



# **Odpornost bakterij proti antibiotikom v Sloveniji in po svetu**

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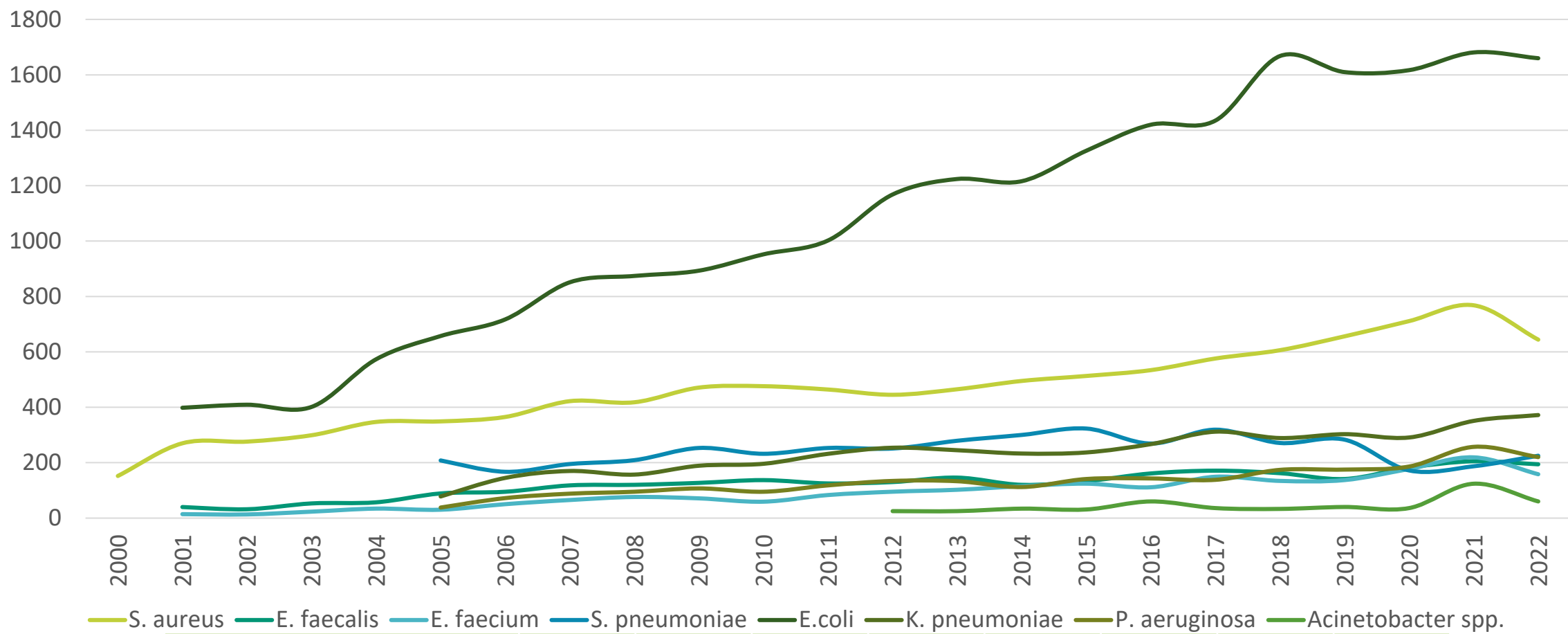
Inštitut za mikrobiologijo in imunologijo, UL MF



## Laboratoriji:

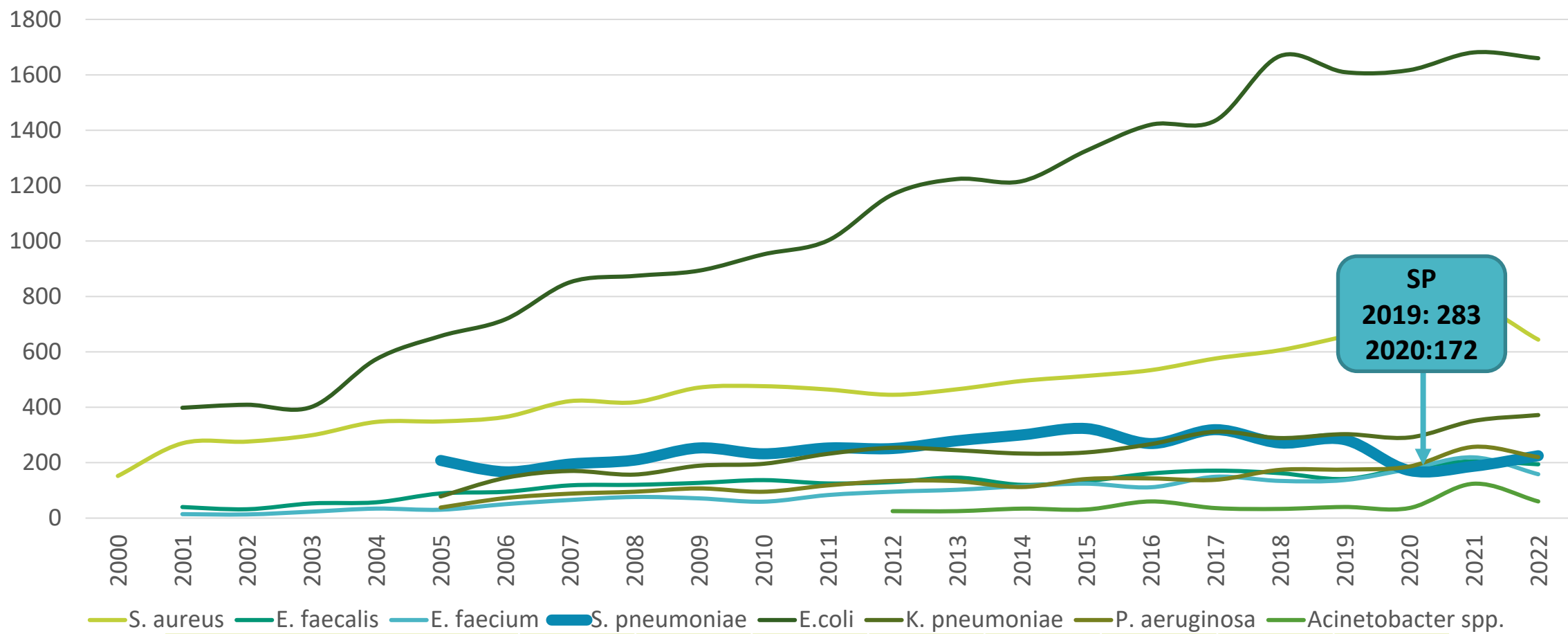
- Inštitut za mikrobiologijo in imunologijo, Medicinska fakulteta v Ljubljani
  - Nacionalni laboratorij za zdravje, okolje in hrano:
    - Maribor
    - Celje
    - Murska Sobota
    - Kranj
    - Koper
    - Nova Gorica
    - Novo Mesto
  - Splošna bolnišnica:
    - Franca Derganca Nova Gorica
    - Slovenj Gradec
  - Univerzitetna klinika za pljučne bolezni in alergijo Golnik
- ECDC
    - EARS–Net
    - Surveillance atlas
  - SKUOPZ poročila 2017
    - Slovenija,
    - 19 bakterijskih vrst, vse klinične kužnine
  - CEASAR - Central Asian and Eastern European Surveillance of Antimicrobial Resistance  
Antimicrobial Resistance Global Report on Surveillance, WHO 2021

# EARS-Net Slovenija



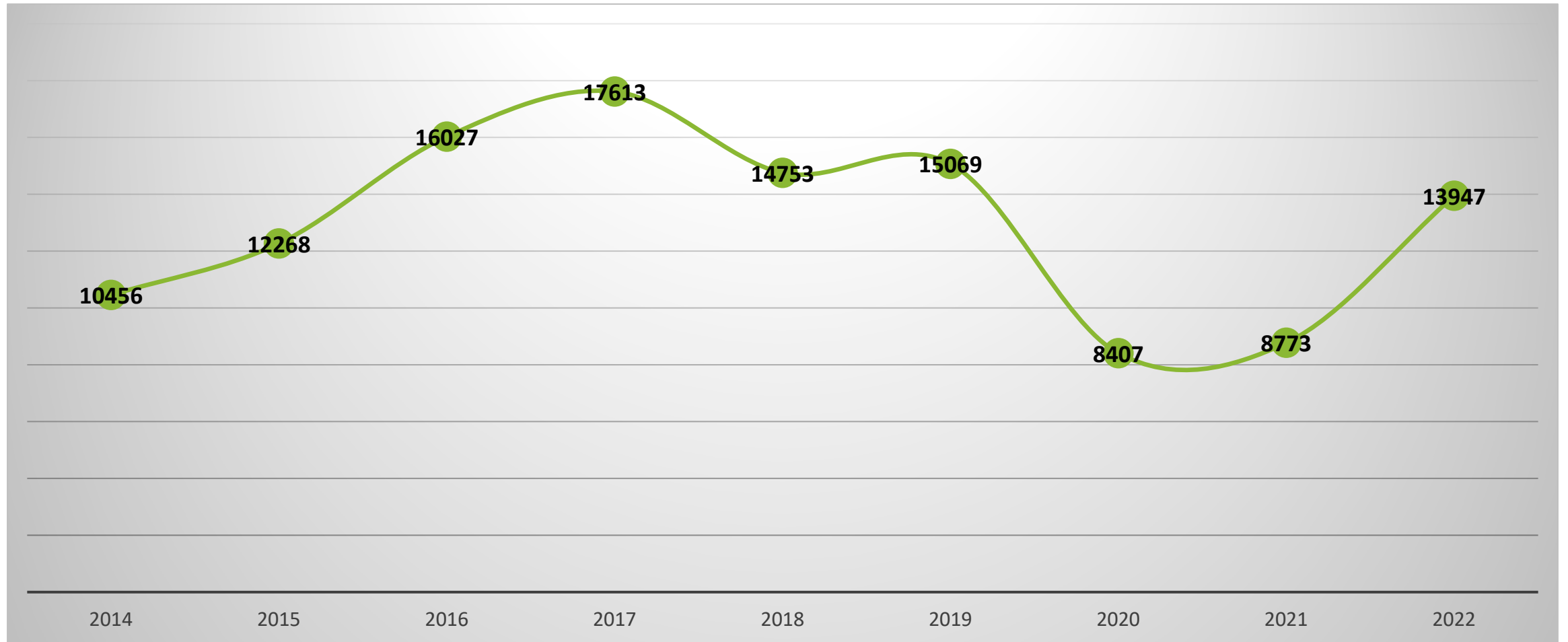
Blood-culture sets/1000 patient days	2015	2016	2017	2018	2019	2020	2021	2022
	35,1	35,0	41,2	36,8	40,4	47,1	56,1	56,4

# EARS-Net Slovenija



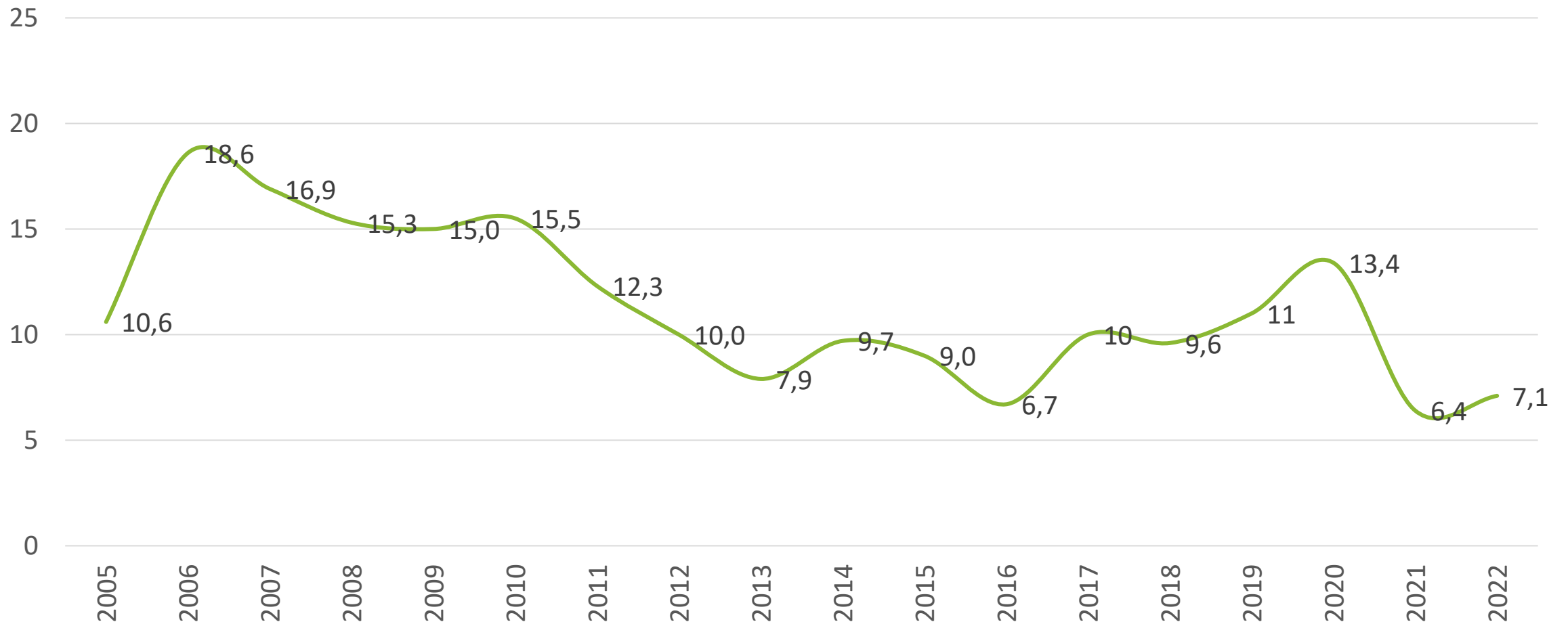
Blood-culture sets/1000 patient days	2015	2016	2017	2018	2019	2020	2021	2022
	35,1	35,0	41,2	36,8	40,4	47,1	56,1	56,4

# EU/EAA EARS-Net: *Streptococcus pneumoniae*



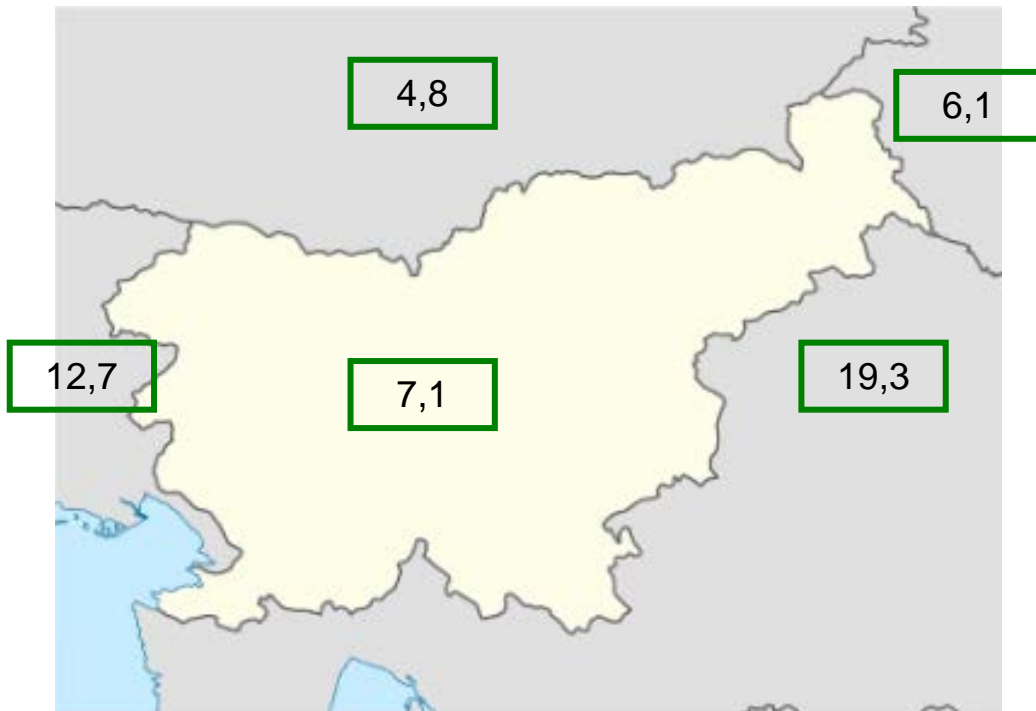
EARS-NET SLOVENIJA: <http://www.nijz.si/sl/ears-net-slovenija>

SKUOPZ: <http://www.imi.si/strokovna-zdruzenja/skuopz/skuopz>

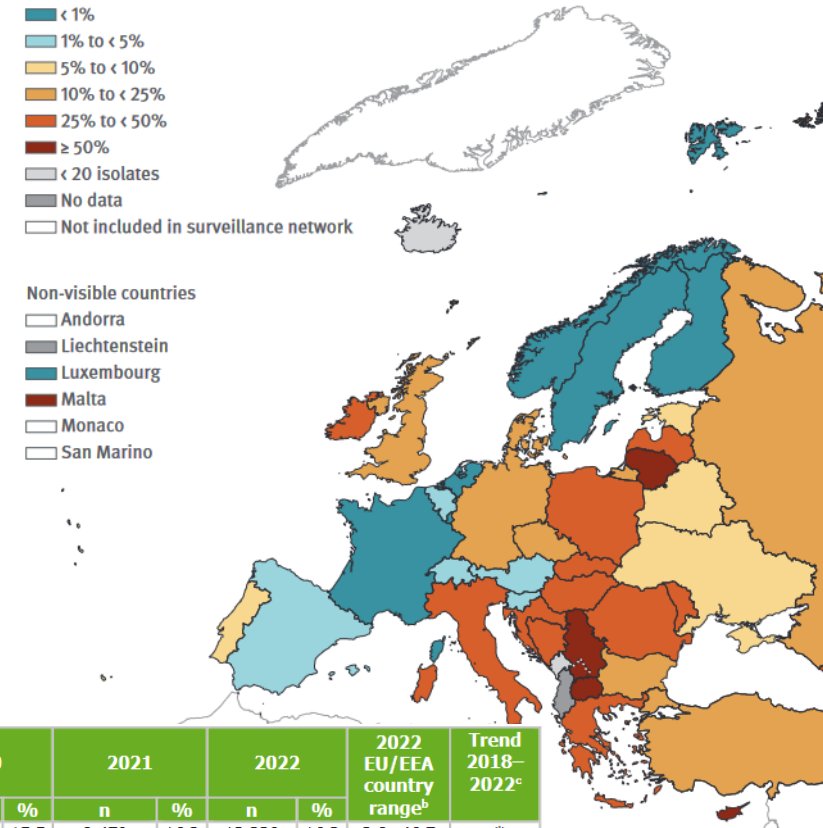


# Proti penicilinu odporni *S. pneumoniae* (PNSP)

## Lokalni podatki - EARS-Net 2022



## EARS-Net/CAESAR 2021

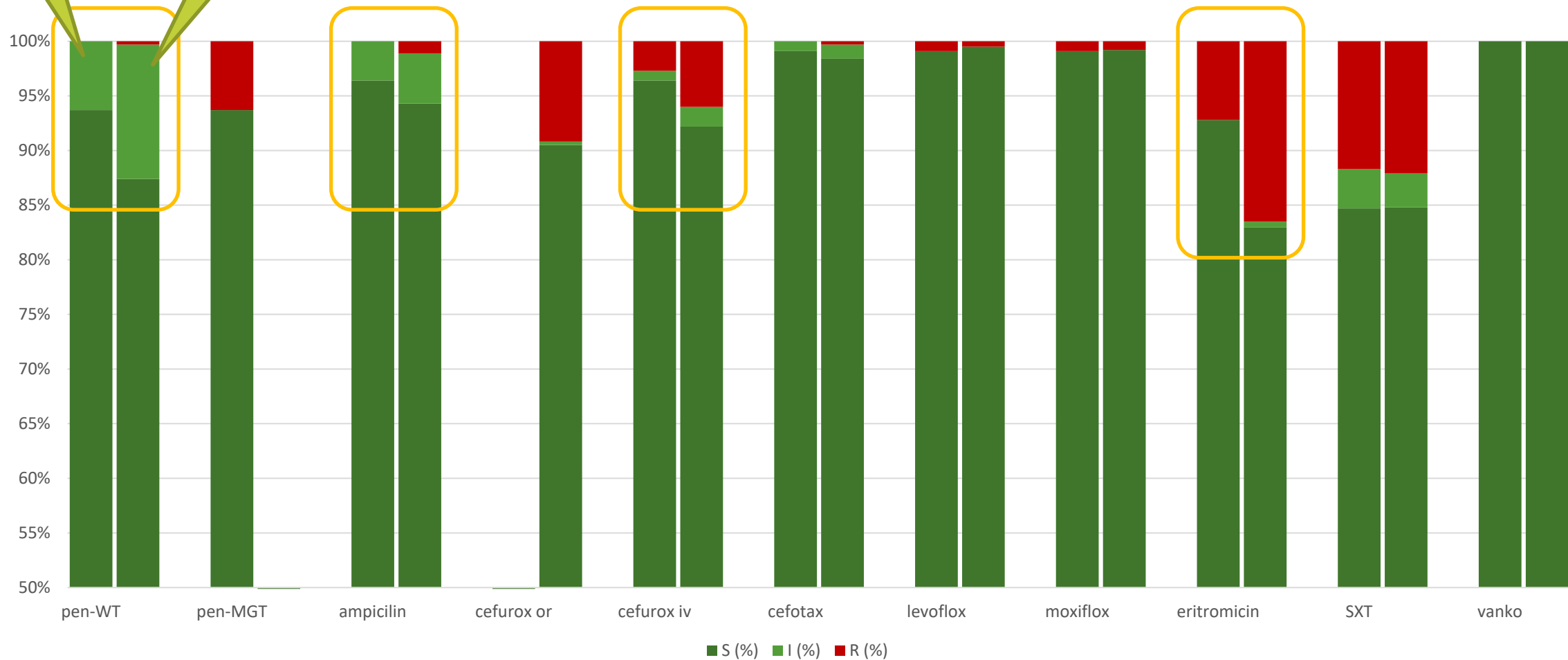


NWT

Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
<i>Streptococcus pneumoniae</i>	Penicillin non-wild-type <sup>a</sup>	14 498	14.0	14 568	13.2	8 076	15.5	8 479	16.2	13 230	16.3	2.8–46.7	↑*
	Macrolide (azithromycin/clarithromycin/erythromycin) resistance	14 753	16.6	15 069	15.9	8 407	16.8	8 773	18.3	13 947	17.9	3.4–36.1	↑*
	Combined penicillin non-wild-type and resistance to macrolides <sup>a</sup>	14 016	8.6	14 102	8.0	7 782	8.9	8 155	9.8	12 694	9.7	0.8–33.3	↑*

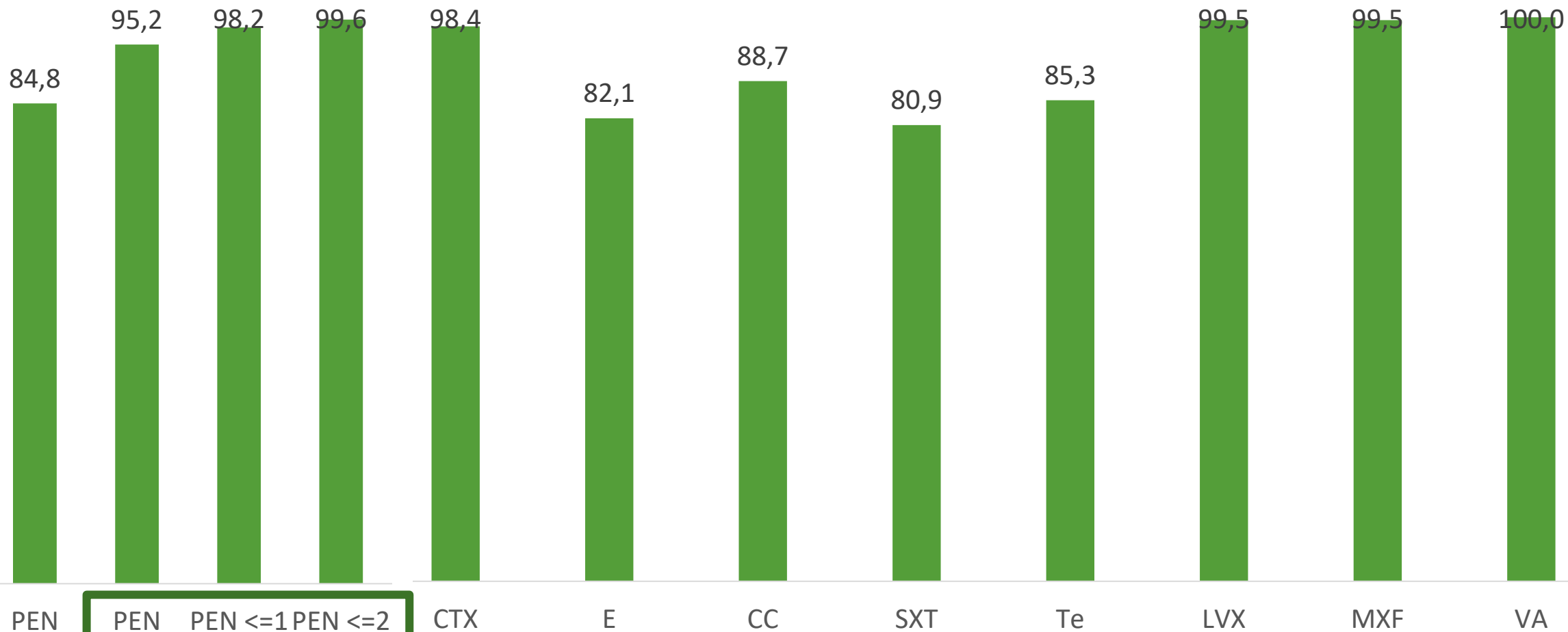
# *S. pneumoniae*

- invazivni : neinvazivni izolati





# Proti penicilinu odporni *S. pneumoniae* (PNSP)



PEN <=0,5  
pljučnica

Vir: SKOUPZ 2017

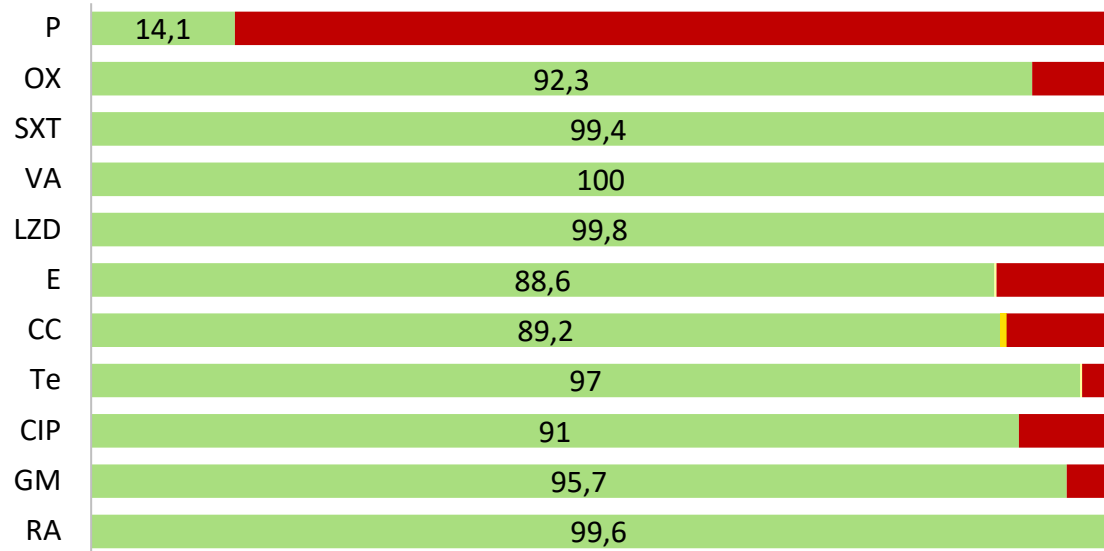
## Antimicrobial resistance: global report on surveillance. 2014

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

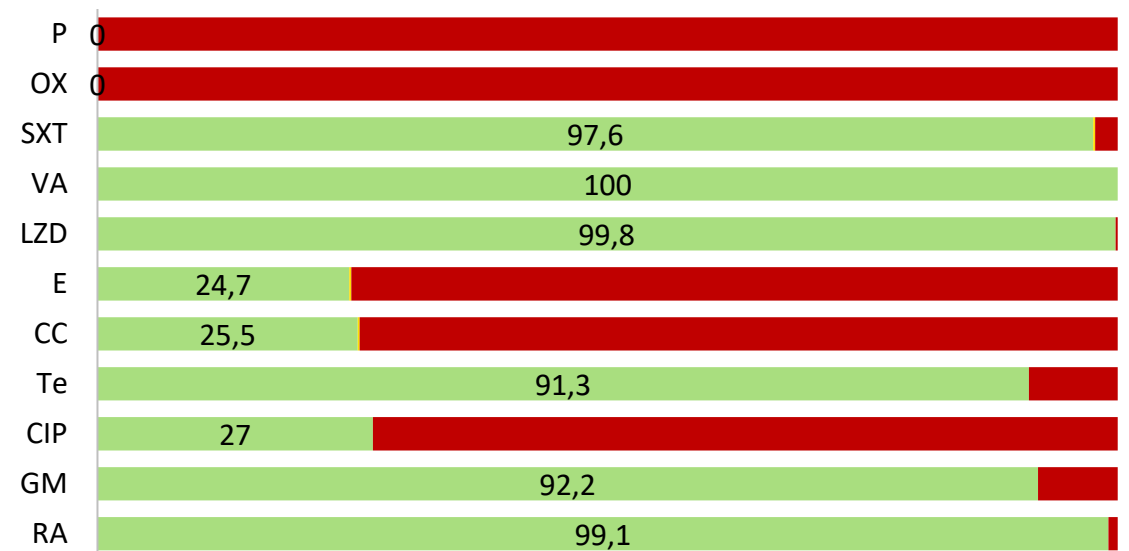
Data sources based on at least 30 tested isolates	Overall reported range of proportion resistant (R) and/or non-susceptible (NS)	Reported range of proportion resistant or non-susceptible in invasive isolates <sup>a</sup> (no. of reports)
African Region – National data (n=5 countries) – Publications (n=16) from 14 additional countries	3–16 (R) or 57–60 (NS) 1–100 (R) or 9–69 NS or 0–79 <sup>b</sup>	3 (R) (n=1) 9–18 (NS) or 24–79 <sup>b</sup> (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 <sup>b</sup> 53 (non-meningitis) (NS)	0–48 <sup>b</sup> (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 <sup>b</sup>	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 <sup>b</sup> (n=27) 13 (NS) (n=1)
South-East Asia Region – National data (n=2 countries) – Publications (n=2) from 2 additional countries	47–48 <sup>b</sup> 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 <sup>b</sup> 0–2 44–96 (R) or 0–69 (NS)	44 (R) or 0 (NS) (n=2)

# Staphylococcus aureus

## S.aureus

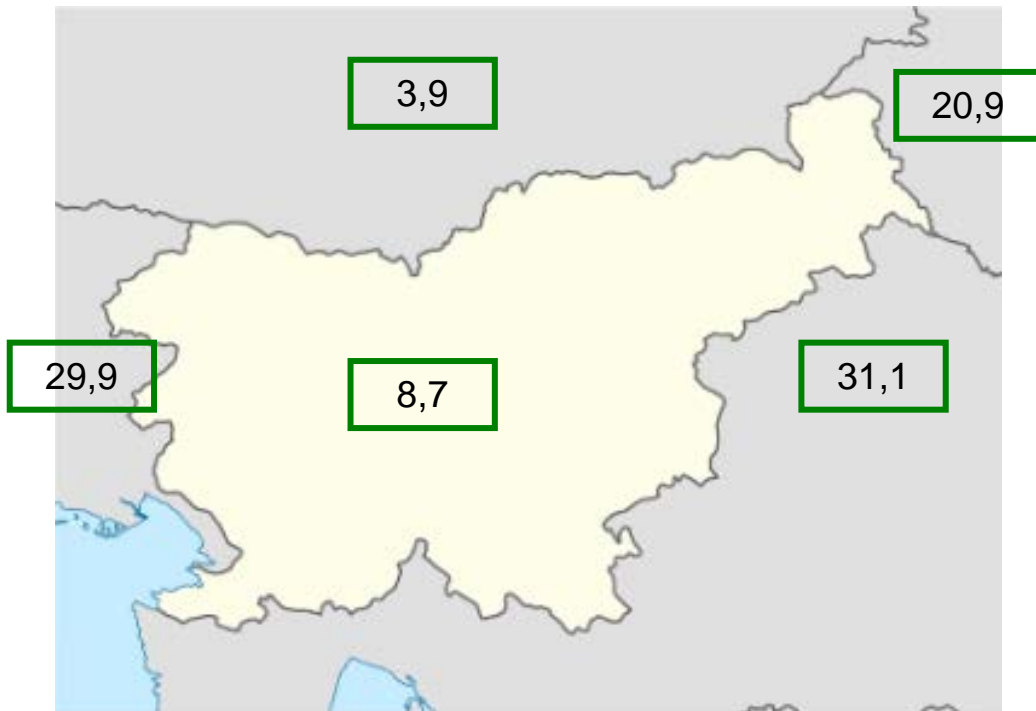


## MRSA

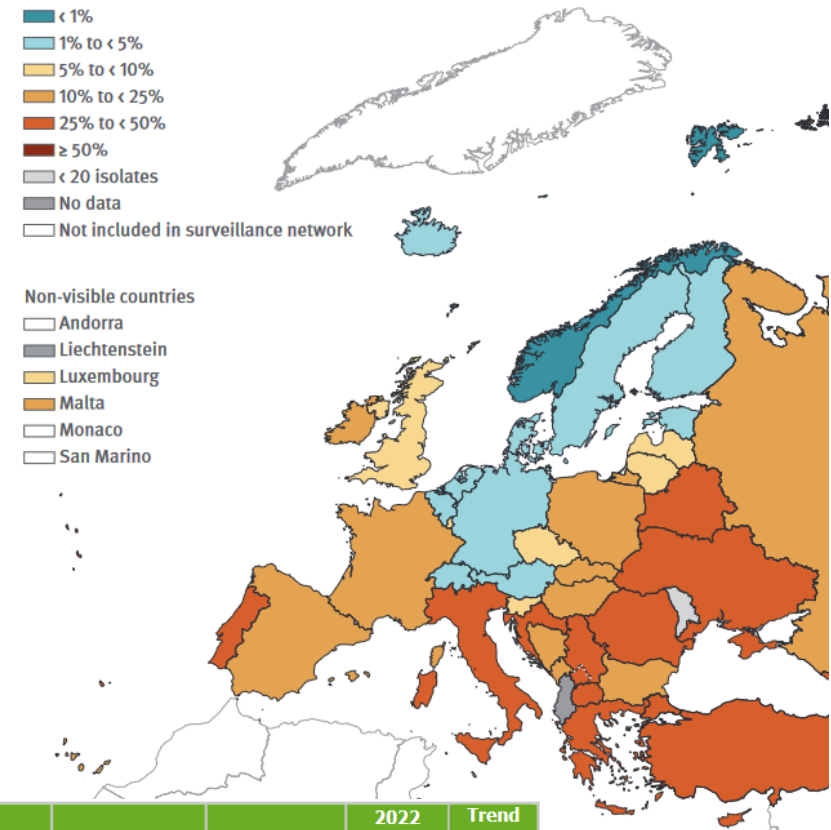


# Staphylococcus aureus - MRSA

## Lokalni podatki - EARS-Net 2022



## EARS-Net/CAESAR 2021



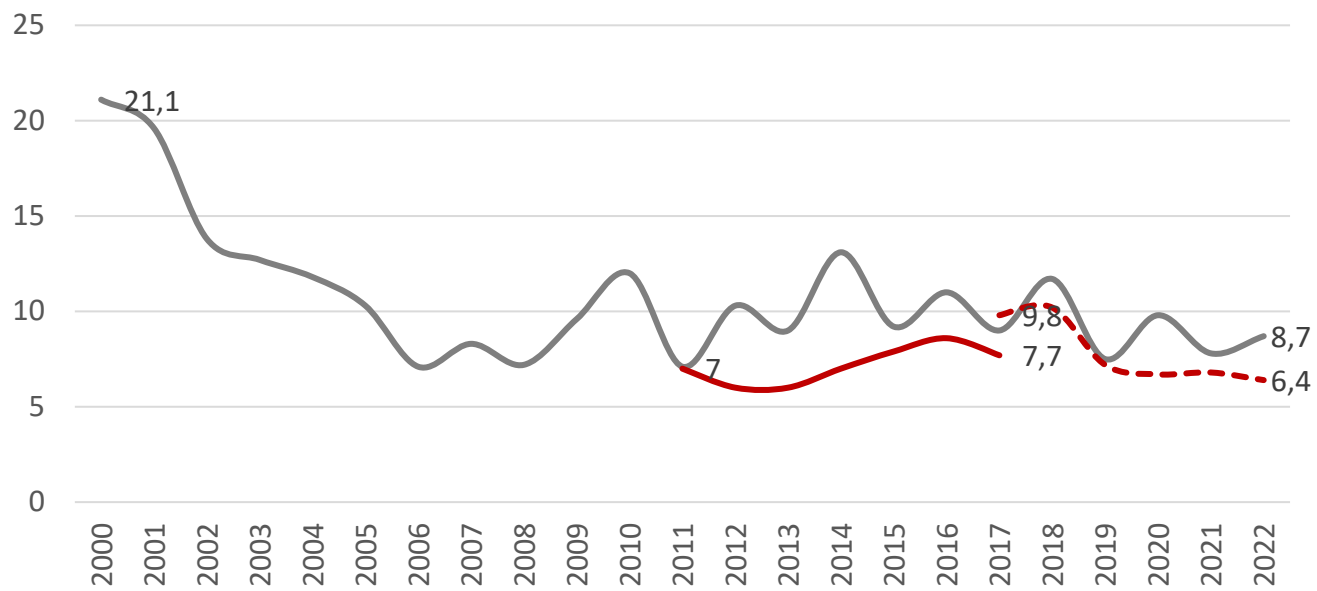
Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
<i>Staphylococcus aureus</i>	MRSA <sup>a</sup>	63 837	17.8	65 604	17.2	72 976	16.7	78 665	15.8	84 397	15.2	1.1–50.8	↓*

# Staphylococcus aureus - MRSA

## EARSS/EARS-Net:

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

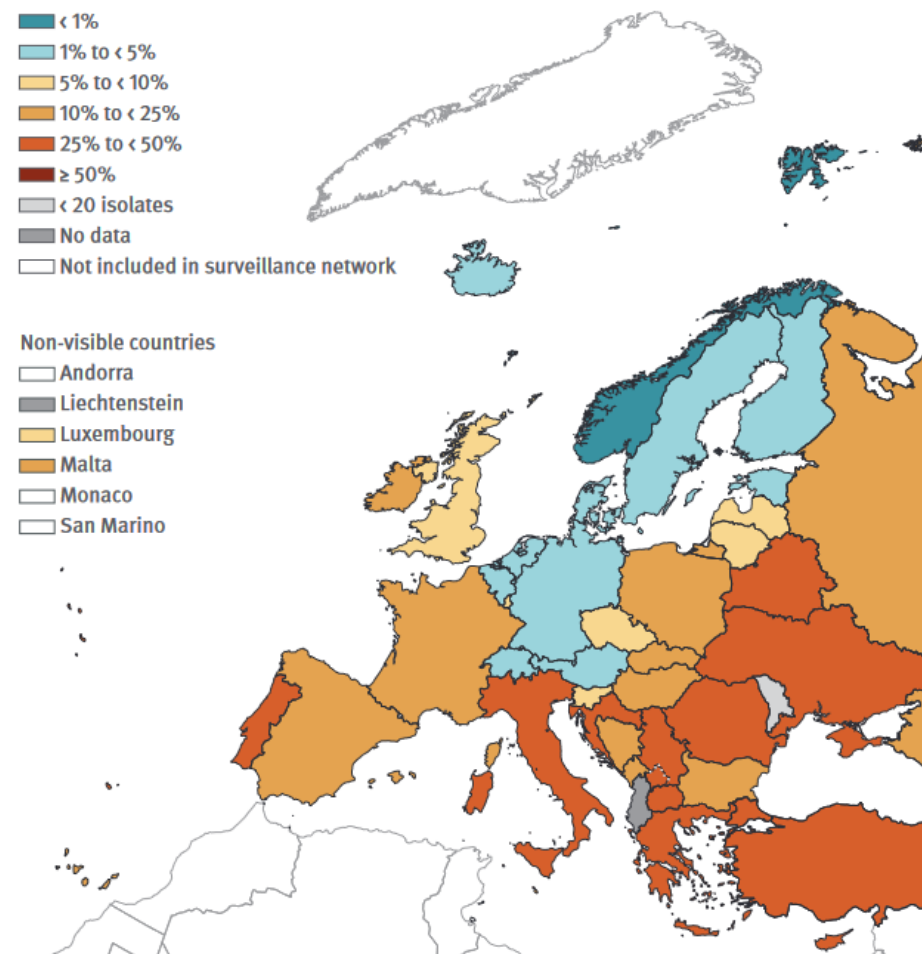
2000=21,4 % → 2006=7,1 %



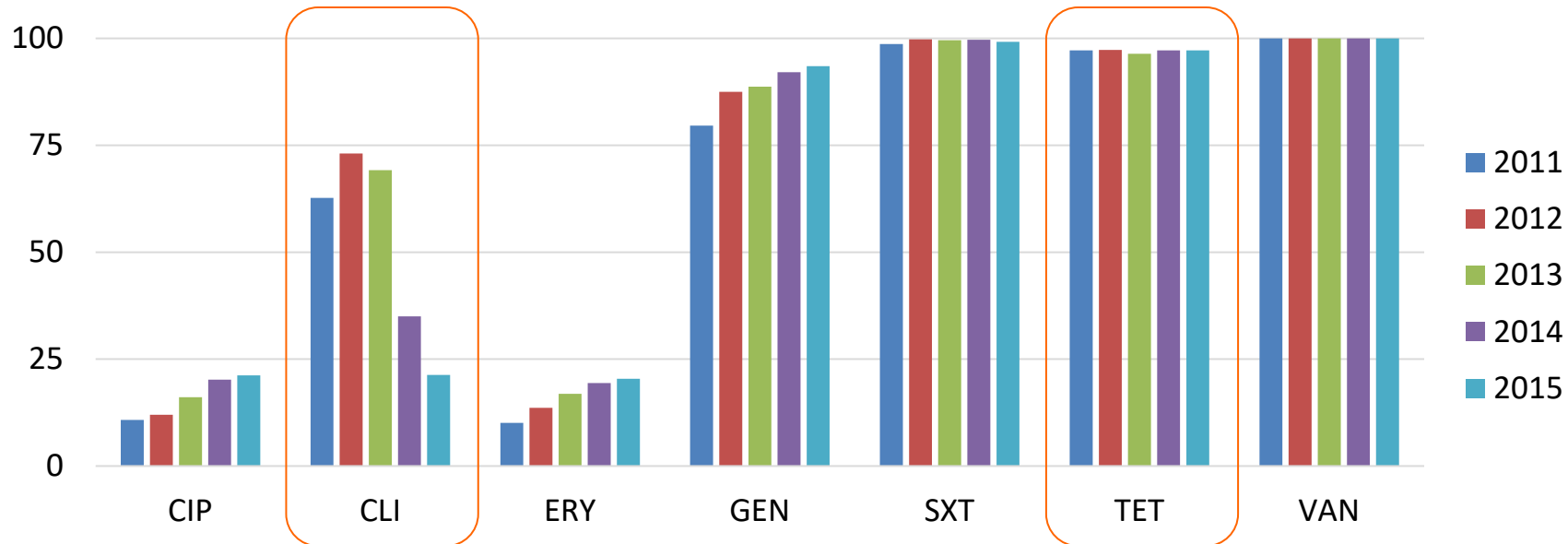
— delež pacientov z MRSA med prvimi izolati bakterije S. aureus iz invazivnih kužnin

— delež pacientov z MRSA med prvimi izolati bakterije S. aureus iz vseh kliničnih kužnin

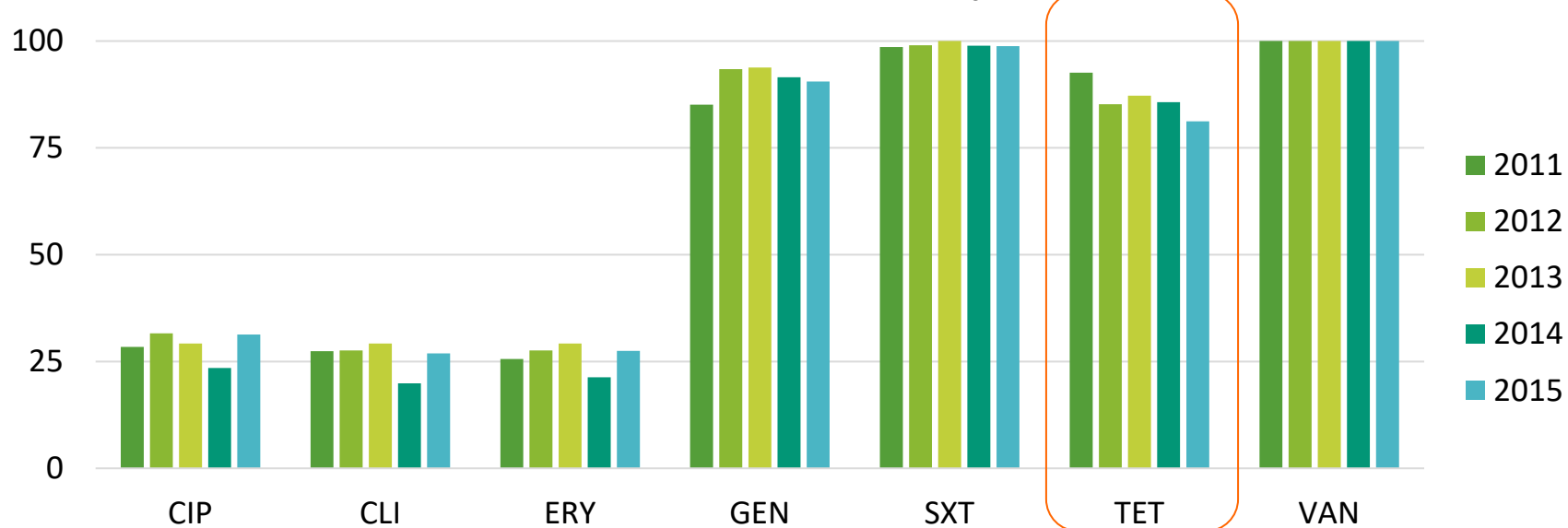
- - - delež pacientov z MRSA med vsemi izolati bakterije S. aureus iz vseh kliničnih kužnin



## Osrednjeslovenska regija



## Severovzhodna Slovenija



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

## Antimicrobial resistance: global report on surveillance. 2014

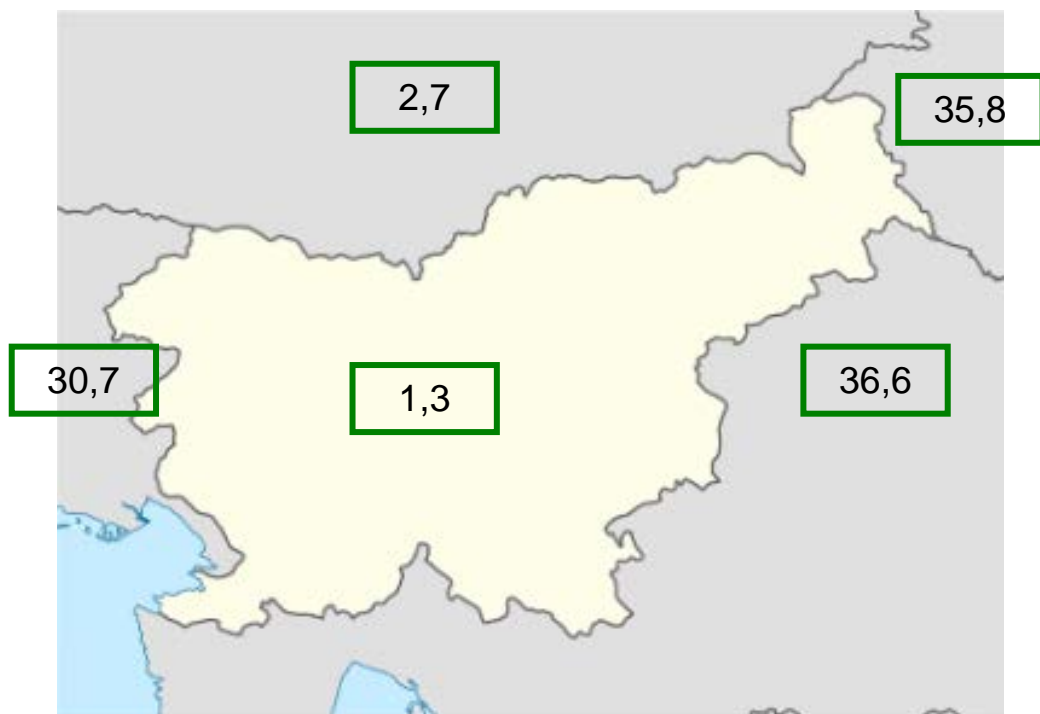
**Table 7** *Staphylococcus aureus*: Resistance to beta-lactam antibacterial drugs (i.e. methicillin-resistant *S. aureus*, MRSA)

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

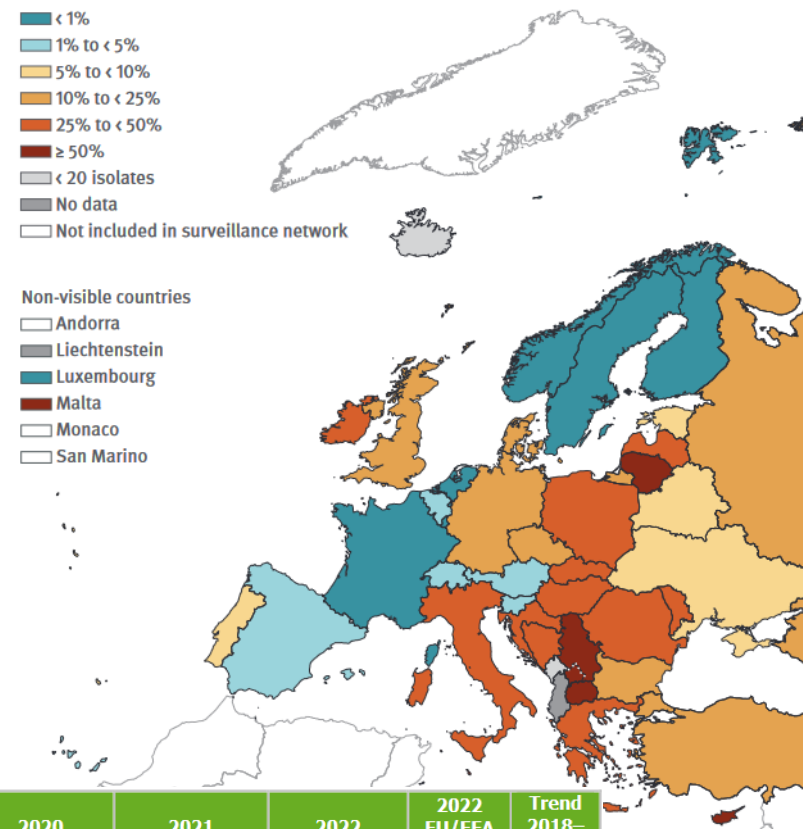
# Proti vankomicinu odporni enterokoki (VRE)

## *E. faecium* - VRE

### Lokalni podatki - EARS-Net 2022



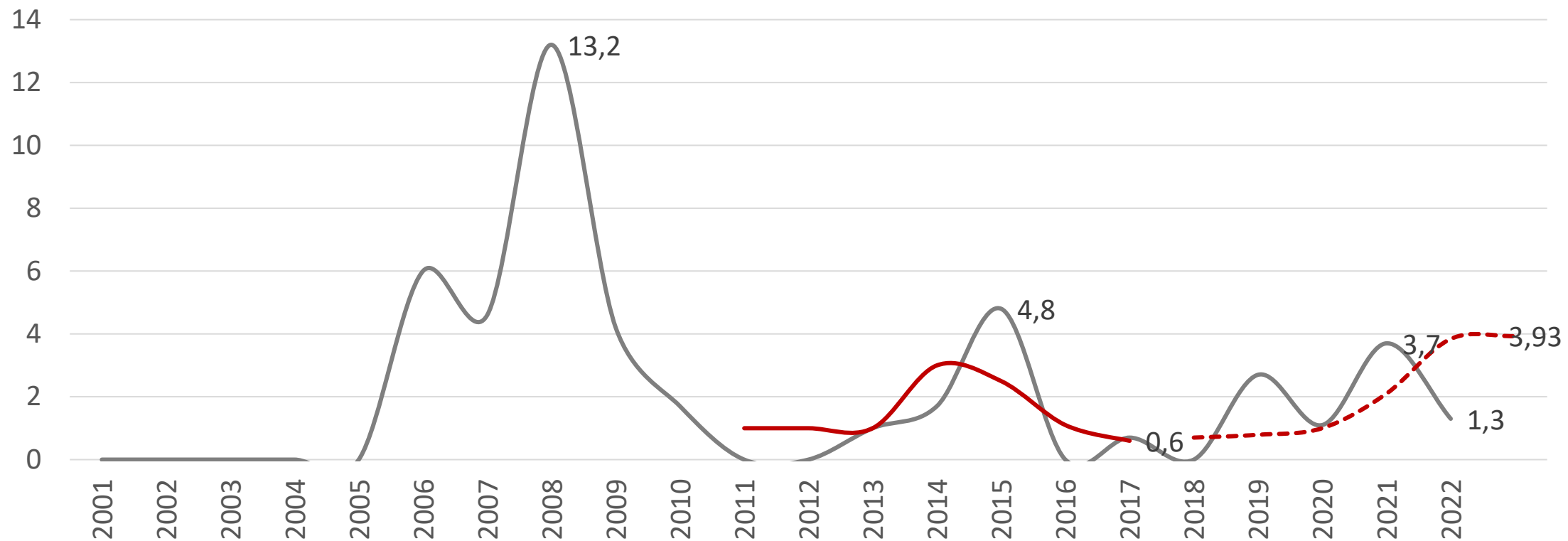
### EARS-Net/CAESAR 2021



Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
<i>Enterococcus faecium</i>	Vancomycin resistance	13 346	16.2	14 095	17.7	18 349	16.8	22 328	17.2	22 709	17.6	0.0–67.7	↑*



# *E. faecium* - VRE



- delež pacientov z VRE med prvimi izolati bakterije *E. faecium* iz invazivnih kužnin
- delež pacientov z VRE med prvimi izolati bakterije *E. faecium* iz vseh kliničnih kužnin
- - - delež pacientov z VRE med vsemi izolati bakterije *E. faecium* iz vseh kliničnih kužnin

# Streptococcus pyogenes

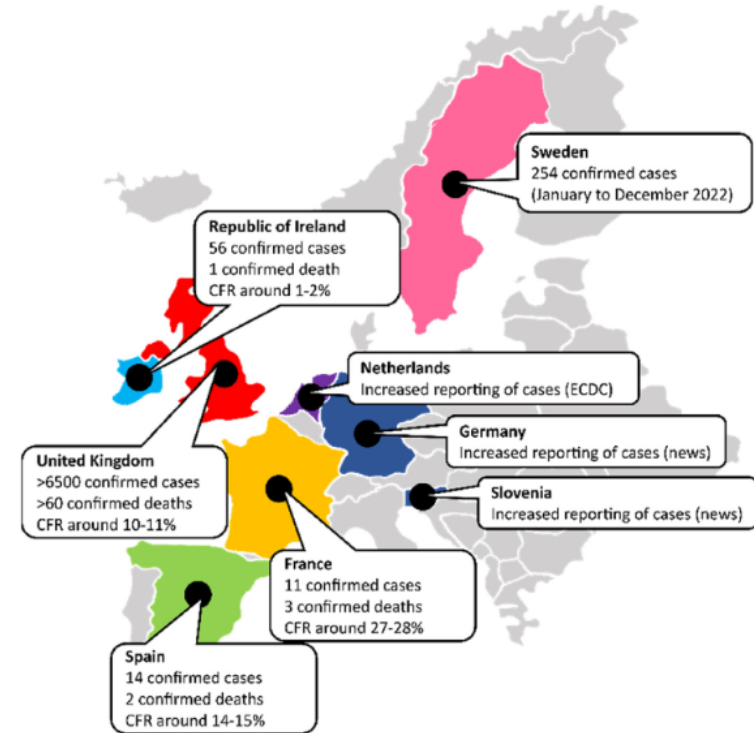
- Občutljivost za penicilin 100 %
- Občutljivost za eritromicin 94 %, za klindamicin 96 %.



## Increase in Invasive Group A streptococcal infections among children in Europe, including fatalities

Press release

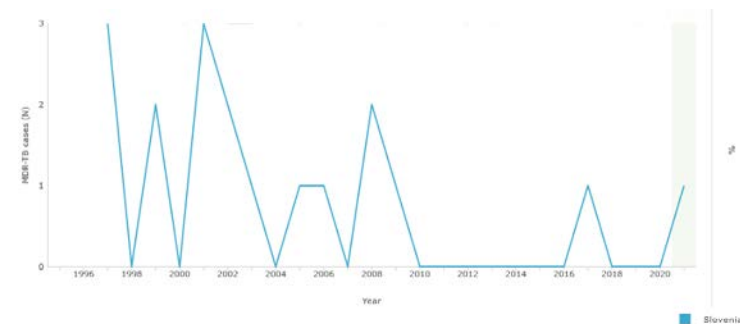
12 Dec 2022



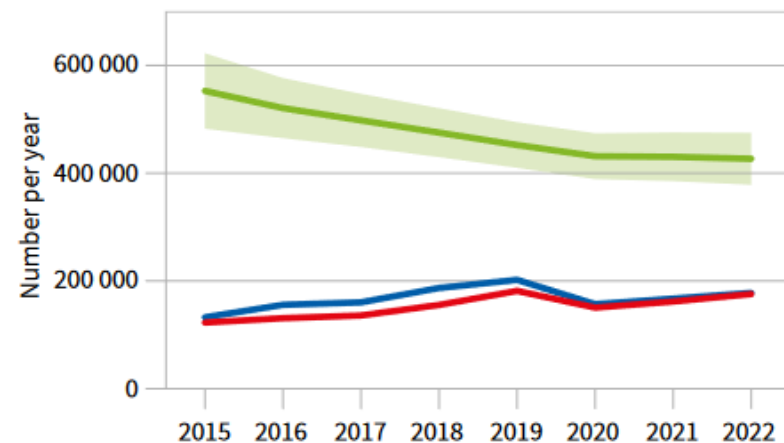
**FIG. 1.** Number of confirmed cases and deaths of Group A Streptococcal infections (both for Scarlet fever and invasive forms combined). CFR: case fatality rate. According to ECDC/WHO (European Centre for Disease Prevention and Control/World Health Organization), Ireland, UK, France, Netherlands, and Sweden are the countries experiencing increased GAS notifications. Spain was removed from this list by ECDC based on a comparison with previous years. GAS notifications are reported to be higher in Germany and Slovenia based on statements from local epidemiologists in newspapers. Note that the authors remain neutral in regards with territorial depictions used in the map. Data source: Ministry of Health of respective countries.

# *Mycobacterium tuberculosis*

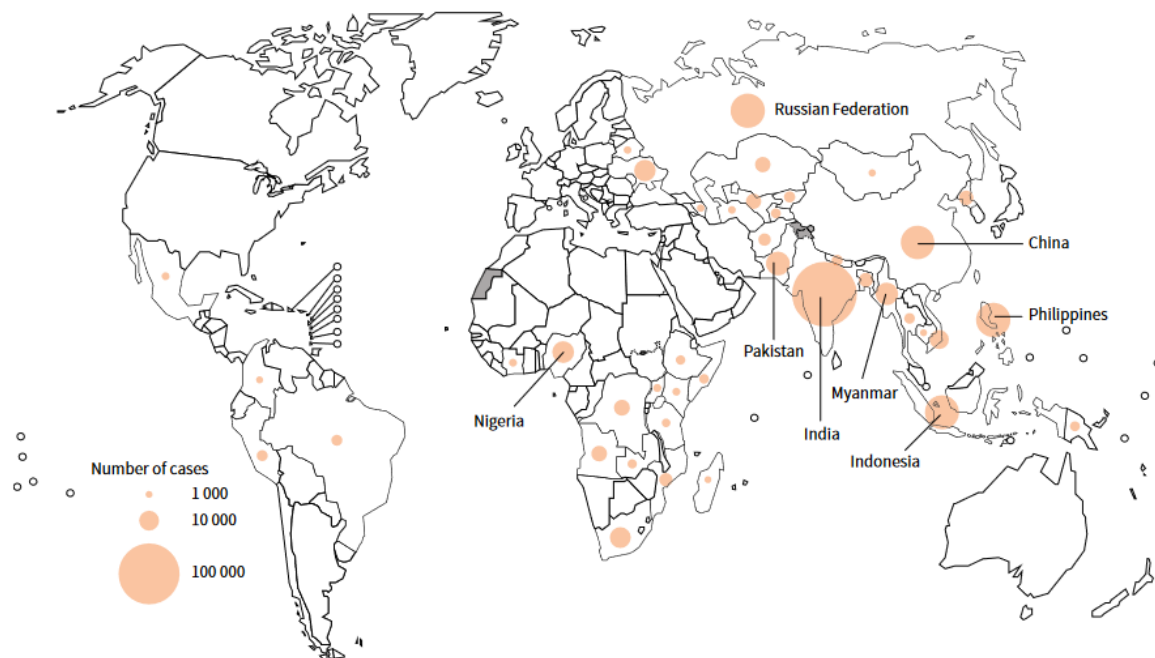
- Večkratno odporni sevi so velik svetovni problem
- Slovenija:
  - Občutljivost za vsa ključna zdravila že nekaj let od 97 do 100 %.
  - 2020 in 2021: 1 primer MDR/RR TB



Global number of people diagnosed with MDR/RR-TB (blue) and number enrolled on an MDR-TB treatment regimen (red), compared with estimates of the global number of incident cases of MDR/RR-TB (95% uncertainty interval shown in green), 2015–2022<sup>a</sup>



Estimated number of people who developed MDR/RR-TB (incident cases) in 2022, for countries with at least 1000 incident cases<sup>a</sup>

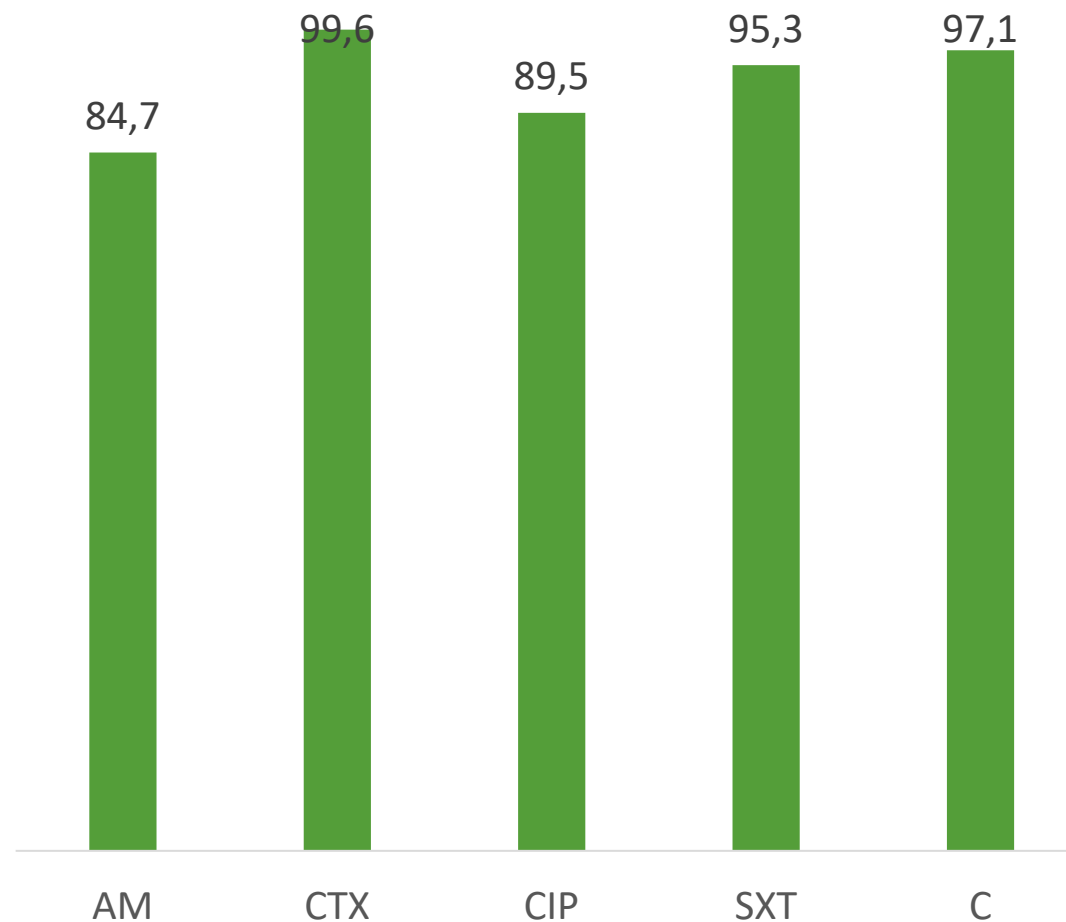


# Salmonella spp.

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

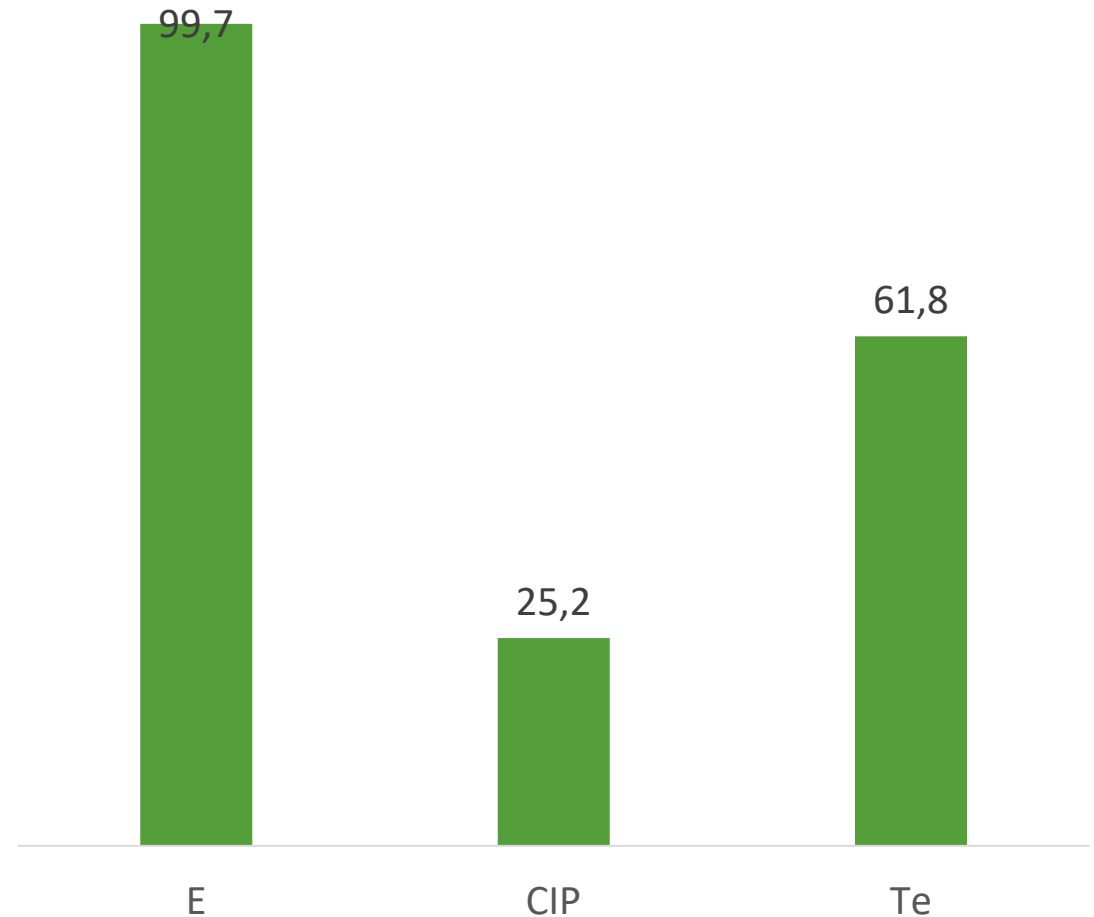
**Table 9** Nontyphoidal *Salmonella*: Resistance to fluoroquinolones<sup>a</sup> (summary of reported or published proportions of resistance, by WHO region)

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) from 1 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.



# Shigella spp.

<i>Shigella sonneii</i> – OSR (%R)	2014-2018	2019-2023
N	39	30
AM	48,7	53,3
CRO	10,3	40
CIP	28,2	40
SXT	94,9	76,7

Increase in extensively-drug resistant *Shigella sonnei* infections in men who have sex with men in the EU/EEA and the UK

**Table 1. Description of confirmed<sup>1</sup> and possible<sup>1</sup> extensively-drug resistant *Shigella sonnei* cases among MSM by country, EU/EEA countries and the United Kingdom, 2020-2022, as of 17 February 2022**

Country	Confirmed cases <sup>1</sup>	Possible cases <sup>1</sup>	Time of sampling or isolation	Genetic relatedness	Demographic data
Austria	9	-	28 June to 16 November 2021	Isolates closely related within cluster and to the representative sequences from the UK (same sequence type by cgMLST; ST152)	Male, age range: 28-41 years
Belgium	4	>30 <sup>2</sup>	19 July and 2 September 2021 (confirmed cases); since September 2021 (possible cases)	Isolates closely related within the cluster (0-2 AD) and to two of the representative sequences from the UK (3-5 AD and 4-6 AD)	Male, age range: 0-66 years (confirmed cases) <sup>3</sup>
Denmark	1	-	November 2021	Isolate closely related to representative sequences from the UK (2-3 AD by cgMLST)	Adult male
France	106	-	September 2020 to 15 February 2022	All isolates closely related to representative sequences from the UK (genotype 3.6.1.1.2 (MSM5) [2])	102 males, age range: 13-68 years; four females
Germany	3 <sup>4</sup>	-	May to October 2021	Isolates closely related to representative sequences from the UK (2-6 AD)	Two cases are males
Ireland	6	-	Since September 2021	Isolates closely related within cluster and to representative sequence from Norway (within 3 to 7 AD by cgMLST)	-
Italy	3	3	July to September 2021	-	Male, age range: 22-67 years
Norway	6	1	21 September to 16 January 2022	Isolates closely related within cluster (within 3 AD by cgMLST) and to representative sequences from the UK (1 AD); ST152	Male,
Spain	8	22	February 2021 to February 2022	Four isolates sequenced, these are closely related within cluster and to the representative sequences from the UK	Male, age range: 18-56 years
United Kingdom	62	-	4 September 2021 to 26 January 2022	All isolates part of the same 10-SNP cluster by WGS	97% male, median age 34 years

# Neisseria gonorrhoeae

**Table 11** *Neisseria gonorrhoeae*: decreased susceptibility to third-generation cephalosporins<sup>a</sup>

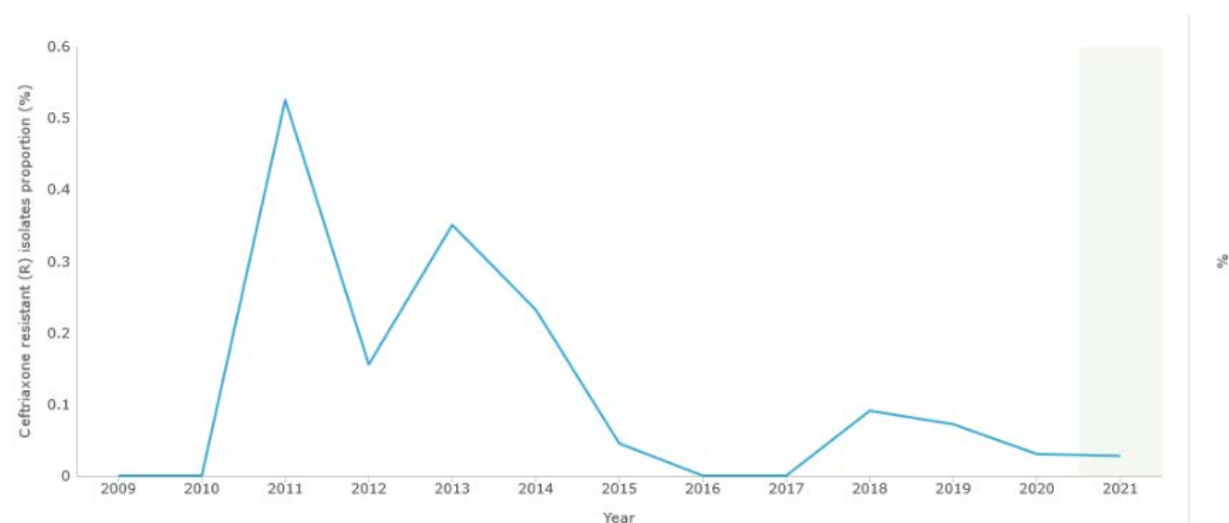
Data sources based on at least 30 tested isolates	Overall reported range of proportion with decreased susceptibility (%)
African Region – National data and/or GASP data (n=2 countries) – Publications (n=5) from 5 additional countries	0–12 0
Region of the Americas – National data and/or GASP/ GISP data (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	%
<b>Penicilin</b>	178	<b>19</b>	11	<b>150</b>	84	<b>9</b>	5
<b>Cefiksim</b>	178	<b>178</b>	100	/		<b>0</b>	0
<b>Ceftriakson</b>	178	<b>178</b>	100	/		<b>0</b>	0
<b>Azitromicin*</b>	178	<b>167</b>	94	/		<b>11</b>	6
<b>Ciprofloksacin</b>	178	<b>73</b>	41	<b>3</b>	2	<b>102</b>	57
<b>Tetraciklin</b>	178	<b>101</b>	57	<b>32</b>	18	<b>45</b>	25
<b>Spektinomycin</b>	178	<b>178</b>	100	<b>0</b>	0	<b>0</b>	0

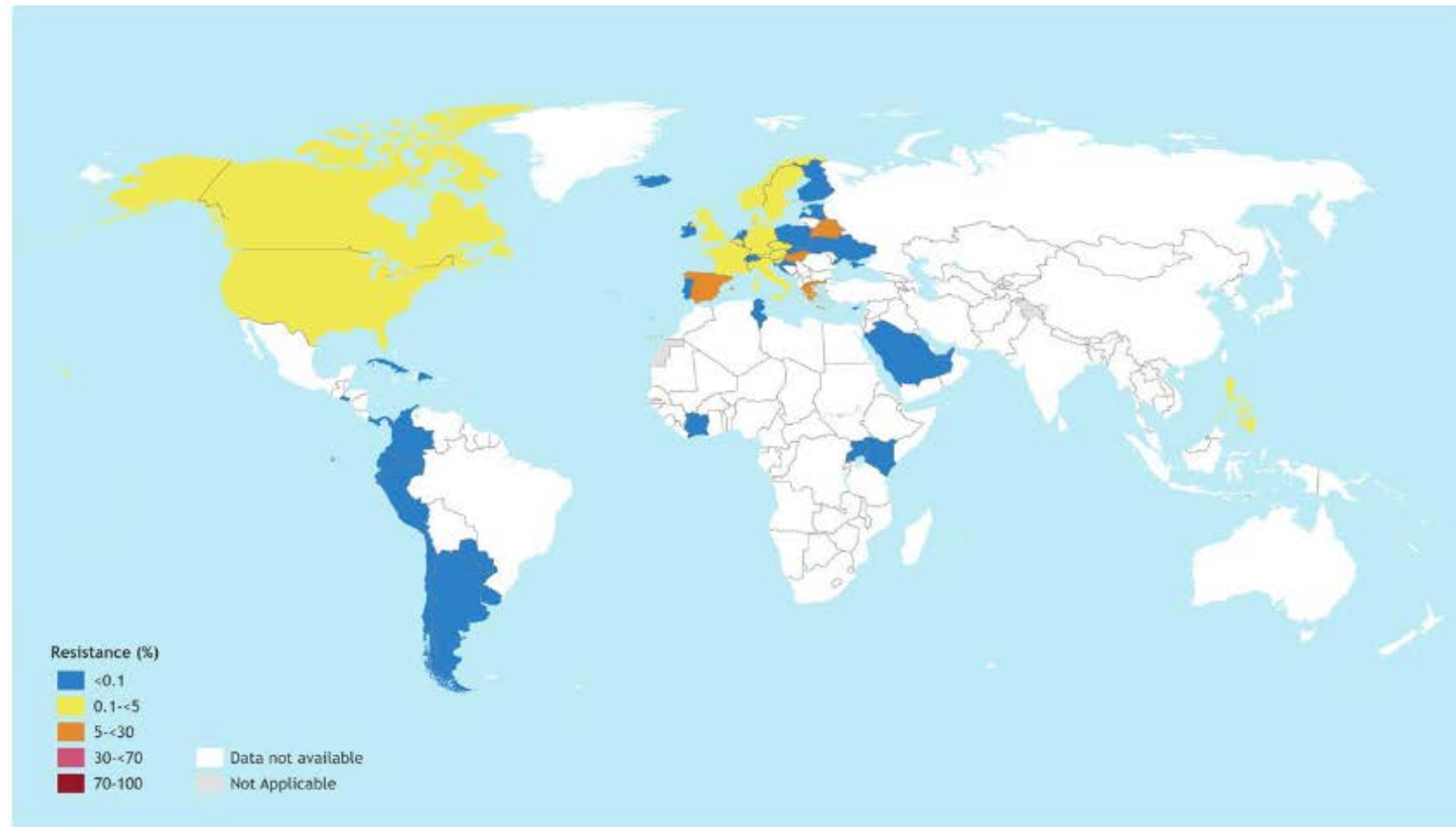
**Betalaktamaza** je bila pozitivna pri **27 (15 %)** izolatih.

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  $MIK \leq 1$  mg/L.



# Countries with reported decreased susceptibility/resistance (DS/R) to ceftriaxone in *N. gonorrhoeae*, WHO GASP 2017-2018



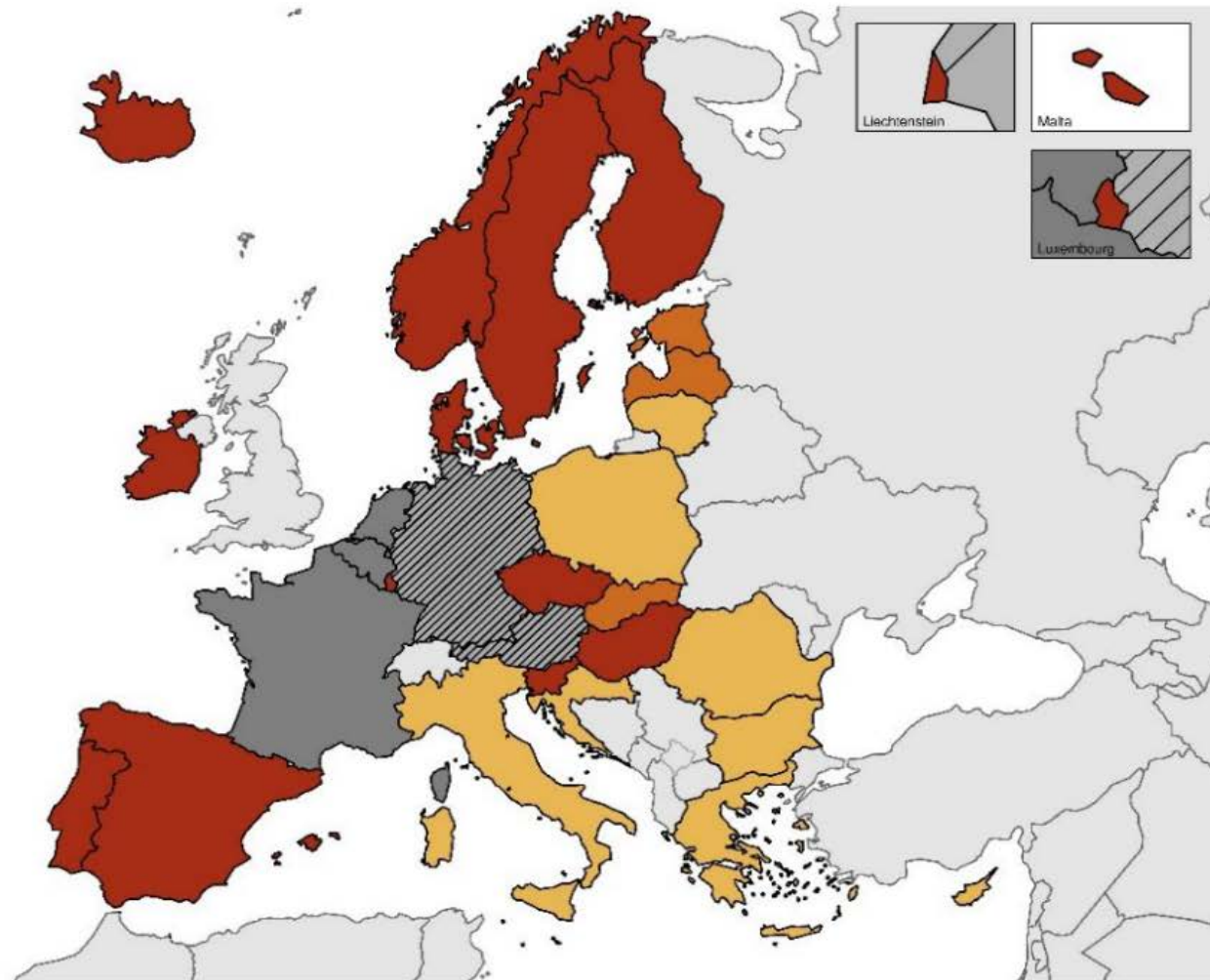
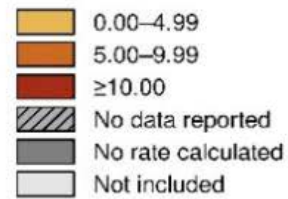
21/68(31%) countries - DS/R to ceftriaxone ; 6 (9%) countries  $\geq 5\%$ ; 15(22%) countries  $\leq 5\%$



## Confirmed gonorrhoea cases per 100 000 population, EU/EEA, 2022.

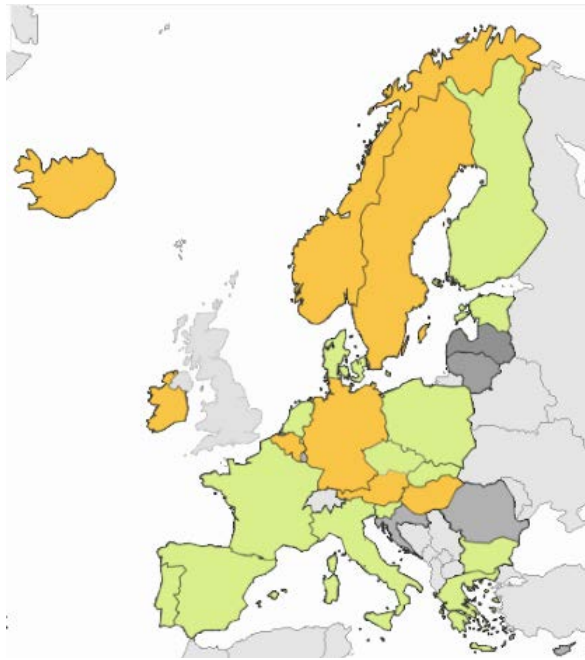


### Notification rate (per 100 000 population)

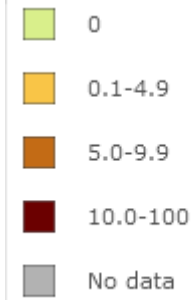


Administration boundaries: © Eurographics  
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 19 February 2024.

*Rates are calculated for countries with comprehensive STI surveillance that reported data for 2022.*



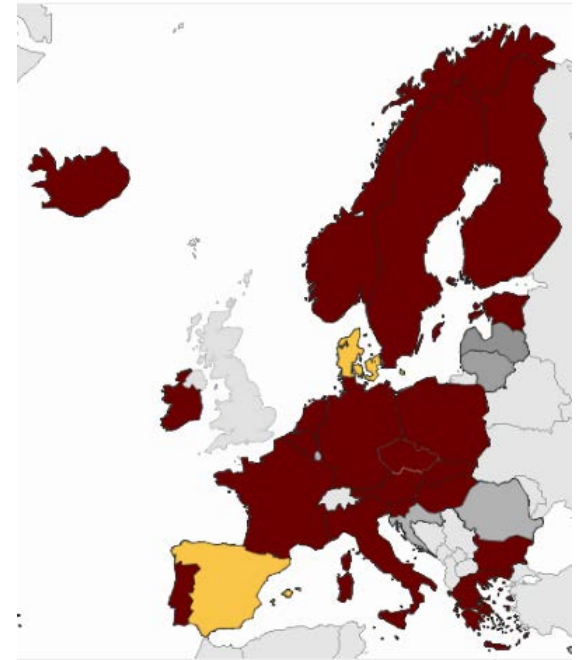
cefiksīm



ceftriakson



azitromicin  
MIK > ECOFF



BRIEF REPORT

## Emergence of Ciprofloxacin-Resistant *Neisseria meningitidis* in North America

Henry M. Wu, M.D., Brian H. Harcourt, Ph.D., Cynthia P. Hatcher, B.S., Stanley C. Wei, M.D., Ryan T. Novak, Ph.D., Xin Wang, Ph.D., Billie A. Juni, M.S., Anita Glennen, B.S., David J. Boxrud, M.S., Jean Rainbow, R.N., M.P.H., Susanna Schmink, B.S., Raydel D. Mair, B.S., M. Jordan Theodore, B.S., Molly A. Sander, M.P.H., Tracy K. Miller, M.P.H., Kirby Kruger, B.S., Amanda C. Cohn, M.D., Thomas A. Clark, M.D., M.P.H., Nancy E. Messonnier, M.D., Leonard W. Mayer, Ph.D., and Ruth Lynfield, M.D.

SUMMARY

We report on three cases of meningococcal disease caused by ciprofloxacin-resistant *Neisseria meningitidis*, one in North Dakota and two in Minnesota. The cases were caused by the same serogroup B strain. To assess local carriage of resistant *N. meningitidis*, we conducted a pharyngeal-carriage survey and isolated the resistant strain from one asymptomatic carrier. Sequencing of the gene encoding subunit A of DNA gyrase (*gyrA*) revealed a mutation associated with fluoroquinolone resistance and suggests that the resistance was acquired by means of horizontal gene transfer with the commensal *N. lactamica*. In susceptibility testing of invasive *N. meningitidis* isolates from the Active Bacterial Core surveillance system between January 2007 and January 2008, an additional ciprofloxacin-resistant isolate was found, in this case from California. Ciprofloxacin-resistant *N. meningitidis* has emerged in North America.



OBSERVATION



## Penicillin- and Ciprofloxacin-Resistant Invasive *Neisseria meningitidis* Isolates from Japan

Ryoichi Saito,<sup>a</sup> Jun Nakajima,<sup>b</sup> Isaac Prah,<sup>a</sup> Masatomo Morita,<sup>c</sup> Samiratu Mahazu,<sup>a</sup> Yusuke Ota,<sup>a</sup> Ayuka Kobayashi,<sup>b</sup> Shuji Tohda,<sup>b</sup> Hajime Kamiya,<sup>d</sup> Hideyuki Takahashi,<sup>c</sup> Makoto Ohnishi<sup>e</sup>

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<sup>e</sup>National Institute of Infectious Diseases, Tokyo, Japan

Morbidity and Mortality Weekly Report


## Detection of Ciprofloxacin-Resistant, $\beta$ -Lactamase-Producing *Neisseria meningitidis* Serogroup Y Isolates — United States, 2019–2020

Lucy A. McNamara, PhD<sup>1</sup>; Caelin Potts, PhD<sup>1</sup>; Amy E. Blain, MPH<sup>1</sup>; Adam C. Retchless, PhD<sup>1</sup>; Natasha Reese, MS<sup>2</sup>; Stephanie Swint, MS<sup>2</sup>; David Lonsway, MMSc<sup>2</sup>; Maria Karlsson, PhD<sup>2</sup>; Kristy Lunquest, ScM<sup>3</sup>; John J. Sweitzer, ScM<sup>3</sup>; Xin Wang, PhD<sup>1</sup>; Susan Hariri, PhD<sup>1</sup>; LeAnne M. Fox, MD<sup>1</sup>; Antimicrobial-Resistant *Neisseria meningitidis* Team

VIEWPOINT | [VOLUME 8, 100098, MARCH 2021](#)

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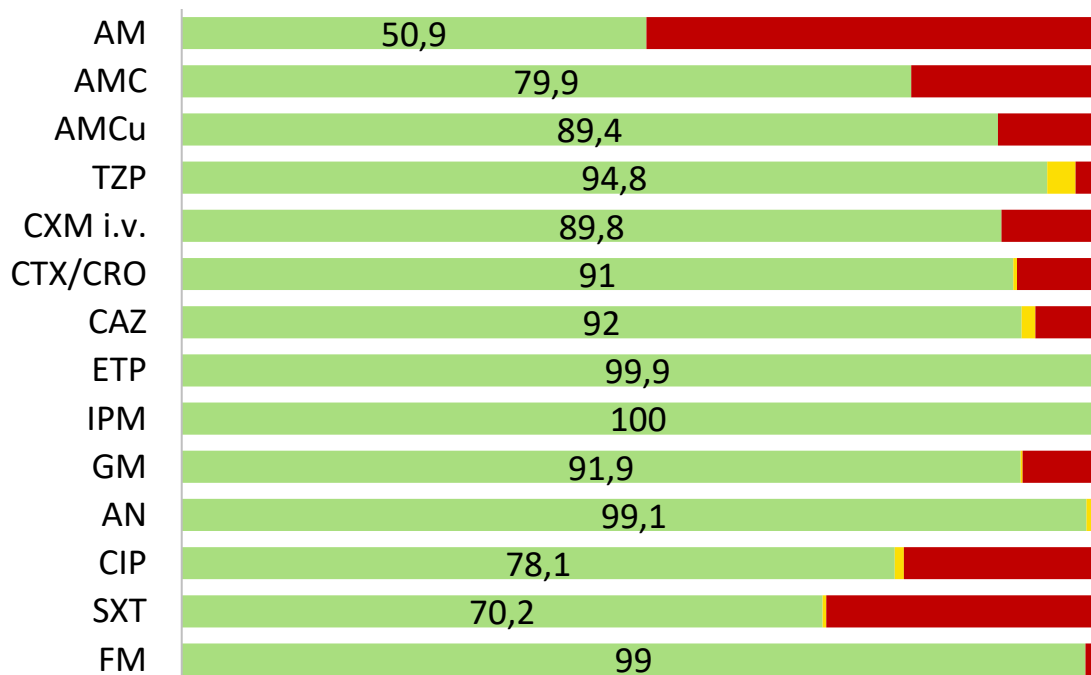
## Emerging macrolide resistance in *Bordetella pertussis* in mainland China: Findings and warning from the global pertussis initiative

[Ye Feng](#) • [Cheng-Hsun Chiu](#)   • [Ulrich Heininger](#) • [Daniela Flavia Hozbor](#) • [Tina Quanbee Tan](#) •  
[Carl-Heinz Wirsing von König](#)

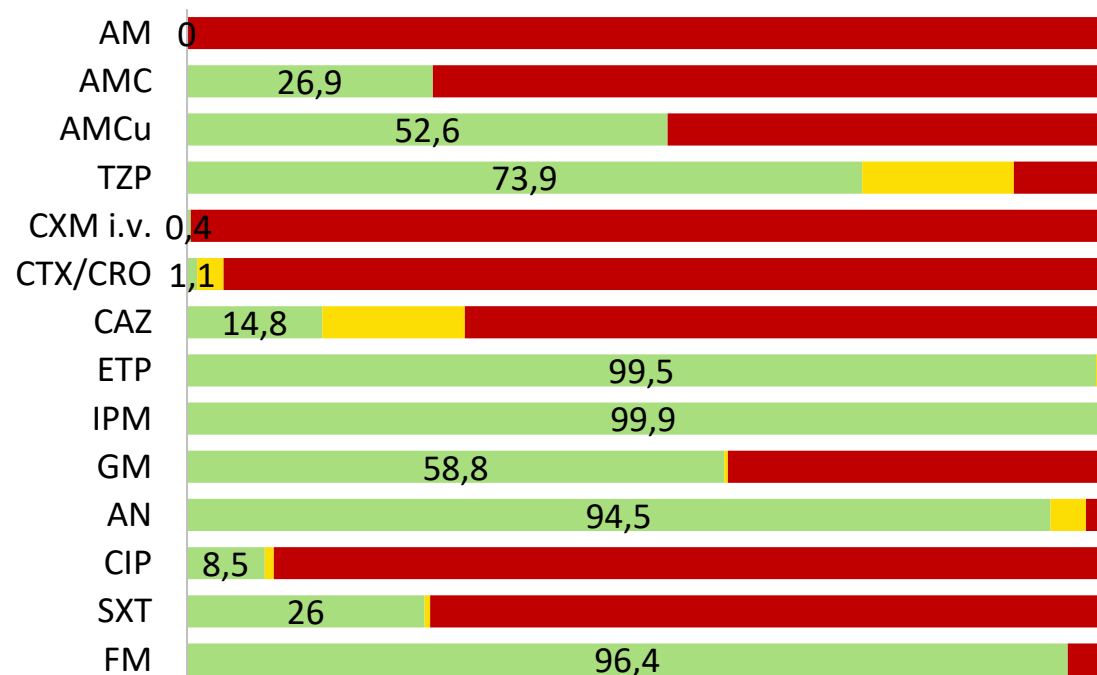
[Open Access](#) • Published: February 05, 2021 • DOI: <https://doi.org/10.1016/j.lanwpc.2021.100098>

# Escherichia coli

## E.coli

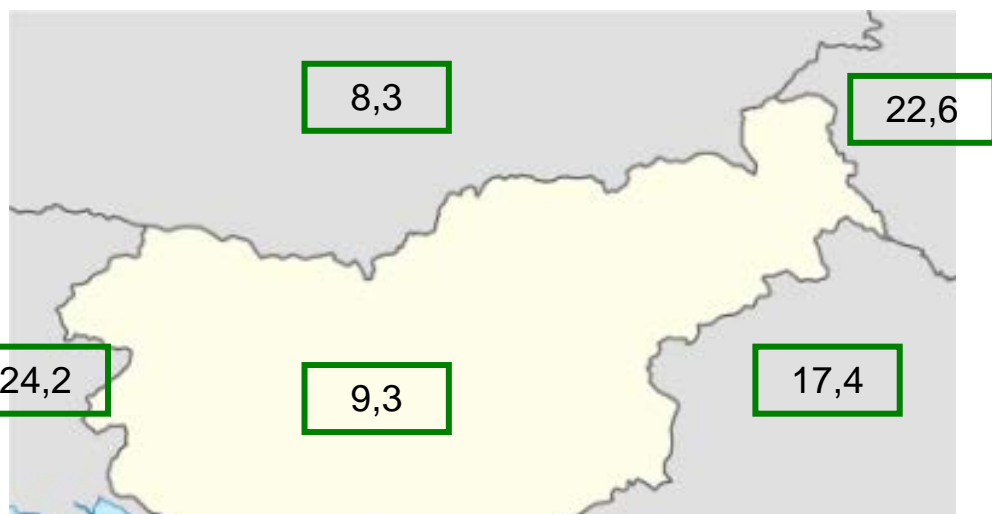


## E.coli - ESBL

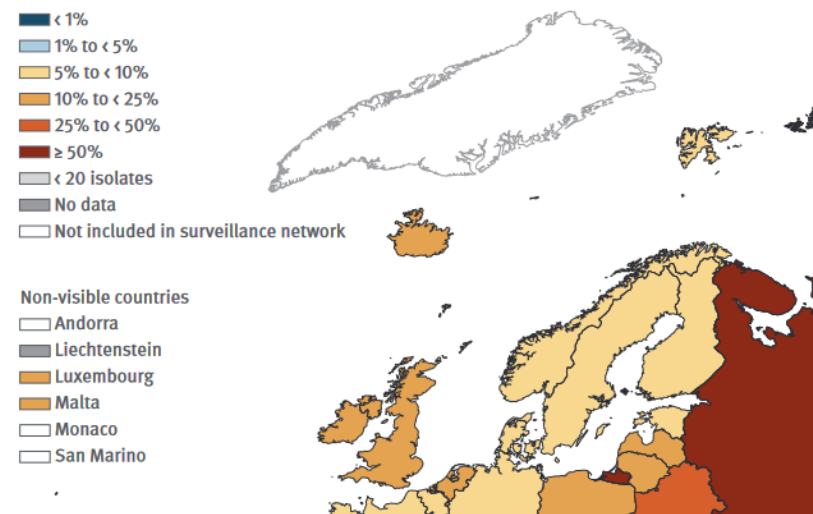


# Escherichia coli – Cef3G NS

## Lokalni podatki - EARS-Net 2022

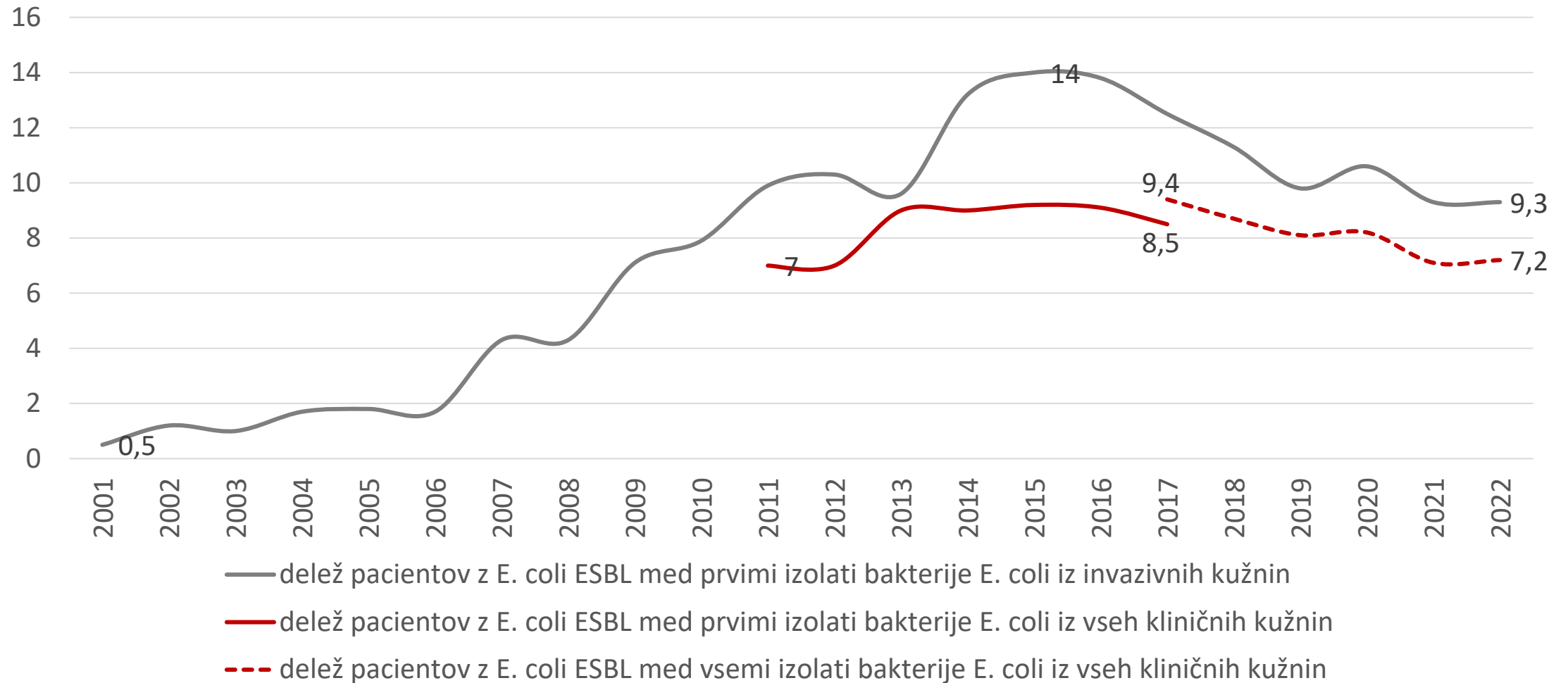


## EARS-Net/CAESAR 2021

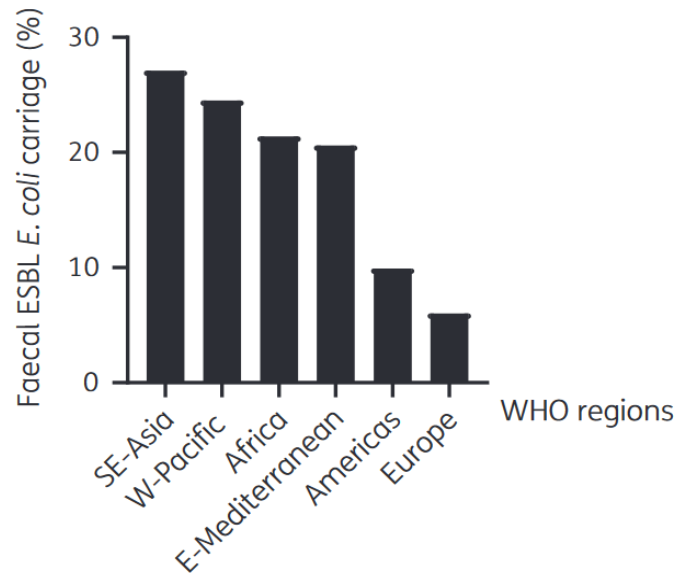


Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
<i>Escherichia coli</i>	Aminopenicillin (amoxicillin/ampicillin) resistance	104 198	57.0	102 375	56.6	107 371	54.6	108 836	53.1	116 543	53.4	32.5–68.6	↓*
	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	124 043	15.7	131 325	15.6	139 057	14.9	143 286	13.8	152 633	14.3	5.8–40.2	↓*
	Carbapenem (imipenem/meropenem) resistance	120 215	0.1	127 262	0.3	135 624	0.2	137 632	0.2	147 793	0.2	0.0–1.5	-
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	123 358	26.4	132 015	24.7	139 372	23.8	143 359	21.9	151 842	22.0	9.9–46.4	↓*
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance <sup>d</sup>	122 147	11.2	130 984	10.8	136 101	10.9	139 541	9.6	147 616	9.7	4.4–24.3	↓*
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides <sup>d</sup>	120 450	6.4	129 083	6.1	134 115	5.7	137 863	5.1	144 919	5.1	1.5–14.2	↓*

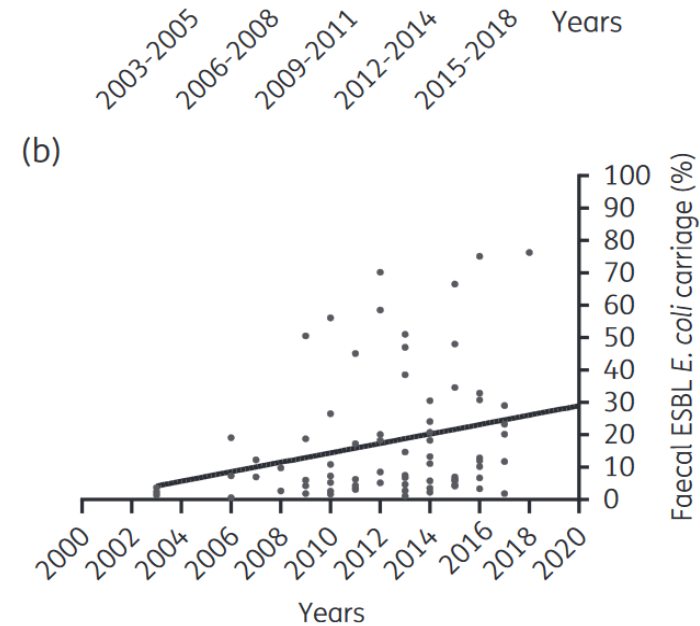
# E. coli - ESBL



# E. coli - ESBL



**Figure 2.** Pooled prevalence of intestinal ESBL *E. coli* carriage among healthy individuals in six WHO regions.<sup>30</sup> E-Mediterranean, Eastern Mediterranean; SE-Asia, South-East Asia; W-Pacific, Western Pacific region.



**Figure 3.** Global trend in faecal ESBL *E. coli* carriage among healthy individuals. (a) Pooled prevalence showing a clear increase from one 3 year interval to another. (b) A simple linear regression plot depicting the trend of carriage (1.5% rise per year,  $P=0.021$ ).

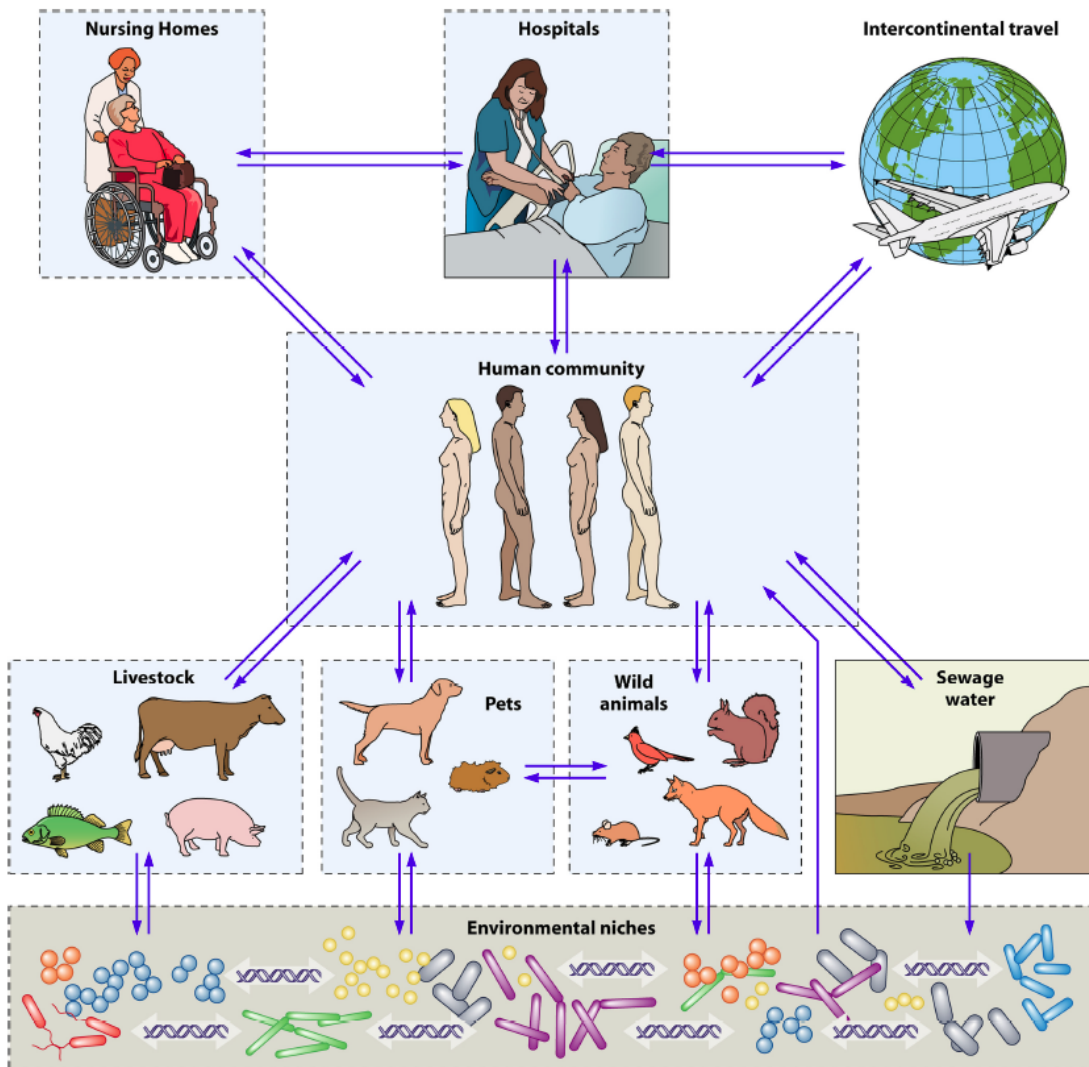
**z *E. coli* – ESBL je kolonizirana vsaj šestina svetovne populacije**



# Trends in Human Fecal Carriage of Extended-Spectrum $\beta$ -Lactamases in the Community: Toward the Globalization of CTX-M

October 2013

Paul-Louis Woerther,<sup>a</sup> Charles Burdet,<sup>b,c</sup> Elisabeth Chachaty,<sup>a</sup> Antoine Andremont<sup>b</sup>



**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  $\beta$ -lactamase-producing bacteria, CMI 2016

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.

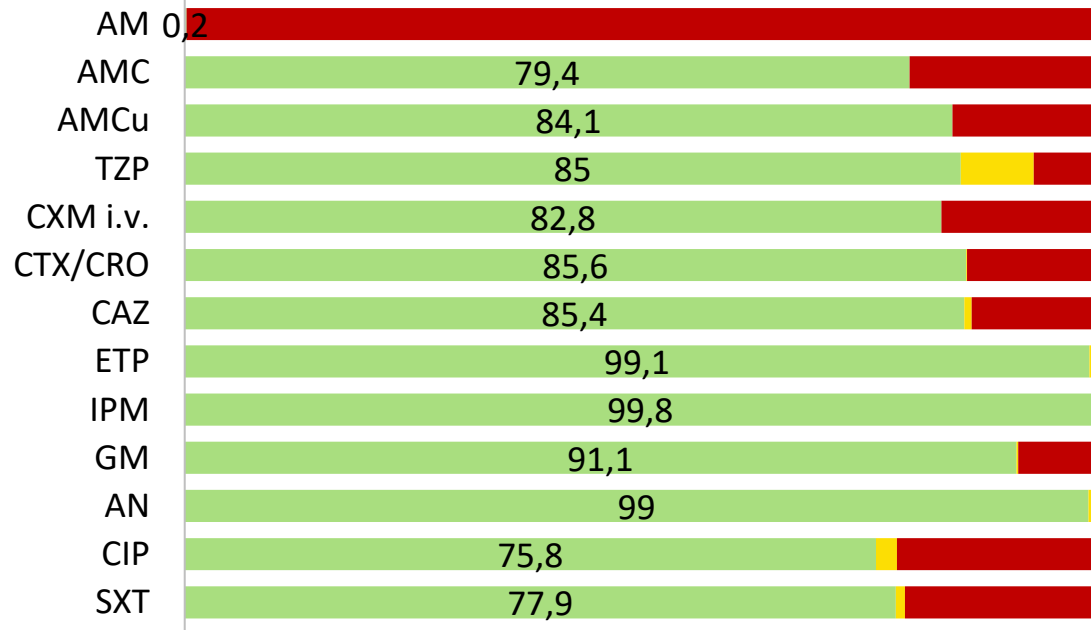
## Antimicrobial resistance: global report on surveillance. 2014

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

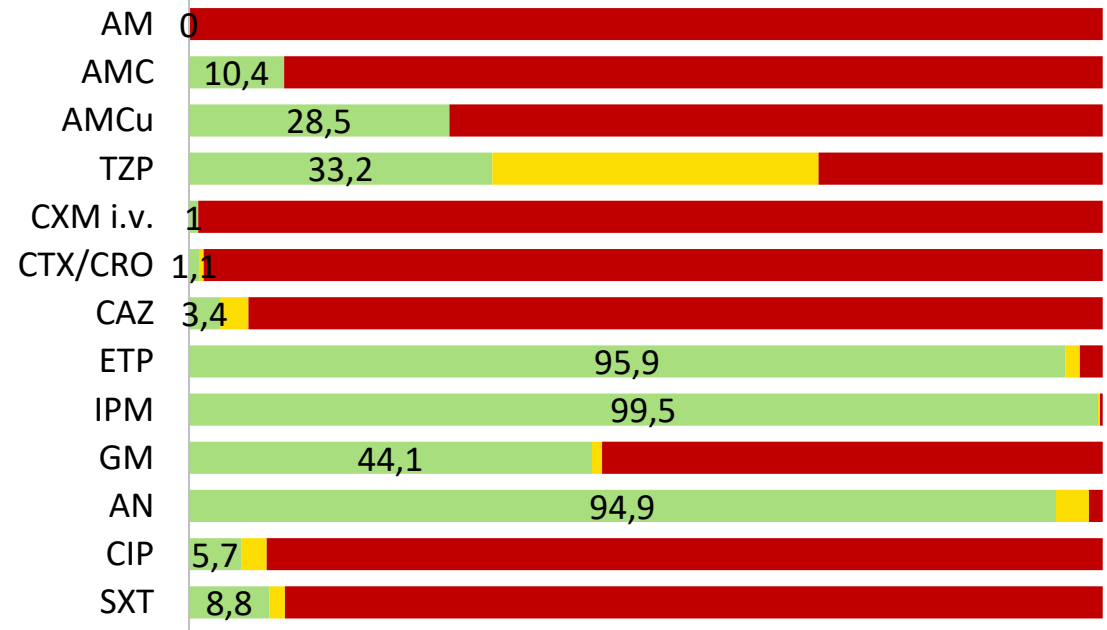
Data sources based on at least 30 tested isolates <sup>b</sup>	Overall reported range of resistant proportion (%)	Reported range of resistant proportion (%) in invasive isolates <sup>c</sup> (no. of reports)
<b>African Region</b> – National data (n=13 countries) – Publications (n=17) from 7 additional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

# *Klebsiella pneumoniae*

## *K. pneumoniae*

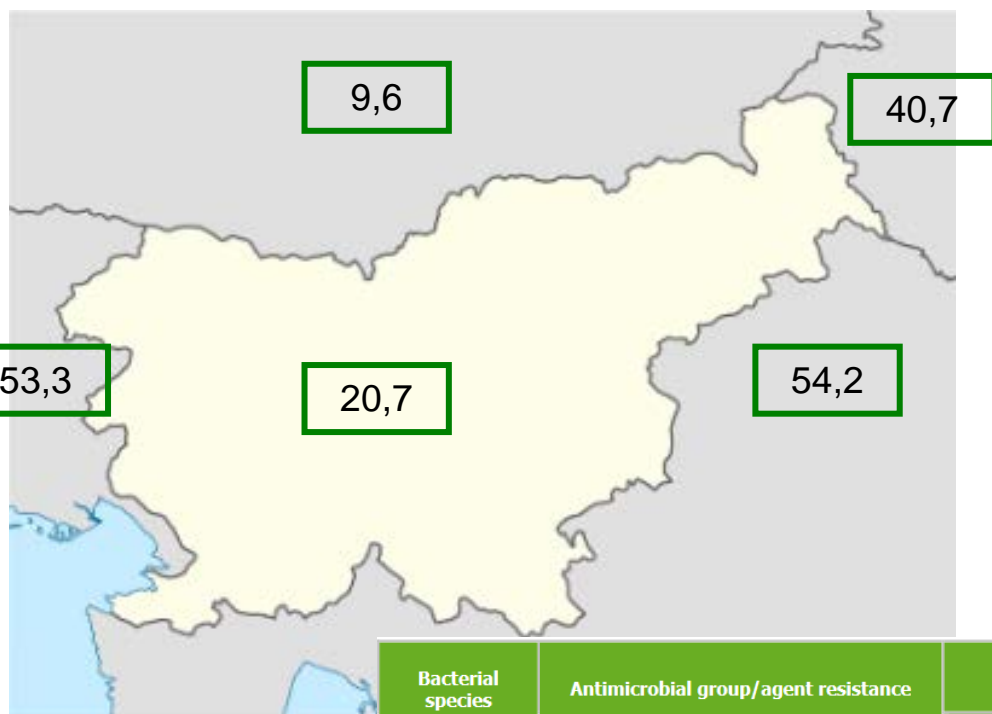


## *K. pneumoniae* - ESBL

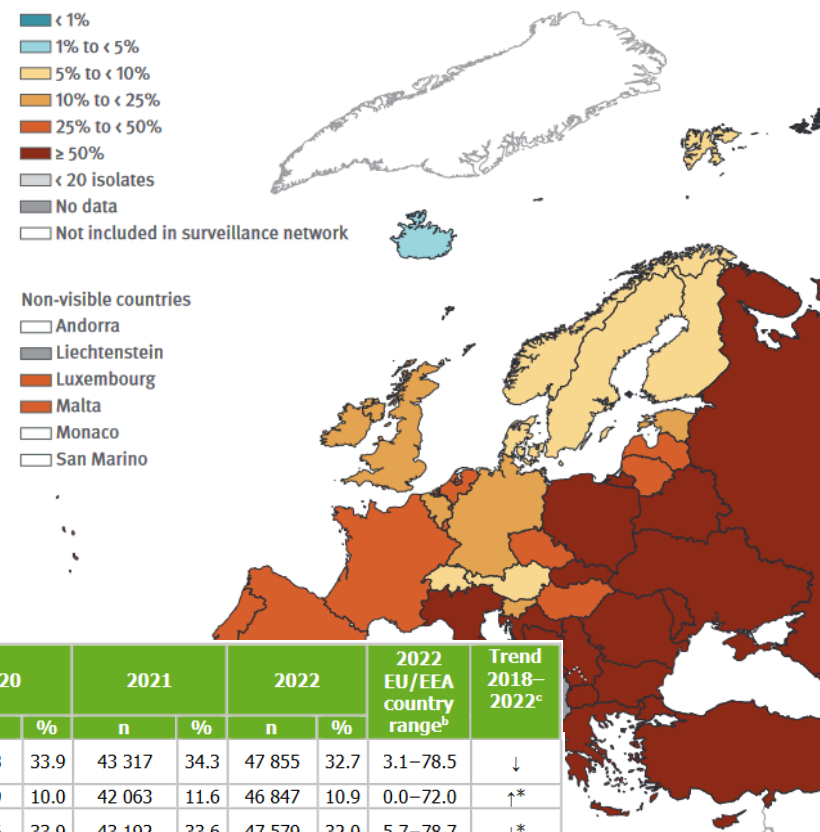


# Klebsiella pneumoniae - Cef3G NS

## Lokalni podatki - EARS-Net 2022

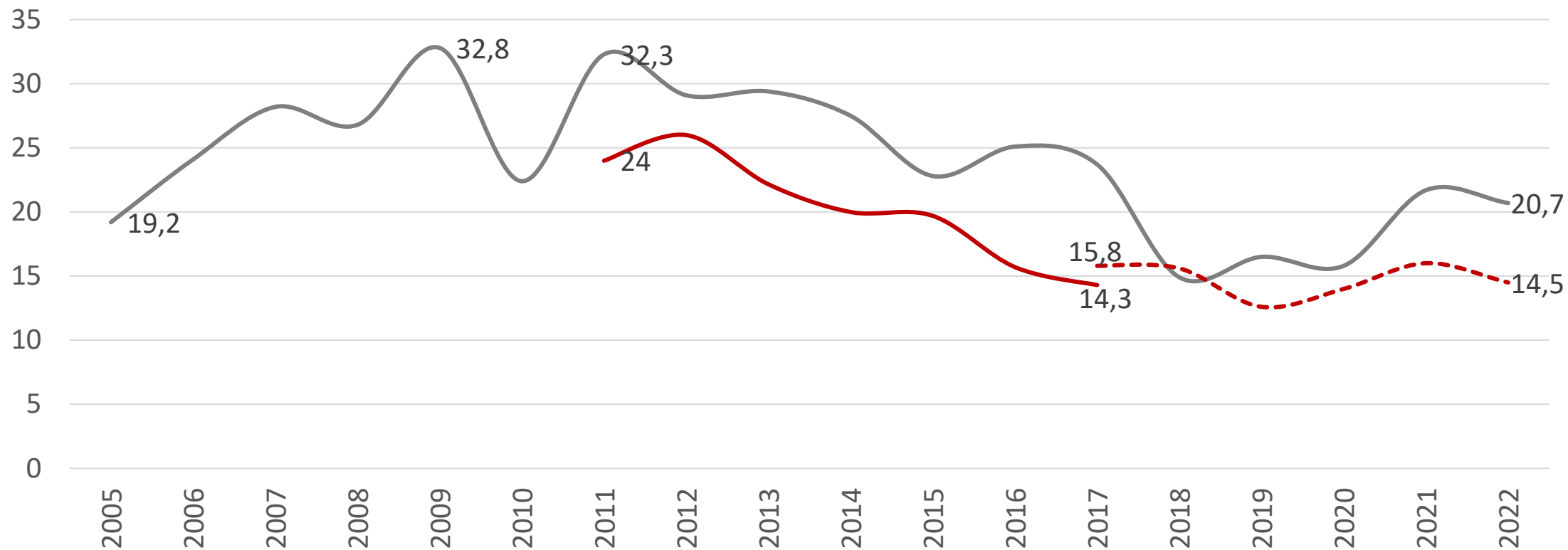


## EARS-Net/CAESAR 2021



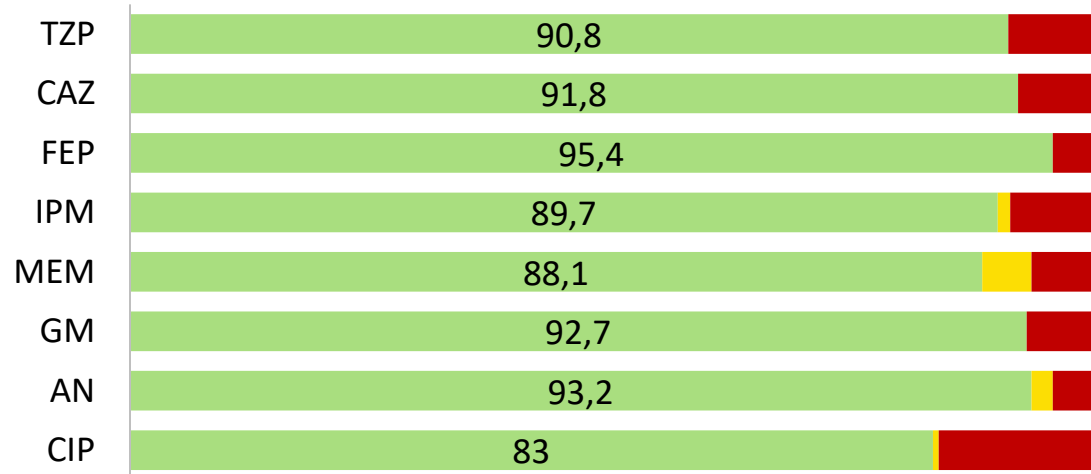
Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
<i>Klebsiella pneumoniae</i>	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	33 239	34.4	36 190	34.1	39 848	33.9	43 317	34.3	47 855	32.7	3.1–78.5	↓
	Carbapenem (imipenem/meropenem) resistance	32 548	8.5	35 439	9.0	39 279	10.0	42 063	11.6	46 847	10.9	0.0–72.0	↑*
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	33 154	34.3	36 315	34.0	40 066	33.9	43 192	33.6	47 579	32.0	5.7–78.7	↓*
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance <sup>d</sup>	32 830	24.7	36 078	24.5	38 977	23.7	42 237	23.7	46 660	22.5	0.0–67.9	↓*
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides <sup>d</sup>	32 381	21.6	35 622	21.5	38 331	21.0	41 646	21.2	45 815	20.0	0.0–66.2	↓

# *K. pneumoniae* - ESBL



- delež pacientov s *K. pneumoniae* ESBL med prvimi izolati bakterije *K. pneumoniae* iz invazivnih kužnin
- delež pacientov s *K. pneumoniae* ESBL med prvimi izolati bakterije *K. pneumoniae* iz vseh kliničnih kužnin
- - - delež pacientov s *K. pneumoniae* ESBL med vsemi izolati bakterije *K. pneumoniae* iz vseh kliničnih kužnin

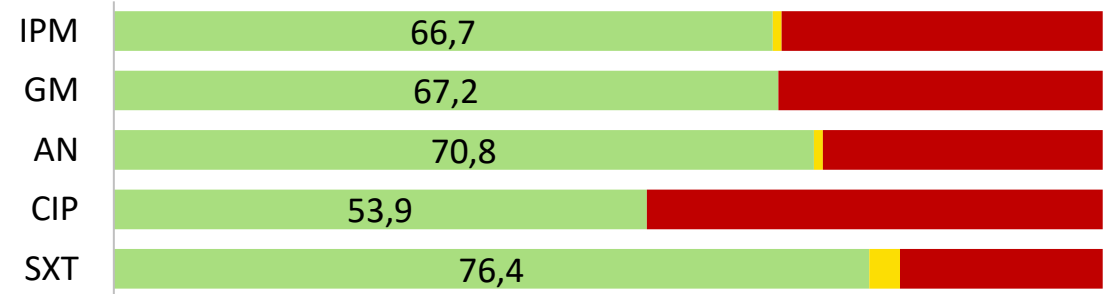
# *Pseudomonas aeruginosa*



- 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.

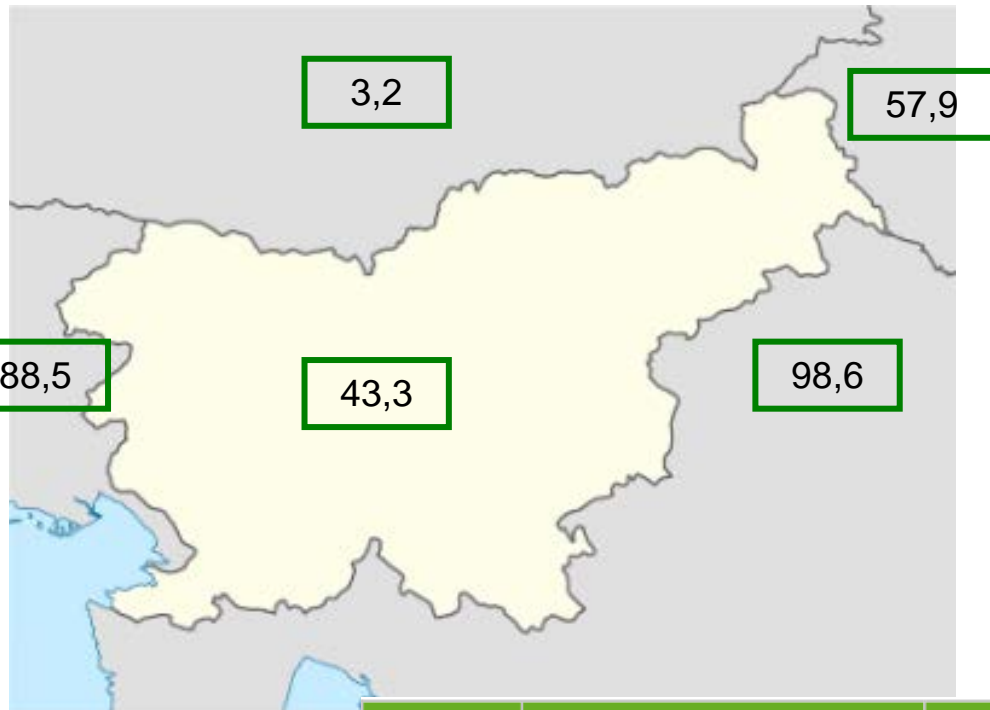
# *Acinetobacter baumannii*

- 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.

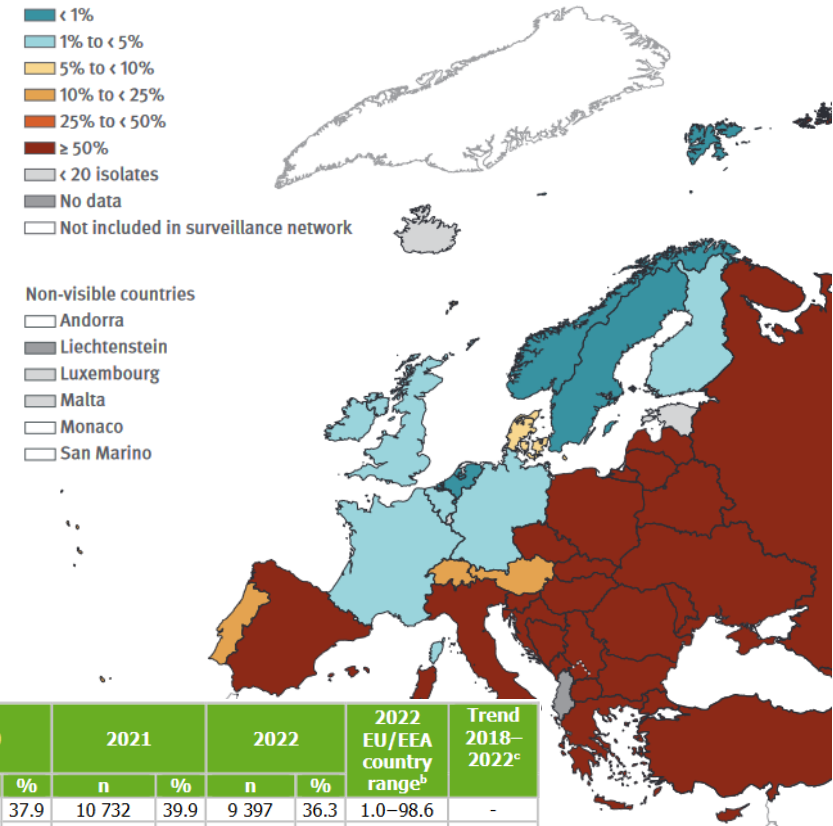


# Acinetobacter spp. - CRAb

## Lokalni podatki - EARS-Net 2022



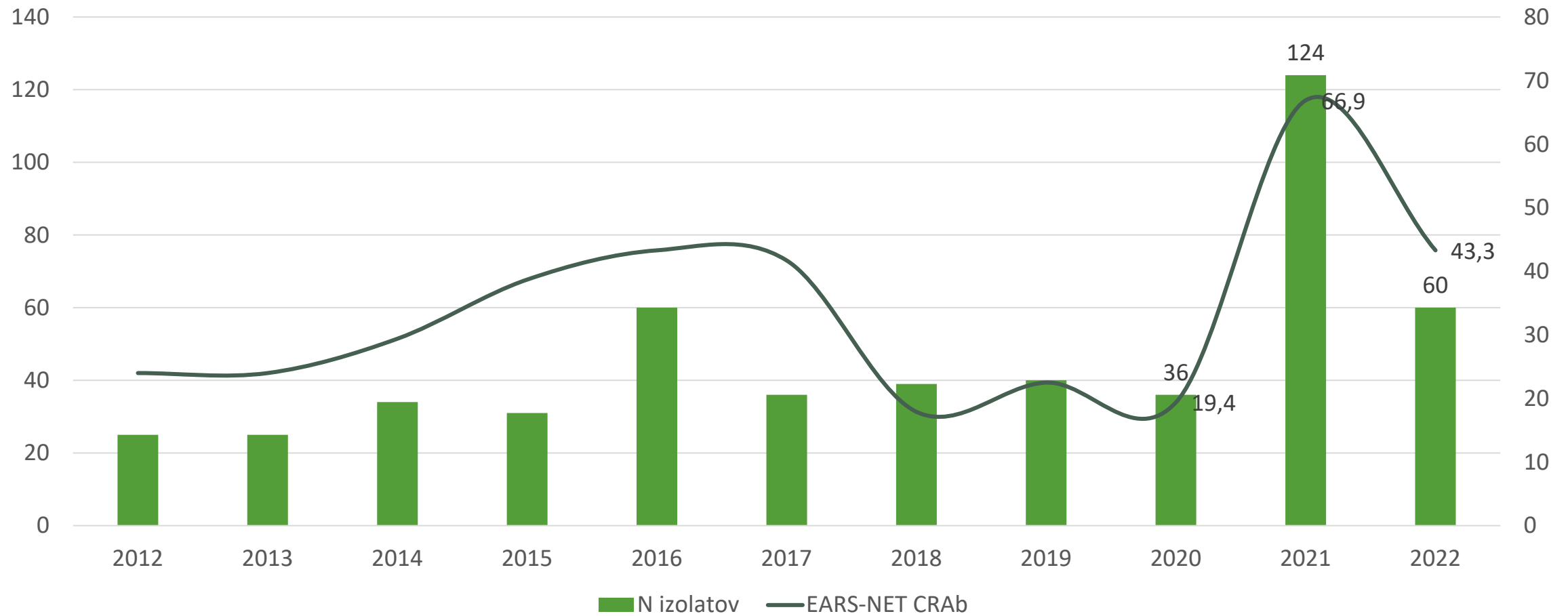
## EARS-Net/CAESAR 2021



Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
<i>Acinetobacter</i> species	Carbapenem (imipenem/meropenem) resistance	5 798	36.4	5 209	36.9	7 507	37.9	10 732	39.9	9 397	36.3	1.0–98.6	-
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	5 754	41.1	5 181	40.9	7 372	41.7	10 626	43.0	9 339	38.8	0.0–98.6	-
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance <sup>d</sup>	5 711	35.2	5 170	36.9	7 275	37.0	10 399	39.6	9 169	34.1	0.0–96.2	-
	Combined resistance to carbapenems, fluoroquinolones and aminoglycosides <sup>d</sup>	5 607	32.4	4 998	33.6	7 111	34.0	10 172	36.8	8 835	31.8	0.0–96.2	-

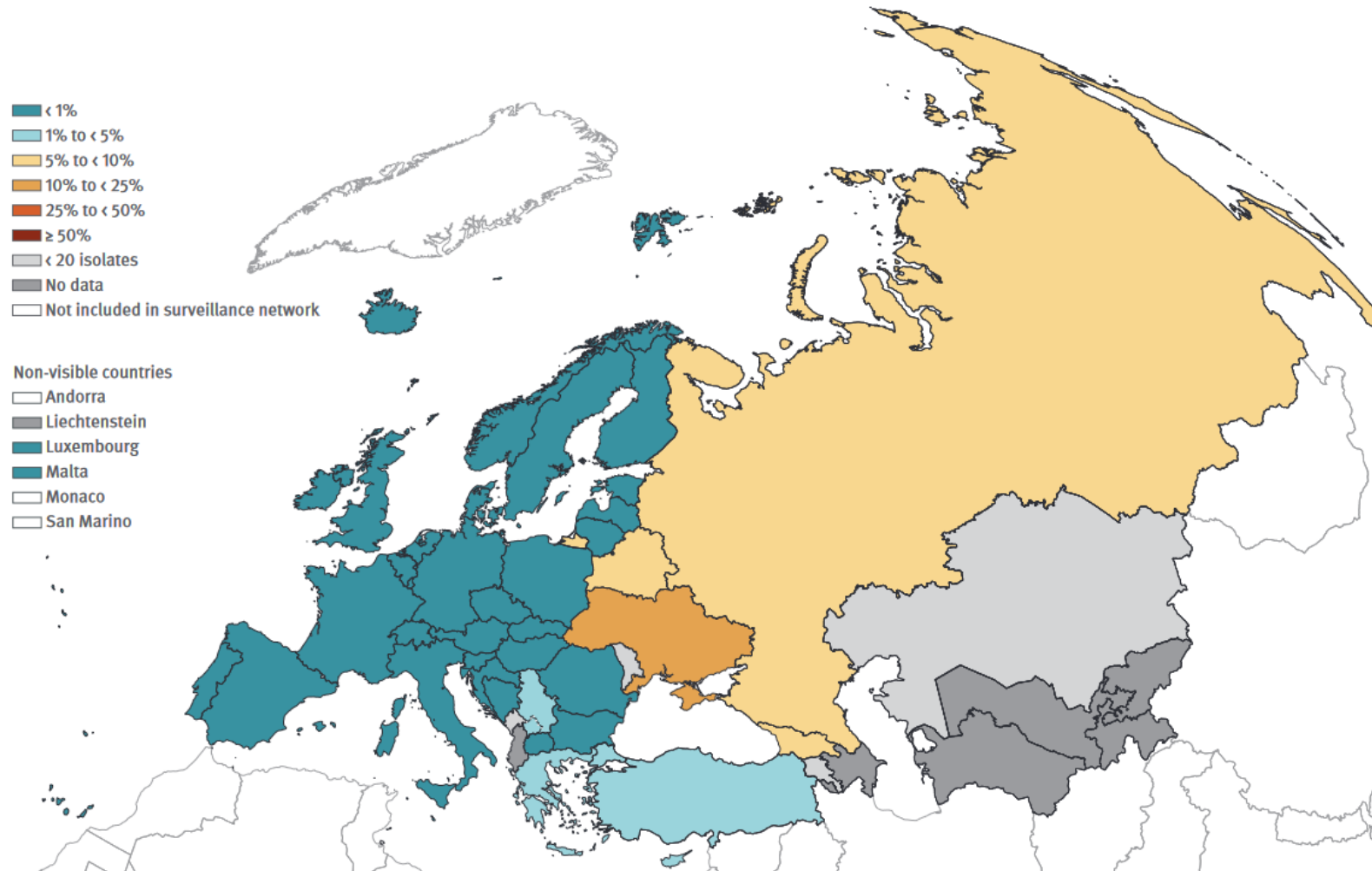


EARS-NET SLOVENIJA: <http://www.nijz.si/sl/ears-net-slovenija>



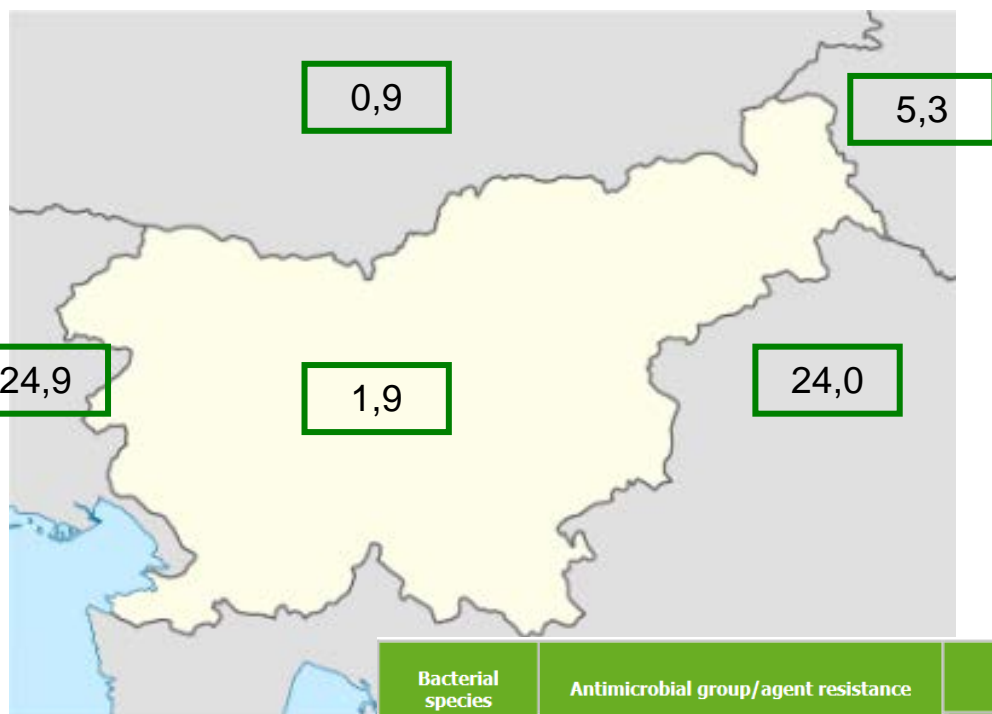
# E. coli - CRE

**Fig. 3** *Escherichia coli*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, WHO European Region, 2021

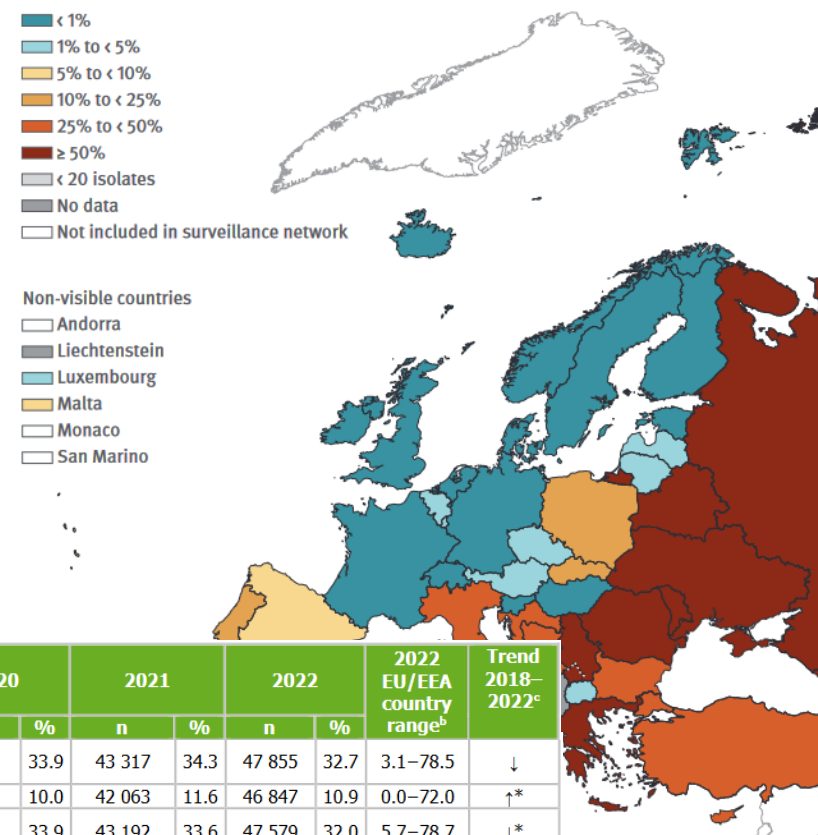


# Klebsiella pneumoniae - CRE

## Lokalni podatki - EARS-Net 2022

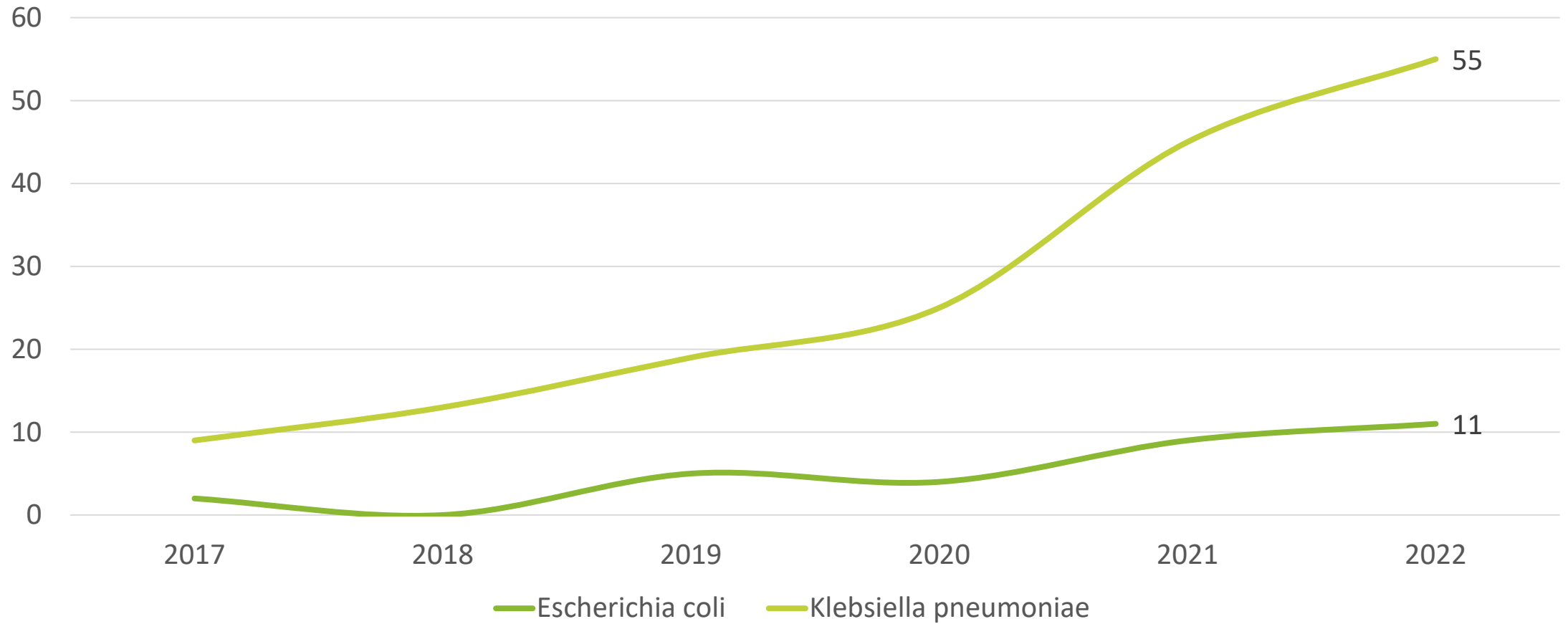


## EARS-Net/CAESAR 2021

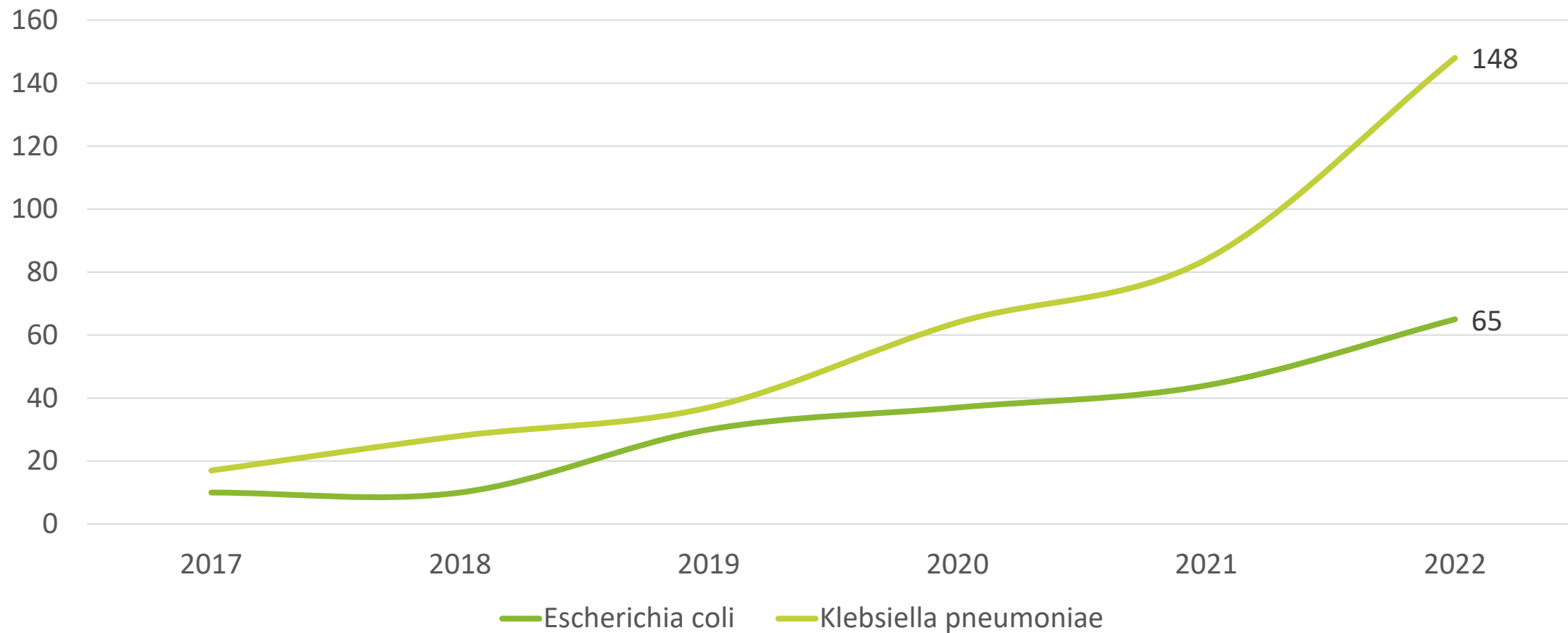


Bacterial species	Antimicrobial group/agent resistance	2018		2019		2020		2021		2022		2022 EU/EEA country range <sup>b</sup>	Trend 2018–2022 <sup>c</sup>
		n	%	n	%	n	%	n	%	n	%		
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# CPE v kliničnih kužninah

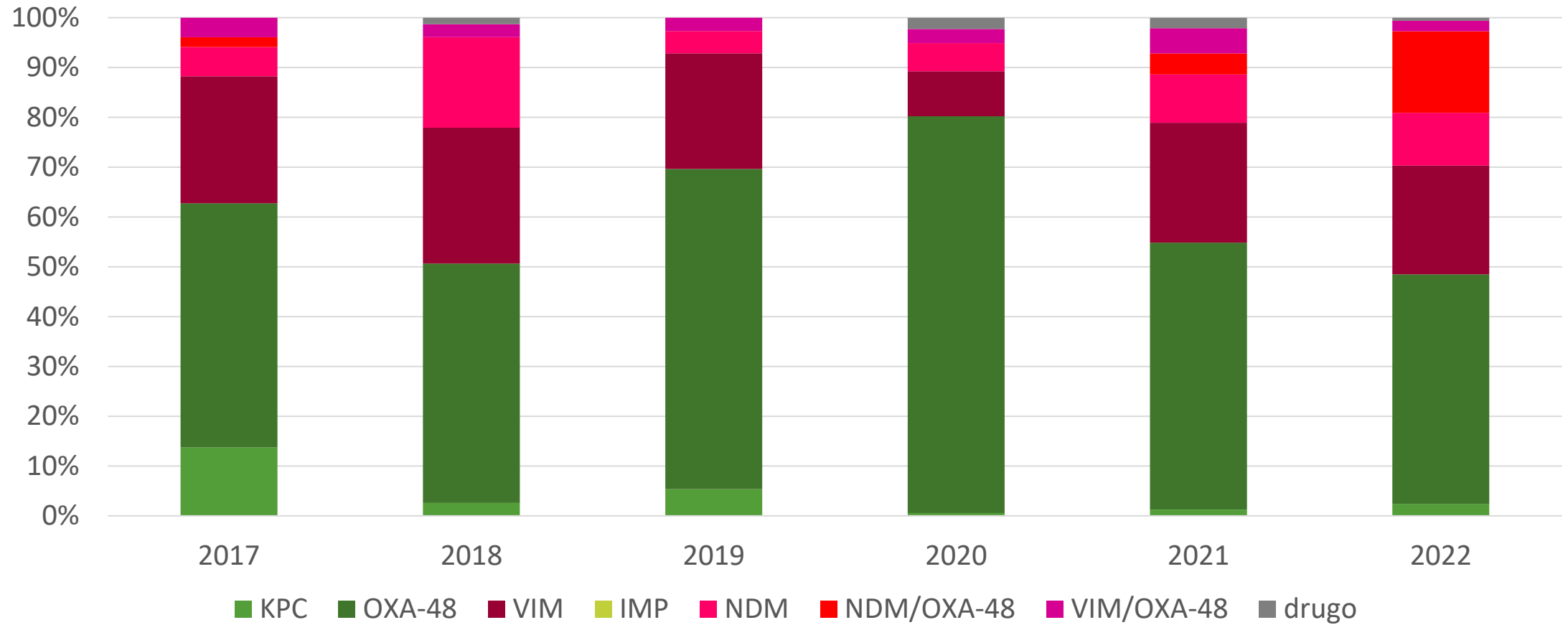


# CPE klinične in nadzorne kužnine

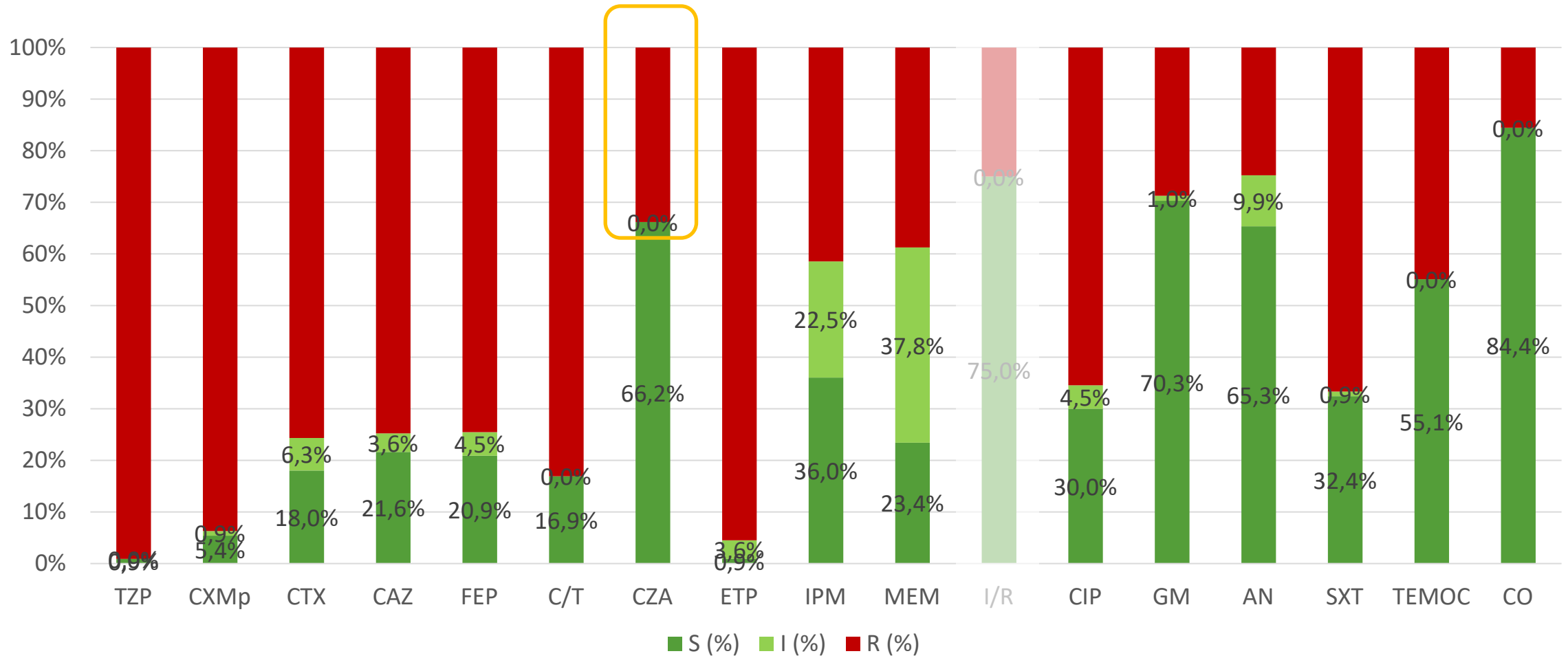


# Spekter karbapenemaz

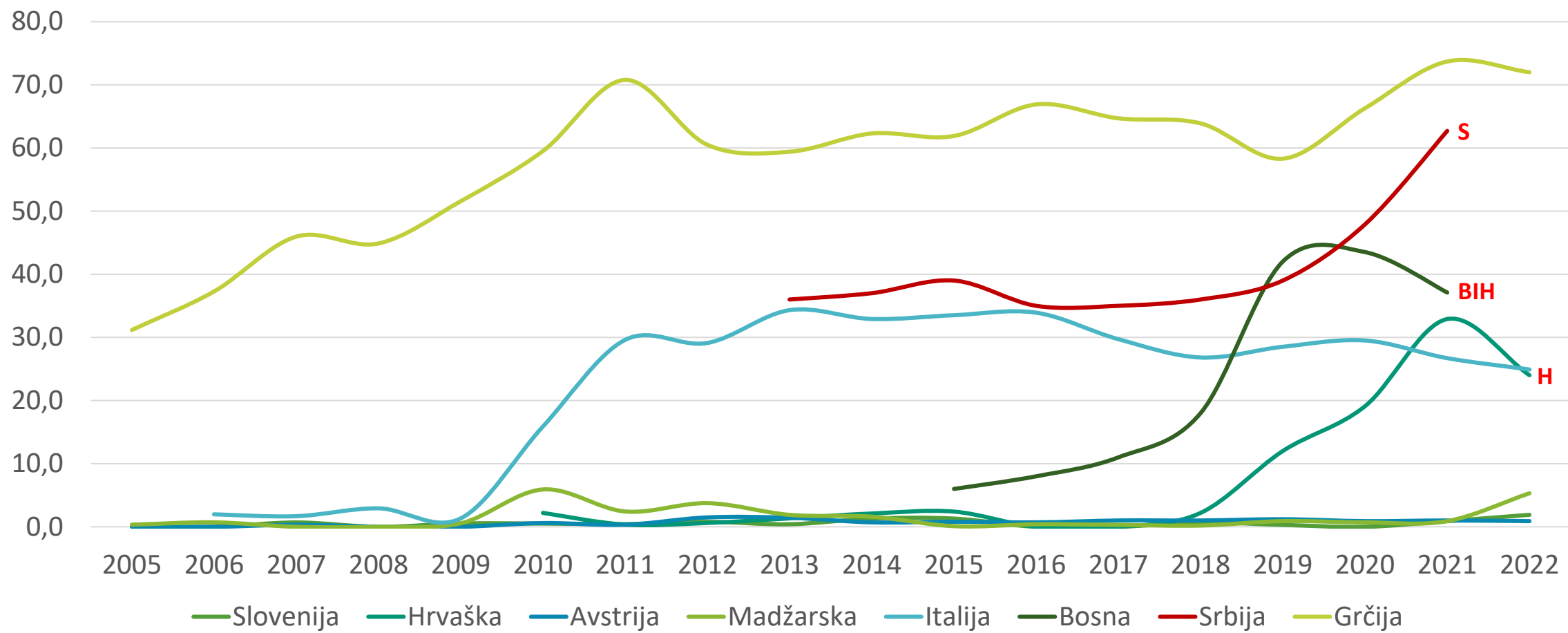
**51 %  
metalobetalaktamaze  
/ kombinacije**



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

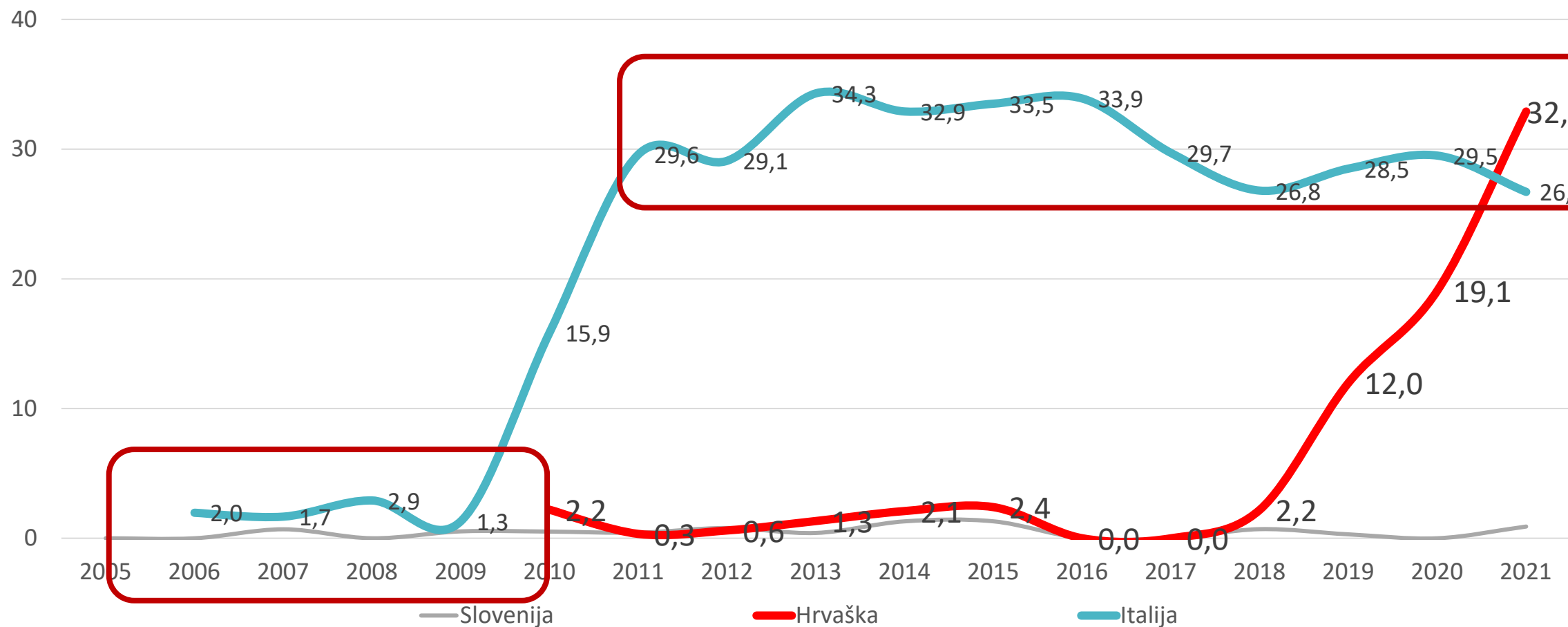


# *Klebsiella pneumoniae* - CRE





# *K. pneumoniae* - CRE



# 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*<sub>OXA-48-like</sub> (*n* = 4), *bla*<sub>KPC-2</sub> (*n* = 3), *bla*<sub>IMP</sub> (*n* = 2), and *bla*<sub>NDM-1</sub> (*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 ( $P < 10^{-6}$ ).

# Trajanje kolonizacije s CPE

- Podobno kot pri nosilstvu ESBL

**Two-year prospective evaluation of colonization with extended-spectrum beta-lactamase-producing Enterobacteriaceae: time course and risk factors**

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#### Abstract

**Background:** We wanted to determine the time course of colonization with extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (EPE), sites of colonization and risk factors for prolonged colonization with EPE to obtain information for successful infection control measures. **Methods:** Rectal swab, urine, throat swab and other clinically relevant samples (wound swab, tracheal aspirate and sputum) were obtained from each participant. Sets of follow-up samples and data about potential risk factors for prolonged colonization with EPE were collected every 3 months for 2 years. Multivariate analysis using a logistic regression model was performed to identify risk factors for prolonged colonization. **Results:** A total of 114 patients were included in the study, 49 completed the 2-year follow-up. In all, 611 sample sets were collected, 309 (50.6%) of which were positive for ESBL. Of the positive sample sets, 90% had a rectal swab positive for ESBL, the throat swab was positive for ESBL in 17.2% of cases and urine in 36.2% of cases; 10% of positive sample sets had negative rectal swabs with EPE isolated from other sites, most often from urine. Immobility was found to be associated with prolonged carriage ( $\geq 12$  months) of EPE. After 2 years, 15/49 (30.6%) patients were colonized with EPE. In 12/49 (24.5%) patients, transient negativity was observed. **Conclusions:** We found that prolonged colonization with EPE was common, especially in bedridden patients. Transient negative samples were often observed during the course of colonization. In some patients, urine can be the only positive site from which EPE are isolated.

čas po odkritju kolonizacije	Delež koloniziranih
3 mesece	75 %
6 mesecev	55 %
12 mesecev	35 %

## Natural history and decolonization strategies for ESBL/carbapenem-resistant Enterobacteriaceae carriage: systematic review and meta-analysis

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**Table 3.** Natural history of colonization without decolonization treatment among healthcare residents at the defined time points

Subgroup	No. of studies <sup>a</sup>	No. of patients <sup>a</sup>	Pooled rate of colonization (%) <sup>b</sup>	95% CI	I <sup>2</sup> (%)	P between subgroups
Total 1 months	12	429	76.7	69.3–82.8	52	
ESBL	6	190	80.2	67.7–88.7	56.9	0.383
CRE	6	239	73.9	64–81.8	47.9	
adult	10	360	74.8	67.7–80.7	39.7	0.306
children	2	69	92.1	46.5–99.4	81.0	
eradication defined as only 1 negative sample	5	86	69.4	59.7–77.7	0.0	0.068
eradication defined as >1 negative sample	7	274	81.5	71.4–88.6	64.7	
presence of MDR-E	9	362	75.0	67.7–81.1	46.5	0.315
persistence same MDR-E	4	128	83.9	65.5–93.5	54.7	
Total 3 months	10	431	75.2	64.6–83.4	74	
ESBL	6	268	76.5	61.1–87.1	76.9	0.852
CRE	4	163	74.6	56.6–86.9	72.7	
adult	8	359	72.5	61.6–81.2	68.9	0.017
children	1	51	96.1	80.7–99.3	0.0	
eradication defined as only 1 negative sample	5	210	69.2	52.3–82.1	62.4	0.168
eradication defined as >1 negative sample	5	221	82.9	67.8–91.8	80.7	
presence of MDR-E	7	294	70.7	56.2–82	65.7	0.496
persistence same MDR-E	4	198	78.0	59–89.7	87.3	
Total 6 months	10	408	55.3	43.7–66.4	76	
ESBL	5	223	56.1	38.7–72.1	83.7	0.945
CRE	5	185	55.2	37.3–71.9	67.3	
adult	7	322	53.0	38.8–66.8	55.6	0.659
children	2	67	67.6	38.4–87.5	95.5	
eradication defined as only 1 negative sample	4	141	43.1	26.9–60.9	4.7	0.079
eradication defined as >1 negative sample	6	267	63.9	48.9–76.5	82.2	
presence of MDR-E	8	302	47.6	35.6–59.8	43.2	0.065
persistence same MDR-E	3	167	68.3	49.9–82.4	90.7	
Total 12 months	12	861	35.2	28.2–42.9	67	
ESBL	7	689	35.7	26.3–46.2	76.9	0.899
CRE	5	172	34.6	22.9–48.5	46.0	
adult	9	782	33.5	26.4–41.5	53.9	0.555
children	2	65	39.4	21.1–61.1	88.0	
eradication defined as only 1 negative sample	6	620	30.9	22.7–40.6	54.1	0.208
eradication defined as >1 negative sample	6	241	39.8	29.9–50.7	62.9	
presence of MDR-E	10	787	32.6	25.8–40.3	60.4	0.328
persistence same MDR-E	3	135	40.0	17.7–53.8	63.3	

## Antimicrobial resistance: global report on surveillance. 2014

**Table 6** *Klebsiella pneumoniae*: Resistance to carbapenems<sup>a</sup> (summary of reported or published proportions of resistance, by WHO region)

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

# 68 letni moški, TX ledvice

## K. pneumoniae OXA-48/NDM

Vzorec: Kri - gojišče BACTEC - II. Periferna vena (Odvzeto 18.07.2023 ob 13:30)

V direktnem preparatu iz pozitivne hemokulture, obarvanem po Gram u, smo videli po Gramu negativne bacile.

Aerobna hemokultura

**Rezultat** 1. *Klebsiella pneumoniae* - CRE-CPE  
Izolirani sev izloča karbapenemazo. Posvetujte se z infektologom ali kliničnim mikrobiologom. Potrebna je dosledna izolacija bolnika.

Anaerobna hemokultura: **NEGATIVNO**. Preiskava je zaključena.

Za pravilno interpretacijo rezultatov antibiograma je potrebno upoštevati komentarje pod tabelo in poznati osnovne opredelitve EUCAST.

	1.
ampicilin	R
amoksisilin+klavulanska kislina	R
piperacilin+tazobaktam	R
cefuroksim (parenteralni)	R
cefotaksim	R
ceftriakson	R
ceftazidim	R
cefepim	R
cefiderocol	R
ceftolozan+tazobaktam	R
	>32/4
ceftazidim+avibaktam	R
	>16/4
ertapenem	R
	>2
meropenem	R
	>16
imipenem	R
	>16
imipenem+relebaktam	R
	32/4
aztreonam	R
	>32
gentamicin	R
amikacin	R
ciprofloksacin	R
levofloksacin	R
trimetoprim+sulfametoksazol	R
tigeciklin	NI
	1
kolistin	(S)
	0,5
fosfomicin (parenteralni)	R
	64

# 1 letna deklica, anomalija sečil

## K. pneumoniae NDM

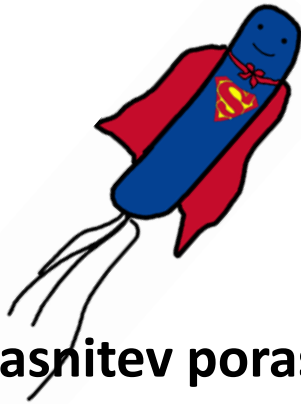
Vzorec: Kultura bakterij iz urina; vzorec v gojišču (Odvzeto 20.07.2023 ob 08:00)

Preiskava na aerobne bakterije

**Rezultat** 1. *Klebsiella pneumoniae* - CRE-CPE  
Izolirani sev izloča karbapenemazo. Posvetujte se z infektologom ali kliničnim mikrobiologom. Potrebna je dosledna izolacija bolnika.

Za pravilno interpretacijo rezultatov antibiograma je potrebno upoštevati komentarje pod tabelo in poznati osnovne opredelitve EUCAST.

	1.
ampicilin	R
amoksisilin+klavulanska kislina - U	R
amoksisilin+klavulanska kislina	R
piperacilin+tazobaktam	R
cefuroksim (parenteralni)	R
cefuroksim (oralni)	R
cefotaksim	R
ceftazidim	R
cefksim	R
cefepim	R
cefiderocol	R*
ceftolozan+tazobaktam	R
	>32/4
ceftazidim+avibaktam	R
	>16/4
ertapenem	R
	>2
meropenem	R
	>16
imipenem	R
	8
gentamicin	R
amikacin	R
norfloksacin	R
ciprofloksacin	R
levofloksacin	R
trimetoprim+sulfametoksazol	R
tigeciklin	NI
	2
nitrofurantoin	NI
kolistin	(S)
	0,5



## 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.