SURVEILLANCE REPORT

Antimicrobial resistance in the EU/EEA (EARS-Net)

Annual Epidemiological Report for 2019

Key facts

- Thirty European Union (EU) or European Economic Area (EEA) countries reported data for 2019 to the European Antimicrobial Resistance Surveillance Network (EARS-Net). Twenty-nine countries reported data for all eight bacterial species under surveillance by EARS-Net (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter* species, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium*), while one country reported data for all bacterial species except *S. pneumoniae*.
- EARS-Net data for 2019 displayed wide variations in the occurrence of antimicrobial resistance (AMR) across the EU/EEA depending on the bacterial species, antimicrobial group and geographical region.
- The most commonly reported bacterial species was *E. coli* (44.2%), followed by *S. aureus* (20.6%), *K. pneumoniae* (11.3%), *E. faecalis* (6.8%), *P. aeruginosa* (5.6%), *S. pneumoniae* (5.3%), *E. faecium* (4.5%) and *Acinetobacter* species (1.7%).
- In 2019, more than half of the *E. coli* isolates reported to EARS-Net and more than a third of the *K. pneumoniae* isolates were resistant to at least one antimicrobial group under surveillance, and combined resistance to several antimicrobial groups was frequent. Resistance percentages were generally higher in *K. pneumoniae* than in *E. coli*. While carbapenem resistance remained rare in *E. coli*, several countries reported carbapenem resistance percentages above 10% in *K. pneumoniae*. Carbapenem resistance was also common in *P. aeruginosa* and *Acinetobacter* species, and at higher percentages than in *K. pneumoniae*. For most gram-negative bacterial species–antimicrobial group combinations, changes in resistance percentages between 2015 and 2019 were moderate, and resistance remained at previously reported high levels.
- For *S. aureus*, the decline in the percentage of meticillin-resistant (i.e. MRSA) isolates reported in previous years continued in 2019. Nevertheless, MRSA remains an important pathogen in the EU/EEA, with levels still high in several countries, and combined resistance to another antimicrobial group was common. Decreases during the same period were also noted for penicillin non-wild type and macrolide resistance in *S. pneumoniae*.
- One development of particular concern was the increase in the percentage of vancomycin-resistant isolates of *E. faecium* in the EU/EEA, from 10.5% in 2015 to 18.3% in 2019 (EU/EEA population-weighted mean percentage).
- For several bacterial species–antimicrobial group combinations, a north-to-south and west-to-east gradient was evident in the EU/EEA. In general, lower percentages of resistance were reported by countries in the north of Europe and higher percentages were reported by countries in the south and east of Europe. However, for vancomycin-resistant *E. faecium,* no distinct geographical pattern was evident.

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Methods

This report is based on data reported to the European Antimicrobial Resistance Surveillance Network (EARS-Net) for the period 2015 to 2019, retrieved from The European Surveillance System (TESSy) and ECDC's decentralised data storage for antimicrobial resistance and healthcare-associated infections (ARHAI) on 10 September 2020. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases in Europe. The ARHAI decentralised data storage is a system allowing EU/EEA countries to store their surveillance data on their national servers in TESSy data format. A subset of the data used for this report is available online from ECDC's online Surveillance Atlas of Infectious Diseases [1].

The antimicrobial resistance (AMR) results presented in this report are based on antimicrobial susceptibility testing (AST) results from invasive (blood or cerebrospinal fluid) isolates of eight bacterial species. These species are all of public health importance in Europe: *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter species, Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecalis* and *Enterococcus faecium.*

Each year, 30 European Union (EU) and European Economic Area (EEA) countries report AST results collected from medical microbiology laboratories to EARS-Net. When it is not possible to include data from all relevant laboratories in the country, countries can report data from sentinel laboratories. In 2019, the estimated national population coverage of the data reported to EARS-Net varied between 11% and 100%, with more than one third of the countries reporting a population coverage of 80% or higher. Data validity, reported as sample representativeness by the National Focal Points for AMR and/or the Operational Contact Points for Epidemiology/Microbiology/TESSY-IT data manager for AMR, was assessed as high by just under two thirds of the countries. However, of the eight countries reporting medium or poor geographical representativeness or hospital sample representativeness, most were countries with a comparatively low population coverage (Table 1).

For several countries, there have been changes in the blood culture rate, population coverage or data representativeness between 2015 and 2019[1], and these differences should be kept in mind when interpreting trends in AMR percentages.

Starting with data collected for 2019, EARS-Net now only accepts AST results generated using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints and methodology [2], thus ensuring compliance with the EU case definition for AMR [3]. In previous years, use of EUCAST breakpoints was encouraged, but results based on other interpretive criteria were accepted. In 2019, a majority of countries had fully implemented the EUCAST methodology among EARS-Net contributing laboratories. However, for a few countries, this new requirement has resulted in a lower number of laboratories included in 2019 compared to previous years.

The ongoing COVID-19 pandemic has challenged the national reporting capacity of some countries, resulting in fewer laboratories reporting compared to previous years. An overview of the number of reporting laboratories and of isolates reported, per country and for the period 2015 to 2019, can be found in a PDF containing all country summaries which is available on the landing page for this report (see footnote 1).

A more detailed description of the methodology is available in the EARS-Net reporting protocol [4]. All laboratories providing data to EARS-Net are offered the opportunity to participate in an annual External Quality Assessment (EQA) to assess the reliability of the laboratory test results [5].

Data analysis

Before data analysis, data were de-duplicated to only include the first isolate per patient, year and bacterial species. The main steps of the data analysis are described in the next sections. For a detailed description of the EARS-Net surveillance system and how the data is interpreted, please refer to the EARS-Net 2018 report [6].

AST categories

For the analysis, an isolate was considered as resistant to an antimicrobial agent when tested and categorised as resistant (R) according to EUCAST clinical breakpoints. For *S. pneumoniae*, the term penicillin non-wild-type was used in this report, referring to *S. pneumoniae* isolates reported by the local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming Minimum Inhibitory Concentrations (MIC)s to benzylpenicillin above those of wild-type isolates (i.e. >0.06 mg/L). Data reported before 2019 may include results obtained using other clinical breakpoints, with different definitions of the cut-off values for the AST categories.

National percentages

Resistance/non-wild-type percentages are presented for a single antibiotic and/or for a group of antibiotics. The bacterial species-antimicrobial agent combinations presented in this report are shown in Table 2. When combining the results for a

[1] A PDF containing all country summaries is available on the landing page for this report at the following link: https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2019

group of antibiotics, the outcome was based on the result for the antibiotic showing the highest level of resistance. For example, when an isolate was 'susceptible, increased exposure' (I) to imipenem and 'resistant' (R) to meropenem, then the susceptibility to the group carbapenems, which comprises imipenem and meropenem, was set to R.

Combined resistance was reported when the isolate was R to at least one antibiotic in each of the antibiotic groups in the definition of combined resistance, with the exception of *S. pneumoniae* for which combined resistance was based on combined penicillin non-wild-type and R to macrolides (Table 3). Isolates with missing data for one or several of the required antibiotic groups were excluded from the analysis of combined resistance. Missing data could be caused by differences in local AST panels or limited reporting of results to local or national surveillance initiatives. The proportion of isolates included should be taken into account when interpreting results for combined resistance.

When fewer than 10 isolates were reported for a specific bacterial species–antimicrobial group combination in a country, the AMR percentage was not displayed on the maps or in the tables presented in this report.

EU/EEA population-weighted mean percentage

An EU/EEA population-weighted mean percentage was determined by multiplying the AMR percentage for each country with the corresponding national population weight and summing up the results; weights were rescaled if AMR percentages were not available for one or more countries. Annual population data were retrieved from the Eurostat online database [7]. To calculate the EU/EEA percentage, country weightings were used to adjust for imbalances in reporting propensity and population coverage, since, in most cases, the number of reported isolates by country was not representative of the total population.

Trend analyses

The statistical significance of temporal trends in AMR percentages by country and for the EU/EEA population-weighted mean was calculated based on data from the last five years (i.e. 2015 to 2019). Countries reporting fewer than 20 isolates for any individual year within the period, or not providing data for all years within the period, were not included in the analysis. The statistical significance of trends was assessed by a chi-square test for trend, and a p-value of <0.05 was considered significant. An additional sensitivity analysis was performed when assessing the significance of the trends by including only laboratories that consistently reported data for the full five-year period, thus minimising bias due to changes in reporting laboratories over time (e.g. by expansion of the surveillance network, or loss of laboratories due to the restriction to only include data from laboratories employing EUCAST clinical breakpoints). In some cases, this restriction results in a considerably lower number of isolates than for the analysis which includes all laboratories.

Table 1. Self-assessed national coverage and sample representativeness* and blood culture sets/1 000 patient-days, EU/EEA countries, 2019

Country	Estimated national population coverage (%)	Geographical representativeness	Hospital representativeness	Patient and isolate representativeness	Blood culture sets/ 1 000 patient-days
Austria	Unknown	High	High	High	Unknown
Belgium	26	Medium	High	High	87.5**
Bulgaria	45	Medium	Medium	Medium	8.6
Croatia	Unknown	Unknown	Unknown	Unknown	Unknown
Cyprus	35	High	High	High	56.9
Czechia	81	High	High	High	16.8
Denmark	100	High	High	High	160.9
Estonia	100	High	High	High	33.4
Finland	96	High	High	High	160.4
France	20**	High	High	High	112.2
Germany	27	High	Medium	High	37.9
Greece	Unknown	Unknown	Unknown	Unknown	Unknown
Hungary	90	High	High	High	12.3
Iceland	100	High	High	High	61.6
Ireland	96	High	High	High	58.9
Italy	41	High	High	High	Unknown
Latvia	90	High	Medium	Medium	9.5
Lithuania	100	High	High	High	6.1
Luxembourg	Unknown	Unknown	Unknown	Unknown	Unknown
Malta	95	High	High	High	28.5
Netherlands	70	High	High	High	Unknown
Norway	94	High	High	High	86.7
Poland	17	Medium	Medium	Medium	39.8
Portugal	97	High	High	High	244.2
Romania	11	Poor	Poor	Poor	21.0
Slovakia	56	High	High	High	36.1
Slovenia	99	High	High	High	40.4
Spain	32	Medium	High	High	67.6
Sweden	78	High	High	High	105.6
United Kingdom	Unknown***	Medium***	High	High	Unknown

* As estimated by the National Focal Points for AMR and/or the Operational Contact Points for Epidemiology/Microbiology/TESSY-IT data manager for AMR.

Estimated population coverage: Mean population coverage (%) of laboratories capable of reporting data on *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium*.

Geographical representativeness: *High*: All main geographical regions are covered and data are considered as representative of the national epidemiology. *Medium*: Most geographical regions are covered and data are considered to provide medium representativeness of the national epidemiology. *Poor*: Only a few geographical areas are covered and data are poorly representative of the national epidemiology. *Unknown*: unknown or no data provided.

Hospital representativeness: *High*: The hospital sample is representative of the acute care hospital distribution in the country. *Medium*: The hospital sample is partly representative of the acute care hospital distribution in the country. *Poor*: The hospital sample is poorly representative of the acute care hospital distribution in the country. *Unknown*: Unknown or no data provided.

Patient and isolate representativeness: *High*: The isolate sample is representative of bacterial species causing invasive infections and of patient case-mix for the hospitals included. *Medium*: The isolate sample is partly representative of bacterial species causing invasive infections and of patient case-mix for the hospitals included. *Poor*: The isolate sample is poorly representative of bacterial species causing invasive infections and of patient case-mix for the hospitals included. *Unknown*: Unknown or no data provided.

** Not including *Streptococcus pneumoniae* network

*** Estimated 100% population coverage and high representativeness in Northern Ireland, Scotland and Wales.

Table 2. Bacterial species-antimicrobial group combinations presented in this report

Bacterial species	Antimicrobial group	Antimicrobial agents
Escherichia coli	Aminopenicillins	Ampicillin or amoxicillin
	Third-generation cephalosporins	Cefotaxime, ceftriaxone or ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin
	Aminoglycosides	Gentamicin, tobramycin or netilimicin
Klebsiella pneumoniae	Third-generation cephalosporins	Cefotaxime, ceftriaxone or ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin
	Aminoglycosides	Gentamicin, tobramycin or netilimicin
Pseudomonas aeruginosa	Piperacillin + tazobactam	Piperacillin + tazobactam
	Ceftazidime	Ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Aminoglycosides	Gentamicin, tobramycin or netilimicin
Acinetobacter species	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Aminoglycosides	Gentamicin, tobramycin or netilimicin
Streptococcus pneumoniae	Penicillins	Oxacillin or penicillin*
	Macrolides	Clarithromycin, erythromycin or azithromycin
	Fluoroquinolones	Levofloxacin or moxifloxacin**
	Third-generation cephalosporins	Cefotaxime or ceftriaxone
Staphylococcus aureus	MRSA	Cefoxitin, oxacillin or molecular MRSA confirmation tests***
	Rifampicin	Rifampin
	Fluoroquinolones	Levofloxacin, ofloxacin or ciprofloxacin****
Enterococcus faecalis and *Enterococcus faecium*	High-level aminoglycoside resistance	Gentamicin high-level resistance
	Vancomycin	Vancomycin

* Priority is given to penicillin susceptibility test results over oxacillin results.

** Susceptibility results for norfloxacin are also accepted as marker for fluoroquinolone susceptibility. Priority is given to levofloxacin and moxifloxacin susceptibility results over norfloxacin results.

*** Detection of the *mecA* gene by PCR or positive PBP2A-agglutionation test is given priority over phenotypic susceptibility results. Reports of cloxacillin or dicloxacillin or flucloxacillin or meticillin resistance are accepted as marker for oxacillin resistance if oxacillin is not reported.

**** Susceptibility results for norfloxacin are also accepted as marker for fluoroquinolone susceptibility. Priority is given to ciprofloxacin, levofloxacin and/or ofloxacin susceptibility results over norfloxacin results.

EU/EEA overview

Epidemiology

Thirty EU/EEA countries reported data for 2019 to EARS-Net. Twenty-nine countries reported data for all eight bacterial species under surveillance by EARS-Net (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* species, *S. pneumoniae*, *S. aureus*, *E. faecalis* and *E. faecium*), while one country (Greece) reported data for all bacterial species except *S. pneumoniae*. The most commonly reported bacterial species was *E. coli* (44.2%), followed by *S. aureus* (20.6%), *K. pneumoniae* (11.3%), *E. faecalis* (6.8%), *P. aeruginosa* (5.6%), *S. pneumoniae* (5.3%), *E. faecium* (4.5%) and *Acinetobacter* species (1.7%).

Country-specific results on data availability and age group, sex and ICU patient proportions are available for each bacterial species[2] , and for age group and sex for specific AMR phenotypes in the ECDC Surveillance Atlas of Infectious Diseases [1].

The AMR situation in bacterial species reported to EARS-Net for 2019 varied widely, depending on the bacterial species, antimicrobial group (Table 3) and geographical region (Figures 1-10 and related PDF in link).

In 2019, more than half of the *E. coli* isolates reported to EARS-Net and more than a third of the *K. pneumoniae* isolates were resistant to at least one antimicrobial group under surveillance, and combined resistance to several antimicrobial groups was frequent. Resistance percentages were generally higher in *K. pneumoniae* than in *E. coli*. While carbapenem resistance remained rare in *E. coli*, several countries reported carbapenem resistance percentages above 10% in *K. pneumoniae*. Carbapenem resistance was also common in *P. aeruginosa* and *Acinetobacter* species, and at higher percentages than in *K. pneumoniae*. For most gram-negative bacteria under surveillance, changes in the EU/EEA mean resistance percentages between 2015 and 2019 were moderate, and resistance remained at previously reported high levels.

For *S. aureus*, the decline in the percentage of meticillin-resistant (i.e. MRSA) isolates reported in previous years continued in 2019. Nevertheless, MRSA remains an important pathogen in the EU/EEA, with levels still high in several countries, and combined resistance to another antimicrobial group was common. Decreases during the same period were also noted for penicillin non-wild type and macrolide resistance percentages in *S. pneumoniae*.

One development of particular concern was the increase in the percentage of vancomycin-resistant isolates of *E. faecium* in the EU/EEA, from 10.5% in 2015 to 18.3% in 2019 (EU/EEA population-weighted mean percentage).

For several bacterial species–antimicrobial group combinations, the reported AMR percentages varied widely between countries, and a north-to-south and west-to-east gradient was evident. In general, the lowest AMR percentages were reported by countries in the north of Europe whereas the highest AMR percentages were reported by countries in the south and east of Europe. However, for vancomycin-resistant *E. faecium,* no distinct geographical pattern could be seen.

Discussion

The considerable variability in AMR percentages across EU/EEA countries highlights opportunities for significant AMR reduction through investments to improve current control and prevention practices. Despite the political prioritisation of AMR as a threat to public health and the availability of evidence-based guidance for antimicrobial stewardship, adequate microbiological capacity and infection prevention and control, it is clear that public health action to tackle AMR remains insufficient.

The major driver behind the occurrence and spread of AMR is the use of antimicrobial agents and transmission of microorganisms with AMR - between humans, between animals, and between humans, animals and the environment. While antimicrobial use exerts an ecological pressure on microorganisms and contributes to the emergence and selection of AMR, poor infection prevention and control practices promote further spread of microorganisms with AMR. Results from the ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals showed that the prevalence of patients receiving antibiotics was positively associated with AMR, and conversely, antibiotic stewardship activities and resources for hospital hygiene were negatively associated with AMR [8]. Prudent antimicrobial use and high standards for infection prevention and control in all healthcare sectors are the cornerstones of an effective response to AMR.

AMR calls for concerted efforts at country level as well as close international cooperation. In 2017, the European Commission adopted a European One Health Action Plan against AMR to support the EU and its Member States in delivering innovative, effective and sustainable responses to AMR [9]. In a 2017 survey, a majority of EU/EEA countries reported having initiated work towards establishing objectives and targets for the reduction of antibiotic use in humans, often in the context of developing a national action plan for AMR. However, only a few countries had published targets in 2017 [10], and a minority had identified specific funding sources to implement their national action plans [8].

[2] A PDF containing all country summaries is available on the landing page for this report at the following link: https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2019

Public health implications

The high levels of AMR for several important bacterial species-antimicrobial group combinations reported to EARS-Net for 2019 show that AMR remains a serious challenge in the EU/EEA. AMR is considered to be one of the biggest threats to public health today, both globally [11] and in the EU/EEA [9]. Recent estimates based on data from EARS-Net show that each year, more than 670 000 infections occur in the EU/EEA due to bacteria resistant to antibiotics, and that approximately 33 000 people die as a direct consequence of these infections [12]. The related cost to the healthcare systems of EU/EEA countries is around EUR 1.1 billion [8].

Rising proportions of AMR will be an increasing concern unless governments respond more robustly to the threat. Further investment in public health interventions to tackle AMR are urgently needed, and would have a significant positive impact on population health and future healthcare expenditures in the EU/EEA. It has been estimated that a mixed intervention package including antibiotic stewardship programmes, enhanced hygiene, mass media campaigns, and the use of rapid diagnostic tests has the potential to prevent approximately 27 000 deaths per year in the EU/EEA. In addition to saving lives, such a public health package could pay for itself within just one year and end up saving around EUR 1.4 billion per year in the EU/EEA [8].

Table 3. Total number of invasive isolates tested (N) and percentage of isolates with resistant phenotype (%), by bacterial species and antimicrobial group, population-weighted EU/EEA mean, 2015–2019

Bacterial species	Antimicrobial group	2015		2016		2017		2018		2019		2019 EU/EEA country range*	Trend 2015-2019**
		N	%	N	%	N	%	N	%	N	%		
Escherichia coli	Aminopenicillin (amoxicillin/ampicillin) resistance	79 507	58.9	108 239	59.0	125 866	58.7	133 700	57.5	129 576	57.1	35.5-71.7	↓
	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	91 822	14.6	123 944	14.9	140 584	14.9	152 720	15.1	156 887	15.1	6.2-38.6	↑#
	Carbapenem (imipenem/meropenem) resistance	88 020	0.2	122 437	0.1	140 438	0.1	151 457	0.1	155 841	0.3	0.0-1.6	↑
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	91 832	24.8	125 161	25.2	141 562	25.7	154 698	25.3	160 692	23.8	11.3-43.5	↓
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance	91 746	11.6	124 480	11.6	141 788	11.4	154 266	11.1	160 406	10.8	4.7-24.4	↓
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides	89 780	6.3	121 582	6.4	135 108	6.3	148 206	6.2	153 818	5.9	0.4-19.0	↓
Klebsiella pneumoniae	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	22 801	31.1	30 633	31.4	32 969	31.2	38 436	31.7	40 764	31.3	4.3-75.7	
	Carbapenem (imipenem/meropenem) resistance	22 063	6.8	30 309	7.4	32 960	7.1	38 140	7.5	40 430	7.9	0.0-58.3	↑
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	22 707	30.1	30 769	30.3	32 924	31.5	38 770	31.6	41 330	31.2	4.3-66.9	↑#
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance	22 650	24.2	30 209	24.4	33 136	24.1	38 555	22.7	41 195	22.3	3.5-57.3	↓
	Combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides	22 220	19.7	29 589	20.6	31 613	20.5	37 402	19.5	39 983	19.3	0.0-53.1	↓
Pseudomonas aeruginosa	Piperacillin + tazobactam resistance	12 498	18.1	15 125	17.5	16 428	16.7	18 607	16.8	19 355	16.9	2.3-52.8	↓
	Ceftazidime resistance	12 498	15.4	15 219	14.4	16 512	14.7	18 960	14.1	19 849	14.3	3.5-52.2	↓#
	Carbapenem (imipenem/meropenem) resistance	12 840	19.3	15 573	18.2	17 109	17.4	19 233	17.2	20 127	16.5	0.0-55.4	↓
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	12 803	20.9	15 504	18.8	16 951	20.2	19 211	19.7	20 273	18.9	4.5-52.2	↓#
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance	12 825	15.3	15 525	14.0	16 979	13.2	19 186	11.8	20 109	11.5	0.3-48.9	↓
	Combined resistance to ≥3 antimicrobial groups (among piperacillin + tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)	12 863	14.6	15 628	13.4	17 129	13.0	19 306	12.6	20 296	12.1	0.0-49.7	↓
***Acinetobacter* species**	Carbapenem (imipenem/meropenem) resistance	5 057	32.1	5 590	32.6	6 186	33.1	6 526	31.9	5 953	32.6	0.0-92.3	
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	5 032	38.5	5 596	37.5	6 098	37.4	6 496	36.2	5 918	36.9	0.0-95.8	↓
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance	5 003	32.4	5 562	32.7	6 042	32.2	6 459	31.3	5 909	33.0	0.0-92.1	

Bacterial species	Antimicrobial group	2015		2016		2017		2018		2019		2019 EU/EEA country range*	Trend 2015-2019**
		N	%	N	%	N	%	N	%	N	%		
	Combined resistance to carbapenems, fluoroquinolones and aminoglycosides	4 908	27.6	5 418	28.3	5 872	28.2	6 294	28.3	5 677	29.7	0.0-91.4	↑#
Staphylococcus aureus	MRSA	46 173	19.0	57 730	17.7	66 279	16.8	72 882	16.4	73 808	15.5	1.1-46.7	↓
Streptococcus pneumoniae	Penicillin non-wild-type***	12 178	14.2	15 666	13.1	17 212	12.9	18 676	12.9	18 112	12.1	4.0-33.3	↓
	Macrolide (erythromycin/clarithromycin/azithromycin) resistance	12 659	16.6	16 027	16.6	17 613	15.7	19 217	15.2	18 832	14.5	3.5-30.4	↓
	Combined penicillin non-wild-type and resistance to macrolides	11 684	8.5	15 182	8.4	16 584	8.2	17 811	7.8	17 420	7.2	1.3-20.0	↓
Enterococcus faecalis	High-level gentamicin resistance	10 887	31.9	12 910	31.8	13 930	29.7	15 343	27.1	13 368	26.6	0.0-44.1	↓
Enterococcus faecium	Vancomycin resistance	9 336	10.5	12 511	12.3	14 213	14.9	15 992	17.3	16 432	18.3	0.0-50.0	↑

* Indicates the lowest and the highest national resistance percentage among reporting EU/EEA countries
** ↑ and ↓ indicate statistically significant increasing and decreasing trends, respectively. # indicates a significant trend in the overall data, but that no trend was detected in data which only included laboratories that reported continuously for all five years.
*** In this report, the term penicillin non-wild-type refers to *S. pneumoniae* isolates reported by local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MICs to benzylpenicillin above those of the wild-type isolates (i.e. >0.06 mg/L). The analysis is based on the qualitative susceptibility categories S, I and R as quantitative susceptibility information was missing for a large part of the data. It should be understood that laboratories not using EUCAST clinical breakpoints during the period 2015–2018 might define the cut-off values for the susceptibility categories differently.

Bacterial species-specific results

Escherichia coli

Epidemiology

For 2019, 30 EU/EEA countries reported 163 005 isolates of *Escherichia coli*. Of these, 129 576 (79%) isolates had AST results for aminopenicillins, 156 887 (96%) isolates had AST results for third-generation cephalosporins, 160 692 (99%) isolates had AST results for fluoroquinolones, 160 406 (98%) isolates had AST results for aminoglycosides, and 155 841 (96%) isolates had AST results for carbapenems (Table 3).

At the EU/EEA level, more than half (57.1%) of the *E. coli* isolates reported to EARS-Net for 2019 were resistant to at least one of the antimicrobial groups under surveillance (i.e. aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) (Table 4). In 2019, the highest EU/EEA population-weighted mean resistance percentage was reported for aminopenicillins (57.1%), followed by fluoroquinolones (23.8%), third-generation cephalosporins (15.1%) and aminoglycosides (10.8%). Resistance to carbapenems remained rare (0.3%) (Table 3).

Between 2015 and 2019, there were significantly increasing trends in the EU/EEA population-weighted mean percentages for third-generation cephalosporin resistance and carbapenem resistance, while the EU/EEA trends for aminopenicillin resistance, fluoroquinolone resistance and aminoglycoside resistance decreased significantly during the same period. When restricting the analysis to only include the laboratories that consistently reported data for all five years, all trends remained significant, with the exception of third-generation cephalosporin resistance (Table 3).

Resistance to multiple antimicrobial groups was common. Among the resistant phenotypes, resistance to aminopenicillins, both as single resistance or in combination with other antimicrobial groups, was the most common at the EU/EEA level (Table 4). In 2019, the percentage of combined resistance, measured as resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, was 5.9% (EU/EEA population-weighted mean) and this had shown a small, but statistically significant, decreasing trend during the period 2015–2019 (Table 3).

With the exception of carbapenem resistance, large inter-country variations were noted for all antimicrobial groups under surveillance (Table 3), with generally higher resistance percentages reported from southern and eastern Europe than from northern Europe (Figure 1, Figure 2, Figure 3 and related PDF link – footnote 1).

Table 4. *Escherichia coli.* Total number of invasive isolates tested (n: 118 399)* and percentage resistance (%) per phenotype, EU/EEA, 2019

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**50 797**	**42.9**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**41 146**	**34.8**
Aminopenicillins	37 854	32.0
Fluoroquinolones	2 783	2.4
Other antimicrobial groups	509	0.4
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**12 456**	**10.5**
Aminopenicillins + fluoroquinolones	7 073	6.0
Aminopenicillins + third-generation cephalosporins	2 986	2.5
Aminopenicillins + aminoglycosides	2 190	1.8
Other antimicrobial group combinations[a]	207	0.2
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**8 620**	**7.3**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones	5 454	4.6
Aminopenicillins + fluoroquinolones + aminoglycosides	2 468	2.1
Other antimicrobial group combinations[a]	698	0.6
Resistance to four antimicrobial groups		
Total (all four-group combinations)	**5 348**	**4.5**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides	5 305	4.5
Other antimicrobial group combinations[a]	43	<0.1
Resistance to five antimicrobial groups		
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	32	<0.1

* Only isolates with complete susceptibility information for aminopenicillins (amoxicillin and/or ampicillin), fluoroquinolones (ciprofloxacin and/or levofloxacin and/or ofloxacin), third-generation cephalosporins (cefotaxime and/or ceftriaxone and/or ceftazidime), aminoglycosides (gentamicin, tobramycin and/or netilmicin) and carbapenems (imipenem and/or meropenem) were included in the analysis. This represented 73% of all reported *E. coli* isolates.

** Not adjusted for population differences in the reporting countries

[a]: Only resistance combinations >1% of the total are specified

Figure 1. *Escherichia coli.* Percentage of invasive isolates resistant to fluoroquinolones (ciprofloxacin or/and levofloxacin or/and ofloxacin), by country, EU/EEA, 2019

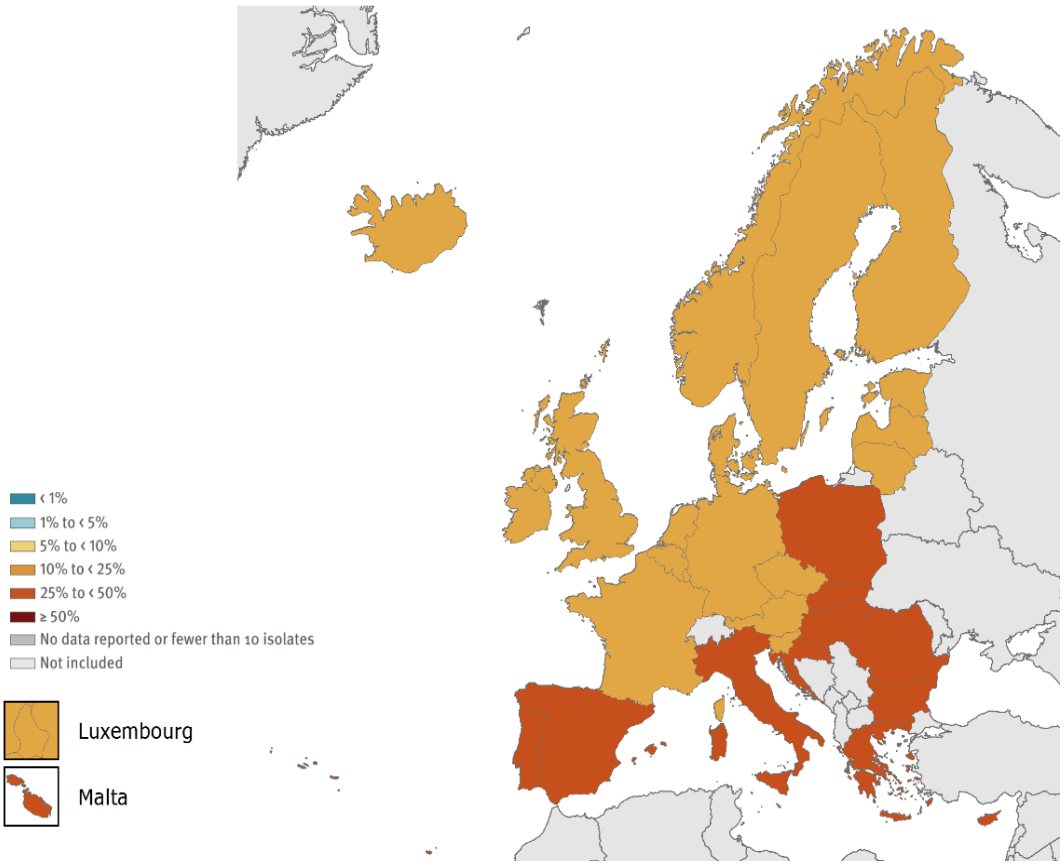


Figure 2. *Escherichia coli*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime or/and ceftriaxone or/and ceftazidime), by country, EU/EEA, 2019

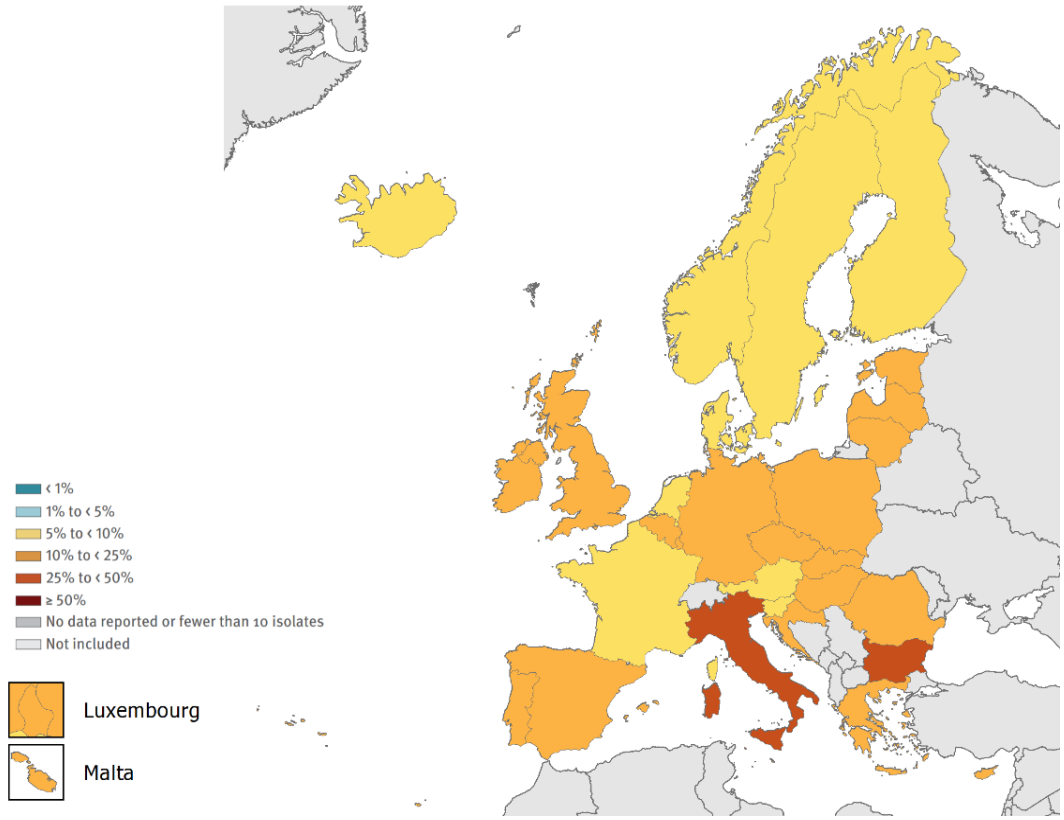
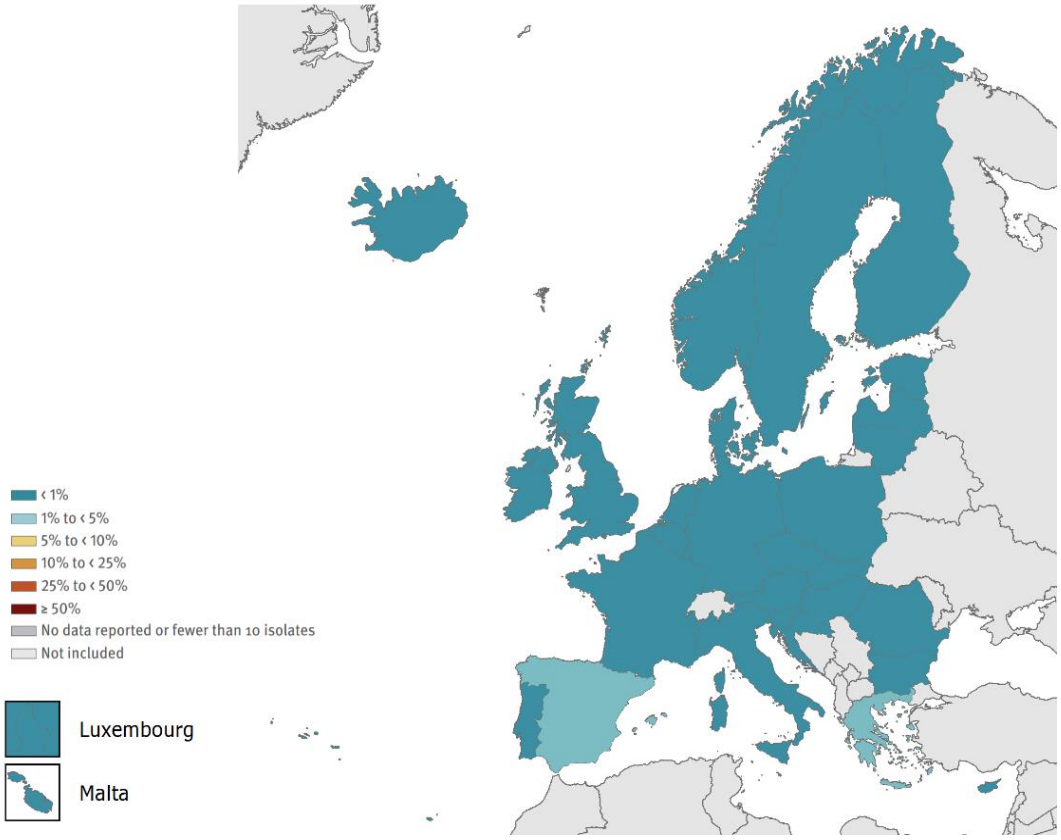


Figure 3. *Escherichia coli*. Percentage of invasive isolates resistant to carbapenems (imipenem or/and meropenem), by country, EU/EEA, 2019



Discussion

E. coli is a major cause of bloodstream infection in Europe, and prompt access to effective antimicrobial treatment is essential to reduce the health-related and economic burden caused by these infections. Infections caused by antimicrobial-resistant *E. coli* proportionally contribute most to the burden of AMR in the EU/EEA, both in terms of the number of cases and the number of attributable deaths [12]. As resistant *E. coli* commonly occur in the community, interventions to reduce the burden of these infections should not be restricted to hospital settings, but should also target primary and community care.

Time series analyses of EU/EEA population-weighted means for third-generation cephalosporin resistance and fluoroquinolone resistance in *E. coli* reported to EARS-Net for the years 2002 to 2018 have shown that although resistance percentages increased substantially during the period, the increase was most prominent up until around 2012. After this, the increase was less pronounced [13]. This was confirmed for the five-year period presented in this report (2015–2019). There was no significant EU/EEA trend for third-generation cephalosporin resistance if only those laboratories that had continuously reported were included. Meanwhile, there was a small, but statistically significant, decreasing EU/EEA trend for fluoroquinolone resistance. Nevertheless, percentages of AMR reported for 2019 were comparatively much higher than in 2002, highlighting the need for further efforts to improve antimicrobial stewardship and infection prevention and control.

Use of broad-spectrum antimicrobials is a known risk factor for the colonisation and spread of antimicrobial-resistant *Enterobacterales*, including *E. coli*. Associations between national resistance percentages in *E. coli* and national antimicrobial consumption rates, in both the hospital and community sector, have been reported [14]. The latest data from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) show large inter-country variations in the use of broad-spectrum antimicrobials [15], indicating a need for increased focus on antimicrobial stewardship [16] and the potential for further reductions in antimicrobial consumption.

As high resistance levels have been reported in *E. coli* isolates from food-producing animals in Europe, including the rare occurrence of isolates with carbapenemase production [17], ensuring cross-sectoral collaboration between the human, veterinary and food production sectors is essential. This work is underpinned by the European Commission's 'One Health' approach, which addresses resistance in both humans and animals. ECDC is working closely with the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) to better understand the interrelationships between antimicrobial use and antimicrobial resistance in humans and animals across Europe.

Although carbapenem-resistant isolates remained rare among the invasive *E. coli* isolates included in EARS-Net, there was a small but significant increase in the EU/EEA population-weighted mean between 2015 and 2019. A further increase in invasive infections caused by carbapenem-resistant *E. coli* would have severe consequences on the burden of AMR in the EU/EEA. Carbapenem-resistant *Enterobacterales* (CRE) infections are associated with high mortality, primarily due to delays in the administration of effective treatment and the limited availability of treatment options. The September 2019 update of ECDC's rapid risk assessment on CRE highlights the need for high standards in infection prevention and control, combined with adequate microbiological capacity to detect and prevent further spread [18].

Carbapenem resistance is most often mediated by a range of carbapenemases, which may in some cases confer resistance to virtually all available beta-lactam antibacterial drugs. However, there are carbapenemase-producing isolates that test susceptible to meropenem and/or imipenem, based on clinical breakpoints. One example is OXA-244-producing *E. coli* that might be classified only as ESBL-producing instead of carbapenemase-producing *E. coli*, unless specifically tested for OXA-48-like carbapenemases. A recent ECDC risk assessment on OXA-244-producing *E. coli* [19] indicated a pan-European problem, with a high risk of further spread of OXA-244-producing *E. coli* in the EU/EEA, given the rapid and simultaneous increase in multiple countries between 2013 and 2020. There is a risk that transmission of OXA-244-producing *E. coli* in the community may contribute to the loss of carbapenems as options for treatment of *E. coli* infections, and therefore there is an urgent need for further investigation to determine the source and routes of transmission for these.

To address the need for enhanced CRE surveillance and complement the phenotypic-based surveillance data available from EARS-Net, a Carbapenem- and/or Colistin-Resistant *Enterobacterales* (CCRE) survey has been incorporated into EURGen-Net for the period 2018 to 2020 [20]. The results of this survey will provide information on the prevalence and distribution of carbapenemases, and contribute to a better understanding of the epidemiology of CRE in Europe and the risk factors associated with CRE infections.

Klebsiella pneumoniae

Epidemiology

For 2019, 30 EU/EEA countries reported 41 814 isolates of *Klebsiella pneumoniae*. Of these, 40 764 (97%) isolates had AST results for third-generation cephalosporins, 41 330 (99%) isolates had AST results for fluoroquinolones, 41 195 (99%) isolates had AST results for aminoglycosides and 40 430 (97%) isolates had AST results for carbapenems (Table 3).

At the EU/EEA level, more than a third (36.6%) of the *K. pneumoniae* isolates reported to EARS-Net for 2019 were resistant to at least one of the antimicrobial groups under surveillance (i.e. fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) (Table 5). In 2019, the highest EU/ EEA population-weighted mean resistance percentage was reported for third-generation cephalosporins (31.3%), followed by fluoroquinolones (31.2%), aminoglycosides (22.3%) and carbapenems (7.9%) (Table 3).

Between 2015 and 2019, there were significantly increasing trends in the EU/EEA population-weighted mean percentages for carbapenem resistance and fluoroquinolone resistance, while the EU/EEA trend for aminoglycoside resistance decreased significantly during the same period. With the exception of fluoroquinolone resistance, all EU/EEA trends remained significant when restricting the analysis to include only those laboratories that consistently reported data (Table 3).

Single resistance was less commonly reported than resistance to two or more antimicrobial groups, with the most common resistance phenotype being combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides (Table 5). The EU/EEA population-weighted mean for combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides was 19.3% in 2019, and showed a small, but statistically significant, decreasing trend during the period 2015–2019 (Table 3).

Large inter-country variations could be noted for all antimicrobial groups under surveillance (Table 3), with generally higher resistance percentages reported from southern and eastern Europe than from northern Europe (Figure 4, Figure 5 and related PDF link – footnote 1). The countries reporting the highest percentages of carbapenem resistance in *K. pneumoniae* were also among those reporting the highest resistance percentages for the other antimicrobial groups.

Table 5. *Klebsiella pneumoniae*. Total number of invasive isolates tested (n: 39 025)* and percentage resistance (%) per phenotype, EU/EEA, 2019

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**24 738**	**63.4**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**3 119**	**8.0**
Fluoroquinolones	1 542	4.0
Third-generation cephalosporins	1 313	3.4
Other antimicrobial groups[a]	264	0.7
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**3 152**	**8.1**
Third-generation cephalosporins + fluoroquinolones	2 148	5.5
Third-generation cephalosporins + aminoglycosides	546	1.4
Fluoroquinolones + aminoglycosides	369	0.9
Other antimicrobial group combinations[a]	89	0.2
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**6 090**	**15.6**
Third-generation cephalosporins + fluoroquinolones + aminoglycosides	5 018	12.9
Third-generation cephalosporins + fluoroquinolones + carbapenems	996	2.6
Other antimicrobial group combinations[a]	76	0.2
Resistance to four antimicrobial groups		
Third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	**1 926**	**4.9**

* Only isolates with complete susceptibility information for fluoroquinolones (ciprofloxacin and/or levofloxacin and/or ofloxacin), third-generation cephalosporins (cefotaxime and/or ceftriaxone and/or ceftazidime), aminoglycosides (gentamicin, tobramycin and/or netilimicin) and carbapenems (imipenem and/or meropenem) were included in the analysis. This represented 93% of all reported *K. pneumoniae* isolates.

** Not adjusted for population differences in the reporting countries.

[a] Only resistance combinations >1% of the total are specified.

Figure 4. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime or/and ceftriaxone or/and ceftazidime), by country, EU/EEA, 2019

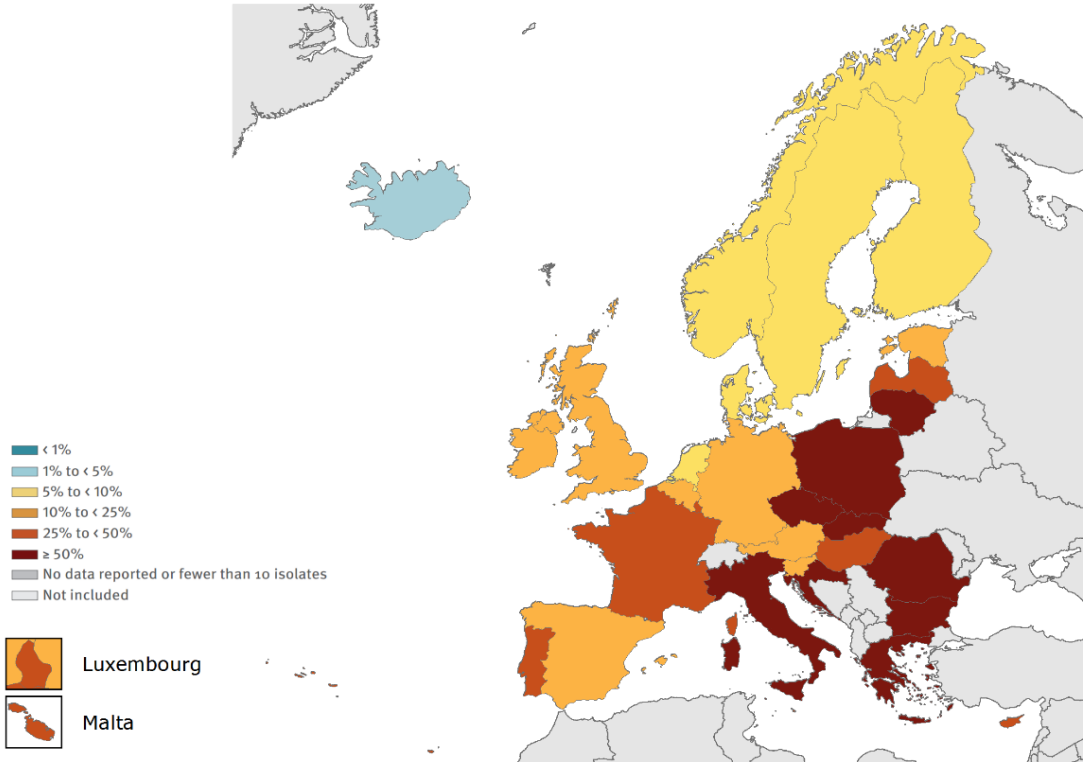
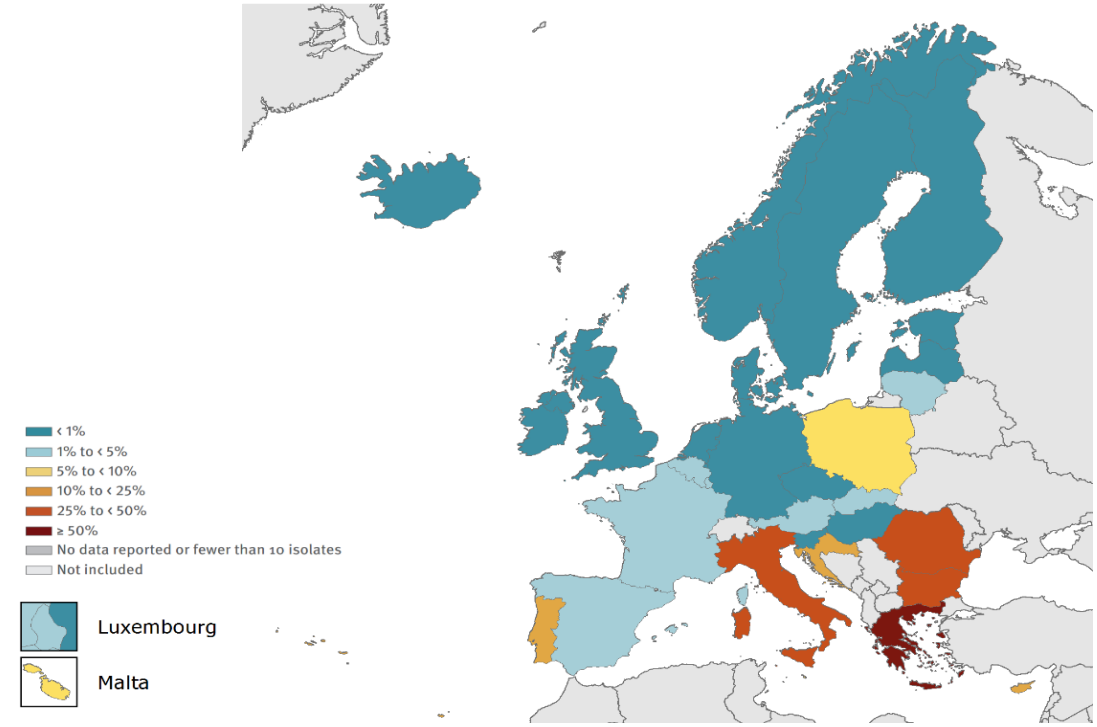


Figure 5. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to carbapenems (imipenem or/and meropenem), by country, EU/EEA, 2019



Discussion

The resistance situation in *K. pneumoniae* in the EU/EEA remains problematic. Although the annual increase in the EU/EEA population-weighted mean carbapenem resistance percentage during the last five years was more moderate than in the previous periods, it has increased more than seven-fold since 2006 [13]. For several individual EU/EEA countries, most notably in the south and south-central parts of Europe, the increase has been substantially larger [1]. Carbapenem resistance was almost always combined with resistance to several other key antimicrobial groups, leading to a severely

limited range of treatment options for invasive infections caused by this type of bacteria. ECDC's study on the health burden of AMR concluded that even in countries with lower levels of carbapenem-resistant *K. pneumoniae*, the impact of AMR on the national health burden is significant because of the high attributable mortality of these infections [12]. This underlines the need for continuous close monitoring and greater efforts to efficiently respond to this public health threat.

The highest percentages of carbapenem resistance observed in south and south-eastern Europe have also been reflected in other European surveillance initiatives, such as the ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals [21] and EURGen-Net [22]. Results from these initiatives also show that the situation in EU/EEA countries has deteriorated in recent years with regard to the epidemiological stage and incidence of these infections. Numerous reports on outbreaks and examples of cross-border spread of CRE demonstrate the transmission potential in EU/EEA healthcare systems [23-25]. Outbreaks in EU/EEA countries have also highlighted the importance of early detection of CRE in settings with low incidence, due to their high transmissibility [22-27].

CRE can be resistant to carbapenems as a result of various mechanisms, but most frequently through production of carbapenemase enzymes. It is not possible to assess the overall presence and spread of carbapenemase-producing *Enterobacterales* through the data available from EARS-Net, as some carbapenemases do not confer a fully carbapenem-resistant phenotype. One example is the OXA-48-like carbapenemase enzymes, presenting a particular problem for laboratory detection because of their weak hydrolysing capacity of carbapenems [23]. This is partly reflected by the substantially higher percentages of *K. pneumoniae* isolates reported as 'susceptible, increased exposure' (I) than reported as 'resistant' (R) in some EU/EEA countries [1].

Although *Klebsiella pneumoniae* carbapenemase (KPC) still plays an important role among the carbapenemases produced by *K. pneumoniae*, recent outbreaks of carbapenemase (NDM-1 and OXA-48)-producing and colistin-resistant *K. pneumoniae* have highlighted the concomitant increase in virulence, transmissibility and antimicrobial resistance among certain *K. pneumoniae* strains, which pose a considerably higher risk to human health than was previously the case with the broader *K. pneumoniae* population. Early detection of such strains and close cooperation between clinicians and public health services is crucial to avoid spread among the patient population in the EU/EEA. There is a need for increased capacity in the EU/EEA to support outbreak investigations and surveillance with real-time whole genome sequencing to identify high-risk clones and to implement enhanced control measures to avoid further spread [26-27]. One initiative addressing this need is the Carbapenem and/or Colistin-Resistant *Enterobacterales* (CCRE) survey (as part of EURGen-Net) that will provide updated and more detailed information on the distribution of carbapenemase-producing *K. pneumoniae* in Europe [20].

As highlighted in the September 2019 update of ECDC's rapid risk assessment on CRE, options for action include timely and appropriate diagnosis, high standards of infection prevention and control, and antimicrobial stewardship [18]. In recent years, many EU/EEA countries have developed and implemented recommendations and guidance documents on multidrug-resistant *Enterobacterales* and/or CRE [28], indicating a trend towards nationally coordinated responses to this public health threat. In 2017, to support countries, ECDC published a guidance document on how to prevent the entry and spread of CRE into healthcare settings. The guidance outlines evidence-based best practices for the prevention of CRE, including measures for intervention that can be adopted or adapted to local needs, depending on the availability of financial and structural resources [29].

Colistin is frequently being used to treat CRE infections, but colistin resistance may develop during treatment. The transferable plasmid-mediated colistin resistance genes that can transmit colistin resistance more easily between bacteria further increase the risk for spread of colistin resistance [30]. Colistin resistance poses a substantial public health risk to the EU/EEA because it further limits treatment options in patients with infections caused by multidrug-resistant gram-negative bacteria, including CRE. The distribution of colistin resistance is difficult to assess through EARS-Net, as colistin susceptibility testing is generally not part of the initial routine AST panel for *Enterobacterales*, being performed instead at national level after referral of multidrug-resistant isolates to a reference laboratory. In addition, colistin susceptibility testing is methodologically challenging, substantially reducing the quality of results from agar dilution, disk diffusion and gradient diffusion. A joint EUCAST and CLSI sub-committee has issued recommendations confirming that broth microdilution is so far the only valid method for colistin susceptibility testing [31]. A survey among EARS-Net participating laboratories in 2017 showed that a majority of the local laboratories that responded did not test for colistin susceptibility locally, or used methods that are not recommended by EUCAST (unpublished data, ECDC/UK NEQAS). This has led to the conclusion that data sources other than EARS-Net are needed for colistin susceptibility surveillance until local laboratory capacity has improved. To better understand the capacity for colistin susceptibility testing and the distribution of colistin-resistant *Enterobacterales* in Europe, ECDC has included colistin in the surveillance panel of the CCRE survey. This survey includes a capacity building component for reference laboratories, which will hopefully also improve diagnostic capacity at the local level [20].

WHO sees a critical need for research and the development of new antibiotics targeting third-generation cephalosporin- and carbapenem-resistant *Enterobacterales*, including *K. pneumoniae* and *E. coli* [32].

Pseudomonas aeruginosa

Epidemiology

For 2019, 30 EU/EEA countries reported 20 536 isolates of *Pseudomonas aeruginosa*. Of these, 19 355 (94%) isolates had AST results for piperacillin+tazobactam, 19 849 (97%) isolates had AST results for ceftazidime, 20 273 (99%) isolates had AST results for fluoroquinolones, 20 109 (98%) isolates had AST results for aminoglycosides and 20 127 (98%) isolates had AST results for carbapenems (Table 3).

In the EU/EEA, 31.8 % of the *P. aeruginosa* isolates reported to EARS-Net for 2019 were resistant to at least one of the antimicrobial groups under surveillance (i.e. piperacillin+tazobactam, fluoroquinolones, ceftazidime, aminoglycosides and carbapenems) (Table 6). The highest EU/EEA population-weighted mean resistance percentage in 2019 was reported for fluoroquinolones (18.9%), followed by piperacillin + tazobactam (16.9%), carbapenems (16.5%), ceftazidime (14.3%) and aminoglycosides (11.5%) (Table 3).

Between 2015 and 2019, EU/EEA trends decreased significantly for all antimicrobial groups under surveillance. When restricting the analysis to include only the laboratories that consistently reported data for all five years, the trends for piperacillin+tazobactam resistance, carbapenem resistance and aminoglycoside resistance remained statistically significant (Table 3).

Resistance to two or more antimicrobial groups was common and seen in 17.6% of all tested isolates (Table 6). Between 2015 and 2019, the EU/EEA population-weighted mean percentage of combined resistance, defined as resistance to at least three of the antimicrobial groups under surveillance, significantly decreased from 14.6% to 12.1% (Table 3). Large inter-country variations could be noted for all antimicrobial groups (Table 3), with generally higher resistance percentages reported from southern and eastern Europe than northern Europe (Figure 6 and related PDF link – footnote 1).

Table 6. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (n: 18 416)* and percentage resistance (%) per phenotype, EU/EEA, 2019

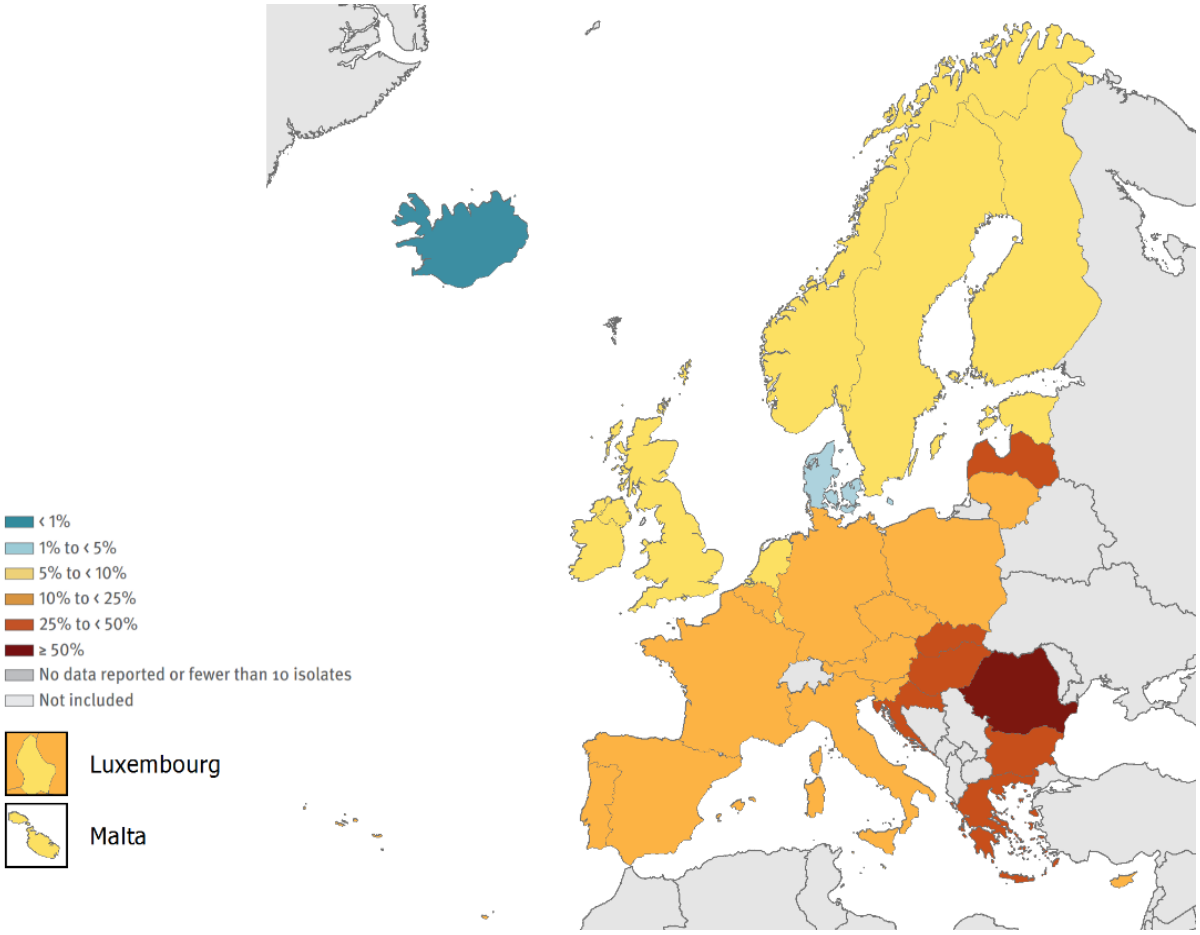
Resistance pattern	Number of isolates	% of total**
Fully susceptible (to tested antibiotics)	**12 735**	**69.2**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance types)	**2 434**	**13.2**
Fluoroquinolones	961	5.2
Carbapenems	759	4.1
[Piperacillin+tazobactam]	309	1.7
Aminoglycosides	267	1.4
Ceftazidime	138	0.7
Resistance to two antimicrobial groups		
Total (all two groups combinations)	**1 405**	**7.6**
[Piperacillin+tazobactam] + ceftazidime	657	3.6
Fluoroquinolones + carbapenems	243	1.3
Other antimicrobial group combinations[a]	505	2.7
Resistance to three antimicrobial groups		
Total (all three group combinations)	**710**	**3.9**
[Piperacillin+tazobactam] + ceftazidime + carbapenems	198	1.1
Other antimicrobial group combinations[a]	512	2.8
Resistance to four antimicrobial groups		
Total (all four group combinations)	**510**	**2.8**
[Piperacillin+tazobactam] + fluoroquinolones + ceftazidime + carbapenems	191	1.0
Other antimicrobial group combinations[a]	319	1.7
Resistance to five antimicrobial groups		
[Piperacillin+tazobactam] + fluoroquinolones + ceftazidime + aminoglycosides + carbapenems	**622**	**3.4**

* Only isolates with complete susceptibility information for at least three antimicrobial groups among piperacillin + tazobactam, fluoroquinolones (ciprofloxacin and/or levofloxacin), ceftazidime, aminoglycosides (gentamicin, tobramycin and/or netilmicin) and carbapenems (imipenem and/or meropenem) were included in the analysis. This represented 90% (18 416/20 536) of all reported *P. aeruginosa* isolates.

** Not adjusted for population differences in the reporting countries.

[a] Only resistance combinations >1% of the total are specified.

Figure 6. *Pseudomonas aeruginosa.* Percentage of invasive isolates with resistance to carbapenems (imipenem or/and meropenem), by country, EU/EEA, 2019



Discussion

EARS-Net data showed that at the EU/EEA level, small but significantly decreasing trends in resistance were noted for *P. aeruginosa* for several antimicrobial groups under surveillance during the period 2015 to 2019. Nevertheless, high resistance percentages and combined resistance persisted in many countries, especially in the eastern and south-eastern parts of Europe. As *P. aeruginosa* is intrinsically resistant to many antimicrobial agents, additional acquired resistance is further complicating the treatment of *P. aeruginosa* infections.

The public health implications of AMR in *P. aeruginosa* should not be neglected, as *P. aeruginosa* remains one of the major causes of healthcare-associated infection in Europe [21,33-34]. *P. aeruginosa* and *Acinetobacter* species bloodstream infections are proportionally far more commonly reported from some EU/EEA countries than others [1]. A recent analysis based on EARS-Net data highlighted that countries reporting high proportions of *P. aeruginosa* and *Acinetobacter*-species bloodstream infections among all reported bloodstream infections were also those where the percentage of isolates with acquired resistance in gram-negative bacteria was generally highest [35]. This finding is probably attributed to shared risk factors, such as a higher consumption of broad-spectrum antimicrobials [15] and sub-standard infection prevention and control measures in healthcare (e.g. lower consumption of alcohol-based hand rub, lower proportions of beds in single rooms and less staff in infection control teams) for these countries [21]. Addressing these factors will probably have a positive impact on both the burden of infections caused by bacteria with high levels of intrinsic resistance, such as *P. aeruginosa* and *Acinetobacter* species, and on the burden caused by bacteria with acquired resistance.

Acinetobacter species

Epidemiology

For 2019, 30 EU/EEA countries reported 6 113 isolates of *Acinetobacter* species. Of these, 5 918 (97%) isolates had AST results for fluoroquinolones, 5 909 (97%) isolates had AST results for aminoglycosides and 5 953 (97%) isolates had AST results for carbapenems (Table 3).

More than half (53.4%) of the *Acinetobacter* species isolates reported by EU/EEA countries to EARS-Net for 2019 were resistant to at least one of the antimicrobial groups under surveillance (i.e. fluoroquinolones, aminoglycosides and carbapenems) (Table 7). The highest EU/EEA population-weighted mean resistance percentage in 2019 was reported for fluoroquinolones (36.9%), followed by aminoglycosides (33.0%) and carbapenems (32.6%) (Table 3).

Between 2015 and 2019, the EU/EEA trend for fluoroquinolone resistance decreased significantly (Table 3).

Resistance to one or two antimicrobial groups was considerably less common than combined resistance to all three groups under surveillance (Table 7). Between 2015 and 2019, the EU/EEA population-weighted mean percentage for combined resistance to fluoroquinolones, aminoglycosides and carbapenems significantly increased from 27.6% to 29.7%, however this trend did not remain statistically significant when restricting the analysis to include only the laboratories that consistently reported data for all five years (Table 3).

Large inter-country variations could be noted for all antimicrobial groups (Table 3), with generally higher resistance percentages reported from southern and eastern Europe than northern Europe (Figure 7 and related PDF link – footnote 1).

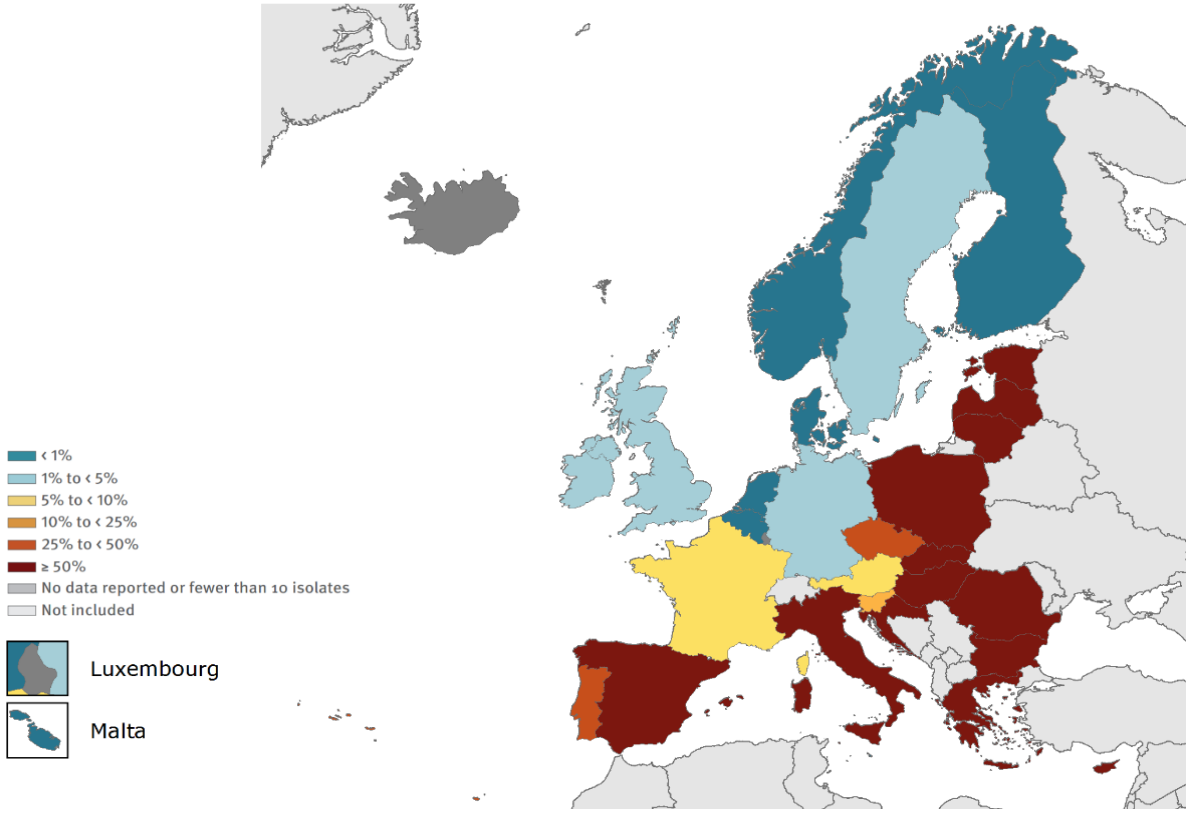
Table 7. *Acinetobacter* species. Total number of invasive isolates tested (n: 5 696)* and percentage resistance (%) per phenotype, EU/EEA, 2019

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**2 652**	**46.6**
Single resistance (to indicated antimicrobial group)		
Total (any single resistance)	**276**	**4.8**
Fluoroquinolones	167	2.9
Aminoglycosides	86	1.5
Carbapenems	23	0.4
Resistance to two antimicrobial groups		
Total (any two-group combinations)	**282**	**5.0**
Fluoroquinolones + carbapenems	159	2.8
Fluoroquinolones + aminoglycosides	115	2.0
Aminoglycosides + carbapenems	8	0.1
Resistance to three antimicrobial groups		
Fluoroquinolones + aminoglycosides + carbapenems	**2 846**	**43.6**

* Only isolates with complete susceptibility information for carbapenems (imipenem and/or meropenem), fluoroquinolones (ciprofloxacin and/or levofloxacin) and aminoglycosides (gentamicin, tobramycin and/or netilimicin) were included in the analysis. This represented 93% (5 696/6 113) of all reported *Acinetobacter* spp. isolates.

** Not adjusted for population differences in the reporting countries

Figure 7. *Acinetobacter* species. Percentage of invasive isolates with resistance to carbapenems (imipenem or/and meropenem), by country, EU/EEA, 2019



Discussion

Of all the bacterial species under surveillance by EARS-Net, *Acinetobacter* species is the one for which the inter-country range in resistance percentages is the widest. In 2019, the percentage of isolates resistant to at least one of the antimicrobial groups under surveillance (fluoroquinolones, aminoglycosides or carbapenems) ranged between 0% and 95.8%, depending on the reporting country. In general, the highest resistance percentages were reported from the Baltic countries and from southern and south-eastern Europe. The high levels of resistance in these countries are of great concern since the most frequently reported resistance phenotype was combined resistance to all three antimicrobial groups under surveillance, severely limiting options for patient treatment.

As *Acinetobacter* species is intrinsically resistant to many antimicrobial agents, additional acquired resistance is further complicating treatment of *Acinetobacter* species infections. The presence of multidrug-resistant *Acinetobacter* species in the healthcare environment is problematic: the bacterium can persist in the environment for long periods and is notoriously difficult to eradicate once established.

ECDC's risk assessment on carbapenem-resistant *Acinetobacter baumannii* in healthcare highlights the need for increased efforts to face this significant threat to patients and healthcare systems in all EU/EEA countries. The document outlines options to reduce risks through clinical management, prevention of transmission in hospitals and other healthcare settings, prevention of cross-border transmission, and improvement in the preparedness of EU/EEA countries. Options for response presented in the risk assessment include timely laboratory reporting; screening and pre-emptive isolation of high-risk patients; high-standard infection control and antimicrobial stewardship programmes [36].

Staphylococcus aureus

Epidemiology

For 2019, 30 EU/EEA countries reported 75 303 isolates of *Staphylococcus aureus*. Of these, 73 808 (97%) isolates had AST results or molecular confirmation test results available to determine meticillin-resistant *S. aureus* (MRSA) (Table 3). A total of 64 596 (85%) isolates had AST results for fluoroquinolones and 60 351 (79%) isolates has AST results for rifampicin.

The EU/EEA population-weighted mean MRSA percentage was 15.5% in 2019. This denotes a significantly decreasing trend for the period 2015 to 2019 (Table 3).

Among MRSA, combined resistance to another antimicrobial group was common. The most common resistance combination was MRSA and resistance to fluoroquinolones. Rifampicin resistance was less common (Table 8).

Large inter-country variations were noted for MRSA (Table 3), with generally higher resistance percentages reported from southern and eastern Europe than northern Europe (Figure 8, and related PDF link – footnote 1).

Table 8. *Staphylococcus aureus*. Total number of invasive isolates tested (n: 53 377)* and percentage resistance (%) per phenotype, EU/EEA, 2019

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**43 469**	**81.4**
Single resistance (to indicated antimicrobial group)		
Total (any single resistance)	**4 368**	**8.2**
Fluoroquinolones	2 670	5.0
MRSA	1 450	2.7
Rifampicin	248	0.5
Resistance to two antimicrobial groups		
Total (any two-group combinations)	**5 199**	**9.7**
MRSA + fluoroquinolones	5 112	9.6
Other resistance combinations[a]	87	0.2
Resistance to three antimicrobial groups		
MRSA + fluoroquinolones + rifampicin	**341**	**0.6**

* Only isolates with complete susceptibility information for MRSA, fluoroquinolones and rifampicin were included in the analysis. This represented 71% of all reported *S. aureus* isolates.

** Not adjusted for population differences in the reporting countries.

[a] Only resistance combinations >1% of the total are specified.

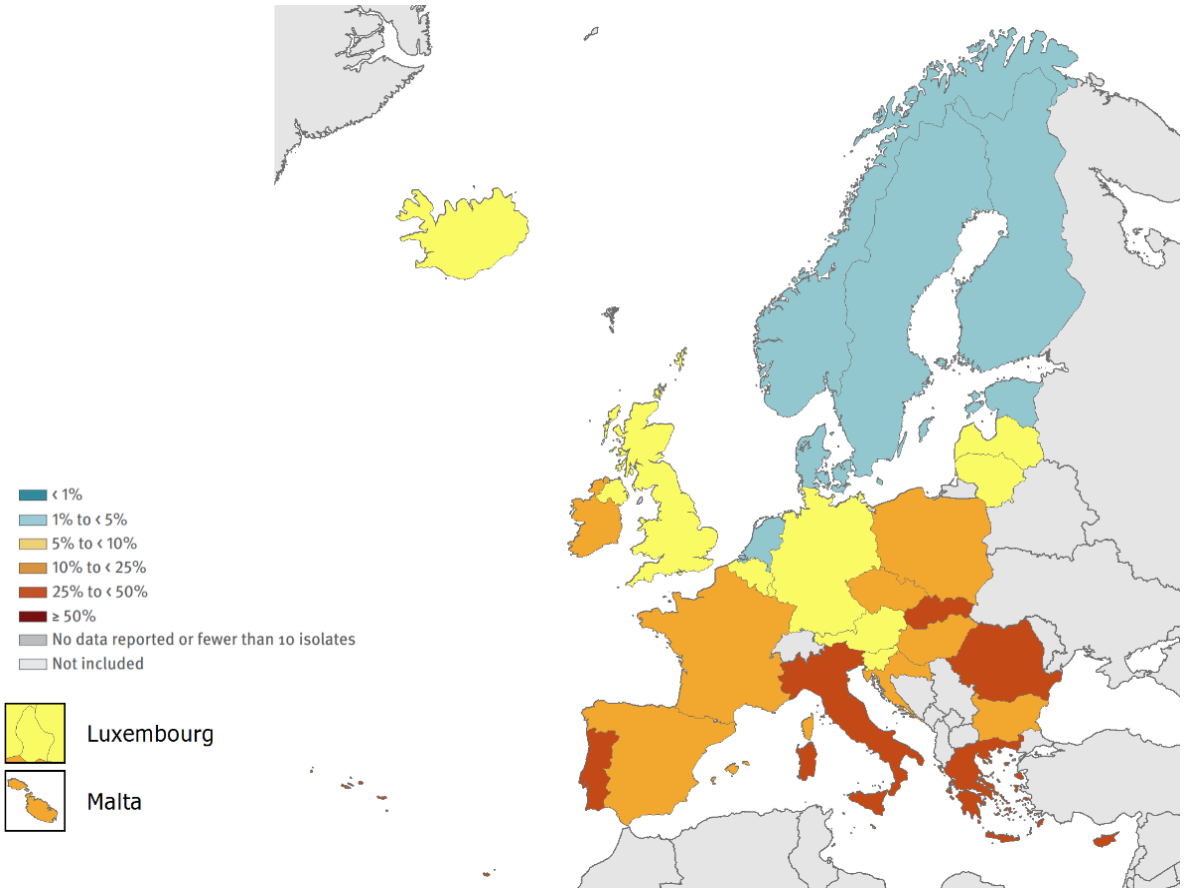
Discussion

As noted in previous EARS-Net reports, MRSA percentages are stabilising or decreasing in a majority of EU/EEA countries, which is also reflected in the continuously decreasing EU/EEA population-weighted mean MRSA percentage. Many countries have developed and implemented national recommendations and guidance documents on preventing the spread of MRSA, focusing on both improved infection prevention and control and prudent antimicrobial use [28].

Despite this positive development, MRSA remains an important pathogen in Europe. *S. aureus* is one of the most common causes of bloodstream infections, exhibiting a high burden in terms of morbidity and mortality [12]. Although the EU/EEA population-weighted MRSA percentage, as reported by EARS-Net, has now been decreasing for many years, ECDC's study on the health burden of AMR reported an increase in the MRSA incidence between 2007 and 2015. Further analysis of the age-group-specific incidence as part of the ECDC study found that this was mainly noted among infants and people aged 55 years or above [12]. The difference in the development over time of the MRSA percentage and the MRSA incidence indicates a need to further study the distribution of *S. aureus* infections in the EU/EEA to obtain a better overview of the current epidemiological situation.

In order to slow down the spread of MRSA in Europe, comprehensive MRSA strategies targeting all healthcare sectors remain essential. The monitoring of MRSA in animals and food is currently voluntary and only performed in a limited number of countries. However, this monitoring shows a constantly evolving situation, including the detection of livestock-associated MRSA (LA-MRSA), healthcare-associated MRSA and community-associated MRSA from companion animals and/or livestock [17]. Recently, LA-MRSA has gained increasing attention, as it poses a zoonotic risk, particularly for those working in close contact with livestock. An ECDC survey has documented the increasing detection and geographical dispersion of LA-MRSA in humans in the EU/EEA during the period 2007–2013 and highlights the veterinary and public health significance of LA-MRSA as a 'One Health' issue [37].

Figure 8. *Staphylococcus aureus.* Percentage of invasive isolates resistant to meticillin (MRSA), by country, EU/EEA, 2019



Streptococcus pneumoniae

Epidemiology

For 2019, 29 EU/EEA countries reported 19 611 isolates of *Streptococcus pneumoniae*. Of these, 18 112 (92%) isolates had AST results for penicillins, and 18 832 (96%) isolates had AST result for macrolides (Table 3).

For this report, the term penicillin non-wild-type refers to *S. pneumoniae* isolates reported by the local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MICs to benzylpenicillin above those of the wild-type isolates (i.e. >0.06 mg/L). The analysis was based on the qualitative susceptibility categories S, I and R, as quantitative susceptibility information was missing for a large proportion of the reported data.

In 2019, the EU/EEA population-weighted mean percentage was 12.1% for penicillin non-wild-type and 14.5% for macrolide resistance. Between 2015 and 2019, EU/EEA trends decreased significantly for both of these phenotypes (Table 3).

The EU/EEA population-weighted mean percentage for combined penicillin non-wild-type and resistance to macrolides was 7.2% in 2019, and decreased significantly during the period 2015 to 2019 (Table 3). Resistance to antimicrobial groups other than penicillin and macrolides was less common (Table 9).

Table 9. *Streptococcus pneumoniae*. Total number of invasive isolates tested (n: 11 170)*, and percentage resistance (%) per phenotype, EU/EEA, 2019

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**8 562**	**76.7**
Single non-wild-type/resistance (to included antimicrobial groups)		
Total (any single resistance)	**1 811**	**16.2**
Macrolides	710	6.4
Fluoroquinolones	551	4.9
Penicillin non-wild-type***	549	4.9
Third-generation cephalosporins	1	<0.1
Non-wild-type/resistance to two antimicrobial groups		
Total (any two-group combinations)	**751**	**6.7**
Penicillin non-wild-type + macrolides	697	6.2
Other antimicrobial group combinations[a]	54	0.5
Non-wild-type/resistance to three antimicrobial groups		
Total (any three-group combinations)	**45**	**0.4**
Non-wild-type/resistance to four antimicrobial groups		
Penicillin non-wild-type + third-generation cephalosporins + fluoroquinolones + macrolides	**1**	**<0.1**

* Only isolates with complete susceptibility information for penicillins, macrolides, fluoroquinolones and third-generation cephalosporins were included in the analysis. This represented 57% (11 170/19 611) of all reported *S. pneumoniae* isolates.

** Not adjusted for population differences in the reporting countries.

*** For this report, the term penicillin non-wild-type refers to *S. pneumoniae* isolates reported by the local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MICs to benzylpenicillin above those of the wild-type isolates (i.e. >0.06 mg/L). The analysis is based on the qualitative susceptibility categories S, I and R as quantitative susceptibility information was missing for a large proportion of the data.

[a] Only resistance combinations >1% of the total are specified.

Discussion

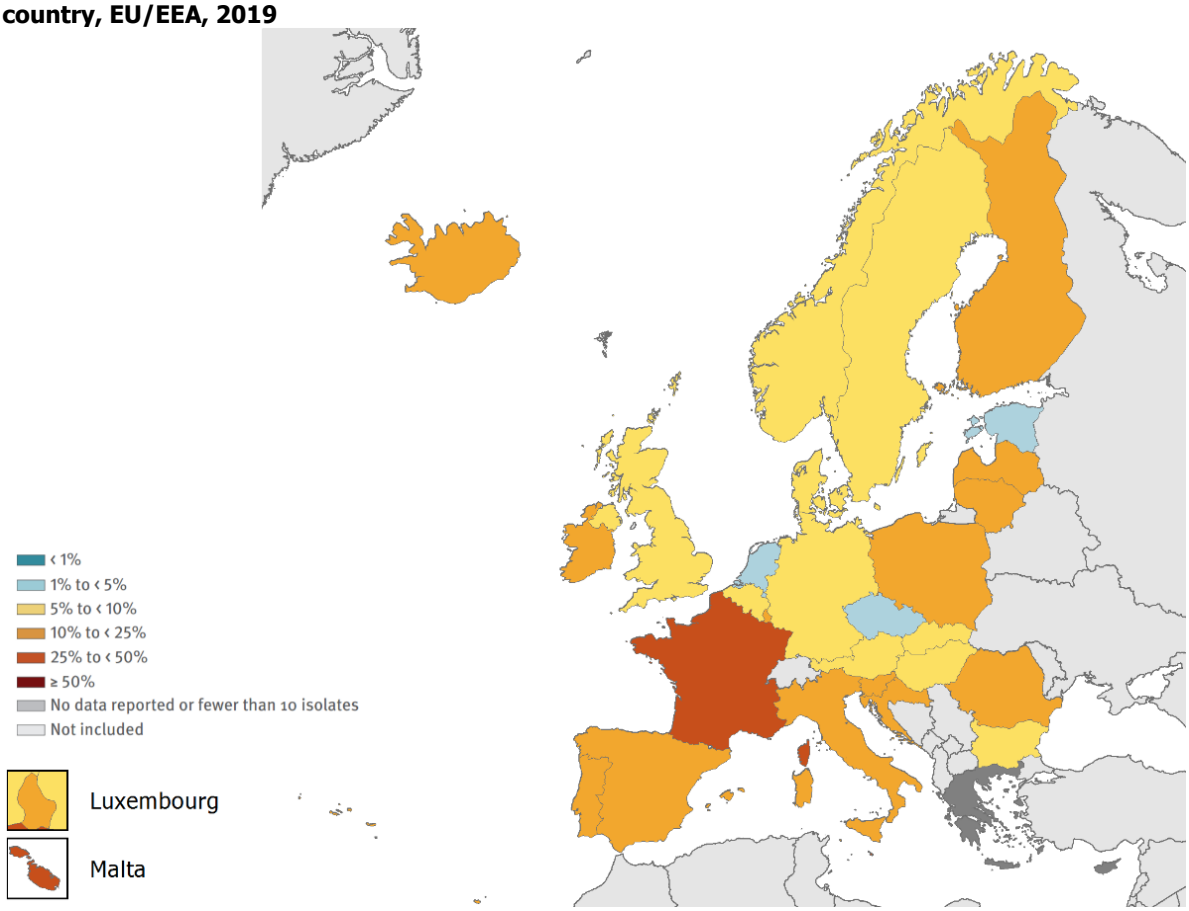
Percentages for penicillin non-wild type and macrolide resistance decreased between 2015 and 2019. As in previous years, there were large inter-country variations. Differences in the clinical breakpoints used historically for determining penicillin susceptibility in *S. pneumoniae* (based on the guidelines used and the sites of infection) introduce bias when comparing national data reported to EARS-Net before 2019. Limited information on the guidelines used for interpretation and incomplete quantitative susceptibility data hamper any assessment of inter-country differences.

In parallel with EARS-Net, the invasive pneumococcal disease (IPD) enhanced surveillance initiative, which is also coordinated by ECDC, collects additional data on IPD cases from reference laboratories throughout the EU/EEA [38]. Data from this surveillance initiative show that the resistance prevalence increased slightly for penicillin and erythromycin in all countries that consistently reported antimicrobial susceptibility data between 2014 and 2016 [39]. It is, however, difficult to compare data from the two surveillance systems due to differences in data sources and

completeness of reporting. The two surveillance systems are currently being harmonised by ECDC to make best use of the available data.

Most EU/EEA countries have implemented routine immunisation for children with multivalent pneumococcal conjugated vaccines (PCVs). In some countries, high-risk adult groups, such as the elderly and immunocompromised individuals, are also targeted with the polysaccharide vaccine or with PCVs [40]. Increased immunisation and better serotype coverage of the available PCVs will probably have an impact on the epidemiology of *S. pneumoniae* in the EU/EEA, both in terms of changes in the age-specific incidence and potential serotype replacement.

Figure 9. *Streptococcus pneumoniae*. Percentage of penicillin non-wild type invasive isolates, by country, EU/EEA, 2019



Enterococcus faecalis and *Enterococcus faecium*

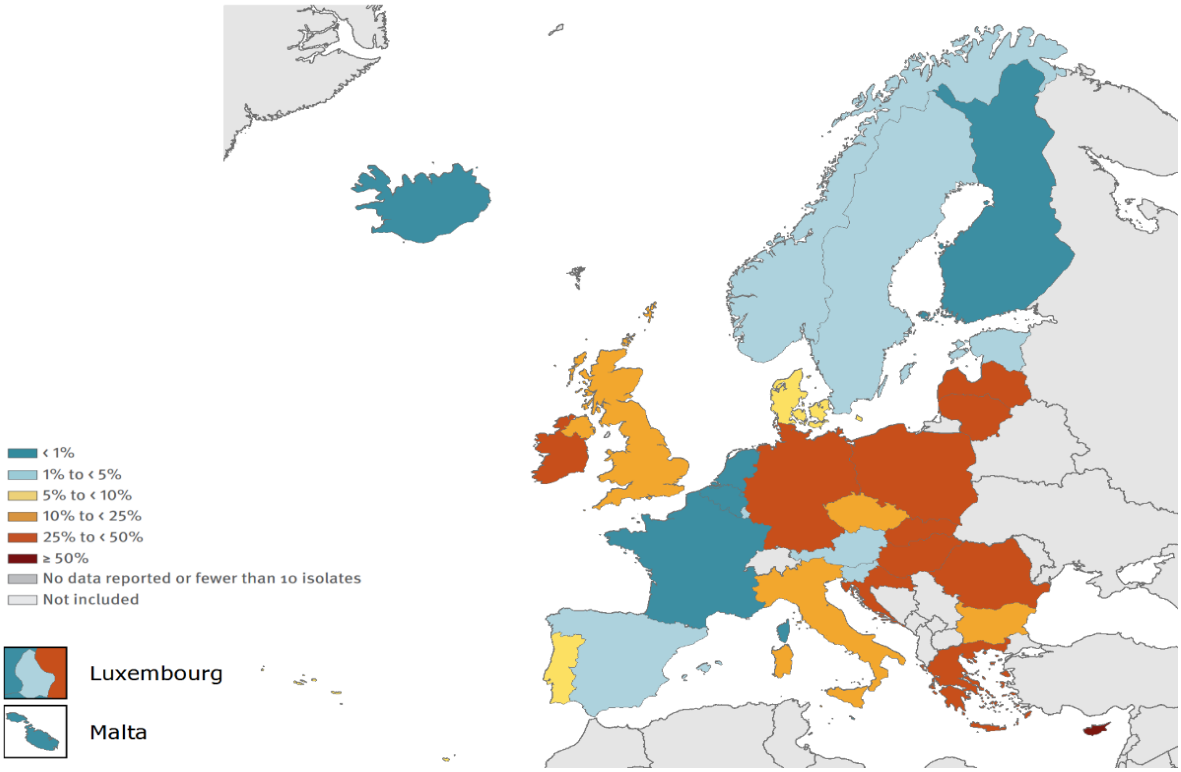
Epidemiology

For 2019, 30 EU/EEA countries reported 25 041 isolates of *Enterococcus faecalis* – 13 368 (53%) with AST results for high-level gentamicin, and 16 632 isolates of *Enterococcus faecium* – 16 432 (99%) with AST results for vancomycin (Table 3).

In 2019, the EU/EEA population-weighted mean percentage of high-level gentamicin resistance in *E. faecalis* was 26.6%, which represents a significant decrease from 2015 when the percentage was 31.9% (Table 3). With few exceptions, national percentages of high-level aminoglycoside resistance in *E. faecium* were higher than for *E. faecalis*. For more information, please refer to ECDC's Surveillance Atlas of Infectious Diseases [1].

The EU/EEA population-weighted mean percentage of vancomycin resistance in *E. faecium* was 18.3% in 2019, which represents a significant increase since 2015 when the percentage was 10.5%. National percentages ranged from 0.0% to 50.0% (Table 3) and only 13 of the 30 reporting countries reported resistance percentages below 5% (Figure 10). In *E. faecalis*, vancomycin resistance remained low in most countries. For more information, please refer to the online ECDC Surveillance Atlas of Infectious Diseases [1].

Figure 10. *Enterococcus faecium*. Percentage of invasive isolates resistant to vancomycin, by country, EU/EEA, 2019



Discussion

The rapid and continuous increase in the percentage of vancomycin resistance in *E. faecium* in the EU/EEA is a cause for concern. ECDC's study on the health burden of AMR estimated that the number of infections and the deaths attributable to vancomycin-resistant enterococci (VRE) almost doubled between 2007 and 2015 [12], and the substantial increase in resistance percentages reported since 2015 contributes to a further increase in the health burden of VRE infections. The significantly increasing trends, observed at EU/EEA level and in many of the individual countries, highlight the urgent need for close monitoring to better understand the epidemiology, clonal diversity and risk factors associated with vancomycin-resistant *E. faecium* infection. Contrary to many other bacterium–antimicrobial group combinations under surveillance by EARS-Net, no distinct geographical pattern could be seen for vancomycin-resistant *E. faecium*, as high resistance levels were reported from countries in both southern, eastern and northern Europe.

Enterococci have intrinsic resistance to several antimicrobial classes, and any additional acquired resistance severely limits the number of treatment options. WHO has listed vancomycin-resistant *E. faecium* as a pathogen with high priority in its global priority list of antibiotic-resistant bacteria, emphasising the paucity of available and effective treatment options [32]. High levels of antimicrobial-resistant enterococci remain a major infection control challenge and an important cause of healthcare-associated infections in Europe. In addition to the fact that infections caused by resistant strains are difficult to treat, enterococci are easily disseminated in healthcare settings.

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