SURVEILLANCE REPORT

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

Annual Epidemiological Report for 2021

Key facts

- Twenty-nine European Union/European Economic Area (EU/EEA) countries reported cases of pathogens with antimicrobial resistance (AMR) to the European Antimicrobial Resistance Surveillance Network (EARS-Net) for 2021, based on data for invasive bacterial isolates (i.e. retrieved from blood or cerebrospinal fluid). Twenty-eight countries reported cases 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 (Greece) reported data for all bacterial species except *S. pneumoniae*.
- During 2020 and 2021, reporting of cases of pathogens with antimicrobial resistance (AMR) coincided with changes in healthcare and the community resulting from the global COVID-19 pandemic, which will have affected infection prevention and control activities targeting these pathogens.
- Overall in 2021, the most commonly reported bacterial species was *E. coli* (39.4% of all reported cases), followed by *S. aureus* (22.1%), *K. pneumoniae* (11.9%), *E. faecalis* (8.8%), *E. faecium* (6.2%), *P. aeruginosa* (6.1%), *Acinetobacter* spp. (3.0%) and *S. pneumoniae* (2.5%). This ranking is different to 2020, since *E. faecium* and *Acinetobacter* spp. are one rank higher.
- Between 2020 and 2021, the number of reported cases increased for all pathogens. The largest increases were observed for *Acinetobacter* spp. (+43%), *E. faecium* (+21%) and *E. faecalis* (+14%), with smaller increases for *S. aureus* (+9.4%), *P. aeruginosa* (+8.2%), *K. pneumoniae* (+8.1%), *S. pneumoniae* (+4.3%), and also for the most frequently reported pathogen - i.e. *E. coli* (+2.8%).
- In 2021, the most striking observation was the overall increase in the number of reported cases of *Acinetobacter* spp. which mostly belong to the *A. baumannii* complex in the EU/EEA. This does not appear to be a feature of improved reporting, as the increase was confirmed among the laboratories that consistently reported data each year during the period 2017–2021 (n=666). On average, there was more than double (+121%) the number of reported cases resistant to each of the three antimicrobial groups (carbapenems, fluoroquinolones and aminoglycosides) in 2021 than the average for 2018–2019. In addition, the population-weighted mean AMR percentage had increased by more than 20% for each of these groups.
- The greatest increases in the number of cases and AMR percentages of *Acinetobacter* spp. were reported by countries that already had high AMR percentages in their reported *Acinetobacter* spp. cases prior to 2020. At country level, among all reporting laboratories in 2021, the percentage of *Acinetobacter* spp. cases resistant to all three antimicrobial groups ranged from 0.0–98.5%.
- Together, these findings imply that the situation with *Acinetobacter* spp. in the EU/EEA has deteriorated for the second year in a row. *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. AMR reduces options for treatment of infections. Options for national preparedness and response include ensuring that hospitals can perform timely screening, laboratory reporting and pre-emptive isolation of high-risk patients; good infection prevention and control; rigorous environmental cleaning and disinfection and antimicrobial stewardship programmes.

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- For *K. pneumoniae*, the percentage of cases resistant to carbapenems continued to increase, and this was also observed among laboratories that continuously reported data from 2017 to 2021. In these laboratories, the percentage remained unchanged from 2017 to 2018, and increased by +8% from 2018 to 2019. Then, in 2020, the percentage of carbapenem-resistant *K. pneumoniae* cases reported by these laboratories increased by a further +31%, and in 2021 by another +20%. The percentages of carbapenem-resistant cases varied widely by country (0–73.7%), implying that there are still further opportunities to counter this AMR threat.
- As in 2020, for *E. faecium,* the increase in the number and percentage of cases with vancomycin resistance continued in 2021, although the relative importance of this finding for public health in the EU/EEA is currently unclear, compared to the trends in other pathogens noted above.
- For *S. pneumoniae*, there had been a large decrease in the number of reported cases in the EU/EEA in 2020 compared to 2019. However, this number remained relatively stable in 2021. In this context, the percentage of penicillin non-wild-type cases increased from 14% in 2017 to 16% in 2021.
- Otherwise, during 2017−2021, for the EU/EEA (excluding the United Kingdom), most of the bacterial species–antimicrobial combinations under surveillance showed either a significantly decreasing trend or no significant trend in the population-weighted mean AMR percentage, in particular *E. coli* (other than carbapenem-resistant)*, K. pneumoniae* (other than carbapenem-resistant), *P. aeruginosa* and meticillin-resistant *S. aureus* (MRSA). Nevertheless, these pathogens remain important in the EU/EEA, with high AMR percentages. For example, more than half (53.1%) of all reported *E. coli* cases in 2021 were resistant to at least one antimicrobial group under surveillance, compared to about a third (34.3%) of *K. pneumoniae* cases and about a fifth (18.7%) of *P. aeruginosa* cases. However, as expected, AMR percentages were generally higher for *K. pneumoniae* and *P. aeruginosa* than for *E. coli* for each reported antimicrobial group/agent.
- The reported AMR percentages varied widely among countries for several bacterial species–antimicrobial group combinations, 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 the EU/EEA, and the highest by countries in the south and east of the EU/EEA.
- The latest country-specific data can be retrieved from the ECDC Surveillance Atlas of Infectious Diseases (https://atlas.ecdc.europa.eu/).
- In 2021, 22 (76%) participating countries classified the national representativeness of their reported EARS-Net data as 'high' for all three recorded standard metrics of national representativeness. These metrics are the geographical areas covered, the included acute care hospitals, and the microorganisms that caused invasive infections in participating hospitals. In the 22 countries, the rate at which blood cultures were obtained from patients was three-fold higher than in the four countries that reported one or none of the metrics of national representativeness as 'high'. Appropriate microbiological testing of blood samples is a pre-requisite for adjusting the appropriateness of antimicrobial prescriptions to treat infections, and for reducing AMR.

Methods

The results presented in this report are based on antimicrobial resistance (AMR) data from invasive isolates (retrieved from blood or cerebrospinal fluid samples) reported to the European Antimicrobial Resistance Surveillance Network (EARS-Net) by 29 European Union (EU) and European Economic Area (EEA) countries in 2022 (data referring to 2021), and trend analyses of data reported by the countries who have participated continuously during the period 2017 to 2021. 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 facilitate action to address AMR.

EARS-Net is based on a network of representatives (ECDC national focal points for AMR, operational contact points[1] for epidemiology, for microbiology and for The European Surveillance System (TESSy) interaction) from EU/EEA countries that collect routine clinical antimicrobial susceptibility test (AST) data from national AMR surveillance initiatives. Scientific guidance and support is 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 2021, all EU Member States and two EEA countries (Iceland and Norway) participated in EARS-Net. A high proportion of laboratories that report data to EARS-Net participate in a regular EARS-Net External Quality Assessment (EQA) exercise, which helps improve data quality and increases the ability of EU/EEA countries to report comparable AMR data. The 2021 EARS-Net EQA included *E. coli* and *K. pneumoniae* samples, whereas previous years also included other species. In 2021, more than 95% of laboratories reported the correct interpretation for 89 (80.23%) of the 111 tested strain-antimicrobial combinations. The difficulties identified in reporting the correct interpretation included the proper characterisation of carbapenem phenotypes in both species, and the detection of decreased susceptibility to fluoroquinolones in *E. coli*. Therefore, in 2021, the EARS-Net laboratories may have over-reported decreased carbapenem susceptibility in both species, and under-reported decreased susceptibility towards fluoroquinolones in *E. coli* [3].

Antimicrobial susceptibility data

Every year, countries report routine AST results collected from local medical microbiology laboratories to EARS-Net. If it is not possible to include data from all of the relevant laboratories, countries can report data from sentinel 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* species, *Campylobacter* species and *Mycobacterium tuberculosis*, are also monitored by ECDC under other surveillance networks but are not included in EARS-Net.

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].

The restriction to invasive isolates aims to reduce the impact of different sampling frames which, 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. However, including routine non-invasive isolates may produce incomparable results for surveillance purposes, because the processing of such samples is heavily influenced by clinical interpretation, and diagnostic and treatment guidelines, which vary 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, and began doing so from 2019 data.

[1] 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

Starting with the data collected for 2019, EARS-Net has only been accepting data generated using EUCAST clinical 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 2017–2021 and retrieved from TESSy on 13 September 2022.

Data analysis

Before data analysis, data are de-duplicated to include only the first isolate per patient, year and bacterial species. Unless otherwise stated, the term 'case' and 'isolate' are used synonymously throughout this report.

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, although laboratories are expected to use current EUCAST standards. As of 2021, EUCAST breakpoints are available for both meningitis and non-meningitis for additional antimicrobial agent combinations that are presented in this report [5]. EARS-Net accepts AST data as it is, but countries are recommended to use non-meningitis breakpoints overall for all 2021 data.

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

AMR/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 2021 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 as 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 20 isolates are reported for a specific bacterial species–antimicrobial group combination in a country, the AMR percentage is not displayed in the tables presented in this report.

Country-specific information for each bacterial species, including results by patient age group and sex for specific AMR phenotypes, are available in ECDC's Surveillance Atlas of Infectious Diseases [1].

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. Unless otherwise stated, comparisons of this percentage between years do not include the United Kingdom (UK).

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 (2017–2021). 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 previous 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, since 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. The categories are listed and described in Table 2. The definition was adjusted, as of data reported in 2021 [2]. For data reported in 2017–2020, the definition of geographical representativeness can be found in the report 'Antimicrobial resistance surveillance in Europe 2022 – 2020 data' [7].

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.

Isolate representativeness

Isolate representativeness is a qualitative indicator referring to the representativeness of data reported by EARS-Net laboratories in relation to the microorganisms causing invasive infections in the included hospitals. The categories are listed and described in Table 2. The collection of data related to 'isolate representativeness' was adjusted, as of the data collection in 2022 [2]. For data reported in the period 2017–2020, 'isolate representativeness' refers to 'patient and isolate representativeness', as defined in the report 'Antimicrobial resistance surveillance in Europe 2022 – 2020 data' [7].

Blood culture rate

Blood culture rate refers to the number of sets of blood cultures (or 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 2021

Bacterial species	Assessed antimicrobial group/agent resistance or specific resistance mechanism	Indicative 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
Enterococcus faecium	Aminopenicillins	Ampicillin or amoxicillin
	High-level aminoglycoside resistance	Gentamicin
	Vancomycin	Vancomycin

MRSA: meticillin-resistant Staphylococcus aureus.

[a] MRSA is based on AST results for cefoxitin or, if not available, oxacillin. AST results reported for cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if oxacillin is not reported. If no phenotypic results are available, data from molecular confirmation tests (detection of mecA *gene PCR or a positive PBP2A-agglutionation test) are accepted as a marker for MRSA.*

[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, 2021 (or latest available data)

Country	Estimated population coverage[a] (%)	Geographical representativeness[b]	Hospital representativeness[c]	Isolate representativeness[d]	Blood culture rate (blood culture sets/ 1 000 patient-days)[e]
Austria	ND	High	High	High	ND
Belgium	43[f]	High	High	High	100.8[f]
Bulgaria	45	Medium	Medium	Medium	11.4
Croatia	100	High	High	High	38.3
Cyprus	75	High	High	High	73.8
Czechia	80	High	High	High	21.3
Denmark	100	High	High	High	251.0
Estonia	100	High	High	High	39.2
Finland	96	High	High	High	143.9
France	55[g]	High	High	High	54.6[g]
Germany	35	High	Medium	High	ND
Greece	42	High	High	Medium	ND
Hungary	90	High	High	High	22.0
Iceland	100	High	High	High	64.4
Ireland	96	High	High	High	56.5
Italy	61	High	High	High	66.6
Latvia	90	High	Medium	Medium	17.0
Liechtenstein	ND	ND	ND	ND	ND
Lithuania	100	High	High	High	9.8
Luxembourg	100	High	High	High	42.1
Malta	95	High	High	High	37.7
Netherlands	68	High	High	High	ND
Norway	94	High	High	High	87.4
Poland	20	Medium	Medium	High	54.7
Portugal	97	High	High	High	256.0
Romania	6	Low	Low	Low	32.7
Slovakia	56	High	High	High	32.1
Slovenia	99	High	High	High	46.8
Spain	31	Medium	High	High	165.4
Sweden	89	High	High	High	ND

[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. Medium: most geographical regions are covered. Low: only a few geographical areas of the country are covered. Unknown: unknown or no data provided.

[c] Hospital representativeness. High: the hospital selection is representative of the acute care hospital distribution in the country. Medium: the hospital selection is partly representative of the acute care hospital distribution in the country. Low: the hospital selection is poorly representative of the acute care hospital distribution in the country.

[d] Isolate representativeness. High: the isolate selection is representative of microorganisms causing invasive infections in the included hospitals. Medium: the isolate selection is partly representative of microorganisms causing invasive infections in the included hospitals. Low: the isolate selection is poorly representative of microorganisms causing invasive infections in the included hospitals.

[e] Blood culture rate (blood culture sets/1 000 patient-days): This refers to the mean of the total number of blood culture sets for Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis and Enterococcus faecium in all hospitals served by laboratories that provide AMR data to EARS-Net divided by the mean of the total number of patient-days in those same hospitals, multiplied by 1 000. The definition of a blood culture set and a patient-day might differ between countries and influence the estimate.

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

[g] The S. pneumoniae network is not included. It has an estimated population coverage of 56%. Its surveillance protocol does not prescribe reporting of the number of blood culture sets.

Overview of EU/EEA country participation in EARS-Net

As in the preceding years, all EU Member States and two EEA countries (Iceland and Norway) reported data for 2021 to EARS-Net [8]. Eighteen (62%) of these 29 countries reported that their participating laboratories had a population coverage of over two-thirds of the national population, including 14 countries that reported having a national population coverage of 90% or more. However, seven countries reported data for less than half of their population (Table 1).

Twenty-two (76%) of the 29 participating countries indicated that their reported data had a high national representativeness, in terms of three metrics: the geographical areas covered, the acute care hospitals included and the microorganisms that caused invasive infections in those hospitals. A further three countries reported that the representativeness was 'high' for two of the three metrics, and one country reported that the representativeness of its national data was 'low' for all three metrics (Table 2).

In hospitals served by the laboratories that reported data to EARS-Net in 2021, the blood culture rate was reported by 24 countries. In the 22 countries that reported a high national representativeness according to all three metrics listed above, the national average blood culture rate was 2.6 times higher than in the four countries reporting a medium or low national representativeness according to at least two of those three metrics (76 versus 29 blood culture sets per 1 000 patient-days, respectively). The reported blood culture rates were highest in Belgium, Denmark, Finland, Portugal, and Spain (>100 sets per 1 000 patient-days), and lowest in Bulgaria, Czechia, Hungary, Latvia and Lithuania (<25 sets per 1 000 patient-days) (Table 2).

All but one country 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 country (Greece) reported data for all bacterial species except *S. pneumoniae*.

The number of laboratories participating in EARS-Net continued to increase, indicating a strengthening of national AMR surveillance systems in the EU/EEA. In 2021, 1 847 laboratories reported data, 1 006 of which were in France. There were 666 laboratories identifiable as having reported data for each year during the period 2017–2021, as the reporting countries were able to provide a consistent laboratory identifier. These do not include >85% of the laboratories in France and Greece that participated in 2021, either because there were major changes in the organisational structure of the national surveillance system (France), or because of the restriction of EARS-Net, starting with 2019 data, to only include laboratories that used EUCAST methods and guidelines (Greece) [2,7].

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

The most commonly reported bacterial species in 2021 were *E. coli* (39.4%), followed by *S. aureus* (22.1%), *K. pneumoniae* (11.9%), *E. faecalis* (8.8%), *E. faecium* (6.2%), *P. aeruginosa* (6.1%), *Acinetobacter* spp. (3.0%) and *S. pneumoniae* (2.5%). This ranking was different to the ranking in 2020, with *E. faecium* and *Acinetobacter* spp. being ranked one place higher in 2021. Both 2020 and 2021 coincided with extreme pandemic-associated pressures on healthcare. Therefore, it is informative to also compare 2021 data with the years immediately pre-2020. In addition, even though the national and EU/EEA representativeness of EARS-Net data is high, restricting analysis to laboratories known to have reported consistently throughout 2017–2021 is a way of verifying trends. This 'restricted' dataset is very similar to the 'full' dataset. To illustrate this point, the overall number of isolates at EU/EEA level, for all bacterial species under surveillance, increased by 7.2% in 2021 compared to 2020 among laboratories that consistently reported data to EARS-Net during 2017–2021, and by 8.8% in all laboratories that reported during that period. Furthermore, among the 'restricted' set of laboratories that consistently reported data during 2017–2021 *S. pneumoniae* was reported more frequently than *Acinetobacter* spp. (3.2% and 2.8% of all reported bacterial species, respectively), but otherwise the ranking remained the same as in the full dataset.

Within that same restricted group of laboratories, comparing 2021 to the average for 2018 and 2019, the largest increases in the number of reported isolates were for *Acinetobacter* spp. (+73.9%; 3 523 and 6 127, respectively) and *E. faecium* (+32.5%; 9 926 and 13 151, respectively) followed by *E. faecalis* (+11.7%; 15 777 and 17 620, respectively). There was almost no change in *K. pneumoniae* (+0.03%; 25 044 and 25 052, respectively) and *P. aeruginosa* (-0.9%; 12 150 and 12 035, respectively), and a decrease in the number of reported isolates of *S. aureus* (-5.5%; 50 267 and 47 487, respectively), *E. coli* (-11.8%; 99 266 and 87 526, respectively), and particularly *S. pneumoniae* (-45.6%; 12 629 and 6 875, respectively) (Table 3c).

Acinetobacter spp. had by far the largest annual increase in the number of reported isolates in both 2020 and 2021. During 2017–2019, the number of isolates had been relatively stable (+/-10%). During 2017–2021, similar

trends were observed for the number of reports of *Acinetobacter* spp. isolates that were resistant to each of the three antimicrobial groups presented in this report (i.e. carbapenems, fluoroquinolones and aminoglycosides) (Table 3b). Among the laboratories that consistently reported data during 2017–2021, the increase in the number of antimicrobial-resistant isolates was more pronounced in 2021 compared to the average for 2018 and 2019 (+121% on average, for each of these three groups), with a large increase in the percentage of isolates resistant to carbapenems, reaching 48% in 2021 (Table 3c). At country level in 2021, the percentage of resistant *Acinetobacter* spp. isolates among all reporting laboratories ranged from 0% to >98%, for each of the three antimicrobial groups individually and for combined resistance to all three groups (Table 3b).

The resistance profiles of both *Enterococcus* species under surveillance continue to be of concern. The percentage of *E. faecium* with vancomycin resistance continued to increase, reaching 17.2% in 2021. The relative importance of this trend in the EU/EEA is currently unclear, compared to the trends in other pathogens noted above. For *E. faecalis*, almost a third of all reported isolates had high-level resistance to gentamicin in 2021.

Otherwise, overall for the EU/EEA (excluding the United Kingdom) and during the period 2017−2021, 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. Exceptions included the trends described for *Acinetobacter* spp., and the EU/EEA population-weighted percentage of carbapenem resistance for both *E. coli* and *K. pneumoniae* which increased during the period 2017–2021 (Table 3b, Table 3c). Reports of carbapenem resistance still remained relatively rare among *E. coli* isolates (0.2% in 2021). By contrast, in 2021, 11.7% *K. pneumoniae* isolates were carbapenem-resistant (country range: 0–80%). The EU/EEA population-weighted mean percentage of carbapenem resistance among *K. pneumoniae* isolates increased each year. The rate of increase, relative to the previous year, also increased each year in the period 2017–2021, by +5%, +6%, +11% and +17%, respectively. The annual relative change in the percentage of carbapenem-resistant *K. pneumoniae* isolates was even striking among the laboratories identified as consistently reporting data each year for 2017–2021 (+0%, +8%, +31% and +20% in 2018–2021, respectively).

In general, the EU/EEA population-weighted AMR percentages were lower in *E. coli* than in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter* spp. Even so, 53.1% of all reported *E. coli* isolates in 2021 had resistance reported for at least one antimicrobial group under surveillance, compared to 34.3% of *K. pneumoniae* isolates and 18.7% of *P. aeruginosa* isolates. Among these three pathogens, combined resistance to several antimicrobial groups/agents remained a frequent occurrence, reported for 5% of *E. coli* isolates, 21% of *K. pneumoniae* isolates, and 13% of *P. aeruginosa* isolates.

For *S. aureus*, a significant decrease in the EU/EEA population-weighted percentage of MRSA isolates was reported during the period 2017−2021, from 18.4% to 15.8% (Table 3b). Nevertheless, MRSA remains an important pathogen in the EU/EEA, with percentages remaining high in several countries.

Country-specific information for each bacterial species, including results by patient age group and sex for specific AMR phenotypes, are available in ECDC's Surveillance Atlas of Infectious Diseases [1]. The reported AMR percentages for several bacterial species–antimicrobial group combinations varied widely among EU/EEA 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.

Discussion

In 2021, the AMR percentages for the bacterial species-antimicrobial group combinations under surveillance continued to be high overall in the EU/EEA. The increasing trends of carbapenem resistance percentages in *K. pneumoniae* and *Acinetobacter* spp. and of vancomycin-resistant *E. faecium* between 2017 and 2021 are of particular concern, and indicate that AMR remains a serious challenge in the EU/EEA. As for previous years, there was a large variability in the percentages across EU/EEA countries in 2021, highlighting the opportunities for significant AMR reduction through interventions to improve infection prevention and control (IPC) and antimicrobial stewardship practices.

The data for the years 2020 and 2021 presented in this report coincide with the first years of the coronavirus disease (COVID-19) pandemic. Changes to human behaviour in 2020 and 2021, resulting from efforts to control the pandemic, modified the risk for infection with pathogens with AMR [9,10]. In the community, non-pharmaceutical interventions (NPIs) for COVID-19 to promote physical distancing reduced the number and duration of person-to-person contacts. During the first part of 2021, countries gradually reduced the intensity of NPI implementation, following vaccine-associated reductions in hospitalisations, intensive care unit (ICU) admissions and deaths due to COVID-19 [11,12]. In autumn and winter 2021, there was a resurgence in hospitalisations and ICU admissions for COVID-19 that led to national authorities reinforcing their public health messaging for COVID-19, and 'pandemic fatigue' was frequently associated with reduced compliance with NPIs [13].

Large decreases in the total consumption of antibacterials for systemic use (ATC group J01) were noted during the first two years of the pandemic, in particular in the community. Changes were less consistent in the hospital sector, with increased consumption of last-line antibiotics such as carbapenems in particular [14].

In 2020–2021, there was delayed access to preventive, primary and elective health care, including surgery. More specialised care, for example for late diagnoses, commonly requires interventions that predispose patients to a higher risk of infection with an antimicrobial-resistant pathogen, such as the use of antimicrobial agents and invasive devices [15]. In addition, ICU admissions due to COVID-19 put a strain on ICU resources which necessitated the re-purposing of non-ICU beds and allocation of non-ICU staff to meet the urgent demand. In healthcare, as in society, recommendations for conscientious IPC for respiratory viral pathogens were the norm. However, compliance with all IPC measures in healthcare is likely to have been adversely affected by high hospital patient loads, staff absenteeism due to COVID-19, and reliance on more junior staff [16-18].

In 2020 and 2021, even though national authorities in EU/EEA countries focussed public health resources on the response to COVID-19 in order to face the acute crisis, EU/EEA countries continued to strengthen their participation in EARS-Net. As a direct result, EARS-Net data can be used to confidently describe the ongoing AMR threat for the EU/EEA, because a majority of countries reported data that are nationally representative.

In 2022, ECDC used the national data reported to EARS-Net for 2016–2020 to estimate the burden of infections with antibiotic-resistant bacteria under surveillance in the EU/EEA [19]. The number of cases of these infections increased from 685 433 (95% uncertainty interval (UI): 589 451 – 792 873 cases) in 2016 to 865 767 (95% UI 742 802 – 1 003 591 cases) in 2019, with a decrease in the estimate for 2020 to 801 517 (95% UI 684 955 – 932 213 cases). These infections resulted in an estimated annual number of attributable deaths that increased from 30 730 (95% UI 26 935 – 34 836 deaths) in 2016 to 38 710 (95% UI 34 053 – 43 748 deaths) in 2019, decreasing slightly to 35 813 (95% UI 31 395 – 40 584 deaths) in 2020.

In 2016–2020, the largest burden of disease was caused by infections with third-generation cephalosporin-resistant *E. coli*, followed by MRSA and third-generation cephalosporin-resistant *K. pneumoniae*. Infections with these three antibiotic-resistant bacteria resulted in the largest health impact, generating 58.2% of the total burden as measured in disability-adjusted life years (DALYs). ECDC estimated that for 2020, 30.9% of the total burden in DALYs was from infections with carbapenem-resistant bacteria, with a similar number of deaths attributable to carbapenem-resistant *K. pneumoniae*, (4 076 (95% UI 3 565 – 4 586) deaths), *Acinetobacter* spp. (3 656 (95% UI 3 036 – 4 289) deaths) and *P. aeruginosa* (3 210 (95% UI 2 513 – 4 004) deaths) [19].

The increase of most concern in the number of reported cases for the period 2020 to 2021 was for *Acinetobacter* spp. (in the EU/EEA, mostly *A. baumannii* complex), including isolates with carbapenem resistance. The increase was the largest of any pathogen under surveillance in EARS-Net, and this for the second consecutive year. Countries with large increases in the number of *Acinetobacter* spp. cases in 2020–2021 had also reported a high percentage of antimicrobial-resistant *Acinetobacter* spp. in the years immediately prior to the COVID-19 pandemic. Conversely, countries that had not reported a high number of cases or AMR percentages prior to 2020 had the lowest numbers and percentages in 2021.

Within the countries that reported increases in the number of reported cases in 2020–2021, most of the newly reported cases were among ICU patients, with the majority of isolates resistant to carbapenems, a common group of antibiotics for empiric treatment of healthcare-associated infections [20]. During the period 2020−2022, *Acinetobacter* spp. has often been reported as being the most frequent bacterial coinfection for COVID-19 patients in hospitals, and particularly ICUs, in Europe, North America and the Middle East, causing clonal outbreaks, with high case fatality rates, often associated with multidrug resistance [21-24].

The reasons for the increased number of *Acinetobacter* spp. infections in many EU/EEA countries warrant further investigation but are probably directly related to pandemic-related changes in healthcare provision. *Acinetobacter* spp., and particularly multidrug-resistant strains, are notoriously difficult to eradicate from the hospital environment once established, surviving on dry surfaces, readily contaminating healthcare providers' hands, and being spread by asymptomatic carriers [21]. Given the unprecedented patient loads in ICUs in EU/EEA countries during 2020–2021, even hospitals that rigorously and conscientiously applied IPC practices may still have had opportunities for IPC breaches sufficient for *Acinetobacter* spp. transmission [9]. This suggests a requirement for *Acinetobacter* spp.-specific control interventions in the affected hospitals [25]. EARS-Net will continue to report annual *Acinetobacter* spp. data in the 'post-pandemic' years to come, to facilitate assessment of trends in this relatively persistent hospital contaminant.

Trends in *P. aeruginosa* cases might have been expected to follow those observed for *Acinetobacter* spp., given that it is also often linked to environmental sources and the rate of ventilator use among hospitalised COVID-19 cases. However, the trends for *P. aeruginosa* cases remained relatively unchanged. Pandemic-related factors may partially explain this – for example, changes in the lengths of hospital stays, and greater shielding of patients at risk of both COVID-19 and *P. aeruginosa* infection, such as cystic fibrosis patients. Nevertheless, ECDC does not have incidence surveillance for pneumonias and lower respiratory tract infections, which, for *P. aeruginosa*, are the site of three times as many healthcare-associated infections [26].

For *S. pneumoniae*, the decrease in the number of cases observed in 2020 continued in 2021, overall and for isolates resistant to the antimicrobials under surveillance. This may be related to reduced risk factors for such infections during the waves of the COVID-19 pandemic such as a decrease in the frequency of inter-personal contacts, influenza incidence, and antibiotic prescriptions, and perhaps a lower incidence of blood cultures for community-acquired infections [14,27].

The monitoring framework for the United Nations Sustainable Development Goals includes two AMR indicators. These monitor the percentage of bloodstream infections due to meticillin-resistant *S. aureus* (MRSA) and *E. coli* resistant to third-generation cephalosporins among patients seeking care whose blood samples have been tested [28]. Among the laboratories in EU/EEA countries that consistently reported data during 2017−2021, the resistance percentages decreased for both pathogens. Among the laboratories that consistently reported data each year during 2017–2021, the decrease in the annual number of reported MRSA isolates reported for 2019–2020 has reversed to some extent in 2020–2021. However, the decreasing trend in the percentage of third-generation cephalosporin-resistant *E. coli* was maintained and it is worth noting that the AMR percentages varied widely between countries, suggesting that opportunities for reduction remain. In particular, pre-2020, the annual reductions in the percentage of *S. aureus* resistant to meticillin (MRSA) were explained by the relatively large and ongoing increase in the number of reported meticillin-susceptible *S. aureus* (MSSA) infections, while the annual number of reported MRSA infections remained relatively stable [29].

When interpreting the EARS-Net data, it is important to be mindful of the structure of this surveillance system, including the large variation in national blood culture rates, and the changes in the surveillance systems over time. Although the restriction of EARS-Net from 2019 onwards, to only accept data generated using EUCAST breakpoints and methodology, should improve the quality and comparability of data in the long term, it has resulted in fewer laboratories participating in many countries in 2019. Moreover, there has not been any systematic assessment of the characteristics and AMR percentages of the EU/EEA laboratories that do not report to EARS-Net. Indeed, seven of 29 countries reported data with less than 50% population coverage. Similarly, the laboratories that were identifiable as having reported data for five consecutive years may also be atypical compared to other laboratories in the same country. Finally, as noted above, trends in AMR percentages are also affected by changes to country surveillance systems, and by changes to EARS-Net itself. For example, the lower percentages of aminoglycoside resistance reported for *P. aeruginosa* in both 2020 and 2021 reflect an update of the EARS-Net reporting protocol for 2020 data. Therefore, the analysis of data from 2020 onwards only includes tobramycin susceptibility test results, whereas previous years include tobramycin, netilmicin and gentamicin. Irrespective of these limitations, overall, EU/EEA-level analyses from EARS-Net surveillance data are probably an accurate reflection of the overall AMR situation in the EU/EEA.

The COVID-19 pandemic has led to several developments that will help the EU address infectious disease threats, including AMR, as well as boosting action on health and health security under the European Health Union [30]. The European Health Union includes strengthened mandates for ECDC and the European Medicines Agency (EMA), creation of the European Health Emergency preparedness and Response Authority (HERA) and a new Regulation on serious cross-border threats to health. A much larger budget is available under the EU4Health programme (EUR 5.3 billion for the period 2021–2027), which is dedicated to wider policy areas but is also one of the main instruments for the European Health Union and includes action on AMR.

The new Regulation on serious cross-border threats to health, adopted by the Council on 24 October 2022 [31], provides a revised regulatory framework for preparedness, surveillance, risk assessment, early warning and responses at EU- and Member-State level in the event of biological, chemical, environmental or other cross-border threats to health, building on and repealing the previous Decision (EU) 1082/2013 [32]. The new elements include the development of a European Union preparedness plan, a system to regularly assess national plans, and a strengthening of Member State interactions in the Health Security Committee. The Regulation also provides for the establishment of EU reference laboratories, coordinated by ECDC, to support national reference laboratories in the Member States, in coordination with the World Health Organization (WHO) Reference Laboratories. The EU reference laboratories will support comparable disease notification and reporting by Member States by promoting good practice and voluntary alignment of Member States diagnostic methodologies. To achieve this, the reference laboratories network activities may be expanded to cover reference diagnostics, including support to outbreak responses; provision of reference materials, external quality assessments and training, scientific advice, collaboration and research.

Public health implications

Public health action to tackle AMR in the EU/EEA 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. Estimates based on data from EARS-Net show that in 2020, more than 800 000 infections occurred in the EU/EEA due to bacteria resistant to antibiotics, and that more than 35 000 people died as a direct consequence of these infections [19].

During the first two years of the COVID-19 pandemic (2020–2021), the most striking increase in the number of cases, compared to pre-2020, was for carbapenem-resistant *Acinetobacter* spp. infections, mostly in countries that had a relatively high percentage of carbapenem-resistant cases pre-pandemic. *Acinetobacter* spp., including carbapenem-resistant isolates, cause outbreaks and are difficult to eradicate once they become endemic. It is therefore likely that carbapenem-resistant *Acinetobacter* spp. will continue to expand in the EU/EEA in 2022. The options for outbreak preparedness, prevention and control described in the ECDC Rapid Risk Assessment

'Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings – 8 December 2016', remain valid for hospitals and national authorities in EU/EEA countries [25,33].

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 including enhanced hygiene, antibiotic stewardship programmes, 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 package could pay for itself within just one year and save around EUR 1.4 billion per year in the EU/EEA [34].

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, 2017–2021

Bacterial species	Antimicrobial group/agent resistance	2017[a]		2018[a]		2019[a]		2020[b]		2021[b]		2021 EU/EEA country range[c]
		N	%	N	%	N	%	N	%	N	%	
Escherichia coli	Aminopenicillin (amoxicillin/ampicillin) resistance	125 866	58.7	133 700	57.5	130 603	57.1	107 371	54.6	108 730	53.1	31.7–70.2
	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	140 584	14.9	152 720	15.1	157 918	15.1	139 057	14.9	143 180	13.8	5.5–37.3
	Carbapenem (imipenem/meropenem) resistance	140 438	0.1	151 444	0.1	156 871	0.3	135 624	0.2	137 526	0.2	0.0–1.1
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	141 562	25.7	154 698	25.3	161 718	23.8	139 372	23.8	143 253	21.9	9.6–51.6
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d]	141 788	11.4	154 266	11.1	161 432	10.8	136 101	10.9	139 435	9.6	4.1–27.0
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[d]	135 108	6.3	148 206	6.2	154 844	5.9	134 115	5.7	137 757	5.1	1.2–14.8
Klebsiella pneumoniae	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	32 952	31.2	38 420	31.7	41 057	31.4	39 848	33.9	43 261	34.3	3.4–81.4
	Carbapenem (imipenem/meropenem) resistance	32 960	7.1	38 140	7.5	40 714	8.0	39 279	10.0	42 007	11.7	0.0–73.7
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	32 908	31.5	38 754	31.6	41 617	31.3	40 066	33.9	43 136	33.6	0.0–80.0
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d]	33 119	24.1	38 539	22.7	41 484	22.4	38 977	23.7	42 181	23.7	0.0–69.1
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[d]	31 597	20.5	37 386	19.6	40 270	19.4	38 331	21.0	41 590	21.2	0.0–67.4
Pseudomonas aeruginosa	Piperacillin-tazobactam resistance	16 414	16.7	18 607	16.8	19 465	17.0	19 799	18.8	21 419	18.7	0.0–47.2
	Ceftazidime resistance	16 481	14.6	18 948	14.1	19 959	14.3	20 122	15.5	21 750	15.8	2.3–46.0
	Carbapenem (imipenem/meropenem) resistance	17 078	17.2	19 221	17.2	20 238	16.6	20 517	17.9	22 267	18.1	3.5–45.9
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	16 920	20.0	19 199	19.7	20 384	18.9	20 425	19.6	22 129	18.7	3.3–48.0
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[e]	16 948	13.1	19 174	11.8	20 344	11.5	12 880	9.4	14 537	8.9	0.0–41.7
	Combined resistance to ≥3 antimicrobial groups (among piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)[e]	15 448	12.7	17 890	12.7	18 630	12.2	12 041	13.6	13 684	12.6	0.0–42.1
Acinetobacter species	Carbapenem (imipenem/meropenem) resistance	6 171	33.1	6 512	31.9	5 927	32.4	7 507	37.9	10 732	39.9	0.0–99.5
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	6 087	37.4	6 474	36.2	5 888	36.6	7 372	41.7	10 626	43.0	1.5–99.8
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d]	6 042	32.2	6 437	31.3	5 891	32.8	7 275	37.0	10 399	39.6	2.1–98.8
	Combined resistance to carbapenems, fluoroquinolones and aminoglycosides[d]	5 872	28.2	6 283	28.3	5 668	29.4	7 111	34.0	10 172	36.8	0.0–98.5

Bacterial species	Antimicrobial group/agent resistance	2017[a]		2018[a]		2019[a]		2020[b]		2021[b]		2021 EU/EEA country range[c]
		N	%	N	%	N	%	N	%	N	%	
Staphylococcus aureus	MRSA[f]	66 279	16.9	72 882	16.4	74 718	15.7	72 976	16.7	78 633	15.8	0.9–42.9
Streptococcus pneumoniae	Penicillin non-wild-type[g]	17 182	12.8	18 660	12.9	18 235	12.2	8 076	15.5	8 465	16.3	3.6–35.7
	Macrolide (azithromycin/clarithromycin/erythromycin) resistance	17 575	15.7	19 203	15.2	18 940	14.5	8 407	16.8	8 758	18.3	0.0–36.0
	Combined penicillin non-wild-type and resistance to macrolides[g]	16 554	8.1	18 068	7.8	17 529	7.3	7 782	8.9	8 141	9.9	0.0–28.0
Enterococcus faecalis	High-level gentamicin resistance	13 930	29.7	15 343	27.1	13 577	25.3	14 316	29.0	16 301	29.0	6.7–55.2
Enterococcus faecium	Vancomycin resistance	14 183	15.0	15 961	17.3	16 523	18.3	18 349	16.8	22 315	17.2	0.0–66.4

[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 2021 (n = 29).
[d] For E. coli, K. pneumoniae and Acinetobacter spp., the aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.
[e] For P. aeruginosa, the aminoglycoside group includes only tobramycin from 2020 onwards.
[f] MRSA is based on AST results for cefoxitin or, if not available, oxacillin. AST results reported for cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if oxacillin is not reported. If no phenotypic results are available, data from molecular confirmation tests (detection of mecA gene PCR or a positive PBP2A-agglutionation test) are accepted as a marker for MRSA.
[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 during 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), 2017–2021

Bacterial species	Antimicrobial group/agent resistance	2017		2018		2019		2020		2021		2021 EU/EEA country range[a]	Trend 2017–2021[b]
		N	%	N	%	N	%	N	%	N	%		
Escherichia coli	Aminopenicillin (amoxicillin/ampicillin) resistance	97 219	58.1	104 198	57.0	102 375	56.6	107 371	54.6	108 730	53.1	31.7–70.2	↓*
	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	112 659	15.6	124 043	15.7	131 325	15.6	139 057	14.9	143 180	13.8	5.5–37.3	↓*
	Carbapenem (imipenem/meropenem) resistance	110 364	0.1	120 215	0.1	127 262	0.3	135 624	0.2	137 526	0.2	0.0–1.1	↑*
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	111 377	26.9	123 358	26.4	132 015	24.7	139 372	23.8	143 253	21.9	9.6–51.6	↓*
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c]	111 049	11.6	122 147	11.2	130 984	10.8	136 101	10.9	139 435	9.6	4.1–27.0	↓*
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[c]	108 300	6.6	120 450	6.4	129 083	6.1	134 115	5.7	137 757	5.1	1.2–14.8	↓*
Klebsiella pneumoniae	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	27 979	34.1	33 239	34.4	36 190	34.1	39 848	33.9	43 261	34.3	3.4–81.4	-
	Carbapenem (imipenem/meropenem) resistance	27 686	8.1	32 548	8.5	35 439	9.0	39 279	10.0	42 007	11.7	0.0–73.7	↑*
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	27 615	34.7	33 154	34.3	36 315	34.0	40 066	33.9	43 136	33.6	0.0–80.0	↓
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c]	27 756	26.4	32 830	24.7	36 078	24.5	38 977	23.7	42 181	23.7	0.0–69.1	↓*
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[c]	26 837	22.9	32 381	21.6	35 622	21.5	38 331	21.0	41 590	21.2	0.0–67.4	↓
Pseudomonas aeruginosa	Piperacillin-tazobactam resistance	13 717	18.3	16 018	18.5	16 894	18.6	19 799	18.8	21 419	18.7	0.0–47.2	-
	Ceftazidime resistance	13 801	16.0	16 327	15.5	17 328	15.7	20 122	15.5	21 750	15.8	2.3–46.0	-
	Carbapenem (imipenem/meropenem) resistance	14 274	18.9	16 473	18.8	17 496	18.1	20 517	17.9	22 267	18.1	3.5–45.9	↓
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	14 118	21.8	16 460	21.2	17 635	20.5	20 425	19.6	22 129	18.7	3.3–48.0	↓*
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d]	14 117	14.4	16 393	12.9	17 552	12.6	12 880	9.4	14 537	8.9	0.0–41.7	↓*
	Combined resistance to ≥3 antimicrobial groups (among piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)[d]	13 022	14.1	15 514	14.1	16 289	13.5	12 041	13.6	13 684	12.6	0.0–42.1	↓
Acinetobacter species	Carbapenem (imipenem/meropenem) resistance	5 389	37.6	5 798	36.4	5 209	36.9	7 507	37.9	10 732	39.9	0.0–99.5	↑*
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	5 294	42.0	5 754	41.1	5 181	40.9	7 372	41.7	10 626	43.0	1.5–99.8	-
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c]	5 252	36.3	5 711	35.2	5 170	36.9	7 275	37.0	10 399	39.6	2.1–98.8	↑*
	Combined resistance to carbapenems, fluoroquinolones and aminoglycosides[c]	5 126	32.1	5 607	32.4	4 998	33.6	7 111	34.0	10 172	36.8	0.0–98.5	↑*

Staphylococcus aureus	MRSA[e]	57 396	18.4	63 837	17.8	65 604	17.2	72 976	16.7	78 633	15.8	0.9–42.9	↓*
Streptococcus pneumoniae	Penicillin non-wild-type[f]	13 219	14.0	14 498	14.0	14 568	13.2	8 076	15.5	8 465	16.3	3.6–35.7	↑*
	Macrolide (azithromycin/clarithromycin/erythromycin) resistance	13 302	17.2	14 753	16.6	15 069	15.9	8 407	16.8	8 758	18.3	0.0–36.0	-
	Combined penicillin non-wild-type and resistance to macrolides[f]	12 669	9.1	14 016	8.6	14 102	8.0	7 782	8.9	8 141	9.9	0.0–28.0	-
Enterococcus faecalis	High-level gentamicin resistance	13 930	29.7	15 343	27.1	13 577	25.3	14 316	29.0	16 301	29.0	6.7–55.2	-
Enterococcus faecium	Vancomycin resistance	11 981	13.4	13 346	16.2	14 095	17.7	18 349	16.8	22 315	17.2	0.0–66.4	↑*

** The trend was confirmed when considering only laboratories that consistently reported data during 2017–2021 (Table 3c).*

[a] Lowest and highest national AMR percentage among reporting EU/EEA countries in 2021 (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] For E. coli, K. pneumoniae and Acinetobacter spp., the aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.

[d] For P. aeruginosa, the aminoglycoside group includes only tobramycin from 2020 onwards.

[e] MRSA is based on AST results for cefoxitin or, if not available, oxacillin. AST results reported for cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if oxacillin is not reported. If no phenotypic results are available, data from molecular confirmation tests (detection of mecA gene PCR or a positive PBP2A-agglutionation test) are accepted as a marker for MRSA.

[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 during the period 2016–2018 might have used different interpretive criteria for the susceptibility categories.

Table 3c. 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), 2017–2021, in laboratories that reported during each year during 2017–2021

Bacterial species	Antimicrobial group/agent resistance	2017		2018		2019		2020		2021		2021 EU/EEA country range[a]	Trend 2017–2021[b]
		N	%	N	%	N	%	N	%	N	%		
Escherichia coli	Aminopenicillin (amoxicillin/ampicillin) resistance	79 488	57.6	83 645	56.7	84 997	56.7	71 426	55.5	70 843	53.4	31.7–65.2	↓
	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	90 982	15.3	96 424	15.5	99 390	15.1	86 083	15.6	86 655	14.1	5.5–36.3	↓
	Carbapenem (imipenem/meropenem) resistance	89 288	0.1	93 684	0.1	97 076	0.4	84 406	0.2	83 392	0.1	0.0–0.5	↑
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	90 271	26.6	95 904	26.2	100 118	24.4	86 641	24.7	87 257	22.7	9.4–46.6	↓
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c]	90 442	11.4	95 726	11.0	99 431	10.7	85 377	11.0	85 037	9.8	4.2–26.3	↓
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[c]	88 389	6.4	94 271	6.3	97 697	5.9	84 092	5.9	84 022	5.0	1.2–14.7	↓
Klebsiella pneumoniae	Third-generation cephalosporin (cefotaxime/ceftriaxone/ceftazidime) resistance	21 867	33.9	24 132	33.8	25 416	33.1	23 133	34.5	24 819	35.9	3.4–86.1	↑
	Carbapenem (imipenem/meropenem) resistance	21 697	8.0	23 667	8.0	25 115	8.6	22 940	11.3	24 138	13.6	0.0–81.3	↑
	Fluoroquinolone (ciprofloxacin/levofloxacin/ofloxacin) resistance	21 770	34.8	24 103	34.1	25 546	33.7	23 338	34.4	24 849	35.2	0.0–84.8	-
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c]	21 927	26.8	24 013	25.2	25 364	24.3	22 907	24.4	24 396	25.3	0.0–77.4	↓
	Combined resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides[c]	21 288	23.3	23 674	22.3	25 024	21.2	22 550	21.8	24 014	22.8	0.0–76.1	-
Pseudomonas aeruginosa	Piperacillin-tazobactam resistance	10 585	18.4	11 333	17.9	11 901	17.3	10 741	17.7	11 584	19.2	0.0–51.6	-
	Ceftazidime resistance	10 667	15.6	11 549	14.8	12 112	14.9	10 871	15.2	11 803	16.3	2.3–46.9	-
	Carbapenem (imipenem/meropenem) resistance	10 992	18.2	11 644	18.4	12 291	17.1	11 082	18.1	11 947	18.7	3.5–48.6	-
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	10 867	21.5	11 647	21.6	12 354	20.3	11 061	20.2	11 931	19.7	3.3–48.6	↓
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[d]	10 875	14.4	11 602	12.8	12 292	12.2	7 634	10.1	8 518	9.5	0.0–42.0	↓
	Combined resistance to ≥3 antimicrobial groups (among piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)[d]	10 173	13.8	10 963	14.1	11 490	12.7	7 110	13.9	8 091	13.4	0.0–41.9	-
Acinetobacter species	Carbapenem (imipenem/meropenem) resistance	3 283	37.1	34 35	38.3	3 451	36.8	3 779	43.5	6 043	47.9	0.0–99.4	↑
	Fluoroquinolone (ciprofloxacin/levofloxacin) resistance	3 249	41.6	3 406	43.0	3 380	40.5	3 711	46.6	5 989	50.2	1.5–99.7	↑
	Aminoglycoside (gentamicin/netilmicin/tobramycin) resistance[c]	3 230	35.9	3 357	36.3	3 355	36.8	3 663	41.9	5 930	47.0	2.2–98.6	↑
	Combined resistance to carbapenems, fluoroquinolones and aminoglycosides[c]	3 163	32.0	3 290	34.0	3 270	33.4	3 582	39.9	5 810	44.1	0.0–98.3	↑

Bacterial species	Antimicrobial group/agent resistance	2017		2018		2019		2020		2021		2021 EU/EEA country range[a]	Trend 2017–2021[b]
		N	%	N	%	N	%	N	%	N	%		
Staphylococcus aureus	MRSA[e]	46 280	18.4	50 134	18.6	49 305	16.6	43 290	17.2	45 889	16.8	0.9–47.5	↓
Streptococcus pneumoniae	Penicillin non-wild-type[f]	11 271	13.6	12 209	13.5	11 762	12.8	6 365	15.8	6 420	16.2	3.6–37.5	↑
	Macrolide (azithromycin/clarithromycin/erythromycin) resistance	11 302	17.1	12 398	16.5	11 995	14.6	6 508	16.1	6 562	17.7	0.0–38.1	-
	Combined penicillin non-wild-type and resistance to macrolides[f]	10 791	9.1	11 845	8.5	11 357	7.5	6 104	8.9	6 175	9.6	0.0–28.6	-
Enterococcus faecalis	High-level gentamicin resistance	10 869	29.3	11 102	26.9	10 087	24.9	10 030	28.6	11 393	28.3	0.0–53.7	-
Enterococcus faecium	Vancomycin resistance	9 510	14.7	9 744	17.0	9 940	18.2	10 757	19.5	13 085	20.0	0.0–66.3	↑

[a] Lowest and highest national AMR percentage among reporting EU/EEA countries in 2021 (n = 29).

[b] ↑ and ↓ indicate statistically significant increasing and decreasing trends, respectively; - indicates no statistically significant trend.

[c] For E. coli, K. pneumoniae and Acinetobacter spp., the aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.

[d] For P. aeruginosa, the aminoglycoside group includes only tobramycin from 2020 onwards.

[e] MRSA is based on AST results for cefoxitin or, if not available, oxacillin. AST results reported for cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if oxacillin is not reported. If no phenotypic results are available, data from molecular confirmation tests (detection of mecA gene PCR or a positive PBP2A-agglutionation test) are accepted as a marker for MRSA..

[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.

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