Surveillance of antimicrobial resistance in Europe

Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net)

2018

The European Centre for Disease Prevention and Control (ECDC) wishes to thank all EARS-Net participating laboratories and hospitals in the EU/EEA countries for providing data for this report.

Furthermore, the National Focal Points for Antimicrobial Resistance and all the Operational Contact Points for Epidemiology, for Microbiology and for TESSy that contribute to EARS-Net are acknowledged for facilitating data transfer and providing valuable comments for this report. John Stelling (WHONET representative) is acknowledged for providing technical support to the countries during data preparation. Carlo Gagliotti (ECDC consultant) is acknowledged for his work in preparing the country summary sheets. In addition, ECDC wishes to thank the EARS-Net Disease Network Coordination Committee: Hanna Billström, Tim Eckmanns, Vincent Jarlier, Jos Monen, Stephen Murchan, Gunnar Skov Simonsen, Maja Šubelj, Arjana Tambić, Dorota Żabicka, Helena Žemličková, Christian Giske (observer, EUCAST), Gunnar Kahlmeter (observer, ESCMID), Marek Gniadkowski (observer ESGARS) and Danilo Lo Fo Wong (observer, WHO/Europe) for providing scientific advice during the production of the report.

Suggested citation: European Centre for Disease Prevention and Control. Surveillance of antimicrobial resistance in Europe 2018. Stockholm: ECDC; 2019.

Stockholm, November 2019

ISBN

doi

Catalogue number

Summary

The results presented in this report are based on antimicrobial resistance (AMR) data from invasive isolates reported to the European Antimicrobial Resistance Surveillance Network (EARS-Net) by 30 European Union (EU) and European Economic Area (EEA) countries in 2019 (data referring to 2018), and on trend analyses of data reported by the participating countries for the period 2015 to 2018.

As in previous years, the AMR situation in Europe displays wide variations depending on bacterial species, antimicrobial group and geographical region. For several bacterial species–antimicrobial group combinations, a north-to-south and west-to-east gradient is evident. In general, lower resistance percentages were reported by countries in the north while higher percentages were reported in the south and east of Europe. The high variability in antimicrobial resistance across EU/EEA countries reinforces the scope for significant reductions in antimicrobial resistance through investments to strengthen current best practice.

In 2018, more than half of the *Escherichia coli* isolates reported to EARS-Net and more than a third of the *Klebsiella pneumoniae* isolates were resistant to at least one antimicrobial agent under regular 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% for *K. pneumoniae*. Carbapenem resistance was also common *in Pseudomonas aeruginosa* and *Acinetobacter* species, and at higher percentages compared with *K. pneumoniae*. For all four gram-negative bacteria, the countries reporting the highest carbapenem resistance percentages were also among the countries reporting the highest resistance percentages for other antimicrobial groups. For most gram-negative bacterial species–antimicrobial group combinations, changes in resistance percentages between 2015 and 2018 were moderate, and resistance remained at previously reported high levels.

For *Streptococcus pneumoniae*, the resistance situation appeared stable, but with large inter-country variations. For *Staphylococcus aureus*, the decline in the percentage of meticillin-resistant, i.e. MRSA, isolates reported in previous years continued in 2018. Nevertheless, MRSA remains an important pathogen in the EU/EEA, as the levels of MRSA were still high in several countries, and combined resistance to other antimicrobial groups was common.

An especially worrying development was reported for vancomycin-resistant *Enterococcus faecium*, with an increase of the EU/EEA population-weighted mean percentage from 10.5% in 2015 to 17.3% in 2018, and corresponding increasing trends were noted in almost half the individual countries. The significantly increasing trends, observed both at EU/EEA level and individual countries highlight the need for close monitoring to better understand the epidemiology, clonal diversity and risk factors associated with infection. Contrary to many other species under surveillance, no distinct geographical pattern could be seen for vancomycin-resistant *E. faecium*, as high percentages were reported from both southern, eastern and northern Europe.

The high levels of AMR for several important bacterial species–antimicrobial group combinations reported to EARS-Net for 2018 show that AMR remains a serious challenge in the EU/EEA. 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 investment of public health actions to tackle the situation is still insufficient.

1 Introduction

Antimicrobial resistance

Antimicrobial resistance (AMR) is the ability of a microorganism to resist the action of one or more antimicrobial agents. The consequences can be severe, as prompt treatment with effective antimicrobials is the most important intervention to reduce the risk of poor outcome of serious infections.

AMR is considered to be one of the biggest threats to public health today, both globally [1] and in the EU/EEA region [2]. Recent estimates based on data from EARS-Net show that each year, more than 670 000 infections due to bacteria resistant to antibiotics occur in the EU/EEA, and that approximately 33 0000 people die as a direct consequence of these types of infection [3]. The related cost to healthcare systems of EU/EEA countries are about 1.1 billion Euros [4].

Acquired resistance is caused by mutations in bacterial genes, or acquisition of exogenous resistance genes carried by mobile genetic elements that can spread horizontally between bacteria. Bacteria can acquire multiple resistance mechanisms and hence become resistant to several antimicrobial agents, which is particularly problematic as it may severely limit the available treatment alternatives for the infection. The major drivers behind the occurrence and spread of AMR are the use of antimicrobial agents and the transmission of antimicrobial-resistant microorganisms between humans; between animals; and between humans, animals and the environment. While antimicrobial use exerts ecological pressure on bacteria and contributes to the emergence and selection of AMR, poor infection prevention and control practices favour the further spread of these bacteria. Prudent antimicrobial use and high standard infection control in all healthcare sectors are therefore cornerstones in an effective response to AMR.

The problem of AMR calls for concerted efforts at the country level as well as close international cooperation. In 2017, the European Commission adopted a new European One Health Action Plan against AMR to support the EU and its Member States in delivering innovative, effective and sustainable responses to AMR. The Action Plan highlights surveillance as a key area to provide better evidence and awareness of the challenges of AMR [2]. AMR is listed as a special health issue in the Commission Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health [5] and the Commission Implementing Decision (EU) 2018/945 of 22 June 2018 on the communicable diseases and related special health issues to be covered by epidemiological surveillance [6].

EARS-Net

The European Antimicrobial Resistance Surveillance Network (EARS-Net) is the main EU surveillance system for AMR in bacteria that cause serious infections. The objective of EARS-Net is to through a network of national surveillance systems collect, analyse and report data on AMR, across EU/EEA Member States and as defined in the EARS-Net protocol, to enable action to address AMR. EARS-Net is the continuation of the European Antimicrobial Resistance Surveillance System (EARSS), which was coordinated by the Dutch National Institute for Public Health and the Environment (RIVM). Established in 1998, EARSS successfully created an international network for AMR surveillance and demonstrated how international AMR data could inform decisions and raise awareness among stakeholders and policymakers. On 1 January 2010, the administration of EARSS was transferred from RIVM to ECDC, and the network was renamed EARS-Net.

All 28 EU Member States and two EEA countries (Iceland and Norway) participate in EARS-Net. The vast majority of the countries regularly report data for all bacteria and antimicrobial groups under surveillance. The number of participating laboratories has continuously increased since the initiation of the network, indicating a strengthening of national AMR surveillance systems in the EU/EEA. The widespread and continuing implementation of European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines for antibacterial susceptibility testing, and the high proportion of laboratories that participate in the annual EARS-Net external quality assessment (EQA) exercise, contribute to improved data quality and an increasing ability of EU/EEA countries to report comparable AMR data.

EARS-Net is based on a network of representatives (National Focal Points for AMR; Operational Contact Points for Epidemiology, for Microbiology and for TESSy interaction) from the EU/EEA countries who collect routine clinical antimicrobial susceptibility data from national AMR surveillance initiatives. Scientific guidance and support is provided by the EARS-Net Disease Network Coordination Committee, which is composed of individual experts elected among the nominated National Focal Points and Operational Contact Points, completed by observers from other organisations involved in AMR surveillance. EARS-Net activities are coordinated in close collaboration with two other major ECDC surveillance networks: the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the Healthcare-associated Infections Surveillance Network (HAI-Net). EARS-Net also collaborates with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), in particular with EUCAST, which is supported by ECDC and ESCMID.

Through close collaboration and by using compatible methodology, the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) Network, coordinated by the World Health Organization Regional Office for Europe (WHO/Europe), complements EARS-Net in non-EU/EEA countries to obtain a pan-European overview of the AMR situation [7] in line with the WHO European strategic action plan on antibiotic resistance [8]. Through WHO/Europe, ECDC also provides data from EARS-Net to the WHO Global Antimicrobial Resistance Surveillance System (GLASS) [9] to support the WHO global action plan on antimicrobial resistance [1].

2 EARS-Net data collection and analysis

A total of 30 countries, including all EU Member States and two EEA countries (Iceland and Norway) reported AMR data for 2018 to EARS-Net before the end of August 2019. Countries provided data for all eight species under surveillance, with the exception of Greece which did not report data on *Streptococcus pneumoniae*.

Only data from invasive (blood and cerebrospinal fluid) isolates are included in EARS-Net. This restriction aims to limit the impact of different sampling frames that would otherwise confound the data analysis if isolates from all anatomical sites were accepted, as it is widely accepted that blood cultures should be obtained prior to initiation of antimicrobial therapy for any patient in whom there is suspicion of bacteraemia. The panels of species/antimicrobial agent combinations under surveillance are defined in the EARS-Net reporting protocol [10]. In addition, the EUCAST guidelines for detection of resistance mechanisms and specific types of resistance of clinical and/or epidemiological importance describe the mechanisms of resistance and recommend methods of detection for key EARS-Net species-antimicrobial group combinations [11].

Routine antimicrobial susceptibility testing (AST) results are collected from clinical laboratories by the national network representatives in each participating country. National data are uploaded directly to The European Surveillance System (TESSy) at ECDC on a yearly basis. Data presented by EARS-Net might diverge slightly from the data presented by the countries themselves, as analysis algorithms and population coverage might differ.

Data analysis

Susceptibility test categories

For the analysis, an isolate was considered resistant to an antimicrobial agent when tested and interpreted as resistant (R) in accordance with the clinical breakpoint criteria used by the local laboratory. An isolate was considered non-susceptible to an antimicrobial agent when tested and interpreted as either resistant (R) or intermediately susceptible (I) with the same local clinical breakpoint criteria. This is in concordance with the old EUCAST definitions of susceptibility test categories, as data were collected before the new S, I and R definitions took effect with EUCAST breakpoint table v9.0 in 2019 [12]. As analyses are based on the qualitative susceptibility categories and quantitative susceptibility data are often missing, no corrections to changes in breakpoints over time are made.

EARS-Net encourages the use of EUCAST breakpoints, but results based on other interpretive criteria used by the reporting countries were accepted for the analysis. The use of EUCAST breakpoints has increased over the years. In 2018, approximately 89% of the participating laboratories used EUCAST, or EUCAST-harmonised, clinical breakpoints, which is an improvement compared to previous years and increases comparability of the reported data [13].

National percentages

As a general rule, results were reported as a resistance percentage, i.e. the percentage of R isolates out of all isolates with AST information for that specific species–antimicrobial group. For some bacteria, results were reported as the percentage of non-susceptible (I+R) isolates out of all isolates with the relevant information. For selected analyses, a 95% confidence interval was determined.

If fewer than 10 isolates were reported for a specific species–antimicrobial group combination in a country, the resistance percentage was not calculated and the results are not displayed on the maps presented in this report.

EU/EEA population-weighted mean percentage

A population-weighted EU/EEA mean percentage was determined by multiplying the percentage resistance for each country with the corresponding national population weight and summing up the results; weights were rescaled if resistance percentages were not available for one or more countries. Annual population data were retrieved from the Eurostat online database [14].

Country weightings were used to adjust for imbalances in reporting propensity and population coverage, as the total number of reported isolates by country does not, in most cases, reflect the population size. The methodology for calculating the EU/EEA population-weighted mean percentage was adjusted in 2018 to better control for increasing differences in the national number of reported isolates. This sometimes results in differences compared with the EU/EEA population-weighted means provided in reports published before 2018.

Trend analyses

The statistical significance of temporal trends of resistance percentages by country and for the EU/EEA population-weighted mean was calculated based on data from the last four years, i.e. 2015 to 2018. Countries reporting fewer than 20 isolates per year, or not providing data for all years within the considered 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 including only laboratories that consistently reported data for the full four-year period, thus minimizing selection bias when assessing the significance of the trends. This restriction might, in some cases, have resulted in a considerably lower number of isolates compared with the analysis including all laboratories.

Data validity

The results, both for inter-country comparison and in some cases national trends, should be interpreted with caution. Several factors might influence the estimates and result in over- as well as underestimation of resistance percentages. Key indicators of the population coverage, data representativeness and comparability are presented in the country summary sheets (Annex), and summarised below.

Data validity in 2018, as measured by sample representativeness by the National Focal Points for AMR and/or Operational Contact Points for AMR, was generally assessed as high. The national population coverage of the data reported to EARS-Net varied between 11% and 100%, with more than half of the countries reporting a population coverage of 80% or higher. A sentinel system without full national coverage does not necessarily imply poor data representativeness as long as the sample size is sufficiently large and caution is taken to avoid systematic error by restricting data collection to certain geographical areas, hospital or patient types. However, out of the seven countries reporting medium or poor population or hospital sample representativeness, most, but not all, were countries with a comparatively low population coverage (Table 2.1).

Although the reported blood culture frequency varied substantially between countries, all but five countries indicated that the isolate samples were representative of the microorganisms causing invasive infections and of patient case-mix of included hospitals (Table 2.1). The impact of the large variation in use of blood cultures between countries on EARS-Net data is difficult to assess. The recent ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals highlights the strong link between diagnostic practices and case ascertainment of patients with healthcare-associated infection as well as detection of AMR, thus confirming the need to harmonise and support diagnostic testing across EU/EEA countries [15].

The use of guidelines for clinical breakpoints varies among EU/EEA countries, and in some instances even between laboratories in the same country (Annex). As a result, the interpretation of AST results may vary, at least for resistance mechanisms resulting in estimates close to the breakpoints. In addition, clinical breakpoints may change over time, as breakpoints may be revised. As quantitative data (i.e. disk diffusion zone diameters or MIC values) are not always provided by participating laboratories, only the reported local interpretations as S, I or R are considered for the analyses.

All laboratories providing data to EARS-Net are offered participation in an annual EQA exercise to assess the reliability of their laboratory test results. The level of performance for EQA specimens is generally high [13].

Table 2.1. Estimated national coverage, sample representativeness* and blood culture sets/1000 patient-days. EU/EEA countries, 2018 (or latest available data)

Country	Estimated national population coverage (%)	Population sample representativeness	Hospital sample representativeness	Isolate sample representativeness	Blood culture sets / 1000 patient-days
Austria	Unknown	High	High	High	24.2
Belgium #	36	Medium	High	High	99.1
Bulgaria	46	Medium	Poor	Medium	8.5
Croatia	80	High	High	High	Unknown
Cyprus	85	High	High	High	51.1
Czech Republic	81	High	High	High	17.0
Denmark	100	High	High	High	142.9
Estonia	100	High	High	High	31.9
Finland	100	High	High	High	150.1
France #	21	High	High	High	105.2
Germany**	30	High	Medium	High	27.2
Greece	68	High	High	Medium	Unknown
Hungary	90	High	High	High	12.2
Iceland	100	High	High	High	50.6
Ireland	100	High	High	High	57.3
Italy	36	High	High	High	55.4
Latvia	90	High	Medium	Medium	8.0
Lithuania	100	High	High	High	5.3
Luxembourg***	100	High	Unknown	Unknown	26.0
Malta	95	High	High	High	29.2
Netherlands	67	High	High	High	Unknown
Norway	94	High	High	High	47.4
Poland	17	Medium	Medium	Medium	38.6
Portugal	97	High	High	High	206.9
Romania	11	Poor	Poor	Poor	34.0
Slovakia	64	High	High	High	23.7
Slovenia	99	High	High	High	36.8
Spain**	37	High	High	High	Unknown
Sweden	51	High	High	High	107.0
United Kingdom	70	Medium	High	High	Unknown

* Population sample 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 of 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 sample 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.
Isolate sample representativeness *High*: The isolate sample is representative of microorganisms causing invasive infections and of patient case-mix of the included hospitals; *Medium*: The isolate sample is partly representative of microorganisms causing invasive infections and of patient case-mix of the included hospitals; *Poor*: The isolate sample is poorly representative of microorganisms causing invasive infections and of patient case-mix of the included hospitals; *Unknown*: Unknown or no data provided.

** Data from 2017. *** Data from 2018.
# Not including *Streptococcus pneumoniae* network

3 Antimicrobial resistance in Europe 2015–2018

3.1 *Escherichia coli*

Escherichia coli is part of the normal intestinal microbiota in humans, but is also a common cause of severe infections. It is the most frequent cause of bloodstream infections and urinary tract infections in the EU/EEA and involved in infections of both community and healthcare origin. In addition, it is associated with intra-abdominal infections and causes neonatal meningitis.

Resistance in *E. coli* readily develops either through mutations, as often seen for fluoroquinolone resistance, or by acquisition of mobile genetic elements encoding resistance mechanisms, such as the production of extended spectrum beta-lactamases (ESBLs) and carbapenemases. ESBLs are enzymes that confer resistance to most beta-lactam antibiotics, including third-generation cephalosporins, and are often seen in combination with other resistance mechanisms, causing multidrug resistance. Carbapenems usually withstand the effect of ESBLs and might remain as one of the few treatment options for severe infections. An increasing threat is carbapenem resistance mediated by a range of carbapenemases, which may confer resistance to virtually all available beta-lactam antibiotics. Carbapenamase genes are often located on plasmids that can be exchanged between Enterobacteriaceae, such as *E. coli*, and other gram-negative bacteria.

Antimicrobial resistance

At the EU/EEA level, more than half (58.3%) of the *E. coli* isolates reported to EARS-Net for 2018 were resistant to at least one of the antimicrobial groups under regular surveillance, i.e. aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems (Table 3.1). In 2018, the highest EU/EEA population-weighted mean resistance percentage was reported for aminopenicillins (57.4%), followed by fluoroquinolones (25.3%), third-generation cephalosporins (15.1%) and aminoglycosides (11.1%) (Tables 3.2–3.5). Resistance to carbapenems remained rare in *E. coli* (Table 3.6).

Between 2015 and 2018, there were small but significant decreasing trends in the EU/EEA population-weighted mean percentages for aminopenicillin resistance, aminoglycoside resistance and carbapenem resistance, while the EU/EEA trends for fluoroquinolone resistance and third-generation cephalosporin resistance increased significantly during the same period. When restricting the analysis to only include the laboratories that consistently reported data during all four years, only the trends for aminopenicillin and aminoglycoside resistance remained statistically significant (Tables 3.2-3.6).

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 3.1). In 2018, the percentage combined resistance, measured as resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides was 6.2% (EU/EEA population-weighted mean) and did not significantly change during the period 2015-2018 (Table 3.7).

Except for carbapenem resistance, large inter-country variations were noted for all antimicrobial groups under regular surveillance, with generally higher resistance percentages reported from the southern and eastern parts of Europe than from northern Europe (Figures 3.2– 3.6). Inter-country differences between the proportions of isolates that were fully susceptible to the included antimicrobial groups were also present (Figure 3.1).

Discussion and conclusion

The recent ECDC study on the health burden of AMR based on EARS-Net data from 2015 showed that infections caused by antimicrobial-resistant *E. coli* proportionally contributed the most to the burden of AMR in the EU/EEA, both as number of cases and as number of attributable deaths [3]. As no or very little reduction in the EU/EEA antimicrobial resistance levels reported to EARS-Net between 2015 and 2018 can be noted, it is clear that antimicrobial resistance in *E. coli* remains a major public health problem and that enhanced containment efforts to reduce the health-related burden of these types of infection are needed. As the ECDC study on the health burden of AMR estimated that more than half of the infections with resistant *E. coli* occurred in the community, interventions to reduce the burden should not be restricted to hospital settings but also target primary and community care.

Use of broad-spectrum antimicrobials is a known risk factor for colonisation and spread of antimicrobial-resistant Enterobacteriaceae, including *E. coli*. Associations between EARS-Net national *E. coli* resistance levels and national antimicrobial consumption in both the hospital and community sector have been found [16]. 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 [17], indicating a need for increased focus on antimicrobial stewardship [18] and room for further reductions in use. In a recent 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, [19] and a minority had identified specific funding sources to implement their national action plans [4].

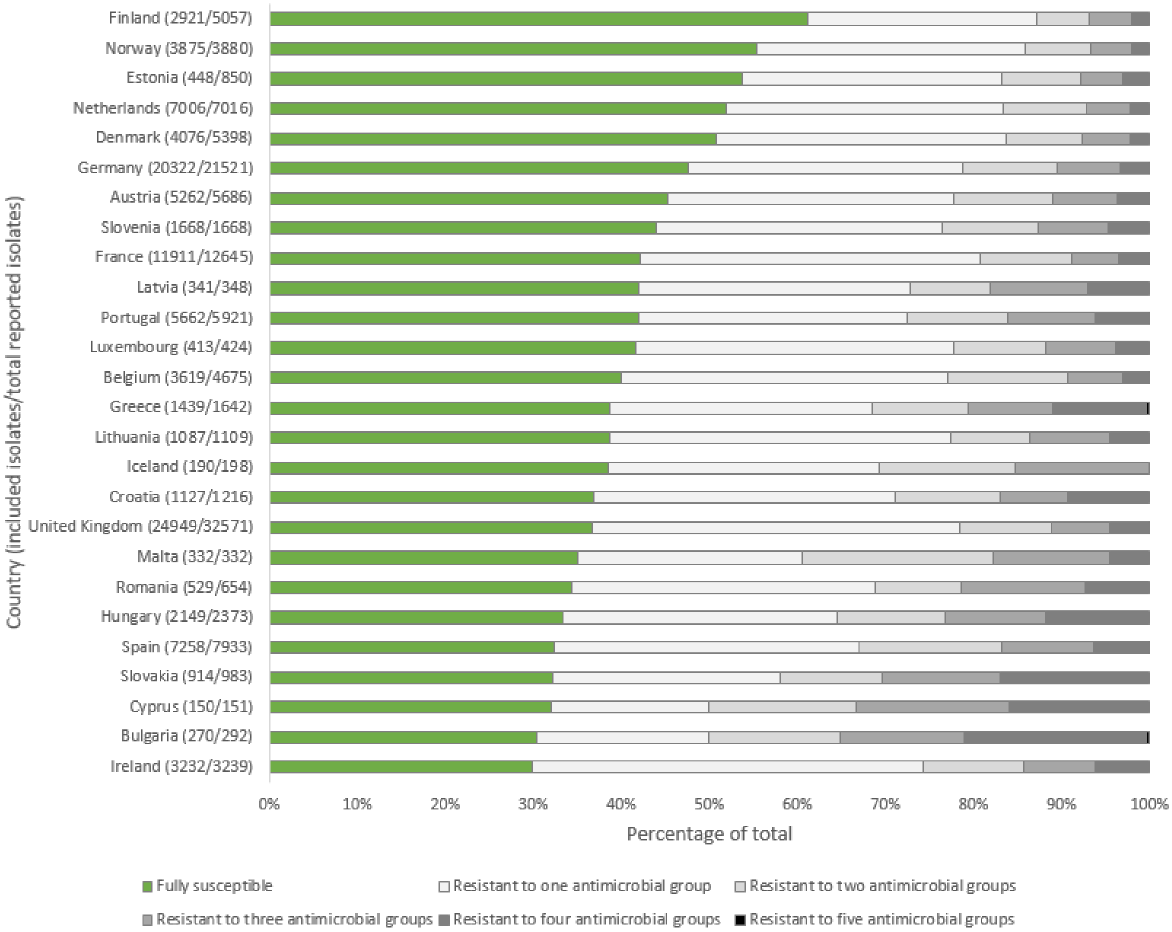
Although carbapenem-resistant *E. coli* was rarely reported in the invasive isolates included in EARS-Net, continued and close monitoring of this type of resistance remains essential. Results from the European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) and its predecessor the European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) show that the general situation for carbapenem-resistant Enterobacteriaceae (CRE), including *E. coli*, has worsened in many EU/EEA countries between 2010 and 2018 [20]. In addition, results from the Central Asian and European Surveillance of Antimicrobial Resistance network (CAESAR), coordinated by WHO/Europe and monitoring AMR in non-EU/EEA European countries, report presence of carbapenem-resistant *E. coli* in several EU/EEA bordering countries [7]. An increase of invasive infections caused by carbapenem-resistant *E. coli* would have severe consequences on the burden of AMR in the EU/EEA, as *E. coli* remains the most commonly cause of bloodstream infections and as CRE are adapted to spread in healthcare settings as well as in the community.

CRE infections are associated with high mortality, primarily due to delays in administration of effective treatment and the limited availability of treatment options. The ECDC rapid risk assessment on CRE highlights the need for high standards in infection prevention and control, combined with adequate microbiological capacity to detected and prevent further spread [21]. 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 Enterobacteriaceae (CCRE) project has been incorporated in EURGen-Net for the period 2018 to 2020 [22]. The results of this project will provide information on the prevalence and distribution of carbapenemases, and contribute to a better understanding of the dissemination of CRE in Europe and the risk factors associated with CRE infections.

Trends in fluoroquinolone resistance might be influenced by the fact that, in 2016, EUCAST lowered its clinical breakpoints for several fluoroquinolones in Enterobacteriaceae [23]. As EARS-Net bases its results on SIR interpretations, it is not possible to assess when or to what degree this change has been implemented by participating laboratories, and how these changes have influenced the results. As a consequence, trend analyses for fluoroquinolone resistance should be interpreted with caution.

As high *E. coli* resistance levels have been reported from food-producing animals in Europe, including the rare occurrence of isolates with carbapenemase production [24], the need to ensure cross-sectoral collaboration between the 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 interrelationship between antimicrobial use and antimicrobial resistance in humans and animals across Europe.

Figure 3.1. *Escherichia coli*. Distribution of isolates: fully susceptible and resistant to one, two, three, four and five antimicrobial groups (among isolates tested against aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems)*, EU/EEA countries, 2018



Data are only displayed for countries providing this information for 50% or more of the isolates.

** Only data from isolates tested against all included antimicrobial groups (aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) were included in the analysis.*

Table 3.1. *Escherichia coli*. Total number of tested isolates* and resistance combinations among invasive isolates tested against aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems (n=119 800), EU/EEA countries, 2018

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**49905**	**41.7**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**41526**	**34.7**
Aminopenicillins	38093	31.8
Fluoroquinolones	3211	2.7
Other antimicrobial groups	222	0.2
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**13056**	**10.9**
Aminopenicillins + fluoroquinolones	7964	6.6
Aminopenicillins + third-generation cephalosporins	2894	2.4
Aminopenicillins + aminoglycosides	2039	1.7
Other antimicrobial group combinations	159	0.1
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**9335**	**7.8**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones	5967	5.0
Aminopenicillins + fluoroquinolones + aminoglycosides	2814	2.3
Other antimicrobial group combinations	554	0.5
Resistance to four antimicrobial groups		
Total (all four-group combinations)	**5938**	**5.0**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides	5904	4.9
Other antimicrobial group combinations	34	<0.1
Resistance to five antimicrobial groups		
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	**40**	**<0.1**

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

** Only data from isolates tested against all five antimicrobials groups (aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) were included in the analysis.*
*** Not adjusted for population differences in the reporting countries.*

Figure 3.2. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.3. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.4. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to aminoglycosides, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.5. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to carbapenems, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.6. *Escherichia coli*. Percentage (%) of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, EU/EEA countries, 2018 *Map to be provided by designer*

Table 3.2. *Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to aminopenicillins (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Finland	2472	36.0	(34-38)	2690	35.8	(34-38)	2874	35.2	(33-37)	3129	35.3	(34-37)	
Norway	3299	45.8	(44-48)	3615	42.9	(41-45)	3731	42.2	(41-44)	3880	42.3	(41-44)	<
Estonia	196	47.4	(40-55)	471	46.7	(42-51)	439	47.8	(43-53)	457	43.5	(39-48)	
Netherlands	5376	47.2	(46-49)	6394	45.9	(45-47)	6684	45.9	(45-47)	7013	45.6	(44-47)	
Denmark	4594	45.3	(44-47)	4698	45.0	(44-46)	4885	45.6	(44-47)	5383	46.0	(45-47)	
Germany	8358	49.4	(48-50)	15957	49.0	(48-50)	21646	48.9	(48-50)	20369	48.9	(48-50)	
Iceland	173	44.5	(37-52)	192	43.8	(37-51)	213	41.3	(35-48)	198	49.0	(42-56)	
Austria	4880	49.9	(48-51)	5094	50.5	(49-52)	5188	49.5	(48-51)	5456	50.7	(49-52)	
Slovenia	1326	54.8	(52-58)	1420	57.1	(54-60)	1435	51.6	(49-54)	1668	53.5	(51-56)	
Czech Republic	3172	54.3	(53-56)	3055	55.1	(53-57)	3198	53.0	(51-55)	3640	54.2	(53-56)	
Portugal	5177	57.8	(56-59)	5772	59.2	(58-61)	6245	56.2	(55-57)	5895	55.1	(54-56)	<
Luxembourg	347	60.2	(55-65)	419	53.2	(48-58)	433	55.9	(51-61)	420	55.2	(50-60)	
France	10946	57.0	(56-58)	11248	57.2	(56-58)	13293	55.6	(55-56)	12553	55.6	(55-56)	<
Belgium	2674	58.0	(56-60)	3736	58.0	(56-60)	4669	57.5	(56-59)	4445	55.8	(54-57)	<#
Latvia	192	53.6	(46-61)	247	55.1	(49-61)	202	60.4	(53-67)	347	56.2	(51-61)	
EU/EEA (population-weighted mean)	**77813**	**58.9**	**(59-59)**	**107383**	**59.0**	**(59-59)**	**125038**	**58.7**	**(58-59)**	**131969**	**57.4**	**(57-58)**	**<**
Greece	1079	56.1	(53-59)	1170	56.9	(54-60)	1306	57.5	(55-60)	1444	57.5	(55-60)	
Croatia	1042	55.3	(52-58)	1043	57.3	(54-60)	1135	58.8	(56-62)	1214	57.7	(55-61)	
Lithuania	582	59.6	(56-64)	794	59.2	(56-63)	845	57.8	(54-61)	1106	59.0	(56-62)	
Malta	238	55.5	(49-62)	328	60.1	(55-65)	314	59.6	(54-65)	332	59.6	(54-65)	
United Kingdom	5117	65.8	(64-67)	21614	62.7	(62-63)	28647	62.5	(62-63)	29502	60.8	(60-61)	<
Slovakia	878	62.8	(59-66)	817	62.3	(59-66)	853	64.9	(62-68)	967	61.7	(59-65)	
Romania	259	73.0	(67-78)	376	72.3	(68-77)	494	68.2	(64-72)	542	62.2	(58-66)	<
Hungary	1970	60.6	(58-63)	1969	57.4	(55-60)	2021	60.3	(58-62)	2312	62.7	(61-65)	>
Spain	6427	63.9	(63-65)	6791	64.1	(63-65)	5947	62.4	(61-64)	7599	62.9	(62-64)	
Poland	346	64.7	(59-70)	1034	64.5	(62-67)	913	69.4	(66-72)	890	64.3	(61-67)	
Italy	3385	67.4	(66-69)	3114	66.9	(65-69)	4078	67.1	(66-69)	7533	64.5	(63-66)	<
Cyprus	123	68.3	(59-76)	149	69.1	(61-76)	156	65.4	(57-73)	151	64.9	(57-72)	
Bulgaria	143	66.4	(58-74)	186	78.0	(71-84)	203	73.9	(67-80)	287	66.6	(61-72)	
Ireland	2646	66.2	(64-68)	2990	68.1	(66-70)	2991	69.8	(68-71)	3237	67.6	(66-69)	
Sweden	396	34.1	(29-39)	-	-	(-)	-	-	(-)	-	-	(-)	N/A

- : No data.

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.3 *Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Finland	4404	11.2	(10-12)	4808	11.5	(11-12)	5305	12.0	(11-13)	5043	11.4	(11-12)	
Norway	3298	10.2	(9-11)	3611	10.9	(10-12)	3731	13.6	(12-15)	3877	12.9	(12-14)	>
Denmark	4570	11.9	(11-13)	4827	11.0	(10-12)	5123	12.8	(12-14)	5386	13.3	(12-14)	>
Netherlands	5379	13.2	(12-14)	6398	12.8	(12-14)	6685	14.2	(13-15)	7015	14.9	(14-16)	>
France	10998	17.7	(17-18)	11251	16.7	(16-17)	13328	15.0	(14-16)	12443	16.3	(16-17)	<
Iceland	162	6.8	(3-12)	178	9.6	(6-15)	199	11.6	(7-17)	192	17.2	(12-23)	>
Estonia	256	15.2	(11-20)	699	13.9	(11-17)	781	17.4	(15-20)	829	17.6	(15-20)	
United Kingdom	5812	15.6	(15-17)	22883	16.3	(16-17)	30185	17.5	(17-18)	31340	17.7	(17-18)	>
Sweden	5525	12.6	(12-14)	6947	13.7	(13-14)	5762	15.8	(15-17)	5378	18.1	(17-19)	N/A
Lithuania	583	20.6	(17-24)	790	19.7	(17-23)	849	25.2	(22-28)	1104	19.7	(17-22)	
Germany	9019	19.4	(19-20)	17196	19.4	(19-20)	22940	20.7	(20-21)	21485	19.8	(19-20)	
Luxembourg	347	24.2	(20-29)	418	28.9	(25-34)	433	22.9	(19-27)	418	21.8	(18-26)	
Belgium	2565	26.6	(25-28)	3854	24.5	(23-26)	4382	23.8	(23-25)	4211	21.8	(21-23)	<
Austria	4808	20.0	(19-21)	5278	19.8	(19-21)	5367	20.5	(19-22)	5679	21.9	(21-23)	>
Slovenia	1325	24.6	(22-27)	1420	25.6	(23-28)	1383	24.9	(23-27)	1668	22.8	(21-25)	
Ireland	2631	23.1	(21-25)	2990	22.9	(21-24)	3119	23.6	(22-25)	3238	23.9	(22-25)	
Latvia	194	27.8	(22-35)	245	27.8	(22-34)	201	30.3	(24-37)	344	24.1	(20-29)	
Czech Republic	3165	22.6	(21-24)	3061	27.6	(26-29)	3199	24.5	(23-26)	3638	24.3	(23-26)	
EU/EEA (population-weighted mean)	**90137**	**24.8**	**(24-25)**	**124306**	**25.2**	**(25-25)**	**140736**	**25.7**	**(25-26)**	**152966**	**25.3**	**(25-25)**	**>#**
Portugal	5371	29.7	(28-31)	5783	28.9	(28-30)	6424	27.3	(26-28)	5868	25.5	(24-27)	<
Romania	371	30.7	(26-36)	418	30.6	(26-35)	518	26.4	(23-30)	646	29.1	(26-33)	
Croatia	1038	24.0	(21-27)	1041	27.9	(25-31)	1150	28.2	(26-31)	1199	30.0	(27-33)	>
Greece	1191	30.6	(28-33)	1304	32.1	(30-35)	1464	32.9	(31-35)	1631	30.8	(29-33)	
Spain	6484	31.6	(30-33)	6793	32.8	(32-34)	5781	32.5	(31-34)	7616	32.1	(31-33)	
Hungary	2021	29.0	(27-31)	1986	26.8	(25-29)	2051	30.6	(29-33)	2364	33.2	(31-35)	>
Poland	1571	27.9	(26-30)	2637	33.1	(31-35)	1832	35.9	(34-38)	2567	34.7	(33-37)	>
Italy	5590	44.4	(43-46)	5950	43.3	(42-45)	6945	44.9	(44-46)	16043	41.7	(41-42)	<
Bulgaria	204	35.3	(29-42)	237	42.2	(36-49)	247	42.1	(36-49)	292	41.8	(36-48)	
Malta	238	37.4	(31-44)	328	41.5	(36-47)	314	43.3	(38-49)	332	41.9	(37-47)	
Slovakia	894	44.2	(41-48)	826	40.4	(37-44)	882	43.2	(40-47)	969	42.1	(39-45)	
Cyprus	123	45.5	(37-55)	149	47.0	(39-55)	156	42.9	(35-51)	151	42.4	(34-51)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.4. *Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to third-generation cephalosporins (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Norway	3301	6.0	(5-7)	3617	5.6	(5-6)	3734	5.9	(5-7)	3879	6.8	(6-8)	
Netherlands	5378	5.7	(5-6)	6397	6.4	(6-7)	6684	6.2	(6-7)	7011	7.3	(7-8)	>
Finland	4342	6.1	(5-7)	4742	6.9	(6-8)	5223	6.9	(6-8)	5020	7.6	(7-8)	>
Denmark	4561	7.5	(7-8)	4659	6.6	(6-7)	4883	6.9	(6-8)	4833	7.7	(7-8)	
Iceland	173	1.7	(0-5)	192	4.2	(2-8)	213	6.1	(3-10)	198	8.1	(5-13)	>
Sweden	5995	6.2	(6-7)	6958	8.3	(8-9)	5790	7.4	(7-8)	5390	8.3	(8-9)	N/A
Belgium	2593	9.7	(9-11)	3737	10.5	(10-12)	4672	9.7	(9-11)	4644	9.0	(8-10)	
France	11051	11.0	(10-12)	11313	11.2	(11-12)	13352	10.2	(10-11)	12614	9.6	(9-10)	<
Estonia	246	11.4	(8-16)	701	9.0	(7-11)	788	8.8	(7-11)	850	9.8	(8-12)	
Austria	4900	9.7	(9-11)	5267	10.0	(9-11)	5129	9.6	(9-10)	5672	10.2	(9-11)	
United Kingdom	5169	11.3	(10-12)	21846	9.2	(9-10)	27925	10.3	(10-11)	28677	11.0	(11-11)	>#
Slovenia	1326	13.7	(12-16)	1420	12.5	(11-14)	1435	12.5	(11-14)	1668	11.3	(10-13)	
Germany	9031	10.3	(10-11)	17190	11.1	(11-12)	22929	12.3	(12-13)	21517	12.2	(12-13)	>
Luxembourg	347	12.7	(9-17)	418	13.6	(10-17)	433	9.7	(7-13)	424	12.5	(10-16)	
Ireland	2638	11.4	(10-13)	2985	11.4	(10-13)	3121	12.0	(11-13)	3237	12.9	(12-14)	>
Spain	6428	11.6	(11-12)	6796	15.0	(14-16)	6027	12.8	(12-14)	7923	13.8	(13-15)	>
Portugal	5376	16.1	(15-17)	5784	16.1	(15-17)	6441	15.6	(15-16)	5881	14.7	(14-16)	<
Croatia	1046	12.5	(11-15)	1045	14.7	(13-17)	1148	16.5	(14-19)	1168	14.8	(13-17)	
EU/EEA (population-weighted mean)	**90126**	**14.6**	**(14-15)**	**123087**	**14.9**	**(15-15)**	**139759**	**14.9**	**(15-15)**	**150989**	**15.1**	**(15-15)**	**>#**
Czech Republic	3172	14.5	(13-16)	3061	15.1	(14-16)	3199	14.2	(13-15)	3641	15.2	(14-16)	
Lithuania	581	16.0	(13-19)	795	14.7	(12-17)	852	16.8	(14-19)	1109	15.3	(13-18)	
Malta	238	11.8	(8-17)	328	14.6	(11-19)	314	15.6	(12-20)	332	15.4	(12-20)	
Poland	1610	11.9	(10-14)	2719	13.7	(12-15)	2866	16.7	(15-18)	2620	17.6	(16-19)	>
Greece	1215	19.8	(18-22)	1304	17.6	(16-20)	1470	18.3	(16-20)	1640	19.3	(17-21)	
Romania	369	26.8	(22-32)	418	23.4	(19-28)	518	18.7	(15-22)	654	20.2	(17-23)	<
Latvia	201	17.9	(13-24)	253	24.1	(19-30)	205	22.0	(16-28)	348	20.4	(16-25)	
Hungary	2026	16.7	(15-18)	1993	16.7	(15-18)	2058	20.1	(18-22)	2370	22.6	(21-24)	>
Italy	5592	30.1	(29-31)	5938	29.8	(29-31)	7077	29.5	(28-31)	16253	28.7	(28-29)	<#
Slovakia	893	30.0	(27-33)	824	29.7	(27-33)	870	30.9	(28-34)	973	30.1	(27-33)	
Cyprus	123	28.5	(21-37)	149	30.2	(23-38)	156	30.8	(24-39)	151	37.1	(29-45)	
Bulgaria	205	38.5	(32-46)	238	41.6	(35-48)	247	41.3	(35-48)	292	38.7	(33-45)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.5. *Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Finland	4135	5.4	(5-6)	4519	4.9	(4-6)	4982	5.0	(4-6)	4815	4.3	(4-5)	<
Norway	3301	6.0	(5-7)	3614	5.5	(5-6)	3732	7.2	(6-8)	3880	5.7	(5-7)	
Denmark	4591	6.8	(6-8)	4846	6.1	(5-7)	5122	6.0	(5-7)	5393	5.7	(5-6)	<
Iceland	173	2.9	(1-7)	192	3.6	(1-7)	213	5.6	(3-10)	197	6.1	(3-10)	
Netherlands	5378	6.0	(5-7)	6397	6.2	(6-7)	6686	5.6	(5-6)	7015	6.2	(6-7)	
Estonia	257	9.3	(6-14)	702	7.4	(6-10)	786	5.7	(4-8)	849	6.2	(5-8)	
Germany	9029	7.1	(7-8)	17023	7.0	(7-7)	22478	7.0	(7-7)	21474	6.9	(7-7)	
Luxembourg	347	8.9	(6-12)	418	9.1	(7-12)	433	10.4	(8-14)	423	7.3	(5-10)	
Belgium	2286	8.4	(7-10)	3499	8.4	(8-9)	3769	8.1	(7-9)	3822	7.4	(7-8)	
France	11055	8.2	(8-9)	11135	7.9	(7-8)	13103	7.0	(7-7)	12283	7.4	(7-8)	<
Sweden	5761	6.4	(6-7)	6949	7.2	(7-8)	5758	6.5	(6-7)	5378	7.7	(7-8)	N/A
Lithuania	583	10.1	(8-13)	791	8.0	(6-10)	848	8.3	(6-10)	1103	7.9	(6-10)	
Austria	4884	7.0	(6-8)	5248	7.8	(7-9)	5318	7.7	(7-8)	5616	8.2	(8-9)	>
Latvia	191	14.1	(10-20)	244	12.7	(9-18)	201	13.4	(9-19)	348	8.9	(6-12)	
Slovenia	1326	12.9	(11-15)	1420	10.6	(9-12)	1435	11.4	(10-13)	1668	9.4	(8-11)	<
Czech Republic	3172	11.3	(10-13)	3061	12.2	(11-13)	3199	10.7	(10-12)	3643	9.5	(9-10)	<
Malta	238	12.2	(8-17)	328	10.4	(7-14)	314	10.8	(8-15)	332	9.9	(7-14)	
United Kingdom	6052	9.9	(9-11)	23166	9.9	(9-10)	30739	10.0	(10-10)	32119	10.5	(10-11)	>
EU/EEA (population-weighted mean)	**90050**	**11.6**	**(11-12)**	**123625**	**11.6**	**(11-12)**	**140962**	**11.4**	**(11-12)**	**152846**	**11.1**	**(11-11)**	**<**
Ireland	2646	11.8	(11-13)	2991	11.2	(10-12)	3123	11.9	(11-13)	3238	11.7	(11-13)	
Portugal	5372	13.8	(13-15)	5765	13.1	(12-14)	6387	11.9	(11-13)	5825	12.2	(11-13)	<
Romania	366	18.3	(14-23)	414	15.0	(12-19)	513	15.2	(12-19)	649	12.8	(10-16)	<
Spain	6489	14.7	(14-16)	6796	14.5	(14-15)	6029	13.7	(13-15)	7924	14.1	(13-15)	
Croatia	1008	12.7	(11-15)	1027	15.7	(14-18)	1154	16.6	(15-19)	1210	14.9	(13-17)	
Poland	1581	11.2	(10-13)	2521	13.3	(12-15)	2719	14.0	(13-15)	2449	15.1	(14-17)	>
Greece	1200	16.1	(14-18)	1301	16.8	(15-19)	1467	17.0	(15-19)	1633	15.5	(14-17)	
Italy	5408	20.2	(19-21)	6079	19.0	(18-20)	7134	18.4	(18-19)	15901	16.0	(15-17)	<
Hungary	2020	13.6	(12-15)	1992	13.3	(12-15)	2060	15.1	(14-17)	2264	17.4	(16-19)	>
Cyprus	123	13.8	(8-21)	149	16.1	(11-23)	156	21.8	(16-29)	151	19.9	(14-27)	
Slovakia	896	24.2	(21-27)	828	20.2	(17-23)	875	22.5	(20-25)	969	21.6	(19-24)	
Bulgaria	182	19.8	(14-26)	210	34.8	(28-42)	229	36.2	(30-43)	275	28.4	(23-34)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.6. *Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Denmark	4046	<0.1	(0-0)	4671	0.0	(0-0)	5117	0.0	(0-0)	4640	0.0	(0-0)	
Croatia	1046	0.0	(0-0)	1045	0.0	(0-0)	1132	0.0	(0-0)	1190	0.0	(0-0)	
Estonia	219	0.0	(0-2)	602	0.0	(0-1)	687	0.0	(0-1)	758	0.0	(0-0)	
Hungary	1922	0.0	(0-0)	1905	0.0	(0-0)	1987	0.1	(0-0)	2279	0.0	(0-0)	
Iceland	162	0.0	(0-2)	192	0.0	(0-0)	198	0.0	(0-0)	190	0.0	(0-0)	
Ireland	2615	<0.1	(0-0)	2989	0.0	(0-0)	3116	0.0	(0-0)	3237	0.0	(0-0)	
Lithuania	579	0.0	(0-1)	793	0.0	(0-0)	849	0.0	(0-0)	1100	0.0	(0-0)	
Latvia	192	0.0	(0-2)	246	0.0	(0-1)	203	0.0	(0-2)	346	0.0	(0-1)	
Luxembourg	347	0.0	(0-1)	418	0.0	(0-1)	433	0.0	(0-1)	424	0.0	(0-1)	
Malta	238	0.0	(0-2)	328	0.0	(0-1)	314	0.0	(0-1)	332	0.0	(0-1)	
Romania	368	1.9	(1-4)	411	1.0	(0-2)	510	0.4	(0-1)	653	0.0	(0-1)	
Slovakia	830	0.0	(0-0)	751	0.0	(0-0)	844	0.0	(0-0)	924	0.0	(0-0)	
Slovenia	1326	0.0	(0-0)	1420	0.0	(0-0)	1435	0.0	(0-0)	1668	0.0	(0-0)	<
Finland	4425	0.0	(0-0)	4832	0.0	(0-0)	5315	0.0	(0-0)	5057	<0.1	(0-0)	
France	10481	<0.1	(0-0)	10929	0.0	(0-0)	12843	0.0	(0-0)	12399	<0.1	(0-0)	
Germany	9032	<0.1	(0-0)	17196	0.0	(0-0)	22940	0.0	(0-0)	21484	<0.1	(0-0)	
Netherlands	5375	<0.1	(0-0)	6394	0.0	(0-0)	6682	0.0	(0-0)	7013	<0.1	(0-0)	
Norway	3297	<0.1	(0-0)	3616	0.1	(0-0)	3733	0.1	(0-0)	3879	<0.1	(0-0)	
United Kingdom	5497	0.3	(0-0)	22762	0.0	(0-0)	30074	0.0	(0-0)	31229	<0.1	(0-0)	<
Spain	6399	<0.1	(0-0)	6790	0.1	(0-0)	6026	0.0	(0-0)	7924	<0.1	(0-0)	
Sweden	5307	0.1	(0-0)	6927	0.1	(0-0)	5769	0.0	(0-0)	5388	<0.1	(0-0)	N/A
Austria	4760	<0.1	(0-0)	5134	0.0	(0-0)	5227	0.0	(0-0)	5564	0.1	(0-0)	
Belgium	2588	0.0	(0-0)	3845	0.1	(0-0)	4672	0.0	(0-0)	4641	0.1	(0-0)	
Poland	1499	0.1	(0-0)	2553	0.0	(0-0)	2741	0.0	(0-0)	2500	0.1	(0-0)	
Czech Republic	1471	0.0	(0-0)	1483	0.0	(0-0)	1431	0.0	(0-0)	1752	0.1	(0-0)	
EU/EEA (population-weighted mean)	**86325**	**0.2**	**(0-0)**	**121582**	**0.1**	**(0-0)**	**139614**	**0.1**	**(0-0)**	**149725**	**0.1**	**(0-0)**	**<#**
Italy	5592	0.2	(0-0)	6106	0.3	(0-0)	7280	0.3	(0-0)	15452	0.4	(0-0)	>##
Portugal	5354	0.1	(0-0)	5760	0.0	(0-0)	6384	0.3	(0-1)	5797	0.5	(0-1)	>
Greece	1215	1.2	(1-2)	1303	0.9	(0-2)	1467	1.6	(1-2)	1640	1.0	(1-2)	
Bulgaria	182	0.0	(0-2)	224	0.9	(0-3)	247	0.0	(0-1)	292	1.4	(0-3)	
Cyprus	123	0.0	(0-3)	149	0.0	(0-2)	156	1.3	(0-5)	150	2.0	(0-6)	>

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.7. *Escherichia coli*. Total number of isolates tested (N) and percentage with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Finland	4103	2.6	(2-3)	4492	2.4	(2-3)	4971	2.4	(2-3)	4798	2.0	(2-2)	
Norway	3298	1.9	(1-2)	3609	1.9	(2-2)	3729	2.4	(2-3)	3876	2.0	(2-3)	
Denmark	4531	2.5	(2-3)	4640	1.8	(1-2)	4883	1.8	(1-2)	4829	2.0	(2-2)	
Iceland	162	0.0	(0-2)	178	1.1	(0-4)	199	1.5	(0-4)	191	2.1	(1-5)	
Netherlands	5377	2.0	(2-2)	6396	2.3	(2-3)	6681	1.9	(2-2)	7009	2.1	(2-3)	
Estonia	233	5.2	(3-9)	698	4.0	(3-6)	780	3.7	(3-5)	828	3.0	(2-4)	
Sweden	5257	2.5	(2-3)	6939	3.1	(3-4)	5746	2.0	(2-2)	5368	3.1	(3-4)	N/A
Belgium	2285	3.5	(3-4)	3496	3.8	(3-4)	3765	3.5	(3-4)	3809	3.1	(3-4)	
Germany	9013	3.0	(3-3)	17013	3.4	(3-4)	22464	3.7	(3-4)	21471	3.4	(3-4)	
France	10988	3.9	(4-4)	11082	3.8	(3-4)	13038	3.0	(3-3)	12107	3.5	(3-4)	<
Austria	4785	2.9	(2-3)	5235	3.5	(3-4)	5071	3.3	(3-4)	5598	3.6	(3-4)	
Luxembourg	347	5.2	(3-8)	418	3.8	(2-6)	433	3.5	(2-6)	417	3.8	(2-6)	
Malta	238	7.1	(4-11)	328	5.5	(3-9)	314	6.4	(4-10)	332	4.5	(3-7)	
United Kingdom	5119	4.5	(4-5)	21101	4.0	(4-4)	26808	4.1	(4-4)	27756	4.5	(4-5)	
Lithuania	581	4.3	(3-6)	783	2.6	(2-4)	845	4.4	(3-6)	1098	4.6	(3-6)	
Slovenia	1325	8.1	(7-10)	1420	6.9	(6-8)	1383	6.3	(5-8)	1668	4.7	(4-6)	<
Ireland	2621	5.4	(5-6)	2984	5.3	(5-6)	3116	5.7	(5-7)	3235	6.1	(5-7)	
Portugal	5366	7.6	(7-8)	5762	7.7	(7-8)	6365	6.6	(6-7)	5746	6.2	(6-7)	<
EU/EEA (population-weighted mean)	**88084**	**6.3**	**(6-6)**	**120727**	**6.4**	**(6-7)**	**134285**	**6.3**	**(6-6)**	**146788**	**6.2**	**(6-6)**	
Czech Republic	3165	6.9	(6-8)	3061	7.9	(7-9)	3199	6.3	(5-7)	3638	6.3	(6-7)	
Spain	6416	5.5	(5-6)	6787	6.2	(6-7)	5774	5.5	(5-6)	7598	6.4	(6-7)	
Latvia	191	10.5	(7-16)	242	10.3	(7-15)	197	11.2	(7-16)	344	7.0	(5-10)	
Romania	364	13.5	(10-17)	410	11.7	(9-15)	513	9.7	(7-13)	641	7.2	(5-9)	<
Croatia	1000	6.9	(5-9)	1023	9.4	(8-11)	1133	9.4	(8-11)	1150	9.2	(8-11)	
Greece	1187	10.7	(9-13)	1300	10.4	(9-12)	1463	9.8	(8-11)	1628	9.8	(8-11)	
Poland	1532	6.1	(5-7)	2411	8.5	(7-10)	1666	8.2	(7-10)	2386	10.5	(9-12)	>
Hungary	2015	6.7	(6-8)	1981	6.4	(5-8)	2047	8.2	(7-9)	2254	11.4	(10-13)	>
Italy	5389	14.6	(14-16)	5763	12.9	(12-14)	6454	13.7	(13-15)	15622	11.4	(11-12)	<
Cyprus	123	9.8	(5-16)	149	11.4	(7-18)	156	15.4	(10-22)	151	14.6	(9-21)	
Slovakia	891	17.1	(15-20)	822	14.8	(12-17)	863	17.7	(15-20)	965	16.6	(14-19)	
Bulgaria	182	12.6	(8-18)	204	22.1	(17-28)	229	24.9	(19-31)	275	19.6	(15-25)	

* *The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

3.2 *Klebsiella pneumoniae*

Klebsiella pneumoniae predominantly colonises hospitalised individuals, where it is mainly found in the gastrointestinal tract, skin and the respiratory tract. The majority of infections caused by *K. pneumoniae* are healthcare-associated and can spread rapidly between patients and via the hands of hospital personnel, leading to nosocomial outbreaks. Infections include urinary tract infections, lower respiratory tract infections, intra-abdominal infections and bloodstream infections.

Similar to *E. coli*, *K. pneumoniae* can be resistant to multiple antimicrobial agents, and resistance traits are frequently acquired through plasmids. In contrast to *E. coli*, *K. pneumoniae* has a chromosomally encoded class A beta-lactamase and is thus intrinsically resistant to aminopenicillins. Many novel ESBL variants were initially identified in *K. pneumoniae* and were only subsequently found in *E. coli*. Carbapenems frequently resist the effect of ESBLs and might remain as one of the few treatment options for severe *K. pneumoniae* infections. An increasing threat is carbapenem resistance mediated by a range of carbapenemases, which may confer resistance to virtually all available beta-lactam antibacterial drugs. Carbapenamase genes are often located on plasmids that can be exchanged between Enterobacteriaceae, including *K. pneumoniae*, and other gram-negative bacteria.

Antimicrobial resistance

At the EU/EEA level, more than a third (37.2%) of the *K. pneumoniae* isolates reported to EARS-Net for 2018 were resistant to at least one of the antimicrobial groups under regular surveillance, i.e. fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems (Table 3.8). In 2018, the highest EU/ EEA population-weighted mean resistance percentage was reported for third-generation cephalosporins (31.7%), followed by fluoroquinolones (31.6%), aminoglycosides (22.7%) and carbapenems (7.5%) (Tables 3.9–3.12).

There were significant increasing trends in the EU/EEA population-weighted mean percentages of fluoroquinolone resistance and carbapenem resistance between 2015 and 2018 (Tables 3.9, 3.12). The corresponding EU/EEA trend for aminoglycoside resistance decreased significantly during the same period (Table 3.6). All EU/EEA trends remained significant when restricting the analysis to only include the laboratories that consistently reported data

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 3.8). The EU/EEA population-weighted mean for combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides was 19.6% in 2018 and did not change significantly between 2015 and 2018 (Table 3.13).

Large inter-country variations could be noted for all antimicrobial groups under regular surveillance, with generally higher resistance percentages reported from the southern and eastern parts of Europe than from northern Europe (Figures 3.8–3.12). The countries reporting the highest percentages of carbapenem resistance in *K. pneumoniae* were also among the countries reporting the highest resistance percentages for the other antimicrobial groups. Similar distinct variations could be seen in the country-specific distributions between fully susceptible isolates and isolates with resistance to one, two, three or four antimicrobial groups (Figure 3.7).

Discussion and conclusion

The resistance situation in *K. pneumoniae* remains problematic Europe. Although the EU/EEA level increase in carbapenem resistance between 2015 and 2018 was more moderate compared to the previous five-year period [25], the results underline the need for continuous close monitoring and increased efforts to curb further increase. Carbapenem resistance was almost always combined with resistance to several other key antimicrobial groups, severely limiting the treatment for infections caused by these type of bacteria.

In general, higher frequency of carbapenem resistance was reported from southern and south-eastern parts of Europe, a pattern that has also been reflected by other European surveillance initiatives such as the ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals

[15], EURGen-Net [20] and the ECDC study on the health burden of AMR [3]. Results from these initiatives also show a deteriorating situation in EU/EEA countries during recent years with regard to epidemiological stage, incidence and related disability-adjusted life years (DALYs). The ECDC study on the health burden of AMR estimated that the number of deaths attributed to infections with *K. pneumoniae* resistant to carbapenems increased six-fold between 2007 and 2015. Even in countries with lower levels of carbapenem-resistant *K. pneumoniae*, the impact on national burden of AMR is high because of the high attributable mortality of these infections [3].

CRE can be resistant to carbapenems as a result of various mechanisms, including and with increasing frequency production of carbapenemase enzymes. The overall presence and spread of carbapenemase-producing Enterobacteriaceae is not possible to assess by 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 [26]. This is partly reflected by the substantially higher percentages of carbapenem non-susceptible *K. pneumoniae* compared to carbapenem-resistant *K. pneumoniae* in some countries in the EU/EEA [27]. The recently launched carbapenem and/or colistin-resistant Enterobacteriaceae (CCRE) project as part of the European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) will provide updated and more detailed information on the distribution of carbapenemase-producing *K. pneumoniae* in Europe [22].

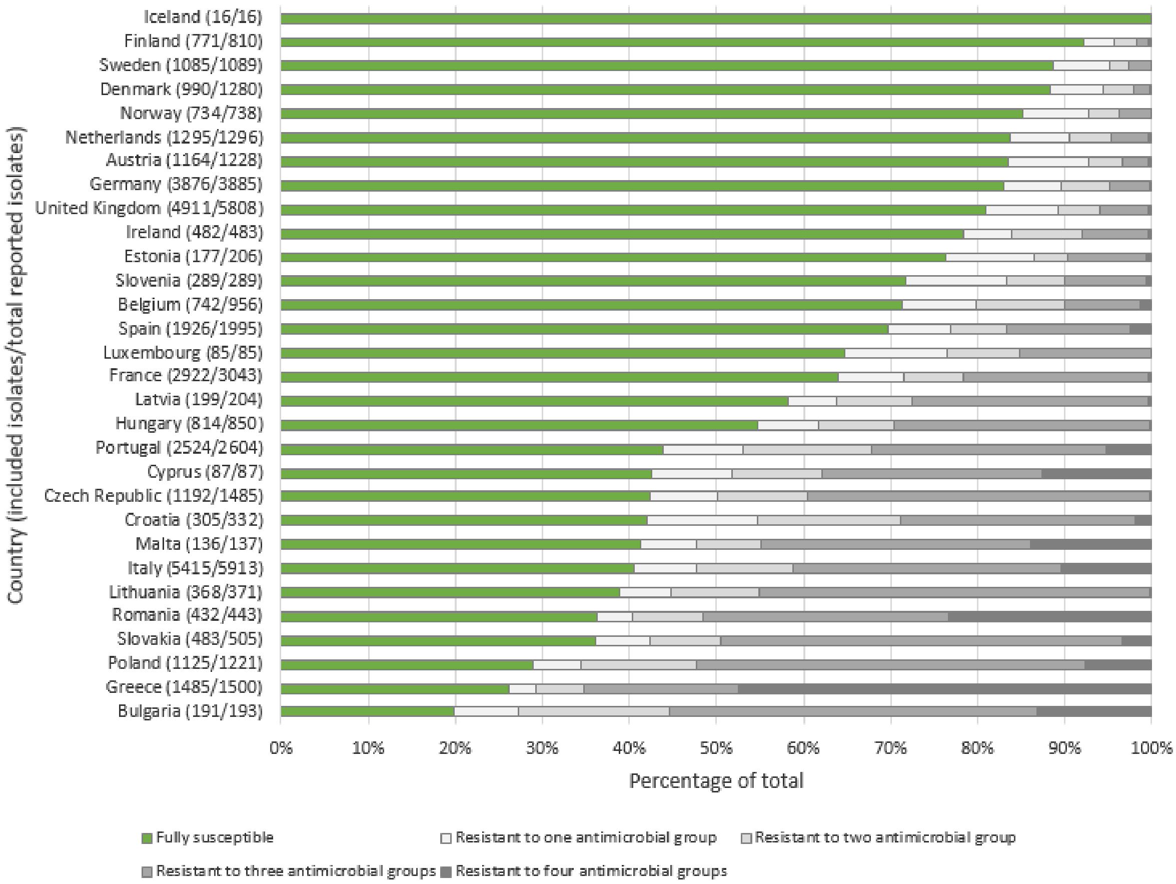
As highlighted in the updated ECDC rapid risk assessment on CRE, options for action include timely and appropriate diagnosis, high standards of infection prevention and control and antimicrobial stewardship [21]. Numerous reports on outbreaks and examples of cross-border transmission of CRE demonstrates the transmission potential in EU/EEA healthcare systems [21, 26, 28]. In recent years, many EU/EEA countries have developed and implemented recommendations and guidance documents on multidrug-resistant Enterobacteriaceae and/or CRE [29], 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 [30].

Colistin is frequently being used to treat CRE infections, but colistin resistance may develop during treatment. The recent discovery of transferable plasmid-mediated colistin resistance genes that can transmit colistin resistance more easily between bacteria further increases the risk for spread of colistin resistance [31]. 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 Enterobacteriaceae, but rather performed 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 subcommittee has issued recommendations confirming that broth microdilution is so far the only valid method for colistin susceptibility testing [32]. A survey among EARS-Net participating laboratories in 2017 showed that a majority of the responding local laboratories did not test for colistin susceptibility locally or used methods that are not recommended by EUCAST (unpublished data, ECDC/UK NEQAS), leading 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 Enterobacteriaceae in Europe, ECDC has included colistin in the surveillance panel of the CCRE project. This project includes a capacity building component for reference laboratories, which hopefully will also improve diagnostic capacity at the local level [22].

A novel antibiotic-enzyme inhibitor combinations, ceftazidime-avibactam, was recently launched as a therapeutic alternative for patients infected with multidrug-resistant gram negative bacteria, including CRE caused by certain, but not all, types of carbapenemase. However, rapidly emerging resistance to ceftazidime-avibactam has been reported from clinical settings and during therapy soon after its launch, both within and outside the EU/EEA [33]. WHO sees a critical need for research and the development of new antibiotics which target third-generation cephalosporin and carbapenem resistance in Enterobacteriaceae, including *K. pneumoniae* and *E. coli* [34].

Similar to *E. coli*, the trends in fluoroquinolone resistance may be influenced by the fact that in 2016, EUCAST lowered its clinical breakpoints for several fluoroquinolones in Enterobacteriaceae. As EARS-Net bases its results on SIR interpretations, it is not possible to assess when or to what degree this change has been implemented by participating laboratories and how these changes have influenced the results. As a consequence, trend analyses for fluoroquinolone resistance should be interpreted with caution.

Figure 3.7. *Klebsiella pneumoniae*. Distribution of isolates: fully susceptible and resistant to one, two, three and four antimicrobial groups (among isolates tested against fluoroquinolone, third-generation cephalosporin, aminoglycoside and carbapenems)*, EU/EEA countries, 2018



** Only data from isolates tested against all included antimicrobial groups were included in the analysis.*

Table 3.8. *Klebsiella pneumoniae*. Total number of invasive isolates tested* and resistance combinations among isolates tested against fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems (n=36 206). EU/EEA countries, 2018

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**22732**	**62.8**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**2624**	**7.2**
Fluoroquinolones	1354	3.7
Third-generation cephalosporins	1064	2.9
Other antimicrobial groups	206	0.6
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**2772**	**7.7**
Third-generation cephalosporins + fluoroquinolones	1750	4.8
Third-generation cephalosporins + aminoglycosides	525	1.5
Fluoroquinolones + aminoglycosides	401	1.1
Other antimicrobial group combinations	96	0.3
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**6279**	**17.3**
Third-generation cephalosporins + fluoroquinolones + aminoglycosides	4978	13.7
Third-generation cephalosporins + fluoroquinolones + carbapenems	1185	3.3
Other antimicrobial group combinations	116	0.3
Resistance to four antimicrobial groups		
Third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	**1799**	**5.0**

Only resistance combinations >1% of the total are specified.
** Only data from isolates tested against all five antimicrobials groups were included in the analysis.*
*** Not adjusted for population differences in the reporting countries.*

Figure 3.8. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.9. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.10. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to aminoglycosides, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.11. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.12. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, EU/EEA countries, 2018 *Map to be provided by designer*

Table 3.9. *Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	35	2.9	(0-15)	21	0.0	(0-16)	16	6.3	(0-30)	16	0.0	(0-21)	N/A
Finland	658	3.3	(2-5)	769	2.7	(2-4)	756	7.9	(6-10)	808	6.3	(5-8)	>
Denmark	935	5.3	(4-7)	1152	5.3	(4-7)	1183	9.1	(8-11)	1279	8.5	(7-10)	>
Sweden	907	4.5	(3-6)	1533	5.4	(4-7)	1034	9.8	(8-12)	1087	10.1	(8-12)	N/A
Netherlands	908	6.8	(5-9)	1134	6.9	(5-9)	1190	11.9	(10-14)	1296	12.2	(10-14)	>
Norway	700	5.0	(4-7)	808	4.3	(3-6)	781	10.2	(8-13)	735	13.1	(11-16)	>
United Kingdom	1011	13.3	(11-16)	4065	7.5	(7-8)	5293	9.3	(9-10)	5600	13.1	(12-14)	>#
Austria	1029	11.7	(10-14)	1246	9.8	(8-12)	1147	14.2	(12-16)	1221	13.2	(11-15)	>
Germany	1580	9.6	(8-11)	3068	12.6	(11-14)	3857	15.3	(14-16)	3881	13.3	(12-14)	>
Ireland	388	17.0	(13-21)	453	11.3	(8-15)	478	14.9	(12-18)	483	18.0	(15-22)	
Estonia	62	33.9	(22-47)	183	29.5	(23-37)	161	24.8	(18-32)	205	21.0	(16-27)	<
Belgium	379	22.7	(19-27)	669	23.6	(20-27)	803	23.7	(21-27)	932	22.6	(20-25)	
Spain	1508	21.6	(20-24)	1676	22.7	(21-25)	1486	22.5	(20-25)	1927	23.8	(22-26)	
Luxembourg	60	20.0	(11-32)	78	35.9	(25-48)	99	28.3	(20-38)	85	24.7	(16-35)	
Slovenia	237	24.5	(19-30)	267	29.6	(24-35)	306	30.4	(25-36)	289	27.3	(22-33)	
France	2332	30.7	(29-33)	2589	27.7	(26-29)	2886	26.8	(25-28)	2997	30.4	(29-32)	
EU/EEA (population-weighted mean)	**22417**	**30.1**	**(30-31)**	**30583**	**30.3**	**(30-31)**	**32784**	**31.5**	**(31-32)**	**38456**	**31.6**	**(31-32)**	**>**
Hungary	700	36.7	(33-40)	713	35.2	(32-39)	685	41.5	(38-45)	842	38.0	(35-41)	
Latvia	112	42.0	(33-52)	91	41.8	(32-53)	116	32.8	(24-42)	200	38.5	(32-46)	
Portugal	2094	38.6	(36-41)	2350	41.7	(40-44)	2736	45.7	(44-48)	2592	43.8	(42-46)	>
Czech Republic	1416	48.9	(46-52)	1384	50.5	(48-53)	1329	49.2	(46-52)	1482	47.2	(45-50)	
Croatia	380	48.7	(44-54)	318	43.4	(38-49)	309	40.8	(35-46)	327	48.6	(43-54)	
Cyprus	62	37.1	(25-50)	75	32.0	(22-44)	71	35.2	(24-47)	87	49.4	(39-60)	
Italy	2000	53.7	(51-56)	2248	56.0	(54-58)	2562	55.7	(54-58)	5752	52.7	(51-54)	
Malta	88	26.1	(17-37)	102	33.3	(24-43)	117	39.3	(30-49)	137	55.5	(47-64)	>
Lithuania	179	45.8	(38-53)	324	54.6	(49-60)	326	64.7	(59-70)	370	56.8	(52-62)	>
Romania	267	61.4	(55-67)	342	60.8	(55-66)	337	64.1	(59-69)	441	57.4	(53-62)	
Slovakia	474	70.0	(66-74)	466	66.3	(62-71)	466	66.7	(62-71)	497	61.0	(57-65)	<
Bulgaria	96	37.5	(28-48)	160	55.6	(48-63)	169	59.8	(52-67)	193	62.7	(55-70)	>
Greece	1161	66.4	(64-69)	1180	68.6	(66-71)	1346	66.9	(64-69)	1488	68.1	(66-70)	
Poland	659	63.9	(60-68)	1119	66.8	(64-70)	739	66.3	(63-70)	1207	68.2	(65-71)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.10. *Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to third-generation cephalosporins (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	36	0.0	(0-10)	25	0.0	(0-14)	17	5.9	(0-29)	16	0.0	(0-21)	N/A
Finland	644	3.0	(2-5)	760	4.1	(3-6)	744	4.6	(3-6)	805	4.5	(3-6)	
Sweden	1001	3.3	(2-5)	1537	4.9	(4-6)	1034	5.6	(4-7)	1089	5.5	(4-7)	N/A
Denmark	929	7.8	(6-10)	1118	7.5	(6-9)	1125	7.3	(6-9)	1159	6.5	(5-8)	
Norway	701	5.0	(4-7)	811	5.8	(4-8)	781	5.8	(4-8)	737	7.5	(6-10)	
Austria	1050	8.4	(7-10)	1245	9.6	(8-11)	1072	8.6	(7-10)	1221	8.4	(7-10)	
Netherlands	908	8.6	(7-11)	1134	10.3	(9-12)	1189	10.9	(9-13)	1295	11.1	(9-13)	
Germany	1581	10.2	(9-12)	3068	13.6	(12-15)	3854	14.6	(14-16)	3884	12.9	(12-14)	
United Kingdom	916	10.5	(9-13)	3914	8.9	(8-10)	4973	11.4	(10-12)	5181	13.0	(12-14)	>#
Estonia	93	23.7	(15-34)	183	32.8	(26-40)	161	21.1	(15-28)	206	13.6	(9-19)	<
Ireland	387	14.7	(11-19)	452	13.5	(10-17)	478	14.6	(12-18)	483	14.5	(11-18)	
Slovenia	237	22.8	(18-29)	267	22.8	(18-28)	312	23.7	(19-29)	289	14.9	(11-20)	<
Belgium	406	19.7	(16-24)	669	22.9	(20-26)	803	19.3	(17-22)	935	21.4	(19-24)	
Spain	1491	20.3	(18-22)	1677	22.4	(20-24)	1513	21.3	(19-23)	1994	25.5	(24-27)	>#
Luxembourg	60	28.3	(17-41)	78	35.9	(25-48)	99	27.3	(19-37)	85	29.4	(20-40)	
France	2338	30.5	(29-32)	2597	28.9	(27-31)	2892	28.8	(27-31)	3033	30.8	(29-32)	
EU/EEA (population-weighted mean)	**22511**	**31.0**	**(30-32)**	**30447**	**31.4**	**(31-32)**	**32829**	**31.2**	**(31-32)**	**38122**	**31.7**	**(31-32)**	
Latvia	115	47.0	(38-56)	95	47.4	(37-58)	116	33.6	(25-43)	204	37.7	(31-45)	<
Hungary	704	37.2	(34-41)	722	37.5	(34-41)	693	41.1	(37-45)	848	40.2	(37-44)	
Croatia	380	46.8	(42-52)	321	48.6	(43-54)	309	41.7	(36-47)	318	44.3	(39-50)	
Cyprus	62	43.5	(31-57)	75	30.7	(21-42)	71	46.5	(35-59)	87	48.3	(37-59)	
Portugal	2094	40.4	(38-43)	2349	46.7	(45-49)	2743	44.9	(43-47)	2579	50.0	(48-52)	>
Czech Republic	1417	54.1	(51-57)	1384	51.8	(49-54)	1329	53.2	(50-56)	1482	50.1	(47-53)	
Malta	88	15.9	(9-25)	102	21.6	(14-31)	117	35.0	(26-44)	137	53.3	(45-62)	>
Italy	1999	55.9	(54-58)	2246	55.8	(54-58)	2546	54.6	(53-57)	5832	53.6	(52-55)	<#
Lithuania	178	51.7	(44-59)	326	56.7	(51-62)	326	63.2	(58-68)	371	55.8	(51-61)	
Slovakia	469	67.2	(63-71)	465	61.3	(57-66)	459	63.2	(59-68)	497	55.9	(51-60)	<
Romania	270	70.7	(65-76)	344	68.0	(63-73)	339	62.5	(57-68)	443	61.4	(57-66)	<
Poland	676	64.2	(60-68)	1142	64.4	(62-67)	1203	63.0	(60-66)	1219	64.6	(62-67)	
Greece	1185	69.5	(67-72)	1181	72.5	(70-75)	1362	69.2	(67-72)	1500	70.7	(68-73)	
Bulgaria	96	75.0	(65-83)	160	72.5	(65-79)	169	76.3	(69-83)	193	77.7	(71-83)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.11. *Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	36	0.0	(0-10)	25	0.0	(0-14)	17	11.8	(1-36)	16	0.0	(0-21)	N/A
Finland	625	1.9	(1-3)	727	2.3	(1-4)	721	2.9	(2-4)	774	2.6	(2-4)	
Sweden	943	3.2	(2-5)	1141	3.4	(2-5)	1033	4.7	(4-6)	1087	3.0	(2-4)	N/A
Denmark	938	2.6	(2-4)	1154	3.2	(2-4)	1186	3.2	(2-4)	1278	3.3	(2-4)	
Austria	959	4.8	(4-6)	1157	4.8	(4-6)	1141	4.8	(4-6)	1214	4.8	(4-6)	
Norway	700	3.6	(2-5)	809	3.3	(2-5)	781	4.2	(3-6)	737	5.3	(4-7)	
Germany	1582	5.6	(5-7)	3042	7.7	(7-9)	3776	8.2	(7-9)	3878	6.2	(5-7)	
Netherlands	908	5.7	(4-7)	1134	6.1	(5-8)	1190	7.6	(6-9)	1296	7.3	(6-9)	
United Kingdom	1070	9.3	(8-11)	4135	6.7	(6-7)	5363	7.9	(7-9)	5709	9.1	(8-10)	>[#]
Estonia	61	21.3	(12-34)	183	21.3	(16-28)	161	12.4	(8-19)	205	10.2	(6-15)	<
Belgium	354	11.6	(8-15)	637	13.8	(11-17)	633	12.5	(10-15)	747	12.4	(10-15)	
Slovenia	237	19.0	(14-25)	267	16.5	(12-21)	312	16.0	(12-21)	289	12.8	(9-17)	
Ireland	389	15.9	(12-20)	453	11.5	(9-15)	479	11.9	(9-15)	483	13.0	(10-16)	
Spain	1509	16.0	(14-18)	1678	15.5	(14-17)	1513	17.4	(16-19)	1995	19.3	(18-21)	>[#]
Luxembourg	60	15.0	(7-27)	78	26.9	(18-38)	99	18.2	(11-27)	85	20.0	(12-30)	
EU/EEA (population-weighted mean)	**22360**	**24.2**	**(24-25)**	**30023**	**24.4**	**(24-25)**	**32996**	**24.1**	**(24-25)**	**38290**	**22.7**	**(22-23)**	**<**
France	2337	26.3	(25-28)	2569	26.2	(25-28)	2857	23.8	(22-25)	2990	24.8	(23-26)	
Italy	1956	34.0	(32-36)	2300	36.1	(34-38)	2571	34.5	(33-36)	5693	27.0	(26-28)	<[#]
Latvia	113	43.4	(34-53)	91	38.5	(28-49)	115	29.6	(21-39)	203	31.0	(25-38)	<
Hungary	706	34.6	(31-38)	720	34.7	(31-38)	693	37.8	(34-42)	845	32.7	(30-36)	
Portugal	2090	32.6	(31-35)	2337	35.0	(33-37)	2717	33.5	(32-35)	2572	34.4	(33-36)	
Croatia	380	43.2	(38-48)	316	36.1	(31-42)	311	30.9	(26-36)	330	36.4	(31-42)	<
Cyprus	62	37.1	(25-50)	75	22.7	(14-34)	71	26.8	(17-39)	87	36.8	(27-48)	
Malta	88	22.7	(14-33)	102	22.5	(15-32)	117	31.6	(23-41)	137	46.7	(38-55)	>
Lithuania	179	46.4	(39-54)	325	49.2	(44-55)	322	53.7	(48-59)	369	48.5	(43-54)	
Czech Republic	1417	51.9	(49-55)	1385	47.1	(44-50)	1330	49.6	(47-52)	1483	48.6	(46-51)	
Romania	266	54.1	(48-60)	336	61.9	(56-67)	338	58.6	(53-64)	436	50.9	(46-56)	
Poland	666	58.6	(55-62)	1075	56.7	(54-60)	1165	55.5	(53-58)	1178	54.2	(51-57)	
Greece	1170	50.7	(48-54)	1171	52.9	(50-56)	1348	53.2	(50-56)	1487	54.4	(52-57)	
Slovakia	475	66.5	(62-71)	466	62.4	(58-67)	468	61.1	(57-66)	496	54.8	(50-59)	<
Bulgaria	84	59.5	(48-70)	135	64.4	(56-72)	168	63.1	(55-70)	191	59.2	(52-66)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.12. *Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	35	0.0	(0-12)	21	0.0	(0-12)	16	0.0	(0-13)	16	0.0	(0-21)	N/A
Luxembourg	60	0.0	(0-6)	78	0.0	(0-5)	99	0.0	(0-4)	85	0.0	(0-4)	
Norway	700	0.1	(0-1)	810	0.0	(0-0)	781	0.0	(0-0)	736	0.1	(0-1)	
Hungary	687	0.1	(0-1)	703	0.4	(0-1)	681	0.3	(0-1)	827	0.2	(0-1)	
Sweden	900	0.0	(0-0)	1531	0.1	(0-0)	1033	0.1	(0-1)	1088	0.2	(0-1)	N/A
Lithuania	177	0.0	(0-2)	325	0.0	(0-1)	325	0.6	(0-2)	371	0.3	(0-1)	
Czech Republic	1100	0.3	(0-1)	1096	0.0	(0-0)	1051	0.4	(0-1)	1194	0.3	(0-1)	
Germany	1583	0.1	(0-0)	3068	0.5	(0-1)	3857	0.5	(0-1)	3879	0.4	(0-1)	
Latvia	112	0.0	(0-3)	90	2.2	(0-8)	116	1.7	(0-6)	204	0.5	(0-3)	
France	2244	0.5	(0-1)	2528	0.4	(0-1)	2807	0.7	(0-1)	2998	0.5	(0-1)	
Denmark	846	0.0	(0-0)	1119	0.3	(0-1)	1185	0.3	(0-1)	1109	0.5	(0-1)	>
Netherlands	907	0.1	(0-1)	1131	0.1	(0-0)	1190	0.5	(0-1)	1295	0.5	(0-1)	>[#]
Estonia	56	0.0	(0-6)	168	0.0	(0-2)	143	0.0	(0-3)	179	0.6	(0-3)	
Finland	658	0.0	(0-1)	770	0.3	(0-1)	758	0.3	(0-1)	810	0.6	(0-1)	>
Ireland	389	0.5	(0-2)	453	0.7	(0-2)	478	0.2	(0-1)	482	0.6	(0-2)	
Slovenia	237	1.3	(0-4)	267	0.0	(0-1)	312	0.0	(0-1)	289	0.7	(0-2)	
United Kingdom	962	0.4	(0-1)	4068	0.3	(0-0)	5274	0.6	(0-1)	5592	0.7	(0-1)	>[#]
Austria	1022	0.8	(0-2)	1198	0.7	(0-1)	1109	1.0	(0-2)	1184	1.0	(1-2)	
Belgium	389	0.5	(0-2)	669	2.4	(1-4)	791	1.1	(1-2)	935	1.4	(1-2)	
Croatia	380	2.4	(1-4)	323	0.0	(0-1)	302	0.0	(0-1)	325	2.2	(1-4)	
Slovakia	436	0.9	(0-2)	435	2.5	(1-4)	450	4.4	(3-7)	488	3.5	(2-6)	>
Spain	1483	2.2	(1-3)	1677	2.1	(1-3)	1510	2.8	(2-4)	1995	3.8	(3-5)	>[#]
EU/EEA (population-weighted mean)	**21773**	**6.8**	**(6-7)**	**30127**	**7.4**	**(7-8)**	**32821**	**7.2**	**(7-7)**	**37826**	**7.5**	**(7-8)**	**>**
Poland	660	0.5	(0-1)	1123	2.1	(1-3)	1161	6.4	(5-8)	1183	8.1	(7-10)	>
Portugal	2085	3.4	(3-4)	2340	5.2	(4-6)	2720	8.6	(8-10)	2563	11.7	(10-13)	>
Malta	88	4.5	(1-11)	102	5.9	(2-12)	117	10.3	(5-17)	136	15.4	(10-23)	>
Bulgaria	95	3.2	(1-9)	159	4.4	(2-9)	169	12.4	(8-18)	193	21.2	(16-28)	>
Cyprus	62	12.9	(6-24)	75	10.7	(5-20)	71	15.5	(8-26)	87	21.8	(14-32)	
Italy	1999	33.5	(31-36)	2307	33.9	(32-36)	2634	29.7	(28-31)	5660	26.8	(26-28)	<
Romania	271	24.7	(20-30)	334	31.4	(26-37)	334	22.5	(18-27)	441	29.5	(25-34)	
Greece	1185	61.9	(59-65)	1180	66.9	(64-70)	1363	64.7	(62-67)	1498	63.9	(61-66)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.13. *Klebsiella pneumoniae*. Total number of isolates tested (N) and percentage with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	35	0.0	(0-10)	21	0.0	(0-16)	16	0.0	(0-21)	16	0.0	(0-21)	N/A
Finland	623	1.1	(0-2)	726	1.2	(1-2)	716	2.4	(1-4)	771	1.6	(1-3)	
Denmark	924	1.1	(1-2)	1112	1.4	(1-2)	1122	2.4	(2-3)	1159	1.9	(1-3)	
Sweden	860	1.9	(1-3)	1141	2.1	(1-3)	1033	3.3	(2-5)	1086	2.6	(2-4)	N/A
Austria	936	3.3	(2-5)	1156	3.5	(3-5)	1062	3.0	(2-4)	1203	3.1	(2-4)	
Norway	699	2.3	(1-4)	807	2.6	(2-4)	781	3.2	(2-5)	735	3.8	(3-5)	
Germany	1578	3.2	(2-4)	3038	5.3	(5-6)	3774	6.3	(6-7)	3878	4.7	(4-5)	
Netherlands	908	3.0	(2-4)	1134	3.5	(3-5)	1189	5.0	(4-6)	1295	4.7	(4-6)	>
United Kingdom	906	4.2	(3-6)	3764	3.7	(3-4)	4760	4.2	(4-5)	5005	5.7	(5-6)	>#
Ireland	387	7.2	(5-10)	452	5.8	(4-8)	477	5.9	(4-8)	483	8.1	(6-11)	
Estonia	36	22.2	(10-39)	183	16.9	(12-23)	161	11.8	(7-18)	204	8.8	(5-14)	<
Belgium	353	9.3	(7-13)	637	9.3	(7-12)	633	8.5	(6-11)	742	9.8	(8-12)	
Slovenia	237	16.9	(12-22)	267	13.1	(9-18)	306	16.0	(12-21)	289	10.0	(7-14)	
Luxembourg	60	13.3	(6-25)	78	24.4	(15-35)	99	17.2	(10-26)	85	15.3	(8-25)	
Spain	1488	11.7	(10-13)	1674	12.4	(11-14)	1484	12.8	(11-15)	1926	15.7	(14-17)	>#
EU/EEA (population-weighted mean)	**21930**	**19.7**	**(19-20)**	**29403**	**20.6**	**(20-21)**	**31473**	**20.5**	**(20-21)**	**37137**	**19.6**	**(19-20)**	
France	2324	22.5	(21-24)	2556	21.3	(20-23)	2844	19.4	(18-21)	2948	21.5	(20-23)	
Italy	1940	29.7	(28-32)	2174	32.7	(31-35)	2352	31.6	(30-34)	5587	24.8	(24-26)	<#
Portugal	2084	25.0	(23-27)	2332	27.2	(25-29)	2711	28.4	(27-30)	2538	26.7	(25-28)	
Latvia	112	36.6	(28-46)	91	31.9	(22-42)	115	24.3	(17-33)	199	27.6	(22-34)	
Croatia	380	32.4	(28-37)	309	27.5	(23-33)	305	23.0	(18-28)	312	28.2	(23-34)	
Hungary	698	30.2	(27-34)	711	30.1	(27-34)	685	33.1	(30-37)	837	28.9	(26-32)	
Cyprus	62	17.7	(9-30)	75	18.7	(11-29)	71	25.4	(16-37)	87	32.2	(23-43)	>
Czech Republic	1416	41.5	(39-44)	1384	40.8	(38-43)	1329	41.8	(39-44)	1482	38.7	(36-41)	
Malta	88	14.8	(8-24)	102	14.7	(8-23)	117	28.2	(20-37)	137	43.8	(35-53)	>
Lithuania	178	39.9	(33-47)	323	42.1	(37-48)	322	48.1	(43-54)	368	45.1	(40-50)	
Romania	261	49.8	(44-56)	335	55.2	(50-61)	336	55.4	(50-61)	434	46.3	(42-51)	
Bulgaria	84	28.6	(19-39)	133	45.9	(37-55)	168	50.0	(42-58)	191	47.6	(40-55)	>
Slovakia	468	59.6	(55-64)	465	55.7	(51-60)	457	57.1	(52-62)	491	49.5	(45-54)	<
Greece	1160	46.7	(44-50)	1171	48.4	(46-51)	1345	47.9	(45-51)	1487	50.4	(48-53)	
Poland	645	54.0	(50-58)	1052	53.6	(51-57)	703	52.6	(49-56)	1162	51.5	(49-54)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

3.3 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a non-fermenting gram-negative bacterium which is ubiquitous in aquatic environments in nature. It is an opportunistic pathogen and a major cause of infection in hospitalised patients with localised or systemic impairment of immune defences. It commonly causes healthcare-associated pneumonia (including ventilator-associated pneumonia), bloodstream infections and urinary tract infections.

P. aeruginosa is intrinsically resistant to the majority of antimicrobial agents due to its selective ability to prevent various antibiotic molecules from penetrating its outer membrane or to extrude them if they enter the cell. The antimicrobial groups that remain active include some fluoroquinolones (e.g. ciprofloxacin and levofloxacin), aminoglycosides (e.g. gentamicin, tobramycin and amikacin), some beta-lactams (e. g. piperacillin-tazobactam, ceftazidime, cefepime, ceftolozane-tazobactam, ceftazidime-avibactam, imipenem, meropenem, doripenem) and polymyxins. Resistance of *P. aeruginosa* to these agents can be acquired through one or more of several mechanisms, including modified antimicrobial targets, efflux, and reduced permeability and degrading enzymes.

Antimicrobial resistance

In the EU/EEA, 32.1% of the *P. aeruginosa* isolates reported to EARS-Net for 2018 were resistant to at least one of the antimicrobial groups under regular surveillance (piperacillin ± tazobactam, fluoroquinolones, ceftazidime, aminoglycosides and carbapenems) (Table 3.14). The highest EU/EEA population-weighted mean resistance percentage in 2018 was reported for fluoroquinolones (19.7%), followed by piperacillin ± tazobactam (18.3%), carbapenems (17.2%), ceftazidime (14.1%) and aminoglycosides (11.8%) (Tables 3.15–3.19). There were significant decreasing trends in the EU/EEA population-weighted mean percentages of piperacillin ± tazobactam resistance, ceftazidime resistance, aminoglycoside resistance and carbapenem resistance between 2015 and 2018 (Tables 3.15–3.19). When only considering the laboratories that consistently reported data during all four years, only the decreasing trends for aminoglycoside resistance and carbapenem resistance remained statistically significant (Tables 3.15–3.19).

Resistance to two or more antimicrobial groups was common and seen in 19.2% of all tested isolates. (Table 3.14). 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 between 2015 and 2018 (Table 3.20). Large inter-country variations could be noted for all antimicrobial groups, with generally higher resistance percentages reported from southern and eastern parts of Europe than northern Europe (Figures 3.13–3.18).

Discussion and conclusion

As in previous years, carbapenem resistance, often combined with resistance to other important antimicrobial groups, was common in *P. aeruginosa* in several EU/EEA countries in 2018. The public health implications of resistant *P. aeruginosa* should not be neglected, as the bacterium remains one of the major causes of healthcare-associated infection in Europe [15, 35-36]. *P. aeruginosa* is intrinsically resistant to many important antimicrobial agents and is a challenging pathogen to control in healthcare environments.

P. aeruginosa and *Acinetobacter* species bloodstream infections are proportionally far more commonly reported from some EU/EEA countries than others [27]. A recent analysis based on EARS-Net data highlighted that countries reporting high proportions of *P. aeruginosa* and *Acinetobacter* spp. bloodstream infections among all reported bloodstream infections were also those where the frequency of resistance in gram-negative bacteria generally was the highest [37]. This finding is likely attributed to shared risk factors such as a higher consumption of broad-spectrum antimicrobials [17] and sub-standard infection prevention and control measures in healthcare, including lower consumption of alcohol-based hand rub, lower proportions of beds in single rooms and lower staffing of infection control teams in these countries [15]. Addressing these factors is likely to 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* spp. as well as caused by bacteria with acquired resistance.

Table 3.14. *Pseudomonas aeruginosa.* Total number of tested isolates and resistance combinations among invasive isolates tested against at least three antimicrobial groups among piperacillin ± tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems (n=17 953), EU/EEA countries, 2018

Resistance pattern	Number of isolates	% of total**
Fully susceptible (to tested antibiotics)	**12196**	**67.9**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance types)	**2311**	**12.9**
Fluoroquinolones	894	5.0
Carbapenems	756	4.2
[Piperacillin ± tazobactam]	346	1.9
Aminoglycosides	211	1.2
Ceftazidime	104	0.6
Resistance to two antimicrobial groups		
Total (all two groups combinations)	**1360**	**7.6**
[Piperacillin ± tazobactam] + ceftazidime	571	3.2
Fluoroquinolones + carbapenems	246	1.4
Fluoroquinolones + aminoglycosides	181	1.0
Other antimicrobial group combinations	362	2.0
Resistance to three antimicrobial groups		
Total (all three group combinations)	**739**	**4.1**
[Piperacillin ± tazobactam] + ceftazidime + carbapenems	169	0.9
Other antimicrobial group combinations	570	3.2
Resistance to four antimicrobial groups		
Total (all four group combinations)	**616**	**3.4**
[Piperacillin ± tazobactam] + fluoroquinolones + ceftazidime + carbapenems	235	1.3
[Piperacillin ± tazobactam] + fluoroquinolones + aminoglycosides + carbapenems	139	0.8
Other antimicrobial group combinations	242	1.3
Resistance to five antimicrobial groups		
[Piperacillin ± tazobactam] + fluoroquinolones + ceftazidime + aminoglycosides + carbapenems	**731**	**4.1**

Only resistance combinations >1% of the total are specified.
** Only data from isolates tested against all five antimicrobials groups were included in the analysis.*
*** Not adjusted for population differences in the reporting countries.*

Figure 3.13. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to piperacillin ± tazobactam, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.14. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.15. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to ceftazidime, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.16. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to aminoglycosides, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.17. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to carbapenems, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.18. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with combined resistance (resistance to three or more antimicrobial groups among piperacillin ± tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems), EU/EEA countries, 2018 *Map to be provided by designer*

Table 3.15. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to piperacillin ± tazobactam (%R), including 95% confidence intervals (95%CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	11	0.0	(0-28)	17	0.0	(0-20)	17	0.0	(0-20)	12	0.0	(0-26)	N/A
Denmark	441	4.1	(2-6)	460	3.5	(2-6)	484	2.9	(2-5)	489	2.9	(2-5)	
Norway	227	5.7	(3-10)	215	7.4	(4-12)	183	6.0	(3-11)	227	5.7	(3-10)	
United Kingdom	493	10.3	(8-13)	2039	6.0	(5-7)	2697	5.3	(4-6)	2631	5.8	(5-7)	<
Finland	333	7.2	(5-11)	351	9.4	(7-13)	377	6.4	(4-9)	391	6.6	(4-10)	
Netherlands	494	6.5	(4-9)	520	4.0	(3-6)	620	7.1	(5-9)	628	6.7	(5-9)	
Sweden	399	5.8	(4-9)	472	7.4	(5-10)	446	6.3	(4-9)	411	7.8	(5-11)	N/A
Ireland	195	9.2	(6-14)	243	12.8	(9-18)	286	14.0	(10-19)	270	8.1	(5-12)	
Estonia	16	6.3	(0-30)	53	17.0	(8-30)	55	14.5	(6-27)	48	8.3	(2-20)	N/A
Belgium	251	8.0	(5-12)	318	9.7	(7-14)	439	10.5	(8-14)	430	10.0	(7-13)	
Spain	871	9.1	(7-11)	817	9.4	(8-12)	814	8.4	(7-10)	1077	10.9	(9-13)	
Croatia	249	24.5	(19-30)	252	18.7	(14-24)	234	16.2	(12-22)	196	11.2	(7-16)	<
Luxembourg	27	0.0	(0-13)	40	12.5	(4-27)	54	11.1	(4-23)	56	12.5	(5-24)	
Germany	972	17.5	(15-20)	1423	17.2	(15-19)	1895	15.5	(14-17)	1742	13.5	(12-15)	<
Austria	675	11.9	(10-15)	689	13.8	(11-17)	721	13.5	(11-16)	729	13.6	(11-16)	
Slovenia	141	9.9	(6-16)	143	19.6	(13-27)	138	13.0	(8-20)	174	16.1	(11-22)	
Malta	25	16.0	(5-36)	40	12.5	(4-27)	37	21.6	(10-38)	29	17.2	(6-36)	
Lithuania	41	29.3	(16-46)	74	13.5	(7-23)	89	18.0	(11-28)	101	17.8	(11-27)	
EU/EEA (population-weighted mean)	**12569**	**19.9**	**(19-21)**	**15152**	**18.8**	**(18-19)**	**16580**	**18.2**	**(18-19)**	**18678**	**18.3**	**(18-19)**	**<#**
France	1915	16.1	(15-18)	1958	17.4	(16-19)	1690	19.2	(17-21)	1897	21.5	(20-23)	>
Portugal	1176	24.5	(22-27)	1230	22.7	(20-25)	1206	24.2	(22-27)	1096	21.9	(19-24)	
Czech Republic	463	25.3	(21-29)	458	25.3	(21-30)	409	23.0	(19-27)	537	23.3	(20-27)	
Cyprus	43	4.7	(1-16)	64	12.5	(6-23)	53	17.0	(8-30)	55	23.6	(13-37)	>
Italy	1074	29.5	(27-32)	1147	30.7	(28-33)	1312	24.2	(22-27)	2938	23.9	(22-26)	<
Greece	638	22.3	(19-26)	692	28.3	(25-32)	813	29.6	(27-33)	844	24.3	(21-27)	
Hungary	747	26.9	(24-30)	720	23.6	(21-27)	721	24.3	(21-28)	791	24.3	(21-27)	
Bulgaria	55	27.3	(16-41)	55	40.0	(27-54)	69	33.3	(22-46)	89	32.6	(23-43)	
Latvia	13	23.1	(5-54)	15	26.7	(8-55)	14	35.7	(13-65)	39	35.9	(21-53)	N/A
Slovakia	257	42.4	(36-49)	168	36.9	(30-45)	187	42.8	(36-50)	236	36.9	(31-43)	
Poland	249	37.8	(32-44)	393	30.0	(26-35)	389	32.1	(28-37)	377	36.9	(32-42)	
Romania	78	59.0	(47-70)	86	48.8	(38-60)	131	53.4	(45-62)	138	49.3	(41-58)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

*** Less than 10 isolates reported, no percentage calculated.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.16. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Malta	25	12.0	(3-31)	40	10.0	(3-24)	37	10.8	(3-25)	29	0.0	(0-12)	
Denmark	420	5.0	(3-8)	460	3.7	(2-6)	484	5.0	(3-7)	489	4.3	(3-6)	
Sweden	382	4.7	(3-7)	469	6.0	(4-9)	445	9.0	(6-12)	408	7.1	(5-10)	N/A
Iceland	12	8.3	(0-38)	17	17.6	(4-43)	17	11.8	(1-36)	12	8.3	(0-38)	N/A
Ireland	194	9.8	(6-15)	243	11.9	(8-17)	287	13.9	(10-18)	272	8.8	(6-13)	
Netherlands	502	5.8	(4-8)	543	6.1	(4-8)	657	9.9	(8-12)	670	9.4	(7-12)	>
United Kingdom	522	8.8	(7-12)	2119	6.9	(6-8)	2802	7.7	(7-9)	2739	9.8	(9-11)	>\#
Norway	230	5.2	(3-9)	227	5.7	(3-10)	205	4.9	(2-9)	250	10.4	(7-15)	>
Germany	970	14.3	(12-17)	1423	12.4	(11-14)	1895	13.9	(12-16)	1739	12.3	(11-14)	
Finland	302	8.9	(6-13)	292	7.9	(5-12)	356	11.2	(8-15)	376	12.8	(10-17)	>\#
Lithuania	41	26.8	(14-43)	73	15.1	(8-25)	89	21.3	(13-31)	101	12.9	(7-21)	
Estonia	18	0.0	(0-19)	56	3.6	(0-12)	56	12.5	(5-24)	45	13.3	(5-27)	N/A
Belgium	261	11.1	(8-16)	366	14.5	(11-19)	430	10.5	(8-14)	451	14.0	(11-18)	
Austria	659	10.3	(8-13)	694	7.2	(5-9)	721	12.3	(10-15)	736	14.0	(12-17)	>
France	1939	19.1	(17-21)	1971	13.6	(12-15)	1709	15.1	(13-17)	1893	15.1	(13-17)	<
EU/EEA (population-weighted mean)	**12681**	**20.9**	**(20-22)**	**15388**	**18.8**	**(18-19)**	**16870**	**20.2**	**(20-21)**	**19023**	**19.7**	**(19-20)**	
Spain	881	23.0	(20-26)	843	23.0	(20-26)	868	19.9	(17-23)	1102	20.1	(18-23)	<
Slovenia	141	14.2	(9-21)	143	20.3	(14-28)	123	20.3	(14-29)	174	21.8	(16-29)	
Luxembourg	28	17.9	(6-37)	40	12.5	(4-27)	56	12.5	(5-24)	59	22.0	(12-35)	
Italy	1080	24.6	(22-27)	1166	24.7	(22-27)	1390	25.1	(23-27)	2994	22.9	(21-24)	
Latvia	13	23.1	(5-54)	16	31.3	(11-59)	14	64.3	(35-87)	39	23.1	(11-39)	N/A
Portugal	1185	22.7	(20-25)	1227	20.1	(18-22)	1208	23.7	(21-26)	1104	23.7	(21-26)	
Cyprus	43	11.6	(4-25)	64	20.3	(11-32)	53	5.7	(1-16)	55	25.5	(15-39)	
Hungary	769	24.7	(22-28)	736	24.3	(21-28)	732	23.4	(20-27)	805	26.0	(23-29)	
Croatia	256	35.2	(29-41)	259	37.5	(32-44)	237	32.9	(27-39)	200	29.0	(23-36)	
Bulgaria	55	36.4	(24-50)	56	35.7	(23-50)	71	28.2	(18-40)	90	30.0	(21-41)	
Greece	662	34.1	(31-38)	702	34.6	(31-38)	816	35.3	(32-39)	856	33.1	(30-36)	
Czech Republic	464	30.0	(26-34)	464	34.7	(30-39)	411	30.2	(26-35)	539	33.4	(29-38)	
Poland	257	36.2	(30-42)	400	31.0	(26-36)	358	37.2	(32-42)	389	39.1	(34-44)	
Romania	92	62.0	(51-72)	89	51.7	(41-62)	132	62.1	(53-70)	155	52.3	(44-60)	
Slovakia	278	52.2	(46-58)	190	47.4	(40-55)	211	46.9	(40-54)	252	52.4	(46-59)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.17. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to ceftazidime (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	11	0.0	(0-28)	17	0.0	(0-20)	17	0.0	(0-20)	12	0.0	(0-26)	N/A
Netherlands	502	4.4	(3-7)	543	3.3	(2-5)	657	3.5	(2-5)	667	2.8	(2-4)	
Denmark	439	3.6	(2-6)	447	4.5	(3-7)	461	3.5	(2-6)	458	3.3	(2-5)	
Estonia	7	-	-	(-)	17.6	(4-43)	47	8.5	(2-20)	47	4.3	(1-15)	N/A
Finland	334	6.9	(4-10)	352	5.4	(3-8)	378	6.1	(4-9)	390	4.4	(3-7)	
United Kingdom	472	6.1	(4-9)	2021	4.3	(3-5)	2680	4.7	(4-6)	2621	4.9	(4-6)	
Sweden	379	4.5	(3-7)	473	7.4	(5-10)	446	4.5	(3-7)	412	6.1	(4-9)	N/A
Norway	216	5.6	(3-10)	224	7.1	(4-11)	197	5.1	(2-9)	240	6.3	(4-10)	
Belgium	226	6.2	(3-10)	320	7.8	(5-11)	431	7.2	(5-10)	441	7.5	(5-10)	
Ireland	195	7.2	(4-12)	243	10.7	(7-15)	272	9.6	(6-14)	261	8.4	(5-12)	
Luxembourg	28	7.1	(1-24)	40	5.0	(1-17)	56	12.5	(5-24)	59	8.5	(3-19)	
Spain	816	10.4	(8-13)	836	10.2	(8-12)	862	9.6	(8-12)	1087	8.7	(7-11)	
Germany	968	8.9	(7-11)	1421	10.1	(9-12)	1883	9.8	(9-11)	1735	9.1	(8-11)	
Austria	577	9.9	(8-13)	628	11.3	(9-14)	620	8.7	(7-11)	729	10.3	(8-13)	
Lithuania	41	19.5	(9-35)	74	10.8	(5-20)	88	14.8	(8-24)	101	11.9	(6-20)	
France	1919	11.6	(10-13)	1956	11.3	(10-13)	1568	12.2	(11-14)	1892	13.0	(12-15)	
Malta	25	8.0	(1-26)	40	7.5	(2-20)	37	13.5	(5-29)	29	13.8	(4-32)	
EU/EEA (population-weighted mean)	**12376**	**15.4**	**(15-16)**	**15102**	**14.4**	**(14-15)**	**16431**	**14.7**	**(14-15)**	**18773**	**14.1**	**(14-15)**	**<#**
Slovenia	141	9.9	(6-16)	143	17.5	(12-25)	138	13.0	(8-20)	174	14.9	(10-21)	
Cyprus	43	4.7	(1-16)	64	10.9	(5-21)	53	13.2	(5-25)	55	16.4	(8-29)	
Croatia	248	18.5	(14-24)	240	20.8	(16-27)	231	19.5	(15-25)	195	17.9	(13-24)	
Portugal	1185	19.2	(17-22)	1228	18.0	(16-20)	1216	18.6	(16-21)	1090	18.6	(16-21)	
Italy	1068	21.7	(19-24)	1160	23.0	(21-26)	1332	20.0	(18-22)	2974	19.9	(18-21)	
Bulgaria	52	26.9	(16-41)	54	38.9	(26-53)	71	38.0	(27-50)	90	20.0	(12-30)	
Czech Republic	464	19.6	(16-24)	464	19.2	(16-23)	411	13.4	(10-17)	539	20.4	(17-24)	
Greece	660	19.4	(16-23)	696	33.6	(30-37)	814	24.9	(22-28)	853	22.3	(20-25)	
Hungary	763	24.2	(21-27)	735	20.7	(18-24)	729	23.9	(21-27)	804	22.5	(20-26)	
Poland	259	27.8	(22-34)	401	19.5	(16-24)	415	24.6	(21-29)	390	26.9	(23-32)	
Slovakia	247	34.8	(29-41)	164	31.1	(24-39)	180	35.6	(29-43)	237	32.1	(26-38)	
Latvia	13	23.1	(5-54)	15	26.7	(8-55)	14	42.9	(18-71)	39	33.3	(19-50)	N/A
Romania	85	65.9	(55-76)	86	44.2	(33-55)	127	55.9	(47-65)	152	46.7	(39-55)	<#

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.18. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Malta	25	16.0	(5-36)	40	7.5	(2-20)	37	10.8	(3-25)	29	0.0	(0-12)	
Iceland	12	0.0	(0-26)	17	0.0	(0-20)	17	0.0	(0-20)	12	0.0	(0-26)	N/A
Denmark	441	2.3	(1-4)	460	1.7	(1-3)	484	1.0	(0-2)	489	0.6	(0-2)	<
Norway	219	0.9	(0-3)	213	0.9	(0-3)	183	0.5	(0-3)	236	0.8	(0-3)	
Finland	341	1.8	(1-4)	352	2.3	(1-4)	378	1.9	(1-4)	391	1.0	(0-3)	
Sweden	387	1.3	(0-3)	471	0.8	(0-2)	444	0.9	(0-2)	411	1.0	(0-2)	N/A
Netherlands	502	2.8	(2-5)	541	2.8	(2-5)	657	4.0	(3-6)	670	2.4	(1-4)	
Germany	966	7.1	(6-9)	1421	6.8	(6-8)	1869	4.8	(4-6)	1739	3.6	(3-5)	<
Luxembourg	28	3.6	(0-18)	40	15.0	(6-30)	56	5.4	(1-15)	53	3.8	(0-13)	
Estonia	17	5.9	(0-29)	54	7.4	(2-18)	56	5.4	(1-15)	48	4.2	(1-14)	N/A
United Kingdom	539	5.2	(3-7)	2140	3.6	(3-4)	2831	3.9	(3-5)	2781	4.5	(4-5)	
Ireland	195	4.1	(2-8)	243	10.3	(7-15)	288	8.7	(6-13)	273	5.5	(3-9)	
Austria	678	6.3	(5-8)	692	6.1	(4-8)	717	5.0	(4-7)	729	6.3	(5-8)	
Slovenia	141	9.2	(5-15)	143	13.3	(8-20)	138	8.7	(5-15)	174	6.9	(4-12)	
Cyprus	43	0.0	(0-8)	64	4.7	(1-13)	53	1.9	(0-10)	55	7.3	(2-18)	
Belgium	218	6.0	(3-10)	327	11.0	(8-15)	377	7.7	(5-11)	406	8.4	(6-12)	
France	1950	14.1	(13-16)	1976	10.7	(9-12)	1713	10.9	(9-12)	1898	9.3	(8-11)	<
Lithuania	41	24.4	(12-40)	74	14.9	(8-25)	89	13.5	(7-22)	101	9.9	(5-17)	<#
Spain	883	16.4	(14-19)	843	15.3	(13-18)	864	12.4	(10-15)	1121	11.6	(10-14)	<
EU/EEA (population-weighted mean)	**12703**	**15.3**	**(15-16)**	**15408**	**14.1**	**(14-15)**	**16898**	**13.2**	**(13-14)**	**18999**	**11.8**	**(11-12)**	**<**
Portugal	1191	13.5	(12-16)	1230	11.6	(10-14)	1210	12.1	(10-14)	1109	11.9	(10-14)	
Italy	1050	17.2	(15-20)	1203	19.1	(17-21)	1428	18.0	(16-20)	2983	12.8	(12-14)	<
Hungary	766	20.5	(18-24)	740	17.6	(15-21)	734	14.6	(12-17)	784	17.9	(15-21)	
Czech Republic	464	21.3	(18-25)	464	18.8	(15-23)	411	14.4	(11-18)	539	19.3	(16-23)	
Croatia	256	34.0	(28-40)	260	33.5	(28-40)	237	26.6	(21-33)	199	21.6	(16-28)	<
Bulgaria	47	27.7	(16-43)	39	48.7	(32-65)	71	28.2	(18-40)	90	24.4	(16-35)	
Poland	258	30.6	(25-37)	367	25.6	(21-30)	384	25.5	(21-30)	384	26.0	(22-31)	
Greece	667	26.4	(23-30)	701	28.0	(25-31)	815	30.2	(27-33)	856	26.5	(24-30)	
Latvia	11	9.1	(0-41)	15	20.0	(4-48)	14	42.9	(18-71)	39	28.2	(15-45)	N/A
Slovakia	277	41.9	(36-48)	191	33.0	(26-40)	211	36.0	(30-43)	254	37.4	(31-44)	
Romania	90	63.3	(53-73)	87	50.6	(40-61)	132	57.6	(49-66)	146	50.7	(42-59)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.19. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	12	0.0	(0-26)	17	5.9	(0-29)	17	0.0	(0-20)	12	0.0	(0-26)	N/A
Malta	25	16.0	(5-36)	40	12.5	(4-27)	37	10.8	(3-25)	29	3.4	(0-18)	
Sweden	398	6.5	(4-9)	472	11.0	(8-14)	446	9.0	(6-12)	412	4.4	(3-7)	N/A
Norway	228	5.7	(3-10)	225	6.7	(4-11)	205	3.4	(1-7)	250	4.8	(3-8)	
Finland	341	4.7	(3-8)	352	6.0	(4-9)	377	6.1	(4-9)	391	4.9	(3-7)	
Netherlands	500	4.0	(2-6)	543	3.7	(2-6)	655	4.4	(3-6)	667	5.1	(4-7)	
Denmark	437	4.6	(3-7)	458	2.4	(1-4)	484	2.5	(1-4)	422	5.2	(3-8)	
United Kingdom	499	2.4	(1-4)	2108	5.1	(4-6)	2804	5.7	(5-7)	2748	6.0	(5-7)	>
Ireland	195	9.2	(6-14)	243	6.2	(3-10)	288	9.0	(6-13)	273	6.6	(4-10)	
Belgium	256	3.9	(2-7)	365	9.6	(7-13)	474	8.2	(6-11)	487	7.4	(5-10)	
Luxembourg	24	8.3	(1-27)	31	6.5	(1-21)	56	10.7	(4-22)	54	11.1	(4-23)	
Germany	971	14.7	(13-17)	1422	14.5	(13-16)	1892	12.6	(11-14)	1740	12.1	(11-14)	<
Cyprus	43	20.9	(10-36)	64	18.8	(10-30)	53	17.0	(8-30)	55	12.7	(5-24)	
Austria	680	12.2	(10-15)	696	12.9	(11-16)	725	13.9	(11-17)	736	12.8	(10-15)	
Slovenia	141	15.6	(10-23)	143	19.6	(13-27)	138	17.4	(11-25)	174	14.9	(10-21)	
Portugal	1191	19.8	(18-22)	1227	19.2	(17-21)	1215	18.3	(16-21)	1108	15.7	(14-18)	<
Italy	1082	23.0	(21-26)	1206	23.5	(21-26)	1434	19.9	(18-22)	3014	15.8	(15-17)	<
France	1925	16.4	(15-18)	1968	15.6	(14-17)	1710	13.9	(12-16)	1896	16.0	(14-18)	
Estonia	16	12.5	(2-38)	54	20.4	(11-34)	55	9.1	(3-20)	48	16.7	(7-30)	N/A
EU/EEA (population-weighted mean)	**12719**	**19.4**	**(19-20)**	**15456**	**18.2**	**(18-19)**	**17029**	**17.4**	**(17-18)**	**19045**	**17.2**	**(17-18)**	**<**
Czech Republic	464	10.6	(8-14)	464	8.8	(6-12)	411	14.8	(12-19)	539	18.0	(15-22)	>
Spain	872	22.7	(20-26)	842	21.4	(19-24)	861	18.4	(16-21)	1120	18.6	(16-21)	<
Lithuania	41	26.8	(14-43)	74	16.2	(9-27)	89	24.7	(16-35)	101	21.8	(14-31)	
Bulgaria	55	25.5	(15-39)	56	30.4	(19-44)	71	25.4	(16-37)	90	25.6	(17-36)	
Croatia	257	38.5	(33-45)	260	42.3	(36-49)	238	30.7	(25-37)	199	27.6	(22-34)	<
Latvia	13	15.4	(2-45)	16	31.3	(11-59)	14	57.1	(29-82)	39	28.2	(15-45)	N/A
Poland	254	37.0	(31-43)	397	26.2	(22-31)	393	24.2	(20-29)	374	33.2	(28-38)	
Hungary	770	35.8	(32-39)	739	33.3	(30-37)	733	36.6	(33-40)	807	37.3	(34-41)	
Greece	675	40.4	(37-44)	699	42.1	(38-46)	821	39.3	(36-43)	856	37.5	(34-41)	
Slovakia	262	51.9	(46-58)	182	42.3	(35-50)	202	47.0	(40-54)	248	44.0	(38-50)	
Romania	92	66.3	(56-76)	93	51.6	(41-62)	131	63.4	(54-72)	156	55.1	(47-63)	

** The symbols > and < indicate significant increasing and decreasing trends, respectively.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.20. *Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) with combined resistance (resistance to three or more antimicrobial groups among piperacillin ± tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems) including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	12	0.0	(0-26)	17	0.0	(0-20)	17	0.0	(0-20)	12	0.0	(0-26)	N/A
Denmark	441	2.3	(1-4)	460	1.3	(0-3)	484	0.4	(0-1)	489	1.2	(0-3)	
Finland	341	4.7	(3-8)	352	3.4	(2-6)	378	3.4	(2-6)	391	1.8	(1-4)	<
Sweden	386	2.6	(1-5)	472	5.3	(3-8)	446	3.1	(2-5)	412	1.9	(1-4)	N/A
Netherlands	502	2.8	(2-5)	543	2.6	(1-4)	657	2.1	(1-4)	670	2.1	(1-3)	
Norway	230	1.3	(0-4)	227	2.6	(1-6)	205	1.5	(0-4)	250	2.4	(1-5)	
United Kingdom	501	3.8	(2-6)	2131	2.5	(2-3)	2830	2.4	(2-3)	2771	3.0	(2-4)	
Ireland	195	5.1	(2-9)	243	8.6	(5-13)	288	7.6	(5-11)	273	3.3	(2-6)	
Malta	25	12.0	(3-31)	40	5.0	(1-17)	37	8.1	(2-22)	29	3.4	(0-18)	
Luxembourg	28	3.6	(0-18)	40	2.5	(0-13)	56	5.4	(1-15)	59	3.4	(0-12)	
Belgium	260	4.6	(2-8)	366	6.3	(4-9)	439	6.6	(4-9)	454	5.3	(3-8)	
Germany	971	7.9	(6-10)	1423	7.6	(6-9)	1895	7.0	(6-8)	1740	6.0	(5-7)	<#
Estonia	15	0.0	(0-22)	56	3.6	(0-12)	57	8.8	(3-19)	48	6.3	(1-17)	N/A
Austria	680	6.8	(5-9)	697	6.7	(5-9)	724	7.0	(5-9)	737	7.2	(5-9)	
Spain	874	14.2	(12-17)	843	14.5	(12-17)	863	10.9	(9-13)	1120	10.9	(9-13)	<
France	1940	12.0	(11-14)	1972	10.7	(9-12)	1709	10.6	(9-12)	1894	11.0	(10-12)	
Slovenia	141	7.1	(3-13)	143	15.4	(10-22)	138	10.9	(6-17)	174	11.5	(7-17)	
Lithuania	41	24.4	(12-40)	74	10.8	(5-20)	89	16.9	(10-26)	101	11.9	(6-20)	
EU/EEA (population-weighted mean)	**12741**	**15.1**	**(14-16)**	**15513**	**13.6**	**(13-14)**	**17051**	**13.3**	**(13-14)**	**19119**	**12.8**	**(12-13)**	**<**
Italy	1082	20.0	(18-22)	1206	20.1	(18-23)	1436	17.5	(16-20)	3006	14.9	(14-16)	<
Portugal	1186	16.9	(15-19)	1230	14.8	(13-17)	1214	16.1	(14-18)	1108	15.3	(13-18)	
Cyprus	43	2.3	(0-12)	64	4.7	(1-13)	53	9.4	(3-21)	55	16.4	(8-29)	>
Croatia	257	28.0	(23-34)	260	31.9	(26-38)	238	21.4	(16-27)	200	19.0	(14-25)	<
Hungary	770	20.9	(18-24)	740.0	19.1	(16-22)	735.0	18.1	(15-21)	807.0	20.2	(17-23)	
Czech Republic	464	19.0	(15-23)	464	19.6	(16-24)	411	17.3	(14-21)	539	21.9	(18-26)	
Bulgaria	55	29.1	(18-43)	56	35.7	(23-50)	71	26.8	(17-39)	90	25.6	(17-36)	
Greece	666	28.4	(25-32)	702	31.6	(28-35)	816	32.4	(29-36)	855	28.7	(26-32)	
Poland	260	29.6	(24-36)	403	20.6	(17-25)	417	22.8	(19-27)	394	29.4	(25-34)	
Latvia	13	15.4	(2-45)	16	18.8	(4-46)	14	42.9	(18-71)	39	30.8	(17-48)	N/A
Slovakia	270	40.7	(35-47)	183	33.9	(27-41)	202	39.1	(32-46)	248	35.9	(30-42)	
Romania	92	63.0	(52-73)	90	48.9	(38-60)	132	59.1	(50-68)	154	49.4	(41-58)	

* *The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

3.4 *Acinetobacter* species

The *Acinetobacter* genus consists of a large number of species which can be divided into two complexes: the *Acinetobacter baumannii* complex – the group including most of the disease-causing species (*A. baumannii*, *A. pittii* and *A. nosocomialis*) – and the generally less pathogenic *Acinetobacter* non-*baumannii* group. The correct identification of *Acinetobacter* isolates at species level is difficult, although possible with mass spectrometry and genotypic methods.

Species belonging to the *Acinetobacter baumannii* group are opportunistic pathogens primarily associated with healthcare-associated infections including ventilator-associated pneumonia, central-line-associated bloodstream infections, urinary tract infections and wound infections. Risk factors for infection include advanced age, presence of serious underlying disease, immune suppression, major trauma or burn injuries, invasive procedures, presence of indwelling catheters, mechanical ventilation, extended hospital stay and previous administration of antibiotics.

Acinetobacter species, particularly those belonging to the *A. baumannii*-complex, are intrinsically resistant to most antimicrobial agents due to their selective ability to prevent various molecules from penetrating their outer membrane. The antimicrobial groups that remain active include some fluoroquinolones (e.g. ciprofloxacin and levofloxacin), aminoglycosides (e.g. gentamicin, tobramycin and amikacin), carbapenems (imipenem and meropenem), polymyxins (colistin and polymyxin B) and, possibly, sulbactam and tigecycline. Acquired resistance results from mutational changes in the chromosome and acquisition of plasmid-mediated resistance genes.

Antimicrobial resistance

More than half of the *Acinetobacter* spp. isolates reported by EU/EEA countries to EARS-Net for 2018 (56.4%) were resistant to at least one of the antimicrobial groups under regular surveillance, i.e. fluoroquinolones, aminoglycosides and carbapenems (Table 3.21). The highest EU/EEA population-weighted mean resistance percentage in 2018 was reported for fluoroquinolones (36.2%), followed by aminoglycosides (31.9%) and carbapenems (31.9%) (Tables 3.22–3.24).

There was a significant decreasing trend in the EU/EEA population-weighted mean percentage of fluoroquinolone resistance; however, the trend did not remain statistically significant when only considering the laboratories that consistently reported data during all four years (Table 3.22).

Resistance to one or two antimicrobial groups was considerably less common than combined resistance to all three groups under surveillance (Table 3.21). In 2018, the population-weighted EU/EEA mean percentage for combined resistance to fluoroquinolones, aminoglycosides and carbapenems was 28.8% (Table 3.25). Large inter-country variations were noted for all antimicrobial groups under regular surveillance, with generally higher resistance percentages reported from southern and eastern Europe than from northern Europe (Figures 3.20–3.23). Single resistance to one antimicrobial group was less common in countries reporting comparatively low proportions of fully susceptible isolates (Figure 3.19).

Discussion and conclusion

Acinetobacter spp. is the microorganism under surveillance by EARS-Net were the inter-country variation in resistance percentages is the most extreme. In 2018, the percentage isolates resistant to any antimicrobial group under regular surveillance (fluoroquinolones, aminoglycosides or carbapenems) ranged between 0% and 95% 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 as the most frequently reported resistance phenotype was combined resistance to all three antimicrobial groups under regular surveillance, severely limiting options for patient treatment. As *Acinetobacter spp.* is intrinsically resistant to many antimicrobial agents, additional acquired resistance is further complicating treatment of serious infections in already vulnerable patient groups.

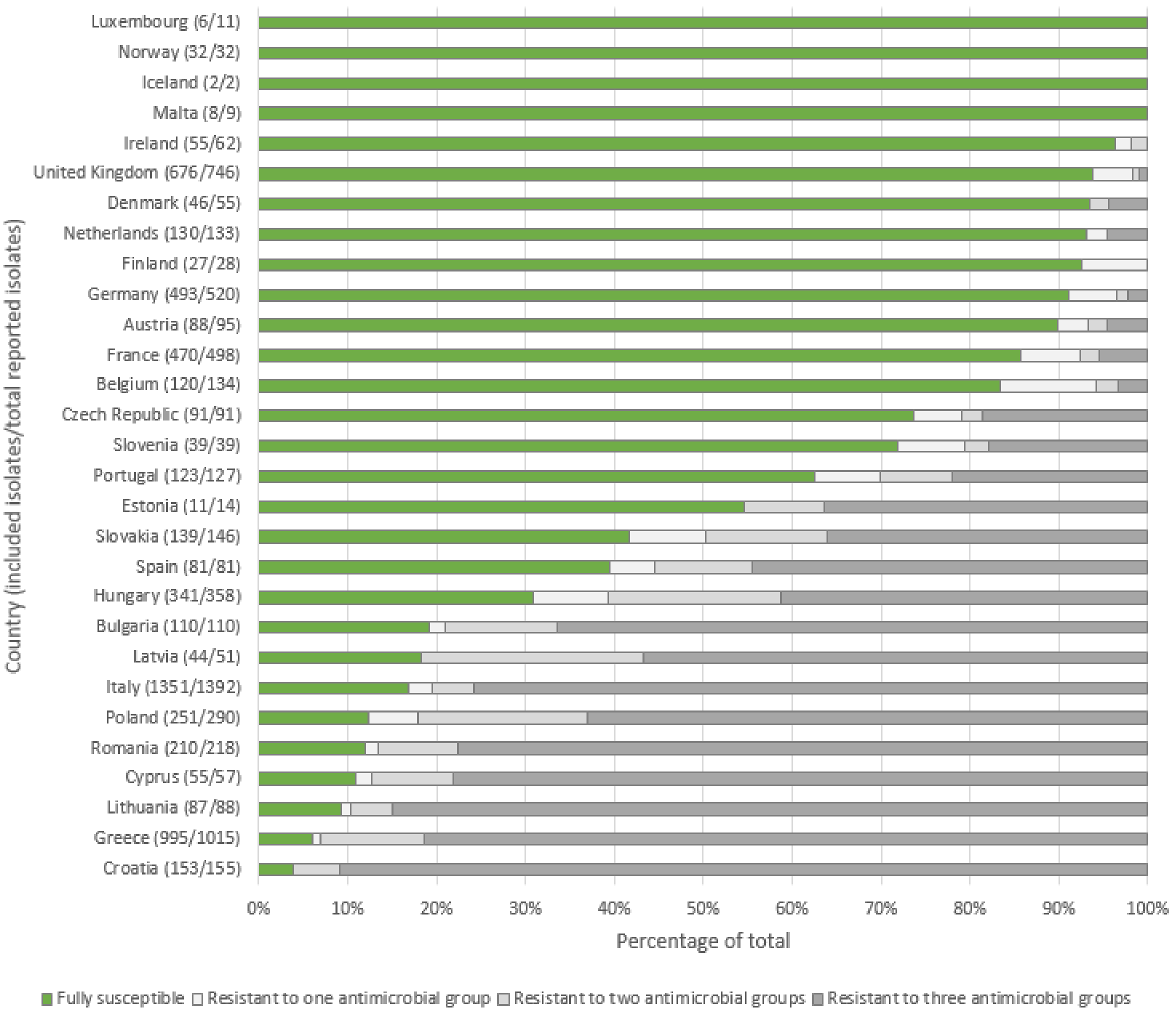
The presence of multidrug-resistant *Acinetobacter* spp. in the healthcare environment is problematic: the bacterium can persist in the environment for long periods and is notoriously difficult to eradicate once established. ECDC's risk assessment on carbapenem-resistant *Acinetobacter baumannii* in healthcare highlights the need of 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 of preparedness of EU/EEA countries. Options for response presented in the risk assessment included timely laboratory reporting, screening and pre-emptive isolation of high-risk patients, high-standard infection control and antimicrobial stewardship programmes [38].

Table 3.21. *Acinetobacter* spp. Overall resistance and resistance combinations among invasive isolates tested to fluoroquinolones, aminoglycosides and carbapenems (n= 6234), EU/EEA countries, 2018

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**2721**	**43.6**
Single resistance (to indicated antimicrobial group)		
Total (any single resistance)	**238**	**3.8**
Fluoroquinolones	134	2.1
Aminoglycosides	67	1.1
Carbapenems	37	0.6
Resistance to two antimicrobial groups		
Total (any two-group combinations)	**427**	**6.8**
Fluoroquinolones + carbapenems	318	5.1
Fluoroquinolones + aminoglycosides	104	1.7
Aminoglycosides + carbapenems	5	0.1
Resistance to three antimicrobial groups		
Fluoroquinolones + aminoglycosides + carbapenems	**2848**	**45.7**

** Only data from isolates tested against all five antimicrobials groups were included in the analysis.*
*** Not adjusted for population differences in the reporting countries.*

Figure 3.19. *Acinetobacter* spp. Distribution of isolates: fully susceptible and resistant to one, two and three antimicrobial groups (among isolates tested against fluoroquinolone, aminoglycoside and carbapenems)*, EU/EEA countries, 2018



** Only data from isolates tested against all included antimicrobial groups (fluoroquinolone, aminoglycoside and carbapenems) were included in the analysis.*

Figure 3.20. *Acinetobacter* spp. Percentage (%) of invasive isolates with resistance to fluoroquinolones, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.21. *Acinetobacter* spp. Percentage (%) of invasive isolates with resistance to aminoglycosides, EU/EEA countries, 2018 Map to be provided by designer

Figure 3.22. *Acinetobacter* spp. Percentage (%) of invasive isolates with resistance to carbapenems, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.23. *Acinetobacter* spp. Percentage (%) of invasive isolates with combined resistance to fluoroquinolones, aminoglycosides and carbapenems, EU/EEA countries, 2018 Map to be provided by designer

Table 3.22. *Acinetobacter* spp. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Norway	32	9.4	(2-25)	33	3.0	(0-16)	31	0.0	(0-11)	32	0.0	(0-11)	<
Ireland	83	4.8	(1-12)	68	1.5	(0-8)	66	7.6	(3-17)	61	0.0	(0-6)	
Finland	43	2.3	(0-12)	28	0.0	(0-12)	37	2.7	(0-14)	28	0.0	(0-12)	
Luxembourg	8	**	(**)	8	**	(**)	8	**	(**)	11	0.0	(0-28)	N/A
United Kingdom	139	7.2	(4-13)	589	4.4	(3-6)	793	6.3	(5-8)	720	2.9	(2-4)	
Germany	339	8.6	(6-12)	460	5.7	(4-8)	536	6.5	(5-9)	511	6.8	(5-9)	
Sweden	26	3.8	(0-20)	86	4.7	(1-11)	54	0.0	(0-7)	55	7.3	(2-18)	N/A
Austria	61	16.4	(8-28)	81	16.0	(9-26)	74	9.5	(4-19)	91	7.7	(3-15)	<
Netherlands	74	6.8	(2-15)	106	2.8	(1-8)	122	3.3	(1-8)	133	8.3	(4-14)	
Denmark	68	5.9	(2-14)	72	2.8	(0-10)	68	1.5	(0-8)	55	9.1	(3-20)	
France	430	13.5	(10-17)	452	15.0	(12-19)	473	12.3	(9-16)	491	12.0	(9-15)	
Belgium	26	0.0	(0-13)	78	7.7	(3-16)	130	10.8	(6-17)	134	12.7	(8-20)	>\#
Czech Republic	60	18.3	(10-30)	57	17.5	(9-30)	55	20.0	(10-33)	91	24.2	(16-34)	
Slovenia	31	58.1	(39-75)	60	55.0	(42-68)	36	47.2	(30-65)	39	28.2	(15-45)	<
Portugal	308	55.8	(50-61)	206	50.5	(43-58)	172	38.4	(31-46)	123	34.1	(26-43)	<
EU/EEA (population-weighted mean)	**5010**	**38.6**	**(37-40)**	**5568**	**37.5**	**(36-39)**	**6088**	**37.4**	**(36-39)**	**6471**	**36.2**	**(35-37)**	**<#**
Estonia	4	**	(**)	5	**	(**)	11	36.4	(11-69)	11	45.5	(17-77)	N/A
Slovakia	154	51.9	(44-60)	115	46.1	(37-56)	126	52.4	(43-61)	141	56.0	(47-64)	
Spain	95	64.2	(54-74)	106	68.9	(59-78)	92	68.5	(58-78)	81	56.8	(45-68)	
Hungary	464	68.1	(64-72)	397	68.0	(63-73)	352	67.0	(62-72)	356	66.0	(61-71)	
Bulgaria	131	78.6	(71-85)	106	67.9	(58-77)	92	95.7	(89-99)	110	78.2	(69-85)	
Latvia	60	78.3	(66-88)	68	85.3	(75-93)	33	81.8	(65-93)	47	80.9	(67-91)	
Italy	664	81.6	(78-85)	697	79.9	(77-83)	804	79.2	(76-82)	1368	81.1	(79-83)	
Poland	243	88.1	(83-92)	393	83.0	(79-87)	348	83.0	(79-87)	268	86.9	(82-91)	
Romania	189	82.5	(76-88)	157	91.1	(85-95)	183	89.1	(84-93)	218	88.1	(83-92)	
Cyprus	60	83.3	(71-92)	28	71.4	(51-87)	50	76.0	(62-87)	55	89.1	(78-96)	
Lithuania	73	93.2	(85-98)	87	87.4	(79-94)	86	91.9	(84-97)	88	90.9	(83-96)	
Greece	946	94.9	(93-96)	862	94.9	(93-96)	1060	96.0	(95-97)	998	93.5	(92-95)	
Croatia	196	92.3	(88-96)	176	94.9	(91-98)	204	98.0	(95-99)	155	96.1	(92-99)	>
Malta	15	13.3	(2-40)	7	**	(**)	9	**	(**)	9	**	(**)	N/A
Iceland	6	**	(**)	3	**	(**)	6	**	(**)	2	**	(**)	N/A

* *The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

*** Less than 10 isolates reported, no percentage calculated.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.23. *Acinetobacter* spp. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Luxembourg	8	**	(**)	8	**	(**)	8	**	(**)	11	0.0	(0-28)	N/A
Norway	32	9.4	(2-25)	32	3.1	(0-16)	31	0.0	(0-11)	32	0.0	(0-11)	<
Germany	331	5.4	(3-8)	436	3.0	(2-5)	498	3.4	(2-5)	493	3.4	(2-5)	
Ireland	80	3.8	(1-11)	63	1.6	(0-9)	62	3.2	(0-11)	56	3.6	(0-12)	
United Kingdom	153	2.0	(0-6)	598	3.3	(2-5)	790	4.6	(3-6)	726	5.1	(4-7)	>#
Netherlands	74	10.8	(5-20)	103	3.9	(1-10)	120	2.5	(1-7)	132	5.3	(2-11)	
Sweden	26	3.8	(0-20)	85	5.9	(2-13)	51	0	(0-7)	55	5.5	(2-15)	N/A
Belgium	15	0.0	(0-22)	66	1.5	(0-8)	99	13.1	(7-21)	122	7.4	(3-14)	N/A
Finland	42	2.4	(0-13)	28	3.6	(0-18)	36	0.0	(0-10)	27	7.4	(1-24)	
Denmark	63	4.8	(1-13)	70	0.0	(0-5)	68	0.0	(0-5)	53	7.5	(2-18)	
Austria	63	6.3	(2-15)	81	16.0	(9-26)	75	9.3	(4-18)	92	8.7	(4-16)	
France	431	11.1	(8-14)	449	12.2	(9-16)	474	9.1	(7-12)	482	8.9	(7-12)	
Slovenia	31	41.9	(25-61)	60	43.3	(31-57)	36	41.7	(26-59)	39	20.5	(9-36)	<
Czech Republic	60	15	(7-27)	57	8.8	(3-19)	55	12.7	(5-24)	91	22.0	(14-32)	
Portugal	310	46.5	(41-52)	206	39.3	(33-46)	168	28.6	(22-36)	126	25.4	(18-34)	<
EU/EEA (population-weighted mean)	**4981**	**32.4**	**(31-34)**	**5534**	**32.8**	**(32-34)**	**6032**	**32.2**	**(31-33)**	**6383**	**31.9**	**(31-33)**	**N/A**
Slovakia	154	42.9	(35-51)	115	40.9	(32-50)	125	40.0	(31-49)	144	44.4	(36-53)	
Estonia	2	**	(**)	5	**	(**)	9	**	(**)	11	45.5	(17-77)	N/A
Hungary	465	60.6	(56-65)	401	59.1	(54-64)	358	56.1	(51-61)	343	48.7	(43-54)	<
Spain	96	49.0	(39-59)	106	50.9	(41-61)	92	52.2	(42-63)	81	49.4	(38-61)	
Latvia	61	59.0	(46-71)	81	77.8	(67-86)	33	78.8	(61-91)	48	60.4	(45-74)	
Poland	245	70.2	(64-76)	387	72.6	(68-77)	344	72.7	(68-77)	285	67.4	(62-73)	
Bulgaria	116	74.1	(65-82)	79	81.0	(71-89)	92	89.1	(81-95)	110	73.6	(64-82)	
Cyprus	59	74.6	(62-85)	28	57.1	(37-76)	50	76.0	(62-87)	57	75.4	(62-86)	
Italy	656	74.7	(71-78)	704	76.4	(73-80)	836	76.1	(73-79)	1369	77.0	(75-79)	
Romania	188	80.9	(74-86)	152	89.5	(83-94)	183	83.6	(77-89)	210	80.0	(74-85)	
Greece	945	83.7	(81-86)	878	85.0	(82-87)	1064	85.6	(83-88)	1003	81.6	(79-84)	
Lithuania	73	90.4	(81-96)	87	82.8	(73-90)	86	81.4	(72-89)	87	85.1	(76-92)	
Croatia	197	88.3	(83-92)	182	83	(77-88)	206	84	(78-89)	153	91.5	(86-95)	
Malta	15	13.3	(2-40)	7	**	(**)	9	**	(**)	8	**	(**)	N/A
Iceland	6	**	(**)	3	**	(**)	6	**	(**)	2	**	(**)	N/A

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
*** Less than 10 isolates reported, no percentage calculated.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.24. *Acinetobacter* spp. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015			2016			2017			2018			Trend
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Finland	43	2.3	(0-12)	28	0.0	(0-12)	37	2.7	(0-14)	28	0.0	(0-12)	
Norway	32	9.4	(2-25)	33	0.0	(0-11)	31	0.0	(0-11)	32	0.0	(0-11)	<
Ireland	84	6.0	(2-13)	65	0.0	(0-6)	63	6.3	(2-15)	60	1.7	(0-9)	
United Kingdom	132	0.8	(0-4)	584	1.5	(1-3)	782	2.8	(2-4)	714	1.8	(1-3)	
Sweden	34	2.9	(0-15)	84	1.2	(0-6)	54	0.0	(0-7)	54	3.7	(0-13)	
Belgium	24	0.0	(0-14)	78	2.6	(0-9)	131	6.9	(3-13)	132	3.8	(1-9)	
Germany	337	6.5	(4-10)	452	4.9	(3-7)	540	4.1	(3-6)	519	4.4	(3-7)	
Austria	64	9.4	(4-19)	81	12.3	(6-22)	75	6.7	(2-15)	91	4.4	(1-11)	
Netherlands	73	4.1	(1-12)	104	0.0	(0-3)	121	0.8	(0-5)	131	4.6	(2-10)	
Denmark	65	4.6	(1-13)	69	0.0	(0-5)	66	0.0	(0-5)	47	6.4	(1-18)	
France	428	5.6	(4-8)	450	7.1	(5-10)	469	6.2	(4-9)	490	6.5	(5-9)	
Slovenia	31	38.7	(22-58)	60	43.3	(31-57)	36	41.7	(26-59)	39	17.9	(8-34)	<
Czech Republic	60	6.7	(2-16)	57	1.8	(0-9)	55	12.7	(5-24)	91	19.8	(12-29)	>
Estonia	3	**	(**)	8	**	(**)	15	33.3	(12-62)	14	28.6	(8-58)	N/A
Portugal	307	57.7	(52-63)	206	51.9	(45-59)	172	40.7	(33-48)	127	30.7	(23-40)	<
EU/EEA (population-weighted mean)	**5036**	**32.1**	**(31-33)**	**5562**	**32.6**	**(31-34)**	**6177**	**33.2**	**(32-34)**	**6501**	**31.9**	**(31-33)**	
Slovakia	142	28.2	(21-36)	109	28.4	(20-38)	120	31.7	(23-41)	141	44.0	(36-53)	>
Spain	95	53.7	(43-64)	106	62.3	(52-71)	92	66.3	(56-76)	81	54.3	(43-65)	
Hungary	467	55.2	(51-60)	401	58.6	(54-63)	358	52.5	(47-58)	357	55.2	(50-60)	
Poland	244	65.6	(59-72)	391	66.0	(61-71)	344	67.4	(62-72)	278	67.3	(61-73)	
Bulgaria	130	73.8	(65-81)	103	74.8	(65-83)	92	80.4	(71-88)	110	74.5	(65-82)	
Latvia	61	68.9	(56-80)	82	73.2	(62-82)	34	79.4	(62-91)	51	78.4	(65-89)	
Italy	664	78.3	(75-81)	702	78.5	(75-81)	868	78.7	(76-81)	1383	79.2	(77-81)	
Cyprus	59	83.1	(71-92)	28	71.4	(51-87)	50	76.0	(62-87)	57	84.2	(72-93)	
Romania	189	81.5	(75-87)	160	85.0	(79-90)	182	87.4	(82-92)	218	85.3	(80-90)	
Lithuania	73	80.8	(70-89)	87	81.6	(72-89)	87	88.5	(80-94)	88	89.8	(81-95)	
Greece	983	93.5	(92-95)	861	95.4	(94-97)	1095	94.8	(93-96)	1013	92.4	(91-94)	
Croatia	200	89.0	(84-93)	181	94.5	(90-97)	208	96.2	(93-98)	155	95.5	(91-98)	>
Iceland	6	**	(**)	3	**	(**)	6	**	(**)	2	**	(**)	N/A
Luxembourg	7	**	(**)	8	**	(**)	8	**	(**)	6	**	(**)	N/A
Malta	15	13.3	(2-40)	7	**	(**)	9	**	(**)	9	**	(**)	N/A

** The symbols > and < indicate significant increasing and decreasing trends, respectively.*
*** Less than 10 isolates reported, no percentage calculated.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.25. *Acinetobacter* spp. Total number of isolates tested (N) and percentage with combined resistance to fluoroquinolones, aminoglycosides and carbapenems (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015 N	2015 %R	2015 (95% CI)	2016 N	2016 %R	2016 (95% CI)	2017 N	2017 %R	2017 (95% CI)	2018 N	2018 %R	2018 (95% CI)	Trend 2015-2018*
Ireland	75	1.3	(0-7)	61	0.0	(0-6)	59	1.7	(0-9)	55	0.0	(0-6)	
Finland	42	2.4	(0-13)	28	0.0	(0-12)	36	0.0	(0-10)	27	0.0	(0-13)	
Norway	32	9.4	(2-25)	32	0.0	(0-11)	31	0.0	(0-11)	32	0.0	(0-11)	<
United Kingdom	131	0.0	(0-3)	558	0.9	(0-2)	746	1.7	(1-3)	676	0.9	(0-2)	
Germany	328	3.7	(2-6)	435	2.3	(1-4)	495	1.2	(0-3)	493	2.2	(1-4)	
Belgium	13	0.0	(0-25)	64	0.0	(0-6)	98	7.1	(3-14)	120	3.3	(1-8)	N/A
Sweden	26	3.8	(0-20)	84	1.2	(0-6)	51	0	(0-7)	54	3.7	(1-13)	N/A
Denmark	60	3.3	(0-12)	67	0.0	(0-5)	66	0.0	(0-5)	46	4.3	(1-15)	
Austria	61	4.9	(1-14)	81	8.6	(4-17)	74	6.8	(2-15)	88	4.5	(1-11)	
Netherlands	73	4.1	(1-12)	100	0.0	(0-4)	120	0.8	(0-5)	130	4.6	(2-10)	
France	424	5.2	(3-8)	447	6.7	(5-9)	468	5.3	(3-8)	470	5.5	(4-8)	
Slovenia	31	35.5	(19-55)	60	38.3	(26-52)	36	41.7	(26-59)	39	17.9	(8-34)	
Czech Republic	60	5.0	(1-14)	57	0.0	(0-6)	55	5.5	(1-15)	91	18.7	(11-28)	>
Portugal	302	45.0	(39-51)	206	37.9	(31-45)	166	24.1	(18-31)	123	22.0	(15-30)	<
EU/EEA (population-weighted mean)	**4887**	**27.7**	**(26-29)**	**5390**	**28.3**	**(27-30)**	**5863**	**28.2**	**(27-29)**	**6218**	**28.8**	**(28-30)**	**N/A**
Slovakia	142	23.2	(17-31)	109	24.8	(17-34)	119	25.2	(18-34)	139	36.0	(28-45)	>
Estonia	1	**	(**)	5	**	(**)	9	**	(**)	11	36.4	(11-69)	N/A
Hungary	462	51.7	(47-56)	397	52.4	(47-57)	352	48.9	(44-54)	341	41.3	(36-47)	<
Spain	94	41.5	(31-52)	106	44.3	(35-54)	92	48.9	(38-60)	81	44.4	(33-56)	
Latvia	60	46.7	(34-60)	67	67.2	(55-78)	32	75.0	(57-89)	44	56.8	(41-72)	
Poland	240	54.6	(48-61)	383	59.3	(54-64)	333	59.5	(54-65)	251	62.9	(57-69)	
Bulgaria	112	66.1	(57-75)	76	72.4	(61-82)	92	78.3	(68-86)	110	66.4	(57-75)	
Italy	650	72.6	(69-76)	692	74.7	(71-78)	763	72.6	(69-76)	1351	75.7	(73-78)	
Romania	186	76.9	(70-83)	152	82.9	(76-89)	182	81.3	(75-87)	210	77.6	(71-83)	
Cyprus	59	72.9	(60-84)	28	57.1	(37-76)	50	76.0	(62-87)	55	78.2	(65-88)	
Greece	943	82.2	(80-85)	838	84.0	(81-86)	1059	84.3	(82-86)	995	81.3	(79-84)	
Lithuania	73	76.7	(65-86)	87	75.9	(65-84)	85	77.6	(67-86)	87	85.1	(76-92)	
Croatia	193	87.0	(81-91)	175	81.1	(75-87)	203	83.7	(78-89)	153	90.8	(85-95)	
Malta	15	6.7	(0-32)	7	**	(**)	9	**	(**)	8	**	(**)	N/A
Iceland	6	**	(**)	3	**	(**)	6	**	(**)	2	**	(**)	N/A
Luxembourg	7	**	(**)	8	**	(**)	8	**	(**)	6	**	(**)	N/A

** The symbols > and < indicate significant increasing and decreasing trends, respectively.*

*** Less than 10 isolates reported, no percentage calculated.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

3.5 *Streptococcus pneumoniae*

Streptococcus pneumoniae is a common cause of infection, especially among young children, elderly people and patients with compromised immune functions. The clinical spectrum ranges from upper airway and middle ear infection to pneumonia, bloodstream infection and meningitis.

The mechanism of penicillin resistance in *S. pneumoniae* consists of alterations in penicillin-binding proteins (PBPs), which may result in reduced affinity to penicillin G and a variable spectrum of other beta-lactams. Alterations in PBPs are due to homologous DNA recombination with PBP gene sequences originating from commensal streptococci. Acquisition of mosaic PBP results in different degrees of resistance, ranging from low-level clinical resistance – conventionally termed intermediate (I) – to full clinical resistance (R). In the absence of meningitis, infections with intermediate isolates are often successfully treated with high doses of benzylpenicillin or of an aminopenicillin.

Macrolide resistance is mainly due to acquisition of either an erythromycin ribosomal methylation gene or a macrolide efflux system gene.

Antimicrobial resistance

In 2018, the national percentages of isolates with penicillin non-susceptibility ranged from 0.1% to 40.0% (Table 3.26, Figure 3.24) and from 2.5% to 32.9% for macrolide non-susceptibility (Table 3.27). Macrolide non-susceptibility was, for most countries, higher than penicillin non-susceptibility. Combined non-susceptibility to both penicillins and macrolides was less common, with a majority of the countries reporting this phenotype for less than 10% of the tested isolates (Table 3.28).

Data might not be comparable between all countries and between the years, as the clinical breakpoints used to determine penicillin susceptibility in *S. pneumoniae* differ depending on the guidelines used for interpretation and the sites of infection. Consequently, a population-weighted EU/EEA mean percentage was not calculated for *S. pneumoniae*.

Discussion and conclusion

Based on EARS-Net data, the resistance situation in *S. pneumoniae* appears stable in the EU/EEA, with few countries reporting increasing or decreasing trends during the period 2015–2018. As in previous years, large inter-country variations could be noted for penicillin non-susceptibility.

Differences in the clinical breakpoints used for determining penicillin non-susceptibility in *S. pneumoniae* with regard to guidelines used and the sites of infection introduce bias when comparing national data reported to EARS-Net. Limited information on the guidelines used for interpretation and incomplete quantitative susceptibility data hamper any assessment of intercountry differences. In parallel to 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 [39]. Data from this surveillance initiative show that the prevalence of non-susceptibility increased slightly for penicillin and erythromycin in all countries that consistently reported antimicrobial susceptibility data between 2014 and 2016 [40]. 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 within ECDC are currently being harmonised to make best use of available data.

Most EU/EEA countries have implemented routine immunisation for children with multivalent pneumococcal conjugated vaccines (PCVs). In some countries, adult high-risk groups such as the elderly and immunocompromised are also targeted with the polysaccharide vaccine or with PCVs [41]. Increased immunisation and better serotype coverage of the available PCVs are likely to impact the epidemiology of non-susceptible *S. pneumoniae* in the EU/EEA, both in terms of changes in the age-specific incidence and potential serotype replacement. Continued long-term monitoring of antimicrobial non-susceptibility is crucial to detect the emergence of non-vaccine, non-susceptible serotypes.

Figure 3.24. *Streptococcus pneumoniae*. Percentage (%) of invasive isolates non-susceptible to macrolides, EU/EEA countries, 2018 *Map to be provided by designer*

Table 3.26. *Streptococcus pneumoniae*. Total number of tested isolates (N) and percentages non-susceptible to penicillin (%IR), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015 N	2015 %IR	2015 (95% CI)	2016 N	2016 %IR	2016 (95% CI)	2017 N	2017 %IR	2017 (95% CI)	2018 N	2018 %IR	2018 (95% CI)	Trend 2015-2018*
Belgium	1361	0.6	(0-1)	1327	0.4	(0-1)	1472	0.2	(0-1)	1526	0.1	(0-0)	<
Estonia	72	2.8	(0-10)	112	3.6	(1-9)	141	2.1	(0-6)	142	2.8	(1-7)	
Netherlands	1163	1.8	(1-3)	1391	2.2	(2-3)	1401	3.4	(3-5)	1498	3.2	(2-4)	>
Czech Republic	284	3.2	(1-6)	266	4.5	(2-8)	366	4.9	(3-8)	378	5.0	(3-8)	
Norway	429	5.4	(3-8)	500	4.4	(3-7)	480	4.8	(3-7)	500	5.0	(3-7)	
Sweden	420	9.8	(7-13)	882	7.1	(6-9)	750	6.1	(5-8)	676	5.2	(4-7)	N/A
Germany	761	6.2	(5-8)	1359	4.6	(4-6)	1989	4.5	(4-5)	1833	5.3	(4-6)	
Denmark	747	4.7	(3-6)	707	6.1	(4-8)	727	3.9	(3-6)	760	5.5	(4-7)	
United Kingdom	1095	7.8	(6-10)	3201	4.9	(4-6)	3963	5.3	(5-6)	4162	5.6	(5-6)	
Austria	444	5.6	(4-8)	440	3.4	(2-6)	463	6.0	(4-9)	523	6.3	(4-9)	
Cyprus	7	**	(**)	10	40.0	(12-74)	11	45.5	(17-77)	16	6.3	(0-30)	N/A
Italy	389	12.3	(9-16)	399	6.5	(4-9)	522	10.5	(8-13)	928	9.2	(7-11)	
Bulgaria	35	22.9	(10-40)	33	27.3	(13-46)	29	27.6	(13-47)	42	9.5	(3-23)	
Slovenia	323	9.0	(6-13)	269	6.7	(4-10)	319	10.0	(7-14)	271	9.6	(6-14)	
Iceland	25	24.0	(9-45)	19	10.5	(1-33)	27	18.5	(6-38)	31	9.7	(2-26)	N/A
Hungary	181	7.2	(4-12)	174	15.5	(10-22)	204	6.9	(4-11)	207	10.1	(6-15)	
Latvia	59	8.5	(3-19)	61	11.5	(5-22)	51	17.6	(8-31)	69	10.1	(4-20)	
Luxembourg	27	3.7	(0-19)	51	13.7	(6-26)	45	6.7	(1-18)	45	11.1	(4-24)	
Finland	677	12.7	(10-15)	706	10.3	(8-13)	698	10.5	(8-13)	600	11.5	(9-14)	
Slovakia	27	22.2	(9-42)	13	7.7	(0-36)	39	25.6	(13-42)	46	13.0	(5-26)	N/A
Portugal	797	11.2	(9-14)	884	12.2	(10-15)	997	12.8	(11-15)	986	13.4	(11-16)	
Poland	217	24.4	(19-31)	337	19.3	(15-24)	290	16.6	(12-21)	343	15.7	(12-20)	<#
Croatia	126	19.0	(13-27)	155	21.9	(16-29)	129	22.5	(16-31)	144	18.1	(12-25)	
Spain	665	23.5	(20-27)	643	25.0	(22-29)	735	22.3	(19-25)	981	18.5	(16-21)	<
Lithuania	87	16.1	(9-26)	99	16.2	(10-25)	109	15.6	(9-24)	93	19.4	(12-29)	
Ireland	303	17.5	(13-22)	363	16.5	(13-21)	412	15.8	(12-20)	455	20.7	(17-25)	
Malta	20	35.0	(15-59)	10	10.0	(0-45)	19	31.6	(13-57)	37	24.3	(12-41)	N/A
France	1068	22.9	(20-26)	1046	25.3	(23-28)	614	25.9	(22-30)	1045	29.1	(26-32)	>
Romania	41	39.0	(24-55)	56	41.1	(28-55)	79	29.1	(19-40)	90	40.0	(30-51)	
Greece	-	-	(-)	-	-	(-)	-	-	(-)	-	-	(-)	N/A

- : No data.
** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
*** Less than 10 isolates reported, no percentage calculated.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.27. *Streptococcus pneumoniae*. Total number of tested isolates (N) and percentages non-susceptible to macrolides (%IR), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015 N	2015 %IR	2015 (95% CI)	2016 N	2016 %IR	2016 (95% CI)	2017 N	2017 %IR	2017 (95% CI)	2018 N	2018 %IR	2018 (95% CI)	Trend 2015-2018*
Denmark	747	5.2	(4-7)	707	4.8	(3-7)	727	3.6	(2-5)	760	2.5	(2-4)	<
Netherlands	1168	3.9	(3-5)	1389	3.1	(2-4)	1406	5.7	(5-7)	1519	4.1	(3-5)	
Sweden	850	6.9	(5-9)	899	5.8	(4-8)	750	4.8	(3-7)	674	4.7	(3-7)	N/A
United Kingdom	1077	7.2	(6-9)	3423	6.5	(6-7)	4273	6.0	(5-7)	4450	5.9	(5-7)	
Cyprus	7	**	(**)	10	60.0	(26-88)	19	26.3	(9-51)	14	7.1	(0-34)	N/A
Germany	758	8.4	(7-11)	1386	8.2	(7-10)	2029	7.1	(6-8)	1849	7.3	(6-9)	
Norway	403	10.7	(8-14)	473	9.5	(7-13)	439	5.9	(4-9)	460	8.0	(6-11)	
Estonia	54	7.4	(2-18)	100	8.0	(4-15)	127	3.9	(1-9)	136	8.1	(4-14)	
Czech Republic	284	6.7	(4-10)	263	7.2	(4-11)	366	9.3	(7-13)	378	10.1	(7-14)	
Slovenia	323	18.9	(15-24)	269	13.8	(10-18)	216	15.7	(11-21)	271	10.3	(7-15)	<
Latvia	58	6.9	(2-17)	52	5.8	(1-16)	28	7.1	(1-24)	66	10.6	(4-21)	
Luxembourg	29	0.0	(0-12)	51	15.7	(7-29)	49	8.2	(2-20)	45	11.1	(4-24)	
Austria	439	8.7	(6-12)	455	8.8	(6-12)	507	11.2	(9-14)	562	11.6	(9-15)	
Finland	765	14.4	(12-17)	791	12.0	(10-14)	808	15.5	(13-18)	653	12.7	(10-16)	
Iceland	25	12.0	(3-31)	19	0.0	(0-18)	27	18.5	(6-38)	31	12.9	(4-30)	N/A
Ireland	296	15.5	(12-20)	354	14.4	(11-19)	396	13.1	(10-17)	419	14.1	(11-18)	
Hungary	170	11.2	(7-17)	166	13.3	(8-19)	187	11.8	(8-17)	190	14.7	(10-21)	
Portugal	822	17.0	(15-20)	912	15.1	(13-18)	1024	15.5	(13-18)	985	15.7	(14-18)	
Belgium	1361	18.7	(17-21)	1327	15.9	(14-18)	1472	15.6	(14-18)	1526	15.8	(14-18)	<#
Spain	631	23.5	(20-27)	630	25.9	(22-29)	717	21.8	(19-25)	1007	18.5	(16-21)	<#
Bulgaria	33	21.2	(9-39)	32	21.9	(9-40)	29	27.6	(13-47)	42	19.0	(9-34)	
Italy	428	24.5	(21-29)	464	23.1	(19-27)	599	23.4	(20-27)	1095	20.6	(18-23)	
France	1068	24.4	(22-27)	1046	26.4	(24-29)	614	23.3	(20-27)	1045	23.9	(21-27)	
Lithuania	72	12.5	(6-22)	94	18.1	(11-27)	107	15.9	(10-24)	92	23.9	(16-34)	
Malta	20	40.0	(19-64)	9	**	(**)	19	36.8	(16-62)	37	24.3	(12-41)	N/A
Poland	206	31.1	(25-38)	277	30.7	(25-36)	253	24.9	(20-31)	309	25.9	(21-31)	
Slovakia	34	35.3	(20-54)	12	8.3	(0-38)	31	35.5	(19-55)	45	26.7	(15-42)	N/A
Romania	20	30.0	(12-54)	59	39.0	(27-53)	76	27.6	(18-39)	93	32.3	(23-43)	
Croatia	126	19.8	(13-28)	154	35.1	(28-43)	127	36.2	(28-45)	143	32.9	(25-41)	>
Greece	-	-	(-)	-	-	(-)	-	-	(-)	-	-	(-)	N/A

- : No data.
** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

** Less than 10 isolates reported, no percentage calculated.
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.28. *Streptococcus pneumoniae*. Total number of tested isolates (N) and percentages non-susceptible to penicillins and macrolides (%IR), including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)	2015-2018*
Belgium	1361	0.4	(0-1)	1327	0.3	(0-1)	1472	0.1	(0-0)	1526	0.1	(0-0)	<#
Netherlands	1030	0.9	(0-2)	1263	0.4	(0-1)	1297	1.1	(1-2)	1374	0.9	(0-2)	
Denmark	747	2.4	(1-4)	707	2.3	(1-4)	727	1.8	(1-3)	760	1.3	(1-2)	
United Kingdom	1060	2.7	(2-4)	3136	2.6	(2-3)	3885	2.0	(2-2)	4052	2.0	(2-3)	
Estonia	27	3.7	(0-19)	100	1.0	(0-5)	127	1.6	(0-6)	136	2.2	(0-6)	
Germany	748	2.7	(2-4)	1342	2.2	(1-3)	1969	2.2	(2-3)	1805	2.5	(2-3)	
Czech Republic	284	1.8	(1-4)	263	1.1	(0-3)	366	3.0	(2-5)	378	2.6	(1-5)	
Sweden	409	5.6	(4-8)	877	4.0	(3-6)	745	3.0	(2-4)	674	2.7	(2-4)	N/A
Austria	433	2.5	(1-4)	438	1.4	(1-3)	457	3.3	(2-5)	519	3.3	(2-5)	
Norway	403	2.5	(1-5)	469	2.8	(1-5)	439	2.5	(1-4)	454	3.5	(2-6)	
Luxembourg	27	0.0	(0-13)	51	7.8	(2-19)	45	4.4	(1-15)	45	4.4	(1-15)	
Italy	347	5.8	(4-9)	361	4.4	(3-7)	474	5.3	(3-8)	879	4.7	(3-6)	
Bulgaria	32	12.5	(4-29)	32	9.4	(2-25)	29	17.2	(6-36)	42	4.8	(1-16)	
Slovenia	323	5.0	(3-8)	269	3.7	(2-7)	216	6.5	(4-11)	271	4.8	(3-8)	
Finland	654	7.0	(5-9)	687	6.1	(4-8)	671	6.7	(5-9)	591	5.8	(4-8)	
Latvia	53	1.9	(0-10)	51	3.9	(0-13)	28	3.6	(0-18)	66	6.1	(2-15)	
Cyprus	7	**	(**)	10	40.0	(12-74)	11	45.5	(17-77)	14	7.1	(0-34)	N/A
Hungary	170	1.8	(0-5)	166	7.8	(4-13)	187	6.4	(3-11)	190	7.9	(4-13)	>
Portugal	776	6.6	(5-9)	868	6.7	(5-9)	978	7.2	(6-9)	922	8.0	(6-10)	
Iceland	25	8.0	(1-26)	19	0.0	(0-18)	27	14.8	(4-34)	31	9.7	(2-26)	N/A
Spain	624	12.0	(10-15)	612	14.4	(12-17)	701	12.4	(10-15)	957	9.8	(8-12)	
Ireland	296	10.8	(8-15)	354	9.9	(7-13)	396	9.6	(7-13)	419	10.0	(7-13)	
Poland	195	19.5	(14-26)	271	16.6	(12-22)	241	14.1	(10-19)	285	10.9	(8-15)	<
Slovakia	27	22.2	(9-42)	12	0.0	(0-26)	30	23.3	(10-42)	44	11.4	(4-25)	N/A
Croatia	126	7.9	(4-14)	154	15.6	(10-22)	126	15.9	(10-23)	141	12.1	(7-19)	
Lithuania	72	11.1	(5-21)	94	12.8	(7-21)	107	11.2	(6-19)	92	13.0	(7-22)	
Malta	20	25.0	(9-49)	9	**	(**)	19	26.3	(9-51)	37	13.5	(5-29)	N/A
France	1068	17.4	(15-20)	1046	18.3	(16-21)	614	17.8	(15-21)	1045	20.4	(18-23)	
Romania	20	25.0	(9-49)	56	30.4	(19-44)	75	24.0	(15-35)	90	26.7	(18-37)	
Greece	-	-	(-)	-	-	(-)	-	-	(-)	-	-	(-)	N/A

- : No data.
* The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.
** Less than 10 isolates reported, no percentage calculated.
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

3.6 *Staphylococcus aureus*

Staphylococcus aureus is a gram-positive bacterium that frequently colonises the skin and nostrils of healthy humans. However, *S. aureus* is also an opportunistic microorganism involved in infections of both community and healthcare origin. Besides being a common cause of skin, soft tissue and bone infections, it is one of the leading causes of bloodstream infections in Europe. *S. aureus* acquires resistance to meticillin and some other beta-lactam agents through expression of the exogenous *mecA*, or less frequently, the *mecC* gene. These genes code for a variant penicillin-binding protein PBP2' (PBP2a) with low affinity for beta-lactams and able to substitute for the function of the other penicillin-binding proteins, thus preventing the inhibition of cell wall synthesis by beta-lactams.

Antimicrobial resistance

The EU/EEA population-weighted mean percentage of meticillin-resistant *S. aureus* (MRSA) was 16.4% in 2018. This is a result of a significantly decreasing trend between 2015 and 2018 (Table 3.30).

In 2018, large differences in national MRSA percentages could be noted, ranging from 0% to 43.0% (Figure 3.30). Close to a third of the countries reported significantly decreasing trends during the period 2015–2018, including countries with both low and high percentages of MRSA (Table 3.30).

Among MRSA, combined resistance to other antimicrobial groups was common. The most common resistance combination was MRSA and resistance to fluoroquinolones. Rifampicin resistance was less common (Table 3.29).

Discussion and conclusion

MRSA percentages continue to be stabilising or still 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 the prevention of 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 serious bacterial infections, exhibiting a high burden in terms of morbidity and mortality [3]. Although the EU/EEA population-weighted MRSA percentage as reported by EARS-Net has decreased since many years, the ECDC 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 on the health burden of AMR found that this was mainly caused by an increase in incidence in infants and people aged 55 years or older [3]. These discrepancies indicate a need to further study the distribution of *S. aureus* in the EU/EEA to get a better overview of the current epidemiological situation.

In order to slow 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, but shows a constantly evolving situation including detection of livestock-associated MRSA (LA-MRSA), HA-MRSA and CA-MRSA from companion animals and/or livestock [24]. 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 documented the increasing detection and geographical dispersion of LA-MRSA in humans in the EU/EEA between 2007 and 2013 and highlights the public health and veterinary importance of LA-MRSA as a One Health issue [42].

Table 3.29. *Staphylococcus aureus*. Total number of tested isolates* and resistance combinations among invasive isolates tested against meticillin, fluoroquinolones and rifampicin (n=17 953), EU/EEA countries, 2018

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**43681**	**80.7**
Single resistance (to indicated antimicrobial group)		
Total (any single resistance)	**4495**	**8.3**
MRSA	1353	2.5
Fluoroquinolones	2927	5.4
Rifampicin	215	0.4
Resistance to two antimicrobial groups		
Total (any two-group combinations)	**5705**	**10.5**
MRSA + fluoroquinolones	5643	10.4
Other resistance combinations	62	0.1
Resistance to three antimicrobial groups		
MRSA + fluoroquinolones + rifampicin	**254**	**0.5**

** Only data from isolates tested against all five antimicrobials groups were included in the analysis*
*** Not adjusted for population differences in the reporting countries*

Figure 3.25. *Staphylococcus aureus*. Percentage (%) of invasive isolates with resistance to meticillin (MRSA), EU/EEA countries, 2018 *Map to be provided by designer*

Table 3.30. *Staphylococcus aureus*. Total number of invasive isolates tested (N) and percentage with resistance to meticillin (MRSA) including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Iceland	88	0.0	(0-4)	76	1.3	(0-7)	69	1.4	(0-8)	82	0.0	(0-4)	
Norway	1453	1.2	(1-2)	1448	1.2	(1-2)	1462	1.0	(1-2)	1547	0.9	(0-2)	
Netherlands	2107	1.3	(1-2)	2699	1.2	(1-2)	2694	1.5	(1-2)	3050	1.2	(1-2)	
Denmark	1876	1.6	(1-2)	1963	2.0	(1-3)	1996	2.5	(2-3)	2181	1.7	(1-2)	
Sweden	3124	0.8	(1-1)	3450	2.3	(2-3)	3787	1.2	(1-2)	3639	1.9	(2-2)	N/A
Finland	2070	1.9	(1-3)	1890	2.2	(2-3)	2439	2.0	(1-3)	2105	2.0	(1-3)	
Estonia	151	4.0	(1-8)	314	3.5	(2-6)	290	2.1	(1-4)	359	3.3	(2-6)	
Latvia	251	5.6	(3-9)	284	4.2	(2-7)	210	5.7	(3-10)	315	5.7	(3-9)	
Austria	2785	7.5	(7-9)	3053	7.1	(6-8)	3158	5.9	(5-7)	3307	6.4	(6-7)	<
United Kingdom	2757	10.8	(10-12)	6717	6.7	(6-7)	8883	6.9	(6-7)	9045	7.3	(7-8)	<
Germany	5020	11.3	(10-12)	9866	10.2	(10-11)	13128	9.1	(9-10)	11611	7.6	(7-8)	<
Luxembourg	135	8.9	(5-15)	187	10.2	(6-15)	200	9.5	(6-14)	181	7.7	(4-13)	
Lithuania	376	8.5	(6-12)	503	11.3	(9-14)	514	8.8	(6-12)	691	8.4	(6-11)	
Belgium	913	12.3	(10-15)	1364	12.2	(10-14)	1511	8.5	(7-10)	1735	9.1	(8-11)	<
Slovenia	513	9.2	(7-12)	534	11.0	(9-14)	576	9.0	(7-12)	606	11.7	(9-15)	
France	5535	15.7	(15-17)	5578	13.8	(13-15)	6472	12.9	(12-14)	6903	12.1	(11-13)	<
Ireland	1057	18.1	(16-21)	1143	14.3	(12-17)	1140	16.3	(14-19)	1188	12.4	(11-14)	<
Czech Republic	1806	13.7	(12-15)	1887	13.9	(12-16)	1944	13.2	(12-15)	2243	13.6	(12-15)	
Poland	958	15.8	(14-18)	1772	16.4	(15-18)	1805	15.2	(14-17)	1959	15.9	(14-18)	
EU/EEA (population-weighted mean)	**45509**	**19.0**	**(19-19)**	**57387**	**17.7**	**(17-18)**	**65928**	**16.8**	**(17-17)**	**72085**	**16.4**	**(16-17)**	**<**
Bulgaria	222	13.1	(9-18)	231	14.3	(10-19)	227	13.7	(9-19)	313	17.6	(14-22)	
Hungary	1517	24.7	(23-27)	1668	25.2	(23-27)	1566	23.6	(22-26)	1721	23.1	(21-25)	
Spain	1968	25.3	(23-27)	1944	25.8	(24-28)	1856	25.1	(23-27)	2444	24.2	(23-26)	
Croatia	486	24.5	(21-29)	458	25.3	(21-30)	520	28.5	(25-33)	458	26.4	(22-31)	
Slovakia	583	28.1	(25-32)	571	27.1	(24-31)	613	29.2	(26-33)	610	26.6	(23-30)	
Italy	3000	34.1	(32-36)	2981	33.6	(32-35)	3591	33.9	(32-35)	8263	34.0	(33-35)	
Malta	87	49.4	(39-60)	97	37.1	(28-48)	95	42.1	(32-53)	88	36.4	(26-47)	
Greece	612	39.4	(35-43)	639	38.8	(35-43)	822	38.4	(35-42)	888	36.4	(33-40)	
Portugal	3619	46.8	(45-48)	3454	43.6	(42-45)	3728	39.2	(38-41)	3836	38.0	(36-40)	<
Cyprus	143	43.4	(35-52)	139	38.8	(31-47)	125	31.2	(23-40)	117	40.2	(31-50)	
Romania	297	57.2	(51-63)	477	50.5	(46-55)	507	44.4	(40-49)	600	43.0	(39-47)	<

** The symbols > and < indicate significant increasing and decreasing trends, respectively.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

3.7 Enterococci

Enterococci belong to the normal bacterial microbiota of the gastrointestinal tract of humans. They are regarded commensals but can cause invasive diseases when the commensal relationship with the host is disrupted. Enterococci can cause a variety of infections, including urinary tract infections, bloodstream infections and endocarditis, and are associated with peritonitis and intra-abdominal abscesses. The vast majority of clinical enterococcal infections in humans are caused by *Enterococcus faecalis* and *E. faecium*.

Enterococci are intrinsically resistant to a broad range of antimicrobial agents including cephalosporins, sulphonamides and low concentrations of aminoglycosides. *E. faecium* is also intrinsically resistant to carbapenems, and enterococci have low susceptibility to many other beta-lactam agents as a consequence of their low-affinity penicillin-binding proteins. However, there is commonly synergy between aminoglycosides and penicillins or glycopeptides against enterococci without acquired high-level glycopeptide resistance. Some enterococci have acquired genes conferring high-level resistance to aminoglycosides, causing loss of any synergistic effect between beta-lactams and aminoglycosides.

Glycopeptide resistance of clinical relevance is mostly mediated through two phenotypes: VanA, with high-level resistance to vancomycin and a variable level of resistance to teicoplanin; and VanB, with a variable level of resistance, in most cases to vancomycin only.

Antimicrobial resistance

Enterococcus faecalis

High-level gentamicin resistance

In 2018, the EU/EEA population-weighted mean percentage of high-level gentamicin resistance in *E. faecalis* was 27.1%, with national percentages ranging from 6.7% to 41.6% (Figure 3.26). The EU/EEA trend decreased significantly between 2015 and 2018, with similar significantly decreasing national trends reported from almost one fourth of the countries (Table 3.31).

Vancomycin resistance

Vancomycin resistance in *E. faecalis* remained low in most countries. For more information, please refer to the online ECDC Surveillance Atlas of Infectious Diseases [26].

Enterococcus faecium

Vancomycin

The EU/EEA population-weighted mean percentage of vancomycin resistance in *E. faecium* was 17.3% in 2018, which represents a significant increase from 2015 when the percentage was 10.5%. In 2018, national percentages ranged from 0.0% to 59.1%. Only 12 out of the 30 reporting countries reported resistance percentages below 5% (Figure 3.27). Several of the countries reporting comparatively high percentages of resistance to vancomycin also reported significantly increasing trends for the last four years (Table 3.32). For several countries, the increase during the four-year period was considerable.

High-level gentamicin resistance

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 [26].

Discussion and conclusion

The rapid and continuous increase in the percentage of vancomycin –resistance in *E. faecium* in the EU/EEA is a cause for concern. The ECDC study on the health burden of AMR estimated that the number of infections and of the deaths attributable to vancomycin-resistant enterococci (VRE) almost doubled between 2007 and 2015 [3], and the substantial increase in resistance percentages reported after 2015 further increase the health burden of VRE infections. The significantly increasing trends, observed at the EU/EEA level and in many of the individual countries, highlight the need for close monitoring and urgent need to better understand the epidemiology, clonal diversity and risk factors associated with 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 [34]. High levels of antimicrobial-resistant enterococci remain a major infection control challenge and an important cause of healthcare-associated infections in Europe. Besides the fact that infections caused by resistant strains are difficult to treat, enterococci easily disseminate in healthcare settings.

Figure 3.26. *Enterococcus faecalis*. Percentage (%) of invasive isolates with high-level resistance to gentamicin, EU/EEA countries, 2018 *Map to be provided by designer*

Figure 3.27. *Enterococcus faecium*. Percentage (%) of invasive isolates with resistance to vancomycin, EU/EEA countries, 2018 *Map to be provided by designer*

Table 3.31. *Enterococcus faecalis*. Total number of invasive isolates tested (N) and percentage with high-level resistance to gentamicin including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

	2015			2016			2017			2018			Trend
Country	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	2015-2018*
Luxembourg	56	14.3	(6-26)	48	12.5	(5-25)	82	22.0	(14-32)	45	6.7	(1-18)	
France	1097	12.2	(10-14)	1057	15.0	(13-17)	795	12.7	(10-15)	1568	9.8	(8-11)	<#
Greece	460	13.3	(10-17)	540	15.9	(13-19)	621	12.2	(10-15)	668	12.0	(10-15)	
Belgium	249	13.3	(9-18)	328	19.8	(16-25)	304	16.4	(12-21)	390	12.3	(9-16)	
Denmark	63	25.4	(15-38)	56	19.6	(10-32)	56	7.1	(2-17)	171	12.3	(8-18)	<
Cyprus	58	8.6	(3-19)	39	20.5	(9-36)	70	8.6	(3-18)	87	12.6	(6-21)	
Sweden	579	12.6	(10-16)	722	13.4	(11-16)	945	13.3	(11-16)	627	12.8	(10-16)	N/A
Norway	163	9.8	(6-15)	221	15.8	(11-21)	216	14.4	(10-20)	216	13.4	(9-19)	
Iceland	21	14.3	(3-36)	24	16.7	(5-37)	33	18.2	(7-35)	30	16.7	(6-35)	
Slovenia	133	32.3	(24-41)	152	43.4	(35-52)	167	33.5	(26-41)	161	20.5	(15-28)	<
Malta	29	27.6	(13-47)	33	39.4	(23-58)	29	34.5	(18-54)	31	22.6	(10-41)	
Germany	1295	30.7	(28-33)	2341	25.2	(23-27)	2930	25.3	(24-27)	2232	22.8	(21-25)	<
Netherlands	343	23.0	(19-28)	451	24.4	(20-29)	537	24.4	(21-28)	543	23.2	(20-27)	
Ireland	261	28.0	(23-34)	265	29.4	(24-35)	302	30.8	(26-36)	292	23.6	(19-29)	
Estonia	26	26.9	(12-48)	56	32.1	(20-46)	71	19.7	(11-31)	87	25.3	(17-36)	
Portugal	872	33.3	(30-36)	851	33.8	(31-37)	931	25.8	(23-29)	783	26.7	(24-30)	<
EU/EEA (population-weighted mean)	**10711**	**31.9**	**(31-33)**	**12698**	**31.8**	**(31-33)**	**13759**	**29.7**	**(29-31)**	**15093**	**27.1**	**(26-28)**	**<**
Lithuania	63	44.4	(32-58)	45	35.6	(22-51)	60	36.7	(25-50)	65	27.7	(17-40)	
Austria	501	33.7	(30-38)	447	33.3	(29-38)	474	33.1	(29-38)	417	28.3	(24-33)	
Latvia	58	36.2	(24-50)	87	46.0	(35-57)	72	45.8	(34-58)	86	32.6	(23-44)	
Croatia	203	35.5	(29-42)	179	33.0	(26-40)	171	33.3	(26-41)	143	33.6	(26-42)	
Czech Republic	544	38.8	(35-43)	515	37.1	(33-41)	526	34.0	(30-38)	594	33.7	(30-38)	<
Spain	936	40.0	(37-43)	950	37.5	(34-41)	873	36.9	(34-40)	1002	34.8	(32-38)	<#
Romania	0		(.-.)	87	56.3	(45-67)	89	44.9	(34-56)	168	37.5	(30-45)	N/A
Hungary	730	45.5	(42-49)	786	42.2	(39-46)	769	41.5	(38-45)	750	38.0	(35-42)	<
Bulgaria	100	42.0	(32-52)	98	46.9	(37-57)	133	43.6	(35-52)	150	39.3	(31-48)	
Italy	1249	47.8	(45-51)	1441	45.3	(43-48)	1630	45.9	(43-48)	2927	39.9	(38-42)	<
Slovakia	234	49.1	(43-56)	213	45.1	(38-52)	213	25.8	(20-32)	215	40.0	(33-47)	<
Poland	388	46.4	(41-51)	666	43.1	(39-47)	660	41.2	(37-45)	645	41.6	(38-45)	
Finland	-	-	(-)	-	-	(-)	-	-	(-)	-	-	(-)	N/A
United Kingdom	-	-	(-)	-	-	(-)	-	-	(-)	-	-	(-)	N/A

- : No data.

** The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*

N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Table 3.32. *Enterococcus faecium*. Total number of invasive isolates tested (N) and percentage with resistance to vancomycin, including 95% confidence intervals (95% CI), EU/EEA countries, 2015–2018

Country	2015 N	2015 %R	2015 (95% CI)	2016 N	2016 %R	2016 (95% CI)	2017 N	2017 %R	2017 (95% CI)	2018 N	2018 %R	2018 (95% CI)	Trend 2015-2018*
Luxembourg	23	0.0	(0-15)	31	0.0	(0-11)	34	0.0	(0-10)	28	0.0	(0-12)	
Slovenia	124	4.8	(2-10)	111	0.0	(0-3)	149	0.7	(0-4)	134	0.0	(0-3)	<
Iceland	20	0.0	(0-17)	16	0.0	(0-21)	17	0.0	(0-20)	16	0.0	(0-21)	N/A
France	849	0.8	(0-2)	808	0.6	(0-1)	986	0.8	(0-2)	987	0.6	(0-1)	
Netherlands	572	1.4	(1-3)	685	0.9	(0-2)	807	1.4	(1-2)	829	1.1	(0-2)	
Sweden	408	0.0	(0-1)	546	0.4	(0-1)	530	0.0	(0-1)	428	1.4	(1-3)	N/A
Finland	298	0.3	(0-2)	294	0.0	(0-1)	301	0.7	(0-2)	289	1.7	(1-4)	>
Belgium	163	0.6	(0-3)	289	1.7	(1-4)	417	5.5	(4-8)	436	1.8	(1-4)	
Austria	483	3.1	(2-5)	533	4.3	(3-6)	570	3.2	(2-5)	524	2.1	(1-4)	
Norway	185	0.0	(0-2)	213	1.9	(1-5)	202	4.5	(2-8)	171	2.3	(1-6)	>
Spain	571	2.5	(1-4)	628	2.1	(1-4)	570	1.8	(1-3)	764	2.5	(2-4)	
Portugal	459	20.3	(17-24)	411	7.5	(5-11)	461	7.2	(5-10)	439	4.3	(3-7)	<
Estonia	27	0.0	(0-13)	64	0.0	(0-6)	52	5.8	(1-16)	64	6.3	(2-15)	>
Bulgaria	41	14.6	(6-29)	44	18.2	(8-33)	84	19.0	(11-29)	91	9.9	(5-18)	
Denmark	690	3.2	(2-5)	679	7.5	(6-10)	785	7.0	(5-9)	779	12.5	(10-15)	>
EU/EEA (population-weighted mean)	**9152**	**10.5**	**(10-11)**	**12330**	**12.3**	**(12-13)**	**14139**	**14.9**	**(14-16)**	**15742**	**17.3**	**(17-18)**	**>**
Italy	756	11.2	(9-14)	941	13.4	(11-16)	1049	14.6	(13-17)	2273	18.9	(17-21)	>
Czech Republic	322	9.6	(7-13)	258	7.8	(5-12)	264	13.3	(9-18)	358	20.7	(17-25)	>
Germany	1347	10.5	(9-12)	2043	11.9	(11-13)	2642	16.5	(15-18)	2382	23.8	(22-26)	>
United Kingdom	218	17.0	(12-23)	1803	17.0	(15-19)	2202	25.8	(24-28)	2615	24.7	(23-26)	>
Croatia	93	25.8	(17-36)	104	22.1	(15-31)	89	19.1	(12-29)	71	25.4	(16-37)	
Malta	6		(-.-)	12	8.3	(0-38)	13	0.0	(0-25)	15	26.7	(8-55)	N/A
Greece	315	19.7	(15-25)	358	27.9	(23-33)	412	30.8	(26-36)	527	28.1	(24-32)	>
Lithuania	52	17.3	(8-30)	61	21.3	(12-34)	80	36.3	(26-48)	99	31.3	(22-41)	>#
Slovakia	143	14.7	(9-22)	125	26.4	(19-35)	122	32.0	(24-41)	161	32.3	(25-40)	>
Latvia	34	17.6	(7-35)	56	28.6	(17-42)	39	25.6	(13-42)	48	35.4	(22-51)	
Poland	215	17.7	(13-23)	405	26.2	(22-31)	400	31.5	(27-36)	374	35.8	(31-41)	>
Hungary	240	16.7	(12-22)	272	22.4	(18-28)	315	28.3	(23-34)	301	39.5	(34-45)	>
Ireland	404	45.8	(41-51)	422	44.1	(39-49)	442	38.2	(34-43)	418	40.2	(35-45)	<
Romania	72	25.0	(16-37)	77	39.0	(28-51)	64	34.4	(23-47)	77	40.3	(29-52)	
Cyprus	28	28.6	(13-49)	41	46.3	(31-63)	41	43.9	(28-60)	44	59.1	(43-74)	>

* *The symbols > and < indicate significant increasing and decreasing trends, respectively. The symbol # indicates a significant trend in the overall data, which was not observed when only data from laboratories consistently reporting for all four years were included.*
N/A: Not applicable as data were not reported for all years, a significant change in data source occurred during the period or number of isolates was below 20 in any year during the period.

Annex 1. Country summaries

The country summaries provide information on the population coverage, hospital coverage and representativeness of data provided by the laboratories reporting data to EARS-Net. The summaries include both quantitative and qualitative measures related to the population under surveillance, the hospitals served by participating laboratories, laboratory practices and the use of blood cultures. For more information on how differences in patient sampling and laboratory practices might impact data validity, please refer to Chapter 2.

In addition, national resistance percentages from 2011 to 2018 are presented together with the EU/EEA population-weighted mean percentages for selected bacterium/antimicrobial group combinations. Data for all bacterium/antimicrobial groups under regular surveillance by EARS-Net for the period 2000–2018 are available in the ECDC Surveillance atlas of Infectious Diseases, available from https://atlas.ecdc. europa.eu

Table 1. Coverage and representativeness of population, hospitals and isolates included in EARS-Net.

Data sources

As the data collected on national surveillance system characteristics was revised in 2019, data for 2018 comes from the European Surveillance System (TESSy), while the data for earlier years combines TESSy data with data from collected through questionnaires distributed to the nominated National Focal Points for Antimicrobial Resistance.

Indicators

Estimated national population coverage is expressed as the estimated percentage of the national population under surveillance by the laboratories contributing data to EARS-Net. It should be considered as an indication of the national coverage, as the exact proportion of the population under surveillance is often difficult to assess. The country coverage was calculated as the mean of the population coverages of the following microorganisms: *E. coli, K. pneumoniae, P. aeruginosa S. aureus, E. faecalis* and *E. faecium*. Due to outliers in some countries, *S. pneumoniae* and *Acinetobacter* spp. were not included in the calculation.

Population sample representativeness is a qualitative indicator referring to the geographical representativeness of data. The categories are:
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 of 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 sample representativeness is a qualitative indicator referring to the representativeness of hospitals served by the EARS-Net participating laboratories, compared to the national distribution of the types of hospitals (specialised, tertiary care, secondary care and primary care). The categories are:
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.

Blood culture sets/1000 patient-days refers to the number of blood culture sets per 1000 inpatient occupied bed-days in hospitals served by EARS-Net laboratories. The definition of an inpatient bed day might differ between countries, and influence the estimate.

Isolate sample representativeness is a qualitative indicator referring to representativeness of blood cultures reported by EARS-Net laboratories. The categories are:
High: The isolate sample is representative of microorganisms causing invasive infections and of patient case-mix of the included hospitals;

Medium: The isolate sample is partly representative of microorganisms causing invasive infections and of patient case-mix of the included hospitals;
Poor: The isolate sample is poorly representative of microorganisms causing invasive infections and of patient case-mix of the included hospitals;
Unknown: Unknown or no data provided.

Table 2. Laboratories contributing data to EARS-Net: participation in EARS-Net EQA exercise and use of EUCAST guidelines

Data source
Data were provided from the annual EARS-Net external quality assessment (EQA) exercise, coordinated by the ECDC contractor United Kingdom National External Quality Assessment Service (UK NEQAS). For more information on the EARS-Net EQA exercise, please refer to the separate EQA report [13].

Indicators
Percentage of laboratories participating in EARS-Net EQA represents the proportion of laboratories invited to participate in the EARS-Net EQA exercise that returned reports within the agreed time.

Percentage of laboratories using EUCAST or EUCAST harmonised guidelines refers to the proportion of laboratories reporting to use EUCAST or EUCAST-harmonised clinical guidelines among laboratories returning reports on the EARS-Net EQA exercise. Guidelines from British Society for Antimicrobial Chemotherapy (BSAC) and the Société Française de Microbiologie (SFM) were considered as harmonised with EUCAST as both have implemented EUCAST breakpoints in their national MIC breakpoint recommendations and adjusted the interpretation of their disk diffusion methods accordingly.

Table 3. Annual number of reporting laboratories, number of reported isolates and proportion of isolates reported from patients in intensive care units (ICU)

Data source
EARS-Net data 2015-2018.

Indicators
Table 3 provides information on the number of laboratories, the number of isolates and the proportion of isolates from patients in intensive care units (ICUs), by year and by pathogen. The percentage of isolates from patients in ICUs is only calculated if information on hospital unit type is available from more than 50% of the isolates. The total number of laboratories participating in EARS-Net could in some countries be higher than the number presented, as only laboratories reporting at least one isolate during each specific year are included.

Figure 1-4. Percentage (%) of invasive isolates with resistance to selected antimicrobial groups

Data source
EARS-Net data 2011-2018. For an explanation on the methodology used for the EU/EEA population-weighted mean, please refer to Chapter 2.

Indicators
Percentage (%) of invasive isolates with resistance to selected antimicrobial groups: *Staphylococcus aureus* with resistance to meticillin (MRSA), *Escherichia coli* with resistance to third-generation cephalosporins, *Klebsiella pneumoniae* with resistance to carbapenems and *Enterococcus faecium* with resistance to vancomycin.

References

1. World Health Organization. Global Action Plan on Antimicrobial Resistance. Geneva: WHO; 2015. Available from: 1. World Health Organization. Global Action Plan on Antimicrobial Resistance. Geneva: WHO; 2015. Available from: https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1.

2. European Commission. A European One Health Action Plan against Antimicrobial Resistance (AMR). Brussels: EC; 2017. Available from: https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf.

3. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis. 2019 Jan;19(1):56-66.

4. Organisation for Economic Co-operation and Development (OECD) and European Centre for Disease Prevention and Control (ECDC). Antimicrobial Resistance. Tackling the burden in the European Union. Briefing note for EU/EEA countries. Paris: OECDC 2019.

5. European Commission. Commission Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32013D1082).

6. European Commission. Commission Implementing Decision (EU) 2018/945 of 22 June 2018 on the communicable diseases and related special health issues to be covered by epidemiological surveillance as well as relevant case definitions. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv%3AOJ.L_.2018.170.01.0001.01.ENG.

7. World Health Organization. Central Asian and European Surveillance of Antimicrobial Resistance. Annual Report 2018. Copenhagen: WHO Regional Office for Europe; 2018. Available from http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/publications/2018/central-asian-and-eastern-european-surveillance-of-antimicrobial-resistance-annual-report-2018-2018.

8. World Health Organization. European strategic action plan on antibiotic resistance. Copenhagen: WHO Regional Office for Europe; 2011 EUR/RC61/14; Available from: http://www.euro.who.int/en/about-us/governance/regional-committee-foreurope/past-sessions/sixty-first-session/documentation/working-documents/wd14-europeanstrategic-action-plan-on-antibiotic-resistance.

9. World Health Organization. Global antimicrobial resistance surveillance system (GLASS) report: early implementation 2017-2018. Geneva: WHO; 2018. Available from: https://apps.who.int/iris/bitstream/handle/10665/279656/9789241515061-eng.pdf?ua=1.

10. European Centre for Disease Prevention and Control. TESSy, The European Surveillance System – Antimicrobial resistance (AMR) reporting protocol 2019 – European Antimicrobial Resistance Surveillance Network (EARS-Net) surveillance data for 2017. Stockholm: ECDC; 2019.

11. European Committee on Antimicrobial Susceptibility Testing. EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance – Version 2.0. Växjö, EUCAST; 2017. Available from: http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Resistance_mechanisms/EUCAST_detection_of_resistance_mechanisms_170711.pdf

12. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 9.0, 2019. http://www.eucast.org/clinical_breakpoints/.

13. European Centre for Disease Prevention and Control. External quality assessment (EQA) of performance of laboratories participating in the European Antimicrobial Resistance Surveillance Network (EARS-Net), 2018. Stockholm: ECDC; 2019. [Publication pending].

14. Eurostat [internet]. Brussels: Eurostat; 2019. Available from: http:// ec.europa.eu/eurostat.

15. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals, 2016-2017. Stockholm: ECDC; 2019. [Publication pending]

16. European Centre for Disease Prevention and Control, European Food Safety Authority and European Medicines Agency. ECDC/EFSA/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals – Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Report. Available from: http://ecdc.europa.eu/publications-data/ecdcefsaema-second-joint-report-integrated-analysisconsumption-antimicrobial.

17.European Centre for Disease Prevention and Control. Antimicrobial consumption. In: ECDC. Annual epidemiological report for 2018. Stockholm: ECDC; 2019 . [Publication pending]

18. European Centre for Disease Prevention and Control. Proposals for EU guidelines on the prudent use of antimicrobials in humans. Stockholm: ECDC; 2017. Available from: https://ecdc.europa. eu/sites/portal/files/media/en/publications/Publications/EU-guidelines-prudent-use-antimicrobials.pdf.

19. D'Atri F, Arthur J, Blix HS, Hicks LA, Plachouras D, Monnet DL et al. Targets for the reduction of antibiotic use in humans in the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) partner countries. Euro Surveill. 2019 Jul;24(28).

20. Brolund A, Lagerqvist N, Byfors S, Struelens MJ, Monnet DL, Albiger B, et al. Worsening epidemiological situation of carbapenemase-producing Enterobacteriaceae in Europe, assessment by national experts from 37 countries, July 2018. Euro Surveill. 2019 Feb;24(9).

21. European Centre for Disease Prevention and Control. Rapid risk assessment: Carbapenem-resistant Enterobacteriaceae – first update 4 June 2018. Stockholm: ECDC; 2018. Available from: http:// ecdc.europa.eu/publications-data/rapid-risk-assessment-carbapenem-resistant-enterobacteriaceae-first-update.

22. European Centre for Disease Prevention and Control. ECDC study protocol for genomic-based surveillance of carbapenem-resistant and/or colistin-resistant Enterobacteriaceae at the EU level. Version 2.0. Stockholm: ECDC; 2018. Available from: http://ecdc.europa. eu/publications-data/ecdc-study-protocol-genomic-based-surveillance-carbapenem-resistant-andor.

23.The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 6.0, 2016. http://www.eucast.org/clinical_breakpoints/.

24. European Food Safety Authority (EFSA) and European Centre for Disease Prevention and Control (ECDC), 2019. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2017. EFSA Journal 2019;17(2):5598, 278 pp. Available from: https://doi.org/10.2903/j.efsa.2019.5598.

25. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2013. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2014. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/antimicrobial-resistance-surveillance-europe-2013.pdf

26. European Centre for Disease Prevention and Control. Rapid risk assessment: Carbapenemase-producing (OXA-48) Klebsiella pneumoniae ST392 in travellers previously hospitalised in Gran Canaria, Spain – 10 July 2018. Stockholm: ECDC; 2018. Available from: http:// www.ecdc.europa.eu/publications-data/rapid-risk-assessmentcarbapenemase-producing-oxa-48-klebsiella-pneumoniae-st392.

27. European Centre for Disease Prevention and Control. Surveillance Atlas of Infectious Diseases [Internet]. Stockholm: ECDC; 2018 [accessed DMY]. Available from: http://atlas.ecdc. europa.eu.

28. European Centre for Disease Prevention and Control. Rapid risk assessment: Regional outbreak of New Delhi metallo-beta-lactamase producing carbapenem-resistant Enterobacteriaceae, Italy, 2018-2019- 4 June 2019. Stockholm: ECDC; 2019. Available from https://ecdc.europa.eu/sites/portal/files/documents/04-Jun-2019-RRA-Carbapenems%2C%20Enterobacteriaceae-Italy.pdf

29. European Centre for Disease Prevention and Control. Directory of online resources for prevention and control of antimicrobial resistance (AMR) and healthcare-associated infections (HAI) [Internet]. Stockholm: ECDC; 2018 [accessed DMY]. Available from: http://ecdc.europa.eu/publications-data/directory-onlineresources-prevention-and-control-antimicrobial-resistance-amr.

30. Magiorakos AP, Burns K, Rodríguez Baño J, Borg M, Daikos G, Dumpis U, *et al*. Infection prevention and control measures and tools for the prevention of entry of carbapenem-resistant Enterobacteriaceae into healthcare settings: guidance from the European Centre for Disease Prevention and Control. Antimicrob Resist Infect Control. 2017 Nov;6:113.

31. European Centre for Disease Prevention and Control. Plasmid mediated colistin resistance in Enterobacteriaceae, 15 June 2016. Stockholm: ECDC; 2016. Available from: http://ecdc.europa.eu/ publications-data/rapid-risk-assessment-plasmid-mediated-colistin-resistance-enterobacteriaceae-15.

32. European Committee on Antimicrobial Susceptibility Testing. Recommendations for MIC determination of colistin (polymyxin E) as recommended by the joint CLSI-EUCAST Polymyxin Breakpoints Working Group. Växjö: EUCAST; 2016. Available from: http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/General_ documents/Recommendations_for_MIC_determination_of_ colis¬tin_March_2016.pdf.

33. European Centre for Disease Prevention and Control. Emergence of resistance to ceftazidime-avibactam in carbapenem-resistant Enterobacteriaceae – 12 June 2018. Stockholm: ECDC; 2018.

34. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Geneva: WHO; 2017. Available from: http://www.who. int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_ NM_WHO.pdf.

35. European Centre for Disease Prevention and Control. Healthcare-associated infections: surgical site infections. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018.

36. European Centre for Disease Prevention and Control. Healthcare-associated infections acquired in intensive care units. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018.

37. Jarlier V, Diaz Högberg L, Heuer OE, Campos J, Eckmanns T, Giske CG. *et al*. Strong correlation between the rates of intrinsically antibiotic-resistant species and the rates of acquired resistance in Gram-negative species causing bacteraemia, EU/EEA, 2016. Euro Surveill. 2019 Aug;24(33).

38. European Centre for Disease Prevention and Control. Rapid risk assessment: Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings – 8 December 2016. Stockholm: ECDC; 2016. Available from: http://ecdc.europa.eu/publications-data/rapidrisk-assessment-carbapenem-resistant-acinetobacter-baumanniihealthcare.

39. European Centre for Disease Prevention and Control. Invasive pneumococcal disease. In: ECDC. Annual epidemiological report for 2017. Stockholm: ECDC; 2019.

40. European Centre for Disease Prevention and Control. Invasive pneumococcal disease. In: Annual epidemiological report for 2016. Stockholm: ECDC, 2018. Available from: http://ecdc.europa.eu/ publications-data/invasive-pneumococcal-disease-annual-epidemiological-report-2016

41. European Centre for Disease Prevention and Control. Vaccine scheduler [Internet]. Stockholm: ECDC; 2019. Available from: http://vaccine-schedule.ecdc.europa.eu.

42. Kinross P, Petersen A, Skov R, Van Hauwermeiren E, Pantosti A, Laurent F, et al. Livestock-associated meticillin-resistant Staphylococcus aureus (MRSA) among human MRSA isolates, European Union/European Economic Area countries, 2013. Euro Surveill. 2017 Nov;22(44).