EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

SURVEILLANCE REPORT

Antimicrobial resistance surveillance in Europe

2012

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Antimicrobial resistance surveillance in Europe

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

2012

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

Furthermore, all EARS-Net participants and National Epidemiological Contact Points are acknowledged for facilitating data transfer and providing valuable comments for this report. The ECDC's staff members Catalin Albu, Gaetan Guyodo and Encarna Gimenez are acknowledged for data management and providing helpdesk support to the participating countries.

John Stelling is acknowledged for his dedicated technical support to the WHONET users among the participating countries.

ECDC staff members Liselotte Diaz Högberg and Ole Heuer are acknowledged for the preparation of the report, and Christine Walton at UK NEQAS is acknowledged for her contribution to Annex 1. In addition, the ECDC wishes to thank EARS-Net Coordination Group members Derek Brown, Jose Campos, Tim Eckmanns, Christian Giske, Hajo Grundmann, Vincent Jarlier, Gunnar Kahlmeter, Jolanta Miciuleviciene, Jos Monen, Gian Maria Rossolini, Gunnar Skov Simonsen, Nienke van de Sande-Bruinsma and Helena Zemlickova for providing valuable comments and scientific advice during the production of the report.

Suggested citation for full report:
European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2012. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2013.

Cover picture © istockphoto

ISSN 1831-9491

ISBN 978-92-9193-511-6

doi 10.2900/93403

Catalogue number TQ-AM-13-001-EN-C

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Abbreviations and acronyms

3GCREC	Third-generation cephalosporin-resistant *Escherichia coli*
3GCRKP	Third generation cephalosporin-resistant *Klebsiella pneumoniae*
AMR	Antimicrobial resistance
AmpC	Ampicillinase C
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*
CRG	Commissie Richtlijnen Gevoeligheidsbepalingen (Dutch)
DIN	Deutsche Industrie Norm (German)
DNA	Deoxyribonucleic acid
EARSS	European Antimicrobial Resistance Surveillance System
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EU	European Union
EQA	External quality assessment
ESBL	Extended-spectrum beta-lactamase
ICU	Intensive care unit
IMP	Imipenemase
KPC	*Klebsiella pneumoniae* carbapenemase
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 gene
PBP	Penicillin-binding protein
PCV	Pneumococcal conjugate vaccine
RNA	Ribonucleic acid
SFM	Comité de l'Antibiogramme de la Société Française de Microbiologie (French)
SIR	Susceptible, intermediate, resistant
SHV	Sulfhydryl-variable extended-spectrum beta-lactamase gene
SRGA	Swedish Reference Group for Antibiotics
TESSy	The European Surveillance System (at ECDC)
TEM	Temoneira extended-spectrum beta-lactamase gene
UK NEQAS	United Kingdom National External Quality Assessment Scheme 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
www.iph.fgov.be
University of Antwerp

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

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

Cyprus
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
Finnish Study Group for Antimicrobial Resistance (FiRe)
www.finres.fi

France
Pitié-Salpêtrière Hospital
National Institute for Public Health Surveillance
www.invs.sante.fr
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.simi.iss.it/antibiotico_resistenza.htm

Latvia
Paul Stradins Clinical University Hospital
State Agency 'Infectology Centre of Latvia'

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

Luxembourg
National Health Laboratory
Microbiology Laboratory, Luxembourg's Hospital Centre

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 Antimicrobial Resistance and Surveillance

Portugal

National Institute of Health Dr. Ricardo Jorge
www.insarj.pt

Ministry of Health

Directorate-General of Health

Romania

National Institute of Research and Development for Microbiology and Immunology 'Cantacuzino'

Institute of Public Health

Slovakia

National Reference Centre for Antimicrobial Resistance

Public Health Authority of Slovakia

Regional Public Health Authority Banska Bystrica

Slovenia

National Institute of Public Health

University of Ljubljana

Spain

Health Institute Carlos III
www.isciii.es

National Centre of Microbiology

Sweden

Swedish Institute for Communicable Disease Control
www.smi.se

United Kingdom

Public Health England
https://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 2013 (data referring to 2012), and on trend analyses of EARSS/EARS-Net data reported by the participating countries during the period 2009 to 2012.

A majority of the *Escherichia coli* and *Klebsiella pneumoniae* isolates reported to EARS-Net in 2012 was resistant to at least one of the antimicrobials under surveillance, and many of these had combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides. This is consistent with the continuously increasing trends of antimicrobial resistance seen in over a third of the reporting counties over the last several years, and a high percentage of extended-spectrum beta-lactamase (ESBL)-positive isolates. The increasing trends can be noted not only for countries that have comparatively low resistance percentages, but also countries with already very high levels.

The percentage of carbapenem resistance among *K. pneumoniae* isolates increased during 2012, further reducing the number of available options for antimicrobial therapy of serious infections with this microorganism. Carbapenem resistance is often seen in combination with resistance to several other antimicrobial groups. This type of combined resistance is most commonly reported from southern Europe.

Carbapenem resistance and resistance to multiple antimicrobial groups were also common in *Pseudomonas aeruginosa* and *Acinetobacter* spp. isolates. *Acinetobacter* spp. were included in EARS-Net surveillance from 2012, after several Member States noticed increasing resistance for this microorganism. Eighteen out of 30 countries were able to report 2012 data and inter-country variation for the percentage of carbapenem resistance in *Acinetobacter* spp. ranged from zero to 88%.

Resistance trends in gram-positive bacteria showed a more diverse pattern across Europe. The trends for *Streptococcus pneumoniae* and enterococci are generally stable, but with large inter-country variations in the percentage of resistant isolates.

For meticillin-resistant *Staphylococcus aureus* (MRSA), the population-weighted EU/EEA mean decreased significantly over the last four years. Despite this, MRSA remains a public health priority as the percentage is still above 25% in seven of the 30 reporting countries, with a population-weighted EU/EEA mean of 17.8%.

For several antimicrobial agent–microorganism combinations, an overall north-to-south and west-to-east gradient is evident in Europe. In general, lower resistance percentages are reported from the north and higher percentages from the south and east of Europe. These geographical differences may reflect differences in infection control practices and antimicrobial use in the reporting countries. Prudent use of antimicrobial agents and comprehensive infection control practices are the cornerstones of effective prevention and control efforts aimed at reducing the selection and transmission of resistant bacteria. The already high percentages and increasing trends of antimicrobial resistance in gram-negative bacteria in Europe described in this report illustrate the continuous loss of effective antimicrobial therapy against these microorganisms and emphasise the need for comprehensive strategies targeting all health sectors.

1 Introduction

Antimicrobial resistance (AMR) is a serious threat to public health in Europe, leading to mounting healthcare costs, treatment failure, and deaths. The issue calls for concerted efforts at Member State level but also close international cooperation in order to preserve future antimicrobial effectiveness and access to effective treatment for bacterial infections.

Surveillance of AMR is a fundamental part of an effective response to this threat, and surveillance results constitute an essential source of information on the magnitude and trends of resistance. Surveillance of AMR at EU level has been assured by European law: AMR is listed as a special health issue in Annex 1 of Commission Decision 2000/96/EC on the communicable diseases to be progressively covered by the Community network under Decision No 2119/98/EC of the European Parliament and of the Council[1]; surveillance of antimicrobial resistance within the EU/EEA is carried out in accordance with Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European Centre for Disease Prevention and Control (ECDC)[2]. Over the years, the need for the Member States to collaborate on AMR surveillance has been reinforced by several council conclusions including the 'Council Conclusion on Antimicrobial Resistance' of 10 June 2008 and the recent 'Council Conclusion on the impact of antimicrobial resistance in the human health sector and in the veterinary sector – a "One Health" perspective' of 22 June 2012[3].

About EARS-Net

The European Antimicrobial Resistance Surveillance Network (EARS-Net) is the continuation of the European Antimicrobial Resistance Surveillance System (EARSS), which was hosted by the Dutch National Institute for Public Health and the Environment (RIVM). Established in 1998, EARSS successfully created a multistate network for AMR surveillance and demonstrated how international AMR data could be provided to inform decisions and raise awareness among stakeholders and policy makers. By 1 January 2010, the management and administration of EARSS was transferred from RIVM to the European Centre for Disease Prevention and Control (ECDC), and the network was renamed EARS-Net. Data collected by the network from EU/EEA Member States since 1999 was 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: page vii). Scientific guidance and support to the network is provided by the EARS-Net Coordination Group. This is composed of individual experts selected from among the nominated disease-specific contact points and experts from other organisations that are involved in surveillance of antimicrobial resistance. EARS-Net activities are coordinated in close collaboration with two other major surveillance networks: the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the Healthcare-associated Infections Surveillance Network (HAI-Net). EARS-Net 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/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 that constitute a basis 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 in the surveillance chain by offering an annual external quality assessment (EQA).

Since 1998, the participating laboratories have collected AMR data on over one million unique invasive bacterial isolates. Being the largest publicly funded system for surveillance of antimicrobial resistance in Europe, data from EARS-Net play an important role in documenting the occurrence and spread of antimicrobial resistance in Europe, and contribute to raising awareness of the problem at the political level, among public health officials, in the scientific community and with the general public. All participating countries have open access to the EARS-Net database. Public access to descriptive data (maps, graphs and tables) is also available through a web-based data query tool[4] and more detailed analyses are presented in the annual reports and in scientific publications.

1 Official Journal of the European Communities. OJ L 28, 3.2.2000, p. 50–53.

2 Official Journal of the European Union. OJ L 142, 30.4.2004, p. 1.

3 Official Journal of the European Union. OJ C 211, 18.7.2012, p. 2–5.

4 EARS-Net interactive database. Available at http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx

2 Data collection and analysis

EARS-Net performs surveillance of AMR in eight bacterial microorganisms of public health importance:

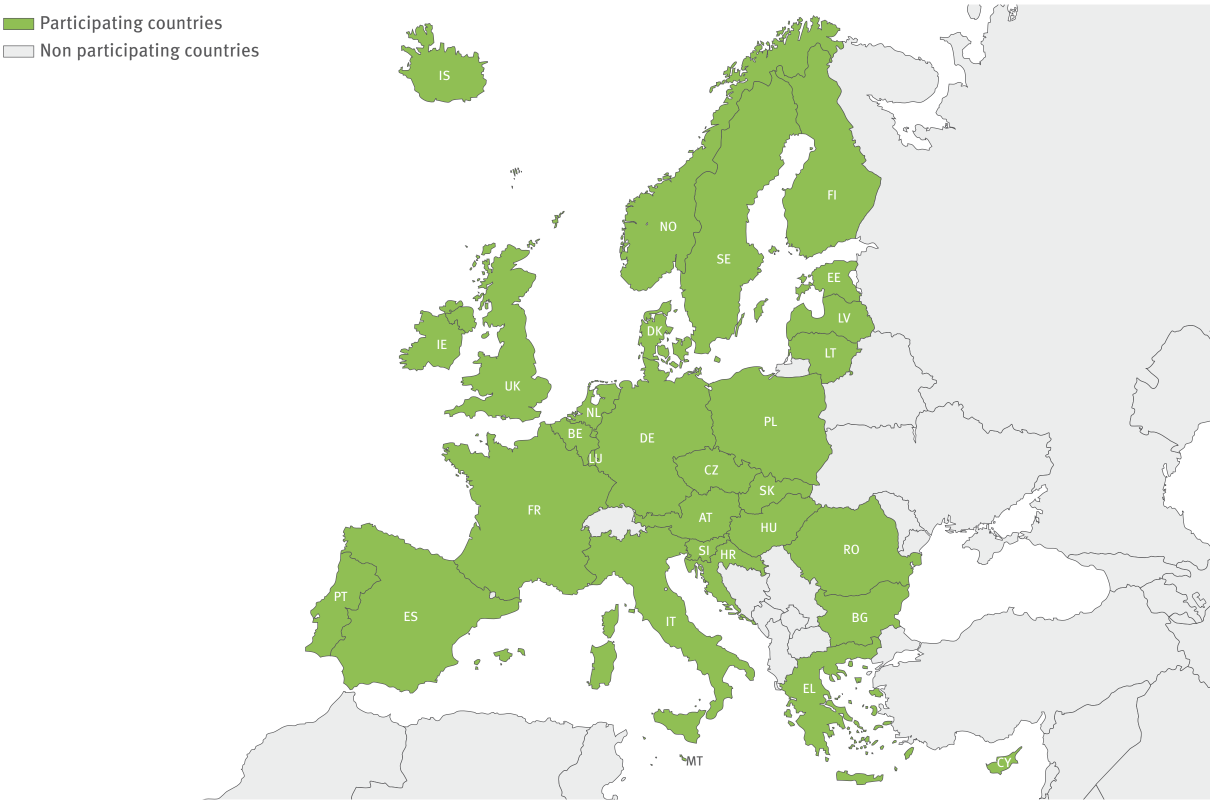
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Acinetobacter* species (data for 2012 and 2013 included as a pilot project).
- *Streptococcus pneumoniae*
- *Staphylococcus aureus*
- *Enterococcus faecalis*
- *Enterococcus faecium*

All 28 EU Member States and two EEA countries (Norway and Iceland) reported AMR data for 2012 to EARS-Net (Figure 2.1). Croatia joined the EU on 1 July 2013 and reported data (2009–2012) to EARS-Net for the first time.

Only data from invasive (blood and cerebrospinal fluid) isolates are included. The panels of antimicrobial agent combinations under surveillance for each bacterium are defined in the EARS-Net Reporting Protocol[5].

5 EARS-Net Reporting Protocol Version 3, 2013. Available from http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/Documents/2013_EARS-Net_Reporting-Protocol.pdf

Figure 2.1. Countries contributing AMR data for 2012 to EARS-Net



AT	Austria	**FI**	Finland	**MT**	Malta
BE	Belgium	**FR**	France	**NL**	Netherlands
BG	Bulgaria	**HR**	Croatia	**NO**	Norway
CY	Cyprus	**HU**	Hungary	**PL**	Poland
CZ	Czech Republic	**IE**	Ireland	**PT**	Portugal
DE	Germany	**IS**	Iceland	**RO**	Romania
DK	Denmark	**IT**	Italy	**SE**	Sweden
EE	Estonia	**LT**	Lithuania	**SI**	Slovenia
EL	Greece	**LU**	Luxembourg	**SK**	Slovakia
ES	Spain	**LV**	Latvia	**UK**	United Kingdom

Routine antimicrobial susceptibility test results are collected from clinical laboratories by the national representative in each participating country. National data are uploaded directly by the national data manager to a central database, TESSy, at ECDC on a yearly basis. TESSy is a web-based system for 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 that are under EU surveillance. TESSy filters the uploaded records according to the list of microorganism/specimen/antimicrobial combinations included in the AMR surveillance and obtains one record per patient, organism, antimicrobial class combination and year (for details please refer to the EARS-Net Reporting Protocol). After uploading data, the national data manager receives a validation report and each country approves its own data before it is included for analysis. Please note that data presented by EARS-Net might diverge slightly from the data presented by the Member States themselves, as data cleaning routines might differ.

In addition to collection of data on AMR, additional 'reference' information from the national networks is collected through questionnaires distributed to participating laboratories and hospitals by the national contact points. Information is 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 national data managers receive the completed questionnaires, compile them and produce the final format suitable for uploading to TESSy. For more information on denominator data, see Annex 2 and the Country Summary Sheets.

2.1 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 found resistant (R) or with intermediate susceptibility (I) using the same clinical breakpoints as interpretive 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.

As a general rule, data are expressed as a resistance percentage, i.e. the percentage of R isolates out of all isolates with antimicrobial susceptibility testing (AST) information on that specific organism–antimicrobial agent combination, 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 is determined for the resistance percentage by applying an exact confidence interval for binomial data.

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. Country weights 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 weight 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 on-line database[6].

If fewer than 10 isolates are reported for a specific organism–antimicrobial agent combination in a country, the results for this country are not displayed on the maps presented in this report.

The statistical significance of temporal trends of antimicrobial resistance percentages by country is 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, are not included in the analysis. The statistical significance of trends is assessed by the Cochran–Armitage test. An additional sensitivity analysis is performed by repeating the Cochran–Armitage test only including laboratories which consistently reported for the full four-year period in order to exclude selection bias when assessing the significance of the trends.

2.2 Interpretation of the results

Interpretation of the results, both for inter-country comparison and in some cases for interpretation of national trends, should be undertaken 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 between reporting countries. Some countries report data from large national surveillance systems with high national coverage, while other countries report data from a smaller subset of local laboratories and hospitals.

For countries only reporting data from a smaller 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 for 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

6 http://epp.eurostat.ec.europa.eu/portal/page/portal/eurostat/home/

previous four years, is provided for all national trend analyses.

For detailed information on the number of reporting laboratories, characteristics of reported data and population under surveillance, see Annex 2 and Country Summary Sheets.

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 indisputable. 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 sources were accepted. However, invasive isolates may, for biological reasons, not be representative for isolates of the same bacterial species from other sites, i.e. urinary tract infections, pneumonia, wound infections, etc.

Case ascertainment of patients with bloodstream infections (BSIs) is strongly linked to diagnostic habits 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 different 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 a serious overestimation of the percentage resistance by not including susceptible BSI isolates in the denominator.

For detailed information on national blood culture frequency, see Annex 2.

Laboratory routines and capacity

The use of guidelines for clinical breakpoints varies between countries in Europe, and in some instances even between laboratories in the same country. At present, there is an ongoing shift among European laboratories from using CLSI (Clinical and Laboratory Standards Institute) to EUCAST clinical guidelines. As a result the interpretation of AST results may vary, at least for resistance mechanisms producing minimum inhibitory concentrations (MICs) close to the breakpoints. In addition, the use of microbiological breakpoints may change over time, when breakpoint protocols are updated or changed. As data on quantitative measures (i.e. zone diameters in disk diffusion tests 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 of the laboratory to identify the microorganism and its associated antimicrobial susceptibility pattern may differ. All laboratories providing data for EARS-Net are offered participation in an annual external quality assessment (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 the gram-negative bacterium most frequently isolated from blood cultures. It is the most frequent cause of bloodstream infections, community- and hospital-acquired urinary tract infections, is associated with spontaneous and post-surgical peritonitis and with skin and soft tissue infections of polymicrobial aetiology, 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 antimicrobials, and are 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, (whereby 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 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, and monobactams. During the past decade, however, these enzymes have largely been replaced by the CTX-M-type ESBLs, which are now the most common ESBLs in *E. coli*. Most ESBLs can be inhibited by beta-lactamase inhibitors such as clavulanic acid, sulbactam or tazobactam. Hundreds of ESBL variants have been identified to date. An important factor in their global dominance is the wide dissemination of bacterial clones producing CTX-M-type ESBLs (e.g., CTX-M-15). Other enzymes affecting the 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 is still less common than ESBLs in *E. coli* in Europe, but 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

Figure 3.1. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins by country, EU/EEA countries, 2012

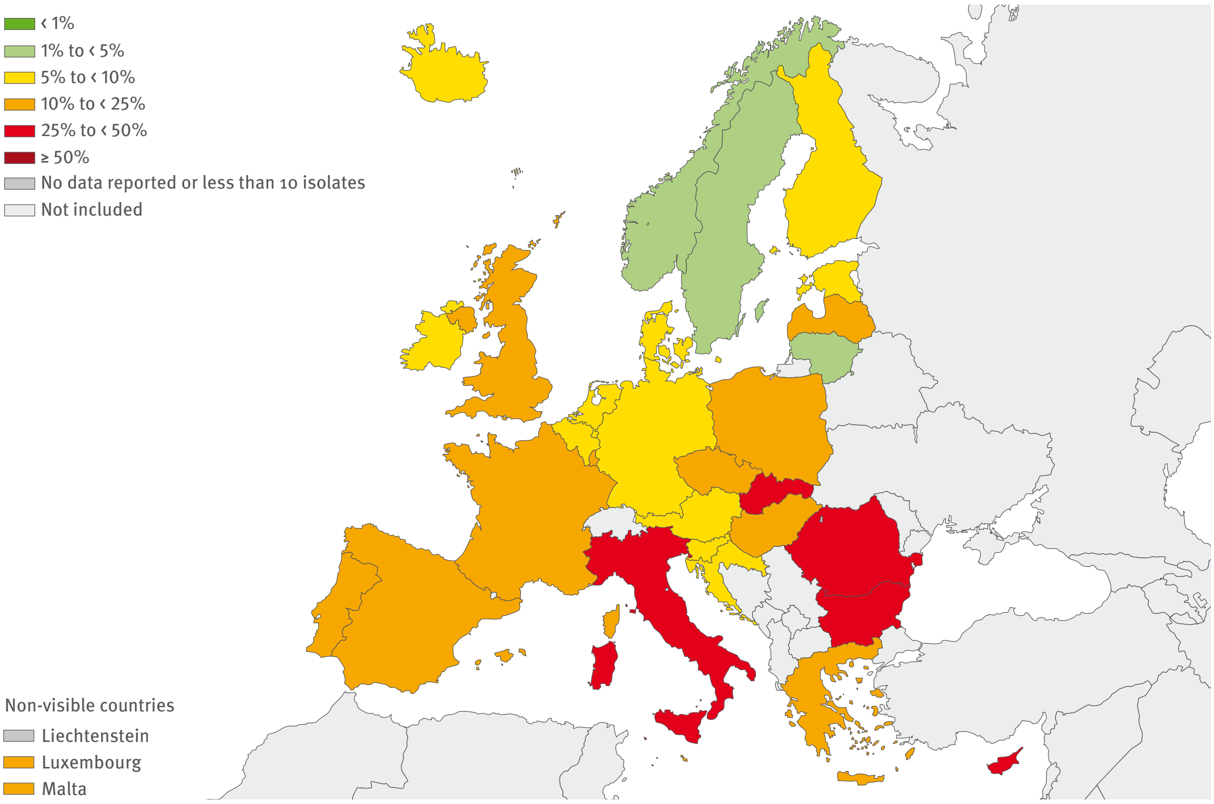
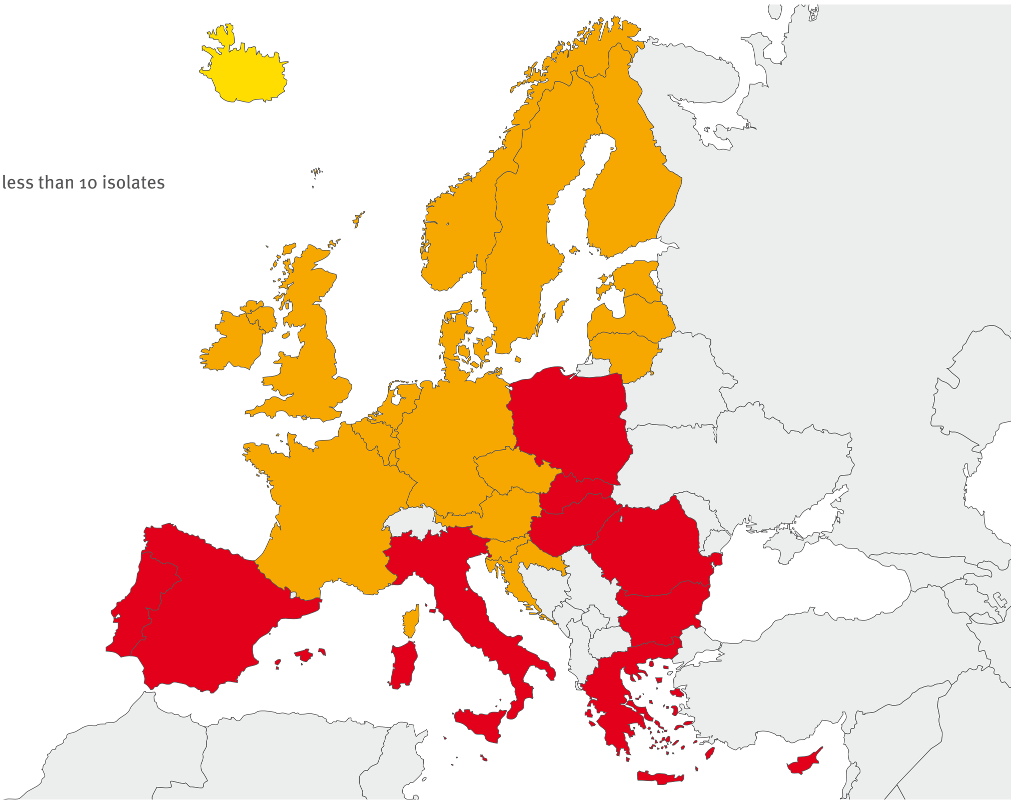


Figure 3.2. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2012**

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

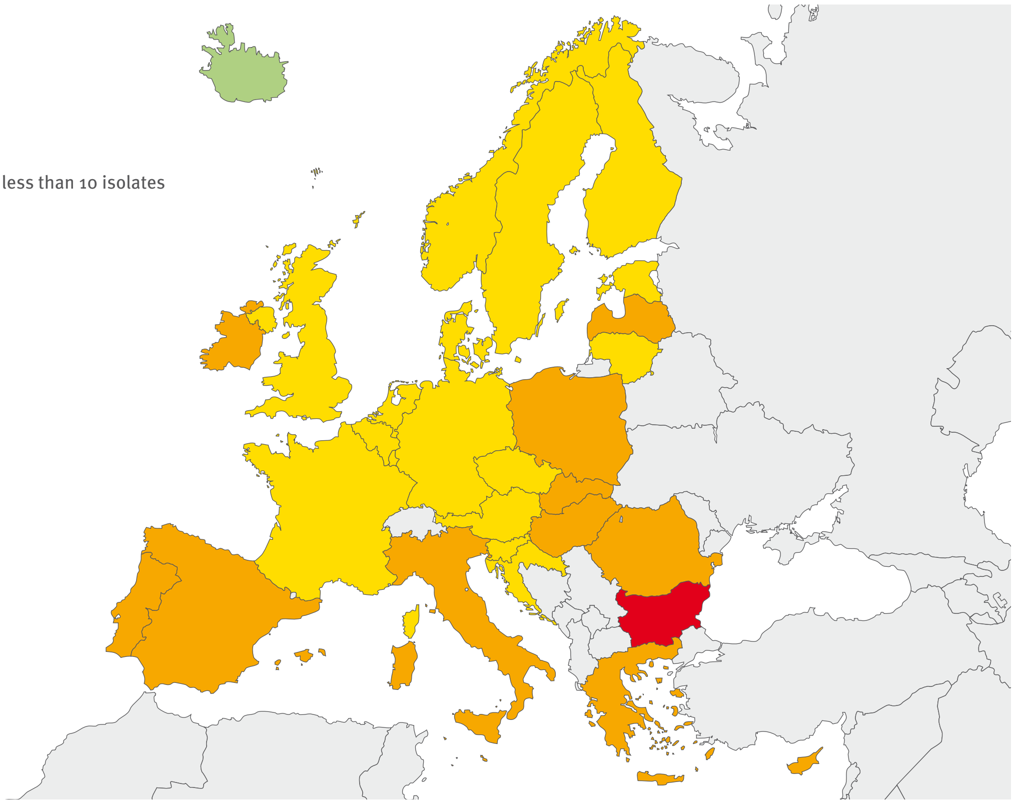


Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

Figure 3.3. ***Escherichia coli*****. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2012**

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included



Non-visible countries

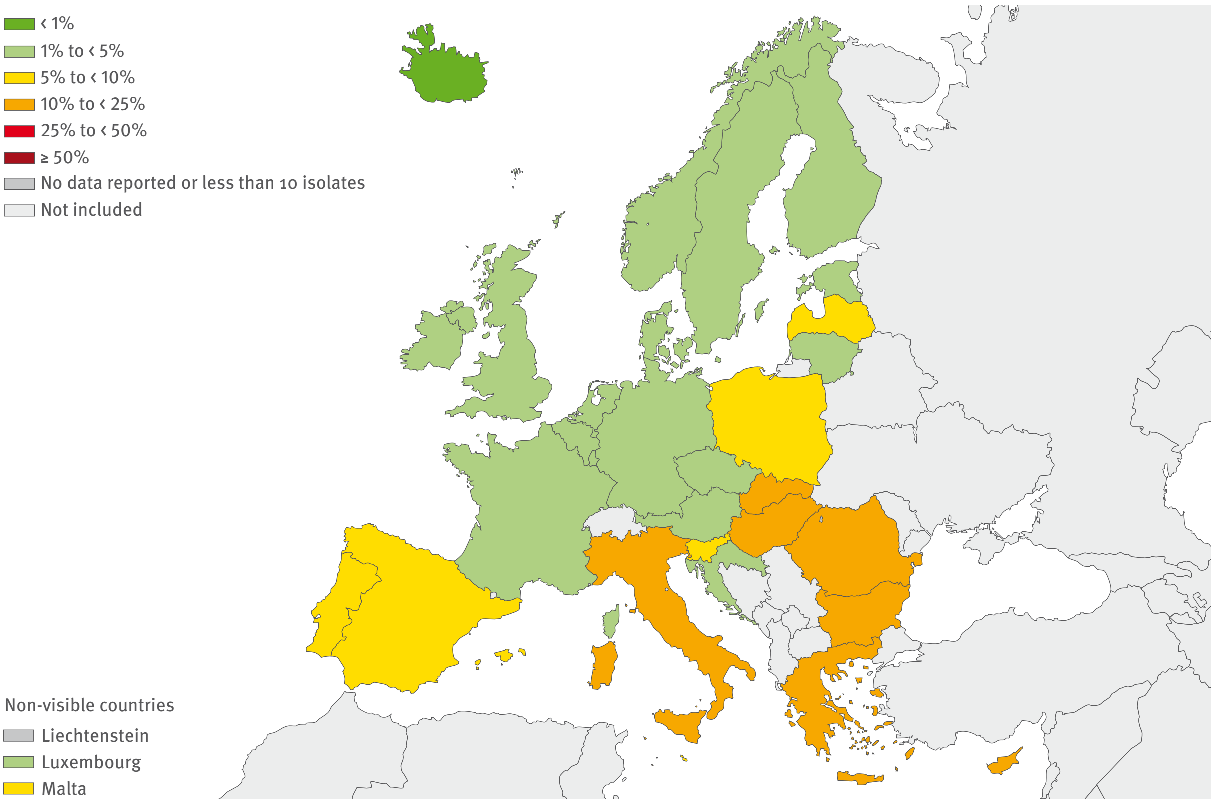
- Liechtenstein
- Luxembourg
- Malta

available beta-lactam agents. Another growing family of beta-lactamases comprises the OXA-type enzymes that confer resistance to ampicillin and cefalotin 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 recently emerged in *E. coli* and other Enterobacteriaceae. When produced alone, they confer reduced susceptibility to carbapenems and resistance to penicillins, but not to the expanded-spectrum cephalosporins. Unfortunately, the finding of *E. coli* strains which produce multiple beta-lactamases is becoming increasingly common, also leading to resistance to the latter cephalosporins.

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 efflux pump, which effluxes 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 rRNA, which excludes 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 pan-resistance to aminoglycosides, and are frequently accompanying carbapenemases.

Figure 3.4. *Escherichia coli*. Percentage (%) of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, by country, EU/ EEA countries, 2012



3.1.3 Antimicrobial susceptibility

- A majority of the *E. coli* isolates reported to EARS-Net in 2012 was resistant to at least one of the antimicrobial groups under surveillance. Aminopenicillin resistance was reported in more than half of the isolates, followed by fluoroquinolone resistance and resistance to third-generation cephalosporins. Many of the isolates resistant to third-generation cephalosporins were ESBL-positive and showed resistance to additional antimicrobial groups.
- During the last four-year period, an increase in the percentages of resistant *E. coli* isolates was observed throughout Europe. Especially worrisome is the increase of resistance to third-generation cephalosporins, aminoglycosides and combined resistance to three major antimicrobial groups, for which a majority of the countries reported significantly increasing trends.
- Carbapenem-resistant *E. coli* remains generally rare, but is reported from southern Europe. The proportion of isolates with resistance to all antimicrobial groups under surveillance by EARS-Net remains very low (< 0.1%).

Full susceptibility

- For 2012, 74 687 *E. coli* isolates were reported to EARS-Net, of which 52 526 isolates (70%) from 28 countries had complete AST information for all antimicrobial groups under surveillance for the bacteria (aminopenicillins, third-generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems).
- The population-weighted EU/EEA mean percentage for isolates fully susceptible to all included antimicrobial groups was 39.5% in 2012, ranging from 22.3% (Bulgaria) to 57.2% (Finland) (Table 3.1).

Aminopenicillins

- For 2012, 29 countries reported 60 138 isolates with AST information for aminopenicillins. The number of isolates with relevant AST information reported per country ranged from 131 to 9 599 (Table 3.1).
- The EU/EEA population-weighted mean percentage for aminopenicillin resistance was 57.4% in 2012. The percentages of resistant isolates in the reporting countries ranged from 39.7% (Finland) to 71.0% (Bulgaria). Seven countries reported resistant percentages of 25–50%, while the remaining 22 countries reported resistant percentages above 50% (Table 3.1).
- Trends for the period 2009–2012 were calculated for 26 countries. Statistically significant increasing trends were observed for six countries (Denmark, Finland, Greece, Italy, the Netherlands and Norway). For Denmark and Italy the trend was not significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for four countries (the Czech Republic, Germany, Lithuania and Luxembourg). For Lithuania this trend was not significant when considering only laboratories reporting consistently for all four years (Figure 3.5).

Third-generation cephalosporins

- For 2012, 30 countries reported 70 857 isolates with AST information for third-generation cephalosporins. The number of isolates reported per country ranged from 138 to 9 563 (Table 3.1).
- The EU/EEA population-weighted mean percentage for third-generation cephalosporin resistance was 11.8% in 2012. The percentages of resistant isolates in the reporting countries ranged from 4.4% (Sweden) to 38.1% (Bulgaria). Three countries reported resistance percentages below 5%, 11 countries reported 5–10%, 11 countries reported 10–25%, and five countries reported above 25% (Table 3.1 and Figure 3.1).
- Trends for the period 2009–2012 were calculated for 28 countries. Statistically significant increasing trends were observed in 19 of 28 countries. For four countries (the Czech Republic, Estonia, Italy and Poland), the trends did not remain significant when considering only data from laboratories reporting consistently for all four years. The EU/EEA population-weighted mean percentage also had a statistically significant increasing trend, from 8.2% in 2009 to 11.8% in 2012. Only Lithuania had a statistically significant decreasing trend of resistance to third-generation cephalosporins during the same period (Figure 3.6).

Extended-spectrum beta-lactamase (ESBL) production

- Twenty-three countries were included in the calculation of ESBL percentages for *E. coli*. Data were only included from laboratories reporting ESBL test results for all isolates identified as resistant to third-generation cephalosporins, and only from countries with at least 10 of such isolates.
- Among *E. coli* isolates resistant to third-generation cephalosporins, a large percentage was ascertained as ESBL-positive. Sixteen of 23 countries reported between 85% and 100% ESBL-positive isolates among isolates resistant to third-generation cephalosporins (Table 3.2).

Fluoroquinolones

- For 2012, 30 countries reported 71 800 isolates with relevant AST information for fluoroquinolones. The number of isolates reported by the countries ranged from 134 to 9 470 (Table 3.1).
- The EU/EEA population-weighted mean percentage for fluoroquinolone resistance was 22.3% in 2012. The percentages of resistant isolates in the reporting countries ranged from 9.7% (Iceland) to 42.0% (Cyprus and Italy). One country reported a resistance percentage below 10%, 18 countries reported 10–25%

and 11 countries reported above 25% (Table 3.1 and Figure 3.2).

- Trends for the period 2009–2012 were calculated for 28 countries. Statistically significant increasing trends were observed for 10 countries. For Italy and Poland, these trends were not significant when considering only data from laboratories reporting consistently during all four years. Statistically significant decreasing trends were observed for Germany and Hungary; the trend for Hungary was not significant when considering only data from laboratories reporting consistently for all four years (Figure 3.7).

Aminoglycosides

- For 2012, 30 countries reported 68 567 isolates with relevant AST information for aminoglycosides. The number of isolates reported by the countries ranged from 138 to 5 750 (Table 3.1).
- The EU/EEA population-weighted mean percentage for aminoglycoside resistance was 10.3% in 2012. The percentages of resistant isolates in the reporting countries ranged from 3.6% (Iceland) to 26.5% (Bulgaria). One country reported resistance percentages below 5%, 16 countries reported 5–10%, 13 countries reported above 10% (Table 3.1 and Figure 3.3).
- Trends for the period 2009–2012 were calculated for 28 countries. Statistically significant increasing trends were observed for 14 countries. For Poland and Romania the trends did not remain significant when considering only data from laboratories consistently reporting for all four years. The EU/EEA population-weighted mean percentage also had a statistically significant increase during the same period, from 8.6% in 2009 to 10.3% in 2012. A statistically significant decreasing trend of aminoglycoside resistance was observed for three countries (Germany, Lithuania and Malta) (Figure 3.8).

Carbapenems

- For 2012, 29 countries reported 68 365 isolates with relevant AST information for carbapenems. The number of isolates reported by the countries ranged from 153 to 9 091 (Table 3.1).

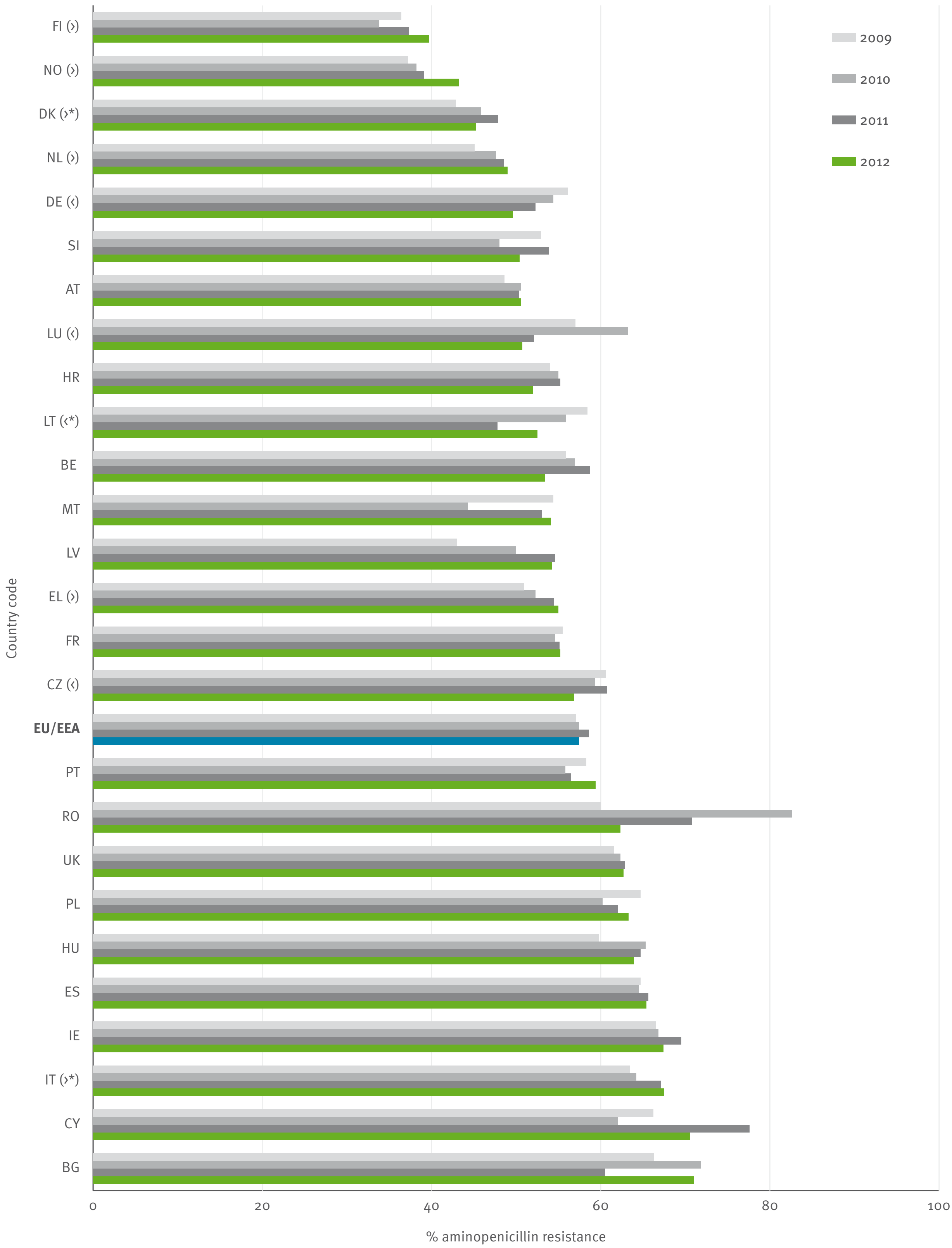
Table 3.1. *Escherichia coli*. Total numbers of isolates tested (N) and percentage susceptible to all antimicrobial groups under EARS-Net surveillance*; total numbers of isolates tested (N) and percentages resistant to aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and combined resistance (%R), including 95% confidence intervals (95% CI), by country, EU/EEA countries, 2012**

Country	Fully susceptible*		Aminopenicillins		Third-gen. cephalosporins		Fluoroquinolones		Aminoglycosides		Carbapenems		Combined** resistance	
	N	% fully S (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)
Austria	3140	45.5 (44-47)	3 625	50.6 (49-52)	3710	8.7 (8-10)	3610	20.6 (19-22)	3713	6.5 (6-7)	3340	0.1 (0-0)	3579	2.5 (2-3)
Belgium	3269	40.1 (38-42)	3898	56.3 (55-58)	4097	6.9 (6-5)	3515	22.2 (21-24)	3689	5.9 (5-7)	4119	< 0.1 (0-0)	3330	1.8 (1-2)
Bulgaria	175	22.3 (16-29)	207	71.0 (64-77)	223	38.1 (32-45)	223	34.1 (28-41)	223	26.5 (21-33)	191	2.6 (1-6)	223	16.1 (12-22)
Croatia	902	43.1 (38-44)	917	51.3 (48-55)	900	6.0 (3-9)	906	17.2 (15-20)	913	7.0 (6-9)	908	0.0 (0-0)	902	2.1 (1-3)
Cyprus	176	26.1 (20-33)	176	70.5 (63-77)	176	31.8 (25-39)	176	42.0 (35-50)	176	21.0 (15-28)	176	0.0 (0-2)	176	14.8 (10-21)
Czech Republic	1725	41.9 (40-44)	2811	56.8 (55-59)	2812	11.5 (10-13)	2809	21.0 (19-23)	2812	8.4 (7-10)	1729	0.1 (0-0)	2809	4.5 (4-5)
Denmark	1678	50.5 (48-53)	3708	45.2 (44-47)	2519	7.9 (7-9)	3923	14.1 (13-15)	3687	7.3 (6-8)	2865	0.0 (0-0)	2285	2.6 (2-3)
Estonia	166	47.6 (40-55)	216	48.1 (41-55)	305	7.9 (5-11)	304	14.1 (10-19)	306	7.5 (5-11)	252	0.0 (0-1)	303	1.7 (1-4)
Finland	1921	57.2 (55-59)	2090	39.7 (38-42)	3162	6.2 (5-7)	3162	11.7 (11-13)	2993	6.1 (5-7)	3161	0.0 (0-0)	2993	3.1 (3-4)
France	5628	42.1 (41-43)	9599	55.2 (54-56)	9563	10.0 (9-11)	9470	17.8 (17-19)	5750	8.2 (7-9)	9091	0.0 (0-0)	5655	3.3 (3-4)
Germany	4140	47.2 (46-49)	4162	49.6 (48-51)	4186	8.8 (8-10)	4188	21.1 (20-22)	4190	7.1 (6-8)	4184	< 0.1 (0-0)	4179	3.2 (3-4)
Greece	1264	40.7 (38-43)	1270	55.0 (52-58)	1393	16.2 (14-18)	1372	29.1 (27-32)	1372	17.9 (16-20)	1396	1.4 (1-2)	1368	10.7 (9-12)
Hungary	1251	31.0 (28-34)	1328	63.9 (61-67)	1411	17.4 (15-20)	1393	28.9 (27-31)	1409	17.2 (15-19)	1307	0.0 (0-0)	1387	10.5 (9-12)
Iceland	0	–	131	44.3 (36-53)	138	5.1 (1-9)	134	9.7 (5-15)	138	3.6 (0-7)	0	–	130	0.7 (0-4)
Ireland	2215	30.4 (29-32)	2329	67.4 (65-69)	2288	9.2 (8-10)	2380	24.3 (23-26)	2378	11.1 (10-12)	2369	0.0 (0-0)	2283	4.0 (3-5)
Italy	1929	29.3 (27-31)	2121	67.5 (65-70)	2994	26.3 (25-28)	2917	42.0 (40-44)	3091	21.4 (20-23)	3018	0.2 (0-0)	2684	14.5 (13-16)
Latvia	150	45.3 (37-54)	153	54.2 (46-62)	154	14.9 (10-22)	152	14.5 (9-21)	154	11.7 (7-18)	153	0.0 (0-2)	152	6.6 (3-12)
Lithuania	442	45.5 (41-50)	461	52.5 (48-57)	462	4.8 (3-7)	456	14.7 (12-18)	461	9.5 (7-13)	450	0.0 (0-1)	455	1.3 (0-3)
Luxembourg	333	46.8 (41-52)	335	50.7 (45-56)	334	11.4 (8-15)	334	24.0 (19-29)	334	6.3 (4-9)	333	0.0 (0-1)	334	2.7 (1-5)
Malta	205	42.9 (36-54)	205	54.1 (47-61)	214	13.6 (9-19)	214	31.3 (25-38)	214	13.6 (9-19)	214	0.0 (0-2)	214	7.9 (5-12)
Netherlands	4640	48.1 (47-50)	4697	49.0 (48-50)	4702	6.0 (5-7)	4697	15.5 (14-17)	4708	7.2 (6-8)	4701	< 0.1 (0-0)	4675	1.8 (1-2)
Norway	2805	54.9 (53-57)	2995	43.2 (41-45)	3019	4.9 (4-6)	2843	11.3 (10-13)	3023	5.8 (5-7)	3023	0.0 (0-0)	2835	1.9 (1-3)
Poland	665	34.4 (31-38)	736	63.3 (60-67)	1037	12.9 (11-15)	1033	29.3 (27-32)	1046	11.9 (10-14)	970	0.0 (0-0)	1011	5.8 (4-7)
Portugal	2037	37.4 (35-40)	2152	59.4 (57-62)	2154	13.5 (12-15)	2158	30.3 (28-32)	2155	16.3 (15-18)	2041	0.1 (0-0)	2152	9.2 (8-11)
Romania	110	36.4 (27-46)	159	62.3 (54-70)	172	25.6 (19-33)	133	27.1 (20-35)	167	24.0 (18-31)	163	0.0 (0-0)	127	14.2 (9-21)
Slovakia	558	29.4 (26-50)	596	64.9 (61-69)	693	30.7 (27-34)	695	41.3 (38-45)	694	21.2 (18-24)	659	0.9 (0-2)	692	13.6 (11-16)
Slovenia	1168	47.3 (44-50)	1168	50.4 (48-53)	1168	9.5 (8-11)	1168	21.4 (19-24)	1168	8.6 (7-10)	1168	0.0 (0-0)	1168	5.1 (4-7)
Spain	5644	30.9 (30-31)	5672	65.4 (64-67)	5672	13.5 (13-14)	5654	33.9 (33-35)	5675	15.6 (15-17)	5670	0.1 (0-0)	5651	5.9 (5-7)
Sweden	0	–	0	–	5536	4.4 (4-5)	5540	11.2 (10-12)	5538	5.0 (4-6)	5532	< 0.1 (0-0)	5532	1.8 (1-2)
United Kingdom	4190	35.0 (34-36)	5846	62.7 (61-64)	5663	12.9 (12-14)	6241	16.6 (16-18)	6390	8.6 (8-9)	5182	0.2 (0-0)	5577	4.1 (4-5)
EU/EEA mean percentage (population-weighted)		**39.5**		**57.4**		**11.8**		**22.3**		**10.3**		**< 0.1**		**4.4**

* Susceptible to aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems. Only isolates tested for all five antimicrobial groups were included in the analysis.

** Resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides. Only isolates tested for all three antimicrobial groups were included in the analysis.

Figure 3.5. ***Escherichia coli*****. Trends of invasive isolates with resistance to aminopenicillins, by country, EU/EEA countries, 2009–2012**

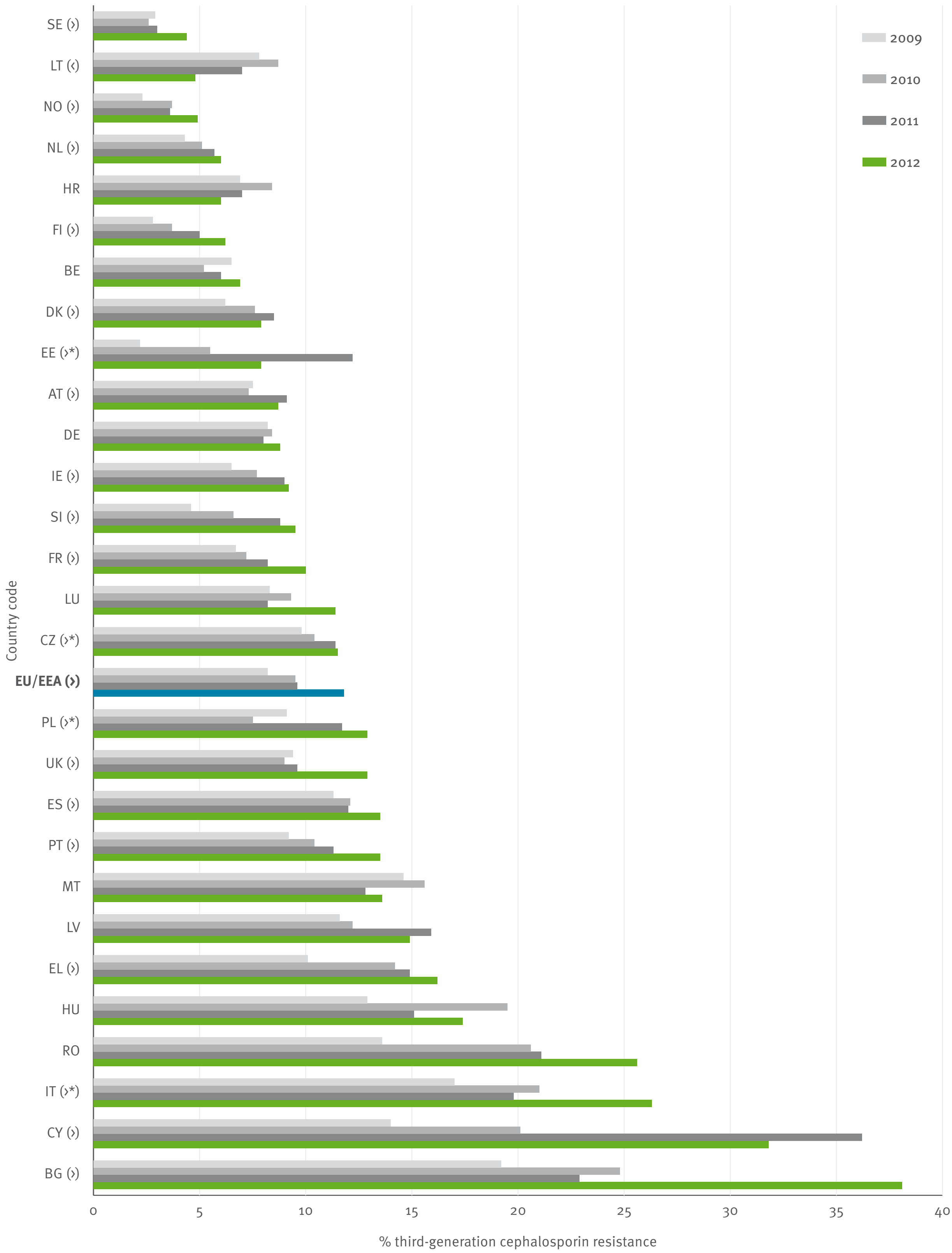


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.6. *Escherichia coli*. Trends of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2009–2012

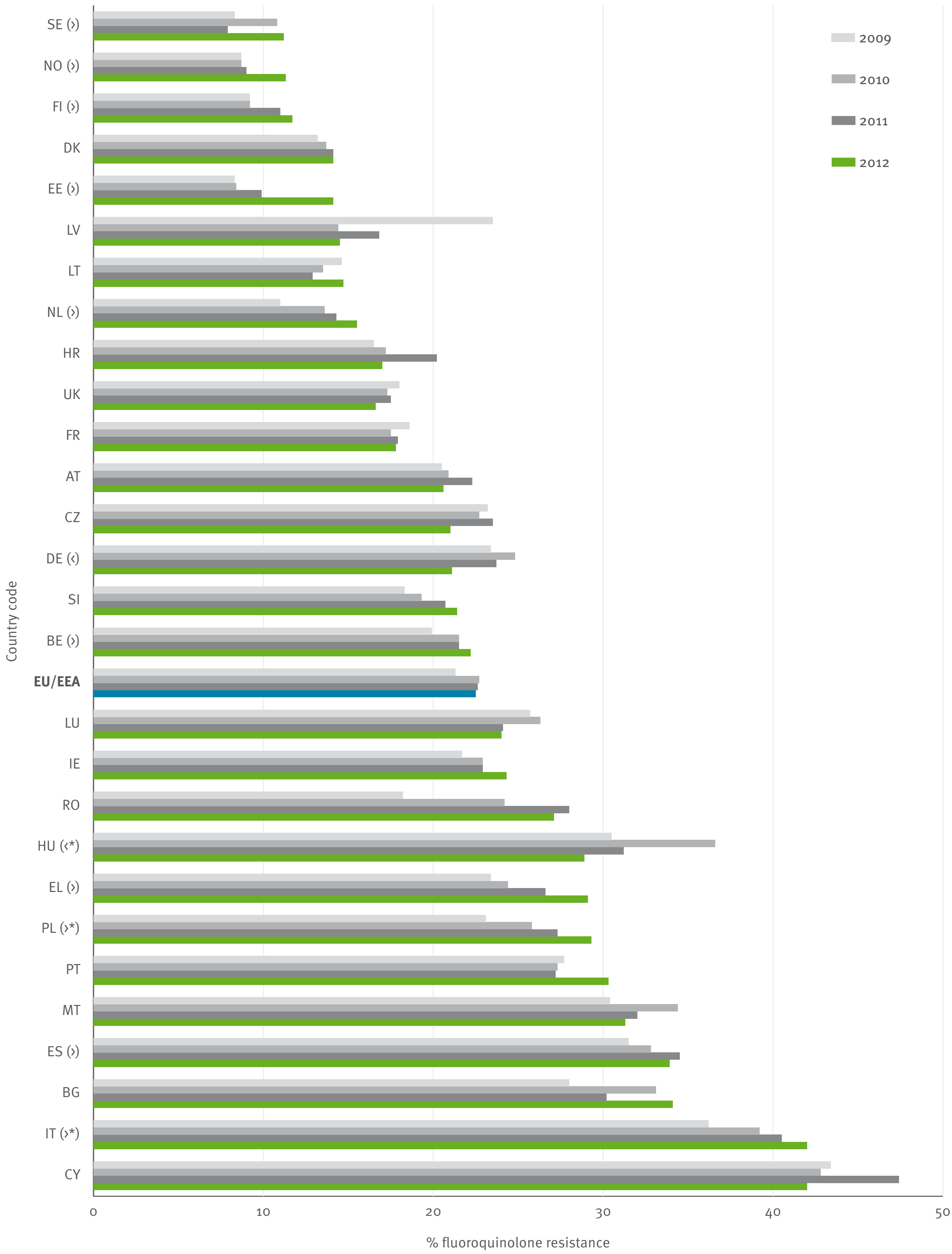


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.7. ***Escherichia coli*. Trends of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2009–2012**

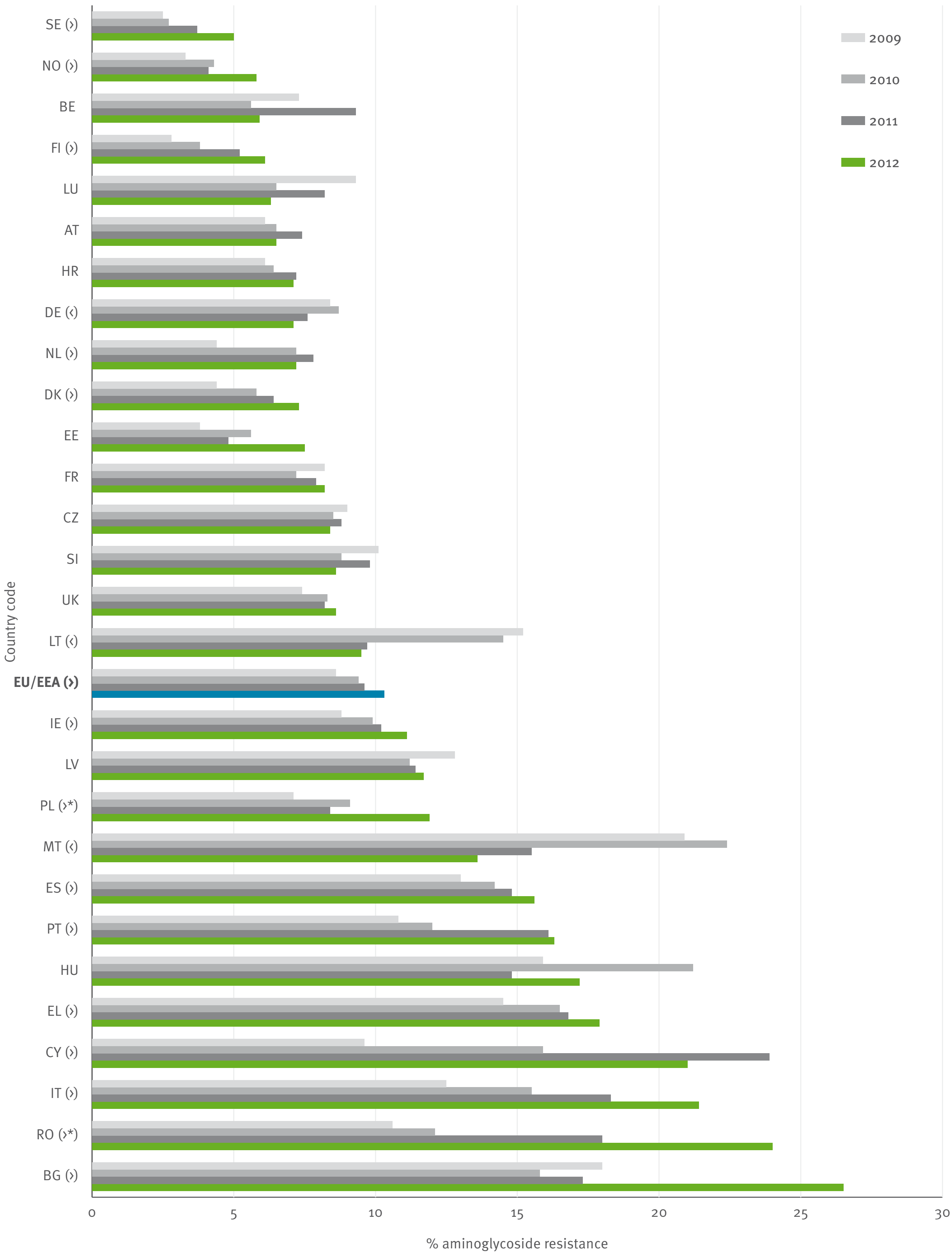


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.8. *Escherichia coli*. Trends of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2009–2012

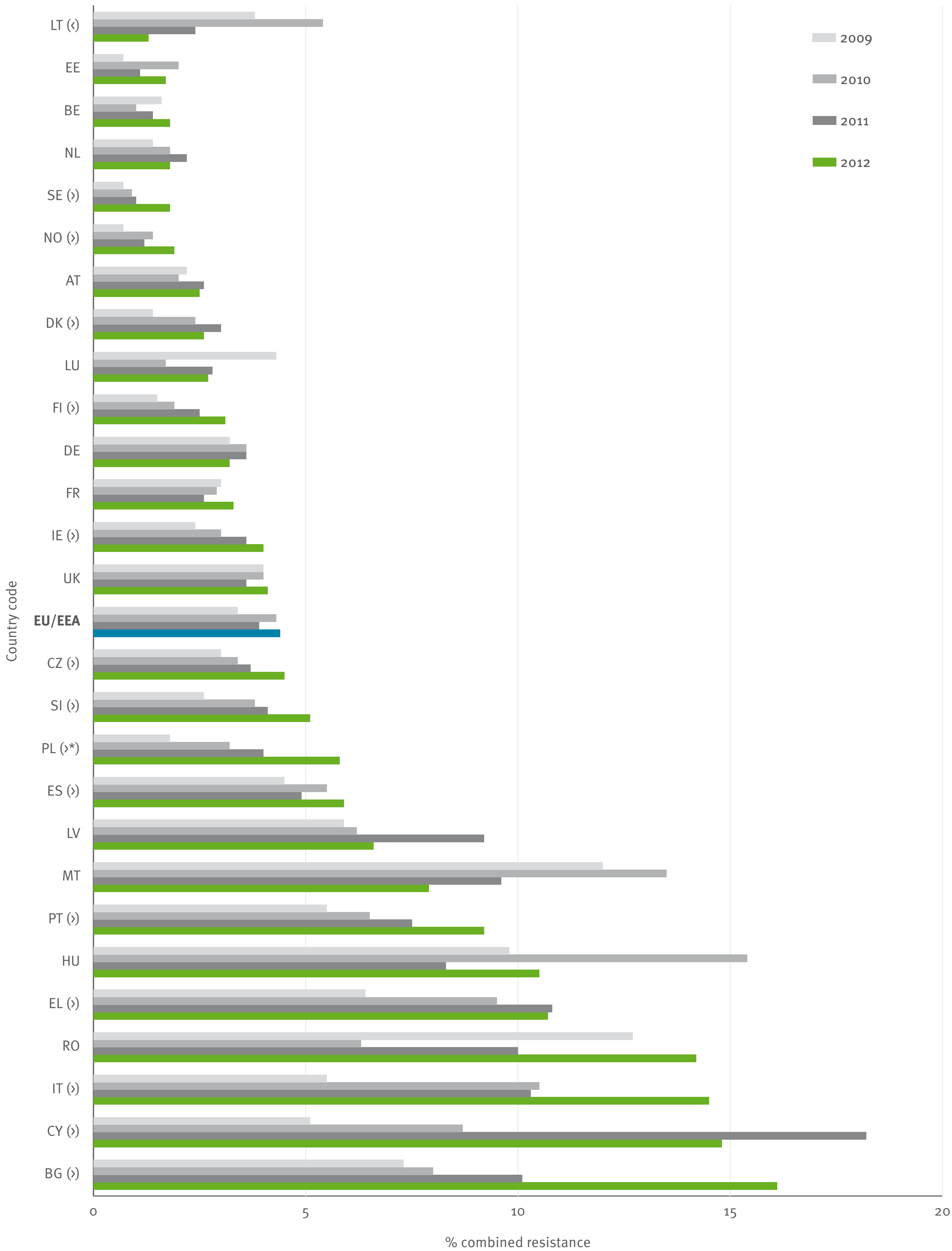


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.9. ***Escherichia coli*. Trends of invasive isolates with combined resistance (resistant to fluoroquinolones, third-generation cephalosporins and aminoglycosides), by country, EU/EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Table 3.2. *Escherichia coli*. Number of reporting laboratories, total numbers of invasive isolates resistant to third-generation cephalosporins (3GCREC) and percentage of extended-spectrum beta-lactamase (ESBL)-positive among these isolates, as ascertained by the participating laboratories, EU/EEA countries, 2012

Country	Number of laboratories	Number of 3GCREC	%ESBL
Austria	29	233	92.7
Bulgaria	14	69	94.2
Croatia	12	79	89.9
Czech Republic	40	322	81.4
Denmark	3	45	91.1
Estonia	6	24	83.3
Finland	17	196	91.8
France	52	915	70.5
Germany	15	260	81.9
Hungary	5	27	100.0
Ireland	30	198	82.3
Italy	3	63	95.2
Latvia	8	23	87.0
Lithuania	10	22	100.0
Luxembourg	5	38	92.1
Netherlands	8	79	96.2
Poland	33	134	85.8
Portugal	16	269	95.9
Romania	6	31	100
Slovakia	14	213	68.1
Slovenia	10	111	91.0
Spain	38	764	82.2
Sweden	17	241	97.1

Only data from laboratories consistently reporting ESBL tests results for all isolates identified as resistant to third-generation cephalosporins and from countries with at least 10 of such isolates were selected for the analysis.

- The EU/EEA population-weighted mean percentage for carbapenem resistance was < 0.1% in 2012. Thirteen countries reported one or more resistant isolate(s) in 2012. The majority of the resistant isolates were reported by Greece (20 isolates; 32% of all carbapenem-resistant *E. coli* isolates) and the United Kingdom (11 isolates; 18%).

Combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides

- For 2012, 30 countries reported 64 861 *E. coli* isolates tested for resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides. The number of isolates with relevant AST information reported by the countries ranged from 127 to 5 655 (Table 3.1).
- The EU/EEA population-weighted mean percentage for combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides was 4.4% in 2012. The percentage of isolates with combined resistance reported by individual countries ranged from 0.7% (Iceland) to 16.1% (Bulgaria). One country reported a resistance percentage below 1%, 16 countries reported 1–5%, six countries reported 5–10%, and seven countries reported above 10% (Table 3.1 and Figure 3.4).
- Trends for the period 2009–2012 were calculated for 27 countries. Statistically significant increasing trends were observed for 14 countries. For Poland, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years. A significantly decreasing trend was observed for Lithuania (Figure 3.9).

Other resistance combinations

- Of the total number of isolates tested for all antimicrobial groups under surveillance for *E. coli*, single resistance was the most common resistance phenotype, of which single aminopenicillin resistance predominated. Of those with resistance to two antimicrobial groups, combined aminopenicillin and fluoroquinolone resistance was most common, and for those with resistance to three antimicrobial groups, aminopenicillin, fluoroquinolone and third-generation cephalosporin resistance was the majority. For isolates with resistance to four antimicrobial groups, combined resistance to aminopenicillin, fluoroquinolones, third-generation cephalosporins and aminoglycosides predominated (Table 3.3).
- As carbapenem resistance remained uncommon, resistance combinations including this antimicrobial group were rare. A total of 19 isolates with resistance to all antimicrobial groups under surveillance by EARS-Net were reported, of which the majority were reported from Greece and France.

3.1.4 Discussion and conclusions

Antimicrobial resistance in *E. coli* requires close attention as the percentages of isolates resistant to commonly used antimicrobials continue to increase throughout Europe. The increase of resistance to third-generation cephalosporins, to aminoglycosides, and of combined resistance to at least three antimicrobial classes, for which many countries had significantly increasing trends during recent years, is especially worrisome.

As *E. coli* is a common cause of bloodstream infections, the high percentage of ESBL-producing isolates and isolates with combined resistance is a public health concern since it limits the number of treatment alternatives for patients with these life-threatening infections. In addition, the increase in combined resistance and spread of ESBL may lead to increased use of carbapenems, thus favouring the further dissemination of carbapenemase-producing Enterobacteriaceae (CPE)[7].

Prudent antimicrobial use and comprehensive infection control measures are the cornerstones of interventions aiming to prevent selection and transmission of resistant bacteria, including *E. coli*. A risk assessment of the spread of CPE, published by ECDC in 2011 , emphasises that the use of standard precautions, especially adherence to hand hygiene policies, is fundamental to prevent transmission of any multidrug-resistant organism, not only CPE, in healthcare settings.

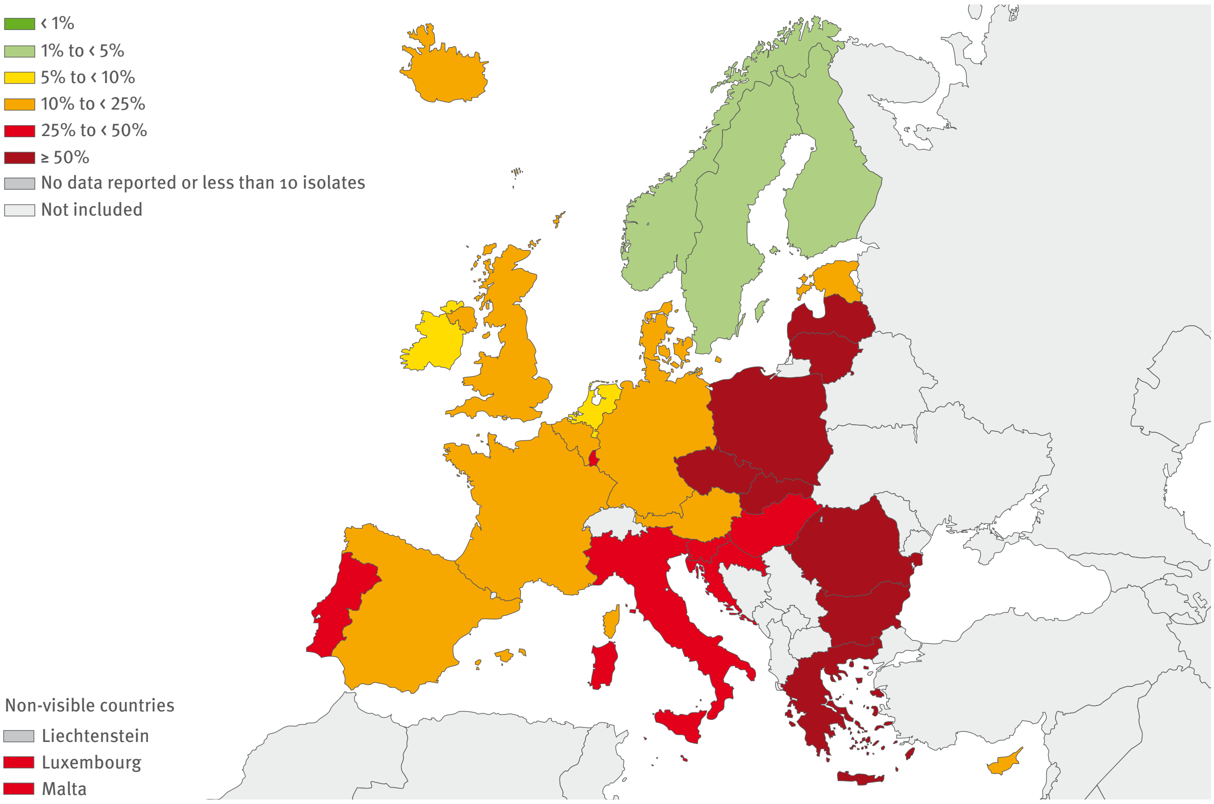
7 European Centre for Disease Prevention and Control. Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between health-care facilities, with special emphasis on cross-border transfer. Stockholm: ECDC; 2011

Table 3.3. ***Escherichia coli*****. Total number of tested isolates and resistance combinations among invasive isolates tested against aminopenicillins, third-generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems (n=52 526), EU/EEA countries, 2012**

Resistance pattern	Number of tested isolates	% of total*
Fully susceptible	21532	41.0
Single resistance (to indicated drug classes)		
Total	**18031**	**34.3**
Aminopenicillins	16631	31.7
Fluoroquinolones	1273	2.4
Aminoglycosides	121	0.2
Carbapenems	6	<0.1
Resistance to two classes of antimicrobial drugs		
Total (any two classes in combination)	**6440**	**12.3**
Aminopenicillins + fluoroquinolones	4268	8.1
Aminopenicillins + third-generation cephalosporins	1277	2.4
Aminopenicillins + aminoglycosides	810	1.5
Fluoroquinolones + aminoglycosides	83	0.2
Aminopenicillins + carbapenems	2	<0.1
Resistance to three classes of antimicrobial drugs		
Total (any three classes in combination)	**3957**	**7.5**
Aminopenicillins + third-generation cephalosporins +fluoroquinolones	1926	3.7
Aminopenicillins + fluoroquinolones + aminoglycosides	1721	3.3
Aminopenicillins + third-generation cephalosporins + aminoglycosides	301	0.6
Aminopenicillins + fluoroquinolones +carbapenems	4	<0.1
Aminopenicillins + third-generation cephalosporin + carbapenems	3	<0.1
Aminopenicillins + aminoglycosides + carbapenems	2	<0.1
Resistance to four classes of antimicrobial drugs		
Total (any four classes in combination)	**2547**	**4.8**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides	2521	4.8
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + carbapenems	14	<0.1
Aminopenicillins + third-generation cephalosporins + aminoglycosides + carbapenems	6	<0.1
Aminopenicillins + fluoroquinolones + aminoglycosides + carbapenems	6	<0.1
Resistance to five classes of antimicrobial drugs		
Aminopenicillins + third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	19	<0.1

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

Figure 3.10. ***Klebsiella pneumoniae*****. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2012**



3.2 *Klebsiella pneumoniae*

3.2.1 Clinical and epidemiological importance

Bacteria of the genus *Klebsiella* are frequent colonisers of the gastrointestinal tract in humans, but may also be found on skin, in the oropharynx and upper airways in hospitalised individuals. *Klebsiella pneumoniae* is associated with opportunistic infections in individuals with impaired immune systems, such as newborns, cancer patients, diabetic, alcoholic and hospitalised patients with indwelling devices. The most common sites of infection are the urinary tract and the respiratory tract. Organisms such as *K. pneumoniae* can spread rapidly, from the gastrointestinal tract of patients and via the hands of hospital personnel to colonise other patients, leading to nosocomial outbreaks. *Klebsiella pneumoniae* is the second most frequent cause of gram-negative bloodstream infections after *E. coli*. The mortality rates for pneumonia caused by *K. pneumoniae* can be high even when appropriate antimicrobial treatment is given. However, this also depends on the severity of the underlying condition.

3.2.2 Resistance mechanisms

Similar to *E. coli*, *K. pneumoniae* can be resistant to multiple antimicrobials, and resistance traits are frequently acquired through plasmids. However, in contrast to *E. coli*, *K. pneumoniae* has a chromosomally encoded SHV 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 with a consequent impact on the emergence of resistance to these antimicrobials, especially in *K. pneumoniae*. KPC carbapenemase-producing clones of *K. pneumoniae* have been observed in the United States, Greece, Italy and Israel, and similar strains are now spreading in several European countries, while plasmids encoding the VIM metallo-carbapenemase are frequent in *K. pneumoniae* in Greece. More recently, strains producing the NDM metallo-carbapenemase have been observed in patients returning from the Indian subcontinent. The $bla_{OXA\text{-}48}$ gene codes for an oxacillinase (OXA-48) that causes resistance to penicillin and reduces susceptibility to carbapenems, but (when produced alone), not to expanded-spectrum cephalosporins. The level of resistance is often low and such strains are thus frequently missed in laboratories using automated AST systems. A combination of OXA-48-like enzymes (OXA-48 and some closely related variants with similar properties) with ESBLs such as CTX-M15 can occur in *Klebsiella* spp. and can result in a highly drug-resistant phenotype. Single clones with such combinations have caused hospital outbreaks in several European countries. OXA-48-producing isolates have

Figure 3.11. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2012

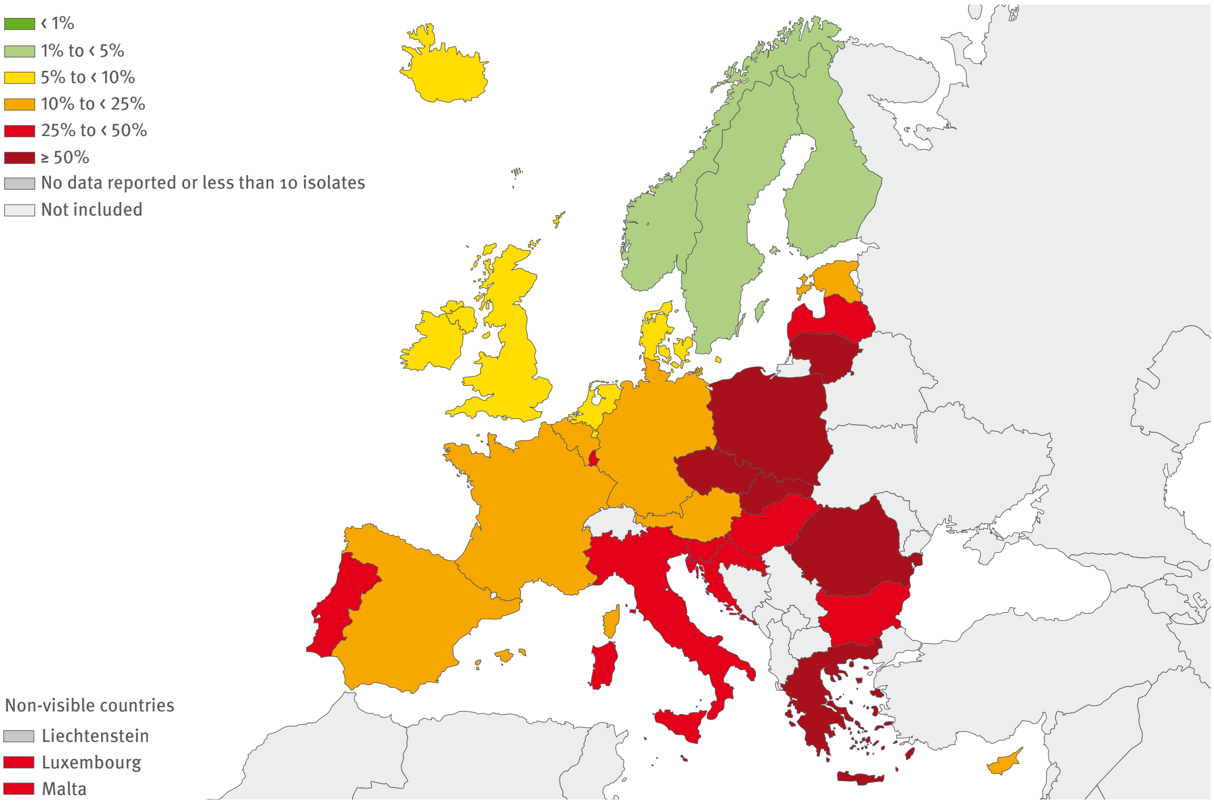


Figure 3.12. ***Klebsiella pneumoniae*****. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2012**

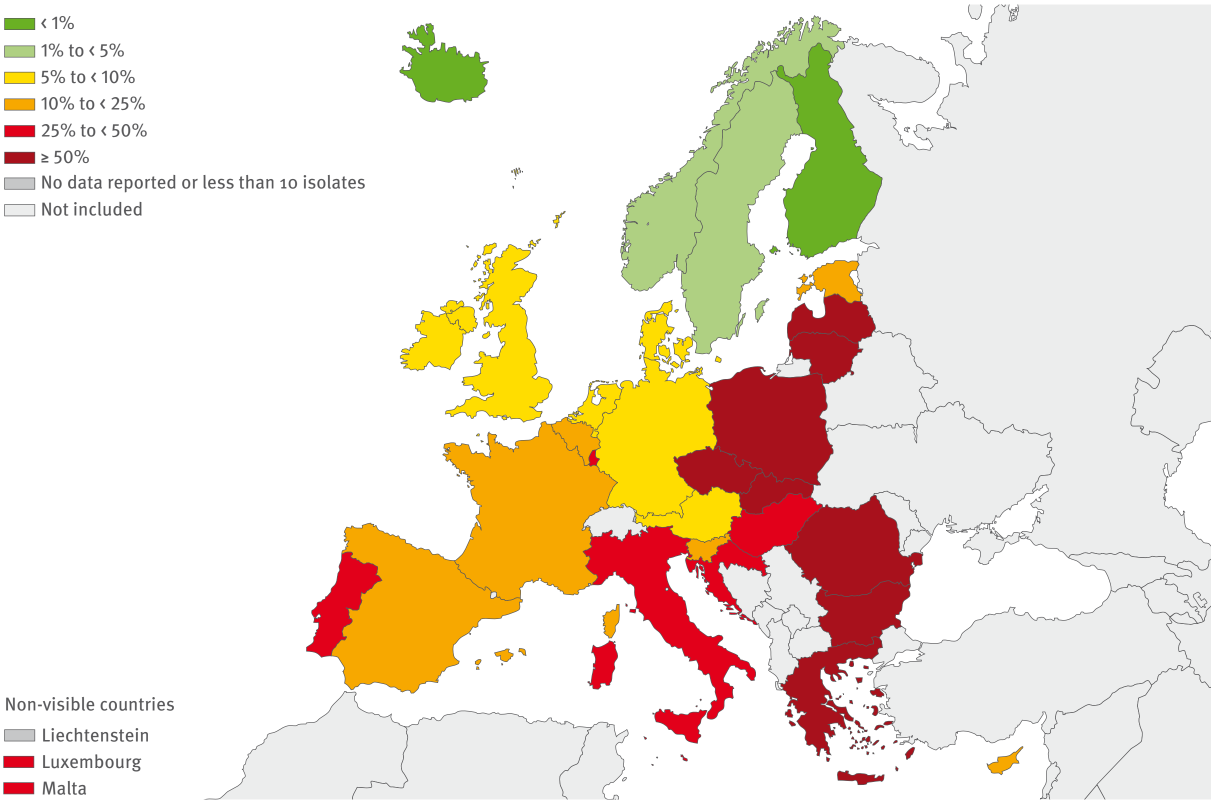
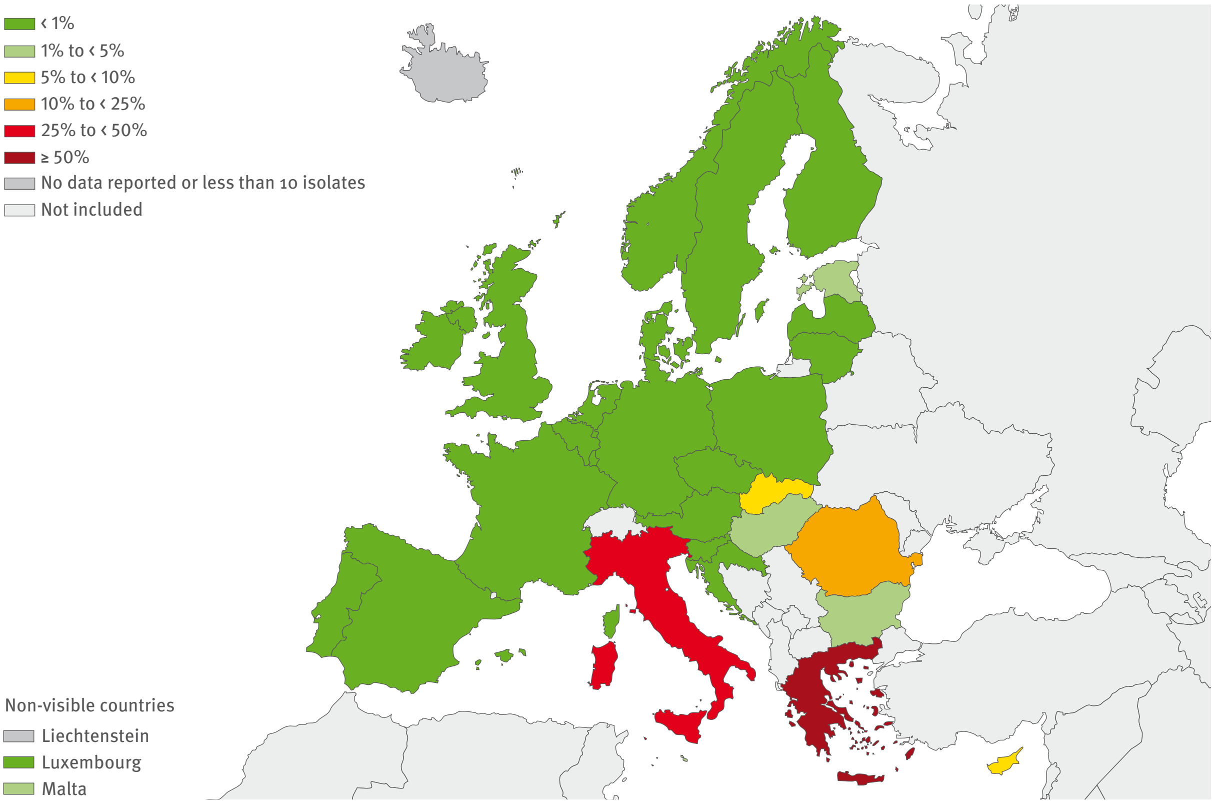


Figure 3.13. ***Klebsiella pneumoniae*****. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2012**



often been observed in patients returning from endemic areas (Turkey, North Africa and the Middle East). OXA-48 has become the most common carbapenemase in carbapenem-resistant Enterobacteriaceae in Spain.

3.2.3 Antimicrobial susceptibility

- A majority of the *K. pneumoniae* isolates reported to EARS-Net in 2012 was resistant to at least one of the antimicrobial agents under surveillance. The most common resistance phenotype was combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides. ESBL was commonly reported for the isolates with third-generation cephalosporin resistance.
- A north-to-east/south gradient could be noted for most antimicrobial groups, with lower resistance percentages reported for the north and higher from the eastern and southern parts of Europe.
- The percentage of isolates resistant to third-generation cephalosporins and with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides has increased significantly in Europe over the last four years. The increase was observed not only for countries with comparatively low resistance percentages, but also for countries with already very high resistance levels.
- Further complicating the situation is the increasing percentage of carbapenem resistance in a number of countries, mainly in the south of Europe.
- The percentage of isolates resistant to all antimicrobial groups under surveillance by EARS-Net for *K. pneumoniae* (including carbapenems) was 7%, mainly reflecting isolates reported from Greece and Italy.

Full susceptibility

- For 2012, 17 410 isolates were reported to EARS-Net, for which 15 059 isolates (86%) from 29 countries had complete AST information for all antimicrobial groups under surveillance for *K. pneumoniae* (third-generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems).
- The population-weighted EU/EEA mean percentage for isolates fully susceptible to all antimicrobials tested was 47.3% in 2012, with national estimates ranging from 20.4% (Bulgaria) to 96.3% (Finland) (Table 3.4).

Third-generation cephalosporins

- For 2012, 30 countries reported 16 704 *K. pneumoniae* isolates with AST information for third-generation cephalosporins. The number of isolates reported by the countries ranged from 14 to 1 711 (Table 3.4).
- The EU/EEA population-weighted mean percentage for third-generation cephalosporin resistance was 25.7% in 2012. The percentages of resistant isolates in the reporting countries ranged from 1.7% (Finland) to 74.8% (Bulgaria). Three countries reported resistance percentages below 5%, two countries reported 5–10%, 10 countries reported 10–25%, seven countries reported 25–50%, and eight countries reported above 50% (Table 3.4, Figure 3.10).
- Trends for the period 2009–2012 were calculated for 28 countries. Statistically significant increasing trends were observed for eight countries. For Luxembourg, the trend did not remain significant when considering only data from laboratories reporting consistently for all four years. The EU/EEA population-weighted mean percentage also increased significantly from 21.5% in 2009 to 25.7% in 2012. None of the reporting countries had statistically significant decreasing trends of resistance to third-generation cephalosporins (Figure 3.15).

Extended-spectrum beta-lactamase (ESBL)

- Twenty countries were included in the calculation of ESBL percentages for *K. pneumoniae*. Data were only included from laboratories reporting ESBL test results for all isolates identified as resistant to third-generation cephalosporins, and only from countries with at least 10 of such isolates.
- Among *K. pneumoniae* isolates resistant to third-generation cephalosporins, a large percentage was ascertained as ESBL-positive by the participating laboratories in 2012. Thirteen of 20 countries reported between 85% and 100% ESBL-positive isolates among isolates resistant to third-generation cephalosporins (Table 3.5).

Fluoroquinolones

- For 2012, 30 countries reported 16 954 isolates with AST information for fluoroquinolones. The number of isolates reported per country ranged from 14 to 1 691 (Table 3.4).
- The EU/EEA population-weighted mean percentage for fluoroquinolone resistance was 25.3% in 2012. The percentages of resistant isolates in the reporting countries ranged from 2.1% (Finland) to 69.7% (Greece). Three countries reported resistance percentages below 5%, five countries reported 5–10%, seven countries reported 10–25%, nine countries reported 25–50%, and six countries reported above 50% (Table 3.4, Figure 3.11).
- Trends for the period 2009–2012 were calculated for 28 countries. Statistically significant increasing trends were observed for ten countries. For Greece and Luxembourg, the trend was not significant when considering only data from laboratories reporting consistently for all four years. Statistically significant decreasing trends were observed for four countries (the Czech Republic, Cyprus, Denmark and Norway) (Figure 3.16).

Aminoglycosides

- For 2012, 30 countries reported 16 474 isolates with relevant AST information for aminoglycosides. The number of isolates reported per country ranged from 16 to 1 432 (Table 3.4).
- The EU/EEA population-weighted mean percentage for aminoglycoside resistance was 22.2% in 2012. The percentages of resistant isolates in the reporting countries ranged from zero (Iceland) to 63.4% (Lithuania). Four countries reported resistance percentages below 5%, six countries reported 5–10%, six countries reported 10–25%, six countries reported 25–50%, and eight countries reported above 50% (Table 3.4, Figure 3.12).
- Trends for the period 2009–2012 were calculated for 27 countries. Statistically significant increasing trends were observed for ten countries. For Luxembourg and France, the trends were not significant when considering only data from laboratories reporting consistently for all four years. The EU/EEA population-weighted mean percentage also increased significantly during the same period, from 18.2% in 2009 to 22.2% in 2012. A statistically significant decreasing trend was only observed for Finland (Figure 3.17).

Carbapenems

- For 2012, 29 countries reported 16 285 isolates with relevant AST information for carbapenems. The number of isolates reported by the countries ranged from 48 to 1 627. Twenty countries reported one or more resistant isolate(s) in 2012. The majority of the resistant isolates (n=1221) were reported by Greece (883 isolates), followed by Italy (242 isolates) (Table 3.4).
- The EU/EEA population-weighted mean percentage for carbapenem resistance was 6.2% in 2012. The percentages of resistant isolates in the reporting countries ranged from zero (seven countries) to 60.5% (Greece). Twenty countries reported resistance percentages below 1%, four countries reported 1–5%, two countries 5–10%, one country reported 10–25%, and two countries reported above 25% (Table 3.4, Figure 3.13).
- Trends for the period 2009–2012 were calculated for 25 countries. Statistically significant increasing trends were observed for five countries (France, Greece, Italy, Norway and Spain). For France and Norway, the trend was not significant when considering only data from laboratories reporting consistently for all four years. The EU/EEA population-weighted mean percentage also increased significantly during the same period, from 3.2% in 2009 to 6.2% in 2012. None of the reporting countries had statistically significant decreasing trends of resistance to carbapenems (Figure 3.18).

Combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides

- For 2012, 30 countries reported 15 690 *K. pneumoniae* isolates tested for resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides.

Figure 3.14. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with combined resistance (resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides), by country, EU/EEA countries, 2012

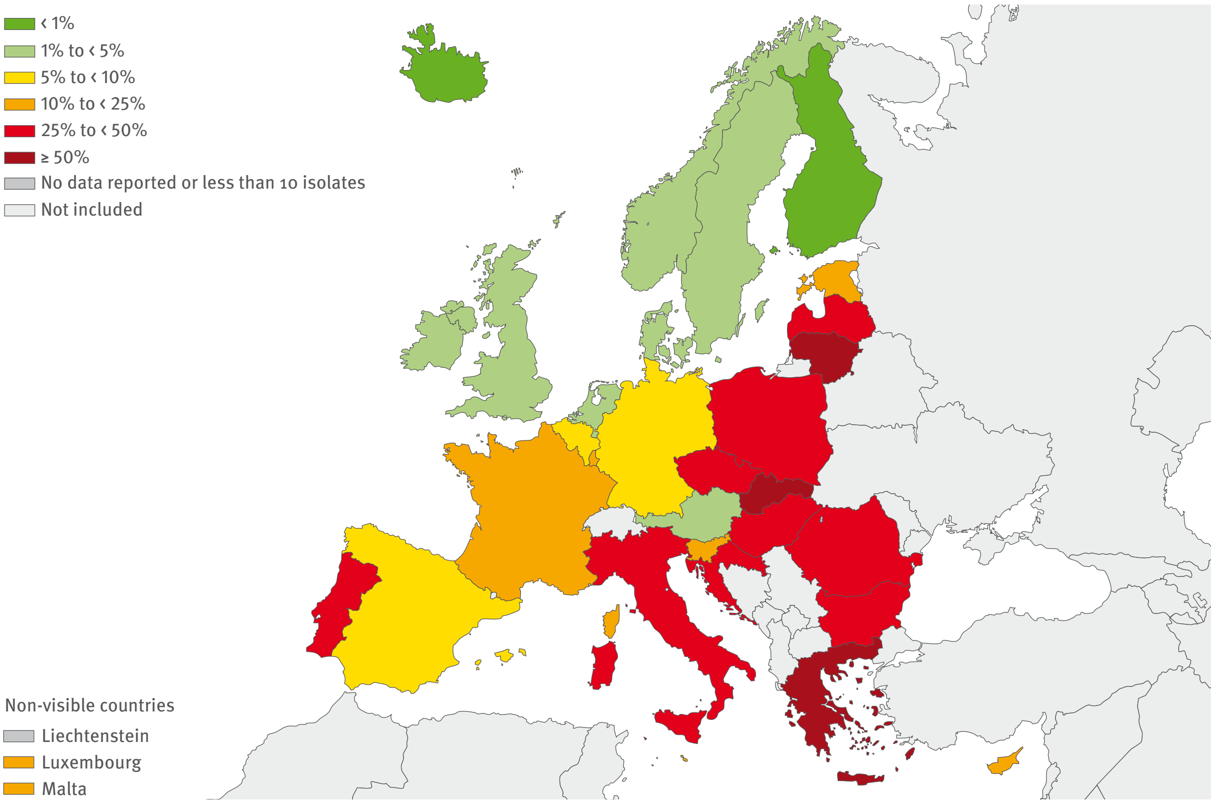


Table 3.4. *Klebsiella pneumoniae*. Total number of isolates tested (N) and percentage susceptible to all antimicrobial groups under EARS-Net surveillance*, total number of isolates tested (N) and percentage resistant to aminopenicillins, fluoroquinolones, third-generation cephalosporins, aminoglycosides and combined resistance (%R), including 95% confidence intervals (95% CI), by country, EU/EEA countries, 2012**

Country	Fully susceptible*		Third-gen. cephalosporins		Fluoroquinolones		Aminoglycosides		Carbapenems		Combined resistance**	
	N	% fully S (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)
Austria	707	81.0 (78-84)	859	11.8 (10-14)	829	15.4 (13-18)	858	5.4 (4-7)	738	0.8 (0-2)	828	4.2 (3-6)
Belgium	477	75.7 (72-79)	540	16.5 (13-20)	532	17.3 (14-21)	503	10.7 (8.13)	545	0.7 (0-2)	477	8.2 (6-11)
Bulgaria	108	20.4 (13-29)	127	74.8 (66-82)	127	47.2 (38-56)	127	54.3 (45-63)	108	1.9 (0-7)	127	36.2 (28-45)
Croatia	342	40.0 (35-45)	342	44.0 (42-51)	342	43.0 (37-48)	344	45.0 (40-51)	343	0.3 (0-2)	342	26.0 (21-31)
Cyprus	65	67.7 (55-79)	65	23.1 (14-35)	65	21.5 (12-33)	65	18.5 (10-30)	65	9.2 (3-19)	65	10.8 (4-21)
Czech Republic	1307	39.6 (37-42)	1399	51.2 (49-54)	1399	50.4 (48-53)	1399	54.4 (52-57)	1307	0.3 (0-1)	1399	41.8 (39-44)
Denmark	473	84.1 (81-87)	621	10.5 (8-13)	941	8.8 (7-11)	902	6.0 (5-8)	680	0.3 (0-1)	577	3.1 (2-5)
Estonia	74	77.0 (66-86)	90	17.8 (11-27)	87	17.2 (10-27)	91	13.2 (7-22)	79	1.3 (0-7)	86	10.5 (5-19)
Finland	516	96.3 (94-98)	536	1.7 (1-3)	536	2.1 (1-4)	516	0.4 (0-1)	536	0.0 (0-1)	516	0.2 (0-1)
France	1093	67.6 (65-70)	1711	22.6 (21-25)	1691	24.4 (22-27)	1119	23.6 (21-26)	1627	0.5 (0-1)	1097	19.4 (17-22)
Germany	661	82.8 (80-86)	664	13.0 (10-16)	663	13.7 (11-17)	663	8.3 (6-11)	661	0.0 (0-1)	663	6.2 (4-8)
Greece	1426	25.9 (24-28)	1459	70.9 (68-73)	1428	69.7 (67-72)	1432	62.9 (60-65)	1460	60.5 (58-63)	1427	59.9 (57-62)
Hungary	466	52.6 (48-57)	500	43.0 (39-47)	485	41.6 (37-46)	500	41.0 (37-45)	481	2.9 (2-5)	485	37.5 (33-42)
Iceland	0	–	14	21.4 (0-43)	14	7.1 (0-21)	16	0.0 (0-22)	0	–	14	0.0 (0-23)
Ireland	326	86.2 (82-90)	326	9.5 (7-13)	338	7.4 (5-11)	338	9.2 (6-13)	338	0.0 (0-1)	326	3.4 (2-6)
Italy	743	46.2 (43-90)	847	47.7 (44-51)	830	49.6 (46-53)	863	42.2 (39-46)	841	28.8 (26-32)	753	40.0 (36-44)
Latvia	76	35.5 (25-47)	78	64.1 (52-75)	78	46.2 (35-58)	78	51.3 (40-63)	76	0.0 (0-5)	78	42.3 (31-54)
Lithuania	183	32.8 (26-40)	186	64.0 (57-71)	184	55.4 (48-63)	186	63.4 (56-70)	185	0.0 (0-2)	184	52.2 (45-60)
Luxembourg	48	56.3 (41-71)	50	34.0 (21-49)	50	32.0 (20-47)	50	26.0 (15-40)	48	0.0 (0-7)	50	20.0 (10-34)
Malta	56	67.9 (54-80)	56	26.8 (16-40)	56	25.0 (14-38)	56	26.8 (16-40)	56	3.6 (0-12)	56	19.6 (10-32)
Netherlands	665	89.3 (87-92)	683	6.7 (5-9)	670	5.4 (4-7)	685	6.3 (5-8)	684	0.1 (0-1)	667	2.7 (2-4)
Norway	593	94.1 (92-96)	621	3.2 (2-5)	596	4.0 (3-6)	622	2.4 (1-4)	623	0.5 (0-1)	593	1.5 (1-3)
Poland	344	34.6 (30-40)	362	60.5 (55-66)	359	60.2 (55-65)	369	51.8 (47-57)	359	0.8 (0-2)	353	48.4 (43-54)
Portugal	745	53.7 (50-57)	781	38.7 (35-42)	777	35.8 (32-39)	780	31.8 (29-35)	749	0.7 (0-2)	776	25.1 (22-28)
Romania	81	35.8 (25-47)	95	57.9 (47-68)	85	51.8 (41-63)	92	54.3 (44-65)	95	13.7 (7-22)	82	41.5 (31-53)
Slovakia	329	29.8 (25-35)	378	62.7 (58-68)	376	66.8 (62-72)	378	63.0 (58-68)	331	6.3 (4-9)	376	55.3 (50-60)
Slovenia	254	65.4 (59-71)	254	28.3 (23-34)	254	33.1 (27-39)	254	20.5 (16-26)	254	0.4 (0-2)	254	17.3 (13-23)
Spain	1149	76.8 (74-79)	1153	16.7 (15-19)	1150	16.5 (14-19)	1153	14.1 (12-16)	1152	0.8 (0-1)	1150	8.9 (7-11)
Sweden	976	92.1 (90-95)	976	2.8 (2-4)	976	3.7 (3-5)	976	2.5 (2-4)	976	0.0 (0-0)	976	1.4 (1-2)
United Kingdom	776	83.9 (81-86)	931	11.7 (10-14)	1036	7.4 (6-9)	1059	6.1 (5-8)	888	0.5 (0-1)	913	2.4 (2-4)
EU/EEA mean percentage (population-weighted)		**47.3**		**25.7**		**25.3**		**22.2**		**6.2**		**18.5**

* Susceptible to fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems. Only isolates tested for all four antimicrobial groups were included in the analysis.

** Resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides. Only isolates tested for all four antimicrobial groups were included in the analysis.

The number of isolates with relevant AST information reported by the countries ranged from 14 to 1427 (Table 3.4).

- The EU/EEA population-weighted mean percentage for combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides was 18.5% in 2012. The percentage of isolates with combined resistance to the above-mentioned antimicrobial groups reported by the countries ranged from zero (Iceland) to 59.9% (Greece). Two countries reported a resistance percentage below 1%, seven countries reported 1–5%, three countries reported 5–10%, six countries reported 10–25%, nine countries reported 25–50% and three countries reported percentages above 50% (Table 3.4 and Figure 3.14).
- Trends for the period 2009–2012 were calculated for 26 countries. Statistically significant increasing trends were observed for 11 countries. For Luxembourg, the trends did not remain significant when considering only data from laboratories reporting consistently for all four years. The EU/EEA population-weighted mean percentage also showed a significant increasing trend during the same period, from 14.3% in 2009 to 18.5% in 2012. A statistically significant decreasing trend was observed for Denmark. (Figure 3.19).

Other resistance combinations

- Of the total number of *K. pneumoniae* isolates tested for all antimicrobial groups under surveillance, combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides was the most common resistance phenotype, more frequent than isolates with single resistance or resistance to two antimicrobial groups together (Table 3.6).
- Close to seven percent of the isolates were resistant to all four antimicrobial groups under surveillance. The majority of these isolates was reported from Greece and Italy (73% and 20%, respectively, of all isolates resistant to all four antimicrobial groups).

3.2.4 Discussion and conclusion

Antimicrobial resistance in *K. pneumoniae* is a public health concern of increasing importance in Europe. Widespread resistance to multiple antimicrobial classes and a high percentage of ESBL-producing isolates are complicating the treatment of serious infections caused by these bacteria. More than half of the *K. pneumoniae* isolates reported in 2012 were resistant to at least one antimicrobial group, and among all the resistant isolates the most common phenotype was a combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides.

Further diminishing the available options for antimicrobial treatment is the increasing percentage of carbapenem-resistant *K. pneumoniae* in some European countries. This increasing trend of carbapenem resistance in *K. pneumoniae* has been confirmed by a separate and more detailed analysis of EARSS/EARS-Net data from 2005 to 2010, showing an increase in progressively more countries in Europe[8]. Even if the increase is currently only observed in a few countries, this is of particular concern as the carbapenems are among the few effective antimicrobials available for the treatment of infections caused by multidrug-resistant *K. pneumoniae*.

Although information on carbapenemase production is very limited in EARS-Net, data from scientific publications and enhanced surveillance established by some EU Member States indicate an increase in the spread of carbapenemase-producing Enterobacteriaceae (CPE) in Europe in recent years, with reports of travel-related cases, autochthonous cases and outbreaks. A recent online survey performed as part of the ECDC-funded European Survey on CPE (EuSCAPE) showed that CPE continue to spread in Europe. Although most countries reported only single hospital outbreaks, the epidemiological situation has deteriorated over the past three years[9].

ECDC issued two risk assessments targeting CPE during 2011[10,11], emphasising the need for implementation of infection control measures such as active patient screening and additional hygiene precautions for the care of CPE-positive patients. In addition, countries are encouraged to develop national guidance on how to stop the spread of CPE within their country, and to actively report cases of CPE by making confirmed cases notifiable to national public health authorities. These interventions would not only target CPE but also affect the general spread of AMR.

Table 3.5. *Klebsiella pneumoniae*. Number of reporting laboratories, total number of invasive isolates resistant to third-generation cephalosporins (3GCRKP) and percentage of extended-spectrum beta-lactamase (ESBL)-positive among these isolates, as ascertained by participating laboratories, by country, EU/EEA countries, 2012

Country	Number of laboratories	Number of 3GCRKP	%ESBL
Austria	24	58	77.6
Bulgaria	9	44	95.5
Croatia	12	175	99.4
Czech Republic	45	675	91.1
Estonia	7	16	81.3
France	48	338	70.7
Germany	14	59	84.7
Hungary	11	60	100
Ireland	13	31	77.4
Latvia	6	45	97.8
Lithuania	11	119	99.2
Luxembourg	4	17	100
Netherlands	15	33	100
Poland	32	219	97.3
Portugal	17	274	94.9
Romania	6	47	95.7
Slovakia	14	237	62
Slovenia	9	72	100
Spain	33	193	81.9
Sweden	9	27	88.9

Only data from laboratories consistently reporting ESBL tests results for all isolates identified as resistant to third-generation cephalosporins and from countries with at least 10 of such isolates were selected for the analysis.

8 Magiorakos AP, Suetens C, Monnet DL, Gagliotti C, Heuer OE; EARS-Net Coordination Group and EARS-Net participants. The rise of carbapenem resistance in Europe: just the tip of the iceberg? Antimicrob Resist Infect Control. 2013 Feb 14;2(1):6.

9 Glasner C, Albiger B, Buist G, Tambić Andrasević A, Canton R, Carmeli Y, et al; European Survey on Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) working group. Carbapenemase-producing Enterobacteriaceae in Europe: a survey among national experts from 39 countries, February 2013. Euro Surveill. 2013 Jul 11;18(28).

10 European Centre for Disease Prevention and Control. Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer. Stockholm: ECDC; 2011.

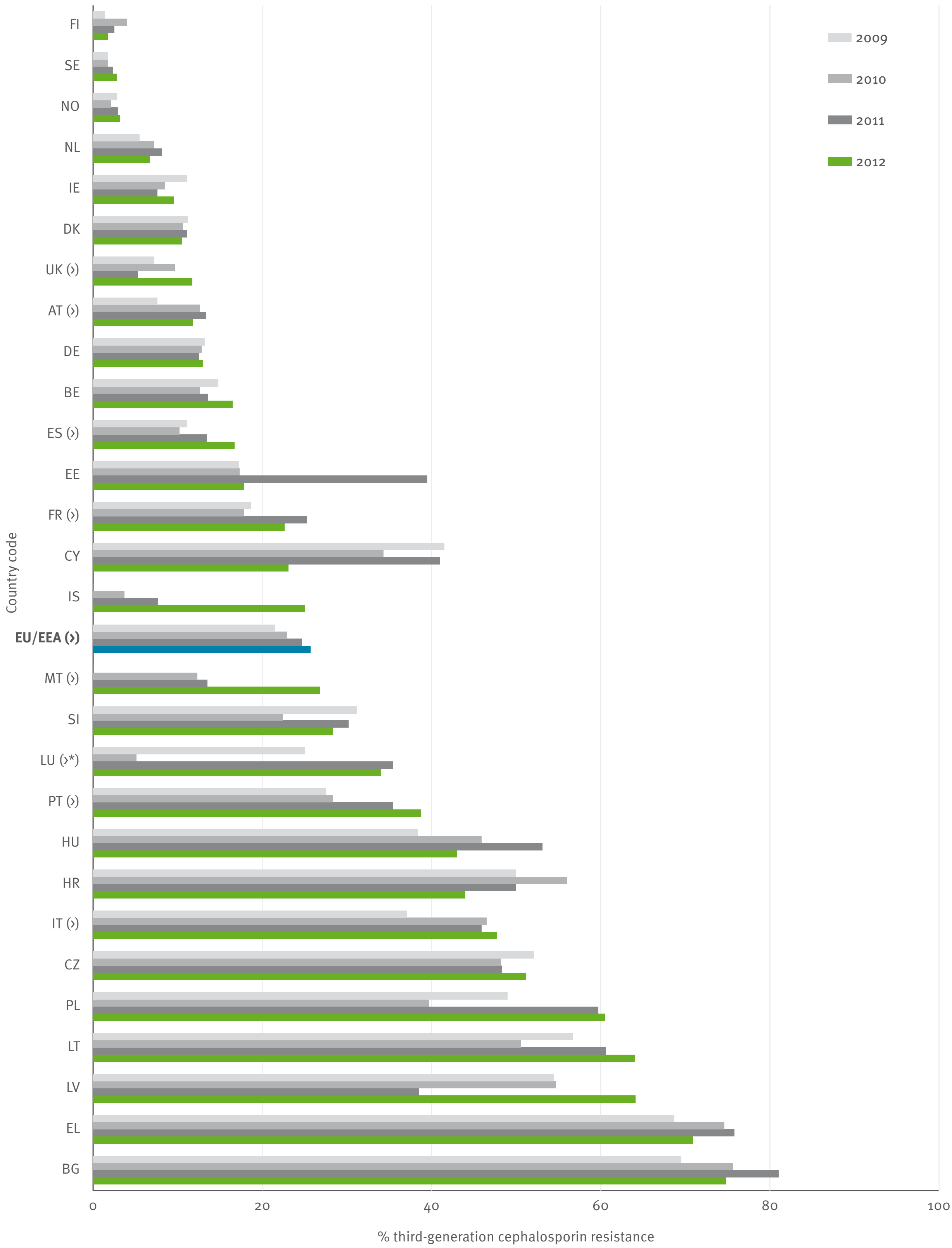
11 European Centre for Disease Prevention and Control. Updated risk assessment on the spread of NDM and its varint within Europe. Stockholm: ECDC; 2011.

Table 3.6. *Klebsiella pneumoniae*. Total number of tested isolates and resistance combinations among invasive isolates tested against third-generation cephalosporins, fluoroquinolones, aminoglycosides and carbapenems (n=15 059), EU/EEA countries, 2012

Resistance pattern	Number of tested isolates	% of total*
Fully susceptible	9410	62.5
Single resistance (to indicated drug classes)		
Total (all single resistance)	**879**	**5.8**
Fluoroquinolones	401	2.7
Third-generation cephalosporins	369	2.5
Aminoglycosides	107	0.7
Carbapenems	2	<0.1
Resistance to two classes of antimicrobial drugs		
Total (any two classes in combination)	**1019**	**6.8**
Third-generation cephalosporins + aminoglycosides	398	2.6
Third-generation cephalosporins + fluoroquinolones	372	2.5
Fluoroquinolones + aminoglycosides	233	1.5
Third-generation cephalosporins + carbapenems	14	0.1
Fluoroquinolones + carbapenems	2	<0.1
Resistance to three classes of antimicrobial drugs		
Total (any three classes in combination)	**2722**	**18.1**
Third-generation cephalosporins + fluoroquinolones + aminoglycosides	2573	17.1
Third-generation cephalosporins + fluoroquinolones + carbapenems	127	0.8
Third-generation cephalosporin + aminoglycosides + carbapenems	22	0.1
Resistance to four classes of antimicrobial drugs		
Third-generation cephalosporins + fluoroquinolones + aminoglycosides + carbapenems	1029	6.8

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

Figure 3.15. *Klebsiella pneumoniae*. Trends of invasive isolates with resistance to third-generation cephalosporins, by country, EU and EEA countries, 2009–2012

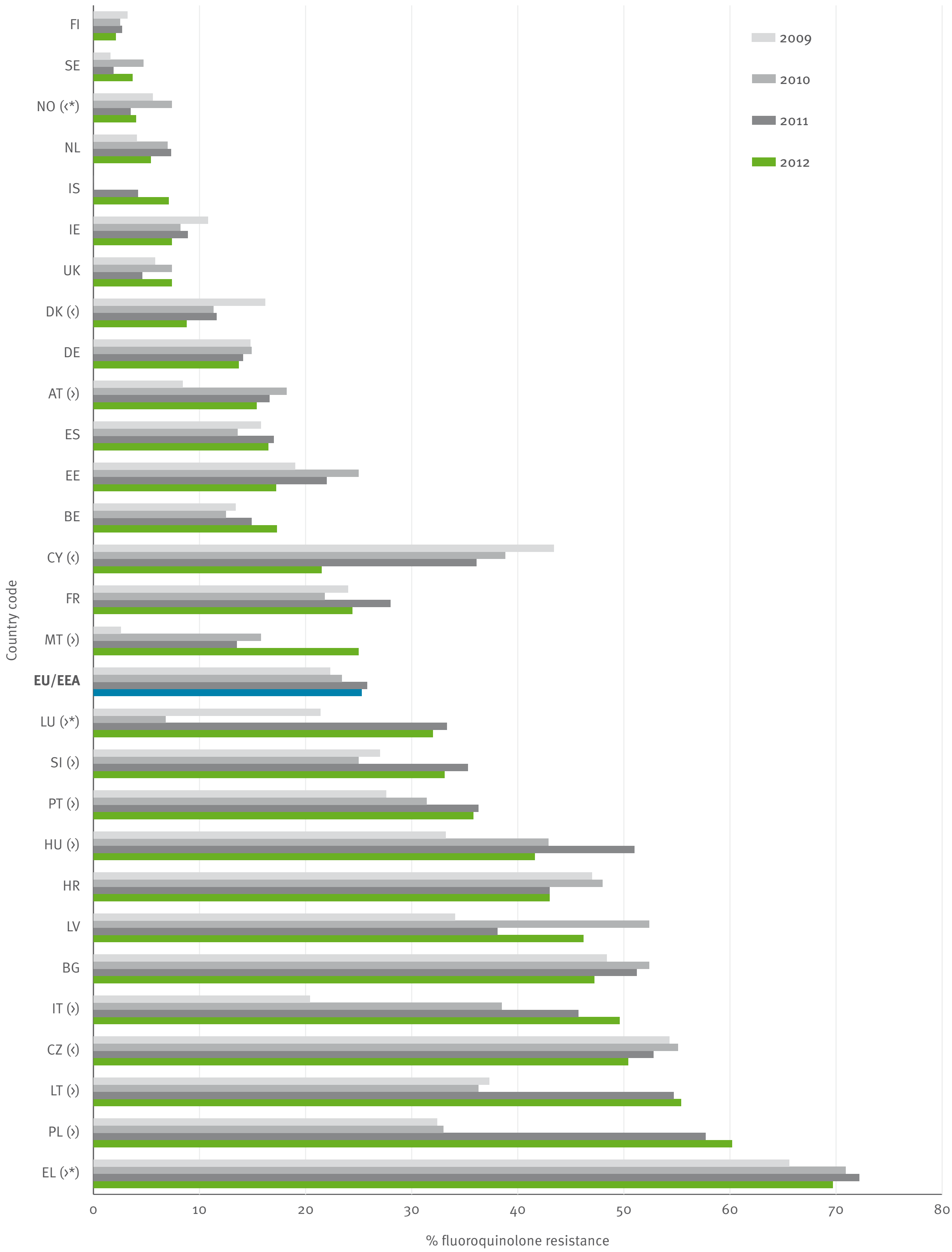


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.16. ***Klebsiella pneumoniae*. Trends of invasive isolates with resistance to fluoroquinolones, by country, EU and EEA countries, 2009–2012**

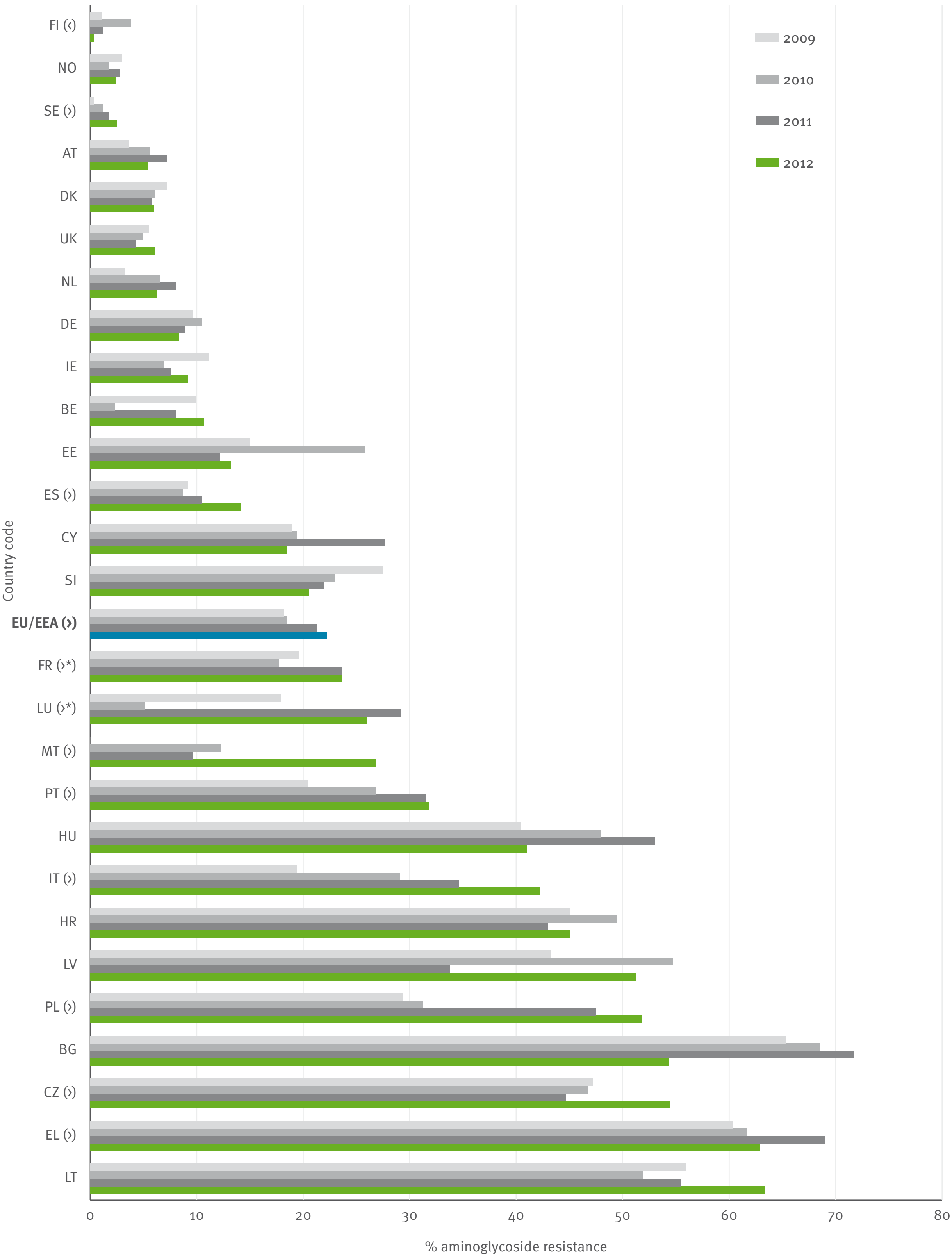


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.17. ***Klebsiella pneumoniae*. Trends of invasive isolates with resistance to aminoglycosides, by country, EU and EEA countries, 2009–2012**

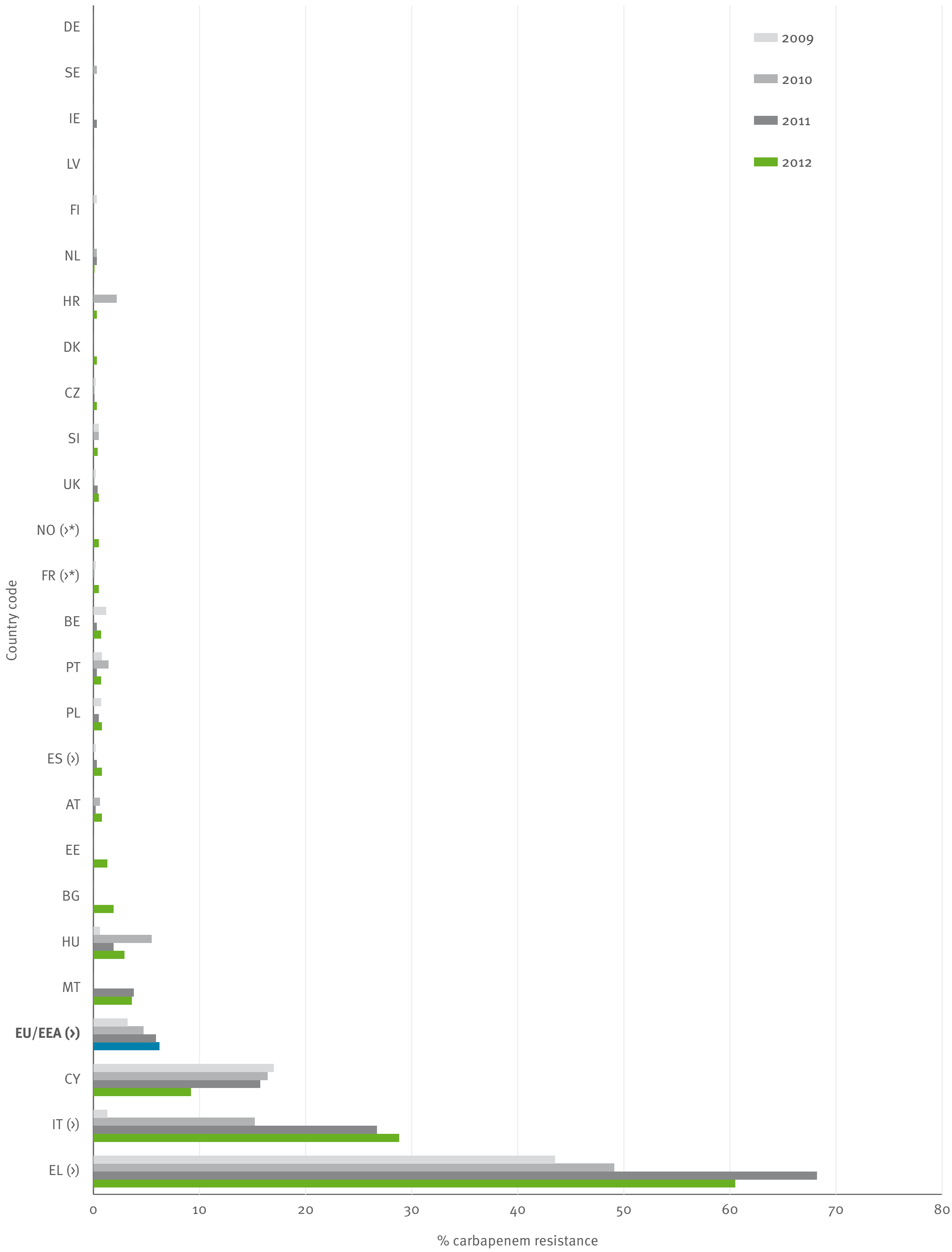


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.18. ***Klebsiella pneumoniae*****. Trends of invasive isolates with resistance to carbapenems, by country, EU and EEA countries, 2009–2012**

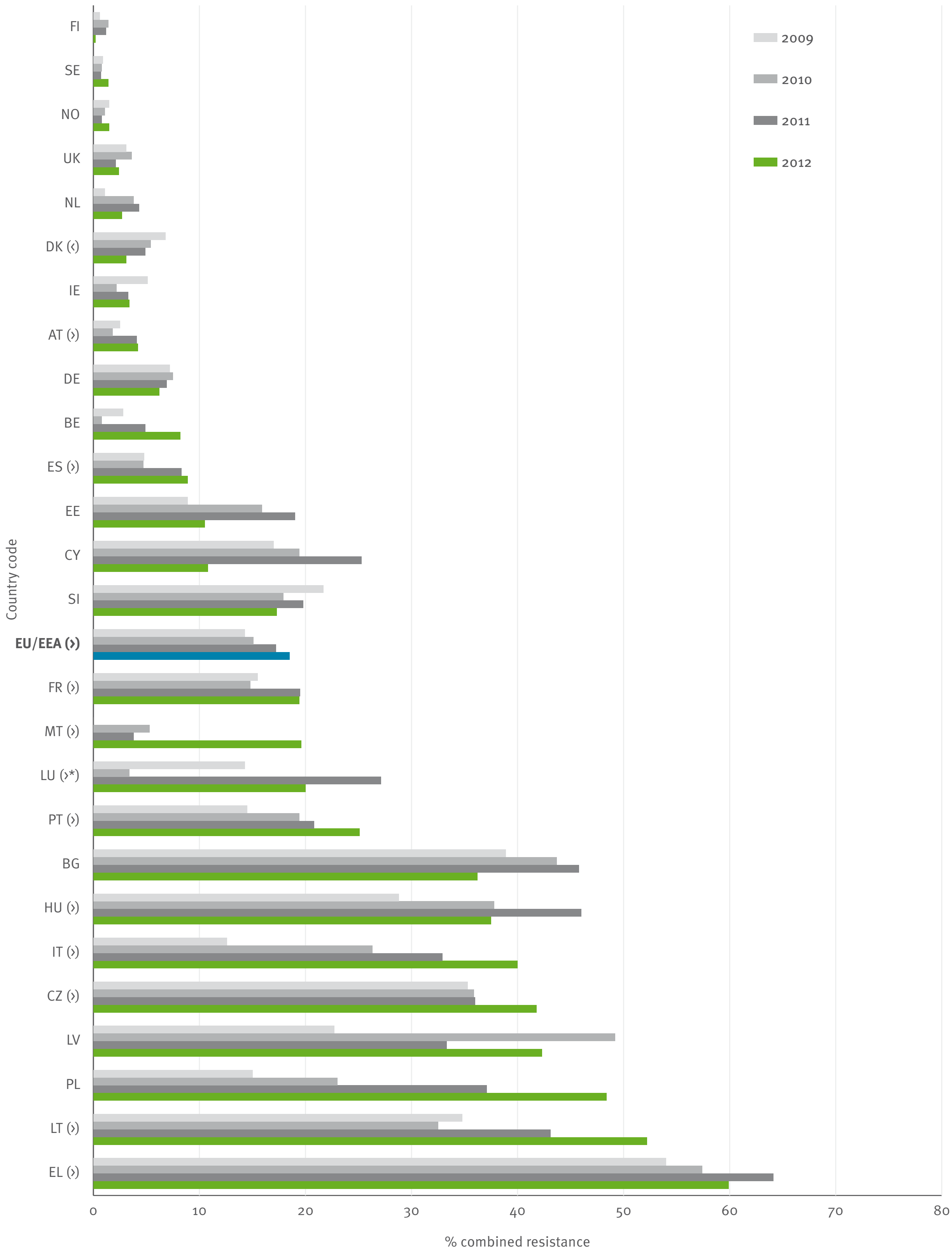


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.19. ***Klebsiella pneumoniae*****. trends of invasive isolates with combined resistance (third-generation cephalosporins, fluoroquinolones and aminoglycosides), by country, EU and EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

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 plants, animals and humans, and is a major and dreaded cause of infection in hospitalised patients with localised or systemic impairment of immune defences, being a common cause of 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* is a frequent cause of skin infections such as folliculitis and otitis externa among recreational and competitive swimmers. In patients with cystic fibrosis, *P. aeruginosa* causes severe bacterial complication leading to chronic colonisation and intermittent exacerbation of the condition with, for example, bronchiolitis and acute respiratory distress syndrome. Finally, *P. aeruginosa* is commonly found in burn units, and in these locations it is almost impossible to eradicate colonising strains with classic infection control procedures.

3.3.2 Resistance mechanism

Pseudomonas aeruginosa is intrinsically resistant to the majority of antimicrobial agents due to its selective ability to exclude various molecules from penetrating its outer membrane. The antimicrobial classes 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 and meropenem) 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 coded 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

Figure 3.20. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to piperacillin (±tazobactam), by country, EU/EEA countries, 2012

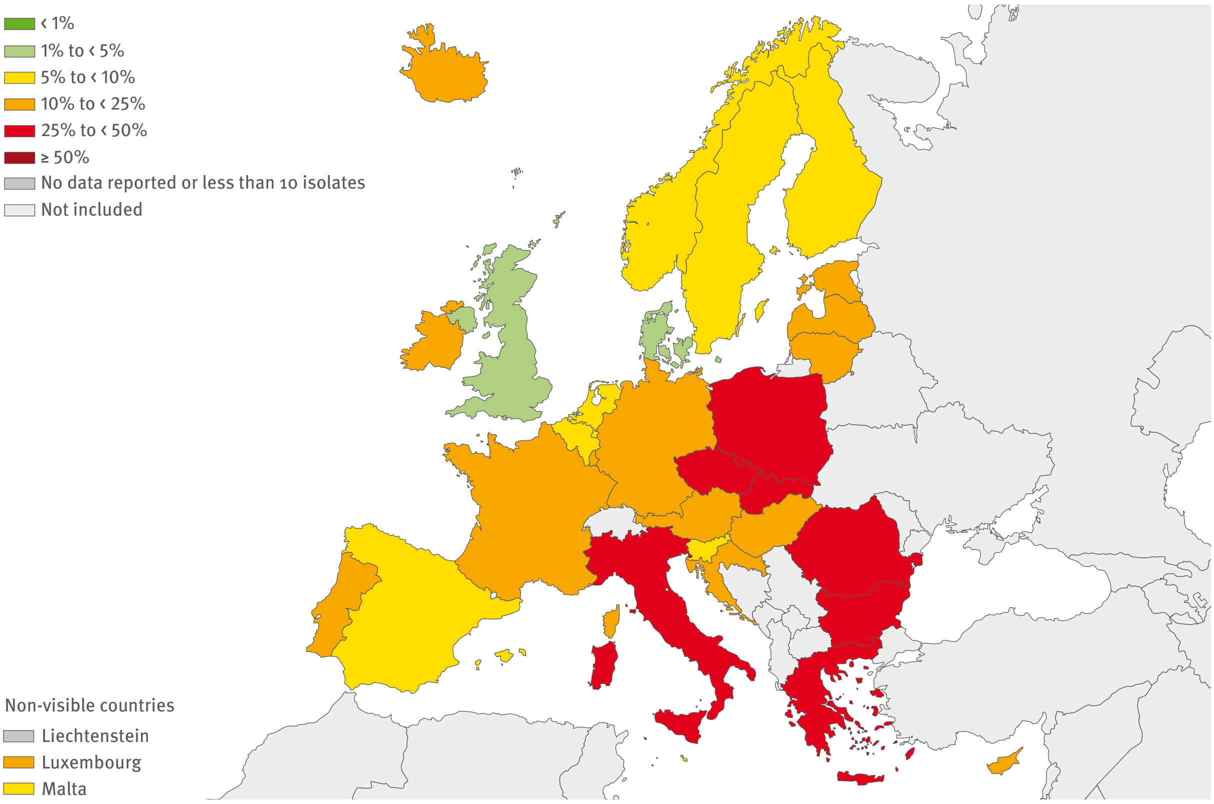


Figure 3.21. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to ceftazidime, by country, EU/EEA countries, 2012

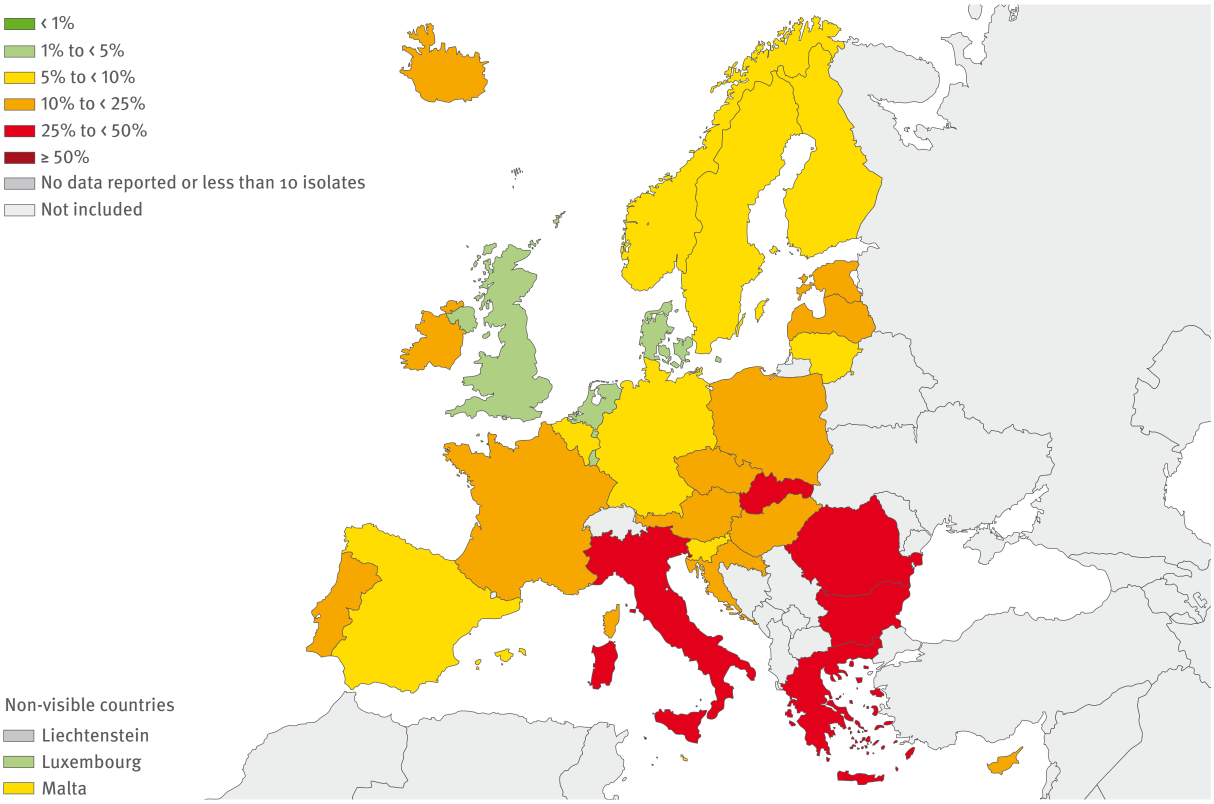
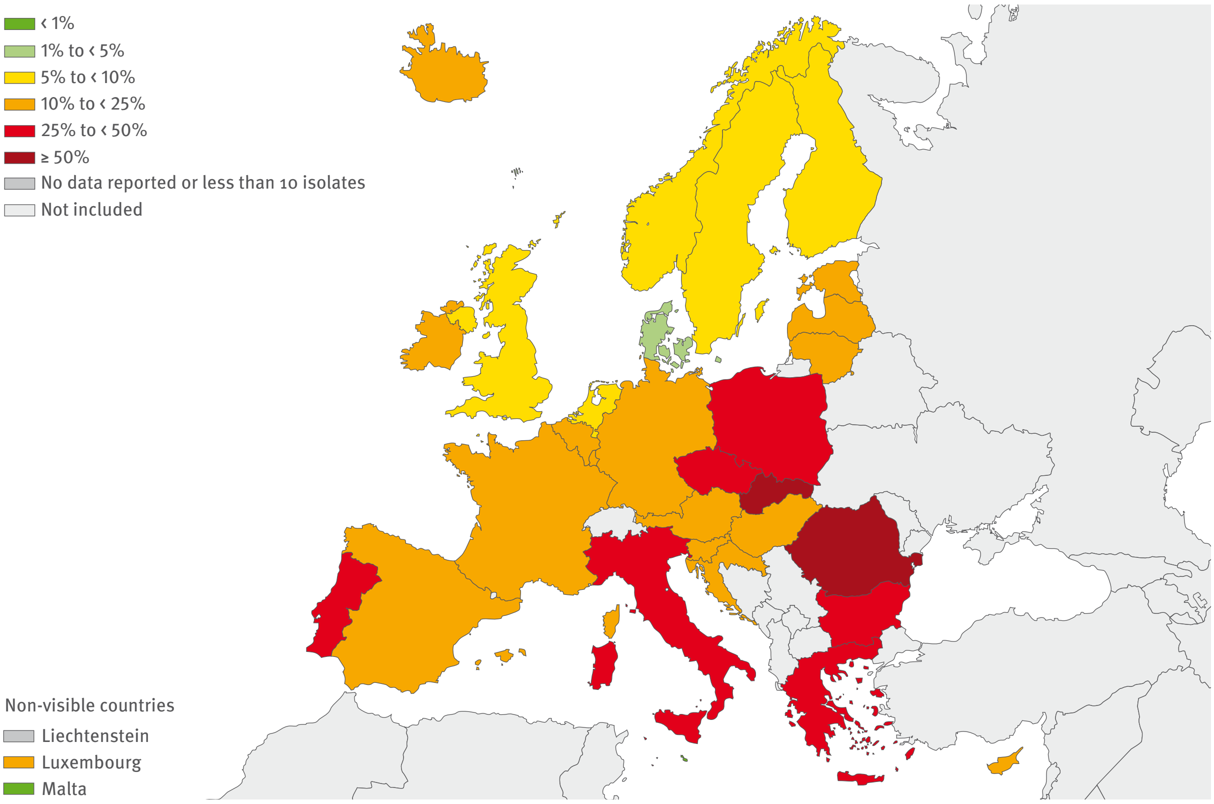


Figure 3.22. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2012



coding for 16S rRNA ribosomal methylases that can confer high-level resistance to all aminoglycosides.

3.3.3 Antimicrobial susceptibility

- High percentages of resistance in *P. aeruginosa* isolates were reported, with a majority of the countries reporting resistance percentages above 10% for all antimicrobial groups under surveillance.
- Carbapenem resistance was common, with an EU/EEA population-adjusted mean percentage of 17.1% and national estimates reported between 3.2% and 51.2%.
- Combined resistance was also common; 13.8% of the isolates were resistant to at least three antimicrobial groups and 5.8% of the isolates were resistant to all five antimicrobial classes under surveillance.
- A north-to-east and east/south gradient was noted for most antimicrobials, with generally lower resistance percentages reported from the north and higher in the eastern and southern parts of Europe.

Full susceptibility

- For 2012, 13 218 isolates were reported to EARS-Net, for which 8 996 isolates (68%) had complete AST information for all antimicrobial groups under surveillance for *P. aeruginosa* (piperacillin ±tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems).
- The population-weighted EU/EEA mean percentage for isolates fully susceptible to all antimicrobials tested was 63.9% in 2012, ranging from 87.8% (the Netherlands and Sweden) to 33.1% (Slovakia) (Table 3.7).

Piperacillin (±tazobactam)

- For 2012, 30 countries reported 10 280 isolates with AST information for piperacillin (±tazobactam). The number of isolates with relevant AST information reported per country ranged from 10 to 1 627.
- The EU/EEA population-weighted mean percentage for piperacillin (±tazobactam) resistance was 19.8%. The percentages of resistant isolates in the reporting countries ranged from 3.1% (the United Kingdom) to 47.5% (Romania). Two countries reported resistance percentages lower than 5%, eight countries reported 5–10%, 13 countries reported 10–25% and seven countries reported 25–50% (Table 3.7 and Figure 3.20).
- Trends for the period 2009–2012 were calculated for 24 countries. Statistically significant increasing trends were observed for five countries (Austria, Denmark, Ireland, Italy and Sweden). For Italy, the trend was not significant when considering only data from laboratories reporting consistently throughout the period. The EU/EEA population-weighted mean percentage

Figure 3.23. ***Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2012**

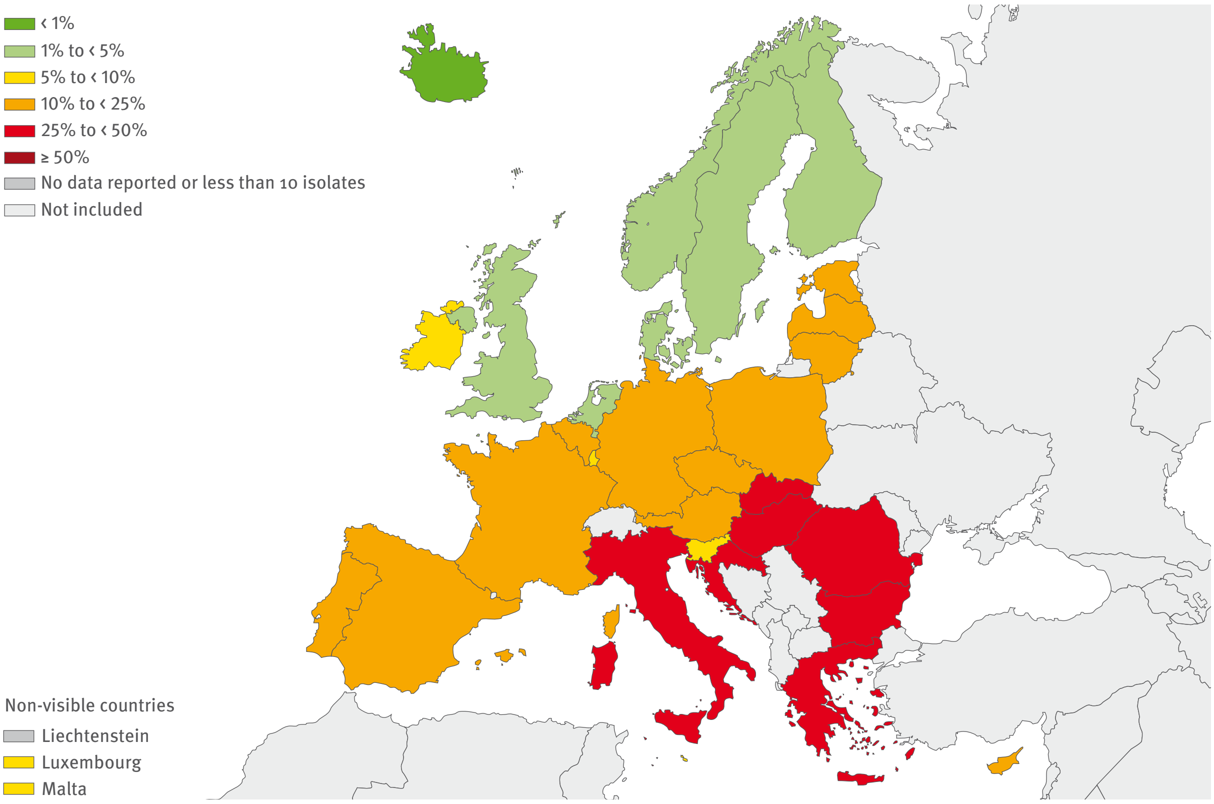


Figure 3.24. ***Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2012**

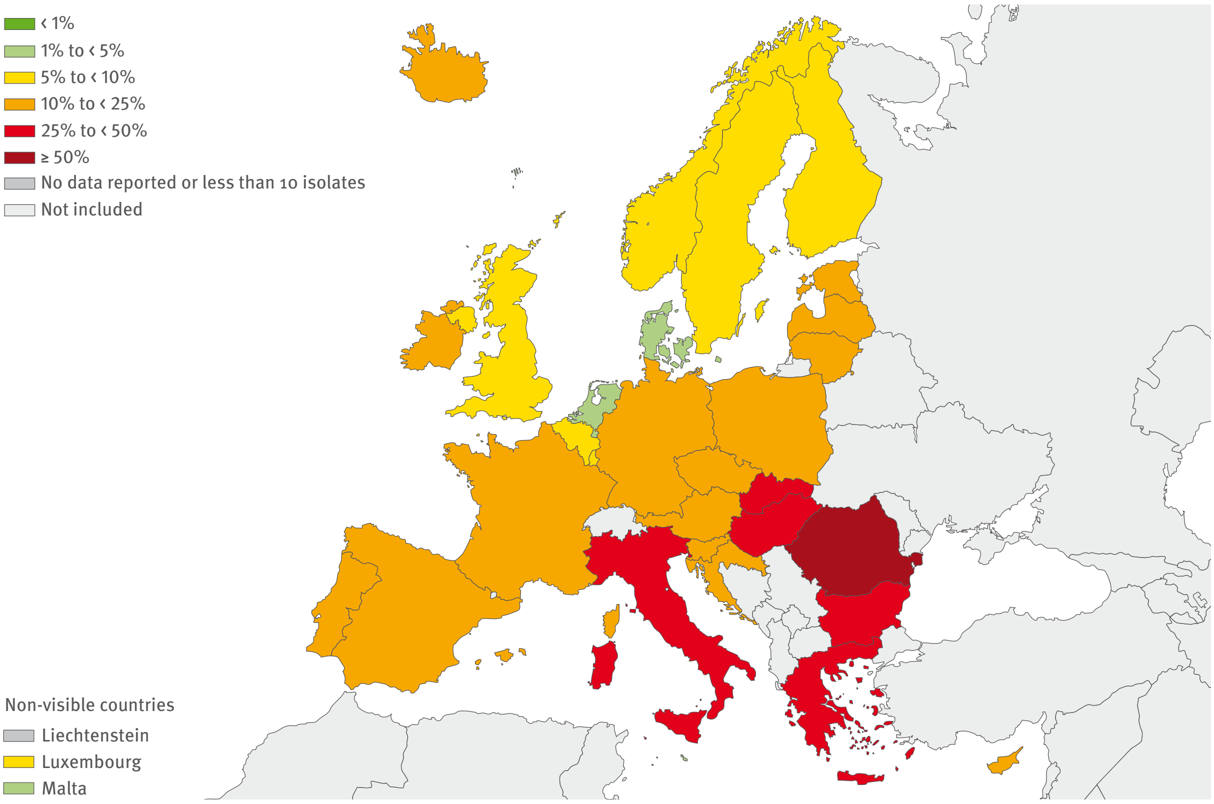
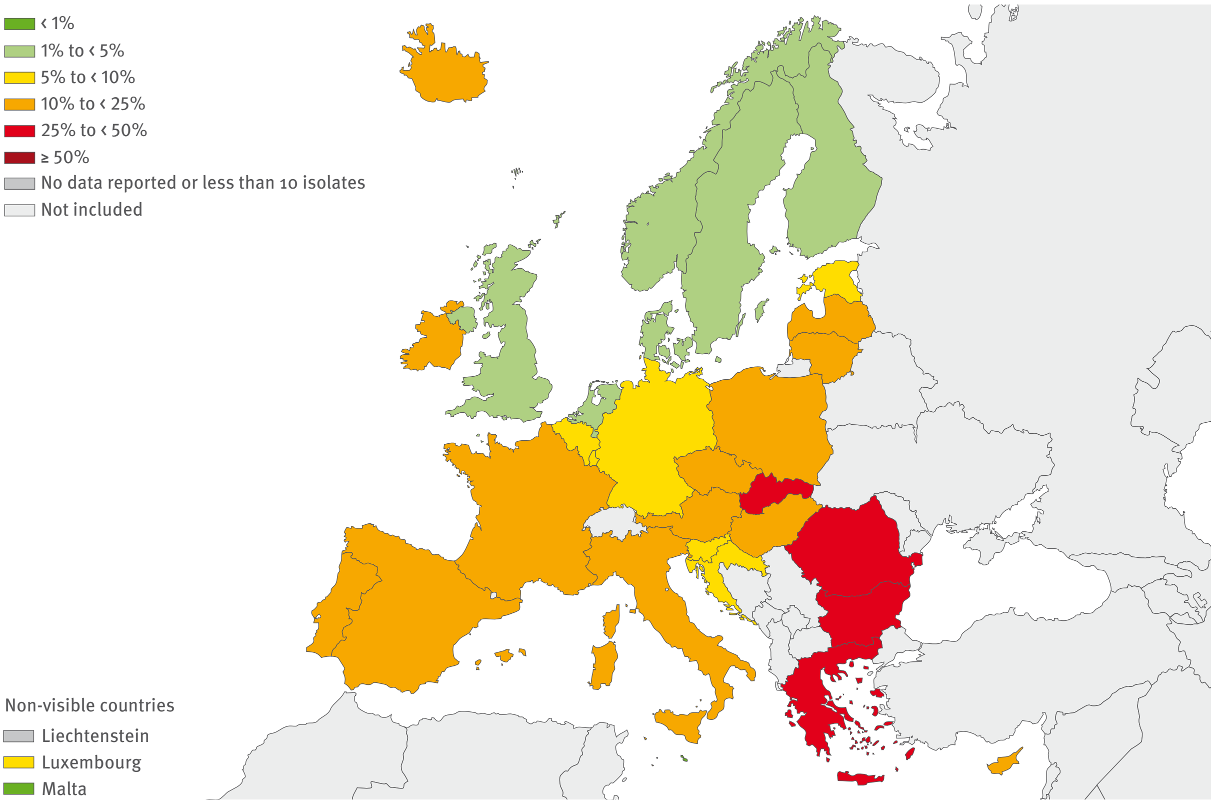


Figure 3.25. ***Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with combined resistance (resistance to three or more antimicrobial classes among piperacillin (±tazobactam), ceftazidime, fluoroquinolones, aminoglycosides and carbapenems), by country, EU/EEA countries, 2012**



also increased significantly during the same period, from 15.8% in 2009 to 19.8% in 2012. Statistically significant decreasing trends were observed for two countries (Slovenia and Malta) (Figure 3.26).

- The ongoing shift from the use of antimicrobial susceptibility breakpoints from the CLSI clinical guidelines to EUCAST guidelines in many countries might introduce bias in trend analyses, as the breakpoint for piperacillin (±tazobactam) resistance is considerably lower in EUCAST than in CLSI (Annex 1).

Ceftazidime

- For 2012, 30 countries reported 10 318 isolates, with relevant AST information for ceftazidime. The number of isolates reported per country ranged from 10 to 1 607.
- The EU/EEA population-weighted mean percentage for ceftazidime resistance was 13.5%. The percentages of resistant isolates reported by the countries ranged from 2.8% (the Netherlands) to 48.6% (Romania). Four countries reported resistance percentages lower than 5%, nine countries reported 5–10%, 12 countries reported 10–25% and five countries reported 25–50% (Table 3.7 and Figure 3.21).
- Trends for the period 2009–2012 were calculated for 25 countries. Statistically significant increasing trends were observed for four countries (Austria, Ireland, Italy and Hungary). For Italy, the trend was not significant when considering only data from laboratories reporting consistently throughout the period. Statistically significant decreasing trends were observed for the Czech Republic and Malta (Figure 3.27).

Fluoroquinolones

- For 2012, 30 countries reported 10 608 isolates with relevant AST information for fluoroquinolones. The number of isolates reported per country ranged from 10 to 1 723.
- The EU/EEA population-weighted mean percentage for fluoroquinolone resistance was 21.0%. The percentages of resistant isolates in the reporting countries ranged from zero (Malta) to 56.3% (Slovakia). Two countries reported resistance percentages lower than 5%, five countries 5–10%, 15 countries reported 10–25%, six countries reported 25–50%, and two countries reported above 50% (Table 3.7 and Figure 3.22).

Table 3.7. *Pseudomonas aeruginosa*. Total number of isolates tested (N) and percentage (%) of invasive isolates susceptible to all antimicrobial groups under EARS-net surveillance*, total number of isolates tested (N) and percentage (%R) with resistance to piperacillin (±tazobactam), ceftazidime, fluoroquinolones, aminoglycosides, carbapenems and combined resistance, including 95% confidence intervals, by country, EU/EEA countries, 2012**

Country	Fully susceptible*		Piperacillin ± tazobactam		Ceftazidime		Fluoroquinolones		Aminoglycosides		Carbapenems		Combined resistance**	
	N	% fully S (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)
Austria	430	71.2 (67-75)	588	18.2 (15-22)	572	14.0 (11-17)	487	14.4 (11-18)	592	11.5 (9-14)	562	14.6 (12-18)	595	10.8 (8-14)
Belgium	306	76.1 (71-81)	342	9.7 (7-13)	326	8.3 (6-12)	329	18.2 (14-22)	286	11.2 (8-15)	391	9.7 (7-13)	346	8.7 (6-12)
Bulgaria	49	51.0 (36-66)	50	26.0 (15-40)	52	34.6 (22-49)	52	32.7 (20-47)	52	32.7 (20-47)	51	31.4 (19-46)	52	34.6 (22-49)
Croatia	196	50.5 (43-58)	201	18.4 (13-25)	196	12.8 (9-19)	201	23.9 (18-31)	203	26.1 (20-33)	201	21.9 (17-28)	196	6.1 (3-9)
Cyprus	50	74.0 (60-85)	50	10.0 (3-22)	52	15.4 (7-28)	52	15.4 (7-28)	52	15.4 (7-28)	52	19.2 (10-33)	52	17.3 (8-30)
Czech Republic	489	60.5 (56-65)	489	26.4 (23-31)	489	20.4 (17-24)	489	30.9 (27-35)	489	23.7 (20-28)	489	15.1 (12-19)	489	21.7 (18-26)
Denmark	304	85.2 (81-89)	389	4.6 (3-7)	325	4.9 (3-8)	389	4.1 (2-7)	372	3.8 (2-6)	355	3.7 (2-6)	388	1.8 (1-4)
Estonia	26	57.7 (37-77)	31	16.1 (5-34)	29	17.2 (6-36)	32	15.6 (5-33)	33	24.2 (11-42)	32	12.5 (4-29)	33	9.1 (2-24)
Finland	313	(85.9 (82-90)	314	7.6 (5-11)	317	5.0 (3-8)	327	8.0 (5-11)	326	2.5 (1-5)	327	6.1 (4-9)	327	4.6 (3-7)
France	1036	56.1 (53-59)	1627	19.9 (18-22)	1607	14.1 (12-16)	1723	22.2 (20-24)	1229	20.0 (18-22)	1722	18.0 (16-20)	1723	14.7 (13-17)
Germany	427	68.1 (63-73)	432	15.5 (12-19)	437	9.6 (7-13)	434	19.6 (16-24)	436	10.6 (8-14)	438	10.7 (8-14)	438	8.4 (6-11)
Greece	790	41.9 (38-45)	849	34.3 (31-38)	883	31.0 (28-34)	864	44.3 (41-48)	897	40.7 (37-44)	907	47.7 (44-51)	898	40.2 (37-43)
Hungary	600	50.0 (46-54)	610	19.2 (16-23)	608	18.1 (15-21)	618	22.3 (19-26)	619	26.7 (23-30)	619	27.5 (24-31)	619	17.6 (15-21)
Iceland	10	80.0 (44-97)	10	10.0 (0-44)	10	10.0 (0-44)	10	10.0 (0-44)	10	0.0 (0-26)	10	10.0 (0-44)	10	10.0 (0-44)
Ireland	208	68.3 (61-75)	216	16.2 (12-22)	210	14.3 (10-20)	215	14.9 (10-20)	215	9.8 (6-15)	213	11.3 (7-16)	215	10.2 (7-15)
Italy	467	48.8 (44-53)	537	30.0 (26-34)	599	25.5 (22-29)	671	31.3 (28-35)	697	30.1 (27-34)	678	25.1 (22-29)	644	23.9 (21-27)
Latvia	17	64.7 (38-86)	17	11.8 (1-36)	18	22.2 (6-48)	18	22.2 (6-48)	18	22.2 (6-48)	18	11.1 (1-35)	18	11.1 (1-35)
Lithuania	28	78.6 (59-92)	28	10.7 (2-28)	28	7.1 (1-24)	28	10.7 (2-28)	28	14.3 (4-33)	28	17.9 (6-37)	28	14.3 (4-33)
Luxembourg	31	71.0 (52-86)	31	16.1 (5-34)	31	3.2 (0-17)	31	19.4 (7-37)	31	6.5 (1-21)	31	6.5 (1-21)	31	6.5 (1-21)
Malta	31	80.6 (63-93)	31	9.7 (2-26)	31	6.5 (1-21)	31	0.0 (0-11)	31	6.5 (1-21)	31	3.2 (0-17)	31	0.0 (0-11)
Netherlands	370	87.8 (84-91)	386	5.2 (3-8)	398	2.8 (1-5)	395	6.1 (4-9)	404	4.0 (2-6)	397	3.3 (2-6)	402	2.5 (1-5)
Norway	180	84.4 (78-89)	198	7.1 (4-12)	202	6.4 (3-11)	209	5.7 (3-10)	197	2.0 (1-5)	208	6.7 (4-11)	209	3.3 (1-7)
Poland	144	50.7 (42-59)	157	29.9 (23-38)	156	23.7 (17-31)	175	26.9 (20-34)	176	24.4 (18-31)	171	22.8 (17-30)	176	21.6 (16-28)
Portugal	564	61.0 (57-65)	586	19.8 (17-23)	587	15.3 (13-19)	587	25.6 (22-29)	586	14.7 (12-18)	568	20.4 (17-24)	587	18.1 (15-21)
Romania	34	41.2 (25-65)	40	47.5 (32-64)	37	48.6 (32-66)	39	51.3 (35-68)	41	48.8 (33-65)	41	51.2 (35-67)	41	46.3 (31-63)
Slovakia	133	33.1 (25-91)	195	38.5 (32-46)	154	35.1 (28-43)	199	56.3 (49-63)	199	41.7 (35-49)	179	40.8 (34-48)	199	39.2 (32-46)
Slovenia	134	69.4 (61-91)	134	7.5 (4-13)	134	6.7 (3-12)	134	14.9 (9-22)	134	9.7 (5-16)	134	21.6 (15-30)	134	9.7 (5-16)
Spain	816	66.4 (63-70)	835	6.7 (5-9)	839	8.9 (7-11)	848	21.0 (18-24)	853	16.5 (14-19)	853	16.4 (14-19)	853	10.8 (9-13)
Sweden	271	87.8 (83-91)	271	5.9 (3-9)	357	6.2 (4-9)	357	6.7 (4-10)	357	1.7 (1-4)	357	5.3 (3-8)	357	2.8 (1-5)
United Kingdom	542	87.3 (84-90)	636	3.1 (2-5)	634	3.9 (3-6)	664	5.0 (3-7)	667	2.2 (1-4)	603	6.3 (4-9)	666	1.7 (1-3)
EU/EEA mean percentage (population-weighted)		**63.9**		**19.8**		**13.5**		**21.0**		**18.4**		**17.1**		**13.8**

* Susceptible to piperacillin (±tazobactam), ceftazidime, fluoroquinolones, aminoglycosides and carbapenems. Only isolates tested for all five antimicrobial groups were included in the analysis.

** Combined resistance defined as being resistant to three or more antimicrobial classes among piperacillin (±tazobactam), ceftazidime, fluoroquinolones, aminoglycosides and carbapenems.

- Trends for the period 2009–2012 were calculated for 25 countries. A statistically significant increasing trend was observed for Portugal. Statistically significant decreasing trends were observed for four countries (the Czech Republic, Hungary, Italy and Malta). For Italy, the trend was not significant when considering only data from laboratories reporting consistently for all four years (Figure 3.28).

Aminoglycosides

- For 2012, 30 countries reported 10 203 isolates with relevant AST information for aminoglycosides. The number of isolates per country ranged from 10 to 1 229.
- The EU/EEA population-weighted mean for aminoglycoside resistance was 18.4%. The percentages of resistant isolates in the reporting countries ranged from 0% (Iceland) to 48.8% (Romania). Seven countries reported resistance percentages lower than 5%, four countries reported 5–10%, 12 countries reported 10–25% and seven countries reported 25–50% (Table 3.7 and Figure 3.23).
- Trends for the period 2009–2012 were calculated for 25 countries. Significantly increasing trends were observed for four countries (Cyprus, Denmark, Norway and Sweden). For Norway and Sweden, the trends were not significant when considering only data from laboratories reporting consistently for all four years. Significantly decreasing trends were observed for two countries (the Czech Republic and Hungary) (Figure 3.29).

Carbapenems

- For 2012, 30 countries reported 10 666 isolates with relevant AST information for carbapenems. The number of isolates per country ranged from 10 to 1 722.
- The EU/EEA population-weighted mean for carbapenem resistance was 17.1%. The percentages of resistant isolates in the reporting countries ranged

Table 3.8. *Pseudomonas aeruginosa*. Total number of tested isolates and resistance combinations among invasive isolates tested against at least three antimicrobial classes among piperacillin±tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems (n=10 750), EU/EEA countries, 2012

Resistance pattern	Number of tested isolates	% of total*
Fully susceptible (to tested antibiotics)	6693	62.3
Single resistance (to indicated drug classes)		
Total (all single resistance types)	**1532**	**14.3**
Carbapenems	620	5.8
Fluoroquinolones	401	3.7
Aminoglycosides	241	2.2
Piperacillin (±tazobactam)	198	1.8
Ceftazidime	72	0.7
Resistance to two classes of antimicrobial drugs		
Total any two classes in combination)	**778**	**7.2**
Piperacillin (±tazobactam) + ceftazidime	309	2.9
Fluoroquinolones + aminoglycosides	242	2.3
Fluoroquinolones + carbapenems	73	0.7
Aminoglycosides +carbapenems	46	0.4
Piperacillin (±tazobactam) +fluoroquinolones	38	0.4
Piperacillin (±tazobactam) + carbapenems	33	0.3
Piperacillin (±tazobactam) + aminoglycosides	14	0.1
Ceftazidime + carbapenems	9	0.1
Fluoroquinolones + ceftazidime	6	0.1
Ceftazidime + aminoglycosides	8	0.1
Resistance to three classes of antimicrobial drugs		
Total (any three classes in combination)	**556**	**5.2**
Fluoroquinolones + aminoglycosides + carbapenems	191	1.8
Piperacillin (±tazobactam) + ceftazidime + carbapenems	106	1.0
Piperacillin (±tazobactam) + fluoroquinolones +aminoglycosides	88	0.8
Piperacillin (±tazobactam) + fluoroquinolones + ceftazidime	68	0.6
Fluoroquinolones +ceftazidime +aminoglycosides	29	0.3
Piperacillin (±tazobactam) + fluoroquinolones + carbapenems	30	0.3
Piperacillin (±tazobactam) + aminoglycosides + carbapenems	12	0.1
Piperacillin (±tazobactam) + ceftazidime +aminoglycosides	17	0.2
Ceftazidime + aminoglycosides + carbapenems	8	0.1
Fluoroquinolones + ceftazidime + carbapenems	7	0.1
Resistance to four classes of antimicrobial drugs		
Total (any four classes in combination)	**569**	**5.3**
Piperacillin (±tazobactam) + fluoroquinolones + aminoglycosides + carbapenems	187	1.7
Piperacillin (±tazobactam) + fluoroquinolones + ceftazidime + aminoglycosides	162	1.5
Fluoroquinolones + ceftazidime + aminoglycosides + carbapenems	107	1.0
Piperacillin (±tazobactam) + fluoroquinolones + ceftazidime + carbapenems	75	0.7
Piperacillin (±tazobactam) + ceftazidime + aminoglycosides + carbapenems	38	0.4
Resistance to five classes of antimicrobial drugs		
Piperacillin (±tazobactam) + fluoroquinolones + ceftazidime + aminoglycosides + carbapenems	622	5.8

* Not adjusted for population differences in the reporting countries.

from 3.2% (Malta) to 51.2% (Romania). Three countries reported resistance percentages below 5%, six countries reported 5–10%, 15 countries reported 10–25%, five countries reported 25–50% and one country reported above 50% (Table 3.7 and Figure 3.24).

- Trends for the period 2009–2012 were calculated for 25 countries. Significantly increasing trends were observed for four countries (Austria, Cyprus, Greece and Portugal). For Portugal, the trend was not significant when considering only data from laboratories reporting consistently for all four years. A significantly decreasing trend was observed for the Czech Republic (Figure 3.30).

Combined resistance (resistance to at least three antimicrobial groups out of piperacillin±tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems)

- For 2012, 30 countries reported 10750 isolates tested for susceptibility to at least three antimicrobial groups under surveillance by EARS-Net for *P. aeruginosa*. The number of isolates with relevant information reported per country ranged from 10 to 1723 (Table 3.7).
- In 2012, 37.7% of the isolates were resistant to one or more of the five considered antimicrobial classes, while 16.3% (population-weighted mean 13.8%) were resistant to three or more. While single resistance was the most common, the most frequent individual resistance phenotype was resistance to all five antimicrobial classes (5.8%) (Table 3.8).
- The percentages of isolates with combined resistance, i.e. resistant to at least three of the five considered antimicrobial groups, were below 1% in one country, 1–5% in six countries, 5–10% in six countries, 10–25% in 13 countries and 25–50% in four countries (Table 3.7 and Figure 3.25).
- Trends for the period 2009–2012 were calculated for 23 countries. Significantly increasing trends of combined resistance were observed for four countries (Austria, Ireland, Portugal and Sweden). For Portugal, the trend was not significant when including only data from laboratories consistently reporting for all four years (Figure 3.31). Significantly decreasing trends of combined resistance were observed for two countries (the Czech Republic and Hungary).

3.3.4 Discussion and conclusions

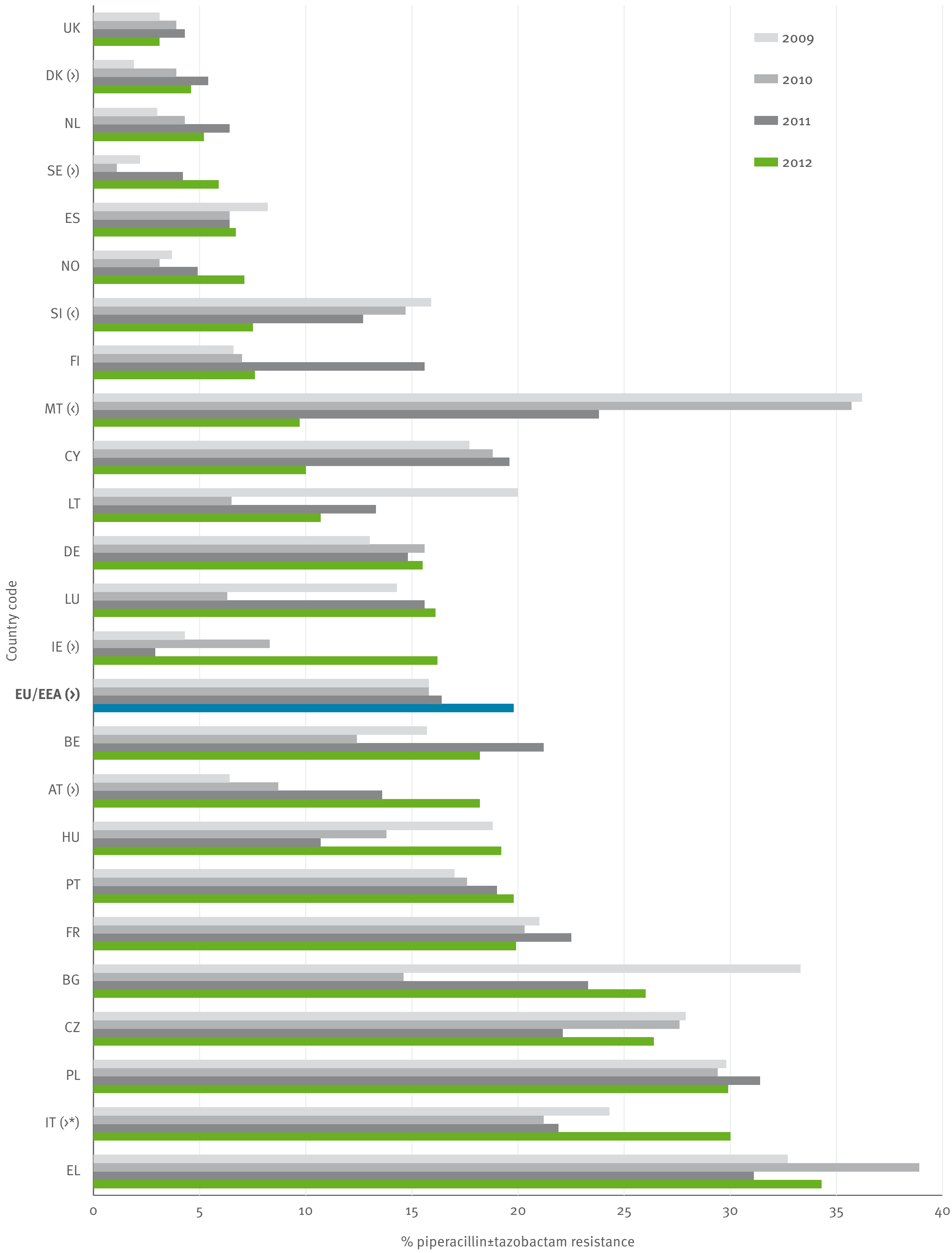
It is important to note that the ongoing change in the use of antimicrobial susceptibility breakpoints from CLSI to EUCAST in many European countries makes trend analysis difficult and sensitive to bias, as there are differences between the antimicrobial breakpoints for *P. aeruginosa* used by the two systems. The change from CLSI to EUCAST guidelines within a country is often gradual and not all laboratories change at the same time.

However, despite use of clinical guidelines, high resistance percentages have been reported from many European countries during the last couple of years. This is a concern as *P. aeruginosa* carries intrinsic resistance to a number of antimicrobial classes and any additional acquired resistance severely limits the therapeutic options for treatment of serious infections.

P. aeruginosa is recognised as a major cause of healthcare-associated infection, and in the recent *Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012*, *P. aeruginosa* was among the five most common bacteria in health-care associated infections, with almost a third of the reported isolates being carbapenem resistant[12]. 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.

12 European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.

Figure 3.26. *Pseudomonas aeruginosa*. Trends of invasive isolates with resistance to piperacillin (±tazobactam), by country, EU/EEA countries, 2009–2012

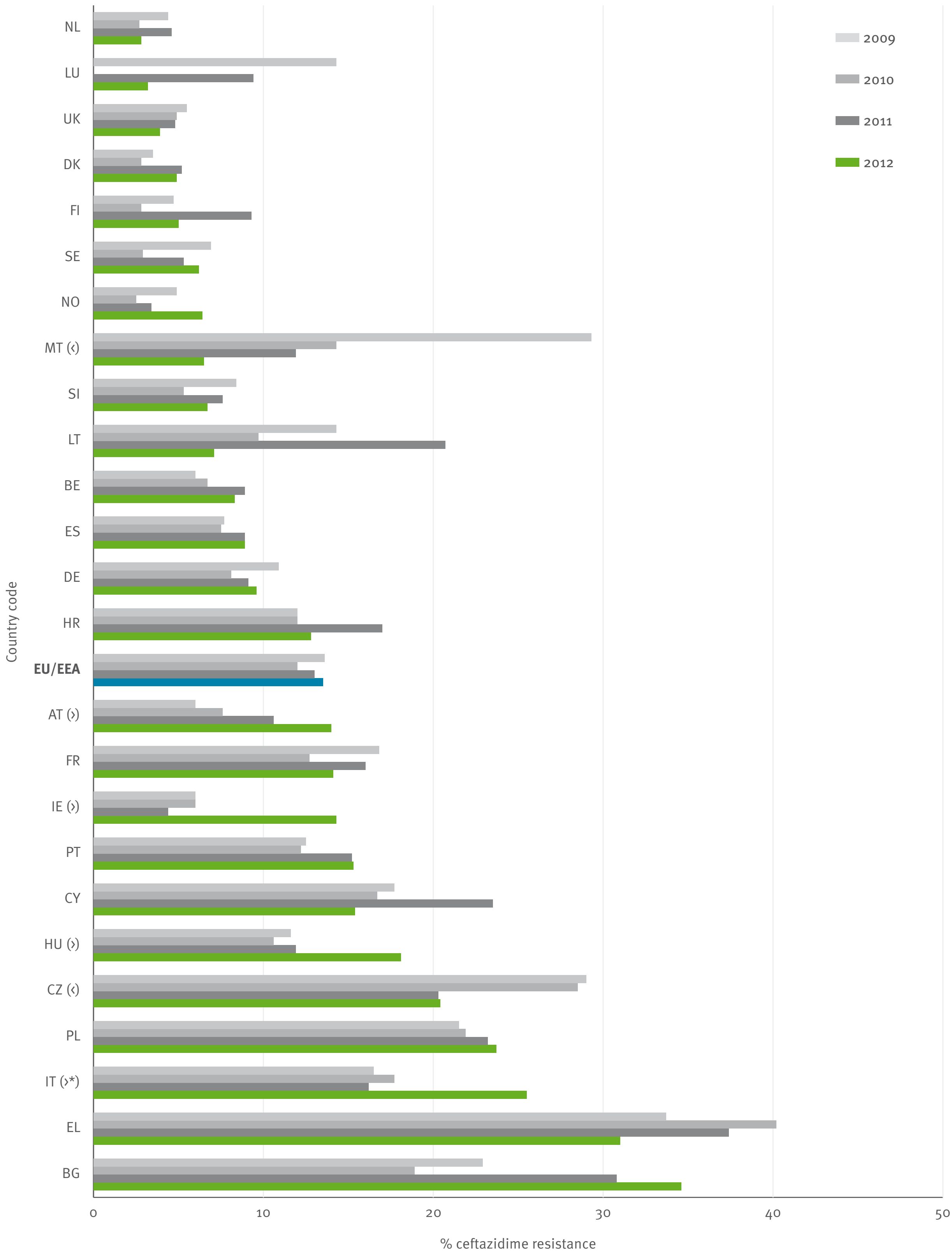


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.27. ***Pseudomonas aeruginosa*. Trends of invasive isolates with resistance to ceftazidime, by country, EU/EEA countries, 2009–2012**

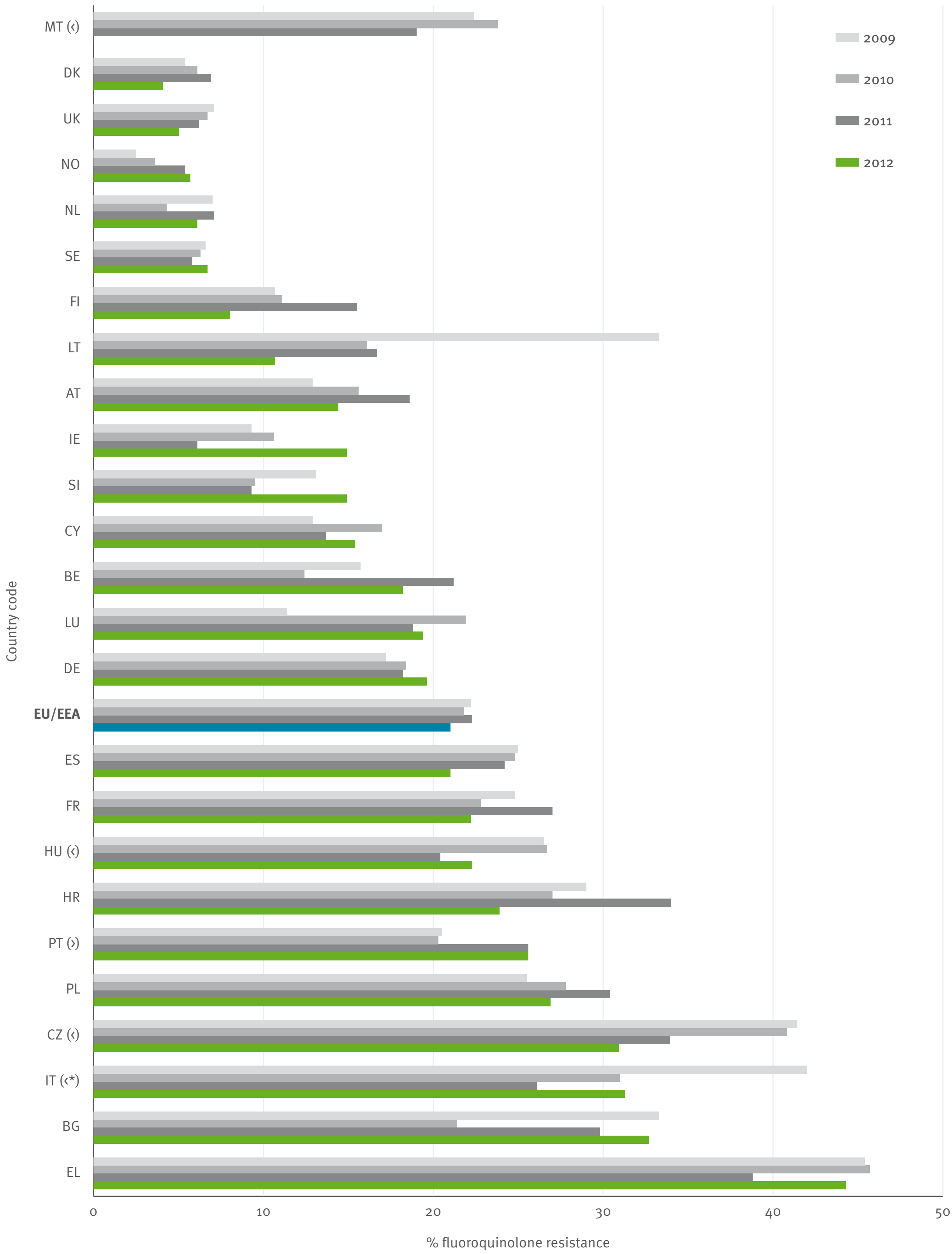


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.28. ***Pseudomonas aeruginosa*****. Trends of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2009–2012**

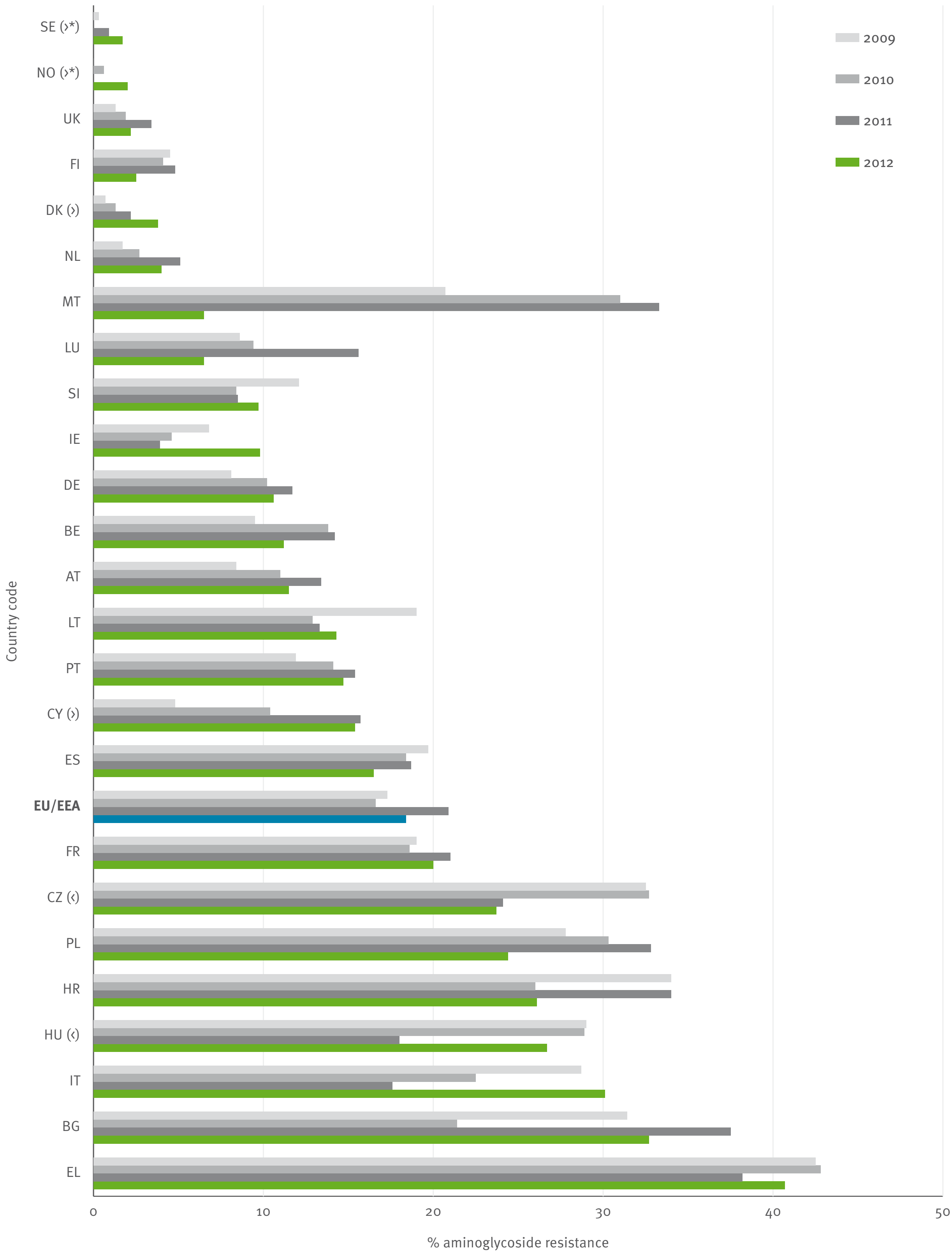


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.29. ***Pseudomonas aeruginosa*****. Trends of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2009–2012**

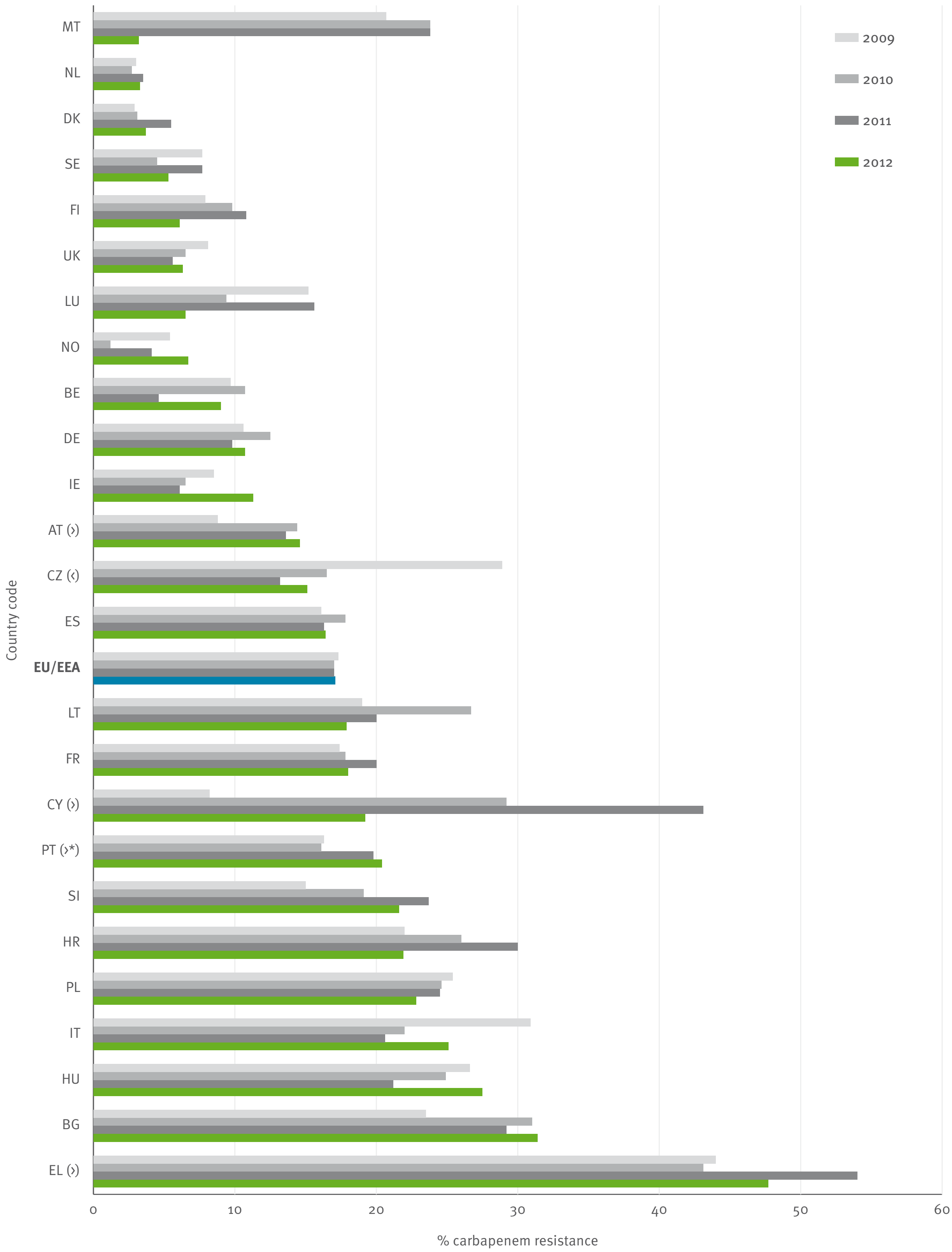


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.30. *Pseudomonas aeruginosa*. Trends of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2009–2012

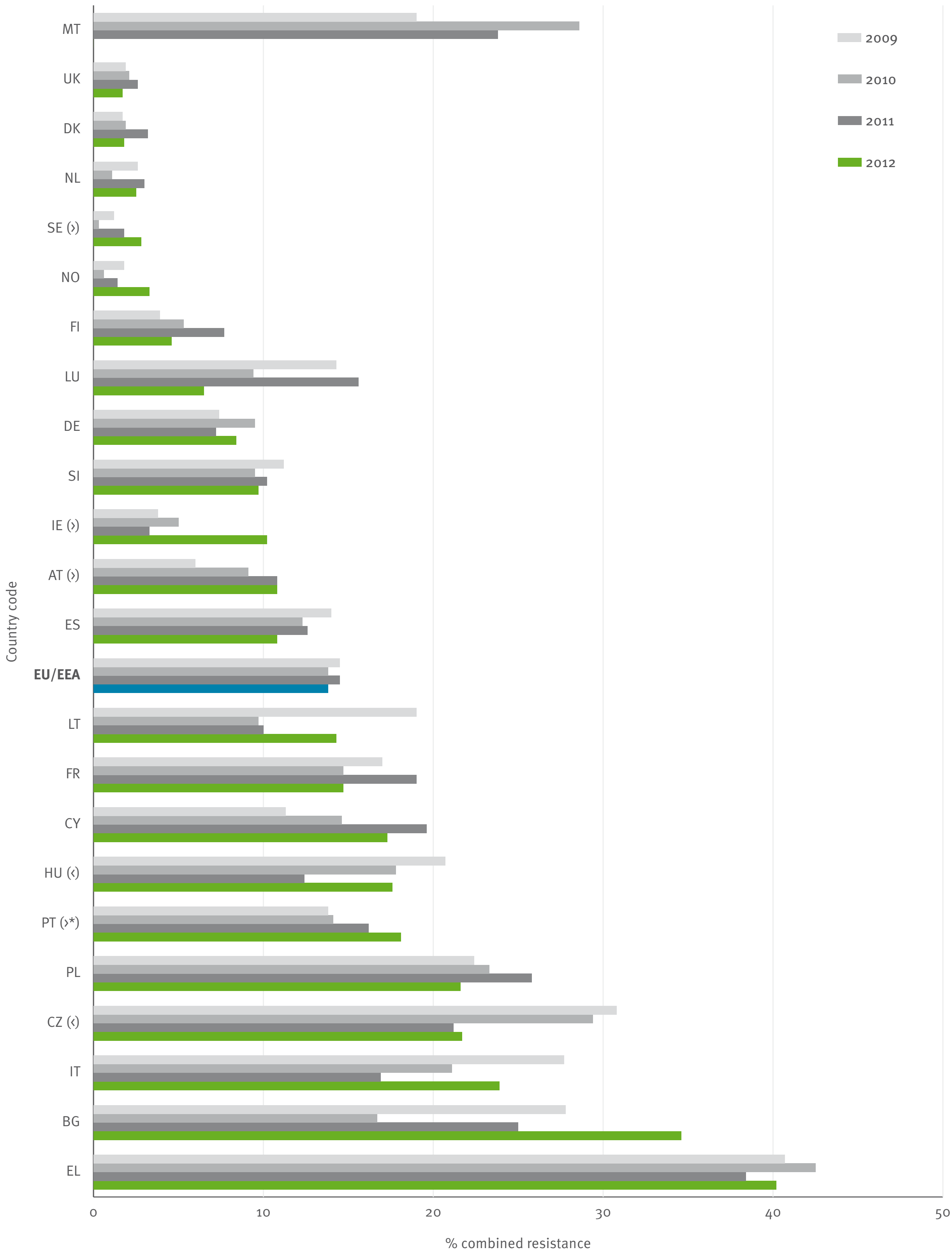


Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

Figure 3.31. ***Pseudomonas aeruginosa*****. trends of invasive isolates with combined (resistance to three or more antimicrobial classes among piperacillin±tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems, by country, EU/EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

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

EU/EEA refers to the population-weighted mean percentage.

3.4 *Acinetobacter* species

3.4.1 Clinical and epidemiological importance

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

Acinetobacter species are gram-negative, strictly aerobic, non-fastidious, non-fermentative, catalase-positive, oxidase-negative 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. *Acinetobacter* species other than *A. baumannii* have been isolated from the skin and mucous membranes of people in the community; however, carriage rates of species belonging to the *A. baumannii* group on the skin and in the faeces have been reported as very low.

The *A. baumannii* group has a limited number of virulence factors, which is why infections due to this

Table 3.9. *Acinetobacter* spp. Total number of tested isolates (N) and percentages susceptible to all antimicrobial groups under EARS-Net surveillance*, total number of tested isolates (N) and percentages of invasive isolates resistant to fluoroquinolones, aminoglycosides, carbapenems and combined resistance, including 95% confidence intervals (95% CI), by country, EU/EEA countries, 2012**

Country	Fully susceptible*		Fluoroquinolones		Aminoglycosides		Carbapenems		Combined resistance**	
	N	% fully S (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)	N	%R (95% CI)
Bulgaria	58	17.2 (9-29)	65	69.2 (57-80)	65	58.5 (46-71)	58	60.3 (47-73)	58	32.8 (21-46)
Cyprus	23	39.1 (20-61)	23	56.5 (34-77)	23	52.2 (31-73)	23	56.5 (34-73)	23	47.8 (27-69)
Denmark	58	81.0 (69-90)	83	12 (6-21)	77	10.4 (5-19)	64	9.4 (4-19)	58	8.6 (3-19)
France	272	82.0 (77-86)	385	15.6 (12-20)	278	12.9 (9-17)	389	3.3 (2-6)	272	4.0 (2-7)
Germany	119	88.2 (81-93)	121	8.3 (4-15)	119	5.9 (2-12)	121	6.6 (3-13)	119	4.2 (1-10)
Greece	1 203	6.4 (5-8)	1 204	93.1 (92-94)	1 234	78.1 (76-80)	1 254	87.8 (86-90)	1 203	74.5 (72-77)
Hungary	394	20.6 (17-25)	405	78 (74-82)	407	68.8 (64-73)	418	48.1 (43-53)	394	41.6 (37-47)
Iceland	2	-	2	-	2	-	2	-	2	-
Italy	214	11.2 (7-16)	233	86.3 (81-90)	231	83.1 (78-88)	228	83.3 (78-88)	214	78 (72-83)
Luxembourg	5	-	6	-	6	-	5	-	5	-
Malta	5	-	6	-	5	-	6	-	5	-
Netherlands	10	100.0 (69-100)	10	0.0 (0-31)	59	1.7 (0-9)	67	6.0 (2-15)	10	0.0 (0-31)
Norway	25	96.0 (80-100)	25	0.0 (0-14)	25	4.0 (0-20)	25	0.0 (0-14)	25	0.0 (0-14)
Poland	197	20.8 (15-27)	209	78 (72-83)	205	63.4 (56-70)	209	38.3 (32-45)	197	35.0 (28-42)
Portugal	168	19.0 (13-26)	168	77.4 (70-83)	169	65.1 (57-72)	168	79.2 (72-85)	168	64.3 (57-72)
Romania	48	4.2 (1-14)	50	90.0 (78-97)	48	54.2 (39-69)	48	81.3 (67-91)	48	45.8 (31-61)
Slovenia	25	68.0 (46-85)	25	28.0 (12-49)	25	20.0 (7-41)	25	24.0 (9-45)	25	12.0 (3-31)
United Kingdom	79	93.7 (86-98)	105	2.9 (1-8)	108	2.8 (1-8)	80	2.5 (0-9)	79	1.3 (0-7)

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

* Susceptible to fluoroquinolones, aminoglycosides and carbapenems. Only isolates tested for all three antimicrobial groups were included in the analysis

** Resistance to fluoroquinolones, aminoglycosides and carbapenems. Only isolates tested for all three antimicrobial groups were included in the analysis.

Table 3.10. *Acinetobacter* spp. Overall resistance and resistance combinations among invasive isolates tested against fluoroquinolones, aminoglycosides and carbapenems (n=2 905), EU/EEA countries, 2012

Resistance pattern	Number of tested isolates	% of total*
Fully susceptible	788	27.1
Single resistance (to indicated drug classes)		
Total (any single resistance)	**143**	**4.9**
Fluoroquinolones	100	3.4
Aminoglycosides	27	0.9
Carbapenems	16	0.6
Resistance to two classes of antimicrobial drugs		
Total (any two classes in combination)	**493**	**17.0**
Fluoroquinolones + aminoglycosides	237	8.2
Fluoroquinolones + carbapenems	247	8.5
Aminoglycosides + carbapenems	9	0.3
Resistance to three classes of antimicrobial drugs		
Fluoroquinolones + aminoglycosides + carbapenems	1 481	51.0

* Not adjusted for population differences in the reporting countries.

bacterium are more likely to occur in critically ill or otherwise debilitated individuals. In fact, outside of the organism's lipopolysaccharide layer, which serves an unknown purpose, the majority of virulence factors, including bacteriocin, encapsulation and a prolonged viability under dry conditions, seem to favour a prolonged survival rather than invasive disease. It can survive for up to five months, and this 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 diseases, 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 (MDR) strain of the *A. baumannii* group are similar, and also 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 antibiotics, especially third-generation cephalosporins, fluoroquinolones and carbapenems.

3.4.2 Resistance mechanisms

Acinetobacter species, particularly those belonging to the *A. baumannii* group, are intrinsically resistant to most antimicrobial agents due to their selective ability to exclude various molecules from penetrating their outer membrane. The antimicrobial classes 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 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 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.

Figure 3.32. *Acinetobacter* spp. Percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2012

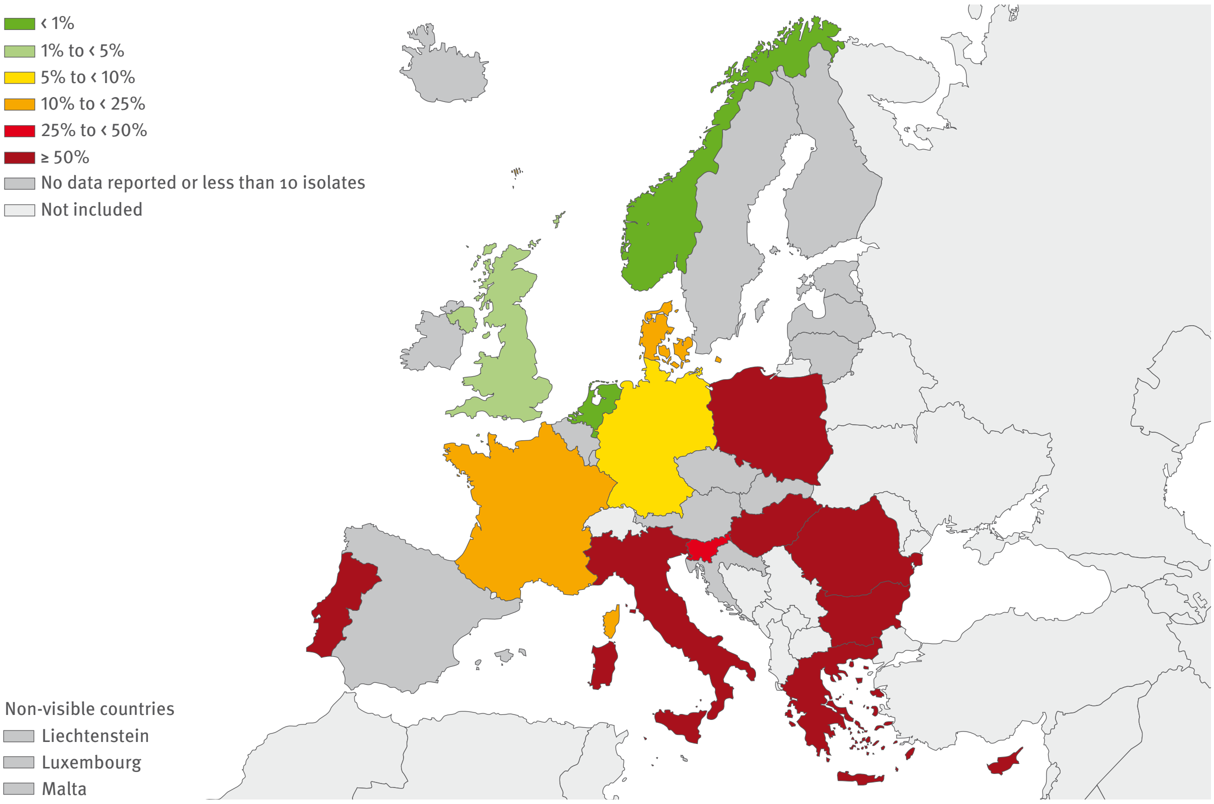


Figure 3.33. ***Acinetobacter*** **spp. Percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2012**

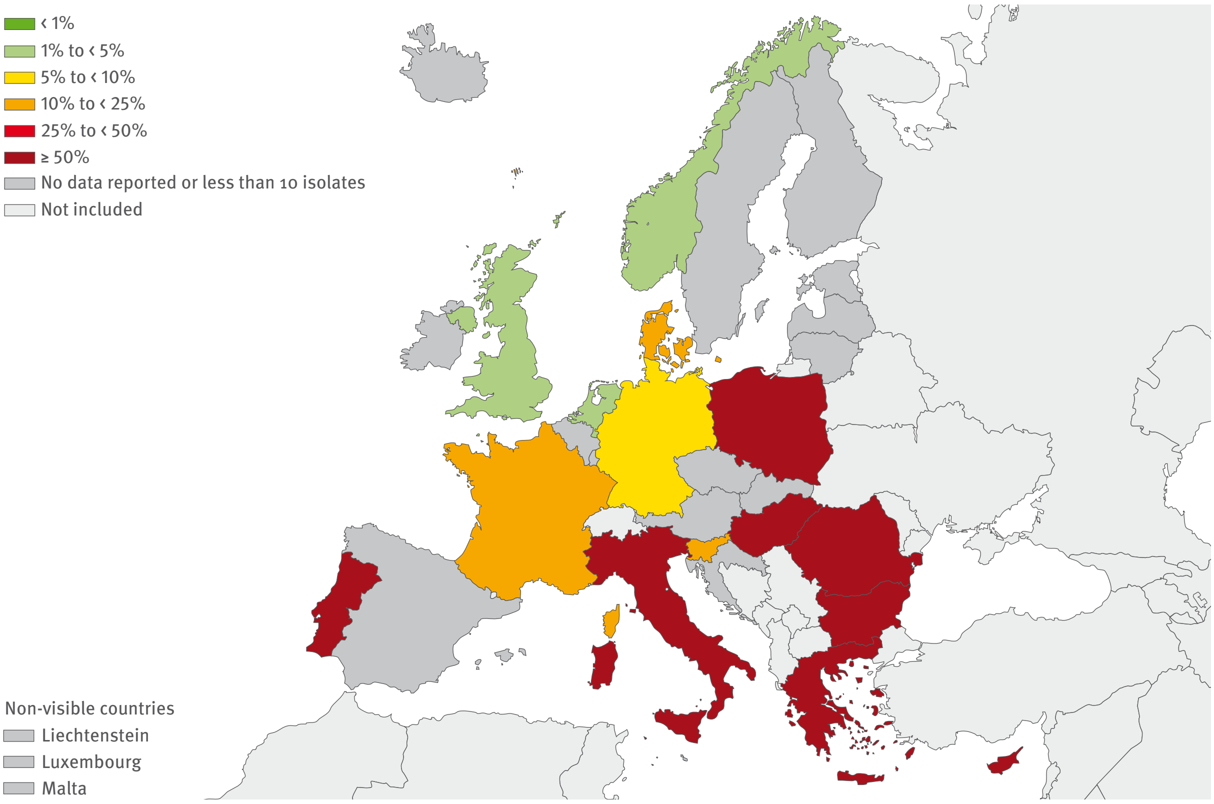
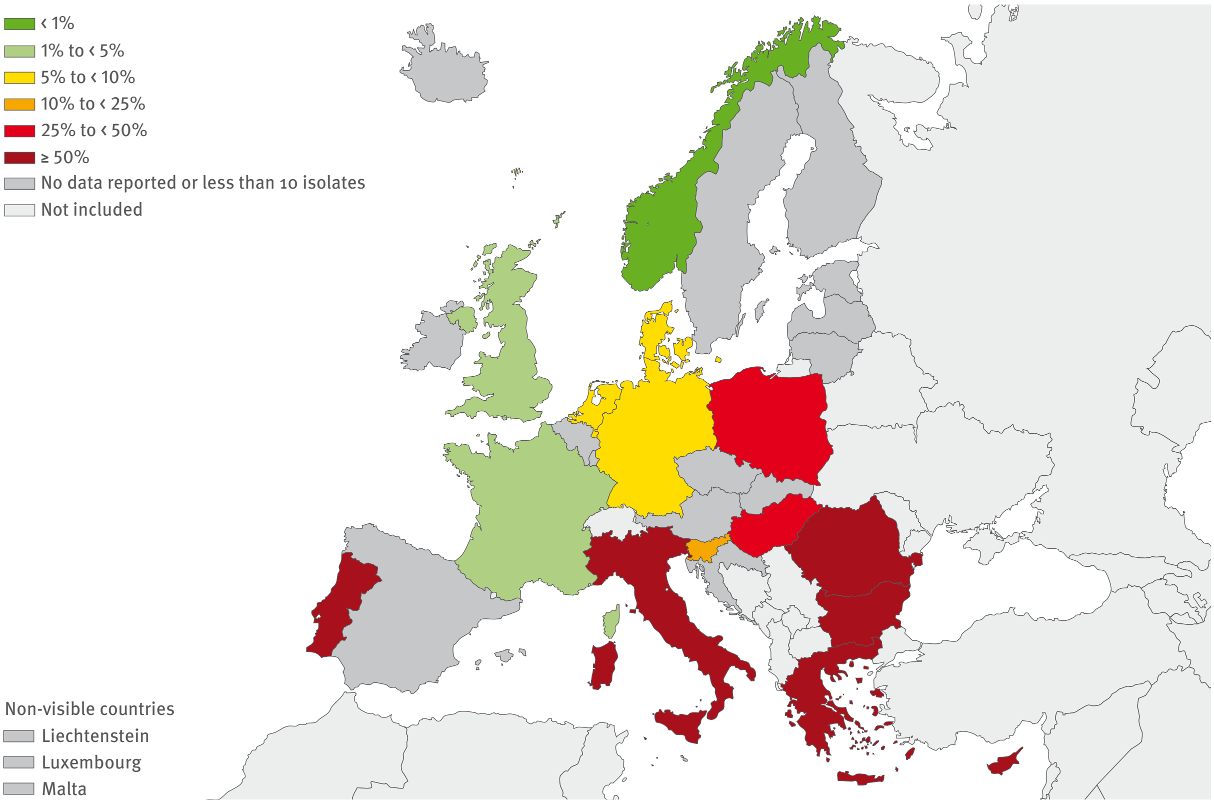


Figure 3.34. ***Acinetobacter*** **spp. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2012**



3.4.3 Inclusion of *Acinetobacter* spp. in EARS-Net 2012

Acinetobacter spp. were included in EARS-Net for the first time this year. Data were collected for 2012, and will be collected for 2013, to test the feasibility of including this bacterium in EARS-Net surveillance. Surveillance is restricted to genus level (i.e., *Acinetobacter* spp.) due to the difficulties of species identification, and the antibiotics under surveillance are limited to a panel for which clear guidelines on susceptibility testing and interpretive criteria exist.

Due to the fact that this was the first year data on *Acinetobacter* were requested from the countries and due to the low number of isolates reported, the results should be interpreted with caution.

3.4.4 Antimicrobial susceptibility

- More than half of *Acinetobacter* spp. isolates reported to EARS-Net in 2012 were resistant to all antibiotic groups included for surveillance. Carbapenem resistance was high, and in most cases combined with resistance to the two other antimicrobial groups under surveillance (fluoroquinolones and aminoglycosides).
- However, large inter-country variation was observed, with generally higher resistance levels reported from southern Europe than northern Europe.

Full susceptibility

- For 2012, 3 277 isolates from 18 countries were reported to EARS-Net, for which 2 905 (89%) isolates had complete AST information for all antimicrobial groups under surveillance for *Acinetobacter* spp. (fluoroquinolones, aminoglycosides and carbapenems).
- The percentage of fully susceptible isolates (out of those tested for all antimicrobials under surveillance) in countries that reported more than 10 isolates, ranged from 100% (the Netherlands) to 4.2% (Romania) (Table 3.9). However, the 100% full susceptibility reported from the Netherlands refers only to the group of isolates tested against the full panel of antimicrobial groups under surveillance by EARS-Net. Resistance to aminoglycosides and carbapenems were reported, but these isolates were not tested against all antimicrobial groups. All isolates reported by the three countries (Iceland, Luxembourg and Malta) that reported fewer than 10 isolates were fully susceptible.

Fluoroquinolones

- For 2012, 18 countries reported 3 125 isolates with relevant AST information for fluoroquinolones. The number of isolates reported per country ranged from two to 1 204. Iceland, Luxembourg and Malta reported fewer than 10 isolates and are therefore not included in Figure 3.32 or the resistance calculations in Table 3.9.
- The percentages of resistant isolates in countries that reported more than 10 isolates ranged from zero (the Netherlands and Norway) to 93.1% (Greece). Among these, two countries reported resistance percentages lower than 1%, one country 1–5%, one country 5–10%, two countries 10–25%, one country 25–50% and eight countries more than 50% (Table 3.9 and Figure 3.32). The three countries (Iceland, Luxembourg and Malta) that reported fewer than 10 isolates did not report any resistant isolates.

Aminoglycosides

- For 2012, 18 countries reported 3 086 isolates with relevant AST information for aminoglycosides. The number of isolates reported per country ranged from two to 1 234. Iceland, Luxembourg and Malta reported fewer than 10 isolates and are therefore not included in Figure 3.33 or the resistance calculations in Table 3.9.
- The percentages of resistant isolates in countries that reported more than 10 isolates ranged from 1.7% (the Netherlands) to 83.1% (Italy). Among these, three countries reported resistance percentages of 1–5%, one country 5–10%, three countries 10–25% and eight countries more than 50% (Table 3.9 and Figure 3.33). The three countries (Iceland, Luxembourg and Malta) that reported less than 10 isolates did not report any resistant isolate.

Carbapenems

- For 2012, 18 countries reported 3 190 isolates with relevant AST information for carbapenems. The number of isolates reported per country ranged from two to 1 234. Iceland, Luxembourg and Malta reported fewer than 10 isolates and are therefore not included in Figure 3.34 or the resistance calculations in Table 3.9.
- The percentages of resistant isolates in countries that reported more than 10 isolates ranged from zero (Norway) to 87.8% (Italy). Among these, one country reported resistance percentages lower than 1%, two countries 1–5%, three countries 5–10%, one country 10–25%, two countries 25–50% and six countries more than 50% (Table 3.9 and Figure 3.34). The three countries (Iceland, Luxembourg and Malta) that reported fewer than 10 isolates did not report any resistant isolates.

Combined resistance (fluoroquinolones, aminoglycosides and carbapenems)

- Single resistance was uncommon (4.9% of all isolates) and resistance to two classes of antimicrobial agents was reported for 17% of all isolates. Within the groups of single resistance and resistance to two antimicrobial groups, single fluoroquinolone resistance and resistance to fluoroquinolones combined with resistance to aminoglycosides or to carbapenems were the most common.

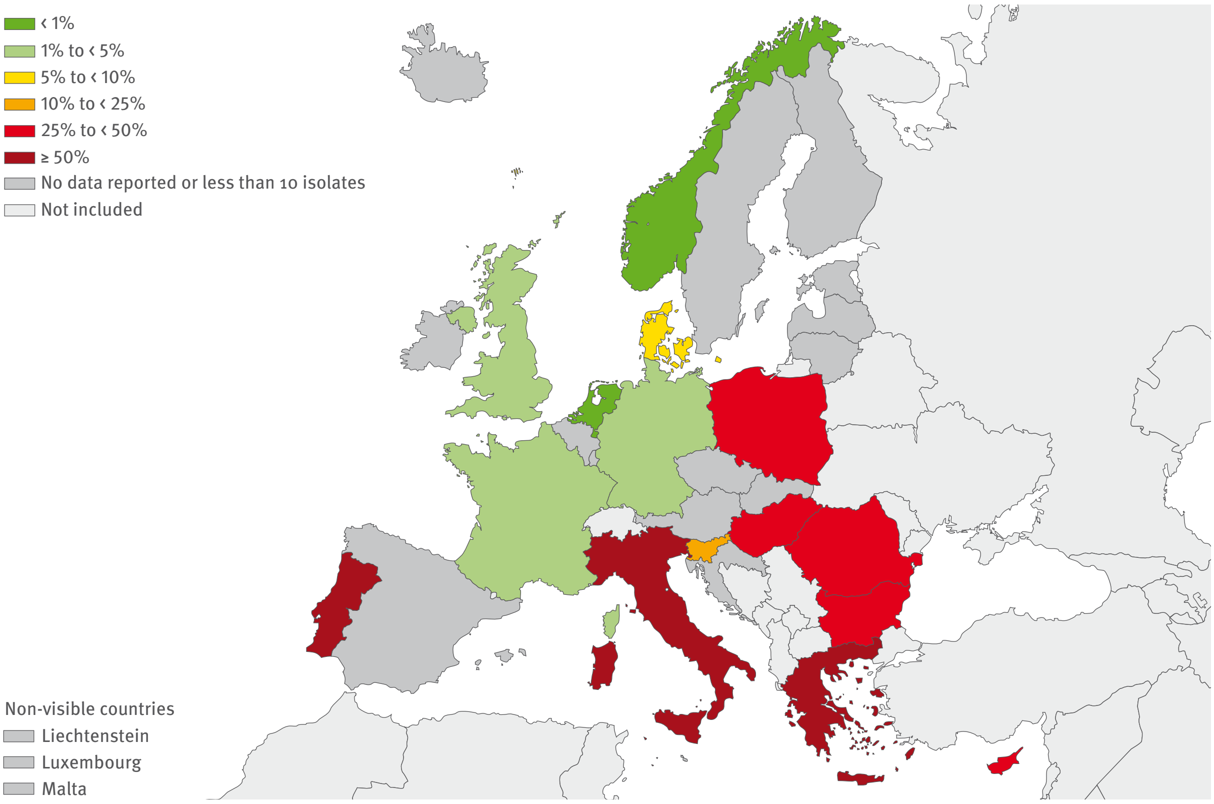
- Overall, the most common resistance phenotype was resistance to all three antimicrobial groups, and was present in 51% of the isolates. The percentage of isolates with this resistance phenotype ranged from zero (the Netherlands and Norway) to 78.0% (Italy). Two countries reported resistance percentages lower than 1%, three countries 1–5%, one country 5–10%, one country 10–25%, five countries 25–50% and three countries more than 50% (Figure 3.35, Table 3.9). The three countries (Iceland, Luxembourg and Malta) that reported fewer than 10 isolates did not report any isolates with combined resistance.

3.4.5 Discussion and conclusions

More than half of the EARS-Net participating countries were able to report data for *Acinetobacter* spp. for 2012. As this is the first year that *Acinetobacter* spp. have been included in EARS-Net and the number of isolates reported from some countries is very low, results must be interpreted with caution.

Nevertheless, there seems to be a large variation in antimicrobial resistance of *Acinetobacter* spp. isolates in Europe, with generally higher resistance percentages reported from countries in the south of Europe than in the north. The high percentage of isolates with combined resistance to fluoroquinolones, aminoglycosides and carbapenems is a concern as it severely limits options for patient treatment.

Figure 3.35. *Acinetobacter* spp. Percentage (%) of invasive isolates with combined resistance (resistance to fluoroquinolones, aminoglycosides and carbapenems), by country, EU/EEA countries, 2012



3.5 *Streptococcus pneumoniae*

3.5.1 Clinical and epidemiological importance

Streptococcus pneumoniae is a common cause of disease, especially among young 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 and bloodstream infections and meningitis. Since *S. pneumoniae* is the most common cause of pneumonia worldwide, morbidity and mortality are high and approximately three million people are estimated to die each year of pneumococcal infections.

Pneumococci carry a variety of virulence factors that facilitate adherence and transcytosis of epithelial cells. The cell wall of pneumococci is coated with a viscous polysaccharide slime layer termed the capsule. This is the most important virulence factor because it protects the bacteria from the adhesion of opsonising antibodies and the destruction by leucocytes. Capsular polysaccharides are highly diverse and play an important role in immune evasion. To date, almost 100 different serotypes have been described. The serotype distribution varies with age, disease and geographical region. 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.

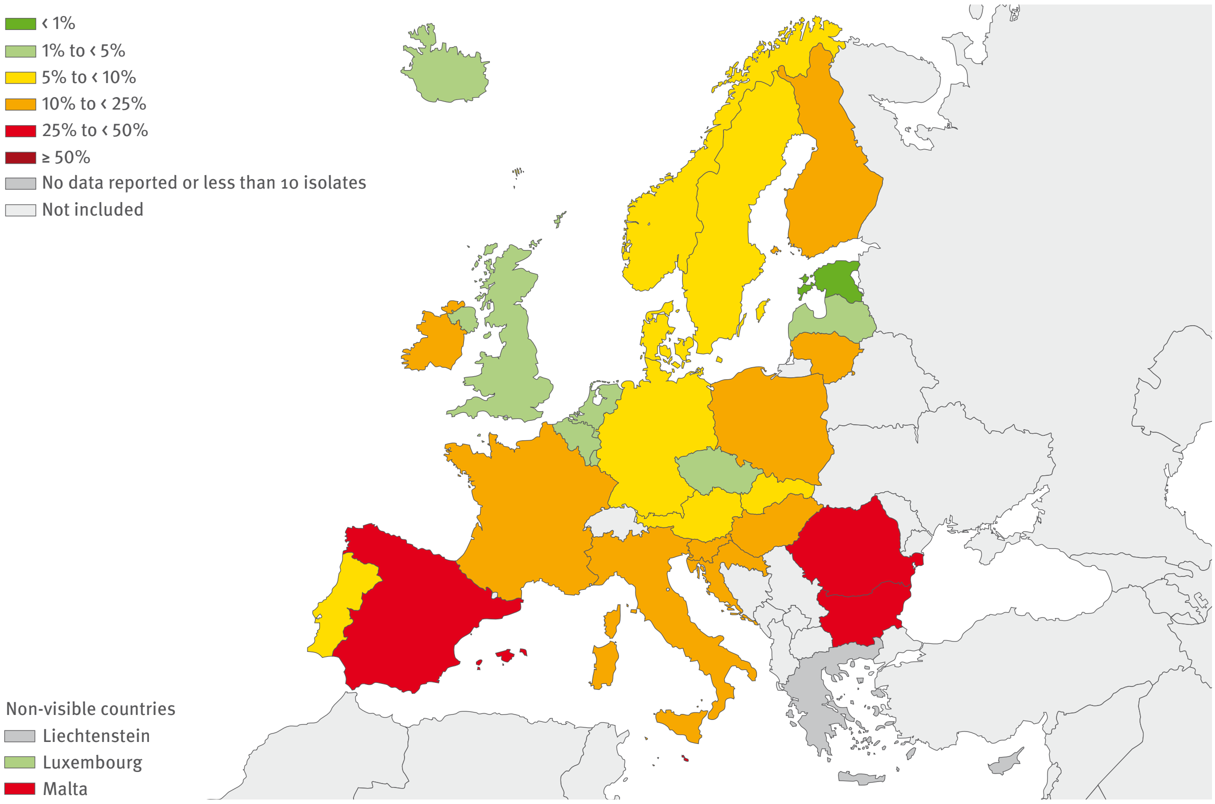
3.5.2 Resistance mechanisms

Beta-lactam antimicrobials bind to cell wall synthesising enzymes, 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 class of antimicrobial. Alterations in PBPs are due to transformation with PBP gene sequences originating from commensal streptococci, and construction of mosaic PBP causes different degrees of resistance proceeding from reduced susceptibility through low-level clinical resistance – conventionally termed intermediate[13] (I) – to full clinical resistance (R). Intermediately susceptible strains are clearly less susceptible than susceptible strains. However, in the absence of meningitis, infections with intermediately resistant strains are often successfully treated with high doses of benzyl penicillin 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 act as protein synthesis inhibitors. There are two predominant resistance mechanisms against MLS antimicrobials in *S. pneumoniae*:

13 Microorganisms are defined as intermediate by a level of antimicrobial activity with uncertain clinical effect. Occasionally, this can be overcome if antibiotics can be administered at a higher dose and/or are concentrated at the infected body site.

Figure 3.36. *Streptococcus pneumoniae*. Percentage (%) of invasive isolates non-susceptible to penicillin (PNSP), by country, EU/EEA countries, 2012



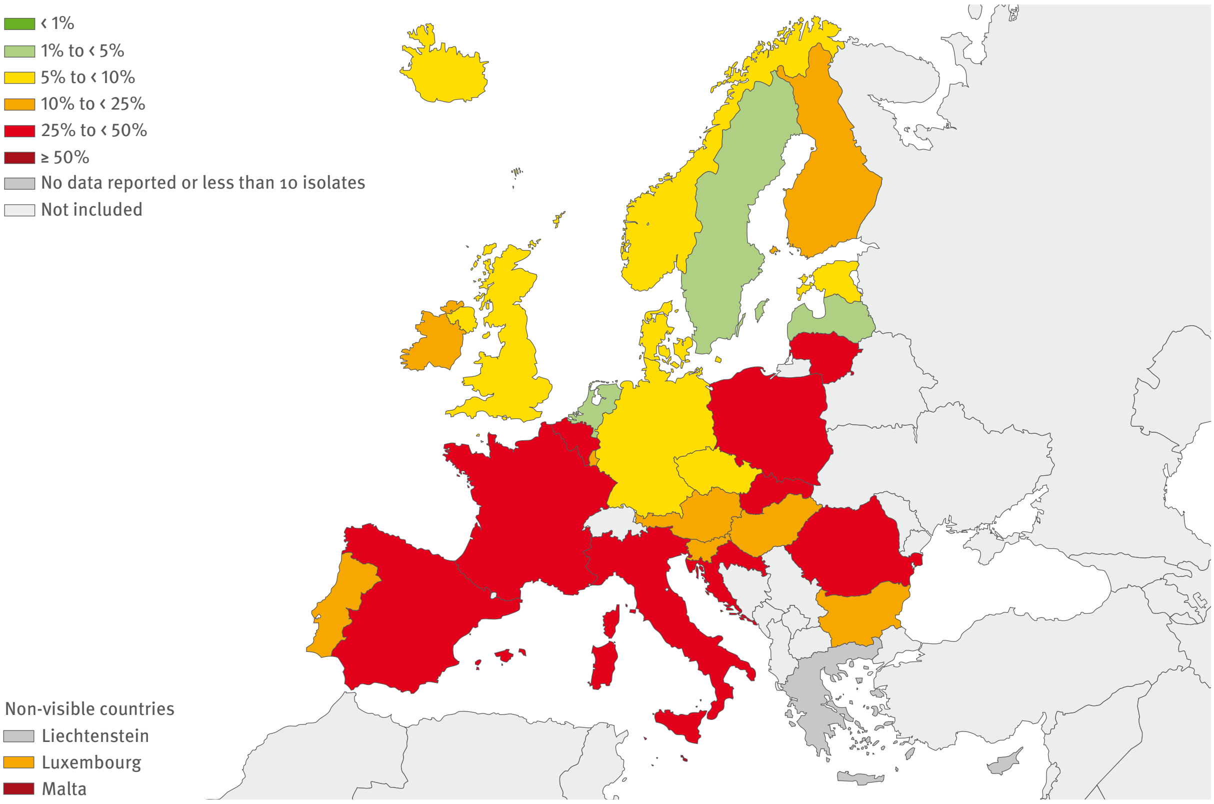
- The acquisition of an erythromycin ribosomal methylation gene (*erm*) results in a post-transcriptional modification of the 23S subunit of ribosomal RNA, which blocks the binding of the macrolide to the ribosome. Once expression of the gene is induced, this often results in high-level resistance (MICs > 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 antimicrobial, and effectively reduces intracellular erythromycin, azithromycin and clarithromycin to sub-inhibitory concentrations. In contrast to beta-lactam resistance, macrolide resistance via these mechanisms (particularly for MLS_B) results in very high MICs, and cannot be overcome by increasing the dosages of antimicrobials.

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

Since *S. pneumoniae* is the most frequent cause of community-acquired pneumonia and cannot clinically be easily distinguished from lower airway infections caused by other pathogens, empirical treatment of community-acquired lower respiratory infections needs to be active against pneumococci and should take the local prevalence of AMR into account. Prescription of non-beta-lactam compounds is therefore typical in countries where penicillin non-susceptibility has been frequently reported. Such prescribing patterns increase the selection pressure of alternative antimicrobials such as macrolides and fluoroquinolones. It is therefore no surprise to see a dynamic AMR picture emerge in different European countries. At the same time, the existence of frequent dual beta-lactam/macrolide resistance, particularly among serotypes commonly found in children, means that in practice the use of agents from either of these classes will result in increasing percentages of resistance to the other class and frequent use of macrolides has been considered as a major driver for the increase in beta-lactam resistance.

Even though a certain small decrease in penicillin resistance had been detected in some countries before the introduction of the PCV, the widespread use of this vaccine is an important factor that may have influenced the decrease in AMR levels, eliminating the infections (and more importantly, the children's carriage) of frequent 'classic' resistant serotypes – 14, 6B, 19F and 23F – all of them covered by the current multivalent PCVs on the market.

Figure 3.37. *Streptococcus pneumoniae*. Percentage (%) of invasive isolates non-susceptible to macrolides by country, EU/EEA countries, 2012



3.5.3 Antimicrobial susceptibility

- As in previous years, the reported susceptibility of *S. pneumoniae* showed large variations between European countries.
- A majority of the reporting countries had percentages of penicillin non-susceptibility below 10%, but four countries reported percentages above 25%.
- Macrolide non-susceptibility was, for most countries, higher than percentages for penicillin non-susceptibility. Dual non-susceptibility to penicillin and macrolides was below 10% in more than half of the reporting countries.
- During the last couple of years, serogroups 1, 3, 7 and 19 have dominated among pneumococcal isolates reported to EARS-Net. A large majority of serogroups 1, 3 and 7 were susceptible to both penicillin and macrolides, but for serogroup 19, 27% of the isolates had a decreased susceptibility to penicillin and/or macrolides.

Penicillin

- For 2012, 29 countries reported 10 900 isolates with relevant AST information for penicillin. The number of isolates reported from the countries ranged between eight (Cyprus) and 1658 (Belgium) (Table 3.11). As Cyprus reported fewer than 10 isolates, it is not included in Figure 3.36 and the resistance calculation in Table 3.11.
- Among countries reporting 10 isolates or more, the percentage of isolates reported as non-susceptible was below 1% in one country, 1–5% in seven countries, 5–10% in seven countries, 10–25% in nine countries and 25–50% in four countries (Figure 3.36 and Table 3.11).
- Trends for the period 2009–2012 were calculated for 25 countries. Five countries (Belgium, Denmark, Finland, Norway and the United Kingdom) had significantly increasing trends. 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 three countries (France, Luxembourg and Portugal) (Figure 3.39).
- Susceptibility breakpoints for penicillin treatment of *S. pneumoniae* infections differ depending on use of clinical guidelines (EUCAST and CLSI) and type of infection (blood infection or meningitis). This might influence both inter-country data comparability and trend analyses. An overview of use of breakpoints for determining penicillin susceptibility in EARS-Net data is given in Table 3.11.

Figure 3.38. *Streptococcus pneumoniae*. Percentage (%) of invasive isolates non-susceptible to penicillins and macrolides by country, EU/EEA countries, 2012

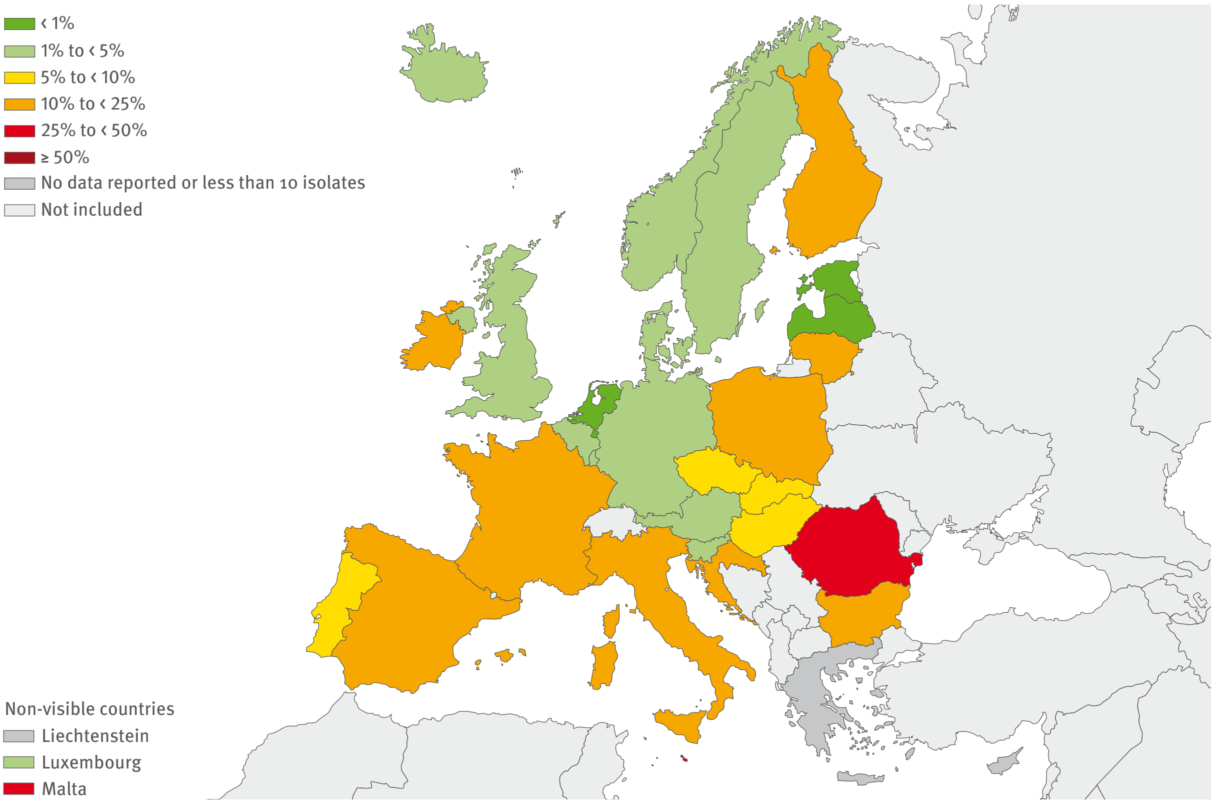
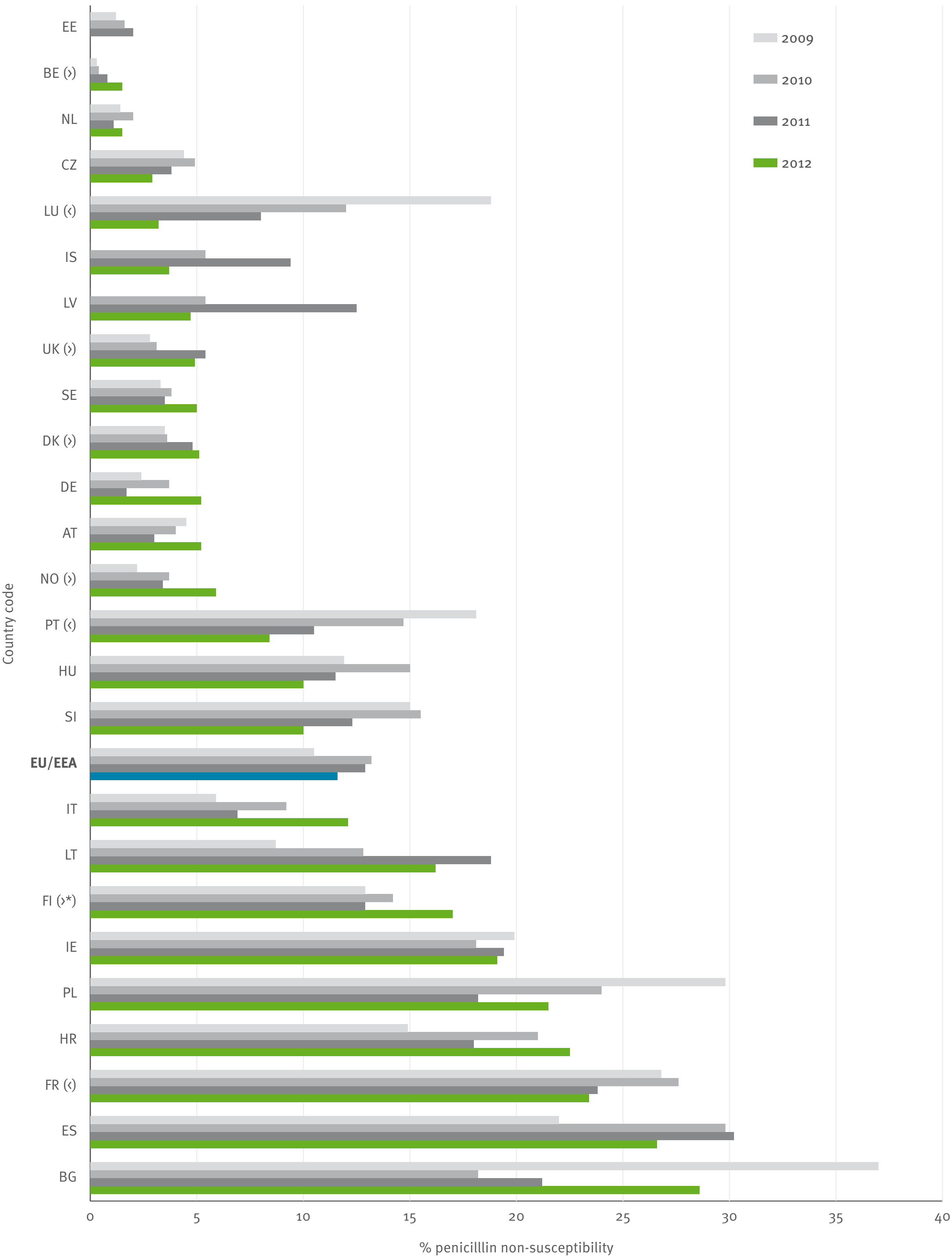


Figure 3.39. ***Streptococcus pneumoniae*. Trends of invasive isolates non-susceptible to penicillin, by country, EU/EEA countries, 2009–2012**

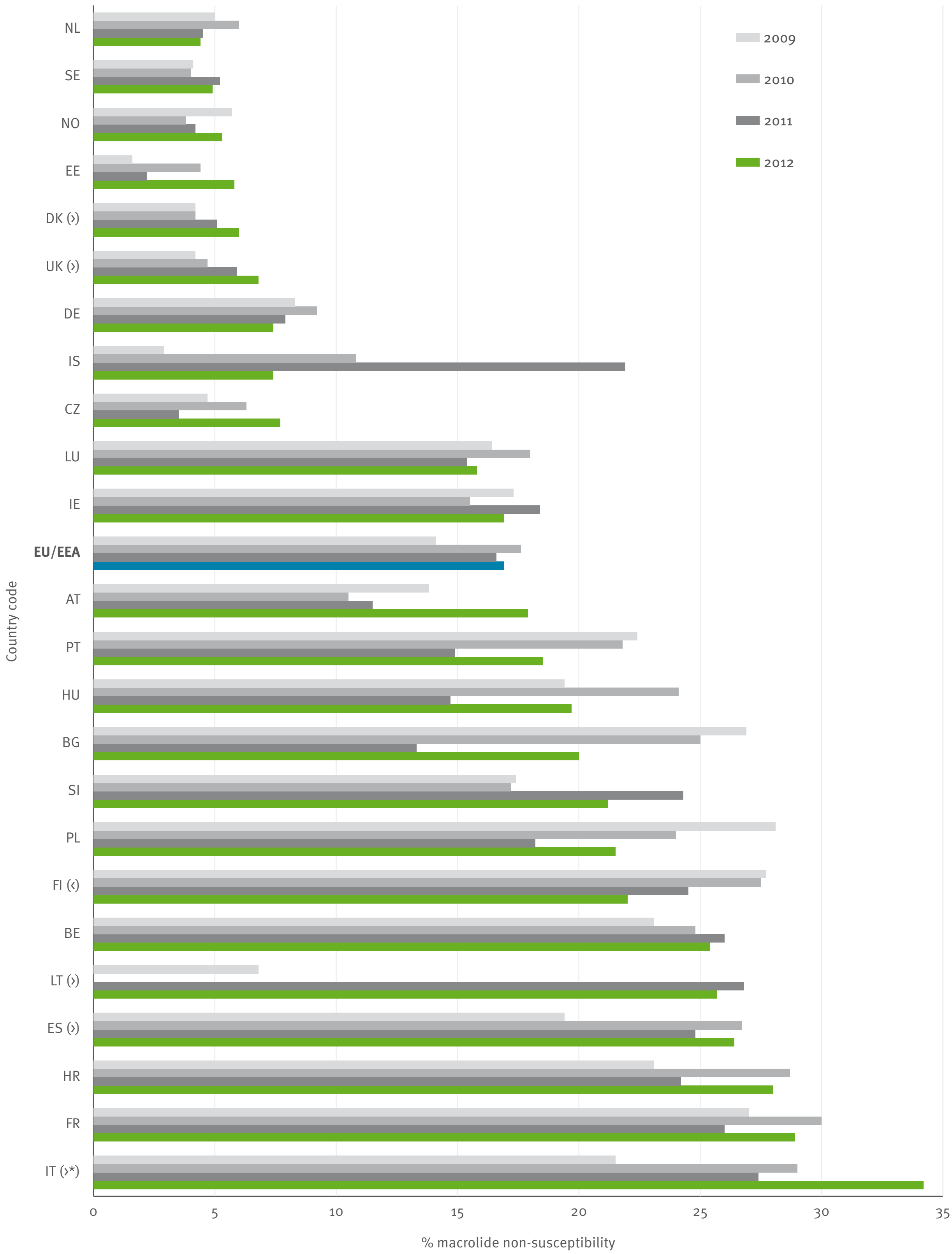


Countries not reporting data for all four years were excluded from the analysis.

The symbols › and ‹ indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.

EU/EEA refers to the population-weighted mean percentage.

Figure 3.40. ***Streptococcus pneumoniae*. Trends of invasive isolates non-susceptible to macrolides, by country, EU/EEA countries, 2009–2012**

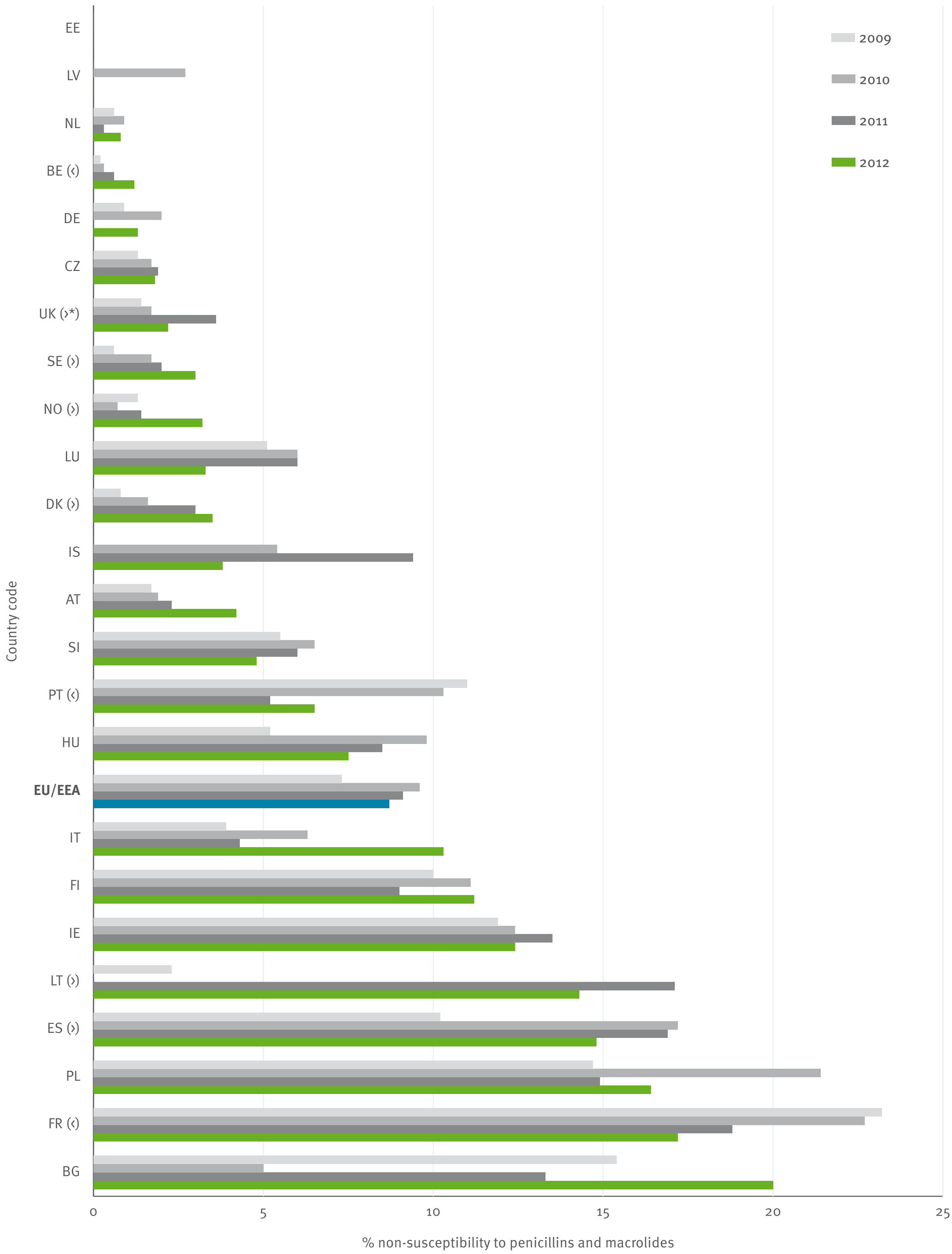


Countries not reporting data for all four years were excluded from the analysis.

The symbols › and ‹ indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.

EU/EEA refers to the population-weighted mean percentage.

Figure 3.41. ***Streptococcus pneumoniae*. Trends of invasive isolates non-susceptible to penicillins and macrolides, by country, EU/EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

The symbols › and ‹ indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.

EU/EEA refers to the population-weighted mean percentage.

Macrolides

- For 2012, 29 countries reported 10 964 isolates with relevant AST information for macrolides. The number of isolates reported from the countries ranged between seven (Cyprus) and 1 662 (Belgium) (Table 3.11). As Cyprus reported fewer than 10 isolates, it is not included in Figure 3.37 or the resistance calculation in Table 3.11.
- Among countries reporting 10 isolates or more, the percentage of isolates reported as non-susceptible ranged from 3.5% (Latvia) to 50% (Malta), and was below 5% in three countries, 5–10% in seven countries, 10–25% in eight countries, and 25–50% in ten countries (Figure 3.37, Table 3.11).
- Trends for the period 2009–2012 were calculated for 24 countries. Significantly increasing trends were observed for Denmark, Italy, Lithuania, Spain and the United Kingdom. For Italy, the trend did not remain significant when considering only data from laboratories reporting consistently throughout the period. A significantly decreasing trend was observed for one country (Finland) (Figure 3.40).

Non-susceptibility to penicillins and macrolides

- For 2012, 29 countries reported 9 928 isolates tested for both penicillin and macrolides. The number of reported *S. pneumoniae* isolates with relevant AST information for both penicillins and macrolides ranged between seven (Cyprus) and 1 614 (Belgium) (Table 3.11). As Cyprus reported fewer than 10 isolates, it is not included in Figure 3.38 or the resistance calculation in Table 3.11.
- Among countries reporting 10 isolates or more, the percentage of isolates reported as non-susceptible to both penicillins and macrolides ranged from zero (Estonia and Latvia) to 38.9% (Malta), and were below 1% in three countries, 1–5% in 11 countries, 5–10% in three countries, 10–25% in nine countries, and 25–50% in two countries (Figure 3.38 and Table 3.11).
- Trends for 2009–2012 were calculated for 24 countries. A significant increase was observed for six countries (Denmark, Lithuania, Norway, Spain, Sweden and the UK). For the UK, the trend did not remain significant when considering only data from laboratories reporting consistently throughout the period. Significant decreasing trends were observed for two countries (France and Portugal) (Figure 3.41).

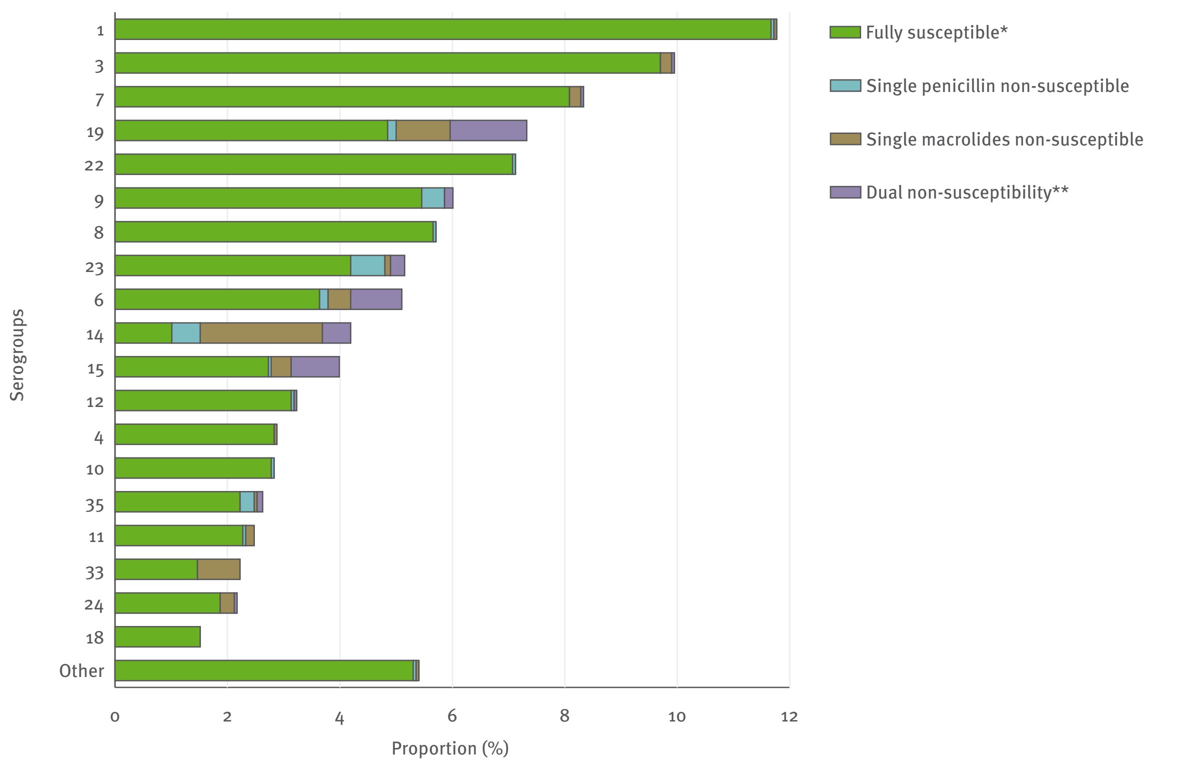
Fluoroquinolones

- For 2012, 24 countries reported susceptibility data for fluoroquinolones in 6 263 isolates (57% of all reported *S. pneumoniae* isolates). Among them, 5.2% were resistant to fluoroquinolones, and 4.4% of the fluoroquinolone-resistant isolates were also penicillin-non-susceptible.

Serogroups

- Fifteen countries reported *S. pneumoniae* isolates with identification of the serotype/serogroup for 2012.

Figure 3.42. ***Streptococcus pneumoniae*. Distribution of serogroups and associated resistance profiles per serogroup, 2012**



Only countries that reported serogroup information for more than 30 isolates were included in the figure.
* Susceptible to at least penicillin and macrolides.
** Non-susceptible to penicillin and macrolides.

- In 2012, serogroups 1 and 3 were the most prevalent (accounting for 12% and 10% of the isolates, respectively), followed by serogroup 7 (8%) and serogroup 19 (7%). These four serogroups have been dominant among EARS-Net isolates during the last couple of years.
- Among the most commonly reported serogroups, dual non-susceptibility to both penicillin and macrolides was mainly observed in serogroups 19, 6, 15 and 14 (by order of decreasing percentage). Single non-susceptibility to penicillin was most common in serogroups 23, 14, 9 and 35, and single non-susceptibility to macrolides was most common in serogroups 14, 19, 33 and 6 (Figure 3.42).

3.5.4 Discussion and conclusions

Although large inter-country variations can be noted, the overall percentages of *S. pneumoniae* with non-susceptibility to commonly used antimicrobials reported to EARS-Net have remained relatively stable in Europe during recent years.

It is important to note that the differences and changes in clinical breakpoints used for determining penicillin susceptibility in *S. pneumoniae* might introduce bias when comparing national data reported to EARS-Net, but also when interpreting trends in countries that changed clinical breakpoints during the observation period. Similar surveillance artefacts have been reported from the United States when *S. pneumoniae* data were analysed with new breakpoints[14]. There is an ongoing shift among many European laboratories from using CLSI guidelines to EUCAST.

Although the number of countries reporting data on serotype distribution to EARS-Net is increasing, data remain incomplete. However, data reported for 2012 support previous observations that most penicillin non-susceptible isolates belong to a few serogroups. Most EU/EEA Member States have, in recent years, implemented routine immunisation for children with the multivalent PCVs[15]. As a limited number of *S. pneumoniae* serotypes are responsible for a considerable percentage of serious pneumococcal infections in both adults and children, introduction of PCVs is likely to change the epidemiology of invasive pneumococcal disease in many European countries.

14 Centers for Disease Control and Prevention (CDC). Effects of new penicillin susceptibility breakpoints for *Streptococcus pneumoniae* – United States 2006-2007. MMWR Morb Mort Wkly Rep 2008;57(50):1353-5.

15 EUVAC-Net. Pneumococcal vaccination (PCV) overview in European countries. [Internet]. Available from http://www.euvac.net/graphics/euvac/vaccination/pcv.html

Table 3.11. *Streptococcus pneumoniae*. Total number of isolates tested for penicillin and macrolide susceptibility, percentage (%) being penicillin-non-susceptible (PNSP), penicillin-resistant (PRSP), macrolide-non-susceptible (MNSP), single penicillin-resistant (PENR), single macrolide-resistant (MACR) and non-susceptible to penicillin and macrolides (DUAL), including 95% confidence intervals, by country, EU/EEA countries, 2012

Country	Number of isolates tested for (PEN/MACR/both)	% PNSP (95% CI)	% PRSP (95% CI)	% MNSP (95% CI)	% single PENR (95% CI)	% single MACR (95% CI)	% DUAL (95% CI)
Austria	291/319/262	5.2 (3-8)	1.4 (0-3)	17.9 (14-23)	1.1 (0-3)	13.0 (9-18)	4.2 (2-7)
Belgium	1658/1662/1614	1.5 (1-2)	0.5 (0-1)	25.4 (23-28)	0.3 (0-1)	24.5 (22-27)	1.2 (1-2)
Bulgaria[2b]	21/20/20	28.6 (11-52)	28.6 (11-52)	20.0 (6-44)	10.0 (1-32)	0.0 (0-17)	20.0 (6-44)
Croatia	98/98/98	22.5 (15-37)	0.0 (0-6)	28.6 (20-40)	1.0 (0-3)	28.5 (20-37)	16.3 (9-24)
Cyprus[2c]	8/7/7	*	*	*	*	*	*
Czech Republic[1a]	274/274/274	2.9 (1-6)	0.4 (0-2)	7.7 (5-11)	1.1 (0-3)	5.8 (3-9)	1.8 (1-4)
Denmark	867/867/867	5.1 (4-7)	0.2 (0-1)	6.0 (5-8)	1.6 (1-3)	2.5 (2-4)	3.5 (2-5)
Estonia	53/52/34	0.0 (0-7)	0.0 (0-7)	5.8 (1-16)	0.0 (0-10)	5.9 (1-20)	0.0 (0-10)
Finland[1a]	553/586/545	17.0 (14-20)	0.5 (0-2)	22.0 (19-26)	7.0 (5-9)	11.6 (9-15)	11.2 (9-14)
France	824/824/824	23.4 (21-26)	0.0 (0-0)	28.9 (26-32)	6.2 (5-8)	11.7 (10-14)	17.2 (15-20)
Germany	310/324/308	5.2 (3-8)	1.3 (0-3)	7.4 (5-11)	3.9 (2-7)	5.8 (4-9)	1.3 (0-3)
Hungary[1c]	160/147/147	10.0 (6-16)	2.5 (1-6)	19.7 (14-27)	2.7 (1-7)	12.2 (7-19)	7.5 (4-13)
Iceland	27/27/26	3.7 (0-19)	3.7 (0-19)	7.4 (1-24)	0.0 (0-13)	3.8 (0-20)	3.8 (0-20)
Ireland[2d]	319/307/307	19.1 (15-24)	4.7 (3-8)	16.9 (13-22)	6.5 (4-10)	4.6 (3-8)	12.4 (9-17)
Italy	141/243/116	12.1 (7-19)	5.7 (2-11)	34.2 (28-40)	1.7 (0-6)	27.6 (20-37)	10.3 (5-17)
Latvia	64/57/57	4.7 (1-13)	4.7 (1-13)	3.5 (0-12)	3.5 (0-12)	3.5 (0-12)	0.0 (0-6)
Lithuania[2b]	37/35/35	16.2 (6-32)	13.5 (5-29)	25.7 (12-43)	2.9 (0-15)	11.4 (3-27)	14.3 (5-30)
Luxembourg	31/38/30	3.2 (0-17)	3.2 (0-17)	15.8 (6-31)	0.0 (0-12)	16.7 (6-35)	3.3 (0-17)
Malta[1c]	18/18/18	38.9 (17-64)	0.0 (0-19)	50.0 (26-74)	0.0 (0-19)	11.1 (1-35)	38.9 (17-64)
Netherlands	1063/1153/972	1.5 (1-2)	0.3 (0-1)	4.4 (3-6)	0.7 (0-1)	3.9 (3-5)	0.8 (0-2)
Norway[1c]	576/533/533	5.9 (4-8)	1.0 (0-2)	5.3 (4-8)	3.0 (2-5)	2.1 (1-4)	3.2 (2-5)
Poland[1c]	121/110/110	21.5 (15-30)	5.0 (2-10)	27.3 (19-37)	6.4 (3-13)	10.9 (6-18)	16.4 (10-25)
Portugal[2c]	299/308/278	8.4 (5-12)	5.4 (3-9)	18.5 (14-23)	1.8 (1-4)	12.2 (9-17)	6.5 (4-10)
Romania	43/43/40	37.2 (23-53)	37.2 (23-53)	37.2 (23-53)	5.0 (1-17)	7.5 (2-20)	32.5 (19-49)
Slovakia[1c]	20/22/20	5.0 (0-25)	5.0 (0-25)	27.3 (11-50)	0.0 (0-17)	15.0 (3-38)	5.0 (0-25)
Slovenia[2d]	251/250/250	10.0 (7-14)	1.2 (0-3)	21.2 (16-27)	5.2 (3-9)	16.4 (12-22)	4.8 (3-8)
Spain	590/579/562	26.6 (23-30)	26.1 (23-30)	26.4 (23-30)	11.9 (9-15)	10.9 (8-14)	14.8 (12-18)
Sweden[1c]	1030/947/947	5.0 (4-6)	4.8 (4-6)	4.9 (4-6)	1.7 (1-3)	1.9 (1-3)	3.0 (2-4)
United Kingdom[3]	1153/1114/627	4.9 (4-6)	0.7 (0-1)	6.8 (5-8)	1.3 (1-2)	4.5 (3-6)	2.2 (1-4)
EU/EEA mean percentage (population-weighted)		**11.6**	**3.9**	**16.9**	**4.6**	**8.5**	**8.7**

* Fewer than 10 isolates, percentage not calculated

Use of clinical guidelines and breakpoints for penicillin susceptibility testing: 1a: EUCAST non-meningitis: S ≤ 0.06 µg/ml, R > 2.0 µg/ml. 1b: EUCAST meningitis: S ≤ 0.06 µg/ml, R ≥ 0.12 µg/ml (no intermediate category). 1c: EUCAST non-meningitis/meningitis depending on site of infection. 2a: CLSI non-meningitis: S ≤ 2 µg/ml, R ≥ 8.0 µg/ml. 2b: CLSI meningitis: S ≤ 0.06 µg/ml, R ≥ 0.12 µg/ml (no intermediate category). 2c: CLSI non-meningitis/meningitis depending on site of infection. 2d: CLSI oral: S ≤ 0.06 µg/ml, R ≥ 2.0 µg/ml. 3: Mix of EUCAST, CLSI or national guidelines.

3.6 *Staphylococcus aureus*

3.6.1 Clinical and epidemiological importance

Staphylococcus aureus is a gram-positive bacterium that colonises the skin of about 30% of healthy humans. Although mainly a harmless coloniser, *S. aureus* 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. Since healthcare-associated MRSA infections add to the number of infections caused by meticillin-susceptible *S. aureus*, a high incidence of MRSA adds to the overall burden of infections caused by *S. aureus* in hospitals. Moreover, infections with MRSA may result in prolonged hospital stay and in higher mortality, owing mainly to a delay in the initiation of appropriate therapy and the inferior effectiveness of alternative treatment regimens. MRSA is still the most commonly identified antimicrobial-resistant pathogen in hospitals in many parts of the world, including Europe, the Americas, North Africa and the Middle- and Far East.

3.6.2 Resistance mechanisms

S. aureus acquires resistance to meticillin and all other beta-lactam antimicrobials through expression of the exogenous *mecA* gene that codes for a variant penicillin-binding protein PBP2' (PBP2a) with low affinity for beta-lactams, thus preventing the inhibition by beta-lactams of cell wall synthesis. A new *mec* gene has been discovered, *mecC* (formerly called mecAlga251), encoding PBP2c, which like PBP2a does not allow for binding of beta-lactams.

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

For rifampicin, the mechanism of resistance is mutation in the *rpoB* gene, leading to production of RNA polymerase with low affinity for rifampicin and other rifamycins. Such resistance easily occurs with rifampicin monotherapy, for which reason the drug should only be used in combination therapy.

Resistance to fluoroquinolones is mediated by the mutations in *parC* or *parE* (subunits of topoisomerase IV) and/or *gyrA* (subunit of DNA gyrase/topoisomerase IV). Additionally, resistance may be conferred by efflux.

The most common mechanism of linezolid resistance is mutation in the 23S rRNA target site. A more recent mechanism is non-mutational and involves acquisition of a natural resistance gene, *cfr* (chloramphenicol–florfenicol resistance). The *cfr* gene has been found primarily in plasmids that can be spread horizontally. The product of the *cfr* gene is a methyltransferase that catalyses methylation of the 23S rRNA gene.

Figure 3.43. *Staphylococcus aureus*. Percentage (%) of invasive isolates resistant to meticillin (MRSA), by country, EU/EEA countries, 2012

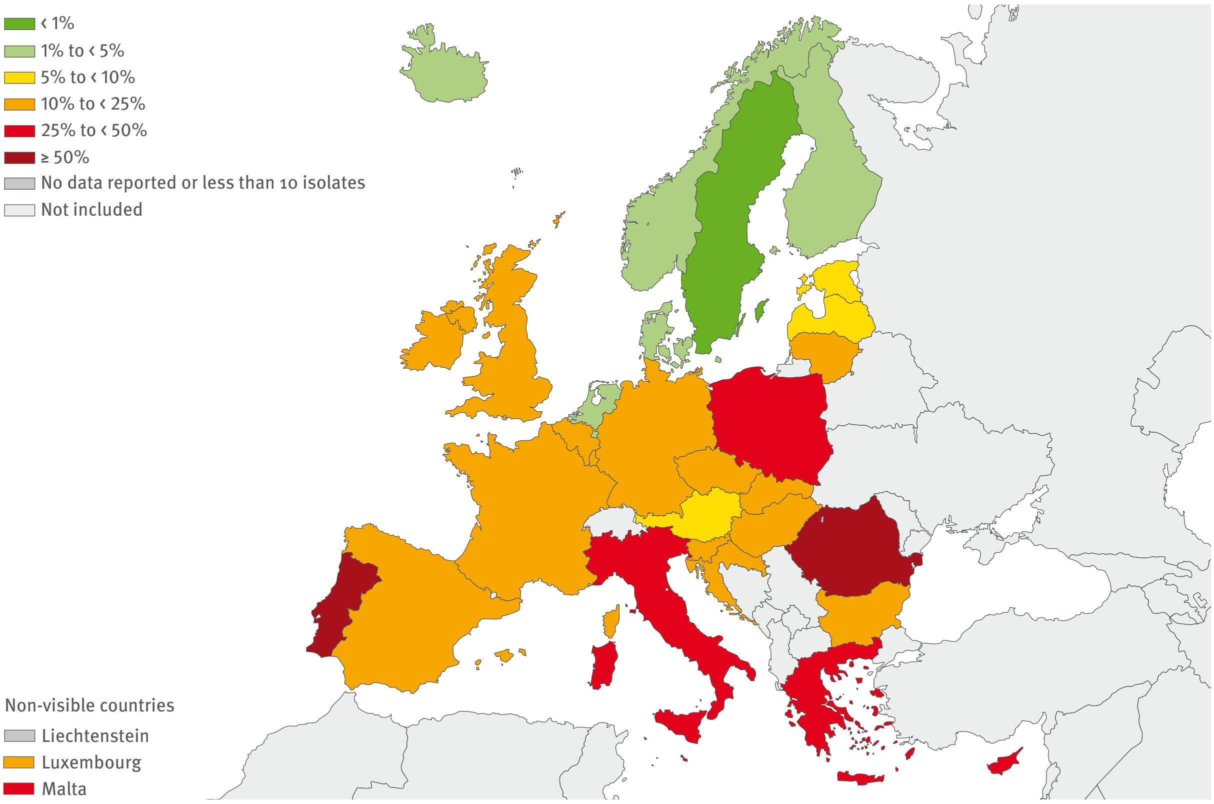
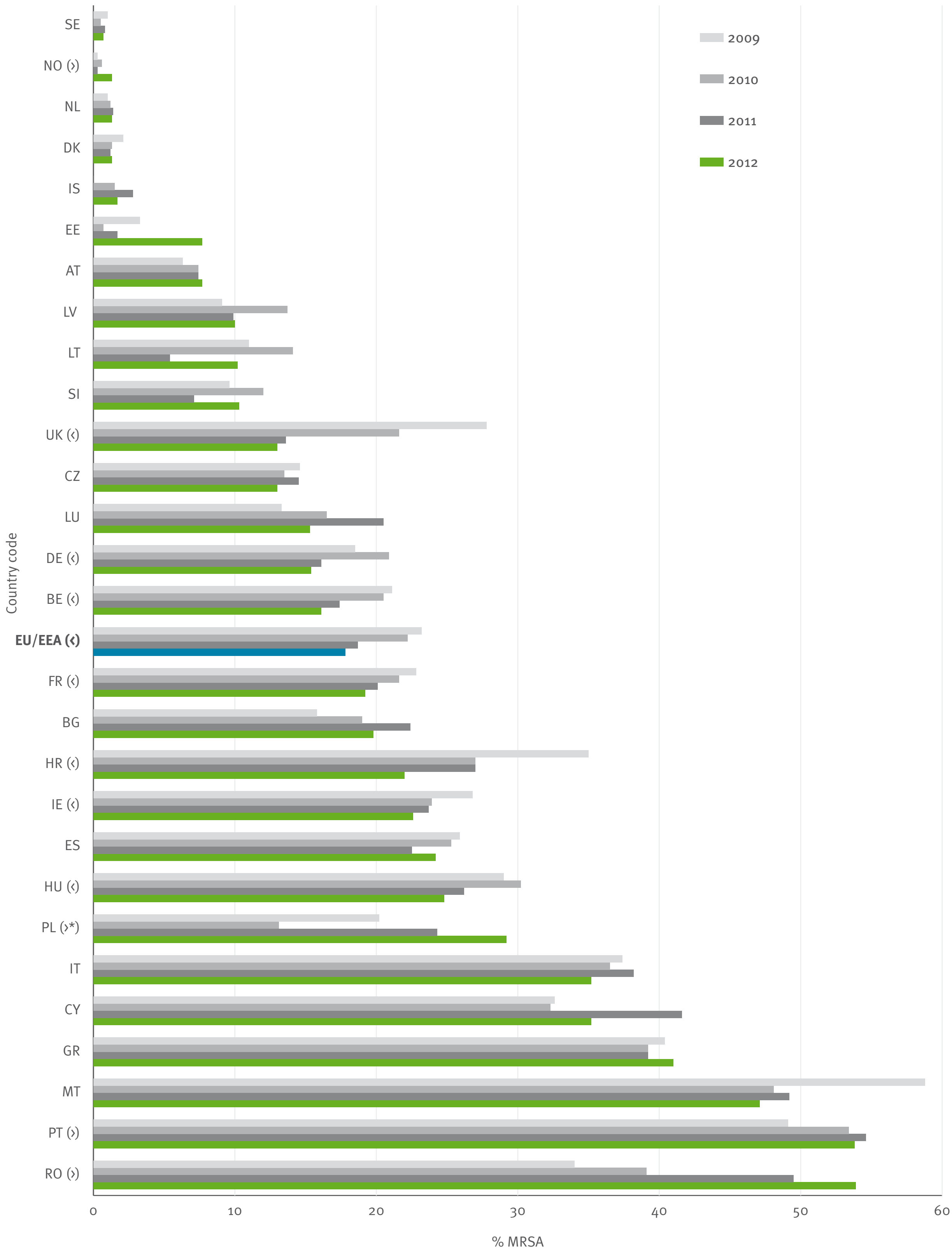


Figure 3.44. ***Staphylococcus aureus*. Trends of invasive isolates resistant to meticillin (MRSA), by country, EU/EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

The symbols › and ‹ indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.

EU/EEA refers to the population-weighted mean percentage.

3.6.3 Antimicrobial susceptibility

- The occurrence of MRSA in Europe displays large inter-country variations. A majority of the countries reported percentages of below 20%. The EU/EEA population-weighted average was 17.8% in 2012, and has decreased significantly over the last four years.
- MRSA percentages are generally lower in northern Europe and higher in the south and south-eastern parts.

Beta-lactams

- For 2012, 30 countries reported 37 495 isolates with relevant information for MRSA classification. The number of isolates reported per country ranged from 58 to 5 228.
- The EU/EEA population-weighted mean percentage for MRSA was 17.8%. The percentage of isolates reported as MRSA ranged from 0.7% (Sweden) to 53.9% (Romania). One country reported a percentage of below 1%, five countries reported 1–5%, three countries reported 5–10%, 14 countries reported 10–25%, five countries reported 25–50%, and two countries reported above 50% (Figure 3.43 and Table 3.12).
- Trends for the period 2009–2012 were calculated for 28 countries. Statistically significant increasing trends were observed for four countries (Norway, Poland, Portugal and Romania). For Poland, the trend did not remain significant when considering only data from laboratories reporting consistently throughout all four years. Statistically significant decreasing trends were observed for seven countries (Belgium, Croatia, France, Germany, Hungary, Ireland and the United Kingdom). The EU/EEA population-weighted mean percentage also decreased significantly during the same period, from 23.2% in 2009 to 17.8% in 2012 (Figure 3.44).

Table 3.12. *Staphylococcus aureus*. Number and percentage (%) of invasive isolates resistant to meticillin (MRSA) and rifampicin including 95% confidence intervals, by country, EU/EEA countries, 2012

Country	Meticillin	
	Number of isolates tested	% MRSA (95%CI)
Austria	2164	7.7 (7-9)
Belgium	2077	16.1 (15-18)
Bulgaria	227	19.8 (15-26)
Croatia	412	22.0 (18-26)
Cyprus	165	35.2 (28-43)
Czech Republic	1611	13.0 (11-15)
Denmark	1431	1.3 (1-2)
Estonia	104	7.7 (3-15)
Finland	1409	2.1 (1-3)
France	5228	19.2 (18-20)
Germany	2558	15.4 (14-17)
Greece	876	41.0 (38-44)
Hungary	1143	24.8 (22-27)
Iceland	58	1.7 (0-5)
Ireland	1038	22.6 (20-25)
Italy	1631	35.2 (33-38)
Latvia	211	9.0 (5-13)
Lithuania	323	10.2 (7-14)
Luxembourg	131	15.3 (10-23)
Malta	102	47.1 (37-57)
Netherlands	1943	1.3 (1-2)
Norway	1430	1.3 (1-2)
Poland	781	29.2 (26-32)
Portugal	1455	53.8 (51-56)
Romania	227	53.9 (47-61)
Slovakia	474	21.7 (18-26)
Slovenia	445	10.3 (8-14)
Spain	1899	24.2 (22-26)
Sweden	3262	0.7 (0-1)
United Kingdom	2680	14.1 (12-15)
EU/EEA mean percentage (population-weighted)		**17.8**

Rifampicin

- For 2012, 29 countries reported 26 541 isolates with relevant AST information for rifampicin. The percentage of rifampicin resistance was 5.7% among the MRSA isolates and 0.6% among the meticillin-susceptible *S. aureus* (MSSA) isolates.

Fluoroquinolones

- For 2012, 29 countries reported AST data for at least one fluoroquinolone in 23 264 isolates. The percentage of fluoroquinolone resistance was 81% among the MRSA isolates and 6% among the MSSA isolates.

Linezolid

- For 2012, 29 countries reported linezolid susceptibility data for 22 653 *S. aureus* isolates, of which 0.2% were resistant to linezolid.

3.6.4 Discussion and conclusions

The decrease in the population-weighted EU/EEA MRSA mean percentage over the past four years, reflecting the decreasing MRSA trends for seven individual countries, provides reason for optimism. This decrease is consistent with what has been reported from a number of European national surveillance programmes and scientific studies in recent years[16,17,18]. In several studies, the decrease has been attributed to improved infection control routines[19,20]. In addition, the decay of some

16 Johnson AP, Davies J, Guy R, Abernethy J, Sheridan E, Pearson A, Duckworth G. Mandatory surveillance of meticillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia in England: the first 10 years. J Antimicrob Chemother. 2012 Apr;67(4):802-9.

17 Anonymous. Recent trends in antimicrobial resistance among *Streptococcus pneumoniae* and *Staphylococcus aureus* isolates: the French experience. Euro Surveill. 2008 Nov 13;13(46).

18 de Kraker ME, Davey PG, Grundmann H; BURDEN study group. Mortality and hospital stay associated with resistant *Staphylococcus aureus* and *Escherichia coli* bacteraemia: estimating the burden of antibiotic resistance in Europe. PLoS Med. 2011 Oct;8(10):e1001104.

19 Rampling A, Wiseman S, Davis L, Hyett AP, Walbridge AN, Payne GC, et al. Evidence that hospital hygiene is important in the control of meticillin-resistant *Staphylococcus aureus*. J Hosp Infect 2001;49(2):109-16.

20 Vos MC, Behrendt MD, Melles DC, Mollema FP, de Groot W, Parlevliet G, et al. 5 years of experience implementing a methicillin-resistant *Staphylococcus aureus* search and destroy policy at the largest university medical center in the Netherlands. Infect Control Hosp Epidemiol. 2009;30(10):977-84.

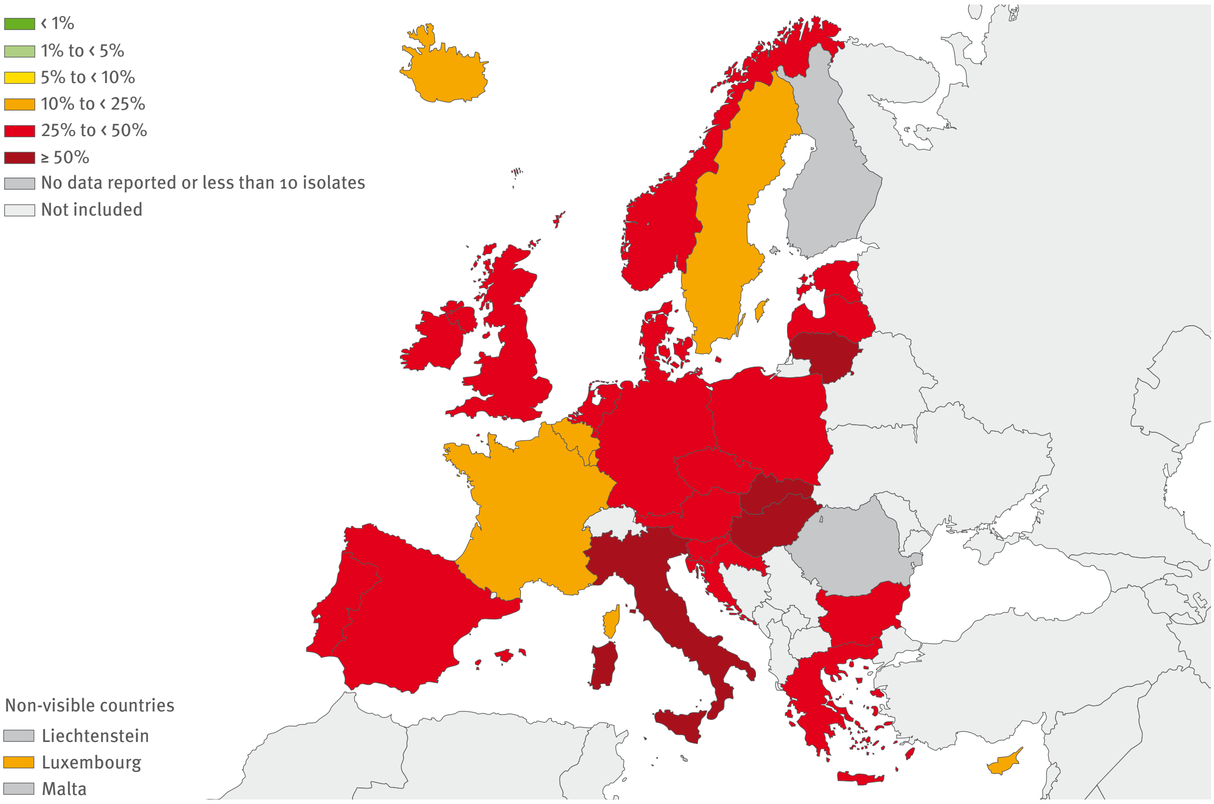
dominant MRSA clones might also have influenced the epidemiology of MRSA in Europe[21].

However, the EU/EEA MRSA population-weighted mean remains at 17.8% and seven out of the 30 reporting countries report MRSA percentages of above 25%, highlighting that MRSA remains a public health priority. To continue to reduce the spread of MRSA in Europe, comprehensive MRSA strategies targeting all healthcare sectors (acute, long-term care facilities and ambulatory care) remain essential.

The large differences between MRSA and MSSA in resistance percentage for rifampicin and fluoroquinolones are most likely due to selective testing of MRSA isolates for additional antimicrobial agents.

21 Thompson DS, Workman R, Strutt M. Decline in the rates of methiicillin-resistant *Staphlococcus aureus* acquisition and bacteraemia in a general intensive care unit between 1996 and 2008. J Hosp Infect 2009;71(4):314-9.

Figure 3.45. *Enterococcus faecalis*. Percentage (%) of invasive isolates with high-level resistance to aminoglycosides, by country, EU/EEA countries, 2012



3.7 Enterococci

3.7.1 Clinical and epidemiological importance

Enterococci belong to the normal bacterial flora of the gastrointestinal tract of humans, other mammals, birds and reptiles. Enterococci are regarded as harmless commensals, and are even believed to have positive effects on a number of gastrointestinal and systemic conditions. However, enterococci can cause invasive diseases. Recently, the recognition of high-risk clones suggests that some particular strains can act as true pathogens, and not only as opportunistic commensals. Enterococci can cause a variety of infections, including endocarditis, bloodstream infections, and urinary tract infections, and are associated with peritonitis and intra-abdominal abscesses. In the United States, three to four nosocomial bloodstream infections per 10 000 hospital discharges are caused by enterococci, and contribute to patient mortality as well as additional hospital stay.

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, exemplified by the expansion of a major hospital-adapted polyclonal subcluster CC17 in *E. faecium*, and by CC2 and CC9 in *E. faecalis*. The latter clones have even been isolated from farm animals. The emergence of particular clones and clonal complexes of *E. faecalis* and *E. faecium* was paralleled by increases in resistance to glycopeptides and high-level resistance to aminoglycosides. These two antimicrobial classes provide the few remaining therapeutic options for treatment of human infections caused by *E. faecium* when resistance has emerged against penicillins. Besides the fact that infections caused by resistant strains are difficult to treat, enterococci are highly tenacious and thus easily disseminate in the hospital setting.

3.7.2 Resistance mechanisms

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

Beta-lactam antimicrobials

By nature, enterococci have low susceptibility to many beta-lactam antimicrobials as a consequence of their low-affinity PBPs. Two possible mechanisms of resistance of enterococci to beta-lactams have been reported: the production of beta-lactamase, which is an extremely rare finding, and the overproduction and modification of PBPs, particularly PBP5, that causes high-level penicillin resistance in *E. faecium*. Resistance to aminopenicillin 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*,

Figure 3.46. *Enterococcus faecium*. Percentage (%) of invasive isolates resistant to vancomycin, by country, EU/EEA countries, 2012

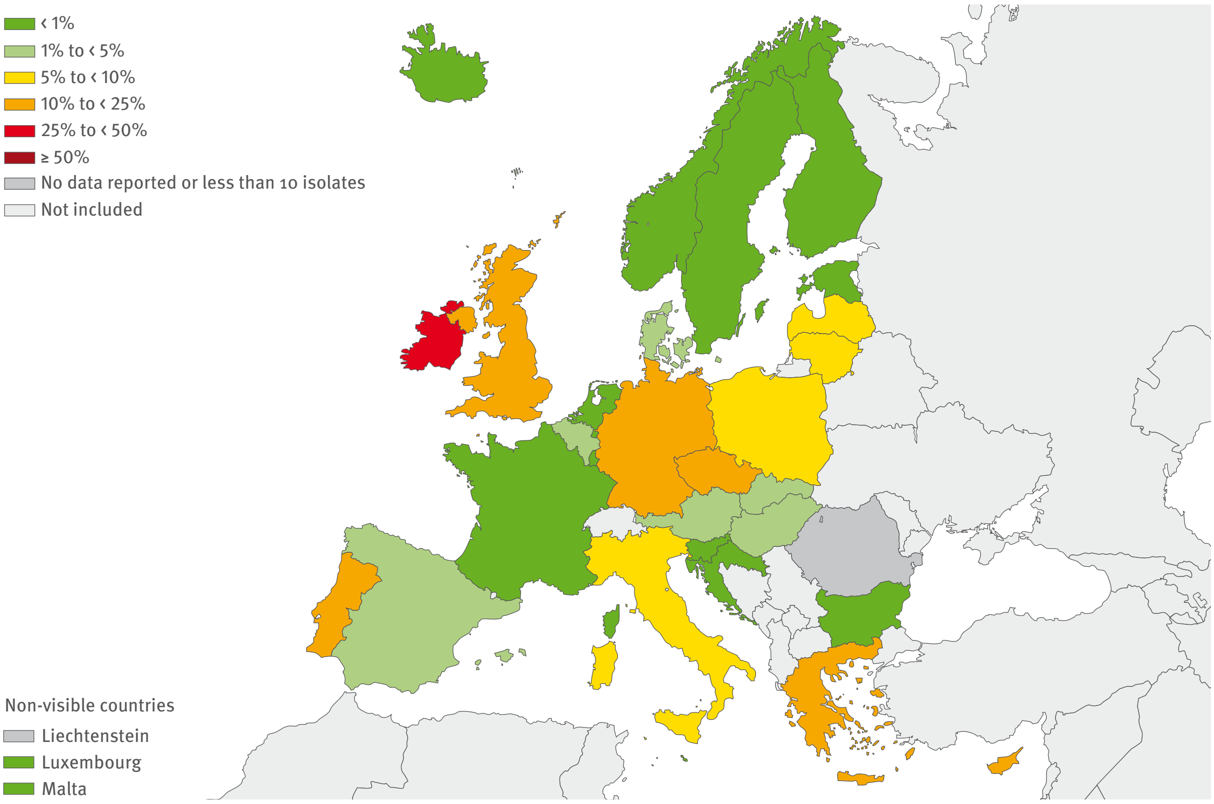
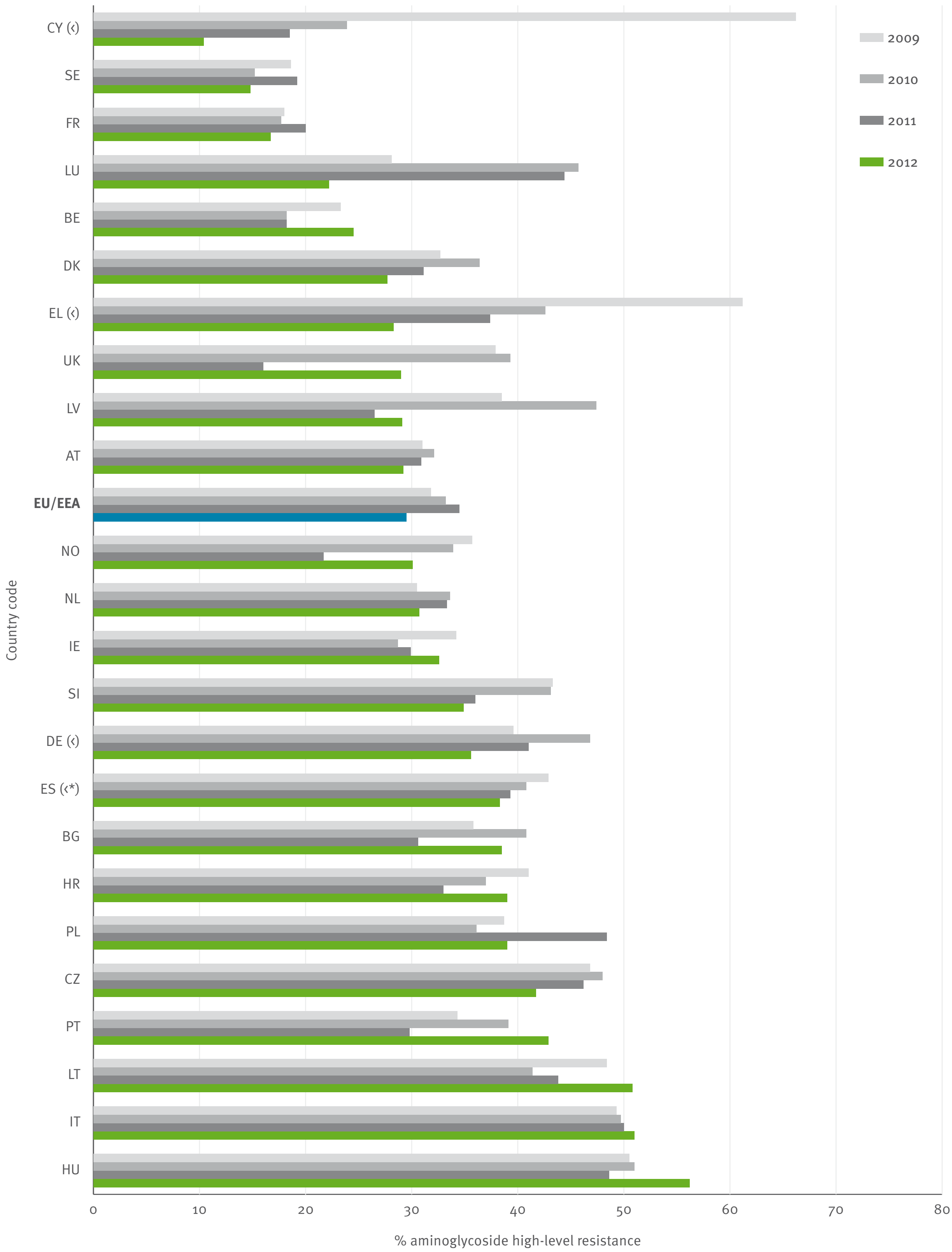


Figure 3.47. ***Enterococcus faecalis*****. Trends of invasive isolates with high-level resistance to aminoglycosides, by country, EU/EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

The symbols › and ‹ indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.

EU/EEA refers to the population-weighted mean percentage.

ampicillin-resistance has increased significantly in recent years, due not least to the wide dissemination of ampicillin-resistant strains belonging to the polyclonal subcluster CC17.

Aminoglycosides

In addition to the intrinsic mechanism of low-level resistance to aminoglycosides, which causes a 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, different aminoglycoside-modifying enzymes have been identified, targeting eight different aminoglycosides. The bi-functional APH(2'')/AAC(6') enzyme confers high-level resistance to all aminoglycosides except streptomycin and is now widespread across Europe. With high-level resistance, any synergistic effect between beta-lactams and glycopeptides is lost.

Glycopeptides

Vancomycin resistance in enterococci was first reported in France and England, but showed the most dramatic increase in the United States and was attributed to the widespread use of vancomycin in US hospitals. While vancomycin consumption was lower in Europe, a closely related glycopeptide, avoparcin, had been widely used as a growth promoter in animal husbandry since the late 1970s until it was banned in the EU by 1998. Glycopeptide resistance is due to the synthesis of modified cell wall precursors that show a decreased affinity for glycopeptides. Six phenotypes have been identified of which two 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 in most cases to vancomycin only. The VanA and VanB phenotypes, mostly found among *E. faecalis* and *E. faecium*, may be transferred by plasmids and through conjugative transposition.

3.7.3 Antimicrobial susceptibility

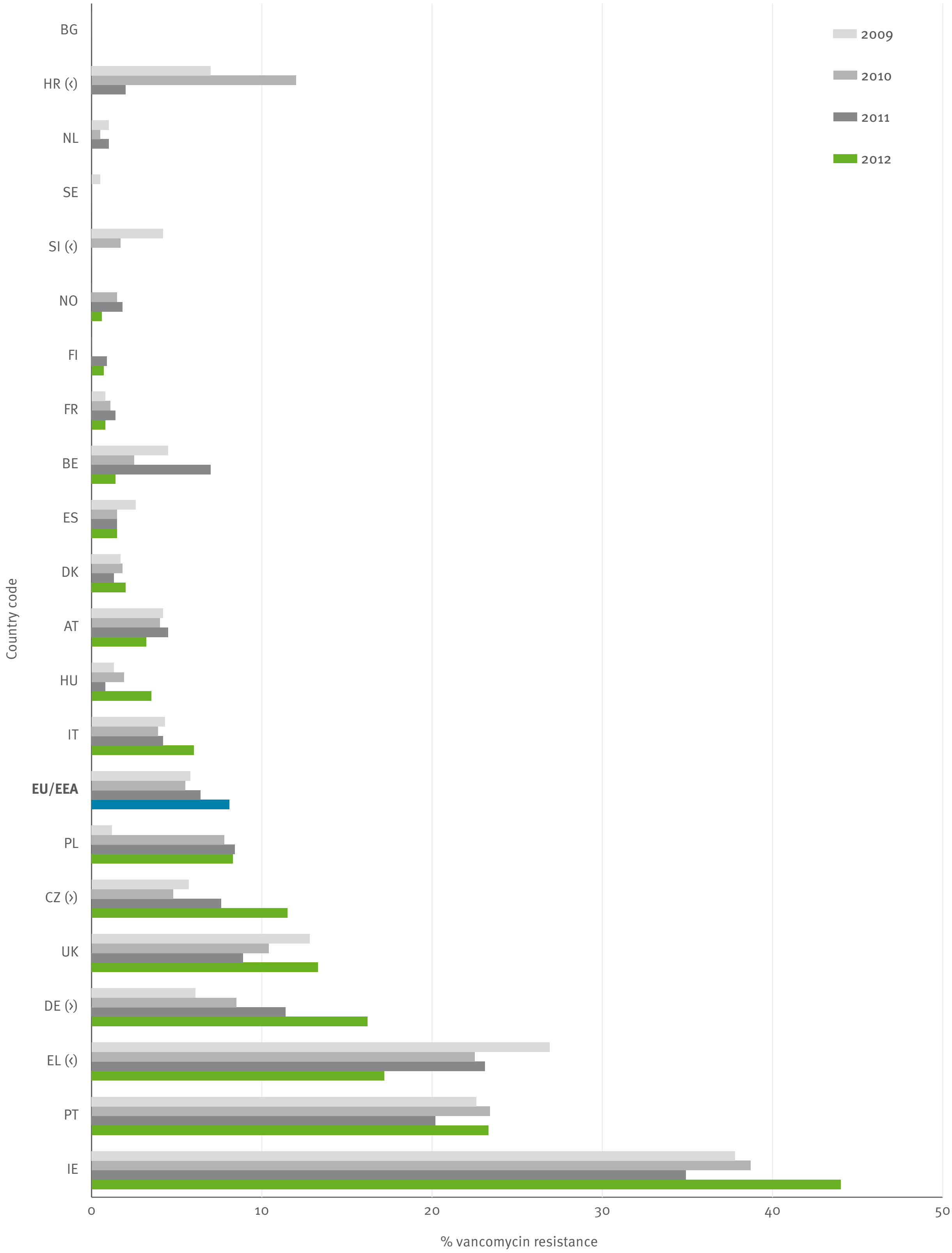
- High-level aminoglycoside resistance in *E. faecalis* seems stable in Europe, but is generally very high with the majority of countries reporting percentages of above 25% over the recent years.
- The percentage of vancomycin resistance in *E. faecium* shows large inter-country variations, with the majority of countries reporting resistance percentages of below 5% during recent years and only a few countries reporting estimates above 10%.

Table 3.13. Total number of invasive isolates and percentages (%) of high-level aminoglycoside-resistant *E. faecalis* and vancomycin-resistant *E. faecium*, including 95% confidence intervals, by country, EU/EEA countries, 2012

Country	High-level aminoglycoside resistant *E. faecalis*		Vancomycin-resistant *E. faecium*	
	Number of isolates	% R (95% CI)	Number of isolates	% R (95% CI)
Austria	425	29.2 (25-34)	376	3.2 (2-6)
Belgium	396	24.5 (20-29)	212	1.4 (0-4)
Bulgaria	78	38.5 (28-50)	42	0.0 (0-8)
Croatia	160	38.8 (31-47)	61	0.0 (0-7)
Cyprus	77	10.4 (5-19)	29	10.3 (2-27)
Czech Republic	581	41.7 (38-46)	262	11.5 (8-16)
Denmark	112	27.7 (20-37)	593	2.0 (1-4)
Estonia	19	42.1 (20-67)	40	0.0 (0-9)
Finland	0	–	274	0.7 (0-3)
France	1528	16.7 (15-19)	614	0.8 (0-2)
Germany	680	35.6 (32-39)	647	16.2 (13-19)
Greece	667	28.3 (25-32)	418	17.2 (14-21)
Hungary	452	56.2 (51-61)	142	3.5 (1-8)
Iceland	20	11.8 (5-28)	14	0.0 (0-20)
Ireland	279	32.6 (27-38)	386	44.0 (39-49)
Italy	300	51.0 (45-57)	435	6.0 (4-9)
Latvia	55	29.1 (18-43)	18	5.6 (0-27)
Lithuania	59	50.8 (37-64)	36	5.6 (1-19)
Luxembourg	45	22.2 (11-37)	20	0.0 (0-17)
Malta	0	–	6	*
Netherlands	287	30.7 (25-36)	484	0.0 (0-1)
Norway	123	30.1 (22-39)	168	0.6 (0-3)
Poland	105	39.0 (30-49)	157	8.3 (4-14)
Portugal	347	42.9 (38-48)	257	23.3 (18-29)
Slovakia	179	50.3 (43-58)	82	4.9 (0-10)
Slovenia	129	34.9 (27-44)	95	0.0 (0-4)
Spain	878	38.3 (35-42)	537	1.5 (1-3)
Sweden	792	14.8 (12-17)	404	0.0 (0-1)
United Kingdom	377	29.4 (22-38)	362	13.3 (10-17)
EU/EEA mean percentage (population-weighted)		**26.5**		**8.1**

* Fewer than 10 isolates, percentage not calculated.

Figure 3.48. ***Enterococcus faecium*. Trends of invasive isolates with resistance to vancomycin, by country, EU/EEA countries, 2009–2012**



Countries not reporting data for all four years were excluded from the analysis.

The symbols › and ‹ indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years.

EU/EEA refers to the population-weighted mean percentage.

Enterococcus faecalis

High-level aminoglycoside resistance

- For 2012, 27 countries reported 9 150 isolates with relevant AST information for high-level aminoglycoside resistance. The number of isolates reported per country ranged from 19 to 1528 (Table 3.13).
- The EU/EEA population-weighted mean percentage for high-level aminoglycoside resistance was 26.5%. The percentages of resistant isolates in the reporting countries ranged from 10.4 (Cyprus) to 56.2% (Hungary). Six countries reported resistance percentages of 10–25%, 17 reported 25–50% and four reported over 50%. (Figure 3.45 and Table 3.13).
- Twenty-four countries have reported more than 20 isolates per year since 2009 and were thus included in the trend analysis for the period 2009–2012.
- Four countries (Cyprus, Germany, Greece and Spain) have had statistically significant decreasing trends of high-level aminoglycoside resistance for the past four years. No country showed a significant increasing trend for the same period (Figure 3.47).

Enterococcus faecium

Vancomycin

- For 2012, 29 countries reported 7 171 isolates with relevant AST information for vancomycin. The number of isolates with relevant AST information reported per country ranged from 6 to 647. Only one country (Malta) reported fewer than 10 isolates and is therefore not included in Figure 3.46 or the resistance calculations in Table 3.13.
- The EU/EEA population-weighted mean percentage for vancomycin resistance was 8.1%. The percentages of vancomycin-resistant isolates ranged from zero (Bulgaria, Croatia, Estonia, Iceland, Luxembourg, Malta, the Netherlands, Slovenia and Sweden) to 44.0% (Ireland). Eleven countries reported resistance percentages of below 1%, six countries reported 1–5%, four countries reported 5–10%, six countries reported 10–25%, and one country reported above 25% (Figure 3.46 and Table 3.13).
- Twenty-one countries have reported more than 20 isolates per year since 2009 and were thus included in the trend analysis for the period 2009–2012. Statistically significant increasing trends were observed for the Czech Republic and Germany. Statistically significant decreasing trends of vancomycin resistance were observed for Croatia, Greece and Slovenia (Figure 3.48).

3.7.4 Discussion and conclusions

High levels of antimicrobial-resistant enterococci remain a major infection control challenge and an important cause of healthcare-associated infections in Europe. In the recent point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012, *Enterococcus* spp. were one of the most commonly isolated microorganisms in healthcare-associated infections and resistance to vancomycin or high-level resistance to aminoglycoside was not unusual[22].

The previously reported[23] large decrease in the percentage of high-level aminoglycoside-resistant *E. faecalis* in Cyprus and Greece continued in 2012. No country reported an increasing trend for the period 2009–2012, and the EU/EEA population-adjusted mean decreased for the first time during the past four years. Despite this positive development, aminoglycoside resistance in *E. faecalis* remained very high at levels above 25% for most European countries.

22 European Centre for Disease Prevention and Control. Point prevalence survey of health-care associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.

23 European Centre for Disease Prevention and Control. Antimicrobial Resistance Surveillance in Europe 2011. Annual report of the European Antimicrobial Resistance Surveillance network (EARS-Net). Stockholm: ECDC; 2012.

Annexes

Annex 1 External quality assessment 2012

Introduction

Since 2000, EARSS/EARS-Net have organised external quality assessment (EQA) of antimicrobial susceptibility testing in collaboration with UK NEQAS (United Kingdom National External Quality Assessment Service). UK NEQAS is based at the Health Protection Agency in London, and is a non-profit organisation with more than 35 years of experience in external quality assessment in different countries (www.ukneqasmicro.org.uk).

The purpose of the EARS-Net EQA is:

- to assess the ability of participating laboratories to identify antimicrobial resistance of clinical and public health importance;
- to determine the accuracy of susceptibility test results reported by individual laboratories;
- to estimate the overall comparability of routinely collected test results between laboratories and countries across Europe.

The strains used for the 2012 EQA were compatible with species under surveillance at ECDC, namely *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Enterococcus faecium*. The reference MICs of strains were each tested in two of three laboratories; Addenbrookes Hospital, Cambridge (UK), University Hospital of Wales, Cardiff (UK) and City Hospital, Birmingham (UK). Reference laboratories confirmed MICs and results were interpreted according to the most frequently used breakpoint criteria (EUCAST and CLSI), as indicated in the summary for each species outlined below.

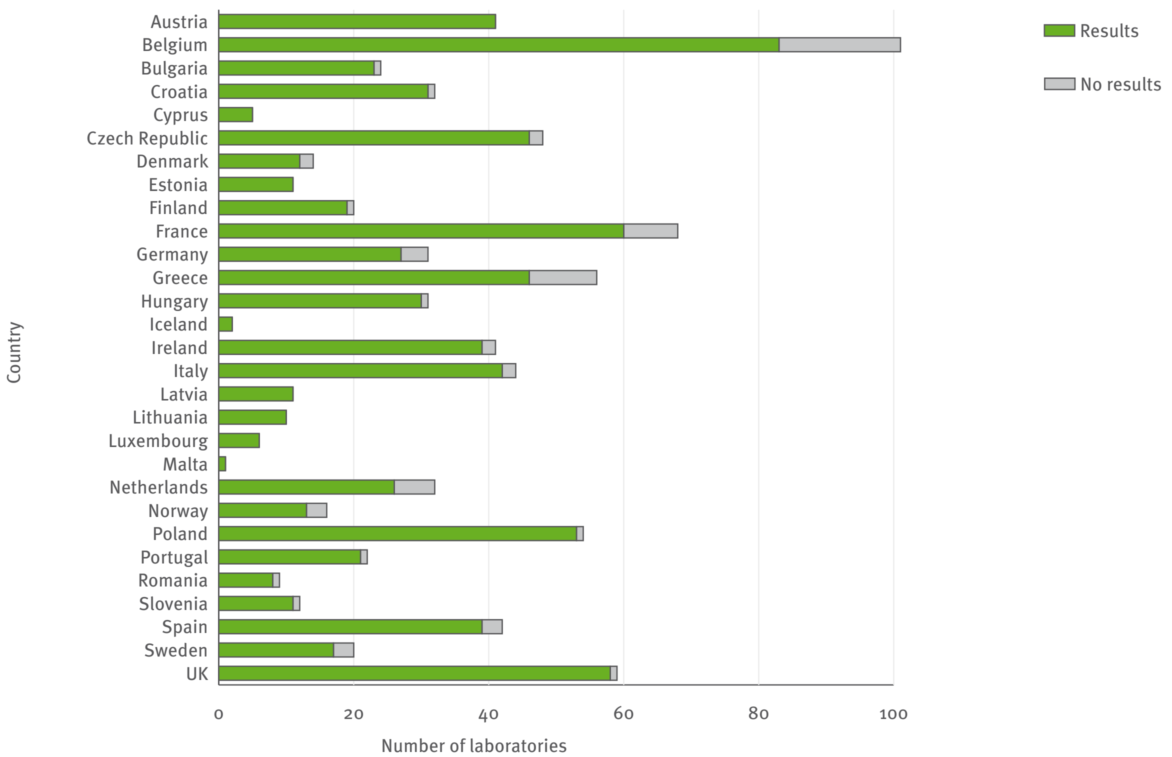
Results

Six strains were distributed to 883 laboratories participating in EARS-Net. Laboratories were asked to report the identification of each organism and clinical susceptibility characterisation – susceptible, intermediate and resistant (S, I, R) – according to guideline used. The return rate was equivalent to previous years; 807 laboratories (91%) 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 (Tables A1.1–A1.6).

For the determination of AST results, laboratories used automated methods (44%), disk diffusion tests (34%), or

Figure A1.1. Number of participating laboratories returning EQA reports 2012, per country



a combination of methods (13%). For species identification, 56% used automated and 44% used conventional methods. Increased use of conventional methods was associated with identification of *S. pneumoniae* and *E. faecalis*.

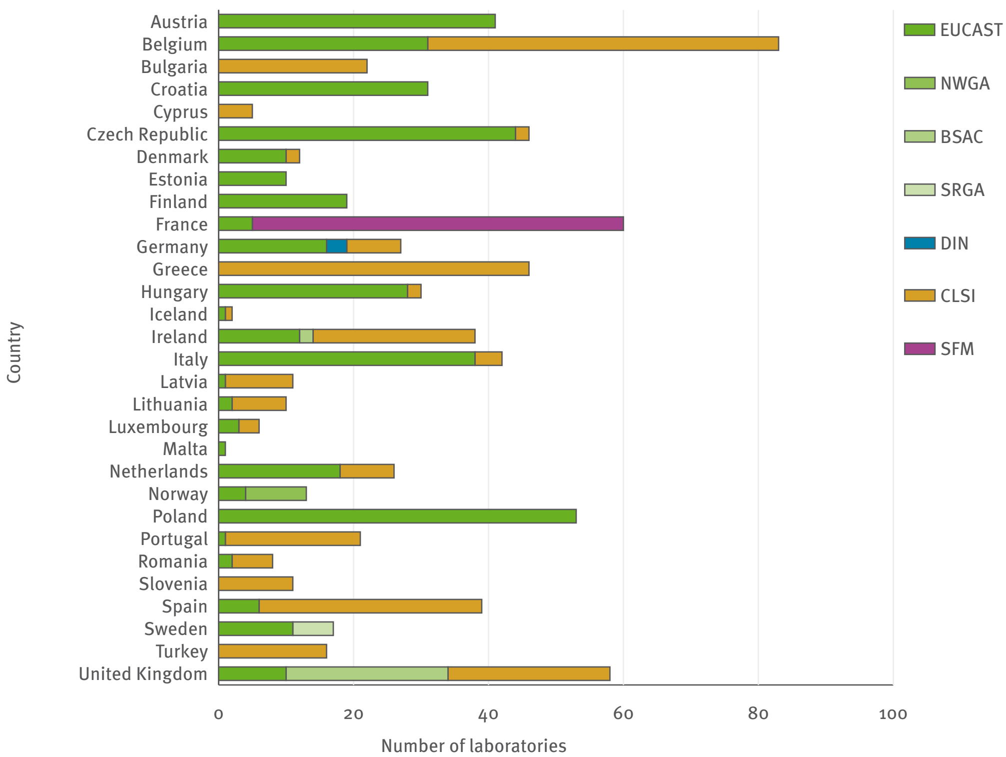
Some 39% of laboratories applied CLSI guidelines; this is a significant reduction from the previous year when the proportion was 47%. Some countries used national guidelines, for example, France (SFM), UK (BSAC), and Sweden (SRGA). EUCAST guidelines were used by 395 (49%) laboratories, this was an increase of 114 laboratories compared to last year (n=281). However, the UK, Sweden, the Netherlands, Germany, France and Norway 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 method accordingly. Therefore, a combined total of some 61% of laboratories used EUCAST breakpoints. Figure A1.2 shows the adherence to (inter)national guidelines by number of laboratories per country.

Specimen 1373 *Enterococcus faecalis*

This organism was an *Enterococcus faecalis* with *vanA*-mediated glycopeptide resistance (resistant to vancomycin and teicoplanin). There were no significant problems detecting vancomycin resistance and only a small minority of participants failed to report reduced susceptibility to teicoplanin (2.9% susceptible, 4.3% intermediate, and 92.8% resistant) (Table A1.1).

Gentamicin monotherapy is ineffective against enterococci. There is, however, synergism between gentamicin and beta-lactam agents against enterococci without mechanisms conferring high-level gentamicin resistance (usually production of the bi-functional enzyme APH(2'')/AAC(6')). This organism was not high-level gentamicin-resistant but 23.7% of participants incorrectly reported it to be so, very similar to error rates for an *Enterococcus*

Figure A1.2. Guidelines reported to be used by laboratories: number of laboratories per country, 2012



BSAC: British Society for Antimicrobial Chemotherapy; DIN: Deutsche Industrie Norm; EUCAST: European Committee on Antimicrobial Susceptibility Testing; CLSI: Clinical and Laboratory Standards Institute; NWGA: Norwegian Working Group on Antimicrobials; SFM: Societe Francaise de Microbiologie; SRGA: Swedish Reference Group for Antimicrobials.

Table A1.1. *Enterococcus faecalis* (1373). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC range (mg/L) ref. lab		Intended interpretation	
	from	to	EUCAST/CLSI	Overall concordance (%)
Amoxicillin	1	1	S	97
Ampicillin	1	2	S	96
High-level gentamicin	8	16	S (not HLR)	76
Teicoplanin	≥128	≥128	R	93
Vancomycin	64	64	R	98

faecium without high-level gentamicin resistance in the 2011 EARS-Net EQA exercise.

Specimen 1374 *Escherichia coli*

This organism was an *Escherichia coli* with a TEM-10 ESBL and there were no significant problems in identifying that the organism was an ESBL-producer (99.1% reported ESBL-positive). While the organism was high-level resistant to ceftazidime (MIC ≥128 mg/L) it displayed borderline resistance to cefotaxime and ceftriaxone (MICs 4 mg/L and 8–16 mg/L, respectively, in reference tests; resistant to both agents with EUCAST and CLSI breakpoints).

As is often the case with borderline susceptibility, reporting of susceptibility categories was variable. For cefotaxime, 47.7% reported resistant, 25.0% intermediate and 27.3% susceptible, and for ceftriaxone, 48.7% reported resistant, 19.4% intermediate and 31.9% susceptible. While the majority of participants reported reduced susceptibility to cefotaxime and ceftriaxone, substantial minorities reported the isolate susceptible.

Cefotaxime MICs were reported by 481 of 703 participants testing cefotaxime susceptibility, most using automated or gradient systems. Reported MICs were more variable than in reference tests, with 248 reporting cefotaxime MICs ≤1 mg/L (susceptible by EUCAST and CLSI breakpoints) and 225 reporting MICs >1 mg/L (intermediate or resistant by EUCAST and CLSI breakpoints). Among participants reporting cefotaxime MICs in the susceptible range, 48.0% interpreted them as susceptible, 17.3% intermediate and 34.7% resistant, indicating that close to half of these laboratories were reporting 'as found' (in line with current EUCAST and CLSI recommendations) and about half were probably editing results of susceptible to intermediate or resistant, presumably because of the presence of an ESBL. Laboratories reporting cefotaxime MICs >1 mg/L would be expected to report intermediate or resistant and 96.5% did so. Similar results were seen with ceftriaxone, for which MICs were reported by 136 of 376 participants testing ceftriaxone susceptibility. Sixty-five participants reported ceftriaxone MICs ≤1 mg/L (susceptible by EUCAST and CLSI breakpoints) and 70 reported MICs >1 mg/L (intermediate or resistant by EUCAST and CLSI breakpoints). Among participants reporting ceftriaxone MICs in the susceptible range, 60.0% interpreted results as susceptible, 9.2% intermediate and 30.8% resistant. Among laboratories reporting ceftriaxone MICs >1 mg/L, 92.8% reported either intermediate or resistant.

The organism was susceptible to piperacillin–tazobactam (MIC 4–8 mg/L) by both EUCAST and CLSI breakpoints. Reports of reduced susceptibility to piperacillin–tazobactam by some participants (11.6%

Table A1.2. *Escherichia coli* (1374). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC range (mg/L) ref. lab.		Intended interpretation	
	from	to	EUCAST/CLSI	Overall concordance (%)
Amikacin	1	1	S	99
Amoxicillin	≥128	≥128	R	98
Ampicillin	≥128	≥128	R	99
Cefotaxime	4	4	R	48
Ceftazidime	≥128	≥128	R	99
Ceftriaxone	8	16	R	49
Ciprofloxacin	0.015	0.015	S	99
Gentamicin	0.5	0.5	S	100
Imipenem	0.25	0.25	S	99
Meropenem	0.03	0.03	S	99
Piperacillin-tazobactam	4	8	S	80
Tobramycin	2	2	S	99
ESBL			POS	99

Table A1.3. *Klebsiella pneumoniae* (1375). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC range (mg/L) ref. lab.		Intended interpretation	
	from	to	EUCAST/CLSI	Overall concordance (%)
Amikacin	1	2	S	99
Amoxicillin	≥128	≥128	R	94
Ampicillin	≥128	≥128	R	99
Cefotaxime	0.03	0.03	S	99
Ceftazidime	0.25	0.25	S	99
Ceftriaxone	0.06	0.06	S	99
Ciprofloxacin	0.06	0.06	S	99
Gentamicin	0.5	0.5	S	99
Imipenem	0.25	0.5	S	100
Meropenem	0.03	0.03	S	100
Piperacillin-tazobactam	8	8	S	98
Tobramycin	1	0.5	S	99
ESBL			NEG	99

resistant, 8.2% intermediate, 80.2% susceptible) may have been because of editing to a more resistant category because of the presence of the ESBL. Guidelines from both EUCAST and CLSI recommend reporting beta-lactamase inhibitor combinations 'as found' in routine tests, although the current EUCAST expert rule 9.1 does recommend that when an organism is intermediate or resistant to any 3rd generation (cefotaxime, ceftriaxone, ceftazidime) or 4th 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 (Table A1.2).

Specimen 1375 *Klebsiella pneumoniae*

This organism was a *Klebsiella pneumoniae* susceptible to all reference agents tested except ampicillin and amoxicillin. *K. pneumoniae* is inherently resistant to ampicillin/amoxicillin so reports of susceptible isolates should always be viewed with caution. Still, 13 (5.7%) participants falsely reported the organism susceptible to amoxicillin, of which 12 correctly reported the organism resistant to ampicillin (Table A.1.3). There is cross-resistance between ampicillin and amoxicillin so a discrepancy in results for these agents should have been recognised as very unlikely.

Specimen 1376 *Pseudomonas aeruginosa*

This organism was a *Pseudomonas aeruginosa* resistant to all agents tested except piperacillin–tazobactam interpreted according to CLSI breakpoints. Reference MICs for piperacillin–tazobactam ranged from 64 to ≥128 mg/L (concentration of tazobactam fixed at 4 mg/L), clearly resistant by EUCAST breakpoints (S ≤16, R >16 mg/L) but borderline with the much higher CLSI resistant breakpoint (S ≤16, R ≥128 mg/L). Reports from participants were largely in line with breakpoints used, in that 95.3% of participants using EUCAST or EUCAST-related breakpoints reported resistant, while only 66.7% of participants using CLSI breakpoints reported resistant (Table A1.4).

Specimen 1377 *Staphylococcus aureus*

This organism was a multi-resistant *Staphylococcus aureus* with dissociated resistance to clindamycin.

Discrepancies with clindamycin were fewer than seen with previous distributions of organisms with dissociated resistance, with 91.1% now reporting resistant, 1.4% intermediate and 7.5% susceptible (Table A1.5). In staphylococci, most resistance to macrolide, lincosamide, streptogramin type B (MLS_B) antibiotics is mediated by the *erm* genes and is induced by erythromycin, clarithromycin and azithromycin, but not by clindamycin (dissociated resistance or MLS_B-inducible resistance). Hence inducible strains are resistant to erythromycin but not to clindamycin in susceptibility tests. Strains with MLS_B-constitutive resistance are resistant to both agents. There has been debate about whether staphylococci with inducible resistance (erythromycin-resistant, clindamycin-susceptible) should be

Table A1.4. ***Pseudomonas aeruginosa*** **(1376). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories**

Antibiotic agent	MIC range (mg/L) ref. lab.		Intended interpretation	
	from	to	EUCAST/CLSI	Overall concordance (%)
Amikacin	64	64	R	99
Ceftazidime	≥128	≥128	R	100
Ciprofloxacin	32	32	R	100
Gentamicin	64	64	R	99
Imipenem	≥128	≥128	R	99
Meropenem	≥128	≥128	R	100
Piperacillin-tazobactam	64	≥128	R	84
Tobramycin	≥128	≥128	R	100

Table A1.5. ***Staphylococcus aureus*** **(1377). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories**

Antibiotic agent	MIC range (mg/L) ref. lab.		Intended interpretation	
	from	to	EUCAST/CLSI	Overall concordance (%)
Cefoxitin	64	64	R	99
Ciprofloxacin	16	16	R	97
Clindamycin	0.12	0.12	dissociated resistance	91
Erythromycin	≥128	≥128	R	99
Fusidic acid	0.12	0.12	S	99
Gentamicin	128	512	R	99
Meticillin	NT*	R	99	99
Oxacillin	≥128	≥128	R	99
Penicillin	64	64	R	99
Rifampicin	0.008	0.008	S	95
Teicoplanin	0.5	0.5	S	99
Tetracycline	≥128	≥128	R	98
Vancomycin	1	1	S	99

* Not tested, result inferred from oxacillin and cefoxitin results

reported as resistant because inducible strains segregate clindamycin-resistant mutants, which may be selected during therapy. The EUCAST expert rules[24] indicate that such strains should either be reported as resistant to clindamycin or reported as susceptible with a warning of possible clinical failure during treatment with clindamycin due to selection of constitutively resistant mutants. EUCAST also states that the use of clindamycin is best avoided in severe infections caused by isolates with dissociated resistance. CLSI suggests that such strains should be reported as resistant but that a comment may be added that clindamycin may still be effective in some patients. Inducible clindamycin resistance is detected in disk diffusion tests with a clindamycin disk placed adjacent to an erythromycin disk: strains with inducible resistance show flattening of the clindamycin zone adjacent to the erythromycin disk.

Specimen 1378 *Streptococcus pneumoniae*

This organism was a *Streptococcus pneumoniae* susceptible to penicillin. Although there were no significant problems in reporting susceptibility to penicillin, 5.8% of participants reported resistance in the oxacillin screening test for penicillin resistance. An additional 0.7% reported oxacillin intermediate despite the fact that there is no intermediate category for the oxacillin screen test (Table A1.6).

Conclusions

The response from the laboratories to the 2012 EARS-Net EQA was very good with a high return rate and very few late responders.

Participants' results were analysed and considered 'concordant' if the reported categorisation agreed with the interpretation of MICs determined in the reference laboratories. For the determination of AST results, on average 43% of laboratories used automated methods and 34% disk diffusion tests. For species identification, on average 55% used automated and 45% used conventional methods, with increased use of conventional methods associated with identification of the *S. pneumoniae* and *E. faecium/faecalis*. National guidelines are commonly followed in some countries e.g. SFM (France), DIN (Germany) and BSAC (UK). However, the BSAC, SRGA, CRG, DIN, SFM and NWGA have been implementing EUCAST breakpoints in their national MIC breakpoint recommendations as harmonised breakpoints have been agreed. Increasing uptake of EUCAST harmonised breakpoints was evident from the guidelines used by participants over the EQA period. The use of CLSI guidelines was reduced from 66% to 39%, whilst the use of EUCAST guidelines increased from 15% to 49%, and when this number was added to users of EUCAST-related guidelines (12% in 2012) this gave a combined total of 61%.

Participant concordance for identification of the organisms was very good. Variation in interpretation of susceptibility results was seen with strain/antimicrobial agent combinations that had borderline MIC values and clear differences in reporting seen where breakpoints and interpretation differ between guidelines.

The design of the EQA was in keeping with the established AST scheme organised by UK NEQAS, which has been established for more than forty years and is currently accredited to ISO 14075.

Discussion

Overall, performance was generally very good and consistent with that seen in previous EQA. Problems, where experienced, were related to borderline susceptibility and when remaining discrepancies between different guidelines resulted in discrepancies in routine susceptibility testing. EQA is a valuable tool in the quality assurance of antimicrobial susceptibility testing and indicates the validity of comparing collated data between laboratories in resistance surveillance studies.

Limitations associated with the design of the EQA panels are largely attributable to the restricted number of isolates distributed in the EARS-Net EQA. It is difficult to cover the full range of strains representative of the epidemiologically important AMR types currently

24 Leclercq R, Cantón R, Brown DF, Giske CG, Heisig P, MacGowan AP, et al. EUCAST expert rules in antimicrobial susceptibility testing. Clin Microbiol Infect. 2013 Feb;19(2):141-60. doi: 10.1111/j.1469-0691.2011.03703.x. Epub 2011 Nov 25. Review.

Table A1.6. *Streptococcus pneumoniae* (1378). Minimum inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories

Antibiotic agent	MIC range (mg/L) ref. lab.		Intended interpretation	
	from	to	EUCAST/CLSI	Overall concordance (%)
Cefotaxime				
Meningitis	≤0.004	≤0.004	S	99
Pneumonia			S	100
Ceftriaxone				
Meningitis	≤0.004	≤0.004	S	99
Pneumonia			S	99
Ciprofloxacin	≥64	≥64	I/no interpretation	96
Clindamycin	-	0.125	S	97
Erythromycin	16	32	R	98
Penicillin				
Meningitis	0.015	0.03	S	97
Pneumonia			S	99

circulating in Europe and equally, to re-circulate isolates that participants found challenging to monitor improvements in resistance detection.

Misunderstanding of language, coupled with differences in the technical terminology used by different AST guidelines and the commercial instruments, was perceived as a potential issue for reporting the detection of high-level gentamicin resistance in enterococci. The differences in terminology can be confusing and, if the participant's first language is not English, this may explain the higher error rates seen for the enterococci isolate without high-level gentamicin resistance.

ECDC would like to thank UK NEQAS, the reference laboratories, the members of the EARS-Net Coordination Group and the country EQA coordinators for their efforts and contribution to the success of this EQA. Special thanks goes to the all involved staff at the participating laboratories for providing timely and high quality responses to the assessment.

Annex 2 EARS-Net laboratory/hospital denominator data 2012

Introduction

For correct interpretation of the EARS-Net data on antimicrobial resistance, accurate background information is important. Therefore, laboratory and hospital denominator data are collected and presented in this Annex.

Methods

Questionnaires (Microsoft Excel files) were sent to the EARS-Net contact points in April 2013. 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, and the number of hospital beds for each participating hospital, the type of hospital, the bed occupancy and the number of admissions. The national data managers received the completed 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 the number of beds.

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

The number of hospitals and laboratories reporting AMR data is defined as the number reporting at least one isolate during the specific year. Please note that the total number of hospitals and laboratories participating in EARS-Net might be higher in some countries.

Participation

Nineteen of the 30 countries reporting AMR data also returned hospital denominator data referring to 2012, while for five countries, hospital denominator data referring to 2011 were available and included in the analysis. Seventeen countries could provide laboratory denominator data (number of blood cultures) for 2012 and five for 2011. Some denominator data for laboratories and hospitals not reporting AMR data, or reporting zero cases, have been included in Figure A2.1, but were not included in other parts of the analysis.

Population coverage

Data on population coverage for AMR data at country level are not reported because of the inherent limitations of these data. Not all laboratories/hospitals reporting AST data also provide denominator data, and this would introduce bias into the calculation of country

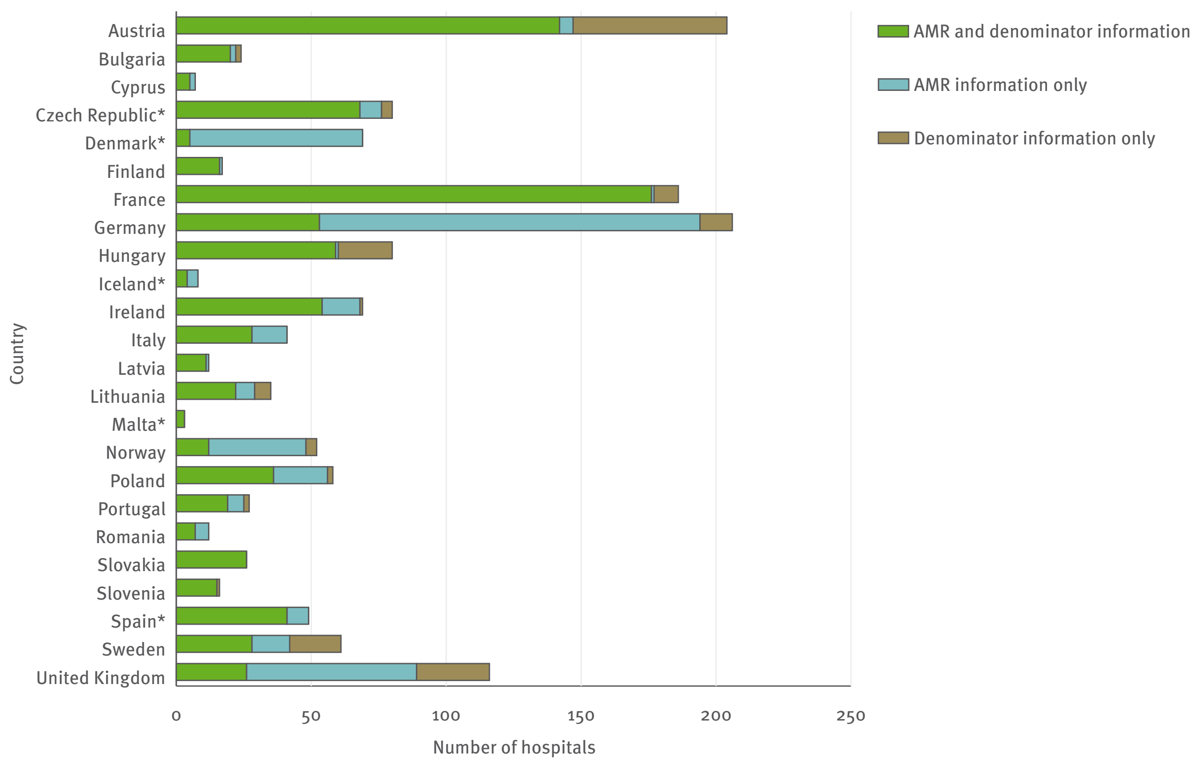
Table A2.1. Hospital denominator data for 2011 or 2012 (using the latest available data)

Country	Hospitals reporting (denominator/AMR data)	Total number of beds	Proportion of ICU beds (%)	Annual occupancy rate (%)	Median length of stay (days)	IQR length of stay (days)
Austria	(142/147)	58276	5	67	4.5	4.0-5.4
Bulgaria	(20/22)	9679	7	73	5.7	5.0-6.3
Cyprus	(5/7)	1330	8	78	5.2	4.9-5.5
Czech Republic*	(68/76)	38911	11	70	7.2	6.1-8.3
Denmark*	(5/69)	3254		82	3.2	2.8-3.6
Finland	(16/17)	9528	3	–	–	–
France	(176/177)	127423	6	81	7.1	5.9-8.5
Germany	(53/194)	18700	7	79	6.7	5.9-8.0
Hungary	(59/60)	43896	2	75	8.4	7.0-9.7
Iceland*	(4/8)	919	5	83	7.7	6.5-14.6
Ireland	(54/68)	12115	–	87	5.1	4.3-6.3
Italy	(28/41)	14892	–	80	–	–
Latvia	(11/12)	5058	3	71	5.5	4.8-6.3
Lithuania	(22/29)	12423	4	74	7.3	6.6-8.5
Malta*	(3/3)	1157	6	87	5.3	4.8-45.0
Norway	(12/48)	5816	3	96	4.8	4.3-5.7
Poland	(36/58)	18811	2	68	5	4.0-6.0
Portugal	(19/25)	8228	6	74	7	5.0-8.7
Romania	(7/12)	5344	8	78	6.2	6.0-7.2
Slovakia	(26/26)	13755	8	69	6.9	6.0-7.5
Slovenia	(15/15)	7377	5	70	5.3	4.9-6.6
Spain*	(41/49)	26646	4	79	–	–
Sweden	(28/42)	9747	5	95	–	–
United Kingdom	(26/89)	18849	–	79	2.8	2.4-4.8

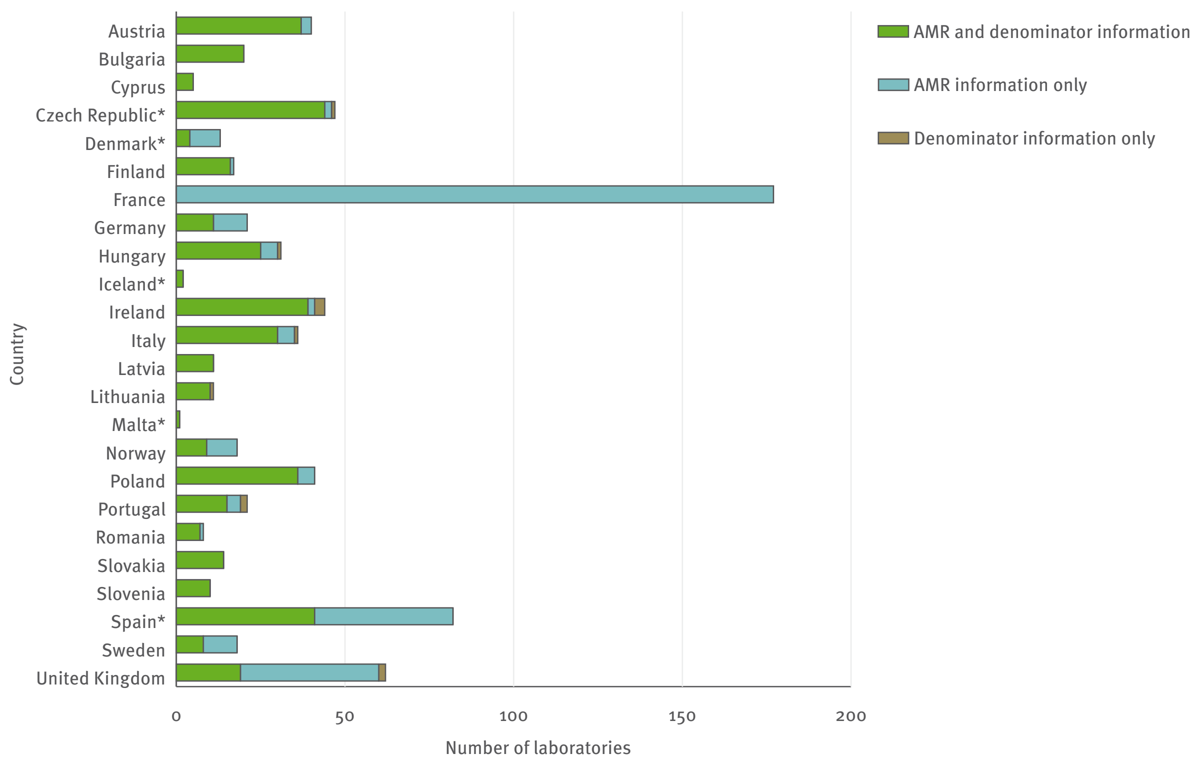
* Data for 2011.

Figure A2.1. **Number of hospitals (A) and laboratories (B) reporting AMR and/or denominator data in 2011 or 2012 (using latest available data)**

A)



B)



* Denominator data from 2011.

population coverage since only laboratories/hospitals reporting denominator data can be included. Secondly, laboratories and hospitals cluster in big cities and, for this reason, some of the catchment areas overlap. This could lead to double counts, which would artificially increase the estimated coverage.

Hospital denominator information

The total number of hospital beds for hospitals reporting both AMR and denominator data in different countries ranged from 919 in Iceland to 127 423 in France, 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, to 11% in the Czech Republic. The overall median length of stay in hospital was 5.6 days with the lowest median in United Kingdom (2.8 days) and the highest in Hungary (8.4 days). The annual occupancy rate was 75 % or higher in 14 out of the 23 countries providing data for this (Table A2.1).

Hospital characteristics

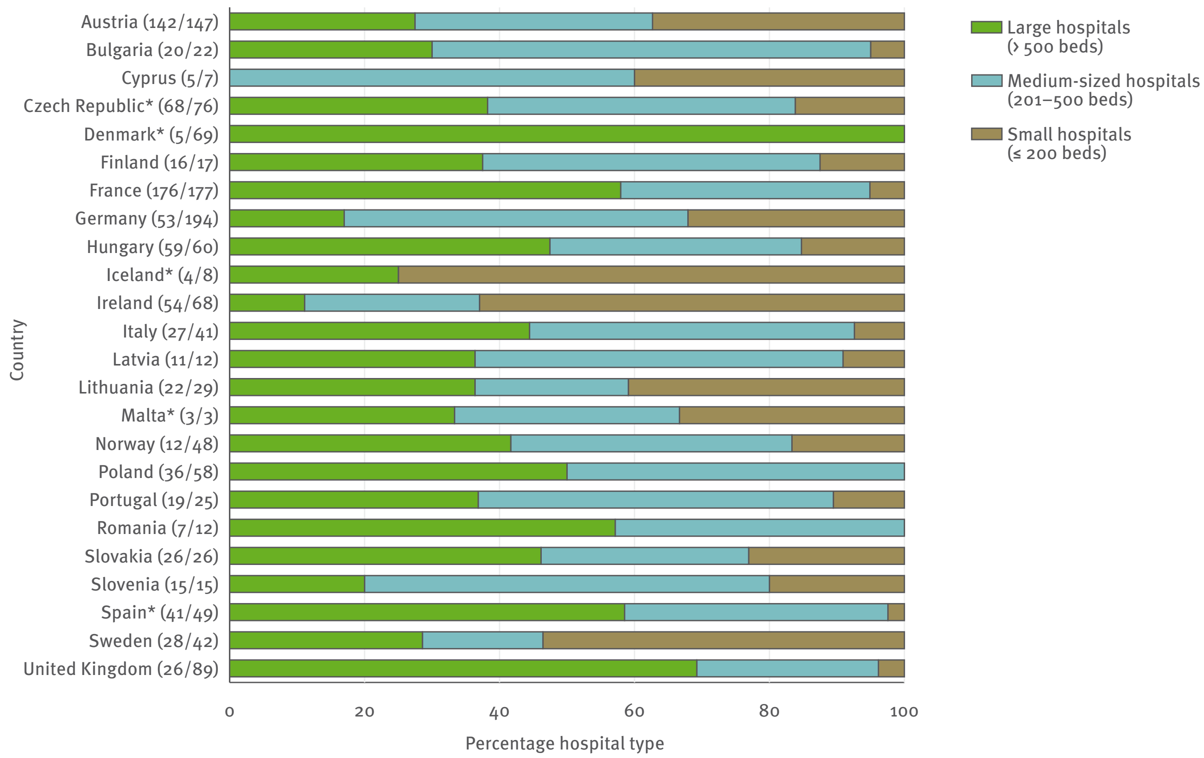
Both the size of a hospital and the level of specialisation may influence the occurrence of antimicrobial resistance in the hospital. As can be seen from Table A2.2 and Figure A2.2, the distribution of size and specialisation level of hospitals varied considerably between the reporting countries. This does not necessarily reflect different distributions of the origin of EARS-Net blood cultures per country, as not all hospitals contribute evenly to the EARS-Net database. On the other hand, this diversity can indicate differences in case-mix, which may confound comparison of AMR results between countries.

The type of hospital and the size of hospital are not always linked and it is not rare, especially in smaller countries, that university hospitals have fewer than 500 beds.

Laboratory denominator information

In 2012/2011 (latest available data), the median blood culture sets per 1000 patient days sets processed in the EARS-Net laboratories responding to the questionnaire was 31.5. The highest rate was reported by Finland (83 cultures per 1000 patient days) and the lowest by Lithuania (7 cultures per 1000 patient days). For the majority of the reporting countries, there are only minor changes in the number of blood culture sets taken per 1000 patient days (Table A2.3) when comparing 2012/2011 (latest available data) data with 2010/2011 (latest available data).

Figure A2.2: Percentage of small, medium and large hospitals per country, based on number of beds, for all hospitals reporting both antimicrobial resistance data and denominator data in 2011 or 2012 (using latest available data)



* Denominator data from 2011.

Table A2.2. Hospital characteristics for 2011 or 2012 (using the latest available data)

Country	Hospitals reporting (denominator/AMR data)	Percentage of hospitals by level of care				
		Tertiary level	Secondary level	Primary level	Other	Unknown
Austria	(142/147)	8	26	41	25	0
Bulgaria	(20/22)	65	30	5	0	0
Cyprus	(5/7)	20	20	40	20	0
Czech Republic*	(68/76)	34	34	29	3	0
Denmark*	(5/69)	40	40	0	0	20
Finland	(16/17)	44	56	0	0	0
France	(176/177)	28	71	0	0	0
Germany	(53/194)	25	40	26	9	0
Hungary	(59/60)	46	27	15	12	0
Iceland*	(4/8)	50	0	50	0	0
Ireland	(54/68)	17	54	11	19	0
Italy	(28/41)	48	41	11	0	0
Latvia	(11/12)	36	27	9	27	0
Lithuania	(22/29)	41	32	23	5	0
Malta*	(3/3)	33	33	0	33	0
Norway	(12/48)	42	0	58	0	0
Poland	(36/58)	33	61	0	6	0
Portugal	(19/25)	63	16	11	5	5
Romania	(7/12)	71	29	0	0	0
Slovakia	(26/26)	54	19	8	19	0
Slovenia	(15/15)	13	67	0	20	0
Spain*	(41/49)	59	37	5	0	0
Sweden	(28/42)	21	25	54	0	0
United Kingdom	(26/89)	54	35	12	0	0

* Data for 2011.

Primary level or district hospital = has few specialties, limited laboratory services; bed capacity ranges from 30 to 200 beds. Secondary level, or provincial hospital = highly differentiated by function with five to 10 clinical specialties; bed capacity ranging from 200 to 800 beds. Tertiary level or central/regional hospital = highly specialised staff and technical equipment; clinical services are highly differentiated by function; may have teaching activities; bed capacity ranges from 300 to 1500 beds. Other = hospitals for a specific patient population, like a military hospital, or hospitals with any single specialty, like a burns unit. Unknown = not available.

Table A2.3. Laboratory denominator information for 2011 or 2012 (using the latest available data)

Country	Laboratories reporting (denominator/AMR data)	Number of hospitals	Total number of blood culture sets	Number of blood culture sets per 1000 patient days
Austria	(37/40)	117	193810	16
Bulgaria	(20/20)	20	19196	7.5
Cyprus	(5/5)	5	14114	37.5
Czech Republic*	(44/46)	68	144615	14.5
Denmark*	(4/13)	4	79269	81
Finland	(16/17)	16	203130	83
Germany	(11/21)	53	90328	16.6
Hungary	(24/30)	47	87931	8.9
Iceland*	(2/2)	4	8906	32.2
Ireland	(39/41)	54	186354	48.5
Latvia	(11/11)	11	10587	8.1
Lithuania	(10/10)	22	20608	7.2
Malta*	(1/1)	3	8796	24
Norway	(9/18)	12	116550	57.3
Poland	(36/41)	36	121633	25.4
Portugal	(15/19)	17	114116	54
Romania	(7/8)	9	26523	27.5
Slovakia	(14/14)	26	56267	16.1
Slovenia	(10/10)	15	59173	31.5
Spain*	(41/41)	41	305229	.
Sweden	(8/18)	28	219380	64.9
United Kingdom	(19/60)	21	187245	45.4

* Data for 2011.

Discussion and conclusions

In summary, the situation for most countries as assessed from denominator data reported to EARS-Net in 2012 appears stable and similar to 2011. This indicates that based on EARS-Net data the comparison of resistance percentages over time remains valid.

The BSIs ascertainment is strongly linked to the blood culture rate. Therefore, the wide range in blood culture rates observed in the countries providing denominator data has implications for inter-country comparisons of both the incidence rate of infections, which could be underestimated in some countries, and of the percentage of 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 hospital and laboratories participating within countries, would be desirable. Furthermore, an improved estimation of the coverage of the EARS-Net surveillance, e.g. by using estimations done at the national level based on knowledge of the country-specific situation, would also be desirable.

Country summary sheets

Explanation to the country summary sheets

General information about EARS-Net participating laboratories and hospitals

Table 1 gives the number of laboratories and isolates reported by year and by pathogen under EARSS/EARS-Net surveillance for the period 2003–2011. 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 2003–2012

Table 2 provides information on the proportion of invasive bacterial isolates non-susceptible (I+R) or resistant (R) to the antibiotics or antibiotic classes mentioned in the EARSS/EARS-Net protocols. When interpreting the results in Table 2, always check the number of isolates provided in Table 1.

Demographic characteristics

Table 3 gives the proportional distribution of the isolates reported by source, gender, age, and hospital department, and the percentage of resistance within the different groups, for the period 2011–2012.

The abbreviations used in this table stand for:

PNSP = penicillin-non-susceptible *S. pneumoniae*;

MRSA = meticillin-resistant *S. aureus*;

FREC = fluoroquinolone-resistant *E. coli*;

VRE = vancomycin-resistant *E. faecalis* or *E. faecium*;

3GCRKP = third-generation cephalosporin-resistant *K. pneumoniae*; and

CRPA = carbapenem-resistant *P. aeruginosa*.

If the number of isolates in a certain category accounts for less than 0.5% of the total number of isolates, the % total is set at <1.

PNSP at laboratory level/MRSA, FREC and 3GCRKP at hospital level

Figures 1, 2, 3 and 4 show the local variation in the percentage of PNSP by laboratory and of MRSA, FREC and 3GCRKP by hospital. These figures are based on data from 2011 and 2012, only including the laboratories and hospitals that reported at least five isolates in these two years. The total number of laboratories or hospitals, the minimum, maximum, median, first and third quartile of the proportion of resistance is displayed in a box in the figures.

Austria

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	1	1	<1	<1	2	<1	3	2	2	1
Penicillin RI	9	5	5	5	5	5	5	4	3	5
Macrolides RI	13	13	15	13	13	12	14	11	12	18
Staphylococcus aureus										
Oxacillin/Meticillin R	15	14	14	9	11	8	6	7	7	8
Escherichia coli										
Aminopenicilins R	41	46	49	53	53	50	49	51	50	51
Aminoglycosides R	5	6	6	8	8	7	6	6	7	6
Fluoroquinolones R	14	17	19	22	26	23	20	21	22	21
3rd gen. Cephalosporins R	2	3	4	7	9	7	8	7	9	9
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	1	<1	1	2	2	2	1	2	<1	<1
HL Gentamicin R	33	23	29	29	30	21	31	32	31	29
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	85	85	85	89	82	91	88	92	91	91
HL Gentamicin R	22	22	30	21	28	19	31	42	49	38
Vancomycin R	<1	<1	1	<1	2	2	4	4	5	3
Klebsiella pneumoniae										
Aminoglycosides R	-	-	3	5	5	6	4	6	7	5
Fluoroquinolones R	-	-	11	8	13	12	8	18	17	15
3rd gen. Cephalosporins R	-	-	6	6	8	8	8	13	13	12
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	13	8	6	8	6	9	14	18
Ceftazidime R	-	-	7	9	5	6	6	8	11	14
Carbapenems R	-	-	10	15	12	11	9	14	14	15
Aminoglycosides R	-	-	6	10	8	8	8	11	13	11
Fluoroquinolones R	-	-	14	15	15	12	13	16	19	14

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.

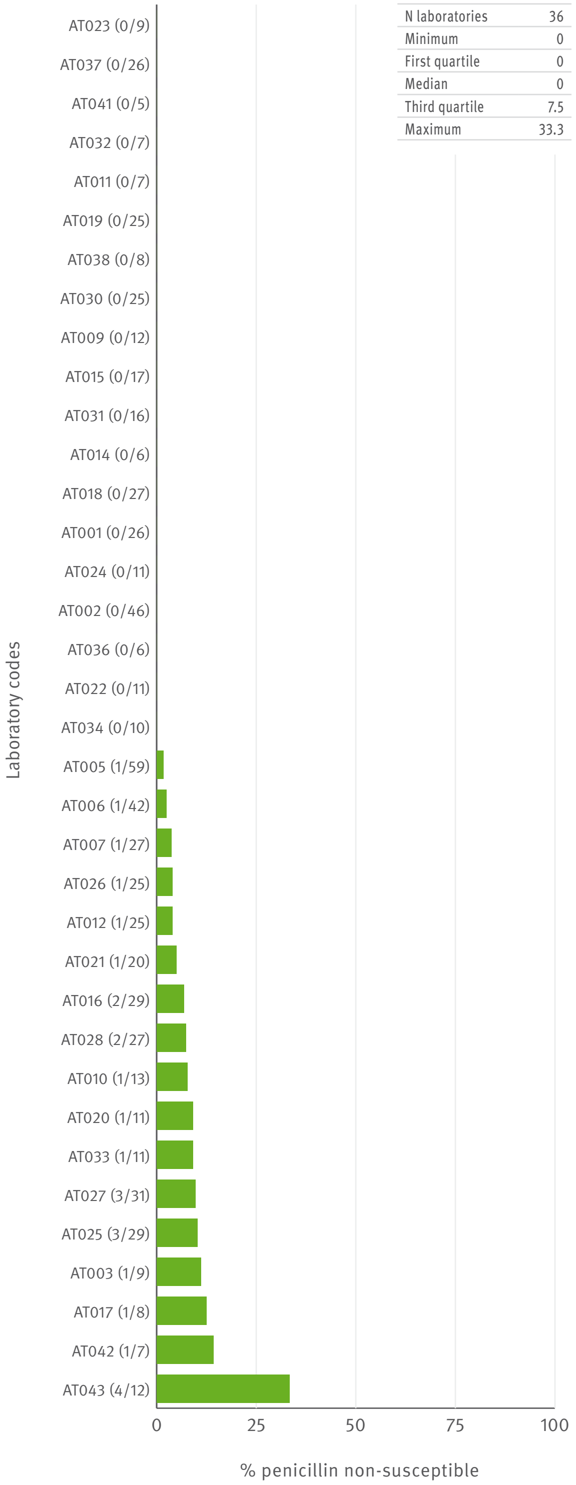
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	97	4	100	8	100	21	100	0	100	4	100	12	99	14
CSF	3	5	-	-	‹1	33	-	-	-	-	‹1	33	1	0
Sex														
Male	55	3	58	8	42	25	65	0	57	4	56	13	60	15
Female	45	5	42	7	57	18	34	1	43	4	43	12	39	13
Unknown	-	-	1	0	1	25	1	0	1	20	1	18	‹1	25
Age (years)														
0–4	4	3	1	5	1	6	2	0	1	0	1	29	1	9
5–19	2	6	1	4	‹1	17	‹1	0	‹1	33	‹1	38	1	43
20–64	36	4	33	6	24	21	28	0	34	5	30	13	31	18
65 and over	58	4	64	8	74	22	70	1	65	3	68	12	68	12
Hospital department														
ICU	16	4	10	12	7	23	14	1	24	3	13	19	15	21
Internal med.	57	4	53	7	58	21	45	0	42	3	48	11	43	12
Surgery	2	0	8	11	7	18	12	1	11	2	10	11	9	12
Other	21	3	23	6	24	24	24	0	20	6	25	13	28	14
Unknown	4	7	5	5	4	24	5	0	3	12	5	11	5	14

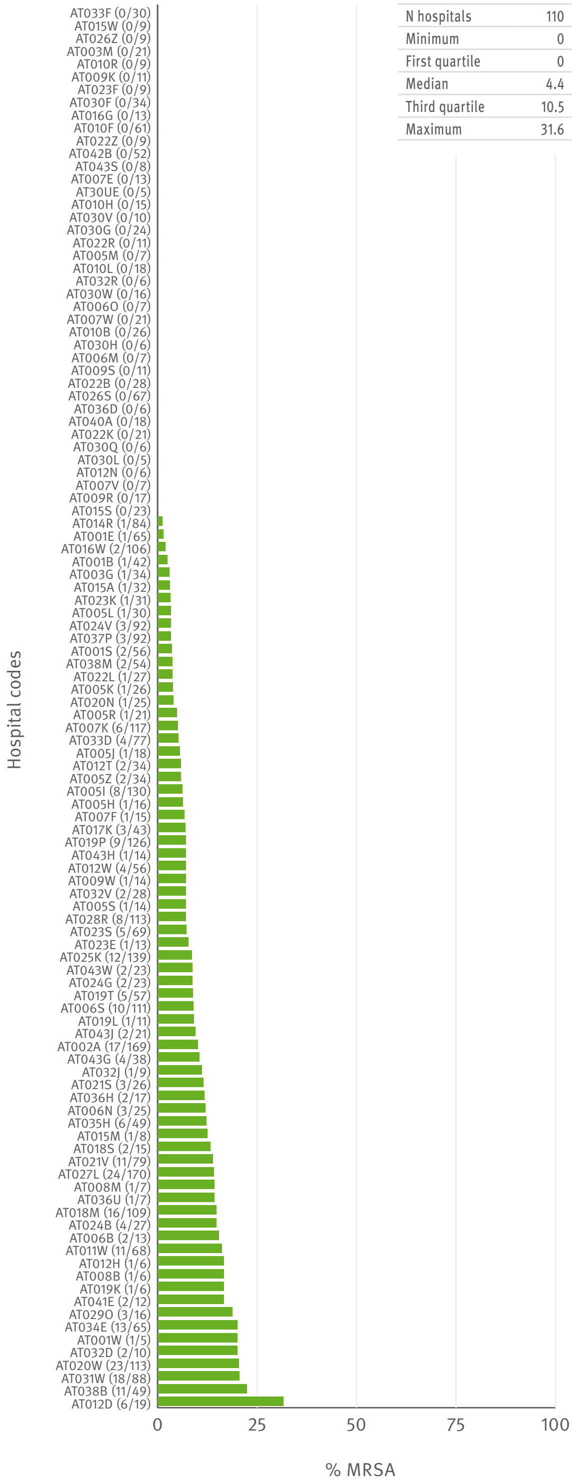
Austria

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**



N laboratories	36
Minimum	0
First quartile	0
Median	0
Third quartile	7.5
Maximum	33.3

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



N hospitals	110
Minimum	0
First quartile	0
Median	4.4
Third quartile	10.5
Maximum	31.6

Figure 3: ***E. coli***: **percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	122
Minimum	0
First quartile	14.3
Median	20.1
Third quartile	25.9
Maximum	57.1

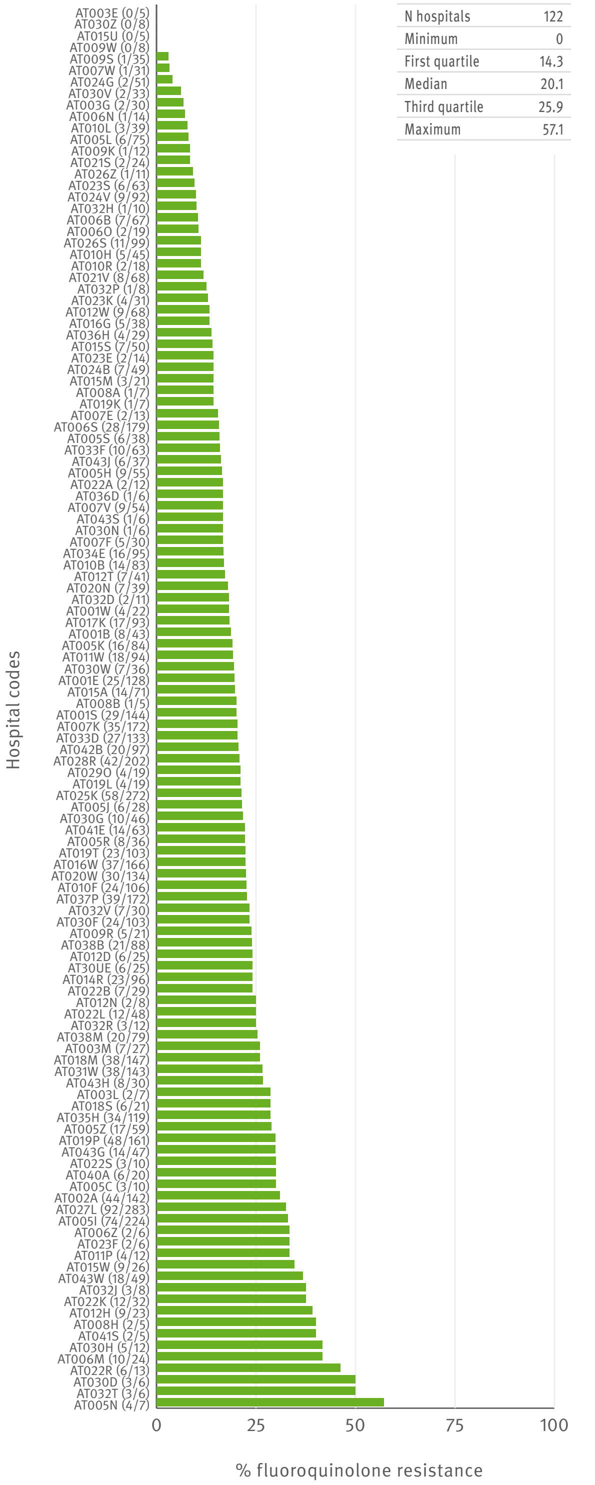
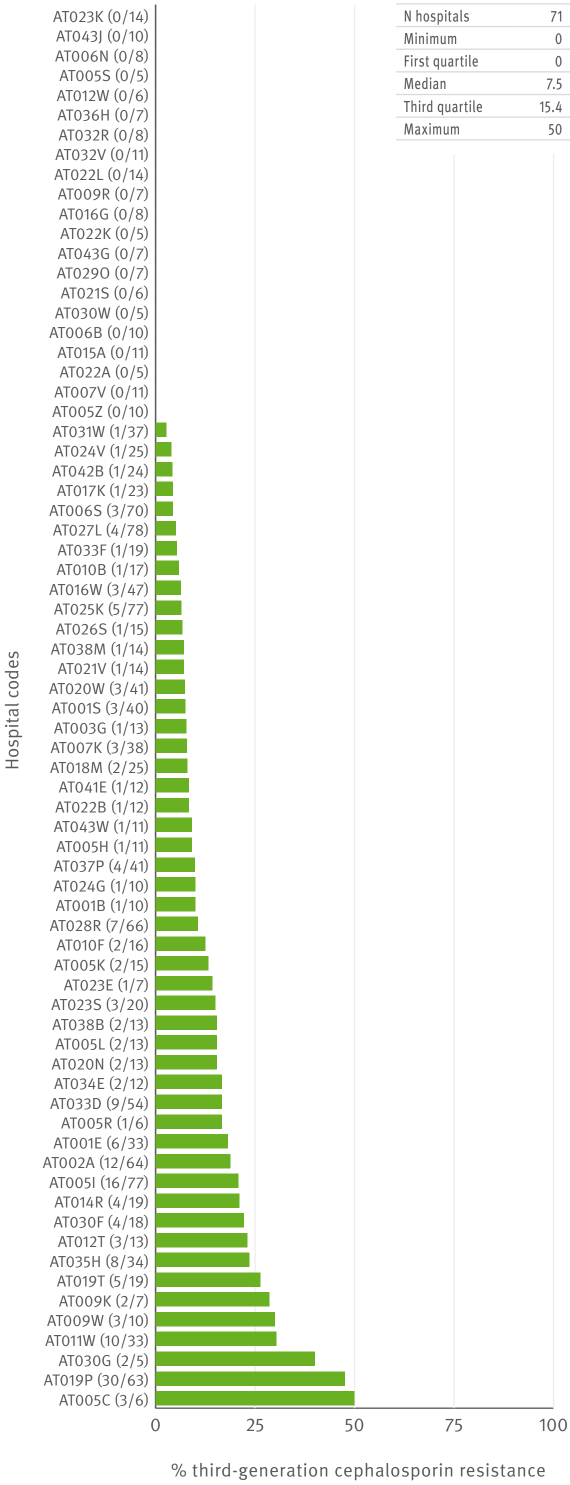


Figure 4: ***K. pneumoniae***: **percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	71
Minimum	0
First quartile	0
Median	7.5
Third quartile	15.4
Maximum	50



Belgium

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	1582	41	4138	41	752	41	549	40	392

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	3	4	3	<1	<1	<1	<1	<1
Penicillin RI	12	9	12	10	9	8	<1	<1	<1	2
Macrolides RI	34	33	31	31	25	24	23	25	26	25
Staphylococcus aureus										
Oxacillin/Meticillin R	30	33	31	22	23	21	21	21	17	16
Escherichia coli										
Aminopenicilins R	50	50	53	54	57	55	56	57	59	56
Aminoglycosides R	5	5	4	6	5	4	7	6	9	6
Fluoroquinolones R	12	15	17	19	19	17	20	22	22	22
3rd gen. Cephalosporins R	3	3	4	3	4	4	6	5	6	7
Carbapenems R	-	-	-	-	-	-	-	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	1	2	<1	<1	<1	3	1	2	2	2
HL Gentamicin R	17	22	26	30	26	30	23	18	18	25
Vancomycin R	1	<1	<1	<1	1	<1	1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	78	63	61	67	68	76	90	89	83	78
HL Gentamicin R	<1	11	22	19	23	17	32	30	33	39
Vancomycin R	<1	5	14	4	<1	5	4	3	7	1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	-	-	-	10	2	8	11
Fluoroquinolones R	-	-	-	-	-	-	13	13	15	17
3rd gen. Cephalosporins R	-	-	-	-	-	-	15	13	14	16
Carbapenems R	-	-	-	-	-	-	1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	-	-	-	7	12	15	10
Ceftazidime R	-	-	-	-	-	-	6	7	9	8
Carbapenems R	-	-	-	-	-	-	9	5	11	10
Aminoglycosides R	-	-	-	-	-	-	12	11	13	11
Fluoroquinolones R	-	-	-	-	-	-	16	12	21	18

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	96	0	100	21	100	21	100	1	100	3	100	14	100	7
CSF	4	8	-	-	0	0	-	-	-	-	0	0	0	0
Gender														
Male	55	0	62	22	46	24	64	1	56	5	57	13	68	4
Female	44	0	37	19	53	18	35	0	42	2	42	15	32	13
Unknown	1	0	1	7	<1	40	1	0	1	0	0	0	-	-
Age (years)														
0–4	17	1	4	16	2	11	3	0	1	0	5	13	3	0
5–19	5	1	2	9	1	26	0	0	-	-	-	-	2	0
20–64	37	0	34	17	30	17	28	0	33	2	29	15	25	9
65 and over	41	0	59	24	67	23	68	1	64	4	65	13	71	6
Unknown	-	-	-	-	-	-	1	0	1	0	-	-	-	-
Hospital department														
ICU	7	1	1	4	1	37	7	0	7	0	-	-	-	-
Internal med.	15	0	2	16	1	27	10	3	10	0	-	-	-	-
Surgery	1	0	1	27	<1	29	3	0	1	0	-	-	-	-
Other	15	0	5	16	1	67	5	0	7	0	-	-	-	-
Unknown	63	0	91	21	97	20	75	0	76	5	100	14	100	7

Belgium

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	94
Minimum	0
First quartile	0
Median	0
Third quartile	1.6
Maximum	28.6

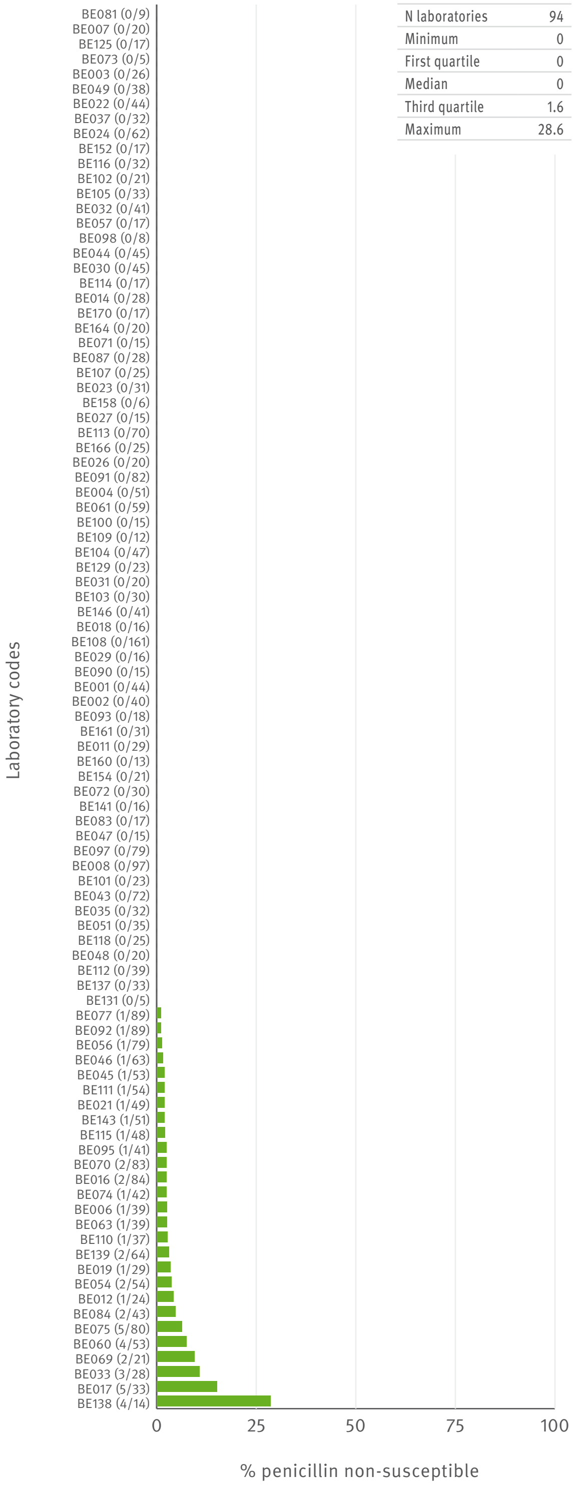


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	55
Minimum	0
First quartile	10.5
Median	16.2
Third quartile	21.4
Maximum	50

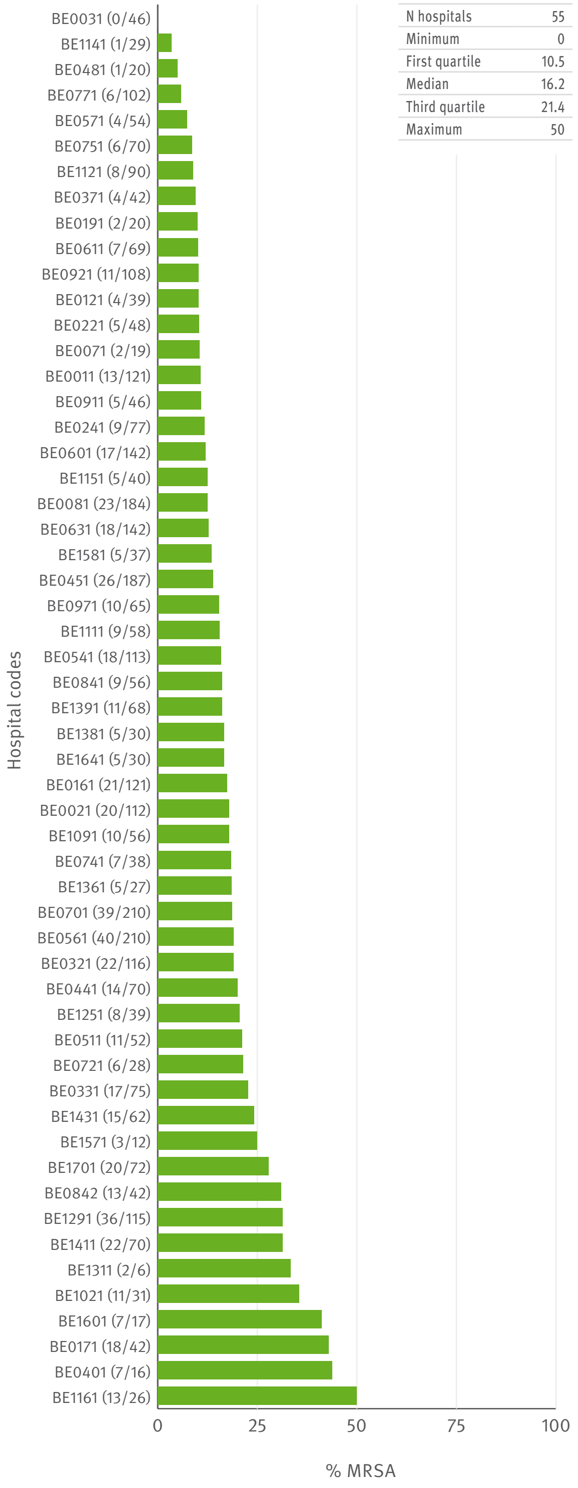
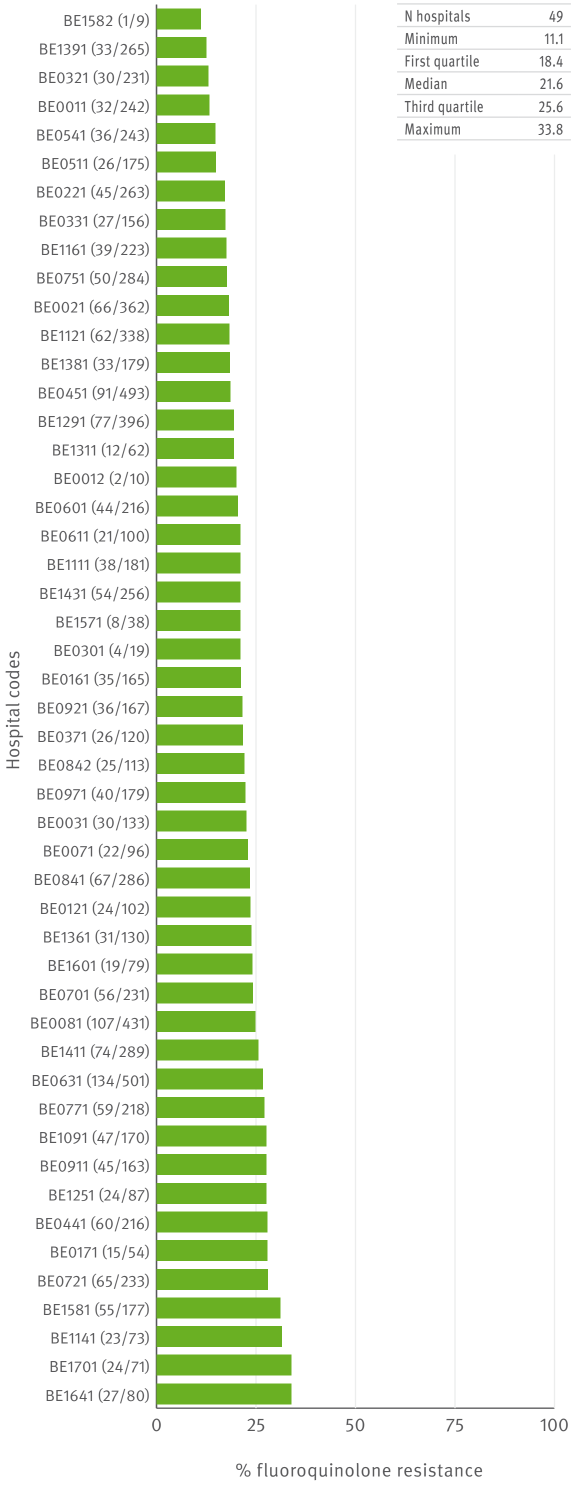
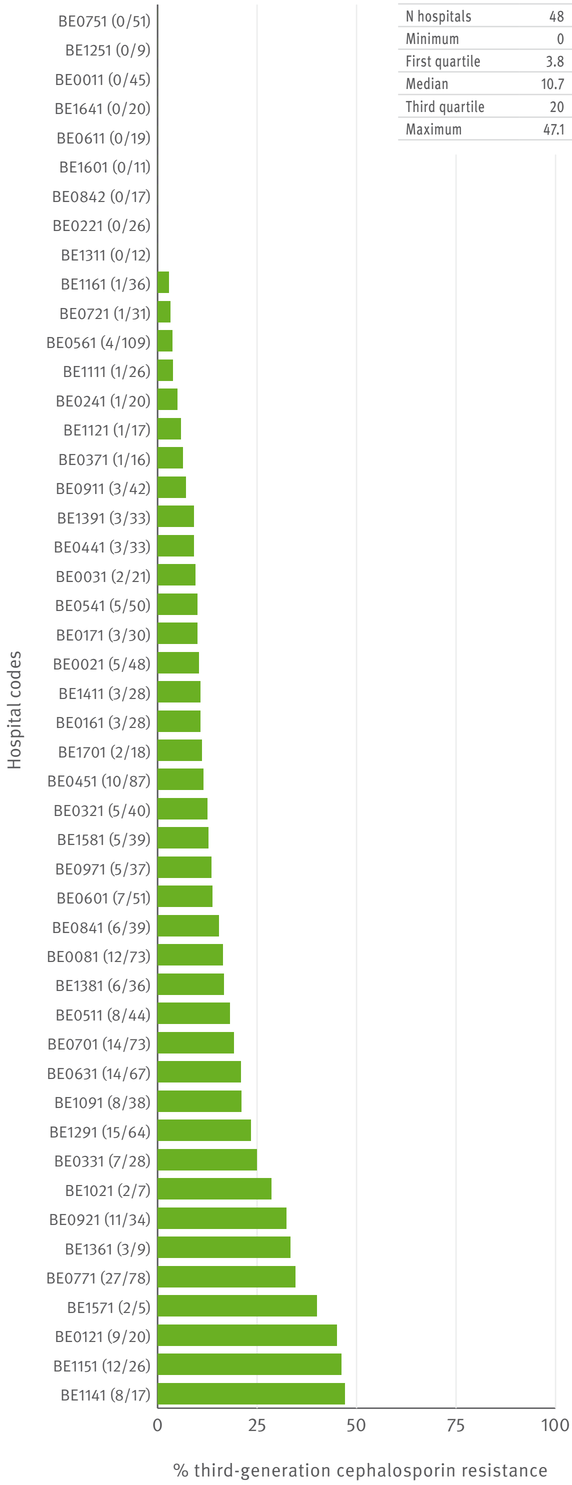


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	49
Minimum	11.1
First quartile	18.4
Median	21.6
Third quartile	25.6
Maximum	33.8

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	48
Minimum	0
First quartile	3.8
Median	10.7
Third quartile	20
Maximum	47.1

Bulgaria

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	9	22	30	7	9	21	22	18	21	29
Penicillin RI	14	22	33	7	16	21	37	18	21	29
Macrolides RI	11	17	8	15	17	4	27	25	13	20
Staphylococcus aureus										
Oxacillin/Meticillin R	31	23	29	28	13	25	16	19	22	20
Escherichia coli										
Aminopenicilins R	54	64	69	64	70	65	66	72	61	71
Aminoglycosides R	22	20	24	28	20	31	18	16	17	26
Fluoroquinolones R	19	24	29	26	35	32	28	33	30	34
3rd gen. Cephalosporins R	18	22	28	29	23	29	19	25	23	38
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	3
Enterococcus faecalis										
Aminopenicilins RI	7	15	8	31	13	8	16	5	6	12
HL Gentamicin R	36	33	24	53	29	44	36	41	31	38
Vancomycin R	<1	2	<1	2	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	60	59	96	97	100	93	96	100	84	95
HL Gentamicin R	60	62	56	79	75	84	65	71	79	71
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	53	60	59	59	65	69	72	54
Fluoroquinolones R	-	-	26	24	41	52	48	52	51	47
3rd gen. Cephalosporins R	-	-	50	60	55	73	69	76	81	75
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	2
Pseudomonas aeruginosa										
Piperacillin R	-	-	50	33	14	48	33	15	23	26
Ceftazidime R	-	-	45	13	21	55	23	19	31	35
Carbapenems R	-	-	38	14	7	17	24	31	29	31
Aminoglycosides R	-	-	53	42	29	48	31	21	38	33
Fluoroquinolones R	-	-	47	17	14	36	33	21	30	33

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	63	29	100	21	99	32	100	0	100	0	99	78	98	31
CSF	37	15	-	-	1	25	-	-	-	-	1	67	2	0
Gender														
Male	52	29	60	23	54	36	61	0	65	0	71	80	63	40
Female	48	19	40	18	46	28	39	0	35	0	29	73	37	14
Unknown	-	-	<1	50	0	0	-	-	-	-	-	-	-	-
Age (years)														
0–4	9	80	2	60	3	21	1	0	5	0	9	91	4	0
5–19	13	14	4	33	2	22	3	0	1	0	3	75	3	0
20–64	52	21	47	23	38	32	40	0	48	0	35	76	40	43
65 and over	20	18	35	15	46	33	48	0	35	0	29	72	39	18
Unknown	6	0	12	18	11	36	9	0	11	0	23	83	13	46
Hospital department														
ICU	22	17	20	40	18	48	24	0	31	0	22	84	36	53
Internal med.	22	17	36	8	44	26	34	0	23	0	21	57	21	10
Surgery	-	-	12	31	11	30	11	0	17	0	13	84	8	0
Other	56	30	32	20	26	34	30	0	27	0	43	83	34	26
Unknown	-	-	0	0	0	0	1	0	1	0	1	67	-	-

Bulgaria

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	4
Minimum	0
First quartile	6.3
Median	14.6
Third quartile	27.1
Maximum	37.5

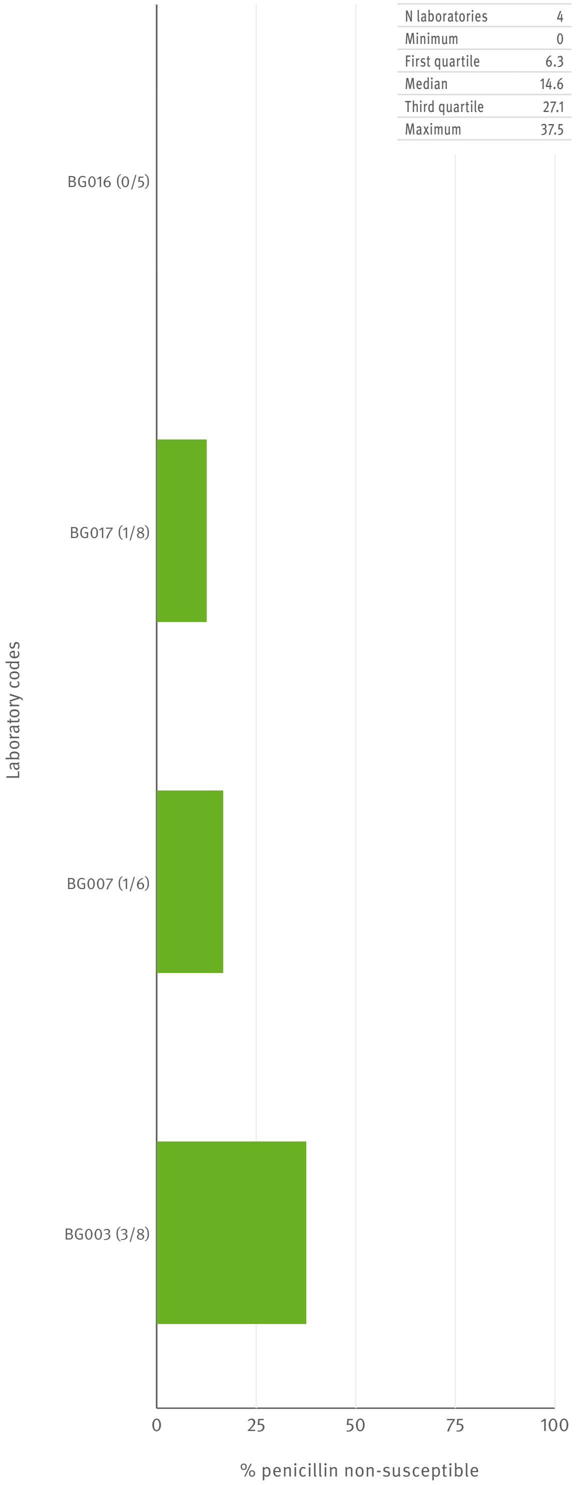


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	20
Minimum	0
First quartile	9.5
Median	13.8
Third quartile	22.5
Maximum	75

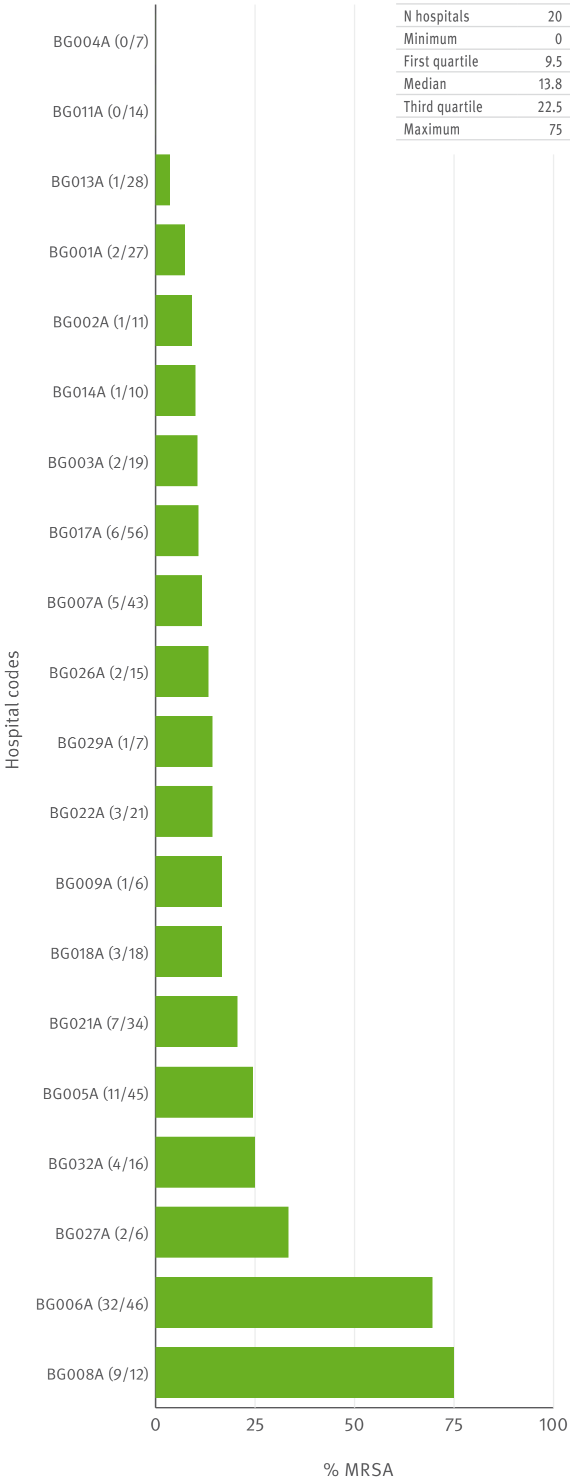
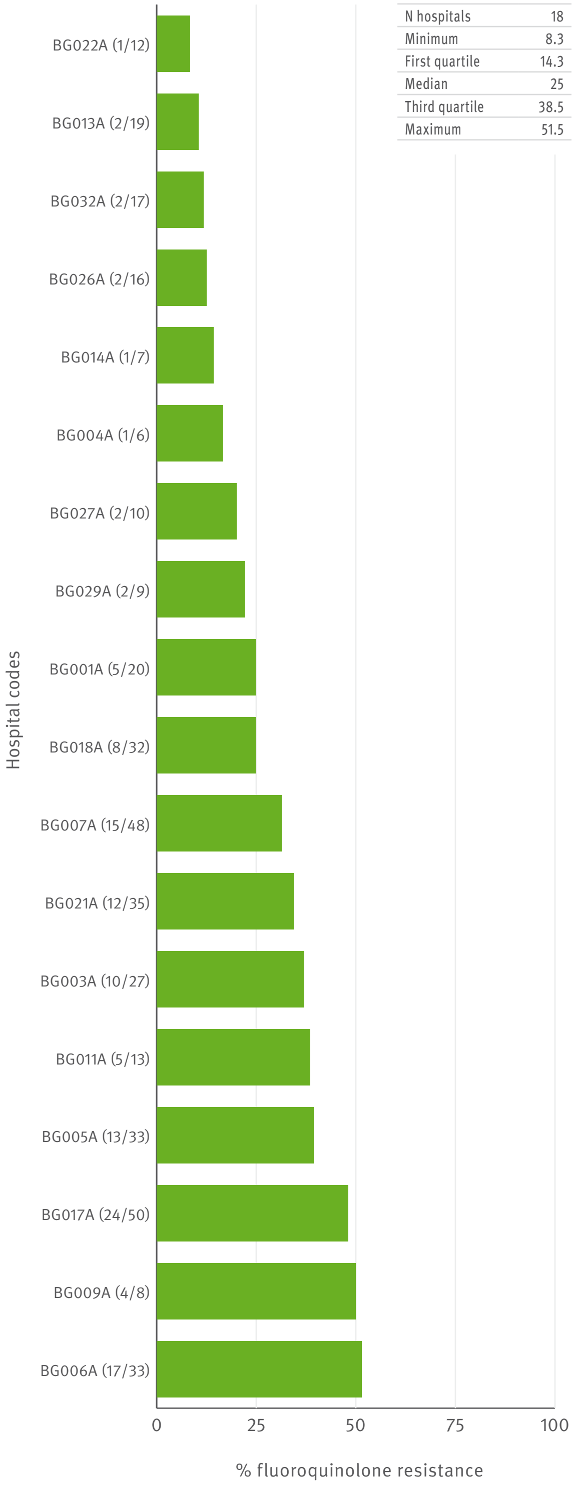
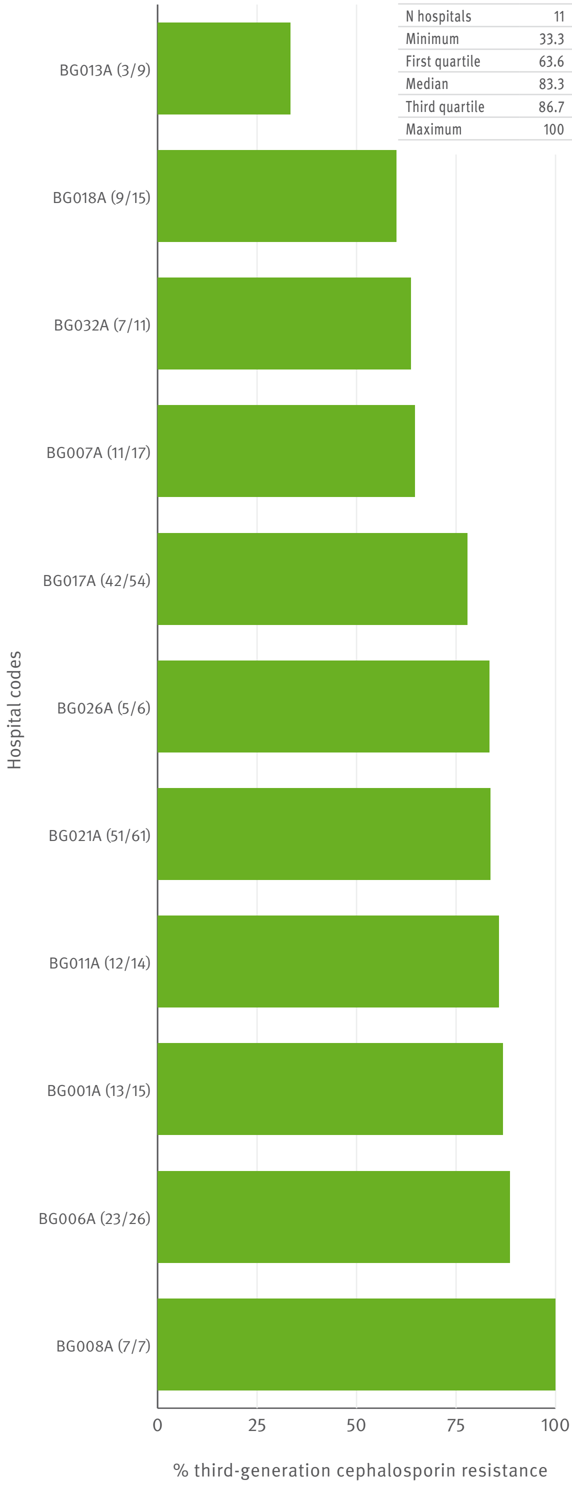


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	18
Minimum	8.3
First quartile	14.3
Median	25
Third quartile	38.5
Maximum	51.5

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	11
Minimum	33.3
First quartile	63.6
Median	83.3
Third quartile	86.7
Maximum	100

Croatia

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2003	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-
2009	14	100	14	463	16	911	20	223	16	318	15	212
2010	11	103	15	363	16	897	12	176	16	286	15	217
2011	16	127	14	451	16	1007	15	244	14	314	15	265
2012	11	98	17	412	17	921	14	219	15	344	14	204

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	-	-	-	-	-	-	3	7	1	1
Penicillin RI	-	-	-	-	-	-	15	21	18	23
Macrolides RI	-	-	-	-	-	-	23	29	24	28
Staphylococcus aureus										
Oxacillin/Meticillin R	-	-	-	-	-	-	35	27	27	22
Escherichia coli										
Aminopenicilins R	-	-	-	-	-	-	54	55	55	51
Aminoglycosides R	-	-	-	-	-	-	6	6	7	7
Fluoroquinolones R	-	-	-	-	-	-	17	17	20	17
3rd gen. Cephalosporins R	-	-	-	-	-	-	7	8	7	6
Carbapenems R	-	-	-	-	-	-	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	-	-	-	-	-	-	10	5	1	5
HL Gentamicin R	-	-	-	-	-	-	41	37	33	39
Vancomycin R	-	-	-	-	-	-	<1	<1	1	<1
Enterococcus faecium										
Aminopenicilins RI	-	-	-	-	-	-	89	82	98	98
HL Gentamicin R	-	-	-	-	-	-	67	60	66	61
Vancomycin R	-	-	-	-	-	-	7	12	2	0
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	-	-	-	45	49	43	45
Fluoroquinolones R	-	-	-	-	-	-	47	48	43	43
3rd gen. Cephalosporins R	-	-	-	-	-	-	50	56	50	44
Carbapenems R	-	-	-	-	-	-	<1	2	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	-	-	-	27	16	-	18
Ceftazidime R	-	-	-	-	-	-	12	12	17	13
Carbapenems R	-	-	-	-	-	-	22	26	30	22
Aminoglycosides R	-	-	-	-	-	-	34	26	34	26
Fluoroquinolones R	-	-	-	-	-	-	29	27	34	24

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	92	21	98	25	99	19	96	1	100	100	97	41	96	22
CSF	8	12	-	33	2	-	3	0	0	0	1	89	3	50
Gender														
Male	54	21	58	22	40	25	61	<1	54	0	55	49	65	22
Female	44	19	37	27	56	14	32	2	42		41	34	29	21
Unknown	<1	0	5	30	4	19	6	0	4	0	33	36	6	39
Age (years)														
0–4	26	25	3	3	3	5	9	0	5	0	12	48	4	35
5–19	7	19	4	3	1	20	3	0	0	0	3	61	2	27
20–64	34	20	37	24	34	21	35	2	39	0	36	45	42	32
65 and over	32	18	56	28	61	18	52	1	54	1	48	51	50	14
Unknown	0	0	1	33	16	1	1	0	1	0	1	17	1	0
Hospital department														
ICU	11	21	10	76	6	19	1	0	0	0	17	61	22	28
Internal med.	17	13	39	18	40	20	31	1	<1	100	35	30	28	14
Surgery	3	33	12	45	6	68	11	3	0	0	11	68	17	25
Other	67	23	38	18	48	15	40	1	99	0	36	38	33	6

Croatia

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	9
Minimum	0
First quartile	16.6
Median	20.5
Third quartile	25
Maximum	50

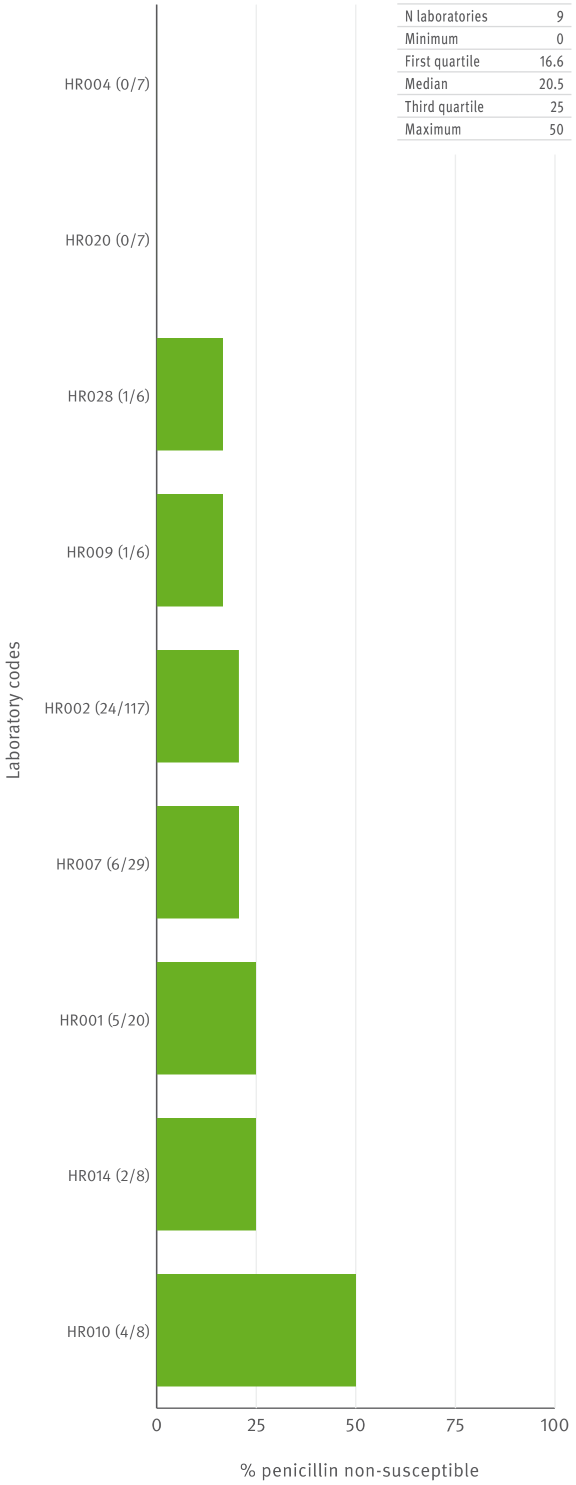


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	15
Minimum	0
First quartile	4.2
Median	20
Third quartile	28.3
Maximum	36.2

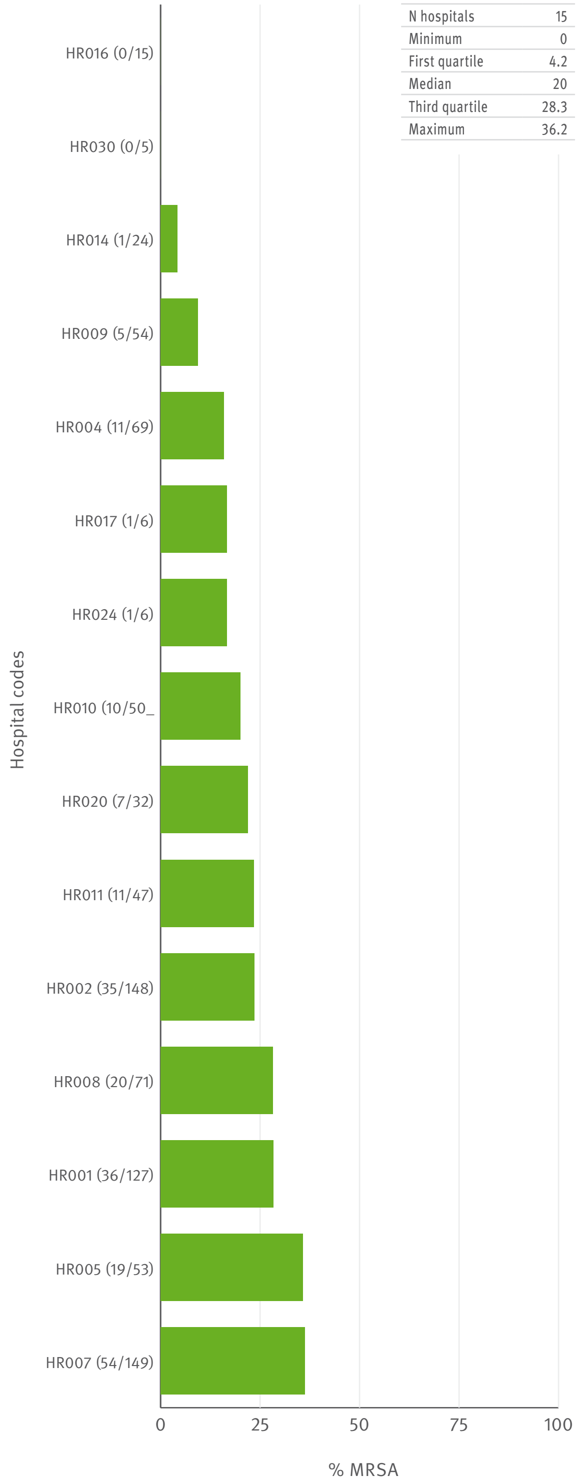


Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	16
Minimum	9.1
First quartile	15.4
Median	18.2
Third quartile	21.9
Maximum	29.9

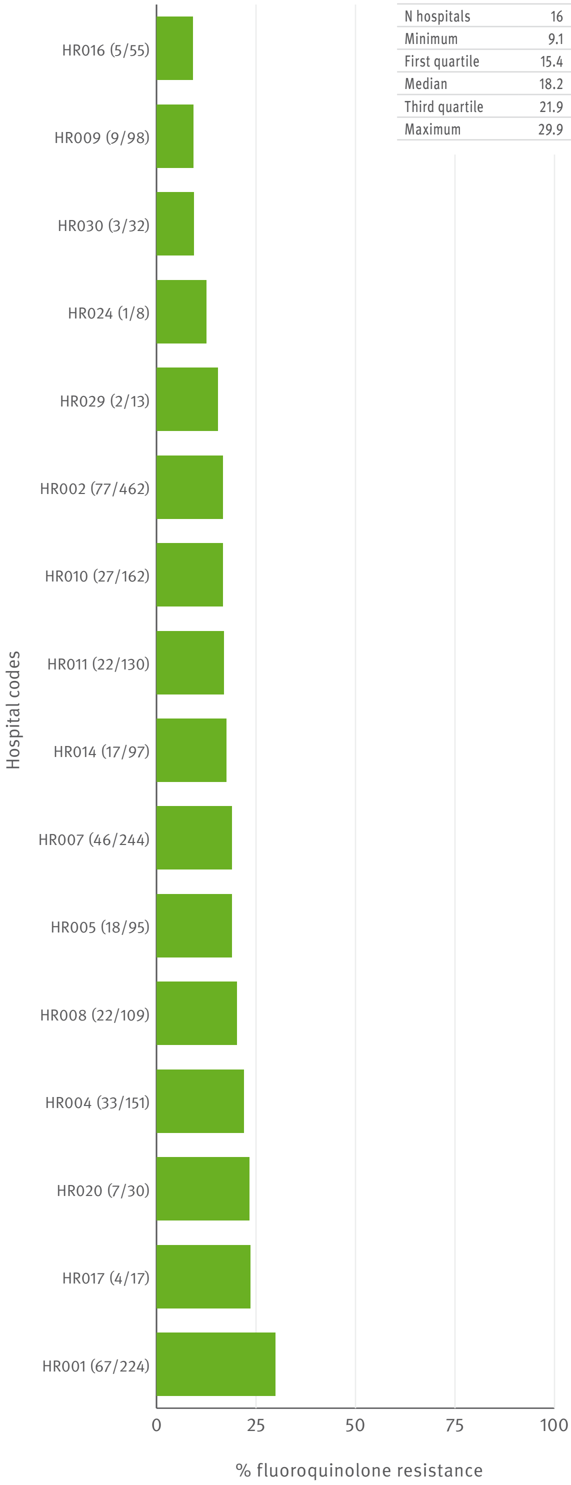


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	12
Minimum	36.8
First quartile	41
Median	42.1
Third quartile	55.6
Maximum	63.6

Cyprus

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	31	7	21	18	33	25	25
Penicillin RI	<1	14	19	38	33	43	36	42	25	25
Macrolides RI	33	<1	13	31	27	29	36	55	25	14
Staphylococcus aureus										
Oxacillin/Meticillin R	64	49	56	34	48	46	33	32	42	35
Escherichia coli										
Aminopenicilins R	63	61	72	62	72	58	66	62	78	70
Aminoglycosides R	11	11	13	10	11	10	10	16	24	21
Fluoroquinolones R	32	22	29	35	39	45	43	43	47	42
3rd gen. Cephalosporins R	11	9	16	16	18	19	14	20	36	32
Carbapenems R	<1	<1	<1	<1	2	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	3	3	5	2	16	32	6	2	1
HL Gentamicin R	43	77	71	44	61	65	66	24	19	10
Vancomycin R	<1	3	<1	<1	<1	1	<1	<1	4	<1
Enterococcus faecium										
Aminopenicilins RI	100	100	80	43	92	60	80	78	82	76
HL Gentamicin R	-	33	<1	14	33	10	13	<1	6	<1
Vancomycin R	<1	33	40	14	25	20	13	<1	<1	10
Klebsiella pneumoniae										
Aminoglycosides R	-	-	11	12	13	21	19	19	28	18
Fluoroquinolones R	-	-	22	12	23	23	43	39	36	22
3rd gen. Cephalosporins R	-	-	33	27	31	35	42	34	41	23
Carbapenems R	-	-	<1	<1	3	10	17	16	16	9
Pseudomonas aeruginosa										
Piperacillin R	-	-	13	27	31	23	18	19	20	10
Ceftazidime R	-	-	38	24	15	9	18	17	24	15
Carbapenems R	-	-	13	11	19	19	8	29	43	19
Aminoglycosides R	-	-	13	11	25	21	5	10	16	15
Fluoroquinolones R	-	-	13	27	23	38	13	17	14	15

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	90	17	100	38	100	44	100	2	100	7	99	33	98	31
CSF	10	100	-	-	<1	100	-	-	-	-	1	50	2	50
Gender														
Male	55	18	62	37	47	58	53	0	50	9	52	39	64	32
Female	40	25	33	38	51	32	44	0	46	5	44	29	32	24
Unknown	5	100	5	50	2	40	4	40	4	0	4	0	4	75
Age (years)														
0–4	10	50	4	33	4	33	5	0	11	0	3	20	4	0
5–19	5	0	1	33	1	50	-	-	-	-	1	0	1	0
20–64	20	0	29	38	22	44	28	0	26	8	35	37	31	38
65 and over	30	50	42	38	47	47	45	0	48	5	34	37	45	24
Unknown	35	14	23	37	27	41	22	7	15	14	26	26	19	45
Hospital department														
ICU	5	0	21	51	10	56	41	2	22	0	32	51	42	33
Internal med.	65	23	56	29	69	46	41	0	48	9	44	23	32	21
Surgery	-	-	11	65	5	69	8	0	2	0	13	47	8	63
Other	15	0	5	29	10	23	4	0	13	17	10	7	13	23
Unknown	15	67	8	33	6	26	6	13	15	0	1	0	6	50

Cyprus

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	2
Minimum	20
First quartile	20
Median	25.4
Third quartile	30.8
Maximum	30.8

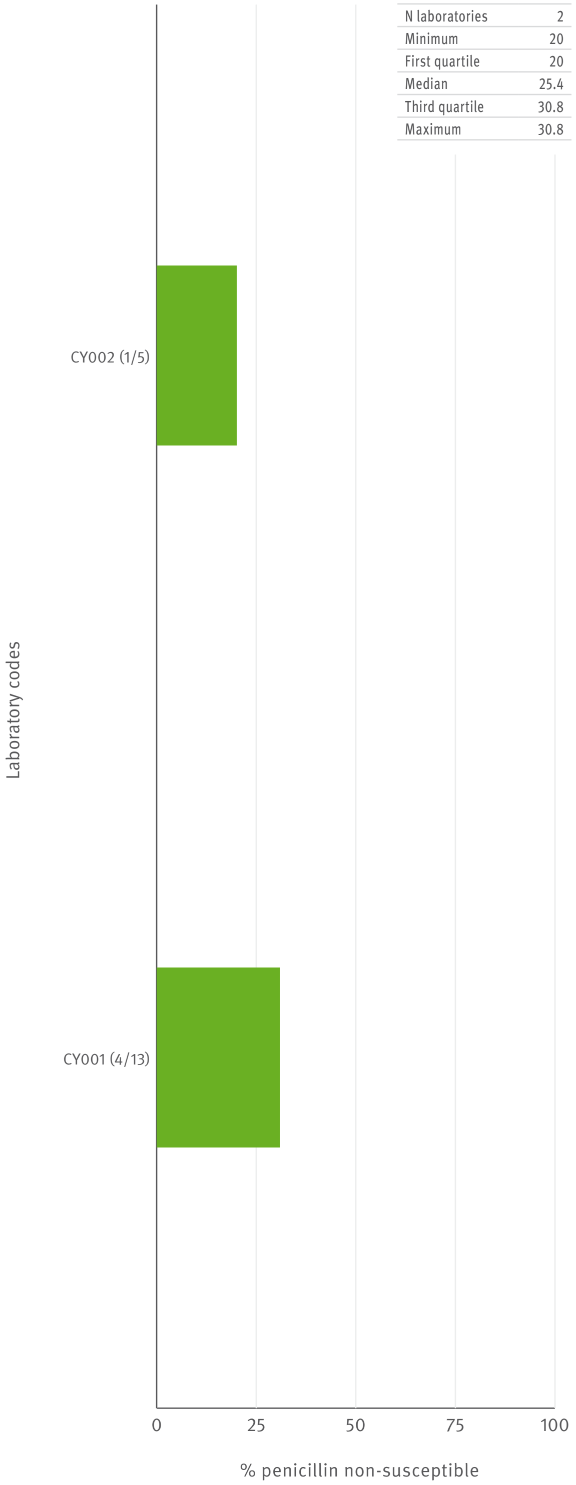


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	5
Minimum	21.4
First quartile	31.3
Median	33.9
Third quartile	41.3
Maximum	46.7

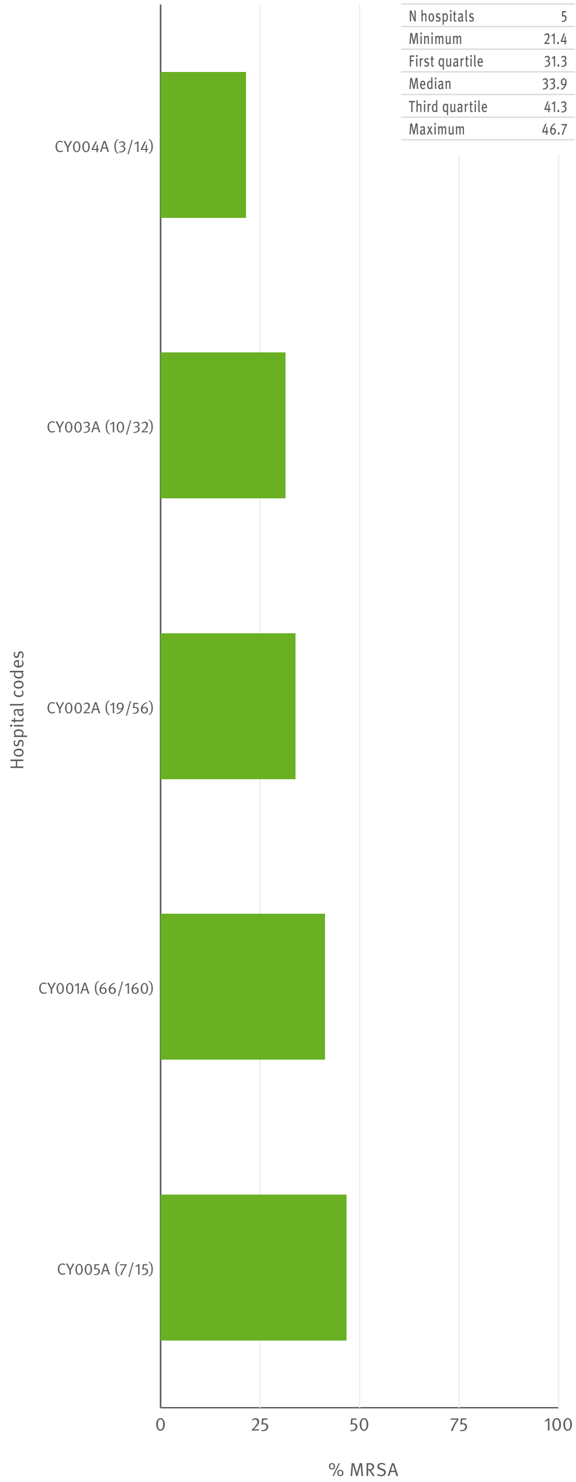
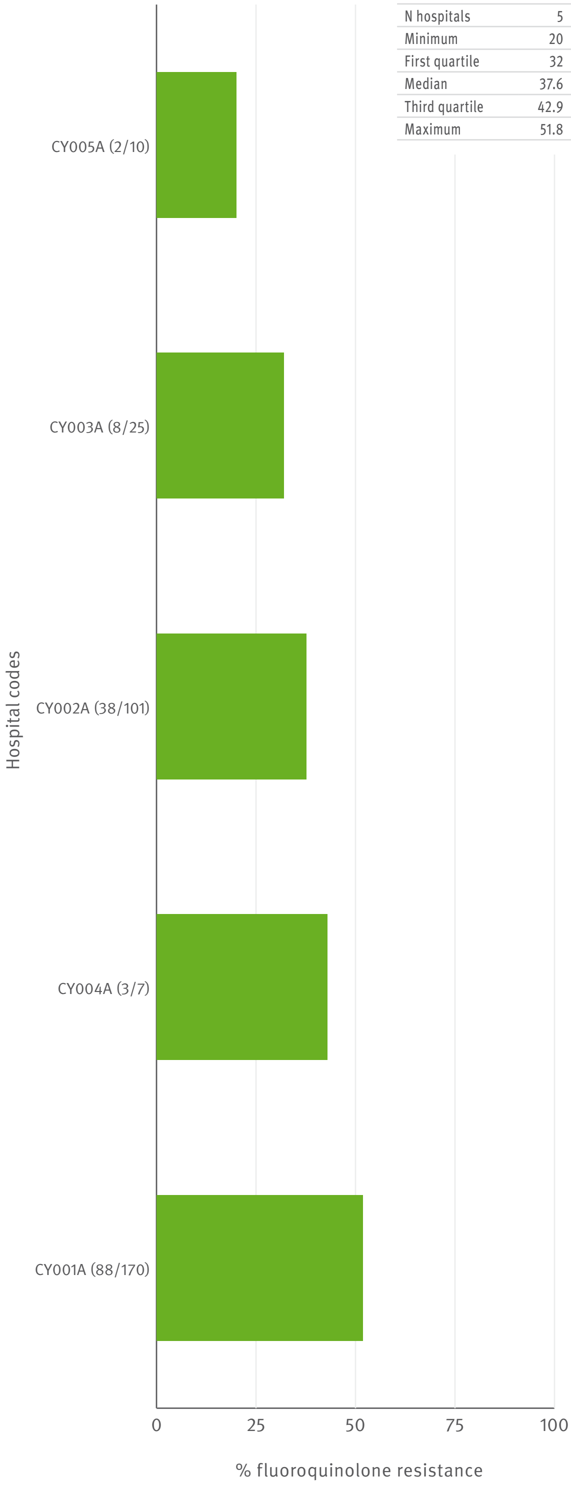
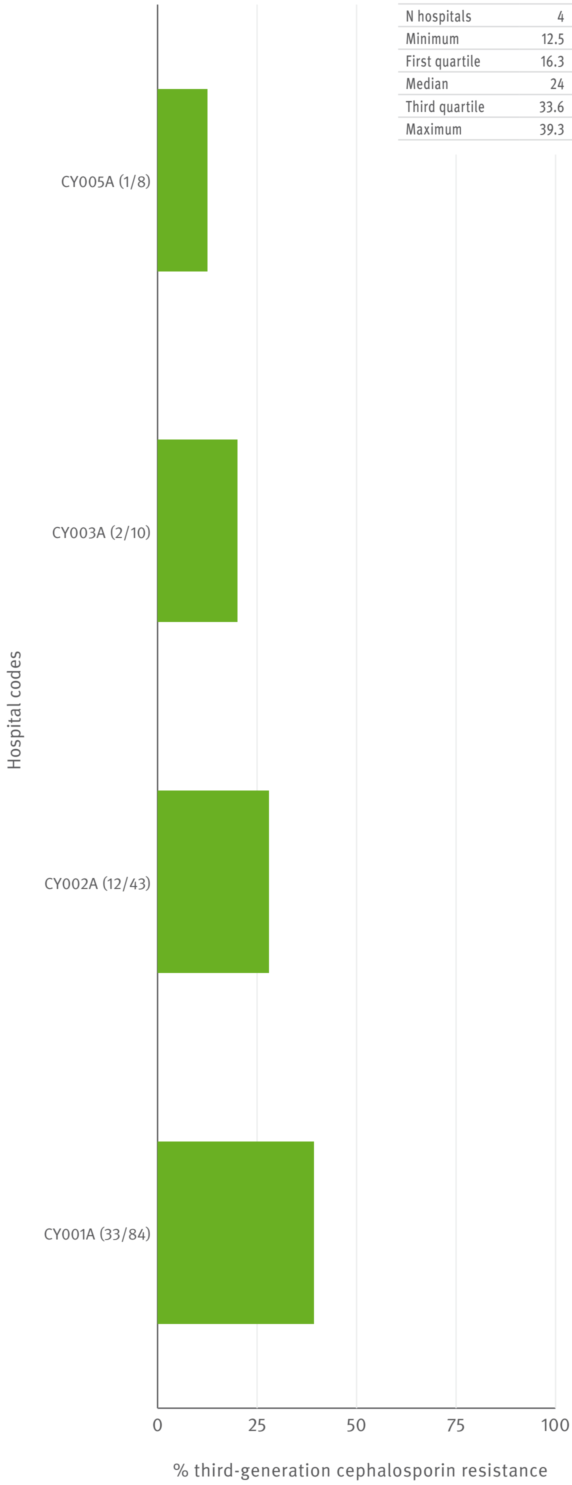


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	5
Minimum	20
First quartile	32
Median	37.6
Third quartile	42.9
Maximum	51.8

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	4
Minimum	12.5
First quartile	16.3
Median	24
Third quartile	33.6
Maximum	39.3

Czech Republic

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	2	<1	<1	<1	<1	<1	<1	<1	<1
Penicillin RI	2	6	4	2	4	3	4	5	4	3
Macrolides RI	2	4	2	3	5	3	5	6	3	8
Staphylococcus aureus										
Oxacillin/Meticillin R	6	9	13	12	13	14	15	13	15	13
Escherichia coli										
Aminopenicilins R	45	47	50	56	56	60	61	59	61	57
Aminoglycosides R	5	5	6	8	7	9	9	8	9	8
Fluoroquinolones R	13	16	20	23	24	26	23	23	23	21
3rd gen. Cephalosporins R	1	2	2	5	7	10	10	10	11	11
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	4	<1	<1	2	3	2	<1	8	4	2
HL Gentamicin R	44	43	45	43	49	49	47	48	46	42
Vancomycin R	<1	<1	<1	<1	1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	80	81	92	90	91	94	98	98	97	98
HL Gentamicin R	48	43	69	74	79	75	65	54	61	69
Vancomycin R	3	3	14	4	6	8	6	5	8	11
Klebsiella pneumoniae										
Aminoglycosides R	-	-	36	38	43	42	47	47	45	54
Fluoroquinolones R	-	-	38	47	48	52	54	55	53	50
3rd gen. Cephalosporins R	-	-	32	35	46	48	52	48	48	51
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	21	29	30	27	28	28	22	26
Ceftazidime R	-	-	40	30	33	44	29	28	20	20
Carbapenems R	-	-	31	33	36	29	29	16	13	15
Aminoglycosides R	-	-	27	29	32	43	33	33	24	24
Fluoroquinolones R	-	-	45	47	43	46	41	41	34	31

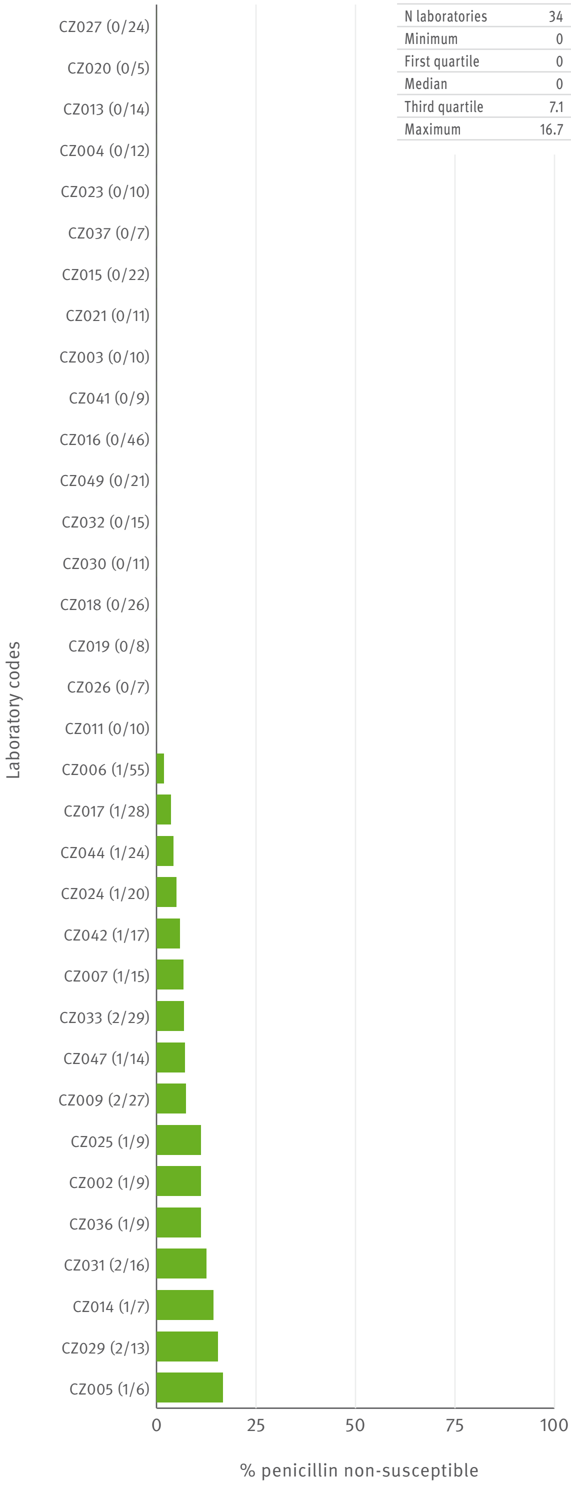
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	84	3	100	14	100	22	100	1	100	10	99	50	99	14
CSF	16	3	-	-	0	0	-	-	-	-	1	57	1	0
Gender														
Male	64	3	62	13	44	27	64	1	59	8	60	51	64	14
Female	36	4	38	15	56	19	36	0	41	12	40	47	36	14
Age (years)														
0–4	5	4	4	1	2	11	4	2	0	0	2	34	2	12
5–19	6	0	2	1	1	18	1	7	2	11	1	63	2	5
20–64	48	2	42	12	29	20	38	1	49	15	39	54	39	18
65 and over	41	5	52	17	67	23	57	1	49	5	58	47	57	12
Hospital department														
ICU	27	3	27	17	20	27	45	1	43	4	41	58	47	17
Internal med.	32	4	42	14	49	20	27	1	19	7	30	39	23	9
Surgery	-	-	7	13	5	25	6	0	6	11	6	39	5	15
Other	32	4	23	10	27	23	23	2	32	18	22	52	25	13
Unknown	9	2	1	17	0	0	0	0	0	0	0	86	1	0

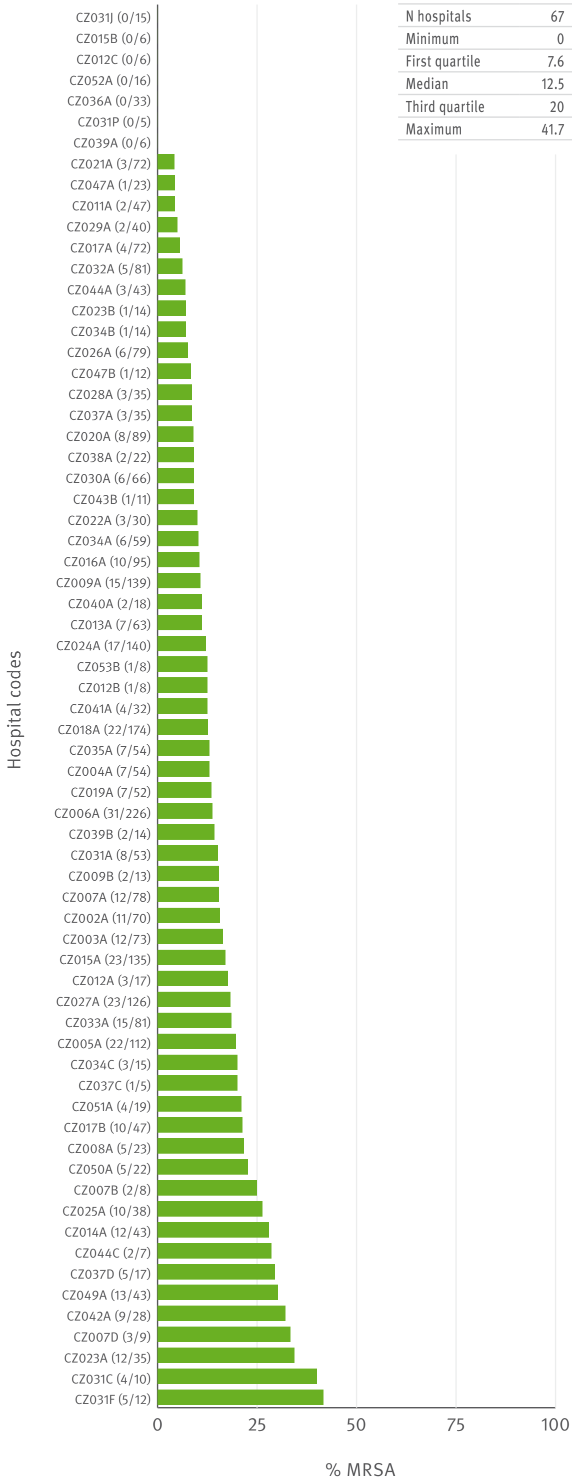
Czech Republic

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**



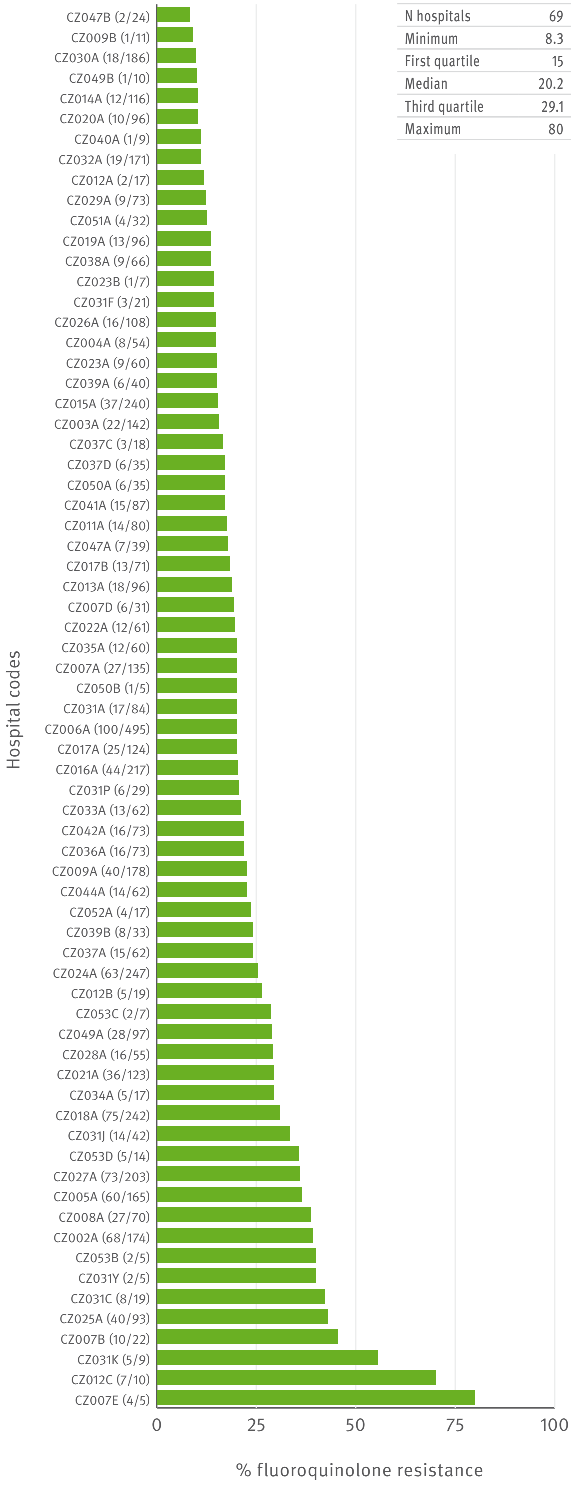
N laboratories	34
Minimum	0
First quartile	0
Median	0
Third quartile	7.1
Maximum	16.7

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



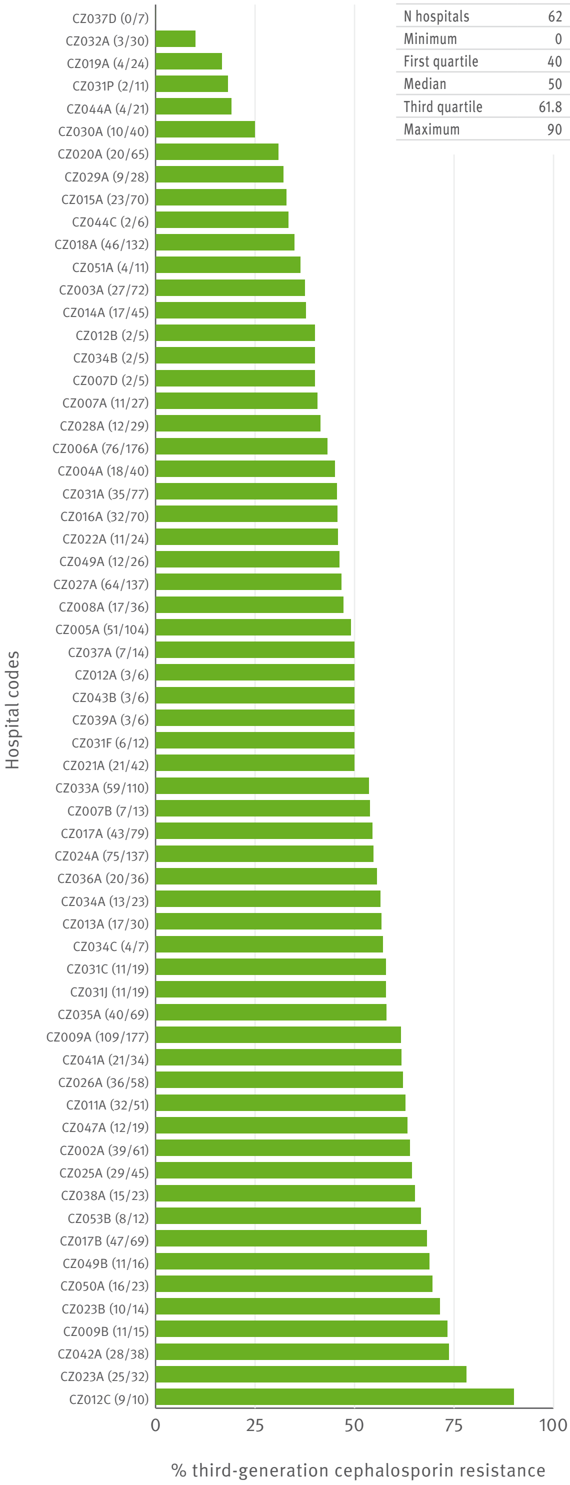
N hospitals	67
Minimum	0
First quartile	7.6
Median	12.5
Third quartile	20
Maximum	41.7

Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	69
Minimum	8.3
First quartile	15
Median	20.2
Third quartile	29.1
Maximum	80

Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	62
Minimum	0
First quartile	40
Median	50
Third quartile	61.8
Maximum	90

Denmark

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Penicillin RI	3	3	4	4	3	3	4	4	5	5
Macrolides RI	5	5	6	6	6	7	4	4	5	6
Staphylococcus aureus										
Oxacillin/Meticillin R	<1	1	2	2	<1	2	2	1	1	1
Escherichia coli										
Aminopenicilins R	-	-	40	42	43	43	43	46	48	45
Aminoglycosides R	-	-	2	3	4	4	4	6	6	7
Fluoroquinolones R	-	-	5	7	9	10	13	14	14	14
3rd gen. Cephalosporins R	-	-	1	2	3	4	6	8	8	8
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	-	-	-	<1	2	2	1	<1	<1	1
HL Gentamicin R	-	-	-	-	-	37	33	36	31	28
Vancomycin R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	-	-	-	87	88	88	88	93	93	94
HL Gentamicin R	-	-	-	-	-	61	52	74	73	62
Vancomycin R	-	-	-	<1	<1	<1	2	2	1	2
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	2	6	7	7	6	6	6
Fluoroquinolones R	-	-	-	6	13	16	16	11	12	9
3rd gen. Cephalosporins R	-	-	-	4	10	9	11	11	11	10
Carbapenems R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	-	3	2	2	4	5	5
Ceftazidime R	-	-	-	-	2	3	4	3	5	5
Carbapenems R	-	-	-	-	2	1	3	3	5	4
Aminoglycosides R	-	-	-	-	1	1	<1	1	2	4
Fluoroquinolones R	-	-	-	-	6	3	5	6	7	4

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	94	5	100	1	100	14	100	0	100	2	100	11	99	5
CSF	6	3	-	-	‹1	3	-	-	-	-	‹1	33	1	14
Gender														
Male	51	5	63	1	48	16	68	0	62	2	60	12	67	6
Female	49	5	37	1	50	12	28	0	36	2	38	9	30	3
Unknown	-	-	-	-	2	15	3	0	2	4	2	4	3	0
Age (years)														
0–4	4	8	3	1	1	9	3	0	1	0	1	29	1	0
5–19	3	2	2	1	1	15	1	0	0	0	2	21	1	9
20–64	37	3	36	2	27	17	26	0	39	2	31	12	28	7
65 and over	56	6	58	1	70	13	70	0	59	1	66	10	70	4
Hospital department														
ICU	-	-	-	-	4	15	8	0	28	2	6	15	6	7
Internal med.	-	-	-	-	40	13	42	0	22	1	41	9	40	6
Surgery	-	-	-	-	14	15	17	0	26	1	17	13	15	7
Other	-	-	-	-	37	15	26	0	19	2	32	11	33	2
Unknown	100	5	100	1	5	18	6	0	5	2	4	8	6	2

Denmark

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

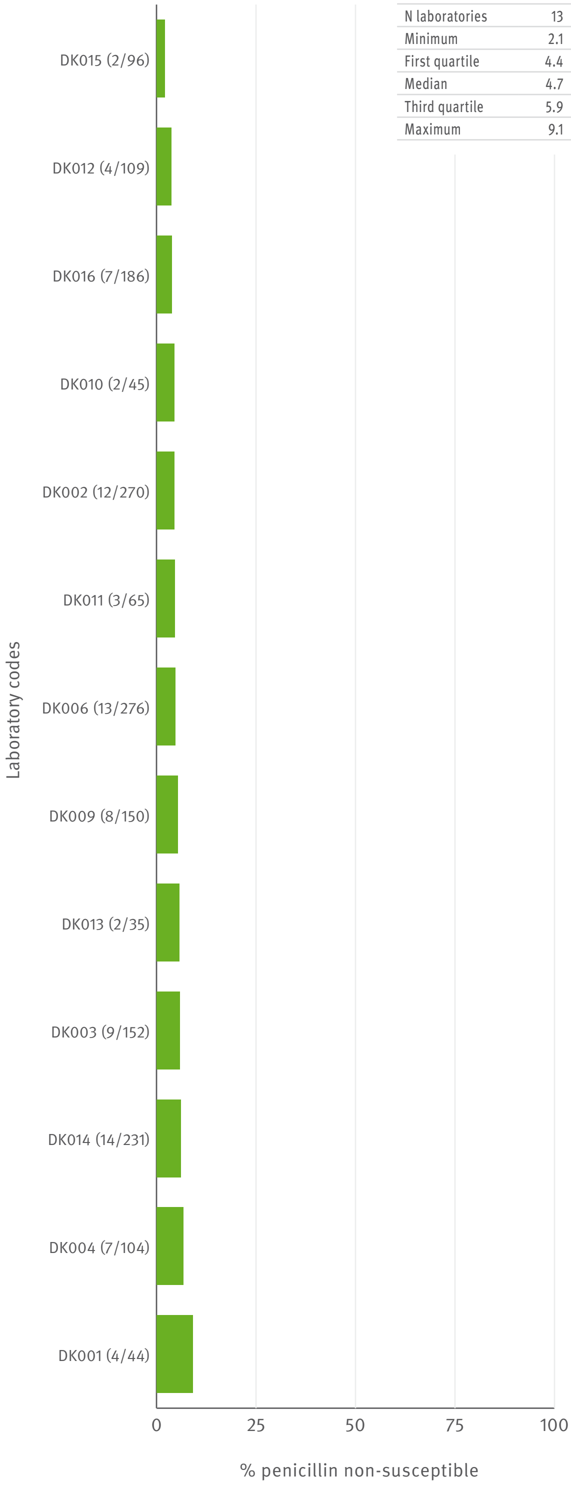


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

Figure 3: *E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)

N hospitals	46
Minimum	0
First quartile	9.6
Median	13.5
Third quartile	15.2
Maximum	30.8

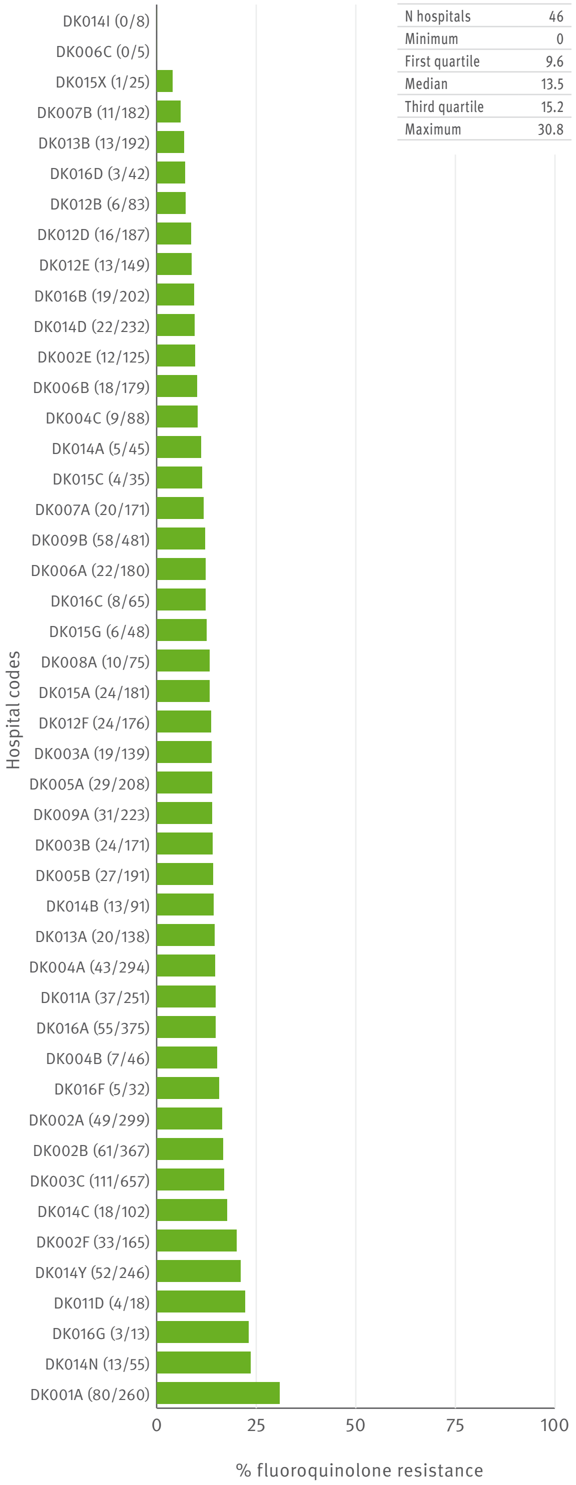
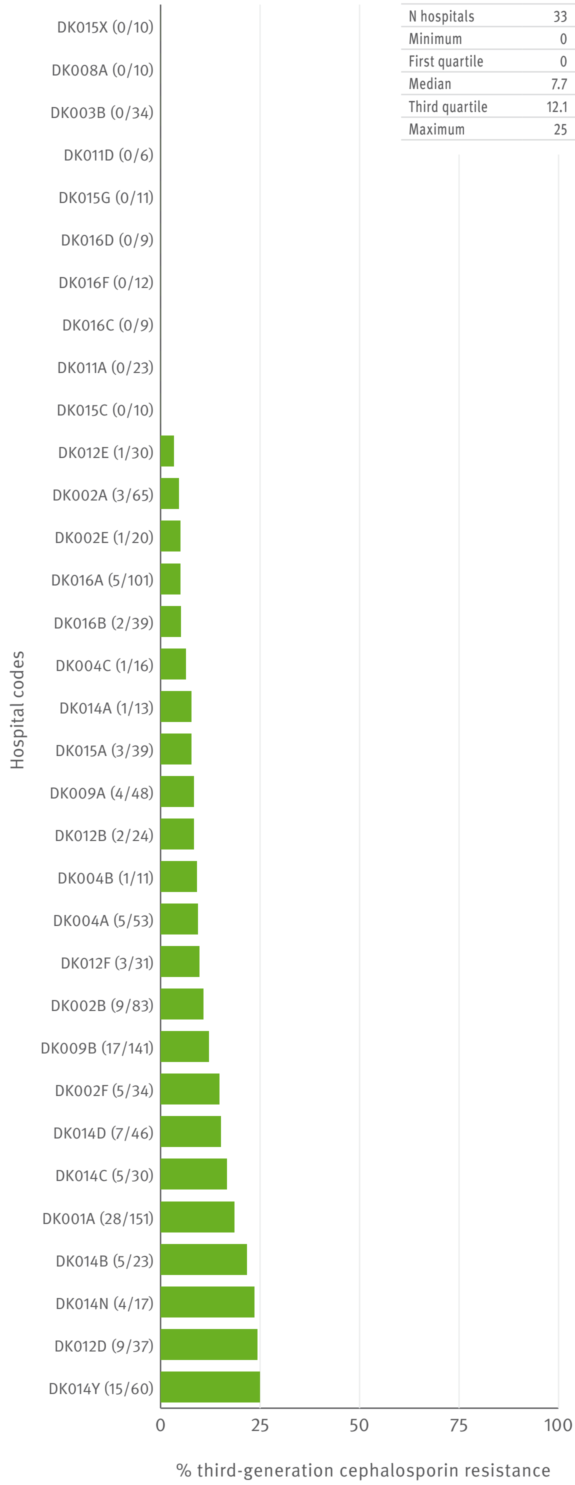


Figure 4: *K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)

N hospitals	33
Minimum	0
First quartile	0
Median	7.7
Third quartile	12.1
Maximum	25



Estonia

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	<1	<1	<1	<1	2	2	<1
Penicillin RI	<1	<1	2	2	<1	5	1	2	2	<1
Macrolides RI	10	6	<1	3	2	4	2	4	2	6
Staphylococcus aureus										
Oxacillin/Meticillin R	4	5	2	3	9	4	3	<1	2	8
Escherichia coli										
Aminopenicilins R	42	55	45	52	50	47	38	37	-	48
Aminoglycosides R	3	2	4	2	6	5	4	6	5	8
Fluoroquinolones R	5	6	5	7	7	7	8	8	10	14
3rd gen. Cephalosporins R	1	4	1	<1	1	5	2	6	12	8
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	4	14	14	9	<1	9	9	14	-	14
HL Gentamicin R	22	32	50	35	23	27	43	27	<1	42
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	75	79	83	84	94	85	90	90	-	89
HL Gentamicin R	50	79	74	78	89	75	79	67	25	63
Vancomycin R	<1	<1	<1	<1	<1	3	<1	<1	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	8	9	2	15	15	26	12	13
Fluoroquinolones R	-	-	<1	5	2	7	19	25	22	17
3rd gen. Cephalosporins R	-	-	8	9	3	12	17	17	40	18
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	1
Pseudomonas aeruginosa										
Piperacillin R	-	-	27	12	9	18	13	25	<1	16
Ceftazidime R	-	-	18	7	7	13	7	11	<1	17
Carbapenems R	-	-	38	29	18	30	17	21	8	13
Aminoglycosides R	-	-	26	7	6	17	9	20	<1	24
Fluoroquinolones R	-	-	14	10	9	18	19	20	6	16

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	97	1	100	5	100	12	100	0	100	0	100	25	100	11
CSF	3	0	-	-	0	0	-	-	-	-	-	-	-	-
Gender														
Male	61	2	57	3	37	15	62	0	45	0	56	16	50	18
Female	39	0	43	6	63	10	38	0	55	0	44	36	50	5
Unknown	-	-	0	0	-	-	-	-	-	-	-	-	-	-
Age (years)														
0–4	6	0	5	8	4	16	12	0	5	0	8	0	5	0
5–19	4	25	4	0	1	0	2	0	-	-	1	0	-	-
20–64	55	0	48	3	38	11	36	0	30	0	53	30	48	10
65 and over	36	0	43	6	57	13	50	0	66	0	39	23	48	14
Unknown	-	-	0	0	-	-	2	0	-	-	-	-	-	-
Hospital department														
ICU	30	3	18	5	15	17	14	0	36	0	24	22	43	11
Internal med.	33	0	40	5	45	8	33	0	27	0	29	33	14	17
Surgery	-	-	10	0	5	12	7	0	9	0	7	44	5	50
Other	38	0	33	5	35	14	45	0	27	0	40	17	39	6
Unknown	-	-	-	-	0	50	-	-	-	-	-	-	-	-

Estonia

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

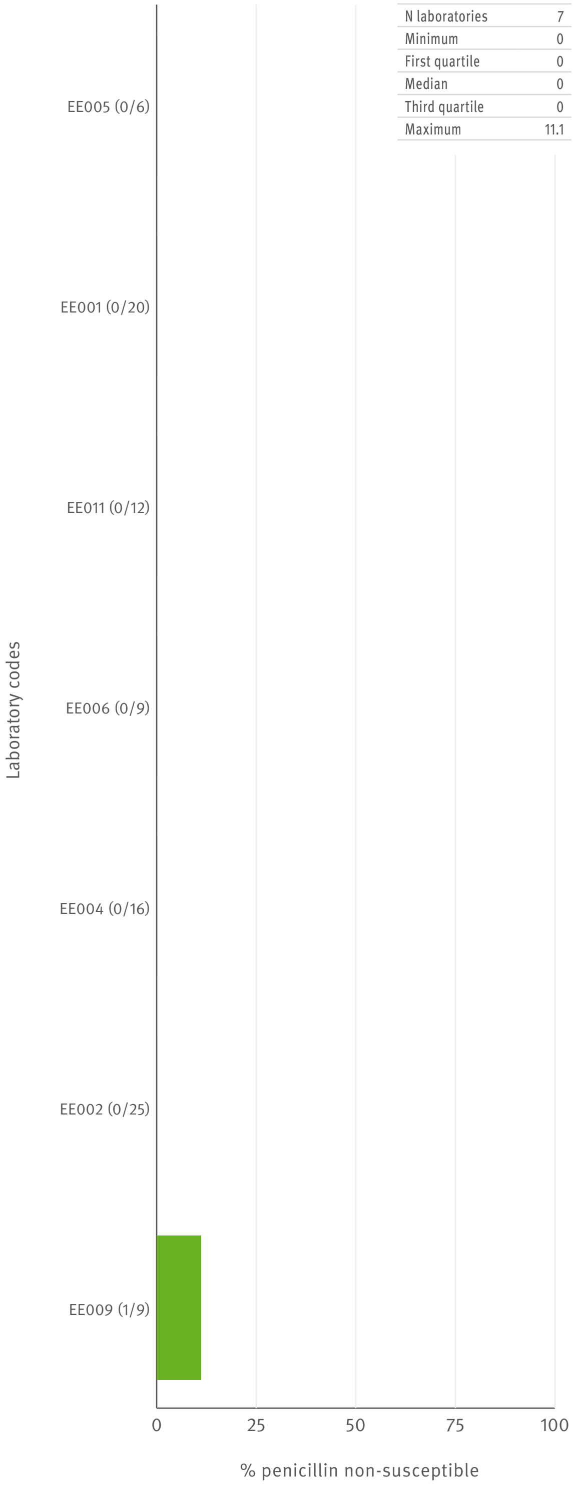


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

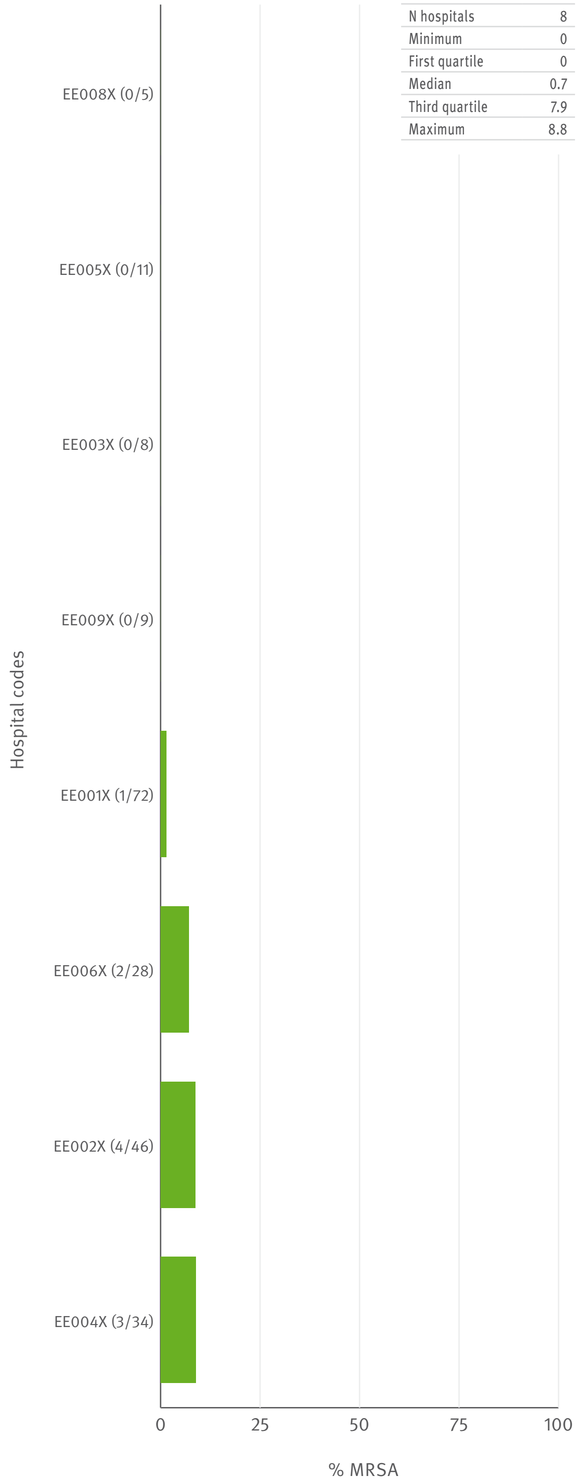


Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

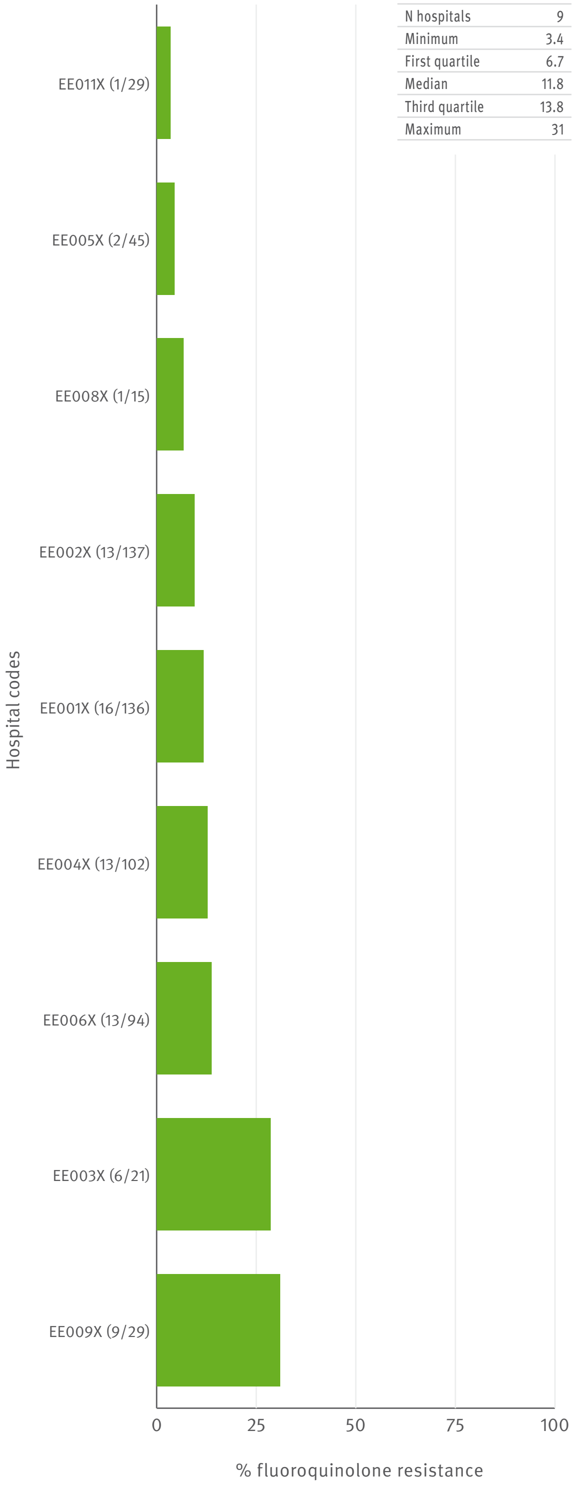
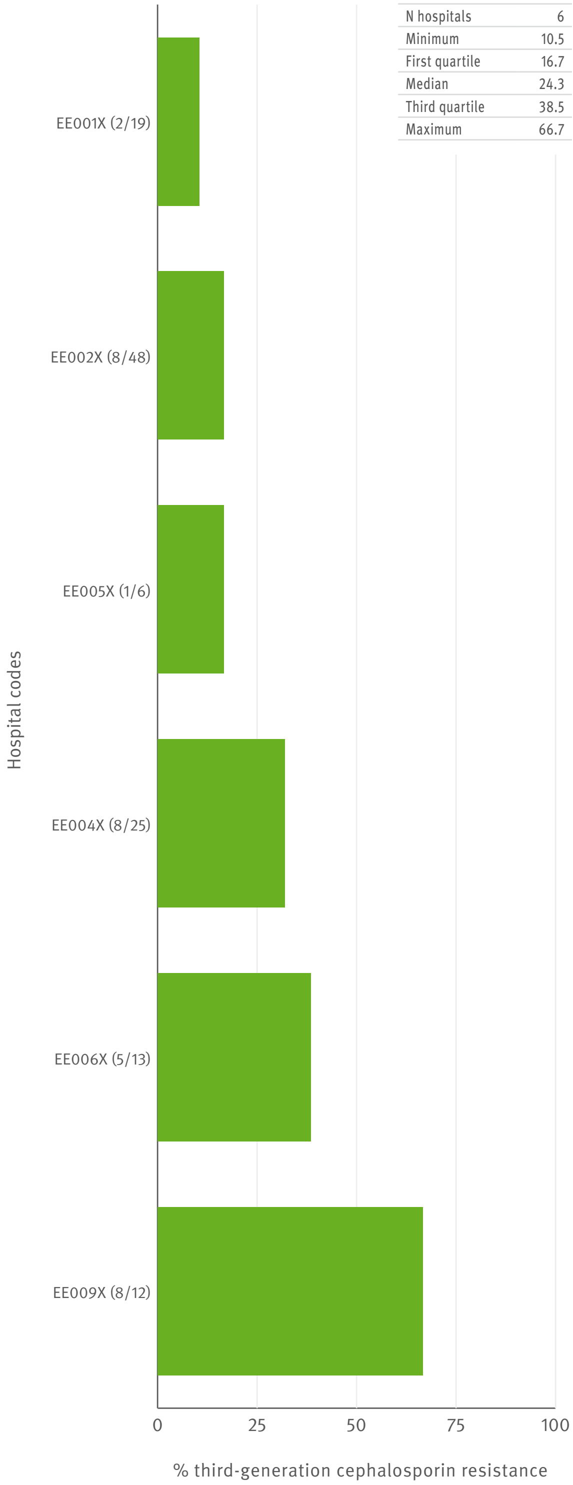


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Finland

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	2	<1	<1	2	1	<1	2	1	<1	<1
Penicillin RI	10	8	7	12	13	11	13	14	13	17
Macrolides RI	20	20	20	24	25	24	28	28	24	22
Staphylococcus aureus										
Oxacillin/Meticillin R	1	3	3	3	2	3	2	2	3	2
Escherichia coli										
Aminopenicilins R	33	33	35	36	34	35	36	34	37	40
Aminoglycosides R	1	2	2	2	3	4	3	4	5	6
Fluoroquinolones R	5	7	7	8	8	9	9	9	11	12
3rd gen. Cephalosporins R	1	2	2	2	2	2	3	4	5	6
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	<1	<1	<1	2	<1	<1	<1	<1	<1
HL Gentamicin R	39	39	27	25	22	13	-	-	-	-
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	79	69	78	80	87	87	87	82	88	85
HL Gentamicin R	4	12	1	16	19	15	-	-	-	-
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	3	1	<1	1	1	4	1	<1
Fluoroquinolones R	-	-	3	4	<1	2	3	2	3	2
3rd gen. Cephalosporins R	-	-	2	<1	1	2	1	4	2	2
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	8	8	7	8	7	7	16	8
Ceftazidime R	-	-	5	3	5	5	5	3	9	5
Carbapenems R	-	-	15	8	9	6	8	10	11	6
Aminoglycosides R	-	-	10	8	8	6	4	4	5	2
Fluoroquinolones R	-	-	16	17	11	15	11	11	15	8

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	97	15	100	3	100	11	100	0	100	1	100	2	99	8
CSF	3	12	-	-	<1	13	-	-	-	-	0	0	1	14
Gender														
Male	56	15	62	2	38	15	68	0	59	1	56	3	63	8
Female	44	15	38	3	62	9	32	0	41	1	44	1	37	9
Age (years)														
0–4	7	18	2	6	1	5	5	0	1	0	1	0	1	0
5–19	3	10	3	2	1	13	1	0	1	0	0	0	1	43
20–64	48	15	41	2	26	11	24	0	33	1	27	3	27	12
65 and over	41	16	53	3	72	12	70	0	65	1	72	2	71	6
Hospital department														
ICU	0	0	1	6	<1	8	1	0	4	5	1	20	2	17
Internal med.	9	10	7	1	5	7	5	0	7	3	6	4	5	13
Surgery	0	0	1	0	1	18	3	0	3	0	2	0	2	0
Other	12	6	11	3	11	13	6	0	4	0	9	2	8	0
Unknown	79	17	80	3	82	11	85	0	83	0	83	2	83	9

Finland

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	16
Minimum	0
First quartile	7.6
Median	11.2
Third quartile	22
Maximum	36.4

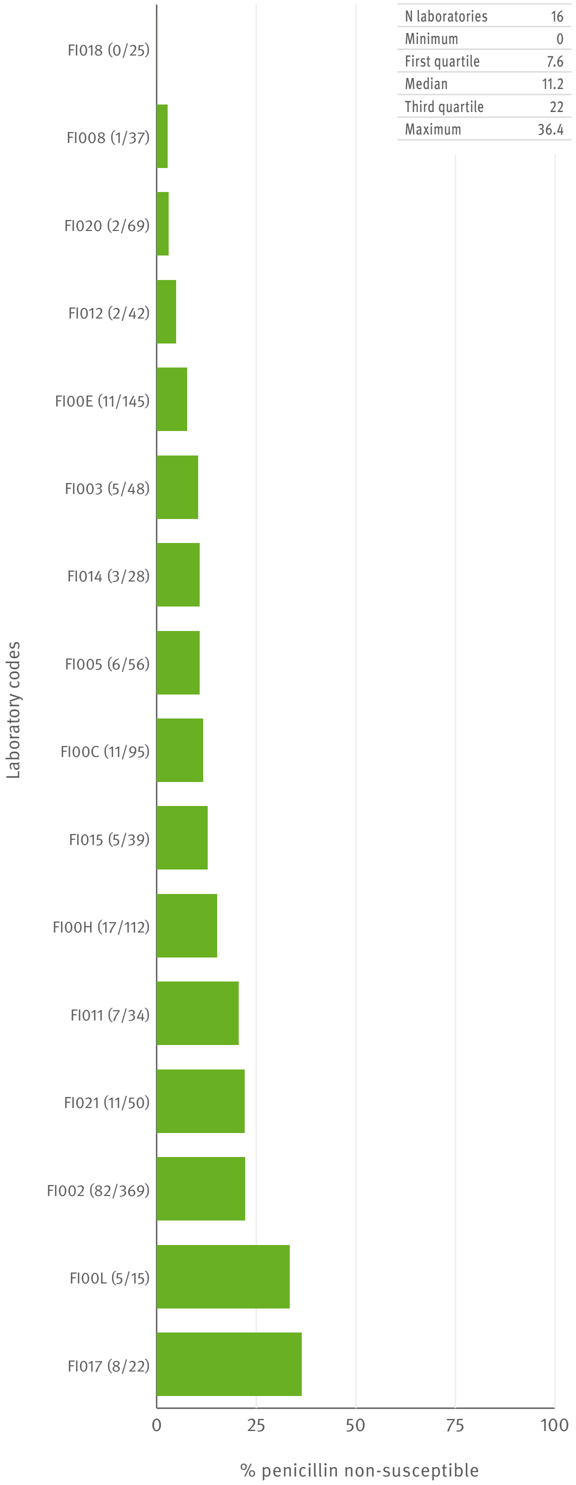


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	18
Minimum	0
First quartile	0
Median	1.4
Third quartile	4.8
Maximum	10.1

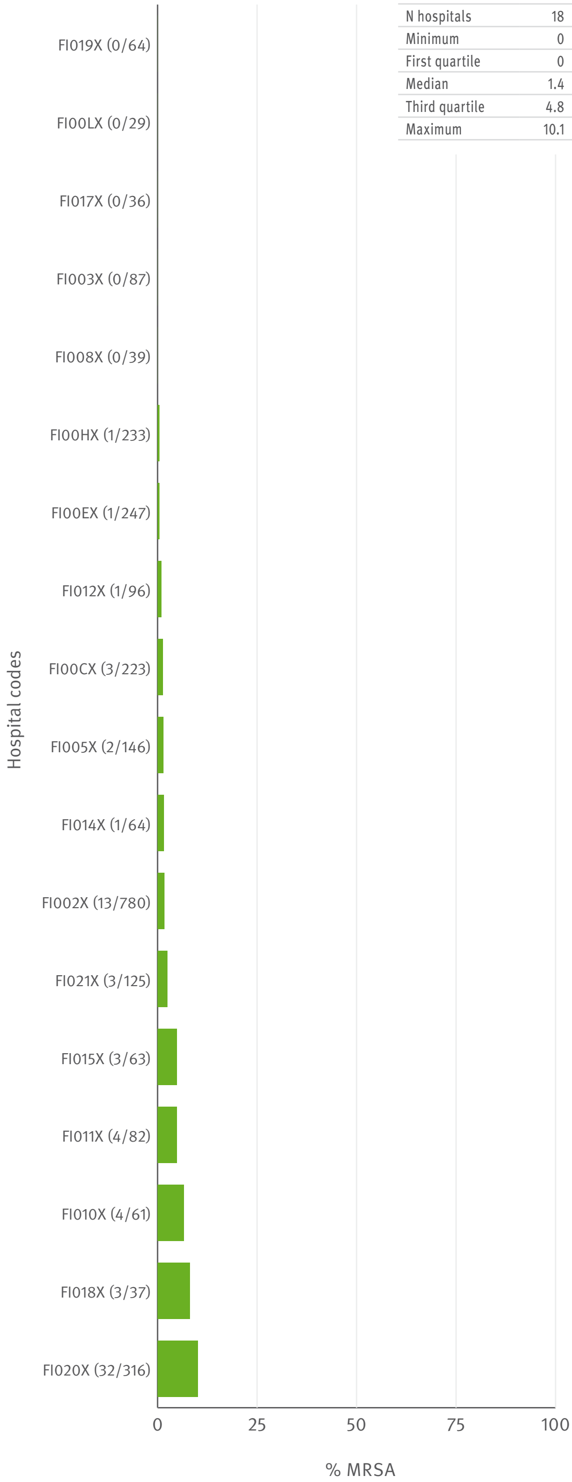
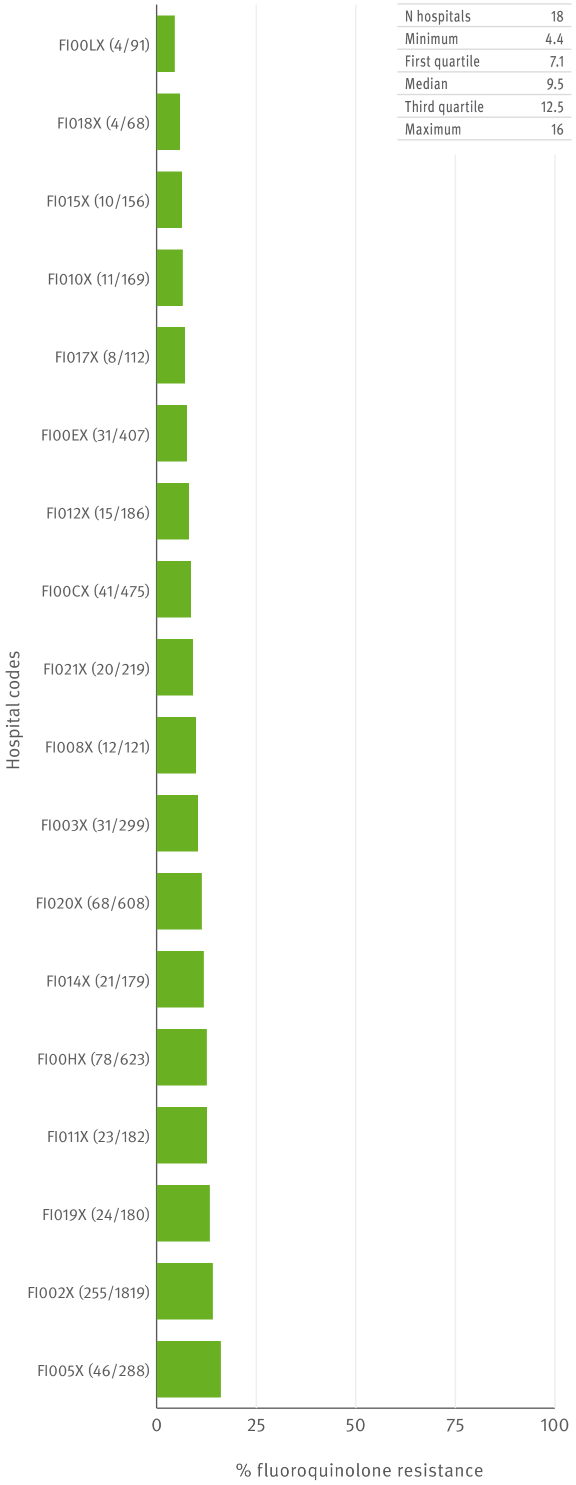


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	18
Minimum	4.4
First quartile	7.1
Median	9.5
Third quartile	12.5
Maximum	16

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	18
Minimum	0
First quartile	0
Median	0.6
Third quartile	2.6
Maximum	9.1

France

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	-	-	5	4	4	7	6	<1	<1	<1
Penicillin RI	-	-	36	32	34	30	27	28	24	23
Macrolides RI	-	-	41	36	37	31	27	30	26	29
Staphylococcus aureus										
Oxacillin/Meticillin R	29	29	27	27	26	24	23	22	20	19
Escherichia coli										
Aminopenicilins R	50	47	50	53	54	54	55	55	55	55
Aminoglycosides R	5	4	5	6	6	7	8	7	8	8
Fluoroquinolones R	9	8	11	14	15	16	19	18	18	18
3rd gen. Cephalosporins R	<1	<1	1	2	2	4	7	7	8	10
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	3	1	<1	1	1	<1	1	<1	<1	<1
HL Gentamicin R	16	17	15	16	15	18	18	18	20	17
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	30	56	64	69	67	68	63	78	81	80
HL Gentamicin R	23	21	24	30	30	30	38	41	43	42
Vancomycin R	<1	5	3	3	1	<1	<1	1	1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	5	7	11	17	20	18	24	24
Fluoroquinolones R	-	-	7	9	14	21	24	22	28	24
3rd gen. Cephalosporins R	-	-	4	6	10	15	19	18	25	23
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	15	11	11	14	21	20	23	20
Ceftazidime R	-	-	9	6	7	8	17	13	16	14
Carbapenems R	-	-	14	12	14	14	17	18	20	18
Aminoglycosides R	-	-	22	16	18	15	19	19	21	20
Fluoroquinolones R	-	-	27	23	24	22	25	23	27	22

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	69	23	100	20	100	18	100	0	100	1	100	24	100	19
CSF	31	26	-	-	-	-	-	-	-	-	-	-	-	-
Gender														
Male	54	24	63	19	49	20	66	0	65	1	61	25	64	19
Female	46	24	36	21	50	16	32	0	34	2	37	23	35	19
Unknown	0	0	1	9	2	16	1	0	1	0	2	15	1	12
Age (years)														
0–4	19	23	4	7	2	8	4	0	2	26	2	22	2	15
5–19	8	12	3	7	1	15	1	0	1	13	1	43	2	11
20–64	38	22	40	13	33	19	37	0	44	1	46	26	46	23
65 and over	35	28	53	25	63	18	58	0	53	0	51	22	49	15
Unknown	<1	25	1	64	<1	25	0	0	0	0	<1	62	<1	50
Hospital department														
ICU	-	-	13	19	8	23	19	0	28	1	16	42	28	32
Internal med.	-	-	34	23	27	19	30	0	28	0	28	21	23	15
Surgery	-	-	14	17	9	19	13	0	13	1	13	27	11	17
Other	-	-	37	18	56	16	37	0	30	2	41	17	36	12
Unknown	100	24	1	24	1	28	1	0	2	0	2	39	2	21

France

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	136
Minimum	0
First quartile	14.3
Median	22.2
Third quartile	32.1
Maximum	80

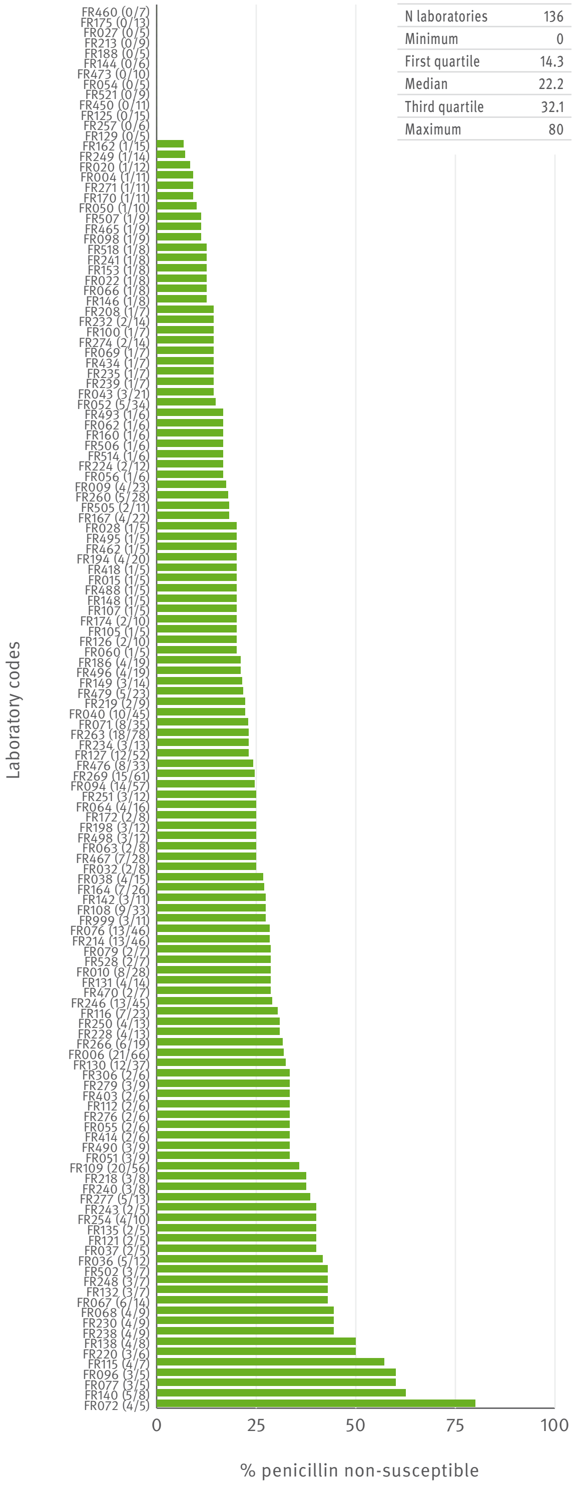


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	58
Minimum	1.2
First quartile	15.8
Median	20.4
Third quartile	24.2
Maximum	35.3

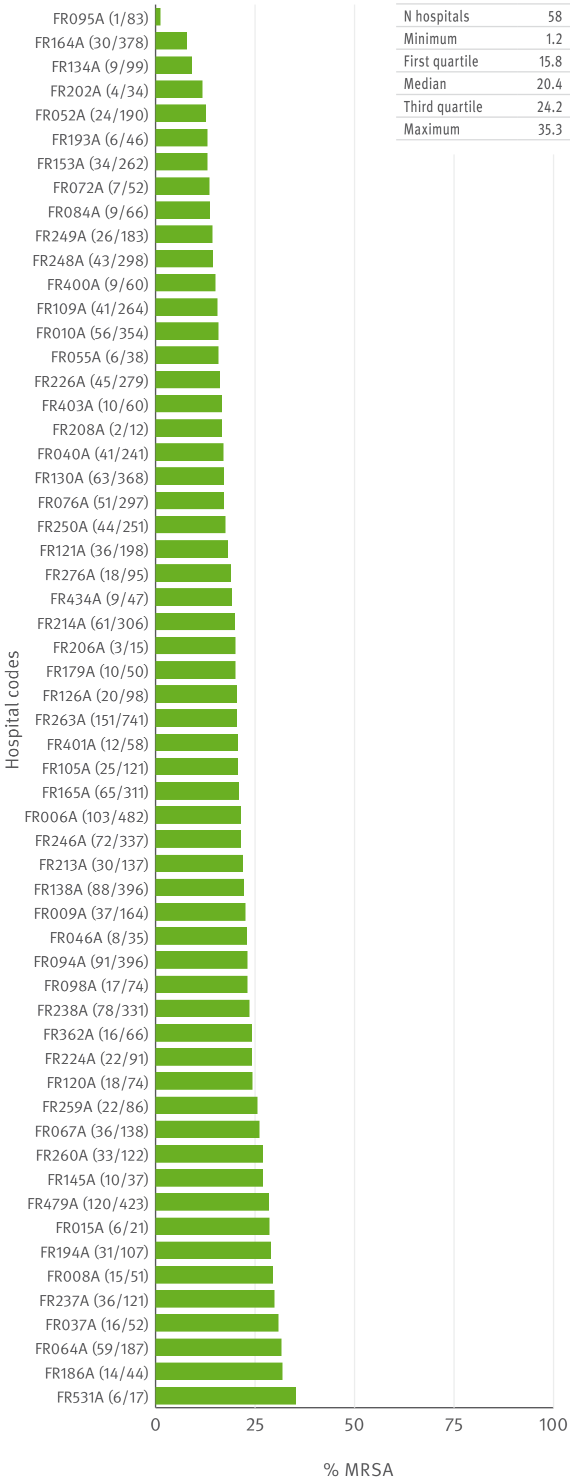


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

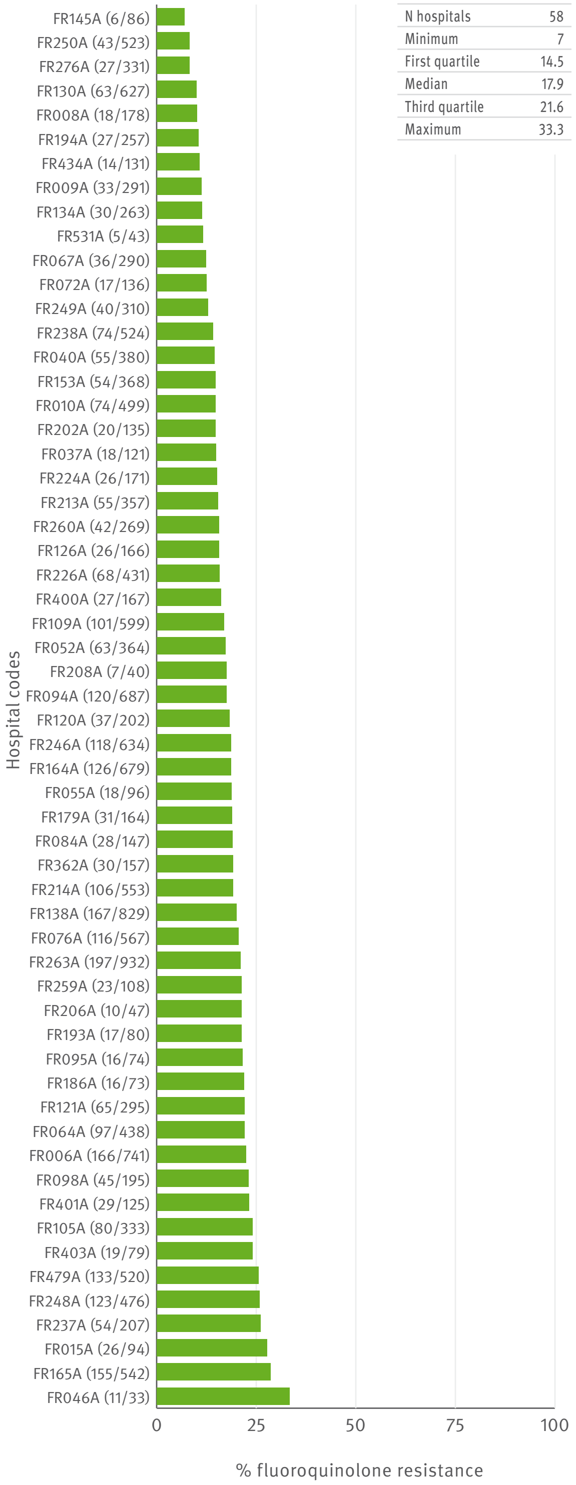
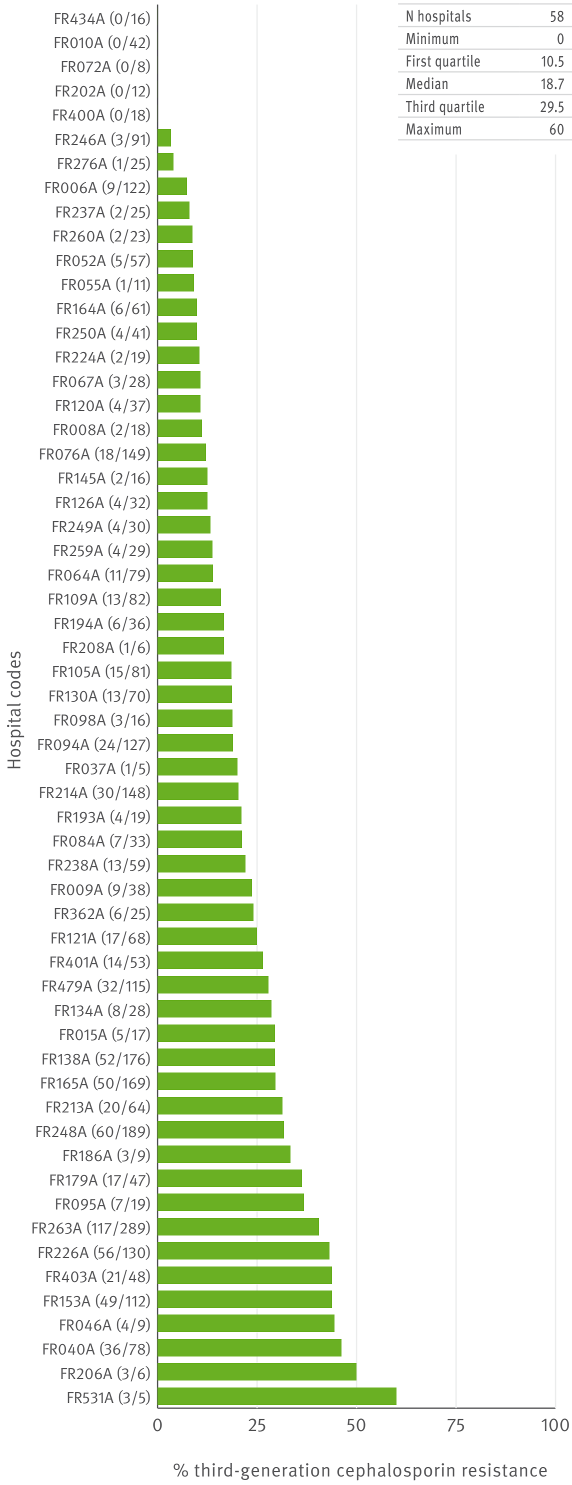


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Germany

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	1	<1	<1	<1	<1	<1	1
Penicillin RI	1	1	4	5	3	5	2	4	2	5
Macrolides RI	11	13	17	12	8	10	8	9	8	7
Staphylococcus aureus										
Oxacillin/Meticillin R	18	20	21	20	16	19	18	21	16	15
Escherichia coli										
Aminopenicilins R	47	55	54	60	55	55	56	54	52	50
Aminoglycosides R	5	4	6	10	6	7	8	9	8	7
Fluoroquinolones R	14	24	23	29	30	23	23	25	24	21
3rd gen. Cephalosporins R	<1	2	2	4	8	5	8	8	8	9
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	7	7	3	3	7	<1	3	<1	<1	<1
HL Gentamicin R	47	42	34	29	67	39	40	47	41	36
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	78	93	96	94	95	95	94	94	96	93
HL Gentamicin R	47	61	52	38	73	35	45	45	42	32
Vancomycin R	3	11	10	8	15	6	6	8	11	16
Klebsiella pneumoniae										
Aminoglycosides R	.	.	10	12	6	10	10	10	9	8
Fluoroquinolones R	.	.	6	12	9	15	15	15	14	14
3rd gen. Cephalosporins R	.	.	7	14	6	11	13	13	13	13
Carbapenems R	.	.	2	<1	2	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	.	<1	18	17	17	9	13	16	15	16
Ceftazidime R	.	<1	11	12	17	8	11	8	9	10
Carbapenems R	.	<1	25	17	22	11	11	13	10	11
Aminoglycosides R	.	<1	12	18	10	10	8	10	12	11
Fluoroquinolones R	.	<1	23	28	28	22	17	18	18	20

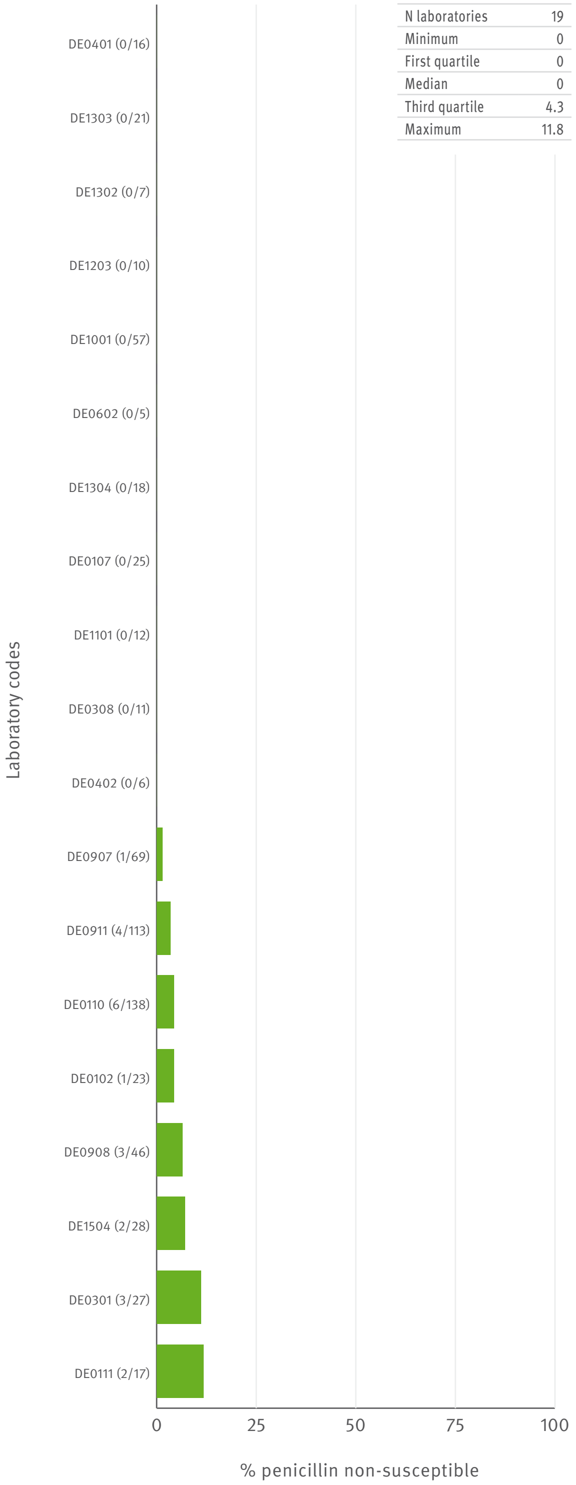
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	94	3	100	16	100	22	100	0	100	14	99	13	98	10
CSF	6	13	-	-	‹ 1	38	-	-	-	-	1	14	2	38
Gender														
Male	39	4	48	16	33	26	52	0	47	16	46	14	52	10
Female	33	3	29	16	42	20	24	0	31	15	34	9	25	13
Unknown	28	3	23	15	25	22	23	1	22	8	21	16	23	9
Age (years)														
0–4	5	6	1	4	1	7	2	0	1	0	2	4	2	15
5–19	2	7	1	6	1	25	0	0	1	22	1	14	1	13
20–64	37	2	28	14	21	25	28	0	35	15	26	14	29	15
65 and over	55	4	69	17	76	22	70	0	64	13	70	13	68	8
Unknown	‹ 1	0	‹ 1	20	‹ 1	0	‹ 1	0	-	-	-	-	-	-
Hospital department														
ICU	20	2	20	19	13	25	25	0	42	16	17	12	23	15
Internal med.	55	3	46	15	53	20	36	0	30	12	45	8	35	8
Surgery	3	6	11	15	7	22	9	0	11	9	8	18	9	12
Other	20	6	20	14	24	27	27	0	17	15	26	18	30	8
Unknown	2	0	2	22	3	18	3	0	1	33	3	27	3	11

Germany

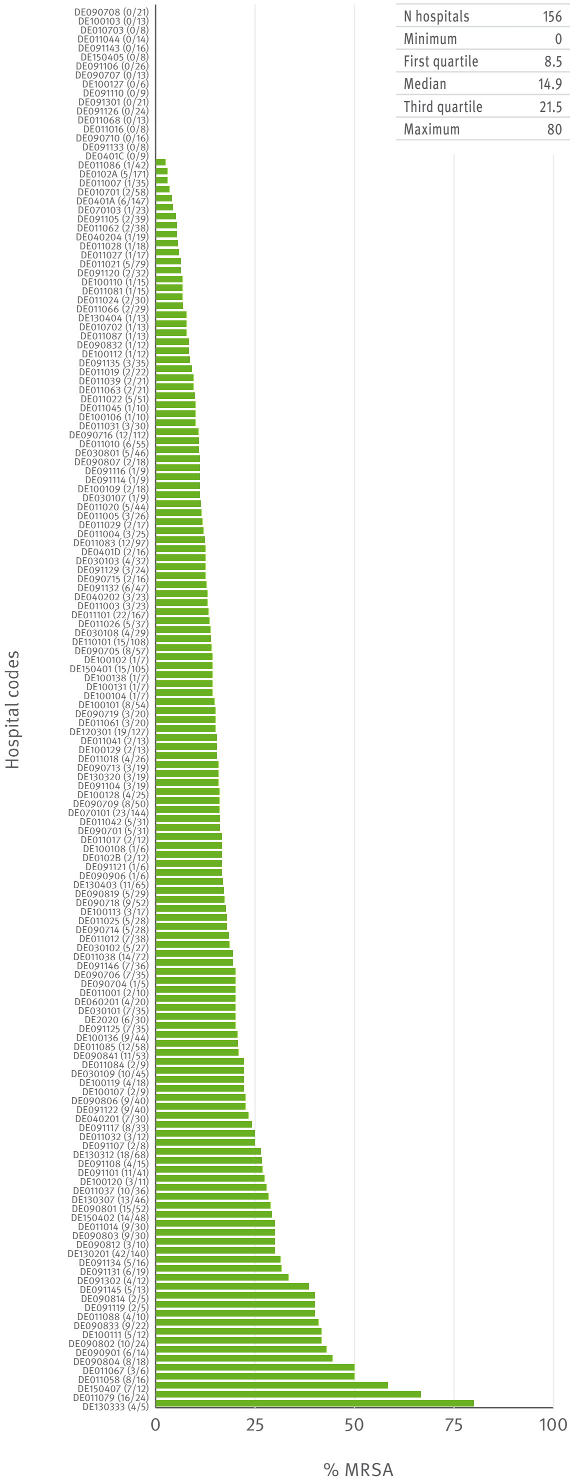
Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**



N laboratories	19
Minimum	0
First quartile	0
Median	0
Third quartile	4.3
Maximum	11.8

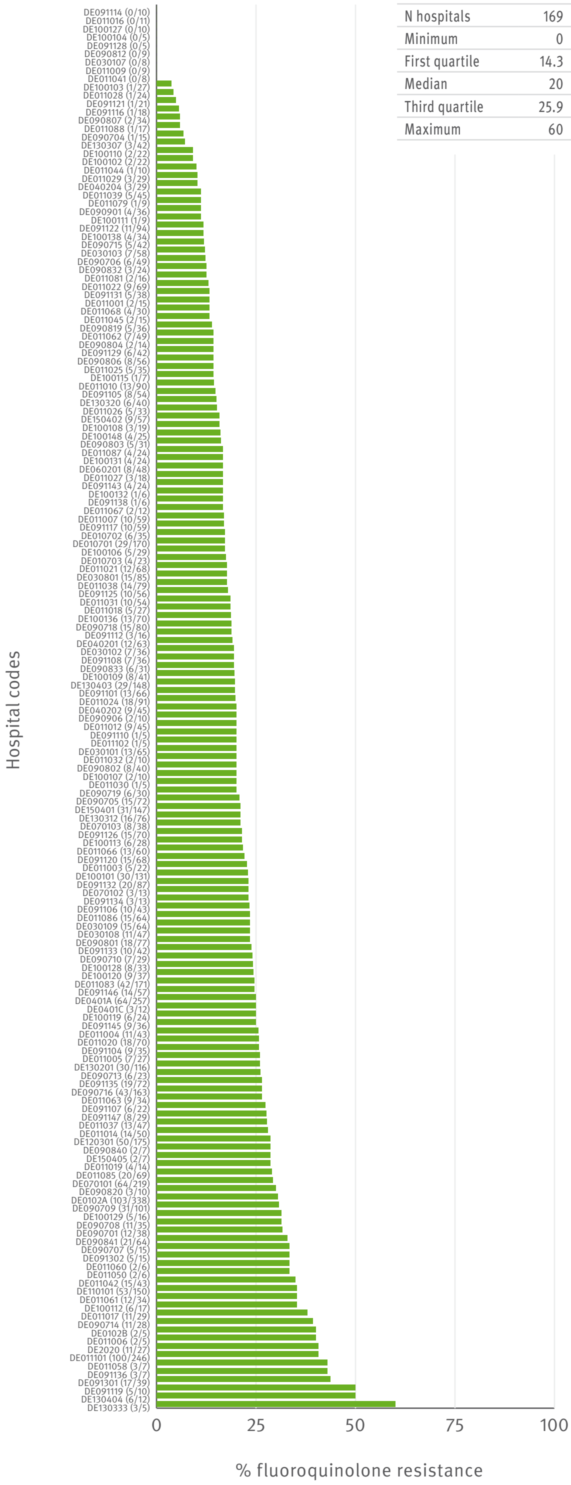
Note. Individual laboratories may serve a large number of hospitals over a wide geographical area within Germany.

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



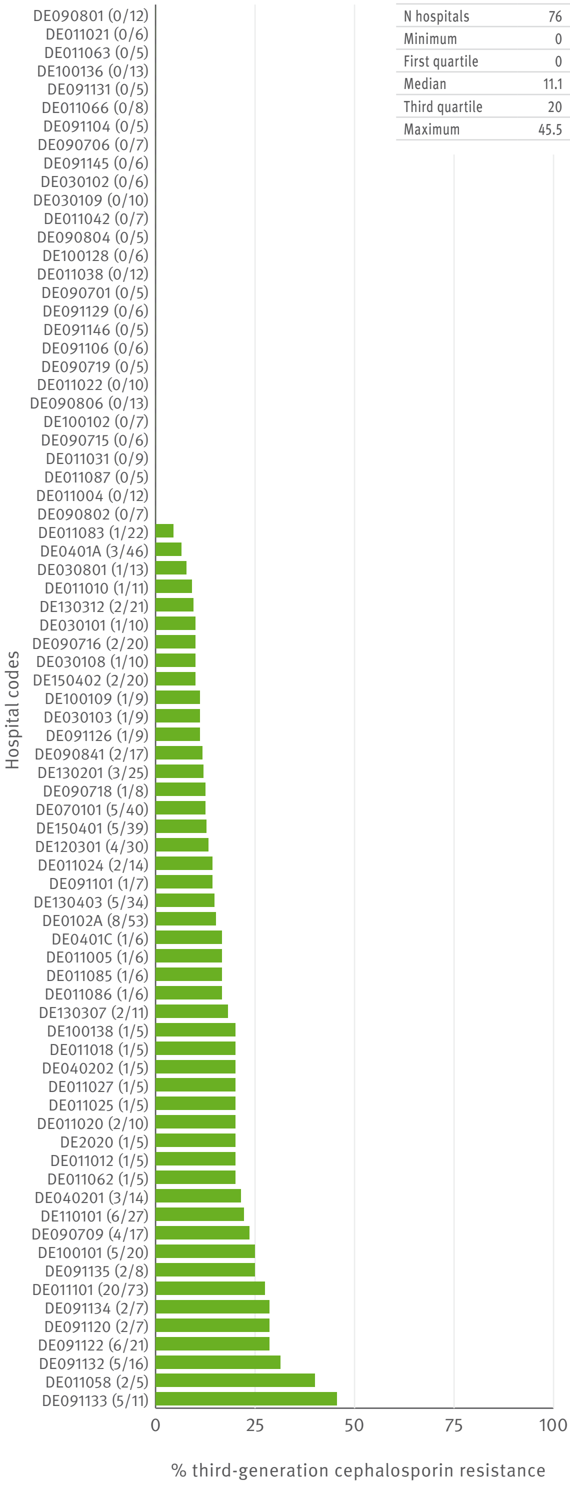
N hospitals	156
Minimum	0
First quartile	8.5
Median	14.9
Third quartile	21.5
Maximum	80

Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	169
Minimum	0
First quartile	14.3
Median	20
Third quartile	25.9
Maximum	60

Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	76
Minimum	0
First quartile	0
Median	11.1
Third quartile	20
Maximum	45.5

Greece

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	-	-	-	-	-	-	-	-	-	-
Penicillin RI	-	-	-	-	-	-	-	-	-	-
Macrolides RI	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus										
Oxacillin/Meticillin R	45	44	42	43	48	41	40	39	39	41
Escherichia coli										
Aminopenicilins R	44	46	46	46	48	50	51	52	55	55
Aminoglycosides R	6	6	7	7	9	15	14	16	17	18
Fluoroquinolones R	12	12	12	14	19	22	23	24	27	29
3rd gen. Cephalosporins R	6	6	7	6	8	10	10	14	15	16
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	1
Enterococcus faecalis										
Aminopenicilins RI	4	4	3	5	4	3	4	3	4	5
HL Gentamicin R	52	59	54	57	65	52	61	43	37	28
Vancomycin R	7	4	4	5	7	7	6	3	6	7
Enterococcus faecium										
Aminopenicilins RI	89	84	85	88	91	85	86	93	93	94
HL Gentamicin R	40	52	34	35	44	52	63	53	43	35
Vancomycin R	18	20	37	42	37	28	27	23	23	17
Klebsiella pneumoniae										
Aminoglycosides R	-	-	60	54	54	55	60	62	69	63
Fluoroquinolones R	-	-	54	50	55	64	66	71	72	70
3rd gen. Cephalosporins R	-	-	61	58	62	66	69	75	76	71
Carbapenems R	-	-	28	33	42	37	44	49	68	60
Pseudomonas aeruginosa										
Piperacillin R	-	-	30	39	38	34	33	39	31	34
Ceftazidime R	-	-	27	34	40	37	34	40	37	31
Carbapenems R	-	-	39	48	47	49	44	43	54	48
Aminoglycosides R	-	-	41	48	50	48	42	43	38	41
Fluoroquinolones R	-	-	39	45	50	48	45	46	39	44

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

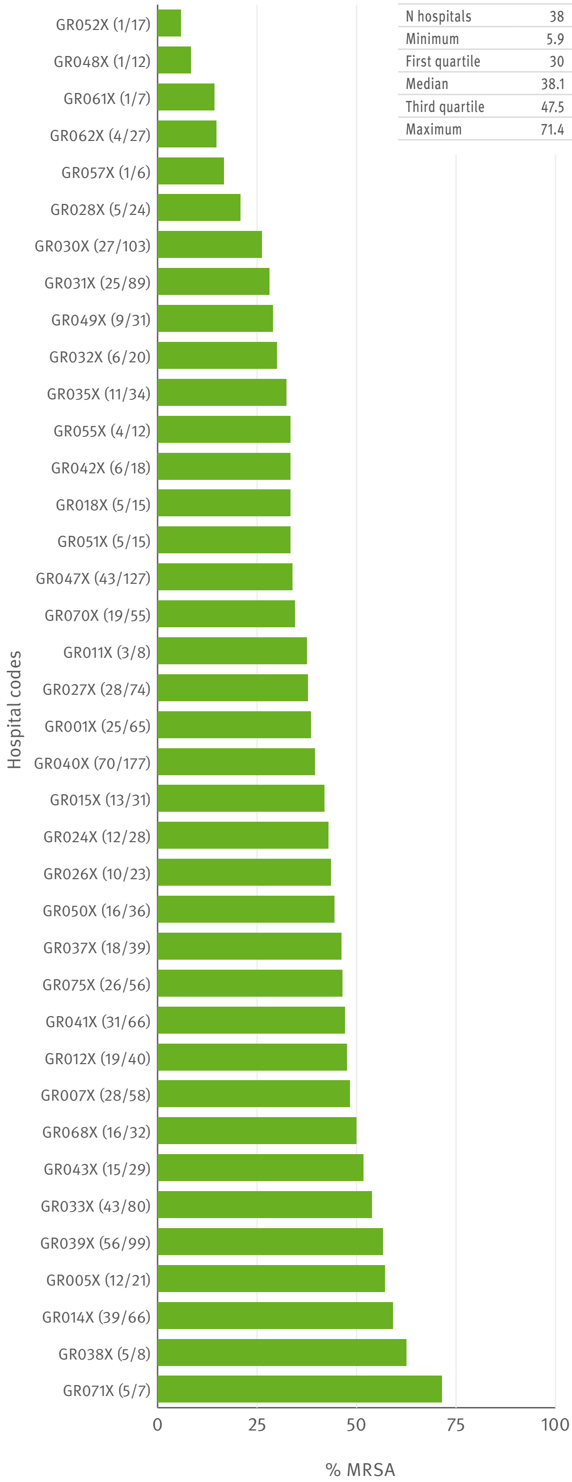
Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	-	-	100	40	100	28	100	7	100	20	97	73	97	50
CSF	-	-	-	-	‹1	46	-	-	-	-	3	90	3	73
Gender														
Male	-	-	10	39	9	29	8	4	12	31	7	61	7	42
Female	-	-	5	45	12	23	7	4	6	33	5	60	5	29
Unknown	-	-	84	40	80	28	85	7	82	18	88	75	88	53
Age (years)														
0–4	-	-	4	25	4	27	6	13	3	15	4	70	4	51
5–19	-	-	‹1	67	‹1	22	-	-	-	-	‹1	17	‹1	25
20–64	-	-	2	32	3	22	2	4	3	17	1	57	2	18
65 and over	-	-	3	37	6	29	3	4	4	41	3	61	2	36
Unknown	-	-	90	41	87	28	89	6	90	20	92	74	92	52
Hospital department														
ICU	-	-	14	52	5	33	33	13	29	22	46	91	44	62
Internal med.	-	-	68	38	74	26	48	3	49	20	35	54	38	40
Surgery	-	-	11	43	11	42	14	2	17	15	14	70	15	47
Other	-	-	2	18	3	9	2	0	3	32	2	15	1	16
Unknown	-	-	5	41	6	27	4	10	2	19	4	73	2	48

Greece

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

No data reported

Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



N hospitals	38
Minimum	5.9
First quartile	30
Median	38.1
Third quartile	47.5
Maximum	71.4

Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	37
Minimum	0
First quartile	19.2
Median	25.3
Third quartile	35
Maximum	50.6

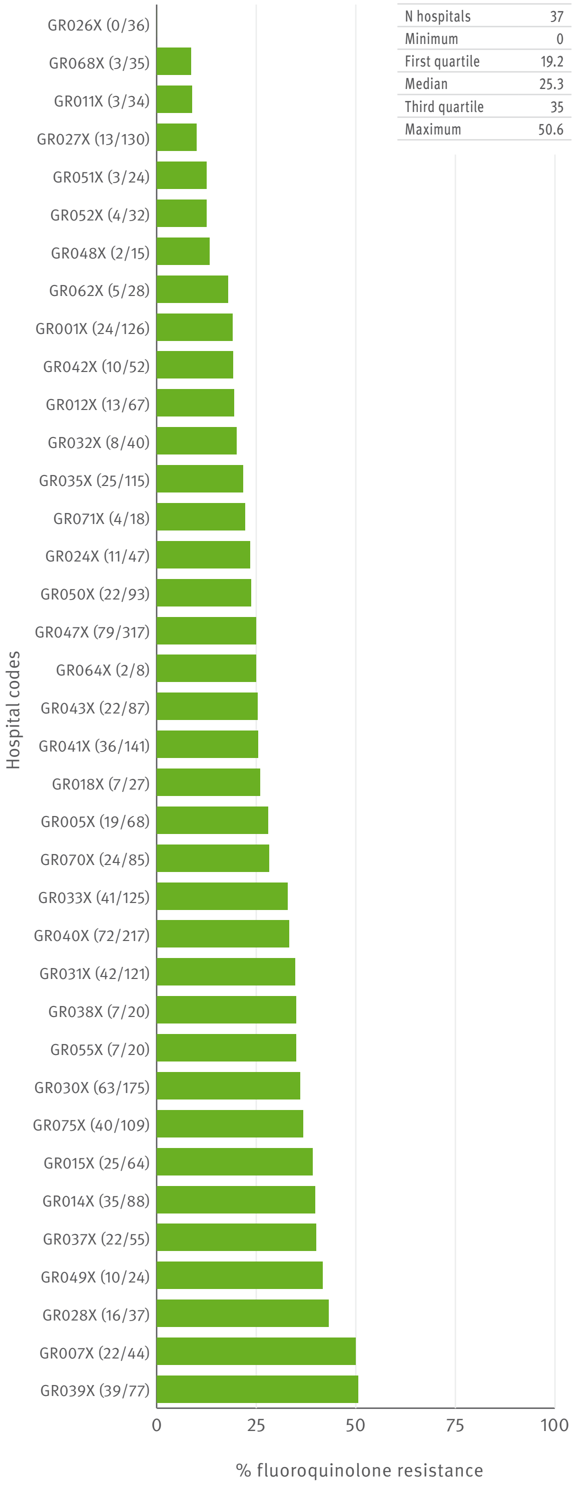
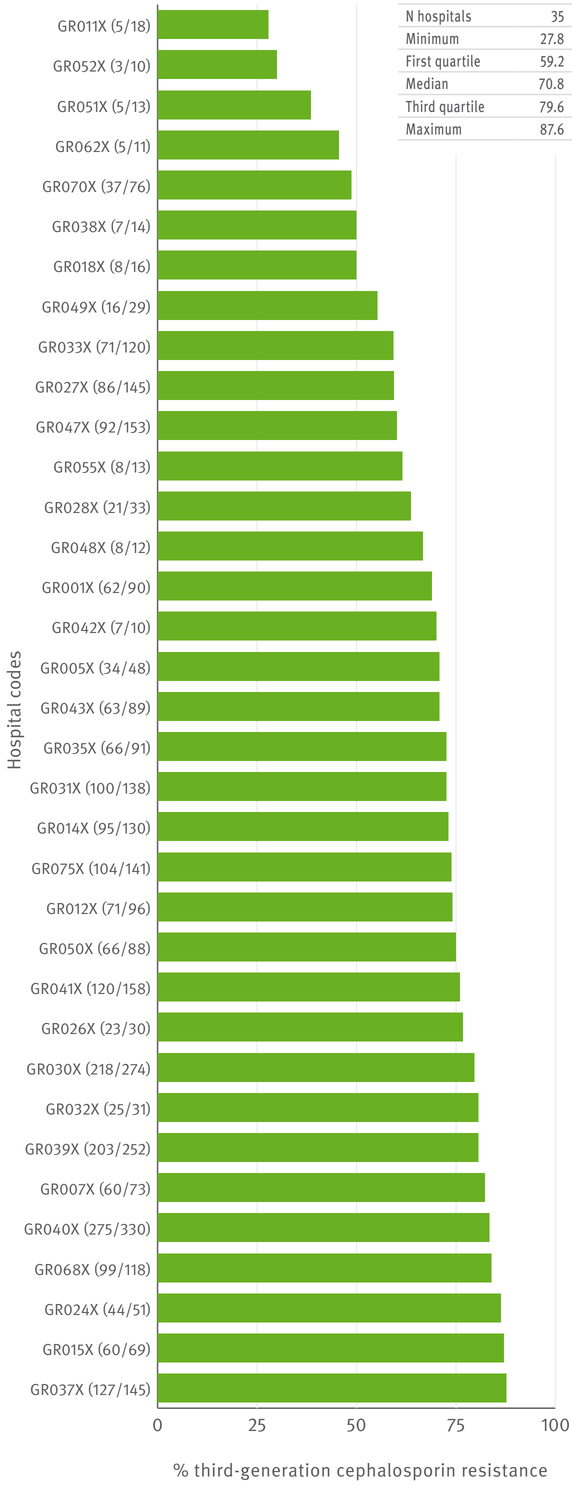


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	35
Minimum	27.8
First quartile	59.2
Median	70.8
Third quartile	79.6
Maximum	87.6



Hungary

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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 Hungary, there are small discrepancies in the data presented by EARS-Net.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	3	<1	4	1	5	8	3	6	6	3
Penicillin RI	24	16	21	18	23	27	12	15	12	10
Macrolides RI	25	25	32	19	36	32	19	24	15	20
Staphylococcus aureus										
Oxacillin/Meticillin R	15	17	20	25	23	23	29	30	26	25
Escherichia coli										
Aminopenicilins R	49	55	51	53	54	59	60	65	65	64
Aminoglycosides R	8	10	9	12	11	13	16	21	15	17
Fluoroquinolones R	15	19	22	27	26	26	30	37	31	29
3rd gen. Cephalosporins R	<1	3	4	5	5	9	13	19	15	17
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	2	1	3	2	3	2	1	1	2
HL Gentamicin R	87	57	43	47	48	53	51	51	49	56
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	91	95	91	88	88	96	97	97	95	99
HL Gentamicin R	96	80	64	67	53	62	70	62	45	51
Vancomycin R	<1	<1	<1	<1	<1	3	1	2	<1	4
Klebsiella pneumoniae										
Aminoglycosides R	-	-	26	20	29	36	40	48	53	41
Fluoroquinolones R	-	-	21	13	22	33	33	43	51	42
3rd gen. Cephalosporins R	-	-	28	20	25	35	38	46	53	43
Carbapenems R	-	-	<1	<1	<1	<1	<1	5	2	3
Pseudomonas aeruginosa										
Piperacillin R	-	-	10	9	11	13	19	14	11	19
Ceftazidime R	-	-	10	8	9	11	12	11	12	18
Carbapenems R	-	-	18	16	19	26	27	25	21	27
Aminoglycosides R	-	-	32	23	26	26	29	29	18	27
Fluoroquinolones R	-	-	28	21	24	26	27	27	20	22

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

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	68	10	100	26	100	30	100	0	100	2	98	48	96	24
CSF	32	13	-	-	-	-	-	-	-	-	2	55	4	22
Gender														
Male	54	9	57	25	44	31	57	0	52	1	59	51	58	26
Female	43	14	42	26	55	29	42	0	47	4	40	41	40	22
Unknown	2	0	2	19	1	28	1	0	2	0	1	80	2	23
Age (years)														
0–4	6	21	2	0	3	13	4	0	4	0	7	47	3	24
5–19	7	0	2	10	1	17	1	0	2	0	1	33	2	22
20–64	49	12	44	23	36	31	38	0	40	3	44	48	48	28
65 and over	37	8	52	29	60	30	57	0	53	2	48	48	48	21
Unknown	<1	100	-	-	-	-	-	-	-	-	-	-	-	-
Hospital department														
ICU	31	11	24	36	14	26	42	0	43	3	30	52	48	34
Internal med.	17	8	22	27	26	31	16	0	12	0	18	37	10	9
Surgery	1	0	10	33	6	32	9	0	5	0	11	61	12	16
Other	46	12	40	19	47	30	27	0	33	3	35	46	25	19
Unknown	4	8	5	12	7	32	7	0	8	0	7	45	5	8

Hungary

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

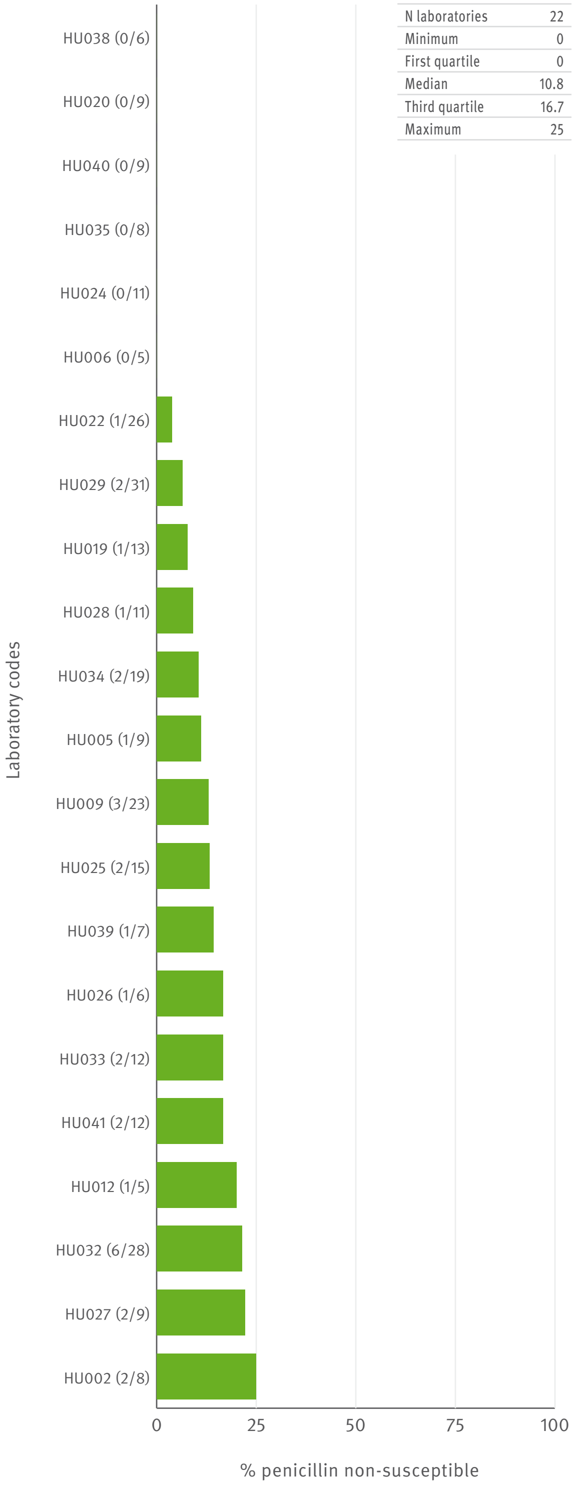


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

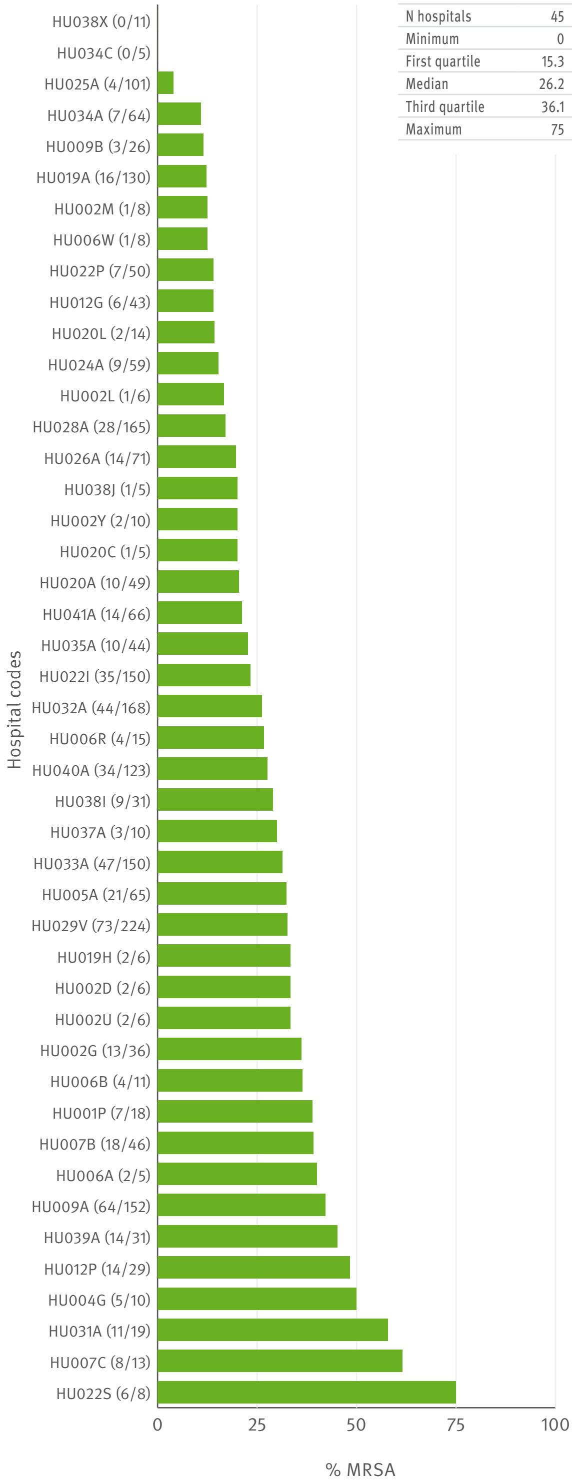
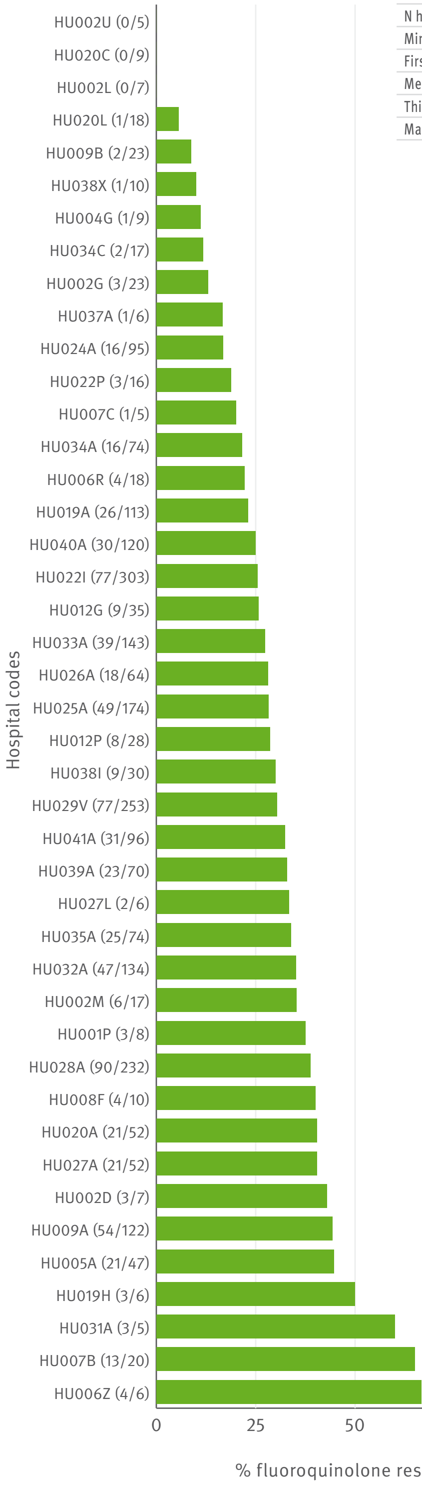
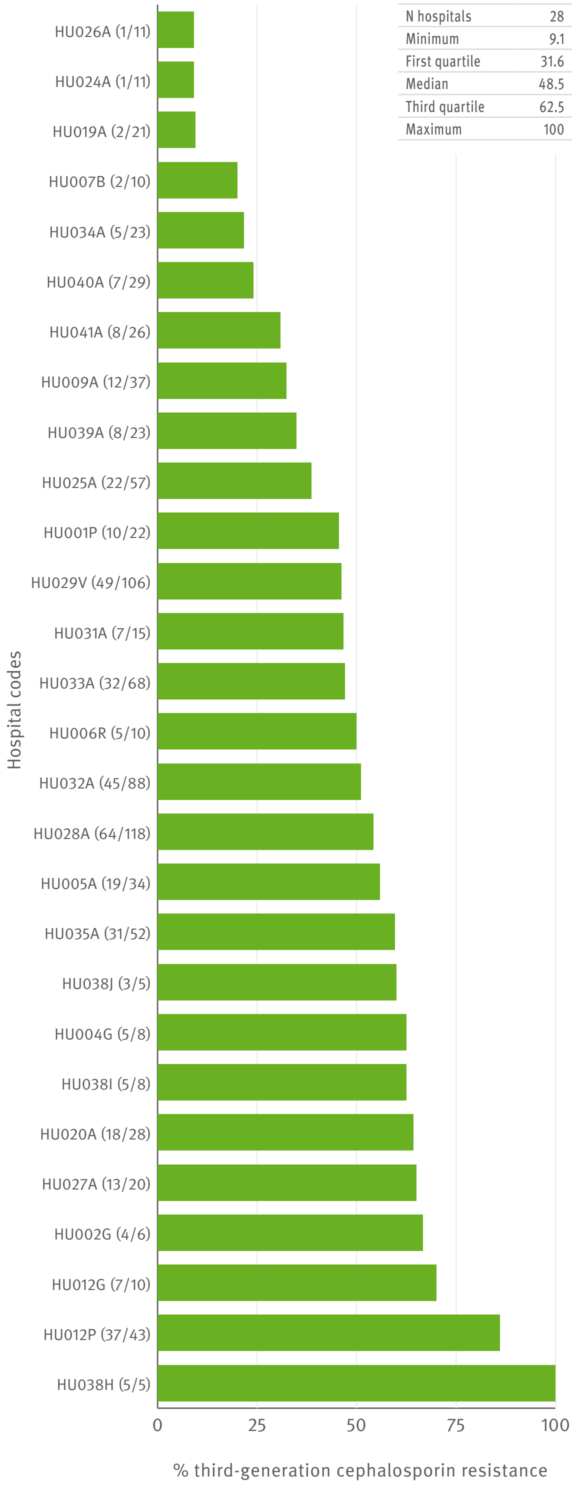


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	43
Minimum	0
First quartile	16.8
Median	28.2
Third quartile	38.8
Maximum	66.7

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	28
Minimum	9.1
First quartile	31.6
Median	48.5
Third quartile	62.5
Maximum	100

Iceland

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	2	<1	<1	2	<1	<1	3	6	4
Penicillin RI	9	17	8	6	7	9	<1	5	9	4
Macrolides RI	20	8	17	10	17	22	9	11	22	7
Staphylococcus aureus										
Oxacillin/Meticillin R	<1	<1	<1	<1	<1	2	<1	2	3	2
Escherichia coli										
Aminopenicilins R	42	43	38	45	46	44	50	46	48	44
Aminoglycosides R	2	<1	<1	7	6	7	7	3	6	4
Fluoroquinolones R	6	2	3	12	17	6	7	11	14	10
3rd gen. Cephalosporins R	1	<1	<1	<1	2	<1	2	4	6	5
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	-	-
Enterococcus faecalis										
Aminopenicilins RI	<1	<1	<1	7	<1	<1	<1	<1	<1	<1
HL Gentamicin R	<1	5	<1	3	13	30	15	13	<1	12
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	57	63	80	56	57	43	68	38	69	67
HL Gentamicin R	<1	13	<1	14	14	43	36	13	15	9
Vancomycin R	<1	<1	<1	<1	<1	<1	8	6	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	<1	<1	<1	4	<1	<1	<1	<1
Fluoroquinolones R	-	-	<1	<1	<1	8	<1	<1	4	7
3rd gen. Cephalosporins R	-	-	<1	<1	<1	4	<1	4	8	21
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	-	-
Pseudomonas aeruginosa										
Piperacillin R	-	-	8	<1	<1	<1	13	8	6	10
Ceftazidime R	-	-	8	<1	<1	<1	6	8	6	10
Carbapenems R	-	-	8	<1	<1	<1	<1	<1	6	10
Aminoglycosides R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Fluoroquinolones R	-	-	<1	<1	<1	<1	13	17	6	10

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	85	2	100	2	100	12	100	0	100	0	100	13	100	7
CSF	15	33	-	-	-	-	-	-	-	-	-	-	-	-
Gender														
Male	61	6	66	2	43	16	51	0	60	0	63	16	70	11
Female	39	9	34	2	57	9	49	0	40	0	38	7	30	0
Age (years)														
0–4	5	33	6	0	3	0	-	-	4	0	-	-	-	-
5–19	2	0	5	0	1	0	-	-	4	0	-	-	-	-
20–64	58	6	40	4	41	10	49	0	48	0	58	9	44	0
65 and over	36	5	49	2	55	14	51	0	44	0	43	18	56	13
Hospital department														
ICU	7	0	2	0	2	25	11	0	24	0	3	0	15	0
Internal med.	8	20	24	0	15	14	24	0	4	0	13	20	19	20
Surgery	2	0	4	0	4	33	11	0	12	0	5	50	4	0
Other	83	6	69	3	80	10	51	0	60	0	75	10	63	6
Unknown	-	-	2	0	-	-	3	0	-	-	5	0	-	-

Iceland

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	2
Minimum	5.7
First quartile	5.7
Median	11.2
Third quartile	16.7
Maximum	16.7

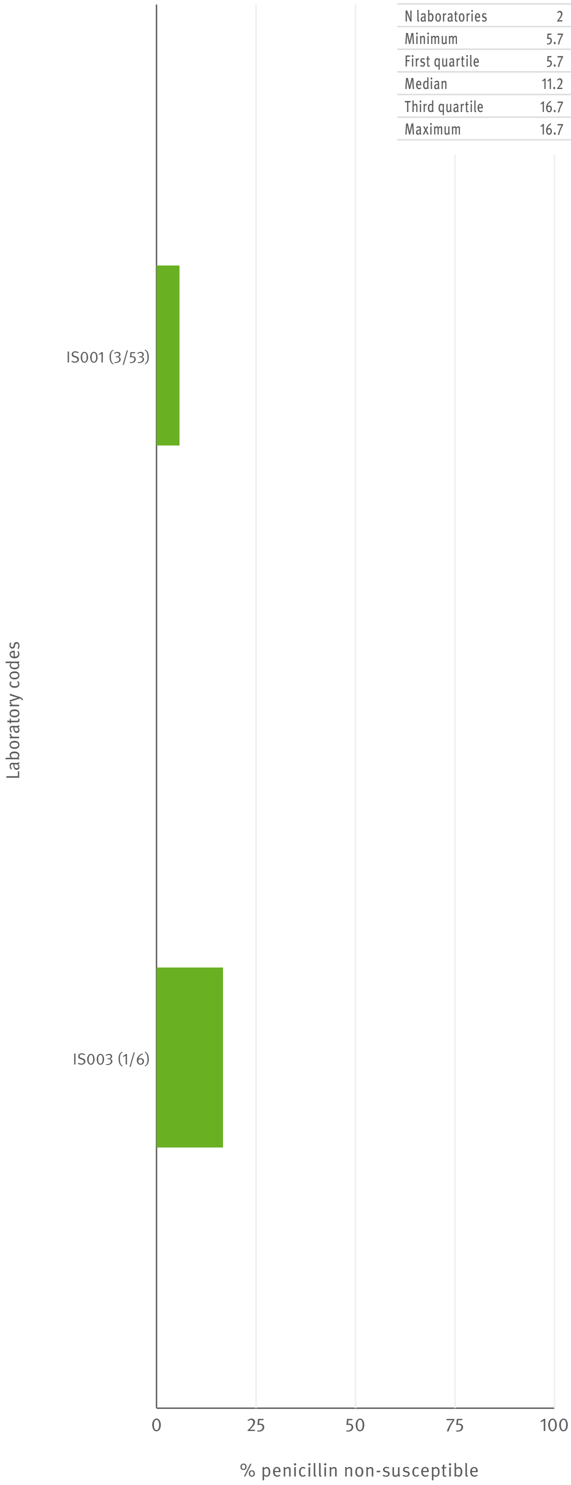


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	2
Minimum	0
First quartile	0
Median	1.4
Third quartile	2.7
Maximum	2.7

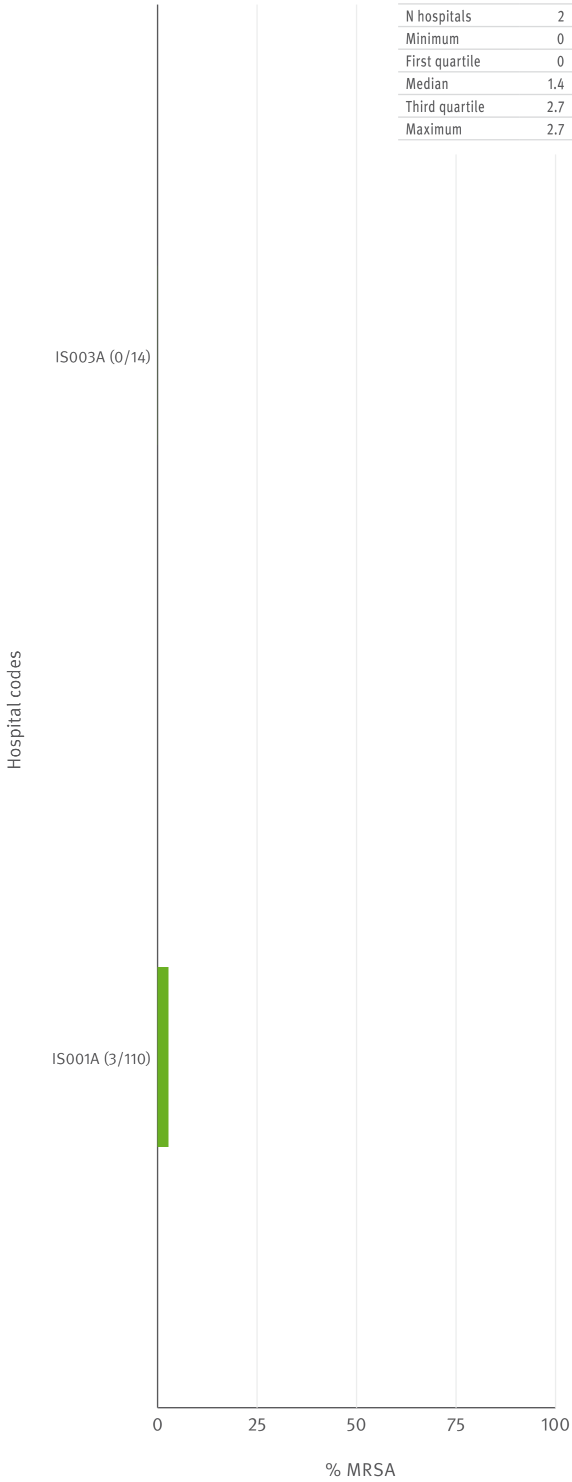


Figure 3: *E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)

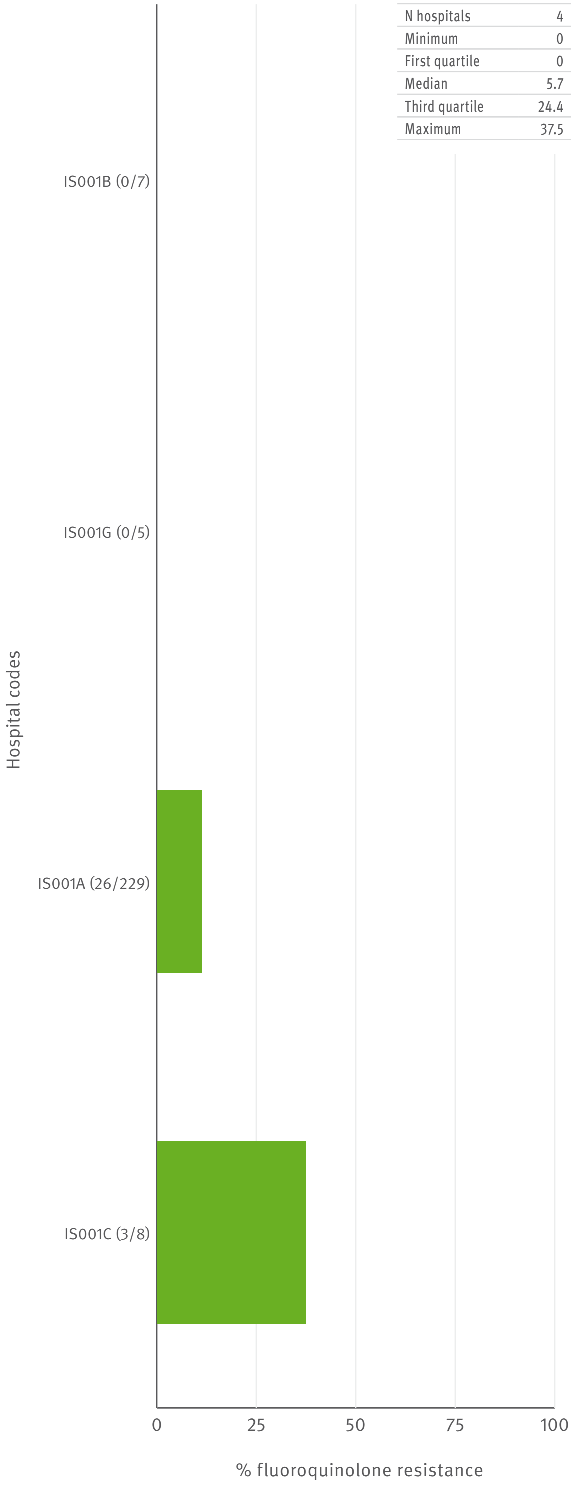
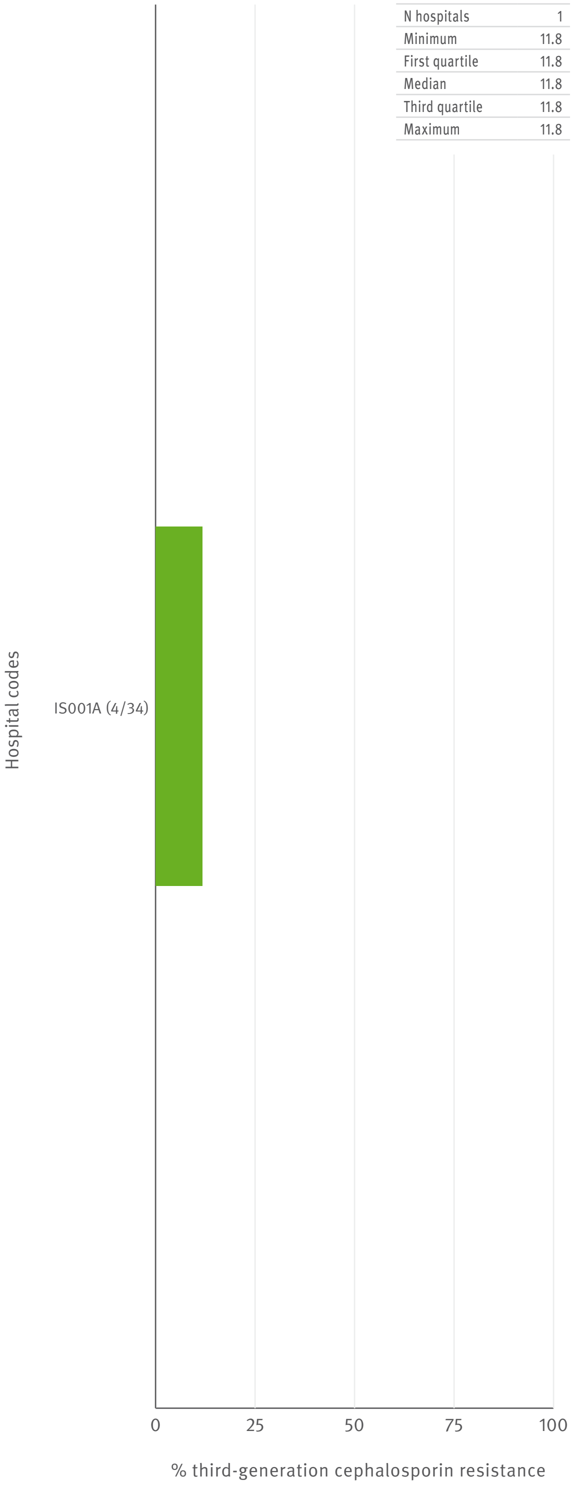


Figure 4: *K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)



Ireland

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	3	3	3	3	6	6	6	5	6	5
Penicillin RI	12	10	11	16	17	23	20	18	19	19
Macrolides RI	12	14	12	16	17	17	17	16	18	17
Staphylococcus aureus										
Oxacillin/Meticillin R	42	41	42	42	38	33	27	24	24	23
Escherichia coli										
Aminopenicilins R	61	65	67	69	65	67	66	67	70	67
Aminoglycosides R	4	5	7	7	10	9	9	10	10	11
Fluoroquinolones R	10	12	17	21	21	23	22	23	23	24
3rd gen. Cephalosporins R	2	2	4	4	5	6	6	8	9	9
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	5	<1	4	5	2	<1	3	2	<1	4
HL Gentamicin R	32	42	42	43	38	31	34	29	30	33
Vancomycin R	<1	1	3	3	3	3	<1	<1	4	3
Enterococcus faecium										
Aminopenicilins RI	91	96	93	94	93	95	93	96	96	93
HL Gentamicin R	54	56	52	44	36	27	38	39	36	39
Vancomycin R	19	22	31	36	33	35	38	39	35	44
Klebsiella pneumoniae										
Aminoglycosides R	-	-	5	9	10	9	11	7	8	9
Fluoroquinolones R	-	-	3	16	17	11	11	8	9	7
3rd gen. Cephalosporins R	-	-	7	9	8	11	11	8	8	10
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	7	7	6	5	4	8	3	16
Ceftazidime R	-	-	10	6	5	4	6	6	4	14
Carbapenems R	-	-	11	9	9	6	8	6	6	11
Aminoglycosides R	-	-	7	9	9	6	7	5	4	10
Fluoroquinolones R	-	-	14	17	18	16	9	11	6	15

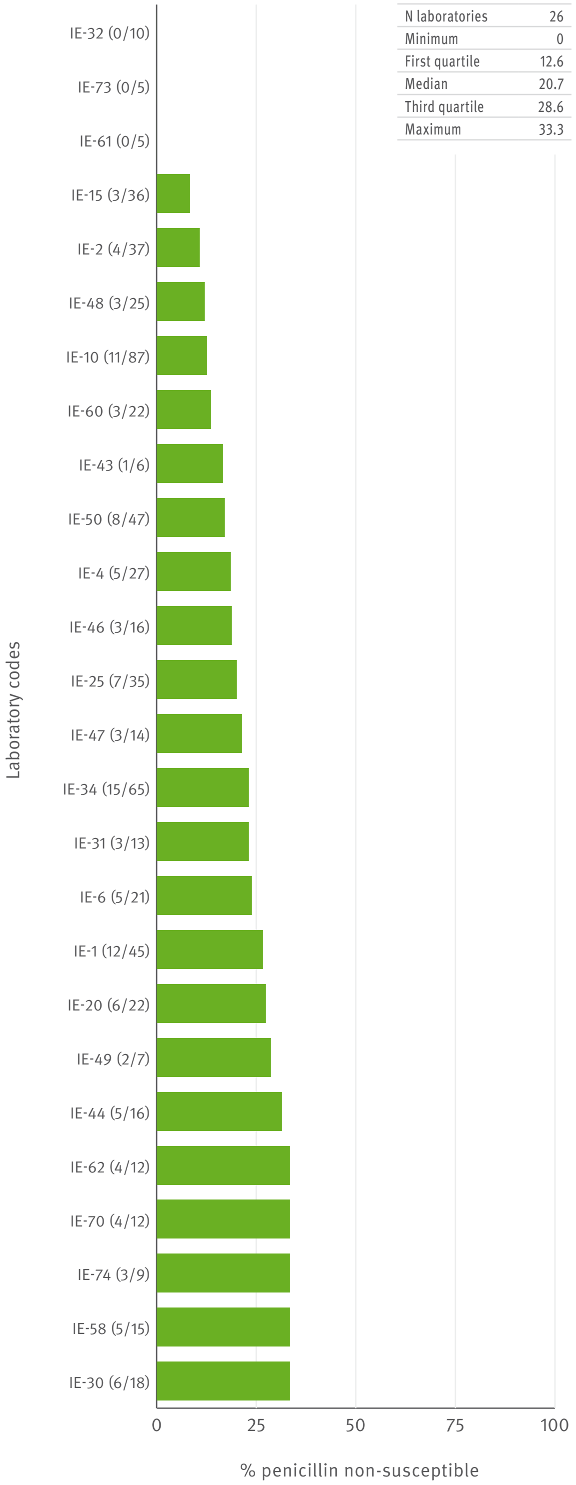
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	98	19	100	23	100	24	100	3	100	40	100	9	99	9
CSF	2	45	-	-	<1	50	-	-	-	-	0	0	1	0
Gender														
Male	54	21	66	23	47	29	66	3	60	39	58	9	63	7
Female	46	17	34	24	53	19	34	3	40	40	42	8	37	12
Age (years)														
0–4	9	25	7	7	3	9	6	0	1	0	3	30	3	0
5–19	2	27	4	11	1	6	1	0	1	29	1	0	2	13
20–64	37	18	38	17	30	20	34	5	40	45	43	8	33	14
65 and over	52	19	50	31	66	26	58	3	58	37	53	8	61	7
Hospital department														
ICU	2	13	3	25	3	29	5	3	9	44	3	10	3	8
Internal med.	10	22	10	29	11	26	7	5	8	29	9	9	9	6
Surgery	1	29	3	38	4	25	5	0	5	23	5	7	4	0
Other	31	16	24	16	27	21	17	2	9	32	22	4	21	12
Unknown	55	21	61	24	55	24	65	4	69	43	62	10	63	9

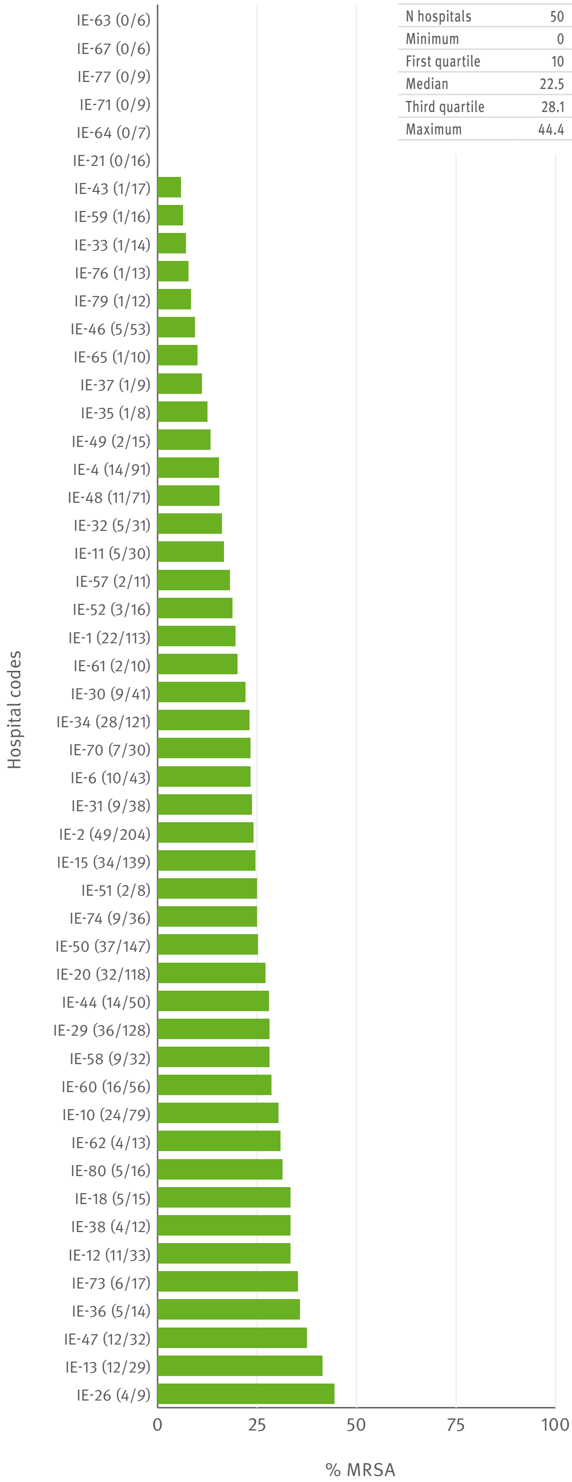
Ireland

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**



N laboratories	26
Minimum	0
First quartile	12.6
Median	20.7
Third quartile	28.6
Maximum	33.3

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



N hospitals	50
Minimum	0
First quartile	10
Median	22.5
Third quartile	28.1
Maximum	44.4

Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

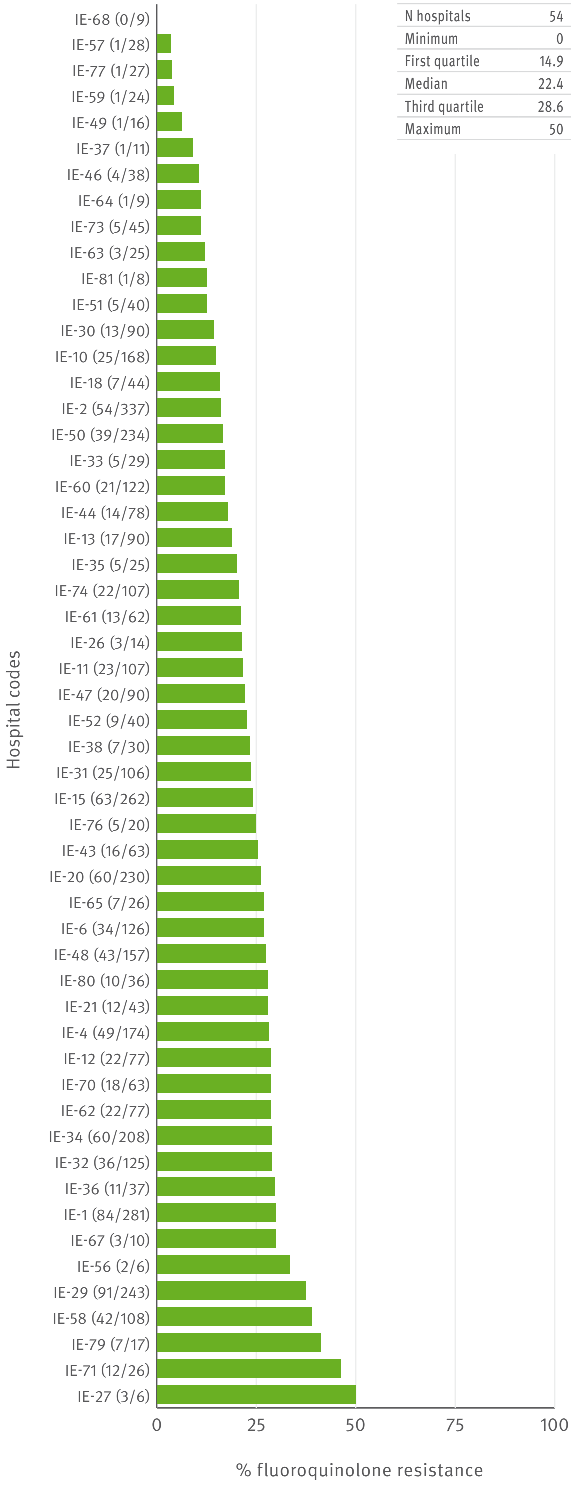
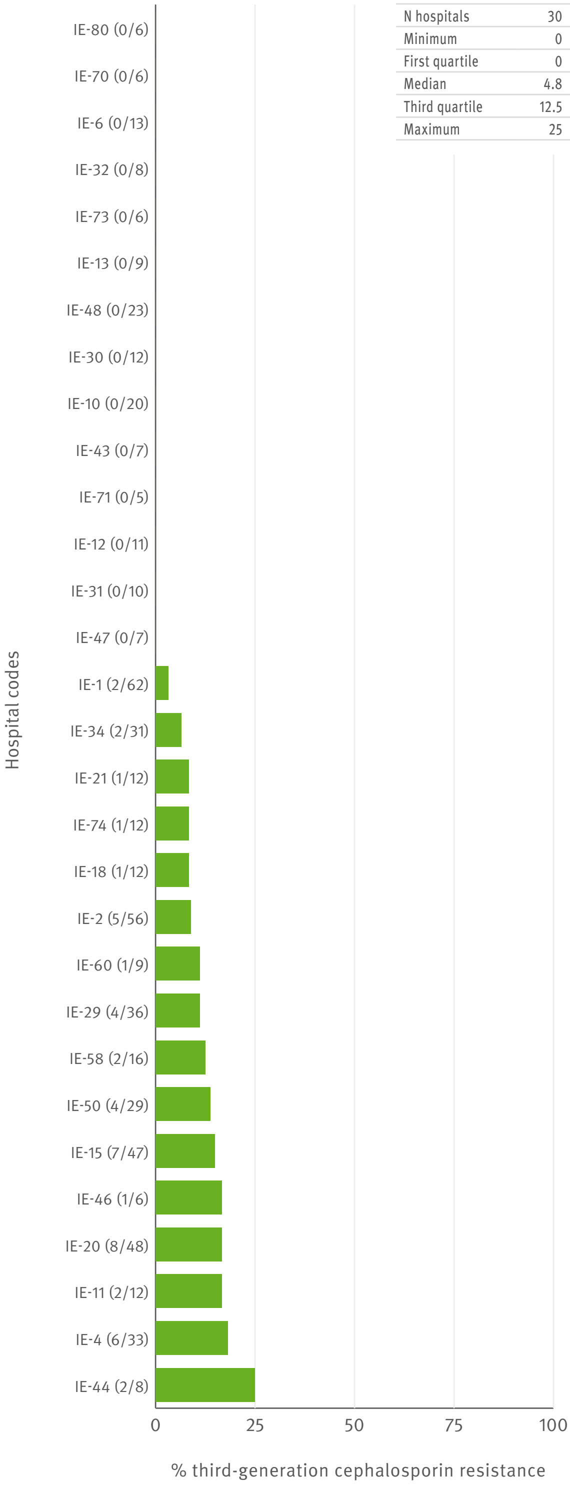


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Italy

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	41	1767	41	3552	41	947	37	979	40	773

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	5	5	5	<1	4	3	3	5	6	6
Penicillin RI	13	14	9	7	15	10	6	9	7	12
Macrolides RI	37	29	31	33	31	26	21	29	27	34
Staphylococcus aureus										
Oxacillin/Meticillin R	39	40	37	38	33	34	37	37	38	35
Escherichia coli										
Aminopenicilins R	52	53	55	56	58	62	63	64	67	68
Aminoglycosides R	10	9	11	8	14	14	13	15	18	21
Fluoroquinolones R	25	28	28	27	32	38	36	39	41	42
3rd gen. Cephalosporins R	6	5	8	7	11	16	17	21	20	26
Carbapenems R	-	-	-	-	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	4	4	4	4	4	13	20	13	11	4
HL Gentamicin R	39	36	38	38	39	47	49	50	50	51
Vancomycin R	2	2	3	3	2	2	3	2	3	1
Enterococcus faecium										
Aminopenicilins RI	80	78	77	86	73	64	60	70	83	87
HL Gentamicin R	44	39	36	48	53	49	52	59	54	62
Vancomycin R	24	21	19	18	11	6	4	4	4	6
Klebsiella pneumoniae										
Aminoglycosides R	-	-	8	26	25	28	19	29	35	42
Fluoroquinolones R	-	-	11	23	27	28	20	39	46	50
3rd gen. Cephalosporins R	-	-	20	33	35	39	37	47	46	48
Carbapenems R	-	-	-	1	1	2	1	15	27	29
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	23	20	20	24	21	22	30
Ceftazidime R	-	-	-	20	25	24	16	18	16	26
Carbapenems R	-	-	-	21	27	33	31	22	21	25
Aminoglycosides R	-	-	-	32	29	30	29	23	18	30
Fluoroquinolones R	-	-	-	36	35	36	42	31	26	31

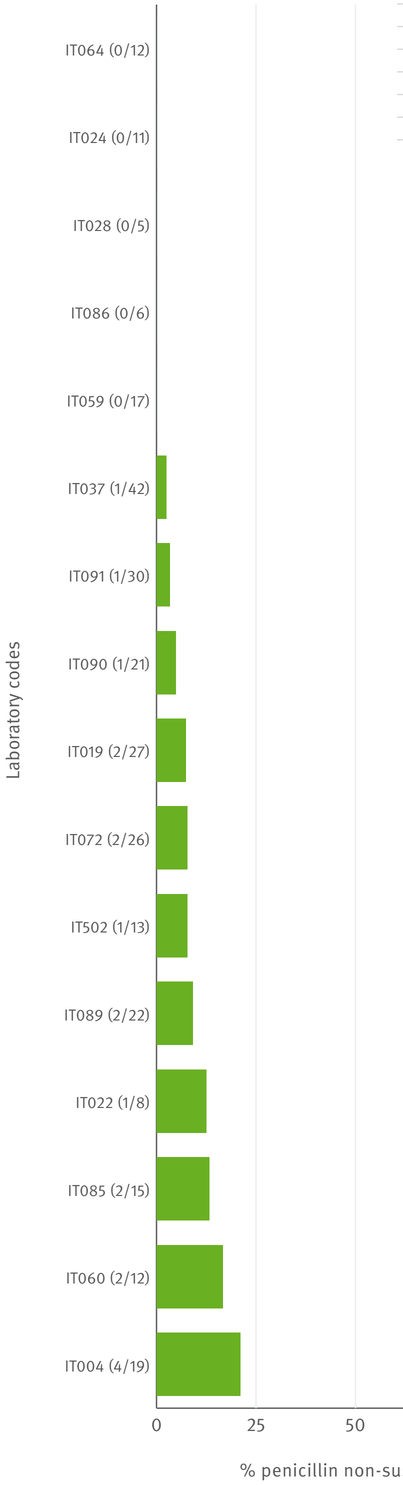
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	89	9	100	37	100	41	100	2	100	5	99	47	98	23
CSF	11	14	-	-	<1	23	-	-	-	-	1	57	2	45
Gender														
Male	46	7	50	36	46	46	46	2	51	6	50	47	51	23
Female	41	9	37	38	44	34	26	2	34	4	35	40	30	22
Unknown	14	19	13	31	9	51	28	3	15	8	15	62	18	28
Age (years)														
0–4	4	15	3	32	1	12	4	0	3	0	3	41	3	18
5–19	3	9	1	26	0	39	1	0	1	0	1	67	1	38
20–64	20	8	17	28	15	39	12	2	16	4	18	49	21	30
65 and over	38	9	37	42	38	41	32	3	34	6	33	47	33	18
Unknown	34	9	42	36	46	43	51	2	46	6	46	46	43	25
Hospital department														
ICU	6	6	10	45	6	41	22	1	19	10	21	63	20	36
Internal med.	35	4	41	38	40	39	35	2	33	5	33	45	29	22
Surgery	4	23	16	38	17	44	14	2	18	2	16	41	18	17
Other	51	13	25	31	34	42	21	2	26	6	24	37	29	20
Unknown	4	7	7	33	3	50	8	4	4	0	6	56	4	30

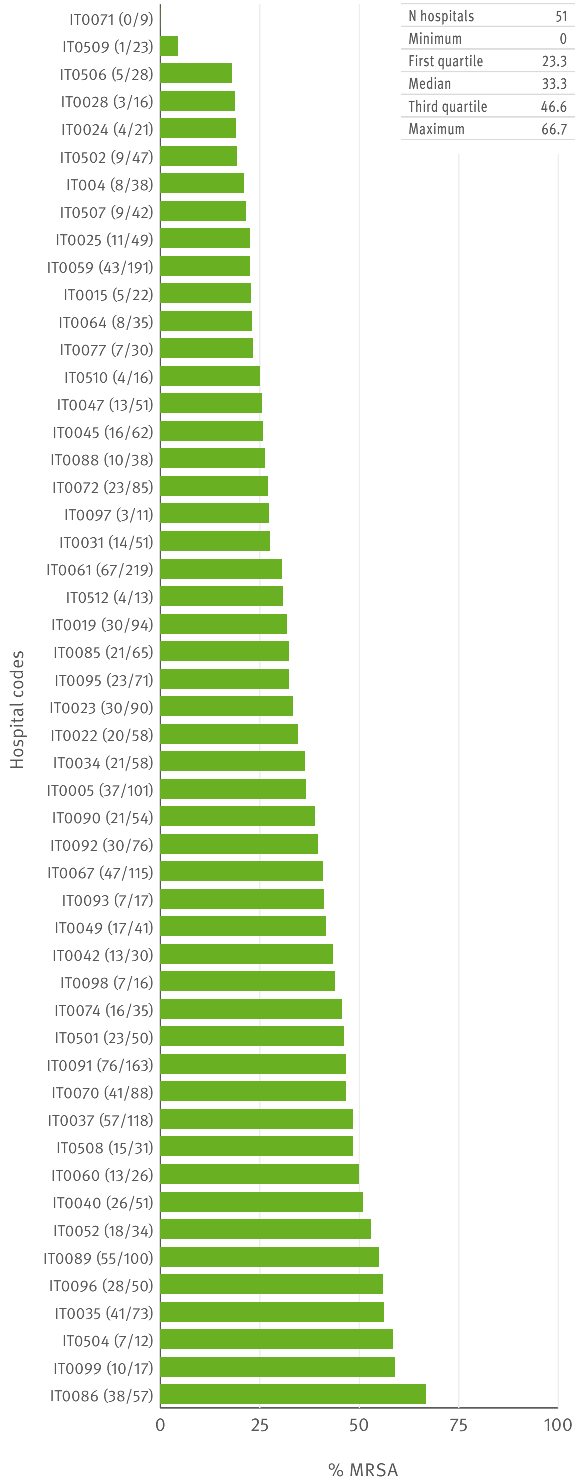
Italy

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**



N laboratories	16
Minimum	0
First quartile	0
Median	6.1
Third quartile	10.8
Maximum	21.1

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



N hospitals	51
Minimum	0
First quartile	23.3
Median	33.3
Third quartile	46.6
Maximum	66.7

Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

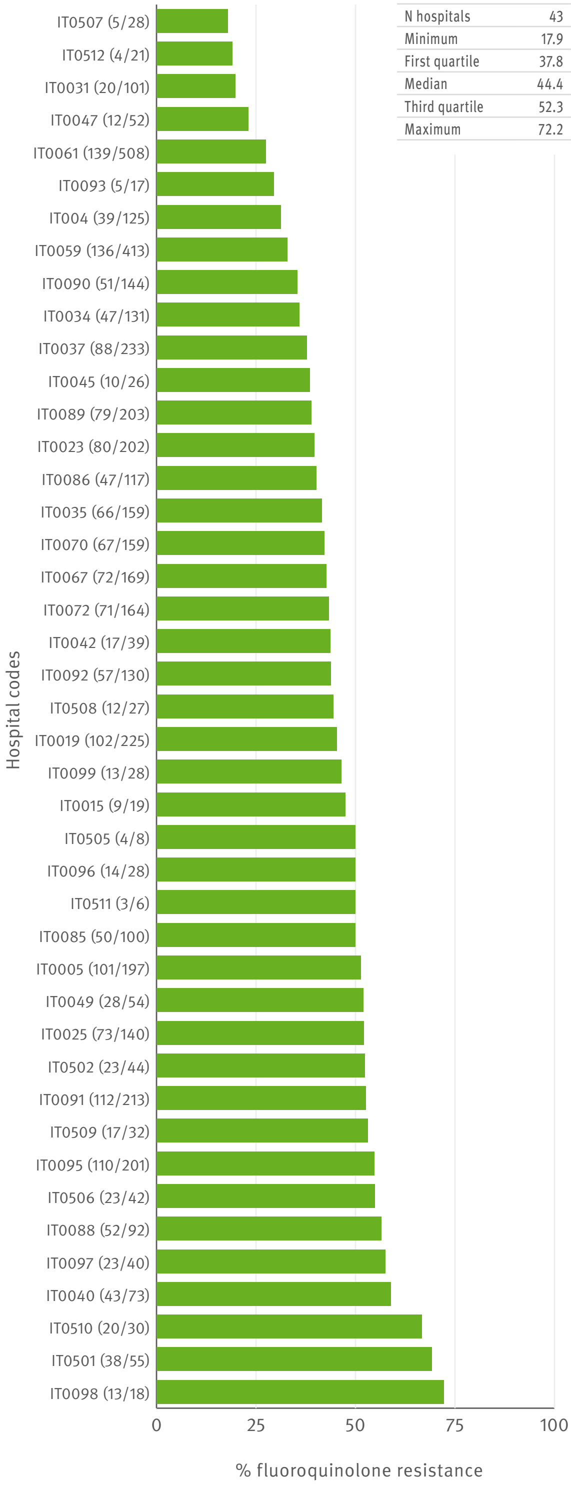
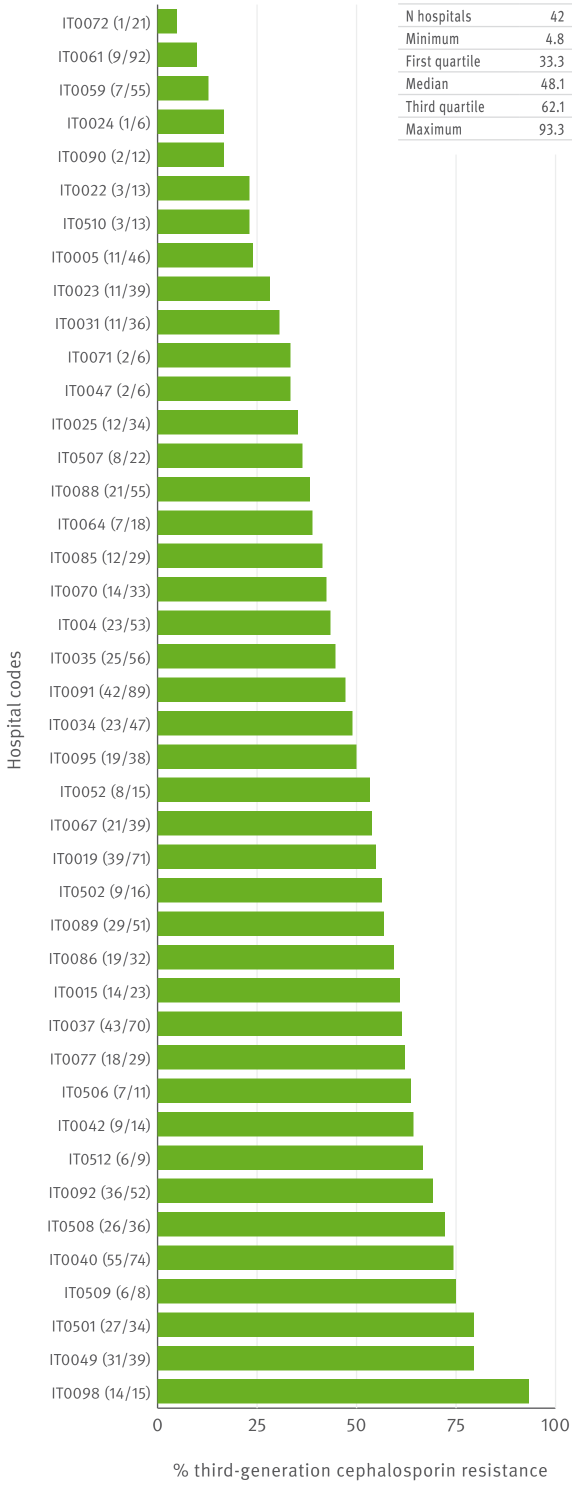


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Latvia

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	-	<1	<1	<1	<1	6	<1	5	10	5
Penicillin RI	-	<1	<1	<1	<1	6	<1	5	13	5
Macrolides RI	-	7	3	3	<1	<1	3	5	<1	4
Staphylococcus aureus										
Oxacillin/Meticillin R	-	26	20	19	8	12	9	14	10	9
Escherichia coli										
Aminopenicilins R	-	-	-	44	43	48	43	50	55	54
Aminoglycosides R	-	-	-	5	14	10	13	11	11	12
Fluoroquinolones R	-	-	-	10	17	14	24	14	17	14
3rd gen. Cephalosporins R	-	-	-	6	14	11	12	12	16	15
Carbapenems R	-	-	-	<1	<1	<1	2	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	-	-	-	9	30	5	12	5	18	7
HL Gentamicin R	-	-	-	50	-	27	38	47	26	29
Vancomycin R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	-	-	-	94	77	90	82	100	96	89
HL Gentamicin R	-	-	-	73	<1	78	79	83	42	28
Vancomycin R	-	-	-	<1	<1	7	18	13	9	6
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	25	22	52	43	55	34	51
Fluoroquinolones R	-	-	-	26	27	45	34	52	38	46
3rd gen. Cephalosporins R	-	-	-	36	44	58	55	55	38	64
Carbapenems R	-	-	-	<1	<1	3	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	17	31	30	17	19	9	12
Ceftazidime R	-	-	-	29	13	36	17	10	9	22
Carbapenems R	-	-	-	13	6	40	7	14	8	11
Aminoglycosides R	-	-	-	47	31	45	22	29	25	22
Fluoroquinolones R	-	-	-	33	13	45	12	19	25	22

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	81	2	100	9	100	16	100	0	100	8	99	52	100	10
CSF	19	30	-	-	0	0	-	-	-	-	1	100	-	-
Gender														
Male	67	6	53	12	40	23	56	0	48	5	59	51	60	11
Female	33	12	47	6	59	11	44	0	53	10	41	54	40	8
Unknown	-	-	-	-	0	0	-	-	-	-	-	-	-	-
Age (years)														
0–4	8	38	8	3	7	0	5	0	-	-	9	46	-	-
5–19	1	100	4	6	2	0	4	0	-	-	1	100	-	-
20–64	62	3	46	10	42	14	44	0	40	13	49	53	33	20
65 and over	30	6	42	9	49	20	48	0	60	4	40	53	67	5
Unknown	-	-	<1	100	-	-	-	-	-	-	1	0	-	-
Hospital department														
ICU	54	5	22	16	28	31	42	0	58	9	41	47	43	8
Internal med.	12	17	43	6	28	11	24	0	23	0	23	55	20	17
Surgery	-	-	9	14	5	21	12	0	10	25	3	50	13	0
Other	35	8	26	9	39	6	22	0	10	0	33	57	23	14
Unknown	-	-	-	-	<1	100	-	-	-	-	1	100	-	-

Latvia

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	5
Minimum	0
First quartile	1.9
Median	12.5
Third quartile	16.7
Maximum	50

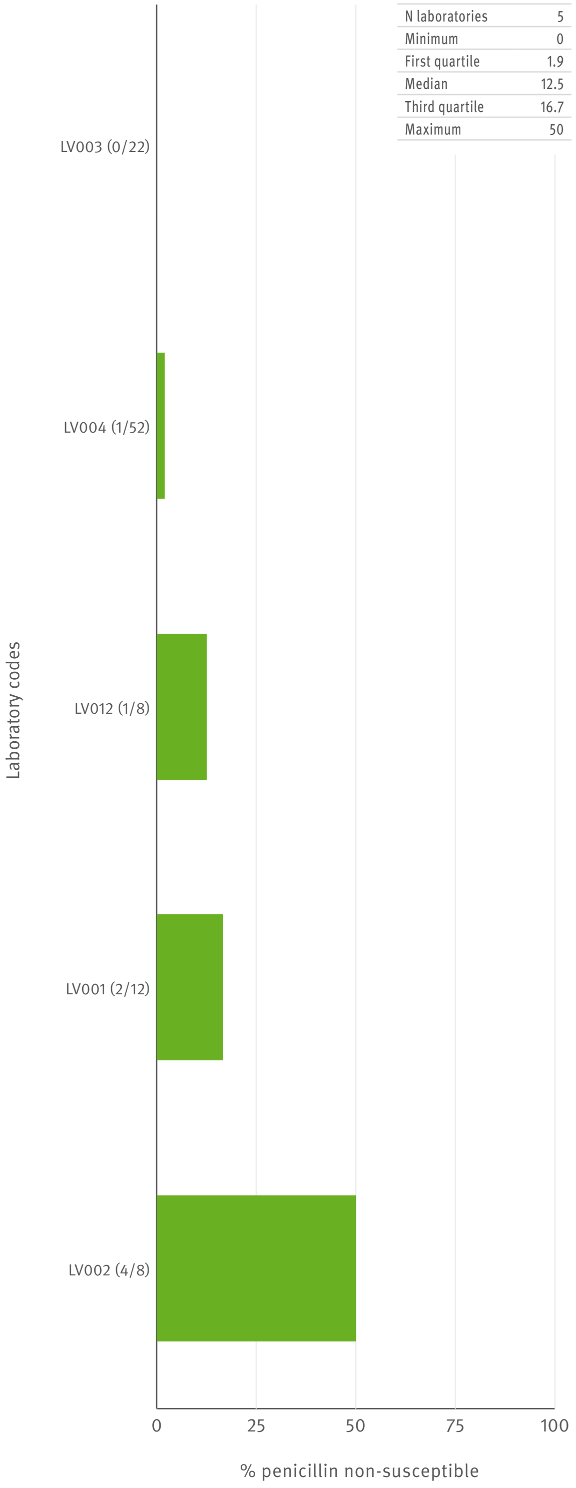


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	11
Minimum	0
First quartile	0
Median	6.3
Third quartile	13.4
Maximum	33.3

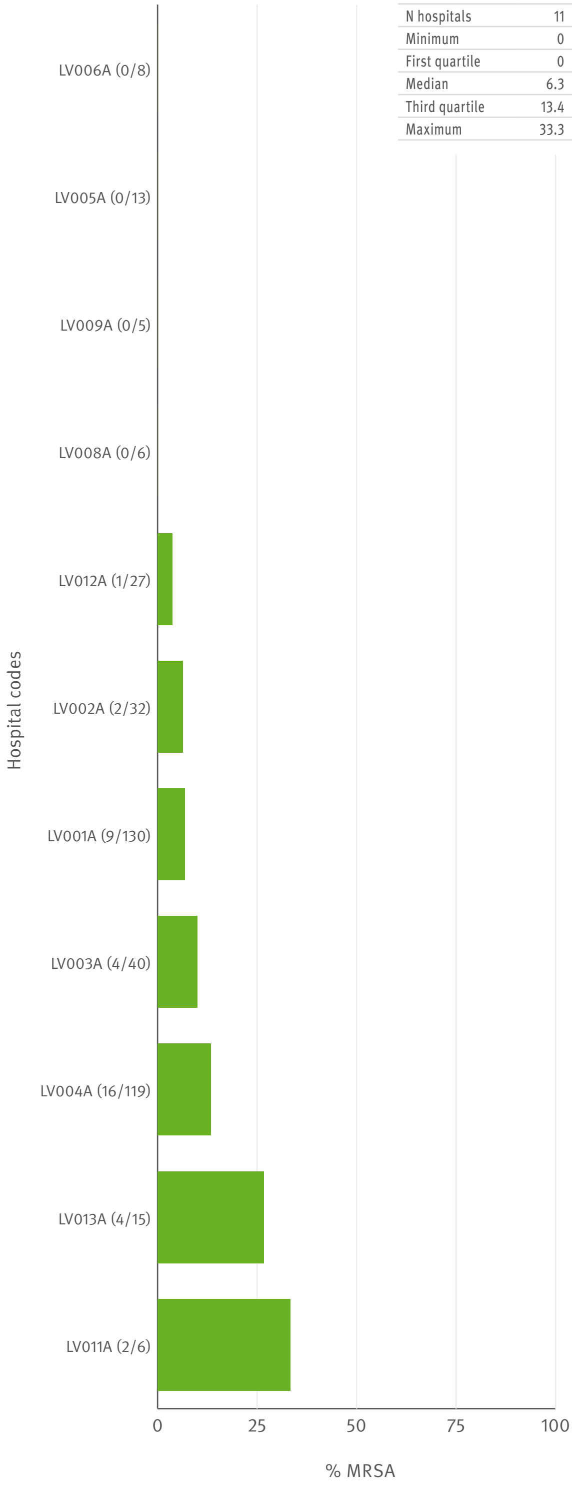
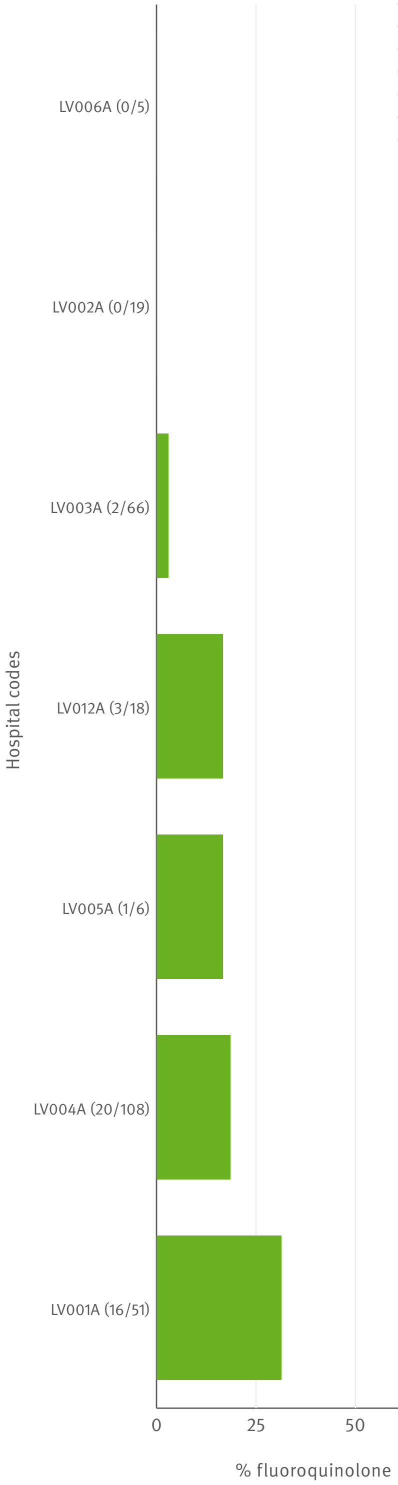
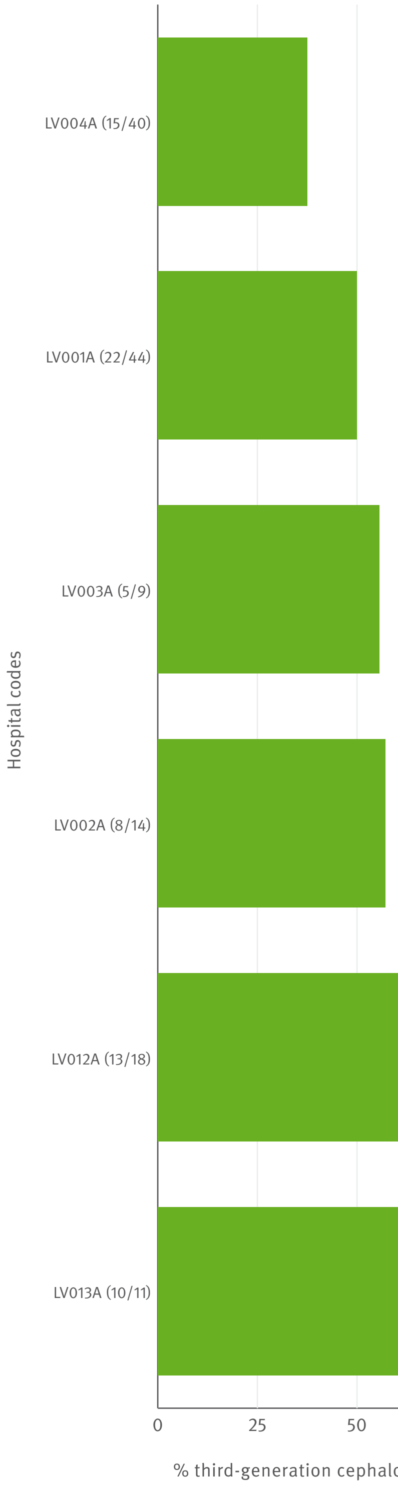


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	7
Minimum	0
First quartile	0
Median	16.7
Third quartile	18.5
Maximum	31.4

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	6
Minimum	37.5
First quartile	50
Median	56.3
Third quartile	72.2
Maximum	90.9

Lithuania

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	96	11	186	9	28

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	-	-	-	<1	1	<1	7	8	2	14
Penicillin RI	-	-	-	16	4	2	9	13	19	16
Macrolides RI	-	-	-	<1	9	6	7	<1	27	26
Staphylococcus aureus										
Oxacillin/Meticillin R	-	-	-	13	9	11	11	14	5	10
Escherichia coli										
Aminopenicilins R	-	-	-	55	50	54	58	56	48	52
Aminoglycosides R	-	-	-	15	12	12	15	15	10	10
Fluoroquinolones R	-	-	-	12	9	14	15	14	13	15
3rd gen. Cephalosporins R	-	-	-	5	7	6	8	9	7	5
Carbapenems R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	-	-	-	5	3	5	3	13	10	5
HL Gentamicin R	-	-	-	50	41	33	48	41	44	51
Vancomycin R	-	-	-	<1	<1	<1	<1	<1	<1	2
Enterococcus faecium										
Aminopenicilins RI	-	-	-	75	100	88	95	88	96	86
HL Gentamicin R	-	-	-	75	81	78	64	87	88	78
Vancomycin R	-	-	-	<1	<1	<1	11	8	8	6
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	26	37	41	56	52	55	63
Fluoroquinolones R	-	-	-	3	8	23	37	36	55	55
3rd gen. Cephalosporins R	-	-	-	23	27	36	57	51	61	64
Carbapenems R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	21	5	14	20	6	13	11
Ceftazidime R	-	-	-	31	<1	10	14	10	21	7
Carbapenems R	-	-	-	21	30	24	19	27	20	18
Aminoglycosides R	-	-	-	29	33	38	19	13	13	14
Fluoroquinolones R	-	-	-	46	38	35	33	16	17	11

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	92	19	100	8	100	14	100	2	100	6	99	62	100	19
CSF	8	0	-	-	-	-	-	-	-	-	1	100	-	-
Gender														
Male	68	21	55	8	35	20	64	1	55	9	63	69	60	11
Female	32	11	44	7	65	11	36	0	45	4	37	52	40	30
Unknown	-	-	0	0	0	0	-	-	-	-	-	-	-	-
Age (years)														
0–4	25	33	4	15	3	4	6	0	2	0	4	75	2	0
5–19	2	0	4	0	1	36	1	0	2	100	1	100	-	-
20–64	49	12	46	7	38	15	39	0	44	11	43	61	43	24
65 and over	24	15	44	9	58	13	54	2	52	0	52	62	55	16
Unknown	-	-	0	0	0	0	-	-	2	0	0	100	-	-
Hospital department														
ICU	36	6	22	12	19	16	31	0	37	4	35	68	45	15
Internal med.	34	31	48	7	48	11	37	0	31	0	28	58	19	36
Surgery	-	-	11	9	6	12	10	0	8	0	10	56	5	0
Other	29	16	19	6	27	18	22	4	24	20	26	64	31	17
Unknown	-	-	0	0	-	-	-	-	-	-	-	-	-	-

Lithuania

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

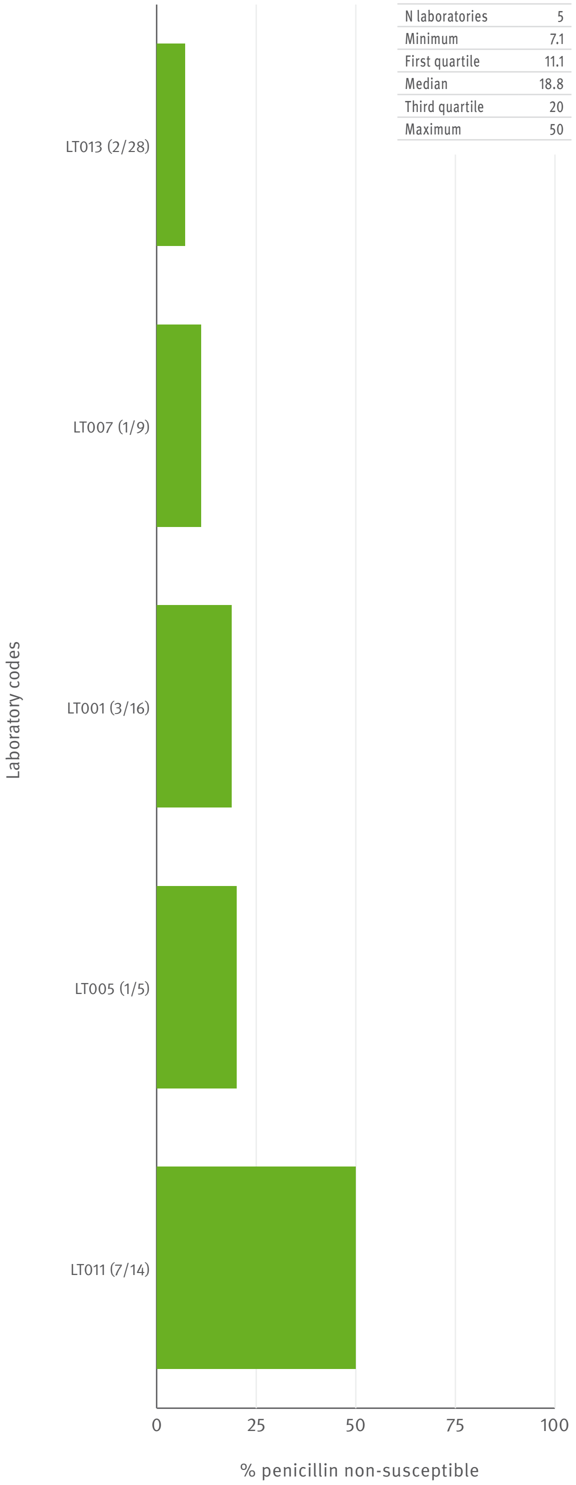


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

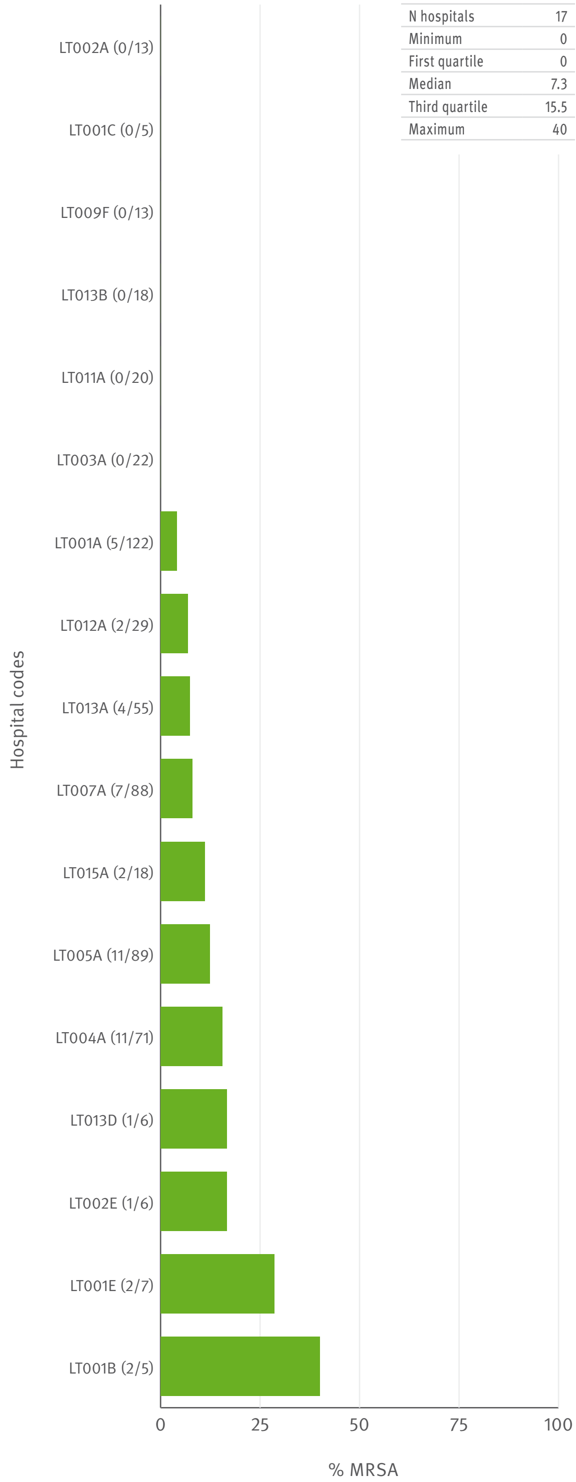


Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	17
Minimum	0
First quartile	6.7
Median	11.1
Third quartile	16.7
Maximum	27.3

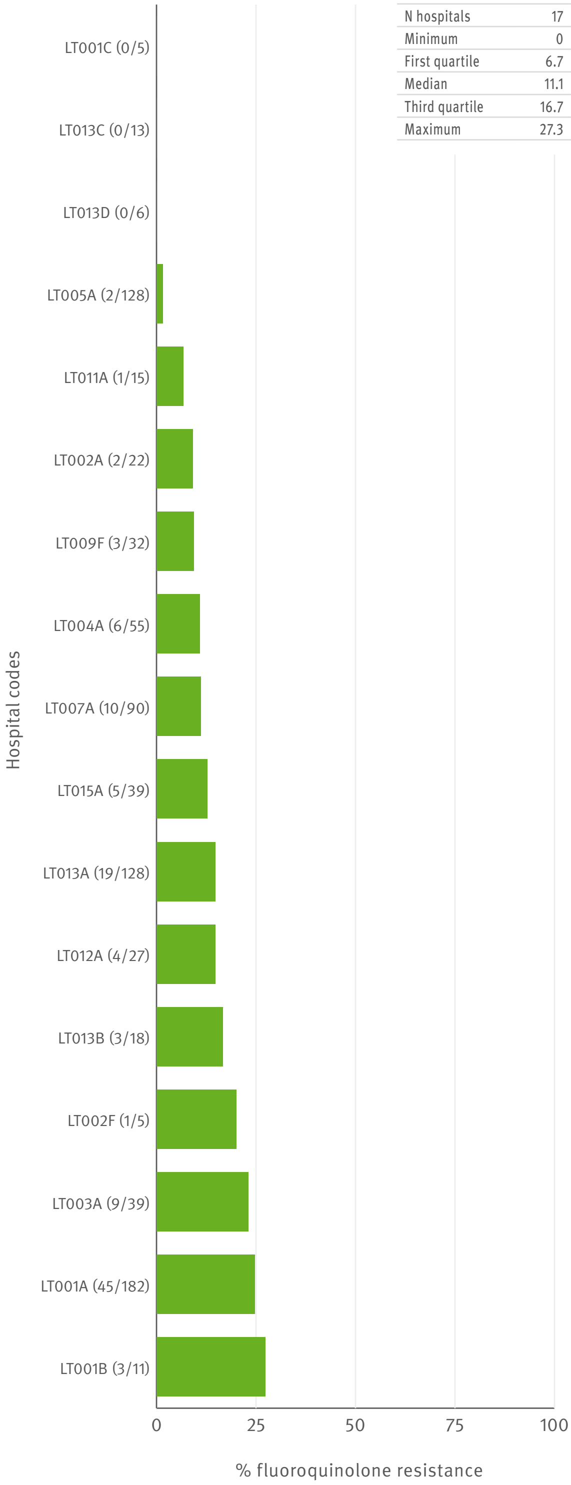
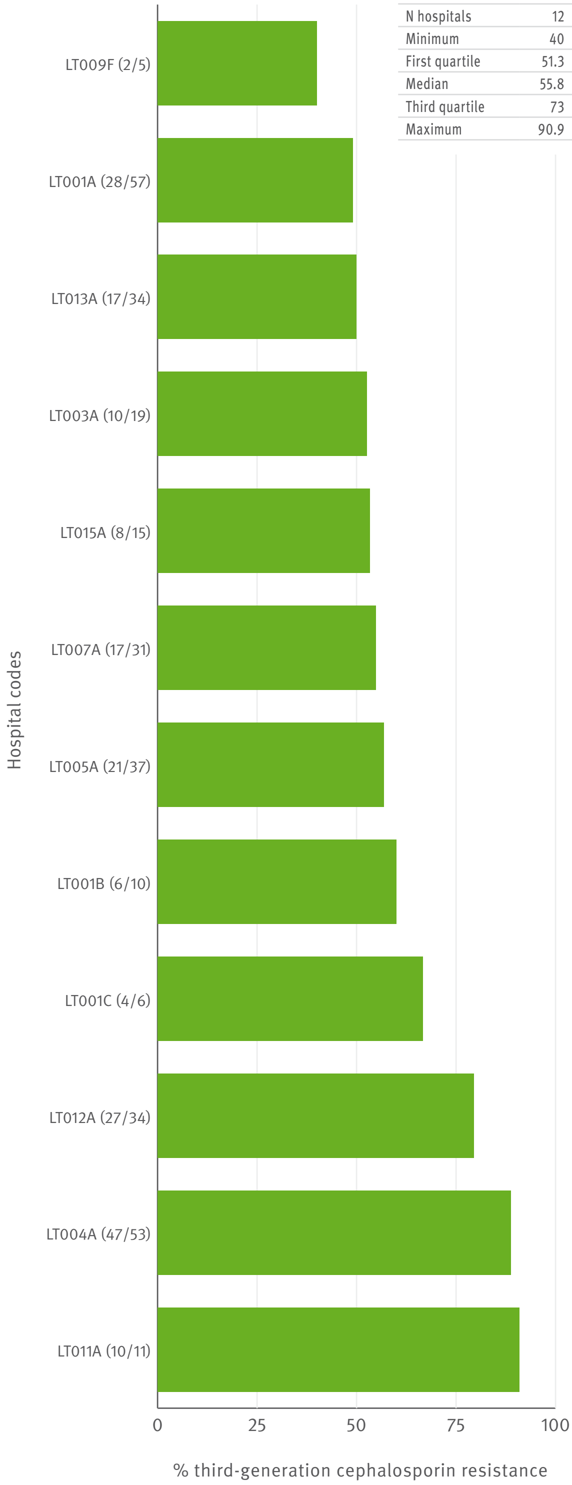


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	12
Minimum	40
First quartile	51.3
Median	55.8
Third quartile	73
Maximum	90.9



Luxembourg

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	301	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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	6	7	5	3	5	11	4	2	3
Penicillin RI	15	11	12	5	6	11	19	12	8	3
Macrolides RI	28	33	24	26	24	14	16	18	15	16
Staphylococcus aureus										
Oxacillin/Meticillin R	21	16	13	19	20	9	13	17	20	15
Escherichia coli										
Aminopenicilins R	49	49	49	46	49	56	57	63	52	51
Aminoglycosides R	4	4	7	6	5	8	9	6	8	6
Fluoroquinolones R	12	18	19	20	21	22	26	26	24	24
3rd gen. Cephalosporins R	<1	<1	3	2	4	6	8	9	8	11
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	5	<1	<1	<1	<1	3	10	6	2	7
HL Gentamicin R	32	18	24	32	44	17	28	46	44	22
Vancomycin R	<1	<1	<1	<1	<1	3	10	4	4	<1
Enterococcus faecium										
Aminopenicilins RI	100	50	36	75	67	76	93	77	71	80
HL Gentamicin R	<1	<1	23	30	10	21	29	19	40	44
Vancomycin R	<1	<1	<1	<1	<1	5	36	32	4	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	<1	4	13	18	5	29	26
Fluoroquinolones R	-	-	-	6	12	12	21	7	33	32
3rd gen. Cephalosporins R	-	-	-	10	2	19	25	5	35	34
Carbapenems R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	<1	9	15	3	14	6	16	16
Ceftazidime R	-	-	<1	10	11	3	14	<1	9	3
Carbapenems R	-	-	<1	7	20	25	15	9	16	6
Aminoglycosides R	-	-	<1	4	22	6	9	9	16	6
Fluoroquinolones R	-	-	<1	10	36	15	11	22	19	19

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	88	7	100	18	100	24	100	2	100	2	99	34	97	11
CSF	12	0	-	-	-	-	-	-	-	-	1	100	3	0
Gender														
Male	57	4	66	17	42	26	74	1	64	4	59	31	51	19
Female	43	9	34	19	58	23	26	4	36	0	41	40	49	3
Age (years)														
0–4	6	0	4	10	2	7	1	0	-	-	6	67	-	-
5–19	7	17	3	11	1	0	-	-	-	-	-	-	3	0
20–64	37	3	38	14	27	18	27	3	23	0	36	43	29	6
65 and over	49	8	55	21	71	27	72	1	75	3	58	26	68	14
Unknown	-	-	-	-	-	-	-	-	2	0	-	-	-	-
Hospital department														
ICU	16	0	13	24	7	36	18	0	34	0	9	56	22	14
Internal med.	7	17	11	18	10	21	10	0	7	0	9	22	13	0
Surgery	4	0	9	14	15	18	10	0	9	0	12	33	8	20
Other	51	7	44	12	41	25	38	0	30	8	45	39	35	14
Unknown	22	6	24	26	27	24	24	8	20	0	24	25	22	7

Luxembourg

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

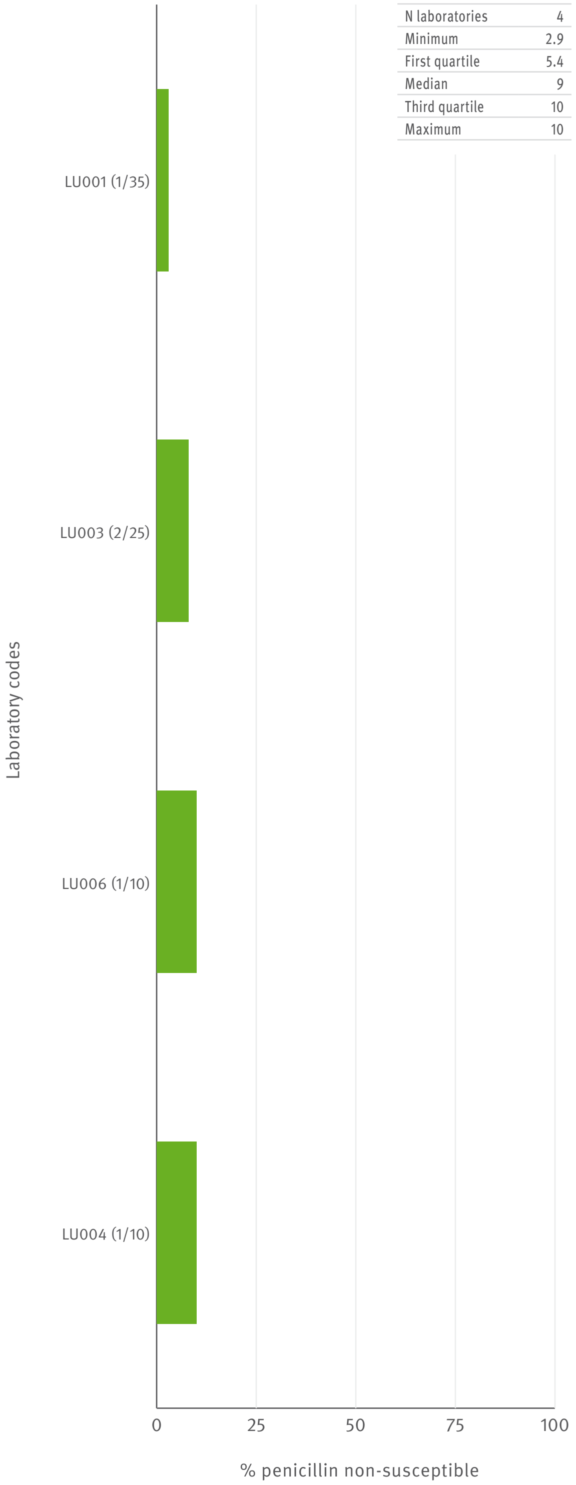


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

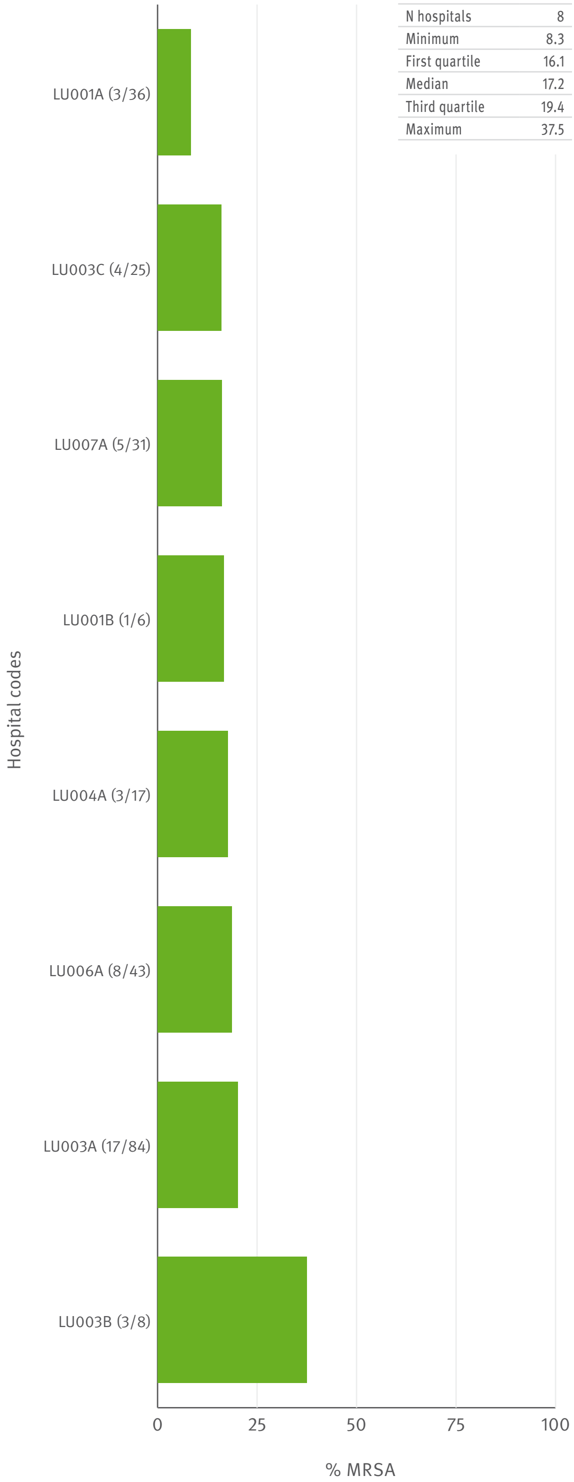


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	11
Minimum	0
First quartile	9.1
Median	23.6
Third quartile	25.2
Maximum	39.1

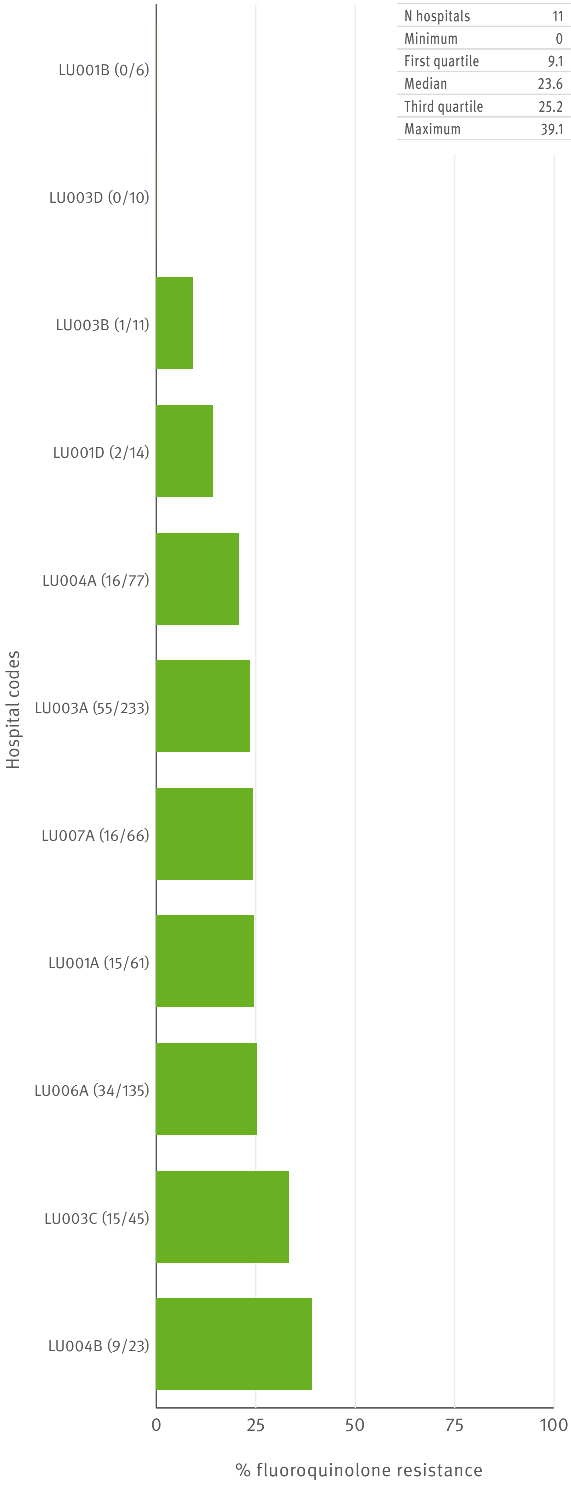
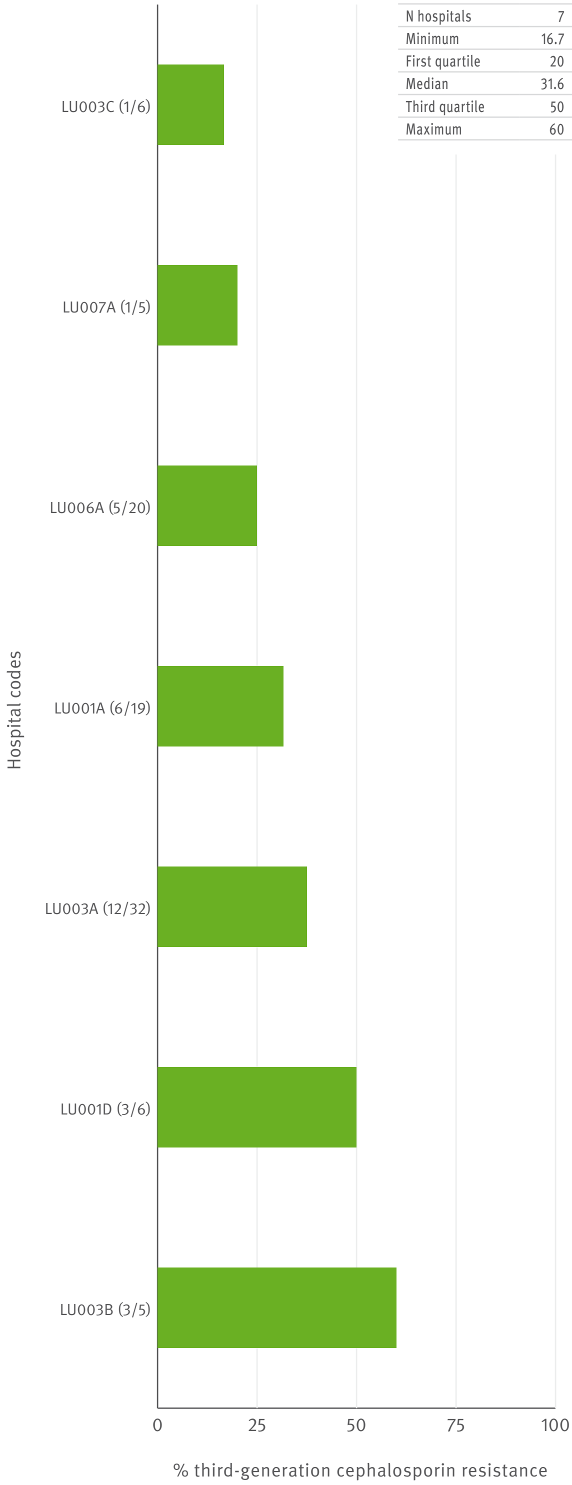


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	7
Minimum	16.7
First quartile	20
Median	31.6
Third quartile	50
Maximum	60



Malta

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	214	1	30	1	56	1	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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	8	3	<1	24	<1	11	10	<1
Penicillin RI	<1	<1	15	7	<1	47	14	22	50	39
Macrolides RI	38	25	46	45	8	35	13	18	13	50
Staphylococcus aureus										
Oxacillin/Meticillin R	43	56	56	67	52	56	59	48	49	47
Escherichia coli										
Aminopenicilins R	39	48	51	56	54	52	54	44	53	54
Aminoglycosides R	18	20	7	15	20	22	21	22	16	14
Fluoroquinolones R	24	36	31	32	35	34	30	34	32	31
3rd gen. Cephalosporins R	2	4	1	4	13	21	15	16	13	14
Carbapenems R	<1	<1	<1	<1	<1	<1	1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	5	<1	3	2	3	<1	5	<1	<1	4
HL Gentamicin R	29	44	32	-	-	-	-	-	-	-
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	33	43	25	14	40	60	75	100	64	67
HL Gentamicin R	50	<1	<1	-	-	-	-	-	-	-
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	17	6	<1	<1	<1	12	10	27
Fluoroquinolones R	-	-	11	6	11	8	3	16	13	25
3rd gen. Cephalosporins R	-	-	6	6	7	<1	<1	12	13	27
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	4	4
Pseudomonas aeruginosa										
Piperacillin R	-	-	22	47	11	45	36	36	24	10
Ceftazidime R	-	-	11	30	3	33	29	14	12	6
Carbapenems R	-	-	18	20	11	30	21	24	24	3
Aminoglycosides R	-	-	16	8	8	23	21	31	33	6
Fluoroquinolones R	-	-	44	24	11	19	22	24	19	<1

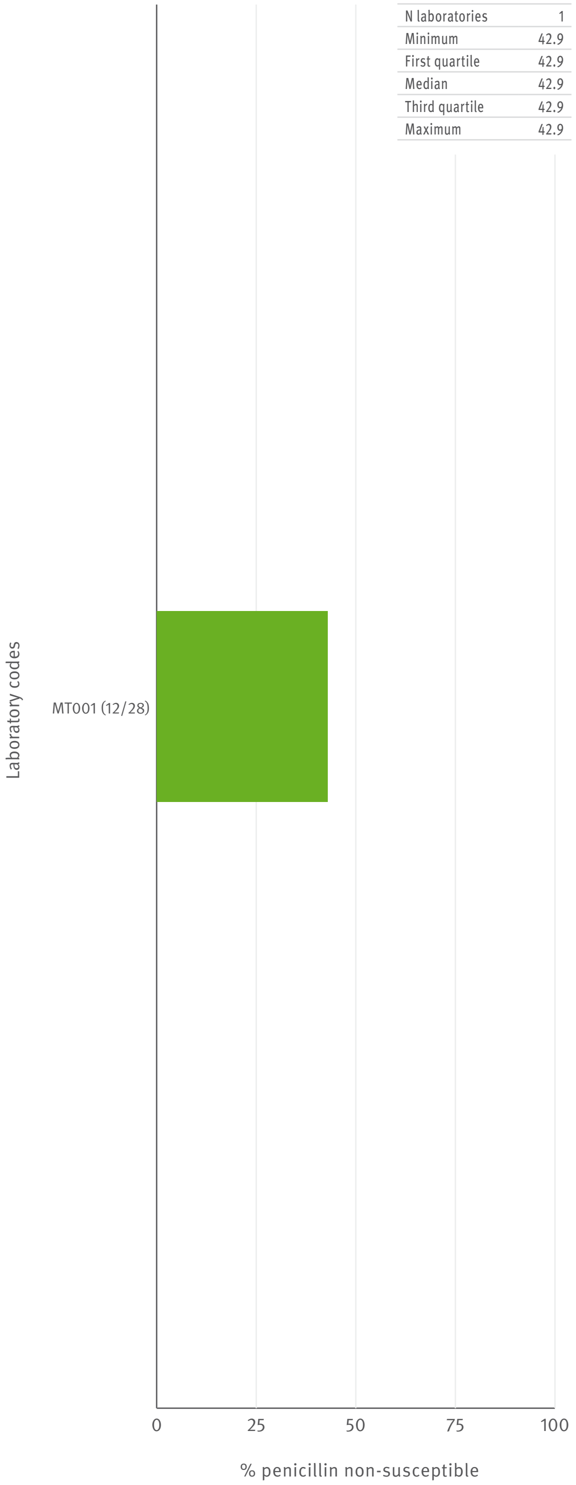
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	96	44	100	48	100	32	100	0	100	0	99	21	99	15
CSF	4	0	-	-	0	0	-	-	-	-	1	0	1	0
Gender														
Male	46	31	56	51	37	41	60	0	70	0	48	27	62	13
Female	46	54	32	42	52	25	33	0	20	0	40	19	30	14
Unknown	7	50	13	52	11	34	6	0	10	0	12	0	8	33
Age (years)														
0–4	21	50	6	50	2	0	14	0	-	-	4	0	3	0
5–19	-	-	2	50	1	0	6	0	5	0	1	0	5	0
20–64	21	50	29	44	22	19	17	0	5	0	35	18	47	21
65 and over	57	38	63	50	75	37	62	0	90	0	60	23	45	12
Hospital department														
ICU	-	-	7	65	2	22	8	0	10	0	8	44	25	39
Internal med.	11	0	33	42	15	32	16	0	30	0	20	23	19	0
Surgery	-	-	9	77	6	35	11	0	15	0	10	18	10	14
Other	89	48	48	44	73	31	62	0	45	0	58	16	41	10
Unknown	-	-	2	60	4	41	3	0	-	-	3	33	5	0

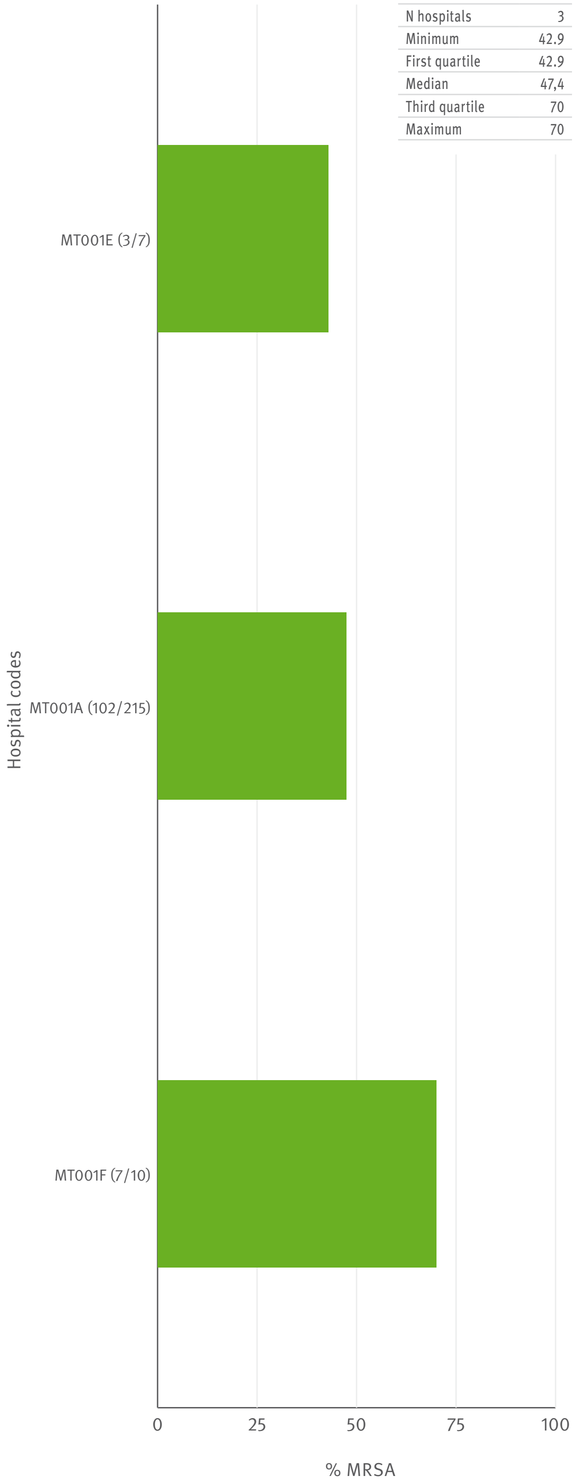
Malta

Figure 1: *S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)



N laboratories	1
Minimum	42.9
First quartile	42.9
Median	42.9
Third quartile	42.9
Maximum	42.9

Figure 2: *S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)



N hospitals	3
Minimum	42.9
First quartile	42.9
Median	47,4
Third quartile	70
Maximum	70

Figure 3: *E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)

N hospitals	3
Minimum	30.7
First quartile	30.7
Median	34.2
Third quartile	39.4
Maximum	39.4

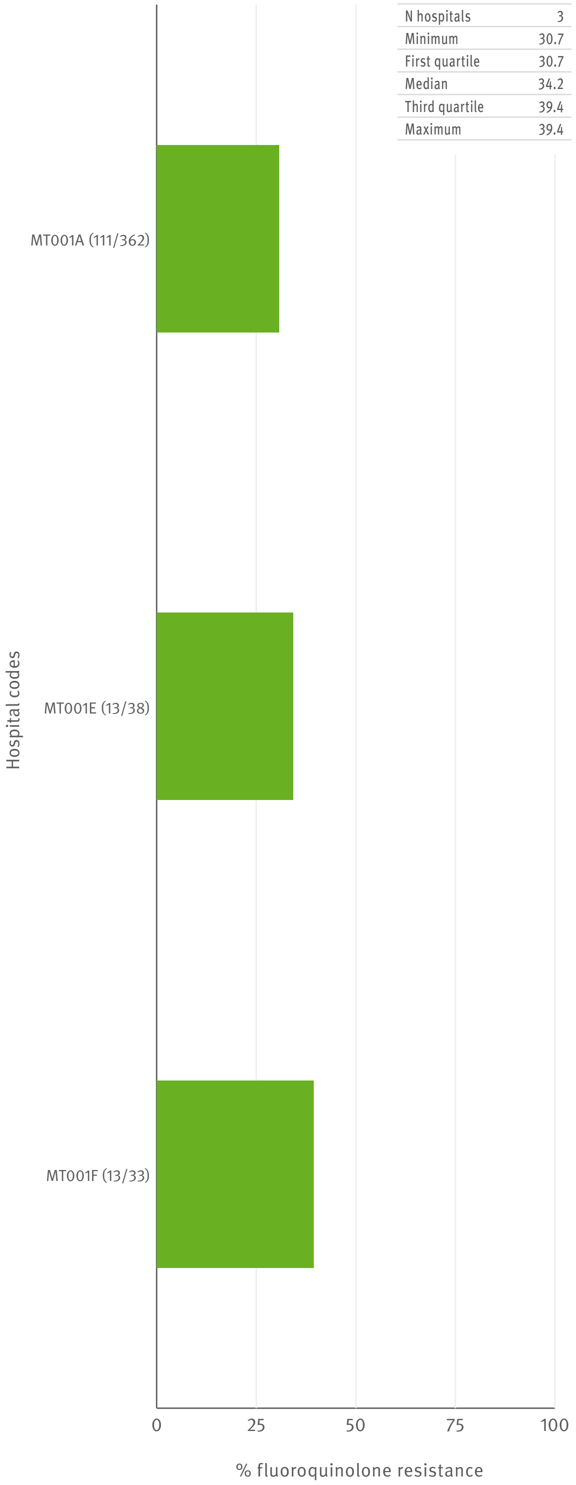
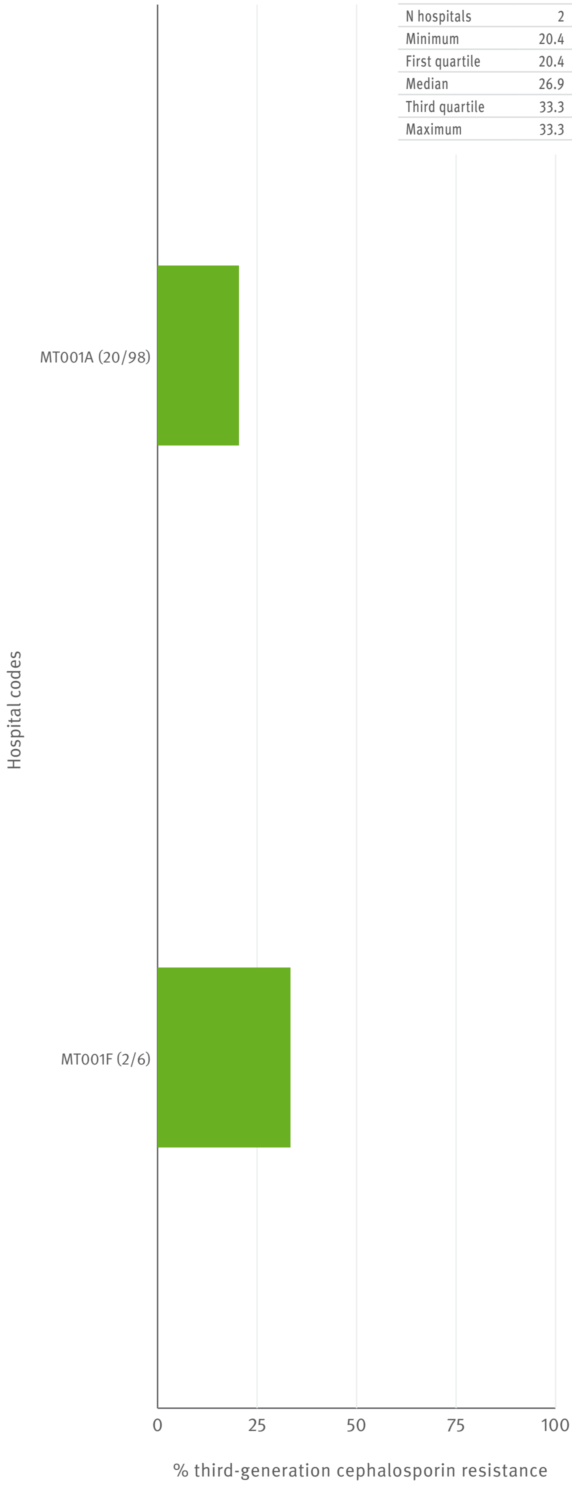


Figure 4: *K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)

N hospitals	2
Minimum	20.4
First quartile	20.4
Median	26.9
Third quartile	33.3
Maximum	33.3



Netherlands

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Penicillin RI	1	2	1	1	2	2	1	2	1	2
Macrolides RI	5	8	11	8	7	7	5	6	5	4
Staphylococcus aureus										
Oxacillin/Meticillin R	1	1	<1	<1	2	<1	<1	1	1	1
Escherichia coli										
Aminopenicilins R	45	43	48	47	49	48	45	48	49	49
Aminoglycosides R	3	3	4	3	5	6	4	7	8	7
Fluoroquinolones R	7	7	10	11	13	14	11	14	14	15
3rd gen. Cephalosporins R	1	1	2	3	4	5	4	5	6	6
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	4	3	3	5	5	<1	2	3	1	1
HL Gentamicin R	29	37	38	28	38	34	31	34	33	31
Vancomycin R	1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	30	42	61	73	83	86	89	89	91	91
HL Gentamicin R	20	20	40	50	62	53	76	65	66	63
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	5	4	5	7	3	7	8	6
Fluoroquinolones R	-	-	6	4	4	7	4	7	7	5
3rd gen. Cephalosporins R	-	-	4	4	7	8	6	7	8	7
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	4	2	2	6	3	4	6	5
Ceftazidime R	-	-	5	5	4	6	4	3	5	3
Carbapenems R	-	-	5	2	2	6	3	3	3	3
Aminoglycosides R	-	-	7	5	3	4	2	3	5	4
Fluoroquinolones R	-	-	9	9	5	8	7	4	7	6

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	95	1	100	1	100	15	100	0	100	1	100	7	99	3
CSF	5	3	-	-	0	0	-	-	-	-	‹1	17	1	10
Gender														
Male	50	1	61	1	50	19	69	0	60	1	59	9	66	4
Female	50	1	39	2	50	11	31	0	40	1	41	6	34	3
Unknown	-	-	-	-	0	0	-	-	-	-	-	-	-	-
Age (years)														
0–4	2	2	5	1	2	6	3	0	2	0	2	4	1	0
5–19	2	0	3	2	1	13	1	0	1	0	1	25	1	17
20–64	40	2	32	2	27	16	26	0	36	1	28	10	28	5
65 and over	55	1	60	1	71	15	70	0	61	1	70	6	70	3
Unknown	-	-	-	-	0	0	0	0	-	-	-	-	-	-
Hospital department														
ICU	10	2	9	4	7	15	14	0	42	0	11	17	16	7
Internal med.	9	3	13	0	15	13	11	0	9	2	14	6	12	2
Surgery	2	2	6	1	4	16	6	0	5	0	5	17	6	2
Other	40	1	30	1	31	15	28	0	14	2	28	6	29	2
Unknown	40	1	41	1	42	16	39	0	29	0	42	6	38	4

Netherlands

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

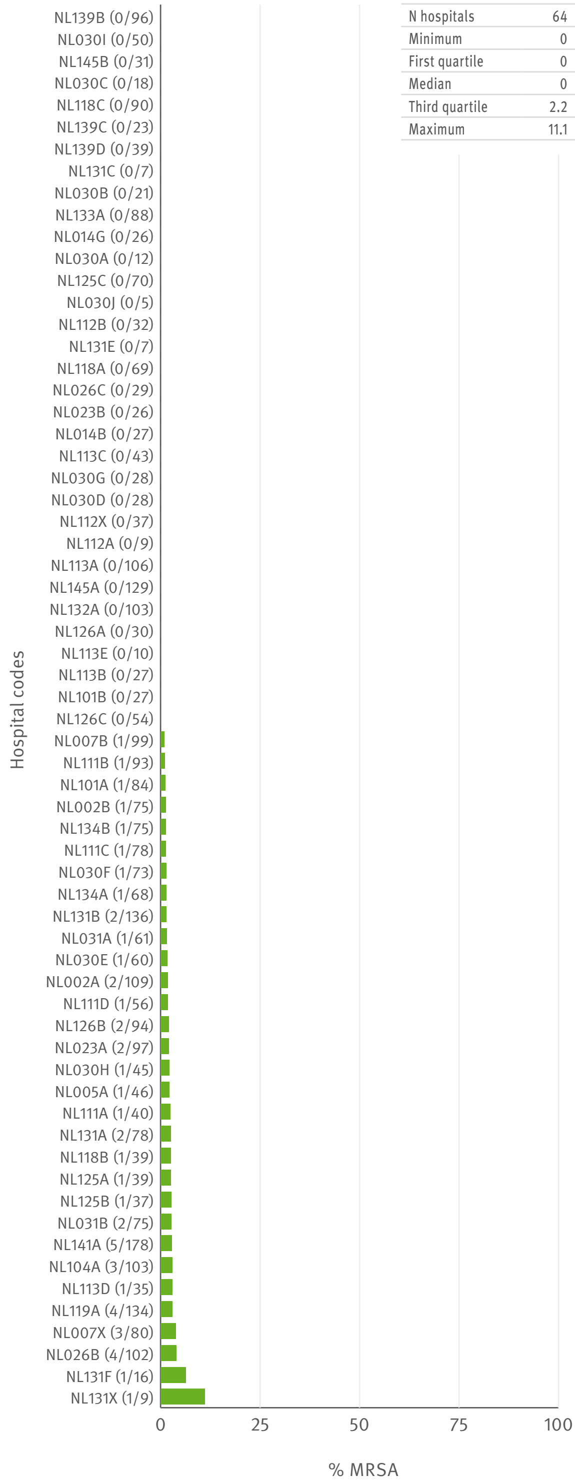
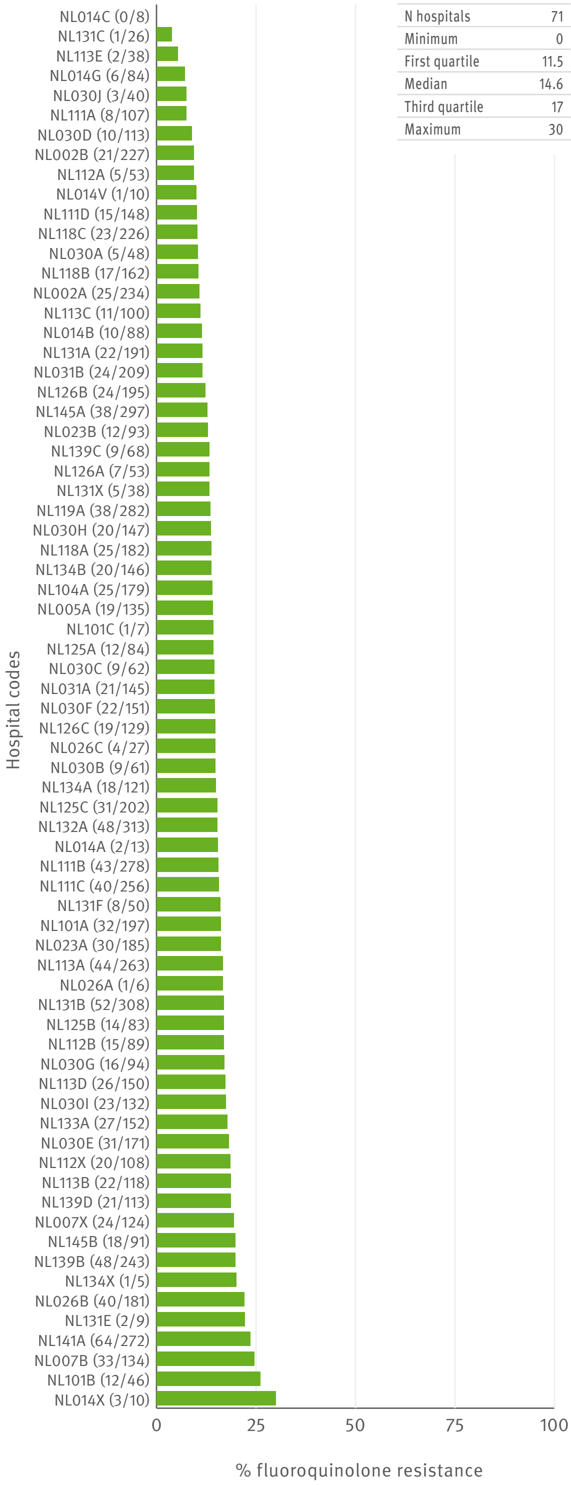
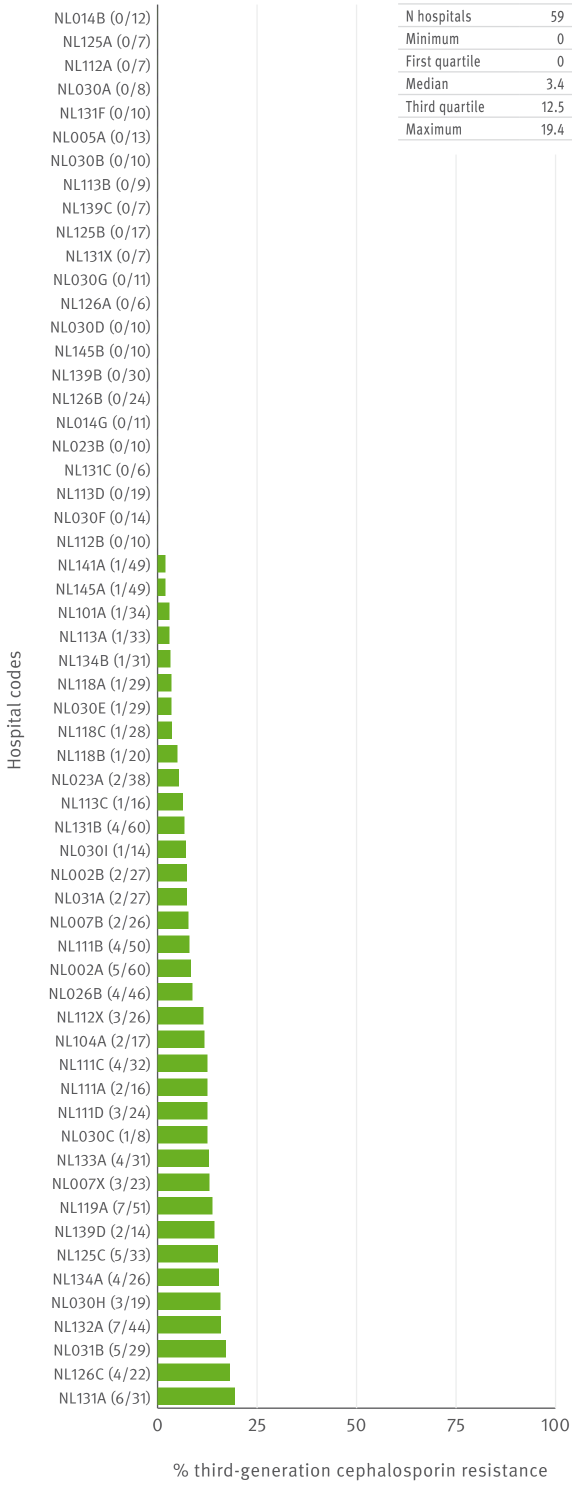


Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	71
Minimum	0
First quartile	11.5
Median	14.6
Third quartile	17
Maximum	30

Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	59
Minimum	0
First quartile	0
Median	3.4
Third quartile	12.5
Maximum	19.4

Norway

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	1
Penicillin RI	<1	2	2	2	2	2	2	4	3	6
Macrolides RI	8	8	14	12	10	7	6	4	4	5
Staphylococcus aureus										
Oxacillin/Meticillin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	1
Escherichia coli										
Aminopenicilins R	34	32	34	35	38	38	37	38	39	43
Aminoglycosides R	<1	<1	2	2	3	3	3	4	4	6
Fluoroquinolones R	2	4	5	5	7	7	9	9	9	11
3rd gen. Cephalosporins R	<1	<1	<1	1	2	3	2	4	4	5
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	4	<1	3	3	2	2	<1	<1	<1	1
HL Gentamicin R	38	27	32	33	34	29	36	34	22	30
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	43	80	72	75	81	78	76	85	75	83
HL Gentamicin R	14	25	44	45	52	54	38	57	43	37
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	1	2	<1
Klebsiella pneumoniae										
Aminoglycosides R	<1	2	3	<1	<1	1	3	2	3	2
Fluoroquinolones R	<1	<1	1	7	5	4	6	7	4	4
3rd gen. Cephalosporins R	<1	<1	2	2	2	2	3	2	3	3
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	<1	13	3	3	2	6	4	3	5	7
Ceftazidime R	<1	<1	3	5	3	4	5	2	3	6
Carbapenems R	<1	4	3	9	9	7	5	1	4	7
Aminoglycosides R	<1	4	<1	1	2	<1	<1	<1	<1	2
Fluoroquinolones R	4	5	4	9	7	3	2	4	5	6

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	96	5	100	1	100	10	100	0	100	1	100	3	100	6
CSF	4	4	-	-	0	0	-	-	-	-	0	0	0	0
Gender														
Male	50	5	64	1	47	14	72	0	60	1	57	4	69	5
Female	50	5	36	1	53	7	28	0	40	1	43	2	31	7
Unknown	0	50	-	-	0	0	0	0	-	-	-	-	-	-
Age (years)														
0–4	4	9	3	5	1	1	3	4	0	0	1	13	2	33
5–19	2	12	3	1	1	6	1	0	1	0	1	0	1	0
20–64	42	4	35	1	27	12	24	0	32	2	28	3	26	10
65 and over	52	4	59	1	71	10	73	0	67	1	70	3	72	4
Hospital department														
ICU	7	4	7	1	5	11	8	0	14	0	5	10	11	13
Internal med.	32	4	31	1	31	9	28	0	28	1	28	3	28	4
Surgery	4	0	14	0	13	11	19	0	21	0	17	1	14	6
Other	56	5	47	1	51	11	44	0	38	2	50	3	47	5
Unknown	1	0	0	0	1	6	0	0	-	-	0	0	0	0

Norway

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

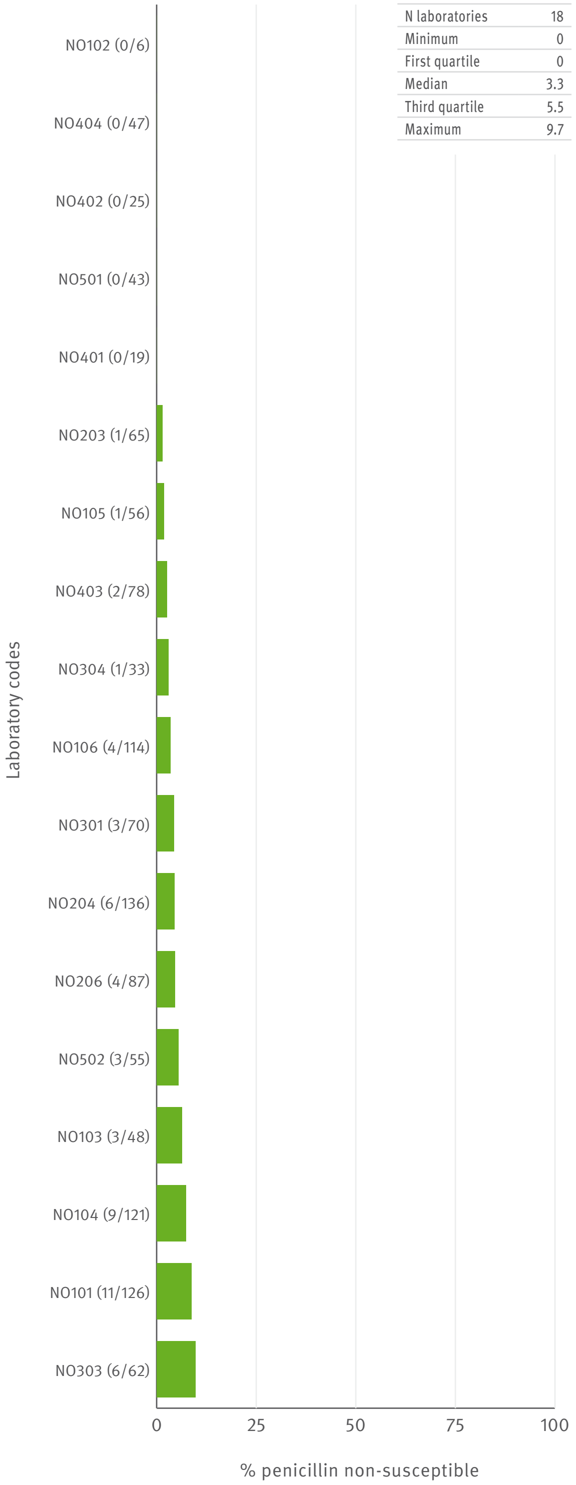


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

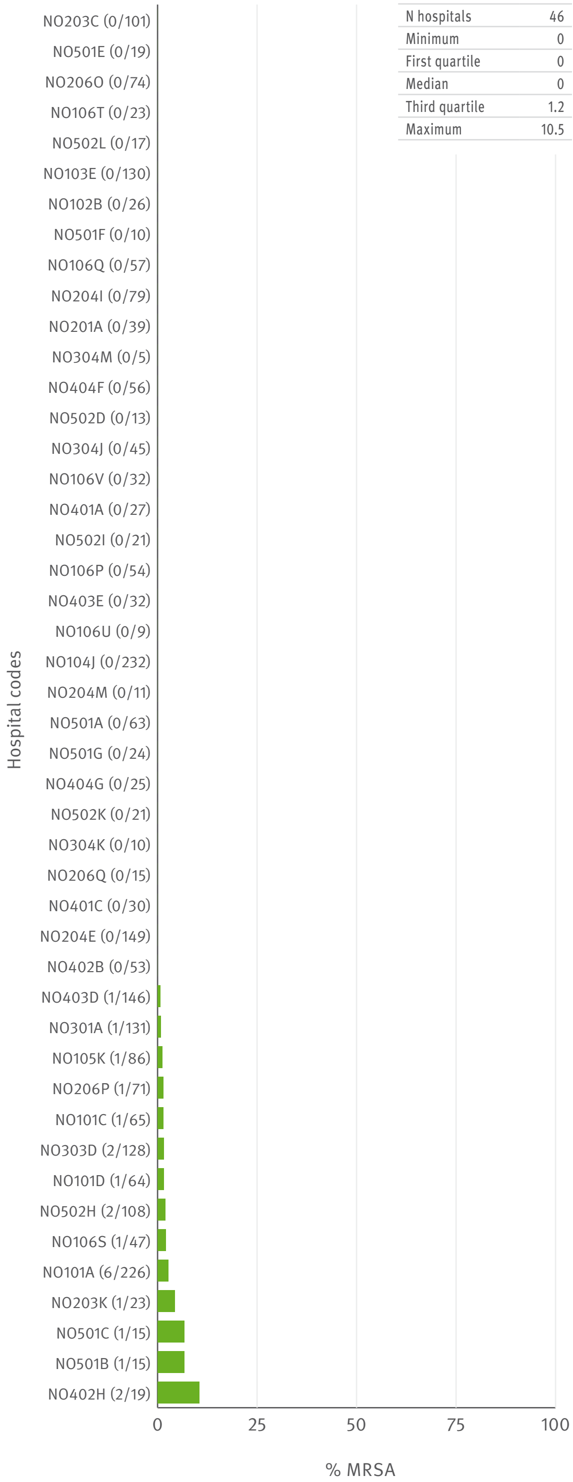


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	47
Minimum	0
First quartile	6.2
Median	8.8
Third quartile	13
Maximum	27.5

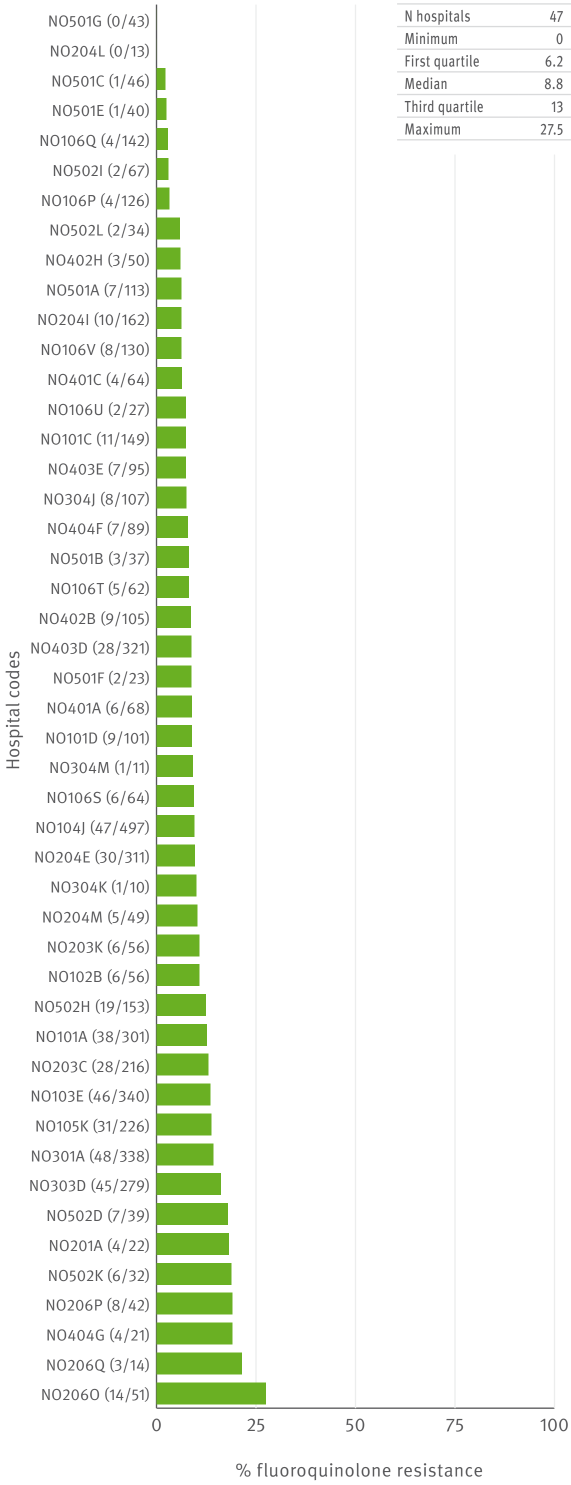
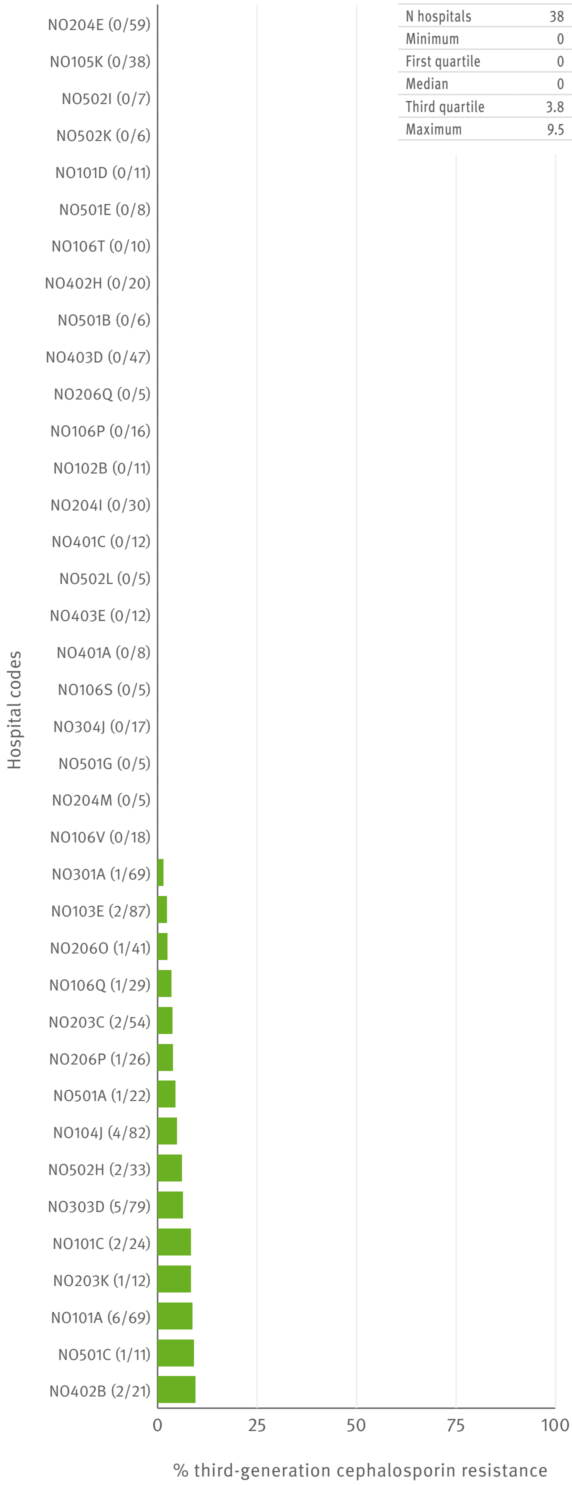


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	38
Minimum	0
First quartile	0
Median	0
Third quartile	3.8
Maximum	9.5



Poland

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	782	41	1056	35	385	37	369	36	177

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	19	<1	17	<1	10	12	30	24	4	5
Penicillin RI	19	<1	33	<1	29	13	30	24	18	21
Macrolides RI	14	19	33	11	-	50	19	39	27	27
Staphylococcus aureus										
Oxacillin/Meticillin R	19	19	24	20	15	12	20	13	24	29
Escherichia coli										
Aminopenicilins R	50	45	56	55	56	54	65	60	62	63
Aminoglycosides R	10	5	7	11	6	7	7	9	8	12
Fluoroquinolones R	7	9	20	20	13	20	23	26	27	29
3rd gen. Cephalosporins R	4	5	5	4	2	2	9	8	12	13
Carbapenems R	-	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	2	9	2	4	6	<1	3	1	1
HL Gentamicin R	48	33	48	50	46	29	39	36	48	39
Vancomycin R	<1	<1	<1	<1	2	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	91	86	95	95	88	78	98	95	93	98
HL Gentamicin R	55	100	62	85	84	67	75	65	70	66
Vancomycin R	<1	<1	5	<1	<1	<1	1	8	8	8
Klebsiella pneumoniae										
Aminoglycosides R	-	-	57	36	31	26	29	31	48	52
Fluoroquinolones R	-	-	34	29	3	32	32	33	58	60
3rd gen. Cephalosporins R	-	-	66	38	34	37	49	40	60	60
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	50	43	36	32	30	29	31	30
Ceftazidime R	-	-	31	42	21	27	21	22	23	24
Carbapenems R	-	-	27	30	18	14	25	25	24	23
Aminoglycosides R	-	-	54	46	40	27	28	30	33	24
Fluoroquinolones R	-	-	31	41	37	13	26	28	30	27

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	85	20	100	27	100	28	100	0	100	8	99	60	98	23
CSF	15	18	-	-	<1	11	-	-	-	-	1	75	2	43
Gender														
Male	56	19	63	27	45	35	63	0	59	9	64	64	63	24
Female	43	21	37	26	55	23	36	1	41	7	36	54	36	22
Unknown	0	0	<1	25	1	15	1	0	1	0	0	0	1	50
Age (years)														
0–4	8	43	5	19	4	9	6	0	5	0	6	57	4	13
5–19	6	41	2	29	1	23	0	0	2	33	3	29	3	36
20–64	48	18	49	27	38	29	42	0	47	13	46	64	48	28
65 and over	31	14	38	29	53	29	44	0	38	4	42	58	38	18
Unknown	7	11	6	15	4	29	7	0	8	0	3	72	7	24
Hospital department														
ICU	8	32	10	40	9	29	24	0	31	3	35	76	30	37
Internal med.	26	16	22	25	27	23	15	0	10	6	10	42	10	12
Surgery	1	33	9	38	6	43	14	0	11	3	8	59	10	35
Other	37	25	30	16	29	30	26	1	35	17	26	56	30	17
Unknown	28	13	29	30	29	28	21	0	13	4	21	48	21	14

Poland

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

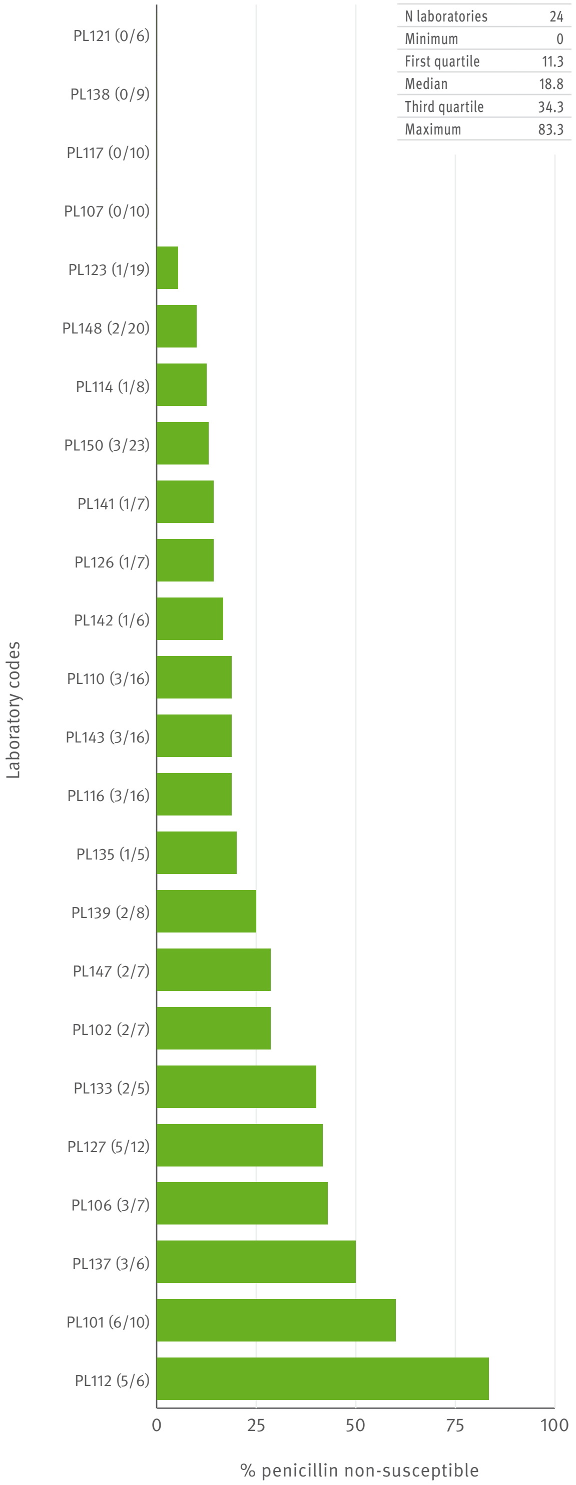


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

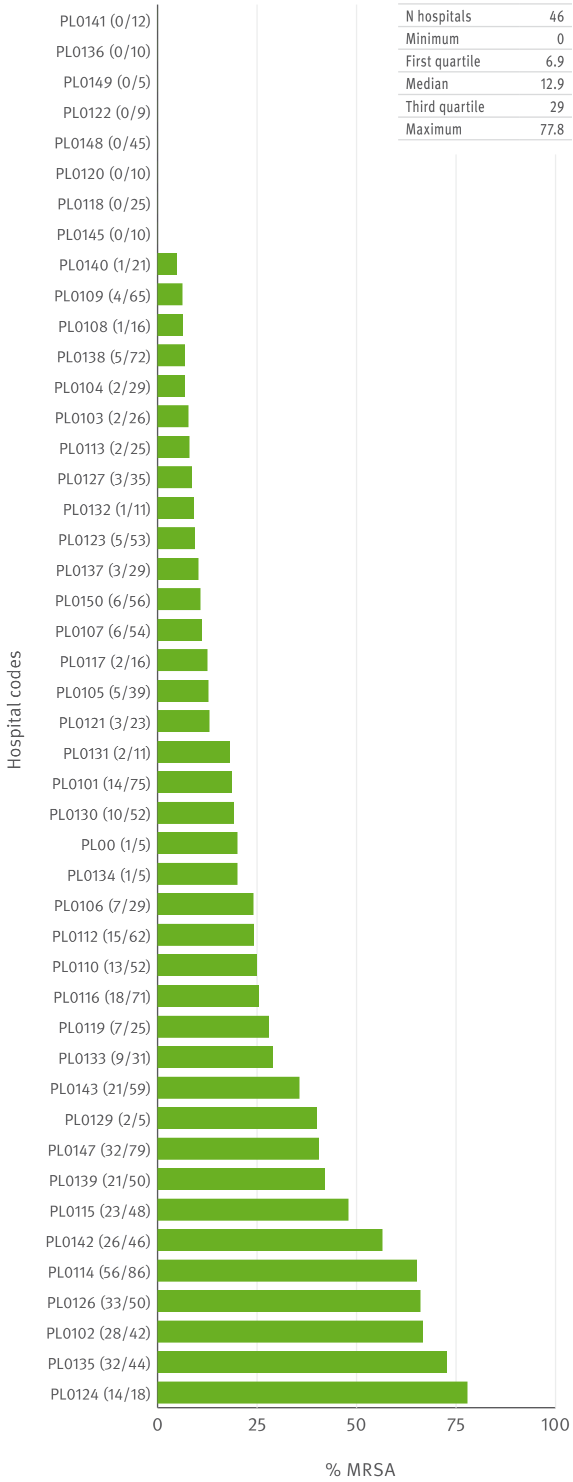
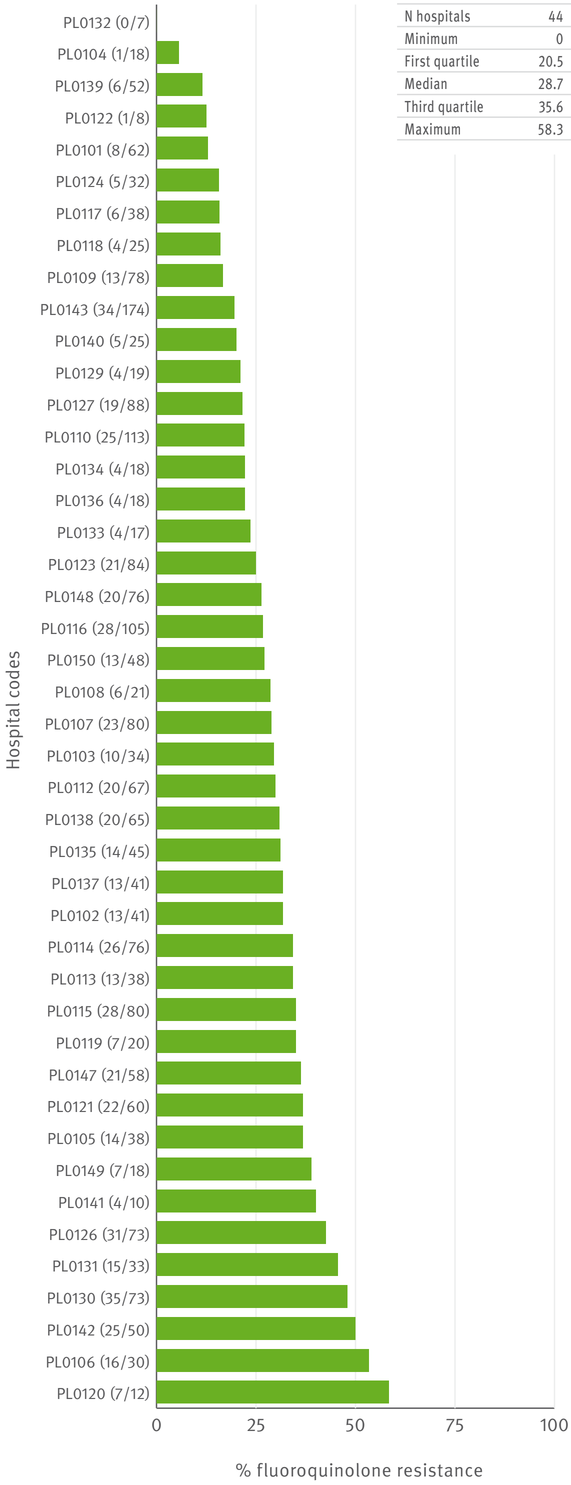
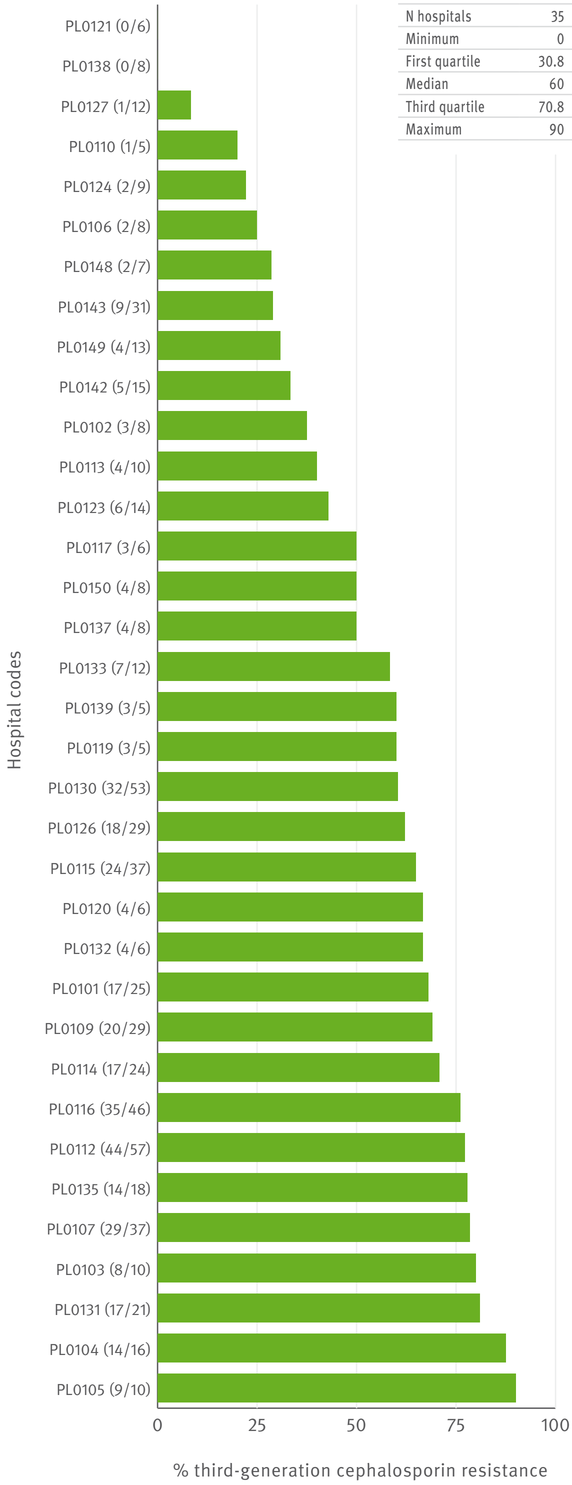


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	44
Minimum	0
First quartile	20.5
Median	28.7
Third quartile	35.6
Maximum	58.3

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	35
Minimum	0
First quartile	30.8
Median	60
Third quartile	70.8
Maximum	90

Portugal

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	<1	<1	<1	18	15	8	5
Penicillin RI	20	27	17	17	16	18	18	15	10	8
Macrolides RI	-	20	19	21	23	22	22	22	15	19
Staphylococcus aureus										
Oxacillin/Meticillin R	45	46	47	48	48	53	49	53	55	54
Escherichia coli										
Aminopenicilins R	53	58	58	59	59	58	58	56	57	59
Aminoglycosides R	9	13	12	12	12	14	11	12	16	16
Fluoroquinolones R	26	27	29	28	30	29	28	27	27	30
3rd gen. Cephalosporins R	7	8	12	10	10	10	9	10	11	14
Carbapenems R	-	-	-	-	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	4	5	<1	2	4	4	7	17	24	12
HL Gentamicin R	34	29	38	41	41	43	34	39	30	43
Vancomycin R	3	6	5	5	4	4	4	2	4	3
Enterococcus faecium										
Aminopenicilins RI	88	83	92	76	93	86	91	91	81	94
HL Gentamicin R	55	66	68	53	49	28	49	53	38	58
Vancomycin R	47	42	34	26	29	24	23	23	20	23
Klebsiella pneumoniae										
Aminoglycosides R	-	-	<1	13	11	19	20	27	32	32
Fluoroquinolones R	-	-	<1	20	18	22	28	31	36	36
3rd gen. Cephalosporins R	-	-	-	21	17	26	28	28	35	39
Carbapenems R	-	-	-	-	<1	<1	<1	1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	15	14	17	17	18	19	20
Ceftazidime R	-	-	-	19	16	16	13	12	15	15
Carbapenems R	-	-	-	21	15	18	16	16	20	20
Aminoglycosides R	-	-	-	17	16	11	12	14	15	15
Fluoroquinolones R	-	-	-	21	19	23	21	20	26	26

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	98	9	100	54	100	29	100	3	100	22	99	37	99	20
CSF	2	29	-	-	0	0	-	-	-	-	1	42	1	38
Gender														
Male	59	10	63	54	45	34	59	4	61	19	61	39	62	21
Female	40	9	37	54	55	25	41	3	39	27	39	34	38	19
Unknown	0	0	-	-	-	-	-	-	-	-	-	-	<1	50
Age (years)														
0–4	9	17	4	21	2	8	4	0	1	0	4	31	1	8
5–19	3	12	2	9	1	17	1	0	2	14	2	48	2	32
20–64	39	10	30	43	30	25	26	4	38	24	36	39	36	24
65 and over	49	8	64	63	67	31	69	3	60	21	55	38	60	18
Unknown	<1	33	0	0	0	0	-	-	-	-	3	11	0	0
Hospital department														
ICU	4	10	10	60	5	34	14	2	18	24	11	37	13	26
Internal med.	18	6	24	63	16	29	18	4	14	21	17	38	16	12
Surgery	1	0	10	62	6	28	13	5	16	30	9	42	12	20
Other	78	10	56	48	72	28	55	3	52	19	63	36	59	21
Unknown	-	-	<1	36	1	28	1	17	-	-	0	0	<1	100

Portugal

Figure 1: ***S. pneumoniae*****: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	19
Minimum	0
First quartile	2
Median	8.3
Third quartile	18.6
Maximum	27.9

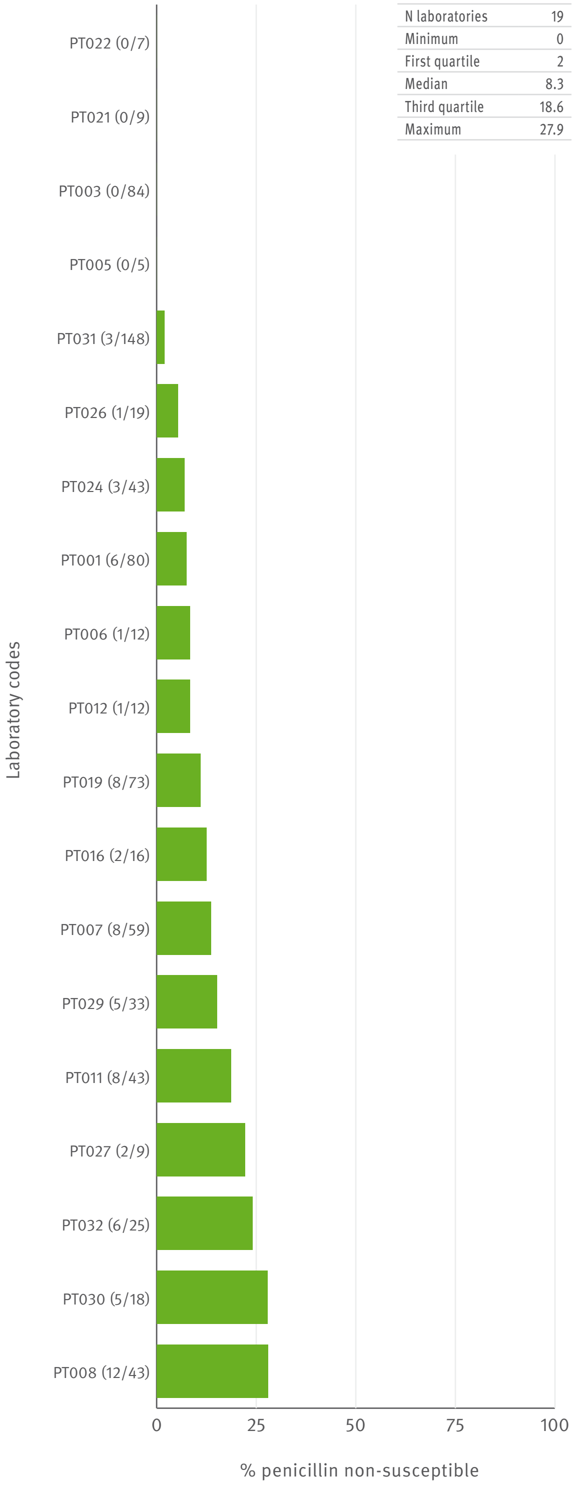


Figure 2: ***S. aureus*****: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	23
Minimum	3.8
First quartile	36
Median	50
Third quartile	62.7
Maximum	80

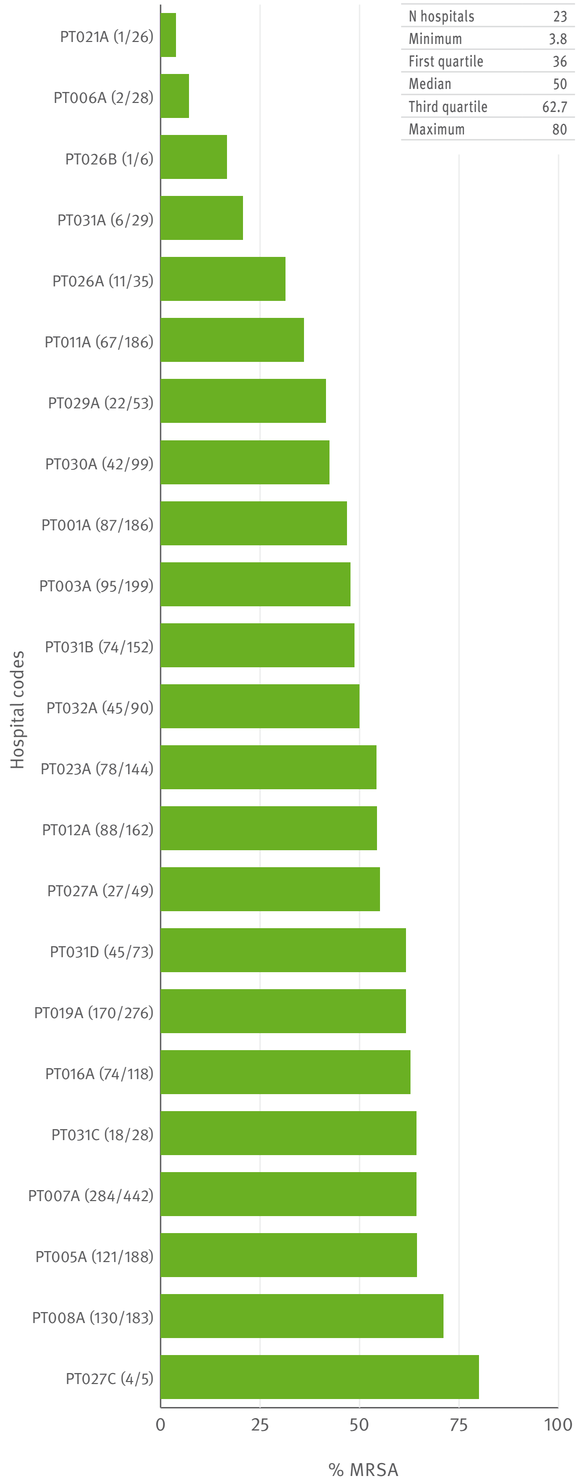


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

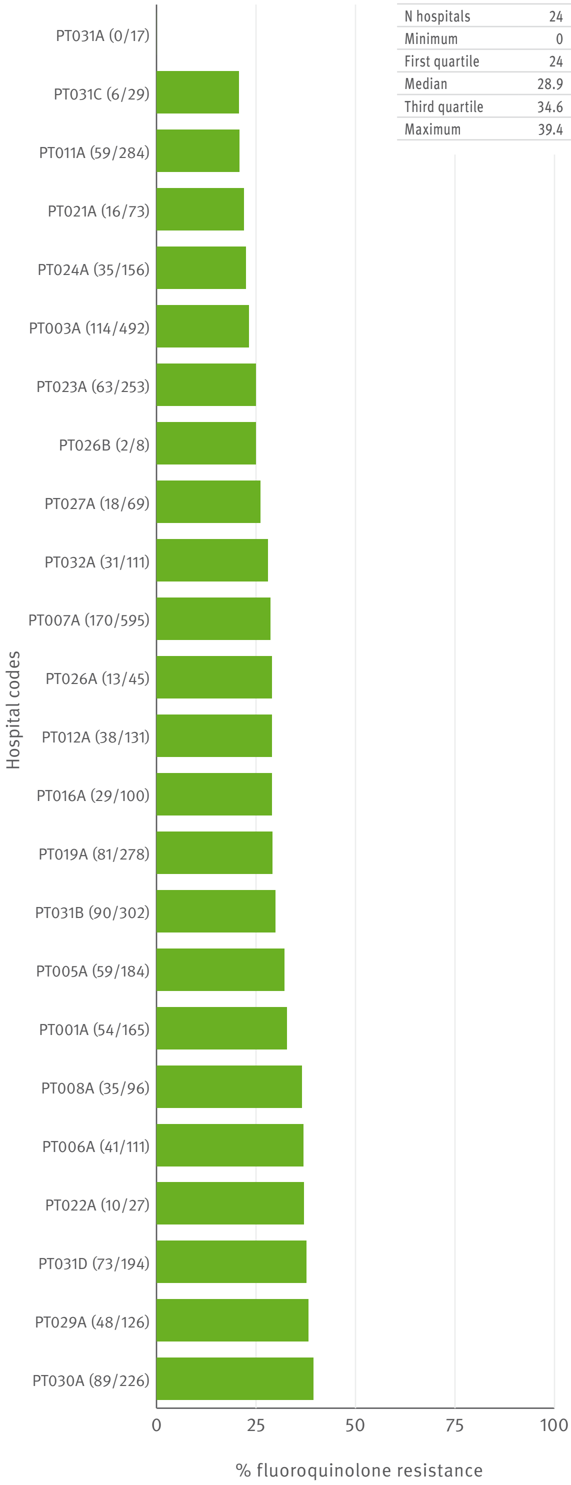
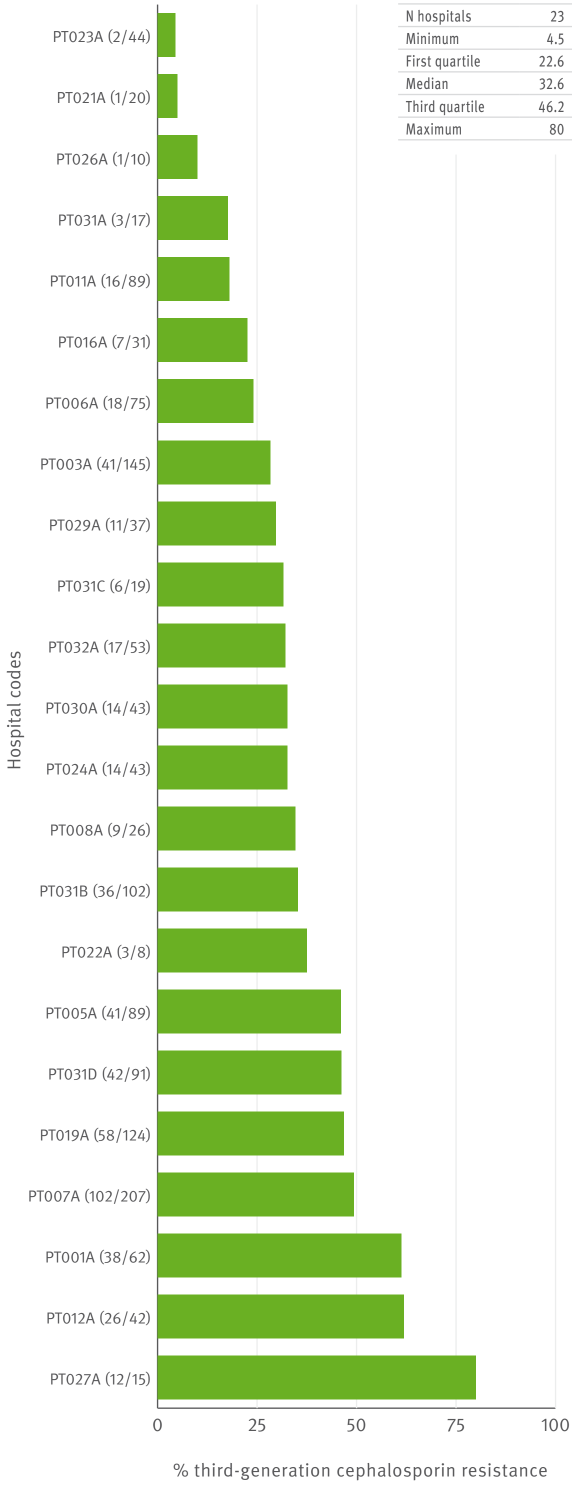


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Romania

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	5	50	8	236	7	178	-	-	8	96	7	41

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	21	11	22	10	22	54	24	31	61	37
Penicillin RI	33	11	39	28	33	69	29	31	61	37
Macrolides RI	29	<1	31	25	19	27	33	36	44	37
Staphylococcus aureus										
Oxacillin/Meticillin R	46	71	60	54	26	33	34	39	50	54
Escherichia coli										
Aminopenicilins R	70	79	78	85	76	55	60	83	71	62
Aminoglycosides R	21	33	14	41	35	24	11	12	18	24
Fluoroquinolones R	14	21	9	41	27	27	18	24	28	27
3rd gen. Cephalosporins R	19	23	17	41	27	24	14	21	21	26
Carbapenems R	<1	3	<1	3	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	29	<1	<1	25	10	13	<1	11	-
HL Gentamicin R	25	<1	50	15	50	22	42	-	-	-
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	-
Enterococcus faecium										
Aminopenicilins RI	86	100	100	100	100	100	100	80	90	-
HL Gentamicin R	63	100	70	80	67	50	71	-	-	-
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	-
Klebsiella pneumoniae										
Aminoglycosides R	-	-	100	91	80	60	32	71	50	54
Fluoroquinolones R	-	-	33	34	23	20	11	29	30	52
3rd gen. Cephalosporins R	-	-	100	94	80	50	65	71	44	58
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	14
Pseudomonas aeruginosa										
Piperacillin R	-	-	61	33	25	25	31	63	57	48
Ceftazidime R	-	-	52	<1	<1	13	30	60	56	49
Carbapenems R	-	-	61	<1	<1	13	46	70	60	51
Aminoglycosides R	-	-	65	33	25	38	38	50	60	49
Fluoroquinolones R	-	-	64	33	25	25	31	56	67	51

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	54	42	100	53	99	27	-	-	-	-	99	55	94	52
CSF	46	56	-	-	1	100	-	-	-	-	1	0	6	67
Gender														
Male	58	48	67	52	40	32	-	-	-	-	64	57	61	52
Female	38	47	31	52	60	25	-	-	-	-	35	52	39	55
Unknown	4	67	1	60	-	-	-	-	-	-	1	0	-	-
Age (years)														
0–4	9	86	6	68	2	0	-	-	-	-	9	64	14	43
5–19	6	60	5	28	3	17	-	-	-	-	2	100	2	100
20–64	33	15	51	45	48	28	-	-	-	-	38	63	51	50
65 and over	25	60	25	68	44	28	-	-	-	-	34	49	27	50
Unknown	27	62	13	57	4	43	-	-	-	-	17	40	6	100
Hospital department														
ICU	5	75	10	83	5	40	3	-	-	-	23	93	25	62
Internal med.	-	-	6	60	11	24	-	-	-	-	4	40	6	0
Surgery	-	-	5	67	2	67	-	-	-	-	7	75	8	75
Other	67	40	64	44	64	26	-	-	-	-	48	40	55	46
Unknown	28	64	15	60	17	28	-	-	-	-	18	43	6	100

Romania

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

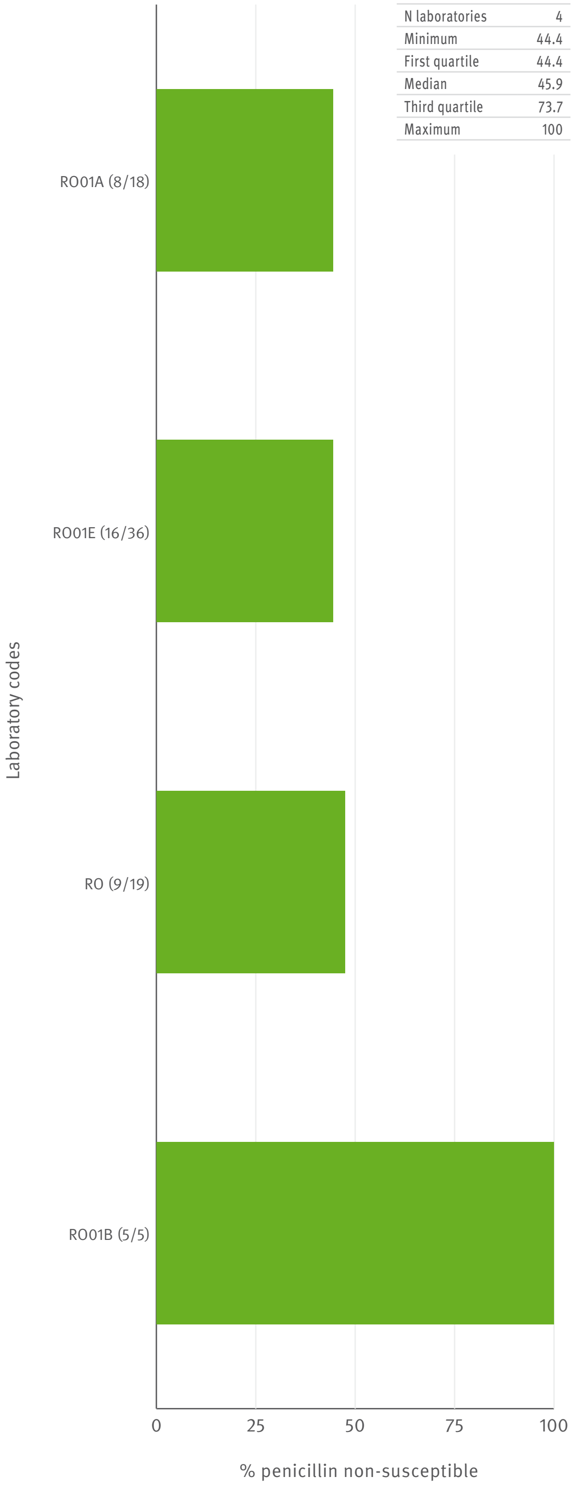


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

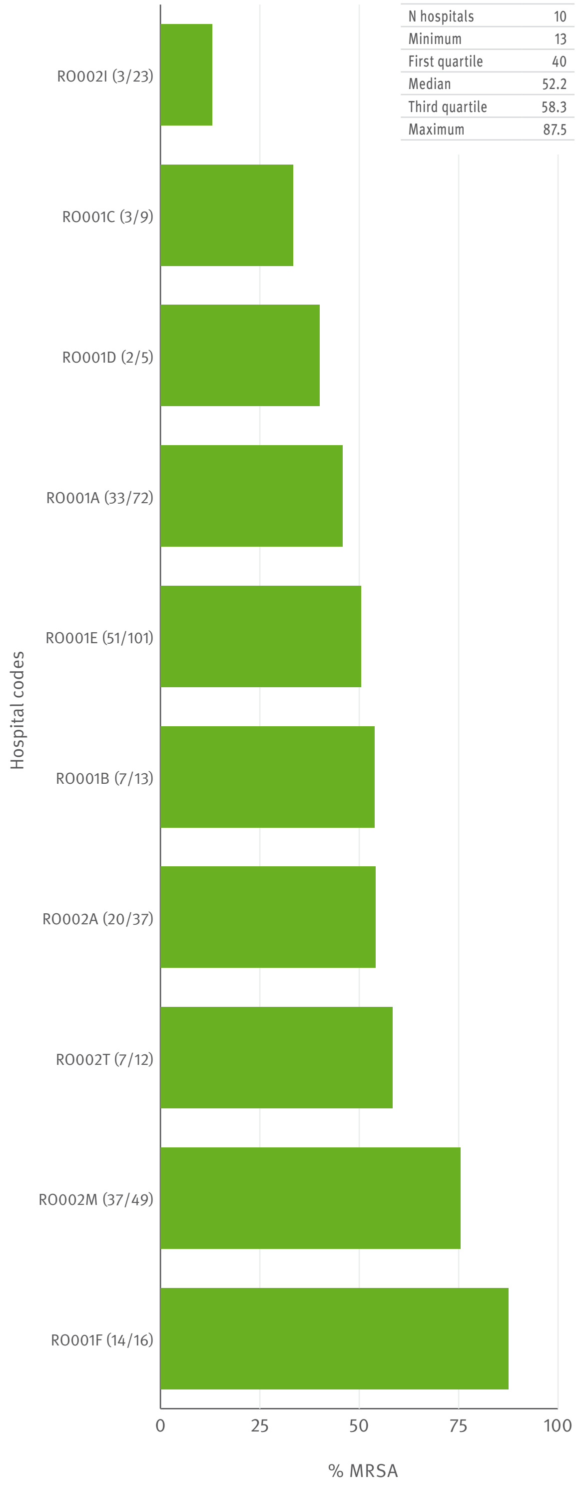


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

N hospitals	5
Minimum	13.2
First quartile	20.8
Median	37.8
Third quartile	38.1
Maximum	42.9

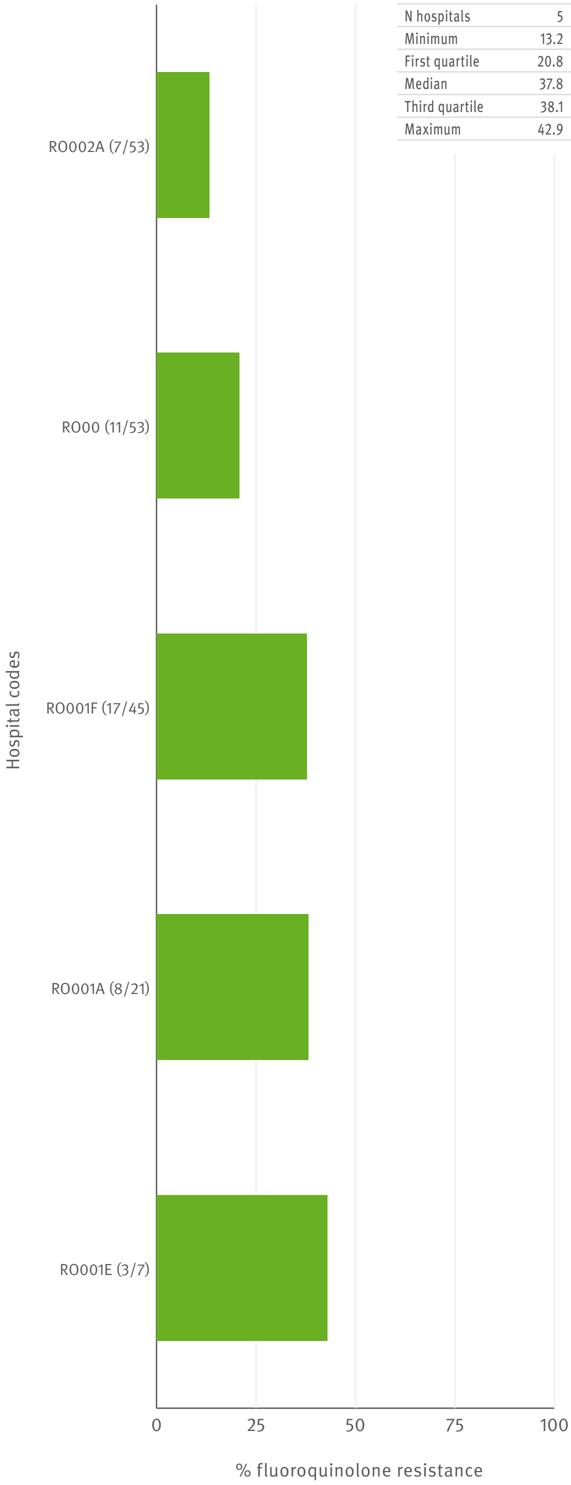


Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**

N hospitals	7
Minimum	33.3
First quartile	40
Median	60.6
Third quartile	87.5
Maximum	100

Slovakia

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	4	24	<1	-	-	-	-	-	4	5
Penicillin RI	11	29	<1	-	-	-	-	-	8	5
Macrolides RI	<1	33	40	-	-	-	-	-	12	27
Staphylococcus aureus										
Oxacillin/Meticillin R	8	14	16	-	-	-	-	-	26	22
Escherichia coli										
Aminopenicilins R	54	62	59	-	-	-	-	-	68	65
Aminoglycosides R	6	11	7	-	-	-	-	-	18	21
Fluoroquinolones R	20	24	14	-	-	-	-	-	42	41
3rd gen. Cephalosporins R	<1	7	8	-	-	-	-	-	31	31
Carbapenems R	<1	<1	<1	-	-	-	-	-	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	7	7	-	-	-	-	-	2	2
HL Gentamicin R	35	37	40	-	-	-	-	-	50	50
Vancomycin R	<1	<1	<1	-	-	-	-	-	<1	<1
Enterococcus faecium										
Aminopenicilins RI	92	91	100	-	-	-	-	-	96	95
HL Gentamicin R	60	45	33	-	-	-	-	-	79	86
Vancomycin R	<1	9	<1	-	-	-	-	-	4	5
Klebsiella pneumoniae										
Aminoglycosides R	-	-	-	-	-	-	-	-	66	63
Fluoroquinolones R	-	-	-	-	-	-	-	-	71	67
3rd gen. Cephalosporins R	-	-	-	-	-	-	-	-	68	63
Carbapenems R	-	-	-	-	-	-	-	-	<1	6
Pseudomonas aeruginosa										
Piperacillin R	-	-	-	-	-	-	-	-	41	38
Ceftazidime R	-	-	-	-	-	-	-	-	25	35
Carbapenems R	-	-	-	-	-	-	-	-	31	41
Aminoglycosides R	-	-	-	-	-	-	-	-	53	42
Fluoroquinolones R	-	-	-	-	-	-	-	-	59	56

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	70	6	100	24	99	42	100	0	100	4	98	65	97	35
CSF	30	7	-	-	1	40	-	-	-	-	2	82	3	43
Gender														
Male	50	4	60	23	46	49	63	0	58	4	63	70	61	35
Female	50	9	40	26	54	35	37	0	42	5	37	59	39	34
Age (years)														
0–4	15	14	5	7	4	8	5	0	3	0	6	72	9	24
5–19	4	0	2	14	2	34	3	0	1	0	3	50	4	53
20–64	57	0	47	23	37	43	47	0	56	5	43	67	48	37
65 and over	24	18	46	27	57	43	46	1	41	4	48	64	39	33
Hospital department														
ICU	28	8	17	30	12	44	28	1	34	2	27	75	30	50
Internal med.	26	0	54	24	44	44	32	0	28	6	30	57	24	24
Surgery	2	0	8	27	10	41	13	0	10	6	10	66	10	35
Other	43	10	20	18	32	37	26	0	28	6	33	65	35	30
Unknown	-	-	2	26	2	39	1	0	1	0	1	75	1	0

Slovakia

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	3
Minimum	0
First quartile	0
Median	9.1
Third quartile	14.3
Maximum	14.3

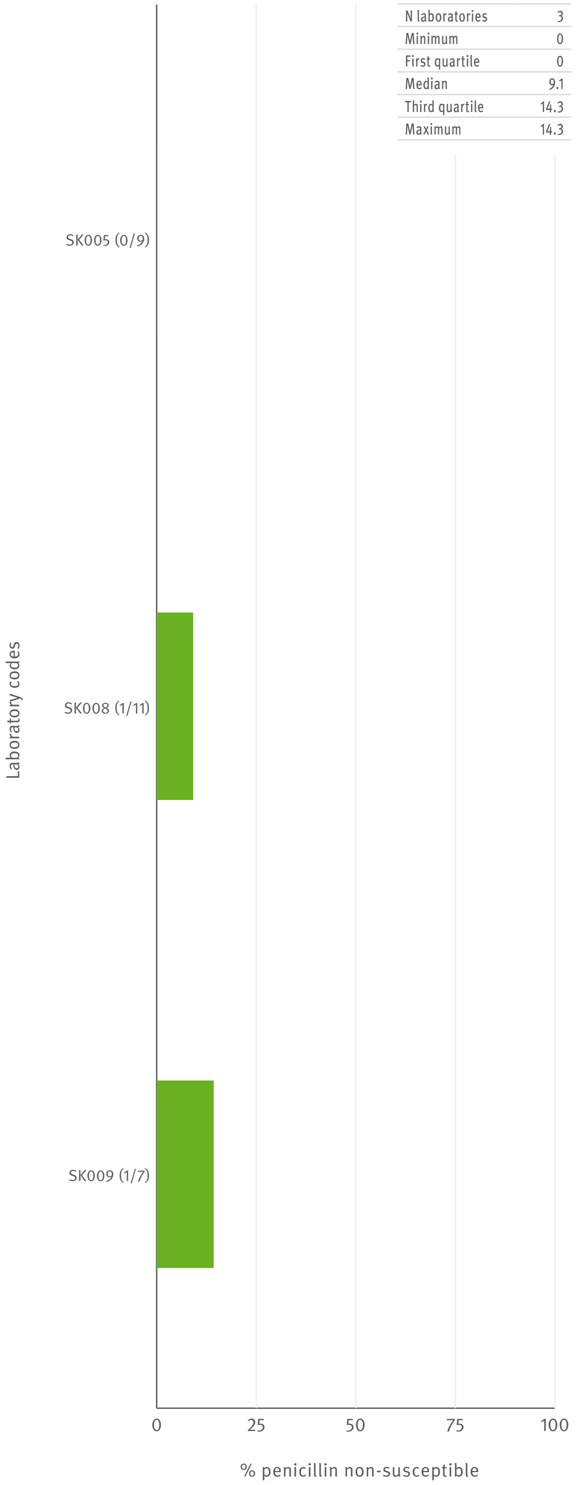


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	24
Minimum	0
First quartile	14
Median	21.2
Third quartile	29.8
Maximum	43.5

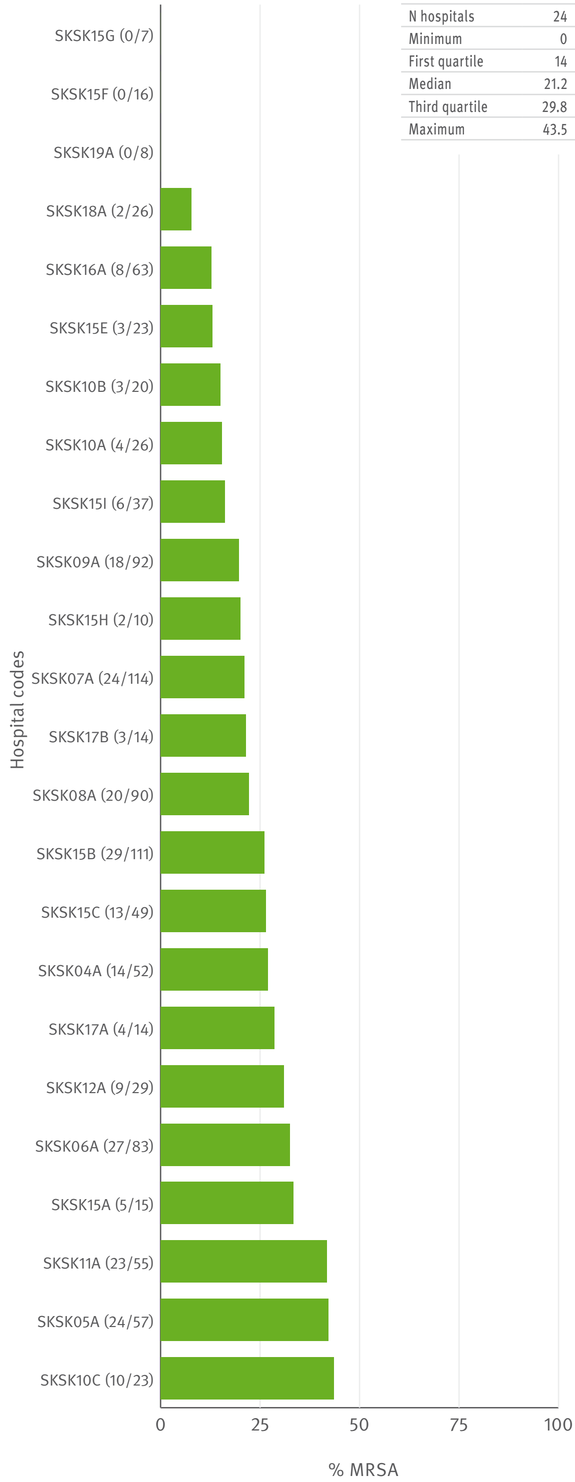


Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

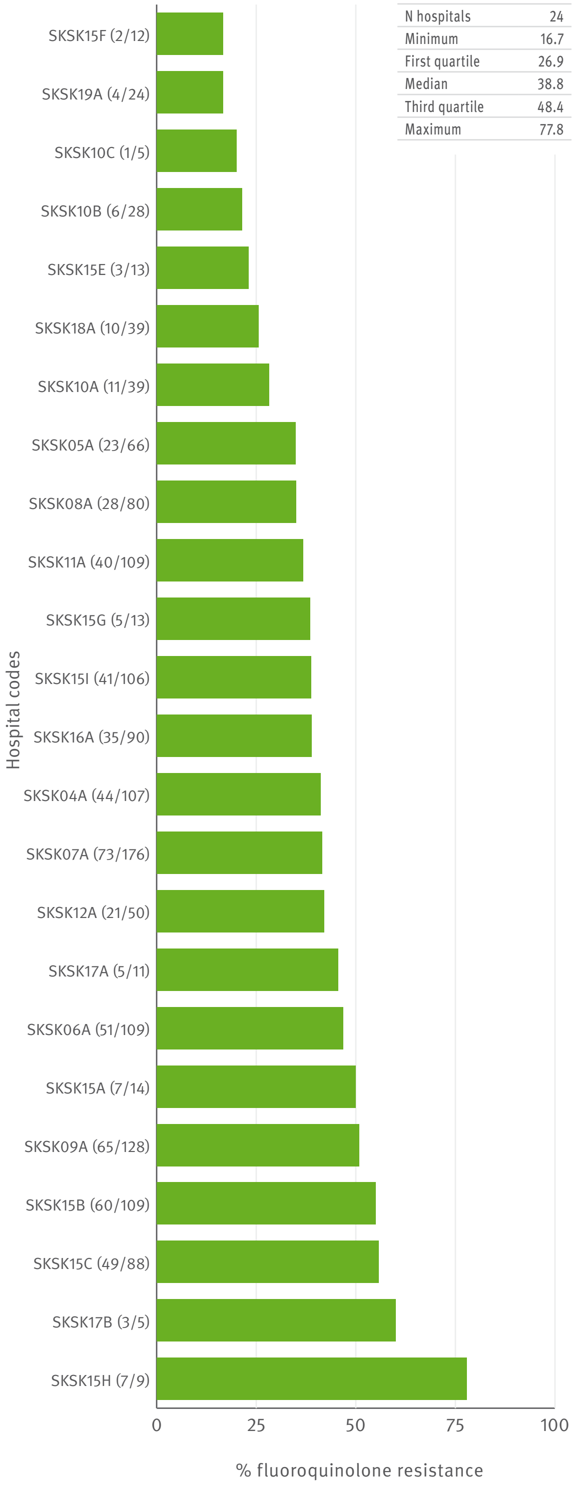
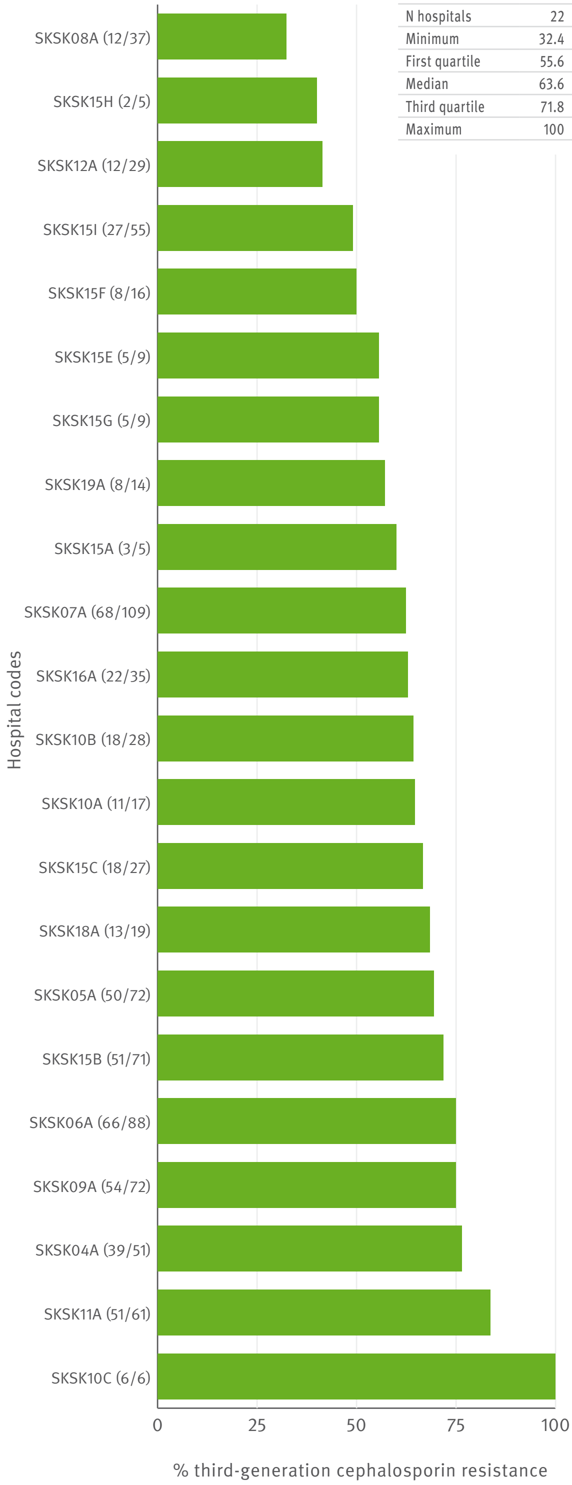


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Slovenia

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	252	10	464	10	1002	10	208	10	232	10	118
2012	10	251	10	445	10	1168	10	225	10	254	10	134

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	2	2	2	5	4	3	1	<1	<1	1
Penicillin RI	15	25	11	19	17	15	15	16	12	10
Macrolides RI	9	11	11	13	17	16	17	17	24	21
Staphylococcus aureus										
Oxacillin/Meticillin R	13	12	10	7	8	7	10	12	7	10
Escherichia coli										
Aminopenicilins R	41	40	42	44	49	49	53	48	54	50
Aminoglycosides R	2	5	4	7	7	7	10	9	10	9
Fluoroquinolones R	11	12	12	15	17	17	18	19	21	21
3rd gen. Cephalosporins R	<1	1	2	2	4	4	5	7	9	10
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	<1	1	1	<1	<1	<1	2	<1	<1
HL Gentamicin R	49	37	46	40	50	40	43	43	36	35
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	83	76	93	86	92	96	94	95	90	93
HL Gentamicin R	82	56	47	54	63	57	56	66	66	63
Vancomycin R	<1	<1	<1	6	5	13	4	2	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	17	19	24	23	28	23	22	20
Fluoroquinolones R	-	-	14	21	26	25	27	25	35	33
3rd gen. Cephalosporins R	-	-	19	24	28	26	31	22	30	28
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	21	18	13	21	16	15	13	7
Ceftazidime R	-	-	11	8	7	14	8	5	8	7
Carbapenems R	-	-	13	6	19	16	15	19	24	22
Aminoglycosides R	-	-	21	15	10	13	12	8	8	10
Fluoroquinolones R	-	-	29	21	17	24	13	9	9	15

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	96	11	100	9	100	21	100	0	100	0	98	29	97	22
CSF	4	15	.	.	0	33	.	.	.	.	2	50	3	43
Gender														
Male	56	11	61	9	42	24	65	0	58	0	58	30	65	22
Female	44	12	39	8	58	19	35	0	42	0	42	29	35	24
Age (years)														
0–4	21	14	2	5	3	3	5	0	1	0	2	0	3	38
5–19	4	0	3	7	1	4	1	0	2	0	1	0	2	25
20–64	37	9	39	9	26	21	27	0	42	0	35	34	35	31
65 and over	38	13	55	9	70	22	67	0	55	0	62	28	61	17
Hospital department														
ICU	13	6	12	14	8	24	19	0	34	0	19	38	27	30
Internal med.	34	11	40	7	47	20	30	0	30	0	37	23	26	18
Surgery	1	17	11	11	6	19	15	0	11	0	12	44	15	27
Other	52	13	37	8	39	22	36	0	25	0	33	26	33	18

Slovenia

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

N laboratories	10
Minimum	3.7
First quartile	6.3
Median	12.1
Third quartile	15
Maximum	21.6

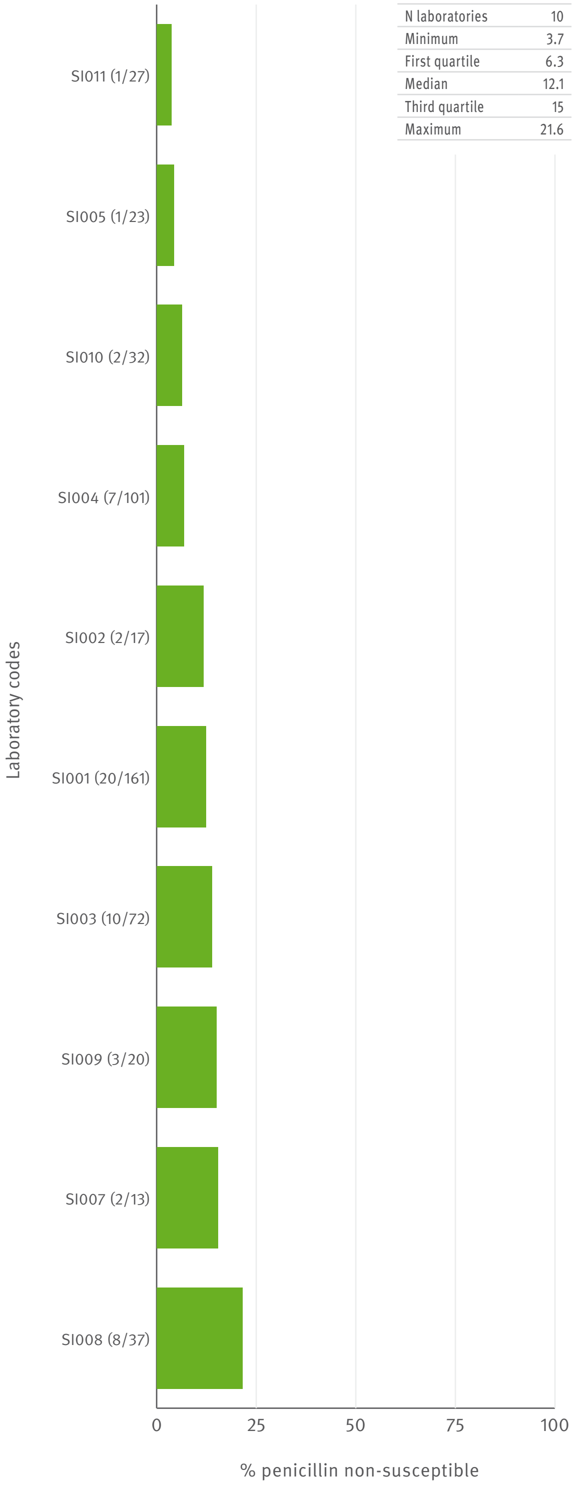


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

N hospitals	15
Minimum	0
First quartile	0
Median	8.8
Third quartile	10.4
Maximum	21.2

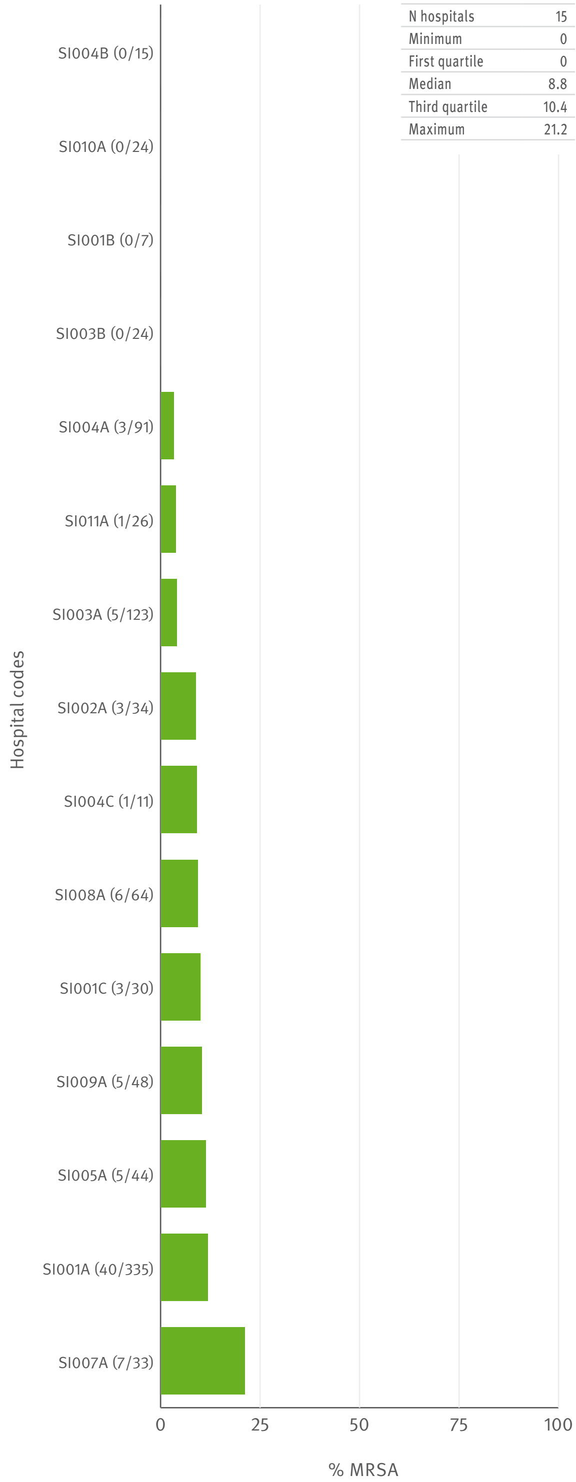


Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

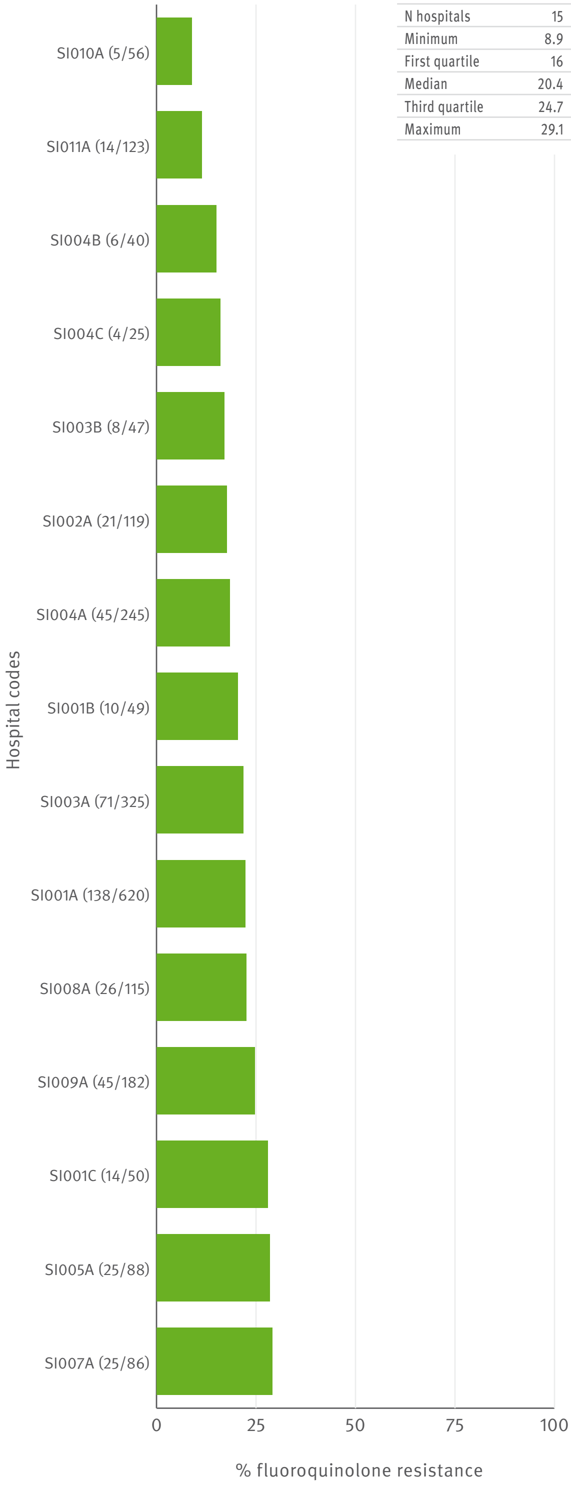
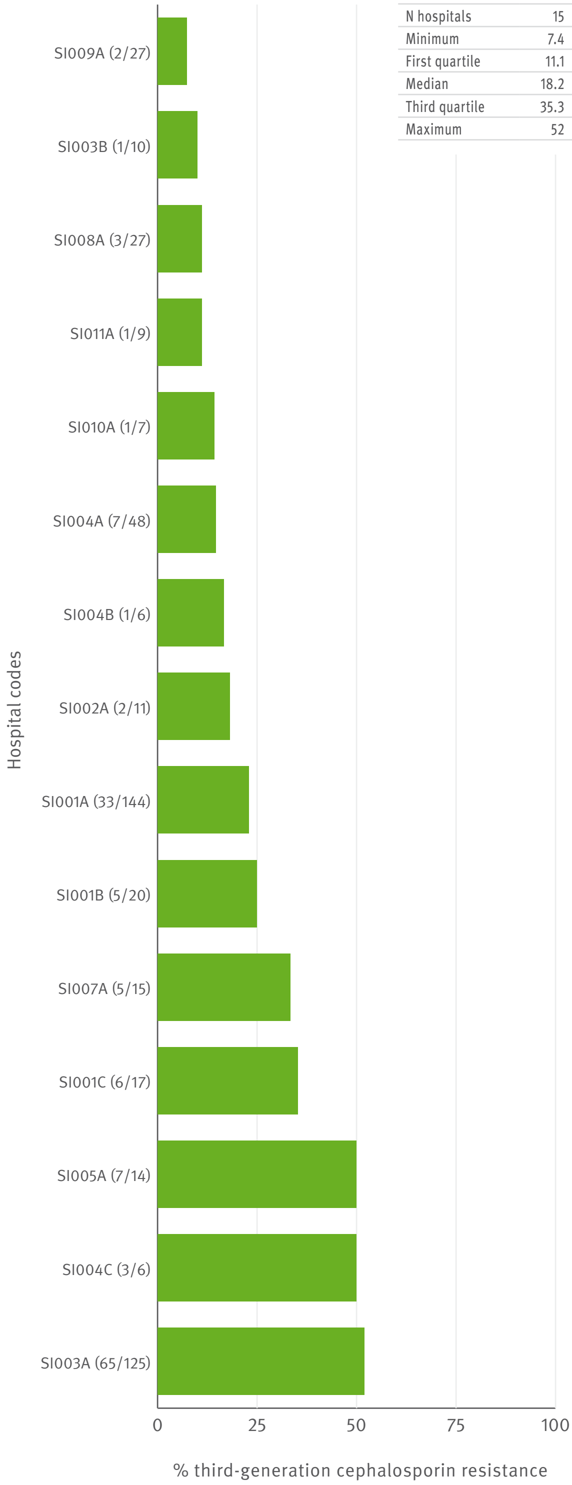


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



Spain

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	619	41	1904	40	5675	41	1508	40	1153	40	853

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	7	9	9	8	8	7	8	10	10	10
Penicillin RI	32	29	25	27	22	23	22	30	30	27
Macrolides RI	27	27	23	22	18	22	19	27	25	26
Staphylococcus aureus										
Oxacillin/Meticillin R	24	26	27	25	25	27	26	25	22	24
Escherichia coli										
Aminopenicilins R	58	60	62	64	62	63	65	65	66	65
Aminoglycosides R	7	7	10	9	10	11	13	14	15	16
Fluoroquinolones R	21	25	28	28	30	33	31	33	34	34
3rd gen. Cephalosporins R	4	7	8	7	7	9	11	12	12	14
Carbapenems R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	1	2	<1	2	1	3	3	1	<1	2
HL Gentamicin R	36	36	36	36	42	41	43	41	39	38
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	64	66	67	73	79	79	83	83	82	87
HL Gentamicin R	11	17	16	21	40	35	38	27	23	26
Vancomycin R	3	2	3	3	2	1	3	1	1	1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	4	7	9	9	9	9	10	14
Fluoroquinolones R	-	-	11	8	17	15	16	14	17	17
3rd gen. Cephalosporins R	-	-	7	9	10	12	11	10	13	17
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	4	9	8	8	8	6	6	7
Ceftazidime R	-	-	6	7	10	11	8	7	9	9
Carbapenems R	-	-	17	12	15	13	16	18	16	16
Aminoglycosides R	-	-	4	11	15	18	20	18	19	17
Fluoroquinolones R	-	-	14	19	25	23	25	25	24	21

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	91	28	100	23	100	34	100	0	100	1	99	15	98	16
CSF	9	38	.	.	‹1	3	.	.	.	.	1	17	2	13
Gender														
Male	62	28	66	24	52	39	65	0	61	1	62	17	66	16
Female	38	30	34	22	48	29	35	0	39	2	38	11	34	17
Unknown	.	.	0	0	‹1	13	.	.	0	0	0	0	0	0
Age (years)														
0–4	10	37	5	11	4	12	12	0	3	0	7	13	4	8
5–19	3	15	3	6	1	30	1	0	1	0	1	5	1	15
20–64	38	24	34	17	28	30	29	0	33	2	35	17	39	23
65 and over	47	31	57	29	68	37	58	0	62	1	57	14	56	13
Unknown	2	19	1	25	‹1	28	‹1	14	0	0	0	22	0	0
Hospital department														
ICU	14	30	9	20	7	35	15	0	16	2	13	20	22	27
Internal med.	29	27	39	26	32	37	29	0	33	2	29	13	28	12
Surgery	1	20	9	33	7	34	11	0	13	1	12	18	10	14
Other	49	29	33	18	45	31	34	0	27	1	35	11	32	13
Unknown	7	28	9	21	9	38	11	0	10	0	11	23	8	16

Spain

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

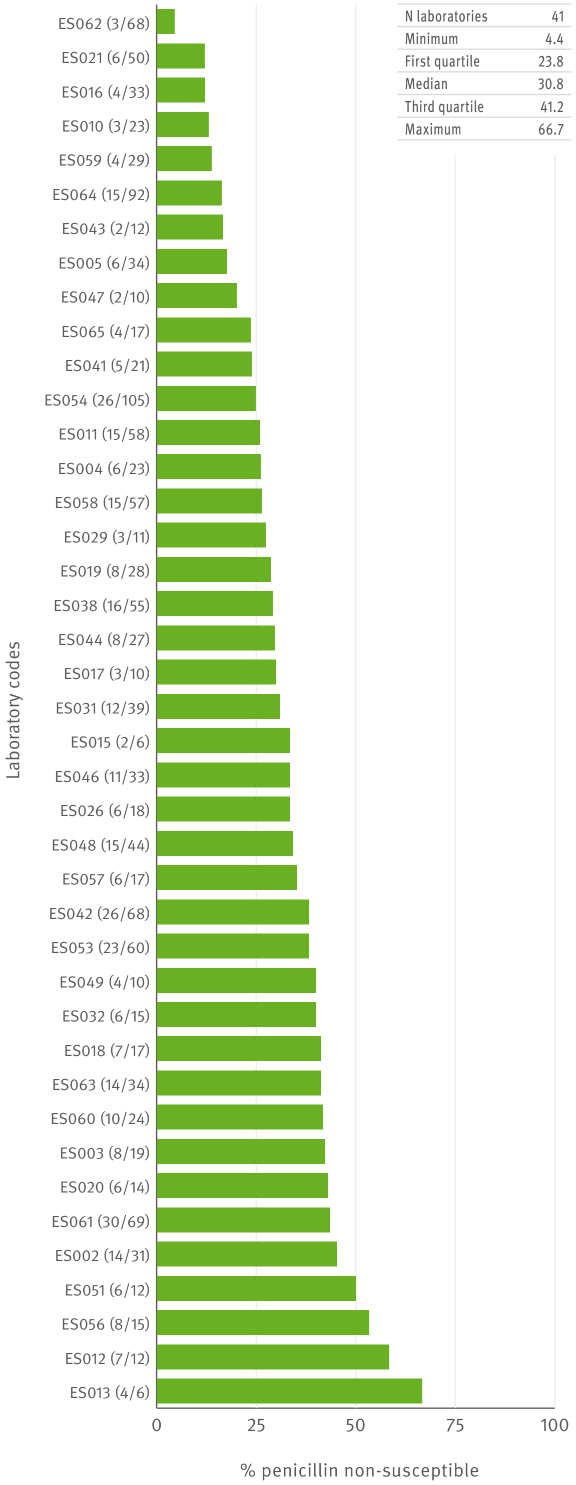


Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

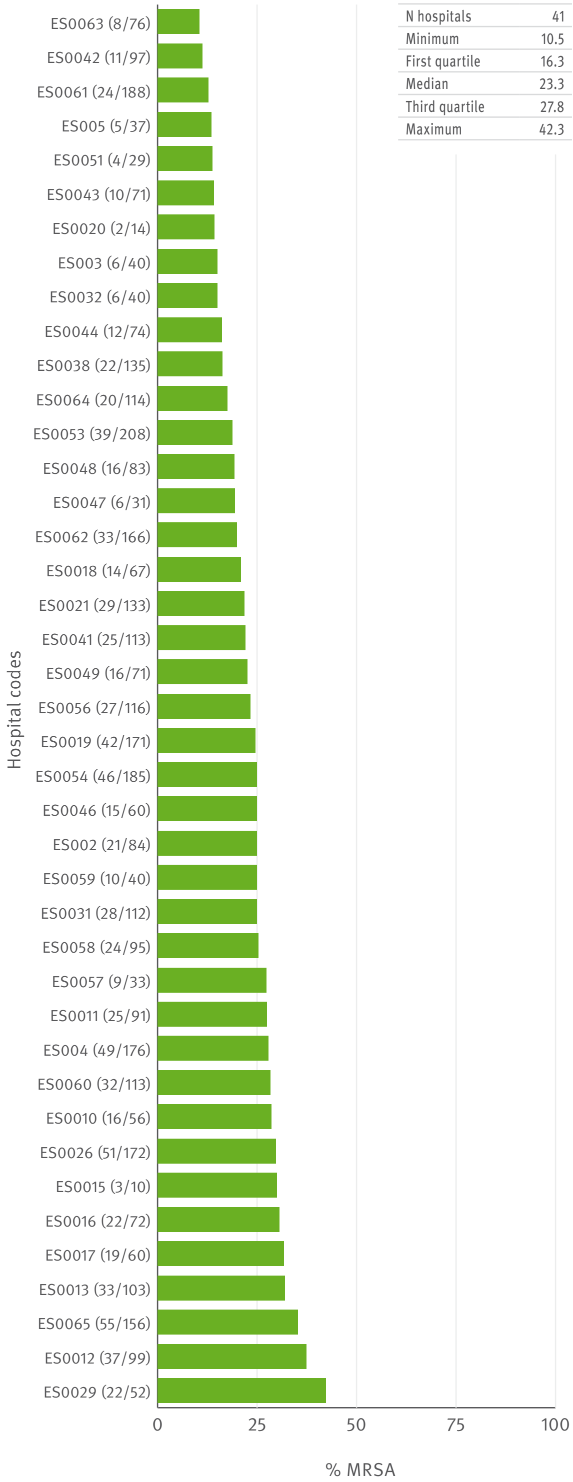
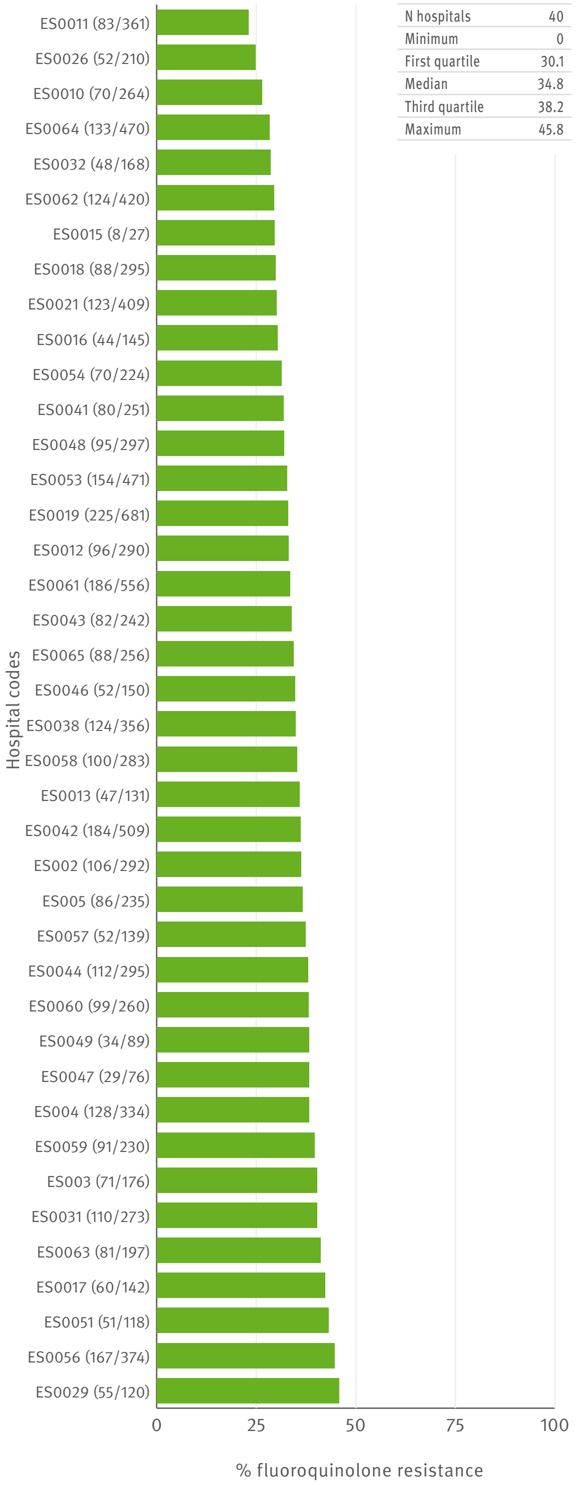
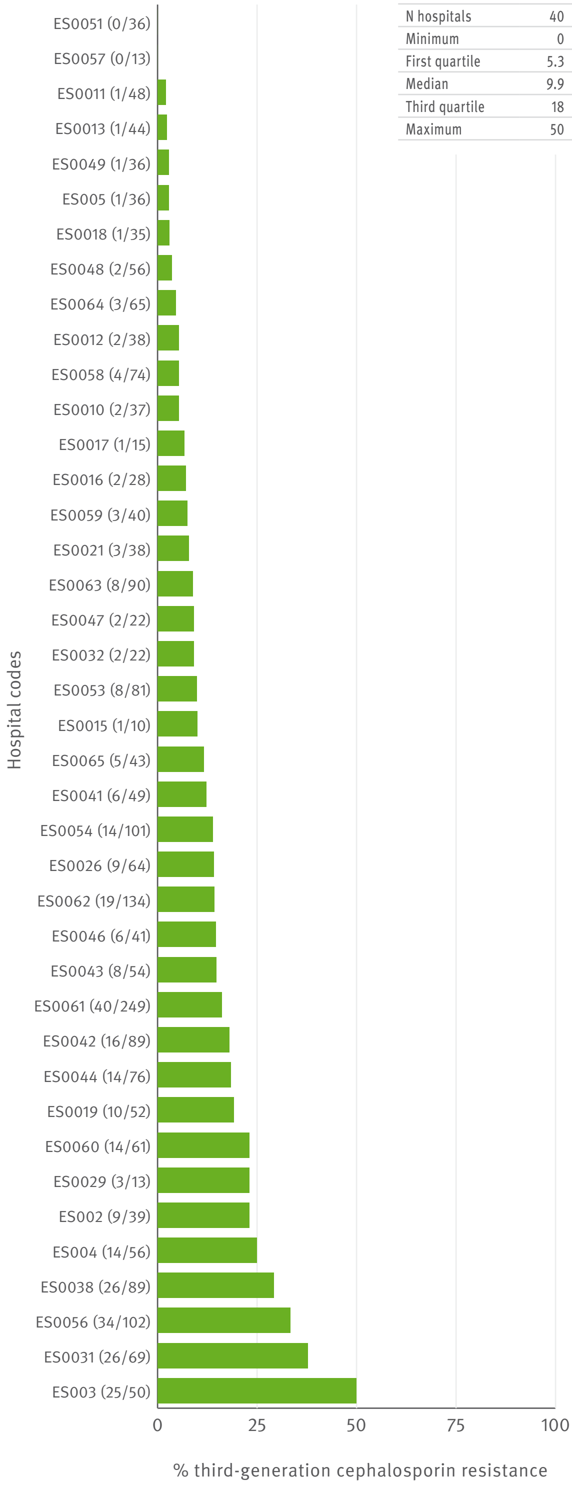


Figure 3: ***E. coli*****: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**



N hospitals	40
Minimum	0
First quartile	30.1
Median	34.8
Third quartile	38.2
Maximum	45.8

Figure 4: ***K. pneumoniae*****: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



N hospitals	40
Minimum	0
First quartile	5.3
Median	9.9
Third quartile	18
Maximum	50

Sweden

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterecocci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	1008	19	2867	18	4846	18	1038	18	878	18	377
2011	18	1015	18	3113	17	5253	18	1239	17	966	17	412
2012	18	1030	18	3262	17	5541	18	1211	17	976	17	357

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	<1	<1	<1	<1	<1	<1	2	2	3	5
Penicillin RI	5	3	4	2	3	2	3	4	3	5
Macrolides RI	5	5	6	5	5	6	4	4	5	5
Staphylococcus aureus										
Oxacillin/Meticillin R	<1	<1	1	<1	<1	<1	1	<1	<1	<1
Escherichia coli										
Aminopenicilins R	29	23	26	28	33	32	33	35	35	-
Aminoglycosides R	1	1	1	2	2	2	3	4	5	5
Fluoroquinolones R	7	8	6	8	10	10	8	11	8	11
3rd gen. Cephalosporins R	<1	<1	1	2	2	2	3	3	4	4
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	<1	<1	<1	<1	<1	<1	<1	2	1	-
HL Gentamicin R	17	16	19	20	16	20	19	15	19	15
Vancomycin R	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecium										
Aminopenicilins RI	77	78	74	76	79	82	76	82	89	-
HL Gentamicin R	11	7	4	12	14	25	24	22	22	20
Vancomycin R	2	1	<1	<1	<1	2	<1	<1	<1	<1
Klebsiella pneumoniae										
Aminoglycosides R	-	-	1	<1	1	1	<1	2	2	2
Fluoroquinolones R	-	-	5	5	6	7	2	5	4	4
3rd gen. Cephalosporins R	-	-	1	1	1	2	2	2	2	3
Carbapenems R	-	-	<1	<1	<1	<1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	9	<1	2	1	2	1	4	6
Ceftazidime R	-	-	5	6	4	5	7	6	5	6
Carbapenems R	-	-	18	5	7	4	8	7	8	5
Aminoglycosides R	-	-	<1	<1	<1	<1	<1	3	1	2
Fluoroquinolones R	-	-	6	5	6	5	7	6	6	7

Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	98	4	100	1	100	10	100	0	100	0	100	3	100	7
CSF	2	6	.	.	0	0	.	.	.	.	.	.	.	.
Gender														
Male	51	5	62	1	48	13	72	0	62	0	59	3	64	7
Female	49	4	38	1	52	7	28	0	38	0	41	2	36	6
Age (years)														
0–4	2	10	3	0	1	3	3	0	1	0	1	0	2	8
5–19	2	3	3	2	1	10	1	0	2	0	1	21	3	15
20–64	39	4	29	1	24	13	23	0	31	0	23	4	26	9
65 and over	55	4	63	1	72	9	71	0	65	0	73	2	68	5
Unknown	2	5	2	0	2	10	2	0	2	0	2	0	2	14
Hospital department														
ICU	6	4	4	0	3	9	5	0	11	0	4	4	5	24
Internal med.	47	3	40	1	37	9	33	0	27	0	33	2	39	4
Surgery	5	2	15	0	19	11	24	0	28	0	24	1	16	4
Other	39	5	35	1	36	11	33	0	31	0	34	3	37	8
Unknown	4	6	5	0	5	7	5	0	3	0	5	2	3	12

Sweden

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**

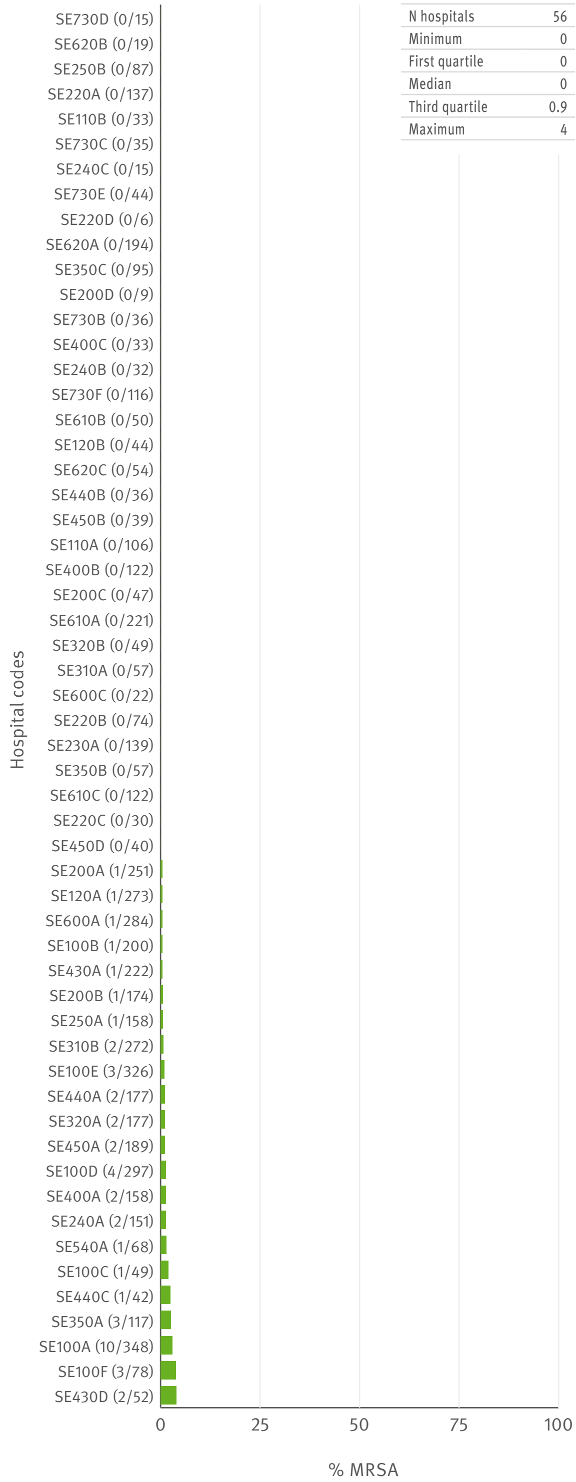
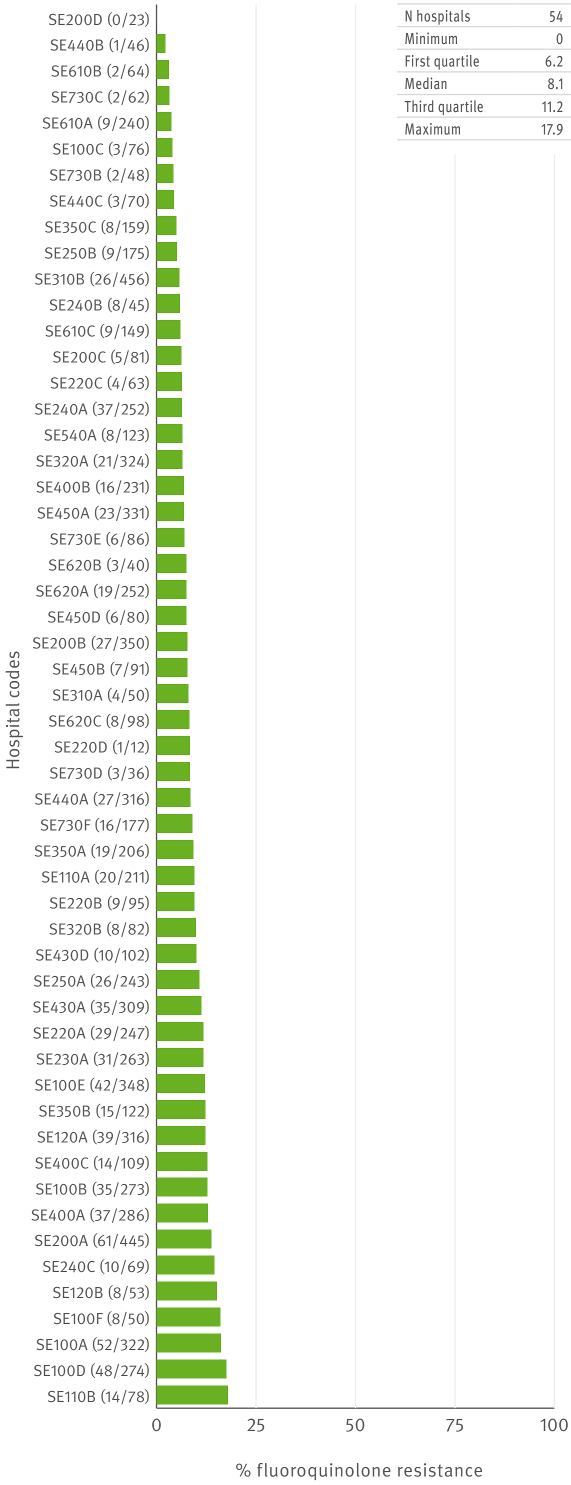
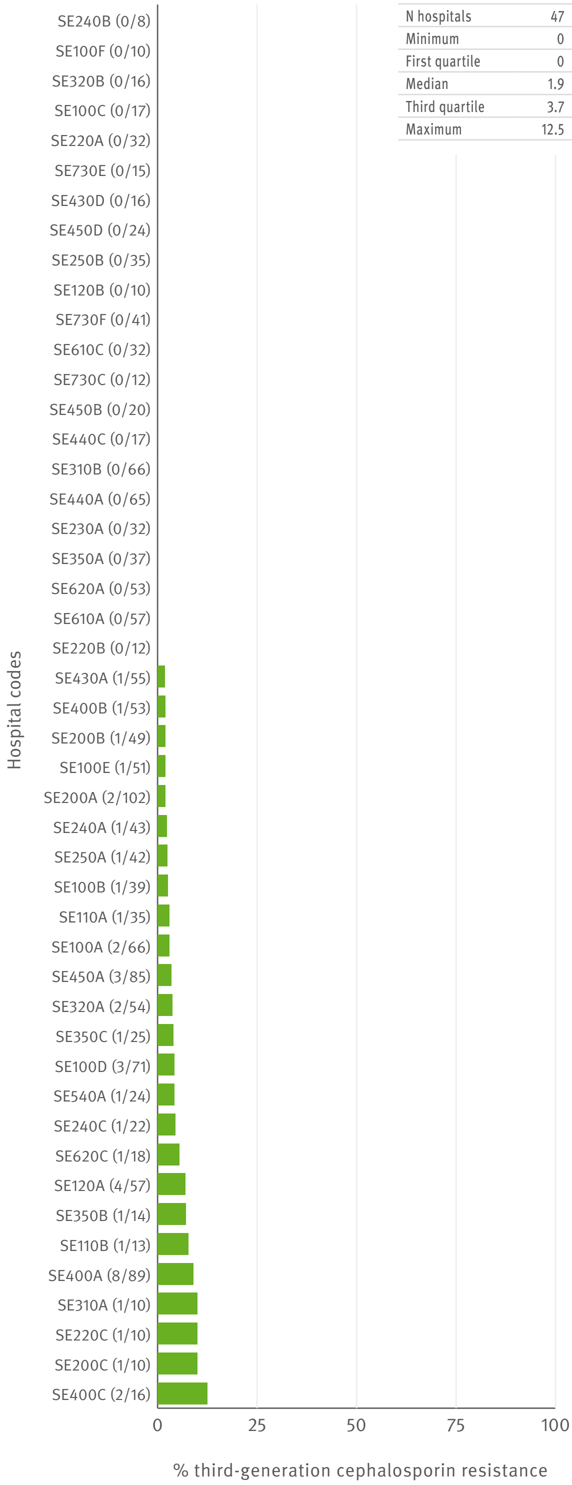


Figure 3: *E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)



N hospitals	54
Minimum	0
First quartile	6.2
Median	8.1
Third quartile	11.2
Maximum	17.9

Figure 4: *K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)



N hospitals	47
Minimum	0
First quartile	0
Median	1.9
Third quartile	3.7
Maximum	12.5

United Kingdom

General information on EARS-Net participating laboratories

Table 1: Annual number of reporting laboratories* and number of reported isolates, 2003-2012

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci		*K. pneumoniae*		*P. aeruginosa*	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
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	2501	55	3285	29	6527	27	887	28	1075	28	681

*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.

Antibiotic resistance from 2003 to 2012

Table 2: Annual percentage (%) of antimicrobial non-susceptible and resistant isolates, 2003-2012

Microorganism by antimicrobial class	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Streptococcus pneumoniae										
Penicillin R	1	<1	2	<1	2	1	1	<1	<1	<1
Penicillin RI	5	3	4	3	4	5	3	3	5	5
Macrolides RI	13	13	11	12	10	6	4	5	6	7
Staphylococcus aureus										
Oxacillin/Meticillin R	44	44	44	42	36	31	28	22	14	13
Escherichia coli										
Aminopenicilins R	55	53	56	57	55	61	62	62	63	63
Aminoglycosides R	4	6	8	7	7	7	7	8	8	9
Fluoroquinolones R	11	14	17	20	18	15	18	17	18	17
3rd gen. Cephalosporins R	3	3	6	8	9	7	9	9	10	13
Carbapenems R	-	-	-	<1	<1	<1	<1	<1	<1	<1
Enterococcus faecalis										
Aminopenicilins RI	-	-	2	3	4	2	2	6	4	4
HL Gentamicin R	-	-	47	52	31	42	38	39	16	29
Vancomycin R	-	-	2	1	2	4	2	1	2	1
Enterococcus faecium										
Aminopenicilins RI	-	-	84	78	82	83	91	84	90	93
HL Gentamicin R	-	-	53	18	35	7	38	31	56	54
Vancomycin R	-	-	33	18	21	28	13	10	9	13
Klebsiella pneumoniae										
Aminoglycosides R	-	-	6	8	9	6	5	5	4	6
Fluoroquinolones R	-	-	12	13	12	7	6	7	5	7
3rd gen. Cephalosporins R	-	-	12	11	13	7	7	10	5	12
Carbapenems R	-	-	<1	<1	<1	1	<1	<1	<1	<1
Pseudomonas aeruginosa										
Piperacillin R	-	-	2	1	5	2	3	4	4	3
Ceftazidime R	-	-	3	3	7	4	5	5	5	4
Carbapenems R	-	-	9	6	10	6	8	6	6	6
Aminoglycosides R	-	-	4	4	5	3	1	2	3	2
Fluoroquinolones R	-	-	8	8	9	8	7	7	6	5

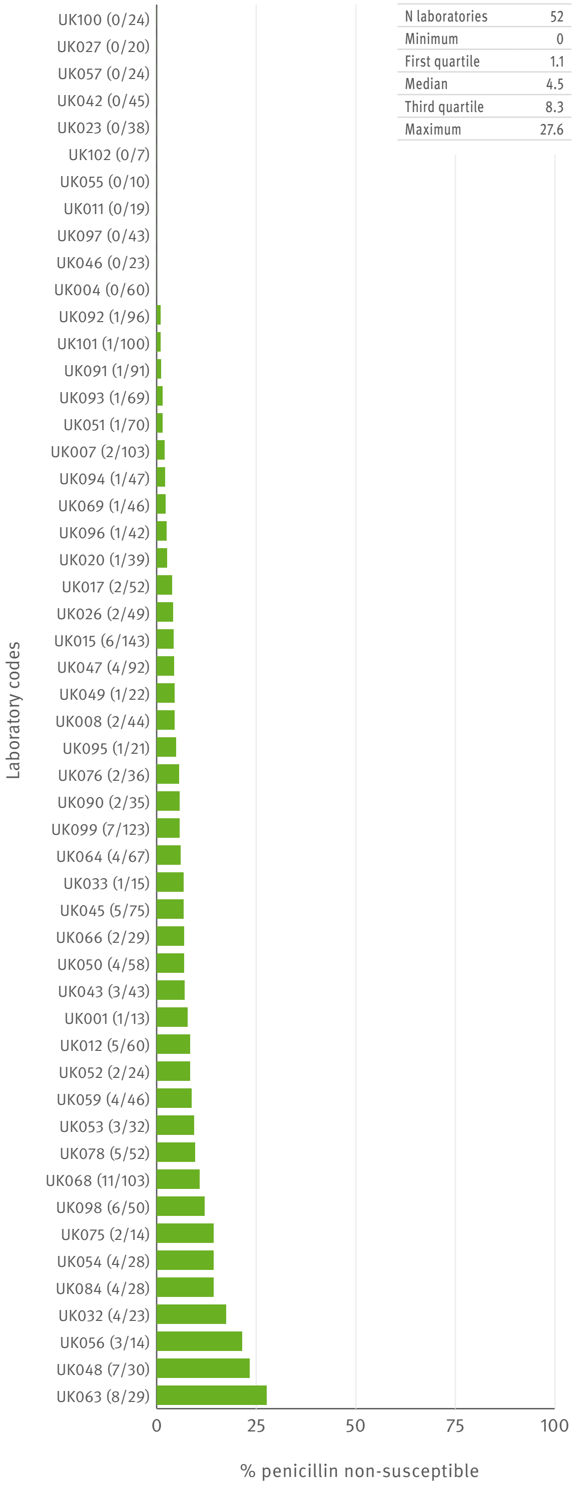
Demographic characteristics

Table 3: Selected details on invasive isolates reported for 2011 and 2012

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*		*K. pneumoniae*		*P. aeruginosa*	
	% total	% PNSP	% total	% MRSA	% total	% FREC	% total	% VRE	% total	% VRE	% total	% 3GCRKP	% total	% CRPA
Isolate source														
Blood	99	5	100	13	100	17	100	2	100	11	100	9	100	6
CSF	1	13	-	-	<1	9	-	-	-	-	0	0	0	0
Gender														
Male	50	5	61	14	47	19	67	1	61	10	60	10	62	6
Female	50	6	39	12	52	15	32	3	39	13	39	6	38	5
Unknown	1	0	0	25	<1	7	1	33	0	0	1	9	<1	67
Age (years)														
0–4	5	6	5	6	2	8	11	5	3	5	3	11	3	12
5–19	4	2	3	4	1	12	2	17	2	25	1	19	1	38
20–64	43	4	41	10	26	15	27	0	40	15	30	9	29	10
65 and over	49	6	47	19	71	18	61	2	55	9	65	8	67	3
Unknown	0	0	4	0	-	-	-	-	-	-	-	-	-	-
Hospital department														
ICU	2	7	1	16	-	-	-	-	-	-	-	-	-	-
Internal med.	8	6	4	28	-	-	-	-	-	-	-	-	-	-
Surgery	1	13	1	22	-	-	-	-	-	-	-	-	-	-
Other	16	5	8	19	-	-	-	-	-	-	-	-	-	-
Unknown	74	5	86	12	100	17	100	2	100	11	100	9	100	6

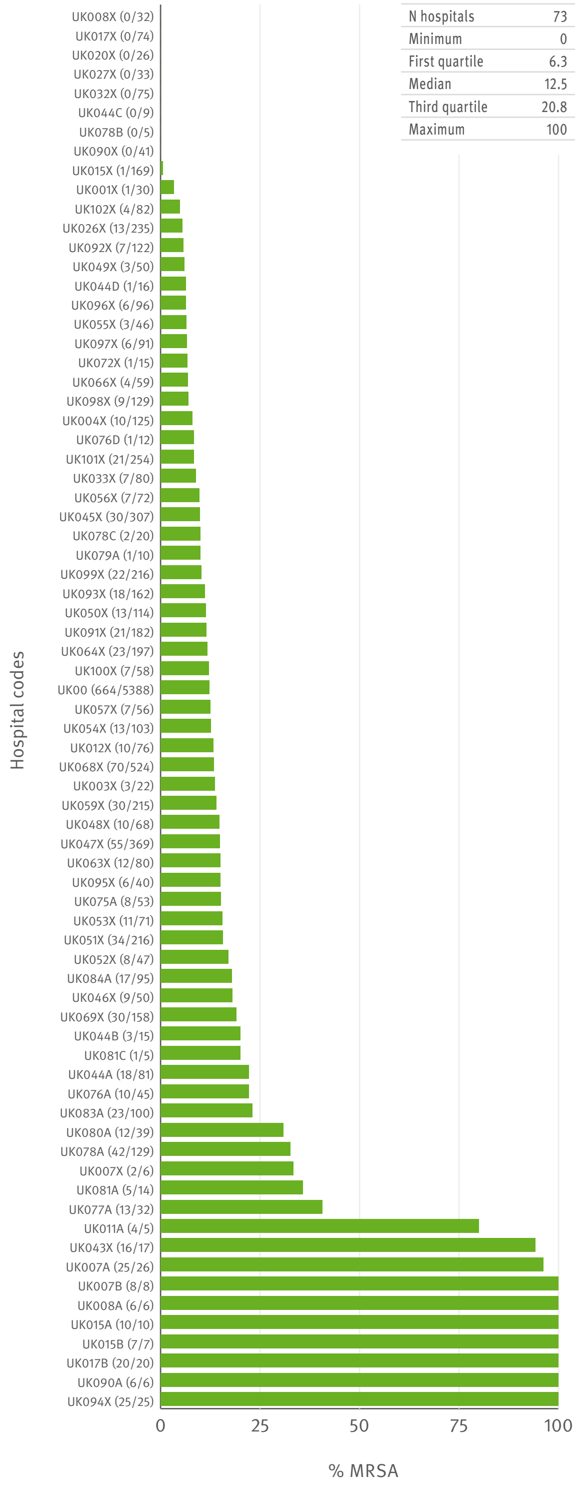
United Kingdom

Figure 1: ***S. pneumoniae*: percentage (%) of invasive isolates with penicillin non-susceptibility by laboratory (2011-2012)**



N laboratories	52
Minimum	0
First quartile	1.1
Median	4.5
Third quartile	8.3
Maximum	27.6

Figure 2: ***S. aureus*: percentage (%) of invasive isolates with resistance to meticillin (MRSA) by hospital (2011-2012)**



N hospitals	73
Minimum	0
First quartile	6.3
Median	12.5
Third quartile	20.8
Maximum	100

100% meticillin resistance rates for isolates of *S. aureus* reflect reporting of MRSA only.

Figure 3: ***E. coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones by hospital (2011-2012)**

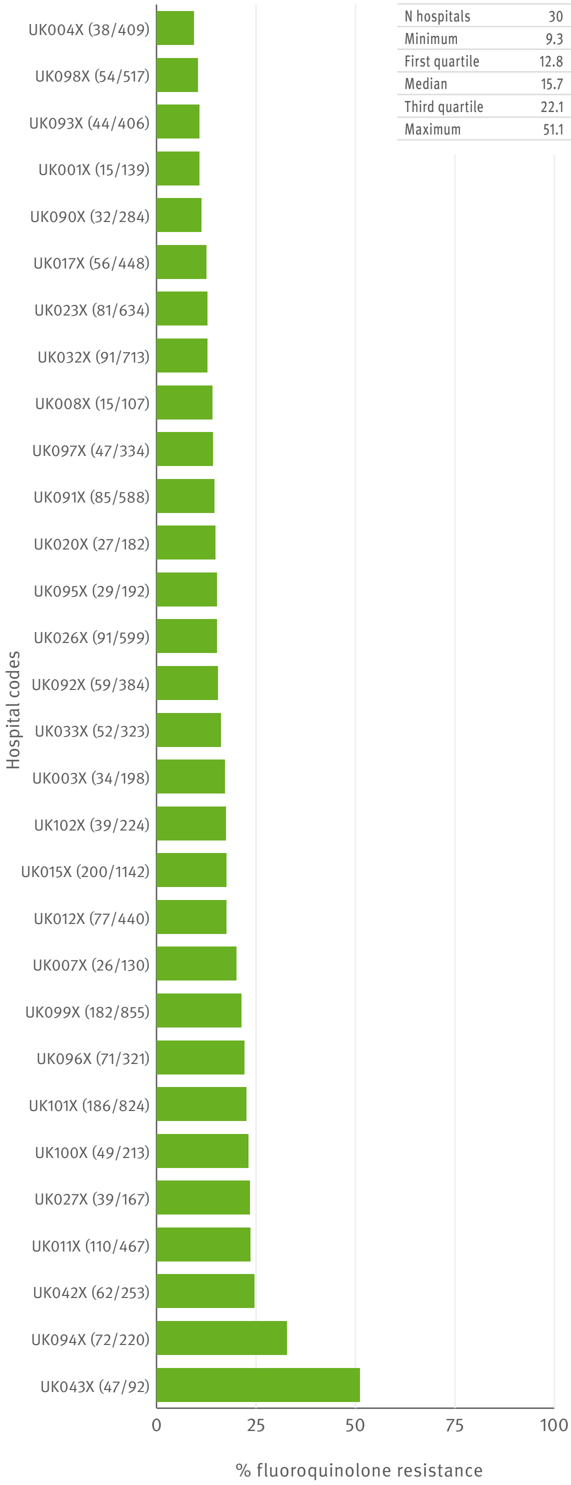
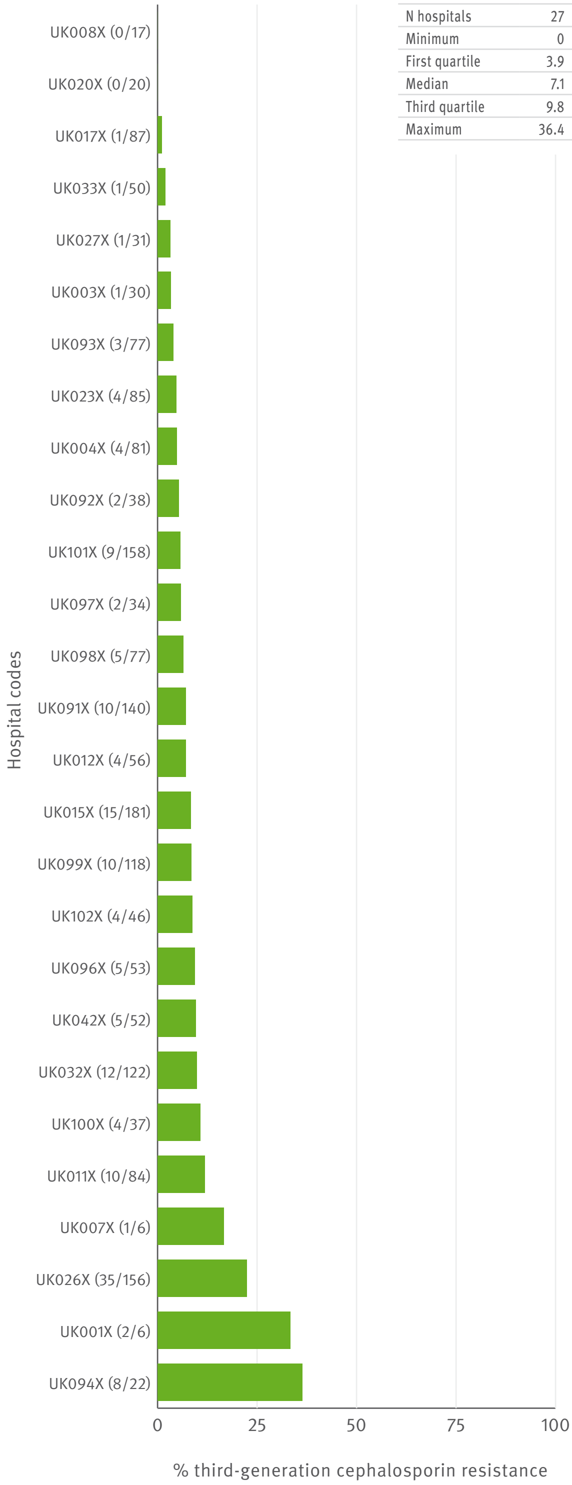


Figure 4: ***K. pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by hospital (2011-2012)**



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TQ-AM-13-001-EN-C

European Centre for Disease Prevention and Control (ECDC)

Postal address:
ECDC, SE-171 83 Stockholm, SWEDEN

Visiting address:
Tomtebodavägen 11a, Solna, SWEDEN

Tel. +46 858601000
Fax +46 858601001
http://www.ecdc.europa.eu

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Publications Office

ISBN: 978-92-9193-511-6