SURVEILLANCE REPORT

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

## Annual Epidemiological Report for 2020

## Key facts

- Twenty-nine European Union/European Economic Area (EU/EEA) countries reported data for 2020 to the European Antimicrobial Resistance Surveillance Network (EARS-Net). Twenty-eight countries reported data for all eight bacterial species under surveillance by EARS-Net (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter* species, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium*), while one country reported data for all bacterial species except *S. pneumoniae*.
- The most commonly reported bacterial species was *E. coli* (41.3%), followed by *S. aureus* (21.9%), *K. pneumoniae* (11.9%), *E. faecalis* (8.4%), *P. aeruginosa* (6.2%), *E. faecium* (5.5%), *S. pneumoniae* (2.6%), and *Acinetobacter* species (2.3%).
- In 2020, the overall number of reported isolates at EU/EEA level increased compared to 2019 for all bacterial species except *S. pneumoniae*. These increases were not always observed at country level. For *S. pneumoniae*, on the other hand, there was both a large decrease in the overall number of isolates at EU/EEA level between 2019 and 2020 (44.3%; from 15 608 in 2019 to 8 689 in 2020) and similarly large decreases of 20% or more reported in all but one country.
- The AMR situation reported by EU/EEA countries to EARS-Net for 2020 varied widely depending on the bacterial species, antimicrobial group and geographical region. Overall, for the EU/EEA (excluding the United Kingdom[1]), most of the bacterial species-antimicrobial combinations in this report showed either a significantly decreasing trend or no significant trend in the population-weighted mean AMR percentage during 2016–2020. The exceptions to this were carbapenem resistance in *E. coli* and *K. pneumoniae*, and vancomycin resistance in *E. faecium,* for which there was a significant increase during this period.
- In 2020, more than half of the *E. coli* isolates reported to EARS-Net and more than a third of the *K. pneumoniae* isolates were resistant to at least one antimicrobial group under surveillance, and combined resistance to several antimicrobial groups was a frequent occurrence. Among antimicrobial groups monitored for both species, AMR percentages were generally higher in *K. pneumoniae* than in *E. coli*. Carbapenem resistance remained rare in *E. coli*, but almost a quarter of EU/EEA countries reported carbapenem resistance percentages above 10% in *K. pneumoniae*. Carbapenem resistance was also common in *P. aeruginosa* and *Acinetobacter* spp., and at a higher percentage than in *K. pneumoniae*. For most gram-negative bacteria under surveillance, changes in the EU/EEA (excluding the United Kingdom) population-weighted mean AMR percentages between 2016 and 2020 were moderate and AMR remained at high levels, as previously reported.

[1] Please note that as ECDC collects data from EU/EEA Member States, 2016-2019 data was collected by ECDC from the United Kingdom (UK) as the UK was still a Member State of the EU at this time. These data are included in EU/EEA estimates unless the contrary is expressly mentioned.

Suggested citation: European Centre for Disease Prevention and Control. Antimicrobial resistance in the EU/EEA (EARS-Net) - Annual Epidemiological Report 2020. Stockholm: ECDC; 2022.

Stockholm, July 2022

- For *S. aureus*, a decrease in the percentage of MRSA isolates was reported during 2016–2020. MRSA nevertheless remains an important pathogen in the EU/EEA, with levels remaining high in several countries, and combined resistance to another antimicrobial group common. A decreasing trend was also seen during 2016–2020 for the percentage of macrolide resistance in *S. pneumoniae*.
- One development of particular concern was the increasing trend in the EU/EEA (excluding the United Kingdom) population-weighted mean percentage of vancomycin-resistant isolates of *E. faecium*, which increased from 11.6% in 2016 to 16.8% in 2020.
- The reported AMR percentages for several bacterial species–antimicrobial group combinations varied widely among countries, often with a north-to-south and west-to-east gradient. In general, the lowest AMR percentages were reported by countries in the north of Europe, and the highest by countries in the south and east of Europe. There was no distinct geographical pattern for vancomycin-resistant *E. faecium*.

# Methods

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 29 European Union (EU) and European Economic Area (EEA) countries in 2021 (data referring to 2020), and on trend analyses of data reported by the continuously participating countries for the period 2016 to 2020. The latest country-specific data can be retrieved from the European Centre for Disease Prevention and Control (ECDC) Surveillance Atlas of Infectious Diseases [1].

## EARS-Net

EARS-Net is coordinated by ECDC with the aim of collecting, analysing and reporting data on AMR through a network of national surveillance systems across EU/EEA countries and, as defined in the EARS-Net protocol [2], to enable action to address AMR.

EARS-Net is based on a network of representatives (ECDC national focal points for AMR, operational contact points[2] for epidemiology, for microbiology and for The European Surveillance System (TESSy) interaction) from EU/EEA countries that collect routine clinical antimicrobial susceptibility data from national AMR surveillance initiatives. Scientific guidance and support are provided by the EARS-Net Disease Network Coordination Committee, which is composed of experts elected from the nominated ECDC national focal points and operational contact points complemented by observers from organisations involved in AMR surveillance. EARS-Net activities are coordinated in close collaboration with two other 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) and with the European Committee on Antimicrobial Susceptibility Testing (EUCAST), which is supported by ECDC and ESCMID.

In 2020, all EU Member States and two EEA countries (Iceland and Norway) participated in EARS-Net. The number of participating laboratories has increased continuously since the initiation of the network, indicating a strengthening of national AMR surveillance systems in the EU/EEA. Although the EARS-Net external quality assessment (EQA) exercise was cancelled in 2020 due to the COVID-19 pandemic, the high proportion of laboratories that have participated in the annual EARS-Net EQA exercise in previous years contributed to improved data quality and an increasing ability of EU/EEA countries to report comparable AMR data [3].

## Antimicrobial susceptibility data

Every year, countries report routine antimicrobial susceptibility testing (AST) results collected from one or more medical microbiology laboratories to EARS-Net. Countries can report data from sentinel laboratories if it is not possible to include data from all their relevant laboratories. The AMR surveillance focuses on invasive isolates of eight key bacterial species (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter* species, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium*). Other notifiable diseases caused by microorganisms with AMR, such as *Neisseria gonorrhoeae*, *Salmonella* spp., *Campylobacter* spp. and *Mycobacterium tuberculosis*, are also monitored by ECDC under other surveillance networks but are not included in EARS-Net.

[2] https://www.ecdc.europa.eu/sites/default/files/media/en/aboutus/governance/competent-bodies/Documents/coordinating-competent-bodies-structures-terms-of-reference-and-interactions-w-Annexes.pdf

EARS-Net collects AMR data from EU/EEA countries through TESSy, a web-based platform for data submission and storage hosted by ECDC [4]. Detailed information on data collection is included in the EARS-Net reporting protocol [2].

Only data from invasive (blood and cerebrospinal fluid) isolates are included in EARS-Net. This restriction aims to reduce the impact of different sampling frames that to some extent hamper data interpretation. Any bacterial isolate of the species under surveillance found in a sample taken from a normally sterile body fluid may be considered a pathogen. Including routine non-invasive isolates may produce incomparable results for surveillance purposes, as the processing of such samples is heavily influenced by clinical interpretation, which varies between countries. Historically, EARS-Net accepted data on isolates from both specimen types for *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* spp. and *S. pneumoniae*, while only isolates from blood were accepted for *S. aureus*, *E. faecalis* and *E. faecium*. To harmonise data collection between the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network and EARS-Net, EARS-Net includes data from both specimen types for all bacterial species, starting with 2019 data.

Starting with the data collected for 2019, EARS-Net only accepts data generated using EUCAST breakpoints and methodology [5]. Before this, the use of EUCAST breakpoints was encouraged, but results based on other interpretive criteria used by reporting countries were also accepted for analysis.

Correction and re-uploading of historical data by reporting countries is possible. The latest published report therefore supersedes previous reports and reflects the most recent available data. This report is based on data reported to EARS-Net for the period 2016–2020 and retrieved from TESSy on 20 September 2021.

# Data analysis

Before data analysis, data are de-duplicated to include only the first isolate per patient, year and bacterial species.

## Susceptibility test categories

For the analysis, the qualitative susceptibility categories – S (susceptible, standard dosing regimen), I (susceptible, increased exposure) and R (resistant) – are used, as reported by the laboratory, since quantitative susceptibility information is missing for a large part of the data. An isolate is considered resistant to an antimicrobial agent when tested and interpreted as R in accordance with the clinical breakpoint criteria used by the local laboratory. The term 'penicillin non-wild-type' is used in this report for *Streptococcus pneumoniae*, referring to *S. pneumoniae* isolates reported by local laboratories as I or R to penicillin, assuming minimum inhibitory concentrations (MIC) to benzylpenicillin above those of wild-type isolates (>0.06 mg/L). Data reported before 2019 may include results obtained using different interpretive criteria for the susceptibility categories.

## National percentages

Resistance/non-wild-type percentages are presented for a single antimicrobial agent and/or for a group of antimicrobial agents. The bacterial species–antimicrobial agent combinations presented in this report for 2020 are shown in Table 1. When combining results for antimicrobial agents representing an antimicrobial group, the outcome is based on the most resistant result. For example, if the AST result of a bacterial species for imipenem is I and AST result for meropenem is R, then the AST result for the group carbapenems, which comprises imipenem and meropenem, is set to R. Combined AMR is determined as R to at least one antimicrobial agent in each of the antimicrobial groups in the definition of combined AMR (with the exception of *S. pneumoniae*, for which combined AMR is calculated as combined penicillin non-wild-type and macrolide resistance). Isolates with missing data for one or more of the required antimicrobial groups are excluded from the analysis of combined AMR. If fewer than 10 isolates are reported for a specific bacterial species–antimicrobial group combination in a country, the AMR percentage is not displayed in the maps or tables presented in this report.

## Population-weighted EU/EEA mean percentage

A population-weighted EU/EEA mean percentage is calculated for each bacterial species–antimicrobial agent combination, based on data reported by EU/EEA countries. Country weightings are used to adjust for imbalances in reporting propensity and population coverage, as in most cases the total number of reported isolates by country does not reflect the population size.

The population-weighted EU/EEA mean percentage is determined by multiplying the AMR percentage for each EU/EEA country with the corresponding national population weight based on the total EU/EEA population and summing up the results. Weights are rescaled if AMR percentages are not available for one or more countries. Annual population data are retrieved from the Eurostat online database [6].

## Trend analyses

The statistical significance of temporal trends in AMR percentages by country and for the population-weighted EU/EEA (excluding the United Kingdom) mean is calculated based on data from the last five years (2016–2020). Countries that did not report data for all years within the period under consideration or which reported fewer than 20 isolates for the specific bacterial species–antimicrobial agent/group combination in any year within the period are not included in the analysis. The statistical significance of trends is assessed by a chi-square test for trend, and a p-value of <0.05 is considered significant. An additional sensitivity analysis is performed when assessing the significance of the trends by including only laboratories that consistently reported data for the full five-year period, thereby minimising bias due to changes in reporting laboratories over time (by expansion of the surveillance network, for instance). In some cases, this restriction results in a considerably lower number of isolates when compared with the analysis that includes all laboratories.

# Coverage and representativeness of population, hospitals and patients included in EARS-Net

## Data sources

Data on coverage, blood-culture sets and representativeness from 2018 onwards are collected via TESSy [2], while data for earlier years combine TESSy data with those collected through questionnaires distributed to the national focal points for AMR.

## Indicators of coverage and representativeness

### *Population coverage*

Population coverage is expressed as the estimated percentage of the population in an entire country covered by the laboratories contributing data to EARS-Net. This value should be considered as an indication of the crude population coverage, as the exact proportion of the population under surveillance is often difficult to assess due to overlapping hospital population catchment areas and patients seeking care in areas where they do not reside. The population coverage is calculated as the mean of the coverage for the following bacterial species: *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *E. faecalis* and *E. faecium*. Due to outliers in some countries, *S. pneumoniae* and *Acinetobacter* spp. are not included in the calculation.

### *Geographical representativeness*

Geographical representativeness is a qualitative indicator referring to geographical coverage and the distribution of urban and regional areas. The categories are listed and described in Table 2.

### *Hospital representativeness*

Hospital representativeness is a qualitative indicator referring to the representativeness of hospitals served by the EARS-Net participating laboratories, compared to the country distribution of hospital types. The categories are listed and described in Table 2.

### *Patient and isolate representativeness*

Patient and isolate representativeness is a qualitative indicator referring to the representativeness of data reported by EARS-Net laboratories in relation to the patient mix in which infections with invasive microorganisms occur and what microorganisms cause these infections. The categories are listed and described in Table 2.

### *Blood-culture rate*

Blood-culture rate refers to the number of blood-culture sets performed per 1 000 patient-days in hospitals served by EARS-Net laboratories. The definition of a blood-culture set and a patient-day may differ between countries and this may influence the estimate. Blood-culture rates are calculated as the mean of blood-culture sets and the mean total number of patient-days for hospitals served by laboratories that provided the number of blood-culture sets performed for the following bacterial species: *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *E. faecalis* and *E. faecium*. Due to outliers in some countries, *S. pneumoniae* and *Acinetobacter* spp. are not included in the calculation. The blood-culture rates are presented as the number of blood-culture sets taken per 1 000 patient-days in hospitals providing AMR data to EARS-Net.

**Table 1. Bacterial species-antimicrobial agent combinations presented in this report for 2020**

| Bacterial species | Antimicrobial group/agent or specific resistance mechanism | Antimicrobial agent(s) |
|---|---|---|
| *Escherichia coli* | Aminopenicillins | Ampicillin or amoxicillin |
| | Third-generation cephalosporins | Cefotaxime, ceftriaxone or ceftazidime |
| | Carbapenems | Imipenem or meropenem |
| | Fluoroquinolones | Ciprofloxacin, levofloxacin or ofloxacin |
| | Aminoglycosides | Gentamicin or tobramycin |
| *Klebsiella pneumoniae* | Third-generation cephalosporins | Cefotaxime, ceftriaxone or ceftazidime |
| | Carbapenems | Imipenem or meropenem |
| | Fluoroquinolones | Ciprofloxacin, levofloxacin or ofloxacin |
| | Aminoglycosides | Gentamicin or tobramycin |
| *Pseudomonas aeruginosa* | Piperacillin-tazobactam | Piperacillin-tazobactam |
| | Ceftazidime | Ceftazidime |
| | Carbapenems | Imipenem or meropenem |
| | Fluoroquinolones | Ciprofloxacin or levofloxacin |
| | Aminoglycosides | Tobramycin |
| *Acinetobacter* species | Carbapenems | Imipenem or meropenem |
| | Fluoroquinolones | Ciprofloxacin or levofloxacin |
| | Aminoglycosides | Gentamicin or tobramycin |
| *Staphylococcus aureus* | MRSA | Oxacillin or cefoxitin[a] |
| | Fluoroquinolones | Ciprofloxacin, levofloxacin, or ofloxacin[b] |
| | Rifampicin | Rifampicin |
| *Streptococcus pneumoniae* | Penicillins | Penicillin or oxacillin[c] |
| | Third-generation cephalosporins | Cefotaxime or ceftriaxone |
| | Fluoroquinolones | Levofloxacin or moxifloxacin[d] |
| | Macrolides | Azithromycin, clarithromycin, or erythromycin |
| *Enterococcus faecalis* | High-level aminoglycoside resistance | Gentamicin high-level resistance |
| *Enterococcus faecium* | Aminopenicillins | Ampicillin or amoxicillin |
| | High-level aminoglycoside resistance | Gentamicin high-level resistance |
| | Vancomycin | Vancomycin |

*MRSA: meticillin-resistant* Staphylococcus aureus.

[a] *MRSA is based on AST results for oxacillin or cefoxitin, but AST results reported as cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if AST results for oxacillin are not reported. Data from molecular confirmation tests (detection of* mecA *gene by polymerase chain reaction (PCR) or a positive PBP2A-agglutionation test) are given priority over phenotypic AST results.*

[b] *AST results for norfloxacin are also accepted if neither ciprofloxacin, levofloxacin nor ofloxacin results are available.*

[c] *Penicillin results are based on penicillin or, if not available, oxacillin.*

[d] *AST results for norfloxacin are also accepted if neither levofloxacin nor moxifloxacin results are available.*

**Table 2. Population and hospitals contributing data: coverage, representativeness and blood culture rate, EU/EEA, 2020 (or latest available data)**

| Country | Estimated population coverage[a] (%) | Geographical representativeness[b] | Hospital representativeness[c] | Patient and isolate representativeness[d] | Blood culture rate (blood culture sets/1 000 patient-days)[e] |
|---|---|---|---|---|---|
| Austria | Unknown | High | High | High | Unknown |
| Belgium | 36[f] | High | High | High | 129.6[f] |
| Bulgaria | 45 | Medium | Medium | Medium | 10.4 |
| Croatia | 80 | High | High | High | 109 |
| Cyprus | 85 | High | High | High | 60.9 |
| Czechia | 80 | High | High | High | 19.7 |
| Denmark | 100 | High | High | High | 202.4 |
| Estonia | 100 | High | High | High | 35.8 |
| Finland | 96 | High | High | High | 175.1 |
| France | 48[f] | High | High | High | 54.5[f] |
| Germany[g] | 27 | High | Medium | High | 37.9 |
| Greece | 60 | High | High | Medium | Unknown |
| Hungary | 90 | High | High | High | 17.2 |
| Iceland | 100 | High | High | High | 61.3 |
| Ireland | 76 | High | High | High | Unknown |
| Italy | 47 | High | High | High | 57 |

| Country | Estimated population coverage[a] (%) | Geographical representativeness[b] | Hospital representativeness[c] | Patient and isolate representativeness[d] | Blood culture rate (blood culture sets/1 000 patient-days)[e] |
|---|---|---|---|---|---|
| Latvia | 90 | High | Medium | Medium | 13.8 |
| Liechtenstein | - | - | - | - | - |
| Lithuania | 100 | High | High | High | 8.1 |
| Luxembourg | 99 | High | High | High | 38.9 |
| Malta | 95 | High | High | High | 35.2 |
| Netherlands | 72 | High | High | High | Unknown |
| Norway | 94 | High | High | High | 91.9 |
| Poland | 16 | Medium | Medium | Medium | 45.6 |
| Portugal | 97 | High | High | High | 244.2 |
| Romania | 21 | Poor | Poor | Poor | 26.4 |
| Slovakia | 56 | High | High | High | 27.0 |
| Slovenia | 99 | High | High | High | 47.1 |
| Spain | 36 | Medium | High | High | 109.5 |
| Sweden | 78 | High | High | High | 105.6 |

[a] *As estimated by the national focal points for AMR and/or operational contact points for AMR. Estimated national population coverage: mean population coverage (%) of laboratories capable of reporting* Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis *and* Enterococcus faecium*. Due to outliers in some countries,* S. pneumoniae *and* Acinetobacter *species are not included in the calculation.*

[b] *Geographical representativeness. High: all main geographical regions are covered and the selection of urban and regional areas are considered to be representative of the country population. Medium: most geographical regions are covered and the selection of urban and regional areas are considered to be partly representative of the country population. Poor: only one or a few geographical areas are covered and the selection of urban and regional areas are considered to be poorly representative of the country population. Unknown: unknown or no data provided.*

[c] *Hospital representativeness. High: the hospital selection is representative of the country distribution of hospital types where blood samples are taken. Medium: the hospital selection is partly representative of the country distribution of hospital types where blood samples are taken. Poor: the hospital selection is poorly representative of the country distribution of hospital types where blood samples are taken. Unknown: unknown or no data provided.*

[d] *Patient and isolate representativeness. High: the patient selection is representative of the patient mix for the hospitals included and of microorganisms causing invasive infections. Medium: the patient selection is partly representative of the patient mix for the hospitals included and of microorganisms causing invasive infections. Poor: the patient selection is poorly representative of the patient mix for the hospitals included and of microorganisms causing invasive infections. Unknown: unknown or no data provided.*

[e] *Blood culture rate (blood culture sets/1 000 patient-days): refers to the number of blood culture sets per 1 000 patient-days in hospitals served by EARS-Net laboratories. The definition of a blood culture set and a patient-day might differ between countries and influence the estimate. Blood culture rates are presented as the number of blood culture sets taken per 1 000 patient-days in hospitals providing AMR data. This is calculated by dividing the mean of blood culture sets with the mean total number of patient-days of hospitals served by laboratories that provided the number of blood culture sets performed for the following bacterial species:* Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis *and* Enterococcus faecium.

[f] *Not including the country's* Streptococcus pneumoniae *network.*

[g] *2019 data*

# Overview of bacterial species under EARS-Net surveillance in the EU/EEA

## Epidemiology

Twenty-nine EU/EEA countries reported data for 2020 to EARS-Net. Twenty-eight reported data for all eight bacterial species under surveillance by EARS-Net (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* spp., *S. pneumoniae*, *S. aureus*, *E. faecalis* and *E. faecium*), while one (Greece) reported data for all bacterial species except *S. pneumoniae*. The most commonly reported bacterial species was *E. coli* (41.3%), followed by *S. aureus* (21.9%), *K. pneumoniae* (11.9%), *E. faecalis* (8.4%), *P. aeruginosa* (6.2%), *E. faecium* (5.5%), *S. pneumoniae* (2.6%) and *Acinetobacter* spp. (2.3%). The overall number of reported isolates at EU/EEA level increased in 2020 compared to 2019 for all bacterial species except *S. pneumoniae*. These increases were not always observed at country level. For *S. pneumoniae*, on the other hand, there was both a large decrease in the overall number of isolates at EU/EEA level between 2019 and 2020 (44.3%; from 15 608 in 2019 to 8 689 in 2020) and similarly large decreases of 20% or more reported in all but one country (Cyprus).

For each bacterial species, country-specific information on data availability and age group, sex and ICU patient percentages is available in the country profiles. Results by age group and sex for specific AMR phenotypes are available in ECDC's Surveillance Atlas of Infectious Diseases [1].

The AMR situation reported by EU/EEA countries to EARS-Net for 2020 varied widely depending on the bacterial species, antimicrobial group and geographical region (Table 3a, Figures 1–10 and country profiles). Overall, for the EU/EEA (excluding the United Kingdom), most of the bacterial species–antimicrobial combinations in this report showed either a significantly decreasing trend or no significant trend in the population-weighted mean AMR percentage during 2016–2020. The exceptions to this were carbapenem resistance in *E. coli* and *K. pneumoniae* and vancomycin resistance in *E. faecium*, for which there was a significant increase during this period (Table 3b).

In 2020, more than half of the *E. coli* isolates reported to EARS-Net and more than a third of the *K. pneumoniae* isolates were resistant to at least one antimicrobial group under surveillance, and combined resistance to several antimicrobial groups was a frequent occurrence. Among antimicrobial groups monitored for both species, AMR percentages were generally higher in *K. pneumoniae* than in *E. coli*. Carbapenem resistance remained rare in *E. coli*, but almost a quarter of EU/EEA countries reported carbapenem resistance percentages above 10% in *K. pneumoniae*. Carbapenem resistance was also common in *P. aeruginosa* and *Acinetobacter* spp., and at a higher percentage than in *K. pneumoniae*. For most gram-negative bacteria under surveillance, changes in the EU/EEA (excluding the United Kingdom) population-weighted mean AMR percentages between 2016 and 2020 were moderate and AMR remained at high levels, as previously reported.

For *S. aureus*, a decrease in the percentage of MRSA isolates was reported during 2016–2020 (Table 3b). MRSA nevertheless remains an important pathogen in the EU/EEA, with levels remaining high in several countries and combined resistance to another antimicrobial group common. A decreasing trend was also seen during 2016–2020 for the percentage of macrolide resistance in *S. pneumoniae* (Table 3b).

One development of particular concern was the increasing trend in the EU/EEA (excluding the United Kingdom) population-weighted mean percentage of vancomycin resistant isolates of *E. faecium*, which increased from 11.6% in 2016 to 16.8% in 2020.

The reported AMR percentages for several bacterial species–antimicrobial group combinations varied widely among countries, often with a north-to-south and west-to-east gradient. In general, the lowest AMR percentages were reported by countries in the north of Europe and the highest by countries in the south and east of Europe. There was no distinct geographical pattern for vancomycin-resistant *E. faecium*.

## Discussion

In March 2020, the World Health Organization (WHO) characterised COVID-19 as a new pandemic [7]. SARS-CoV-2 presented the world with a new and globally distributed infectious agent that affected public health across the planet, albeit with vaccines developed and recommended for authorisation towards the end of 2020 [8]. Despite the pandemic, all EU/EEA countries that regularly report AMR data reported 2020 data in 2021.

The COVID-19 pandemic and the related public health interventions may have affected 2020 AMR data in different ways and to varying degrees over time. Examples of this include changes in hospital admission patterns and patient case-mix [9], antimicrobial prescription patterns [9], laboratory reporting capacity, and the implementation of non-pharmaceutical interventions (NPIs) introduced to reduce SARS-CoV-2 transmission [9]. Decreased circulation of pathogens in the community because of NPIs could for example potentially explain the decrease in the number of *S. pneumoniae* isolates reported by EU/EEA countries for 2020.

The decreasing AMR trends in the EU/EEA (excluding the United Kingdom) during 2016–2020 for several bacterial species-antimicrobial group combinations under surveillance by EARS-Net had in most cases already been noted in the annual epidemiological report for 2019 [10]. Significantly increasing trends for carbapenem resistance in *E. coli* and *K. pneumoniae* and vancomycin resistance in *E. faecium* were observed for the period 2016–2020 (excluding the United Kingdom), similar to the previously reported trends for 2015–2019 when the United Kingdom was included [10].

A large decrease in community antibiotic consumption in the EU/EEA was reported by ESAC-Net for 2020 [11]. Concomitant large changes in the AMR percentages were not observed at EU/EEA level in EARS-Net. For *E. coli*, there was a larger decrease in the percentages of resistance to aminopenicillins and third-generation cephalosporins in the EU/EEA in 2020 than for each year during the period 2016–2019. For a few other bacterial species-antimicrobial group combinations, there were large increases in AMR percentages at EU/EEA level between 2019 and 2020, although an increasing trend during 2016–2020 (excluding the United Kingdom) was reported only for carbapenem resistance in *K. pneumoniae*.

Limitations to the quality of AMR data and interpretation of AMR percentages should be taken into consideration. For example, there have been changes in the reporting of data to EARS-Net over time within countries and at EU/EEA level. This could have influenced the results, and this fact should be borne in mind when interpreting trends. The analysis for *P. aeruginosa* and aminoglycoside resistance, for instance, changed: previously the analysis included netilmicin, gentamicin and tobramycin, but from 2020 onwards it only includes tobramycin. This hampers interpretation of the decrease in aminoglycoside resistance percentages observed for 2020. Other examples are changes to country surveillance systems, which may affect the interpretation of the AMR percentages over time (country profiles), and restriction on data generated using EUCAST breakpoints and methodology, starting with data collected for 2019. The restriction to EUCAST breakpoints and methodology should, however, improve quality and comparability of data in the long term.

Antimicrobial resistance (AMR) percentages for the bacterial species-antimicrobial group combinations under surveillance continue to be high overall in the EU/EEA and the large variability in the percentages across EU/EEA countries remained in 2020. This highlights the opportunities for significant AMR reduction through interventions to improve interventions on infection prevention and control (IPC) and antimicrobial stewardship practices.

For healthcare settings, results from the ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals showed that the prevalence of patients receiving antibiotics was positively associated with AMR and, conversely, higher antibiotic stewardship activities and resources for IPC were associated with lower AMR percentages [12]. Another study showed that knowledge and perceived knowledge about antibiotics, antibiotic use and antibiotic resistance was high among healthcare workers in EU/EEA countries, while highlighting areas where there was a need for educational interventions [13]. Prudent antimicrobial use and high standards of IPC in all healthcare sectors remain the cornerstones of an effective response to AMR, and these studies highlight areas for improvement in healthcare settings across the EU/EEA.

The long-term effects on AMR of the large decrease in community antibiotic consumption observed in almost all EU/EEA countries in 2020 [11] remain to be seen. 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. Antimicrobial use exerts an ecological pressure on microorganisms and contributes to the emergence and selection of AMR, and poor IPC practices promote further spread of antimicrobial-resistant microorganisms. Prudent use of antimicrobials is therefore advisable, and relevant EU guidelines have been published by the European Commission [14]. Moreover, the importance of infection prevention in society as a whole through, for example, appropriate hand hygiene and vaccination should not be overlooked.

Reducing AMR calls for concerted efforts at country level and close international cooperation. In 2017, the European Commission adopted a European One Health Action Plan against AMR to support the EU and its Member States in delivering innovative, effective and sustainable responses to this issue[15]. A majority of EU/EEA countries in a 2017 survey reported having implemented or initiated work towards establishing objectives and targets for the reduction of antibiotic use in humans, often through the development of a national action plan (NAP) on AMR. Only a few, however, had published these targets in 2017 [16] and had identified specific funding sources to implement their NAPs [12]. As of 2020, 25 out of 29 EU/EEA countries had reported having a NAP on AMR and three others were in the process of developing a NAP [17].

# Public health implications

The high levels of AMR for several important bacterial species-antimicrobial group combinations reported to EARS-Net for 2020 show that AMR remains a serious challenge in the EU/EEA. Indeed, AMR is a considerable threat to public health, both in the EU/EEA [15] and worldwide [18]. Estimates based on data from EARS-Net show that each year, more than 670 000 infections occur in the EU/EEA due to bacteria resistant to antibiotics, and that approximately 33 000 people die as a direct consequence of these infections [19]. The related cost to the healthcare systems of EU/EEA countries is estimated to be around €1.1 billion [12].

Public health action to tackle AMR remains insufficient, despite the increased awareness of AMR as a threat to public health and the availability of evidence-based guidance for IPC, antimicrobial stewardship and adequate microbiological capacity. AMR will be an increasing concern unless governments respond more robustly to the threat. Further investment in public health interventions is urgently needed to tackle AMR. This would have a significant positive impact on population health and future healthcare expenditure in the EU/EEA. It has been estimated that a mixed intervention package that included antibiotic stewardship programmes, enhanced hygiene, mass media campaigns, and the use of rapid diagnostic tests would have the potential to prevent approximately 27 000 deaths each year in the EU/EEA. In addition to saving lives, such a public health package could pay for itself within just one year and save around €1.4 billion per year in the EU/EEA [12].

**Table 3a. Total number of invasive isolates tested (N) and percentage of isolates with AMR phenotype (%) in the EU/EEA, by bacterial species and antimicrobial group/agent, population-weighted EU/EEA mean, 2016–2020**

| Bacterial species | Antimicrobial group/agent | 2016[a] | | 2017[a] | | 2018[a] | | 2019[a] | | 2020[b] | | 2020 EU/EEA country range[c] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % | N | % | |
| ***Escherichia coli*** | Aminopenicillin (amoxicillin/ampicillin) resistance | 108 239 | 59.0 | 125 866 | 58.7 | 133 700 | 57.5 | 130 603 | 57.1 | 105 827 | 54.6 | 34.1-67.5 |
| | Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance | 123 944 | 14.9 | 140 584 | 14.9 | 152 720 | 15.1 | 157 918 | 15.1 | 137 465 | 14.9 | 5.8-41.4 |
| | Carbapenem (imipenem/meropenem) resistance | 122 437 | 0.1 | 140 438 | 0.1 | 151 457 | 0.1 | 156 871 | 0.3 | 134 032 | 0.2 | 0.0-0.8 |
| | Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance | 125 161 | 25.2 | 141 562 | 25.7 | 154 698 | 25.3 | 161 718 | 23.8 | 137 785 | 23.8 | 10.0-48.2 |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d] | 124 480 | 11.6 | 141 788 | 11.4 | 154 266 | 11.1 | 161 432 | 10.8 | 134 683 | 10.9 | 5.5-34.2 |
| | Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[d] | 121 582 | 6.4 | 135 108 | 6.3 | 148 206 | 6.2 | 154 844 | 5.9 | 132 705 | 5.7 | 1.6-18.7 |
| ***Klebsiella pneumoniae*** | Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance | 30 633 | 31.4 | 32 969 | 31.2 | 38 436 | 31.7 | 41 057 | 31.4 | 39 579 | 33.9 | 0.0-79.1 |
| | Carbapenem (imipenem/meropenem) resistance | 30 309 | 7.4 | 32 960 | 7.1 | 38 140 | 7.5 | 40 714 | 8.0 | 39 006 | 10.0 | 0.0-66.3 |
| | Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance | 30 769 | 30.3 | 32 924 | 31.5 | 38 770 | 31.6 | 41 617 | 31.3 | 39 794 | 33.8 | 0.0-74.4 |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d] | 30 209 | 24.4 | 33 136 | 24.1 | 38 555 | 22.7 | 41 484 | 22.4 | 38 733 | 23.7 | 0.0-67.0 |
| | Combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides[d] | 29 589 | 20.6 | 31 613 | 20.5 | 37 402 | 19.5 | 40 270 | 19.4 | 38 094 | 21.0 | 0.0-58.3 |
| ***Pseudomonas aeruginosa*** | Piperacillin-tazobactam resistance | 15 125 | 17.5 | 16 428 | 16.7 | 18 607 | 16.8 | 19 465 | 17.0 | 19 695 | 18.8 | 4.4-64.3 |
| | Ceftazidime resistance | 15 219 | 14.4 | 16 512 | 14.7 | 18 960 | 14.1 | 19 959 | 14.3 | 20 014 | 15.5 | 2.9-54.3 |
| | Carbapenem (imipenem/meropenem) resistance | 15 573 | 18.2 | 17 109 | 17.4 | 19 233 | 17.2 | 20 238 | 16.6 | 20 414 | 17.8 | 3.6-48.9 |
| | Fluoroquinolone (ciprofloxacin/levofloxacin) resistance | 15 504 | 18.8 | 16 951 | 20.2 | 19 211 | 19.7 | 20 384 | 18.9 | 20 279 | 19.6 | 3.2-52.9 |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[e] | 15 525 | 14.0 | 16 979 | 13.2 | 19 186 | 11.8 | 20 344 | 11.5 | 12 840 | 9.4 | 0.0-37.1 |
| | Combined resistance to ≥3 antimicrobial groups (among piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)[e] | 15 628 | 13.4 | 17 129 | 13.0 | 19 306 | 12.6 | 20 406 | 12.1 | 20 421 | 12.1 | 0.0-47.1 |
| ***Acinetobacter* species** | Carbapenem (imipenem/meropenem) resistance | 5 590 | 32.6 | 6 186 | 33.1 | 6 526 | 31.9 | 5 958 | 32.4 | 7 542 | 38.0 | 0.0-96.4 |
| | Fluoroquinolone (ciprofloxacin/levofloxacin) resistance | 5 596 | 37.5 | 6 098 | 37.4 | 6 496 | 36.2 | 5 923 | 36.6 | 7 392 | 41.8 | 0.0-98.2 |

| Bacterial species | Antimicrobial group/agent | 2016[a] | | 2017[a] | | 2018[a] | | 2019[a] | | 2020[b] | | 2020 EU/EEA country range[c] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % | N | % | |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d] | 5 562 | 32.7 | 6 042 | 32.2 | 6 459 | 31.3 | 5 915 | 32.7 | 7 306 | 37.1 | 0.0-96.4 |
| | Combined resistance to carbapenems, fluoroquinolones and aminoglycosides[d] | 5 418 | 28.3 | 5 872 | 28.2 | 6 294 | 28.3 | 5 682 | 29.4 | 7 140 | 34.1 | 0.0-95.1 |
| ***Staphylococcus aureus*** | MRSA[f] | 57 730 | 17.7 | 66 279 | 16.8 | 72 882 | 16.4 | 74 718 | 15.7 | 72 314 | 16.7 | 1.4-49.1 |
| ***Streptococcus pneumoniae*** | Penicillin non-wild-type[g] | 15 666 | 13.1 | 17 212 | 12.9 | 18 676 | 12.9 | 18 235 | 12.2 | 8 032 | 15.6 | 3.9-56.3 |
| | Macrolide (azithromycin/clarithromycin/erythromycin) resistance | 16 027 | 16.6 | 17 613 | 15.7 | 19 217 | 15.2 | 18 940 | 14.5 | 8 362 | 16.9 | 3.5-43.8 |
| | Combined penicillin non-wild-type and resistance to macrolides[g] | 15 182 | 8.4 | 16 584 | 8.2 | 18 082 | 7.8 | 17 529 | 7.3 | 7 739 | 9.0 | 0.0-37.5 |
| ***Enterococcus faecalis*** | High-level gentamicin resistance | 12 910 | 31.8 | 13 930 | 29.7 | 15 343 | 27.1 | 13 596 | 26.8 | 14 279 | 29.0 | 4.1-51.6 |
| ***Enterococcus faecium*** | Vancomycin resistance | 12 511 | 12.3 | 14 213 | 14.9 | 15 992 | 17.3 | 16 549 | 18.2 | 18 151 | 16.8 | 0.0-56.6 |

*[a] Number of EU/EEA countries: 30 (2016-2019).*
*[b] Number of EU/EEA countries: 29, i.e. excluding the United Kingdom (2020).*
*[c] Lowest and highest national AMR percentage among reporting EU/EEA countries in 2020 (n = 29).*
*[d] The aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.*
*[e] The aminoglycoside group includes only tobramycin from 2020 onwards.*
*[f] MRSA is based on AST results for oxacillin or cefoxitin, but AST results reported as cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if AST results for oxacillin are not reported. Data from molecular confirmation tests (detection of* mecA *gene by PCR or a positive PBP2A-agglutionation test) are given priority over phenotypic AST results.*
*[g] Penicillin results are based on penicillin or, if not available, oxacillin. For* Streptococcus pneumoniae*, the term penicillin non-wild-type is used in this report, referring to* S. pneumoniae *isolates reported by local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MIC to benzylpenicillin above those of wild-type isolates (>0.06 mg/L). The qualitative susceptibility categories (S/I/R) as reported by the laboratory are used, since quantitative susceptibility information is missing for a large part of the data. Laboratories not using EUCAST clinical breakpoints in the period 2016–2018 might have used different interpretive criteria for the susceptibility categories.*

**Table 3b. Total number of invasive isolates tested (N) and percentages isolates with AMR phenotype (%) in the EU/EEA (excluding the United Kingdom), by bacterial species and antimicrobial group/agent, population-weighted EU/EEA mean and trend (excluding the United Kingdom), 2016–2020**

| Bacterial species | Antimicrobial group/agent | 2016 | | 2017 | | 2018 | | 2019 | | 2020 | | 2020 EU/EEA country range[a] | Trend 2016-2020[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % | N | % | N | % | | |
| ***Escherichia coli*** | Aminopenicillin (amoxicillin/ampicillin) resistance | 86 625 | 58.4 | 97 219 | 58.1 | 104 198 | 57.0 | 102 375 | 56.6 | 105 827 | 54.6 | 34.1-67.5 | ↓ |
| | Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance | 102 098 | 15.7 | 112 659 | 15.6 | 124 043 | 15.7 | 131 325 | 15.6 | 137 465 | 14.9 | 5.8-41.4 | ↓ |
| | Carbapenem (imipenem/meropenem) resistance | 99 675 | 0.1 | 110 364 | 0.1 | 120 228 | 0.1 | 127 262 | 0.3 | 134 032 | 0.2 | 0.0-0.8 | ↑ |
| | Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance | 102 278 | 26.4 | 111 377 | 26.9 | 123 358 | 26.4 | 132 015 | 24.7 | 137 785 | 23.8 | 10.0-48.2 | ↓ |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c] | 101 314 | 11.8 | 111 049 | 11.6 | 122 147 | 11.2 | 130 984 | 10.8 | 134 683 | 10.9 | 5.5-34.2 | ↓ |
| | Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[c] | 100 481 | 6.7 | 108 300 | 6.6 | 120 450 | 6.4 | 129 083 | 6.1 | 132 705 | 5.7 | 1.6-18.7 | ↓ |
| ***Klebsiella pneumoniae*** | Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance | 26 719 | 34.7 | 27 996 | 34.1 | 33 255 | 34.4 | 36 190 | 34.1 | 39 579 | 33.9 | 0.0-79.1 | - |
| | Carbapenem (imipenem/meropenem) resistance | 26 241 | 8.4 | 27 686 | 8.1 | 32 548 | 8.5 | 35 439 | 9.0 | 39 006 | 10.0 | 0.0-66.3 | ↑ |
| | Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance | 26 704 | 33.6 | 27 631 | 34.7 | 33 170 | 34.3 | 36 315 | 34.0 | 39 794 | 33.8 | 0.0-74.4 | - |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c] | 26 074 | 27.0 | 27 773 | 26.4 | 32 846 | 24.7 | 36 078 | 24.5 | 38 733 | 23.7 | 0.0-67.0 | ↓ |
| | Combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides[c] | 25 825 | 23.0 | 26 853 | 22.9 | 32 397 | 21.6 | 35 622 | 21.5 | 38 094 | 21.0 | 0.0-58.3 | ↓ |
| ***Pseudomonas aeruginosa*** | Piperacillin-tazobactam resistance | 13 086 | 19.2 | 13 731 | 18.4 | 16 018 | 18.5 | 16 894 | 18.6 | 19 695 | 18.8 | 4.4-64.3 | - |
| | Ceftazidime resistance | 13 198 | 15.9 | 13 832 | 16.1 | 16 339 | 15.5 | 17 328 | 15.7 | 20 014 | 15.5 | 2.9-54.3 | - |
| | Carbapenem (imipenem/meropenem) resistance | 13 465 | 20.1 | 14 305 | 19.1 | 16 485 | 18.8 | 17 496 | 18.1 | 20 414 | 17.8 | 3.6-48.9 | ↓ |
| | Fluoroquinolone (ciprofloxacin/levofloxacin) resistance | 13 385 | 20.6 | 14 149 | 22.0 | 16 472 | 21.2 | 17 635 | 20.5 | 20 279 | 19.6 | 3.2-52.9 | ↓ |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d] | 13 385 | 15.6 | 14 148 | 14.5 | 16 405 | 12.9 | 17 552 | 12.6 | 12 840 | 9.4 | 0.0-37.1 | ↓ |
| | Combined resistance to ≥3 antimicrobial groups (among piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)[d] | 13 497 | 15.0 | 14 299 | 14.5 | 16 535 | 14.1 | 17 628 | 13.5 | 20 421 | 12.1 | 0.0-47.1 | ↓ |
| ***Acinetobacter* species** | Carbapenem (imipenem/meropenem) resistance | 5 006 | 37.1 | 5 404 | 37.6 | 5 812 | 36.3 | 5 240 | 36.9 | 7 542 | 38.0 | 0.0-96.4 | - |
| | Fluoroquinolone (ciprofloxacin/levofloxacin) resistance | 5 007 | 42.3 | 5 305 | 41.9 | 5 776 | 41.1 | 5 216 | 41.0 | 7 392 | 41.8 | 0.0-98.2 | - |
| | Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c] | 4 964 | 37.0 | 5 252 | 36.3 | 5 733 | 35.2 | 5 194 | 36.8 | 7 306 | 37.1 | 0.0-96.4 | - |
| | Combined resistance to carbapenems, fluoroquinolones and aminoglycosides[c] | 4 860 | 32.3 | 5 126 | 32.1 | 5 618 | 32.4 | 5 012 | 33.6 | 7 140 | 34.1 | 0.0-95.1 | ↑ # |
| ***Staphylococcus aureus*** | MRSA[e] | 51 013 | 19.3 | 57 396 | 18.3 | 63 837 | 17.7 | 65 604 | 17.1 | 72 314 | 16.7 | 1.4-49.1 | ↓ |
| ***Streptococcus pneumoniae*** | Penicillin non-wild-type[f] | 12 465 | 14.3 | 13 249 | 14.0 | 14 514 | 14.0 | 14 568 | 13.2 | 8 032 | 15.6 | 3.9-56.3 | - |
| | Macrolide (azithromycin/clarithromycin/erythromycin) resistance | 12 604 | 18.2 | 13 340 | 17.2 | 14 767 | 16.6 | 15 069 | 15.9 | 8 362 | 16.9 | 3.5-43.8 | ↓ |
| | Combined penicillin non-wild-type and resistance to macrolides[f] | 12 046 | 9.2 | 12 699 | 9.2 | 14 030 | 8.6 | 14 102 | 8.0 | 7 739 | 9.0 | 0.0-37.5 | ↓ |
| ***Enterococcus faecalis*** | High-level gentamicin resistance | 12 910 | 31.8 | 13 930 | 29.7 | 15 343 | 27.1 | 13 577 | 25.3 | 14 279 | 29.0 | 4.1-51.6 | ↓ |
| ***Enterococcus faecium*** | Vancomycin resistance | 10 708 | 11.6 | 12 011 | 13.3 | 13 377 | 16.2 | 14 121 | 17.7 | 18 151 | 16.8 | 0.0-56.6 | ↑ |

[a] *Lowest and highest national AMR percentage among reporting EU/EEA countries in 2020 (n = 29).*

[b] *↑ and ↓ indicate statistically significant increasing and decreasing trends, respectively; # indicates a significant trend in the overall data, but not in data that only included laboratories reporting continuously for all five years; - indicates no statistically significant trend.*

[c] *The aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.*

[d] *The aminoglycoside group includes only tobramycin from 2020 onwards.*

[e] *MRSA is based on AST results for oxacillin or cefoxitin, but AST results reported as cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if AST results for oxacillin are not reported. Data from molecular confirmation tests (detection of* mecA *gene by PCR or a positive PBP2A-agglutionation test) are given priority over phenotypic AST results.*

[f] *Penicillin results are based on penicillin or, if not available, oxacillin. For* Streptococcus pneumoniae*, the term penicillin non-wild-type is used in this report, referring to* S. pneumoniae *isolates reported by local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MIC to benzylpenicillin above those of wild-type isolates (>0.06 mg/L). The qualitative susceptibility categories (S/I/R) as reported by the laboratory are used, since quantitative susceptibility information is missing for a large part of the data. Laboratories not using EUCAST clinical breakpoints in the period 2016–2018 might have used different interpretive criteria for the susceptibility categories.*

# Bacterial species-specific results

## *Escherichia coli*

### Epidemiology

For 2020, 29 EU/EEA countries reported 138 793 isolates of *E. coli*. Of these, 105 827 (76%) isolates had AST results for aminopenicillins, 137 465 (99%) for third-generation cephalosporins, 137 785 (99%) for fluoroquinolones, 134 683 (97%) for aminoglycosides and 134 032 (97%) for carbapenems (Table 3a).

At EU/EEA level, more than half (54.0%) of the *E. coli* isolates reported to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) (Table 4). In 2020, the highest EU/EEA population-weighted mean AMR percentage was reported for aminopenicillins (54.6%), followed by fluoroquinolones (23.8%), third-generation cephalosporins (14.9%) and aminoglycosides (10.9%). Resistance to carbapenems remained rare (0.2%) (Table 3a).

There was a significantly increasing trend between 2016 and 2020 in the EU/EEA (excluding the United Kingdom) population-weighted mean percentage for carbapenem resistance, while the trends for aminopenicillin resistance, third-generation cephalosporin resistance, fluoroquinolone resistance and aminoglycoside resistance decreased significantly during the same period. When restricting the analysis to include only laboratories that consistently reported data for all five years, all trends remained significant (Table 3b). Larger annual decreases in EU/EEA-level resistance percentages were seen in 2020 than in the period 2016–2019 for aminopenicillin (−2.0 percentage points) and third-generation cephalosporins (−0.7 percentage point) (Table 3b). The former was also reflected at country level by annual decreases in more than 80% of the countries reporting data on the species–antimicrobial group [1].

Resistance to multiple antimicrobial groups was common. At EU/EEA level, resistance to aminopenicillins, both as single resistance or in combination with other antimicrobial groups, was the most common (Table 4). In 2020, the percentage of combined resistance, measured as resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, was 5.7% (EU/EEA, excluding the United Kingdom, population-weighted mean) and there was a statistically significant decreasing trend during the period 2016–2020 (Table 3b).

Except for carbapenem resistance, large intercountry variations were noted for all antimicrobial groups under surveillance (Table 3a), with generally higher AMR percentages reported from southern and eastern Europe than from northern Europe (Figures 1–3).

**Table 4. *Escherichia coli*: total number of invasive isolates tested (n = 98 567)[a] and AMR percentage (%) per phenotype, EU/EEA, 2020**

| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **45 338** | **46.0** |
| **Single resistance (to indicated antimicrobial group)** | | |
| **Total (any single resistance)** | **32 535** | **33.0** |
| Aminopenicillins | 29 512 | 29.9 |
| Fluoroquinolones | 2 547 | 2.6 |
| Other antimicrobial groups | 476 | 0.5 |
| **Resistance to two antimicrobial groups** | | |
| **Total (any two-group combinations)** | **10 026** | **10.2** |
| Aminopenicillins + fluoroquinolones | 5 660 | 5.7 |
| Aminopenicillins + third-generation cephalosporins | 2 493 | 2.5 |
| Aminopenicillins + aminoglycosides | 1 710 | 1.7 |
| Other antimicrobial group combinations | 163 | 0.2 |
| **Resistance to three antimicrobial groups** | | |
| **Total (any three-group combinations)** | **6 742** | **6.8** |
| Aminopenicillins + third-generation cephalosporins + fluoroquinolones | 4 417 | 4.5 |
| Aminopenicillins + fluoroquinolones + aminoglycosides | 1 830 | 1.9 |
| Other antimicrobial group combinations | 495 | 0.5 |
| **Resistance to four antimicrobial groups** | | |
| **Total (any four-group combinations)** | **3 902** | **4.0** |

| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides | 3 873 | 3.9 |
| Other antimicrobial group combinations | 29 | <0.1 |
| **Resistance to five antimicrobial groups** | | |
| Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems | **24** | **<0.1** |

[a] *Only isolates with complete susceptibility information for aminopenicillins (amoxicillin or ampicillin), third-generation cephalosporins (cefotaxime, ceftriaxone or ceftazidime), carbapenems (imipenem or meropenem), fluoroquinolones (ciprofloxacin, levofloxacin or ofloxacin) and aminoglycosides (gentamicin or tobramycin) were included in the analysis. This represented 71% (98 567/138 793) of all reported* E. coli *isolates.*
[b] *Only AMR combinations >1% of the total are specified.*
[c] *Not adjusted for population differences in the reporting countries.*

**Figure 1.** ***Escherichia coli.*** **Percentage of invasive isolates resistant to fluoroquinolones (ciprofloxacin /levofloxacin/ofloxacin), by country, EU/EEA, 2020**

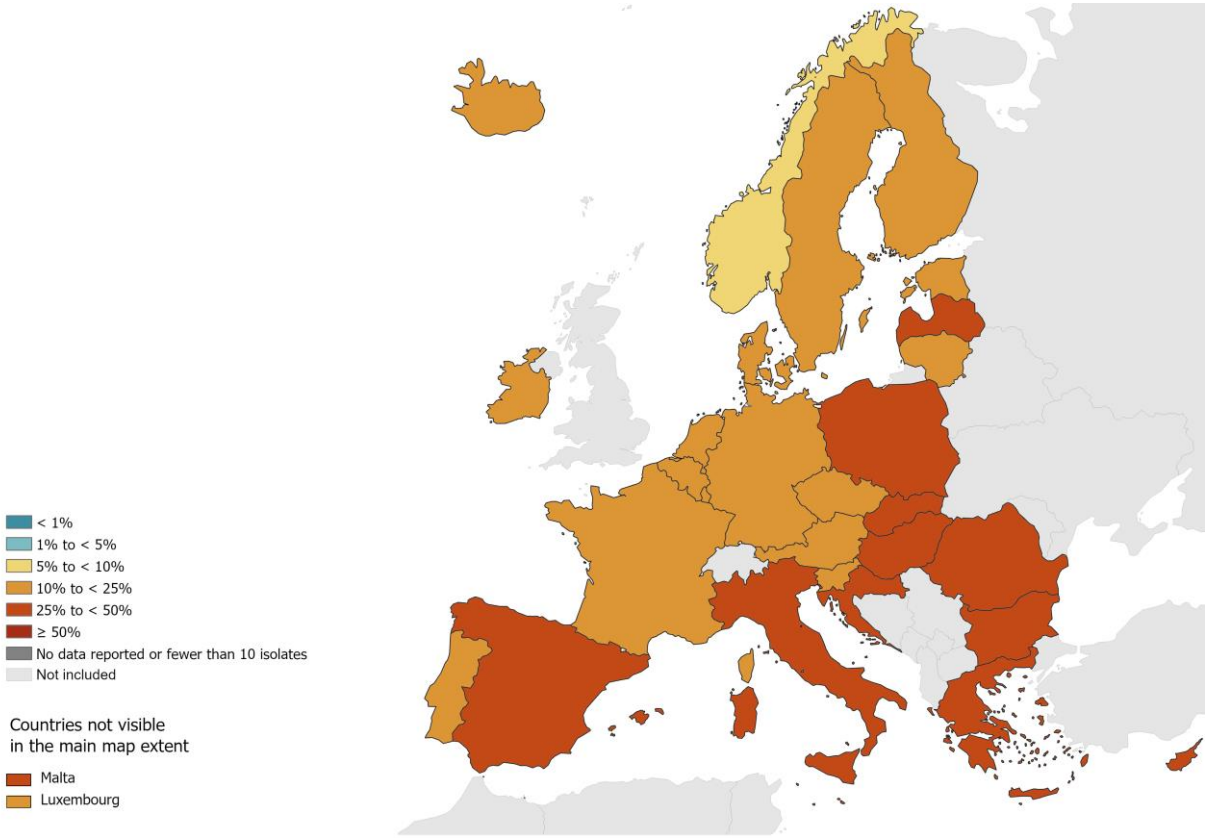


**Figure 2. *Escherichia coli*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2020**

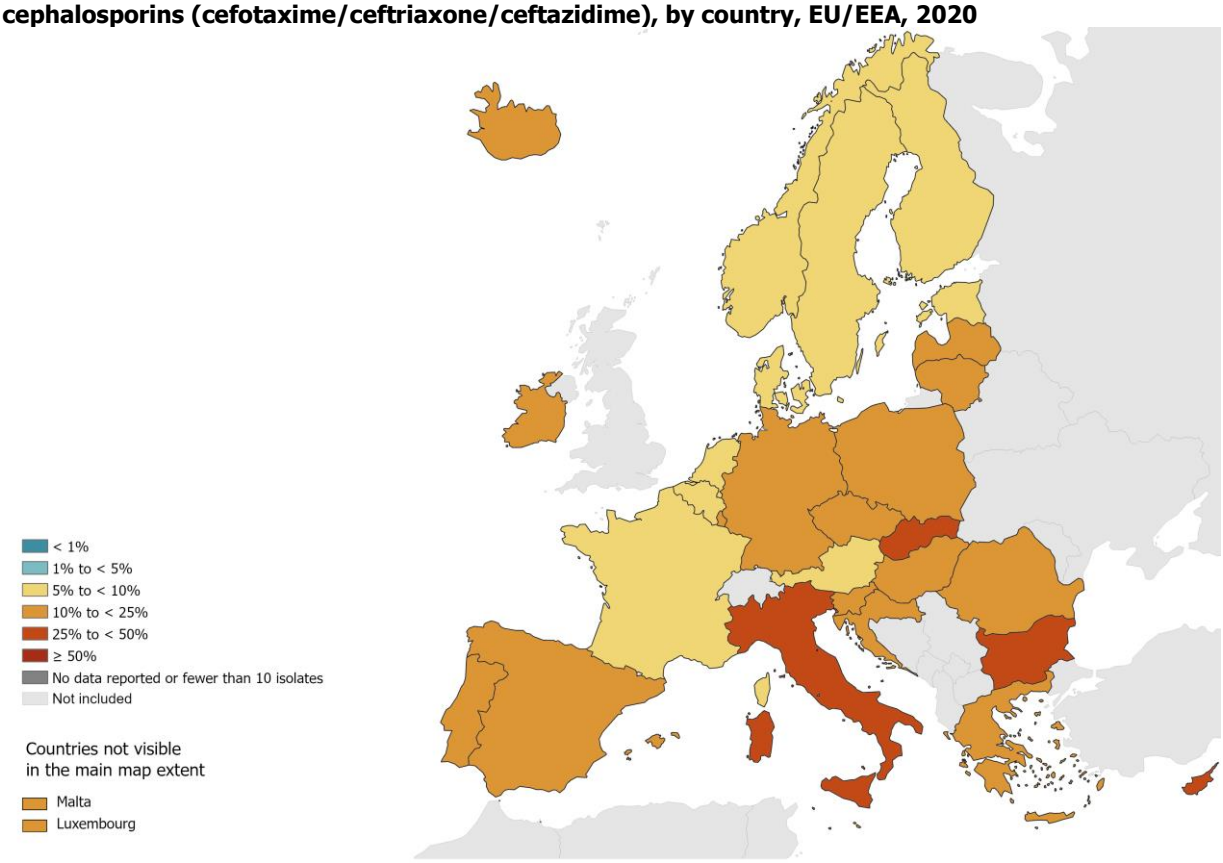
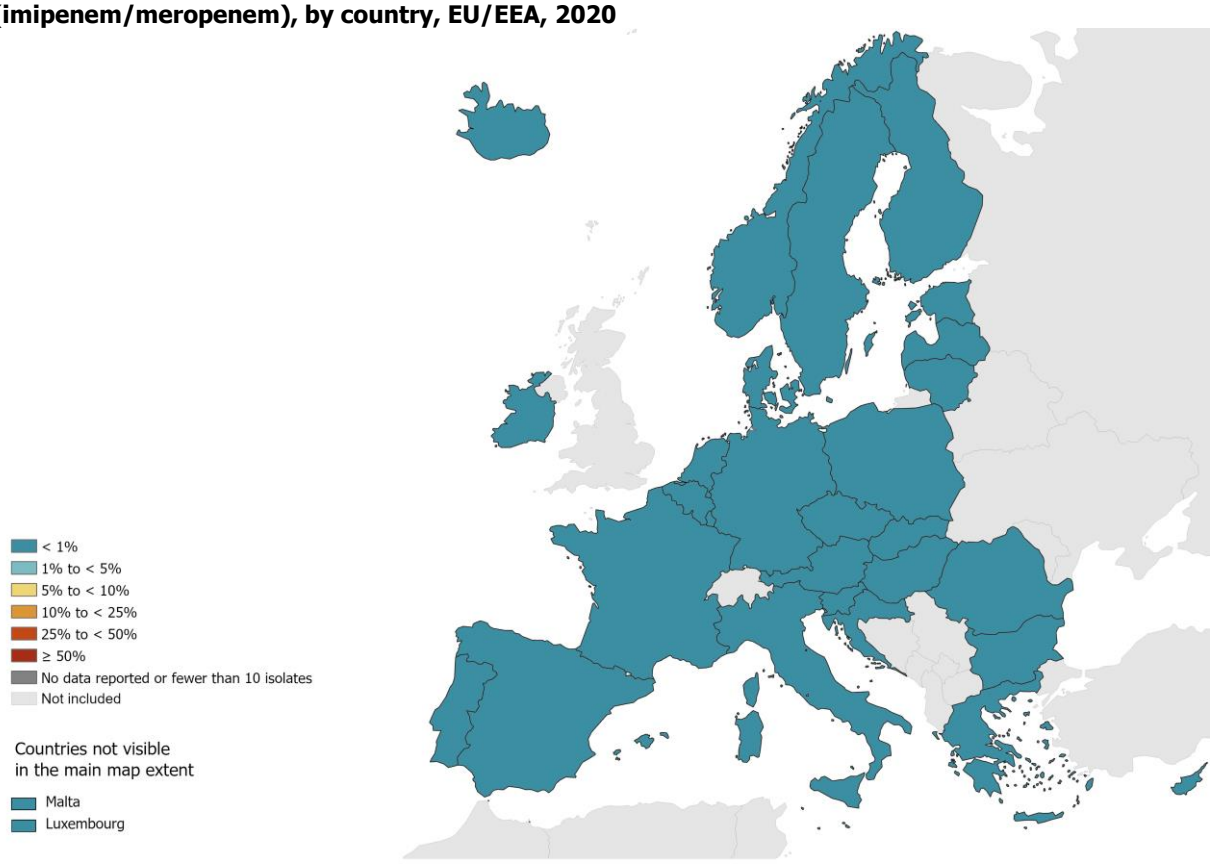



**Figure 3. *Escherichia coli*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, EU/EEA, 2020**



# Discussion

*E. coli* is a major cause of bloodstream infection in Europe, and prompt access to effective antimicrobial treatment is essential to reduce the health-related and economic burden caused by *E. coli* infections. Infections caused by antimicrobial-resistant *E. coli* proportionally contribute most to the burden of AMR in the EU/EEA, both in terms of the number of cases and the number of attributable deaths [19]. As antimicrobial-resistant *E. coli* infections commonly occur in the community, interventions to reduce the burden of infection should not be restricted to hospital settings, but should also target primary and community care.

Time-series analyses of EU/EEA population-weighted means for third-generation cephalosporin resistance and fluoroquinolone resistance in *E. coli* reported to EARS-Net for the years 2002–2018 showed that while AMR percentages increased substantially during the period, the increase was most prominent up until around 2012. After this, it was less pronounced [20]. A significantly decreasing EU/EEA (excluding the United Kingdom) trend was noted for the five-year period presented in this report (2016–2020). Percentages of AMR reported for 2020 nevertheless remain at a high level, highlighting the need for further efforts to improve antimicrobial stewardship and IPC.

Use of broad-spectrum antimicrobials is a known risk factor for the colonisation and spread of antimicrobial-resistant Enterobacterales, including *E. coli*. Associations between national AMR percentages in *E. coli* and national antimicrobial consumption rates have been reported [21]. The latest data from ESAC-Net show a considerable decrease in antimicrobial consumption in 2020 [11]. However, the 2020 AMR percentages at EU/EEA level are not all showing a similar decrease. The latest data from ESAC-Net also show that large intercountry variations in the use of broad-spectrum antimicrobials remain [11], indicating a need for increased focus on antimicrobial stewardship and highlighting the potential for further reductions in antimicrobial consumption.

As high AMR levels have been reported in *E. coli* isolates from food-producing animals in Europe, including the rare occurrence of isolates with carbapenemase production [22], ensuring cross-sectoral collaboration between the human, veterinary and food-production sectors is essential in a One Health approach, which addresses AMR in both humans and food-producing animals. ECDC is working closely with the European Food Safety Authority and the European Medicines Agency to better understand the interrelationships between antimicrobial use and AMR in humans and animals across Europe, and published the third joint interagency report on integrated analysis of antimicrobial agent consumption and occurrence of AMR in bacteria from humans and food-producing animals in 2021 [21].

Although carbapenem-resistant isolates remained rare among the invasive *E. coli* isolates included in EARS-Net, there was a small but significant increase in the EU/EEA (excluding the United Kingdom) population-weighted mean between 2016 and 2020. A further increase in serious infections caused by carbapenem-resistant *E. coli* would have severe consequences on the burden of AMR in the EU/EEA. Carbapenem-resistant Enterobacterales (CRE) infections are associated with high mortality, primarily due to delays in the administration of effective treatment and the limited availability of treatment options. The 2019 update of ECDC's rapid risk assessment on CRE highlights the need for high standards in IPC, combined with adequate microbiological capacity to detect and prevent further spread [23].

Carbapenem resistance is most often mediated by a range of carbapenemases and there are carbapenemase-producing isolates that test susceptible to meropenem and/or imipenem, based on clinical breakpoints. One example is OXA-244-producing *E. coli* that, in routine clinical microbiology laboratories, may only be classified as extended-spectrum beta-lactamase-producing rather than carbapenemase-producing *E. coli*, unless specifically tested for OXA-48-like carbapenemases. A recent ECDC risk assessment on OXA-244-producing *E. coli* [24] indicated a pan-European problem, with a high risk of further spread of OXA-244-producing *E. coli* in the EU/EEA, given the rapid and simultaneous increase in multiple countries between 2016 and 2019. There is a risk that spread of OXA-244-producing *E. coli* in the community may further contribute to the loss of carbapenems as options for treatment of multidrug-resistant *E. coli* infections. This highlights the need to further investigate the sources and routes of transmission for carbapenemase-producing *E. coli*.

To address this need and to complement the phenotypic-based surveillance data available from EARS-Net, the periodic carbapenem- and/or colistin-resistant Enterobacterales (CCRE) surveys are now incorporated into a new network, i.e. the European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) [25]. The latest survey results will provide information on the prevalence and distribution of carbapenemases and contribute to a better understanding of the epidemiology of CRE in Europe and risk factors associated with CRE infection and colonisation. ECDC, to a limited extent, is also able to provide Member States with access to whole-genome sequencing services, primarily for investigating potential multi-country outbreaks. By way of example, these services were provided for a combined clonal and plasmid-mediated outbreak of carbapenemase-producing Enterobacterales in Lithuania in 2019–2020 [26].

# *Klebsiella pneumoniae*

## Epidemiology

For 2020, 29 EU/EEA countries reported 40 075 isolates of *K. pneumoniae*. Of these, 39 579 (99%) isolates had AST results for third-generation cephalosporins, 39 794 (99%) for fluoroquinolones, 38 733 (97%) for aminoglycosides and 39 006 (97%) for carbapenems (Table 3a).

At EU/EEA level, more than a third (38.0%) of the *K. pneumoniae* isolates reported to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) (Table 5). In 2020, the highest EU/EEA population-weighted mean AMR percentage was reported for third-generation cephalosporins (33.9%), followed by fluoroquinolones (33.8%), aminoglycosides (23.7%) and carbapenems (10.0%) (Table 3a).

Between 2016 and 2020, there was a significantly increasing trend in the EU/EEA (excluding the United Kingdom) population-weighted mean percentage for carbapenem resistance, while the trend for aminoglycoside resistance decreased significantly during the same period. All observed trends remained significant when restricting the analysis to include only laboratories that consistently reported data (Table 3b). Notably, the annual change in resistance percentage at EU/EEA level indicated a quite large increase in 2020 (+1.0 percentage point) for carbapenems compared with the period 2016–2019 (Table 3b).

Single resistance was less commonly reported than resistance to two or three antimicrobial groups, with the most common AMR phenotype being combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides (Table 5). In 2020, the EU/EEA (excluding the United Kingdom) population-weighted mean for combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides was 21.0% and showed a statistically significant decreasing trend during the period 2016–2020 (Table 3b).

Large intercountry variations were noted for all antimicrobial groups under surveillance (Table 3a), with generally higher AMR percentages reported from southern and eastern Europe than from northern Europe (Figures 4 and 5). Several countries reported carbapenem resistance percentages above 10% for *K. pneumoniae*. The countries reporting the highest percentages of carbapenem resistance in *K. pneumoniae* were also among those reporting the highest AMR percentages for the other antimicrobial groups.

**Table 5. *Klebsiella pneumoniae*: total number of invasive isolates tested (n = 37 187)[a] and AMR percentage (%) per phenotype, EU/EEA, 2020**

| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **23 069** | **62.0** |
| **Single resistance (to indicated antimicrobial group)** | | |
| **Total (any single resistance)** | **2 839** | **7.6** |
| Fluoroquinolones | 1 400 | 3.8 |
| Third-generation cephalosporins | 1 212 | 3.3 |
| Other antimicrobial groups | 227 | 0.6 |
| **Resistance to two antimicrobial groups** | | |
| **Total (any two-group combinations)** | **3 082** | **8.3** |
| Third-generation cephalosporins + fluoroquinolones | 2 195 | 5.9 |
| Third-generation cephalosporins + aminoglycosides | 412 | 1.1 |
| Other antimicrobial group combinations | 475 | 1.3 |
| **Resistance to three antimicrobial groups** | | |
| **Total (any three-group combinations)** | **5 828** | **15.7** |
| Third-generation cephalosporins + fluoroquinolones + aminoglycosides | 4 652 | 12.5 |
| Third-generation cephalosporins + fluoroquinolones + carbapenems | 1 101 | 3.0 |
| Other antimicrobial group combinations | 75 | 0.2 |
| **Resistance to four antimicrobial groups** | | |
| Third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems | **2 369** | **6.4** |

[a] *Only isolates with complete susceptibility information for third-generation cephalosporins (cefotaxime, ceftriaxone or ceftazidime), carbapenems (imipenem or meropenem), fluoroquinolones (ciprofloxacin, levofloxacin or ofloxacin) and aminoglycosides (gentamicin or tobramycin) were included in the analysis. This represented 93% (37 187/40 075) of all reported* K. pneumoniae *isolates.*
[b] *Only AMR combinations >1% of the total are specified.*
[c] *Not adjusted for population differences in the reporting countries.*

**Figure 4. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime / ceftriaxone / ceftazidime), by country, EU/EEA, 2020**

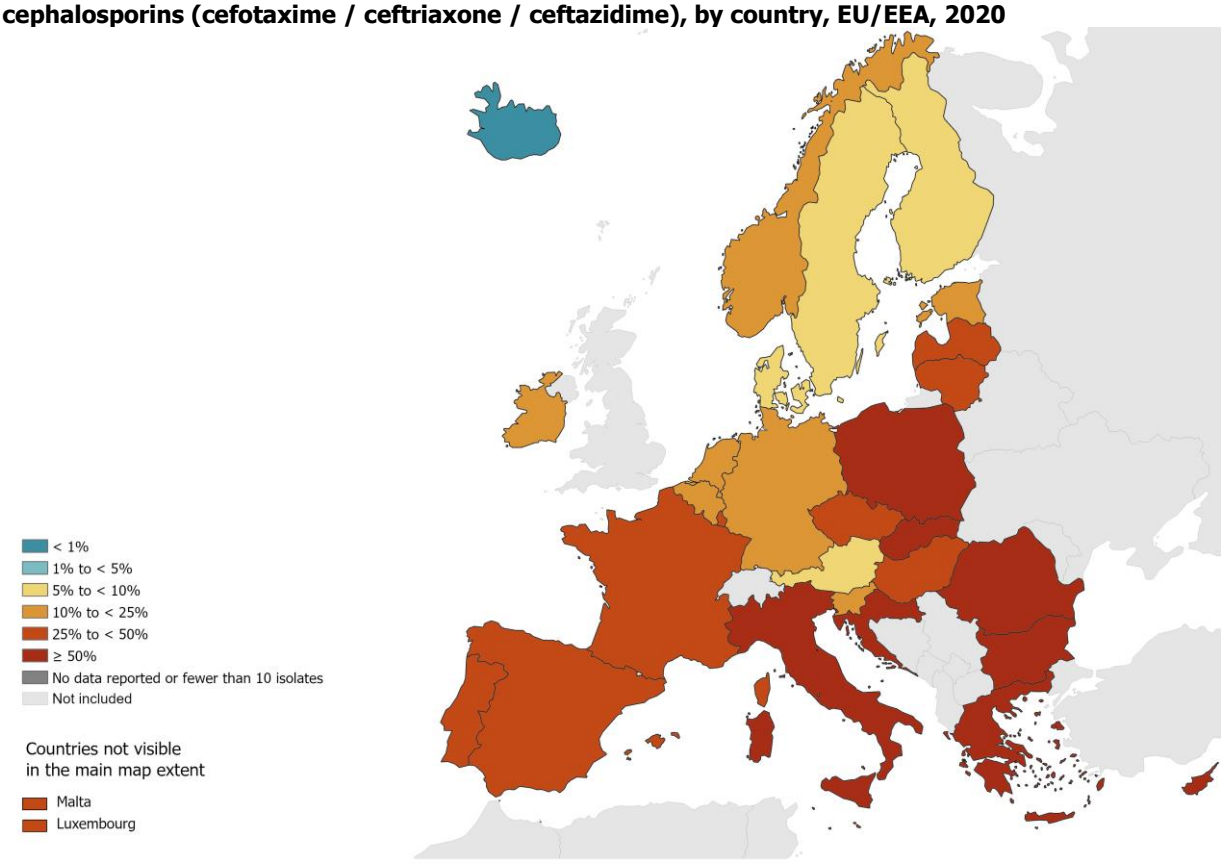
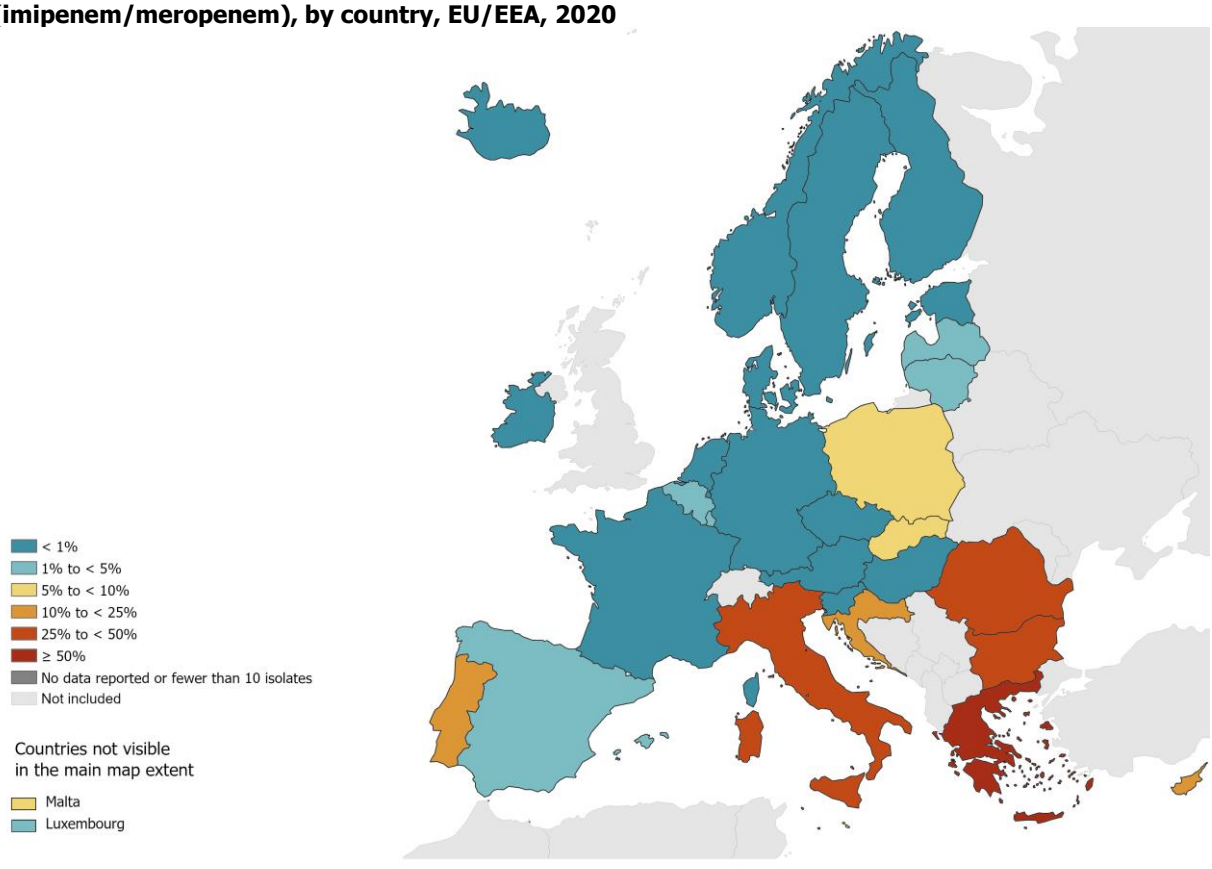



**Figure 5. *Klebsiella pneumoniae*. Percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country, EU/EEA, 2020**



# Discussion

The AMR situation in *K. pneumoniae* in the EU/EEA remains problematic. In addition to the significantly increasing trend in the EU/EEA (excluding the United Kingdom) population-weighted mean percentage of carbapenem resistance during the period 2016 to 2020, a proportionally larger increase was noted from 2019 to 2020 compared to the annual change in the previous years covered by this report. Carbapenem resistance was almost always combined with resistance to several other key antimicrobial groups, leading to a severely limited range of treatment options for serious infections caused by this type of bacteria. ECDC's study of the health burden of AMR found that even though the level of carbapenem-resistant *K. pneumoniae* was relatively low, the impact of AMR on the EU/EEA health burden was large because of the high attributable mortality of these infections [19]. This underlines the need for continuous close monitoring and greater efforts to respond efficiently to this public health threat.

The highest percentages of carbapenem resistance were observed in south and south-eastern Europe, similar to the distribution of carbapenemase-producing Enterobacterales reflected in a survey conducted by EURGen-Net [27]. Results from EURGen-Net also show that in several EU/EEA countries, the situation deteriorated between 2010 and 2018 with regards to the epidemiological stage of the spread of carbapenemase-producing Enterobacterales [27]. Numerous reports on outbreaks with varying potential for, or recorded cross-border spread of CRE, demonstrate the transmission potential in the healthcare systems of EU/EEA countries [28–30]. Outbreaks and clusters in EU/EEA countries also highlight the importance of detecting CRE early in settings with low incidence, due to their high transmissibility [28–32].

CRE can be resistant to carbapenems as a result of various mechanisms, but most frequently through production of carbapenemase enzymes. It is not possible to assess the overall presence and spread of carbapenemase-producing Enterobacterales through the data available from EARS-Net, as some carbapenemases do not confer a fully carbapenem-resistant phenotype. One example is the OXA-48-like carbapenemase enzymes, which present a particular problem for laboratory detection because of their weak capacity to hydrolyse carbapenems [28].

Recent outbreaks of carbapenemase (NDM-1 and OXA-48)-producing and colistin-resistant *K. pneumoniae* have highlighted the concomitant increase in virulence, transmissibility and AMR of certain *K. pneumoniae* strains. These strains pose a considerably higher risk to human health than was previously the case with circulating *K. pneumoniae* strains. A 2021 rapid risk assessment by ECDC raised the issue of emerging hypervirulent *K. pneumoniae* ST23 carrying carbapenemase genes [33]. The limited information available so far indicates that very few cases and clusters have been reported in the EU/EEA. Early detection of such strains and close cooperation between clinicians and public health services nevertheless are crucial to avoiding spread among the patient population in the EU/EEA.

There is a need for increased capacity in the EU/EEA to support outbreak investigations and surveillance with real-time whole genome sequencing to identify high-risk clones and implement enhanced control measures to avoid further spread [31,32]. One initiative to address this need is the CCRE surveys (part of EURGen-Net) that will provide updated and more detailed information on the distribution of carbapenemase-producing *K. pneumoniae* in Europe [25].

As highlighted in the 2019 update of ECDC's rapid risk assessment on CRE, options for action include timely and appropriate diagnosis, high standards of IPC and antimicrobial stewardship [23]. Many EU/EEA countries have developed and implemented recommendations and guidance documents on multidrug-resistant Enterobacterales and/or CRE [34], indicating a trend towards nationally coordinated responses to this public health threat. To support countries, ECDC published in 2017 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 [35].

Resistance to newly released antimicrobials has turned out to be a challenge for the optimal treatment of infections with CRE that are resistant to these new antimicrobials [36]. This highlights the need to also monitor for resistance to new antimicrobials. In addition, WHO sees a critical need for research and development of new antibiotics targeting third-generation cephalosporin-resistant Enterobacterales and CRE, including *K. pneumoniae* and *E. coli* [37].

# *Pseudomonas aeruginosa*

## Epidemiology

For 2020, 29 EU/EEA countries reported 20 675 isolates of *P. aeruginosa*. Of these, 19 695 (95%) isolates had AST results for piperacillin-tazobactam, 20 014 (97%) for ceftazidime, 20 279 (98%) for fluoroquinolones, 12 840 (62%) for aminoglycosides, 20 414 (99%) for carbapenems (Table 3a).

In the EU/EEA, 30.1% of the *P. aeruginosa* isolates reported to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (piperacillin-tazobactam, fluoroquinolones, ceftazidime, aminoglycosides and carbapenems) (Table 6). The highest EU/EEA population-weighted mean AMR percentage in 2020 was reported for fluoroquinolones (19.6%), followed by piperacillin-tazobactam (18.8%), carbapenems (17.8%), ceftazidime (15.5%) and aminoglycosides (9.4%) (Table 3a).

Between 2016 and 2020, EU/EEA (excluding the United Kingdom) trends decreased significantly for all but two antimicrobial groups under surveillance (piperacillin-tazobactam and ceftazidime). When restricting the analysis to include only laboratories that consistently reported data for all five years, the trends for carbapenem resistance, fluoroquinolone and aminoglycoside resistance remained statistically significant (Table 3b). For *P. aeruginosa* and aminoglycosides, there was a considerable change in the analysis for 2020 (previously the analysis included netilmicin, gentamicin and tobramycin, but from 2020 onwards it only includes tobramycin) and a relatively large annual decrease in the resistance percentage for 2020 (−3.2 percentage points) compared to annual changes observed during the period 2016−2019 (Table 3b).

Resistance to two or more antimicrobial groups was common, being observed in 17.3% of all tested isolates (Table 6). Between 2016 and 2020, the EU/EEA (excluding the United Kingdom) population-weighted mean percentage of combined resistance, defined as resistance to at least three of the antimicrobial groups under surveillance, significantly decreased from 15.0% to 12.1% (Table 3b). Large intercountry variations were noted for all antimicrobial groups (Table 3a), with generally higher AMR percentages reported from southern and eastern Europe than northern Europe (Figure 6).

**Table 6. *Pseudomonas aeruginosa*: total number of invasive isolates tested (n = 11 967)[a] and AMR percentage (%) per phenotype, EU/EEA, 2020**

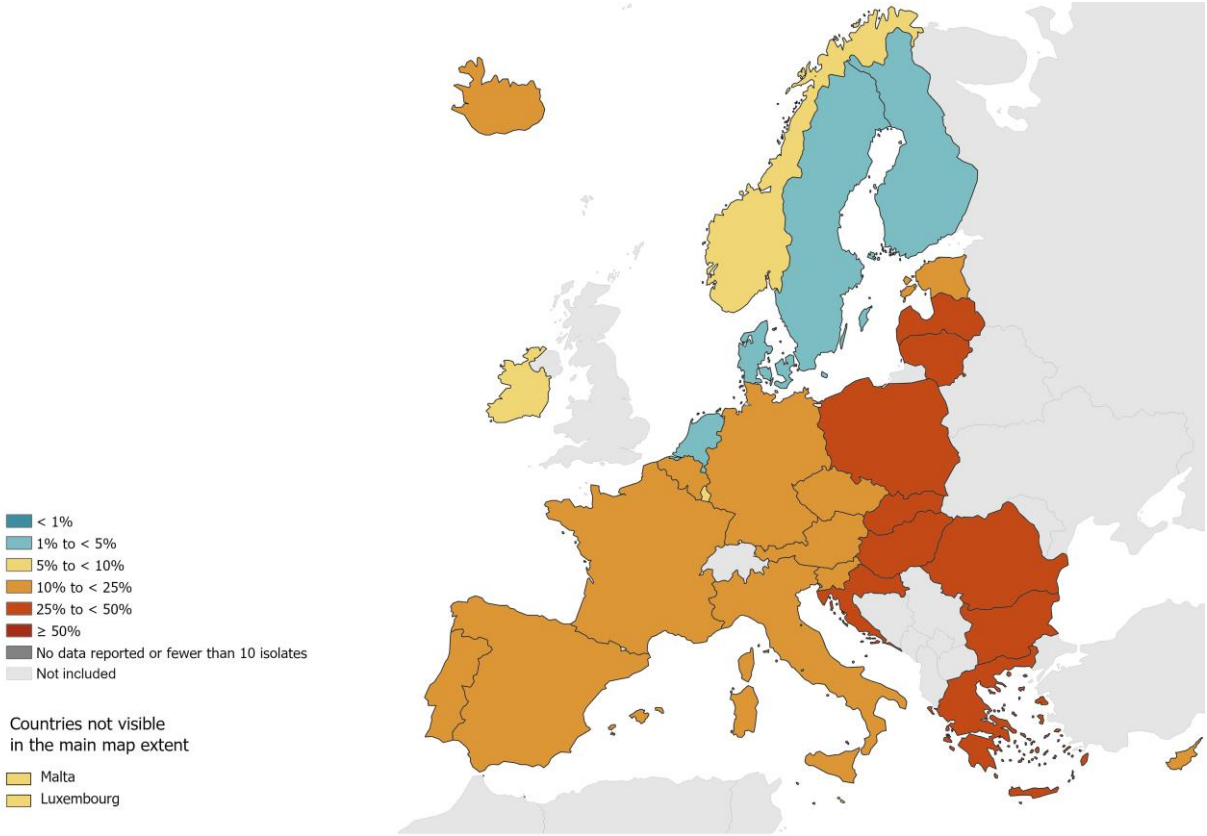
| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **8 367** | **69.9** |
| **Single resistance (to indicated antimicrobial group)** | | |
| **Total (any single resistance)** | **1 529** | **12.8** |
| Fluoroquinolones | 635 | 5.3 |
| Carbapenems | 598 | 5.0 |
| Piperacillin-tazobactam | 182 | 1.5 |
| Other antimicrobial groups | 114 | 1.0 |
| **Resistance to two antimicrobial groups** | | |
| **Total (any two group combinations)** | **908** | **7.6** |
| Piperacillin-tazobactam + ceftazidime | 423 | 3.5 |
| Fluoroquinolones + carbapenems | 212 | 1.8 |
| Other antimicrobial group combinations | 273 | 2.3 |
| **Resistance to three antimicrobial groups** | | |
| **Total (any three group combinations)** | **477** | **4.0** |
| Piperacillin-tazobactam + ceftazidime + carbapenems | 163 | 1.4 |
| Piperacillin-tazobactam + ceftazidime + fluoroquinolones | 139 | 1.2 |
| Other antimicrobial group combinations | 175 | 1.5 |
| **Resistance to four antimicrobial groups** | | |
| **Total (any four group combinations)** | **321** | **2.7** |
| Piperacillin-tazobactam + fluoroquinolones + ceftazidime + carbapenems | 170 | 1.4 |
| Other antimicrobial group combinations | 151 | 1.3 |
| **Resistance to five antimicrobial groups** | | |
| Piperacillin-tazobactam + fluoroquinolones + ceftazidime + aminoglycosides + carbapenems | **365** | **3.1** |

*[a] Only isolates with complete susceptibility information for piperacillin-tazobactam, ceftazidime, carbapenems (imipenem or meropenem), fluoroquinolones (ciprofloxacin or levofloxacin) and aminoglycosides (tobramycin) were included in the analysis. This represented 58% (11 967/20 675) of all reported* P. aeruginosa *isolates.*

*[b] Only AMR combinations >1% of the total are specified.*

*[c] Not adjusted for population differences in the reporting countries.*

**Figure 6. *Pseudomonas aeruginosa.* Percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country, EU/EEA, 2020**




# Discussion

EARS-Net data showed that at EU/EEA (excluding the United Kingdom) level, trends in resistance decreased significantly for *P. aeruginosa* in relation to several antimicrobial groups under surveillance during the period 2016 to 2020. High AMR percentages and combined AMR nevertheless persisted in many countries, especially in the eastern and south-eastern parts of Europe. As *P. aeruginosa* is intrinsically resistant to many antimicrobial agents, additional acquired resistance is further complicating the treatment of *P. aeruginosa* infections.

The public health implications of AMR in *P. aeruginosa* should not be ignored, as *P. aeruginosa* remains one of the major causes of healthcare-associated infection in Europe [38]. *P. aeruginosa* and *Acinetobacter* spp. bloodstream infections are proportionally far more commonly reported from some EU/EEA countries than others [1]. An analysis based on 2016 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 percentage of isolates with acquired AMR in gram-negative bacteria generally was the highest [39]. This finding is probably attributable to shared risk factors, such as a high proportion of consumption of broad-spectrum antimicrobials and varying infection prevention and control practices in healthcare [40]. Addressing these factors and implementing high standards of IPC in healthcare across these countries would probably have a positive impact on not only the burden of infections caused by bacteria with high levels of intrinsic AMR, such as *P. aeruginosa* and *Acinetobacter* spp., but most likely also bacteria with acquired AMR.

At the global level, WHO has listed carbapenem-resistant *P. aeruginosa* as a pathogen of critical priority that requires research and the development of new antibiotics [37].

# *Acinetobacter* species

## Epidemiology

For 2020, 29 EU/EEA countries reported 7 622 isolates of *Acinetobacter* spp., with four EU/EEA countries each reporting fewer than 30 isolates. Of these, 7 392 (97%) isolates had AST results for fluoroquinolones, 7 306 (96%) for aminoglycosides and 7 542 (99%) for carbapenems (Table 3a).

Almost two thirds (65.6%) of the *Acinetobacter* spp. isolates reported by EU/EEA countries to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (fluoroquinolones, aminoglycosides and carbapenems) (Table 7). In 2020, the highest EU/EEA population-weighted mean AMR percentage was reported for fluoroquinolones (41.8%), followed by carbapenems (38.0%) and aminoglycosides (37.1%) (Table 3a).

Between 2016 and 2020, no significant trend was detected for carbapenem, fluoroquinolone or aminoglycoside resistance respectively in the EU/EEA (excluding the United Kingdom) (Table 3b). A quite large annual increase in resistance percentage nevertheless was seen for carbapenems at EU/EEA level in 2020 (+1.1 percentage points) compared with the period 2016–2019 (Table 3b).

Resistance to one or two antimicrobial groups was considerably less common than combined resistance to all three groups under surveillance (Table 7). Between 2016 and 2020, the EU/EEA (excluding the United Kingdom) population-weighted mean percentage for combined resistance to carbapenems, fluoroquinolones and aminoglycosides significantly increased from 32.3% to 34.1%. However, this trend did not remain statistically significant when restricting the analysis to include only laboratories consistently reporting data for all five years (Table 3b).

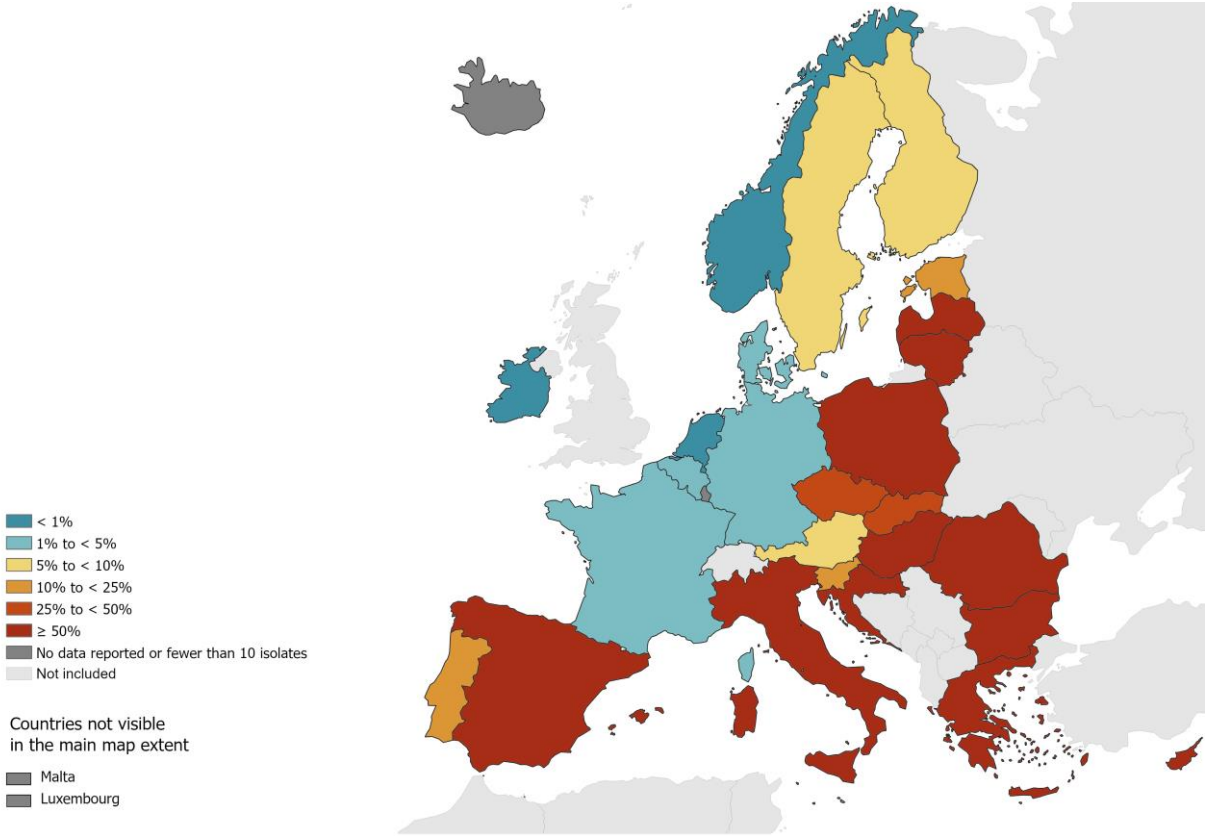
Large intercountry variations were noted for all antimicrobial groups (Table 3a), with generally higher AMR percentages reported from southern and eastern Europe than northern Europe (see country profiles and Figure 7).

**Table 7. *Acinetobacter* species: total number of invasive isolates tested (n = 7 162)[a] and AMR percentage (%) per phenotype, EU/EEA, 2020**

| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **2 461** | **34.4** |
| **Single resistance (to indicated antimicrobial group)** | | |
| **Total (any single resistance)** | **238** | **3.3** |
| Fluoroquinolones | 146 | 2.0 |
| Other antimicrobial groups | 92 | 1.3 |
| **Resistance to two antimicrobial groups** | | |
| **Total (any two-group combinations)** | **358** | **5.0** |
| Fluoroquinolones + carbapenems | 242 | 3.4 |
| Fluoroquinolones + aminoglycosides | 103 | 1.4 |
| Other antimicrobial group combinations | 13 | 0.2 |
| **Resistance to three antimicrobial groups** | | |
| Fluoroquinolones + aminoglycosides + carbapenems | **4 105** | **57.3** |

[a] *Only isolates with complete susceptibility information for carbapenems (imipenem or meropenem), fluoroquinolones (ciprofloxacin or levofloxacin) and aminoglycosides (gentamicin or tobramycin) were included in the analysis. This represented 94% (7 162/7 622) of all reported* Acinetobacter *spp. isolates.*
[b] *Only AMR combinations >1% of the total are specified.*
[c] *Not adjusted for population differences in the reporting countries.*

**Figure 7. *Acinetobacter* species. Percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country, EU/EEA, 2020**




# Discussion

Of all the bacterial species under surveillance by EARS-Net, *Acinetobacter* spp. is the least commonly reported and the one for which the intercountry range in AMR percentages is the widest. In 2020, the percentage of isolates resistant to at least one of the antimicrobial groups under surveillance (fluoroquinolones, aminoglycosides or carbapenems) ranged between 0.0% and 98.2%, depending on the reporting country. In general, the highest AMR percentages were reported from southern and eastern Europe. The high levels of AMR in these countries are of great concern since the most frequently reported AMR phenotype was combined resistance to all three antimicrobial groups under surveillance, severely limiting options for patient treatment.

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

ECDC's risk assessment on carbapenem-resistant *Acinetobacter baumannii* (*A. baumannii*) in healthcare settings highlights the need for increased efforts to face this significant threat to patients and healthcare systems in all EU/EEA countries. The document outlines options to reduce risks through clinical management, prevention of transmission in hospitals and other healthcare settings, prevention of cross-border transmission and improvement in the preparedness of EU/EEA countries. Options for response presented in the risk assessment include timely laboratory reporting, screening and pre-emptive isolation of high-risk patients, good infection prevention and control, rigorous environmental cleaning and disinfection, and antimicrobial stewardship programmes [41].

WHO has listed carbapenem-resistant *A. baumannii* as a pathogen of critical priority in its global priority list of antibiotic-resistant bacteria requiring research and the development of new antibiotics [37].

# *Staphylococcus aureus*

## Epidemiology

For 2020, 29 EU/EEA countries reported 73 518 isolates of *S. aureus*. Of these, 72 314 (98%) isolates had AST results or molecular confirmation test results available to determine MRSA (Table 3a).

One fifth (20.1%) of the *S. aureus* isolates reported by EU/EEA countries to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (meticillin/MRSA, fluoroquinolones and rifampicin) (Table 8).

The EU/EEA population-weighted mean MRSA percentage was 16.7% in 2020. There was a significantly decreasing trend, from 19.3% to 16.7%, for the period 2016–2020 (excluding the United Kingdom); a trend that remained statistically significant when restricting the analysis to include only laboratories that consistently reported data for all five years (Table 3b).

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

Large intercountry variations were noted for MRSA (Table 3a), with generally higher MRSA percentages reported from southern and eastern Europe than northern Europe (Figure 8).

**Table 8. *Staphylococcus aureus*: total number of invasive isolates tested (n = 49 773)[a] and AMR percentage (%) per phenotype, EU/EEA, 2020**

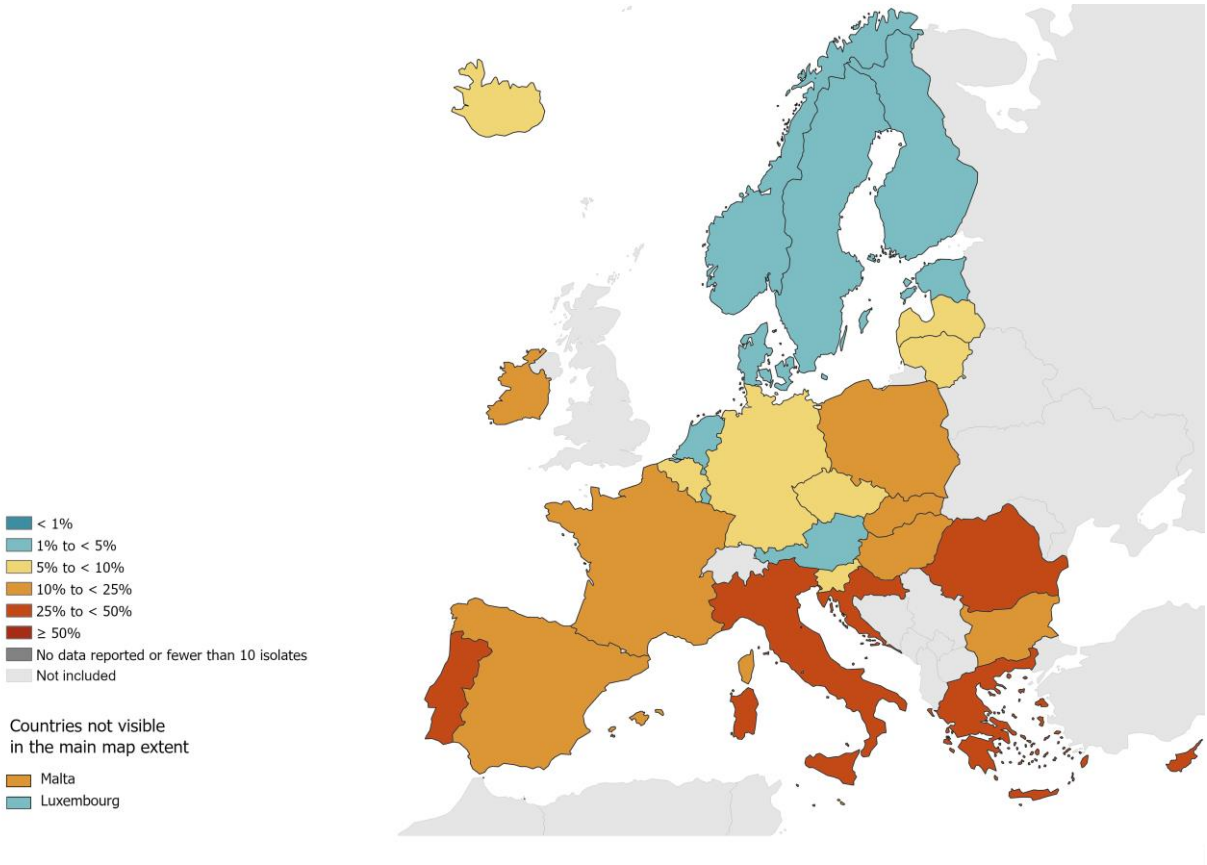
| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **39 769** | **79.9** |
| **Single resistance (to indicated antimicrobial group)** | | |
| **Total (any single resistance)** | **4 272** | **8.6** |
| Fluoroquinolones | 2 446 | 4.9 |
| Meticillin/MRSA | 1 605 | 3.2 |
| Other antimicrobial groups | 221 | 0.4 |
| **Resistance to two antimicrobial groups** | | |
| **Total (any two-group combinations)** | **5 388** | **10.8** |
| Meticillin/MRSA + fluoroquinolones | 5 298 | 10.6 |
| Other resistance combinations | 90 | 0.2 |
| **Resistance to three antimicrobial groups** | | |
| Meticillin/MRSA + fluoroquinolones + rifampicin | **344** | **0.7** |

[a] *Only isolates with complete susceptibility information for MRSA, fluoroquinolones and rifampicin were included in the analysis. This represented 68% (49 773/73 518) of all reported* S. aureus *isolates. MRSA is based on AST results for oxacillin or cefoxitin, but AST results reported as cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if AST results for oxacillin are not reported. Data from molecular confirmation tests (detection of* mecA *gene by PCR or a positive PBP2A-agglutionation test) are given priority over phenotypic AST results. For fluoroquinolones (ciprofloxacin, levofloxacin or ofloxacin), AST results for norfloxacin are also accepted if neither ciprofloxacin, levofloxacin nor ofloxacin results are available.*

[b] *Only AMR combinations >1% of the total are specified.*

[c] *Not adjusted for population differences in the reporting countries.*

**Figure 8. *Staphylococcus aureus.* Percentage of invasive isolates resistant to meticillin (MRSA),[a] by country, EU/EEA, 2020**




*[a] MRSA is based on AST results for oxacillin or cefoxitin, but AST results reported as cloxaciilin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if AST results for oxacillin or cefoxitin are not reported. Data from molecular confirmation tests (detection of* mecA *gene by PCR or a positive PBP2A-agglutination test), are given priority over phenotypic AST results.*

# Discussion

In 2020, MRSA percentages were stable or decreasing in several EU/EEA countries [1], and a decreasing EU/EEA (excluding the United Kingdom) population-weighted mean MRSA percentage was noted. Several countries have developed and implemented national recommendations and guidance documents on preventing the spread of MRSA, focusing on improved IPC and prudent antimicrobial use [34].

Despite this positive development, MRSA remains an important pathogen in Europe. *S. aureus* is one of the most common causes of bloodstream infection, exhibiting a high burden in terms of morbidity and mortality [19]. Although the EU/EEA (excluding the United Kingdom) population-weighted MRSA percentage, as reported by EARS-Net, has been decreasing for many years, ECDC's study of the health burden of AMR reported an increase in estimated MRSA incidence between 2007 and 2015. Further analysis of the age-group-specific incidence as part of the ECDC study found that this mainly related to infants and people aged 55 years or above [19]. A separate study based on EARS-Net data for the period 2005 to 2018 highlighted that the decrease in the percentage of MRSA among *S. aureus* bloodstream infections was mainly due to the increasing number of meticillin-susceptible *S. aureus* (MSSA) bloodstream infections. The seemingly conflicting results highlight the need to improve surveillance of AMR by reporting not only AMR percentages but also the number and the incidence of infections with antimicrobial-resistant bacteria such as MRSA [42].

Comprehensive MRSA strategies targeting all healthcare sectors are essential to slow down the spread of MRSA in Europe. Monitoring of MRSA in food-producing animals and food currently is voluntary and is only performed in a limited number of countries. This monitoring nevertheless reported the detection of MRSA, mainly livestock-associated MRSA (LA-MRSA) isolates, in food and food-producing animals in 2018–2019 [22]. LA-MRSA has gained attention, as it poses a zoonotic risk, particularly for those working in close contact with livestock. Although data collected through EARS-Net do not allow identification of LA-MRSA isolates, an ECDC survey documented an increasing detection and geographical dispersion of LA-MRSA in humans in the EU/EEA during the period 2007–2013 and highlighted the veterinary and public health significance of LA-MRSA as a One Health issue [43].

# *Streptococcus pneumoniae*

## Epidemiology

For 2020, 28 EU/EEA countries reported 8 689 isolates of *S. pneumoniae*. There was a decrease of 20% or more in the number of reported isolates in 2020 compared to 2019 in all of the reporting countries apart from Cyprus. Such a uniform decrease was not seen for the other bacterial species under EARS-Net surveillance. The decrease compared to previous years was also reflected in the number of reported isolates with AMR phenotype in the EU/EEA (excluding the United Kingdom) (Table 3b). Of the reported isolates, 8 032 (92%) had AST results for penicillins and 8 362 (96%) had AST results for macrolides (Table 3a).

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

More than one fifth (22.6%) of the *S. pneumoniae* isolates reported by EU/EEA countries to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (penicillins, third-generation cephalosporins, fluoroquinolones and macrolides) (Table 9). In 2020, the EU/EEA population-weighted mean percentage was 15.6% for penicillin non-wild-type and 16.9% for macrolide resistance (Table 3a).

Between 2016 and 2020, the EU/EEA (excluding the United Kingdom) trend decreased significantly for resistance to macrolides, from 18.2% to 16.9% (Table 3b). Although no significant increase in trend was noted for penicillin non-wild-type resistance, there nevertheless was a relatively large annual increase in AMR percentage at EU/EEA level in 2020 (+2.4 percentage points) compared with the period 2016–2019 (Table 3b).

The EU/EEA population-weighted mean percentage for combined penicillin non-wild-type and macrolide resistance was 9.0% in 2020 and decreased significantly during the period 2016 to 2020 (excluding the United Kingdom) (Table 3b). Resistance to antimicrobial groups other than penicillin and macrolides was less common (Table 9).

Large intercountry variations were noted for all antimicrobial groups (Table 3a, Figure 9), with generally higher macrolide resistance percentages reported from southern and eastern Europe than northern Europe.

**Table 9. *Streptococcus pneumoniae*: total number of invasive isolates tested (n = 5 755)[a] and percentage non-wild-type/ AMR (%) per phenotype, EU/EEA, 2020**

| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **4 452** | **77.4** |
| **Single non-wild-type/resistance (to indicated antimicrobial groups)** | | |
| **Total (any single resistance)** | **844** | **14.7** |
| Macrolides | 411 | 7.1 |
| Penicillin non-wild-type[d] | 360 | 6.3 |
| Fluoroquinolones | 73 | 1.3 |
| **Non-wild-type/resistance to two antimicrobial groups** | | |
| **Total (any two-group combinations)** | **439** | **7.6** |
| Penicillin non-wild-type + macrolides | 421 | 7.3 |
| Other antimicrobial group combinations | 18 | 0.3 |
| **Non-wild-type/resistance to three antimicrobial groups** | | |
| **Total (any three-group combinations)** | **19** | **0.3** |
| Other antimicrobial group combinations | 19 | 0.3 |
| **Non-wild-type/resistance to four antimicrobial groups** | | |
| Penicillin non-wild-type + third-generation cephalosporins + fluoroquinolones + macrolides | **1** | **<0.1** |

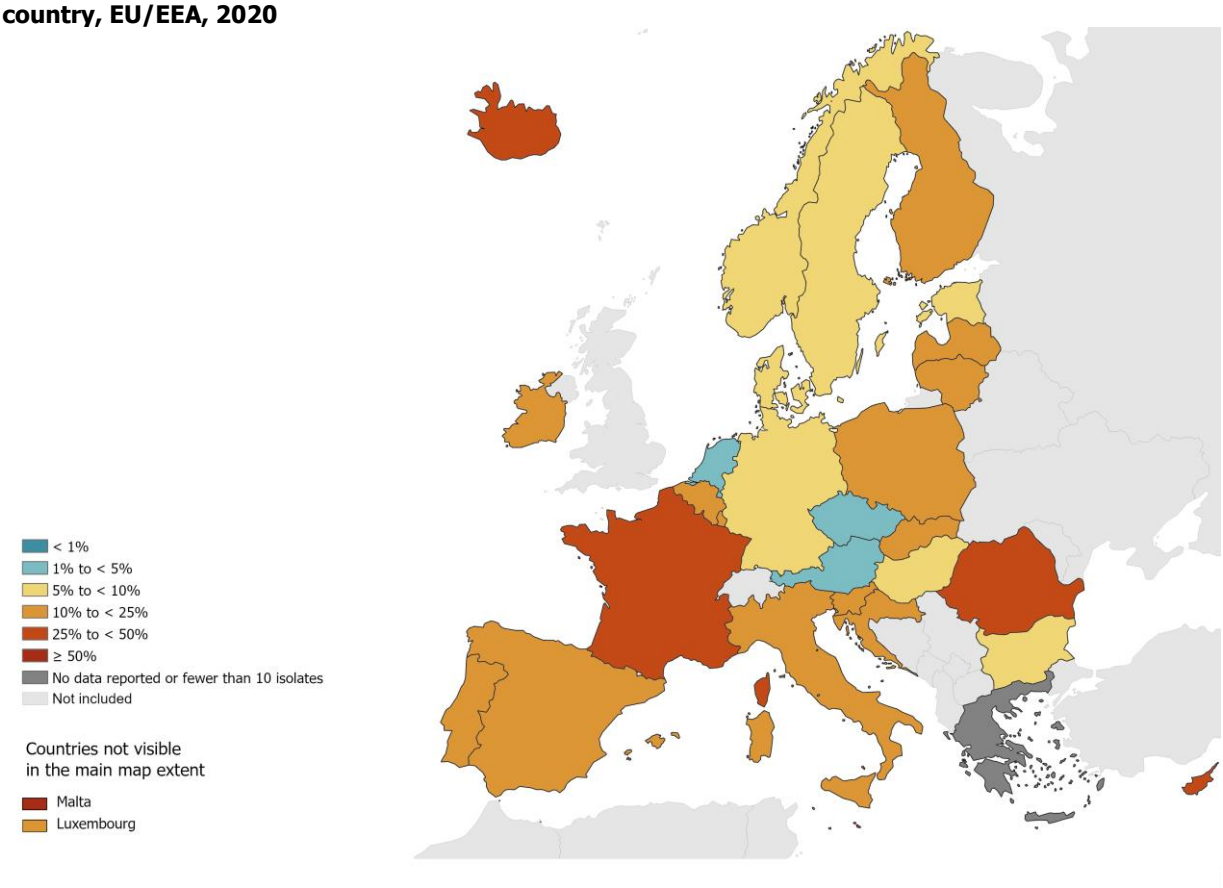
[a] *Only isolates with complete susceptibility information for penicillins (based on penicillin or, if not available, oxacillin), third-generation cephalosporins (cefotaxime or ceftriaxone) and fluoroquinolones (levofloxacin or moxifloxacin - AST results for norfloxacin are also accepted if neither levofloxacin nor moxifloxacin results are available) and macrolides (azithromycin, clarithromycin or erythromycin) were included in the analysis. This represented 66% (5 755/8 689) of all reported* S. pneumoniae *isolates.*

[b] *Only AMR combinations >1% of the total are specified.*

[c] *Not adjusted for population differences in the reporting countries.*

[d] *For* Streptococcus pneumoniae*, the term penicillin non-wild-type is used in this report, referring to* S. pneumoniae *isolates reported by local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MIC to benzylpenicillin above those of wild-type isolates (>0.06 mg/L). The qualitative susceptibility categories (S/I/R) as reported by the laboratory are used, since quantitative susceptibility information is missing for a large part of the data.*

**Figure 9. *Streptococcus pneumoniae*. Percentage of penicillin[a] non-wild type[b] invasive isolates, by country, EU/EEA, 2020**




[a] *Penicillin results are based on penicillin or, if not available, oxacillin.*

[b] *For* S. pneumoniae*, the term penicillin non-wild-type is used in this report, referring to* S. pneumoniae *isolates reported by local laboratories as 'susceptible, increased exposure' (I) or resistant (R) to penicillin, assuming MIC to benzylpenicillin above those of wild-type isolates (>0.06 mg/L). The qualitative susceptibility categories (S/I/R) as reported by the laboratory are used, since quantitative susceptibility information is missing for a large part of the data. Laboratories not using EUCAST clinical breakpoints might define the cut-off values for the susceptibility categories differently.*

# Discussion

As mentioned elsewhere in this report, decreased circulation of pathogens in the community as a result of NPIs introduced to reduce SARS-CoV-2 transmission could potentially explain the decrease in the number of *S. pneumoniae* isolates reported by EU/EEA countries for 2020.

However, the population-weighted EU/EEA (excluding the United Kingdom) mean percentages for penicillin non-wild-type and macrolide resistance did not uniformly decrease between 2016 and 2020. As in previous years, there were large intercountry variations. Differences in the clinical breakpoints used historically to determine penicillin susceptibility in *S. pneumoniae* (based on the guidelines used and the sites of infection) could introduce bias when comparing national data reported to EARS-Net before 2020. Limited information on the guidelines and breakpoints used for interpretation as well as incomplete quantitative susceptibility data hamper assessment of intercountry differences to some extent and may also thwart the assessment of changes over time.

In parallel to EARS-Net, surveillance of invasive pneumococcal disease is covered by another surveillance network, i.e. the European Invasive Bacterial Disease Surveillance Network (EU-IBD), also coordinated by ECDC. This network collects additional data on invasive pneumococcal disease cases throughout the EU/EEA on, for example, outcome [44]. Data from this surveillance show that the percentage of resistance to penicillin was 2% and to erythromycin 18%, based on reporting of antimicrobial susceptibility data by 10 EU/EEA countries in 2018 [44]. It is, however, difficult to compare data from the two surveillance systems due to differences in, for instance, the number of reporting countries.

Most EU/EEA countries have implemented routine immunization for children with multivalent pneumococcal conjugated vaccines (PCVs). In some countries, high-risk adult groups, such as elderly people and immunocompromised individuals, are also targeted with the polysaccharide vaccine or with PCVs [45]. Changes in immunisation and serotype coverage of the available PCVs will probably have an impact on the epidemiology of *S. pneumoniae* in the EU/EEA, both in terms of changes in the age-specific incidence and potential serotype replacement. It is also conceivable that the ongoing COVID-19 pandemic and related public health interventions and changes in antibiotic consumption [46] may additionally affect *S. pneumoniae* epidemiology in the EU/EEA.

# *Enterococcus faecalis*

## Epidemiology

For 2020, 29 EU/EEA countries reported 28 163 isolates of *E. faecalis*. Of these, 14 279 (51%) had AST results for high-level gentamicin (Table 3a).

In 2020, the EU/EEA population-weighted mean percentage of high-level gentamicin resistance in *E. faecalis* was 29.0%, which represents a significant decrease from 2016, when the percentage was 31.8% (excluding the United Kingdom) (Table 3b). There nevertheless was a quite large annual increase in AMR percentage at EU/EEA level in 2020 (+3.7 percentage points) for high-level gentamicin resistance compared with the period 2016−2019 (Table 3b).

Large intercountry variations were noted for high-level gentamicin resistance in *E. faecalis* (Table 3a), with generally higher high-level gentamicin resistance percentages reported from southern and eastern Europe than northern Europe, with a few exceptions (see country profiles). More information is provided in ECDC's Surveillance Atlas of Infectious Diseases [1].

## Discussion

Despite the decreasing trend in high-level gentamicin resistance in *E. faecalis* noted by EARS-Net, high levels of AMR in enterococci remain a major infection control challenge and an important cause of healthcare-associated infections in Europe. In addition to the fact that infections caused by resistant strains are difficult to treat, enterococci are also easily disseminated in healthcare settings.

# *Enterococcus faecium*

## Epidemiology

For 2020, 29 EU/EEA countries reported 18 548 isolates of *E. faecium*. Of these, 18 151 (98%) had AST results for vancomycin (Table 3a).

More than nine tenths (92.0%) of the *E. faecium* isolates reported by EU/EEA countries to EARS-Net for 2020 were resistant to at least one of the antimicrobial groups under surveillance (aminopenicillins, gentamicin (high-level resistance) and vancomycin) (Table 10).

Resistance to two or more antimicrobial groups was common, being seen in 52.4% of all tested isolates (Table 10).

The EU/EEA population-weighted mean percentage of vancomycin resistance in *E. faecium* was 16.8% in 2020, representing a significant increase since 2016 when the percentage was 11.6% (excluding the United Kingdom). National percentages ranged from 0.0% to 56.6% (Table 3a) and only 11 of the 29 EU/EEA countries reported AMR percentages below 5% (Figure 10).

**Table 10. *Enterococcus faecium*: total number of invasive isolates tested (n = 9 354)[a] and AMR percentage (%) per phenotype, EU/EEA, 2020**

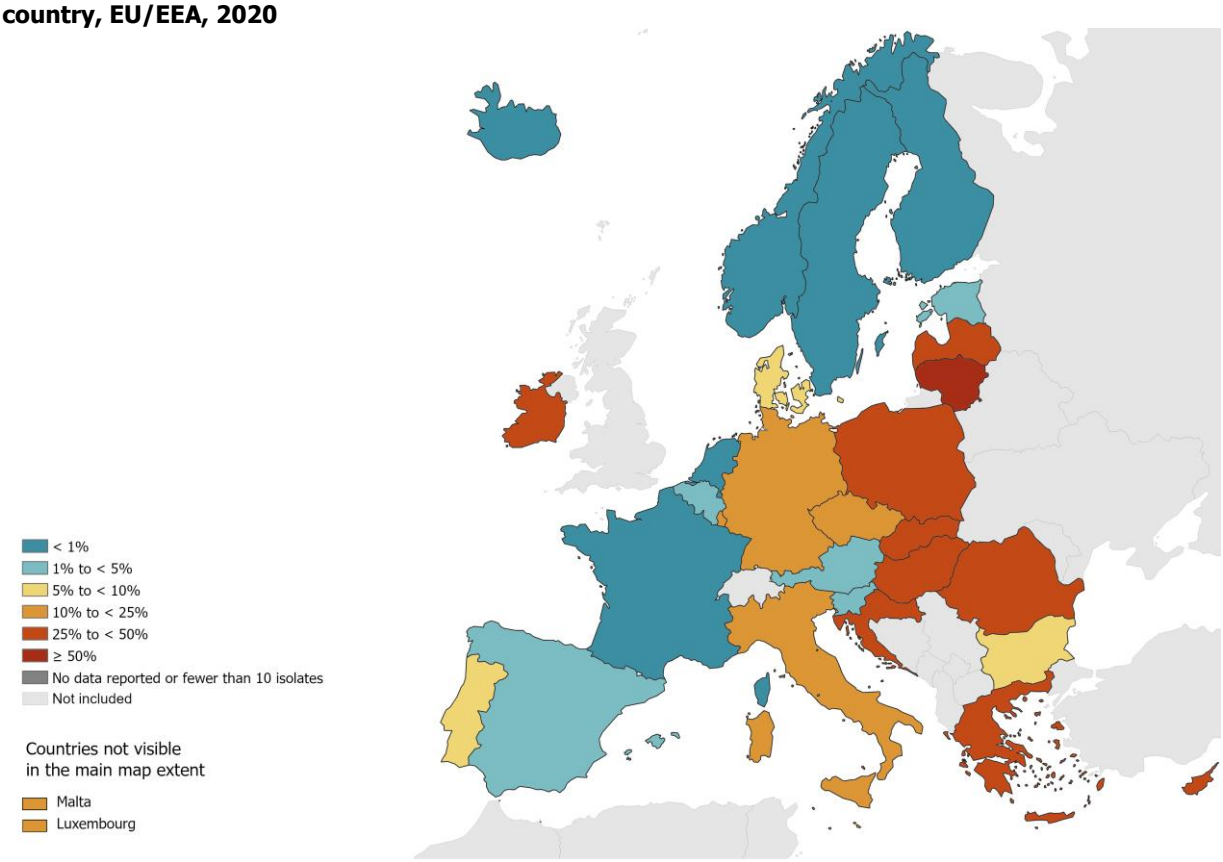
| AMR pattern[b] | Number of isolates | Percentage of total[c] |
|---|---|---|
| **Fully susceptible (to included antimicrobial groups)** | **745** | **8.0** |
| **Single resistance (to indicated antimicrobial group)** | | |
| **Total (any single resistance)** | **3 710** | **39.7** |
| Aminopenicillins | 3 656 | 39.1 |
| Other antimicrobial groups | 54 | 0.6 |
| **Resistance to two antimicrobial groups** | | |
| **Total (any two-group combinations)** | **3 987** | **42.6** |
| Aminopenicillins + gentamicin (high level resistance) | 3 209 | 34.3 |
| Aminopenicillins + vancomycin | 774 | 8.3 |
| Other resistance combinations | 4 | <0.1 |
| **Resistance to three antimicrobial groups** | | |
| Aminopenicillins + gentamicin (high level resistance) + vancomycin | **912** | **9.7** |

[a] *Only isolates with complete susceptibility information for aminopenicillins (ampicillin or amoxicillin), gentamicin (high-level resistance) and vancomycin were included in the analysis. This represented 50% (9 354/18 548) of all reported* E. faecium *isolates.*

[b] *Only AMR combinations >1% of the total are specified.*

[c] *Not adjusted for population differences in the reporting countries.*

**Figure 10. *Enterococcus faecium*. Percentage of invasive isolates resistant to vancomycin, by country, EU/EEA, 2020**




# Discussion

The rapid and continuous increase in the percentage of vancomycin resistance in *E. faecium* in the EU/EEA is a cause for concern. ECDC's study of the health burden of AMR estimated that the median number of infections and deaths attributable to vancomycin-resistant enterococci almost doubled between 2007 and 2015 [19], and the increase in resistance percentages reported since 2016 contributes to a further increase in the health burden of vancomycin-resistant enterococci infections. The significantly increasing trend, observed at EU/EEA (excluding the United Kingdom) level and in several individual countries, highlights the urgent need for close monitoring to better understand the epidemiology, clonal diversity and risk factors associated with vancomycin-resistant *E. faecium* infection. Contrary to many other bacterial species–antimicrobial group combinations under surveillance by EARS-Net, no distinct geographical pattern could be seen for vancomycin-resistant *E. faecium*, with high AMR levels reported from countries in southern, eastern and western Europe.

Enterococci have intrinsic resistance to several antimicrobial classes, and any additional acquired AMR severely limits the number of treatment options. WHO has listed vancomycin-resistant *E. faecium* as a pathogen of high priority in its global priority list of antibiotic-resistant bacteria, emphasising the paucity of available and effective treatment options [37]. High levels of antimicrobial-resistant enterococci remain a major infection control challenge and an important cause of healthcare-associated infections in Europe. In addition to the fact that infections caused by resistant strains are difficult to treat, enterococci are also easily disseminated in healthcare settings.

# References


1. European Centre for Disease Prevention and Control. Surveillance atlas of infectious diseases. In: European Centre for Disease Prevention and Control [website]. Stockholm: ECDC; 2021. Available at: https://www.ecdc. europa.eu/en/surveillance-atlas-infectious-diseases
2. European Centre for Disease Prevention and Control. TESSy – The European Surveillance System – antimicrobial resistance (AMR) reporting protocol 2021 – European Antimicrobial Resistance Surveillance Network (EARS-Net) surveillance data for 2020. Stockholm: ECDC; 2021. Available at:
3. 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), 2019. Stockholm: ECDC; 2020. Available at: https://www.ecdc.europa.eu/en/publications-data/antibiotic-resistance-external-quality-assessment-laboratories-earsnet
4. European Centre for Disease Prevention and Control. ECDC activities on surveillance. In: European Centre for Disease Prevention and Control [website]. Stockholm: ECDC; 2018 Available at: https://www.ecdc.europa.eu/en/about-us/what-we-do/ecdc-activities-surveillance
5. European Committee on Antimicrobial Susceptibility Testing. Clinical breakpoints – breakpoints and guidance. In: European Committee on Antimicrobial Susceptibility Testing [website]. Basel: EUCAST; 2021. Available at: http://www.eucast.org/clinical_breakpoints/
6. Eurostat [website]. Brussels: European Commission; 2021. Available at: https://ec.europa.eu/eurostat
7. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020. In: World Health Organization [website]. Geneva: WHO; 2020. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
8. European Medicines Agency. EMA recommends first COVID-19 vaccine for authorisation in the EU. In: European Medicines Agency [website]. Amsterdam: EMA; 2020. Available at: https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu
9. Monnet DL, Harbarth S. Will coronavirus disease (COVID-19) have an impact on antimicrobial resistance? Euro Surveill. 2020;25(45):pii=2001886. Available at: https://doi.org/10.2807/1560-7917.ES.2020.25.45.2001886
10. European Centre for Disease Prevention and Control. Antimicrobial resistance in the EU/EEA (EARS-Net). Annual epidemiological report 2019. Stockholm: ECDC; 2020. Available at: https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2019
11. European Centre for Disease Prevention and Control. Antimicrobial consumption. Annual epidemiological report for 2020. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-consumption-europe-2020
12. Organisation for Economic Co-operation and Development, European Centre for Disease Prevention and Control. Antimicrobial resistance. Tackling the burden in the European Union. Briefing note for EU/EEA countries. Paris: OECD; 2019. Available at: https://www.oecd.org/health/health-systems/AMR-Tackling-the-Burden-in-the-EU-OECD-ECDC-Briefing-Note-2019.Pdf
13. Ashiru-Oredope D, Hopkins S, Vasandani S, Umoh E, Oloyede O, Nilsson A et al. Healthcare workers' knowledge, attitudes and behaviours with respect to antibiotics, antibiotic use and antibiotic resistance across 30 EU/EEA countries in 2019. Euro Surveill. 2021;26(12):pii=1900633. Available at: www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.12.1900633
14. European Commission. European Commission notice — EU guidelines for the prudent use of antimicrobials in human health (2017/C 212/01). Brussels: EC; 2017. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52017XC0701(01)&from=ET
15. European Commission. A European One Health Action Plan against Antimicrobial Resistance (AMR). Brussels: EC; 2017. Available at: https ://ec.europa.eu/health/sites/health/files/antimicrobial_resistance/docs/amr_2017_action-plan.pdf
16. 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;24(28):pii=1800339. Available at: https://doi.org/10.2807/1560-7917.ES.2019.24.28.1800339
17. WHO Regional Office for Europe/European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2022 – 2020 data. Copenhagen: WHO Regional Office for Europe; 2022. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/ECDC-WHO-AMR-report.pdf
18. World Health Organization. Global action plan on antimicrobial resistance. Geneva: WHO; 2015 Available at: https://www.who.int/publications/i/item/9789241509763

19. 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;19(1):56–66. Available at: https://doi.org/10.1016/S1473-3099(18)30605-4
20. Peñalva G, Högberg LD, Weist K, Vlahović-Palčevski V, Heuer O, Monnet DL et al. Decreasing and stabilising trends of antimicrobial consumption and resistance in *Escherichia coli* and *Klebsiella pneumoniae* in segmented regression analysis, European Union/European Economic Area, 2001 to 2018. Euro Surveill. 2019;24(46):1900656. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.46.1900656
21. European Centre for Disease Prevention and Control, European Food Safety Authority, European Medicines Agency. Third joint inter-agency report on the integrated analysis of consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals in the EU/EEA, JIACRA III. 2016-20118. Stockholm, Parma, Amsterdam: ECDC, EFSA, EMA; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/third-joint-interagency-antimicrobial-consumption-and-resistance-analysis-report
22. European Food Safety Authority, European Centre for Disease Prevention and Control. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2019-2020. EFSA Journal 2022;20(3):7209. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/efs2_7209_Rev2.pdf
23. European Centre for Disease Prevention and Control. Rapid risk assessment: carbapenem-resistant Enterobacteriaceae, second update – 26 September 2019. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/carbapenem-resistant-enterobacteriaceae-second-update
24. European Centre for Disease Prevention and Control. Rapid risk assessment: increase in OXA-244-producing *Escherichia coli* in the European Union/European Economic Area and the UK since 2013 – first update 20 July 2021. Stockholm: ECDC; 2021 Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-increase-oxa-244-producing-escherichia-coli-eu-eea
25. 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 at: https://www.ecdc.europa.eu/en/publications-data/ecdc-study-protocol-genomic-based-surveillance-carbapenem-resistant-andor
26. European Centre for Disease Prevention and Control. Rapid risk assessment: combined clonal and plasmid-mediated outbreak of carbapenemase-producing Enterobacterales in Lithuania, 2019–2020 – 3 February 2020. Stockholm: ECDC; 2020. Available at: https://www.ecdc.europa.eu/en/publications-data/combined-clonal-and-plasmid-mediated-outbreak-carbapenemase-producing
27. 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;24(9):1900123. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.9.1900123
28. 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 at: .https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-carbapenemase-producing-oxa-48-klebsiella-pneumoniae-st392
29. European Centre for Disease Prevention and Control. Rapid risk assessment: regional outbreak of New Delhi metallo-betalactamase-producing carbapenem-resistant Enterobacteriaceae, Italy, 2018–2019 – 4 June 2019. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/RRA-new-delhi-metallo-beta-lactamase-producing-CRE
30. European Centre for Disease Prevention and Control. Rapid risk assessment: outbreak of carbapenemase-producing Enterobacterales in Lithuania, 2019 – 18 December 2019. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-outbreak-carbapenemase-producing-enterobacterales-lithuania
31. Ludden C, Lötsch F, Alm E, Kumar N, Johansson K, Albiger B et al. Cross-border spread of blaNDM-1- and blaOXA-48-positive *Klebsiella pneumoniae*: a European collaborative analysis of whole genome sequencing and epidemiological data, 2014 to 2019. Euro Surveill. 2020;25(20):2000627. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.20.2000627
32. European Centre for Disease Prevention and Control. Rapid risk assessment: outbreak of carbapenemase-producing (NDM-1 and OXA-48) and colistin-resistant *Klebsiella pneumoniae* ST307,

north-east Germany, 2019. 28 October 2019. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/outbreak-Klebsiella-pneumoniae-Germany

33. European Centre for Disease Prevention and Control. Rapid risk assessment: emergence of hypervirulent *Klebsiella pneumoniae* ST23 carrying carbapenemase genes in EU/EEA countries. 17 March 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/risk-assessment-emergence-hypervirulent-klebsiella-pneumoniae-eu-eea
34. European Centre for Disease Prevention and Control. Directory of online resources for the prevention and control of antimicrobial resistance (AMR) and healthcare-associated infections (HAI). Stockholm: ECDC; 2018. Available at: https://www.ecdc.europa.eu/en/publications-data/directory-online-resources-prevention-and-control-antimicrobial-resistance-amr
35. 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;6:113.
36. European Centre for Disease Prevention and Control. Rapid risk assessment Emergence of resistance to ceftazidime-avibactam in carbapenem-resistant Enterobacteriaceae, 12 June 2018. Stockholm: ECDC; 2018. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/RRA-Emergence-of-resistance-to%20CAZ-AVI-in-CRE-Enterobacteriaceae.pdf
37. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Geneva: WHO; 2017. Available at: https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf
38. European Centre for Disease Prevention and Control. Healthcare-associated infections acquired in intensive care units. Annual epidemiological report for 2017. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/healthcare-associated-infections-intensive-care-units-annual-epidemiological-1
39. 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;24(33):1800538. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.33.1800538
40. Plachouras D, Kärki T, Hansen S, Hopkins S, Lyytikäinen O, Moro ML et al. Antimicrobial use in European acute care hospitals: results from the second point prevalence survey (PPS) of healthcare-associated infections and antimicrobial use, 2016 to 2017. Euro Surveill. 2018;23(46):1800393. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.23.46.1800393
41. European Centre for Disease Prevention and Control. Rapid risk assessment: carbapenem-resistant *Acinetobacter baumannii* in healthcare settings – 8 December 2016. Stockholm: ECDC; 2016. Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-carbapenem-resistant-acinetobacter-baumannii-healthcare
42. Gagliotti C, Diaz Högberg L, Billström H, Eckmanns T, Giske CG, Heuer OE, et al. *Staphylococcus aureus* bloodstream infections: diverging trends of meticillin-resistant and meticillin-susceptible isolates, EU/EEA, 2005 to 2018. Euro Surveill. 2021 Nov;26(46):2002094. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.46.2002094
43. 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;22(44):16-00696. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2017.22.44.16-00696
44. European Centre for Disease Prevention and Control. Invasive pneumococcal disease. Annual epidemiological report for 2018. Stockholm: ECDC; 2020. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2018_IPD.pdf
45. European Centre for Disease Prevention and Control. Vaccine scheduler. In: European Centre for Disease Prevention and Control [website]. Stockholm: ECDC; 2019. Available at: https://vaccine-schedule.ecdc.europa.eu/
46. Diaz Högberg L, Vlahović-Palčevski V, Pereira C, Weist K, Monnet DL. Decrease in community antibiotic consumption during the COVID-19 pandemic, EU/EEA, 2020. Euro Surveill. 2021 Nov;26(46):2101020. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.46.2101020