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Antimicrobial resistance surveillance in Europe

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

2015

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Abbreviations and acronyms

AmpC	Ampicillinase C
AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
BSAC	British Society for Antimicrobial Chemotherapy
BSI	Bloodstream infection
CC	Clonal complex
CLSI	Clinical and Laboratory Standards Institute
CMY	Cephamycinase
CPE	Carbapenemase-producing *Enterobacteriaceae*
DNA	Deoxyribonucleic acid
EARSS	European Antimicrobial Resistance Surveillance System
EARS-Net	European Antimicrobial Resistance Surveillance Network
EEA	European Economic Area
EQA	External quality assessment
ESBL	Extended-spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EUSCAPE	European survey on carbapenemase-producing Enterobacteriaceae
ICU	Intensive care unit
IMP	Imipenemase
KPC	*Klebsiella pneumoniae* carbapenemase
LA-MRSA	Livestock-associated MRSA
MIC	Minimum inhibitory concentration
MLS	Macrolide, lincosamide and streptogramin
MRSA	Meticillin-resistant *Staphylococcus aureus*
MSSA	Meticillin-susceptible *Staphylococcus aureus*
NDM	New Delhi metallo-beta-lactamase
NWGA	Norwegian Working Group on Antimicrobials
OXA	Oxacillinase
PBP	Penicillin-binding protein
PCV	Pneumococcal conjugate vaccine
RNA	Ribonucleic acid
SFM	Comité de l'Antibiogramme de la Société Française de Microbiologie
SHV	Sulfhydryl-variable beta-lactamase
SIR	Susceptible, intermediate, resistant
ST	Sequence type
TEM	Temoneira beta-lactamase
TESSy	The European Surveillance System (ECDC)
UK NEQAS	United Kingdom National External Quality Assessment Service for Microbiology
VIM	Verona integron-encoded metallo-beta-lactamase

National institutions/organisations participating in EARS-Net

Austria
Federal Ministry of Health
Medical University Vienna
Elisabethinen Hospital, Linz
www.elisabethinen.or.at

Belgium
Scientific Institute of Public Health
https://www.wiv-isp.be/Nsih

Bulgaria
Alexander University Hospital, Sofia
National Center of Infectious and Parasitic Diseases

Croatia
Reference Center for Antimicrobial Resistance Surveillance, Ministry of Health
Zagreb University Hospital for Infectious Diseases 'Dr. Fran Mihaljević'

Cyprus
Microbiology Department, Nicosia General Hospital

Czech Republic
National Institute of Public Health
www.szu.cz
National Reference Laboratory for Antibiotics

Denmark
Statens Serum Institut, Danish Study Group for Antimicrobial Resistance Surveillance (DANRES)
www.danmap.org

Estonia
Health Board
East-Tallinn Central Hospital
Tartu University Hospital

Finland
National Institute for Health and Welfare, Finnish Hospital Infection Program (SIRO)
www.thl.fi/siro and Bacterial infections unit
Finnish Study Group for Antimicrobial Resistance (FiRe)
www.finres.fi

France
Santé Publique France, the French National Public Health Agency
www.santepubliquefrance.fr
Pitié-Salpêtrière Hospital
French National Observatory for the Epidemiology of Bacterial Resistance to Antimicrobials (ONERBA): Azay-Résistance, Île-de-France and Réussir networks
www.onerba.org
National Reference Centre for Pneumococci (CNRP)

Germany
Robert Koch Institute
www.rki.de

Greece
Hellenic Pasteur Institute
National School of Public Health
National and Kapodistrian University of Athens, Medical School
www.mednet.gr/whonet

Hungary
National Centre for Epidemiology
www.oek.hu

Iceland
National University Hospital of Iceland
Centre for Health Security and Infectious Disease Control

Ireland
Health Protection Surveillance Centre (HPSC)
www.hpsc.ie

Italy
National Institute of Health
www.iss.it

Latvia
Disease Prevention and Control Center of Latvia
www.spkc.gov.lv

Lithuania
National Public Health Surveillance Laboratory
www.nvspl.lt
Institute of Hygiene
www.hi.lt

Luxembourg
National Health Laboratory
Microbiology Laboratory, Centre Hospitalier de Luxembourg

Malta
Mater Dei Hospital, Msida

Netherlands
National Institute for Public Health and the Environment
www.rivm.nl

Norway
University Hospital of North Norway
Norwegian Institute of Public Health
St. Olav University Hospital, Trondheim

Poland
National Medicines Institute
Department of Epidemiology and Clinical Microbiology
National Reference Centre for Susceptibility Testing

Portugal
National Institute of Health Doutor Ricardo Jorge
www.insarj.pt
Ministry of Health
Directorate-General of Health

Romania
National Institute of Public Health

Slovakia
National Reference Centre for Antimicrobial Resistance
Public Health Authority of the Slovak Republic
Regional Public Health Authority Banska Bystrica

Slovenia
National Institute of Public Health
www.nijz.si
Medical faculty, University of Ljubljana
National Laboratory of Health, Environment and Food

Spain
Health Institute Carlos lll
www.isciii.es
National Centre for Microbiology

Sweden
The Public Health Agency of Sweden
www.folkhalsomyndigheten.se

United Kingdom
Public Health England
www.gov.uk/government/organisations/public-health-england
Health Protection Scotland
Public Health Agency Northern Ireland

Summary

The results presented in this report are based on antimicrobial resistance data from invasive isolates reported to EARS-Net by 30 EU/EEA countries in 2016 (data referring to 2015), and on trend analyses of data reported by the participating countries for the period 2012–2015.

As in previous years, the antimicrobial resistance situation in Europe displays wide variations depending on the bacterial species, antimicrobial group and geographical region. For several species–antimicrobial group combinations, a north-to-south and west-to-east gradient is evident in Europe. In general, lower resistance percentages are reported by countries in the north and higher percentages by countries in the south and east of Europe. These differences are most likely related to differences in antimicrobial use, infection prevention, infection control practices, and healthcare utilisation patterns in the countries.

This report highlights an especially worrying situation with regard to gram-negative bacteria: resistance percentages reported from many parts of Europe are high and, in many cases, on the increase. Over the last four years (2012–2015), resistance to third-generation cephalosporins in both *Escherichia coli* and *Klebsiella pneumoniae* increased significantly at EU/EEA level as well as in many of the individual Members States. A large proportion of the isolates resistant to third-generation cephalosporins produced an extended-spectrum beta-lactamase (ESBL). Third-generation cephalosporin resistance was often seen in combination with fluoroquinolone and aminoglycoside resistance. This type of combined resistance also increased significantly in the EU/EEA between 2012 and 2015, for both *E. coli* and *K. pneumoniae*. Increasing trends were observed in countries with both high and low levels of resistance. The observed increase in combined resistance to multiple antimicrobial groups, as well as the high proportion of ESBL-producing isolates, is especially worrying, as this leaves few treatment alternatives for patients suffering from infections caused by these pathogens. Besides its impact on treatment outcome of individual patients, frequent resistance in gram-negative bacteria may lead to an increased use of carbapenems, thus further favouring the emergence and spread of carbapenem-resistant bacteria.

While the EU/EEA population-weighted mean for carbapenem resistance was 8.1% for *K. pneumoniae*, the carbapenem resistance levels remained very low in *E. coli* (0.1%). Wide inter-country variations were noted for carbapenem-resistant *K. pneumoniae*, for which resistance percentages ranged between zero and 61.9%, with a majority of the countries reporting resistance levels below 1%. With a few exceptions, countries reporting the highest levels of combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides also reported the highest percentages of carbapenem resistance. While the trend for carbapenem resistance appeared fairly stable in *E. coli*, with few changes observed in national data between 2012 and 2015, a more dynamic pattern was observed for *K. pneumoniae*, for which the EU/EEA population-weighted mean percentage of carbapenem resistance increased significantly for the period 2012–2015.

Carbapenem resistance and resistance to multiple antimicrobial groups were also common in *Pseudomonas aeruginosa* and *Acinetobacter* spp. Among all species–antimicrobial group combinations monitored by EARS-Net, the highest levels of resistance were reported for *Acinetobacter* spp., for which carbapenem resistance percentages in some countries in the south and south-eastern parts of Europe and in the Baltic States reached levels of over 80% in 2015; carbapenem resistance was often seen in combination with resistance to other key antimicrobial groups.

Treatment alternatives for patients infected with bacteria resistant to both carbapenems and other important antimicrobial groups are often limited to combination therapy and to older antimicrobial agents with lower efficacy such as polymyxins, e.g. colistin. Although data on polymyxin susceptibility as part of EARS-Net surveillance are not complete, and testing susceptibility to polymyxins is technically difficult, the fact that some countries, especially countries with already high percentages of carbapenem resistance, reported large numbers of isolates with polymyxin resistance is an indication of the further loss of effective antimicrobial treatment options for gram-negative bacterial infections.

The increase in carbapenem resistance in *K. pneumoniae* observed in the EARS-Net surveillance data is most likely the result of an increase in isolates producing a carbapenemase, as previously reported from the ECDC-funded *European survey on carbapenemase-producing Enterobacteriaceae* (EuSCAPE). The continuous spread of carbapenemase-producing Enterobacteriaceae (CPE), mostly *K. pneumoniae*, represents a serious threat to healthcare and patient safety in European hospitals, to which many European countries have reacted by intensifying their containment efforts. However, results from EuSCAPE have highlighted that gaps still remain, and many countries are still lacking national guidance for CPE prevention and control.

Resistance trends in gram-positive bacteria showed a more diverse pattern across Europe. For meticillin-resistant *Staphylococcus aureus* (MRSA), the EU/EEA population-weighted mean percentage continued to decrease during the last four-year period, from 18.8%

in 2012 to 16.8 % in 2015. The decline in recent years has, however, been less pronounced compared with 2009–2012.

For *Streptococcus pneumoniae*, resistance percentages were generally stable during the period 2012–2015, but with wide inter-country variations. Macrolide non-susceptibility in *S. pneumoniae* was, for most countries, higher than penicillin non-susceptibility.

For enterococci, a significantly increasing trend for vancomycin-resistant *Enterococcus faecium* could be noted in almost half of the reporting countries between 2012 and 2015. Although the overall trend was not significant in EU/EEA countries, this development needs to be monitored carefully.

Antimicrobial resistance is a serious threat to public health in Europe. For invasive bacterial infections, prompt treatment with effective antimicrobial agents is especially important and is one of the single most effective interventions to reduce the risk of fatal outcome. The ongoing increase in antimicrobial resistance to a number of key antimicrobial groups in invasive bacterial isolates reported to EARS-Net is therefore of great concern and constitutes a serious threat to patient safety in Europe. Prudent antimicrobial use and comprehensive infection prevention and control strategies targeting all healthcare sectors are the cornerstones of effective interventions aiming to prevent selection and transmission of bacteria resistant to antimicrobial agents.

1 Introduction

Antimicrobial resistance

Antimicrobial resistance (AMR) is the ability of a microorganism to resist the action of one or more antimicrobial agents. The consequences can be severe, as prompt treatment with effective antimicrobial agents is the most effective intervention to reduce the risk of poor outcome of serious infections. Effective antimicrobial agents ensuring the prevention and treatment of bacterial complications are also crucial for many medical interventions such as major surgery, solid organ and stem cell transplantations, intensive care, implantation of devices, and aggressive treatment of cancer.

Increasing resistance to key antimicrobial groups is reported from many parts of the world, including Europe. AMR is a serious threat to public health and patient safety in Europe, leading to mounting healthcare costs, patient treatment failure, and deaths. Analyses from the European Centre for Disease Prevention and Control (ECDC) in 2009 estimated that infections caused by a subset of resistant bacteria are responsible for about 25 000 deaths in Europe annually. In addition to these avoidable deaths, healthcare costs and productivity losses have been estimated to be at least EUR 1.5 billion [1]. With the increase in AMR noted since these estimates were produced, the numbers are most likely to be considerably higher today.

Development of AMR is a natural phenomenon caused by mutations in bacterial genes, or acquisition of exogenous resistance genes carried by mobile genetic elements that can spread horizontally between bacteria. A bacterium can acquire several different resistance mechanisms and hence be resistant to several antimicrobial agents, which is particularly problematic as it may severely limit the available treatment alternatives for the infection. For a detailed description of resistance mechanisms, please refer to the resistance mechanism section for each bacterial species in Chapter 3.

The major drivers behind the occurrence and spread of AMR are the use of antimicrobial agents and the transmission of antimicrobial-resistant microorganisms between humans; between animals; and between humans, animals and the environment. While antimicrobial use exerts ecological pressure on bacteria and contributes to the emergence and selection of AMR, poor infection prevention and control practices and inadequate sanitary conditions favour the further spread of these bacteria.

The problem of AMR calls for concerted efforts at Member State level as well as close international cooperation. In 2008, the European Council adopted conclusions calling upon the European Commission to promote cooperation between the Commission, Agencies and the Member States against AMR [2]. In the Action Plan issued by the Commission in 2011, surveillance of AMR is pointed out as one of the areas where measures are required the most, together with appropriate use of antimicrobial agents, infection prevention and control, and development of new effective antimicrobial agents or alternatives for treatment [3]. AMR is listed as a special health issue in Annex 1 of Commission Decision 2000/96/EC on the communicable diseases to be covered by the Community network under Decision No 1082/2013/EU of the European Parliament and of the Council on serious cross-border threats to health [4].

EARS-Net

The European Antimicrobial Resistance Surveillance Network (EARS-Net) is the main EU surveillance system for AMR, and data reported from the network serve as important indicators on the occurrence and spread of AMR in European countries. All 28 EU Member States and two of the remaining three EEA countries (Iceland and Norway) participate in EARS-Net. The vast majority of the countries regularly report data for all bacteria and antimicrobial groups under surveillance. The number of participating laboratories has continuously increased since the initiation of the network, indicating a strengthening of national AMR surveillance systems in Europe. The widespread and continuing implementation of EUCAST guidelines for antibacterial susceptibility testing in Europe, and the high proportion of laboratories that participate in the annual EARS-Net EQA exercise, contribute to improved data quality and an increasing ability in the Member States to report comparable AMR data.

EARS-Net is the continuation of the European Antimicrobial Resistance Surveillance System (EARSS), which was coordinated by the Dutch National Institute for Public Health and the Environment (RIVM). Established in 1998, EARSS successfully created an international network for AMR surveillance and demonstrated how international AMR data could inform decisions and raise awareness among stakeholders and policymakers. On 1 January 2010, the administration of EARSS was transferred from RIVM to ECDC, and the network was renamed EARS-Net. Data collected by the network from EU/EEA Member States since 1999 were transferred to The European Surveillance System (TESSy) database at ECDC.

EARS-Net is based on a network of representatives from the Member States collecting routine clinical antimicrobial susceptibility data from national AMR surveillance initiatives (for details, please refer to the list of national institutions and organisations participating in EARS-Net on page viii). Scientific guidance and

support to the network is provided by the EARS-Net Coordination Committee. This group is composed of individual experts selected from among the appointed disease-specific contact points and experts from other organisations that are involved in AMR surveillance. EARS-Net activities are coordinated in close collaboration with two other major ECDC surveillance networks: the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the Healthcare-associated Infections Surveillance Network (HAI-Net). EARS-Net also collaborates with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), in particular with the European Committee on Antimicrobial Susceptibility Testing (EUCAST), which is supported by ECDC and ESCMID.

The objectives of EARS-Net are:

- to collect comparable, representative and accurate AMR data;
- to analyse temporal and spatial trends of AMR in Europe;
- to provide timely AMR data for policy decisions;
- to encourage the implementation, maintenance and improvement of national AMR surveillance programmes; and
- to support national systems in their efforts to improve diagnostic accuracy by offering an annual External Quality Assessment (EQA).

EARS-Net is the largest publicly funded system for AMR surveillance in Europe, so data from EARS-Net play an important role in raising awareness at the political level, among public health officials, in the scientific community and among the general public. All participating countries have open access to the EARS-Net database. Public access to descriptive data (maps, graphs and tables) is available through a web-based data query tool [5], and more detailed analyses are presented in annual reports and scientific publications.

2 EARS-Net data collection and analysis

A total of 30 countries, including all EU Member States, and two of the three remaining EEA countries (Iceland and Norway) reported AMR data for 2015 to EARS-Net before August 2016. The number of participating laboratories and unique isolates has increased in recent years, indicating improved population coverage of the network. Only data from invasive (blood and cerebrospinal fluid) isolates are included in EARS-Net. The panels of antimicrobial agent combinations under surveillance for each species are defined in the EARS-Net reporting protocol [6]. In addition, the EUCAST guidelines for detection of resistance mechanisms and specific types of resistance of clinical and/or epidemiological importance have been developed to describe the mechanisms of resistance and recommended methods of detection for key EARS-Net species–antimicrobial group combinations [7].

Routine antimicrobial susceptibility test (AST) results are collected from clinical laboratories by the national network representative in each participating country. National data are uploaded directly by the national data manager to The European Surveillance System (TESSy) at ECDC on a yearly basis. TESSy is a web-based system for the collection, validation and cleaning of data and is intended to be the single point for Member States to submit and retrieve data on all communicable diseases under EU surveillance. TESSy filters the uploaded records according to the list of bacteria/specimens/antimicrobial agents under AMR surveillance and creates one record per patient, bacterium, antimicrobial agent and year. After uploading data, the national data manager receives a validation report, and each country approves its own data before they are used for analysis. Data presented by EARS-Net might diverge slightly from the data presented by the Member States themselves, as analysis algorithms and population coverage might differ.

Data analysis

For the analysis, an isolate is considered resistant to an antimicrobial agent when tested and interpreted as resistant (R) in accordance with the clinical breakpoint criteria used by the local laboratory. An isolate is considered non-susceptible to an antimicrobial agent when tested and interpreted as either resistant (R) or intermediately susceptible (I) with the same local clinical breakpoint criteria. EARS-Net encourages the use of EUCAST breakpoints but results based on other interpretive criteria used by the reporting countries are accepted for the analysis. The use of EUCAST breakpoints has increased over the years [8], and in 2015 approximately 84 % of the participating laboratories used EUCAST clinical breakpoints (Annex 1), which improved the comparability of the data.

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

A population-weighted EU/EEA mean percentage was determined by applying population-based weights to each country's data before calculating the arithmetic mean for all reporting countries. Only countries reporting data for the last four years were included in the EU/EEA mean. Country weightings were used to adjust for imbalances in reporting propensity and population coverage, as the total number of reported isolates per country in most cases does not reflect the population size. The weighting applied to each national data point represented the proportion of the country's population out of the total population of all countries included in the calculation. Annual population data were retrieved from the Eurostat online database [9].

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

The statistical significance of temporal trends of antimicrobial resistance percentages by country was calculated based on data from the last four years. Countries reporting fewer than 20 isolates per year, or not providing data for all years within the considered period, were not included in the analysis. Statistical significance of trends was assessed by the Cochran–Armitage test, and a p-value of ≤ 0.05 was considered significant. An additional sensitivity analysis was performed by repeating the Cochran–Armitage test, including only laboratories that consistently reported for the full four-year period in order to exclude selection bias when assessing the significance of the trends. This restriction might in some cases result in a considerably lower number of isolates compared with the non-restricted analysis.

Interpretation of the results

The results, both for inter-country comparison and in some cases national trends, should be interpreted with caution. A number of factors might influence and introduce bias to the data, resulting in over- as well as underestimation of resistance percentages. Some of the most important potential sources of bias in EARS-Net are explained below.

Population coverage

Population coverage varies among reporting countries. Some countries report data from large national surveillance systems with a high national coverage, while other countries report data from a smaller subset of local laboratories and hospitals.

For countries reporting data from only a small number of hospitals and laboratories located in one specific geographical area, the sample may not be representative for the whole country. Likewise, national trends may not be representative of regional situations as pooled data could mask variations at local level.

For some countries, the population under surveillance is not constant and may change over the years due to variations in the number of participating laboratories. To control for this potential bias in trend analyses, an additional sensitivity analysis including a subset of data originating only from laboratories reporting for all the previous four years is provided for all national trend analyses.

For an overview of the number of reporting laboratories, see Annex 3.

Sampling

EARS-Net data are exclusively based on invasive isolates from blood or cerebrospinal fluid. The clinical relevance of indicator organisms isolated from these sites is undisputable. This restriction prevents some of the inconsistencies that arise from differences in clinical case definitions, different sampling frames or heterogeneous healthcare utilisation that would otherwise confound the data analysis if isolates from all anatomical sites were accepted. However, invasive isolates may not be representative of isolates of the same bacterial species from other type of infections, i.e. urinary tract infections, pneumonia, wound infections, etc.

Case ascertainment of patients with bloodstream infections (BSIs) is strongly linked to diagnostic practices and the frequency with which blood cultures are taken. Therefore, variations in blood culture frequency (non-differential sampling) result in an increasing uncertainty when comparing resistance percentages between hospitals and countries. Extrapolations of EARS-Net data as a measure of BSI incidence could therefore underestimate the true value in countries with low blood culture frequency.

Differential sampling can occur if blood cultures are typically only performed after empirical treatment shows no adequate therapeutic response. Predictably, this will lead to an overestimation of the resistance percentage by not including susceptible BSI isolates from the denominator.

Laboratory routines and capacity

The use of guidelines for clinical breakpoints varies among countries in Europe, and in some instances even between laboratories in the same country. At present, many European laboratories are changing from using CLSI to EUCAST clinical guidelines (Annex 1). As a result, the interpretation of AST results may vary, at least for resistance mechanisms, resulting in MICs close to the breakpoints. In addition, clinical breakpoints may change over time, as breakpoints may be revised. As quantitative data (i.e. disk diffusion zone diameters or MIC values) are not provided by all participating laboratories, only the reported S, I, and R results are considered for the analyses.

The ability to identify the microorganism and its associated antimicrobial susceptibility pattern may differ among laboratories. All laboratories providing data for EARS-Net are offered participation in an annual EQA to assess the reliability of the laboratory test results. For more information on the EARS-Net EQA and laboratory performance, see Annex 1.

3 Antimicrobial resistance in Europe

3.1 *Escherichia coli*

3.1.1 Clinical and epidemiological importance

Escherichia coli is part of the normal intestinal microbiota in humans but also a common cause of bacterial infections. It is the most frequent cause of bloodstream and urinary tract infections in Europe and involved in infections of both community and healthcare origin. In addition, *E. coli* is associated with intra-abdominal infections, causes neonatal meningitis and is one of the leading causative agents in food-borne infections worldwide.

3.1.2 Resistance mechanisms

In *E. coli*, resistance to beta-lactams is mostly due to production of beta-lactamases. These enzymes hydrolyse the beta-lactam ring of beta-lactam agents that is crucial for inhibition of the penicillin-binding protein (PBP) targets. Resistance to broad-spectrum penicillins, such as ampicillin or amoxicillin, is usually conferred by plasmid-coded beta-lactamases mainly of the TEM type and to a lesser extent of the SHV type (TEM-1 accounts for up to 60% of aminopenicillin resistance), while resistance to third-generation cephalosporins is mostly conferred by extended-spectrum beta-lactamases (ESBLs). The most common resistance mechanisms detected in amoxicillin-clavulanic-acid-resistant *E. coli* are OXA-1 production, hyperproduction of penicillinase, production of plasmidic AmpC, hyperproduction of chromosomal AmpC and production of inhibitor-resistant TEM (IRT). The first ESBLs spreading in *E. coli* were variants of the TEM or SHV enzymes, in which single or multiple amino acid substitutions expand their hydrolysing ability to include third-generation cephalosporins (in this report referring to cefotaxime, ceftriaxone and ceftazidime), fourth-generation cephalosporins, the new anti-MRSA cephalosporins (ceftaroline and ceftobiprole), and monobactams.

During the past decade, however, these enzymes have largely been replaced by the CTX-M-type ESBLs, which are now by far the most common ESBLs in *E. coli*. Most ESBLs can be inhibited by beta-lactamase inhibitors such as clavulanic acid, sulbactam, tazobactam, or avibactam.

Hundreds of ESBL variants are known to date. An important factor in their global dominance is the wide dissemination of bacterial clones producing CTX-M-type ESBLs (e.g. the ST131 pandemic clone producing CTX-M-15, particularly the H30-Rx subclone). Other enzymes affecting susceptibility to third-generation cephalosporins include plasmid-encoded variants derived from some chromosomal AmpC-type beta-lactamases. CMY-2 is the most widespread enzyme belonging to this group, which remains less common than ESBLs in *E. coli* in Europe, and is more frequently seen in the United States. An important threat that will require close surveillance in the future, is the emergence of carbapenem resistance in *E. coli*, mediated by metallo-beta-lactamases (such as the VIM, and NDM enzymes) or serine-carbapenemases (such as the KPC enzymes), providing resistance to most or all available beta-lactam agents.

Another growing family of beta-lactamases comprises the OXA-type enzymes that confer resistance to ampicillin and cephalothin and are characterised by their high hydrolytic activity against oxacillin and cloxacillin and the fact that they are poorly inhibited by clavulanic acid. This family also includes some enzymes with carbapenemase activity (OXA-48-like enzymes), which have emerged in *E. coli* and other Enterobacteriaceae. When produced alone, they confer reduced susceptibility to carbapenems and resistance to penicillins, but usually not to the extended-spectrum cephalosporins. Unfortunately, *E. coli* strains producing multiple beta-lactamases are becoming increasingly common, leading to complex resistance patterns which may include most beta-lactams.

Fluoroquinolones interact with DNA gyrase and topoisomerase IV, which are enzymes that regulate conformational changes in the bacterial chromosome during replication and transcription. This interaction leads to the irreversible inhibition of the enzyme activity followed by DNA fragmentation and eventually to cell death. Resistance to fluoroquinolones arises through stepwise mutations in some specific regions (the so-called quinolone-resistance determining regions, QRDRs) of the DNA gyrase subunits (*gyrA* and *gyrB*) and DNA topoisomerase IV subunits (*parC*). Accumulation of mutations in several of these genes increases the MIC in a stepwise manner. Low-level resistance to fluoroquinolones may also arise through changes in outer membrane porins or from upregulation of efflux pumps, resulting in lower outer membrane permeability and higher efflux, respectively. In recent years, several plasmid-mediated quinolone resistance mechanisms have also been identified, including the Qnr proteins, which protect DNA topoisomerases from quinolone binding, the AAC(6')-Ib-cr enzyme, which inactivates some fluoroquinolones by acetylation, and the QepA and OqxAB efflux pumps, which reduce the intracellular concentration of hydrophilic quinolones. These mechanisms are a concern because this type of resistance is transferable and because of their frequent association with CTX-M and CMY-type enzymes inactivating third-generation cephalosporins. Additionally, their presence is believed to facilitate evolution to resistance by chromosomal mutations.

Aminoglycosides block protein synthesis by binding to the ribosomes, which are involved in the translation of RNA into proteins, and are also able to damage the outer membrane of gram-negative bacteria. Resistance to aminoglycosides can be due to targeted modification (methylation) of the 16S ribosomal RNA (rRNA), which prevents aminoglycoside molecules from binding the small ribosomal subunit, or by aminoglycoside-modifying enzymes that acetylate, adenylate or phosphorylate their target molecules and thereby neutralise the biological effect of aminoglycosides. Of particular concern are the 16S ribosomal methylases that confer resistance to all aminoglycosides and frequently accompany carbapenemases, most notably of NDM-type carbapenemases.

Polymyxin resistance is mostly mediated through chromosomal mutations in regulators of the endogenous lipid A modification systems. The resulting effects are an increase in positive charge in the LPS, which reduces interaction with the positively charged polymyxins. Recently, plasmid-mediated polymyxin resistance has also emerged. The *mcr-1* gene encodes a phosphoethanolamine transferase. When phosphoethanolamine is added to lipid A, this will lead to an increased positive charge in the LPS as in the case of the two-component regulatory system mutations. Lately, two variants of *mcr-1* have also been described, *mcr-1.2* and *mcr-2*. MCR-encoding genes have mostly been described in *E. coli*.

3.1.3 Antimicrobial susceptibility

- More than half of the *E. coli* isolates reported to EARS-Net in 2015 were resistant to at least one antimicrobial group under surveillance. As in previous years, resistance to aminopenicillin and fluoroquinolones were most frequently reported, both as single resistance and in combination with other antimicrobial groups.
- The EU/EEA population-weighted mean percentage for third-generation cephalosporin resistance and combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides in *E. coli* both increased significantly between 2012 and 2015.
- Carbapenem resistance remained rare in *E. coli* in Europe.
- The highest resistance percentages in *E. coli* were generally reported from southern and south-eastern Europe.

Aminopenicillins

- For 2015, 30 countries reported 77 528 *E. coli* isolates with AST information for aminopenicillins (amoxicillin or ampicillin). The number of isolates reported per country ranged from 123 to 10 946 (Table 3.1).

The EU/EEA population-weighted mean percentage for aminopenicillin resistance was 57.2 % in 2015. No significant trend was noted between 2012 and 2015 (Table 3.1).

National percentages of resistant isolates ranged from 34.1 % (Sweden) to 73.0 % (Romania) in 2015. Trends for the period 2012–2015 were calculated for the 29 countries reporting data for at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for seven countries (Belgium, France, Lithuania, Luxembourg, Slovenia, Romania and the United Kingdom). For Belgium, the trend did not remain significant when considering only data from laboratories that reported consistently for all four years. Significantly decreasing trends were observed for four countries (the Czech Republic, Finland, Hungary and the Netherlands). For the Czech Republic and the Netherlands, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years (Table 3.1).

Fluoroquinolones

For 2015, 30 countries reported 89 850 *E. coli* isolates with AST information for fluoroquinolones (ciprofloxacin, levofloxacin or ofloxacin). The number of isolates reported per country ranged from 123 to 10 998 (Table 3.2).

The EU/EEA population-weighted mean percentage for fluoroquinolone resistance was 22.8 % in 2015. No significant trend was noted between 2012 and 2015 (Table 3.2).

National percentages of resistant isolates ranged from 6.8 % (Iceland) to 45.5 % (Cyprus) in 2015 (Table 3.2 and Figure 3.1). All 30 countries reported data for at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for seven countries (Belgium, Croatia, Italy, Latvia, Lithuania, Slovenia and Sweden). For Sweden, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for four countries (Denmark, Germany, the Netherlands and Spain). For Germany, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years (Table 3.2).

Third-generation cephalosporins

For 2015, 30 countries reported 89 839 *E. coli* isolates with AST information for third-generation cephalosporins (cefotaxime, ceftriaxone or ceftazidime). The number of isolates reported per country ranged from 123 to 11 051 (Table 3.3).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 11.9 % in 2012 to 13.1 % in 2015 (Table 3.3).

National percentages of resistant isolates ranged from 1.7 % (Iceland) to 38.5 % (Bulgaria) in 2015 (Table 3.3 and Figure 3.2). All 30 countries reported data for at

Figure 3.1. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2015**

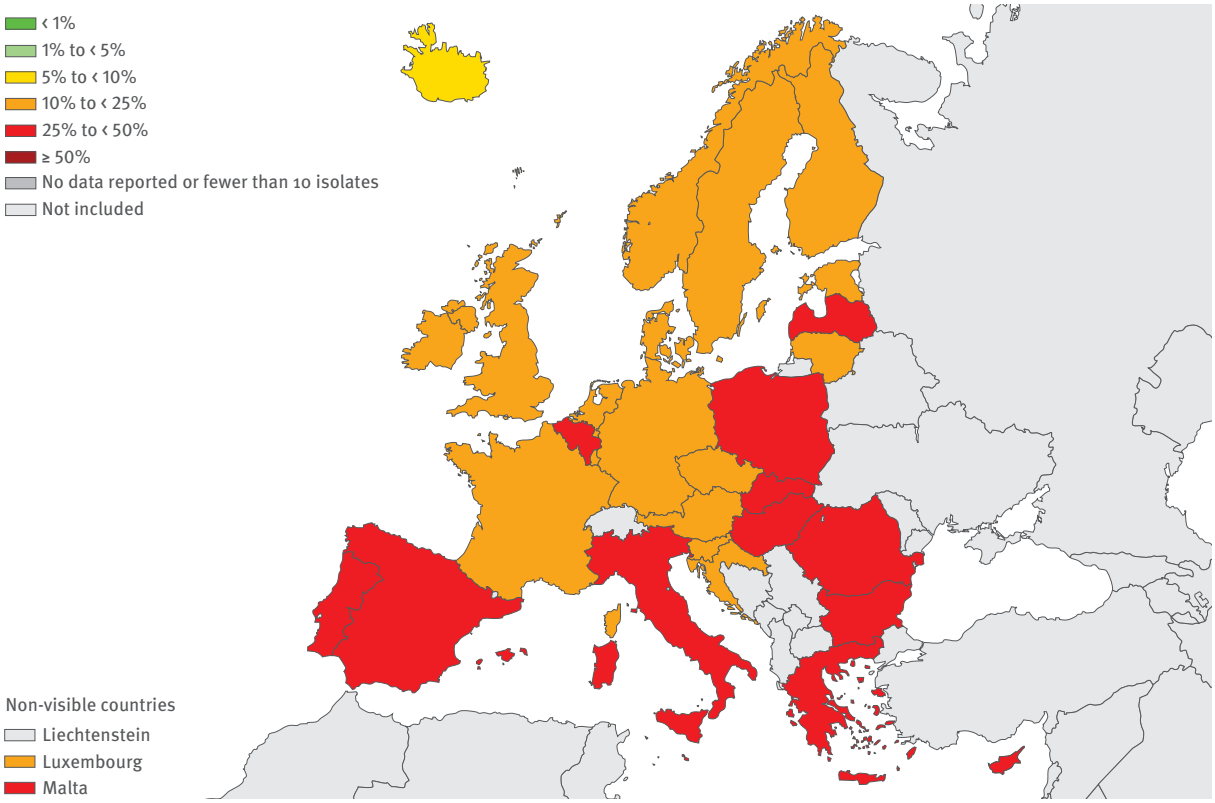
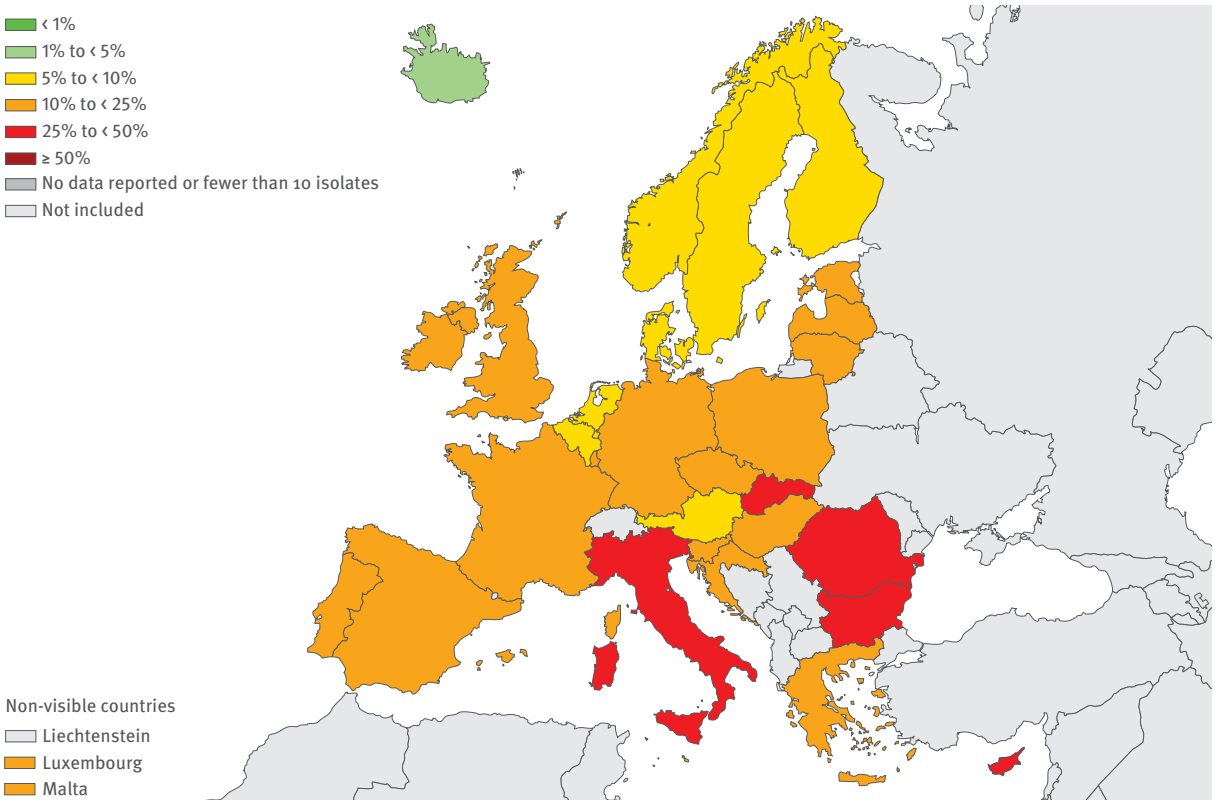


Figure 3.2. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2015**



least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for 12 countries (Belgium, Croatia, the Czech Republic, France, Greece, Ireland, Italy, Lithuania, Norway, Portugal, Slovenia and Sweden). For Greece and Portugal, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for Spain and the United Kingdom. These trends remained significant when considering only data from laboratories reporting consistently for all four years (Table 3.3).

ESBL percentages for *E. coli* were calculated based on data from 24 countries. Only data from laboratories reporting ESBL results for all isolates identified as resistant to third-generation cephalosporins (56% of the laboratories reporting AST data for third-generation cephalosporin in *E. coli*), and only data from countries reporting at least 10 such isolates were included. Among the *E. coli* isolates resistant to third-generation cephalosporins and meeting the inclusion criteria, 88.6% were ascertained as ESBL-positive by the laboratories in 2015. ESBL results might not be directly comparable between countries as there are national differences in the definition of ESBL. The presence of ESBL might also be masked by some carbapenemases such as MBLs and KPC and/or severe permeability defects [10].

Aminoglycosides

For 2015, 30 countries reported 89764 *E. coli* isolates with AST information for aminoglycosides (gentamicin or tobramycin). The number of isolates reported per country ranged from 123 to 11055 (Table 3.4).

The EU/EEA population-weighted mean percentage for aminoglycoside resistance was 10.4% in 2015. No significant trend was noted between 2012 and 2015 (Table 3.4).

National percentages of resistant isolates ranged from 2.9% (Iceland) to 24.2% (Slovakia) in 2015 (Table 3.4 and Figure 3.3). All 30 countries reported data for at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for five countries (Belgium, Croatia, the Czech Republic, Slovenia and the United Kingdom). For Belgium, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for four countries (Finland, Hungary, the Netherlands and Portugal). For Finland and the Netherlands, these trends did not remain significant when considering only data from laboratories reporting consistently for all four years (Table 3.4).

Susceptibility data for amikacin were less frequently reported than for gentamicin and/or tobramycin and generally showed lower resistance levels. A total of 52637 isolates had susceptibility data for both for amikacin and gentamicin and/or tobramycin (58.6% of the isolates included in the aminoglycoside group analysis). Among isolates with resistance to either gentamicin or tobramycin, 5.1% of the isolates were also resistant to amikacin.

Carbapenems

For 2015, 30 countries reported 86200 *E. coli* isolates with AST information for carbapenems (doripenem, imipenem or meropenem). The number of isolates reported per country ranged from 123 to 10481 (Table 3.5).

The EU/EEA population-weighted mean percentage for carbapenem resistance was 0.1% in 2015. No significant trend was noted between 2012 and 2015 (Table 3.5).

E. coli with resistance to carbapenems remained rare in Europe. Twenty-three countries reported carbapenem resistance percentages ‹0.01% in 2015 (Table 3.5 and Figure 3.4). Only two countries – Greece (1.2%) and Romania (1.9%) – reported percentages above 1%. All 30 countries reported data for at least 20 isolates per year during the full reporting period. A significantly increasing trend was observed for Romania, but the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for Bulgaria, Italy and Slovakia. For Slovakia, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years (Table 3.5).

Combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides

For 2015, 30 countries reported 87798 *E. coli* isolates with sufficient AST information to determine combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides. The number of isolates reported per country ranged from 123 to 10988 (Table 3.6).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 4.9% in 2012 to 5.3% in 2015 (Table 3.6).

National percentages of resistant isolates ranged from zero (Iceland) to 17.1% (Slovakia) in 2015 (Table 3.6 and Figure 3.5). All 30 countries reported data for at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for 10 countries (Belgium, Croatia, the Czech Republic, Estonia, France, Ireland, Lithuania, Luxembourg, Slovenia and Sweden). For Belgium, France and Sweden, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for Finland, Hungary and Portugal. For Finland, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years (Table 3.6).

Other resistance combinations and resistance to other antimicrobial groups

Of the 72123 isolates (78.2% of all *E. coli* isolates) tested for all antimicrobial groups under regular EARS-Net surveillance (aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) in 2015, more than half (53.7%) were resistant to at least one antimicrobial group. Among the resistant isolates, single resistance to one antimicrobial

Figure 3.3. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2015**

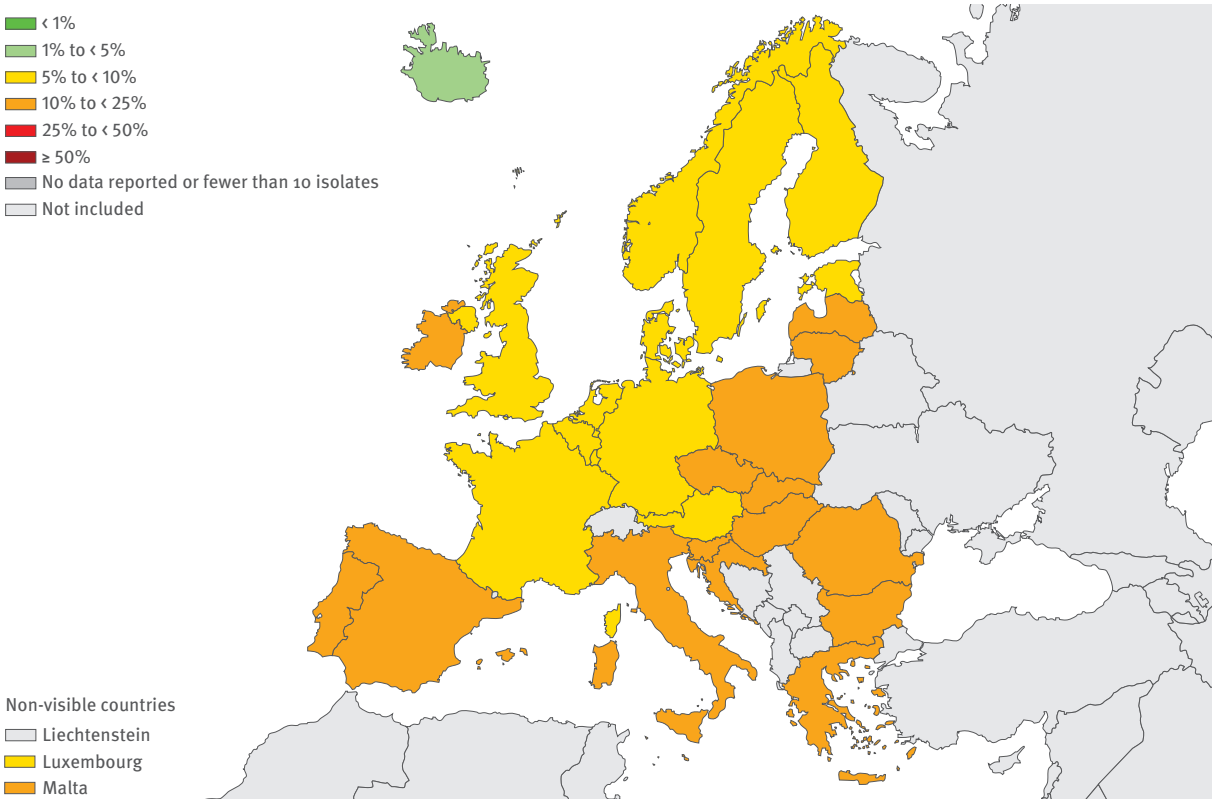
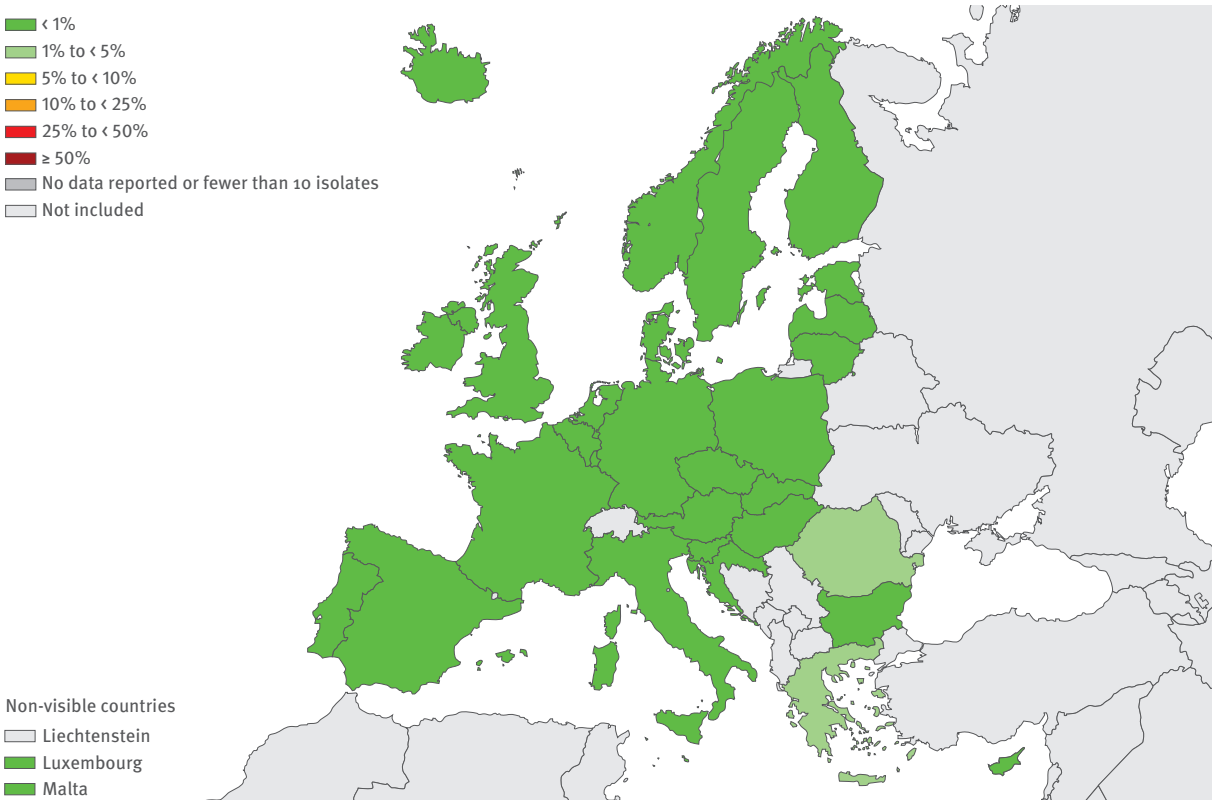


Figure 3.4. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015**



group (mainly aminopenicillins) was the most common (34.2 %). For isolates with resistance to two antimicrobial groups (11.4 %), combined aminopenicillin and fluoroquinolone resistance was the most common, and for those with resistance to three antimicrobial groups (7.6 %), combined aminopenicillin, fluoroquinolone and third-generation cephalosporin resistance accounted for the majority. Antimicrobial resistance to four antimicrobial groups were less frequent (5.2 %), the vast majority of these isolates was resistant to aminopenicillins, third-generation cephalosporins, fluoroquinolones and aminoglycosides. As carbapenem resistance remained rare in *E. coli*, resistance combinations including this antimicrobial group were uncommon (Table 3.7).

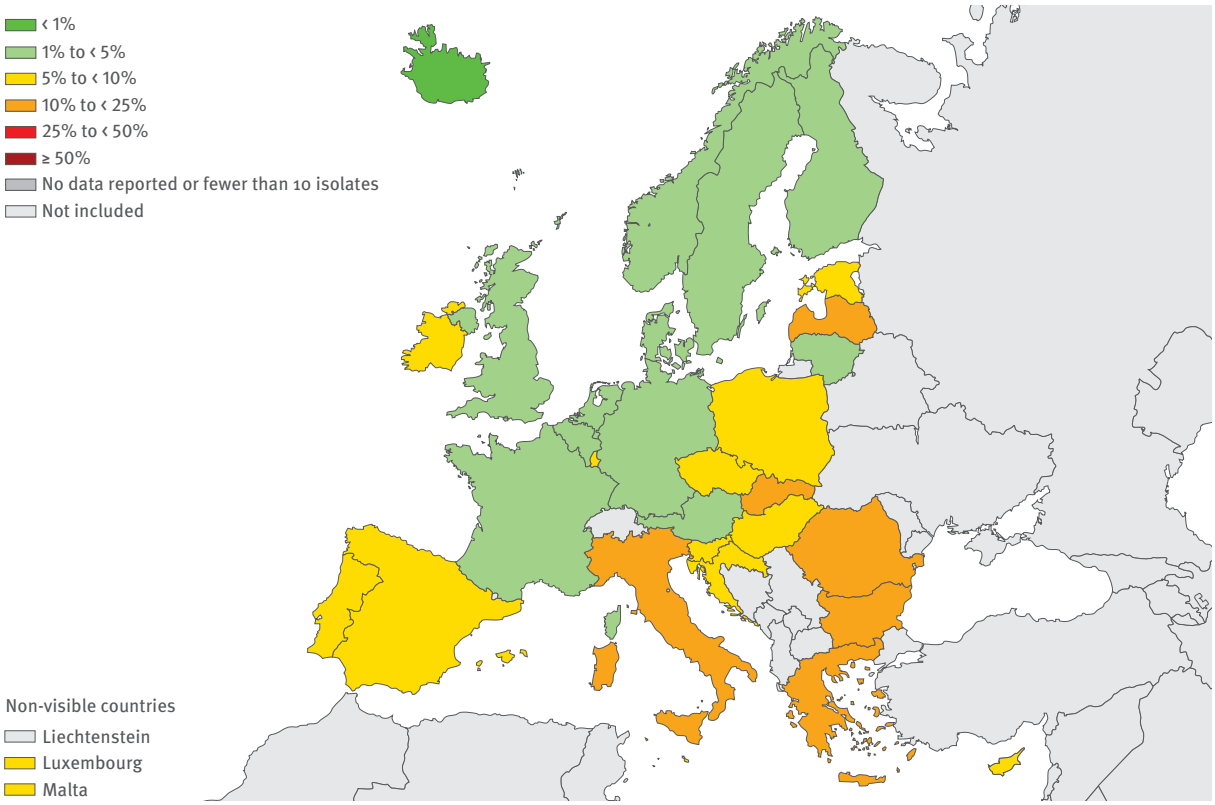
Twenty countries reported AST data for polymyxins for a total of 14 518 isolates (15.7 % of all reported *E. coli* isolates) in 2015. Only five countries reported polymyxin AST data for more than half of the reported *E. coli* isolates. Only a small proportion (1.1 %) was resistant to polymyxin. Among carbapenem-resistant isolates also tested for resistance to polymyxins (30 out of 69 isolates), 6.2 % were resistant to polymyxins, whereas only 1.1 % of the carbapenem-susceptible isolates were resistant to polymyxins. The small number of isolates, the rare occurrence of both carbapenem and polymyxin resistance in *E. coli*, and potential differences in the use of laboratory methodology used to determine susceptibility mean that these findings should be interpreted with caution and may not be representative for Europe as a whole.

3.1.4 Discussion and conclusions

Antimicrobial resistance in *E. coli* is common: more than half of the isolates were resistant to at least one of the isolates under surveillance. As *E. coli* is the most common cause of bloodstream infection in Europe, prompt access to effective antimicrobial treatment is essential to reduce the health-related and economic burden caused by this type of infection.

As in previous years, the highest EU/EEA population-weighted mean resistance percentages were reported for aminopenicillins (57.2 %), followed by fluoroquinolones (22.8 %). The EU/EEA trends for resistance to these two antimicrobial groups have remained stable between 2012 and 2015, with very little variation between years. By contrast, the EU/EEA trends for resistance to third-generation cephalosporins, and combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides continued to increase significantly in 2015. As in previous years [11-12], similar increasing

Figure 3.5. *Escherichia coli*. Percentage (%) of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, by country, EU/EEA countries, 2015



trends were also reported at a national level by more than a third of the countries, including countries with both high and low resistance levels.

The increase in combined resistance and the high frequency of ESBL-producing isolates may lead to an increased use of carbapenems, thus favouring dissemination of carbapenemase-producing Enterobacteriaceae (CPE). Although carbapenem resistance in blood isolates of *E. coli* remains very rare in Europe, with resistance percentages <0.1% reported by the majority of countries, it requires close monitoring as CPE are becoming more widespread in Europe [13]. In response to this development, ECDC issued a rapid risk assessment on carbapenem-resistant Enterobacteriaceae in 2016 [14], in addition to two risk assessments published in 2011 [15-16] and a 2014 systematic review on the effectiveness of infection control measures to prevent cross-border transmission [17].

High-standards in infection prevention and control, combined with an adequate microbiological laboratory capacity, are essential to detect and prevent the transmission of multidrug-resistant bacteria, including carbapenem resistance. The previous use of broad-spectrum antimicrobials from various classes, and in particular carbapenems, is a known risk factor for colonisation by carbapenem-resistant Enterobacteriaceae. Therefore, the implementation of comprehensive antimicrobial stewardship programmes is recommended to prevent and control the emergence and spread of carbapenem-resistant *E. coli* [14].

Table 3.1. ***Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to aminopenicillins (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95%CI)	N	%R	(95%CI)	N	%R	(95%CI)	N	%R	(95%CI)			Comment*
Sweden	230	28.3	(23–35)	452	34.1	(30–39)	–	–	(.–.)	396	34.1	(29–39)		N/A	
Finland	2090	39.7	(38–42)	2124	37.3	(35–39)	2365	34.7	(33–37)	2472	36.0	(34–38)			‹
Iceland	131	44.3	(36–53)	121	46.3	(37–56)	151	43.0	(35–51)	173	44.5	(37–52)			
Denmark	3708	45.2	(44–47)	3965	46.3	(45–48)	4490	44.9	(43–46)	4594	45.3	(44–47)			
Norway	2995	43.2	(41–45)	3016	43.0	(41–45)	3404	41.8	(40–43)	3299	45.8	(44–48)			
Netherlands	4697	49.0	(48–50)	4656	47.5	(46–49)	6458	46.0	(45–47)	5376	47.2	(46–49)			‹ #
Estonia	216	48.1	(41–55)	235	46.4	(40–53)	261	47.1	(41–53)	196	47.4	(40–55)			
Germany	4162	49.6	(48–51)	5306	52.9	(52–54)	5543	51.7	(50–53)	8053	49.3	(48–50)			
Austria	3625	50.6	(49–52)	4379	51.3	(50–53)	4742	50.4	(49–52)	4880	49.9	(48–51)			
Latvia	153	54.2	(46–62)	135	51.9	(43–61)	182	48.4	(41–56)	192	53.6	(46–61)			
Czech Republic	2811	56.8	(55–59)	2954	54.9	(53–57)	2978	54.4	(53–56)	3172	54.3	(53–56)			‹ #
Slovenia	1168	50.4	(48–53)	1224	51.5	(49–54)	1216	52.6	(50–55)	1326	54.8	(52–58)			›
Malta	207	54.6	(48–62)	248	54.8	(48–61)	279	53.4	(47–59)	258	55.0	(49–61)			
Croatia	904	51.4	(48–55)	1036	53.7	(51–57)	1077	54.0	(51–57)	1042	55.3	(52–58)			
Greece	1270	55.0	(52–58)	1149	56.4	(53–59)	1057	55.7	(53–59)	1079	56.1	(53–59)			
France	9599	55.2	(54–56)	10146	55.1	(54–56)	10325	55.9	(55–57)	10946	57.0	(56–58)			›
EU/EEA population–weighted mean)	**64010**	**57.4**	**(57–58)**	**69170**	**57.7**	**(57–58)**	**73892**	**57.2**	**(57–58)**	**77528**	**57.2**	**(57–57)**			
Portugal	2152	59.4	(57–62)	2677	59.4	(58–61)	4899	58.9	(57–60)	5177	57.8	(56–59)			
Belgium	3898	56.3	(55–58)	4350	56.8	(55–58)	2876	58.9	(57–61)	2674	58.0	(56–60)			› #
Lithuania	461	52.5	(48–57)	434	54.1	(49–59)	590	57.8	(54–62)	582	59.6	(56–64)			›
Luxembourg	335	50.7	(45–56)	299	54.5	(49–60)	371	59.6	(54–65)	347	60.2	(55–65)			›
Hungary	1328	63.9	(61–67)	1411	60.9	(58–64)	1603	59.1	(57–61)	1970	60.6	(58–63)			‹
Slovakia	596	64.9	(61–69)	786	61.5	(58–65)	866	64.5	(61–68)	878	62.8	(59–66)			
Spain	5672	65.4	(64–67)	5720	65.1	(64–66)	5817	64.9	(64–66)	6427	63.9	(63–65)			
Poland	736	63.3	(60–67)	277	65.3	(59–71)	268	59.7	(54–66)	346	64.7	(59–70)			
United Kingdom	5846	62.7	(61–64)	6648	63.1	(62–64)	6637	62.7	(62–64)	5117	65.8	(64–67)			›
Ireland	2329	67.4	(65–69)	2465	69.4	(68–71)	2694	68.7	(67–70)	2646	66.2	(64–68)			
Bulgaria	207	71.0	(64–77)	160	74.4	(67–81)	159	73.0	(65–80)	143	66.4	(58–74)			
Italy	2123	67.5	(66–70)	2356	65.7	(64–68)	2178	65.4	(63–67)	3385	67.4	(66–69)			
Cyprus	176	70.5	(63–77)	162	77.2	(70–83)	153	71.2	(63–78)	123	68.3	(59–76)			
Romania	185	58.9	(51–66)	279	67.4	(62–73)	253	68.0	(62–74)	259	73.0	(67–78)			›

–: No data

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

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

Table 3.2. ***Escherichia coli*. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015			Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)		Comment*
Iceland	134	9.7	(5–16)	116	14.7	(9–22)	141	7.8	(4–14)	162	6.8	(3–12)		
Norway	2843	11.3	(10–13)	2975	10.9	(10–12)	3415	11.0	(10–12)	3298	10.2	(9–11)		
Finland	3162	11.7	(11–13)	3618	13.2	(12–14)	3987	11.0	(10–12)	4404	11.2	(10–12)		
Denmark	3923	14.1	(13–15)	3963	12.4	(11–14)	4489	12.3	(11–13)	4570	11.9	(11–13)		‹
Sweden	5537	11.1	(10–12)	7356	11.6	(11–12)	5142	11.3	(10–12)	5525	12.6	(12–14)		› #
Netherlands	4697	15.5	(14–17)	4730	14.1	(13–15)	6444	13.3	(12–14)	5379	13.2	(12–14)		‹
Estonia	304	14.1	(10–19)	338	11.8	(9–16)	407	12.3	(9–16)	256	15.2	(11–20)		
United Kingdom	6241	16.6	(16–18)	6998	16.3	(15–17)	6921	16.8	(16–18)	5812	15.6	(15–17)		
France	9470	17.8	(17–19)	10069	16.7	(16–17)	10307	17.6	(17–18)	10998	17.7	(17–18)		
Germany	4188	21.1	(20–22)	5296	22.1	(21–23)	6163	20.6	(20–22)	8712	19.5	(19–20)		‹ #
Austria	3610	20.6	(19–22)	4279	22.0	(21–23)	4642	19.8	(19–21)	4808	20.0	(19–21)		
Lithuania	456	14.7	(12–18)	433	15.9	(13–20)	592	12.8	(10–16)	583	20.6	(17–24)		›
Czech Republic	2809	21.0	(19–23)	2953	20.8	(19–22)	2976	21.6	(20–23)	3165	22.6	(21–24)		
EU/EEA population–weighted mean)*	**71841**	**22.3**	**(22–23)**	**80345**	**22.5**	**(22–23)**	**83874**	**22.5**	**(22–23)**	**89850**	**22.8**	**(23–23)**		
Ireland	2380	24.3	(23–26)	2478	24.2	(22–26)	2703	24.5	(23–26)	2631	23.1	(21–25)		
Croatia	892	17.0	(15–20)	1026	20.2	(18–23)	1072	20.1	(18–23)	1038	24.0	(21–27)		›
Luxembourg	334	24.0	(19–29)	295	27.8	(23–33)	368	24.7	(20–29)	347	24.2	(20–29)		
Slovenia	1168	21.4	(19–24)	1224	19.9	(18–22)	1216	23.3	(21–26)	1325	24.6	(22–27)		›
Belgium	3515	22.2	(21–24)	4113	23.0	(22–24)	2599	26.7	(25–28)	2565	26.6	(25–28)		›
Latvia	152	14.5	(9–21)	134	18.7	(12–26)	181	17.7	(12–24)	194	27.8	(22–35)		›
Poland	1033	29.3	(27–32)	1035	27.3	(25–30)	1057	29.2	(27–32)	1571	27.9	(26–30)		
Hungary	1393	28.9	(27–31)	1432	30.3	(28–33)	1614	28.4	(26–31)	2021	29.0	(27–31)		
Portugal	2158	30.3	(28–32)	2685	31.6	(30–33)	5027	32.4	(31–34)	5371	29.7	(28–31)		
Greece	1372	29.1	(27–32)	1240	30.9	(28–34)	1105	32.8	(30–36)	1191	30.6	(28–33)		
Romania	186	29.0	(23–36)	300	31.0	(26–37)	307	31.3	(26–37)	371	30.7	(26–36)		
Spain	5654	33.9	(33–35)	5926	34.9	(34–36)	5818	34.0	(33–35)	6484	31.6	(30–33)		‹
Bulgaria	223	34.1	(28–41)	187	37.4	(30–45)	215	38.6	(32–45)	204	35.3	(29–42)		
Malta	216	31.9	(26–39)	248	29.8	(24–36)	279	29.0	(24–35)	258	38.8	(33–45)		
Slovakia	695	41.3	(38–45)	808	40.3	(37–44)	887	43.0	(40–46)	894	44.2	(41–48)		
Italy	2920	42.1	(40–44)	3928	42.2	(41–44)	3647	43.9	(42–46)	5590	44.4	(43–46)		›
Cyprus	176	42.0	(35–50)	162	51.9	(44–60)	153	46.4	(38–55)	123	45.5	(37–55)		

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

Table 3.3. ***Escherichia coli.*** **Total number of invasive isolates tested (N) and percentage with resistance to third-generation cephalosporins (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	138	5.1	(2–10)	121	5.0	(2–10)	152	3.3	(1–8)	173	1.7	(0–5)			
Netherlands	4702	6.0	(5–7)	4740	5.8	(5–7)	6497	5.7	(5–6)	5378	5.7	(5–6)			
Norway	3019	4.9	(4–6)	3077	5.5	(5–6)	3421	5.8	(5–7)	3301	6.0	(5–7)			›
Finland	3162	6.2	(5–7)	3720	7.1	(6–8)	4009	5.4	(5–6)	4342	6.1	(5–7)			
Sweden	5537	4.5	(4–5)	7532	5.2	(5–6)	6546	5.6	(5–6)	5995	6.2	(6–7)			›
Denmark	2519	7.9	(7–9)	2451	8.1	(7–9)	4410	7.0	(6–8)	4561	7.5	(7–8)			
Austria	3710	8.7	(8–10)	4376	9.8	(9–11)	4739	9.4	(9–10)	4900	9.7	(9–11)			
Belgium	4097	6.9	(6–8)	4051	8.0	(7–9)	2802	9.7	(9–11)	2593	9.7	(9–11)			›
Germany	4186	8.8	(8–10)	5335	10.7	(10–12)	6246	10.5	(10–11)	8724	10.4	(10–11)			
France	9563	10.0	(9–11)	10154	9.5	(9–10)	10349	9.9	(9–11)	11051	11.0	(10–12)			›
Malta	216	13.9	(10–19)	248	8.9	(6–13)	279	10.8	(7–15)	258	11.2	(8–16)			
United Kingdom	5663	13.1	(12–14)	6586	14.7	(14–16)	6221	10.3	(10–11)	5169	11.3	(10–12)			‹
Estonia	305	7.9	(5–11)	340	7.4	(5–11)	410	9.3	(7–12)	246	11.4	(8–16)			
Ireland	2288	9.2	(8–10)	2480	10.6	(9–12)	2691	10.7	(10–12)	2638	11.4	(10–13)			›
Spain	5672	13.5	(13–14)	5932	13.3	(12–14)	5821	12.3	(12–13)	6428	11.6	(11–12)			‹
Poland	1037	12.9	(11–15)	1036	10.9	(9–13)	1085	10.5	(9–12)	1610	11.9	(10–14)			
Croatia	906	7.6	(6–10)	1040	8.8	(7–11)	1079	10.8	(9–13)	1046	12.5	(11–15)			›
Luxembourg	334	11.4	(8–15)	301	10.6	(7–15)	368	12.0	(9–16)	347	12.7	(9–17)			
EU/EEA population–weighted mean)	**70888**	**11.9**	**(12–12)**	**79082**	**12.6**	**(12–13)**	**85103**	**12.0**	**(12–12)**	**89839**	**13.1**	**(13–13)**			›
Slovenia	1168	9.5	(8–11)	1224	8.7	(7–10)	1216	12.7	(11–15)	1326	13.7	(12–16)			›
Czech Republic	2812	11.5	(10–13)	2954	13.1	(12–14)	2978	14.0	(13–15)	3172	14.5	(13–16)			›
Lithuania	462	4.8	(3–7)	434	7.6	(5–11)	594	8.1	(6–11)	581	16.0	(13–19)			›
Portugal	2154	13.5	(12–15)	2678	14.9	(14–16)	5024	16.4	(15–17)	5376	16.1	(15–17)			› #
Hungary	1411	17.4	(15–20)	1437	18.9	(17–21)	1619	16.4	(15–18)	2026	16.7	(15–18)			
Latvia	154	13.0	(8–19)	136	14.0	(9–21)	165	10.9	(7–17)	201	17.9	(13–24)			
Greece	1393	16.2	(14–18)	1255	17.2	(15–19)	1122	21.0	(19–24)	1215	19.8	(18–22)			› #
Romania	191	25.1	(19–32)	298	22.8	(18–28)	306	29.4	(24–35)	369	26.8	(22–32)			
Cyprus	176	31.8	(25–39)	162	38.9	(31–47)	153	28.8	(22–37)	123	28.5	(21–37)			
Slovakia	693	30.7	(27–34)	807	29.7	(27–33)	889	31.8	(29–35)	893	30.0	(27–33)			
Italy	2997	26.3	(25–28)	3990	26.2	(25–28)	3694	28.7	(27–30)	5592	30.1	(29–31)			›
Bulgaria	223	38.1	(32–45)	187	39.6	(33–47)	218	40.4	(34–47)	205	38.5	(32–46)			

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

Table 3.4. ***Escherichia coli*****. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	138	3.6	(1–8)	121	4.1	(1–9)	152	5.3	(2–10)	173	2.9	(1–7)		5.4 4.2 3.0	
Finland	2993	6.1	(5–7)	3561	6.5	(6–7)	3817	4.6	(4–5)	4135	5.4	(5–6)		6.6 5.6 4.6	‹ #
Netherlands	4706	7.2	(6–8)	4741	6.2	(6–7)	6485	6.3	(6–7)	5378	6.0	(5–7)		7.2 6.6 6.0	‹ #
Norway	3023	5.8	(5–7)	3079	6.4	(6–7)	3419	5.9	(5–7)	3301	6.0	(5–7)		6.4 6.1 5.8	
Sweden	5537	5.8	(5–6)	7100	6.0	(5–7)	5606	6.1	(5–7)	5761	6.4	(6–7)		6.4 6.1 5.8	
Denmark	3687	7.3	(6–8)	3887	6.5	(6–7)	4493	7.3	(7–8)	4591	6.8	(6–8)		7.5 7.0 6.5	
Austria	3702	6.3	(6–7)	4367	7.2	(6–8)	4726	7.1	(6–8)	4884	7.0	(6–8)		7.2 6.7 6.2	
Germany	4190	7.1	(6–8)	5337	7.0	(6–8)	6244	6.9	(6–8)	8723	7.2	(7–8)		7.2 7.1 6.9	
France	5749	8.1	(7–9)	10156	7.8	(7–8)	10341	7.7	(7–8)	11055	8.2	(8–9)		8.2 8.0 7.7	
Belgium	3010	7.3	(6–8)	3309	7.3	(6–8)	2045	8.9	(8–10)	2286	8.4	(7–10)		8.9 8.1 7.3	› #
Luxembourg	334	6.3	(4–9)	299	7.0	(4–11)	367	7.9	(5–11)	347	8.9	(6–12)		8.9 7.6 6.3	
Estonia	304	7.6	(5–11)	341	7.3	(5–11)	411	6.8	(5–10)	257	9.3	(6–14)		9.3 8.0 6.7	
United Kingdom	6390	8.6	(8–9)	7166	9.0	(8–10)	7274	8.9	(8–10)	6052	9.9	(9–11)		10.0 9.3 8.6	›
Lithuania	460	9.6	(7–13)	429	10.7	(8–14)	584	10.6	(8–13)	583	10.1	(8–13)		10.7 10.2 9.7	
EU/EEA (population-weighted mean)	**67669**	**10.5**	**(10–11)**	**79537**	**9.9**	**(10–10)**	**84026**	**9.7**	**(10–10)**	**89764**	**10.4**	**(10–11)**		10.5 10.1 9.7	
Poland	1025	12.1	(10–14)	1049	10.7	(9–13)	1068	9.8	(8–12)	1581	11.2	(10–13)		12.0 11.0 10.0	
Czech Republic	2812	8.2	(7–9)	2957	9.1	(8–10)	2979	10.7	(10–12)	3172	11.3	(10–13)		12.0 10.0 8.0	›
Malta	216	13.0	(9–18)	248	9.3	(6–14)	279	10.4	(7–15)	258	11.6	(8–16)		13.0 11.0 9.0	
Ireland	2375	10.7	(9–12)	2481	11.2	(10–12)	2705	12.1	(11–13)	2646	11.8	(11–13)		12.1 11.4 10.7	
Croatia	901	7.0	(5–9)	1016	7.7	(6–9)	1077	10.9	(9–13)	1008	12.7	(11–15)		13.0 10.0 7.0	›
Slovenia	1168	8.4	(7–10)	1224	9.3	(8–11)	1216	11.3	(10–13)	1326	12.9	(11–15)		13.0 10.5 8.0	›
Hungary	1404	17.1	(15–19)	1427	17.0	(15–19)	1610	14.7	(13–17)	2020	13.6	(12–15)		17.2 15.4 13.6	‹
Cyprus	176	21.0	(15–28)	162	24.7	(18–32)	153	17.6	(12–25)	123	13.8	(8–21)		25.0 19.5 14.0	
Portugal	2154	16.2	(15–18)	2684	15.2	(14–17)	4991	15.1	(14–16)	5372	13.8	(13–15)		16.5 15.0 13.5	‹
Latvia	154	11.7	(7–18)	134	5.2	(2–10)	181	8.3	(5–13)	191	14.1	(10–20)		14.0 9.5 5.0	
Spain	5675	15.6	(15–17)	5929	15.3	(14–16)	5820	15.1	(14–16)	6489	14.7	(14–16)		15.7 15.2 14.7	
Greece	1372	17.8	(16–20)	1239	16.9	(15–19)	1110	15.6	(14–18)	1200	16.1	(14–18)		17.8 16.7 15.6	
Romania	185	24.3	(18–31)	298	14.8	(11–19)	303	17.2	(13–22)	366	18.3	(14–23)		25.0 20.0 15.0	
Bulgaria	219	26.5	(21–33)	187	31.0	(24–38)	189	29.1	(23–36)	182	19.8	(14–26)		31.0 25.5 20.0	
Italy	2916	22.3	(21–24)	3802	19.0	(18–20)	3493	19.4	(18–21)	5408	20.2	(19–21)		23.0 21.0 19.0	
Slovakia	694	20.7	(18–24)	807	24.0	(21–27)	888	22.7	(20–26)	896	24.2	(21–27)		24.0 22.0 20.0	

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

Table 3.5. ***Escherichia coli*****. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Belgium	4119	0.0	(0–0)	4246	<0.1	(0–0)	2614	<0.1	(0–0)	2588	0.0	(0–0)			
Bulgaria	191	2.6	(1–6)	176	2.8	(1–7)	197	0.5	(0–3)	182	0.0	(0–2)			<
Croatia	900	0.0	(0–0)	1038	0.0	(0–0)	1079	0.0	(0–0)	1046	0.0	(0–0)			
Cyprus	176	<0.1	(0–2)	162	0.0	(0–2)	153	0.0	(0–2)	123	0.0	(0–3)			
Czech Republic	1729	0.1	(0–0)	1733	0.0	(0–0)	1702	0.0	(0–0)	1471	0.0	(0–0)			
Estonia	252	<0.1	(0–1)	283	0.0	(0–1)	254	0.0	(0–1)	219	0.0	(0–2)			
Finland	3161	0.0	(0–0)	3721	0.0	(0–0)	4013	0.0	(0–0)	4425	0.0	(0–0)			
Hungary	1307	0.0	(0–0)	1355	0.1	(0–1)	1517	0.0	(0–0)	1922	0.0	(0–0)			
Iceland	138	0.0	(0–3)	121	0.0	(0–3)	140	0.0	(0–3)	162	0.0	(0–0)			
Latvia	153	<0.1	(0–2)	135	0.0	(0–3)	182	0.0	(0–2)	192	0.0	(0–2)			
Lithuania	450	<0.1	(0–1)	433	0.0	(0–1)	593	0.0	(0–1)	579	0.0	(0–1)			
Luxembourg	333	<0.1	(0–1)	295	0.0	(0–1)	368	0.3	(0–2)	347	0.0	(0–1)			
Malta	216	<0.1	(0–2)	248	0.0	(0–1)	279	0.0	(0–1)	258	0.0	(0–1)			
Slovakia	659	0.9	(0–2)	588	0.0	(0–1)	820	0.0	(0–0)	830	0.0	(0–0)			< #
Slovenia	1168	0.0	(0–0)	1224	0.1	(0–0)	1216	0.0	(0–0)	1326	0.0	(0–0)			
Austria	3340	0.1	(0–0)	4257	<0.1	(0–0)	4600	<0.1	(0–0)	4760	<0.1	(0–0)			
Denmark	2865	0.0	(0–0)	2832	<0.1	(0–0)	3946	<0.1	(0–0)	4046	<0.1	(0–0)			
France	9091	0.0	(0–0)	9585	0.1	(0–0)	9693	<0.1	(0–0)	10481	<0.1	(0–0)			
Germany	4184	0.0	(0–0)	5333	0.1	(0–0)	6247	0.1	(0–0)	8725	<0.1	(0–0)			
Ireland	2369	0.0	(0–0)	2476	<0.1	(0–0)	2697	<0.1	(0–0)	2615	<0.1	(0–0)			
Netherlands	4701	0.0	(0–0)	4726	<0.1	(0–0)	6475	0.0	(0–0)	5375	<0.1	(0–0)			
Norway	3023	0.0	(0–0)	3079	0.1	(0–0)	3420	0.0	(0–0)	3297	<0.1	(0–0)			
Spain	5670	0.1	(0–0)	5921	0.7	(1–1)	5817	0.1	(0–0)	6399	<0.1	(0–0)			
Poland	970	0.0	(0–0)	938	0.0	(0–0)	979	0.2	(0–1)	1499	0.1	(0–0)			
Portugal	2041	0.1	(0–0)	2668	0.1	(0–0)	4998	<0.1	(0–0)	5354	0.1	(0–0)			
Sweden	5529	<0.1	(0–0)	7347	<0.1	(0–0)	6298	0.0	(0–0)	5307	0.1	(0–0)			
EU/EEA (population-weighted mean)	**68516**	**0.1**	**(0–0)**	**76715**	**0.2**	**(0–0)**	**81787**	**0.1**	**(0–0)**	**86200**	**0.1**	**(0–0)**			
Italy	3021	0.3	(0–1)	3989	0.6	(0–1)	3696	0.2	(0–0)	5592	0.2	(0–0)			<
United Kingdom	5182	0.2	(0–0)	6251	<0.1	(0–0)	6367	0.1	(0–0)	5497	0.3	(0–0)			
Greece	1396	1.4	(1–2)	1256	1.4	(1–2)	1122	1.2	(1–2)	1215	1.2	(1–2)			
Romania	182	0.0	(0–2)	299	0.0	(0–1)	305	0.7	(0–2)	368	1.9	(1–4)			> #

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

Table 3.6. ***Escherichia coli*. Total number of isolates tested (N) and percentage with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	134	1.5	(0–5)	116	0.9	(0–5)	141	1.4	(0–5)	162	0.0	(0–2)			
Norway	2835	1.9	(1–3)	2971	2.5	(2–3)	3413	2.0	(2–2)	3298	1.9	(1–2)			
Netherlands	4675	1.8	(1–2)	4722	1.9	(2–2)	6425	2.1	(2–3)	5377	2.0	(2–2)			
Denmark	2285	2.6	(2–3)	2377	2.2	(2–3)	4406	1.9	(1–2)	4531	2.5	(2–3)			
Sweden	5534	1.8	(1–2)	7094	2.0	(2–2)	4203	2.0	(2–2)	5257	2.5	(2–3)			› #
Finland	2993	3.1	(3–4)	3457	3.2	(3–4)	3787	2.2	(2–3)	4103	2.6	(2–3)			‹ #
Austria	3573	2.3	(2–3)	4258	3.1	(3–4)	4609	2.6	(2–3)	4785	2.9	(2–3)			
Germany	4179	3.2	(3–4)	5282	2.7	(2–3)	6158	3.0	(3–3)	8707	3.0	(3–3)			
Belgium	2998	2.0	(2–3)	3138	2.7	(2–3)	2045	3.9	(3–5)	2285	3.5	(3–4)			› #
France	5655	3.3	(3–4)	10068	3.2	(3–4)	10299	3.5	(3–4)	10988	3.9	(4–4)			› #
Lithuania	454	1.3	(0–3)	428	1.9	(1–4)	582	2.6	(1–4)	581	4.3	(3–6)			›
United Kingdom	5577	4.2	(4–5)	6535	4.4	(4–5)	6191	4.4	(4–5)	5119	4.5	(4–5)			
Estonia	301	1.7	(1–4)	335	3.3	(2–6)	404	3.5	(2–6)	233	5.2	(3–9)			›
Luxembourg	334	2.7	(1–5)	283	2.1	(1–5)	367	3.8	(2–6)	347	5.2	(3–8)			›
EU/EEA (population-weighted mean)	**64514**	**4.9**	**(5–5)**	**76499**	**4.6**	**(4–5)**	**80907**	**4.7**	**(5–5)**	**87798**	**5.3**	**(5–5)**			›
Ireland	2282	3.6	(3–4)	2477	4.7	(4–6)	2689	4.7	(4–6)	2621	5.4	(5–6)			›
Spain	5651	5.8	(5–6)	5921	5.8	(5–6)	5814	5.3	(5–6)	6416	5.5	(5–6)			
Poland	990	6.1	(5–8)	978	5.0	(4–7)	1026	5.6	(4–7)	1532	6.1	(5–7)			
Hungary	1382	10.6	(9–12)	1418	11.0	(9–13)	1599	8.2	(7–10)	2015	6.7	(6–8)			‹
Croatia	885	2.7	(2–4)	1003	3.5	(2–5)	1070	6.0	(5–8)	1000	6.9	(5–9)			›
Czech Republic	2809	4.3	(4–5)	2953	4.9	(4–6)	2976	6.4	(6–7)	3165	6.9	(6–8)			›
Malta	216	7.4	(4–12)	248	5.2	(3–9)	279	6.8	(4–10)	258	7.0	(4–11)			
Portugal	2151	9.2	(8–10)	2676	8.1	(7–9)	4989	8.2	(7–9)	5366	7.6	(7–8)			‹
Slovenia	1168	5.0	(4–6)	1224	4.5	(3–6)	1216	7.1	(6–9)	1325	8.1	(7–10)			›
Cyprus	176	14.8	(10–21)	162	20.4	(14–27)	153	13.1	(8–19)	123	9.8	(5–16)			
Latvia	152	6.6	(3–12)	132	3.8	(1–9)	163	2.5	(1–6)	191	10.5	(7–16)			
Greece	1368	10.7	(9–12)	1234	10.3	(9–12)	1102	10.7	(9–13)	1187	10.7	(9–13)			
Bulgaria	219	16.0	(11–22)	187	18.7	(13–25)	188	20.2	(15–27)	182	12.6	(8–18)			
Romania	179	15.6	(11–22)	292	9.2	(6–13)	298	14.4	(11–19)	364	13.5	(10–17)			
Italy	2667	14.3	(13–16)	3724	12.5	(11–14)	3428	13.7	(13–15)	5389	14.6	(14–16)			
Slovakia	692	13.4	(11–16)	806	17.2	(15–20)	887	17.0	(15–20)	891	17.1	(15–20)			

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

Table 3.7. ***Escherichia coli*****. Total number of tested isolates* and resistance combinations among invasive isolates tested against aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems (n=72 123), EU/EEA countries, 2015**

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**30 074**	**41.7**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**24 660**	**34.2**
Aminopenicillins	22 820	31.6
Fluoroquinolones	1 713	2.4
Aminoglycosides	126	0.2
Carbapenems	1	<0.1
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**8 198**	**11.4**
Aminopenicillins + fluoroquinolones	5 294	7.3
Aminopenicillins + third-generation cephalosporins	1 626	2.3
Aminopenicillins + aminoglycosides	1 155	1.6
Fluoroquinolones + aminoglycosides	121	0.2
Aminopenicillins + carbapenems	1	<0.1
Aminoglycosides + carbapenems	1	<0.1
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**5 450**	**7.6**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones	3 118	4.3
Aminopenicillins + fluoroquinolones + aminoglycosides	2 005	2.8
Aminopenicillins + third-generation cephalosporins + aminoglycosides	322	0.4
Aminopenicillins + third-generation cephalosporins + carbapenems	5	<0.1
Resistance to four antimicrobial groups		
Total (all four-group combinations)	**3 720**	**5.2**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides	3 707	5.1
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + carbapenems	8	<0.1
Aminopenicillins + third-generation cephalosporins + aminoglycosides + carbapenems	5	<0.1
Resistance to five antimicrobial groups		
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	**21**	**<0.1**

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

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

3.2 *Klebsiella pneumoniae*

3.2.1 Clinical and epidemiological importance

Klebsiella pneumoniae predominantly colonise hospitalised individuals, where it is mainly found in the gastrointestinal tract, skin, the oropharynx and upper airways. The majority of infections caused by *K. pneumoniae* are healthcare-associated and can spread rapidly between colonised or infected patients and via the hands of hospital personnel, leading to nosocomial outbreaks. Infections include urinary tract infections, lower respiratory tract infections and bloodstream infections. Some hypervirulent strains can cause severe invasive infections (often liver abscesses with bacteraemia and metastatic infections) also occurring in healthy subjects.

3.2.2 Resistance mechanisms

Similar to *E. coli*, *K. pneumoniae* can be resistant to multiple antimicrobial agents, and resistance traits are frequently acquired through plasmids. In contrast to *E. coli*, *K. pneumoniae* has a chromosomally encoded class A beta-lactamase and is thus intrinsically resistant to aminopenicillins. Moreover, this organism readily acquires plasmid-mediated resistance determinants. Many novel ESBL variants were initially identified in *K. pneumoniae* and were only subsequently found in *E. coli*. Since the resistance mechanisms do not differ significantly from those described for *E. coli*, readers should refer to the *E. coli* section (3.1, above) for further details.

Carbapenems have been widely used in many countries due to the increasing rate of ESBL-producing Enterobacteriaceae, resulting in the emergence of resistance to these agents, especially in *K. pneumoniae*. In Europe, *K. pneumoniae* with carbapenemase KPC, NDM, OXA-48-like, or VIM production has been reported, although with greatly varying prevalence. The highest rates were reported in Mediterranean and Balkan countries.

3.2.3 Antimicrobial susceptibility

- More than a third of the *K. pneumoniae* isolates reported to EARS-Net in 2015 were resistant to at least one antimicrobial group under surveillance, and combined resistance to multiple antimicrobial groups was common. The most common resistance phenotype was combined resistance to three key antimicrobial groups: fluoroquinolones, third-generation cephalosporins and aminoglycosides.
- The EU/EEA population-weighted mean percentages of resistance in *K. pneumoniae* to fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems, as well as combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, all increased significantly between 2012 and 2015.
- There were wide inter-country differences in the percentage of carbapenem-resistant *K. pneumoniae*. The three countries with the highest of carbapenem resistance (Greece, Italy and Romania) also contributed the vast majority of the isolates with combined carbapenem and polymyxin resistance.
- A north to east/south gradient was noted for most antimicrobial groups, with lower resistance percentages in *K. pneumoniae* reported from northern countries and higher percentages from the eastern and southern parts of Europe.

Fluoroquinolones

For 2015, 30 countries reported 22 358 *K. pneumoniae* isolates with AST information for fluoroquinolones (ciprofloxacin, levofloxacin or ofloxacin). The number of isolates reported per country ranged from 35 to 2 332 (Table 3.7).

The EU/EEA population-weighted mean percentage showed a significantly increased trend for the period 2012–2015, from 25.3% in 2012 to 29.7% in 2015 (Table 3.7).

National percentages of resistant isolates ranged from 2.9% (Iceland) to 70.0% (Slovakia) in 2015 (Table 3.7 and Figure 3.6). Trends for the period 2012–2015 were calculated for the 29 countries reporting at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for five countries (France, Ireland, Romania, Spain and the United Kingdom). These trends remained significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for Austria, Denmark and Germany. These trends remained significant when considering only data from laboratories reporting consistently for all four years.

Third-generation cephalosporins

For 2015, 30 countries reported *K. pneumoniae* isolates with AST information for third-generation cephalosporins (cefotaxime, ceftriaxone or ceftazidime). The number of isolates reported per country ranged from 36 to 2 338 (Table 3.8).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 25.8 % in 2012 to 30.3 % in 2015 (Table 3.8).

National percentages of resistant isolates ranged from zero (Iceland) to 75.0 % (Bulgaria) in 2015 (Table 3.8, Figure 3.7). Trends for the period 2012–2015 were calculated for the 29 countries reporting at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for Cyprus, Finland and the United Kingdom. For Finland, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Significantly decreasing trends were observed for five countries (Denmark, Germany, Greece, Hungary and Lithuania). For Germany, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

ESBL percentages for *K. pneumoniae* were calculated based on data from 23 countries. Only data from laboratories reporting ESBL results for all isolates identified as resistant to third-generation cephalosporins (51 % of the laboratories reporting AST data for third-generation cephalosporin in *K. pneumoniae*), and only data from countries reporting at least 10 such isolates were included. Among the *K. pneumoniae* isolates resistant to third-generation cephalosporins and meeting the inclusion criteria, 85.3 % were ascertained as ESBL-positive by the laboratories in 2015. ESBL results might not be directly comparable between countries as there are national differences in the definition of ESBL. The presence of ESBL might also be masked by carbapenemases such as MBLs and KPCs, and/or severe permeability defects [18].

Aminoglycosides

For 2015, 30 countries reported 22 301 *K. pneumoniae* isolates with AST information for aminoglycosides (gentamicin and/or tobramycin). The number of isolates reported per country ranged from 36 to 2 337 (Table 3.9).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 21.5 % in 2012 to 22.5 % in 2015 (Table 3.9).

National percentages of resistant isolates ranged from zero (Iceland) to 66.5 % (Slovakia) in 2015 (Table 3.9 and Figure 3.8). Trends for the period 2012–2015 were calculated for the 29 countries reporting at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for Cyprus, Finland and the United Kingdom. For Finland, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for five countries (Denmark, Germany, Greece, Hungary and Lithuania). For Germany, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Susceptibility data for amikacin were less frequently reported than for gentamicin and/or tobramycin and generally showed lower resistance. A total of 15 421 isolates had susceptibility data for both amikacin and gentamicin and/or tobramycin (69.1 % of the isolates included in the aminoglycoside group analysis). Among isolates with resistance to either gentamicin or tobramycin, 17.2 % of the isolates were also resistant to amikacin.

Carbapenems

For 2015, 30 countries reported 21 749 *K. pneumoniae* isolates with AST information for carbapenems (doripenem, imipenem or meropenem). The number of isolates reported per country ranged from 35 to 2 244 (Table 3.10).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 6.2 % in 2012 to 8.1 % in 2015 (Table 3.10).

The national percentages of resistant isolates ranged from zero (Denmark, Estonia, Finland, Iceland, Latvia, Lithuania, Luxembourg and Sweden) to 61.9 % (Greece) (Table 3.10, Figure 3.9). Trends for the period 2012–2015 were calculated for the 29 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for four countries (Croatia, Portugal, Romania and Spain). For Romania, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for Hungary and Slovakia. For Slovakia, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides

For 2015, 30 countries reported 21 871 *K. pneumoniae* isolates with sufficient AST information to determine combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides. The number of isolates reported per country ranged from 35 to 2 324 (Table 3.11).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 17.7 % in 2012 to 18.6 % in 2015 (Table 3.11).

National percentages of resistant isolates ranged from zero (Iceland) to 59.6 (Slovakia) in 2015 (Table 3.11 and Figure 3.10). Trends for the period 2012–2015 were calculated for the 29 countries reporting at least 20 isolates per year during the full four-year period. A significantly increasing trend was observed for Finland, a trend that did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for five countries (Denmark, Germany, Greece, Hungary

Figure 3.6. ***Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2015**

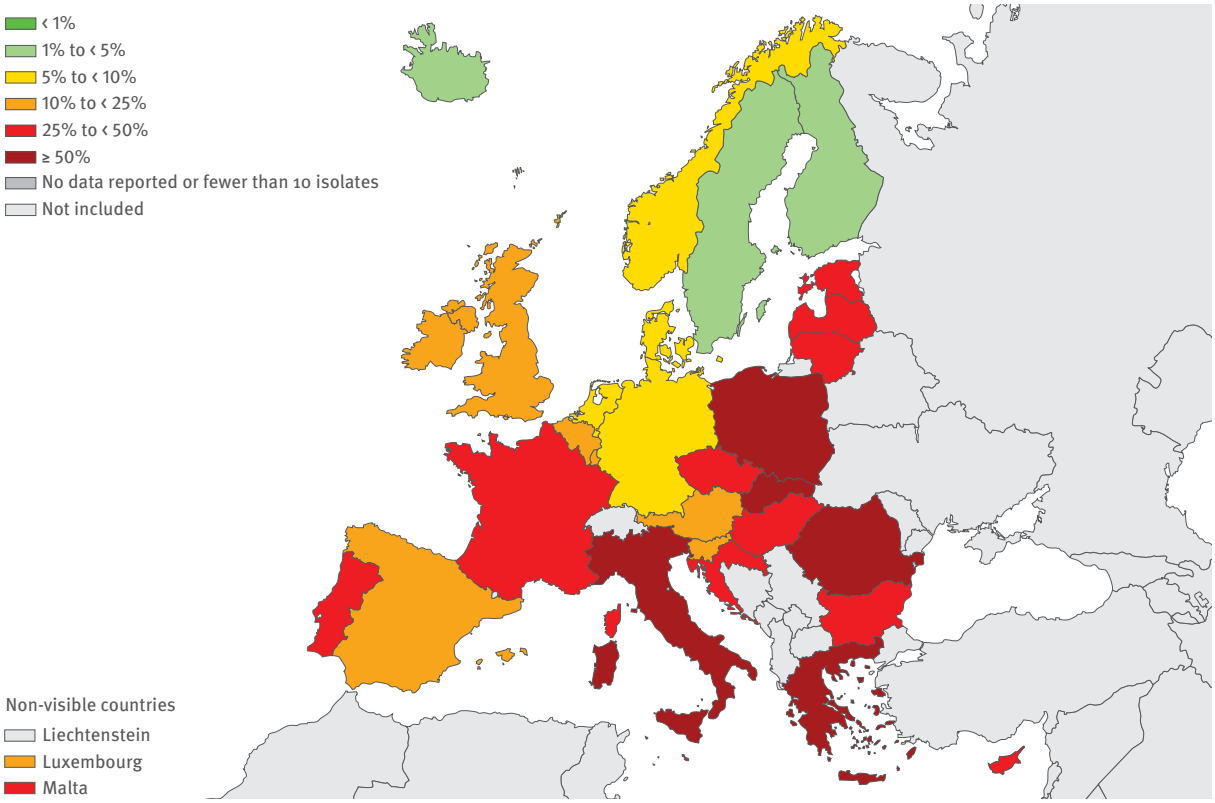
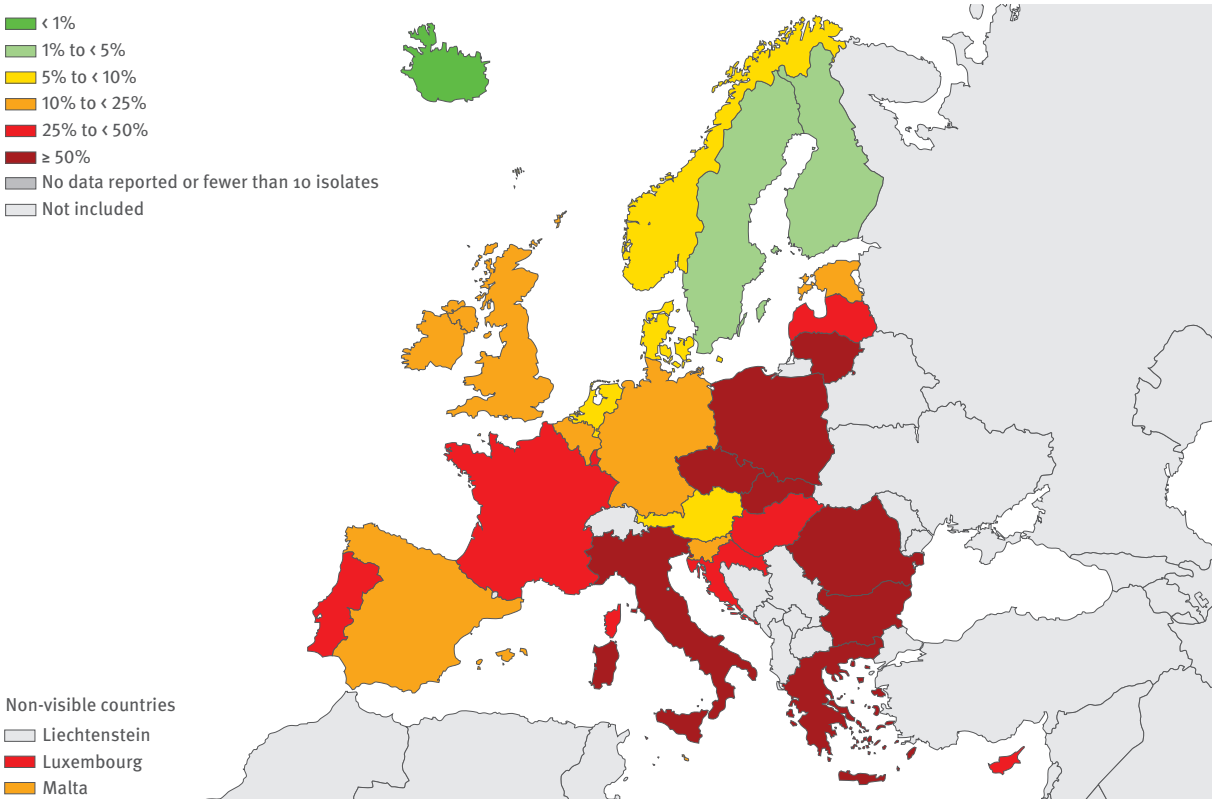


Figure 3.7. ***Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2015**



and Lithuania). For Denmark, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 17.7% in 2012 to 18.6% in 2015 (Table 3.11).

Other resistance combinations and resistance to other antimicrobial groups

Of the 21141 isolates (92.3% of all *K. pneumoniae* isolates) tested for all antimicrobial groups under regular EARS-Net surveillance (fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems) in 2015, more than one third (36.6%) were resistant to at least one antimicrobial group. Among the resistant isolates, combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides was the most common resistance phenotype, more frequent than isolates with single resistance to antimicrobial group or two antimicrobial groups together. Overall, 4.7% of all *K. pneumoniae* isolates were resistant to all groups under EARS-Net surveillance (Table 3.12).

Twenty-one countries reported AST data for polymyxins for a total of 6 029 isolates (26.3% of all reported *K. pneumoniae* isolates) in 2015. Only six countries reported polymyxin AST data for more than half of the reported *K. pneumoniae* isolates. Overall, 8.8% of the *K. pneumoniae* isolates were resistant to polymyxins. Among carbapenem-resistant isolates also tested for resistance to polymyxins (26.5% of all isolates with carbapenem AST information), 31.9% were resistant to polymyxins, whereas only 2.6% of the carbapenem-susceptible isolates were resistant to polymyxins. The vast majority (95%) of the isolates with combined carbapenem and polymyxin resistance were reported from Greece and Italy.

Due to the low number of isolates tested, potential sequential testing and differences in the use of laboratory methodology used to determine susceptibility, these findings should be interpreted with caution and may not be representative of Europe as a whole.

3.2.4 Discussion and conclusion

The high and increasing percentages of antimicrobial-resistant *K. pneumoniae* are a public health concern of growing importance in Europe. More than one third of the *K. pneumoniae* isolates reported in 2015 were resistant to at least one antimicrobial group under surveillance (fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems). Among the resistant isolates, the most common phenotype was combined resistance to fluoroquinolone, third-generation cephalosporins and aminoglycosides.

The EU/EEA population-weighted mean percentage for resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides as well as for combined resistance to all three of these antimicrobial groups all increased significantly during the period 2012–2015. This is a continuation of the worrying trends described in previous reports [19-20]. Increasing resistance trends were noted for countries with both low and high resistance percentages.

The percentage of third-generation cephalosporin-resistant isolates with ESBL production was high, and combined resistance to more than one antimicrobial group was common. As for *E. coli*, the increase in combined resistance to more antimicrobial groups and the high frequency of ESBL-producing isolates may lead to an increased use of carbapenems, thus favouring the further dissemination of carbapenemase-producing bacteria.

Carbapenemases are a group of enzymes that can hydrolyse most beta-lactams, including carbapenems, meaning that treatment options are limited to few alternative agents which retain activity (such as colistin, tigecycline, fosfomycin and gentamicin or amikacin) or new drugs like ceftazidime plus avibactam (a new beta-lactamase inhibitor active against some carbapenemases). Information on carbapenemase production is very limited in the EARS-Net data, but recent information from the European Survey on Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) project indicates that carbapenemase-producing Enterobacteriaceae (CPE) continue to spread in Europe, creating an especially problematic situation with regard to *K. pneumoniae* [21].

The significantly increasing trend of the EU/EEA population-weighted mean percentage for carbapenem resistance between 2009 and 2014 continued in 2015. National carbapenem resistance percentages ranged from zero to 61.9% in 2015, with a majority of the countries (20) reporting percentages lower than 1%. Five countries reported resistance percentages between 1 and 5%, and three countries reported between 5 and 15%. Three countries (Greece, Italy and Romania) reported carbapenem resistance percentages considerably higher than any other country (61.9%, 33.5% and 24.7%, respectively). With only a few exceptions, the countries reporting the highest carbapenem resistance percentages were those that also reported the highest levels of combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides. The 2016 ECDC rapid risk assessment on carbapenem-resistant Enterobacteriaceae, including *K. pneumoniae*, highlights that carbapenem-resistant bacteria pose a significant threat to patients and healthcare systems in all EU/EEA Member States: carbapenem-resistant Enterobacteriaceae are associated with higher healthcare costs, prolonged hospital stays, treatment failure and mortality.

Recommendations include timely and appropriate laboratory reporting, screening/pre-emptive isolation of high-risk patients, good infection control (including environmental cleaning and adequate reprocessing of medical devices), and antimicrobial stewardship programmes. Measures related to enhanced surveillance and the screening/pre-emptive isolation of patients who were transferred from hospitals and other healthcare settings in high-prevalence countries are an immediate

Figure 3.8. ***Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2015**

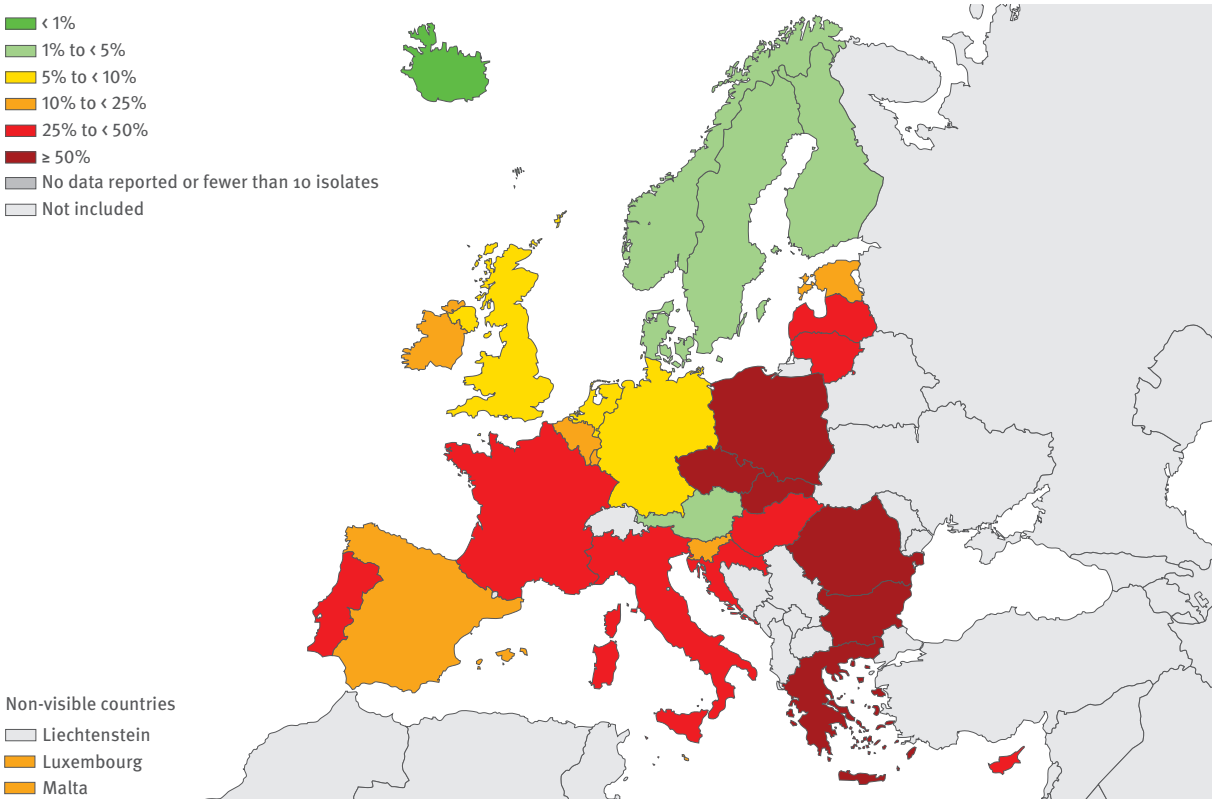
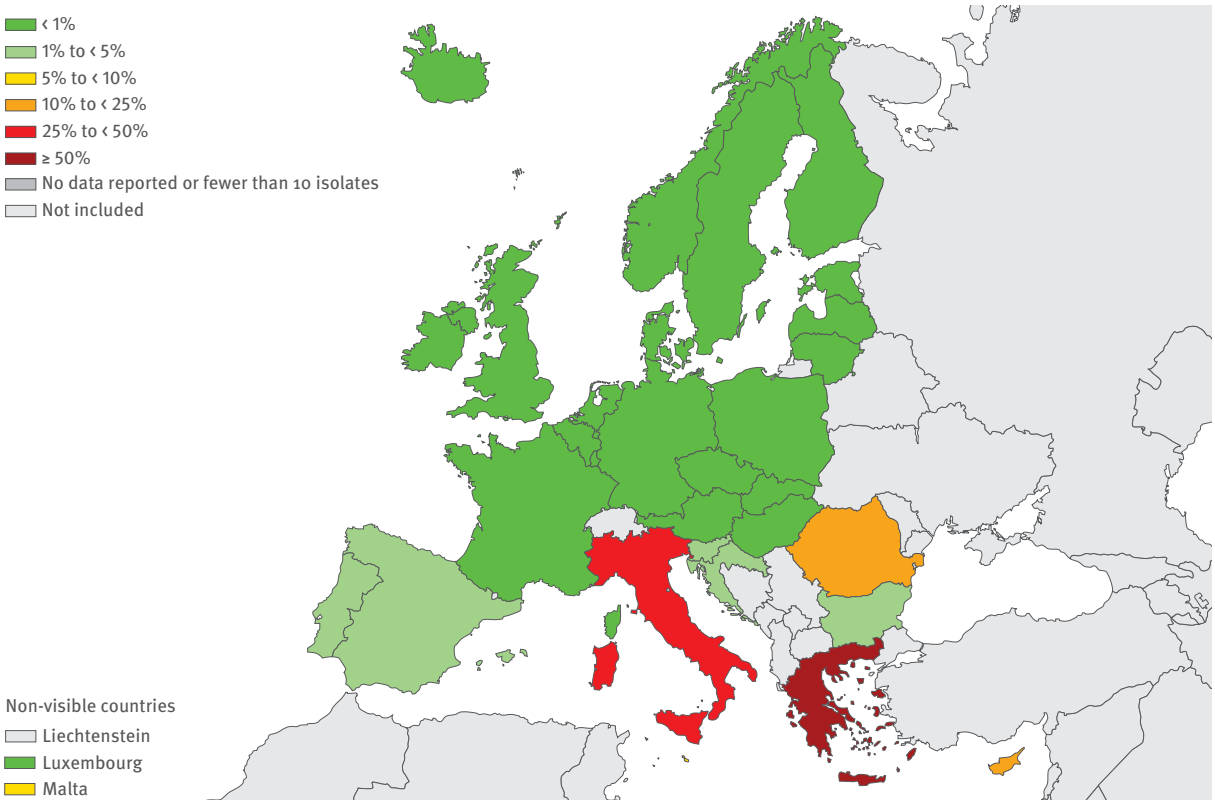


Figure 3.9. ***Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015**



measure to reduce transmission in healthcare and prevent outbreaks. Although many European countries recently upgraded their level of management for carbapenem-resistant Enterobacteriaceae, gaps still remain, and many countries still lack national guidance for infection prevention and control of these infections [22].

The emergence of resistance to polymyxins, especially in countries with already high percentages of multidrug and carbapenem resistance, is a special concern, as these antimicrobial agents remain one of the very few treatment options for these types of infections.

Data on polymyxin susceptibility from EARS-Net should be interpreted with caution due to potential selective testing targeted at high-risk patients and methodological problems with MIC determination. To overcome the latter problem, the joint CLSI–EUCAST Polymyxin Breakpoints Working Group has published a method to determine colistin MICs in 2016. Susceptibility testing by other methods, including agar dilution, disk diffusion and gradient diffusion, is not recommended until historical data have been reviewed or new study data have been generated [23]. As data on methods used for determining colistin susceptibility are incomplete in EARS-Net, the impact of the various testing methods on the results is unknown.

The ECDC rapid risk assessment on carbapenem-resistant Enterobacteriaceae concluded that it is likely that most countries could still control the spread through proportionate investments in control measures as long as prevalence is still low. Once an endemic situation is reached, control efforts will be more costly and less likely to be effective. Many of the recommended interventions would not only target carbapenem-resistant bacteria, but also affect the general spread of antimicrobial-resistant bacteria.

Figure 3.10. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, by country, EU/EEA countries, 2015

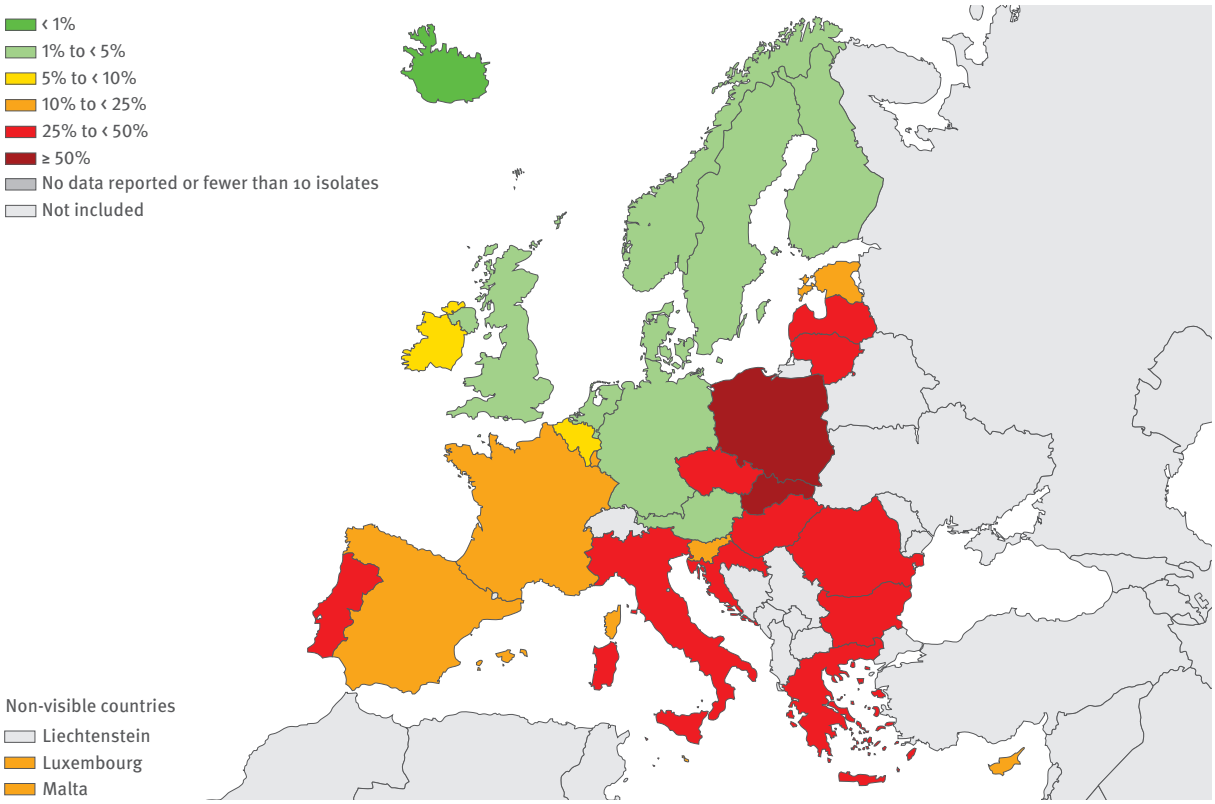


Table 3.8. ***Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	14	7.1	(0–34)	28	0.0	(0–12)	28	3.6	(0–18)	35	2.9	(0–15)		N/A	
Finland	536	2.1	(1–4)	537	2.6	(1–4)	581	4.6	(3–7)	658	3.3	(2–5)			
Sweden	977	3.7	(3–5)	1270	3.9	(3–5)	763	4.1	(3–6)	907	4.5	(3–6)			
Norway	596	4.0	(3–6)	616	4.9	(3–7)	746	6.2	(5–8)	700	5.0	(4–7)			
Denmark	941	8.8	(7–11)	874	8.9	(7–11)	943	6.9	(5–9)	935	5.3	(4–7)			‹
Netherlands	670	5.4	(4–7)	638	6.1	(4–8)	886	4.7	(3–6)	908	6.8	(5–9)			
Germany	663	13.7	(11–17)	756	15.1	(13–18)	980	12.7	(11–15)	1517	9.6	(8–11)			‹
Austria	829	15.4	(13–18)	925	15.8	(13–18)	971	10.4	(9–12)	1029	11.7	(10–14)			‹
United Kingdom	1036	7.4	(6–9)	1155	8.7	(7–10)	1130	7.7	(6–9)	1011	13.3	(11–16)			›
Ireland	338	7.4	(5–11)	316	14.6	(11–19)	355	13.5	(10–18)	388	17.0	(13–21)			›
Luxembourg	50	32.0	(20–47)	53	22.6	(12–36)	66	31.8	(21–44)	60	20.0	(11–32)			
Spain	1150	16.5	(14–19)	1241	21.8	(20–24)	1266	18.6	(17–21)	1508	21.6	(20–24)			›
Belgium	532	17.3	(14–21)	639	22.2	(19–26)	506	18.2	(15–22)	379	22.7	(19–27)			
Slovenia	254	33.1	(27–39)	245	32.7	(27–39)	233	32.6	(27–39)	237	24.5	(19–30)			
Malta	57	26.3	(16–40)	69	27.5	(17–40)	101	33.7	(25–44)	92	26.1	(17–36)			
EU/EEA (population-weighted mean)	**16965**	**25.3**	**(25–26)**	**18612**	**29.3**	**(29–30)**	**19992**	**28.6**	**(28–29)**	**22358**	**29.7**	**(29–30)**			**›**
France	1691	24.4	(22–27)	1916	29.4	(27–32)	2175	31.0	(29–33)	2332	30.7	(29–33)			›
Estonia	87	17.2	(10–27)	90	26.7	(18–37)	133	21.8	(15–30)	62	33.9	(22–47)			
Hungary	485	41.6	(37–46)	555	37.7	(34–42)	641	34.9	(31–39)	700	36.7	(33–40)			
Cyprus	65	21.5	(12–33)	68	23.5	(14–35)	80	26.3	(17–37)	62	37.1	(25–50)			
Bulgaria	127	47.2	(38–56)	138	45.7	(37–54)	151	50.3	(42–59)	96	37.5	(28–48)			
Portugal	777	35.8	(32–39)	911	35.7	(33–39)	1712	36.5	(34–39)	2094	38.6	(36–41)			
Latvia	78	46.2	(35–58)	88	43.2	(33–54)	116	44.8	(36–54)	112	42.0	(33–52)			
Lithuania	184	55.4	(48–63)	144	45.1	(37–54)	154	45.5	(37–54)	179	45.8	(38–53)			
Croatia	331	42.9	(38–48)	373	43.2	(38–48)	330	44.8	(39–50)	380	48.7	(44–54)			
Czech Republic	1399	50.4	(48–53)	1291	47.7	(45–50)	1382	48.0	(45–51)	1416	48.9	(46–52)			
Italy	835	49.9	(46–53)	1428	54.4	(52–57)	1295	55.7	(53–58)	2000	53.7	(51–56)			
Romania	100	50.0	(40–60)	213	51.6	(45–59)	257	66.5	(60–72)	267	61.4	(55–67)			›
Poland	359	60.2	(55–65)	374	70.1	(65–75)	455	67.9	(63–72)	659	63.9	(60–68)			
Greece	1428	69.7	(67–72)	1172	67.6	(65–70)	1063	67.6	(65–70)	1161	66.4	(64–69)			
Slovakia	376	66.8	(62–72)	489	66.9	(63–71)	493	70.8	(67–75)	474	70.0	(66–74)			

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

Table 3.9. ***Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to third-generation cephalosporins (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	14	21.4	(5–51)	30	0.0	(0–12)	28	0.0	(0–12)	36	0.0	(0–10)		N/A	
Finland	536	1.7	(1–3)	550	2.2	(1–4)	582	2.4	(1–4)	644	3.0	(2–5)			
Sweden	977	2.9	(2–4)	1300	3.6	(3–5)	1000	4.5	(3–6)	1001	3.3	(2–5)			
Norway	621	3.2	(2–5)	645	4.0	(3–6)	746	5.9	(4–8)	701	5.0	(4–7)			
Denmark	621	10.5	(8–13)	529	11.5	(9–15)	925	7.6	(6–9)	929	7.8	(6–10)			‹ #
Austria	859	11.8	(10–14)	941	10.7	(9–13)	996	8.2	(7–10)	1050	8.4	(7–10)			‹
Netherlands	683	6.7	(5–9)	644	7.5	(6–10)	911	5.5	(4–7)	908	8.6	(7–11)			
Germany	664	13.0	(10–16)	766	16.1	(14–19)	1006	12.7	(11–15)	1518	10.1	(9–12)			‹ #
United Kingdom	931	11.8	(10–14)	1077	13.6	(12–16)	978	9.3	(8–11)	916	10.5	(9–13)			
Ireland	326	9.5	(7–13)	316	19.3	(15–24)	354	11.6	(8–15)	387	14.7	(11–19)			
Malta	57	26.3	(16–40)	69	27.5	(17–40)	101	29.7	(21–40)	92	16.3	(9–25)			
Belgium	540	16.5	(13–20)	594	15.3	(13–18)	485	16.3	(13–20)	406	19.7	(16–24)			
Spain	1153	16.7	(15–19)	1241	19.8	(18–22)	1265	18.0	(16–20)	1491	20.3	(18–22)			
Slovenia	254	28.3	(23–34)	245	29.0	(23–35)	233	26.6	(21–33)	237	22.8	(18–29)			
Estonia	90	17.8	(11–27)	90	23.3	(15–33)	135	20.7	(14–29)	93	23.7	(15–34)			
Luxembourg	50	34.0	(21–49)	53	34.0	(22–48)	66	34.8	(24–48)	60	28.3	(17–41)			
EU/EEA population–weighted mean)	**16708**	**25.8**	**(25–26)**	**18333**	**30.1**	**(29–31)**	**20190**	**29.3**	**(29–30)**	**22452**	**30.3**	**(30–31)**			›
France	1711	22.6	(21–25)	1938	28.0	(26–30)	2192	29.6	(28–32)	2338	30.5	(29–32)			›
Hungary	500	43.0	(39–47)	557	37.3	(33–42)	644	35.6	(32–39)	704	37.2	(34–41)			‹
Portugal	781	38.7	(35–42)	911	37.0	(34–40)	1712	40.9	(39–43)	2094	40.4	(38–43)			
Cyprus	65	23.1	(14–35)	68	30.9	(20–43)	80	32.5	(22–44)	62	43.5	(31–57)			›
Croatia	332	52.1	(47–58)	376	50.0	(45–55)	334	47.9	(42–53)	380	46.8	(42–52)			
Latvia	78	62.8	(51–74)	92	66.3	(56–76)	104	52.9	(43–63)	115	47.0	(38–56)			‹ #
Lithuania	186	64.0	(57–71)	145	44.1	(36–53)	154	52.6	(44–61)	178	51.7	(44–59)			
Czech Republic	1399	51.2	(49–54)	1291	52.0	(49–55)	1383	52.9	(50–56)	1417	54.1	(51–57)			
Italy	852	47.9	(44–51)	1441	55.1	(52–58)	1319	56.5	(54–59)	1999	55.9	(54–58)			›
Poland	362	60.5	(55–66)	376	65.2	(60–70)	465	68.2	(64–72)	676	64.2	(60–68)			
Slovakia	378	62.7	(58–68)	488	66.4	(62–71)	493	69.4	(65–73)	469	67.2	(63–71)			
Greece	1459	70.9	(68–73)	1208	70.1	(67–73)	1092	72.5	(70–75)	1185	69.5	(67–72)			
Romania	102	60.8	(51–70)	214	67.3	(61–74)	256	73.8	(68–79)	270	70.7	(65–76)			
Bulgaria	127	74.8	(66–82)	138	69.6	(61–77)	151	74.8	(67–82)	96	75.0	(65–83)			

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

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

Table 3.10. ***Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	16	0.0	(0–21)	30	0.0	(0–12)	28	3.6	(0–18)	36	0.0	(0–10)		N/A	
Finland	516	0.4	(0–1)	527	1.7	(1–3)	559	2.3	(1–4)	625	1.9	(1–3)			› #
Denmark	902	6.0	(5–8)	864	4.4	(3–6)	943	4.9	(4–6)	938	2.6	(2–4)			‹
Sweden	977	2.5	(2–4)	1235	2.9	(2–4)	860	3.3	(2–5)	943	3.2	(2–5)			
Norway	622	2.4	(1–4)	644	2.3	(1–4)	744	4.8	(3–7)	700	3.6	(2–5)			
Austria	857	5.0	(4–7)	865	5.0	(4–7)	925	5.5	(4–7)	959	4.8	(4–6)			
Germany	663	8.3	(6–11)	763	10.0	(8–12)	1006	7.1	(6–9)	1519	5.5	(4–7)			‹ #
Netherlands	685	6.3	(5–8)	652	6.1	(4–8)	898	3.9	(3–5)	908	5.7	(4–7)			
United Kingdom	1059	6.1	(5–8)	1163	6.4	(5–8)	1174	5.5	(4–7)	1070	9.3	(8–11)			›
Belgium	414	11.6	(9–15)	486	11.9	(9–15)	341	10.9	(8–15)	354	11.6	(8–15)			
Luxembourg	50	26.0	(15–40)	53	28.3	(17–42)	66	19.7	(11–31)	60	15.0	(7–27)			
Ireland	338	9.2	(6–13)	317	17.4	(13–22)	354	12.1	(9–16)	389	15.9	(12–20)			
Spain	1153	14.1	(12–16)	1241	15.9	(14–18)	1264	13.8	(12–16)	1509	16.0	(14–18)			
Slovenia	254	20.5	(16–26)	245	20.0	(15–26)	233	20.2	(15–26)	237	19.0	(14–25)			
Estonia	91	13.2	(7–22)	89	10.1	(5–18)	135	18.5	(12–26)	61	21.3	(12–34)			
EU/EEA (population-weighted mean)	**16331**	**21.5**	**(21–22)**	**18362**	**22.5**	**(22–23)**	**19830**	**22.4**	**(22–23)**	**22301**	**22.5**	**(22–23)**			›
Malta	57	26.3	(16–40)	69	26.1	(16–38)	101	29.7	(21–40)	92	22.8	(15–33)			
France	1119	23.2	(21–26)	1938	26.6	(25–29)	2188	27.7	(26–30)	2337	26.3	(25–28)			
Portugal	780	31.8	(29–35)	912	29.4	(26–32)	1706	30.5	(28–33)	2090	32.6	(31–35)			
Italy	830	37.0	(34–40)	1383	32.5	(30–35)	1190	36.2	(33–39)	1956	34.0	(32–36)			
Hungary	492	41.5	(37–46)	554	37.0	(33–41)	639	31.8	(28–36)	706	34.6	(31–38)			‹
Cyprus	65	15.4	(8–26)	68	22.1	(13–34)	80	28.8	(19–40)	62	37.1	(25–50)			›
Croatia	332	46.1	(41–52)	370	50.8	(46–56)	334	48.8	(43–54)	380	43.2	(38–48)			
Latvia	78	51.3	(40–63)	92	48.9	(38–60)	118	43.2	(34–53)	113	43.4	(34–53)			
Lithuania	185	63.8	(56–71)	145	47.6	(39–56)	152	49.3	(41–58)	179	46.4	(39–54)			‹
Greece	1429	59.9	(57–62)	1169	55.2	(52–58)	1067	59.3	(56–62)	1170	50.7	(48–54)			‹
Czech Republic	1399	54.4	(52–57)	1291	51.0	(48–54)	1383	50.7	(48–53)	1417	51.9	(49–55)			
Romania	99	54.5	(44–65)	213	57.3	(50–64)	250	67.6	(61–73)	266	54.1	(48–60)			
Poland	366	53.6	(48–59)	364	60.4	(55–65)	455	59.1	(54–64)	666	58.6	(55–62)			
Bulgaria	126	54.0	(45–63)	132	50.8	(42–60)	143	65.7	(57–73)	84	59.5	(48–70)			
Slovakia	377	63.1	(58–68)	488	63.9	(59–68)	494	68.2	(64–72)	475	66.5	(62–71)			

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

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

Table 3.11. ***Klebsiella pneumoniae*. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Denmark	680	0.3	(0–1)	645	0.2	(0–1)	830	0.2	(0–1)	846	0.0	(0–0)			
Estonia	79	1.3	(0–7)	74	2.7	(0–9)	92	0.0	(0–4)	56	0.0	(0–6)			
Finland	536	0.0	(0–1)	550	0.0	(0–1)	583	0.0	(0–1)	658	0.0	(0–1)			
Iceland	16	0.0	(0–19)	28	0.0	(0–12)	28	0.0	(0–12)	35	0.0	(0–11)		N/A	
Latvia	77	0.0	(0–5)	92	0.0	(0–4)	118	1.7	(0–6)	112	0.0	(0–3)			
Lithuania	185	0.0	(0–2)	144	0.0	(0–3)	154	1.3	(0–5)	177	0.0	(0–2)			
Luxembourg	48	0.0	(0–7)	53	1.9	(0–10)	66	1.5	(0–8)	60	0.0	(0–6)			
Sweden	977	0.1	(0–1)	1269	0.0	(0–0)	978	0.0	(0–0)	900	0.0	(0–0)			
Germany	661	0.0	(0–1)	763	0.7	(0–2)	1006	0.7	(0–1)	1520	0.1	(0–0)			
Hungary	481	2.9	(2–5)	531	1.7	(1–3)	621	1.1	(0–2)	687	0.1	(0–1)			‹
Netherlands	684	0.1	(0–1)	646	0.2	(0–1)	903	0.2	(0–1)	907	0.1	(0–1)			
Norway	623	0.5	(0–1)	645	0.2	(0–1)	746	0.0	(0–0)	700	0.1	(0–1)			
Czech Republic	1307	0.3	(0–1)	1133	0.5	(0–1)	1148	0.1	(0–0)	1100	0.3	(0–1)			
United Kingdom	888	0.5	(0–1)	1051	0.5	(0–1)	1069	0.8	(0–2)	962	0.4	(0–1)			
Belgium	545	0.7	(0–2)	618	0.3	(0–1)	429	0.5	(0–2)	389	0.5	(0–2)			
France	1627	0.5	(0–1)	1842	0.7	(0–1)	2103	0.5	(0–1)	2244	0.5	(0–1)			
Ireland	338	0.0	(0–1)	317	0.3	(0–2)	353	0.6	(0–2)	389	0.5	(0–2)			
Poland	359	0.8	(0–2)	370	0.8	(0–2)	451	1.3	(0–3)	660	0.5	(0–1)			
Austria	738	0.8	(0–2)	910	1.2	(1–2)	971	0.6	(0–1)	1022	0.8	(0–2)			
Slovakia	331	6.3	(4–10)	342	0.6	(0–2)	456	2.6	(1–5)	436	0.9	(0–2)			‹ #
Slovenia	254	0.4	(0–2)	245	0.4	(0–2)	233	0.9	(0–3)	237	1.3	(0–4)			
Spain	1152	0.8	(0–1)	1241	1.6	(1–2)	1266	2.3	(2–3)	1483	2.2	(1–3)			›
Croatia	331	0.0	(0–1)	376	0.5	(0–2)	334	0.9	(0–3)	380	2.4	(1–4)			›
Bulgaria	108	1.9	(0–7)	129	0.0	(0–3)	139	7.2	(4–13)	95	3.2	(1–9)			
Portugal	749	0.7	(0–2)	904	1.8	(1–3)	1701	1.8	(1–3)	2085	3.4	(3–4)			›
Malta	57	3.5	(0–12)	69	5.8	(2–14)	101	9.9	(5–17)	92	5.4	(2–12)			
EU/EEA (population-weighted mean	**16287**	**6.2**	**(6–7)**	**17932**	**8.2**	**(8–9)**	**19619**	**7.1**	**(7–7)**	**21749**	**8.1**	**(8–8)**			›
Cyprus	65	9.2	(3–19)	68	5.9	(2–14)	80	5.0	(1–12)	62	12.9	(6–24)			
Romania	102	13.7	(8–22)	215	20.5	(15–26)	257	31.5	(26–38)	271	24.7	(20–30)			› #
Italy	845	29.1	(26–32)	1453	34.3	(32–37)	1315	32.9	(30–36)	1999	33.5	(31–36)			
Greece	1460	60.5	(58–63)	1209	59.4	(57–62)	1088	62.3	(59–65)	1185	61.9	(59–65)			

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

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

Table 3.12. ***Klebsiella pneumoniae*. Total number of isolates tested (N) and percentage with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015			Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)		Comment*
Iceland	14	0.0	(0–23)	28	0.0	(0–12)	28	0.0	(0–12)	35	0.0	(0–10)	N/A	
Denmark	577	3.1	(2–5)	519	3.5	(2–5)	925	3.1	(2–4)	924	1.1	(1–2)		‹ #
Finland	516	0.2	(0–1)	514	0.4	(0–1)	556	1.4	(1–3)	623	1.1	(0–2)		› #
Sweden	977	1.4	(1–2)	1235	1.7	(1–3)	623	1.4	(1–3)	860	1.9	(1–3)		
Norway	593	1.5	(1–3)	616	1.8	(1–3)	744	3.9	(3–6)	699	2.3	(1–4)		
Netherlands	667	2.7	(2–4)	630	2.2	(1–4)	865	2.0	(1–3)	908	3.0	(2–4)		
Germany	663	6.2	(4–8)	753	7.0	(5–9)	979	5.3	(4–7)	1515	3.1	(2–4)		‹
Austria	827	4.0	(3–6)	837	3.6	(2–5)	900	3.2	(2–5)	936	3.3	(2–5)		
United Kingdom	913	2.3	(1–3)	1070	4.8	(4–6)	975	3.1	(2–4)	906	4.2	(3–6)		
Ireland	326	3.4	(2–6)	316	7.9	(5–11)	353	7.4	(5–11)	387	7.2	(5–10)		
Belgium	411	8.5	(6–12)	464	8.2	(6–11)	341	7.9	(5–11)	353	9.3	(7–13)		
Spain	1150	8.9	(7–11)	1241	11.2	(9–13)	1263	10.1	(8–12)	1488	11.7	(10–13)		
Luxembourg	50	20.0	(10–34)	53	17.0	(8–30)	66	16.7	(9–28)	60	13.3	(6–25)		
Malta	57	19.3	(10–32)	69	20.3	(12–32)	101	26.7	(18–36)	92	15.2	(9–24)		
Slovenia	254	17.3	(13–23)	245	15.9	(12–21)	233	18.9	(14–25)	237	16.9	(12–22)		
Cyprus	65	9.2	(3–19)	68	5.9	(2–14)	80	15.0	(8–25)	62	17.7	(9–30)		
EU/EEA (population-weighted mean)	**15 617**	**17.7**	**(17–18)**	**17 711**	**18.9**	**(18–20)**	**19 195**	**19.1**	**(19–20)**	**21 871**	**18.6**	**(18–19)**		›
Estonia	86	10.5	(5–19)	87	9.2	(4–17)	131	11.5	(7–18)	36	22.2	(10–39)		
France	1097	19.2	(17–22)	1916	22.9	(21–25)	2172	23.7	(22–26)	2324	22.5	(21–24)		
Portugal	776	25.1	(22–28)	909	21.7	(19–24)	1705	22.8	(21–25)	2084	25.0	(23–27)		
Bulgaria	126	36.5	(28–46)	132	35.6	(27–44)	143	44.1	(36–53)	84	28.6	(19–39)		
Italy	752	33.9	(31–37)	1360	29.6	(27–32)	1164	32.0	(29–35)	1940	29.7	(28–32)		
Hungary	480	37.9	(34–42)	549	32.2	(28–36)	636	28.6	(25–32)	698	30.2	(27–34)		‹
Croatia	331	30.8	(26–36)	367	30.0	(25–35)	330	30.6	(26–36)	380	32.4	(28–37)		
Latvia	78	42.3	(31–54)	88	39.8	(29–51)	104	41.3	(32–51)	112	36.6	(28–46)		
Lithuania	184	52.2	(45–60)	144	33.3	(26–42)	152	35.5	(28–44)	178	39.9	(33–47)		‹
Czech Republic	1399	41.8	(39–44)	1291	38.3	(36–41)	1382	38.7	(36–41)	1416	41.5	(39–44)		
Greece	1426	57.0	(54–60)	1164	51.5	(49–54)	1061	55.1	(52–58)	1160	46.7	(44–50)		‹
Romania	97	42.3	(32–53)	210	42.9	(36–50)	247	56.3	(50–63)	261	49.8	(44–56)		
Poland	350	50.3	(45–56)	350	54.3	(49–60)	443	54.6	(50–59)	645	54.0	(50–58)		
Slovakia	375	55.5	(50–61)	486	57.8	(53–62)	493	63.3	(59–68)	468	59.6	(55–64)		

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

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

Table 3.13. ***Klebsiella pneumoniae*. Total number of invasive isolates tested* and resistance combinations among isolates tested against fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems (n=21 141). EU/EEA countries, 2015**

Resistance pattern	Number of isolates	% of total**
Fully susceptible	**13 402**	**63.4**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**1 365**	**6.5**
Fluoroquinolones	663	3.1
Third-generation cephalosporins	545	2.6
Aminoglycosides	151	0.7
Carbapenems	6	<0.1
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**1 501**	**7.1**
Third-generation cephalosporins + fluoroquinolones	675	3.2
Third-generation cephalosporins + aminoglycosides	510	2.4
Fluoroquinolones + aminoglycosides	281	1.3
Third-generation cephalosporins + carbapenems	32	0.2
Fluoroquinolones + carbapenems	3	<0.1
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**3 883**	**18.4**
Third-generation cephalosporins + fluoroquinolones + aminoglycosides	3 314	15.7
Third-generation cephalosporins + fluoroquinolones + carbapenems	531	2.5
Third-generation cephalosporins + aminoglycoside + carbapenems	36	0.2
Fluoroquinolones + aminoglycosides + carbapenems	2	<0.1
Resistance to four antimicrobial groups		
Third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	**990**	**4.7**

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

3.3 *Pseudomonas aeruginosa*

3.3.1 Clinical and epidemiological importance

Pseudomonas aeruginosa is a non-fermentative gram-negative bacterium that is ubiquitous in aquatic environments in nature. It is an opportunistic pathogen for human, animals and plants, and is a major cause of infection in hospitalised patients with localised or systemic impairment of immune defences. It commonly causes hospital-acquired pneumonia (including ventilator-associated pneumonia), bloodstream and urinary tract infections. Because of its ubiquity, its enormous versatility and intrinsic tolerance to many detergents, disinfectants and antimicrobial compounds, it is difficult to control *P. aeruginosa* in hospitals and institutional environments. Moreover, *P. aeruginosa* can cause skin infections such as folliculitis and external otitis among recreational and competitive swimmers. *P. aeruginosa* may chronically colonise the respiratory tract of patients with cystic fibrosis, causing severe intermittent exacerbation of the condition.

3.3.2 Resistance mechanism

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

- mutational modification of antimicrobial targets such as topoisomerases or ribosomal proteins, which confer resistance to fluoroquinolones and aminoglycosides, respectively;
- mutational derepression of the chromosomally encoded AmpC beta-lactamase that can confer resistance to penicillins and cephalosporins active against *Pseudomonas* spp., and which is not inhibited by tazobactam;
- mutational loss of outer membrane proteins preventing the uptake of antimicrobial agents such as carbapenems;
- mutational upregulation of efflux systems that can confer resistance to beta-lactams, fluoroquinolones and aminoglycosides; and
- acquisition of plasmid-mediated resistance genes coding for various beta-lactamases and aminoglycoside-modifying enzymes that can confer resistance to various beta-lactams including carbapenems (e.g. metallo-beta-lactamases) and aminoglycosides, or coding for 16S rRNA ribosomal methylases that can confer high-level resistance to all aminoglycosides.

3.3.3 Antimicrobial susceptibility

- Antimicrobial resistance in *P. aeruginosa* is common in Europe, with a majority of the countries reporting resistance percentages above 10% for all antimicrobial groups under surveillance.
- The significantly decreasing trends for fluoroquinolone and aminoglycoside resistance and the significantly increasing trend for piperacillin + tazobactam resistance in *P. aeruginosa* observed between 2011 and 2014 in the EU/EEA continued in 2015.
- Combined resistance was common in *P. aeruginosa*: 13.7% of the isolates were resistant to at least three antimicrobial groups, and 5.5% were resistant to all five antimicrobial groups under regular EARS-Net surveillance.

Piperacillin-tazobactam

For 2015, 30 countries reported 11362 isolates with AST information for piperacillin-tazobactam. The number of isolates reported per country ranged from 11 to 1915 (Table PA1).

The trend for the EU/EEA population-weighted mean percentage increased significantly for the period 2012–2015, from 16.7 % in 2012 to 18.1 % in 2015 (Table 3.14).

National percentages of resistant isolates ranged from zero (Iceland and Luxemburg) to 57.0 % (Romania) in 2015. Trends for the period 2012–2015 were calculated for the 27 countries reporting data for at least 20 isolates per year during the full reporting period. Significantly increasing trends were observed for four countries (Hungary, Lithuania, Poland and the United Kingdom). These trends remained significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for four countries (Austria, France, Greece and Ireland). For France, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Fluoroquinolones

For 2015, 30 countries reported 12651 isolates with AST information for fluoroquinolones (ciprofloxacin or levofloxacin). The number of isolates reported per country ranged from 12 to 1939 (Table 3.15).

The trend for the EU/EEA population-weighted mean percentage decreased significantly for the period 2012–2015, from 20.9 % in 2012 to 19.3 % in 2015 (Table 3.15).

National percentages of resistant isolates ranged from zero (Estonia) to 62.0.0 % (Romania) in 2015. Trends for the period 2012–2015 were calculated for the 27 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for four countries (Croatia, Lithuania, Poland and the United Kingdom). For Lithuania and Poland, the

Figure 3.11. ***Pseudomonas aeruginosa*****. Percentage (%) of invasive isolates with resistance to piperacillin-tazobactam, by country, EU/EEA countries, 2015**

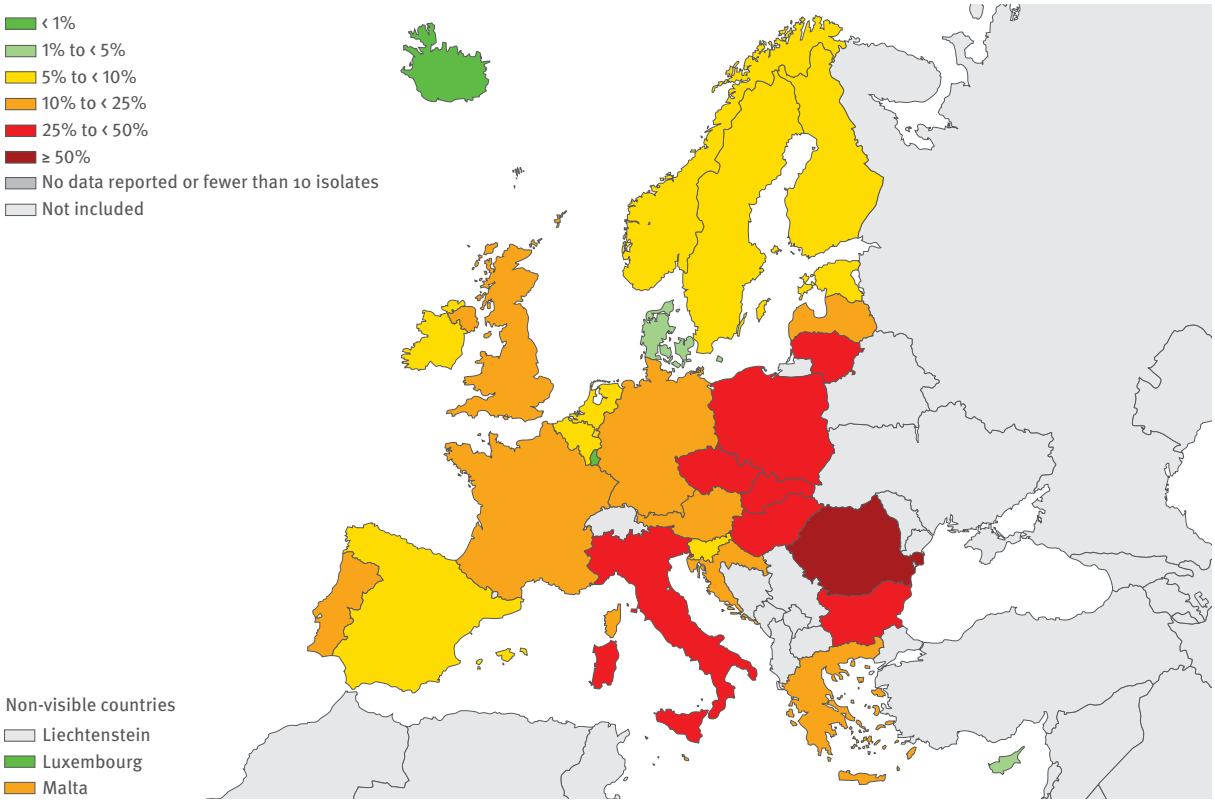


Figure 3.12. ***Pseudomonas aeruginosa*****. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2015**

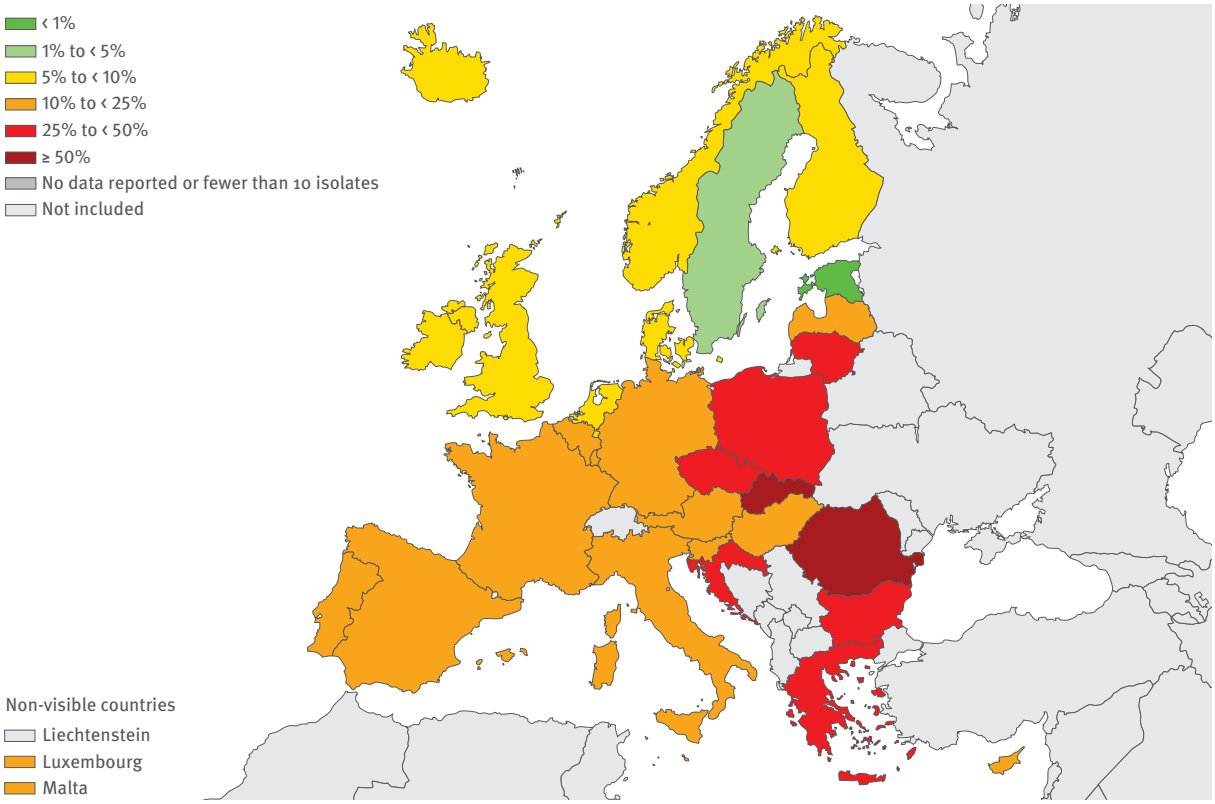


Figure 3.13. ***Pseudomonas aeruginosa*****. Percentage (%) of invasive isolates with resistance to ceftazidime, by country, EU/EEA countries, 2015**

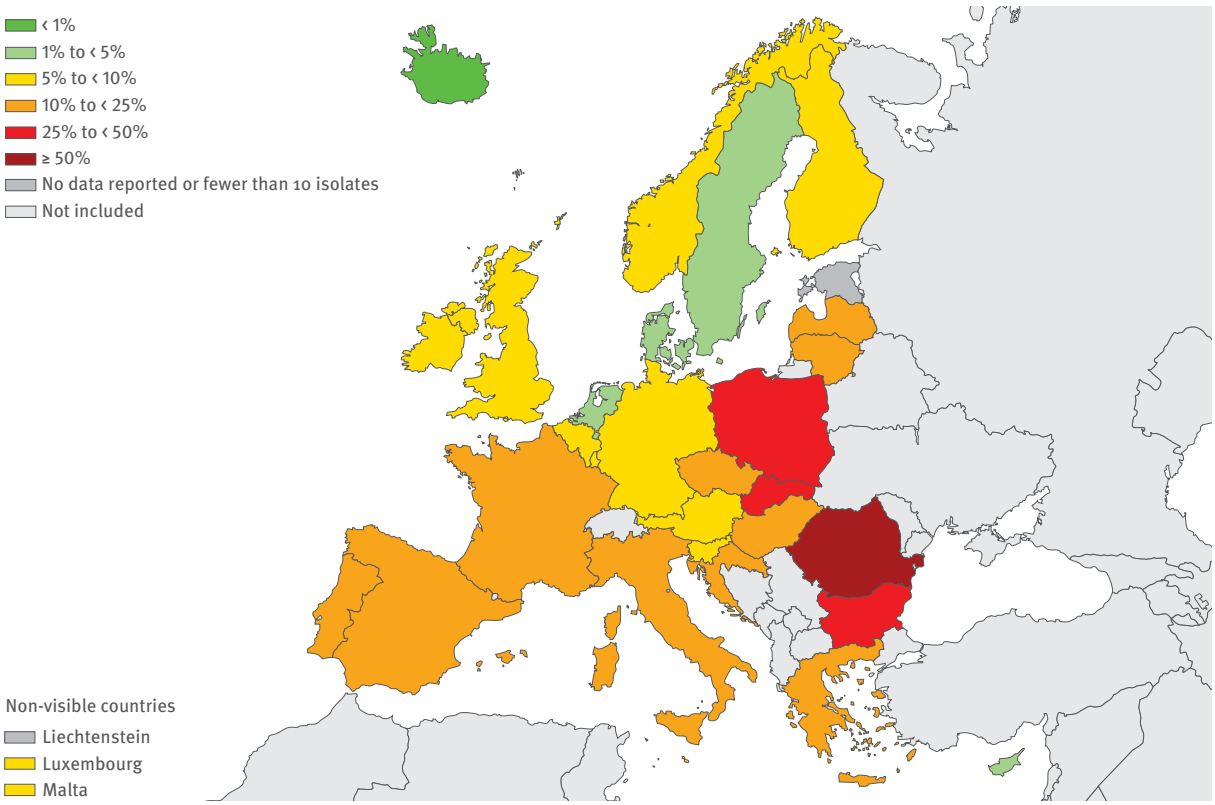
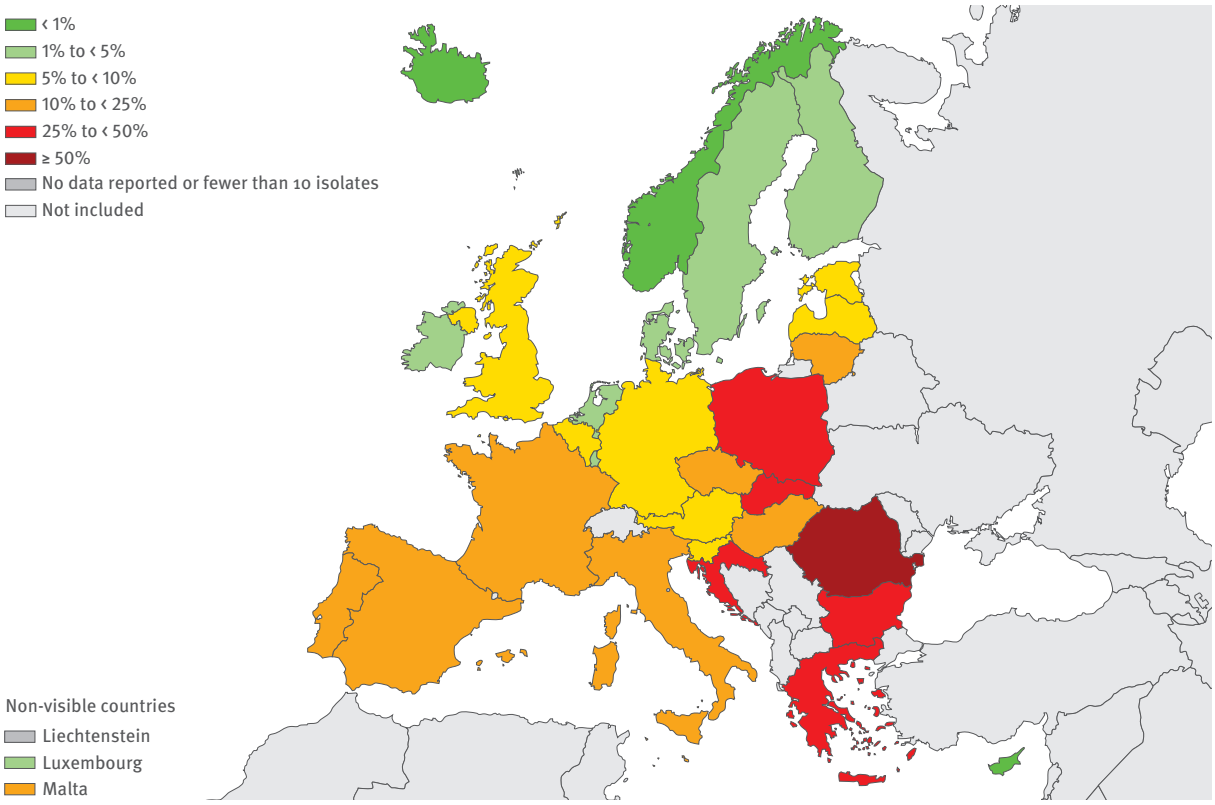


Figure 3.14. ***Pseudomonas aeruginosa*****. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2015**



trends did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for six countries (Austria, Belgium, France, Germany, Greece and Italy). For Belgium and Italy, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years.

Ceftazidime

For 2015, 30 countries reported 12 353 isolates with AST information for ceftazidime. The number of isolates reported per country ranged from 7 to 1 910 (Table 3.16).

No significant change in the trend for the EU/EEA population-weighted mean percentage could be noted for the period 2012–2015 (Table 3.16).

National percentages of resistant isolates ranged from 0 (Iceland) to 65.9 % (Romania) in 2015. Trends for the period 2012–2015 were calculated for the 27 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for Hungary, Portugal and Romania. For Romania, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for Austria, Greece and Ireland, trends that remained significant when considering only data from laboratories reporting consistently for all four years.

Aminoglycosides

For 2015, 30 countries reported 12 673 isolates with AST information for aminoglycosides (gentamicin, and/or tobramycin). The number of isolates reported per country ranged from 11 to 1 941 (Table 3.17).

The trend for the EU/EEA population-weighted mean percentage decreased significantly for the period 2012–2015, from 17.1 % in 2012 to 13.3 % in 2015 (Table 3.17).

National percentages of resistant isolates ranged from zero (Cyprus and Iceland) to 63.3 % (Romania) in 2015. Trends for the period 2012–2015 were calculated for the 27 countries reporting at least 20 isolates per year during the four-year period. Significantly increasing trends were observed for Croatia and the United Kingdom. For Croatia, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for eight countries (Austria, Belgium, Cyprus, France, Greece, Hungary, Italy and Ireland). For Belgium, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Susceptibility data for amikacin were less frequently reported than for gentamicin and/or tobramycin and generally showed lower resistance levels. A total of 9 303 isolates had susceptibility data for both amikacin and gentamicin and/or tobramycin (73.4 % of the isolates included in the aminoglycoside group analysis). Among isolates with resistance to either gentamicin or tobramycin, 43.5 % of the isolates were also resistant to amikacin.

Carbapenems

For 2015, 30 countries reported 12 689 isolates with AST information for carbapenems (imipenem or meropenem). The number of isolates reported per country ranged from 12 to 1 925 (Table 3.18 and Figure 3.15).

The population-weighted EU/EEA mean percentage was 17.8 % in 2015. No significant change in the trend could be noted for the period 2012–2015 (Table 3.18).

National percentages of resistant isolates ranged from 0 (Iceland) to 66.3 % (Romania) in 2015. Trends for the period 2012–2015 were calculated for the 27 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for Croatia, Hungary, Poland and Spain. For all four countries, the trend remained significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for four countries (Belgium, the Czech Republic, Greece and the United Kingdom). For the Czech Republic, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Combined resistance: resistance to at least three antimicrobial groups out of piperacillin with tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems

For 2015, 30 countries reported 21 871 *P. aeruginosa* isolates with AST information on at least three antimicrobial groups out piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems. The number of isolates reported per country ranged from 12 to 1 934 (Table 3.19).

The population-weighted EU/EEA mean percentage was 12.9 % in 2015. No significant change in the trend could be noted for the period 2012–2015 (Table 3.19).

National percentages of isolates resistant to at least three antimicrobial groups ranged from zero (Iceland and Estonia) to 66.0 % (Romania) in 2015 (Table 3.19 and Figure 3.16). Trends for the period 2012–2015 were calculated for the 27 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for four countries (Croatia, Poland, Romania and Spain). For Croatia and Romania, the trends did not remain significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for seven countries (Austria, Belgium, France, Greece, Ireland, Italy and Portugal). For Belgium, Italy and Portugal, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years.

Figure 3.15. ***Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015**

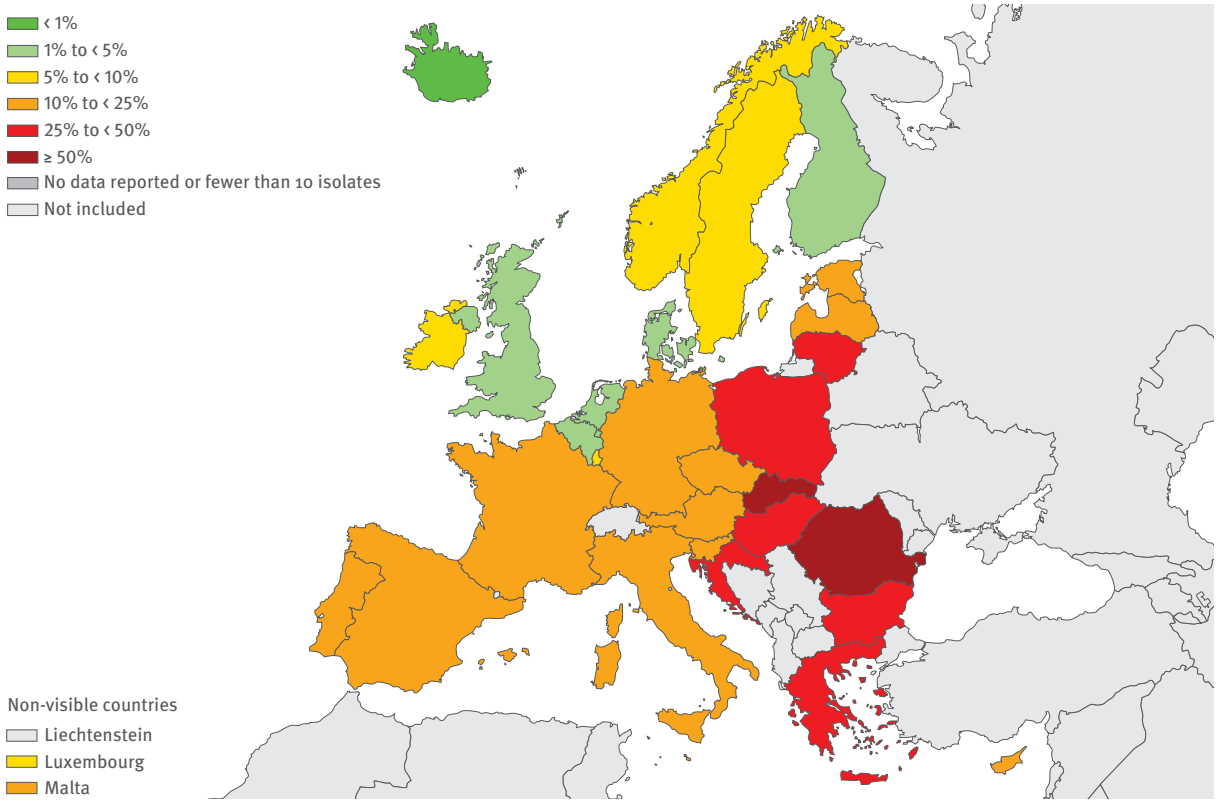
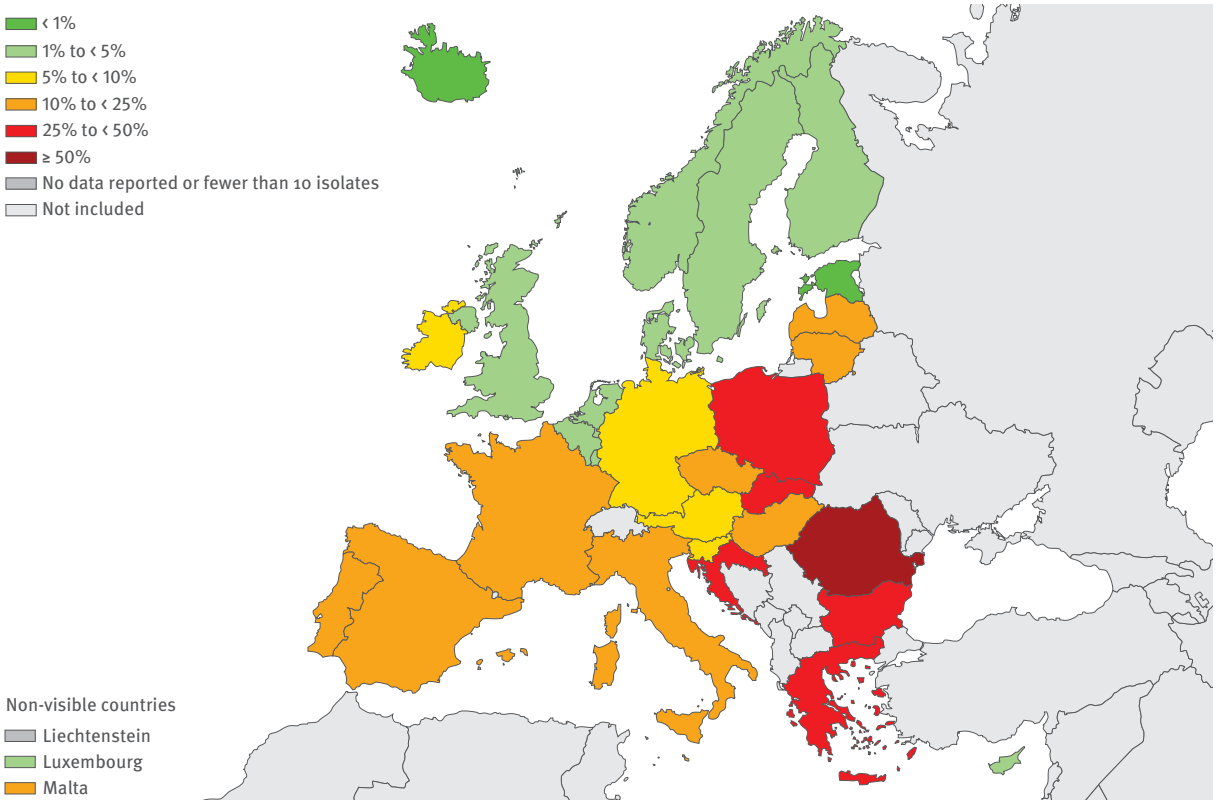


Figure 3.16. ***Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with combined resistance (resistance to three or more antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems), by country, EU/EEA countries, 2015**



Other resistance combinations and resistance to other antimicrobial groups

Of all *P. aeruginosa* isolates tested for all antimicrobial groups under EARS-Net surveillance (piperacillin with tazobactam, fluoroquinolones, ceftazidime, aminoglycosides and carbapenems), 66.1% were susceptible to all tested antimicrobial groups. Single resistance to carbapenems (5.0%) followed by resistance to all five antimicrobial groups (4.4%) was the most common resistance phenotypes (Table 3.20).

Twenty-one countries reported AST data for polymyxins for a total of 9303 isolates (43.7% of all reported *P. aeruginosa* isolates in 2015). Ten countries reported polymyxins AST data for more than half of their reported *P. aeruginosa* isolates. Overall, 0.83% of the isolates were resistant to polymyxins.

3.3.4 Discussion and conclusions

In 2015, high percentages of resistance in *P. aeruginosa* were reported, especially from eastern and south-eastern parts of Europe. Combined resistance to multiple antimicrobial groups was common, with 14.9% of the isolates being resistant to at least three antimicrobial groups and 5.5% being resistant to all five groups under regular EARS-Net surveillance. This is a concern as *P. aeruginosa* is intrinsically resistant to a number of antimicrobial groups and any additional acquired resistance severely limits the therapeutic options for treatment of infections caused by this pathogen.

The decrease in fluoroquinolone and aminoglycoside resistance reported in previous years continued in 2015; fluoroquinolone resistance in *E. coli* and *K. pneumoniae* reported to EARS-Net has not shown the same positive development in recent years.

Carbapenem resistance was common, with national percentages ranging between zero and 66.3% in 2015. With a few exceptions, the countries reporting high carbapenem resistance percentages in *P. aeruginosa* also reported high percentages for *E. coli*, *K. pneumoniae* and *Acinetobacter* spp. The EU/EEA population-weighted mean percentage for carbapenem resistance was 17.8% in 2015, but the significantly increasing trend noted previously did not continue in 2015.

P. aeruginosa is recognised as a major cause of healthcare-associated infections. Due to its ubiquitous nature and potential virulence, *P. aeruginosa* is a challenging pathogen to control in healthcare settings. Prudent antimicrobial use and high standards of infection control are essential to prevent the situation from deteriorating.

Table 3.14. ***Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to piperacillin–tazobactam (%R), including 95 % confidence intervals (95 %CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	10	10.0	(0–45)	11	0.0	(0–28)	11	9.1	(0–41)	11	0.0	(0–28)		N/A	
Luxembourg	31	16.1	(5–34)	34	11.8	(3–27)	37	10.8	(3–25)	27	0.0	(0–13)			
Denmark	389	4.6	(3–7)	414	2.4	(1–4)	388	4.4	(3–7)	441	4.1	(2–6)			
Cyprus	50	10.0	(3–22)	47	8.5	(2–20)	42	16.7	(7–31)	43	4.7	(1–16)			
Norway	198	7.1	(4–12)	198	9.1	(5–14)	254	7.9	(5–12)	227	5.7	(3–10)			
Sweden	271	5.9	(3–9)	531	7.3	(5–10)	337	4.7	(3–8)	399	5.8	(4–9)			
Estonia	31	16.1	(5–34)	17	11.8	(1–36)	39	10.3	(3–24)	16	6.3	(0–30)		N/A	
Netherlands	386	5.2	(3–8)	381	6.6	(4–10)	530	8.1	(6–11)	494	6.5	(4–9)			
Finland	314	7.6	(5–11)	327	8.6	(6–12)	306	6.9	(4–10)	333	7.2	(5–11)			
Belgium	342	9.6	(7–13)	431	13.2	(10–17)	294	9.5	(6–13)	251	8.0	(5–12)			
Spain	835	6.7	(5–9)	818	8.6	(7–11)	870	7.8	(6–10)	871	9.1	(7–11)			
Ireland	216	16.2	(12–22)	202	11.4	(7–17)	178	11.2	(7–17)	195	9.2	(6–14)			‹
Slovenia	134	7.5	(4–13)	133	13.5	(8–21)	112	25.9	(18–35)	141	9.9	(6–16)			
United Kingdom	636	3.1	(2–5)	671	4.8	(3–7)	610	4.8	(3–7)	493	10.3	(8–13)			›
Austria	588	18.2	(15–22)	616	13.3	(11–16)	636	11.8	(9–15)	675	11.9	(10–15)			‹
Malta	31	9.7	(2–26)	24	20.8	(7–42)	38	10.5	(3–25)	25	16.0	(5–36)			
France	1627	19.9	(18–22)	1815	15.4	(14–17)	1783	17.0	(15–19)	1915	16.1	(15–18)			‹ #
Germany	432	15.5	(12–19)	629	18.8	(16–22)	642	17.4	(15–21)	941	17.7	(15–20)			
EU/EEA (population-weighted mean)	**10284**	**16.7**	**(16–17)**	**11043**	**16.4**	**(16–17)**	**11527**	**17.2**	**(17–18)**	**11362**	**18.1**	**(17–19)**			›
Greece	849	34.3	(31–38)	863	29.9	(27–33)	666	31.4	(28–35)	638	22.3	(19–26)			‹
Latvia	17	17.6	(4–43)	24	20.8	(7–42)	3	66.7	(9–99)	13	23.1	(5–54)		N/A	
Croatia	194	24.2	(18–31)	233	23.6	(18–30)	216	24.5	(19–31)	249	24.5	(19–30)			
Portugal	586	19.8	(17–23)	87	24.1	(16–35)	1061	28.5	(26–31)	1176	24.5	(22–27)			
Czech Republic	489	26.4	(23–31)	516	27.5	(24–32)	429	23.1	(19–27)	463	25.3	(21–29)			
Hungary	610	19.2	(16–23)	657	19.8	(17–23)	736	23.5	(20–27)	747	26.9	(24–30)			›
Bulgaria	50	26.0	(15–40)	59	13.6	(6–25)	48	31.3	(19–46)	55	27.3	(16–41)			
Lithuania	28	10.7	(2–28)	35	8.6	(2–23)	31	32.3	(17–51)	41	29.3	(16–46)			›
Italy	541	30.1	(26–34)	754	30.9	(28–34)	686	31.5	(28–35)	1074	29.5	(27–32)			
Poland	160	30.0	(23–38)	171	31.6	(25–39)	185	32.4	(26–40)	249	37.8	(32–44)			›
Slovakia	195	38.5	(32–46)	265	41.5	(36–48)	269	36.1	(30–42)	257	42.4	(36–49)			
Romania	44	50.0	(35–65)	80	55.0	(43–66)	90	62.2	(51–72)	78	59.0	(47–70)			

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

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

Table 3.15. ***Pseudomonas aeruginosa.*** **Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Estonia	32	15.6	(5–33)	20	25.0	(9–49)	39	10.3	(3–24)	18	0.0	(0–19)		N/A	
Sweden	357	6.7	(4–10)	531	6.0	(4–8)	338	7.7	(5–11)	382	4.7	(3–7)			
Denmark	389	4.1	(2–7)	408	3.2	(2–5)	388	3.6	(2–6)	420	5.0	(3–8)			
Norway	209	5.7	(3–10)	205	8.8	(5–14)	257	3.1	(1–6)	230	5.2	(3–9)			
Netherlands	395	6.1	(4–9)	370	6.2	(4–9)	541	6.7	(5–9)	502	5.8	(4–8)			
Iceland	10	10.0	(0–45)	11	0.0	(0–28)	11	0.0	(0–28)	12	8.3	(0–38)		N/A	
United Kingdom	664	4.8	(3–7)	711	5.8	(4–8)	629	5.4	(4–7)	522	8.8	(7–12)			›
Finland	327	8.0	(5–11)	317	11.4	(8–15)	289	10.0	(7–14)	302	8.9	(6–13)			
Ireland	215	14.9	(10–20)	205	12.2	(8–17)	178	8.4	(5–14)	194	9.8	(6–15)			
Austria	487	14.4	(11–18)	533	15.2	(12–19)	599	10.9	(8–14)	659	10.3	(8–13)			‹
Belgium	329	18.2	(14–23)	486	16.9	(14–21)	309	12.6	(9–17)	261	11.1	(8–16)			‹ #
Cyprus	52	15.4	(7–28)	47	10.6	(4–23)	42	16.7	(7–31)	43	11.6	(4–25)			
Malta	31	0.0	(0–11)	25	8.0	(1–26)	38	5.3	(1–18)	25	12.0	(3–31)			
Slovenia	134	14.9	(9–22)	133	11.3	(6–18)	112	22.3	(15–31)	141	14.2	(9–21)			
Germany	434	19.6	(16–24)	611	16.4	(14–20)	623	13.0	(10–16)	940	14.4	(12–17)			‹
Luxembourg	31	19.4	(7–37)	34	20.6	(9–38)	41	9.8	(3–23)	28	17.9	(6–37)			
France	1723	22.2	(20–24)	1863	21.2	(19–23)	1779	20.6	(19–23)	1939	19.1	(17–21)			‹
EU/EEA (population-weighted mean)	**10612**	**20.9**	**(20–22)**	**11805**	**20.2**	**(19–21)**	**11631**	**19.7**	**(19–20)**	**12651**	**19.3**	**(19–20)**			‹
Portugal	587	25.6	(22–29)	735	23.9	(21–27)	1062	26.3	(24–29)	1185	22.7	(20–25)			
Spain	848	21.0	(18–24)	825	22.7	(20–26)	873	24.6	(22–28)	881	23.0	(20–26)			
Latvia	18	22.2	(6–48)	25	24.0	(9–45)	18	16.7	(4–41)	13	23.1	(5–54)		N/A	
Italy	675	31.4	(28–35)	773	28.7	(26–32)	739	28.3	(25–32)	1080	24.6	(22–27)			‹ #
Hungary	618	22.3	(19–26)	667	23.4	(20–27)	743	24.6	(22–28)	769	24.7	(22–28)			
Lithuania	28	10.7	(2–28)	37	10.8	(3–25)	31	25.8	(12–45)	41	26.8	(14–43)			› #
Czech Republic	489	30.9	(27–35)	516	33.7	(30–38)	447	32.7	(28–37)	464	30.0	(26–34)			
Greece	864	44.3	(41–48)	853	43.5	(40–47)	676	37.7	(34–41)	662	34.1	(31–38)			‹
Croatia	194	25.3	(19–32)	240	21.7	(17–27)	230	30.0	(24–36)	256	35.2	(29–41)			›
Poland	176	26.7	(20–34)	194	29.4	(23–36)	184	35.3	(28–43)	257	36.2	(30–42)			› #
Bulgaria	52	32.7	(20–47)	60	18.3	(10–30)	48	27.1	(15–42)	55	36.4	(24–50)			
Slovakia	199	56.3	(49–63)	286	53.1	(47–59)	275	45.5	(39–52)	278	52.2	(46–58)			
Romania	45	53.3	(38–68)	84	45.2	(34–56)	92	55.4	(45–66)	92	62.0	(51–72)			

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

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

Table 3.16. ***Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to ceftazidime (%R), including 95% confidence intervals (95% CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	10	10.0	(0–45)	11	0.0	(0–28)	11	9.1	(0–41)	11	0.0	(0–28)		N/A	
Denmark	325	4.9	(3–8)	357	3.1	(2–5)	386	3.9	(2–6)	439	3.6	(2–6)			
Netherlands	398	2.8	(1–5)	371	3.8	(2–6)	534	4.9	(3–7)	502	4.4	(3–7)			
Sweden	357	6.4	(4–10)	531	6.8	(5–9)	433	5.5	(4–8)	379	4.5	(3–7)			
Cyprus	52	15.4	(7–28)	47	12.8	(5–26)	42	23.8	(12–39)	43	4.7	(1–16)			
Norway	202	6.4	(3–11)	193	6.2	(3–11)	251	5.2	(3–9)	216	5.6	(3–10)			
United Kingdom	634	3.9	(3–6)	695	3.7	(2–5)	588	4.6	(3–7)	472	6.1	(4–9)			
Belgium	326	8.3	(6–12)	459	9.4	(7–12)	316	8.9	(6–13)	226	6.2	(3–10)			
Finland	317	5.0	(3–8)	322	5.0	(3–8)	307	6.2	(4–9)	334	6.9	(4–10)			
Luxembourg	31	3.2	(0–17)	34	11.8	(3–27)	41	2.4	(0–13)	28	7.1	(1–24)			
Ireland	210	14.3	(10–20)	204	7.8	(5–12)	175	8.0	(4–13)	195	7.2	(4–12)			‹
Malta	31	6.5	(1–21)	25	8.0	(1–26)	38	5.3	(1–18)	25	8.0	(1–26)			
Germany	437	9.6	(7–13)	628	10.2	(8–13)	638	9.9	(8–12)	938	9.1	(7–11)			
Austria	572	14.0	(11–17)	608	9.5	(7–12)	631	8.7	(7–11)	577	9.9	(8–13)			‹
Slovenia	134	6.7	(3–12)	133	13.5	(8–21)	112	20.5	(13–29)	141	9.9	(6–16)			
Spain	839	8.9	(7–11)	825	9.0	(7–11)	864	9.6	(8–12)	816	10.4	(8–13)			
France	1607	14.1	(12–16)	1868	11.5	(10–13)	1778	12.0	(11–14)	1919	11.6	(10–13)			
EU/EEA (population-weighted mean)	**10324**	**13.5**	**(13–14)**	**11571**	**12.3**	**(12–13)**	**11590**	**13.2**	**(13–14)**	**12353**	**13.3**	**(13–14)**			
Estonia	29	17.2	(6–36)	19	0.0	(0–18)	28	7.1	(1–24)	7	**	**		N/A	
Croatia	189	13.2	(9–19)	239	18.8	(14–24)	227	24.2	(19–30)	248	18.5	(14–24)			
Portugal	587	15.3	(13–19)	737	15.5	(13–18)	1061	22.0	(20–25)	1185	19.2	(17–22)			›
Greece	883	31.0	(28–34)	849	27.9	(25–31)	649	26.7	(23–30)	660	19.4	(16–23)			‹
Lithuania	28	7.1	(1–24)	37	8.1	(2–22)	30	16.7	(6–35)	41	19.5	(9–35)			
Czech Republic	489	20.4	(17–24)	516	22.9	(19–27)	446	21.5	(18–26)	464	19.6	(16–24)			
Italy	603	25.5	(22–29)	722	23.7	(21–27)	683	24.9	(22–28)	1068	21.7	(19–24)			
Latvia	18	22.2	(6–48)	25	24.0	(9–45)	3	66.7	(9–99)	13	23.1	(5–54)		N/A	
Hungary	608	18.1	(15–21)	662	20.8	(18–24)	739	24.1	(21–27)	763	24.2	(21–27)			›
Bulgaria	52	34.6	(22–49)	56	12.5	(5–24)	47	29.8	(17–45)	52	26.9	(16–41)			
Poland	163	22.7	(17–30)	49	22.4	(12–37)	183	21.9	(16–29)	259	27.8	(22–34)			
Slovakia	154	35.1	(28–43)	285	30.9	(26–37)	261	29.5	(24–35)	247	34.8	(29–41)			
Romania	39	51.3	(35–68)	64	43.8	(31–57)	88	59.1	(48–69)	85	65.9	(55–76)			› #

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

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

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

Table 3.17. ***Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Cyprus	52	15.4	(7–28)	47	4.3	(1–15)	42	9.5	(3–23)	43	0.0	(0–8)			‹
Iceland	10	0.0	(0–31)	11	0.0	(0–28)	11	0.0	(0–28)	12	0.0	(0–26)		N/A	
Norway	197	2.0	(1–5)	194	1.5	(0–4)	240	1.3	(0–4)	219	0.9	(0–3)			
Sweden	351	1.7	(1–4)	519	2.9	(2–5)	313	0.6	(0–2)	387	1.3	(0–3)			
Finland	326	2.5	(1–5)	327	3.1	(1–6)	305	2.3	(1–5)	341	1.8	(1–4)			
Denmark	372	3.8	(2–6)	408	4.9	(3–7)	388	2.3	(1–4)	441	2.3	(1–4)			
Netherlands	404	4.0	(2–6)	374	2.9	(1–5)	544	2.9	(2–5)	502	2.8	(2–5)			
Luxembourg	31	6.5	(1–21)	34	23.5	(11–41)	39	7.7	(2–21)	28	3.6	(0–18)			
Ireland	215	9.8	(6–15)	205	10.7	(7–16)	178	5.6	(3–10)	195	4.1	(2–8)			‹
United Kingdom	667	2.2	(1–4)	715	2.4	(1–4)	641	1.7	(1–3)	539	5.2	(3–7)			›
Estonia	32	25.0	(11–43)	19	10.5	(1–33)	40	7.5	(2–20)	17	5.9	(0–29)		N/A	
Belgium	286	11.2	(8–15)	407	12.3	(9–16)	258	8.5	(5–13)	218	6.0	(3–10)			‹ #
Austria	592	10.6	(8–13)	618	7.4	(6–10)	638	6.6	(5–9)	678	6.3	(5–8)			‹
Germany	436	10.6	(8–14)	630	7.6	(6–10)	643	5.9	(4–8)	936	7.3	(6–9)			
Latvia	18	22.2	(6–48)	25	20.0	(7–41)	18	5.6	(0–27)	11	9.1	(0–41)		N/A	
Slovenia	134	6.7	(3–12)	133	6.0	(3–12)	112	8.9	(4–16)	141	9.2	(5–15)			
France	1229	20.0	(18–22)	1863	16.0	(14–18)	1767	15.7	(14–18)	1941	12.8	(11–14)			‹
EU/EEA (population-weighted mean)	**10189**	**17.1**	**(16–18)**	**11792**	**14.6**	**(14–15)**	**11578**	**14.2**	**(14–15)**	**12673**	**13.3**	**(13–14)**			‹
Portugal	586	14.5	(12–18)	737	14.2	(12–17)	1064	17.6	(15–20)	1191	13.5	(12–16)			
Malta	31	6.5	(1–21)	25	0.0	(0–14)	38	13.2	(4–28)	25	16.0	(5–36)			
Spain	853	16.3	(14–19)	825	14.9	(13–18)	873	16.5	(14–19)	883	16.4	(14–19)			
Italy	675	29.9	(26–34)	741	24.7	(22–28)	704	23.2	(20–26)	1050	17.2	(15–20)			‹
Hungary	618	26.4	(23–30)	661	24.8	(22–28)	741	21.1	(18–24)	766	20.5	(18–24)			‹
Czech Republic	489	22.7	(19–27)	516	25.8	(22–30)	446	20.6	(17–25)	464	21.3	(18–25)			
Lithuania	28	14.3	(4–33)	37	13.5	(5–29)	30	26.7	(12–46)	41	24.4	(12–40)			
Greece	895	38.7	(35–42)	858	38.7	(35–42)	676	35.8	(32–40)	667	26.4	(23–30)			‹
Bulgaria	51	29.4	(17–44)	60	20.0	(11–32)	44	31.8	(19–48)	47	27.7	(16–43)			
Poland	172	27.3	(21–35)	194	23.7	(18–30)	185	31.9	(25–39)	258	30.6	(29–37)			
Croatia	196	28.1	(22–35)	244	23.8	(19–30)	231	35.1	(29–42)	256	34.0	(28–40)			› #
Slovakia	198	41.9	(35–49)	285	38.6	(33–45)	276	37.0	(31–43)	277	41.9	(36–48)			
Romania	45	51.1	(36–66)	80	51.3	(40–63)	93	63.4	(53–73)	90	63.3	(53–73)			

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

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

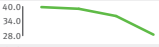
Table 3.18. ***Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	10	10.0	(0–45)	11	9.1	(0–41)	11	9.1	(0–41)	12	0.0	(0–26)		N/A	
United Kingdom	603	6.3	(4–9)	671	5.2	(4–7)	590	6.3	(4–9)	499	2.4	(1–4)			‹
Belgium	391	9.7	(7–13)	518	11.0	(8–14)	344	10.2	(7–14)	256	3.9	(2–7)			‹
Netherlands	397	3.3	(2–6)	375	3.5	(2–6)	543	4.4	(3–7)	500	4.0	(2–6)			
Denmark	355	3.7	(2–6)	410	2.9	(2–5)	386	4.7	(3–7)	437	4.6	(3–7)			
Finland	327	6.1	(4–9)	327	10.4	(7–14)	307	7.2	(5–11)	341	4.7	(3–8)			
Norway	208	6.7	(4–11)	206	5.8	(3–10)	256	5.9	(3–9)	228	5.7	(3–10)			
Sweden	357	5.9	(4–9)	517	7.2	(5–10)	408	7.1	(5–10)	398	6.5	(4–9)			
Luxembourg	31	6.5	(1–21)	34	17.6	(7–35)	42	4.8	(1–16)	24	8.3	(1–27)			
Ireland	213	11.3	(7–16)	204	9.3	(6–14)	177	8.5	(5–14)	195	9.2	(6–14)			
Czech Republic	489	15.1	(12–19)	516	15.7	(13–19)	448	14.1	(11–18)	464	10.6	(8–14)			‹ #
Austria	562	14.6	(12–18)	616	12.3	(10–15)	636	12.7	(10–16)	680	12.2	(10–15)			
Estonia	32	12.5	(4–29)	20	10.0	(1–32)	39	15.4	(6–31)	16	12.5	(2–38)		N/A	
Germany	438	10.7	(8–14)	630	15.4	(13–18)	642	17.0	(14–20)	941	15.0	(13–17)			
Latvia	18	11.1	(1–35)	25	28.0	(12–49)	18	16.7	(4–41)	13	15.4	(2–45)		N/A	
Slovenia	134	21.6	(15–30)	133	25.6	(18–34)	112	31.3	(23–41)	141	15.6	(10–23)			
Malta	31	3.2	(0–17)	25	16.0	(5–36)	38	15.8	(6–31)	25	16.0	(5–36)			
France	1722	18.0	(16–20)	1862	17.2	(15–19)	1780	18.7	(17–21)	1925	16.4	(15–18)			
EU/EEA (population-weighted mean)	**10669**	**17.2**	**(16–18)**	**11864**	**17.8**	**(17–18)**	**11791**	**18.4**	**(18–19)**	**12689**	**17.8**	**(17–18)**			
Portugal	568	20.4	(17–24)	733	20.6	(18–24)	1064	22.5	(20–25)	1191	19.8	(18–22)			
Cyprus	52	19.2	(10–33)	47	19.1	(9–33)	42	33.3	(20–50)	43	20.9	(10–36)			
Spain	853	16.4	(14–19)	825	17.6	(15–20)	872	18.5	(16–21)	872	22.7	(20–26)			›
Italy	682	25.1	(22–29)	788	25.9	(23–29)	753	25.1	(22–28)	1082	23.0	(21–26)			
Bulgaria	51	31.4	(19–46)	59	13.6	(6–25)	48	29.2	(17–44)	55	25.5	(15–39)			
Lithuania	28	17.9	(6–37)	37	18.9	(8–35)	31	29.0	(14–48)	41	26.8	(14–43)			
Hungary	619	27.5	(24–31)	668	30.2	(27–34)	744	33.5	(30–37)	770	35.8	(32–39)			›
Poland	172	22.7	(17–30)	189	32.3	(26–39)	185	27.6	(21–35)	254	37.0	(31–43)			›
Croatia	195	29.2	(23–36)	241	25.3	(20–31)	232	35.3	(29–42)	257	38.5	(33–45)			›
Greece	907	47.7	(44–51)	877	49.3	(46–53)	699	42.9	(39–47)	675	40.4	(37–44)			‹
Slovakia	179	40.8	(34–48)	214	58.9	(52–66)	250	38.4	(32–45)	262	51.9	(46–58)			
Romania	45	57.8	(42–72)	86	60.5	(49–71)	94	58.5	(48–69)	92	66.3	(56–76)			

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

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

Table 3.19. ***Pseudomonas aeruginosa*. Total number of invasive isolates tested (N) with combined resistance (resistance to three or more antimicrobial groups among piperacillin–tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems) including 95% confidence intervals (95% CI), by country, EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015			Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)		Comment*
Estonia	33	9.1	(2–24)	21	0.0	(0–16)	40	0.0	(0–9)	15	0.0	(0–22)	N/A	
Iceland	10	10.0	(0–45)	11	0.0	(0–28)	11	0.0	(0–28)	12	0.0	(0–26)	N/A	
Norway	209	3.3	(1–7)	205	3.4	(1–7)	257	1.6	(0–4)	230	1.3	(0–4)		
Cyprus	52	17.3	(8–30)	47	4.3	(1–15)	42	14.3	(5–29)	43	2.3	(0–12)		
Denmark	388	1.8	(1–4)	414	1.7	(1–3)	388	1.5	(1–3)	441	2.3	(1–4)		
Sweden	357	3.4	(2–6)	531	4.1	(3–6)	436	1.6	(1–3)	386	2.6	(1–5)		
Netherlands	402	2.5	(1–5)	375	2.4	(1–5)	542	2.8	(2–5)	502	2.8	(2–5)		
Luxembourg	31	6.5	(1–21)	34	5.9	(1–20)	41	4.9	(1–17)	28	3.6	(0–18)		
United Kingdom	666	1.7	(1–3)	711	2.4	(1–4)	627	1.6	(1–3)	501	3.8	(2–6)		
Belgium	335	9.0	(6–13)	486	10.9	(8–14)	297	8.4	(6–12)	260	4.6	(2–8)		‹ #
Finland	327	4.6	(3–7)	327	4.6	(3–7)	306	3.9	(2–7)	341	4.7	(3–8)		
Ireland	215	10.2	(7–15)	205	7.3	(4–12)	178	5.6	(3–10)	195	5.1	(2–9)		‹
Austria	595	10.4	(8–13)	617	8.3	(6–11)	638	7.1	(5–9)	680	6.8	(5–9)		‹
Slovenia	134	7.5	(4–13)	133	11.3	(6–18)	112	18.8	(12–27)	141	7.1	(3–13)		
Germany	438	8.4	(6–11)	630	9.2	(7–12)	643	8.9	(7–11)	941	8.2	(7–10)		
Portugal	587	18.1	(15–21)	737	11.9	(10–15)	1064	20.6	(18–23)	1186	11.8	(10–14)		‹ #
France	1723	14.7	(13–16)	1869	12.5	(11–14)	1784	13.2	(12–15)	1940	12.0	(11–14)		‹
Malta	31	0.0	(0–11)	25	8.0	(1–26)	38	7.9	(2–21)	25	12.0	(3–31)		
EU/EEA (population-weighted mean)	**10751**	**13.6**	**(13–14)**	**11940**	**13.0**	**(12–14)**	**11812**	**13.3**	**(13–14)**	**12711**	**12.9**	**(12–14)**		
Spain	853	10.8	(9–13)	825	12.2	(10–15)	873	12.4	(10–15)	874	14.2	(12–17)		›
Latvia	18	11.1	(1–35)	25	24.0	(9–45)	18	11.1	(1–35)	13	15.4	(2–45)	N/A	
Czech Republic	489	21.3	(18–25)	516	23.3	(20–27)	446	20.2	(17–24)	464	19.0	(15–23)		
Italy	645	23.7	(20–27)	774	24.3	(21–27)	746	22.9	(20–26)	1082	20.0	(18–22)		‹ #
Hungary	619	17.6	(15–21)	667	18.7	(16–22)	746	21.7	(19–25)	770	20.9	(18–24)		
Lithuania	28	14.3	(4–33)	37	8.1	(2–22)	31	25.8	(12–45)	41	24.4	(12–40)		
Croatia	197	23.4	(18–30)	244	18.4	(14–24)	232	31.5	(26–38)	257	28.0	(23–34)		› #
Greece	896	39.8	(37–43)	859	39.1	(36–42)	679	36.1	(32–40)	666	28.4	(25–32)		‹
Bulgaria	52	30.8	(19–45)	60	8.3	(3–18)	48	29.2	(17–44)	55	29.1	(18–43)		
Poland	177	21.5	(16–28)	188	14.4	(10–20)	187	26.7	(21–34)	260	29.6	(24–36)		›
Slovakia	199	39.2	(32–46)	285	36.1	(31–42)	268	37.3	(32–43)	270	40.7	(35–47)		
Romania	45	48.9	(34–64)	82	50.0	(39–61)	94	59.6	(49–70)	92	63.0	(52–73)		› #

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

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

Table 3.20. ***Pseudomonas aeruginosa*. Total number of tested isolates and resistance combinations among invasive isolates tested against at least three antimicrobial groups among piperacillin–tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems (n = 12 711), EU/EEA countries, 2015**

Resistance pattern	Number of isolates	% of total*
Fully susceptible (to tested antibiotics)	**8 402**	**66.1**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance types)	**1 620**	**12.7**
Carbapenems	638	5.0
Fluoroquinolones	489	3.8
[Piperacillin–tazobactam]	220	1.7
Aminoglycosides	152	1.2
Ceftazidime	121	1.0
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**961**	**7.6**
[Piperacillin–tazobactam] + ceftazidime	302	2.4
Fluoroquinolones + aminoglycosides	190	1.5
Fluoroquinolones + carbapenems	177	1.4
[Piperacillin–tazobactam] + carbapenems	69	0.5
[Piperacillin–tazobactam] + fluoroquinolones	58	0.5
Aminoglycosides + carbapenems	52	0.4
Fluoroquinolones + ceftazidime	41	0.3
Ceftazidime + carbapenems	41	0.3
[Piperacillin–tazobactam] + aminoglycosides	20	0.2
Ceftazidime + aminoglycosides	11	0.1
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**620**	**5.0**
Fluoroquinolones + aminoglycosides + carbapenems	191	1.5
[Piperacillin–tazobactam] + ceftazidime + carbapenems	98	0.8
[Piperacillin–tazobactam] + fluoroquinolones + aminoglycosides	78	0.6
[Piperacillin–tazobactam] + fluoroquinolones + ceftazidime	70	0.6
Fluoroquinolones + ceftazidime + carbapenems	64	0.5
[Piperacillin–tazobactam] + fluoroquinolones + carbapenems	51	0.4
Fluoroquinolones + ceftazidime + aminoglycosides	26	0.2
[Piperacillin–tazobactam] + ceftazidime + aminoglycosides	21	0.2
[Piperacillin–tazobactam] + aminoglycosides + carbapenems	13	0.1
Ceftazidime + aminoglycosides + carbapenems	8	0.1
Resistance to four antimicrobial groups		
Total (all four-group combinations)	**543**	**4.3**
[Piperacillin–tazobactam] + fluoroquinolones + aminoglycosides + carbapenems	148	1.2
Fluoroquinolones + ceftazidime + aminoglycosides + carbapenems	139	1.1
[Piperacillin–tazobactam] + fluoroquinolones + ceftazidime + carbapenems	112	0.9
[Piperacillin–tazobactam] + fluoroquinolones + ceftazidime + aminoglycosides	108	0.8
[Piperacillin–tazobactam] + ceftazidime + aminoglycosides + carbapenems	36	0.3
Resistance to five antimicrobial groups		
[Piperacillin–tazobactam] + fluoroquinolones + ceftazidime + aminoglycosides + carbapenems	**565**	**4.4**

* Not adjusted for population differences in the reporting countries

3.4 *Acinetobacter* species

3.4.1 Clinical and epidemiological importance

The *Acinetobacter* genus consists of a large number of species, most being environmental species with low pathogenicity. The correct identification of *Acinetobacter* isolates to species level is challenging and usually only possible with genotypic methods. Recently, mass spectrometry has offered the possibility of at least identifying isolates that belong to the *A. baumannii* group (consisting of the species *A. baumannii*, *A. pittii* and *A. nosocomialis*), which is by far the clinically most important group of species within this genus.

Acinetobacter species are gram-negative, strictly aerobic, non-fastidious, non-fermentative opportunistic pathogens. Species belonging to the *A. baumannii* group have been identified as pathogens in nosocomial pneumonia (particularly ventilator-associated pneumonia), central line-associated bloodstream infections, urinary tract infections, surgical site infections and other types of wound infection. While many members of the *Acinetobacter* genus are considered ubiquitous in nature, this is not the case with the species that belong to the *A. baumannii* group.

The *A. baumannii* group has a limited number of virulence factors, which is why infections due to this bacterium are more likely to occur in critically ill or otherwise debilitated individuals. In fact, outside of the organism's lipopolysaccharide layer, the majority of virulence factors, including bacteriocin production, encapsulation and a prolonged viability under dry conditions, seem to favour a prolonged survival rather than invasive disease. Prolonged survival in the environment is likely to be a major contributing factor to nosocomial spread, particularly in intensive care units (ICUs).

Risk factors for infection with the *A. baumannii* group include advanced age, presence of serious underlying disease, immune suppression, major trauma or burn injuries, invasive procedures, presence of indwelling catheters, mechanical ventilation, extended hospital stay and previous administration of antibiotics. The risks for acquiring a multidrug-resistant strain of the *A. baumannii* group are similar and include prolonged mechanical ventilation, prolonged ICU or hospital stay, exposure to infected or colonised patients, increased frequency of interventions, increased disease severity and receipt of broad-spectrum agents, especially third-generation cephalosporins, fluoroquinolones and carbapenems.

3.4.2 Resistance mechanisms

Acinetobacter species, particularly those belonging in the *A. baumannii* group, are intrinsically resistant to most antimicrobial agents due to their selective ability to prevent various molecules from penetrating their outer membrane. The antimicrobial groups that remain active include some fluoroquinolones (e.g. ciprofloxacin and levofloxacin), aminoglycosides (e.g. gentamicin, tobramycin and amikacin), carbapenems (imipenem, doripenem and meropenem), polymyxins (polymyxin B and colistin) and, possibly, sulbactam and tigecycline. Resistance of *Acinetobacter* spp. to these agents can be acquired through one or more of the following mechanisms:

- mutational modification of antimicrobial targets such as topoisomerases or ribosomal proteins, which confers resistance to fluoroquinolones and aminoglycosides, respectively;
- mutational loss of outer membrane proteins, which prevents the uptake of antimicrobial agents such as carbapenems;
- mutational upregulation of efflux systems that can confer resistance to beta-lactams, fluoroquinolones and aminoglycosides, and reduced susceptibility to tigecycline; and
- acquisition of plasmid-mediated resistance genes coding for various beta-lactamases that can confer resistance to carbapenems (OXA carbapenemases and metallo-beta-lactamases), for aminoglycoside-modifying enzymes that may confer resistance to various aminoglycosides, or for 16S rRNA ribosomal methylases that can confer high-level resistance to all aminoglycosides.

3.4.3 Antimicrobial susceptibility

- Wide variations in antimicrobial resistance of *Acinetobacter* spp. isolates in Europe were reported, with generally higher resistance percentages observed in countries in the east, south and south-east of Europe than in the north.
- Carbapenem resistance was common in *Acinetobacter* spp. and was in most cases combined with resistance to fluoroquinolones and aminoglycosides.

Fluoroquinolones

For 2015, 30 countries reported 5 025 isolates with AST information for fluoroquinolones (ciprofloxacin or levofloxacin). The number of isolates reported per country ranged from 4 to 946 (Table 3.21).

The percentages of resistant isolates in countries which reported more than 10 isolates ranged from zero (Belgium) to 94.9 % (Greece) (Table 3.21 and Figure 3.17). Estonia, Iceland and Luxembourg reported fewer than 10 isolates and are therefore not included in Figure AC1. Trends for the period 2012–2015 were calculated for the 16 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for five countries (Cyprus, Norway, Poland, Slovenia and the United Kingdom). For Norway and the United Kingdom, the trends did not remain significant when only data from laboratories reporting

Figure 3.17. ***Acinetobacter*** **spp. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2015**

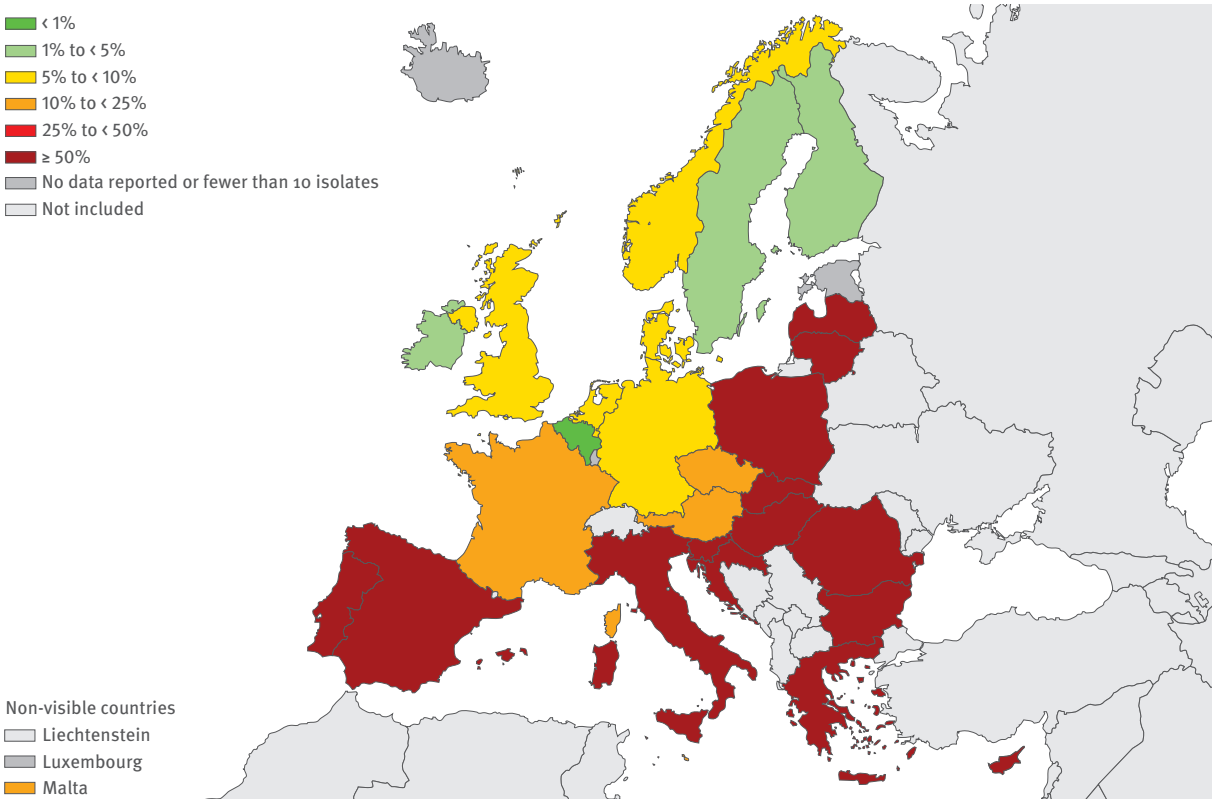
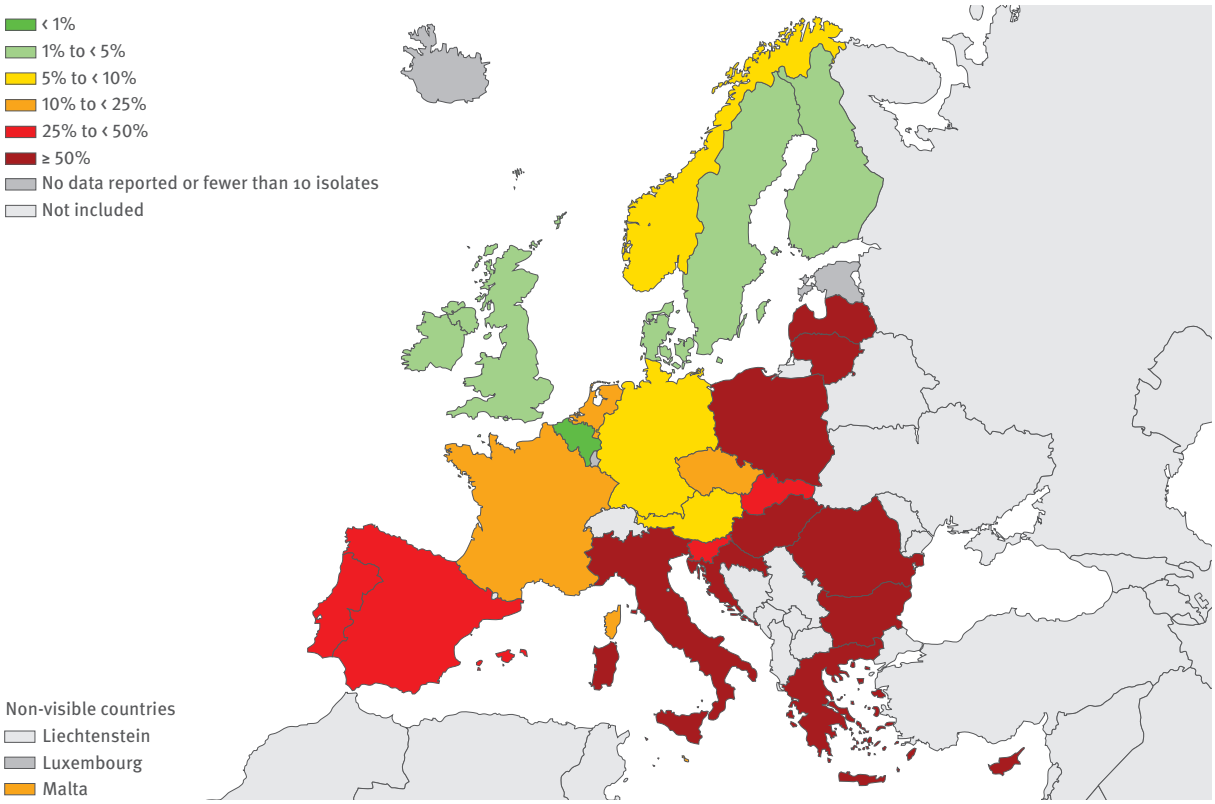


Figure 3.18. ***Acinetobacter*** **spp. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2015**



for the whole period were considered. Significantly decreasing trends were observed for Hungary, Portugal and Romania. For Romania, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Aminoglycosides

For 2015, 30 countries reported 4 994 isolates with AST information for aminoglycosides (gentamicin, tobramycin and netilmicin). The number of isolates reported per country ranged from 2 to 945 (Table 3.22).

The percentages of resistant isolates in countries which reported more than 10 isolates ranged from zero (Belgium) to 90.4% (Lithuania). Estonia, Iceland and Luxembourg reported fewer than 10 isolates and are therefore not included in Figure 3.18.

Trends for the period 2012–2015 were calculated for the 14 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for five countries (Bulgaria, Cyprus, Greece, Romania and Slovenia). For all countries the trends remained significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for Hungary, Italy and Portugal. For Italy, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Carbapenems

For 2015, 30 countries reported 5 049 isolates with AST information for carbapenems (imipenem and/or meropenem). The number of isolates reported per country ranged from 3 to 983 (Table 3.23).

The percentages of resistant isolates in countries which reported more than 10 isolates ranged from 0.0% (Belgium) to 93.5% (Greece). Estonia, Iceland and Luxembourg reported fewer than 10 isolates and are therefore not included in Figure 3.19. Trends for the period 2012–2015 were calculated for the 15 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for five countries (Bulgaria, Cyprus, Greece, Norway and Poland). For Norway, the trend did not remain significant when only data from laboratories reporting for the whole period were considered. A significantly decreasing trend was observed for Portugal, a trend that remained when considering only data from laboratories reporting consistently for all four years.

Combined resistance (fluoroquinolones, aminoglycosides and carbapenems)

For 2015, 30 countries reported 4 898 isolates with sufficient AST information to determine combined resistance to fluoroquinolones, aminoglycosides and carbapenems. The number of isolates reported per country ranged from 1 to 943 (Table 3.24).

The percentage of isolates with combined resistance in countries that reported more than 10 isolates ranged from zero (Belgium and the United Kingdom) to 87.0% (Croatia). Trends for the period 2012–2015 were calculated for the 14 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for eight countries (Bulgaria, Cyprus, Greece, Hungary, Norway, Poland, Romania and Slovenia). For Norway and Slovenia the trends did not remain significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for Italy and Portugal. For Italy, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

Polymyxins

Twenty-five countries reported AST data for polymyxins for a total of 3 037 isolates (59.1% of all reported *Acinetobacter* spp. isolates). Eleven of those countries reported polymyxin AST data for more than half of all their reported *Acinetobacter* spp. isolates. Overall, 4.1% of the isolates were resistant to polymyxins, with 47.3% of these resistant isolates reported from Greece and Italy.

Due to the low number of isolates tested, the relatively high proportion of isolates from high-resistance areas and differences in the use of laboratory methodology used to determine susceptibility, these findings should be interpreted with caution and may not be representative of Europe as a whole.

3.4.5 Discussion and conclusions

Antimicrobial resistance in *Acinetobacter* spp. is common in Europe, as is combined resistance to multiple antimicrobial groups. In 2015, combined resistance to fluoroquinolones, aminoglycosides and carbapenems was the most frequently reported resistance phenotype and accounted for almost half of the reported isolates.

Antimicrobial resistance of *Acinetobacter* spp. in Europe shows wide variation, with especially high resistance percentages reported from the Baltic countries and from countries in southern and south-eastern Europe. The high levels of antimicrobial resistance reported from these regions are of great concern, especially when last-line treatment alternatives such as carbapenems or polymyxins also show high resistance levels.

For the first time since *Acinetobacter* spp. was included in an EARS-Net survey in 2012, a four-year trend analysis could be performed for countries which reported at least 20 isolates per year during the full four-year period. More than half of the 14 countries showed significantly increasing trends for the period 2012–2015 with regard to combined resistance to all three antimicrobial groups under EARS-Net surveillance. Increasing trends were mainly noted for countries with comparatively high resistance frequency. Due to the lower number of countries reporting data during the first part of the 2012–2015 period, no EU/EAA population-weighted mean was calculated.

Figure 3.19. ***Acinetobacter*** **spp. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015**

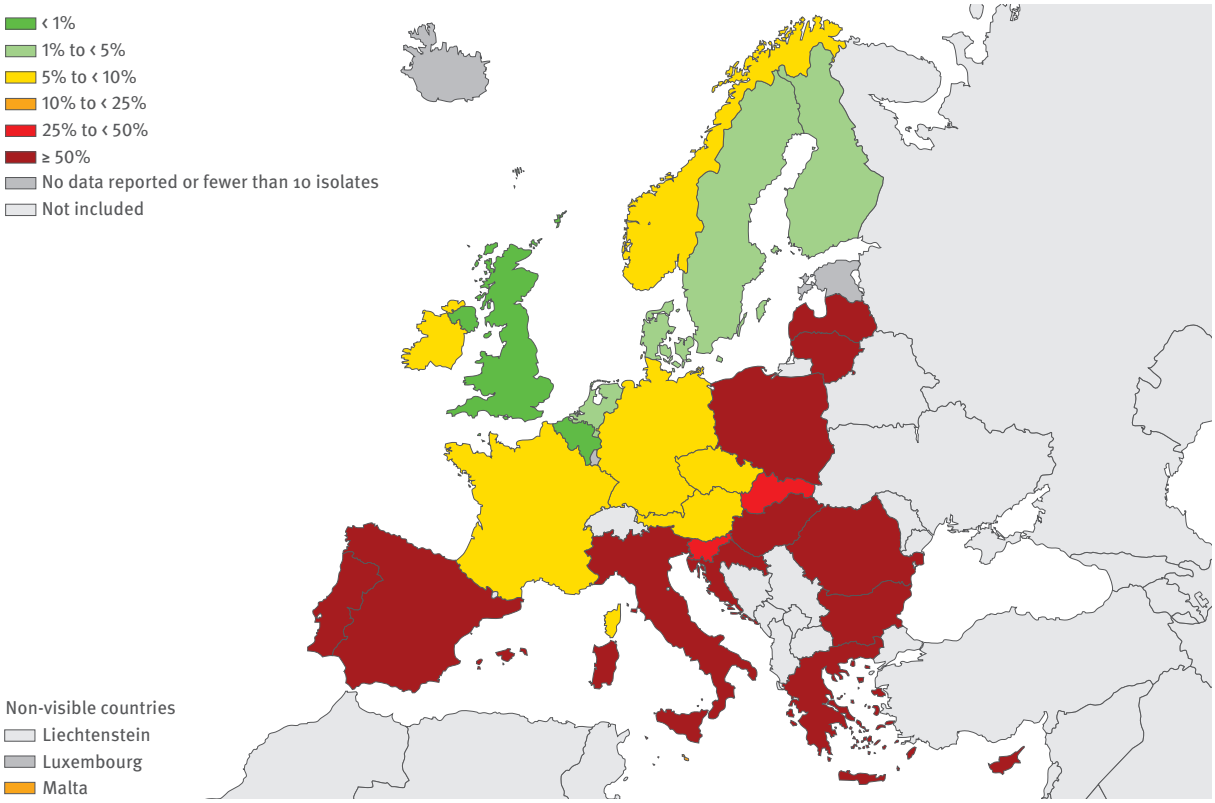


Figure 3.20. ***Acinetobacter*** **spp. Percentage (%) of invasive isolates with combined resistance to fluoroquinolones, aminoglycosides and carbapenems, by country, EU/EEA countries, 2015**

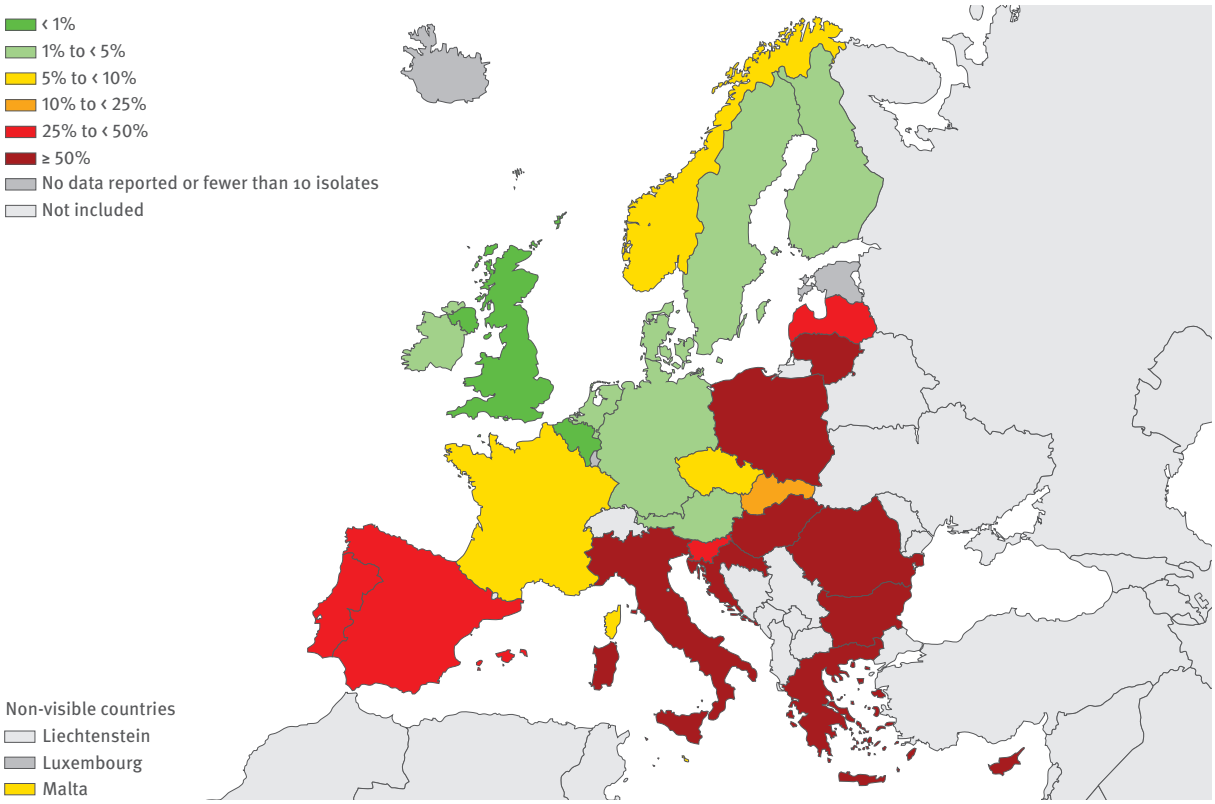


Table 3.21. ***Acinetobacter*** **spp. Total number of invasive isolates tested (N) and percentage with resistance to fluoroquinolones (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Belgium	–	–	(–)	3	**	(**)	4	**	(**)	**26**	**0.0**	**(0–13)**		N/A	
Finland	–	–	(–)	36	2.8	(0–15)	31	6.5	(1–21)	**43**	**2.3**	**(0–12)**		N/A	
Sweden	–	–	(–)	74	5.4	(1–13)	52	11.5	(4–23)	**26**	**3.8**	**(0–20)**		N/A	
Ireland	–	–	(–)	88	1.1	(0–6)	86	4.7	(1–11)	**83**	**4.8**	**(1–12)**		N/A	
Denmark	83	12.0	(6–21)	79	6.3	(2–14)	69	2.9	(0–10)	**68**	**5.9**	**(2–14)**		12.0 7.0 2.0	
Netherlands	10	0.0	(0–31)	69	2.9	(0–10)	72	4.2	(1–12)	**74**	**6.8**	**(2–15)**		7.0 3.5 0.0	
United Kingdom	105	2.9	(1–8)	165	3.6	(1–8)	123	11.4	(6–18)	**139**	**7.2**	**(4–13)**		12.0 7.5 3.0	› #
Germany	121	8.3	(4–15)	175	9.7	(6–15)	199	6.0	(3–10)	**336**	**8.6**	**(6–12)**		10.0 8.0 6.0	
Norway	25	0.0	(0–14)	36	0.0	(0–10)	34	5.9	(1–20)	**32**	**9.4**	**(2–25)**		10.0 5.0 0.0	› #
Malta	6	**	(**)	7	**	(**)	10	30.0	(7–65)	**15**	**13.3**	**(2–40)**		N/A	
France	385	15.6	(12–20)	397	13.6	(10–17)	395	11.9	(9–16)	**430**	**13.5**	**(10–17)**		16.0 13.5 11.0	
Austria	–	–	(–)	51	21.6	(11–35)	75	5.3	(1–13)	**61**	**16.4**	**(8–28)**		N/A	
Czech Republic	–	–	(–)	91	19.8	(12–29)	59	15.3	(7–27)	**60**	**18.3**	**(10–30)**		N/A	
Slovakia	–	–	(–)	188	58.5	(51–66)	170	51.8	(44–59)	**154**	**51.9**	**(44–60)**		N/A	
Portugal	168	77.4	(70–83)	225	68.9	(62–75)	264	52.7	(46–59)	**308**	**55.8**	**(50–61)**		77.0 66.0 55.0	‹
Slovenia	25	28.0	(12–49)	25	28.0	(12–49)	34	41.2	(25–59)	**31**	**58.1**	**(39–75)**		58.0 43.0 28.0	›
Spain	–	–	(–)	76	72.4	(61–82)	79	67.1	(56–77)	**95**	**64.2**	**(54–74)**		N/A	
Hungary	405	78.0	(74–82)	472	73.5	(69–77)	441	66.4	(62–71)	**464**	**68.1**	**(64–72)**		78.0 72.0 66.0	‹
Latvia	–	–	(–)	–	–	(–)	52	88.5	(77–96)	**60**	**78.3**	**(66–88)**		88.5 83.3 78.0	
Bulgaria	65	69.2	(57–80)	94	70.2	(60–79)	115	73.9	(65–82)	**131**	**78.6**	**(71–85)**		79.0 74.0 69.0	
Italy	236	86.0	(81–90)	472	83.1	(79–86)	469	92.1	(89–94)	**664**	**81.6**	**(78–85)**		92.0 87.0 82.0	
Romania	54	88.9	(77–96)	137	90.5	(84–95)	123	83.7	(76–90)	**189**	**82.5**	**(76–88)**		90.0 86.0 82.0	‹ #
Cyprus	23	56.5	(34–77)	33	60.6	(42–77)	58	77.6	(65–87)	**60**	**83.3**	**(71–92)**		83.0 70.0 57.0	›
Poland	209	78.0	(72–83)	188	81.4	(75–87)	185	82.7	(76–88)	**243**	**88.1**	**(83–92)**		88.0 83.0 78.0	›
Croatia	–	–	(–)	112	92.9	(86–97)	164	92.1	(87–96)	**196**	**92.3**	**(88–96)**		N/A	
Lithuania	–	–	(–)	–	–	(–)	66	84.8	(74–92)	**73**	**93.2**	**(85–98)**		N/A	
Greece	1204	93.1	(92–94)	812	95.0	(93–96)	806	95.3	(94–97)	**946**	**94.9**	**(93–96)**		96.0 94.5 93.0	
Estonia	–	–	(–)	–	–	(–)	–	–	(–)	**4**	******	**(**)**		N/A	
Iceland	2	**	(**)	–	–	(–)	3	**	(**)	**6**	******	**(**)**		N/A	
Luxembourg	6	**	(**)	3	**	(**)	6	**	(**)	8	**	(**)		N/A	

–: No data

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

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

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

Table 3.22. ***Acinetobacter*** **spp. Total number of invasive isolates tested (N) and percentage with resistance to aminoglycosides (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	Comment*
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			
Belgium	–	–	(–)	1	**	(**)	2	**	(**)	15	0.0	(0–22)		N/A	
United Kingdom	108	2.8	(1–8)	163	2.5	(1–6)	129	10.1	(5–17)	153	2.0	(0–6)		10.0 6.0 2.0	
Finland	–	–	(–)	36	0.0	(0–10)	31	3.2	(0–17)	42	2.4	(0–13)		N/A	
Ireland	–	–	(–)	88	1.1	(0–6)	89	2.2	(0–8)	80	3.8	(1–11)		N/A	
Sweden	–	–	(–)	74	8.1	(3–17)	36	2.8	(0–15)	26	3.8	(0–20)		N/A	
Denmark	77	10.4	(5–19)	75	1.3	(0–7)	60	1.7	(0–9)	63	4.8	(1–13)		11.0 6.0 1.0	
Germany	119	5.9	(2–12)	180	6.1	(3–11)	197	4.1	(2–8)	328	5.5	(3–9)		6.0 5.0 4.0	
Austria	–	–	(–)	51	9.8	(3–21)	79	8.9	(4–17)	63	6.3	(2–15)		N/A	
Norway	25	4.0	(0–20)	36	2.8	(0–15)	33	3.0	(0–16)	32	9.4	(2–25)		10.0 6.5 3.0	
Netherlands	59	1.7	(0–9)	67	4.5	(1–13)	73	5.5	(2–13)	74	10.8	(5–20)		N/A	
France	278	12.9	(9–17)	409	11.2	(8–15)	409	8.3	(6–11)	431	11.1	(8–14)		13.0 10.5 8.0	
Malta	5	**	(**)	7	**	(**)	10	30.0	(7–65)	15	13.3	(2–40)		N/A	
Czech Republic	–	–	(–)	91	15.4	(9–24)	59	10.2	(4–21)	60	15.0	(7–27)		N/A	
Slovenia	25	20.0	(7–41)	25	16.0	(5–36)	34	32.4	(17–51)	31	41.9	(25–61)		42.0 29.0 16.0	›
Slovakia	–	–	(–)	187	42.8	(36–50)	170	40.6	(33–48)	154	42.9	(35–51)		N/A	
Portugal	169	65.1	(57–72)	231	56.3	(50–63)	265	42.3	(36–48)	310	46.5	(41–52)		66.0 54.0 42.0	‹
Spain	–	–	(–)	77	68.8	(57–79)	80	58.8	(47–70)	96	49.0	(39–59)		N/A	
Latvia	–	–	(–)	–	–	(–)	52	69.2	(55–81)	61	59.0	(46–71)		N/A	
Hungary	407	68.8	(64–73)	473	63.2	(59–68)	444	59.5	(55–64)	465	60.6	(56–65)		69.0 64.0 59.0	‹
Poland	211	70.1	(63–76)	191	73.3	(66–79)	188	58.5	(51–66)	245	70.2	(64–76)		74.0 66.0 58.0	
Bulgaria	65	58.5	(46–71)	91	58.2	(47–68)	87	60.9	(50–71)	116	74.1	(65–82)		74.0 66.0 58.0	›
Cyprus	23	52.2	(31–73)	33	60.6	(42–77)	57	73.7	(60–84)	59	74.6	(62–85)		74.0 63.0 52.0	›
Italy	234	83.3	(78–88)	456	81.8	(78–85)	444	88.3	(85–91)	656	74.7	(71–78)		88.0 81.0 74.0	‹ #
Romania	54	57.4	(43–71)	137	80.3	(73–87)	122	77.0	(69–84)	188	80.9	(74–86)		81.0 69.0 57.0	›
Greece	1234	78.1	(76–80)	813	82.0	(79–85)	800	83.9	(81–86)	945	83.7	(81–86)		84.0 81.0 78.0	›
Croatia	–	–	(–)	113	84.1	(76–90)	166	82.5	(76–88)	197	88.3	(83–92)		N/A	
Lithuania	–	–	(–)	–	–	(–)	65	80.0	(68–89)	73	90.4	(81–96)		N/A	
Estonia	–	–	(–)	–	–	(–)	–	–	(–)	2	**	(**)		N/A	
Iceland	2	**	(**)	–	–	(–)	3	**	(**)	6	**	(**)		N/A	
Luxembourg	6	**	(**)	3	**	(**)	6	**	(**)	8	**	(**)		N/A	

–: No data

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

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

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

Table 3.23. ***Acinetobacter*** **spp. Total number of invasive isolates tested (N) and percentage with resistance to carbapenems (%R), including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Belgium	–	–	(–)	3	**	(**)	4	**	(**)	24	0.0	(0–14)		N/A	
United Kingdom	80	2.5	(0–9)	149	2.0	(0–6)	120	1.7	(0–6)	132	0.8	(0–4)		2.5 1.3 0.0	
Finland	–	–	(–)	35	0.0	(0–10)	32	3.1	(0–16)	43	2.3	(0–12)		N/A	
Sweden	–	–	(–)	72	5.6	(2–14)	52	3.8	(0–13)	34	2.9	(0–15)		N/A	
Netherlands	67	6.0	(2–15)	65	1.5	(0–8)	74	0.0	(0–5)	73	4.1	(1–12)		6.0 3.0 0.0	
Denmark	64	9.4	(4–19)	61	1.6	(0–9)	62	1.6	(0–9)	65	4.6	(1–13)		10.0 5.5 1.0	
France	389	3.3	(2–6)	406	5.9	(4–9)	401	2.5	(1–5)	428	5.6	(4–8)		6.0 4.0 2.0	
Ireland	–	–	(–)	85	2.4	(0–8)	79	1.3	(0–7)	84	6.0	(2–13)		N/A	
Germany	121	6.6	(3–13)	180	8.9	(5–14)	201	5.5	(3–10)	334	6.6	(4–10)		9.0 7.0 5.0	
Czech Republic	–	–	(–)	91	4.4	(1–11)	59	5.1	(1–14)	60	6.7	(2–16)		N/A	
Austria	–	–	(–)	51	7.8	(2–19)	78	6.4	(2–14)	64	9.4	(4–19)		N/A	
Norway	25	0.0	(0–14)	36	0.0	(0–10)	34	2.9	(0–15)	32	9.4	(2–25)		10.0 5.0 0.0	› #
Malta	6	**	(**)	7	**	(**)	10	10.0	(0–45)	15	13.3	(2–40)		N/A	
Slovakia	–	–	(–)	142	45.8	(37–54)	161	32.9	(26–41)	142	28.2	(21–36)		N/A	
Slovenia	25	24.0	(9–45)	25	24.0	(9–45)	34	26.5	(13–44)	31	38.7	(22–58)		40.0 32.0 24.0	
Spain	–	–	(–)	95	75.8	(66–84)	78	65.4	(54–76)	95	53.7	(43–64)		N/A	
Hungary	418	48.1	(43–53)	481	50.1	(46–55)	443	44.5	(40–49)	467	55.2	(51–60)		56.0 50.0 44.0	
Portugal	168	79.2	(72–85)	229	69.0	(63–75)	262	53.1	(47–59)	307	57.7	(52–63)		79.0 66.0 53.0	‹
Poland	212	38.2	(32–45)	189	49.7	(42–57)	189	53.4	(46–61)	244	65.6	(59–72)		66.0 52.0 38.0	›
Latvia	–	–	(–)	–	–	(–)	52	78.8	(65–89)	61	68.9	(56–80)		N/A	
Bulgaria	58	60.3	(47–73)	89	59.6	(49–70)	110	59.1	(49–68)	130	73.8	(65–81)		73.0 66.0 59.0	›
Italy	231	83.1	(78–88)	468	79.5	(76–83)	477	89.9	(87–92)	664	78.3	(75–81)		90.0 84.0 78.0	
Lithuania	–	–	(–)	–	–	(–)	66	69.7	(57–80)	73	80.8	(70–89)		N/A	
Romania	54	81.5	(69–91)	137	85.4	(78–91)	123	81.3	(73–88)	189	81.5	(75–87)		86.0 83.0 80.0	
Cyprus	23	56.5	(34–77)	33	60.6	(42–77)	58	77.6	(65–87)	59	83.1	(71–92)		83.0 70.0 57.0	›
Croatia	–	–	(–)	114	89.5	(82–94)	166	87.3	(81–92)	200	89.0	(84–93)		N/A	
Greece	1254	87.8	(86–90)	848	90.6	(88–92)	841	93.2	(91–95)	983	93.5	(92–95)		94.0 91.0 88.0	›
Estonia	–	–	(–)	–	–	(–)	–	–	(–)	3	**	(**)		N/A	
Iceland	2	**	(**)	–	–	(–)	3	**	(**)	6	**	(**)		N/A	
Luxembourg	5	**	(**)	1	**	(**)	6	**	(**)	7	**	(**)		N/A	

–: No data

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

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

**Percentage resistance not calculated as number of isolates was below 10.

Table 3.24. ***Acinetobacter*** **spp. Total number of isolates tested (N) and percentage with combined resistance to fluoroquinolones, aminoglycosides and carbapenems (%R), including 95 % confidence intervals (95 % CI), by country, EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Belgium	–	–	(–)	1	**	(**)	2	**	(**)	13	0.0	(0–25)		N/A	
United Kingdom	79	1.3	(0–7)	149	1.3	(0–5)	119	1.7	(0–6)	131	0.0	(0–3)		2.0 1.0 0.0	
Ireland	–	–	(–)	84	0.0	(0–4)	79	1.3	(0–7)	75	1.3	(0–7)		N/A	
Finland	–	–	(–)	34	0.0	(0–10)	30	0.0	(0–12)	42	2.4	(0–13)		N/A	
Denmark	58	8.6	(3–19)	57	1.8	(0–9)	49	0.0	(0–7)	60	3.3	(0–12)		10.0 5.0 0.0	
Germany	119	4.2	(1–10)	174	5.2	(2–10)	188	2.1	(1–5)	325	3.7	(2–6)		6.0 4.0 2.0	
Sweden	–	–	(–)	71	5.6	(2–14)	36	2.8	(0–15)	26	3.8	(0–20)		N/A	
Netherlands	10	0.0	(0–31)	64	1.6	(0–8)	69	0.0	(0–5)	73	4.1	(1–12)		N/A	
Austria	–	–	(–)	51	5.9	(1–16)	74	2.7	(0–9)	61	4.9	(1–14)		N/A	
Czech Republic	–	–	(–)	91	4.4	(1–11)	59	5.1	(1–14)	60	5.0	(1–14)		N/A	
France	272	4.0	(2–7)	389	4.1	(2–7)	391	1.5	(1–3)	424	5.2	(3–8)		5.0 3.0 1.0	
Malta	5	**	(**)	7	**	(**)	10	10.0	(0–45)	15	6.7	(0–32)		N/A	
Norway	25	0.0	(0–14)	36	0.0	(0–10)	33	3.0	(0–16)	32	9.4	(2–25)		10.0 5.0 0.0	› #
Slovakia	–	–	(–)	141	24.8	(18–33)	160	24.4	(18–32)	142	23.2	(17–31)		N/A	
Slovenia	25	12.0	(3–31)	25	16.0	(5–36)	34	20.6	(9–38)	31	35.5	(19–55)		36.0 24.0 12.0	› #
Spain	–	–	(–)	71	66.2	(54–77)	78	55.1	(43–66)	94	41.5	(31–52)		N/A	
Portugal	168	64.3	(57–72)	222	56.3	(50–63)	260	39.2	(33–45)	302	45.0	(39–51)		65.0 52.0 39.0	‹
Latvia	–	–	(–)	–	–	(–)	52	61.5	(47–75)	60	46.7	(34–60)		N/A	
Hungary	394	41.6	(37–47)	465	42.8	(38–47)	438	38.4	(34–43)	462	51.7	(47–56)		52.0 45.0 38.0	›
Poland	206	36.9	(30–44)	184	46.2	(39–54)	184	38.0	(31–45)	240	54.6	(48–61)		55.0 46.0 37.0	›
Bulgaria	58	32.8	(21–46)	86	39.5	(29–51)	85	47.1	(36–58)	112	66.1	(57–75)		66.0 49.0 32.0	›
Italy	217	77.4	(71–83)	444	78.8	(75–83)	437	86.3	(83–89)	650	72.6	(69–76)		86.0 79.0 72.0	‹ #
Cyprus	23	47.8	(27–69)	33	60.6	(42–77)	57	73.7	(60–84)	59	72.9	(60–84)		74.0 61.0 48.0	›
Lithuania	–	–	(–)	–	–	(–)	65	60.0	(47–72)	73	76.7	(65–86)		N/A	
Romania	54	50.0	(36–64)	137	74.5	(66–82)	121	76.9	(68–84)	186	76.9	(70–83)		78.0 64.0 50.0	›
Greece	1203	74.5	(72–77)	809	79.6	(77–82)	793	82.6	(80–85)	943	82.2	(80–85)		83.0 79.0 75.0	›
Croatia	–	–	(–)	111	78.4	(70–86)	162	80.9	(74–87)	193	87.0	(81–91)		N/A	
Iceland	2	**	(**)	–	–	(–)	3	**	(**)	6	**	(**)		N/A	
Luxembourg	5	**	(**)	1	**	(**)	6	**	(**)	7	**	(**)		N/A	
Estonia	–	–	(–)	–	–	(–)	–	–	(–)	1	**	(**)		N/A	

–: No data

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

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

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

Table 3.25. ***Acinetobacter*** **spp. Overall resistance and resistance combinations among invasive isolates tested to fluoroquinolones, aminoglycosides and carbapenems (n=4898), EU/EEA countries, 2015**

Resistance pattern	Number of isolates	% of total*
Fully susceptible	**1809**	**36.9**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance)	**212**	**4.3**
Fluoroquinolones	134	2.7
Aminoglycosides	51	1.0
Carbapenems	27	0.6
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**476**	**9.7**
Fluoroquinolones + carbapenems	283	5.8
Fluoroquinolones + aminoglycosides	183	3.7
Aminoglycosides + carbapenems	10	0.2
Resistance to three antimicrobial groups		
Fluoroquinolones + aminoglycosides + carbapenems	**2401**	**49**

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

* Not adjusted for population differences in the reporting countries.

As for *E. coli* and *K. pneumoniae*, resistance to carbapenems is often associated with production of carbapenemases. Results from the EuSCAPE project show that carbapenem-resistant *Acinetobacter* spp. might be more widely disseminated in Europe than CPE [24]. The high levels of carbapenem resistance in *Acinetobacter* spp. reported from many countries in EARS-Net support this assumption. The EuSCAPE project also showed that in 2013, several EU/EEA countries did not routinely engage in the surveillance and reporting of carbapenem-resistant *A. baumannii*. In general, less information and more limited data were available on the national capacity for surveillance and containment of carbapenem-resistant *A. baumannii* compared to carbapenem-resistant Enterobacteriaceae, but the increasing number of countries and laboratories that report data on *Acinetobacter* spp. to EARS-Net might indicate that surveillance of this pathogen in Europe has indeed improved.

An ECDC rapid risk assessment on carbapenem-resistant *A. baumannii* published in 2016 [25] concluded that carbapenem-resistant *A. baumannii* poses a significant threat to patients and healthcare systems in all EU/EEA Member States. As *Acinetobacter* spp. in the healthcare environment can persist for long periods and is notoriously difficult to eradicate once established, increased efforts are needed for the detection of cases and the control of outbreaks to prevent *Acinetobacter* spp. from becoming endemic in European health facilities and regions. Options for response include timely laboratory reporting, screening/pre-emptive isolation of high-risk patients, good infection control, and antimicrobial stewardship programmes [25].

3.5 *Streptococcus pneumoniae*

3.5.1 Clinical and epidemiological importance

Streptococcus pneumoniae is a common cause of disease, especially among young non-vaccinated children, elderly people and patients with compromised immune functions. The clinical spectrum ranges from upper airway infections, such as sinusitis, and otitis media to pneumonia, bloodstream infections and meningitis. Since *S. pneumoniae* is the most common cause of pneumonia worldwide, morbidity and mortality are high.

Pneumococci carry a variety of virulence factors that facilitate adherence to, and transcytosis of, epithelial cells, including a polysaccharide capsule preventing phagocytosis by the host's immune cells. More than 90 different capsular serotypes are known, differing in virulence, prevalence, and extent of drug resistance. Interestingly, serotypes most frequently involved in pneumococcal disease or colonisation in infants are also most frequently associated with AMR. However, serotype replacement due to increased use of the pneumococcal conjugate vaccine (PCV) has been reported.

3.5.2 Resistance mechanisms

Beta-lactam antimicrobials bind to cell wall synthesising enzymes, the so-called penicillin-binding proteins (PBPs), and interfere with the biosynthesis and remodelling of the bacterial cell wall during cell growth and division. The mechanism of penicillin resistance in *S. pneumoniae* consists of alterations in PBPs, which result in reduced affinity to this antimicrobial group. Alterations in PBPs are due to transformation with PBP gene sequences originating from commensal streptococci. Acquisition of mosaic PBP results in different degrees of resistance ranging from low-level clinical resistance, conventionally termed intermediate (I), to full clinical resistance (R). However, except meningitis, respiratory infections with intermediate strains are often successfully treated with high doses of benzylpenicillin or aminopenicillins.

Macrolide, lincosamide and streptogramin (MLS) antimicrobials are chemically distinct, but all bind to a ribosomal subunit, inhibiting the initiation of mRNA binding and thus inhibiting protein synthesis. There are two predominant resistance mechanisms to MLS agents in *S. pneumoniae*:

- The acquisition of an erythromycin ribosomal methylation gene (commonly *ermB*) results in a post-transcriptional modification of the 23S subunit of rRNA, which blocks the binding of the macrolide to the ribosome. This often results in high-level resistance (MICs › 128 mg/L) to macrolides, lincosamide and streptogramin B, termed MLS_B resistance.
- The acquisition of a macrolide efflux system gene *(mef)* results in the excretion of the agent and effectively reduces intracellular erythromycin, azithromycin and clarithromycin to subinhibitory concentrations. In contrast to beta-lactam resistance, macrolide resistance via these mechanisms (particularly for MLS_B) confers very high MICs and cannot be overcome by increasing dosages of the antimicrobial agents.

The two fluoroquinolones with acknowledged clinical activity against pneumococci are levofloxacin and moxifloxacin. Resistance to fluoroquinolones is mediated by mutations in *ParC* (subunit of topoisomerase IV) and/or *GyrA* (subunit of DNA gyrase/topoisomerase IV). Additionally, resistance may be conferred by efflux.

3.5.3 Antimicrobial susceptibility

- Susceptibility of *S. pneumoniae* showed wide variations between European countries.
- Macrolide non-susceptibility in *S. pneumoniae* was, for most countries, higher than penicillin non-susceptibility.
- While little variation over time was noted for penicillin non-susceptibility, macrolide non-susceptibility in *S. pneumoniae* decreased significantly in 8 out of 26 countries between 2012 and 2015.

Penicillin

For 2015, 29 countries reported 12 274 isolates with AST information for penicillins (penicillin or if no penicillin information was available, oxacillin). The number of isolates reported by country ranged from 7 to 1 361.

Among the 28 countries reporting 10 isolates or more, the percentages of penicillin-non-susceptible isolates ranged from 0.6 % (Belgium) to 39.0 % (Romania). Trends for the period 2012–2015 were calculated for the 26 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for Portugal and the United Kingdom. For Portugal, the trend did not remain significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for Belgium and Finland. For Belgium, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years.

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

Macrolides

For 2015, 29 countries reported 12 268 isolates with AST information for macrolides (azithromycin, clarithromycin or erythromycin). The number of isolates reported by country ranged from 7 to 1 361.

Among the 28 countries reporting 10 isolates or more, the percentages of penicillin-non-susceptible isolates ranged from zero (Luxembourg) to 40.0 % (Malta). Trends for the period 2012–2015 were calculated for the

26 countries reporting at least 20 isolates per year during the full four-year period. A significantly increasing trend was observed for Norway, a trend that remained significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for eight countries (Austria, Belgium, Croatia, Finland, France, Hungary, Italy, and Luxembourg). For Belgium, Croatia, France, Hungary and Italy, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years.

Combined non-susceptibility to penicillins and macrolides

For 2015, 29 countries reported 12 268 isolates with AST information for both penicillins and macrolides. The number of isolates reported by country ranged from 7 to 1 361.

Among the 28 countries reporting 10 isolates or more, the percentages of penicillin-non-susceptible isolates ranged from zero (Luxembourg) to 25.0 % (Malta and Romania). Trends for the period 2012–2015 were calculated for the 26 countries reporting at least 20 isolates per year during the full four-year period. Significantly increasing trends were observed for Slovakia, a trend that did not remain significant when only data from laboratories reporting for the whole period were considered. Significantly decreasing trends were observed for Belgium, Croatia, Finland and Spain. For Belgium and Croatia, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years.

3.5.4 Discussion and conclusions

As in previous years, wide inter-country variations can be noted in *S. pneumoniae* susceptibility to penicillins and macrolides. Differences in clinical breakpoints used for determining penicillin susceptibility in *S. pneumoniae* with regard to guidelines used and site of infection might introduce bias when comparing national data reported to EARS-Net. However, limited information on use of guidelines and incomplete quantitative susceptibility data hamper an assessment of the impact of these differences on the data.

In parallel to EARS-Net, the invasive pneumococcal disease (IPD) enhanced surveillance network, also coordinated by ECDC, collects additional data on IPD cases from reference laboratories throughout Europe [26]. For most countries, antimicrobial susceptibility testing results reported to EARS-Net correspond with the data reported for the IPD enhanced surveillance. However, for a few countries, there seem to be differences in antimicrobial susceptibility testing results between the two systems. For some countries, this may be due to differences in data sources, or a low number of cases and large confidence intervals may not allow appropriate comparison.

Figure 3.21. *Streptococcus pneumoniae*. Percentage (%) of invasive isolates non-susceptible to macrolides, by country, EU/EEA countries, 2015

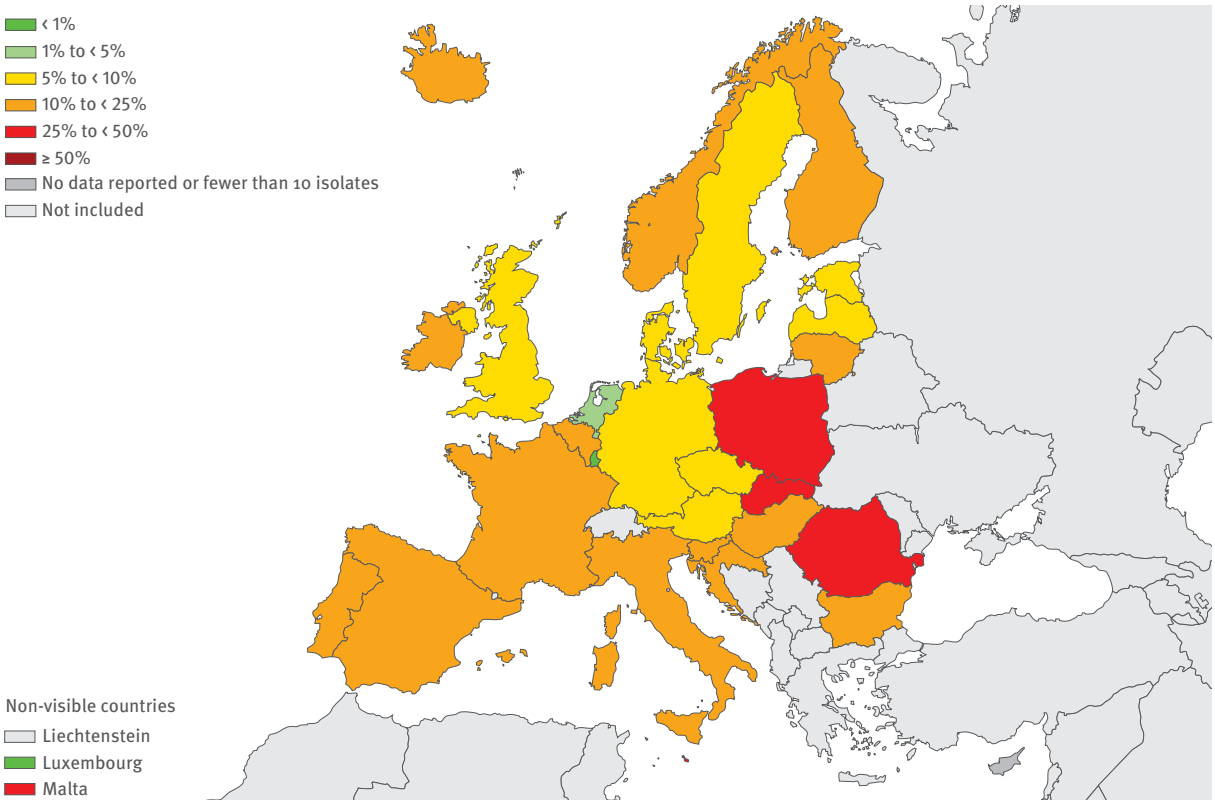


Table 3.26. ***Streptococcus pneumoniae.*** **Total number of tested isolates (N) and percentages non-susceptible to penicillin (%IR), including 95 % confidence intervals (95 % CI), by country, EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015			Trend 2012–2015	
	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)		Comment*
Belgium	1658	1.5	(1–2)	1536	1.7	(1–2)	1110	1.3	(1–2)	1361	0.6	(1–2)		#
Netherlands	1063	1.5	(1–2)	1032	1.1	(1–2)	1139	2.1	(1–3)	1163	1.8	(1–2)		
Estonia	53	0.0	(0–7)	78	1.3	(0–7)	72	4.2	(1–12)	72	2.8	(0–7)		
Czech Republic	274	2.9	(1–6)	333	2.1	(1–4)	274	5.8	(3–9)	284	3.2	(1–6)		
Luxembourg	31	3.2	(0–17)	44	15.9	(7–30)	32	6.3	(1–21)	27	3.7	(0–17)		
Denmark	867	5.1	(4–7)	789	6.6	(5–9)	709	5.6	(4–8)	747	4.7	(4–7)		
Norway	576	5.9	(4–8)	549	3.3	(2–5)	534	5.1	(3–7)	429	5.4	(4–8)		
Austria	291	5.2	(3–8)	385	2.1	(1–4)	361	5.3	(3–8)	444	5.6	(3–8)		
Germany	310	5.2	(3–8)	475	6.9	(5–10)	499	4.4	(3–7)	725	6.2	(3–8)		
Sweden	997	5.1	(4–7)	696	6.8	(5–9)	696	7.9	(6–10)	882	6.8	(5–9)		
Hungary	160	10.0	(6–16)	154	5.8	(3–11)	128	11.7	(7–19)	181	7.2	(6–16)		
United Kingdom	1153	4.9	(4–6)	1207	4.9	(4–6)	1288	5.1	(4–6)	1095	7.8	(4–6)		›
Latvia	64	6.3	(2–15)	67	11.9	(5–22)	48	4.2	(1–14)	59	8.5	(2–15)		
Slovenia	251	10.0	(7–14)	279	7.9	(5–12)	300	9.7	(7–14)	323	9.0	(7–14)		
Portugal	299	8.4	(5–12)	475	7.6	(5–10)	610	10.2	(8–13)	797	11.2	(5–12)		› #
Italy	141	12.1	(7–19)	268	14.6	(11–19)	183	15.3	(10–21)	389	12.3	(7–19)		
Finland	553	17.0	(14–20)	617	13.9	(11–17)	593	12.5	(10–15)	677	12.7	(14–20)		‹
Lithuania	37	16.2	(6–32)	59	23.7	(14–37)	67	16.4	(8–27)	87	16.1	(6–32)		
Ireland	319	19.1	(15–24)	310	20.3	(16–25)	328	17.7	(14–22)	303	17.5	(15–24)		
Croatia	97	22.7	(15–32)	116	25.9	(18–35)	130	26.4	(19–35)	124	19.4	(13–27)		
Slovakia	20	5.0	(0–25)	28	10.7	(2–28)	29	20.7	(8–40)	27	22.2	(0–25)		
Bulgaria	21	28.6	(11–52)	28	21.4	(8–41)	32	25.0	(11–43)	35	22.9	(11–52)		
France	824	23.4	(21–26)	919	22.4	(20–25)	656	22.3	(19–26)	1068	22.9	(21–26)		
Spain	604	27.0	(23–31)	569	30.1	(26–34)	551	27.9	(24–32)	665	23.5	(23–31)		
Iceland	27	3.7	(0–19)	18	16.7	(4–41)	25	8.0	(1–26)	25	24.0	(0–19)	N/A	
Poland	121	23.1	(16–32)	167	32.3	(25–40)	130	29.2	(22–38)	217	24.4	(16–32)		
Malta	18	38.9	(17–64)	7	**	(**)	8	37.5	(9–76)	20	35.0	(17–64)	N/A	
Romania	44	38.6	(24–55)	44	25.0	(13–40)	45	46.7	(32–62)	41	39.0	(24–55)		
Cyprus	8	**	(**)	15	40.0	(16–68)	12	0.0	(0–26)	7	**	(**)	N/A	

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

**Resistance percentage not calculated as total number of isolates was <10.

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

Table 3.27. ***Streptococcus pneumoniae*. Total number of tested isolates (N) and percentages non-susceptible to macrolides (%IR), including 95 % confidence intervals (95 % CI), by country, EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015			Trend 2012–2015	
	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)		Comment*
Luxembourg	38	15.8	(6–31)	49	26.5	(15–41)	35	14.3	(5–30)	29	0.0	(0–12)		‹
Netherlands	1153	4.4	(3–6)	1155	4.8	(4–6)	1287	4.3	(3–6)	1168	3.9	(3–5)		
Denmark	867	6.0	(5–8)	789	4.8	(3–7)	709	6.6	(5–9)	747	5.2	(4–7)		
Sweden	1030	4.9	(4–6)	1164	6.5	(5–8)	788	6.7	(5–9)	878	6.6	(5–9)		
Czech Republic	274	7.7	(5–11)	333	8.7	(6–12)	274	7.7	(5–11)	284	6.7	(4–10)		
Latvia	64	4.7	(1–13)	66	1.5	(0–8)	49	4.1	(0–14)	58	6.9	(2–17)		
United Kingdom	1114	6.8	(5–8)	935	7.5	(6–9)	1260	7.1	(6–9)	1077	7.2	(6–9)		
Estonia	52	5.8	(1–16)	59	3.4	(0–12)	54	5.6	(1–15)	54	7.4	(2–18)		
Germany	324	7.4	(5–11)	481	10.6	(8–14)	494	7.1	(5–10)	724	8.1	(6–10)		
Austria	319	17.9	(14–23)	421	10.2	(7–14)	400	10.5	(8–14)	439	8.7	(6–12)		‹
Norway	533	5.3	(4–8)	499	4.4	(3–7)	492	7.5	(5–10)	403	10.7	(8–14)		›
Hungary	147	19.7	(14–27)	139	14.4	(9–21)	123	14.6	(9–22)	170	11.2	(7–17)		‹ #
Iceland	27	7.4	(1–24)	18	16.7	(4–41)	24	12.5	(3–32)	25	12.0	(3–31)	N/A	
Lithuania	35	25.7	(12–43)	56	25.0	(14–38)	62	22.6	(13–35)	72	12.5	(6–22)		
Finland	586	22.0	(19–26)	657	18.6	(16–22)	636	14.5	(12–17)	765	14.4	(12–17)		‹
Ireland	307	16.9	(13–22)	305	18.0	(14–23)	317	13.9	(10–18)	296	15.5	(12–20)		
Portugal	308	18.5	(14–23)	496	20.6	(17–24)	658	16.0	(13–19)	822	17.0	(15–20)		
Croatia	97	28.9	(20–39)	116	32.8	(24–42)	130	27.7	(21–36)	126	18.4	(13–26)		‹ #
Belgium	1662	25.4	(23–28)	1574	22.9	(21–25)	1108	17.9	(16–20)	1361	18.7	(17–21)		‹ #
Slovenia	250	21.2	(16–27)	279	10.4	(7–15)	300	19.3	(15–24)	323	18.9	(15–24)		
Bulgaria	20	20.0	(6–44)	27	18.5	(6–38)	30	26.7	(12–46)	33	21.2	(9–39)		
Spain	579	26.4	(23–30)	560	25.7	(22–30)	544	20.0	(17–24)	631	23.5	(20–27)		
France	824	28.9	(26–32)	919	29.8	(27–33)	656	23.0	(20–26)	1068	24.4	(22–27)		‹ #
Italy	243	34.2	(28–40)	394	24.6	(20–29)	252	28.6	(23–35)	428	24.5	(21–29)		‹ #
Romania	43	39.5	(25–56)	42	38.1	(24–54)	50	48.0	(34–63)	20	30.0	(12–54)		
Poland	110	27.3	(19–37)	142	31.7	(24–40)	121	29.8	(22–39)	206	31.1	(25–38)		
Slovakia	22	27.3	(11–50)	29	17.2	(6–36)	29	41.4	(24–61)	34	35.3	(20–54)		
Malta	18	50.0	(26–74)	9	**	(**)	8	**	(**)	20	40.0	(19–64)	N/A	
Cyprus	7	**	(**)	15	26.7	(8–55)	12	0.0	(0–28)	7	**	(**)	N/A	

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

**Resistance percentage not calculated as total number of isolates was ‹ 10.

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

Table 3.28. ***Streptococcus pneumoniae*. Total number of tested isolates (N) and percentages non-susceptible to penicillins and macrolides (%IR), including 95 % confidence intervals (95 % CI), by country, EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)	N	%IR	(95% CI)			Comment*
Luxembourg	30	3.3	(0–17)	44	11.4	(4–25)	32	6.3	(1–21)	27	0.0	(0–13)			
Belgium	1614	1.2	(1–2)	1534	0.9	(0–2)	1069	0.7	(0–1)	1361	0.4	(0–1)			‹ #
Netherlands	972	0.8	(0–2)	921	0.4	(0–1)	1025	1.2	(1–2)	1030	0.9	(0–2)			
Czech Republic	274	1.8	(1–4)	333	1.2	(0–3)	274	3.3	(2–6)	284	1.8	(1–4)			
Hungary	147	7.5	(4–13)	139	3.6	(1–8)	123	7.3	(3–13)	170	1.8	(0–5)			
Latvia	64	1.6	(0–8)	66	0.0	(0–5)	46	4.3	(1–15)	53	1.9	(0–10)			
Denmark	867	3.5	(2–5)	789	4.2	(3–6)	709	3.9	(3–6)	747	2.4	(1–4)			
Austria	262	4.2	(2–7)	380	1.6	(1–3)	351	2.8	(1–5)	433	2.5	(1–4)			
Germany	308	1.3	(0–3)	467	2.6	(1–4)	491	1.4	(1–3)	714	2.5	(2–4)			
Norway	533	3.2	(2–5)	497	1.4	(1–3)	490	2.2	(1–4)	403	2.5	(1–5)			
United Kingdom	1029	3.3	(2–5)	867	3.1	(2–4)	1190	2.9	(2–4)	1060	2.7	(2–4)			
Estonia	34	0.0	(0–10)	59	0.0	(0–6)	54	1.9	(0–10)	27	3.7	(0–19)			
Sweden	997	3.1	(2–4)	694	3.2	(2–5)	693	4.2	(3–6)	764	3.7	(3–5)			
Slovenia	250	4.8	(3–8)	279	2.9	(1–6)	300	4.7	(3–8)	323	5.0	(3–8)			
Italy	116	10.3	(5–17)	248	8.1	(5–12)	163	11.0	(7–17)	347	5.8	(4–9)			
Portugal	278	6.5	(4–10)	467	4.3	(3–7)	601	5.8	(4–8)	776	6.6	(5–9)			
Finland	532	10.7	(8–14)	599	7.7	(6–10)	570	6.5	(5–9)	654	7.0	(5–9)			‹
Croatia	97	16.5	(10–25)	116	15.5	(9–23)	116	10.3	(5–17)	126	7.9	(4–14)			‹ #
Iceland	26	3.8	(0–20)	18	16.7	(4–41)	24	8.3	(1–27)	25	8.0	(1–26)		N/A	
Ireland	307	12.4	(9–17)	305	13.1	(10–17)	317	11.4	(8–15)	296	10.8	(8–15)			
Lithuania	35	14.3	(5–30)	56	14.3	(6–26)	62	16.1	(8–28)	72	11.1	(5–21)			
Spain	551	15.1	(12–18)	556	16.0	(13–19)	526	12.2	(9–15)	624	12.0	(10–15)			‹
Bulgaria	20	20.0	(6–44)	26	7.7	(1–25)	30	10.0	(2–27)	32	12.5	(4–29)			
France	824	17.2	(15–20)	919	18.9	(16–22)	656	15.9	(13–19)	1068	17.4	(15–20)			
Poland	110	16.4	(10–25)	139	24.5	(18–32)	119	24.4	(17–33)	195	19.5	(14–26)			
Slovakia	20	5.0	(0–25)	28	7.1	(1–24)	26	19.2	(7–39)	27	22.2	(9–42)			› #
Malta	18	38.9	(17–64)	7	**	(**)	8	**	(**)	20	25.0	(9–49)		N/A	
Romania	43	32.6	(19–49)	42	21.4	(10–37)	45	37.8	(24–53)	20	25.0	(9–49)			
Cyprus	7	**	(**)	15	26.7	(8–55)	11	0.0	(0–28)	7	**	(**)		N/A	

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

**Resistance percentage not calculated as total number of isolates was ‹ 10.

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

Most EU/EEA Member States have implemented routine immunisation for children with the multivalent pneumococcal conjugate vaccines (PCVs), and in some instances they also target adult high-risk groups, such as the elderly and the immunocompromised, with the polysaccharide vaccine [27].

Data from the IPD network have shown that the highest IPD notification rates were among children under one year of age and among adults 65 years and over, providing supporting scientific evidence for the recommendations for targeting these age groups for vaccination. Increased immunisation and better serotype coverage of the available PCVs are likely to impact the epidemiology of IPD in Europe, both in terms of changes in age-specific incidence and potential serotype replacement. Continued surveillance of IPD in Europe is therefore essential to monitor serotype replacement and the prevalence of antimicrobial-resistant strains to document changes in characteristics of the disease, guide treatment decisions, and inform future vaccine development. The IPD surveillance initiatives within ECDC are currently being harmonised to make the best use of available data.

3.6 *Staphylococcus aureus*

3.6.1 Clinical and epidemiological importance

Staphylococcus aureus is a gram-positive bacterium that frequently colonises the nasal vestibule and the skin of healthy humans. However, *S. aureus* is an opportunistic microorganism and can cause severe infection. Its oxacillin-resistant form (meticillin-resistant *S. aureus*, MRSA) has been the most important cause of antimicrobial-resistant healthcare-associated infections worldwide. Most healthcare-associated MRSA in Europe belong to only five clonal lineages, which have distinctive geographical patterns of occurrence, whereas the background populations of meticillin-susceptible S. aureus (MSSA) are highly diverse, consisting of many lineages that have been widely disseminated. In addition to healthcare-associated infections, MRSA infections may spread and occur in the community. MRSA also occurs in livestock animals, from where it can be transmitted to humans as LA-MRSA (livestock-associated MRSA).

MRSA infections add to, rather than replace, infections caused by MSSA. A high incidence of MRSA thus adds to the overall clinical and economic burden in hospitals, causing prolonged hospital stay and higher mortality, mainly due to delayed initiation of appropriate therapy and less effective alternative treatment regimens.

3.6.2 Resistance mechanisms

S. aureus acquires resistance to meticillin and all other beta-lactam agents through expression of the exogenous *mecA* gene. It codes for a variant penicillin-binding protein (PBP2a) with low affinity for beta-lactams, thus preventing the inhibition by beta-lactams of cell wall synthesis. In some methicillin/oxacillin resistant *mecA*-negative MRSA, a novel *mec* gene, *mecC* (formerly called $mecA_{lga251}$), was described in 2010.

The level of meticillin resistance, as defined by the MIC, depends on the amount of PBP2' production. The PBP2' production is influenced by various genetic factors. Resistance levels of *mec*-positive strains can thus occasionally range from phenotypically susceptible to highly resistant. Upon challenge with beta-lactam agents, a highly resistant subpopulation may rapidly be selected from a heterogeneously resistant MRSA population.

MRSA strains are variably resistant to other antibiotics, including fluoroquinolones, macrolides, lincosamides, rifampicin and tetracycline. Resistance to trimethoprim-sulphamethoxazole and anti-MRSA agents (glycopeptides, oxazolidinones, daptomycin, tigecycline and the new anti-MRSA cephalosporins) remains uncommon.

3.6.3 Antimicrobial susceptibility

- Wide inter-country variations in the occurrence of MRSA were evident across Europe, with percentages ranging from zero to 57.2%. MRSA percentages were generally lower in northern Europe and higher in the southern and south-eastern parts.
- The EU/EEA population-weighted mean MRSA percentage continued to decrease significantly from 18.8% in 2011 to 16.8% in 2015.

Beta-lactams

For 2015, 30 countries reported 45 364 isolates with AST information or molecular information sufficient to discern MRSA.

The percentages of MRSA isolates ranged from zero (Iceland) to 57.2 % (Romania). Trends for the period 2012–2015 were calculated for the 30 countries reporting at least 20 isolates per year during the full four-year period. A significantly increasing trend was observed for Slovakia, a trend that also remained significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for seven countries (Belgium, France, Germany, Ireland, Poland, Portugal and the United Kingdom). For Belgium, the trend did not remain significant when only data from laboratories reporting for the whole period were considered.

The EU/EEA population-weighted mean percentage for MRSA decreased significantly from 18.8 % in 2012 to 16.8 % in 2015.

Resistance to other antimicrobial groups

AST data for fluoroquinolones (ciprofloxacin, levofloxacin, norfloxacin or ofloxacin) were available for a total of 40 068 isolates (85.2 % of all reported *S. aureus* isolates) in 2015. Overall, 19.5 % *S. aureus* isolates were resistant to fluoroquinolones. Among isolates with information sufficient to discern MRSA and MSSA and results of antimicrobial susceptibility testing for fluoroquinolones (85.6 % of all isolates with MRSA/MSSA information), 85.2 % of the MRSA isolates were also resistant to fluoroquinolones, while only 6.7 % of the MSSA isolates were resistant to fluoroquinolones.

AST data for linezolid were available for a total of 34 277 isolates (75.6 % of all reported *S. aureus* isolates) in 2015. Resistance for linezolid was very low (0.1 %).

3.6.4 Discussion and conclusions

MRSA percentages in the EU/EEA continued to decline in 2015 and reached their lowest level since population-weighted data for EU/EEA were first presented in 2009. Despite this positive development, MRSA remains a public health priority in Europe, as MRSA percentages remain high in several countries. MRSA isolates are often also resistant to fluoroquinolones, further limiting the treatment options available for severe infections.

In order to further reduce the spread of MRSA in Europe, comprehensive MRSA strategies targeting all health-care sectors (acute care, long-term care and ambulatory care) remain essential. Despite MRSA still being a major cause of healthcare-associated infections, community-associated MRSA are increasingly being reported from many parts of the world, including Europe. In addition, the proportion of community-onset infections caused by MRSA clones that are usually associated with health-care-associated infections has increased, indicating transfer of healthcare-associated MRSA clones into the community [28].

Figure 3.22. *Staphylococcus aureus*. Percentage (%) of invasive isolates with resistance to meticillin (MRSA), by country, EU/EEA countries, 2015

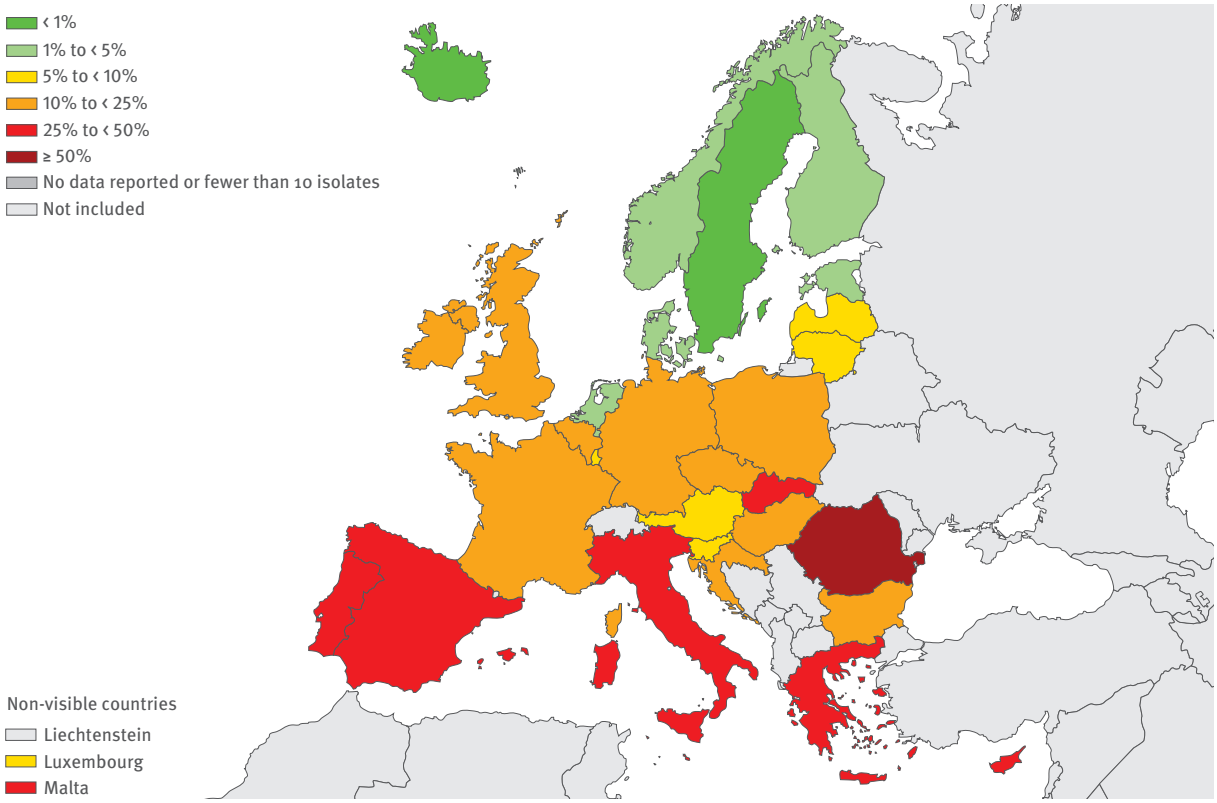


Table 3.29. ***Staphylococcus aureus*. Total number of invasive isolates tested (N) and percentage with resistance to meticillin (MRSA) including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Iceland	58	1.7	(0–9)	69	0.0	(0–5)	61	3.3	(0–11)	88	0.0	(0–4)			
Sweden	3263	0.7	(0–1)	4099	1.0	(1–1)	2745	1.0	(1–1)	3124	0.8	(1–1)			
Norway	1430	1.3	(1–2)	1473	0.7	(0–1)	1544	1.0	(1–2)	1453	1.2	(1–2)			
Netherlands	1944	1.3	(1–2)	2062	1.2	(1–2)	2524	1.0	(1–1)	2107	1.3	(1–2)			
Denmark	1431	1.3	(1–2)	1685	1.7	(1–2)	1874	2.5	(2–3)	1876	1.6	(1–2)			
Finland	1409	2.1	(1–3)	1580	1.8	(1–3)	1831	2.6	(2–3)	2070	1.9	(1–3)			
Estonia	104	7.7	(3–15)	170	3.5	(1–8)	223	3.1	(1–6)	151	4.0	(1–8)			
Latvia	211	9.0	(6–14)	172	7.0	(4–12)	220	8.2	(5–13)	251	5.6	(3–9)			
Austria	2164	7.7	(7–9)	2534	9.2	(8–10)	2651	7.8	(7–9)	2785	7.5	(7–9)			
Lithuania	323	10.2	(7–14)	267	9.7	(6–14)	383	7.8	(5–11)	376	8.5	(6–12)			
Luxembourg	131	15.3	(10–23)	135	8.9	(5–15)	125	12.0	(7–19)	135	8.9	(5–15)			
Slovenia	445	10.3	(8–14)	465	9.0	(7–12)	495	13.1	(10–16)	513	9.2	(7–12)			
United Kingdom	2676	14.0	(13–15)	2117	13.7	(12–15)	2400	11.3	(10–13)	2757	10.8	(10–12)			‹
Germany	2563	15.4	(14–17)	3128	12.8	(12–14)	3146	12.9	(12–14)	4871	11.2	(10–12)			‹
Belgium	1568	16.6	(15–19)	1612	16.9	(15–19)	988	13.5	(11–16)	913	12.3	(10–15)			‹ #
Bulgaria	227	19.8	(15–26)	214	19.2	(14–25)	216	20.8	(16–27)	222	13.1	(9–18)			
Czech Republic	1611	13.0	(11–15)	1707	13.2	(12–15)	1695	13.0	(11–15)	1806	13.7	(12–15)			
France	5228	19.2	(18–20)	5431	17.1	(16–18)	5484	17.4	(16–18)	5535	15.7	(15–17)			‹
Poland	783	25.4	(22–29)	743	16.0	(13–19)	490	20.6	(17–24)	958	15.8	(14–18)			‹
EU/EEA (population-weighted mean)	**36989**	**18.8**	**(18–19)**	**40976**	**18.1**	**(18–18)**	**40910**	**17.5**	**(17–18)**	**45364**	**16.8**	**(17–17)**			‹
Ireland	1038	22.6	(20–25)	1069	19.9	(18–22)	1075	19.4	(17–22)	1057	18.1	(16–21)			‹
Croatia	403	21.3	(17–26)	520	24.0	(20–28)	484	21.3	(18–25)	486	24.5	(21–29)			
Hungary	1143	24.8	(22–27)	1200	24.0	(22–27)	1279	23.1	(21–25)	1517	24.7	(23–27)			
Spain	1899	24.2	(22–26)	1777	22.6	(21–25)	1920	22.1	(20–24)	1970	25.3	(23–27)			
Slovakia	474	21.7	(18–26)	552	26.6	(23–31)	640	28.0	(25–32)	583	28.1	(25–32)			›
Italy	1636	35.2	(33–38)	2394	35.8	(34–38)	2134	33.6	(32–36)	3000	34.1	(32–36)			
Greece	876	41.0	(38–44)	757	40.3	(37–44)	556	37.1	(33–41)	612	39.4	(35–43)			
Cyprus	165	35.2	(28–43)	157	32.5	(25–40)	136	36.0	(28–45)	143	43.4	(35–52)			
Portugal	1455	53.8	(51–56)	2390	46.8	(45–49)	3193	47.4	(46–49)	3619	46.8	(45–48)			‹
Malta	102	47.1	(37–57)	114	51.8	(42–61)	82	42.7	(32–54)	89	48.3	(38–59)			
Romania	229	53.3	(47–60)	383	64.5	(59–69)	316	56.0	(50–62)	297	57.2	(51–63)			

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

3.7 Enterococci

3.7.1 Clinical and epidemiological importance

Enterococci belong to the normal microbiota of the gastrointestinal tract of humans and animals. Enterococci are regarded harmless commensals, however they can cause invasive diseases when the commensal relationship with the host is disrupted. Enterococci can cause a variety of infections, including endocarditis, bloodstream infections, and urinary tract infections, and are associated with peritonitis and intra-abdominal abscesses.

The vast majority of clinical enterococcal infections in humans are caused by *Enterococcus faecalis* and *E. faecium*. Epidemiological data collected over the last two decades have documented the emergence of enterococci as important nosocomial pathogens.

3.7.2 Resistance mechanisms

Enterococci are intrinsically resistant to a broad range of antimicrobial agents, including cephalosporins, sulphonamides and aminoglycosides at therapeutic concentrations. Patient safety in hospitals is challenged by the ability of enterococci to acquire additional resistance through the transfer of plasmids and transposons, or mutation.

Beta-lactams

By nature, enterococci have low susceptibility to many beta-lactam agents as a consequence of their low-affinity penicillin-binding proteins (PBPs). Two possible mechanisms of resistance of enterococci to beta-lactams have been reported: the production of a beta-lactamase, which is an extremely rare finding, and the overproduction and modification of PBPs, particularly PBP5, which causes high-level aminopenicillins resistance in *E. faecium*. Resistance to aminopenicillins is currently rare in *E. faecalis*. Therefore, the first choice for treatment of infections caused by this microorganism is still an aminopenicillin such as ampicillin. In *E. faecium*, ampicillin resistance has increased significantly in recent years due to the wide dissemination of ampicillin-resistant strains.

Aminoglycosides

In addition to the intrinsic low-level resistance to aminoglycosides due to low uptake of the drug, enterococci have acquired genes conferring high-level resistance to aminoglycosides. High-level resistance to streptomycin can be mediated by single mutations within a protein of the 30S ribosomal subunit, the target of aminoglycoside activity. In addition, several different aminoglycoside-modifying enzymes have been identified, targeting various amino and hydroxyl groups on aminoglycoside molecules. The bifunctional APH(2'')/AAC(6') enzyme confers high-level resistance to all aminoglycosides except streptomycin and is now widespread across Europe. With high-level aminoglycoside resistance, any synergistic effect between beta-lactams and aminoglycosides is lost.

Glycopeptides

Glycopeptide resistance is due to the synthesis of modified cell wall precursors that show a decreased affinity for glycopeptides. Two genotypes have clinical relevance: VanA, with high-level resistance to vancomycin and a variable level of resistance to teicoplanin; and VanB, with a variable level of resistance to vancomycin only. The VanA and VanB phenotypes, mostly found among *E. faecalis* and *E. faecium*, may be transferred by plasmids and through conjugative transposons.

3.7.3 Antimicrobial susceptibility

- Although no significant difference in high-level gentamicin resistance in *E. faecalis* was observed at the EU/EEA level between 2012 and 2015, national resistance percentages decreased in nearly a third of the countries during the same period.
- For vancomycin-resistant *E. faecium*, a significant increase was observed in 12 of 26 countries. Although the increase at the EU/EEA level (from 8.1% in 2012 to 8.3% in 2015) was not statistically significant, vancomycin resistance needs to be monitored carefully.

Enterococcus faecalis

High-level gentamicin resistance

For 2015, 27 countries reported 10 665 isolates with AST information on high-level gentamicin resistance. The number of isolates reported per country ranged from 21 to 1 249.

The EU/EEA population-weighted mean percentage for high-level gentamicin resistance was 31.3 % in 2015 and has not changed significantly since 2012.

Among the 27 countries reporting 10 isolates or more, the percentages of high-level gentamicin resistance ranged from 8.6 % (Cyprus) to 49.1 % (Slovakia). Trends for the period 2012–2015 were calculated for the 24 countries that reported at least 20 isolates per year during the full four-year period. A significantly decreasing trend was observed for seven countries (Belgium, France, Germany, Greece, Hungary, Norway and Portugal). For Belgium, Germany and Portugal, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years. None of the countries reported a significantly increasing trend.

Figure 3.23. ***Enterococcus faecalis*. Percentage (%) of invasive isolates with high-level resistance to gentamicin, by country, EU/EEA countries, 2015**

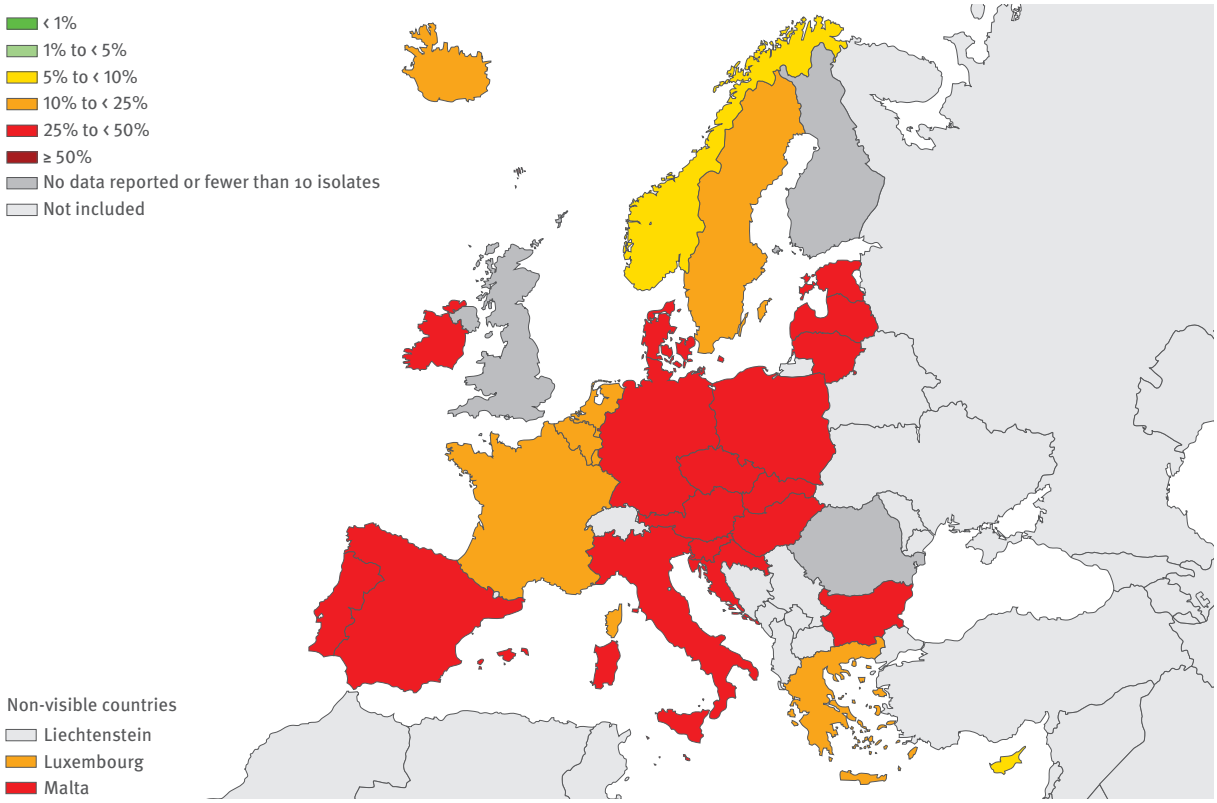


Figure 3.24. ***Enterococcus faecium*. Percentage (%) of invasive isolates with resistance to vancomycin, by country, EU/EEA countries, 2015**

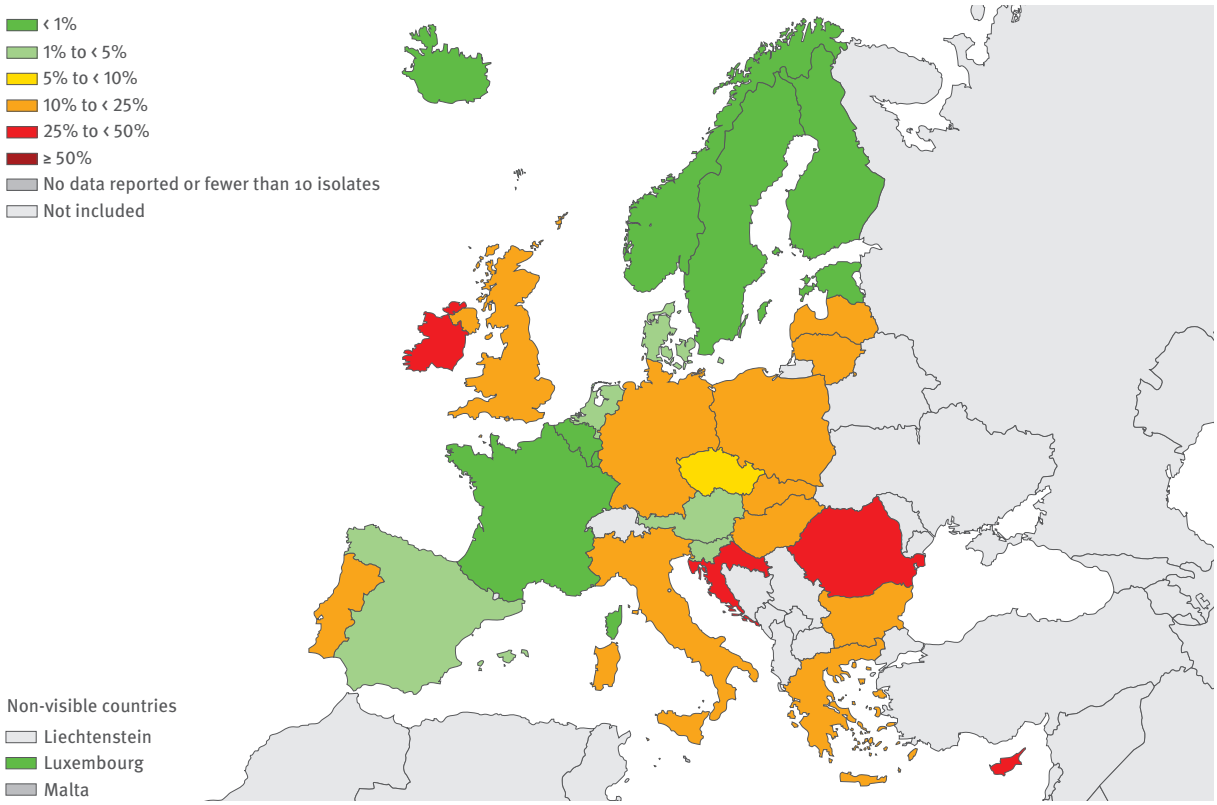


Table 3.30. ***Enterococcus faecalis.*** **Total number of invasive isolates tested (N) and percentage with high-level resistance to gentamicin including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

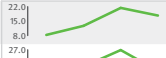
Country	2012			2013			2014			2015			Trend 2012–2015	
	N	%R	(95%CI)	N	%R	(95%CI)	N	%R	(95%CI)	N	%R	(95%CI)		Comment*
Cyprus	77	10.4	(5–19)	67	26.9	(17–39)	80	17.5	(10–28)	58	8.6	(3–19)		
Norway	123	30.1	(22–39)	168	26.8	(20–34)	270	20.7	(16–26)	163	9.8	(6–15)		‹
France	1528	16.7	(15–19)	1639	14.7	(13–17)	1741	13.7	(12–15)	1097	12.2	(10–14)		‹
Sweden	791	14.8	(12–17)	605	16.4	(14–20)	723	15.8	(13–19)	579	12.6	(10–16)		
Belgium	395	24.6	(20–29)	398	27.6	(23–32)	170	22.9	(17–30)	249	13.3	(9–18)		‹ #
Greece	667	28.3	(25–32)	548	23.5	(20–27)	407	20.1	(16–24)	460	13.3	(10–17)		‹
Iceland	17	11.8	(1–36)	15	33.3	(12–62)	12	8.3	(0–38)	21	14.3	(3–36)	N/A	
Luxembourg	45	22.2	(11–37)	36	27.8	(14–45)	39	30.8	(17–48)	56	14.3	(6–26)		
Netherlands	287	30.7	(25–36)	279	26.9	(22–32)	403	28.8	(24–33)	343	23.0	(19–28)		
Denmark	112	27.7	(20–37)	48	27.1	(15–42)	60	30.0	(19–43)	63	25.4	(15–38)		
Estonia	19	42.1	(20–67)	10	20.0	(3–56)	19	36.8	(16–62)	26	26.9	(12–48)	N/A	
Malta	25	40.0	(23–59)	31	29.0	(16–47)	28	25.0	(13–43)	29	27.6	(15–46)		
Ireland	279	32.6	(27–38)	277	32.1	(27–38)	290	31.4	(26–37)	261	28.0	(23–34)		
Germany	680	35.6	(32–39)	836	39.7	(36–43)	903	33.6	(30–37)	1249	31.1	(29–34)		‹ #
EU/EEA (population-weighted mean)	**8989**	**29.6**	**(29–31)**	**9815**	**31.2**	**(30–32)**	**9737**	**29.2**	**(28–30)**	**10665**	**31.3**	**(30–33)**		
Slovenia	129	34.9	(27–44)	146	32.2	(25–40)	119	36.1	(28–45)	133	32.3	(24–41)		
Portugal	347	42.9	(38–48)	545	37.2	(33–41)	607	32.6	(29–37)	872	33.3	(30–36)		‹ #
Austria	425	29.2	(25–34)	503	31.4	(27–36)	421	37.1	(32–42)	501	33.7	(30–38)		
Croatia	152	37.5	(30–46)	167	34.7	(28–42)	149	32.9	(25–41)	203	35.5	(29–42)		
Latvia	55	29.1	(18–43)	54	61.1	(47–74)	13	46.2	(19–75)	58	36.2	(24–50)	N/A	
Czech Republic	581	41.7	(38–46)	603	40.0	(36–44)	525	38.7	(34–43)	544	38.8	(35–43)		
Spain	878	38.3	(35–42)	899	42.6	(39–46)	970	38.9	(36–42)	936	40.0	(37–43)		
Bulgaria	78	38.5	(28–50)	102	47.1	(37–57)	105	40.0	(31–50)	100	42.0	(32–52)		
Lithuania	59	50.8	(37–64)	44	54.5	(39–70)	65	29.2	(19–42)	63	44.4	(32–58)		
Hungary	452	56.2	(51–61)	602	51.7	(48–56)	659	49.8	(46–54)	730	45.5	(42–49)		‹
Poland	122	45.9	(37–55)	184	45.1	(38–53)	148	43.9	(36–52)	388	46.4	(41–51)		
Italy	301	50.8	(45–57)	584	46.2	(42–50)	516	55.2	(51–60)	1249	47.8	(45–51)		
Slovakia	179	50.3	(43–58)	209	57.4	(50–64)	261	41.0	(35–47)	234	49.1	(43–56)		
Finland	–	–	(–)	–	–	(–)	–	–	(–)	–	–	(–)	N/A	
Romania	51	56.9	(42–71)	80	58.8	(47–70)	34	76.5	(59–89)	–	–	(–)	N/A	
United Kingdom	135	29.6	(22–38)	136	30.9	(23–39)	–	–	(–)	–	–	(–)	N/A	

–: No data

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

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

Table 3.31. ***Enterococcus faecium*****. Total number of invasive isolates tested (N) and percentage with resistance to vancomycin, including 95 % confidence intervals (95 % CI), EU/EEA countries, 2012–2015**

Country	2012			2013			2014			2015				Trend 2012–2015	
	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)	N	%R	(95% CI)			Comment*
Estonia	40	0.0	(0–9)	40	0.0	(0–9)	48	0.0	(0–7)	27	0.0	(0–13)			
Iceland	12	0.0	(0–26)	17	5.9	(0–29)	11	0.0	(0–28)	20	0.0	(0–17)		N/A	
Luxembourg	20	0.0	(0–17)	19	5.3	(0–26)	31	3.2	(0–17)	23	0.0	(0–15)		N/A	
Norway	168	0.6	(0–3)	211	2.4	(1–5)	227	1.8	(0–4)	185	0.0	(0–2)			
Sweden	404	0.0	(0–1)	575	0.0	(0–1)	452	0.4	(0–2)	408	0.0	(0–1)			
Finland	274	0.7	(0–3)	304	0.3	(0–2)	368	0.0	(0–1)	298	0.3	(0–2)			
Belgium	212	1.4	(0–4)	235	1.7	(0–4)	195	3.1	(1–7)	163	0.6	(0–3)			
France	614	0.8	(0–2)	733	0.1	(0–1)	737	0.5	(0–1)	849	0.8	(0–2)			
Netherlands	484	0.0	(0–1)	439	0.5	(0–2)	532	1.1	(0–2)	572	1.4	(1–3)			›
Spain	537	1.5	(1–3)	553	0.9	(0–2)	546	2.4	(1–4)	571	2.5	(1–4)			›
Austria	376	3.2	(2–6)	437	5.9	(4–9)	480	4.4	(3–7)	483	3.1	(2–5)			
Denmark	593	2.0	(1–4)	644	3.4	(2–5)	715	4.5	(3–6)	690	3.2	(2–5)			
Slovenia	95	0.0	(0–4)	102	1.0	(0–5)	115	1.7	(0–6)	124	4.8	(2–10)			›
EU/EEA (population-weighted mean)	**7203**	**8.1**	**(7–9)**	**8307**	**9**	**(8–10)**	**8324**	**8.2**	**(8–9)**	**9123**	**8.3**	**(8–9)**			
Czech Republic	262	11.5	(8–16)	268	9.0	(6–13)	250	4.4	(2–8)	322	9.6	(7–13)			
Germany	647	16.2	(13–19)	855	14.6	(12–17)	882	9.1	(7–11)	1312	10.2	(9–12)			‹
Italy	435	6.0	(4–9)	563	4.4	(3–6)	472	8.5	(6–11)	756	11.2	(9–14)			›
Bulgaria	42	0.0	(0–8)	44	2.3	(0–12)	60	13.3	(6–25)	41	14.6	(6–29)			›
Slovakia	82	4.9	(1–12)	132	7.6	(4–13)	129	10.1	(5–17)	143	14.7	(9–22)			›
Hungary	142	3.5	(1–8)	210	7.1	(4–12)	224	8.5	(5–13)	240	16.7	(12–22)			›
United Kingdom	362	13.3	(10–17)	442	23.3	(19–28)	423	21.3	(17–25)	218	17.0	(12–23)			
Lithuania	37	5.4	(1–18)	25	0.0	(0–14)	44	4.5	(1–15)	52	17.3	(8–30)			›
Latvia	18	5.6	(0–27)	25	12.0	(3–31)	15	13.3	(2–40)	34	17.6	(7–35)		N/A	
Poland	157	8.3	(4–14)	173	12.7	(8–19)	182	21.4	(16–28)	215	17.7	(13–23)			› #
Greece	418	17.2	(14–21)	345	21.2	(17–26)	264	26.9	(22–33)	315	19.7	(15–25)			
Portugal	257	23.3	(18–29)	350	22.0	(18–27)	363	20.1	(16–25)	459	20.3	(17–24)			
Romania	34	2.9	(0–15)	54	11.1	(4–23)	56	25.0	(14–38)	72	25.0	(16–37)			›
Croatia	60	0.0	(0–6)	74	6.8	(2–15)	67	10.4	(4–20)	93	25.8	(17–36)			›
Cyprus	29	10.3	(2–27)	30	23.3	(10–42)	35	40.0	(24–58)	28	28.6	(13–49)			›
Ireland	386	44.0	(39–49)	398	42.7	(38–48)	390	45.1	(40–50)	404	45.8	(41–51)			
Malta	6	~	(~)	10	0.0	(0–31)	11	0.0	(0–28)	6	~	(~)	~	N/A	

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

**Resistance percentage not calculated as total number of isolates was ‹ 10.

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

Enterococcus faecium

Vancomycin

For 2015, 30 countries reported 9123 isolates with AST information on vancomycin. The number of isolates reported per country ranged from 6 to 1312.

Among the 29 countries reporting 10 isolates or more, the percentages of vancomycin resistance ranged from zero (Estonia, Iceland, Luxembourg, Norway and Sweden) to 45.8% (Ireland). Trends for the period 2012–2015 were calculated for the 26 countries that reported at least 20 isolates per year during the full four-year period. A significantly increasing trend was observed for 12 countries (Bulgaria, Croatia, Cyprus, Hungary, Italy, Lithuania, the Netherlands, Poland, Romania, Slovakia, Slovenia and Spain). For Poland, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. A significantly decreasing trend was observed for Germany, a trend that remained significant when only data from laboratories reporting for the whole period were considered.

The EU/EEA population-weighted mean percentage for vancomycin resistance was 8.3% in 2015 and has not changed significantly since 2012.

3.7.4 Discussion and conclusions

Although the EU/EEA trend for high-level aminoglycoside resistance in *E. faecalis* did not change significantly during the period, significant decreasing trends were reported from almost one third of the countries.

By contrast, a significant increase in the percentage of vancomycin-resistant *E. faecium* invasive isolates was observed in 12 of the 26 countries that reported more than 20 isolates per year between 2012 and 2015. Although the increase at the EU/EEA level (from 8.1% in 2012 to 8.3% in 2015) was not statistically significant, trends for individual countries may indicate a change in the epidemiology of vancomycin-resistant *E. faecium* in Europe.

The further development of resistance in enterococci, especially to vancomycin, requires close attention. Enterococci have intrinsic resistance to several antimicrobial classes and the ability to acquire additional resistance, which severely limits the number of treatment options. High levels of antimicrobial-resistant enterococci remain a major infection control challenge and an important cause of healthcare-associated infections in Europe. Besides the fact that infections caused by resistant strains are difficult to treat, enterococci easily disseminate in healthcare settings.

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Annexes

Annex 1. External quality assessment 2015

Since 2000, EARSS/EARS-Net have organised external quality assessments (EQA) of antimicrobial susceptibility testing in collaboration with the United Kingdom National External Quality Assessment Service (UK NEQAS). UK NEQAS is based at Public Health England in London and is a non-profit organisation with more than 40 years of experience in conducting EQAs in different countries.

The purpose of the EARS-Net EQA was to determine the accuracy of antimicrobial susceptibility test (AST) results reported by individual laboratories and thereby estimate the overall comparability of routinely collected test results between laboratories and countries across Europe. A panel of six lyophilised strains was prepared and found fully compliant during in-house quality control testing, and confirmed by two expert reference laboratories. The panel included one strain of each of the following species: *Enterococcus faecalis, Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli* and *Pseudomonas aeruginosa*, as agreed with ECDC. The strains were characterised and tested in two reference laboratories: Specialist Antimicrobial Chemotherapy Unit, Cardiff (UK), and EUCAST Reference and Development Laboratory, Växjö (Sweden). Both reference laboratories confirmed MICs and interpreted the results in accordance with the most frequently used breakpoint criteria (CLSI and EUCAST), as indicated in the summary for each species outlined in the results section below.

Results

The EQA panels were dispatched to a total of 974 participants in 30 countries. Participants were asked to report the identification of each organism and clinical susceptibility characterisation – susceptible, intermediate or resistant (S, I, R) – in accordance with the guideline used. The return rate was equivalent to previous years; 902 (92.6 %) laboratories returned reports. Figure A1.1 shows the proportion of participating laboratories returning results per country. Participants' results were analysed and considered concordant if the reported categorisation agreed with the interpretation of the reference laboratories.

Figure A1.1. Number of participating laboratories returning EQA reports 2015, by country

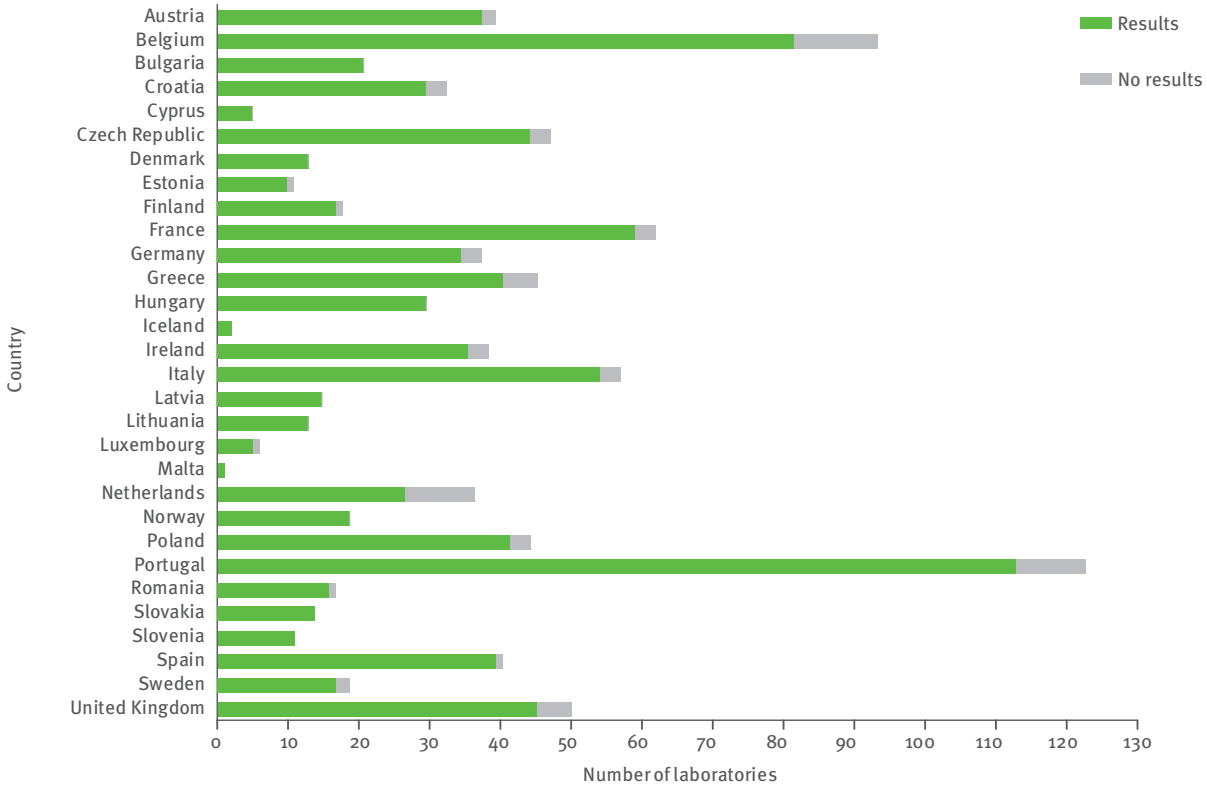
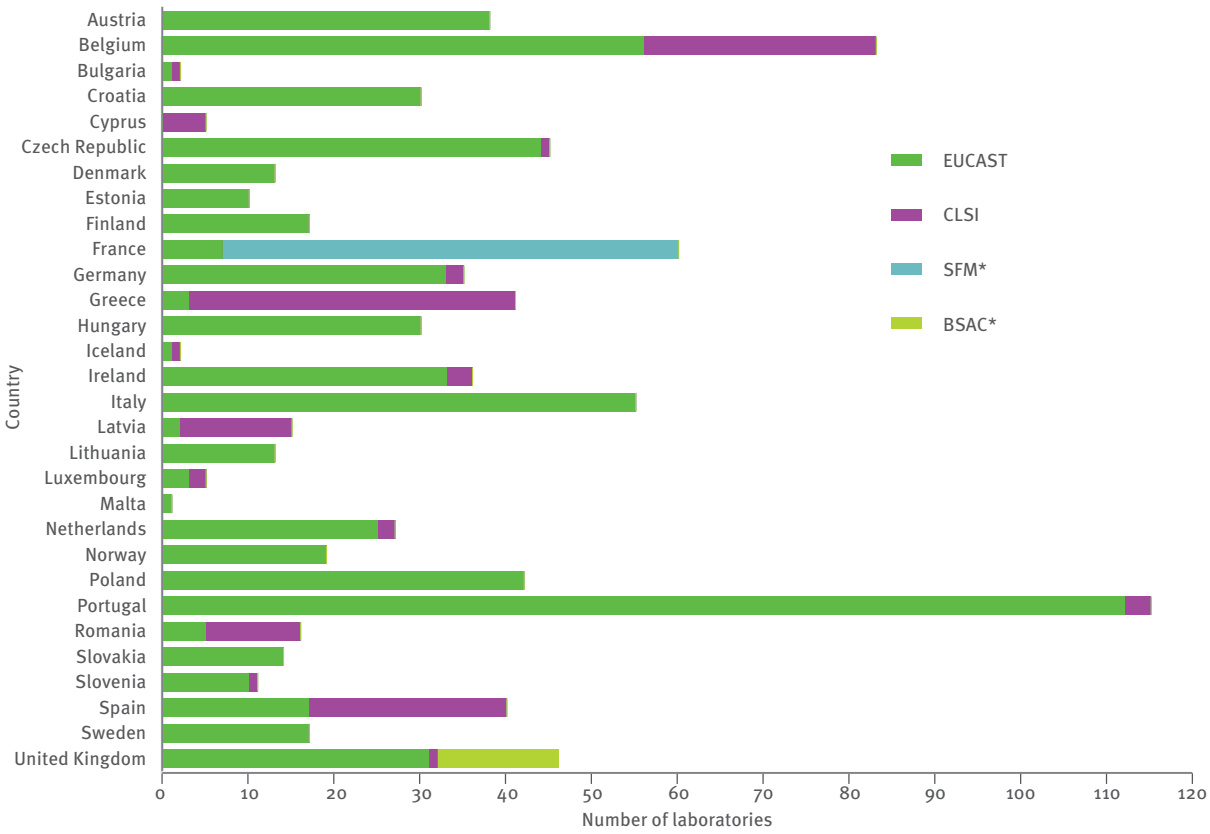


Figure A1.2. Clinical guidelines reported to be used by laboratories: number of laboratories per country, 2015



* National guidelines harmonised with EUCAST: BSAC: British Society for Antimicrobial Chemotherapy; SFM: Société Française de Microbiologie.

Table A1.1. *Enterococcus faecalis* (3 082). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC (mg/L)		Result	
	Reference laboratory 1	Reference laboratory 2	EUCAST/CLSI	Overall concordance (%)
Amoxicillin	–		S	97.6
Ampicillin	1		S	96.8
High-level resistance to gentamicin	› 512		Positive (detected)	94.3
Teicoplanin	0.25	0.5	S	98.7
Vancomycin	8		R/I	88.3

Table A1.2. Vancomycin susceptibility reports for *Enterococcus faecalis* specimen 3 082

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	11 (7.4)	4 (2.7)	133 (89.9)
	Automated	5 (1.8)	0	278 (98.2)
	MIC	15 (4.9)	8 (2.7)	281 (92.4)
	Multi/other	1	0	14
	Total	**32 (4.3)**	**12 (1.6)**	**706 (94.1)**
CLSI	Disk diffusion	6 (20.7)	9 (31.0)	14 (48.3)
	Automated	2 (2.8)	21 (29.6) 48 (67.6)	48 (67.6)
	MIC	5 (11.9)	17 (40.5)	20 (47.6)
	Multi/other	1	0	1
	Total	**14 (9.8)**	**47 (32.6)**	**83 (57.6)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Use of methods and clinical guidelines

For the determination of AST results, laboratories used automated methods (51.9%), disk diffusion tests (39.2%), MIC (7.9%), gradient strip, or a combination of methods (1.0%). For species identification, 79.5% used an automated instrument and 20.5% used conventional methods. Increased use of conventional methods was associated with identification of *S. pneumoniae*. There was an increase (23.5%) in the number of participants using an automated instrument to confirm the identity of the isolates compared to the EQA exercise in 2014.

Some 16.2% of laboratories applied CLSI guidelines; this represented a reduction from the previous year when the proportion was 19.6%. EUCAST guidelines were reported by 76.4% of laboratories. France (SFM) and the United Kingdom (BSAC) used national guidelines; however, both have been implementing EUCAST breakpoints in their national MIC breakpoint recommendations as harmonised breakpoints have been agreed, and have adjusted the interpretation of their disk diffusion methods accordingly. Therefore, a combined total of 83.8% of laboratories used EUCAST, or EUCAST-related, breakpoints. This represented an increase of 3.8% compared to 2014. Figure A1.2 shows the national and international guidelines used by laboratories in different countries.

Antimicrobial susceptibility results

Specimen 3082 – *Enterococcus faecalis*

This organism was an *Enterococcus faecalis* resistant to vancomycin (VanB), which also showed high-level resistance to gentamicin. Vancomycin MICs can be low for VanB strains, as in this case (MIC 8 mg/L), which means that according to EUCAST breakpoints the isolate would be interpreted as 'resistant'; if CLSI breakpoints were applied, the result would be 'intermediate'. Borderline susceptibility makes detection of reduced susceptibility more difficult, particularly if disk diffusion methods are used, where the difference in zone diameter between susceptible and resistant isolates may be small and the appearance of a fuzzy zone edge, or colonies just within the zone edge, may be the best indication of resistance. Reduced susceptibility to vancomycin was detected by 94.9% of 894 participants (5.1% reported susceptible, 6.6% intermediate and 88.3% resistant) (Table A1.1).

Failure to detect reduced susceptibility was more common among participants if they followed the CLSI guidelines rather than EUCAST and EUCAST-related guidelines. Failure was also more common among those using disk diffusion and MIC (mostly gradient) methods than among those using automated methods. In line with the differences in breakpoints between EUCAST and CLSI, participants following CLSI breakpoints were more likely to report intermediate resistance to vancomycin than participants following EUCAST guidelines (Table A1.2). As there is no intermediate category for vancomycin in EUCAST guidelines, it was clear that participants reporting 'intermediate' were following a different set of guidelines.

There were small numbers of incorrect reports of 'intermediate' or 'resistant' with regard to ampicillin (3.2% non-susceptible) and amoxicillin (2.4% non-susceptible). The MIC of ampicillin (1 mg/L) was typical for susceptible *E. faecalis* (amoxicillin was not included in reference tests). Resistance to ampicillin/amoxicillin in *E. faecalis* is very rare worldwide, and any isolate of *E. faecalis* appearing resistant to ampicillin or amoxicillin should be retested for identification and antimicrobial susceptibility. If resistance is confirmed, the isolate should be sent to a reference laboratory.

Specimen 3083 – *Klebsiella pneumoniae*

This organism was a *Klebsiella pneumoniae* which produces an OXA-48 carbapenemase that confers reduced susceptibility to carbapenems. OXA-48 hydrolyses third-generation cephalosporins very weakly or not at all. While the current isolate is susceptible to third-generation cephalosporins, OXA-48-producing strains are often resistant to cephalosporins due to the concomitant production of ESBLs (most commonly CTX-M). It is typical for OXA-48-producing isolates to be resistant to piperacillin + tazobactam and amoxicillin-clavulanic acid. Overall, 99.8% of 849 participants reported the isolate as piperacillin + tazobactam resistant, and all 840 participants reported the isolate as amoxicillin-clavulanic acid resistant. Susceptibility to third-generation cephalosporins was reduced compared with wild-type isolates, but the MICs, although borderline, were within the susceptible category. The borderline susceptibility was reflected in the high discrepancy rates for cefotaxime (64.3% of 788 participants reported susceptible, 27.4% intermediate and 8.3% resistant), ceftriaxone (79.6% of 388 participants reported susceptible, 13.9% intermediate and 6.5% resistant), and ceftazidime (84.1% of 876 participants reported susceptible, 11.3% intermediate and 4.6% resistant) (Table A1.3)

There was little overall difference among participants in the reporting of third-generation cephalosporins, regardless of observed guidelines, but participants that used disk diffusion methods were more likely to report 'intermediate' or 'resistant' to cefotaxime and ceftriaxone than those using automated or MIC methods (Tables A1.4 to A1.6).

OXA-48 carbapenemases generally hydrolyse carbapenems weakly. In the presence of OXA-48, MICs of carbapenems are commonly raised, often resulting in resistance to ertapenem, while the effect on other carbapenems is less pronounced, sometimes resulting in reports of intermediate or even susceptible. This isolate was resistant to ertapenem (MIC 8 mg/L), and 99.2% of 740 participants reported it as resistant. The isolate was borderline intermediate–resistant to imipenem (MIC 4-8 mg/L) by EUCAST breakpoints and resistant by CLSI breakpoints. This was reflected by the fact that reporting was variable (overall, 31.1% of 700 participants reported susceptible, 35.3% intermediate and 33.6% resistant).

Table A1.3. *Klebsiella pneumoniae* (3083). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC (mg/L)		Result	
	Reference laboratory 1	Reference laboratory 2	EUCAST/CLSI	Overall concordance (%)
Amikacin	1		S	99.5
Amoxicillin	≥ 128		R	98.9
Amoxicillin-clavulanic acid	≥ 128 (≥ 128)**		R	100
Ampicillin	≥ 128		R	99.9
Cefotaxime	1		S	64.3
Ceftazidime	0.5	1	S	84.1
Ceftriaxone	1		S	79.6
Ciprofloxacin	0.03		S	99.8
Ertapenem	8		R	99.2
Gentamicin	0.25	0.5	S	99.5
Imipenem	4	8	I/R	35.3
Levofloxacin	–		S*	99.6
Meropenem	2	4	I/(I/R)	38.5
Ofloxacin	–		S*	98.7
Piperacillin–tazobactam	≥ 128		R	99.8
Tobramycin	0.25	0.5	S	99.6

* Results based on participant consensus, as no reference laboratory results available for these organism/antibiotic combinations
** Amoxicillin-clavulanic acid MIC determined with a fixed 2mg/L concentration of clavulanic acid (with a 2:1 ratio of amoxicillin : clavulanic acid)

Table A1.4. Cefotaxime susceptibility reports for *Klebsiella pneumoniae* specimen 3083

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	97 (53.9)	60 (33.3)	23 (12.8)
	Automated	221 (69.5)	81 (25.5)	16 (5.0)
	MIC	98 (64.9)	43 (28.5)	10 (6.6)
	Multi/other	6	1	0
	Total	**422 (64.3)**	**185 (28.2)**	**49 (7.5)**
CLSI	Disk diffusion	15 (42.9)	15 (42.9)	5 (14.2)
	Automated	56 (74.6)	14 (18.7)	5 (6.7)
	MIC	14 (66.7)	2 (9.5)	5 (23.8)
	Multi/other	0	0	1
	Total	**85 (64.4)**	**31 (23.5)**	**16 (12.1)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.5. Ceftriaxone susceptibility reports for *Klebsiella pneumoniae* specimen 3083

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	97 (78.2)	19 (15.3)	8 (6.5)
	Automated	75 (81.5)	13 (14.1)	4 (4.4)
	MIC	80 (84.2)	10 (10.5)	5 (5.3)
	Multi/other	1	0	1
	Total	**253 (80.8)**	**42 (13.4)**	**7 (9.2)**
CLSI	Disk diffusion	19 (67.9)	7 (25.0)	2 (7.1)
	Automated	25 (80.6)	3 (9.7)	3 (9.7)
	MIC	12	2	2
	Multi/other	0	0	0
	Total	**56 (74.7)**	**12 (16.0)**	**7 (9.3)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.6. Ceftazidime susceptibility reports for *Klebsiella pneumoniae* specimen 3083

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	212 (86.5)	23 (9.4)	10 (4.1)
	Automated	290 (81.5)	51 (14.3)	15 (4.2)
	MIC	111 (88.8)	9 (7.2)	5 (4.0)
	Multi/other	7	0	0
	Total	**620 (84.6)**	**83 (11.3)**	**30 (4.1)**
CLSI	Disk diffusion	33 (82.5)	3 (7.5)	4 (10.0)
	Automated	70 (81.4)	13 (15.1)	3 (3.5)
	MIC	14	0	3
	Multi/other	0	0	0
	Total	**117 (81.8)**	**16 (11.2)**	**10 (7.0)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.7. Imipenem susceptibility reports for *Klebsiella pneumoniae* specimen 3083

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	63 (31.7)	92 (46.2)	44 (22.1)
	Automated	82 (31.2)	95 (36.1)	86 (32.7)
	MIC	41 (34.7)	48 (40.7)	29 (24.6)
	Multi/other	3	0	2
	Total	**189 (32.3)**	**235 (40.2)**	**161 (27.5)**
CLSI	Disk diffusion	3 (11.1)	1 (3.7)	23 (85.2)
	Automated	22 (33.8)	9 (13.9)	34 (52.3)
	MIC	4 (17.4)	2 (8.7)	17 (73.9)
	Multi/other	0	0	0
	Total	**29 (25.2)**	**12 (10.5)**	**74 (64.3)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.8. Meropenem susceptibility reports for *Klebsiella pneumoniae* specimen 3083

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	54 (24.2)	113 (50.7)	56 (25.1)
	Automated	142 (47.3)	110 (36.7)	48 (16.0)
	MIC	52 (33.1)	56 (35.7)	49 (31.2)
	Multi/other	2	2	2
	Total	**250 (36.4)**	**281 (41.0)**	**155 (22.6)**
CLSI	Disk diffusion	2 (4.9)	11 (26.8)	28 (68.3)
	Automated	24 (35.8)	16 (23.9)	27 (40.3)
	MIC	3 (15.0)	6 (30.0)	11 (55.0)
	Multi/other	0	0	1
	Total	**29 (22.5)**	**33 (25.6)**	**67 (51.9)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

A significant number of participants incorrectly reported the isolate as imipenem susceptible. In line with the differences in breakpoints, reports of intermediate were more common among participants following EUCAST or EUCAST-related guidelines, and reports of resistant were more common among those following CLSI guidelines. If CLSI guidelines were applied, reports of susceptible were more common among participants using automated methods than among those using other methods (Table A1.7).

The isolate was borderline susceptible–intermediate to meropenem (MIC 2-4 mg/L) according to EUCAST breakpoints, and intermediate–resistant according to CLSI breakpoints. This was again reflected by the fact that reporting was variable (34.2 % of 815 participants reported susceptible, 38.5 % intermediate and 27.3 % resistant). In line with differences in breakpoints, reports of the isolate as susceptible and intermediate were more common among participants following EUCAST or EUCAST-related guidelines, and reports of resistant were more common among those following CLSI guidelines. Reports of the isolate as susceptible were more common among participants using automated methods than among those using other methods (Table A1.8). Despite borderline susceptibility to meropenem, the presence of a carbapenemase in this isolate can be detected with the EUCAST carbapenemase screening breakpoint (meropenem MIC >0.25 mg/L).

Specimen 3084 – *Staphylococcus aureus*

This organism was a *Staphylococcus aureus* with low-level resistance to vancomycin and teicoplanin (or VISA) (Table A1.9). It was the same strain of VISA that was distributed in the EARS-Net EQA exercise in 2014, and there is little evidence of change in the participants' performance.

Detection of reduced susceptibility to glycopeptides in *S. aureus* is difficult, which was again reflected in the failure of many participants to detect reduced susceptibility. Of 877 participants reporting vancomycin susceptibility, only 41.6 % reported the isolate as resistant and 9.2 % as intermediate, while 49.2 % incorrectly reported the isolate as susceptible. This is very similar to reports in 2014, when 42.1 % of 819 participants reported the isolate as resistant, 9.8 % as intermediate and 48.1 % as susceptible. As noted in the 2014 report, isolates of *S. aureus* with vancomycin MICs of 4–8 mg/L were originally termed 'vancomycin-intermediate *S. aureus*' (VISA) because the level of resistance is low and is distinguishable from the high-level resistance displayed by *S. aureus* carrying the mecA gene (MICs >8 mg/L). While CLSI maintained this distinction, EUCAST does not have an intermediate category because VISA strains are clinically resistant to glycopeptides. Reports as susceptible were less frequent among the 738 participants that followed the EUCAST or EUCAST-related guidelines (48 % susceptible) than among the

Table A1.9. *Staphylococcus aureus* (3084). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC (mg/L)		Result	
	Reference laboratory 1	Reference laboratory 2	EUCAST/CLSI	Overall concordance (%)
Cefoxitin	≥ 128		R	99.9
Ciprofloxacin	16		R	99.5
Clindamycin	≥ 128		R	100
Erythromycin	≥ 128		R	99.9
Fusidic acid	0.06	0.12	S/–	99.2
Gentamicin	128	256	R	99.8
Oxacillin	≥ 128		R	100
Penicillin	64		R	100
Rifampicin	≥ 128		R	99.9
Teicoplanin	8	16	R/(S/I)	82.6
Tetracycline	64		R	98.2
Vancomycin	4		R/I	41.6

Table A1.10. Vancomycin susceptibility reports for *Staphylococcus aureus* specimen 3084

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion**	56 (40.3)	5 (3.6)	78 (56.1)
	Automated	172 (60.6)	9 (3.1)	103 (36.3)
	MIC	118 (39.3)	10 (3.3)	172 (57.4)
	Multi/other	8	2	5
	Total	**354 (48.0)**	**26 (3.5)**	**358 (48.5)**
CLSI	Disk diffusion	19 (73.1)	5 (19.2)	2 (7.7)
	Automated	38 (55.1)	26 (37.7)	5 (7.2)
	MIC	19 (45.2)	23 (54.8)	0 (0)
	Multi/other	1	1	0
	Total	**77 (55.4)**	**55 (39.6)**	**7 (5.0)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.
** As reported by laboratories. However, EUCAST and CLSI do not recommend disk diffusion for determining vancomycin susceptibility in *S. aureus*. EUCAST provides no disk diffusion breakpoints for vancomycin and *S. aureus*, and CLSI only lists susceptible disk diffusion interpretive criteria.

Table A1.11. Teicoplanin susceptibility reports for *Staphylococcus aureus* specimen 3084

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	11 (10.0)	2 (1.8)	97 (88.2)
	Automated	5 (1.6)	1 (0.3)	304 (98.1)
	MIC	7 (3.1)	2 (0.9)	218 (96.0)
	Multi/other	0	0	8
	Total	**23 (3.5)**	**5 (0.8)**	**627 (95.7)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

139 that relied on CLSI guidelines (55.4% susceptible) (Table A1.10). In line with the differences in breakpoints, most non-susceptible reports with CLSI guidelines were in the intermediate category (39.6% intermediate, 5.0% resistant) while reports based on EUCAST guidelines were mostly in the resistant category (3.5% intermediate, 48.5% resistant).

Reduced susceptibility to glycopeptides in *S. aureus* cannot be reliably detected by disk diffusion methods, and EUCAST, CLSI and BSAC disk diffusion methods all state that disk diffusion should not be used for *S. aureus*. In total, 165 participants that reported susceptibility to vancomycin stated that they used disk diffusion, but only 46 participants reported disk diffusion zone diameters; 143 reported an MIC value and set up an MIC test instead of, or together with, disk diffusion. Of 18 participants apparently ignoring international guidelines and, inappropriately, using only a disk diffusion method (report of zone diameter, no MIC), 16 (88.9%) incorrectly reported the isolate as vancomycin susceptible. Of the 143 participants that reported use of a disk diffusion method, but also reporting an MIC value, 39.9% reported the isolate as vancomycin susceptible, similar to the 40.1% of 342 participants reporting use of an MIC method. Of the 353 participants reporting use of an automated method, 59.8% reported the isolate as vancomycin susceptible. As already seen in 2014, MIC methods were the most reliable method for detecting reduced susceptibility. However, none of the methods performed well, and there was no evidence of improved performance with regard to the problems we pointed out a year ago: serious concerns remain regarding the ability of many participants to detect vancomycin resistance in VISA isolates. MICs of teicoplanin for VISA are usually higher than vancomycin MICs, and reduced susceptibility to glycopeptides may be more readily detected with teicoplanin than with vancomycin. There

are significant differences in breakpoints between EUCAST and CLSI. EUCAST breakpoints for teicoplanin are set to report all VISA isolates as teicoplanin resistant (S ‹2 mg/L, R ›2 mg/L), and among 627 participants following EUCAST or EUCAST-related guidelines, 3.5 % reported the isolate as teicoplanin susceptible, 0.8 % classified it as intermediate, and 95.7 % reported it as resistant. CLSI breakpoints are significantly higher (S ‹8 mg/L, R ›32 mg/L) and VISA isolates are borderline susceptible–intermediate. In line with the differences in breakpoints, among 126 participants following CLSI guidelines, 31.7 % reported the isolate as teicoplanin susceptible, 54.0 % as intermediate and 14.3 % as resistant. Similar results were seen with this isolate in the 2014 EQA exercise.

Laboratory performance for different methods for teicoplanin is shown in Table A1.11. In view of the significant differences in breakpoints, the analysis of the ability of different methods to detect reduced susceptibility to teicoplanin applies only to EUCAST and EUCAST-related guidelines. In total, 11 participants following EUCAST or EUCAST-related guidelines and reporting susceptibility to teicoplanin stated that a disk diffusion method was used, but only 24 participants reported disk diffusion zone diameters; 98 reported an MIC value and set up an MIC test instead of, or together with, disk diffusion. Of the 10 participants apparently ignoring guidelines and using only a disk diffusion method (report of zone diameter, no MIC), seven incorrectly reported the isolate as teicoplanin susceptible. Of 98 participants reporting use of a disk diffusion method, but also reporting a MIC value, 3.0 % reported the isolate as teicoplanin susceptible, similar to the 3.1 % of 227 participants that reported the use of an MIC method. Of 310 participants reporting use of an automated method, only 1.6 % reported the isolate as teicoplanin susceptible. Non-susceptibility to teicoplanin was reliably detected in tests that relied on automated and MIC methods.

Specimen 3085 – *Streptococcus pneumoniae*

This organism was a *Streptococcus pneumoniae* with reduced susceptibility to penicillin (MIC 0.25 mg/L) (Table A1.12).

For *S. pneumoniae* with no mechanism of resistance to penicillin, MICs are ≤ 0.06 mg/L. For isolates with higher MICs, the interpretation of susceptibility to penicillin depends on the site of infection and the route of administration of antibiotics. Patients with pneumonia caused by isolates with intermediate susceptibility (MIC 0.12–2 mg/L) are, depending on the parenteral dosage, treatable with penicillin, ampicillin or amoxicillin. Hence, such isolates may be reported susceptible if from pneumonia. Patients with meningitis caused by isolates with penicillin MIC › 0.06 mg/L are unlikely to respond to therapy and such isolates should be reported as resistant in this situation. Both EUCAST and CLSI guidelines include options for reporting susceptibility depending on the site of infection. In this distribution, data were collected on results of the oxacillin screen test, penicillin reporting without a site of infection, and the interpretation that would be reported if the isolate was from a case of pneumonia and if the isolate was from a case of meningitis. Irrespective of recommendations by EUCAST and CLSI, reporting practices vary considerably and, as noted previously for distributions of *S. pneumoniae* with intermediate susceptibility to penicillin, this is reflected in the variability of responses.

Of the 532 participants reporting a result for oxacillin (screening test for penicillin resistance), 93.4 % reported the isolate as resistant, 1.5 % as intermediate and 5.1 % as susceptible. There were no significant differences in reporting oxacillin susceptibility between those using EUCAST and EUCAST-related guidelines and those following CLSI guidelines (Table A1.13), but 27.0 % of the 37 participants that followed SFM guidelines failed to report reduced susceptibility, which seems to indicate an accuracy issue with the SFM guidelines. EUCAST and CLSI guidelines do not include an intermediate category for oxacillin because the oxacillin screening test is not considered to distinguish reliably between isolates with different degrees of reduced susceptibility; consequently, reports as intermediate would be pointless.

It is unclear how different participants interpreted the result for penicillin without a site of infection. Overall, 75.8 % of 690 participants reported the isolate as being intermediate to penicillin, with 7.7 % reporting resistant and 16.5 % susceptible. As seen in previous EARS-Net EQA distributions, participants following CLSI guidelines were more likely than participants using EUCAST and EUCAST-related guidelines to report ‘susceptible to penicillin’ when the site of infection was not stated (Table A1.14). These differences may partly relate to national or local differences in reporting practices.

Isolates from a case of pneumonia were mostly reported as susceptible: 53.0 % of 836 participants reported ‘susceptible to penicillin’, 44.4 % reported ‘intermediate’, and only 2.6 % said ’resistant’. As seen in previous EARS-Net EQA distributions, participants following CLSI guidelines were more likely than those using EUCAST and EUCAST-related guidelines to report susceptible to penicillin when the infection was pneumonia (Table A1.15).

The differences in reporting for pneumonia may again partly relate to differences in reporting practices. Some participants may apply the guidelines for isolates other than meningitis without making an allowance for the high doses used to treat pneumonia. Some may report susceptible because higher doses are always used to treat pneumonia and variation in dosing listed by EUCAST would not affect reporting if the MIC was 0.25mg/L. Some may report intermediate because susceptibility is dose-dependent, and clinicians are left to interpret the results based on the dose they use.

If the isolate was from a case of meningitis, 94.9 % of 829 participants would report resistant, 1.8 % intermediate and 3.3 % susceptible. EUCAST and CLSI guidelines both indicate that the isolate should be reported as resistant to penicillin, and there was little difference in reporting between participants following EUCAST guidelines and those following CLSI guidelines (Table A1.16).

Table A1.12. ***Streptococcus pneumoniae*** **(3085). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories**

Antibiotic agent	MIC (mg/L)		Result	
	Reference laboratory 1	Reference laboratory 2	EUCAST/CLSI	Overall concordance (%)
Cefotaxime				
meningitis	0.12	0.25	S	98.6
pneumonia				98.8
non-meningitis				99.2
Ceftriaxone				
meningitis	0.25	0.5	S	98.0
pneumonia				98.9
non-meningitis				98.7
Clindamycin			S*	97.2
Erythromycin	4	8	R	96.9
Levofloxacin	1		S	98.7
Moxifloxacin	0.12		S	99.4
Norfloxacin	–		S*	95.3
Oxacillin	Screening test		R	93.4
Penicillin				
meningitis	0.25		R	94.9
pneumonia			S/–	53.0
non-meningitis			–/S	–

* Results based on participant consensus, as no reference laboratory results available for these organism/antibiotic combinations.

Table A1.13. Oxacillin susceptibility reports for ***Streptococcus pneumoniae*** **specimen 3085**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	17 (5.5)	6 (1.9)	287 (92.6)
	Automated	7 (7.6)	2 (2.2)	83 (90.2)
	MIC	0 (0)	0 (0)	44 (100)
	Multi/other	0	0	5
	Total	**24 (5.3)**	**8 (1.8)**	**419 (92.9)**
CLSI	Disk diffusion	2 (4.0)	0 (0)	48 (96.0)
	Automated	0 (0)	0 (0)	29 (100)
	MIC	1	0	1
	Multi/other	0	0	0
	Total	**3 (3.7)**	**0 (0)**	**78 (96.3)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.14. Penicillin susceptibility reports (no site of infection) for ***Streptococcus pneumoniae*** **specimen 3085**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	16 (11.3)	117 (82.4)	9 (6.3)
	Automated	26 (11.2)	188 (80.7)	19 (8.1)
	MIC	27 (13.0)	170 (81.7)	11 (5.3)
	Multi/other	1	4	0
	Total	**70 (11.9)**	**479 (81.5)**	**39 (6.6)**
CLSI	Disk diffusion	8	6	2
	Automated	19 (35.8)	27 (50.9)	7 (13.3)
	MIC	16 (50.0)	11 (34.4)	5 (15.6)
	Multi/other	1	0	0
	Total	**44 (43.1)**	**44 (43.1)**	**14 (13.8)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.15. Penicillin susceptibility reports (pneumonia isolate) for ***Streptococcus pneumoniae*** **specimen 3085**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	121 (54.5)	98 (44.1)	3 (1.4)
	Automated	101 (33.8)	185 (61.9)	13 (4.3)
	MIC	99 (57.2)	70 (40.5)	4 (2.3)
	Multi/other	5	2	0
	Total	**326 (46.5)**	**355 (50.6)**	**20 (2.9)**
CLSI	Disk diffusion	22 (88.0)	3 (12.0)	0 (0)
	Automated	63 (86.3)	8 (11.0)	2 (2.7)
	MIC	31 (86.1)	5 (13.9)	0 (0)
	Multi/other	1	0	0
	Total	**117 (86.7)**	**16 (11.9)**	**2 (1.4)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.16. Penicillin susceptibility reports (meningitis isolate) for *Streptococcus pneumoniae* specimen 3085

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	5 (2.2)	8 (3.6)	212 (94.2)
	Automated	7 (2.4)	2 (0.7)	281 (96.9)
	MIC	5 (2.9)	3 (1.7)	166 (95.4)
	Multi/other	1	0	6
	Total	**18 (2.6)**	**13 (1.9)**	**665 (95.5)**
CLSI	Disk diffusion	4 (15.4)	1 (3.8)	21 (80.8)
	Automated	5 (6.8)	1 (1.3)	68 (91.9)
	MIC	0 (0)	0 (0)	32 (100)
	Multi/other	0	0	1
	Total	**9 (6.8)**	**2 (1.5)**	**122 (91.7)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Specimen 3086 – *Escherichia coli*

This organism was an *Escherichia coli* with a TEM-3 extended-spectrum beta-lactamase. Resistance to aminopenicillins and third-generation cephalosporins was clear, and there were no significant problems in detecting resistance. Susceptibility to amoxicillin-clavulanic acid (MIC 16 mg/L) was borderline, and the isolate was resistant by EUCAST breakpoints (S ≤ 8, R › 8 mg/L) and intermediate by CLSI breakpoints (S ≤ 8, R ≥ 32 mg/L). Overall, 14.7 % of 598 participants reported the isolate as susceptible to amoxicillin-clavulanic acid, 12.8 % as intermediate, and 72.5 % as resistant (Table A1.17).

The difference in breakpoints was reflected in the reported results: participants following EUCAST or EUCAST-related breakpoints were more likely to report resistant while those following CLSI breakpoints were more likely to report intermediate. Participants using automated methods were more likely to report resistant if they followed EUCAST guidelines, and more likely to report intermediate if they used CLSI guidelines (Table A1.18).

The organism was susceptible to piperacillin + tazobactam (MIC 4 mg/L) by both EUCAST and CLSI breakpoints. Overall, 81.8 % of 844 participants reported the isolate as susceptible to piperacillin + tazobactam, 11.4 % as intermediate and 6.8 % as resistant. There was no association of guidelines or methods with reported susceptibility (Table A1.19). Some participants may have edited susceptible test results to intermediate or resistant because of the presence of the ESBL; but guidelines from both EUCAST and CLSI recommend reporting beta-lactamase inhibitor combinations 'as found' in routine tests. The current EUCAST expert rules recommend that when an isolate is intermediate or resistant to any third-generation (cefotaxime, ceftriaxone, ceftazidime) or fourth-generation (cefepime) oxyimino-cephalosporin, reports of susceptible to beta-lactamase inhibitor combinations should include a warning of uncertain therapeutic outcome for infections other than urinary tract infections.

Aminoglycoside susceptibility was typical for an organism producing AAC(6')I in that the organism was susceptible to gentamicin (MIC 0.5–1 mg/L), borderline susceptible to amikacin (MIC 8 mg/L), and borderline resistant to tobramycin (MIC 8–16 mg/L; resistant by EUCAST breakpoints, intermediate–resistant by CLSI breakpoints). For tobramycin, 90.0 % of 708 participants reported the isolate as resistant, 8.3 % as intermediate and 1.7 % as susceptible. In line with the differences in breakpoints between EUCAST and CLSI, among participants using CLSI guidelines, reports of intermediate were more common than among those following EUCAST guidelines (Table A1.20).

For amikacin, 27.2 % of 767 participants reported the isolate as susceptible, 57.9 % as intermediate and 14.9 % as resistant. In line with the differences in breakpoints between EUCAST and CLSI, reports as susceptible were most common among those following CLSI guidelines, and reports as intermediate were most common among participants using EUCAST or EUCAST-related guidelines. Participants following EUCAST or EUCAST-related guidelines were more likely to report the isolate as amikacin susceptible if they used disk diffusion methods rather than automated or MIC methods (Table A1.21).

The EUCAST expert rules note that acquired AAC(6')I may not confer phenotypic resistance to amikacin despite the modification of amikacin by enzymes, and that such isolates should be reported as intermediate to amikacin even if they appear susceptible. It would therefore be reasonable to report 'intermediate' if EUCAST expert rules are followed, and some participants may indeed have edited their test results from susceptible to intermediate. This rule is currently under review by EUCAST and is likely to be removed from the next version because of the lack of clinical evidence.

The ciprofloxacin MIC (0.25 mg/L) was raised slightly compared with wild type *E. coli* but the organism was within the susceptible category by both EUCAST and CLSI breakpoints. Most (94.0 %) of the 884 participants reported the isolate as susceptible, with 4.9 % reporting intermediate and 1.1 % resistant. Reference MICs were not available for the other fluoroquinolones listed, levofloxacin and ofloxacin, but most (97.1 %) of the 484 participants reporting susceptibility to levofloxacin reported the isolate as susceptible, with 1.7 % reporting intermediate and 1.2 % resistant. Among 205

Table A1.17. ***Escherichia coli*** **(3086). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories**

Antibiotic agent	MIC (mg/L)		Result	
	Reference laboratory 1	Reference laboratory 2	EUCAST/CLSI	Overall concordance (%)
Amikacin	8		S	27.2
Amoxicillin	› 128		R	99.3
Amoxicillin-clavulanic acid	16(16)**		R	72.5
Ampicillin	› 128		R	99.8
Cefotaxime	32		R	98.5
Ceftazidime	64		R	99.4
Ceftriaxone	32		R	96.8
Ciprofloxacin	0.25		S	94.0
Ertapenem	0.06		S	98.6
Gentamicin	0.5	1	S	99.2
Imipenem	0.25		S	99.6
Levofloxacin	–		S*	97.1
Meropenem	0.03		S	99.5
Ofloxacin	–		S*	62.9
Piperacillin-tazobactam	4		S	81.9
Tobramycin	8	16	R/ (I/R)	90.0

* Results based on participant consensus, as no reference laboratory results available for these organism/antibiotic combinations

** Amoxicillin-clavulanic acid MIC determined with a fixed 2mg/L concentration of clavulanic acid (with a 2:1 ratio of amoxicillin:clavulanic acid)

Table A1.18. Amoxicillin-clavulanic acid susceptibility reports for ***Escherichia coli*** **specimen 3086**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	50 (18.4)	24 (8.8)	198 (72.8)
	Automated	16 (4.7)	1 (0.3)	324 (95.0)
	MIC	21 (33.3)	1 (1.6)	41 (65.1)
	Multi/other	2	0	5
	Total	**89 (13.0)**	**26 (3.8)**	**568 (83.2)**
CLSI	Disk diffusion	9 (20.9)	20 (46.5)	14 (32.6)
	Automated	18 (21.4)	53 (63.1)	13 (15.5)
	MIC	5	7	1
	Multi/other	0	0	0
	Total	**32 (22.9)**	**80 (57.1)**	**28 (20.0)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.19. Piperacillin-tazobactam susceptibility reports for ***Escherichia coli*** **specimen 3086**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	231 (87.5)	23 (8.7)	10 (3.8)
	Automated	243 (75.2)	53 (16.4)	27 (8.4)
	MIC	96 (85.7)	6 (5.4)	10 (8.9)
	Multi/other	4	3	1
	Total	**574 (81.2)**	**85 (12.0)**	**48 (6.8)**
CLSI	Disk diffusion	36 (90.0)	2 (5.0)	2 (5.0)
	Automated	67 (84.8)	9 (11.4)	3 (3.8)
	MIC	13	0	5
	Multi/other	0	0	0
	Total	**116 (84.7)**	**11 (8.0)**	**10 (7.3)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.20. Tobramycin susceptibility reports for ***Escherichia coli*** **specimen 3086**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	5 (2.0)	7 (2.9)	233 (95.1)
	Automated	1 (0.4)	5 (1.7)	281 (97.9)
	MIC	0 (0)	5 (8.1)	57 (91.9)
	Multi/other	0	0	6
	Total	**6 (1.0)**	**17 (2.8)**	**577 (96.2)**
CLSI	Disk diffusion	1 (3.3)	9 (29.0)	21 (67.7)
	Automated	3 (4.8)	32 (50.8)	28 (44.4)
	MIC	2	1	11
	Multi/other	0	0	0
	Total	**6 (5.5)**	**42 (38.9)**	**60 (55.6)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.21. Amikacin susceptibility reports for *Escherichia coli* specimen 3086

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	80 (32.5)	136 (55.3)	30 (12.2)
	Automated	32 (10.9)	203 (69.3)	58 (19.8)
	MIC	14 (16.7)	56 (66.6)	14 (16.7)
	Multi/other	0	4	3
	Total	**126 (20.0)**	**399 (63.3)**	**105 (16.7)**
CLSI	Disk diffusion	25 (61.0)	14 (34.1)	2 (4.9)
	Automated	50 (63.3)	25 (31.6)	4 (5.1)
	MIC	8	6	3
	Multi/other	0	0	0
	Total	**83 (60.6)**	**45 (32.8)**	**9 (6.6)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.22. Ofloxcin susceptibility reports for *Escherichia coli* specimen 3086

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	58 (61.1)	28 (29.4)	9 (9.5)
	Automated	17 (41.5)	7 (17.1)	17 (41.4)
	MIC	12 (60.0)	4 (20.0)	4 (20.0)
	Multi/other	0	0	4
	Total	**87 (54.3)**	**39 (24.4)**	**34 (21.3)**
CLSI	Disk diffusion	19 (95.0)	1 (5.0)	0 (0)
	Automated	21 (91.3)	2 (8.7)	0 (0)
	MIC	2	0	0
	Multi/other	0	0	0
	Total	**42 (93.3)**	**3 (6.7)**	**0 (0)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

participants reporting ofloxacin susceptibility, only 62.9% reported the isolate as susceptible, with 20.5% reporting intermediate and 16.6% resistant. CLSI breakpoints are only available for urinary tract infections (S ≤ 2 mg/L, R ≥ 8 mg/L) and are higher than the EUCAST systemic breakpoints (S ≤ 0.5 mg/L, R >1 mg/L). It is likely that participants that followed CLSI guidelines applied the UTI breakpoints and, in line with the differences in these breakpoints, participants following EUCAST or EUCAST-related guidelines were more likely to report intermediate or resistant than those following CLSI guidelines (Table A1.22).

Specimen 3087 – *Pseudomonas aeruginosa*

This organism was a *Pseudomonas aeruginosa* resistant to ciprofloxacin, gentamicin, tobramycin, carbapenems, and piperacillin + tazobactam (Table A1.23).

Detecting carbapenem resistance was straightforward, which is likely to be mediated by porin loss/efflux as no carbapenemase enzyme was present. The ceftazidime MIC (8 mg/L) was borderline susceptible with both EUCAST (S ≤ 8, R >8 mg/L) and CLSI (S ≤ 8, R ≥ 32 mg/L) breakpoints. Overall, 55.3% of the 893 participants reported the isolate as ceftazidime resistant, 8.6% as intermediate and 36.1% as susceptible. The majority (63.8%) of the 748 participants following EUCAST or EUCAST-related guidelines reported the isolate as ceftazidime resistant, with 2.0% reporting as intermediate and 34.2% as susceptible. Among 145 participants following CLSI guidelines, reports as susceptible (45.5%) or intermediate (42.8%) were more common, with only 11.7% reporting the isolate as ceftazidime resistant.

The CLSI guidelines include an intermediate category, but EUCAST guidelines do not, and a significant proportion (42.8%) of laboratories following CLSI guidelines reported the isolate as intermediate; only 2.0% of the laboratories that followed EUCAST or EUCAST-related guidelines reported the isolate as intermediate. As the susceptible breakpoint is the same in EUCAST and CLSI guidelines, it is not clear why participants following EUCAST guidelines were less likely to report susceptible than those following CLSI guidelines, regardless of disk diffusion or automated methods (Table A1.24).

The piperacillin + tazobactam MIC (64 mg/L) was clearly in the resistant category by EUCAST breakpoints (S ≤ 8, R >16 mg/L) but intermediate by CLSI breakpoints (S ≤ 16, R ≥ 128mg/L).

Overall, 85.3% of 880 participants reported the isolate as resistant, 8.8% as intermediate and 5.9% as susceptible. In line with the differences in breakpoints, participants following CLSI guidelines were more likely to report intermediate (49.3% of 144) or susceptible (25.0%) than those following EUCAST guidelines (0.8% of 736 reported intermediate and 2.2% reported susceptible). There was no clear correlation of methods with results (Table A1.25).

Table A1.23. ***Pseudomonas aeruginosa*** **(3087). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories**

Guideline	MIC (mg/L)		Result	
	Reference laboratory 1	Reference laboratory 2	EUCAST/CLSI	Overall concordance (%)
Amikacin	4		S	96.3
Ceftazidime	8		S	36.1
Ciprofloxacin	32		R	99.7
Gentamicin	› 128		R	99.5
Imipenem	32		R	99.7
Levofloxacin	–		R*	100
Meropenem	32		R	99.5
Piperacillin-tazobactam	64		R	85.3
Tobramycin	› 128		R	99.5

* Results based on participant consensus, as no reference laboratory results available for these organism/antibiotic combinations

Table A1.24. Ceftazidime susceptibility reports for ***Pseudomonas aeruginosa*** **specimen 3087**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	96 (38.2)	2 (0.8)	153 (61.0)
	Automated	93 (25.7)	10 (2.8)	259 (71.5)
	MIC	62 (48.8)	3 (2.4)	62 (48.8)
	Multi/other	5	0	3
	Total	**256 (34.2)**	**15 (2.0)**	**477 (63.8)**
CLSI	Disk diffusion	25 (59.5)	12 (28.6)	5 (11.9)
	Automated	30 (34.9)	44 (51.2)	12 (13.9)
	MIC	11	6	0
	Multi/other	0	0	0
	Total	**66 (45.5)**	**62 (42.8)**	**17 (11.7)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Table A1.25. Piperacillin-tazobactam susceptibility reports for ***Pseudomonas aeruginosa*** **specimen 3087**

Guideline	Method	N (%) of laboratories reporting		
		S	I	R
EUCAST and EUCAST-related*	Disk diffusion	13 (4.9)	6 (2.2)	247 (92.9)
	Automated	1 (0.3)	0 (0)	345 (99.7)
	MIC	2 (1.7)	0 (0)	114 (98.3)
	Multi/other	0	0	8
	Total	**16 (2.2)**	**6 (0.8)**	**714 (97.0)**
CLSI	Disk diffusion	9 (22.5)	21 (52.5)	10 (25.0)
	Automated	24 (28.6)	42 (50.0)	18 (21.4)
	MIC	3 (15.0)	8 (40.0)	9 (45.0)
	Multi/other	0	0	0
	Total	**36 (25.0)**	**71 (49.3)**	**37 (25.7)**

* EUCAST-related methods include BSAC and SFM methods, which are calibrated to EUCAST breakpoints.

Annex 2. EARS-Net laboratory/hospital denominator data 2015

Laboratory and hospital denominator data have been collected and presented in this Annex to aid the correct interpretation of the EARS-Net data on antimicrobial resistance.

Methods

Questionnaires were sent to the EARS-Net-appointed contact points for AMR in March 2016. The contact points distributed the questionnaires to the participating laboratories and hospitals in their country. Information was collected on the total number of blood culture sets processed in the laboratories, the number of hospital beds for each participating hospital, the type of hospital, the bed occupancy, and the number of admissions. The appointed contact points and/or national focal points for antimicrobial resistance completed the questionnaires, compiled them and produced the final format suitable for uploading to The European Surveillance System (TESSy).

Laboratories were defined as reporting denominator data if they provided the number of blood culture sets performed for one or more hospitals. Hospitals were defined as reporting denominator data if they provided at least the number of beds.

Organisation of healthcare systems and affiliation between laboratories and hospitals differ considerably between countries, which might influence data comparability. For countries submitting denominator data for a small percentage of the hospitals and/or laboratories that contributed data to EARS-Net, the reported figures might not be representative for the overall country profile.

Participation

Seventeen of the 30 countries reporting AMR data for 2015 also returned hospital denominator data referring to the same year, while for four countries, hospital denominator data referring to 2014 were available and included in the analysis. Sixteen countries could provide sufficient laboratory denominator data for calculating the number of blood culture sets per 1000 patient-days for 2015 and four for 2014.

Hospital denominator information

The total number of hospital beds for hospitals reporting both AMR and denominator data in different countries ranged from 1362 in Cyprus to 128 154 in the United Kingdom, reflecting the size of the country as well as the rate of participation in EARS-Net and the rate of response to the questionnaires.

The percentage of ICU beds over total hospital beds shows wide variation by country, ranging from 2% in Hungary and Poland, to 12% in the Czech Republic. The annual occupancy rate was 85% or higher in three of the 21 countries that provided data for this variable (Table A2.1).

Hospital characteristics

Both the size of a hospital and the level of specialisation may influence the occurrence of antimicrobial resistance in the hospital. As can be seen from Table A2.1, the distribution of size and specialisation level of hospitals varied considerably between the reporting countries. This does not necessarily reflect different distributions of the origin of blood culture results reported to EARS-Net in each country, as not all hospitals contribute evenly to the EARS-Net database. On the other hand, this diversity can indicate differences in the patient case mix, which may confound comparison of AMR results between countries.

Type and size of hospitals were not always linked, and it was not rare, especially in smaller countries, that university hospitals have fewer than 500 beds.

Laboratory denominator information

In 2015/2014 (latest available data), a median of 27.2 blood culture sets per 1 000 patient-days were processed in the EARS-Net laboratories responding to the questionnaire. The highest rate was reported by the United Kingdom (65.4 cultures per 1000 patient-days) and the lowest by Latvia (6.7 cultures per 1000 patient-days) (Table A2.1). For the majority of the reporting countries, there are only minor changes in the number of blood culture sets per 1000 patient-days when comparing 2015/2014 (latest available data) data with 2013/2012 (latest available data).

Discussion and conclusions

In summary, the situation for most countries as assessed from denominator data reported to EARS-Net in 2015/2014 appears stable and similar to that of 2013/2012. This indicates that based on EARS-Net data, the comparison of AMR percentages over time remains valid.

Case ascertainment of patients with bloodstream infections is strongly linked to diagnostic practices and the frequency with which blood cultures are taken. Therefore, the wide range in blood culture rates observed in the countries providing denominator data has implications for inter-country comparisons of both

Table A2.1. Hospital denominator data for 2014 or 2015 (latest available data)

Country	Number of hospitals reporting		Total number of beds	Percentage of ICU beds (%)	Annual occupancy rate (%)	Percentage of hospitals by level of care				
	Denominator data	AMR data				Tertiary level	Secondary level	Primary level	Other	Unknown
Austria	155	155	58299	5	67	8	22	39	32	0
Bulgaria	20	20	9553	7	72	60	30	5	5	0
Cyprus	5	5	1362	9	71	20	20	40	20	0
Czech Republic	66	70	38144	12	74	38	41	18	3	0
Estonia	12	12	5218	5	77	33	58	8	0	0
Finland*	20	20	12481	4	–	54	36	11	0	0
France	195	214	104796	7	80	41	59	0	0	0
Germany	108	336	37358	6	75	23	39	19	14	5
Hungary	68	68	54051	2	75	48	23	12	17	0
Ireland	53	80	11291	–	85	17	47	15	21	0
Italy*	40	48	24321	4	80	58	35	5	0	2
Latvia	27	27	8438	3	69	19	44	19	17	0
Malta	3	3	1545	3	78	33	33	0	33	0
Norway	15	46	10311	3	79	60	20	20	0	0
Poland	44	60	23848	2	71	34	52	0	14	0
Romania*	16	16	6305	–	70	21	36	0	43	0
Slovakia	26	25	13637	9	67	54	15	8	23	0
Slovenia	16	15	7407	5	71	13	44	25	19	0
Spain*	39	43	23689	5	75	59	23	18	0	0
Sweden	47	49	15482	4	95	17	40	43	0	0
United Kingdom	33	93	128154	5	86	50	32	12	6	0

– No information available
* Data from 2014

Table A2.2. Laboratory denominator information for 2014 or 2015 (latest available data)

Country	Number of laboratories reporting		Total number of blood culture sets	Number of blood culture sets per 1000 patient days
	Denominator data	AMR data		
Austria	38	39	220277	15.7
Bulgaria	19	20	19608	8.2
Cyprus	5	5	15337	41.4
Czech Republic	50	48	166403	16.6
Estonia	11	11	28539	17.8
Finland*	20	20	204157	63.5
France**	50	54	905880	81
Germany	20	29	253666	24.9
Hungary	32	30	119231	8.4
Ireland	37	39	197751	52.9
Italy*	34	47	280875	41.9
Latvia	17	16	14513	6.7
Malta	1	1	9635	22.7
Norway	15	18	168416	56.9
Poland	40	48	196541	32.4
Portugal	37	122	251961	64.6
Romania*	9	16	39992	24.9
Slovakia	14	14	68428	20.1
Slovenia	10	10	67039	35.1
Spain*	39	40	330347	46.2
United Kingdom	25	52	272385	65.4

– No information available
* Data from 2014
** Observatoire National de l'Epidémiologie de la Résistance (Onerba) laboratories only

the incidence of bloodstream infections, which could be underestimated in some countries, and of the percentage of antimicrobial resistance. In particular, the percentage of resistance could be overestimated if blood cultures are not systematically performed before starting empiric therapy and if blood cultures are more likely to be performed in patients not responding to initial empiric treatment.

For future improvement of the denominator data collection and analysis, a further increase in the number of countries reporting denominator data, as well as an increased number of hospitals and laboratories participating within countries, would be desirable. Furthermore, an improved estimation of the coverage of the EARS-Net surveillance, e.g. by using national estimations based on knowledge of the country-specific situation, would also be desirable.

Annex 3. General information on EARS-Net participating laboratories

Country summary sheets

General information on EARS-Net participating laboratories and hospitals

This section provides the number of laboratories and isolates reported by year and by pathogen under EARSS/EARS-Net surveillance for the period 2000–2015. The total number of laboratories participating in EARS-Net could in some countries be higher than the number presented in Table 1, as only laboratories reporting at least one isolate during each specific year are included.

Antibiotic resistance 2000–2015

For an overview of antimicrobial susceptibility results for the period 2000–2015, please refer to the antimicrobial resistance section of the ECDC Surveillance atlas of infectious diseases, available from http://atlas.ecdc.europa.eu

Austria

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	9	63	10	385	–	–	–	–	–	–	–	–	–	–
2001	8	53	9	278	8	260	6	67	–	–	–	–	–	–
2002	10	80	11	456	10	479	10	181	–	–	–	–	–	–
2003	20	163	20	871	21	985	19	327	–	–	–	–	–	–
2004	28	257	30	1453	31	1862	28	604	–	–	–	–	–	–
2005	31	298	32	1481	33	2058	30	568	7	89	8	77	–	–
2006	32	293	33	1640	33	2483	33	699	30	434	31	405	–	–
2007	35	322	34	1577	34	2545	33	688	33	445	33	411	–	–
2008	38	380	38	1899	38	2985	38	864	38	583	38	510	–	–
2009	38	379	38	1794	38	2625	36	825	37	622	36	525	–	–
2010	35	375	39	1840	39	2937	39	944	39	722	39	504	–	–
2011	39	438	40	1982	40	3174	40	894	40	799	40	544	–	–
2012	38	356	40	2173	40	3766	39	1049	40	859	39	596	–	–
2013	37	426	38	2543	38	4390	38	1113	38	947	38	618	18	51
2014	39	410	39	2662	39	4757	39	1140	39	996	39	638	21	79
2015	38	450	39	2815	39	4919	39	1170	39	1065	39	680	21	64

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Note: National data analysis allows for a more accurate validation. Due to differences in the validation algorithms used by EARS-Net and Austria, there are small discrepancies in the data presented by EARS-Net.

Belgium

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	90	964	42	657	–	–	–	–	–	–	–	–	–	–
2001	89	1093	47	941	23	226	19	42	–	–	–	–	–	–
2002	98	1210	48	1092	27	1184	23	205	–	–	–	–	–	–
2003	107	1488	47	1133	24	1326	16	146	–	–	–	–	–	–
2004	95	1443	49	1227	25	1601	18	228	–	–	–	–	–	–
2005	97	1539	41	1048	25	1592	19	223	–	–	–	–	–	–
2006	98	1427	33	858	21	1632	22	267	–	–	–	–	–	–
2007	105	1511	34	855	17	1460	20	245	–	–	–	–	–	–
2008	101	1647	38	906	16	1430	19	236	–	–	–	–	–	–
2009	101	1885	34	949	18	1610	14	227	8	142	8	136	–	–
2010	97	1797	40	1088	23	1966	22	323	14	145	15	130	–	–
2011	91	1829	50	1771	43	4039	46	754	44	676	43	460	–	–
2012	96	1739	44	1569	41	4137	41	742	41	549	40	392	–	–
2013	93	1612	41	1683	41	4408	39	922	41	639	40	518	2	3
2014	96	1181	27	1034	27	2895	25	558	26	506	27	357	3	4
2015	91	1361	25	994	25	2685	25	550	24	406	25	263	8	26

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Bulgaria

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	8	13	16	102	–	–	–	–	–	–	–	–	–	–
2001	8	16	17	103	15	98	11	30	–	–	–	–	–	–
2002	11	25	21	116	20	135	16	42	–	–	–	–	–	–
2003	13	22	20	157	20	158	16	49	–	–	–	–	–	–
2004	13	32	22	170	20	167	16	75	–	–	–	–	–	–
2005	16	43	26	160	23	203	21	95	15	34	9	34	–	–
2006	11	29	23	159	20	196	19	98	15	55	13	31	–	–
2007	10	32	14	121	15	127	13	65	9	29	6	14	–	–
2008	13	29	21	160	22	147	18	70	11	49	10	23	–	–
2009	10	27	20	221	17	194	16	92	12	95	11	36	–	–
2010	13	22	20	200	21	153	16	108	15	127	11	42	–	–
2011	16	33	19	214	19	179	16	117	15	121	12	48	–	–
2012	12	21	19	227	19	223	20	129	14	127	11	52	11	65
2013	14	29	20	214	17	187	19	154	17	138	13	60	13	94
2014	12	32	20	216	20	218	19	182	17	151	12	48	15	115
2015	10	36	20	222	19	205	19	156	16	96	13	55	18	133

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Croatia

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	10	20	14	149	13	182	7	33	–	–	–	–	–	–
2002	14	90	14	279	15	490	13	96	–	–	–	–	–	–
2003	12	88	14	360	16	570	11	101	–	–	–	–	–	–
2004	12	103	13	392	14	535	11	115	–	–	–	–	–	–
2005	15	129	17	354	16	638	11	120	14	112	10	72	–	–
2006	14	116	17	391	17	780	16	178	15	205	15	170	–	–
2007	15	137	15	375	17	860	13	174	17	280	16	189	–	–
2008	13	100	18	474	17	914	16	232	17	334	14	221	–	–
2010	11	103	15	359	16	883	12	174	16	281	15	210	–	–
2011	16	125	13	417	15	986	14	226	13	300	14	227	–	–
2012	10	97	17	404	16	907	15	216	15	332	14	197	–	–
2013	16	116	19	520	18	1040	17	248	18	376	18	246	13	114
2014	14	129	16	485	18	1080	16	220	16	334	16	232	15	167
2015	15	126	16	488	18	1046	16	298	17	380	17	257	17	200

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Cyprus

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2002	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2003	1	3	1	28	1	19	1	28	–	–	–	–	–	–
2004	1	7	3	39	4	46	3	38	–	–	–	–	–	–
2005	4	16	5	54	5	75	3	40	4	9	4	8	–	–
2006	5	13	5	62	5	90	4	48	4	26	4	37	–	–
2007	4	15	4	85	5	109	3	63	4	39	3	52	–	–
2008	4	14	5	92	4	119	5	85	5	62	5	43	–	–
2009	4	11	5	89	5	136	5	80	5	53	5	62	–	–
2010	4	12	5	99	5	139	5	91	4	67	5	48	–	–
2011	2	12	4	113	5	138	4	71	4	83	4	51	–	–
2012	3	8	5	165	5	176	5	106	5	65	5	52	5	23
2013	4	15	5	160	5	162	5	97	5	68	5	47	5	33
2014	4	12	5	138	5	153	5	115	5	80	5	42	5	58
2015	4	7	5	145	5	123	5	86	5	62	5	43	5	61

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Czech Republic

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	26	111	31	516	–	–	–	–	–	–	–	–	–	–
2001	32	154	39	1075	36	1176	34	461	–	–	–	–	–	–
2002	34	144	41	1168	40	1587	39	587	–	–	–	–	–	–
2003	32	204	45	1387	43	1766	44	630	–	–	–	–	–	–
2004	37	162	45	1444	44	1966	41	660	–	–	–	–	–	–
2005	39	195	47	1553	47	2234	45	758	37	478	36	257	–	–
2006	39	172	47	1527	47	2176	45	697	45	1130	43	490	–	–
2007	41	205	47	1653	48	2407	47	816	48	1230	41	517	–	–
2008	40	244	47	1715	46	2738	44	883	45	1493	42	568	–	–
2009	41	297	46	1695	45	2759	44	835	45	1415	45	575	–	–
2010	41	288	44	1593	43	2484	41	759	44	1264	41	511	–	–
2011	42	316	46	1555	45	2696	44	767	44	1287	42	448	–	–
2012	39	274	47	1611	44	2812	42	843	46	1399	44	489	–	–
2013	44	333	47	1707	46	2962	43	875	45	1291	43	516	19	91
2014	45	274	44	1695	45	2981	42	775	44	1383	40	448	18	59
2015	44	284	46	1806	45	3174	44	869	46	1418	44	464	15	60

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Denmark

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	5	410	4	501	–	–	–	–	–	–	–	–	–	–
2001	5	506	4	520	–	–	–	–	–	–	–	–	–	–
2002	5	366	5	752	–	–	–	–	–	–	–	–	–	–
2003	5	606	5	671	–	–	–	–	–	–	–	–	–	–
2004	15	1188	15	1436	–	–	–	–	–	–	–	–	–	–
2005	14	1081	15	1350	5	1283	–	–	–	–	–	–	–	–
2006	15	872	15	1279	11	2723	11	711	11	607	–	–	–	–
2007	15	1030	14	1315	12	3021	13	927	13	784	13	417	–	–
2008	15	934	15	1295	14	3283	14	1005	14	793	14	420	–	–
2009	15	996	15	1395	14	3532	14	1100	14	822	14	429	–	–
2010	15	954	15	1362	14	3418	14	1112	14	799	14	376	–	–
2011	13	896	13	1452	12	3642	12	1197	12	910	12	407	–	–
2012	13	867	13	1431	12	3925	12	1248	12	948	12	390	10	83
2013	12	789	12	1685	11	3967	11	1224	11	875	11	414	11	79
2014	11	709	11	1874	10	4496	10	1308	10	943	10	388	10	72
2015	11	747	11	1876	11	4597	11	1303	11	939	11	442	10	68

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Estonia

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	1	1	–	–	–	–	–	–	–	–
2001	5	20	6	79	4	52	4	21	–	–	–	–	–	–
2002	5	21	8	82	6	67	3	13	–	–	–	–	–	–
2003	8	26	9	98	9	98	6	27	–	–	–	–	–	–
2004	6	40	9	104	10	167	5	63	–	–	–	–	–	–
2005	7	53	8	141	10	156	7	66	7	38	5	38	–	–
2006	8	52	9	154	9	215	8	85	6	47	6	43	–	–
2007	8	64	10	206	11	219	8	66	9	63	8	48	–	–
2008	10	66	11	185	11	267	11	86	10	72	8	41	–	–
2009	8	82	11	213	11	320	8	72	7	60	6	43	–	–
2010	10	64	9	152	11	317	8	66	9	82	8	43	–	–
2011	9	54	11	121	11	315	3	10	6	91	6	17	–	–
2012	9	71	10	163	11	306	8	76	9	91	7	33	–	–
2013	10	79	11	171	11	342	9	77	11	91	8	21	–	–
2014	10	72	11	226	11	412	9	81	10	136	7	40	–	–
2015	10	102	11	231	11	513	10	103	9	133	7	38	5	8

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Finland

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	11	238	12	367	–	–	–	–	–	–	–	–	–	–
2001	13	468	13	607	14	1283	13	273	–	–	–	–	–	–
2002	15	454	15	721	15	1330	14	278	–	–	–	–	–	–
2003	16	517	16	727	15	1450	15	266	–	–	–	–	–	–
2004	17	548	17	883	17	1749	17	336	–	–	–	–	–	–
2005	17	543	17	790	17	1924	17	340	14	175	13	108	–	–
2006	15	501	15	894	15	1875	15	348	14	228	14	162	–	–
2007	16	547	16	814	16	1949	16	400	15	273	14	183	–	–
2008	15	643	15	923	15	2111	15	381	12	288	12	175	–	–
2009	20	688	20	978	20	2224	20	506	20	375	18	233	–	–
2010	20	622	20	1094	20	2551	20	521	20	401	20	281	–	–
2011	17	662	18	1319	17	3021	16	479	17	404	16	269	–	–
2012	16	607	17	1409	17	3162	17	651	17	536	17	327	–	–
2013	18	675	18	1580	18	3721	18	698	18	550	18	327	11	37
2014	19	659	19	1831	19	4013	19	844	19	583	19	307	14	32
2015	20	788	20	2070	20	4425	20	777	20	658	20	341	16	43

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

France

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	–	–	21	1714	–	–	–	–	–	–	–	–	–	–
2002	–	–	21	1664	21	2495	21	467	–	–	–	–	–	–
2003	–	–	21	1710	21	2266	20	468	–	–	–	–	–	–
2004	–	–	50	3355	50	5678	46	871	–	–	–	–	–	–
2005	195	632	50	3484	50	6056	47	1023	49	838	48	993	–	–
2006	97	371	50	3824	50	6718	50	1152	50	963	47	1006	–	–
2007	168	663	57	4265	57	8093	56	1545	56	1187	56	1305	–	–
2008	127	557	56	4380	56	7993	54	1555	54	1138	54	1225	–	–
2009	225	826	54	4727	54	8451	54	1969	52	1378	32	1221	–	–
2010	181	1127	56	4883	56	9028	54	1970	56	1542	36	1191	–	–
2011	255	1413	52	4740	52	8790	46	2163	52	1691	52	1634	–	–
2012	160	824	55	5242	55	9610	52	2263	55	1712	54	1731	44	391
2013	229	919	54	5439	54	10157	53	2538	54	1940	54	1878	51	413
2014	150	656	53	5498	53	10350	53	2693	53	2196	53	1789	49	409
2015	198	1068	54	5597	54	11067	53	2852	53	2350	53	1956	48	434

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Germany

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	18	204	19	890	1	180	1	28	–	–	–	–	–	–
2001	21	212	22	1220	21	1269	20	294	–	–	–	–	–	–
2002	17	248	18	1067	16	1068	14	290	–	–	–	–	–	–
2003	17	175	20	920	19	997	17	347	–	–	–	–	–	–
2004	16	145	22	1107	22	1217	22	606	–	–	1	1	–	–
2005	15	119	17	827	17	961	17	569	12	105	12	117	–	–
2006	15	85	18	799	18	850	16	529	14	148	12	162	–	–
2007	11	75	12	853	12	977	12	648	10	173	11	197	–	–
2008	11	209	14	1090	14	1615	13	451	11	235	11	167	–	–
2009	16	346	17	1893	17	2803	17	952	15	479	16	287	–	–
2010	16	363	17	1980	17	3024	16	1009	15	478	15	315	–	–
2011	18	359	19	2388	19	3650	17	1231	17	519	17	389	–	–
2012	20	326	21	2563	21	4194	21	1499	20	664	20	438	11	121
2013	21	492	23	3129	23	5345	23	1901	22	766	22	630	13	181
2014	21	502	21	3417	21	6251	21	2035	20	1008	20	643	17	208
2015	28	736	29	4876	29	8729	29	2991	28	1521	28	941	24	337

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Greece

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	17	366	18	398	12	197	–	–	–	–	–	–
2001	–	–	25	363	26	620	25	304	–	–	–	–	–	–
2002	–	–	33	368	35	588	28	292	–	–	–	–	–	–
2003	–	–	34	682	35	1076	32	621	–	–	–	–	–	–
2004	–	–	35	610	39	1131	34	565	–	–	–	–	–	–
2005	–	–	35	682	35	1140	34	737	33	774	33	699	–	–
2006	–	–	42	828	41	1253	39	949	38	841	38	818	–	–
2007	–	–	41	819	43	1234	39	999	38	972	37	802	–	–
2008	–	–	46	907	44	1462	42	992	41	1093	42	920	–	–
2009	–	–	48	1025	49	1831	47	1190	47	1649	47	1123	–	–
2010	–	–	44	902	45	1549	43	1105	40	1703	42	1014	–	–
2011	–	–	39	826	37	1437	36	1122	38	1671	35	948	–	–
2012	–	–	38	877	37	1397	36	1121	37	1462	34	913	37	1254
2013	–	–	32	776	31	1258	31	930	30	1212	30	886	29	849
2014	–	–	27	575	26	1123	26	725	27	1093	26	700	26	844
2015	–	–	29	635	29	1218	28	826	28	1187	28	680	29	1001

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Hungary

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	16	64	18	301	18	264	17	121	–	–	–	–	–	–
2002	17	61	24	416	24	354	23	169	–	–	–	–	–	–
2003	20	134	27	858	27	842	25	279	–	–	–	–	–	–
2004	26	143	30	1020	28	967	26	366	–	–	–	–	–	–
2005	23	133	28	1083	27	1046	27	476	21	314	24	507	–	–
2006	23	151	27	1127	26	1135	25	453	24	302	25	546	–	–
2007	22	146	26	1199	25	1179	26	400	23	322	24	518	–	–
2008	22	166	26	1181	25	1057	21	428	23	369	25	513	–	–
2009	22	143	26	1068	25	1057	27	444	24	361	25	518	–	–
2010	27	140	30	1224	29	1385	29	591	29	514	28	636	–	–
2011	27	139	28	1156	30	1227	28	582	27	432	29	606	–	–
2012	26	160	28	1143	28	1415	28	594	27	500	29	619	27	418
2013	26	154	26	1201	30	1440	29	813	28	559	30	670	28	482
2014	25	129	26	1279	30	1622	28	883	28	644	29	746	27	446
2015	27	181	27	1517	30	2026	28	970	27	706	29	770	25	467

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Iceland

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	1	36	1	40	–	–	–	–	–	–	–	–	–	–
2001	2	48	2	63	2	86	2	18	–	–	–	–	–	–
2002	2	43	2	60	2	83	2	25	–	–	–	–	–	–
2003	2	35	2	64	2	100	2	22	–	–	–	–	–	–
2004	2	54	2	55	2	119	1	27	–	–	–	–	–	–
2005	2	37	2	78	2	130	2	31	2	22	1	13	–	–
2006	2	52	2	57	2	130	2	40	2	13	1	9	–	–
2007	2	42	2	65	2	105	1	29	2	27	1	11	–	–
2008	2	46	2	63	2	123	2	17	1	24	2	7	–	–
2009	2	36	2	59	2	111	2	51	2	27	2	16	–	–
2010	2	37	2	65	2	104	2	31	2	27	2	12	–	–
2011	2	32	2	71	2	130	2	32	2	26	2	17	–	–
2012	2	28	2	58	2	143	2	30	2	16	1	10	1	2
2013	2	18	2	69	2	121	1	32	2	30	1	11	–	–
2014	2	25	2	61	2	152	1	23	1	28	1	11	1	3
2015	1	25	2	88	2	173	2	41	2	36	2	12	1	6

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Ireland

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	17	131	18	549	–	–	–	–	–	–	–	–	–	–
2001	21	182	18	713	–	–	–	–	–	–	–	–	–	–
2002	20	277	22	998	20	736	15	250	–	–	–	–	–	–
2003	24	363	26	1108	26	978	21	348	–	–	–	–	–	–
2004	28	399	38	1286	37	1235	29	418	–	–	–	–	–	–
2005	31	397	38	1360	39	1424	33	502	15	42	11	29	–	–
2006	32	406	38	1347	39	1638	32	550	28	211	23	128	–	–
2007	33	435	41	1332	42	1750	37	598	31	237	29	172	–	–
2008	35	442	38	1242	41	1875	37	685	33	307	29	191	–	–
2009	34	356	41	1261	41	2012	38	671	37	316	30	236	–	–
2010	32	310	39	1207	40	2121	38	670	34	318	30	219	–	–
2011	32	324	39	1057	38	2167	36	608	34	304	28	181	–	–
2012	30	319	40	1038	40	2386	37	677	32	338	34	216	–	–
2013	33	310	39	1069	40	2482	38	726	32	317	33	205	22	89
2014	34	328	37	1075	39	2705	34	698	34	355	31	178	24	89
2015	30	303	37	1057	39	2649	36	697	30	389	29	195	21	86

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Italy

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	37	118	51	473	–	–	–	–	–	–	–	–	–	–
2001	40	129	53	839	–	–	42	297	–	–	–	–	–	–
2002	51	300	53	1343	17	618	49	602	–	–	–	–	–	–
2003	44	293	46	1480	17	923	44	634	–	–	–	–	–	–
2004	37	271	42	1225	14	645	40	576	–	–	–	–	–	–
2005	38	331	41	1479	16	1195	40	714	38	344	–	–	–	–
2006	34	269	38	1164	13	910	35	650	32	321	12	183	–	–
2007	34	298	38	1167	14	1052	36	656	37	391	10	185	–	–
2008	27	194	30	939	14	957	31	580	27	331	11	168	–	–
2009	21	216	23	987	9	863	22	509	22	313	10	195	–	–
2010	33	323	35	1886	23	2623	35	1106	34	739	23	517	–	–
2011	29	294	31	1372	21	2098	31	841	30	688	21	355	–	–
2012	32	293	42	1772	42	3555	42	949	38	984	42	777	27	249
2013	43	436	52	2540	43	4097	50	1386	48	1486	42	796	38	480
2014	42	284	46	2270	38	3802	47	1421	45	1352	37	760	31	483
2015	39	479	46	3300	45	5605	46	2393	43	2015	41	1083	40	667

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Latvia

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2002	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2003	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2004	4	17	7	87	–	–	–	–	–	–	–	–	–	–
2005	5	36	7	127	–	–	–	–	–	–	–	–	–	–
2006	7	37	11	172	10	62	10	56	6	28	9	16	–	–
2007	6	31	12	169	9	76	8	57	7	27	6	16	–	–
2008	3	18	12	164	10	90	9	51	11	40	6	11	–	–
2009	7	30	12	188	9	86	8	48	10	44	7	18	–	–
2010	4	38	10	155	8	98	8	61	8	64	6	21	–	–
2011	5	51	11	197	9	132	8	59	9	65	4	12	–	–
2012	7	64	11	211	10	154	7	73	8	78	6	18	–	–
2013	10	67	13	207	12	136	10	83	10	92	6	25	–	–
2014	7	51	13	222	10	182	10	79	12	118	6	18	6	52
2015	9	64	15	253	11	201	12	94	11	115	6	13	6	61

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Lithuania

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2002	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2003	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2004	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2005	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2006	9	35	13	167	11	171	8	30	8	35	7	14	–	–
2007	10	67	12	240	13	235	10	56	10	41	7	21	–	–
2008	11	48	12	278	12	304	10	67	11	54	7	21	–	–
2009	10	46	13	258	13	297	11	57	12	68	8	21	–	–
2010	9	40	11	257	10	333	10	59	9	81	8	31	–	–
2011	8	48	10	279	10	385	9	74	10	137	6	30	–	–
2012	9	37	11	323	11	462	11	97	11	186	9	28	–	–
2013	9	59	11	267	11	434	9	72	11	145	10	37	–	–
2014	10	67	13	383	13	594	12	122	12	154	9	31	11	66
2015	14	87	14	376	15	583	12	133	12	179	9	41	11	73

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Luxembourg

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	5	22	4	67	–	–	–	–	–	–	–	–	–	–
2001	8	41	8	85	8	193	7	31	–	–	–	–	–	–
2002	9	33	9	97	9	193	8	30	–	–	–	–	–	–
2003	7	54	8	95	8	227	7	41	–	–	–	–	–	–
2004	6	36	7	96	7	216	5	28	–	–	–	–	–	–
2005	5	47	5	83	5	188	5	31	–	–	1	1	–	–
2006	5	31	5	77	5	167	4	42	4	21	4	23	–	–
2007	6	48	6	117	6	275	5	37	6	52	5	36	–	–
2008	6	59	5	117	6	303	5	61	6	52	4	33	–	–
2009	6	67	6	113	6	302	5	54	3	28	6	35	–	–
2010	6	50	6	134	6	354	6	70	6	59	6	32	–	–
2011	5	52	5	127	5	354	5	76	4	48	5	32	–	–
2012	6	39	6	131	6	335	5	74	4	50	5	31	2	6
2013	5	50	5	135	8	322	5	61	4	53	5	34	2	3
2014	5	35	5	125	5	371	5	77	4	66	5	42	3	6
2015	5	29	7	135	5	347	5	81	4	60	4	28	2	8

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Malta

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	1	11	1	76	–	–	–	–	–	–	–	–	–	–
2001	1	13	1	82	1	129	1	24	–	–	–	–	–	–
2002	1	12	1	87	1	74	1	33	–	–	–	–	–	–
2003	1	9	1	121	1	91	1	26	–	–	–	–	–	–
2004	1	18	1	94	1	91	1	41	–	–	–	–	–	–
2005	1	13	1	77	1	85	1	38	1	18	1	45	–	–
2006	1	31	1	90	1	94	1	53	1	32	1	51	–	–
2007	1	13	1	105	1	117	1	37	1	28	1	36	–	–
2008	1	17	1	108	1	128	1	32	1	36	1	31	–	–
2009	1	8	1	85	1	158	1	36	1	38	1	58	–	–
2010	1	11	1	108	1	192	1	37	1	57	1	42	–	–
2011	1	11	1	130	1	219	1	53	1	52	1	42	–	–
2012	1	18	1	102	1	216	1	31	1	57	1	31	1	6
2013	1	9	1	116	1	248	1	41	1	69	1	25	1	7
2014	1	8	1	83	1	279	1	41	1	101	1	38	1	10
2015	1	20	1	89	1	258	1	37	1	92	1	25	1	15

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Netherlands

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	23	728	23	1282	12	1312	8	81	–	–	–	–	–	–
2001	19	734	19	1291	20	1864	13	254	–	–	–	–	–	–
2002	23	892	23	1550	22	2427	22	530	–	–	–	–	–	–
2003	24	891	23	1422	23	2133	23	480	–	–	–	–	–	–
2004	22	758	22	1339	21	2111	22	444	–	–	–	–	–	–
2005	23	815	23	1407	23	2201	23	563	16	301	16	210	–	–
2006	22	1006	23	1636	22	2905	23	776	18	458	19	330	–	–
2007	21	940	21	1471	21	2801	21	827	19	497	19	338	–	–
2008	17	723	16	1191	16	2283	17	632	15	463	15	345	–	–
2009	17	746	16	1035	16	2398	16	522	15	408	15	235	–	–
2010	22	971	21	1565	21	3422	20	834	20	647	21	376	–	–
2011	25	1289	23	1815	23	4436	23	1108	23	729	23	434	–	–
2012	26	1246	25	1963	25	4738	24	1062	25	694	24	408	18	70
2013	27	1269	25	2088	27	4758	26	1019	25	663	25	381	22	70
2014	35	1406	35	2580	35	6514	35	1256	35	926	35	555	26	75
2015	27	1301	27	2107	27	5380	27	1220	27	908	27	502	21	74

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Norway

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	11	429	11	401	11	922	11	110	3	22	4	9	–	–
2001	11	429	11	413	11	966	11	154	4	26	4	20	–	–
2002	11	453	11	502	11	1119	11	177	4	29	4	27	–	–
2003	11	512	11	506	11	1179	11	192	4	46	4	25	–	–
2004	11	600	11	516	11	1212	11	235	4	51	4	27	–	–
2005	11	606	11	553	11	1331	11	304	11	193	11	97	–	–
2006	12	601	12	734	12	1574	12	349	12	263	12	96	–	–
2007	13	616	13	794	13	1713	13	416	13	320	13	105	–	–
2008	13	576	13	837	13	1799	13	403	13	349	13	148	–	–
2009	12	554	12	909	12	1846	12	478	12	396	12	166	–	–
2010	15	576	15	1050	15	2277	15	563	15	479	15	168	–	–
2011	17	622	17	1223	17	2620	17	588	17	450	17	148	–	–
2012	18	576	18	1430	18	3025	18	672	16	623	18	209	10	25
2013	18	551	18	1473	18	3080	18	710	17	645	18	206	12	36
2014	19	536	19	1546	19	3422	19	764	18	746	19	257	13	34
2015	18	429	18	1457	18	3302	18	625	18	701	18	230	11	32

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Poland

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	4	6	19	151	20	103	16	57	–	–	–	–	–	–
2002	7	10	21	186	22	135	19	56	–	–	–	–	–	–
2003	11	16	24	166	25	124	16	64	–	–	–	–	–	–
2004	11	16	30	262	29	192	23	52	–	–	–	–	–	–
2005	6	6	30	198	30	176	21	54	17	53	14	26	–	–
2006	4	9	24	174	26	206	21	68	15	42	16	37	–	–
2007	10	22	24	185	27	256	20	71	18	32	23	67	–	–
2008	34	84	15	99	14	84	11	26	11	19	8	22	–	–
2009	21	71	30	551	29	625	28	267	25	151	27	153	–	–
2010	26	76	35	527	35	771	32	286	33	246	29	169	–	–
2011	41	166	45	868	45	1188	44	484	45	391	35	199	–	–
2012	30	121	41	791	41	1056	35	385	37	370	37	178	35	214
2013	38	170	38	750	38	1072	37	460	35	383	30	198	33	192
2014	31	133	32	750	32	1096	31	457	32	466	30	187	27	189
2015	40	230	48	1192	48	1616	48	648	47	679	40	260	38	246

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Portugal

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	11	97	8	151	–	–	–	–	–	–	–	–	–	–
2001	16	155	16	521	13	418	12	185	–	–	–	–	–	–
2002	14	185	16	544	17	444	13	101	–	–	–	–	–	–
2003	12	95	22	1033	21	792	18	398	–	–	–	–	–	–
2004	14	166	23	1063	19	761	19	410	–	–	–	–	–	–
2005	13	202	19	1153	19	1171	17	405	1	1	–	–	–	–
2006	15	183	17	1306	18	1331	17	464	13	315	11	266	–	–
2007	12	202	20	1383	20	1432	19	518	18	370	16	340	–	–
2008	14	260	20	1557	21	1625	20	588	21	543	19	467	–	–
2009	17	237	20	1824	20	2040	19	675	20	564	18	536	–	–
2010	12	156	18	1633	19	1980	19	621	19	596	19	548	–	–
2011	17	455	18	1507	18	1963	18	684	18	619	18	526	–	–
2012	16	330	18	1455	18	2158	18	687	19	781	18	588	15	169
2013	37	504	44	2450	34	2687	41	963	32	913	40	737	34	234
2014	50	668	53	3241	56	5027	51	1958	53	1714	51	1064	40	266
2015	51	843	57	3645	58	5377	54	1440	58	2099	56	1192	43	312

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Romania

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2002	6	10	10	80	8	28	4	11	–	–	–	–	–	–
2003	5	26	9	85	9	50	5	12	–	–	–	–	–	–
2004	4	9	15	95	12	48	4	9	–	–	–	–	–	–
2005	5	18	13	93	13	84	7	14	1	3	2	23	–	–
2006	8	29	11	83	9	41	9	28	5	32	2	3	–	–
2007	5	27	9	42	9	63	5	14	6	30	2	4	–	–
2008	4	14	5	39	4	58	4	16	3	6	3	8	–	–
2009	3	17	6	48	7	90	5	27	4	27	4	24	–	–
2010	2	13	5	47	5	35	2	19	3	17	5	10	–	–
2011	3	36	5	109	3	95	3	31	4	25	4	10	–	–
2012	7	44	10	230	10	192	9	86	10	102	8	45	4	54
2013	8	44	15	384	14	302	14	135	16	221	15	94	16	138
2014	12	50	15	399	16	309	15	158	16	258	15	94	16	124
2015	9	70	13	424	12	371	12	185	13	271	11	92	13	190

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Slovakia

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2001	4	6	7	37	8	45	6	17	–	–	–	–	–	–
2002	9	16	14	259	14	215	12	79	–	–	–	–	–	–
2003	14	27	16	269	16	239	10	75	–	–	–	–	–	–
2004	9	17	15	289	15	310	12	82	–	–	–	–	–	–
2005	4	8	12	147	13	134	8	46	–	–	–	–	–	–
2006	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2007	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2008	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2009	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2010	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2011	7	26	11	572	11	740	11	305	11	466	11	267	–	–
2012	10	22	14	478	14	696	14	274	14	378	14	199	–	–
2013	8	29	14	558	14	809	14	366	14	490	14	286	14	188
2014	9	32	14	640	14	889	13	411	14	494	14	276	14	171
2015	9	34	14	583	14	896	14	401	14	475	14	278	14	154

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Slovenia

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	7	37	10	152	–	–	–	–	–	–	–	–	–	–
2001	10	156	10	270	10	398	10	54	–	–	–	–	–	–
2002	11	101	11	276	11	409	9	45	–	–	–	–	–	–
2003	11	172	11	299	11	401	10	76	–	–	–	–	–	–
2004	10	166	11	347	11	573	9	91	–	–	–	–	–	–
2005	11	208	11	349	11	657	11	119	10	78	8	38	–	–
2006	11	167	11	365	11	717	10	145	10	145	10	72	–	–
2007	10	195	10	422	10	851	9	183	10	170	9	88	–	–
2008	10	209	10	418	10	874	10	196	9	157	10	95	–	–
2009	10	253	10	471	10	893	10	198	10	189	10	107	–	–
2010	10	232	10	476	10	952	10	196	10	196	10	95	–	–
2011	10	253	10	464	10	1002	10	208	10	232	10	118	–	–
2012	10	251	10	445	10	1168	10	225	10	254	10	134	3	25
2013	10	279	10	465	10	1224	10	248	10	245	10	133	5	25
2014	10	300	10	495	10	1216	10	235	10	233	9	112	8	34
2015	10	323	10	513	10	1326	10	257	10	237	10	141	7	31

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Spain

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	33	621	31	857	–	–	–	–	–	–	–	–	–	–
2001	36	652	35	949	27	1944	26	371	–	–	–	–	–	–
2002	35	658	36	1196	29	2484	35	566	–	–	–	–	–	–
2003	35	656	36	1391	29	2650	36	608	–	–	–	–	–	–
2004	36	684	36	1527	36	3471	36	710	–	–	–	–	–	–
2005	34	740	34	1337	34	2997	35	623	14	56	13	70	–	–
2006	35	625	35	1483	35	3364	34	755	33	564	32	405	–	–
2007	35	862	35	1645	35	3678	35	885	33	618	35	448	–	–
2008	31	695	32	1505	32	3626	32	1002	30	639	32	548	–	–
2009	32	708	33	1715	33	3821	33	1093	32	628	33	544	–	–
2010	41	862	41	1986	41	5696	41	1467	41	1161	41	749	–	–
2011	40	763	40	1965	40	5605	39	1478	40	1145	40	839	–	–
2012	40	644	41	1904	40	5675	41	1508	40	1153	40	853	–	–
2013	38	596	39	1856	39	5933	39	1506	38	1241	39	825	19	100
2014	38	583	39	1943	38	5824	39	1552	39	1266	39	874	23	83
2015	36	672	39	2004	40	6493	39	1572	40	1510	40	884	26	96

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

Sweden

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	19	810	19	1478	1	1	–	–	–	–	–	–	–	–
2001	20	790	20	1634	20	2798	20	671	–	–	–	–	–	–
2002	21	830	21	1837	21	3066	21	695	–	–	–	–	–	–
2003	21	919	21	1855	21	3350	21	850	–	–	–	–	–	–
2004	21	955	21	1906	21	3372	21	856	–	–	–	–	–	–
2005	21	1025	21	1774	21	3241	21	821	18	282	17	149	–	–
2006	21	996	21	1968	20	3539	21	884	20	621	18	300	–	–
2007	21	1032	21	2163	20	3749	21	932	20	649	20	343	–	–
2008	21	1219	21	2410	20	4032	21	1059	20	826	20	315	–	–
2009	19	1063	19	2460	18	4247	19	967	18	706	18	338	–	–
2010	19	1007	19	2792	18	4859	19	1132	18	886	18	378	–	–
2011	18	1016	18	3045	17	5273	18	1254	17	972	17	416	–	–
2012	18	1030	18	3263	17	5542	18	1211	17	977	17	357	–	–
2013	18	1166	18	4124	18	7538	18	1697	18	1300	18	533	9	75
2014	16	792	16	3501	16	6549	16	1358	16	1000	16	438	10	52
2015	17	867	17	3415	17	6768	17	1280	17	1141	17	435	9	35

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

United Kingdom

General information on EARS-Net participating laboratories

Annual number of reporting laboratories* and number of reported isolates, 2000–2015

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*		*Acinetobacter* spp	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2000	28	512	27	1419	–	–	–	–	–	–	–	–	–	–
2001	26	573	25	1422	20	1424	–	–	–	–	–	–	–	–
2002	23	617	21	1588	20	1958	–	–	–	–	–	–	–	–
2003	50	1334	51	3548	19	2253	–	–	–	–	–	–	–	–
2004	54	1059	54	3562	20	2091	–	–	–	–	–	–	–	–
2005	53	1375	58	3971	23	2359	27	591	23	420	25	438	–	–
2006	51	1514	55	4132	26	2438	22	547	22	404	24	353	–	–
2007	50	1785	55	4865	20	2374	18	435	18	382	19	370	–	–
2008	51	1223	55	3355	15	2456	14	274	15	350	14	345	–	–
2009	59	1396	69	2977	28	4712	26	712	27	725	26	639	–	–
2010	50	1459	55	2730	29	5389	28	651	28	840	28	588	–	–
2011	53	1513	53	3430	29	5971	28	723	28	1007	28	599	–	–
2012	54	1295	55	2696	29	6527	27	877	28	1075	28	681	24	109
2013	54	1337	56	3049	31	7294	30	964	31	1169	31	715	27	165
2014	56	1418	56	3569	31	7369	29	945	29	1180	29	649	27	129
2015	44	1126	47	3125	22	6117	22	776	22	1077	22	541	20	153

* Number of laboratories reporting at least one isolate during the specific year. Please note that the total number of laboratories participating in EARS-Net might be higher.

European Centre for Disease Prevention and Control (ECDC)

Postal address:
Granits väg 8, SE-171 65 Solna, Sweden

Visiting address:
Tomtebodavägen 11A, SE-171 65 Solna, Sweden

Tel. +46 858601000
Fax +46 858601001
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