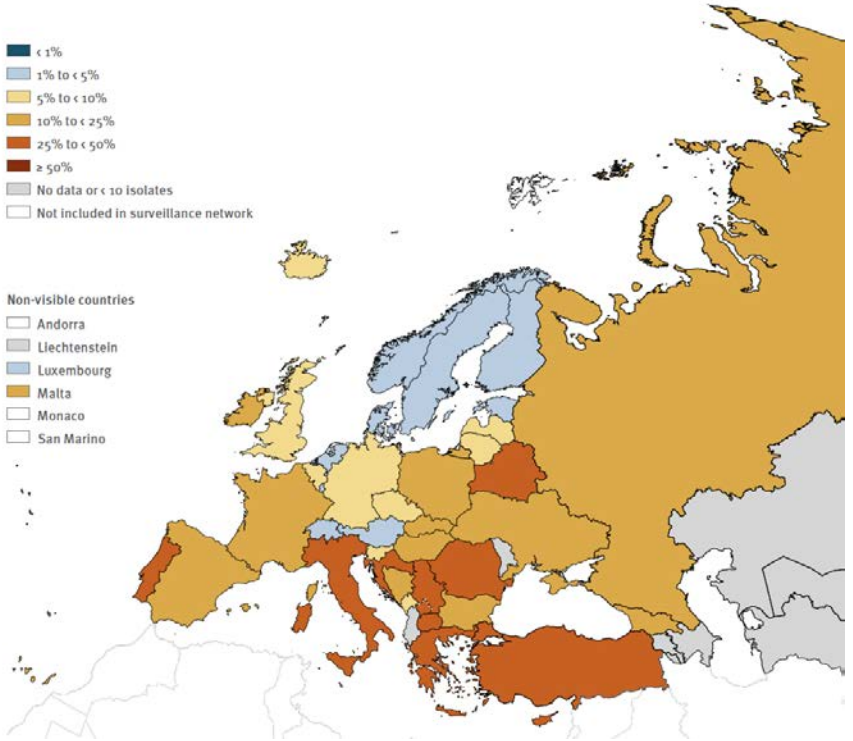
Vir: SKOUPZ 2017

Staphylococcus aureus - MRSA

Lokalni podatki



EARS-Net/CAESAR 2020



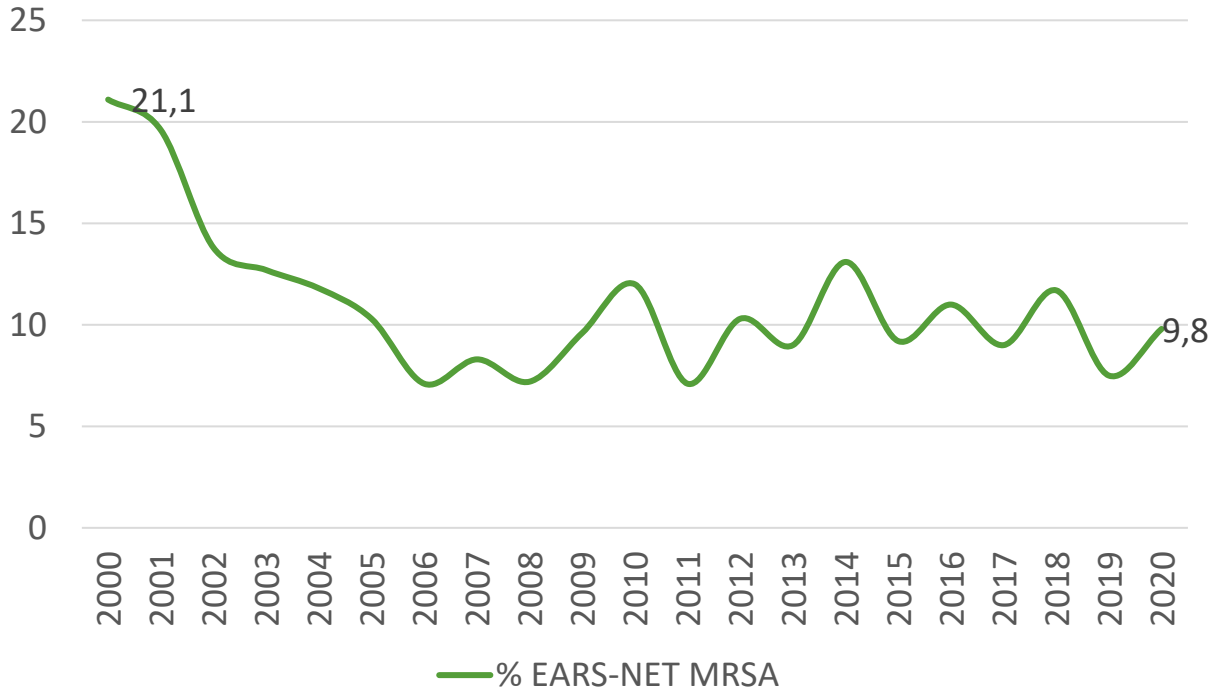
Bacterial species	Antimicrobial group/agent	2016		2017		2018		2019		2020		2020 EU/EEA countryrange[a]	Trend 2016–2020[b]
		N	%	N	%	N	%	N	%	N	%		
S. aureus	MRSA*	51 013	19.3	57 396	18.3	63 837	17.7	65 604	17.1	72 314	16.7	1.4–49.1	↓

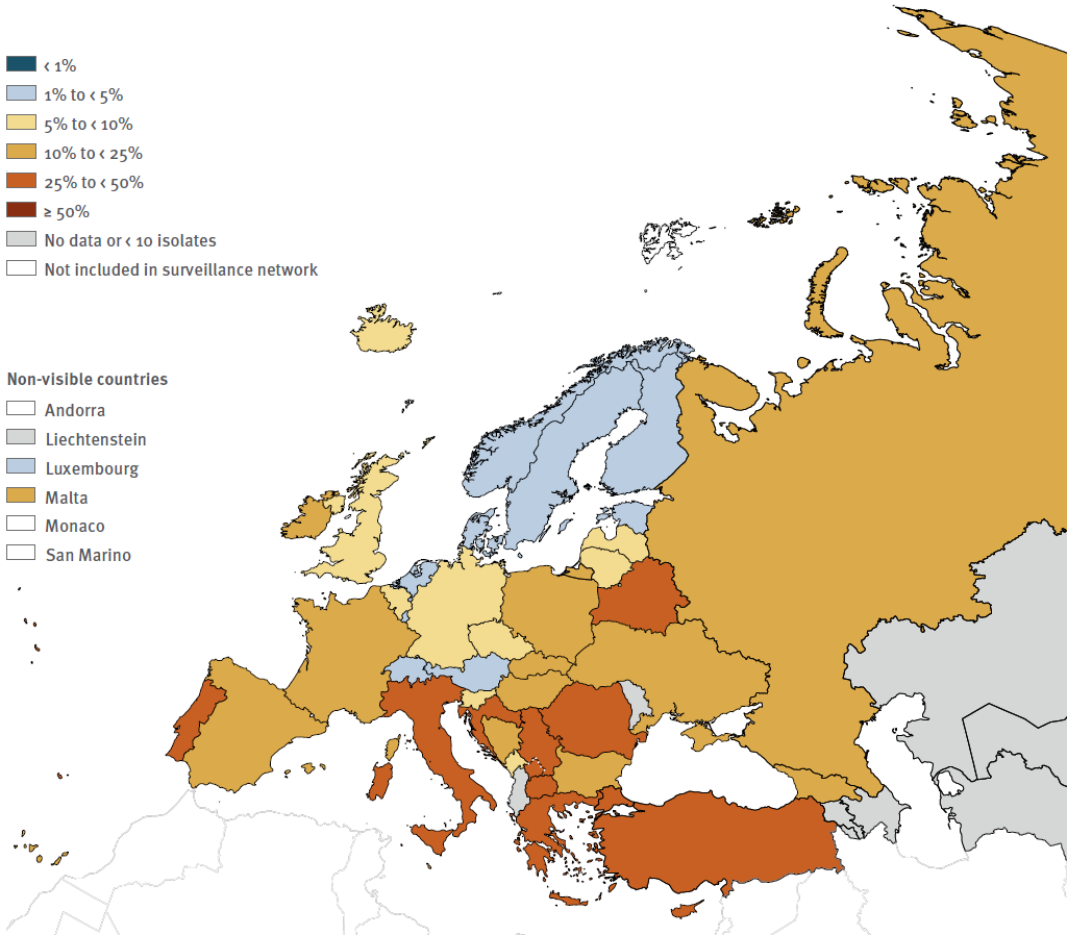
Staphylococcus aureus - MRSA

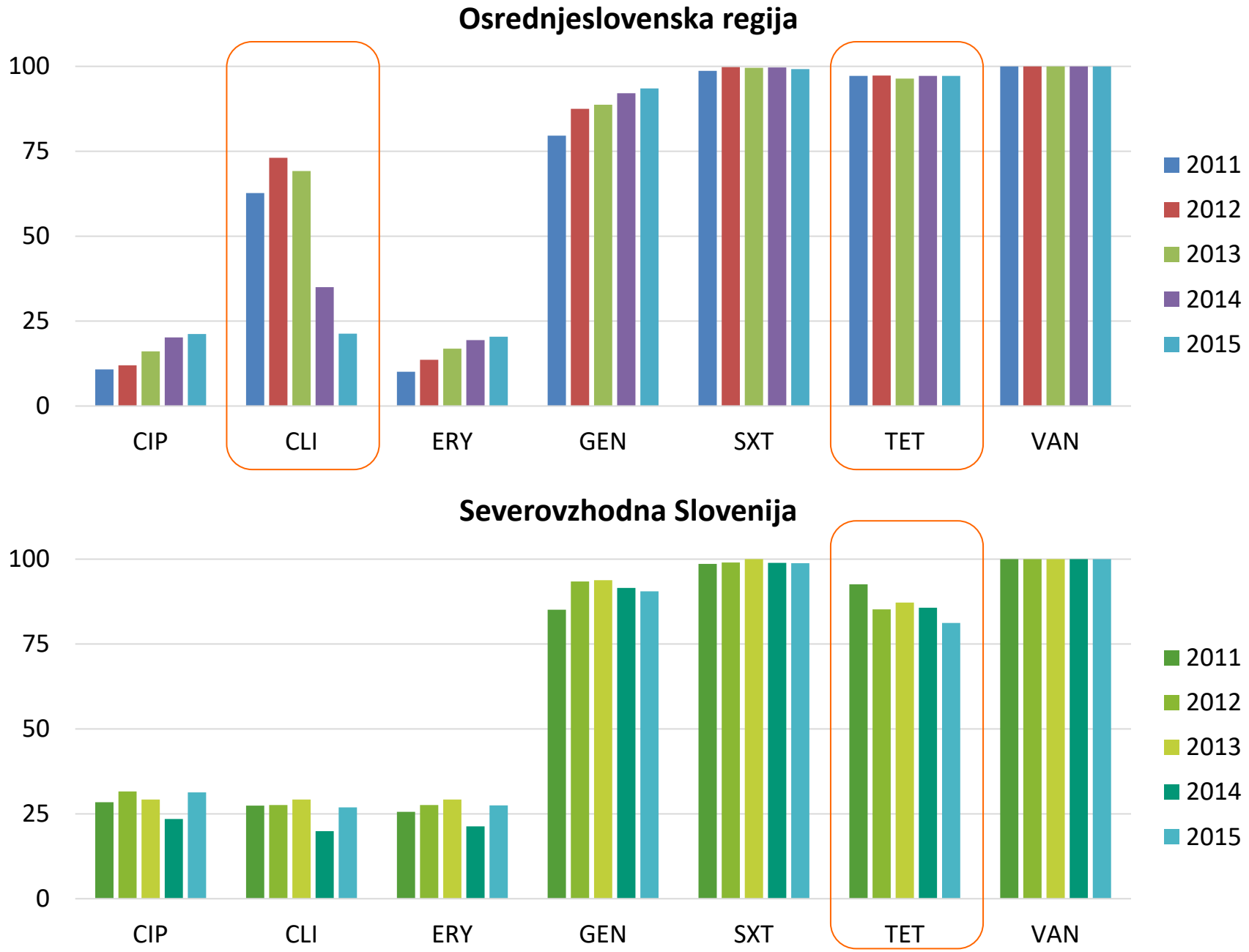
EARSS/EARS-Net:

•Slovenija prva država v Evropi, ki ji je uspelo **znižati delež MRSA v** hemokulturah:

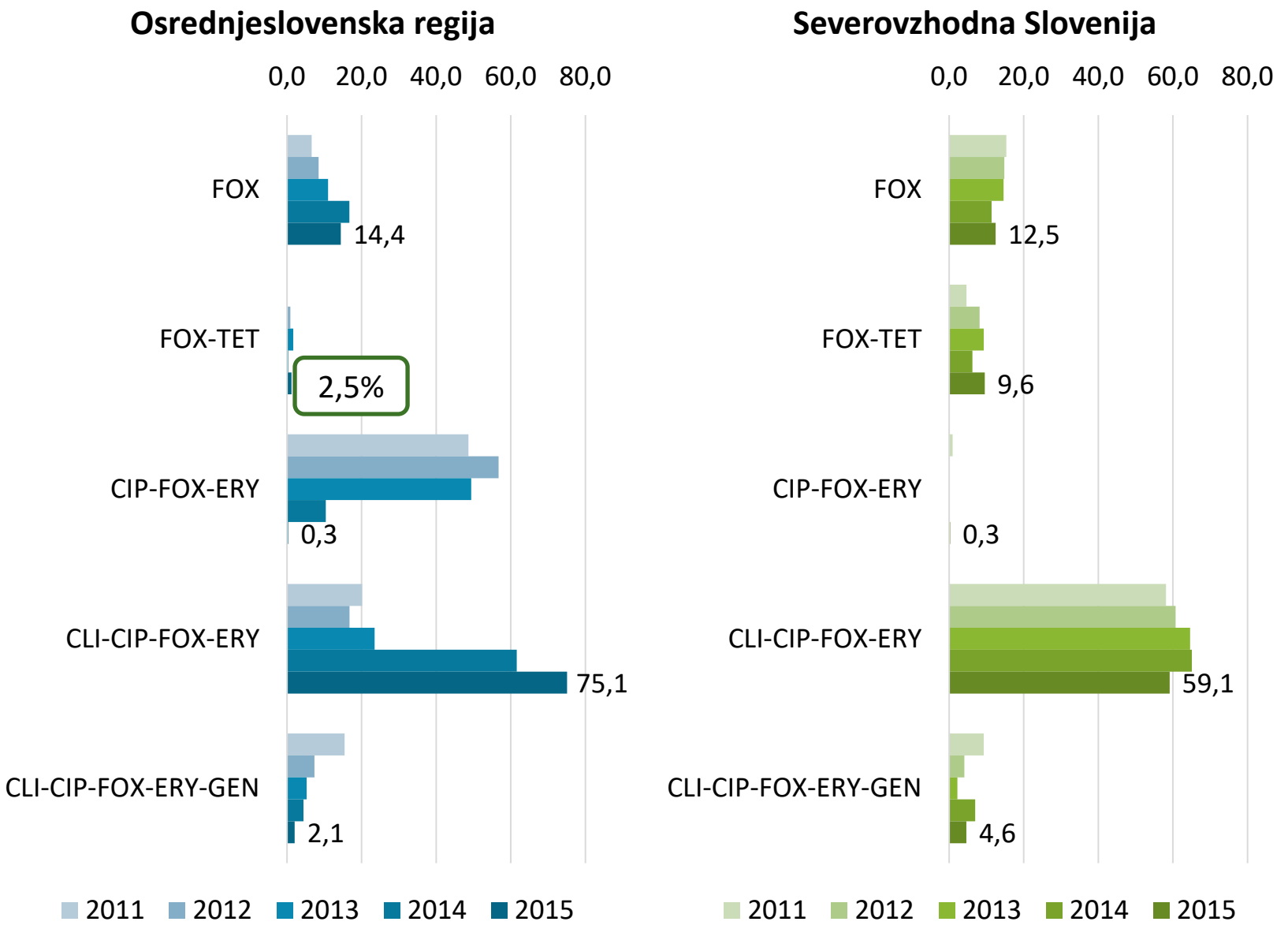
2000=21,4 % → 2006=7,1 %







Pirš M in sod. Vzorci občutljivosti za antibiotike in odpornosti proti njim pri MRSA v dveh slovenskih regijah v obdobju 2011–2015. Likarjev simpozij 2016



V celotni Sloveniji opažamo nižanje deleža proti tetraciklinu občutljivih MRSA, kar nakazuje na vdor LA-MRSA

World Health Organization

Antimicrobial resistance: global report on surveillance. 2014

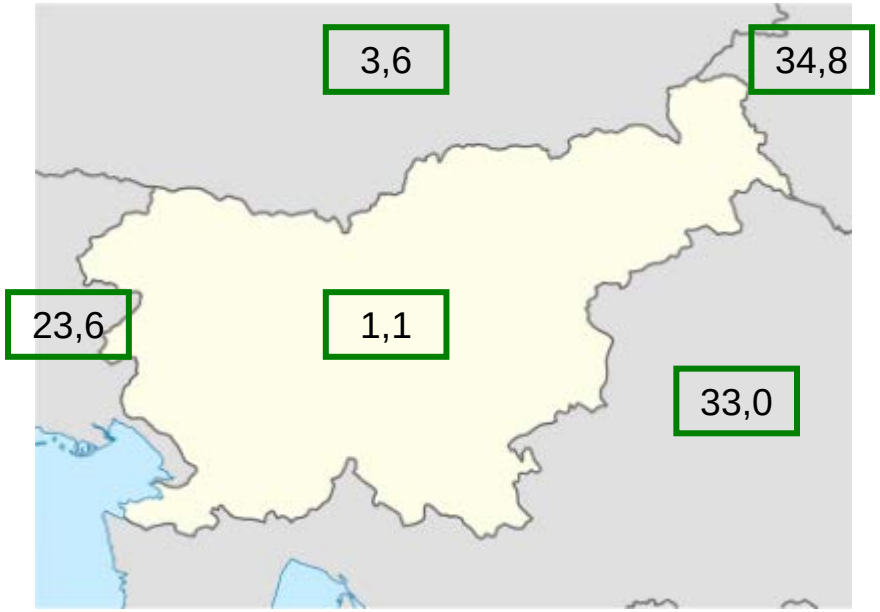
Table 7 *Staphylococcus aureus:* **Resistance to beta-lactam antibacterial drugs (i.e. methicillin-resistant *S. aureus*, MRSA)**

Data sources based on at least 30 tested isolates[a]	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in invasive isolates[b] (no. of reports)
African Region		
– National data (n=9 countries)	12–80	52 (n=1)
– Publications (n=27) from 10 additional countries	0–100	33–95 (n=3)
Region of the Americas		
– National data or report to ReLAVRA (n=15 countries)	21–90	
– National networks (n=2) no additional country	21–84	
– Publications (n=17) from 7 additional countries	2.4–90	43–45 (n=2)
Eastern Mediterranean Region		
– National data (n=4 countries)	10–53	53 (n=1)
– Hospital network[c] (n=1) from 1 additional country	46	
– Publications (n=31) from 10 additional countries	0–92	13–18 (n=3)
European Region		
– National data or report to EARS-Net n=36 countries)	0.3–60	0.3–6 (n=32)
– Publications (n=5) from 2 additional countries	27–80	27–50 (n=3)
South-East Asia Region		
– National reports (n=3 countries)	10–26	
– Publications (n=25) from 4 additional countries	2–81	37 (n=1)
Western Pacific Region		
– National data (n=16 countries)	4–84	
– Institute surveillance (n=2 from one additional country)	1–4	
– Publications (n=1) from one additional country	60	

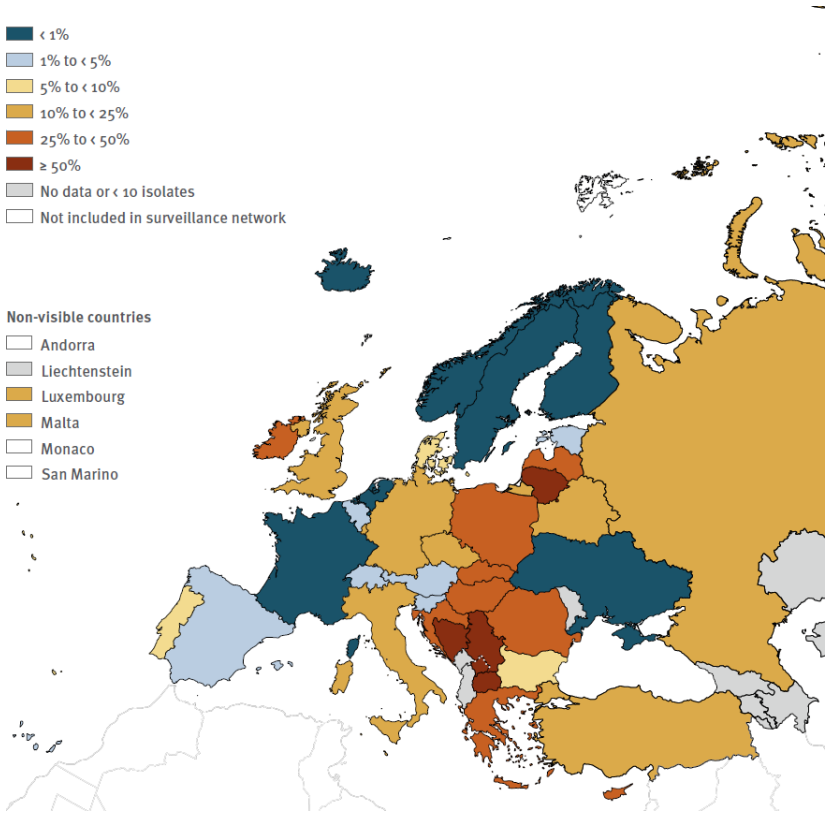
Proti vankomicinu odporni enterokoki (VRE)

E. faecium - VRE

Lokalni podatki



EARS-Net/CAESAR 2020

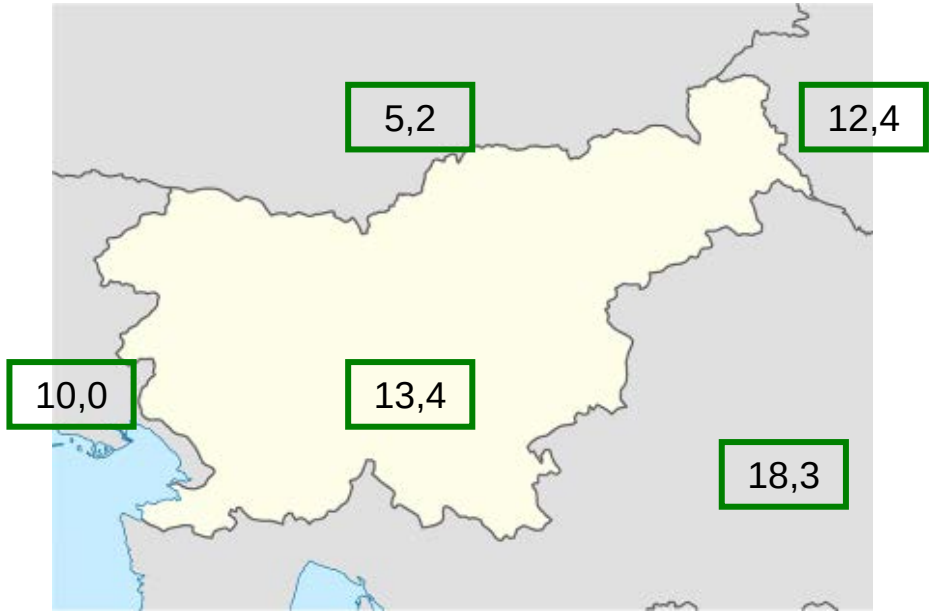


Bacterial species	Antimicrobial group/agent	2016		2017		2018		2019		2020		2020 EU/EEA countryrange[a]	Trend 2016–2020[b]
		N	%	N	%	N	%	N	%	N	%		
E. faecium	Vancomycin resistance	10 708	11.6	12 011	13.3	13 377	16.2	14 121	17.7	18 151	16.8	0.0–56.6	↑

EARS-NET SLOVENIJA: http://www.nijz.si/sl/ears-net-slovenija
SKUOPZ: http://www.imi.si/strokovna-zdruzenja/skuopz/skuopz

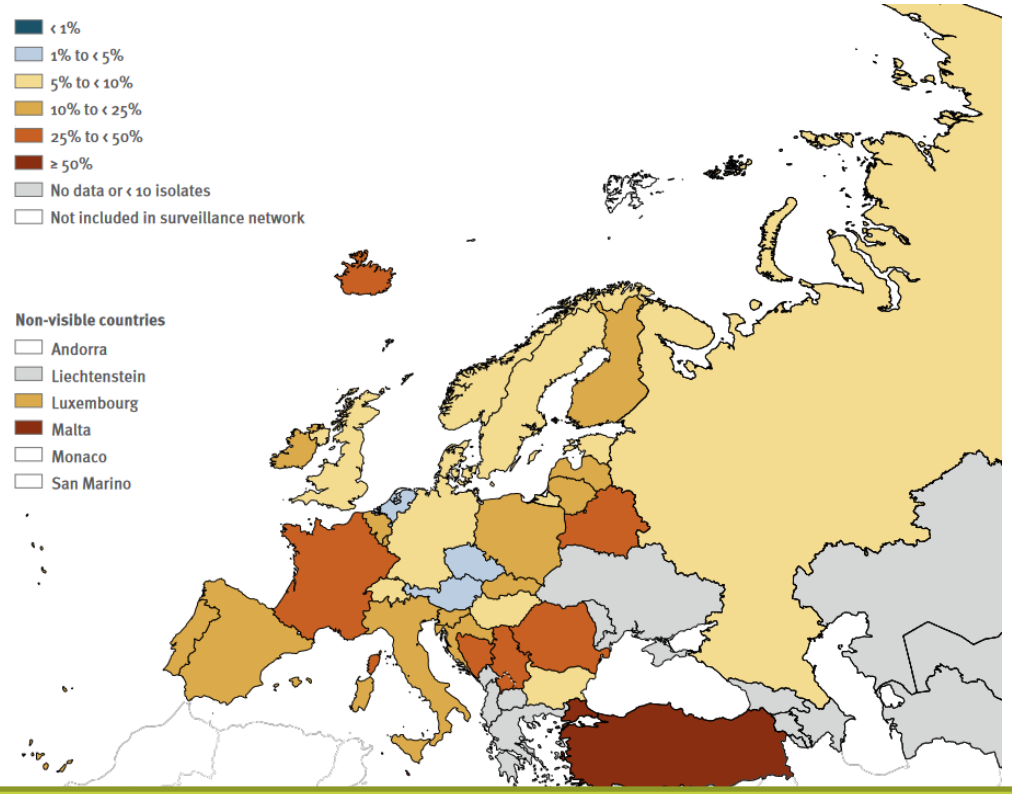
Proti penicilinu odporni *S. pneumoniae* (PNSP)

Lokalni podatki



NWT izolati!

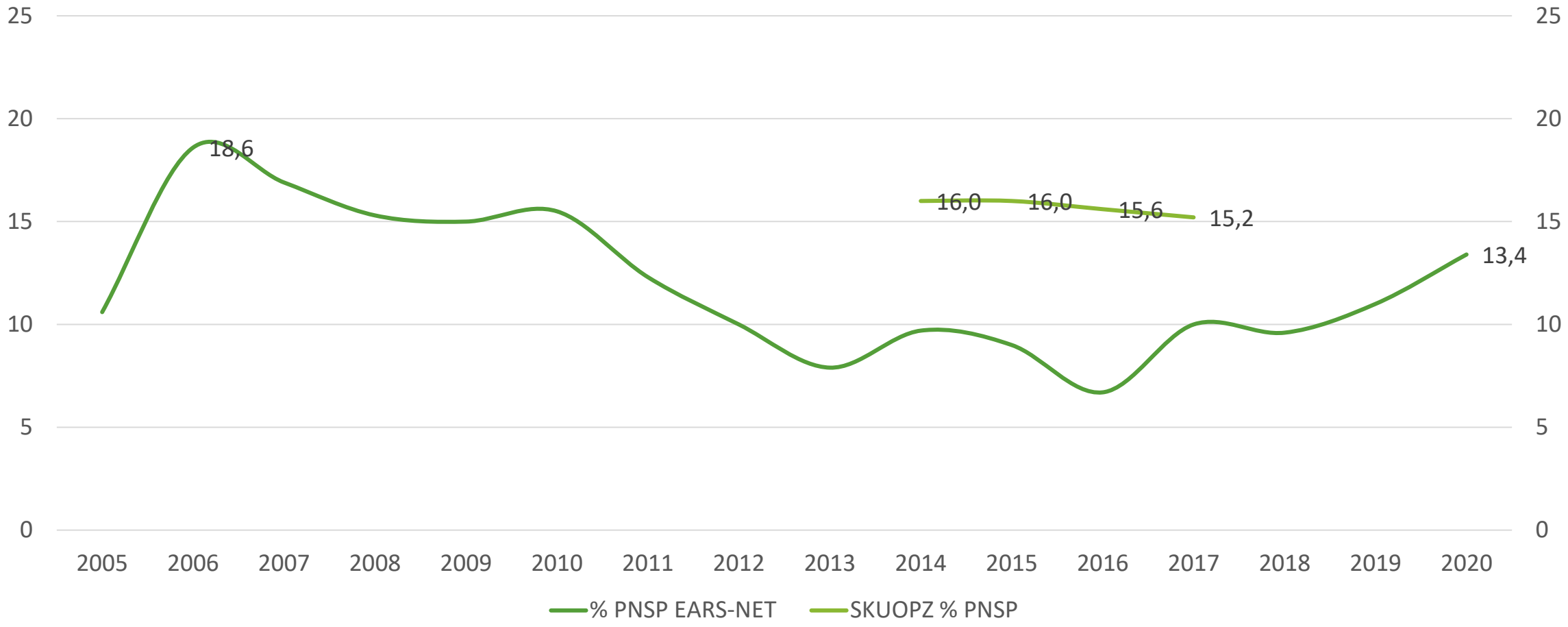
EARS-Net/CAESAR 2020



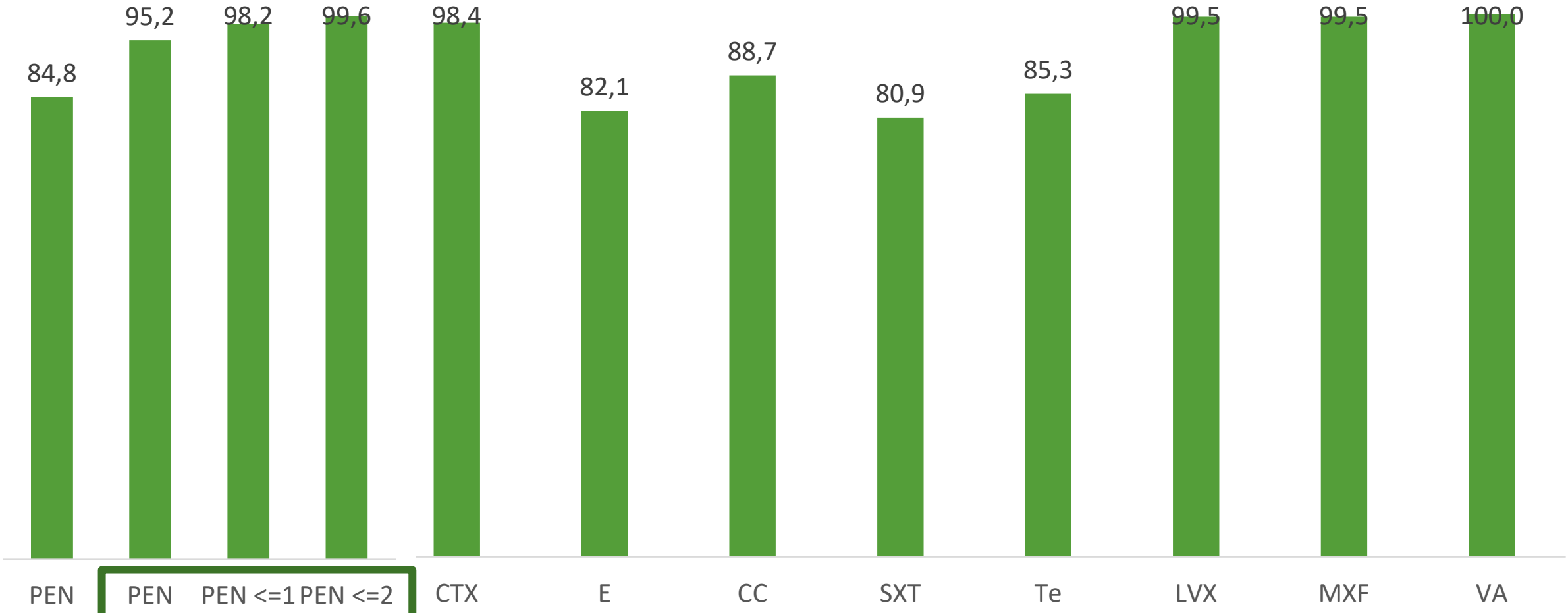
PNSP:

- EU/EEA 2015 14,2 % → 2019 12,1 % (4.0-33.3) ↓
- Slovenija 2015 9,0 % → 2019 11,0 % ≈

EARS-NET SLOVENIJA: http://www.nijz.si/sl/ears-net-slovenija
SKUOPZ: http://www.imi.si/strokovna-zdruzenja/skuopz/skuopz



Proti penicilinu odporni *S. pneumoniae* (PNSP)



Vir: SKOUPZ 2017

World Health Organization

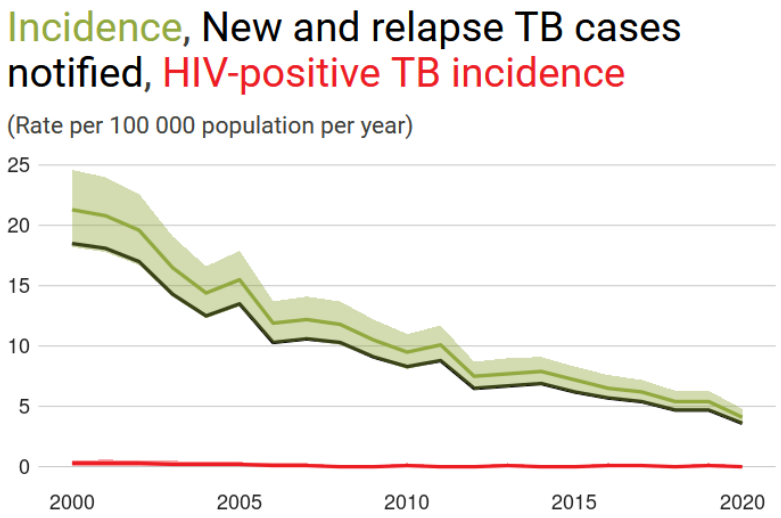
Antimicrobial resistance: global report on surveillance. 2014

Table 8 *Streptococcus pneumoniae*: Resistance or non-susceptibility to penicillin

Data sources based on at least 30 tested isolates	Overall reported range of proportion resistant (R) and/or non-susceptible (NS)	Reported range of proportion resistant or non-susceptible in invasive isolates[a] (no. of reports)
African Region – National data (n=5 countries) – Publications (n=16) from 14 additional countries	 3–16 (R) or 57–60 (NS) 1–100 (R) or 9–69 NS or 0–79 [b]	 3 (R) (n=1) 9–18 (NS) or 24–79 [b] (n=5)
Region of the Americas – National data or report to ReLAVRA or SIREVA (n=15 countries) – Publications (n=1) from 1 additional country	 0–48 [b] 53 (non-meningitis) (NS)	 0–48 [b] (n=14) 64 (meningitis) (NS)
Eastern Mediterranean Region – National data (n=3 countries) – Publications (n=17) from 9 additional countries	 13–34 (R) or 5 (NS) 0.3–64 (R) or 17–48 (NS) or 0–93 [b]	 34 (R) (n=1) 2–14 (R) or 17–40 (NS) (n=10)
European Region – National data or report to EARS-Net (n=31 countries) – Publications (n=1) from 1 additional country	 0–61 (R) or 0.9–73 (NS) 13–68 (NS)	 0.9–61 (NS) or 32–45 [b] (n=27) 13 (NS) (n=1)
South-East Asia Region – National data (n=2 countries) – Publications (n=2) from 2 additional countries	 47–48 [b] 0–6 (R)	 0 (R) (n=1)
Western Pacific Region – National data (n=10 countries) – Hospital data (two hospitals in 1 country) – Publications (n=4) from 2 additional countries	 17–64 (NS) or 0–47 [b] 0–2 44–96 (R) or 0–69 (NS)	 44 (R) or 0 (NS) (n=2)

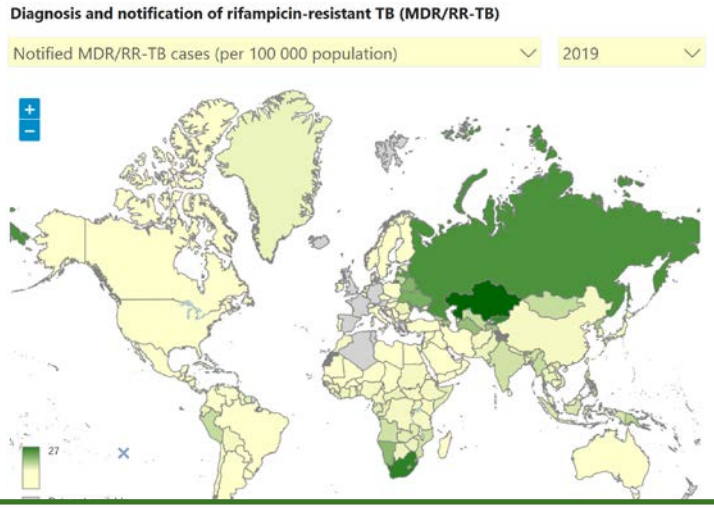
Mycobacterium tuberculosis

- Večkratno odporni sevi so velik svetovni problem, v Sloveniji jih ni!
- Občutljivost vseh ključnih zdravil že nekaj let od 97 do 100 %.
- 2020: 1 primer MDR/RR TB



Streptococcus pyogenes

- Občutljivost za penicilin 100 %
- Občutljivost za eritromicin 94 %, za klindamicin 96 %.



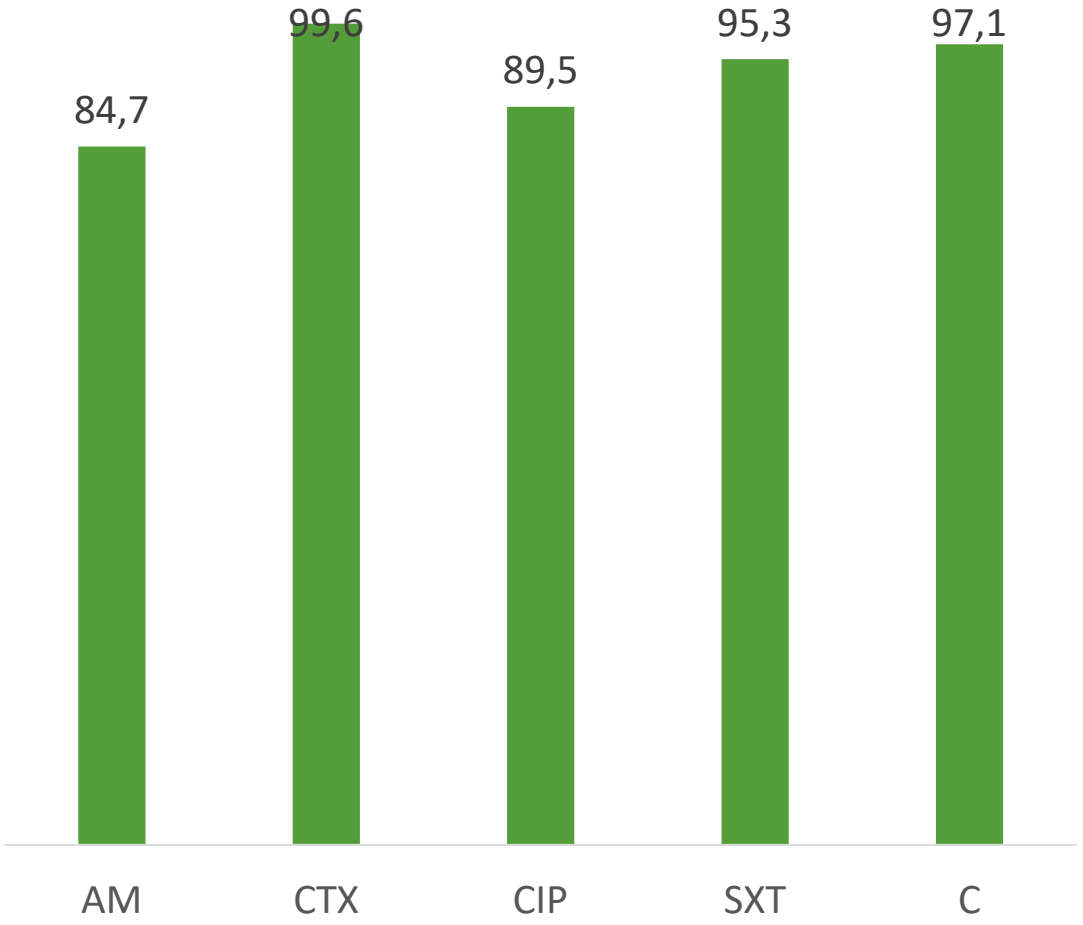
WHO: porast TB prvič v več kot 15 letih → nazaj na raven 2017!

Salmonella spp.

- Prevladujoči serovari!
- ↓ občutljivega serovara *S*. Enteritidis,
- Δ občutljivost predvsem za ciprofloksacin.

Table 9 Nontyphoidal *Salmonella*: Resistance to fluoroquinolones[a] (summary of reported or published proportions of resistance, by WHO region)

Data sources based on at least 30 tested isolates	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in blood isolates (no. of reports)
African Region – National data (n=9 countries) – Publications (n=11) from 8 additional countries	 0–35 0–30	 0–30 (n=4)
Region of the Americas – National data (n=13 countries) – Publications (n=1) from 1 additional country	 0–96 0	
Eastern Mediterranean Region – National data (n=4 countries) – Publications (n=4) from 4 additional countries	 2–49 0–46	 6 (n=1)
European Region – National data or report to FWD-Net, (n=29 countries) – Publications (n=1) from1 additional country	 2–3 13	
South-East Asia Region – National data (n=2 countries) – Publication (n=1) from 1 additional country	 0.2–4 1.4	
Western Pacific Region – National data (n=9 countries) – Network/institution data (n=4 from 2 countries) – Publications from remaining countries (n=0)	 0–14 0–0.3	

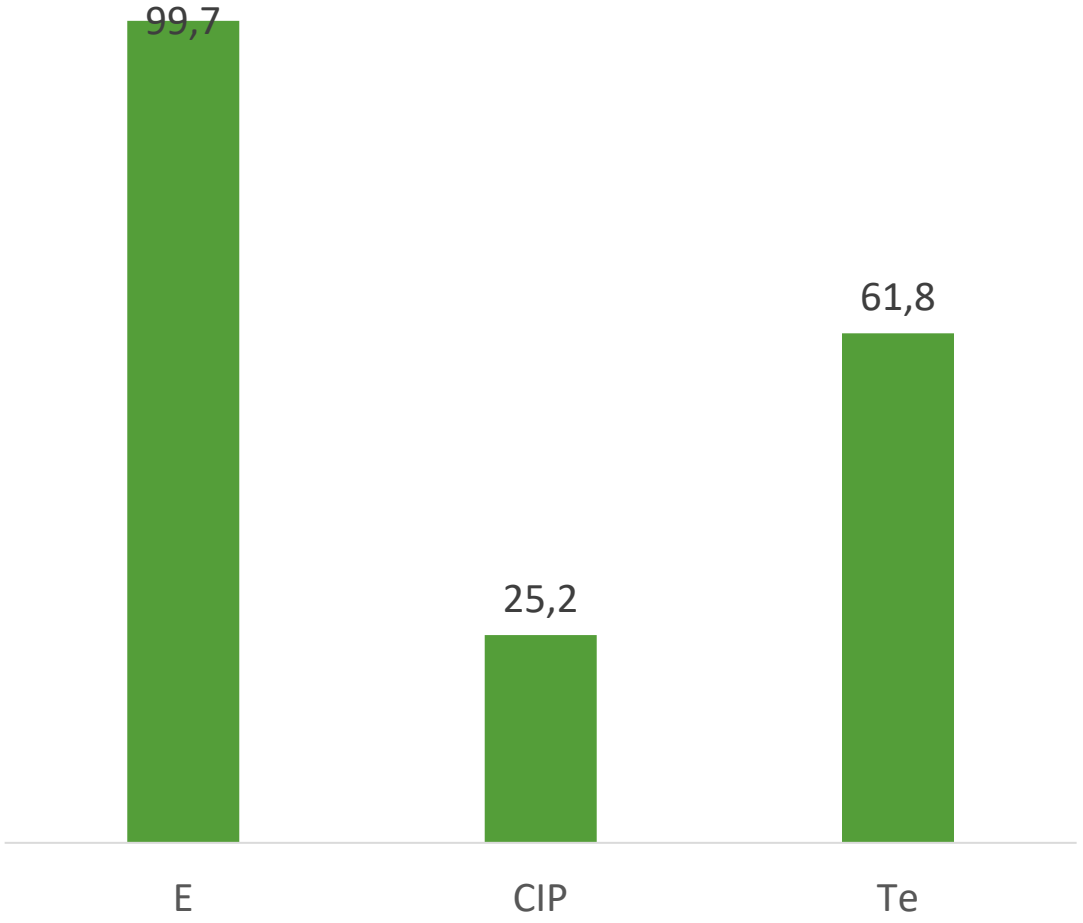


Campylobacter jejuni

- Slaba občutljivost za ciprofloksacin 25 %
- Dobra občutljivost za eritromicin >99 %
- Podobno velja za *C. coli*

- Posamezni večkratno odporni izolati, odporni proti vsem antibiotikom, ki jih je po EUCAST mogoče testirati:

  CIP R + ERI R + TET R.



Neisseria gonorrhoeae

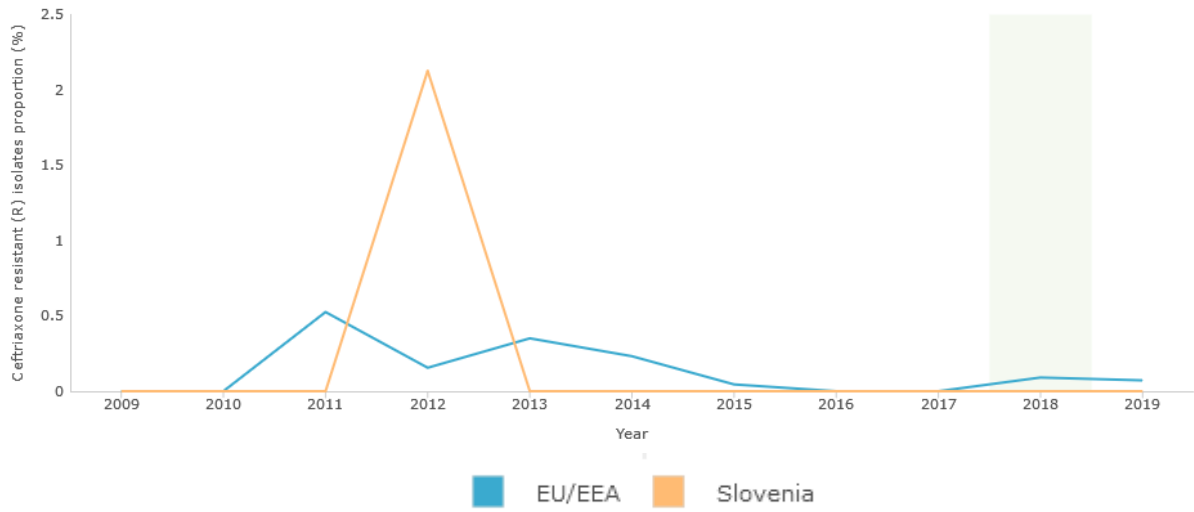
Table 11 *Neisseria gonorrhoeae*: decreased susceptibility to third-generation cephalosporins[a]

Data sources based on at least 30 tested isolates	Overall reported range of proportion with decreased susceptibility (%)
African Region – National data and/or GASP data (n=2 countries) – Publications (n=5) from 5 additional countries	 0–12 0
Region of the Americas – National data and/or GASP/ GISP data (n=4 countries) – Publications from remaining countries (n=0)	0–31
Eastern Mediterranean Region – National data and/or GASP data (n=2 countries) – Publications (n=1) from 1 additional country	0–12 0
European Region – National data and/or EURO-GASP/GRASP data (n=17) – Publications (n=3) from 3 additional countries	0–36 0
South-East Asia Region – National data and/or GASP data (n=5 countries) – Publications from remaining countries (n=0)	0–5
Western Pacific Region – National data and/or GASP data (n=12 countries) – Publications from remaining countries (n=0)	0–31

	Število izolatov	S		I		R	
		n	%	n	%	n	%
Penicilin	178	**19**	11	**150**	84	**9**	5
Cefiksim	178	**178**	100	/		**0**	0
Ceftriakson	178	**178**	100	/		**0**	0
Azitromicin*	178	**167**	94	/		**11**	6
Ciprofloksacin	178	**73**	41	**3**	2	**102**	57
Tetraciklin	178	**101**	57	**32**	18	**45**	25
Spektinomicin	178	**178**	100	**0**	0	**0**	0
Betalaktamaza je bila pozitivna pri **27** (15 %) izolatih.							

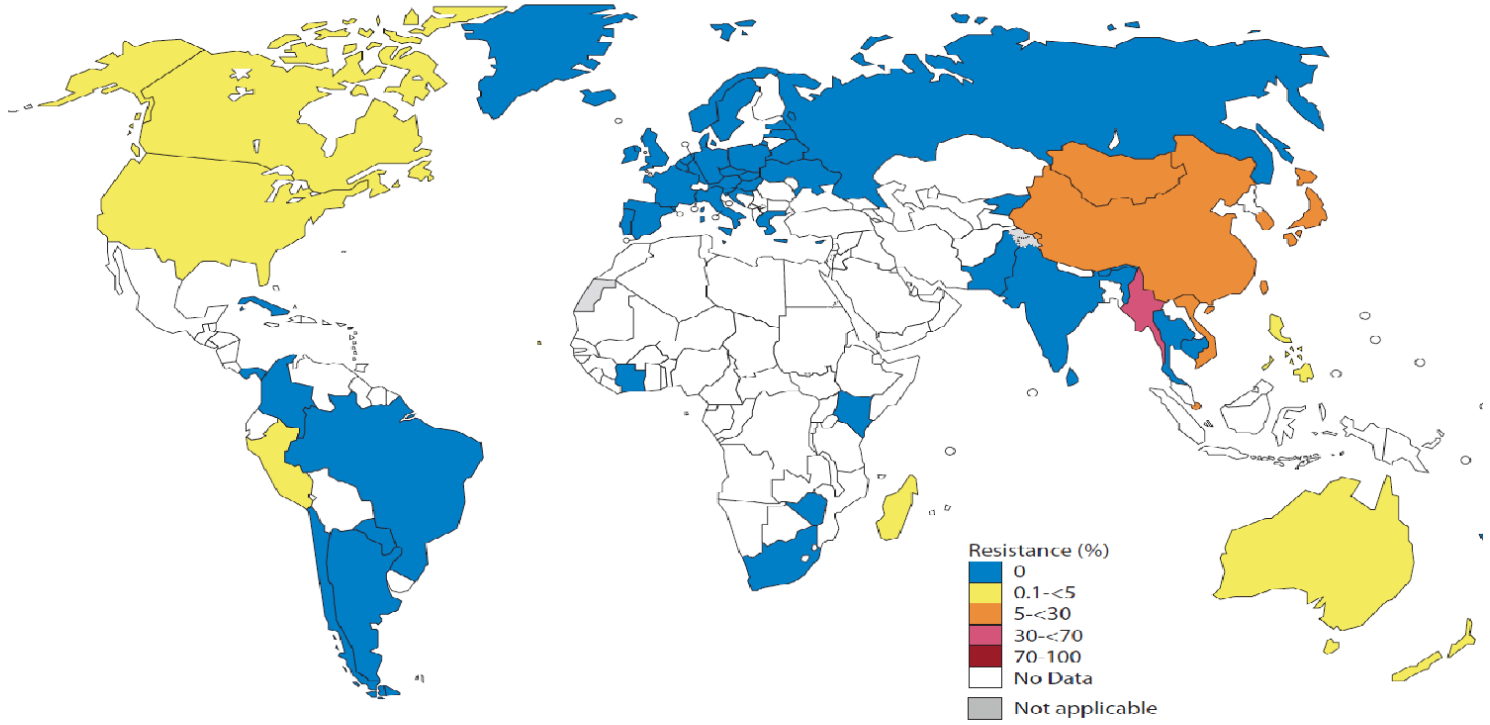
Občutljivost je izračunana po standardu EUCAST; upoštevali smo prvi izolat znotraj ene epizode bolezni (epizoda=30 dni).

* Mejne vrednosti pri azitromicinu so izračunane glede na standard EUCAST 2019. Epidemiološka mejna vrednost (ECOFF), ki razlikuje divje seve od izolatov z zmanjšano občutljivostjo, je MIK ≤ 1 mg/L.

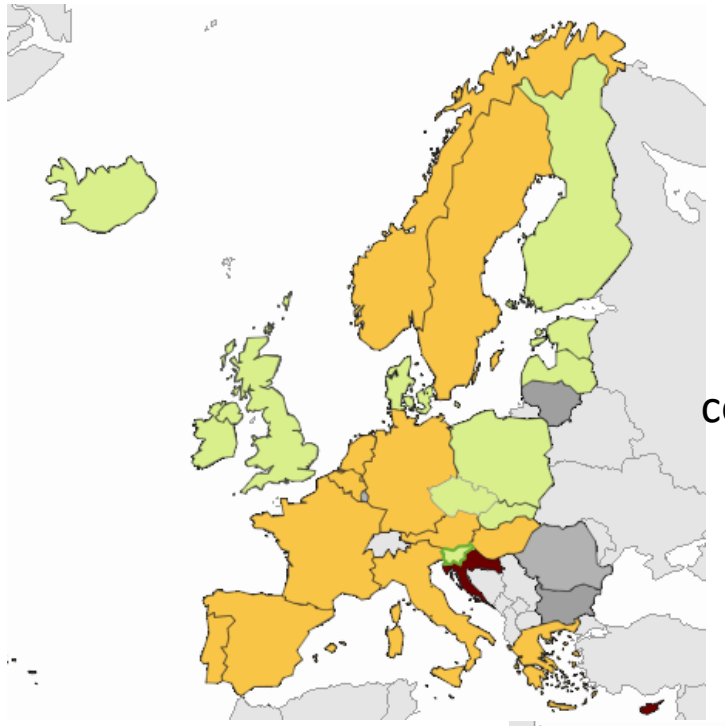


World Health Organization

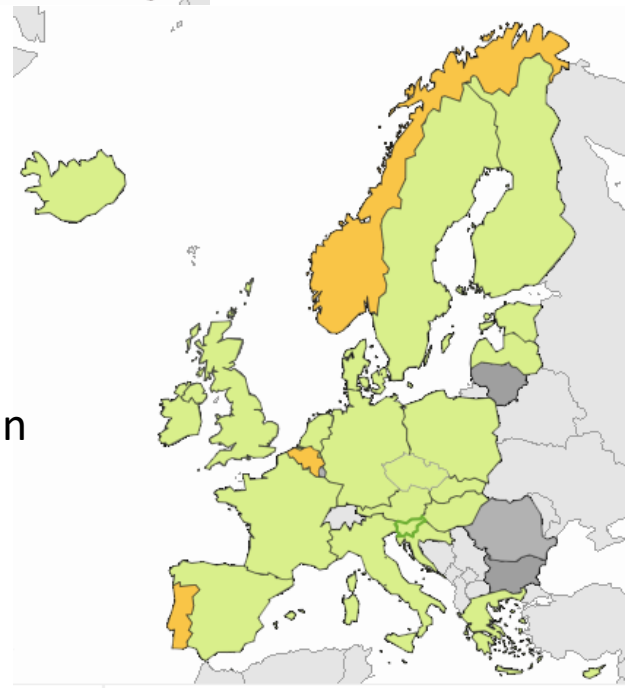
Countries with reported decreased susceptibility/resistance (DS/R) to ceftriaxone in *N. gonorrhoeae*, WHO GASP 2015-2016



15/63 (30%) countries - DS/R to ceftriaxone ; 8 (15 %) countries ≥ 5%; 8(15%) countries ≤ 5%



cefiksim

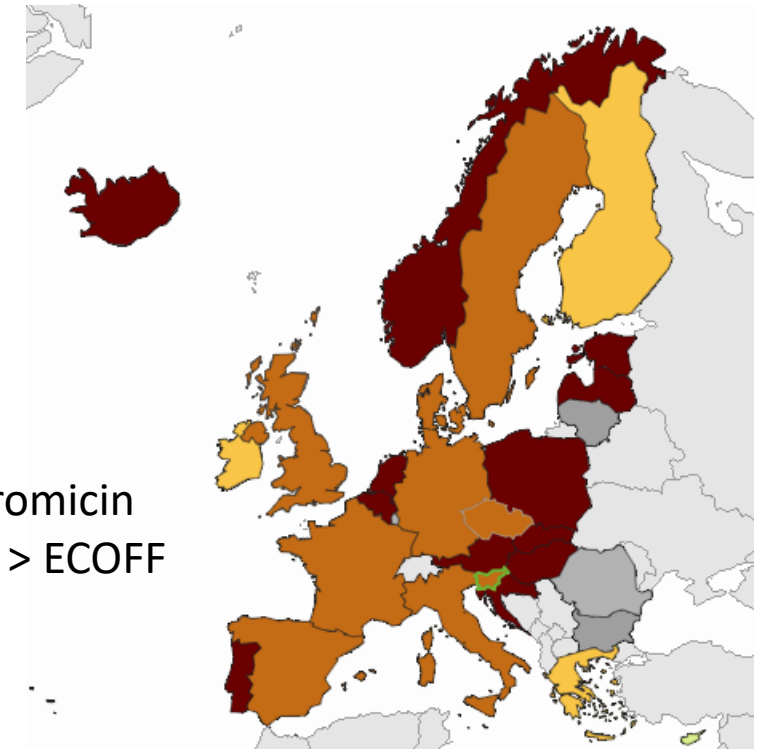


ceftriakson

Surveillance Atlas of Infectious Diseases

zadnji podatki 2019

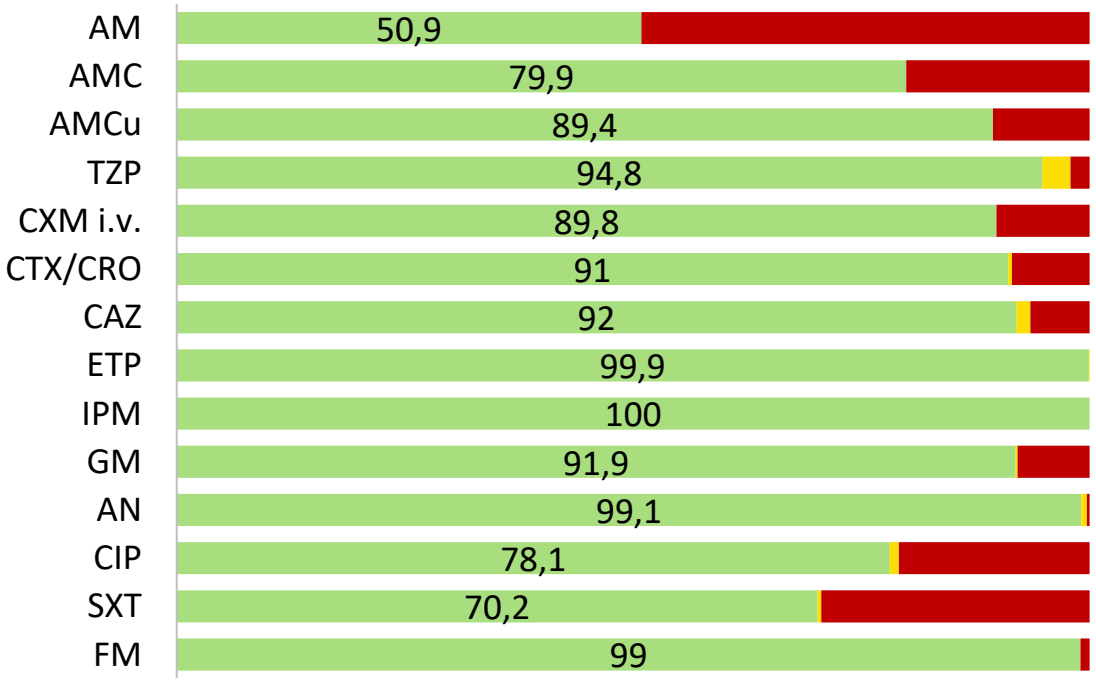
- 0
- 0.1-4.9
- 5.0-9.9
- 10.0-100
- No data



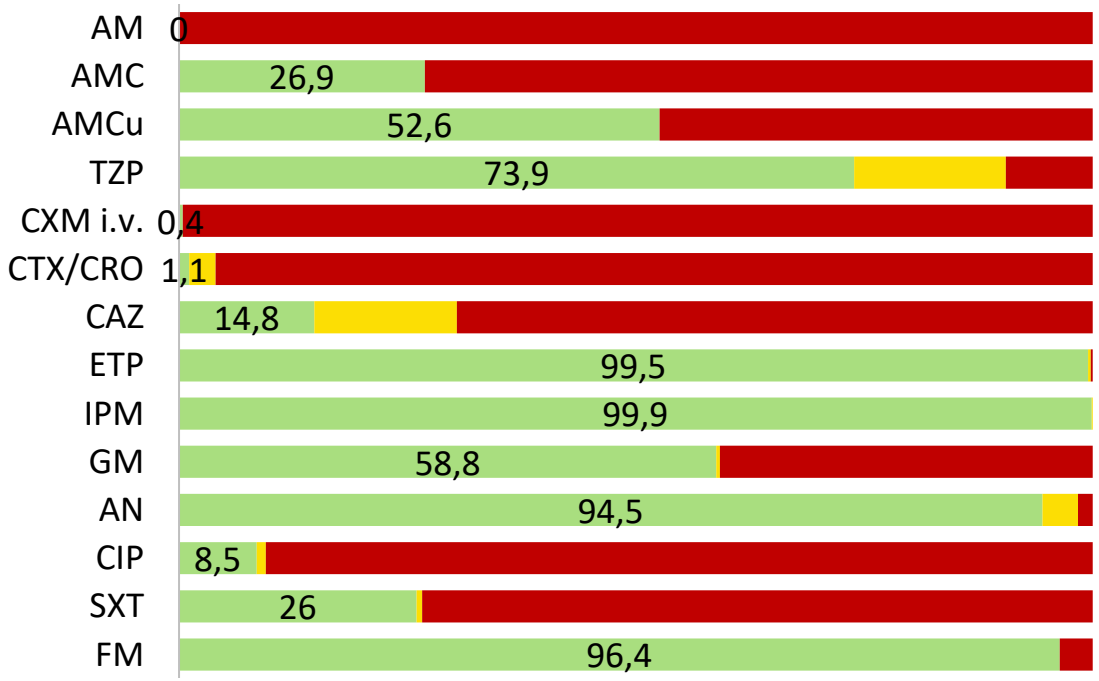
azitromicin
MIK > ECOFF

Escherichia coli

E.coli



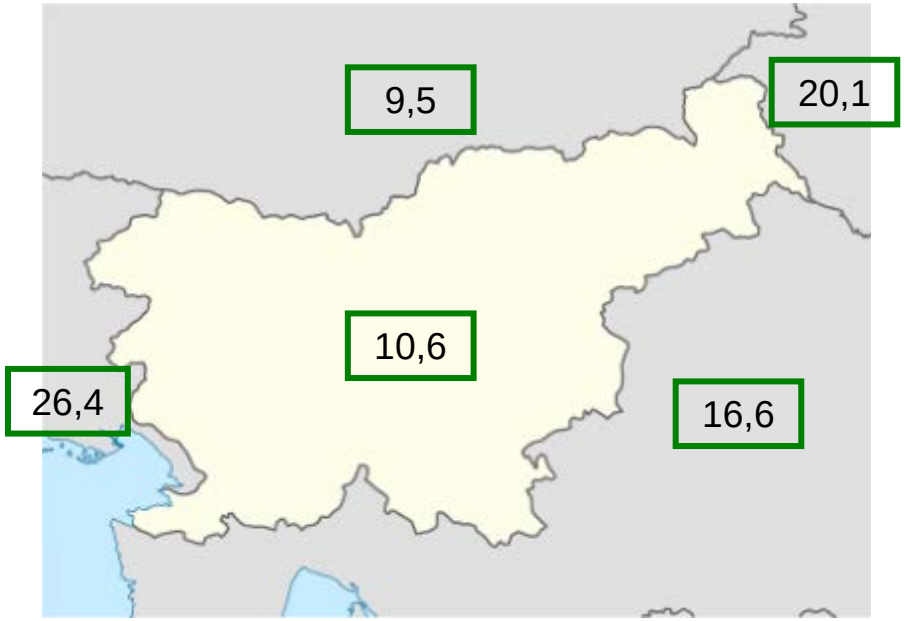
E.coli - ESBL



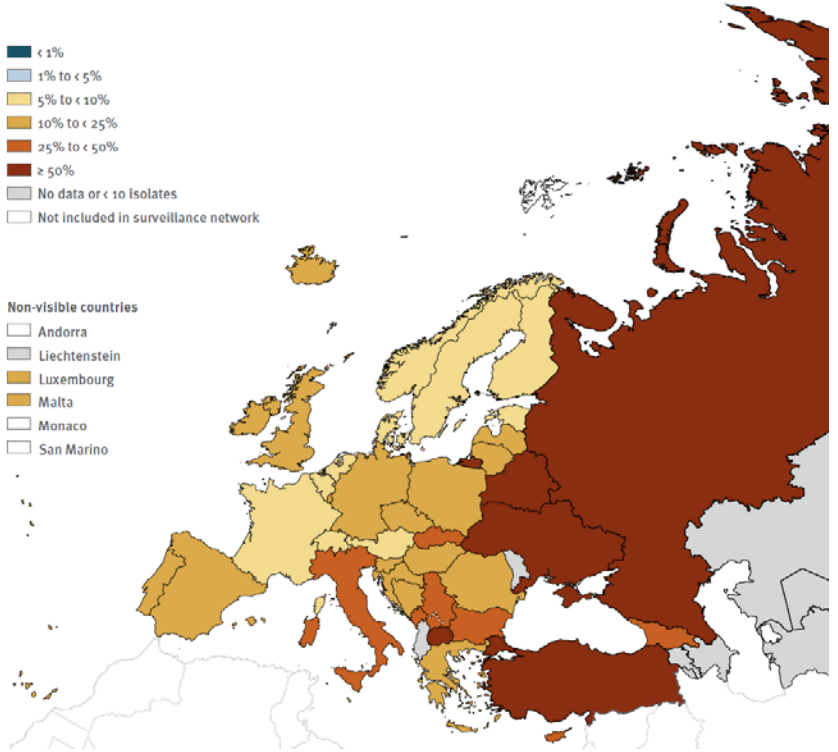
Vir: SKOUPZ 2017

Escherichia coli – Cef3G NS

Lokalni podatki

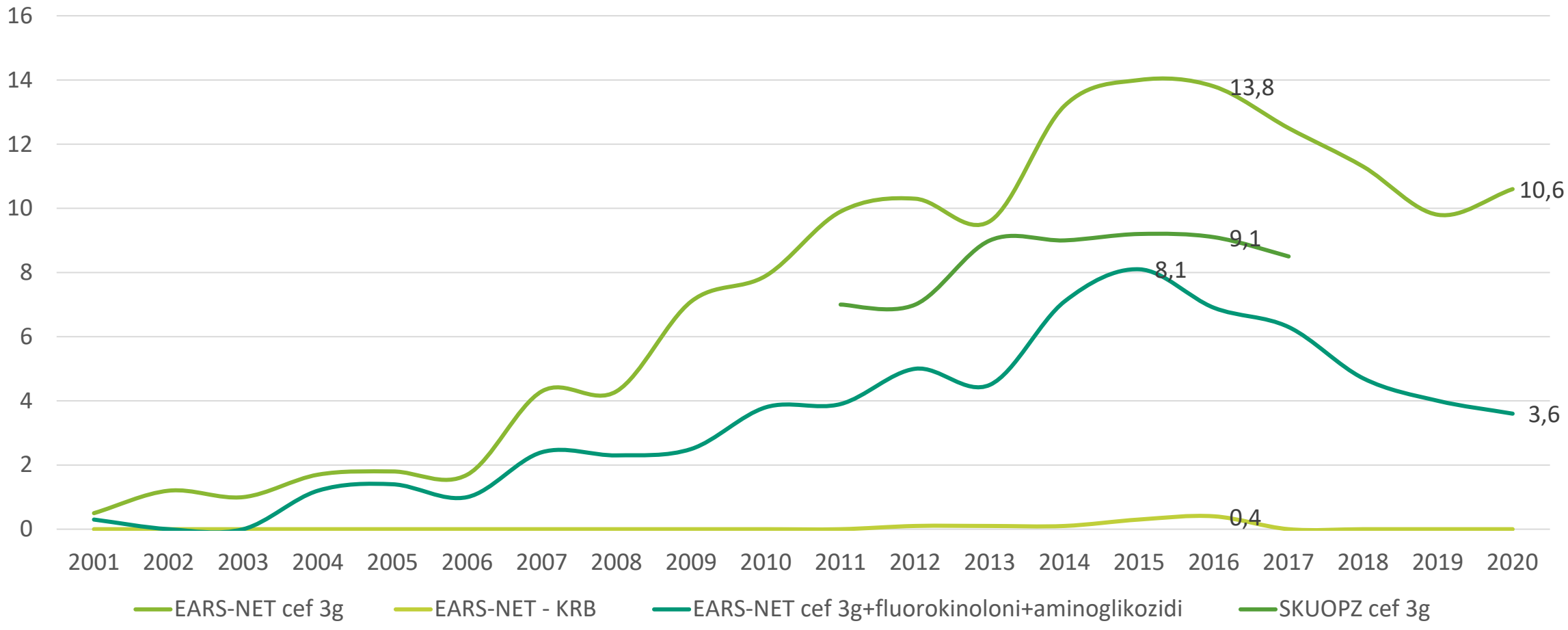


EARS-Net / CAESAR 2020



EU/EEA Trend 2016-2020 ↓

EARS-NET SLOVENIJA: http://www.nijz.si/sl/ears-net-slovenija
SKUOPZ: http://www.imi.si/strokovna-zdruzenja/skuopz/skuopz



- Švedska - Nosilstvo ESBL v skupnosti / pri bolnikih z invazivnimi okužbami.

- Zdravi nosilci, kolonizirani z ESBL 4,7 %; večinoma malo patogeni sevi;
- Invazivne kužnine - prevladuje ST 131.

Journal of Antimicrobial Chemotherapy Advance Access published October 24, 2016

J Antimicrob Chemother
doi:10.1093/jac/dkw419

Journal of Antimicrobial Chemotherapy

Community carriage of ESBL-producing *Escherichia coli* is associated with strains of low pathogenicity: a Swedish nationwide study

Sofia Ny[1,2], Sonja Löfmark[1], Stefan Börjesson[3], Stina Englund[3], Maj Ringman[1], Jakob Bergström[1], Pontus Nauclér[4,5], Christian G. Giske[2,6*] and Sara Byfors[1]

[1]Public Health Agency of Sweden, Stockholm, Sweden; [2]Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Stockholm, Sweden; [3]National Veterinary Institute, Uppsala, Sweden; [4]Infectious Disease Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden; [5]Department of Infectious Diseases, Karolinska University Hospital, Stockholm, Sweden; [6]Department of Clinical Microbiology, Karolinska University Hospital, Stockholm, Sweden

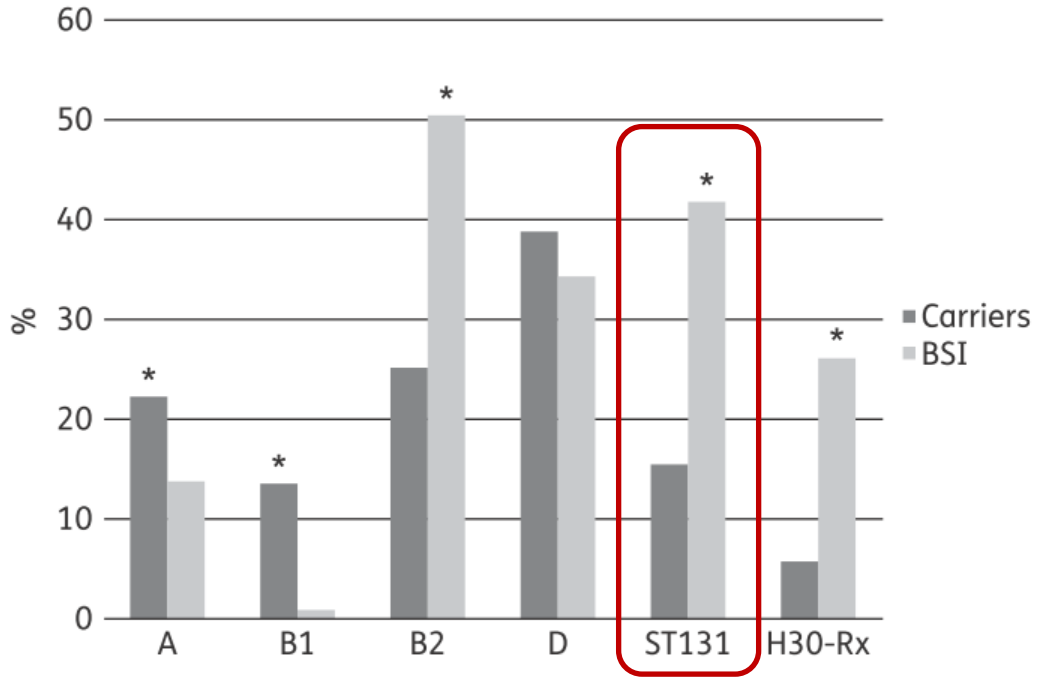


Figure 1. Distribution of phylogroups, ST131 and H30-Rx among ESBL- and pAmpC-producing *E. coli* isolates from BSI and carriers. Significant differences are marked with an asterisk. See Table 3 for statistical data.

World Health Organization

Antimicrobial resistance: global report on surveillance. 2014

Table 3 *Escherichia coli:* Resistance to third-generation cephalosporins[a] (summary of reported or published proportions of resistance, by WHO region)

Data sources based on at least 30 tested isolates[b]	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in invasive isolates[c] (no. of reports)
African Region		
– National data (n=13 countries)	2–70	28–36 (n=4)
– Publications (n=17) from 7 additional countries	0–87	0–17 (n=5)
Region of the Americas		
– National data or report to ReLAVRA (n=14 countries)	0–48	
– Publications (n=10) from 5 additional countries	0–68	
Eastern Mediterranean Region		
– National data (n=4 countries)	22–63	41 (n=1)
– Surveillance network in 1 country[d]	39 (caz)–50 (cro)	
– Publications (n=44) from 11 additional countries	2–94	11–33 (n=6)
European Region		
– National data or report to EARS-Net (n=35 countries)	3–82	3–43 (n=32)
– Publications (n=5) from 2 additional countries	0–8	0–8 (n=2)
South-East Asia Region		
– National data (n=5 countries)	16–68	
– Publications (n=26) from 2 additional countries	19–95	20–61 (n=2)
Western Pacific Region		
– National data (n=13 countries)	0–77	
– Institute surveillance (data from 3 hospitals in one country)	4–14	
– Publications (n=4) from 2 additional countries	8–71	

CMR
Journals.ASM.org

Trends in Human Fecal Carriage of Extended-Spectrum β-Lactamases in the Community: Toward the Globalization of CTX-M

October 2013

Paul-Louis Woerther,[a] Charles Burdet,[b,c] Elisabeth Chachaty,[a] Antoine Andremont[b]

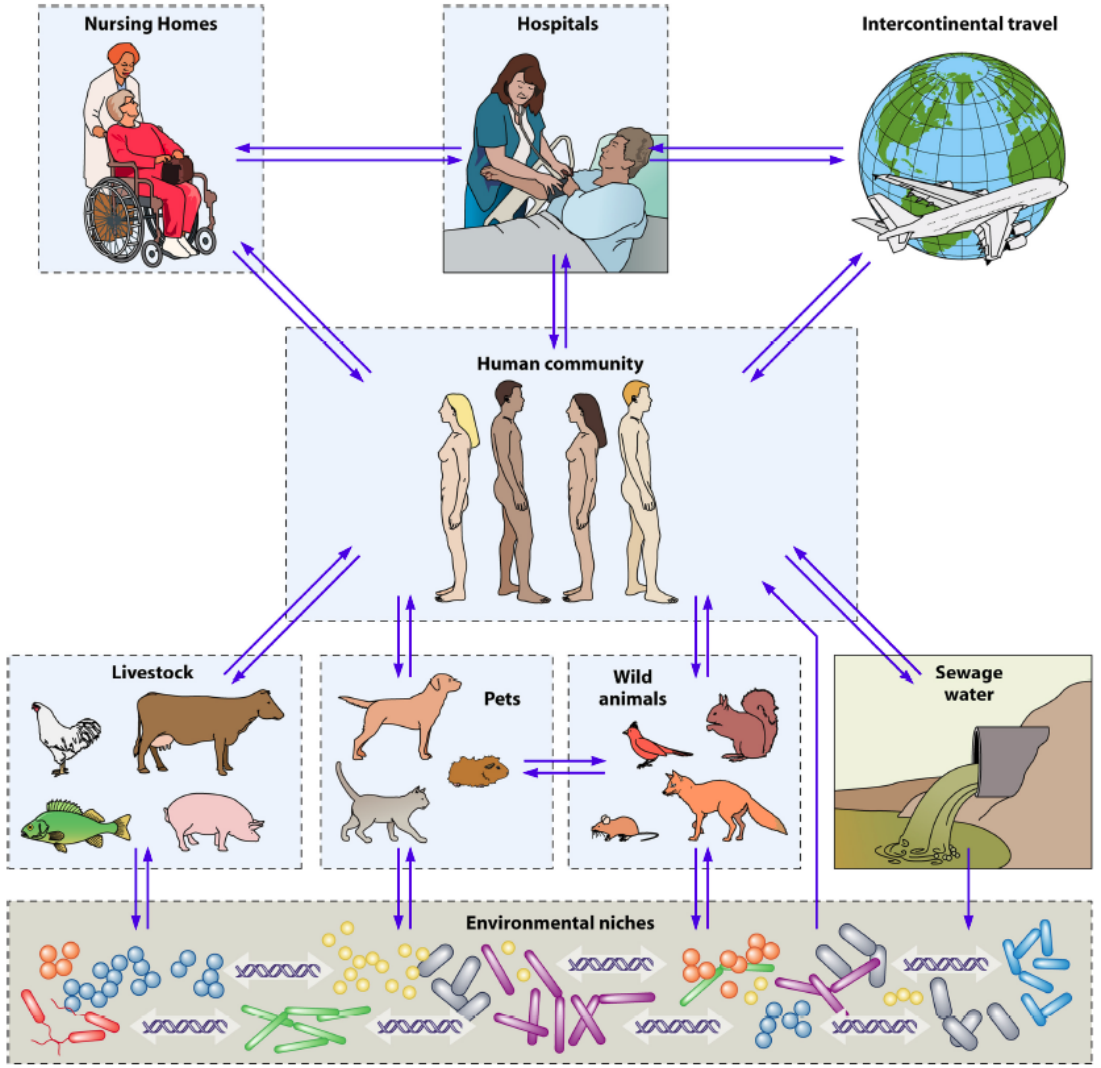


FIG 3 Representation of the main digestive or environmental reservoirs of ESBL-E to which the worldwide human community belongs and is also exposed. Each independent reservoir is included in a dashed black outline, inside which cross-transmission may occur. Arrows show the flux of ESBL-E from one reservoir to another. Environmental niches comprise mainly water, soils, and plants, where genetic material exchanges between bacteria of digestive and/or environmental origin occur.

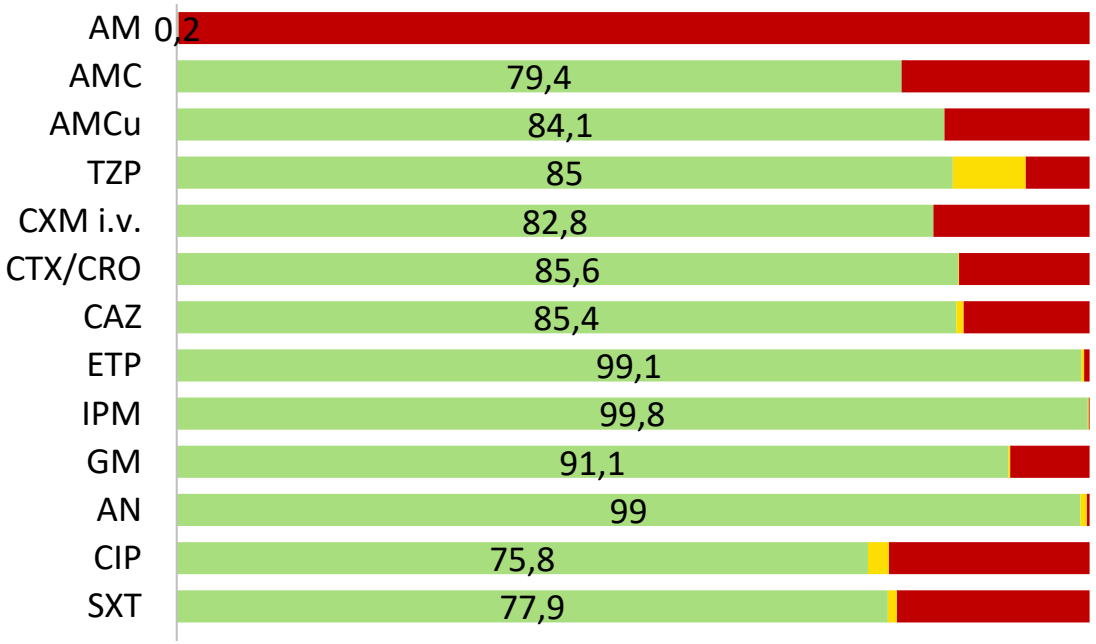
Znotraj gospodinjstva:

- **Pacient prenese ESBL na 67 % članov gospodinjstva.**
- **Navadno nosilstvo članov ni dolgotrajno.**

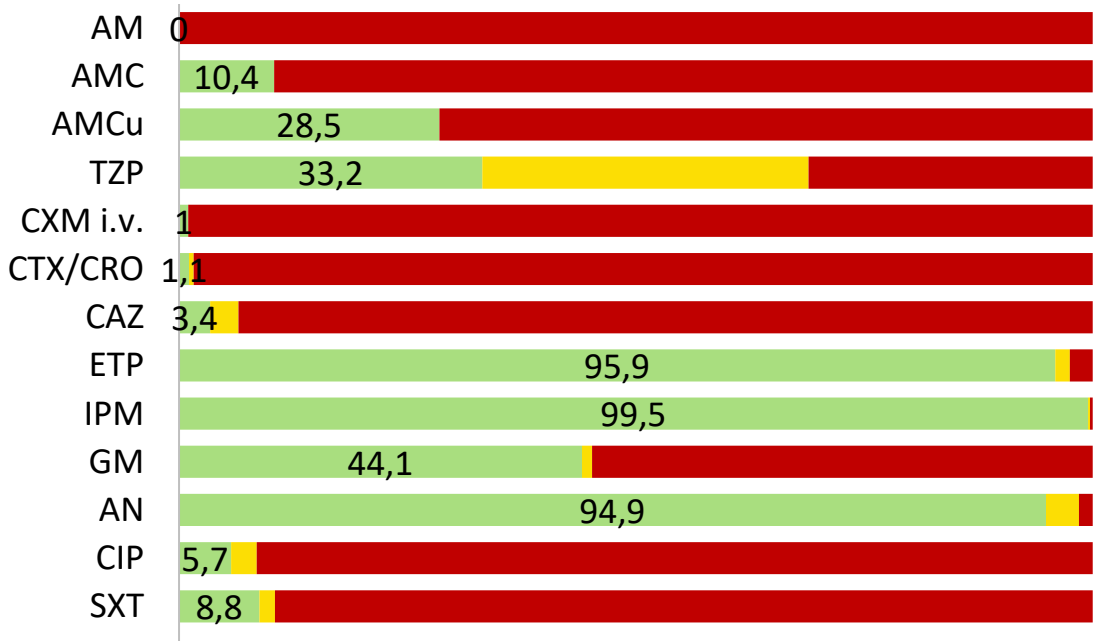
Haverkate MR, et al., Quantifying within-household transmission of extended-spectrum b -lactamase-producing bacteria, CMI 2016

Klebsiella pneumoniae

K. pneumoniae



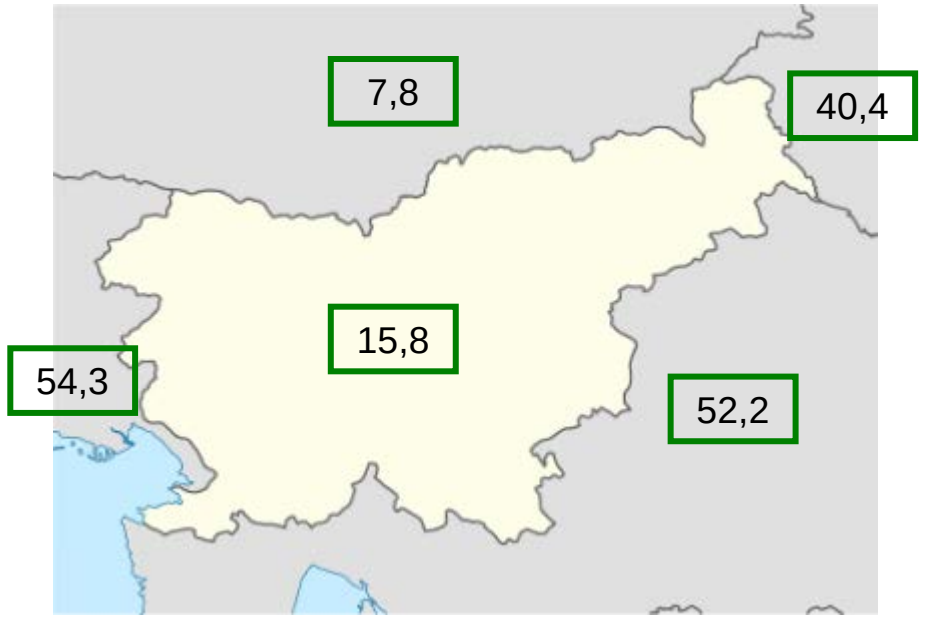
K. pneumoniae - ESBL



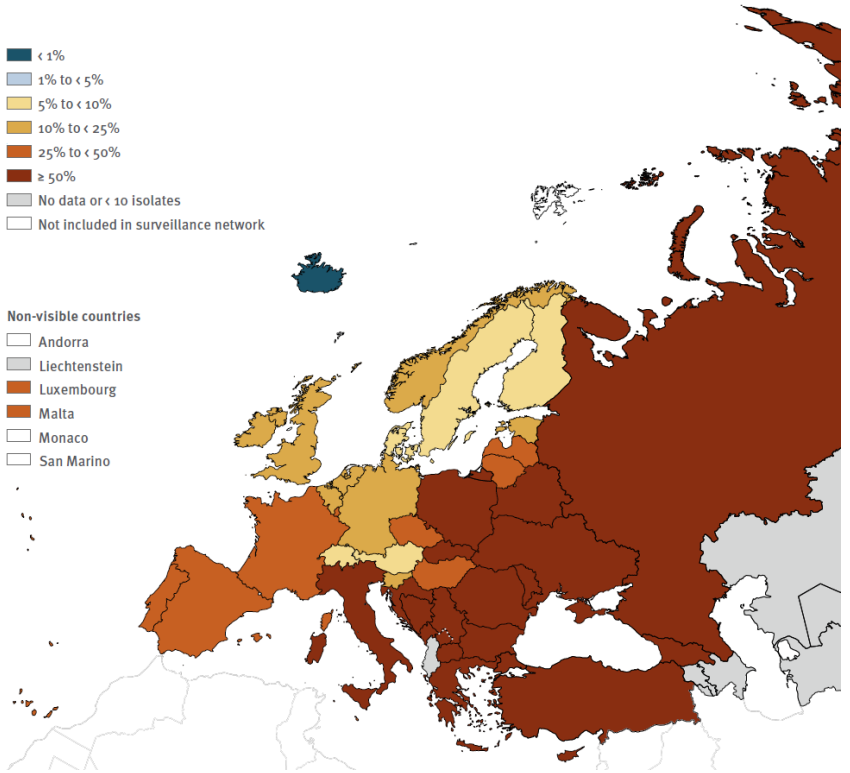
Vir: SKOUPZ 2017

Klebsiella pneumoniae - Cef3G NS

Lokalni podatki

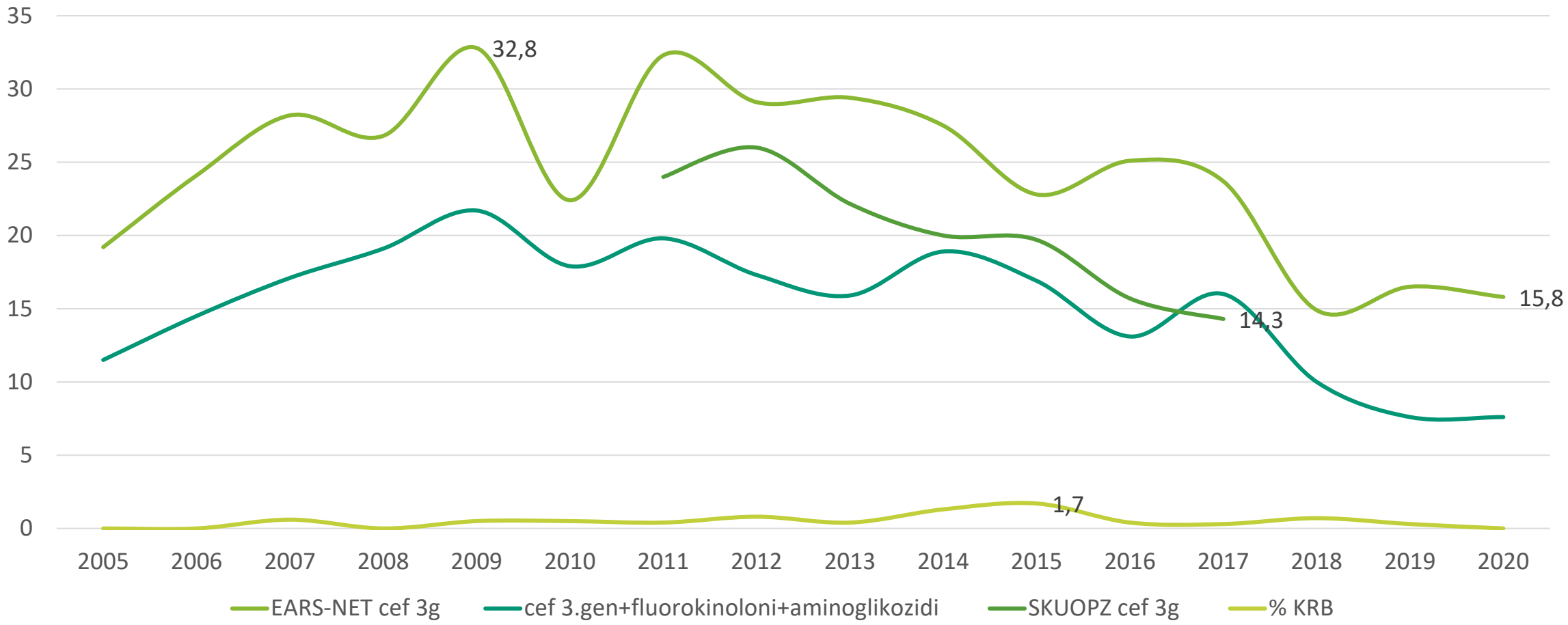


EARS-Net / CAESAR 2020

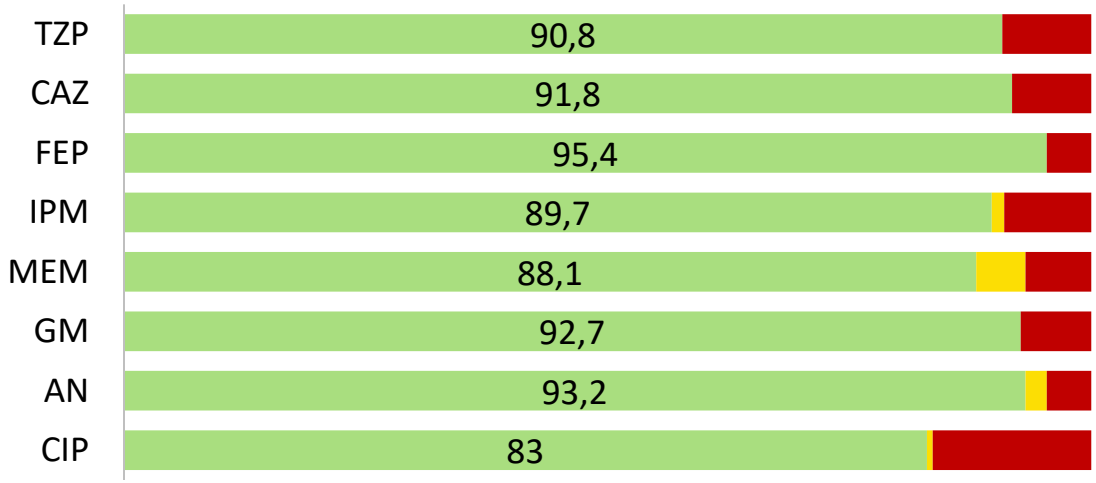


EU/EEA Trend 2016-2020 -

EARS-NET SLOVENIJA: http://www.nijz.si/sl/ears-net-slovenija
SKUOPZ: http://www.imi.si/strokovna-zdruzenja/skuopz/skuopz

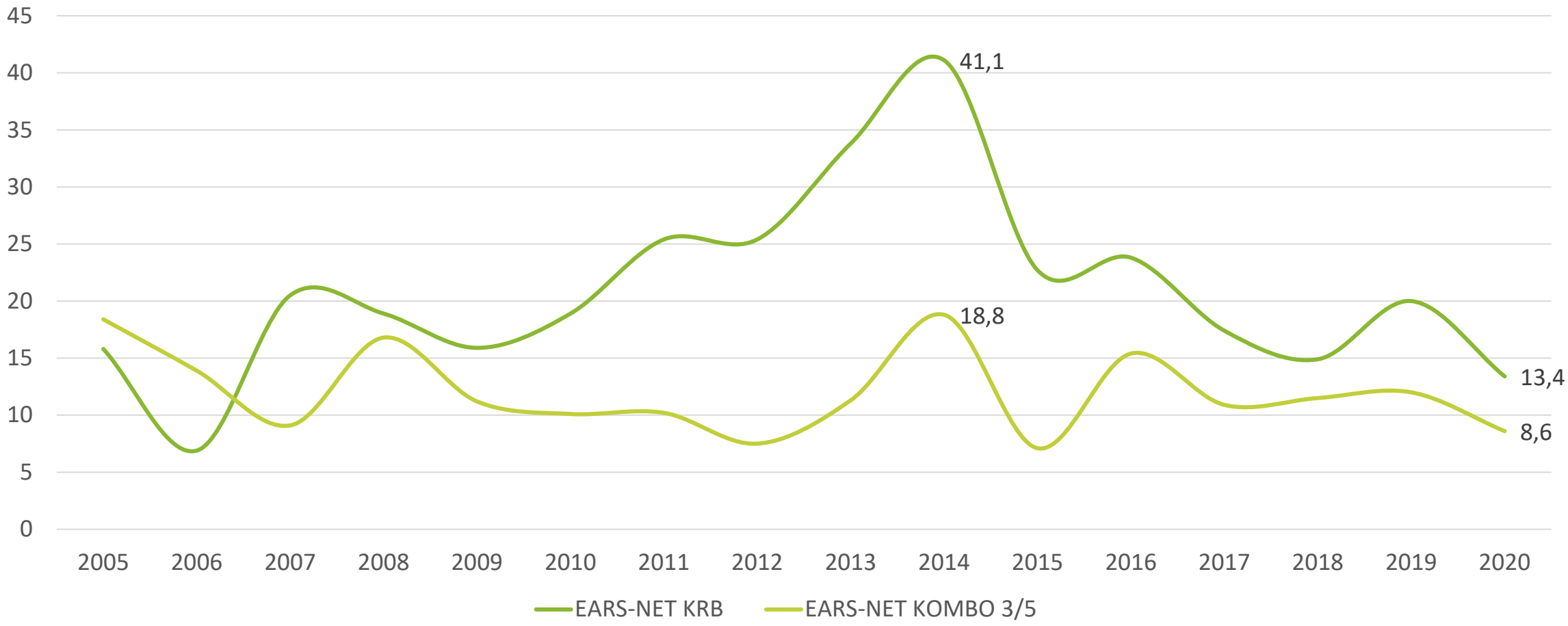


Pseudomonas aeruginosa



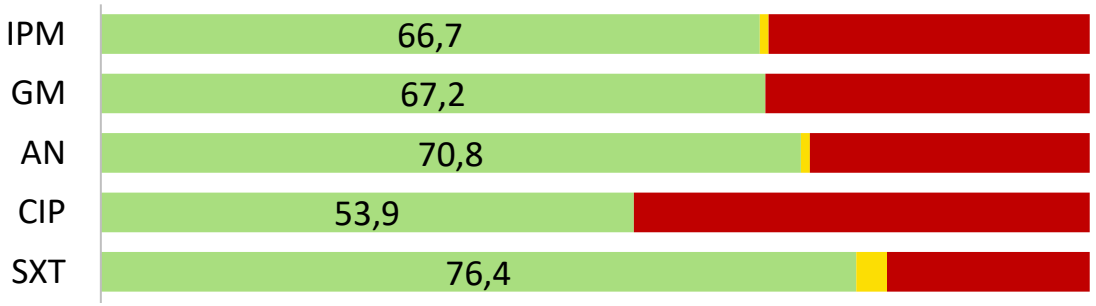
- Ni večjih sprememb
- Problem so izolati, odporni proti vsem BL antibiotikom (lahko tudi drugim razredom), nekateri izločajo karbapenemaze VIM,
- Občutljivost za protipseudomonasne cefalosporine je boljša kot občutljivost za karbapeneme.

EARS-NET SLOVENIJA: http://www.nijz.si/sl/ears-net-slovenija



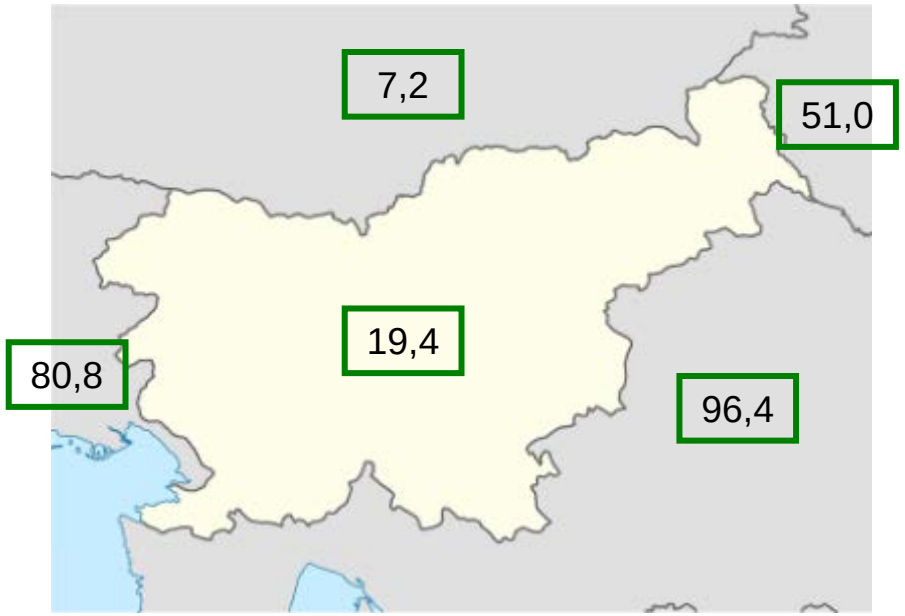
Acinetobacter baumannii

- Naraščajoč delež CRAb
- večkratno odporni izolati, ki izločajo karbapenemaze (OXA-40/OXA-23), pogosto odporni tudi proti drugim antibiotičnim razredom
- V več regijah, različno pogosti.

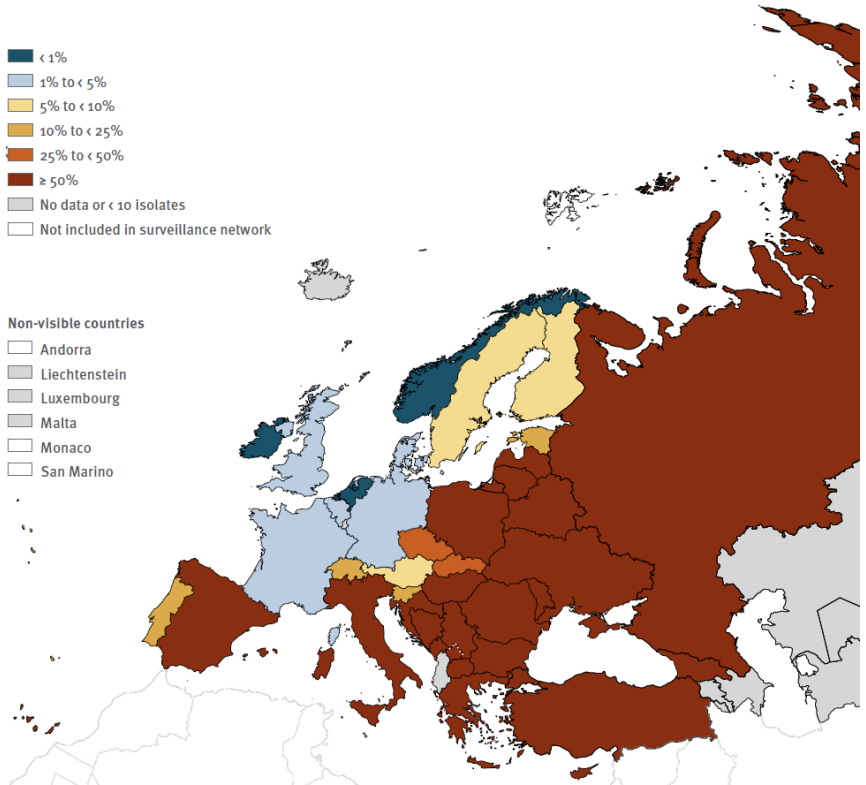


Acinetobacter spp. - CRAb

Lokalni podatki

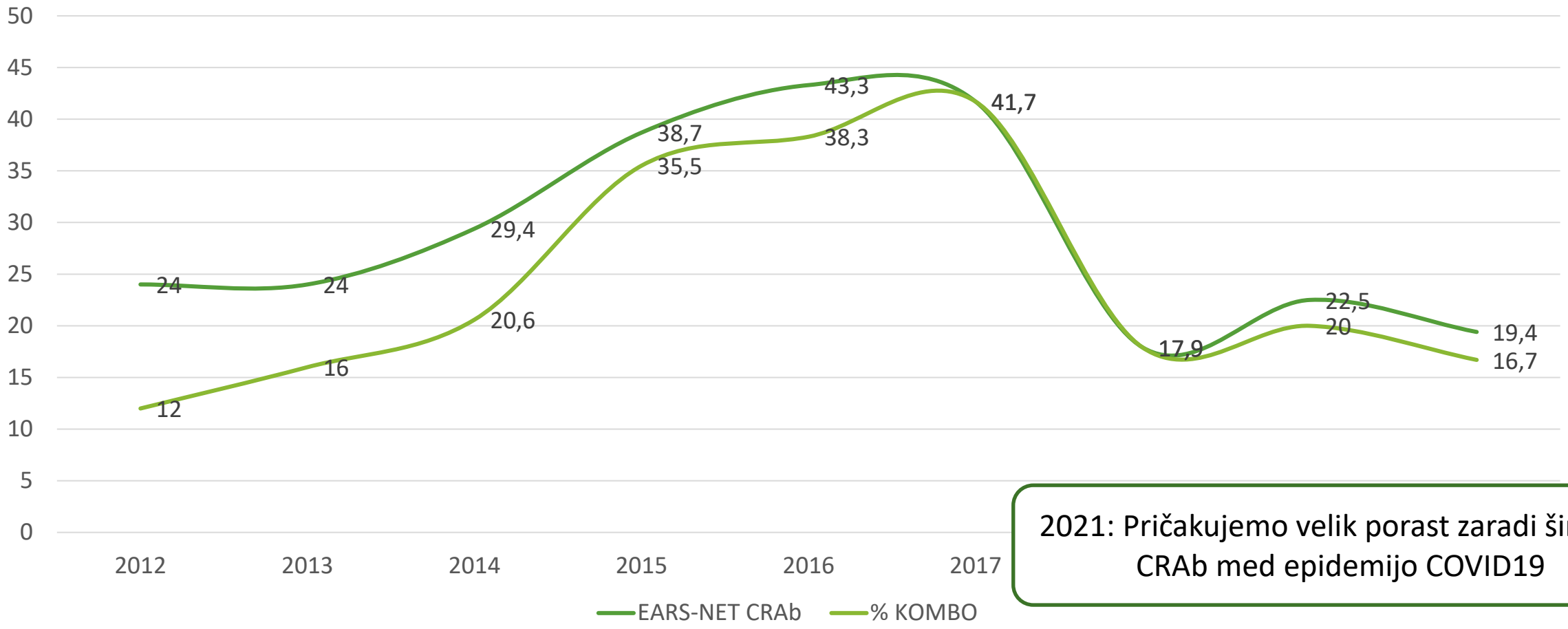


EARS-Net / CAESAR 2020



EU/EEA Trend 2015-2019 -

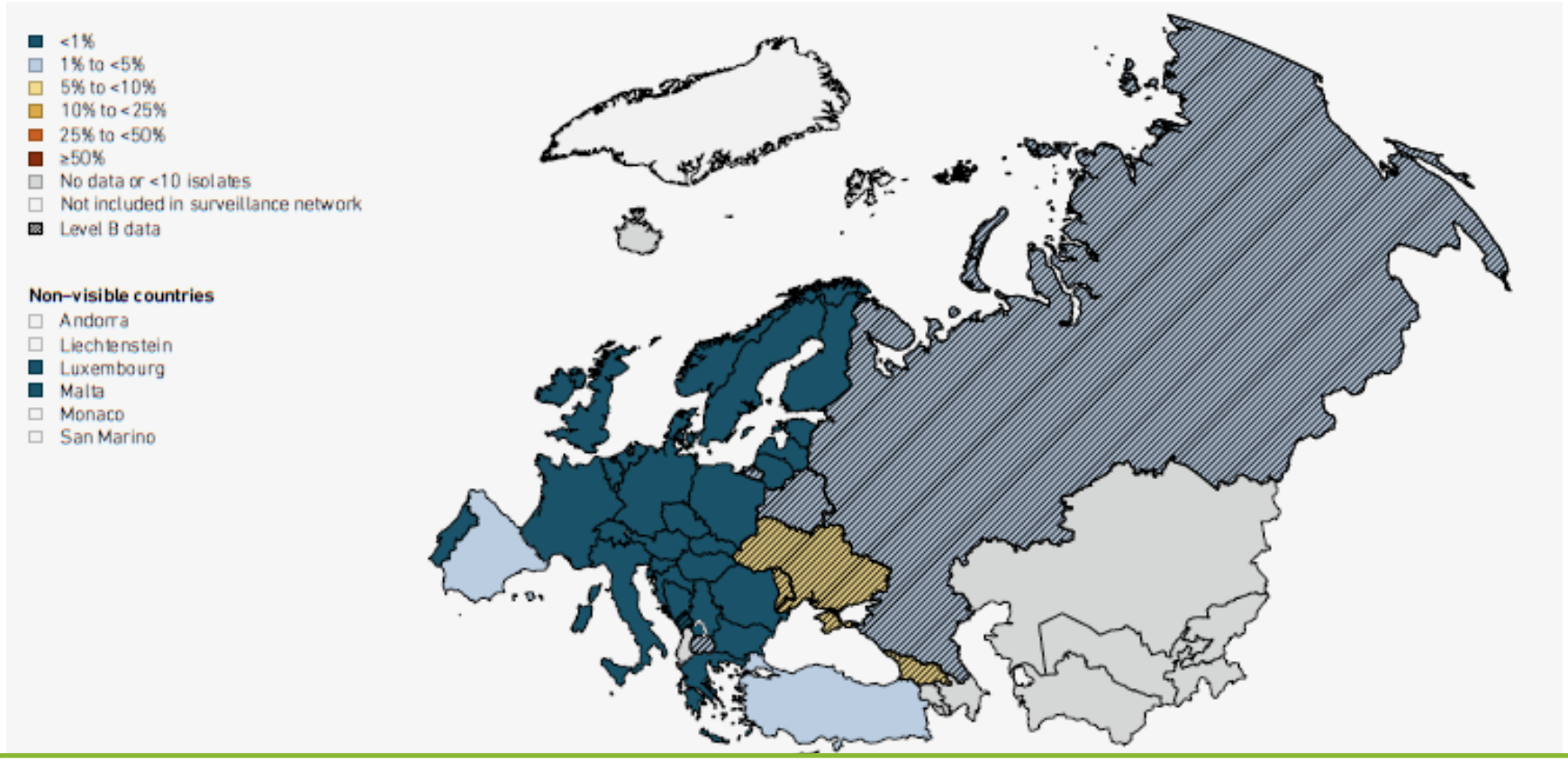
EARS-NET SLOVENIJA: http://www.nijz.si/sl/ears-net-slovenija



2021: Pričakujemo velik porast zaradi širjenja CRAb med epidemijo COVID19

E. coli - CRE

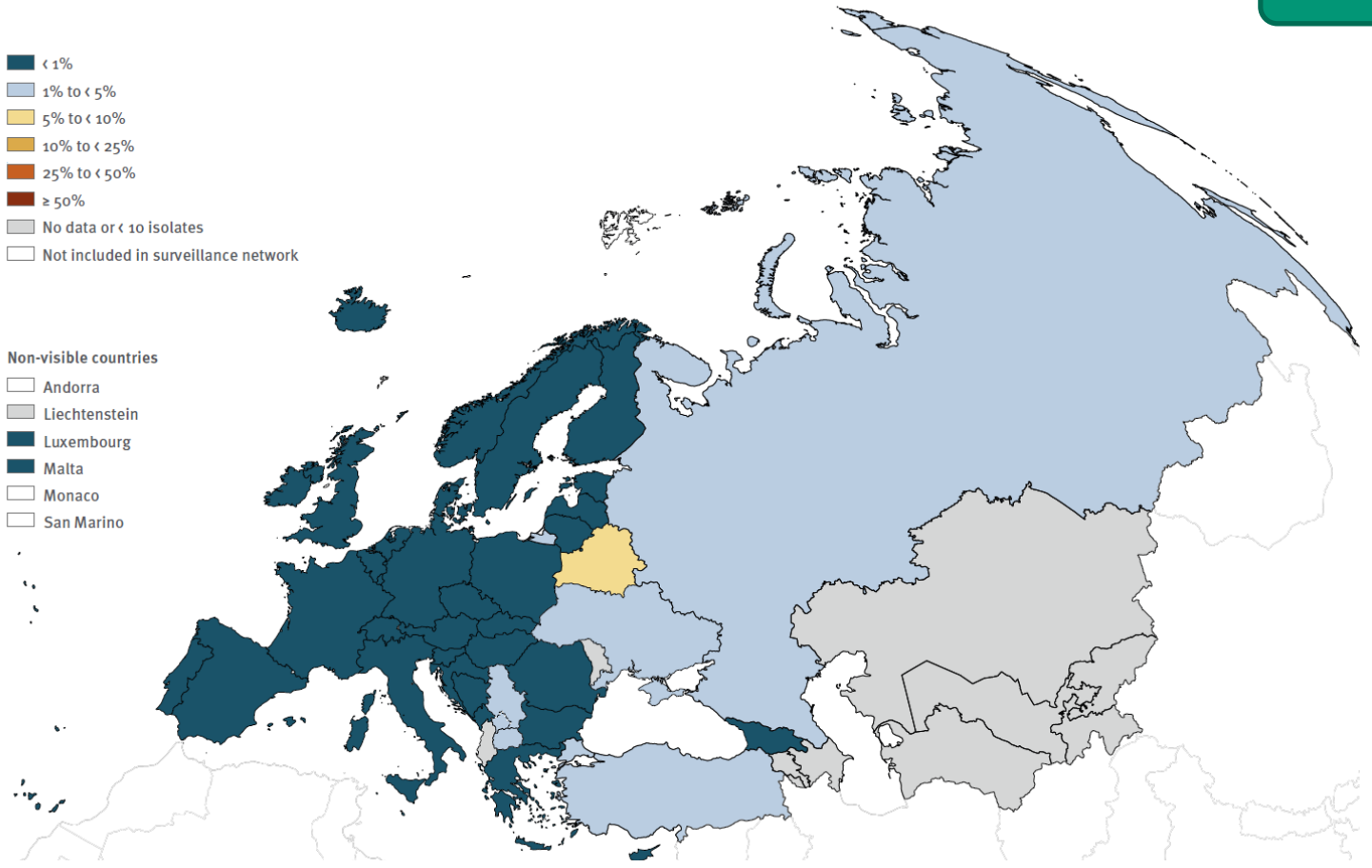
2019



The recent emergence of *E. coli* – CRE is of serious concern. Belarus (4%), Georgia (8%), North Macedonia (1%), the Republic of Moldova, the Russian Federation (S%), Spain (1,6%), Turkey (3%) and Ukraine (6%) reported resistance proportions of 1% or higher in 2019.

E. coli - CRE

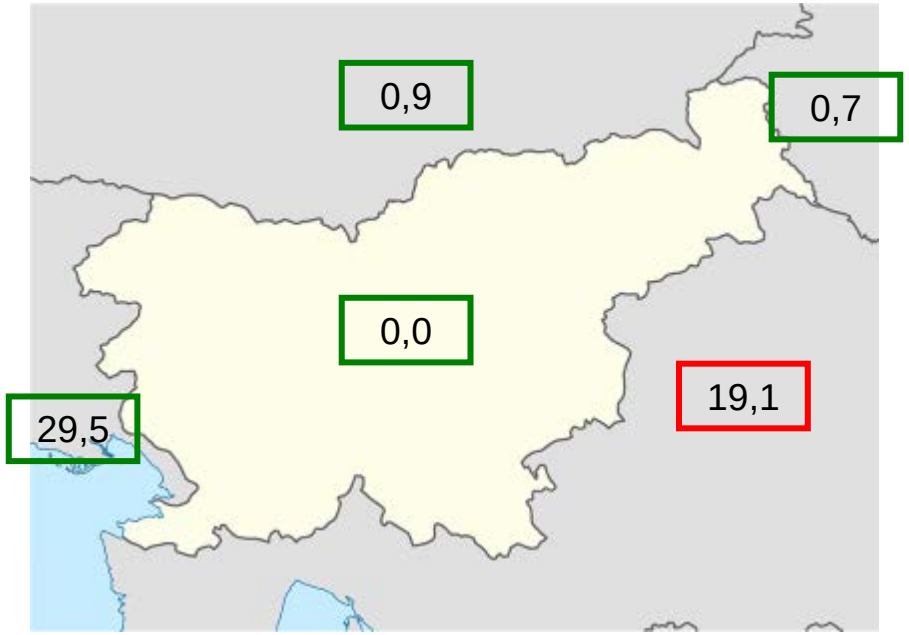
2020



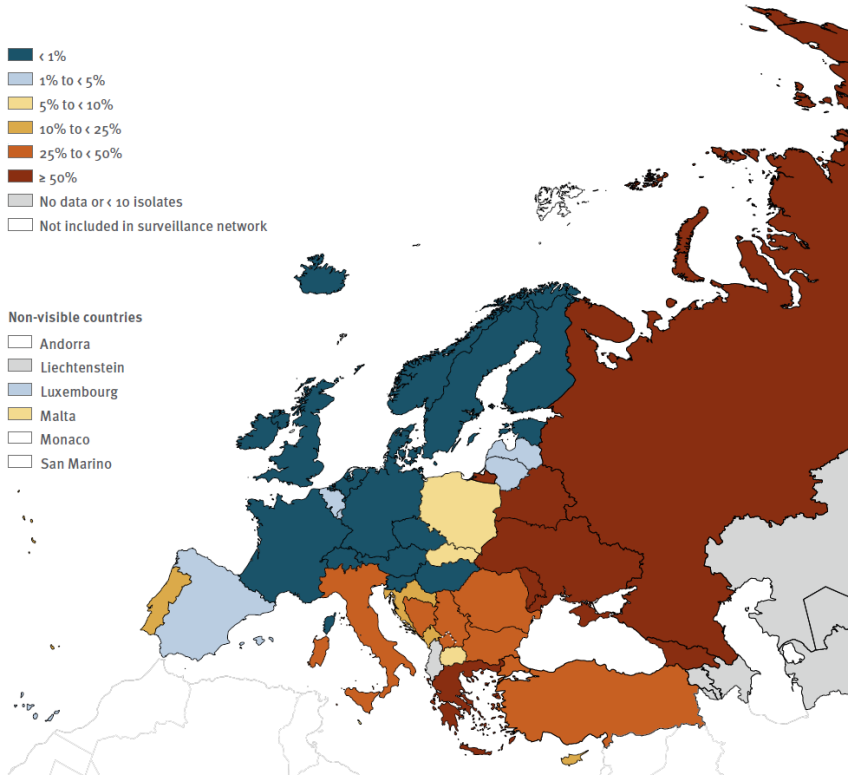
Bacterial species	Antimicrobial group/agent	2016		2017		2018		2019		2020		2020 EU/EEA countryrange[a]	Trend 2016–2020[b]
		N	%	N	%	N	%	N	%	N	%		
E. coli	Aminopenicillin (amoxicillin/ampicillin) resistance	86 625	58.4	97 219	58.1	104 198	57.0	102 375	56.6	105 827	54.6	34.1–67.5	⇣
	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	102 098	15.7	112 659	15.6	124 043	15.7	131 325	15.6	137 465	14.9	5.8–41.4	⇣
	Carbapenem (imipenem/meropenem) resistance	99 675	0.1	110 364	0.1	120 228	0.1	127 262	0.3	134 032	0.2	0.0–0.8	⇡

Klebsiella pneumoniae - CRE

Lokalni podatki



EARS-Net / CAESAR 2020



EU/EEA Trend 2016-2020 ↑ (10%)

1. izbruh CPE

- 40 znanih bolnikov v UKCL
- Okužbe ali kolonizacije s CPE

- 5 bolnikov premeščenih v druge bolnišnice (v štirih regijah)
- vsaj 2 bolnika → prehodna hospitalizacija na negovalnih oddelkih
- 4 → DSO
- Vsaj 2 bolnika → zdravilišče.

8

kri	urin	Spodnja dihala	Rane/tkivo	Abdominalna/plevralna votlina	črevesje
3 (7,5%)*	10 (25%)	8 (20%)	5 (12,5%)	2 (5%)	36 (90%)*
*2 KPN-OXA48 1 PM-NDM					*21 (52,5%) samo NDZ

Occurrence of carbapenemase-producing *Klebsiella pneumoniae* and *Escherichia coli* in the European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE): a prospective, multinational study

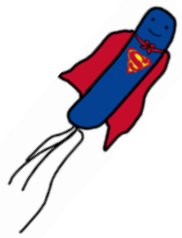
Lancet Infect Dis 2016
Published Online
November 17, 2016

- **E. coli – CRE**:
  - KPC 7,2%, NDM 10,3%, VIM 0%, OXA-48 22,2% (other 60,3%)

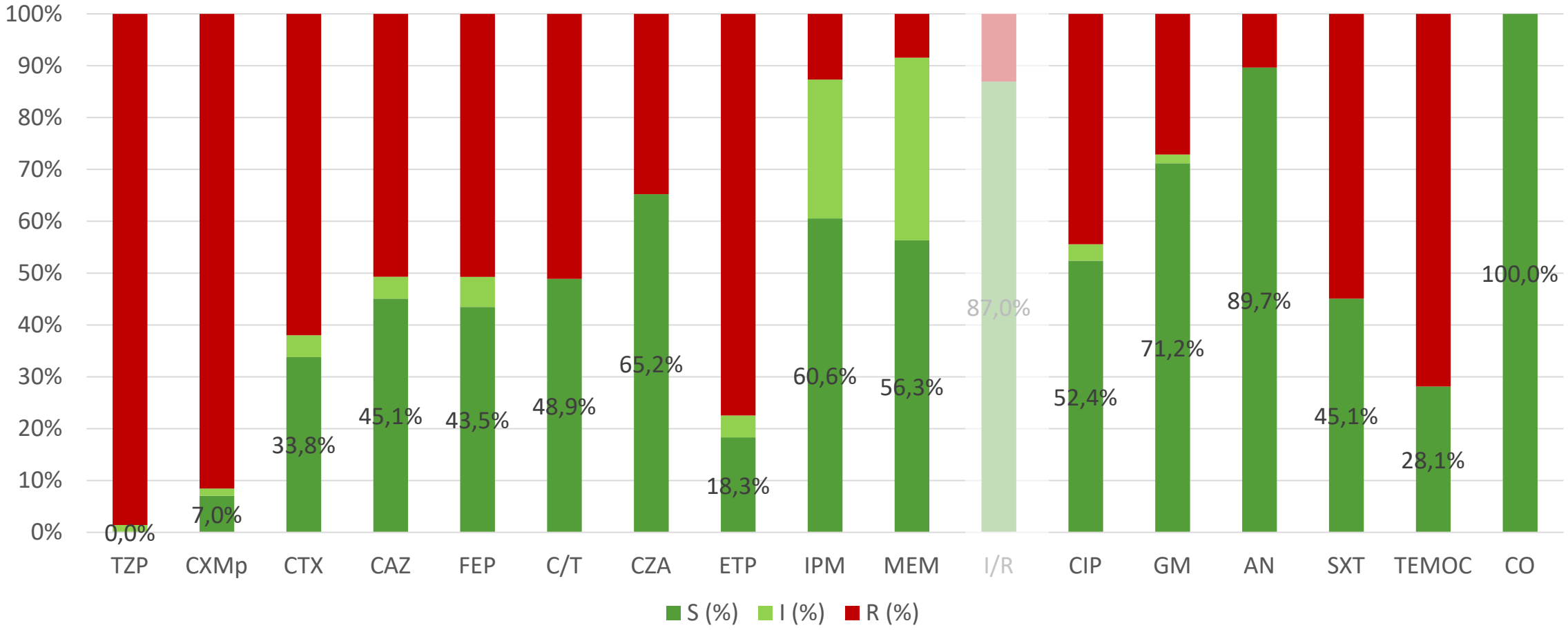
ceftazidim/avibactam
Imipenem/relebaktam

- **K. pneumoniae – CRE**:
  - KPC 31,5%, NDM 7,7%, VIM 5,7%, OXA-48 25,8% (other 29,3%)

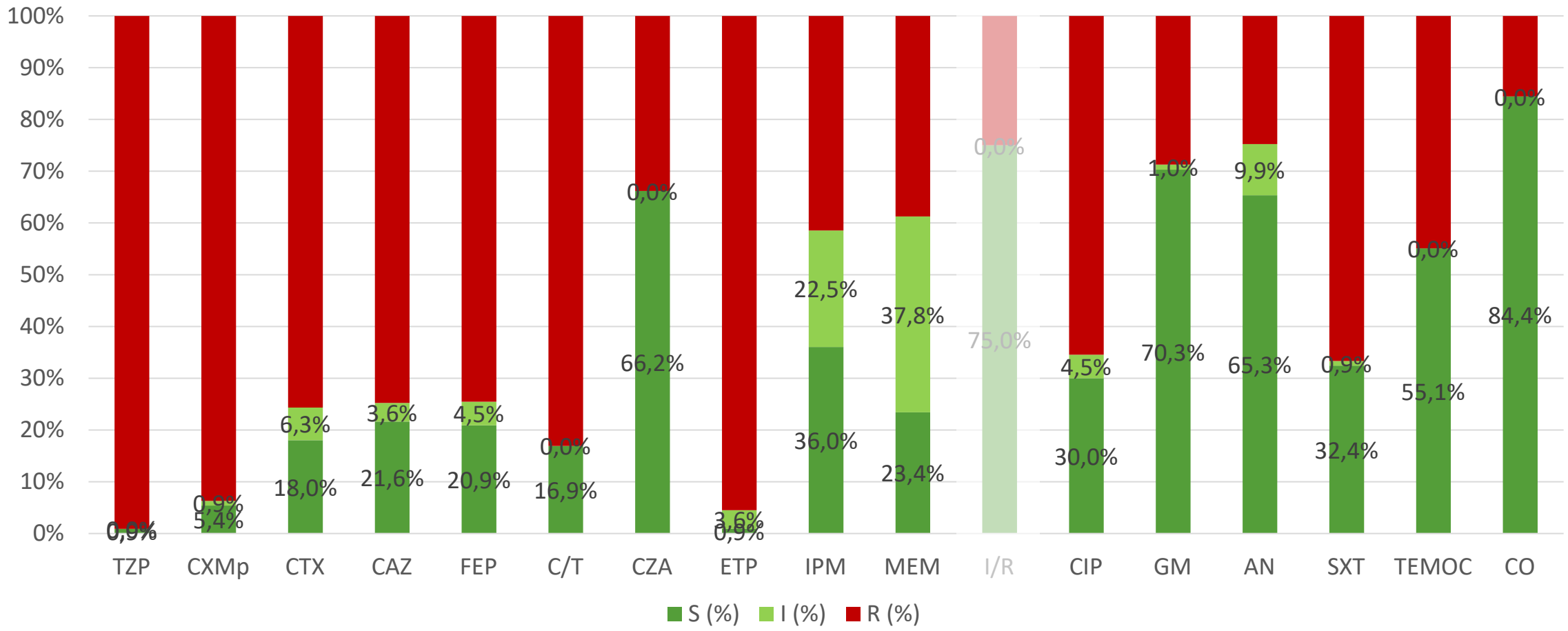
- **CRE – CPE**:
  - Izolati so običajno XDR – odporni proti BL, FQ, TMP/SXT
  - kolistin 28,3% R
  - fosfomicin: 54% R
  - tigecicline: 5,2% R
  - **Pan-rezistentni izolati: 9,3%**

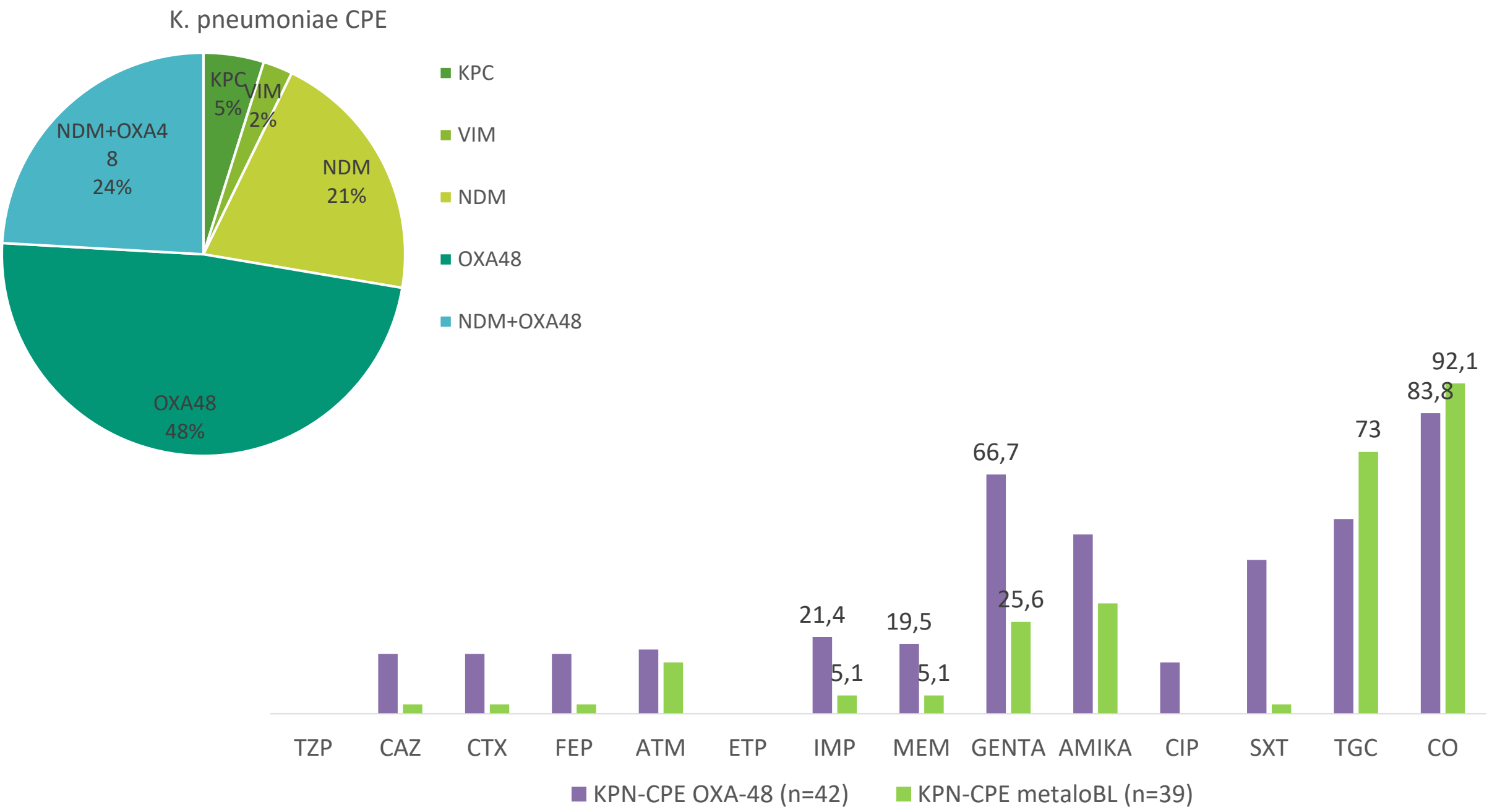


E. coli CRE+/-CPE N=71
klinični + nadzorni primoizolati

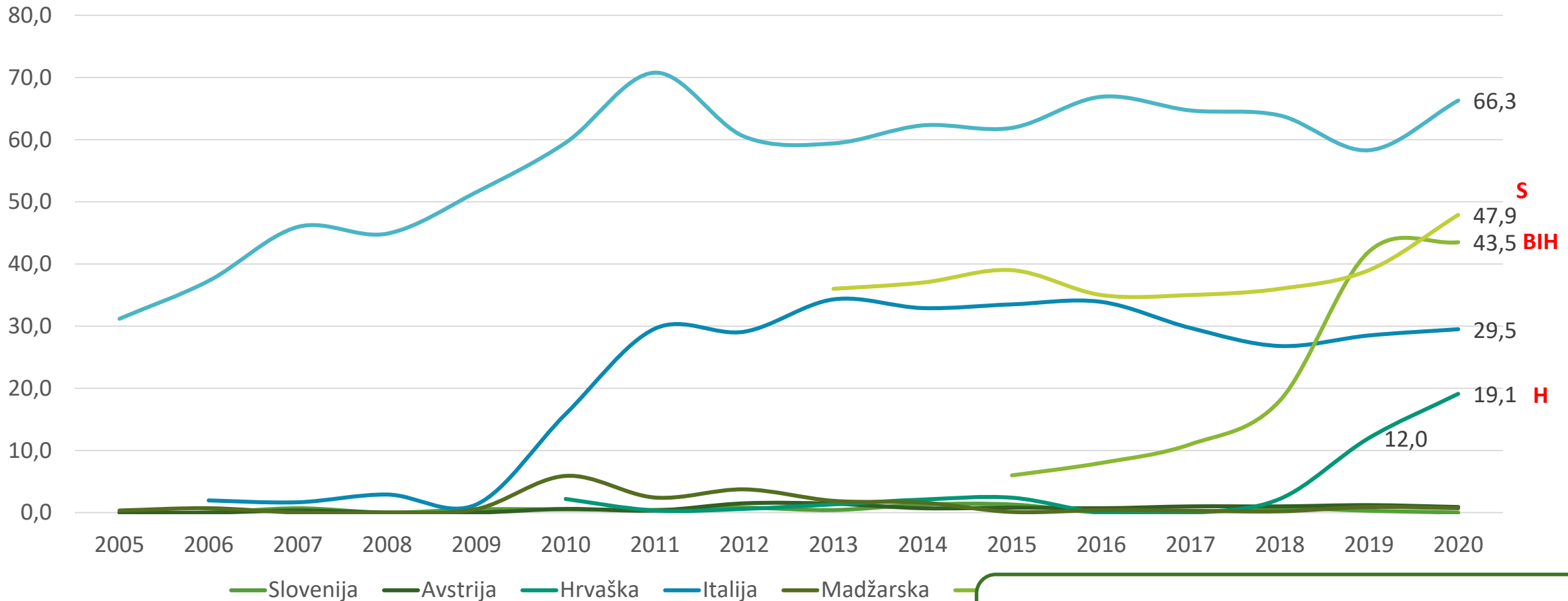


K. pneumoniae CRE+/-CPE N=111
klinični + nadzorni primoizolati




K. pneumoniae CPE
KPC 5%
VIM 2%
NDM 21%
OXA48 48%
NDM+OXA48 24%
KPC
VIM
NDM
OXA48
NDM+OXA48
21,4
5,1
19,5
5,1
66,7
25,6
73
83,8
92,1
TZP
CAZ
CTX
FEP
ATM
ETP
IMP
MEM
GENTA
AMIKA
CIP
SXT
TGC
CO
KPN-CPE OXA-48 (n=42)
KPN-CPE metaloBL (n=39)

Klebsiella pneumoniae - CRE



2021: Pričakujemo porast zaradi širjenja KPN-CRE med epidemijo COVID19

Household transmission of carbapenemase-producing Enterobacteriaceae: a prospective cohort study

J Antimicrob Chemother 2021; **76**: 1299–1302
doi:10.1093/jac/dkaa561 Advance Access publication 8 January 2021

Objectives: To estimate the transmission rate of carbapenemase-producing Enterobacteriaceae (CPE) in households with recently hospitalized CPE carriers.

Methods: We conducted a prospective case-ascertained cohort study. We identified the presence of CPE in stool samples from index subjects, household contacts and companion animals and environmental samples at regular intervals. Linked transmissions were identified by WGS. A Markov model was constructed to estimate the household transmission potential of CPE.

Results: Ten recently hospitalized index patients and 14 household contacts were included. There were seven households with one contact, two households with two contacts, and one household with three contacts. Index patients were colonized with $bla_{\text{OXA-48-like}}$ ($n=4$), $bla_{\text{KPC-2}}$ ($n=3$), bla_{IMP} ($n=2$), and $bla_{\text{NDM-1}}$ ($n=1$), distributed among divergent species of Enterobacteriaceae. After a cumulative follow-up time of 9.0 years, three family members (21.4%, 3/14) acquired four different types of CPE in the community (hazard rate of 0.22/year). The probability of CPE transmission from an index patient to a household contact was 10% (95% CI 4%–26%).

Conclusions: We observed limited transmission of CPE from an index patient to household contacts. Larger studies are needed to understand the factors associated with household transmission of CPE and identify preventive strategies.

Household transmission of NDM-producing *E. coli* in New Zealand

Matthew R Blakiston, Helen Heffernan, Sally A Roberts, Joshua T Freeman

ABSTRACT

This report describes the introduction of an extensively antibiotic-resistant carbapenemase-producing *Escherichia coli* into a hospital in Auckland, New Zealand, by a patient who was a household contact of recent travellers to the Indian subcontinent. The carbapenemase was identified as New Delhi metallo-β-lactamase (NDM) and reflects probable household transmission in the context of a recent upsurge in NDM-producing *Enterobacteriaceae* isolation in New Zealand. The observations in this report suggest that hospital screening practices to identify carbapenemase-producing *Enterobacteriaceae* (CPE) colonised patients may need to be extended to include travellers to high-risk countries who were not hospitalised during their trip, and possibly also their close contacts.

Risk factors for acquisition of multidrug-resistant Enterobacterales among international travellers: a synthesis of cumulative evidence

Results: A total of 20 studies (5253 travellers from high-income countries) were included in the meta-analysis. South Asia [58.7%; 95% confidence interval (CI), 44.5–72.5%] and Northern Africa (43.9%; 95% CI 37.6–50.3%) were the travel destinations with the highest proportion of MRE acquisition. Inflammatory bowel disease (OR 2.1; 95% CI 1.2–3.8), use of antibiotics (OR 2.4; 95% CI 1.9–3.0), traveller's diarrhoea (OR 1.7; 95% CI 1.3–2.3) and contact with the healthcare system overseas (OR 1.5; 95% CI 1.1–2.2) were associated with MRE colonization. Vegetarians (OR 1.4; 95% CI 1.0–2.0) and backpackers (OR 1.5; 95% CI 1.2–1.8) were also at increased odds of MRE colonization. Few studies ($n = 6$) investigated preventive measures and found that consuming only bottled water/beverages, meticulous hand hygiene and probiotics had no protective effect on MRE colonization.

Conclusions: International travel is an important driver for MRE spread worldwide. Future research needs to identify effective interventions to reduce the risk of MRE acquisition as well as design strategies to reduce local transmission on return.

Carbapenemase-producing Enterobacterales and vancomycin-resistant *Enterococcus faecium* carriage in patients who have traveled in foreign countries: A single center 5-year prospective study

Methods: From 2014 to 2018, patients who had travelled abroad in the previous year before their admission underwent microbiological screening and were pre-emptively isolated. Contact precautions were verified and CPE/VRE cross-transmission events investigated.

Results: Among 1,780 screened patients, 59 (3.3%) were colonized with CPE and/or VRE, of whom 17 (29.3%) (Table 1). Among the 17 carriers not hospitalized abroad, 16 carried only CPE and one only VRE. Among the patients hospitalized abroad, 11.5% were carriers versus 1.5% of the patients not hospitalized abroad ($P < 10^{-6}$).

Infection Control: Infection control

Importance of introduction of multidrug-resistant organisms to UMC Ljubljana by repatriates and foreign citizens – a 7-year retrospective analysis

M. Pirs[1], T. Lejko Zupanc[2], B. Beovic[3], B. ?nidar?ic[2], M. Mueller Premru[1]

[1]Faculty of Medicine, Institute of clinical microbiology and immunology, Ljubljana, Slovenia ; [2]University Medical Centre, Infection Control Unit, Ljubljana, Slovenia ; [3]University Medical Centre, Department of Infectious Diseases, Ljubljana, Slovenia

Methods: Retrospectiveanalysis of laboratory and patient data was performed for patients that were repatriated from foreign hospitals and foreign citizens treated at UMCbetween 2007 and November of 2013 that were colonized or infected with MDRO.

Results: Intotal, 100 patients, colonized or infected with MDRO, were repatriatesor foreign citizens. In 36 of them (36.0%)colonization or infection with multiple (up to 8) MDRO was noted, 17 (17.0%) were colonized or infected with two,12 (12.0%) with three, 2 (2%) with four, 4 (4.0%) with five MDRO, one patientwas colonized with 8 different MDRO (Table 1).ESBL-producing *Enterobacteriaceae*were founc

Table 1. MDRO isolated from repatriates and foreign citizens in UMC Ljubljana between 2007 to November 2013.

	SA-MRSA	VRE	ESBL	CPE	CRAb	PA – BLNS
No of patients (total)	39	7	62	7	20	6
Clinical samples	24	2	45	3	15	6
blood cultures	2	0	4	0	2	0
surveillance samples	34	6	51	6	11	1

SA-MRSA –methicillin-resistant *S. aureus*, VRE – vancomycin-resistant *E. faecium* or *E. faecalis*, CPE carbapenemase-producing *Enterobacteriaceae*, CRAb – carbapenem resistant *A. baumannii*, PA – BLNS - *P. aeruginosa* nonsusceptible to antipseudomonal betalactam antibiotics

Odpornost proti karbapenemom pri enterobakterijah in gramnegativnih nefermentativnih bacilih

MALO alternativnih zdravil:

- Usmerjeno zdravljenje → lahko zakasnela uvedba ustreznega antibiotika
- Problem odpornosti → XDR/PDR izolati

„Rezervni“ antibiotiki:

n

- Ceftolozan/tazobaktam (ne CP)
- Ceftazidim/avibactam (ne metaloK)
- Imipenem/relebaktam

Large Nosocomial Outbreak of Colistin-Resistant, Carbapenemase-Producing *Klebsiella pneumoniae* Traced to Clonal Expansion of an *mgrB* Deletion Mutant

Tommaso Giani,[a] Fabio Arena,[a] Guendalina Vaggelli,[b] Viola Conte,[a] Adriana Chiarelli,[a] Lucia Henrici De Angelis,[a] Rossella Fornaini,[c] Maddalena Grazzini,[d] Fabrizio Niccolini,[d] Patrizia Pecile,[b] Gian Maria Rossolini[a,b,e,f]

October 2015 Volume 53 Journal of Clinical Microbiology

TABLE 1 Observed BSI caused by *K. pneumoniae* during the study period[a]

Yr	No. of *K. pneumoniae* BSI	No. (%) of *K. pneumoniae* isolates that were:			
		Carbapenemase sensitive	Carbapenemase resistant[b]	COL^r CRKP[b,c]	Colistin consumption[d]
2009	29	28 (97)	1 (3)	0 (0; 0)	0.004
2010	49	38 (78)	11 (22)*	1 (3; 9)	0.013
2011	76	44 (58)	32 (42)*	4 (5; 12)	0.018
2012	128	46 (36)	82 (64)*	53 (41; 65)*	0.014
2013	93	32 (34)	61 (66)	35 (38; 57)	0.015
Total	375	188 (50)	187 (50)	93 (25; 50)	

[a] Numbers and proportions of BSI cases caused by carbapenem-susceptible, carbapenem-resistant, and carbapenem- and colistin-resistant (COL^r CRKP) strains. For patients with recurrent BSI episodes, only the first episode was considered.

[b] An asterisk indicates that the difference in the proportion of resistant isolates was statistically significantly different ($P < 0.05$) from that for the previous year. For statistical analysis, the chi-squared test with Yates' correction or Fisher's exact test (as appropriate) was used.

[c] Proportions are reported in relation to both *K. pneumoniae* BSI and CRKP BSI. (Values are shown in parentheses and separated by semicolons.) COL^r *K. pneumoniae* was only observed among CRKP cases.

[d] Data on colistin consumption in the hospital during the study period, expressed as the defined daily dose per 1,000 inhabitants per day, are also reported.

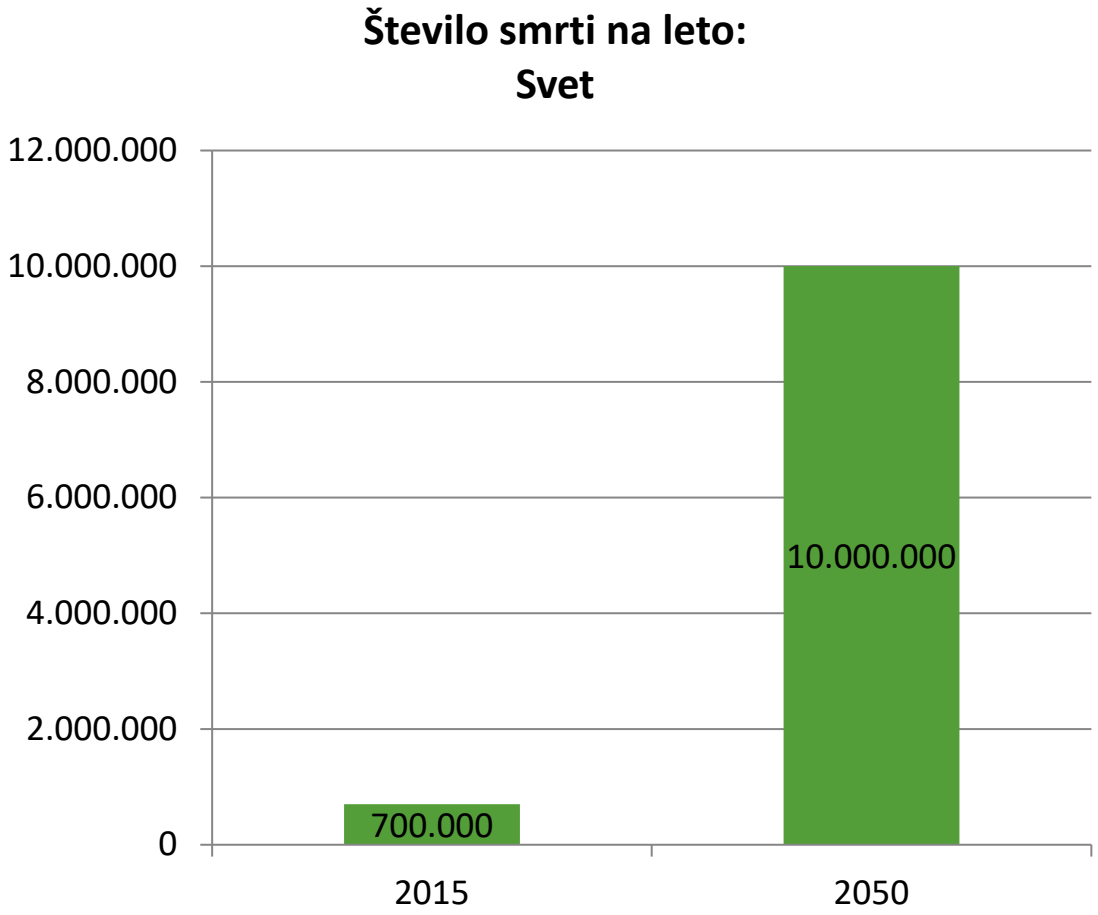
World Health Organization

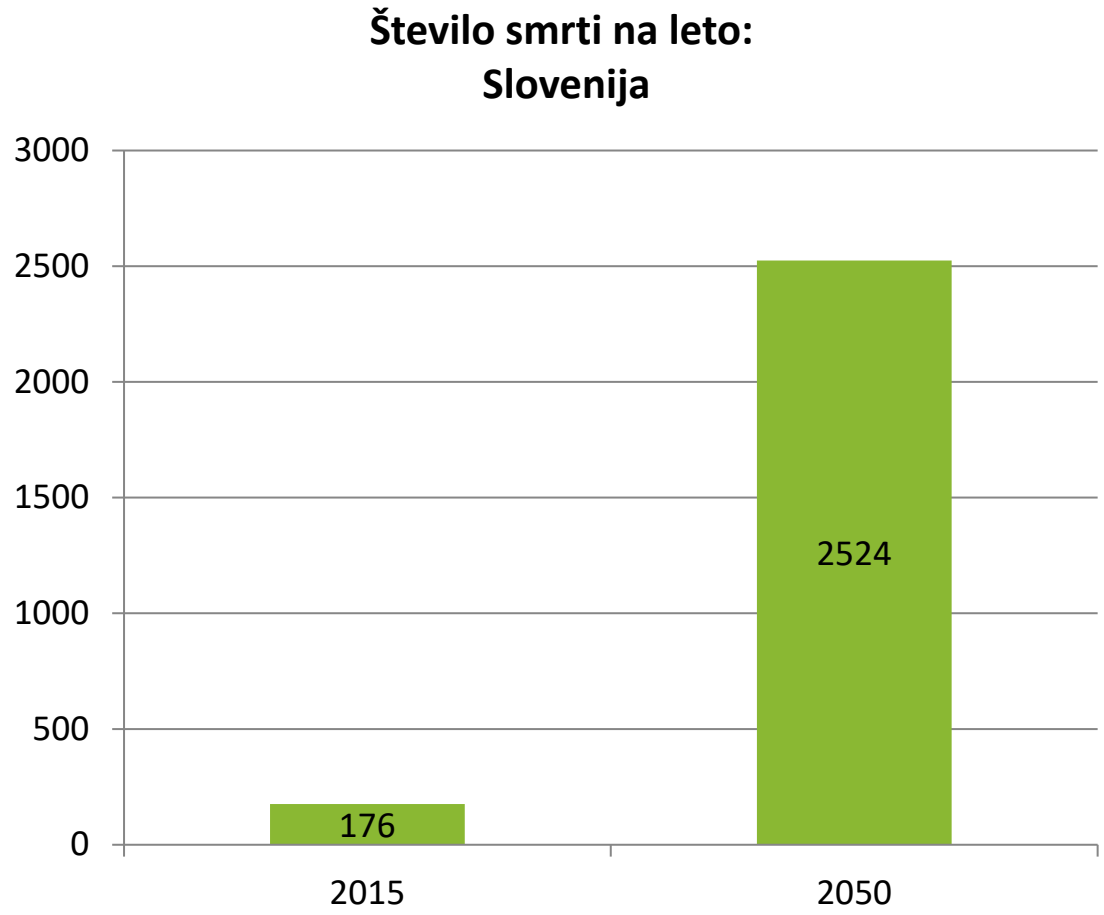
Antimicrobial resistance: global report on surveillance. 2014

Table 6 *Klebsiella pneumoniae:* **Resistance to carbapenems[a] (summary of reported or published proportions of resistance, by WHO region)**

Data sources based on at least 30 tested isolates[b]	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in invasive isolates[c] (no. of reports)
African Region		
– National data (n=4 countries)	0–4	
– Publications (n=0)		
Region of the Americas		
– National data or report to ReLAVRA (n=17 countries)	0–11	
– Publications (n=2) from 2 additional countries	0–2	
Eastern Mediterranean Region		
– National data (n=4 countries)	0–54	54 (n=1)
– Surveillance network[d] (n=1) in 1 additional country	6	
– Publications (n=9) from 5 additional countries	0–21	0 (n=1)
European Region		
– National data or report to EARS-Net (n=31 countries)	0–68	0–68 (n=30)
– Publications (n=3) from 2 additional countries	2–7	2 (n=1)
South-East Asia Region		
– National data (n=4 countries)	0–8	
– Publications (n=15) from 2 additional countries	0–55	0–52 (n=3)
Western Pacific Region		
– National data (n=9 countries)	0–8	
– Institute surveillance (data from 2 hospitals in 1 country)	0–1	
– Publications (n=2) from 2 additional countries	0–11	

Štrumbelj I. Strokovno srečanje ob Evropskem dnevu antibiotikov 2016: Število smrti zaradi odpornosti mikrobov na leto v Sloveniji - izračun po globalni projekciji UK Review on Antimicrobial Resistance (UK R AMR).

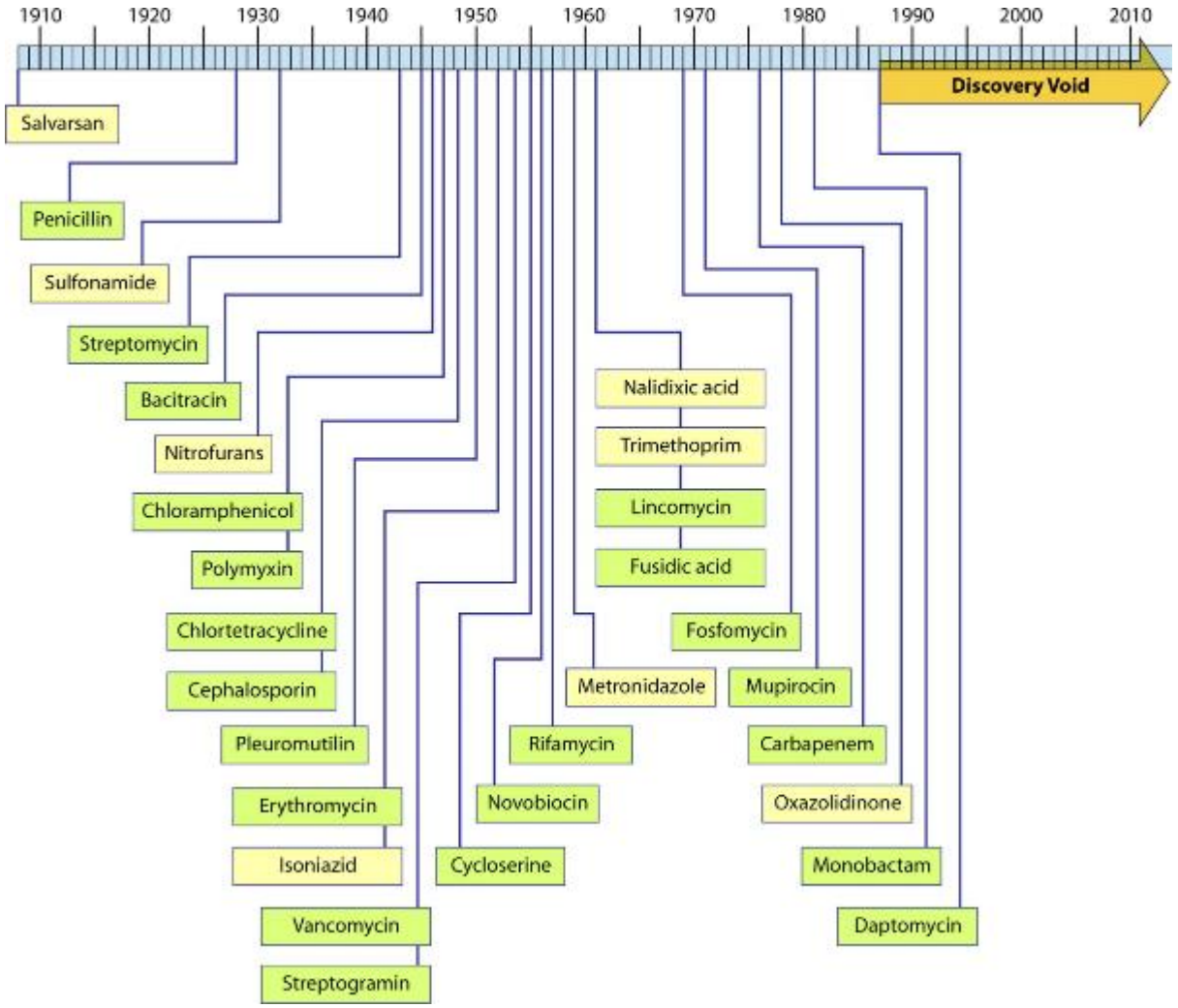




Predpostavka nespremenjenih globalnih trendov ter: izračun UK R AMR velja za vse države enako.
Glede na prebivalstvo, Svet 7.835.639.694, Slovenija 1.978.029 (0,025 %), vir CIA World Factbook.

V Sloveniji umre letno približno 19.000 ljudi.

Illustration of the “discovery void.” Dates indicated are those of reported initial discovery or patent.



Silver L L Clin. Microbiol. Rev. 2011;24:71-109

Kaj lahko naredimo?

- Za **upočasnitev porasta** odpornosti proti antibiotikom in **preprečevanje širjenja** večkratno odpornih bakterijskih klonov z visokim tveganjem za širjenje so bistvenega pomena:
  - **smotrna uporaba antibiotikov**
  - **dobra bolnišnična higiena:** higiena rok, aktivno iskanje nosilcev, ukrepi kontaktne izolacije, razkuževanje opreme in pripomočkov, ki pridejo v stik s koloniziranim bolnikom
  - **zmanjševanje možnost vnosa novih rezistenčnih determinant** iz bakterij okoljskega in živalskega izvora.

Primer 1 – vnos VOB iz tujine
mlajša bolnica iz Slovenije, Prometna nesreča v Srbiji, 14 dni hospitalizirana v UKC Beograd → premestitev v UKCL

Izolat	K. pneumoniae	P. stuartii	P.mirabilis	E.raffinosus	E.faecalis	E.faecium	S.aureus	A.baumannii
	- CRE	- CRE	- CRE	- VRE	- VRE	- VRE	- MRSA	- CRAb
oksacilin							R	
amoksicilin/klav.k.	R	R	R				R	
ampicilin/sulbakt.								R
piperacilin/tazob.	R	R	R					R
ceftazidim/cefotaksim	R	R	R					R
cefepim	R	R	R					
ertapenem	R	R	R					
imipenem	R	R	R					R
meropenem	R	R	R					
ciprofloksacin	R	R	R	S	R	R	R	R
amikacin	S	R	S					R
gentamicin	R	R	S				R	R
trimetoprim/sulfam.	R	R	R				S	
teikoplanin				I	R	R	S	
vankomicin				R	R	R	S	
kolistin	S	R	R					S
daptomicin							R	
linezolid				S	S	S	S	
rifampin				S	R	R	R	
tigeciklin	I	R	R					

Primer 2 – vnos VOB iz tujine

- Imunokompromitiran bolnik
- Bosna
- Črevesna kolonizacija:

  1. *E. faecium* - VRE

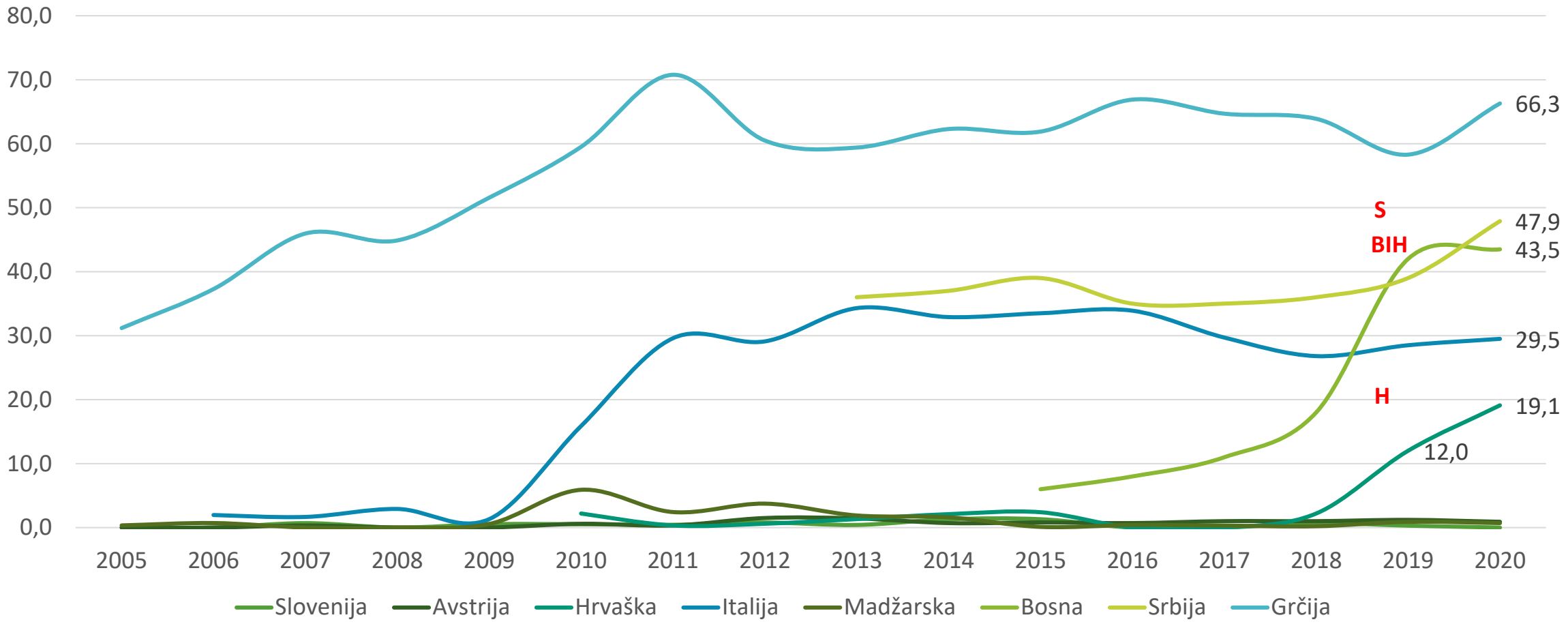
  2. *K. pneumoniae* – ESBL, CRE-CPE (**OXA-48**)

  3. *K. pneumoniae* – CRE-CPE (**NDM**)

1. ***Enterococcus faecium*** **- VRE**
2. ***Klebsiella pneumoniae*** **- ESBL, - CRE-CPE**
3. ***Klebsiella pneumoniae*** **- CRE-CPE**

	1.	2.	3.
penicilin			
ampicilin	R	R	R
oksacilin			
amoksicilin+klavulanska kislina		R	R
piperacilin+tazobaktam		R	R
cefuroksim (parenteralni)		R	R
cefotaksim		R	R
ceftriakson		R	R
ceftazidim		R	R
cefepim		R	R
cefiderocol		R	S
ceftolozan+tazobaktam		R >32/4	R >32/4
ceftazidim+avibaktam		S 1/4	R >16/4
ertapenem		R >2	R >2
meropenem		R 16	R >16
imipenem	R	R 8	R >16
imipenem+relebaktam		S 2/4	R 32/4
aztreonam		R	R 256
vankomicin	R 256		
teikoplanin	R 128		
gentamicin		R	S
gentamicin HL	HLR		
amikacin		R	I
eritromicin			
klindamicin			
tetraciklin			
ciprofloksacin		R	R
levofloksacin		R	R
trimetoprim+sulfametoksazol		R	R
rifampin			
linezolid	S		
tigeciklin	S	NI 0,5	NI 1
kolistin		S 0,5	S 0,5
kvinupristin+dalfopristin	S		
fosfomicin (parenteralni)		R 256	R 128
fucidinska kislina			
kloramfenikol		R >32	R >32

Klebsiella pneumoniae - CRE



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