

European Antimicrobial Resistance Surveillance System



EARSS Annual Report 2008

On-going surveillance of
S. Pneumoniae, *S. aureus*, *E. coli*, *E. faecium*, *E. faecalis*, *K. pneumoniae*, *P. aeruginosa*

Funded by The European Centre for Disease Prevention and Control (ECDC)

EARSS

EUROPEAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM



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EARSS Annual Report 2008

The European Antimicrobial Resistance Surveillance System (EARSS), funded by the European Centre for Disease Prevention and Control (ECDC) of the European Commission, the Dutch Ministry of Health, Welfare and Sports, and the Dutch National Institute for Public Health and the Environment, is an international network of national surveillance systems which collects comparable and validated antimicrobial susceptibility data for public health action.

EARSS performs on-going surveillance of antimicrobial susceptibility in *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis/faecium*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* causing invasive infections and monitors variations of antimicrobial resistance over time and place.

In December 2008, almost 900 microbiological laboratories serving more than 1500 hospitals from 33 countries had provided susceptibility data of more than 700,000 invasive isolates.

An interactive website is available at www.rivm.nl/earss, where up-to-date details can be found on country-specific resistance levels for important groups of antibiotics.

Period of data collection: January 1999 – December 2008

This document was prepared by the EARSS Management Team, members of the Advisory Board, and national representatives of EARSS, Bilthoven, The Netherlands, October 2009.

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Acknowledgements

Ten years of EARSS

In 1963, Alexander Langmuir defined surveillance as the “systematic collection, consolidation, analysis and dissemination” of health information for public health practice. For antimicrobial resistance, surveillance can address public health demands from different angles. It may therefore be useful to divide AMR surveillance systems into three different levels depending on their objectives and the gaps in our knowledge that they are able to cover. The division that I suggest also mirrors the professional contribution from different disciplines such as biology, medicine and public health and are a reflection of the interaction of the major players in antimicrobial resistance namely the pathogen, host and population.

Surveillance at pathogen level utilises the genetic information of microorganisms to map and track the geographical and evolutionary trajectories with the aim to explain the reservoirs and origins of emerging virulence, transmissibility, antimicrobial resistance and the abundance of certain human pathogens. Data at this level can provide answers about the relationship between the emergence of resistance in different ecological niches such as humans, animals, or the environment and their spread across the interfaces between these respective habitats. Importantly, this information can directly influence infection control measures in the community and in hospitals.

Host level surveillance is the most pervasive argument for patient safety, as it guides treatment by local epidemiology. At this level, the individual patient is the unit of interest and the collation of case-based AMR data provide the decision basis for appropriate empirical therapy and can guide the judicious use of antibiotics. Obviously for the data to be relevant for treatment decisions they need to be generated locally (health centre-based), in a timely fashion, and should be syndrome-based.

Population level surveillance measures the national and international scale of AMR and thus puts AMR into context with other public health threats. Information gathered at this level will lead to the public recognition of antimicrobial agents as scarce or non-renewable resources, support policy changes and eventually redirect investment into drug development.

In 1999, EARSS was implemented with the clear vision of the current Director General of the Dutch National Institute for Public Health and the Environment (RIVM), Marc Sprenger, to address the information needs *at the population level* and since then surveillance of antimicrobial resistance in Europe has come a long way. Despite initial scepticism of the microbiological community over the validity of comparing hetero-consistent susceptibility data across national boundaries, the EARSS initiative was readily taken up by countries eager to contribute to scientific community building with the sense for the urgent need of protecting antimicrobial effectiveness and in anticipation of the enlargement of the European Union. Since the publication of first Annual Report in 1999 EARSS has increased in scope, size and coverage, starting with two pathogens and four pathogen-compound combinations, now up to seven and twenty pathogen-compound combinations; increasing from 13 to 33 participating countries, from 320 to 888 laboratories, from 396 to 1578 hospitals and from 12916 to 130293 isolates reported annually to the central database in Bilthoven. Ever since the implementation of an interactive website that made the recorded data publicly available, the “EARSS maps” have become a trademark and an apparently indispensable part of any scientific presentation on international conferences devoted to bacterial infections.

Largely due to the support of already existing or new national initiatives, EARSS national networks have been thriving in several countries and are now able to address the surveillance demands at the *host level surveillance* and help practitioners in their daily choice of appropriate therapy. When in 2003 the data from the European Surveillance of Antimicrobial Consumption (ESAC) network became available as the logical next step, the combination of population data on consumption and resistance became the strongest and clearly the ultimate advocacy tool for antimicrobial stewardship at the European level.

It also became clear that the gradient between countries puts low resistance/consumption countries under heavy colonisation pressure and a new offspring of the EARSS network was borne with the decision to utilise standardised genetic typing approaches for the mapping of the distribution of clones with public health importance across the European region. In the winter 2006-2007 a structured survey was carried out whereby 450 hospitals in 26 countries collected almost 3000 isolates of *S. aureus* from blood stream infections that were genetically characterised by *spa* sequence typing at the Staphylococcal Reference Laboratories (SRLs) in each country, being the crucial step towards *surveillance at the pathogen level* and leading to the first interactive mapping tool (at www.spatial-epidemiology.net/srl-maps) that describes the dissemination of MRSA and MSSA clones of major public health importance across a continental scale.

Twenty-one advisory board meetings, 10 annual plenary meetings, 5 data manager-workshops and 5 SRL workshops and 74 publications after the launch of EARSS ten year ago, EARSS is now ready to be taken over by its new foster institution the ECDC which will host this prolific network on behalf of the European Commission from January 2010.

All of this being the result of the enthusiasm and exceptionally professional collaborative spirit to of all national representatives, national data managers and their ability to continuously keep up the motivation of participating laboratories and their willingness to share the antimicrobial susceptibility data over the last ten years.

I thank UK-NEQAS for their major role in preparing and organising the eight successive external QA exercises. I would also like to thank the different members of the EARSS Advisory Board and the EARSS Management Team for sharing their expertise, for their contribution to this report and also for making the activities organised within EARSS a beacon that is clearly recognized far beyond the European boundaries. Furthermore, I would like to thank John Stelling for visiting many participating countries and spreading the gospel for WHONET and for EARSS, Alex Friedrich and Dag Harmsen for their support of the staphylococcal *spa*-typing initiative and David Aanensen for the development of the interactive web-based mapping tool. Finally, I would like to thank the Directorate General for Health and Consumer Protection of the European Commission (DG-SANCO), the ECDC and the Ministry of Health, Welfare and Sports of the Netherlands for the financial and moral support without which this initiative had never come to fruition.



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Summary

The European Antimicrobial Resistance Surveillance System (EARSS) is an international initiative funded by the European Centre for Disease Prevention and Control (ECDC) of the European Union, the Dutch Ministry of Health, Welfare and Sports and the Dutch National Institute for Public Health and the Environment (RIVM). It maintains a comprehensive surveillance and information system that links national networks by providing comparable and validated data on the prevalence and spread of major invasive bacteria with clinically and epidemiologically relevant antimicrobial resistance in Europe.

EARSS collects routinely generated antimicrobial susceptibility (AST) data, provides spatial trend analyses and makes timely feedback available via an interactive website at www.rivm.nl/earss. Routine data for major indicator pathogens (*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) are quarterly submitted by almost 900 laboratories serving more than 1500 hospitals in 33 European countries.

Based on the denominator data reported through the laboratory/hospital questionnaire, the overall hospital catchment population of the EARSS network is estimated to include at least 20% of EU population; including accession countries and Israel, and with national coverage rates between 20-100% for most countries. The comparability of MRSA incidence rates and proportions indicates that the resistance proportions as reported by EARSS are a good approximation of the incidence rates, and comparison of resistance proportions between countries thus provides useful information. The resistance profile of *S. pneumoniae* has a dynamic character. Although penicillin non-susceptibility is increasing in two countries, four countries are on the decrease, among those the high endemic countries Israel and France, strongly decreasing over the past years. Erythromycin non-susceptibility is becoming more prevalent in two countries, but against that, six countries are on the decrease. For dual non-susceptibility more increasing trends than decreasing trends were found. In 2008, again 12 countries have reported serogroup information for *S. pneumoniae* isolates, and data from seven countries were included for analysis. Compared to 2007, changes were small. Serogroup 1 and 19 are still the most prevalent ones, whereas serogroup 7 and serogroup 3 became slightly more prevalent, and serogroup 14 became less prevalent in the population.

For the first time, more countries showed decreasing MRSA proportions instead of increasing trends, so the MRSA problem seems to stabilize for many European countries. Nevertheless, MRSA proportions are still above 25% in one third of countries. The highest rates were reported from the Mediterranean, with Malta and Portugal showing MRSA proportions of over 50%. With the ongoing spread of clonal complex 17 in Europe, outbreaks of vancomycin resistant *E. faecium* continues to afflict hospitals in various countries. The spread of these hospital-adapted strains occurs on the background of high-level aminoglycoside resistance. The control of glycopeptide resistant enterococci is a formidable task and these problematic pathogens will continue to remain a challenge for hospital infection control practitioners.

The Europe-wide increase of resistance of *Escherichia coli* to all of the antimicrobial classes recorded by EARSS is a disturbing development with seemingly relentless vigor. The highest resistance proportions have been reported for aminopenicillins and these cannot be regarded as a useful option for empirical treatment. For fluoroquinolones the situation becomes progressively dire. The speed with which fluoroquinolones lose their activity against *E. coli* is next to no other compound pathogen combination in the EARSS database. Combined resistance is a frequent occurrence, with co-resistance to 4 antimicrobial classes including 3rd generation cephalosporins and expected to become the dominant combined resistance phenotype for invasive *E. coli* in Europe.

In *K. pneumoniae* a high prevalence of resistant strains to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides becomes evident in central and south-eastern Europe. Many of these strains have combined resistance and the most frequent phenotype shows resistance to all three antimicrobial classes recorded by EARSS. Although carbapenems are still effective in most countries, the rapid emergence and dissemination of strains with carbapenemase production are threatening the effectiveness of this last line therapeutic option. It is thus necessary to closely monitor the effectiveness of carbapenems and be aware that carbapenemase-positive isolates may not be detected by automated systems. EARSS therefore recommends to be further scrutinise all isolates with MIC ≥ 0.5 mg/l or meropenem and ≥ 1 mg/L for imipenem.

Combined resistance is the dominant threat imposed by invasive *P. aeruginosa* on Europe. Since resistance in *P. aeruginosa* emerges readily during antibiotic treatment, the time when blood cultures are taken is crucial as any isolate sampled after prolonged exposure with antimicrobial chemotherapy will predictably be a multi-resistant phenotype. Assuming the diagnostic habits in Europe are comparable, the picture that our data suggest is that the geographical gradient observed for all other gram-negative pathogens, namely lower resistance in the Northwest and increasing resistance towards the Southeast also holds for *P. aeruginosa*.

In conclusion, the data that EARSS has gathered over the years bring an unpleasant, but important truth: the loss of effective antimicrobial therapy increasingly threatens the delivery of crucial health services in hospitals and in the community.

List of abbreviations and acronyms

AMR	Antimicrobial resistance
ARMed	Antibiotic Resistance Surveillance and Control in the Mediterranean region
AST	Antimicrobial susceptibility testing
CC	Clonal Complex
CSF	Cerebrospinal fluid
DCFP	Data Check and Feedback Programme
DEFS	Data Entry & Feedback Software
DG-SANCO	Directorate General for Health and Consumer Protection
DNA	Deoxyribonucleic Acid
EARSS	European Antimicrobial Resistance Surveillance System
EARSS-MT	EARSS Management Team
EARSS-NR	EARSS National Representatives
ECDC	European Centre for Disease Prevention and Control
ENSP	Erythromycin nonsusceptible <i>Streptococcus pneumoniae</i>
EU	European Union
EQA	External quality assessment
ESAC	European Surveillance of Antimicrobial Consumption
ESBL	Extended-spectrum beta-lactamase
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
ESGARS	ESCMID Study Group for Antimicrobial Resistance Surveillance
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GISA	Glycopeptide intermediate resistant <i>Staphylococcus aureus</i>
ICU	Intensive care unit
MIC	Minimum Inhibitory Concentration
MLS	Macrolide-Lincosamide-Streptogramin
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
NRL	National reference laboratories
OXA	Oxacillinase gene
PBP	Penicillin binding protein
PCV	Pneumococcal conjugate vaccin
PNSP	Penicillin nonsusceptible <i>Streptococcus pneumoniae</i>
PRSP	Penicillin resistant <i>Streptococcus pneumoniae</i>
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment)
RNA	Ribonucleic Acid
SeqNet.org	European Network of Laboratories for Sequence Based Typing of Microbial Pathogens
Spa-typing	<i>S. aureus</i> protein A-gene sequence typing
TESSy	The European Surveillance System from ECDC
UK-NEQAS	United Kingdom National External Quality Assessment Scheme for Microbiology
VISA	Vancomycin intermediate <i>Staphylococcus aureus</i>
VRE	Vancomycin resistant enterococci
VREF	Vancomycin resistant <i>Enterococcus faecalis</i>
VRSA	Vancomycin resistant <i>Staphylococcus aureus</i>
WHO	World Health Organization
WHONET	WHO microbiology laboratory database software

The EARSS network from January 2008 till August 2009

I. Countries participating in EARSS

Austria	AT	Italy	IT
Belgium	BE	Latvia	LV
Bosnia Herzegovina	BA	Lithuania	LT
Bulgaria	BG	Luxembourg	LU
Croatia	HR	Malta	MT
Cyprus	CY	Netherlands	NL
Czech Republic	CZ	Norway	NO
Denmark	DK	Poland	PL
Estonia	EE	Portugal	PT
Finland	FI	Romania	RO
France	FR	Slovenia	SI
Germany	DE	Spain	ES
Greece	GR	Sweden	SE
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VII. EARSS related publications

Scientific papers in peer reviewed journals

EARSS management team

- Bronzwaer SL, Cars O, Buchholz U, Molstad S, Goettsch W, Veldhuijzen IK, Kool JL, Sprenger MJ, Degener JE. European Antimicrobial Resistance Surveillance System. A European study on the relationship between antimicrobial use and antimicrobial resistance. *Emerg Infect Dis* **2002**; 8: 278-82.
- Bronzwaer S, Buchholz U, Courvalin P, Snell J, Cornaglia G, de Neeling A, Aubry-Damon H, Degener J; EARSS participants. Comparability of antimicrobial susceptibility test results from 22 European countries and Israel: an external quality assurance exercise of the European Antimicrobial Resistance Surveillance System (EARSS) in collaboration with the United Kingdom National External Quality Assurance Scheme (UK NEQAS). *J Antimicrob Chemother* **2002**; 50: 953-64.
- Bronzwaer SL, Cars O, Buchholz U, Mólstad S, Goettsch W, Veldhuijzen IK, Kool JL, Sprenger MJW, Degener JE, and participants in the European Antimicrobial Resistance Surveillance System A European Study on the Relationship between Antimicrobial Use and Antimicrobial Resistance. *Emerg Infect Dis* **2002**; 6: 278-282.
- Tiemersma EW, Bronzwaer SL, Lyytikäinen O, Degener JE, Schrijnemakers P, Bruinsma N, Monen J, Witte W, Grundmann H, and EARSS Participants. Methicillin-resistant *Staphylococcus aureus* in Europe, 1999–2002. *Emerging Infect Dis* **2004**; 10: 1627-1634.
- Bruinsma N, Kristinsson K, Bronzwaer S, Schrijnemakers P, Degener J, Tiemersma E, Hryniewicz W, Monen J, Grundmann H, and the EARSS participants. Trends of penicillin and erythromycin resistance among invasive *Streptococcus pneumoniae* in Europe. *J Antimicrobial Chemother* **2004**; 54: 1045-1050.
- Tiemersma EW, Monnet DL, Bruinsma N, Skov R, Monen JCM, Grundmann H, and EARSS participants. *Staphylococcus aureus* bacteremia, Europe. *Emerging Infect Dis* **2005**; 11: 1798-9.
- Grundmann H, Aires-de-Sousa M, Boyce J, Tiemersma E. Emergence and resurgence of methicillin-resistant *Staphylococcus aureus* as a public health threat. *The Lancet* **2006**; 368: 874-885.
- Foster KR, Grundmann H. Do we need to put society first? The potential for tragedy in antimicrobial resistance. *PloS Medicine* **2006**; 3: 29.
- Van de Sande-Bruinsma N, Grundmann H, Verloo D, Tiemersma E, Monen J, Goossens H, Ferech M; European Antimicrobial Resistance Surveillance System Group; European Surveillance of Antimicrobial Consumption Project Group. Antimicrobial Drug Use and Resistance in Europe. *Emerging Infect Dis* **2008**; 14(11):1722-30.
- Borg MA, van de Sande-Bruinsma N, Scicluna E, de Kraker M, Tiemersma E, Monen J, Grundmann H; ARMed Project Members and Collaborators. Antimicrobial resistance in invasive strains of *Escherichia coli* from southern and eastern Mediterranean laboratories. *Clin Microbiol Infect* **2008**; 14(8): 789-96.
- Borg M, Tiemersma E, Scicluna E, Van de Sande-Bruinsma N, De Kraker M, Monen J, Grundmann H; ARMed Project members and collaborators. Prevalence of penicillin and erythromycin resistance among *Streptococcus pneumoniae* isolates reported by laboratories in the southern and eastern Mediterranean region. *Clin Microbiol Infect* **2009**; 15(3): 232-7.

Austria

- Metz-Gercek S, Mittermayer H. The European surveillance activities EARSS and ESAC in the context of ABS International. *Wien Klin Wochenschr.* **2008**; 120(9-10): 264-7.
- Metz-Gercek S, Maieron A, Strauss R, Wieninger P, Apfalter P, Mittermayer H. Ten years of antibiotic consumption in ambulatory care: trends in prescribing practice and antibiotic resistance in Austria. *BMC Infect Dis.* **2009**;13; 9-61.

Belgium

- Goossens H, Ferech M, Vander Stichele R, Elseviers M; ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* **2005**; 9459: 579-587.

Croatia

- Budimir A, Duerenberg RH, Plecko V, Vink C, Kalenic S, Stobberingh E. Molecular characterization of methicillin-resistant *Staphylococcus aureus* bloodstream isolates from Croatia. *J Antimicrob Chemother.* **2006**; 57: 331-334.

Czech Republic

- Urbášková P, Macková B, Jakubu V, Žemlicková H a CZ-EARSS. Resistance to clindamycin among 1373 *Staphylococcus aureus* isolates from blood. *Zprávy CEM (Bulletin of the Centre of Epidemiology and Microbiology)* **2006**; 15(3-4):156-158, ISSN 1211-7358.
- Urbášková P, Macková B, Jakubu V, Žemlicková H a CZ-EARSS. Antimicrobial resistance surveillance in invasive *Staphylococcus aureus* isolates within EARSS. *Zprávy CEM (Bulletin of the Centre of Epidemiology and Microbiology)* **2006**; 15(5):200-203, ISSN 1211-7358.
- Urbášková P, Jakubu V, Žemlicková H a účastníci CZ-EARSS. Antimicrobial resistance in seven invasive bacterial species monitored within EARSS in the Czech Republic (CR) from 2000 - 2006. *CzMa JEP Prakticky lékař* No. 1, **2007**.
- Hrabák J, Fridrichová M, Stolbová M, Bergerová T, Žemlicková, Urbášková P. First identification of metallo-beta-lactamase-producing *Pseudomonas aeruginosa* in the Czech Republic. *Euro Surveill.* **2009** 29; 14(4). pii: 19102.

Denmark

- Lester CH, Sandvang D, Olsen SS, Schønheyder HC, Jarløv JO, Bangsborg J, Hansen DS, Jensen TG, Frimodt-Møller N, Hammerum AM; DANRES Study Group. Emergence of ampicillin-resistant *Enterococcus faecium* in Danish hospitals. *J Antimicrob Chemother.* **2008**; 62(6): 1203-6. Epub 2008 Sep 1.
- Jensen US, Skjöt-Rasmussen L, Olsen SS, Frimodt-Møller N, Hammerum AM; DANRES Study Group. Consequences of increased antibacterial consumption and change in pattern of antibacterial use in Danish hospitals. *J Antimicrob Chemother.* **2009**; 63(4): 812-5. Epub 2009 Feb 24.

Estonia

- Lõivukene K, Kermes K, Sepp E, Adamson V, Mitt P, Kallandi Ü, Otter K, Naaber P. The surveillance of antimicrobial resistance of invasive pathogens: Estonian experience. *Eurosurveillance monthly* **2006**; 11; Issues 1-3: 47-49.
- Lõivukene K, Kermes K, Sepp E, Adamson V, Mitt P, Jürna M, Mägi H, Kallandi Ü, Otter K, Naaber P. The comparison of susceptibility of gram-negative invasive and nosocomial pathogens in Estonian hospitals. *Antonie van Leeuwenhoek.* **2006**; 89:367-71.
- Lõivukene K, Sepp E, Adamson V, Kallandi Ü, Otter K, Naaber P. Importance and antimicrobial susceptibility of *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* in intensive care units. Estonian study compared with other European data. *Scand J Infect Dis.* **2006**; 38: 1001-1008.

Finland

- Lyytikäinen O, Möttönen T, Nissinen A. Mikrobilääkeresistenssin seuranta Euroopassa: EARSS-tuloksia 2002. *Kansanterveys* **2003**; 10: 13-14.
- Lyytikäinen O, Möttönen T, Nissinen A. Mikrobilääkeresistenssin seuranta Euroopassa: EARSS-tuloksia 2002. *Sairaalahygienialehti* **2003**; 6: 282-283.
- Lyytikäinen O, Nissinen A. Mikrobilääkeresistentit sairaalainfektioiden aiheuttajat meillä ja muualla. *Sairaala* **2004**; 3: 14-15.
- Lyytikäinen O, Agthe N, Virolainen-Julkunen A, Vuopio-Varkila J. MRSA-tilanne yhä huonontunut – nyt myös vaikeissa yleisinfektioissa. *Kansanterveys* **2004**; 7: 9.
- Lyytikäinen O, Agthe N, Virolainen-Julkunen A, Vuopio-Varkila A. MRSA cases continue to increase in Finland. *Eurosurveillance weekly* 16 September **2004**.

- Virolainen-Julkunen A, Vuopio-Varkila J, Huovinen P, Lyytikäinen O, Ruutu P. Lisämääräraha MRSA:n torjuntaan. *Kansanterveys* **2005**; 2-3: 7-8.
- Lyytikäinen O. Onko Suomen MRSA-tilanteen huononeminen pysähtynyt? *Kansanterveys* **2005**; 7: 3-4.
- Vuopio-Varkila J, Lyytikäinen O. Mikä on avohoidon MRSA? *Kansanterveys* **2005**; 7:4.
- Kainulainen K, Lyytikäinen O, Vuopio-Varkila J, Syrjälä H. Vankomysiinierokokki (VRE) Suomessa. *Kansanterveys* **2006**; 5-6: 22-23.
- Kerttula A-M, Lyytikäinen O, Virolainen-Julkunen A, Vuopio-Varkila J. Perimätutkimukset valaisevat Suomen huonontuneen MRSA-tilanteen taustaa. *Suomen Lääkärelehti* **2006**; 61: 2383-7.
- Säilä P, Lyytikäinen O, Möttönen T, Nissinen A. Bakteerilääkeresistenssin seuranta Euroopassa: EARSS-tuloksia. *Kansanterveys* **2007**; 5-6: 18-19.
- Salmenlinna S, Lyytikäinen O, Kanerva M, Vuopio-Varkila J. MRSA:n epidemiologia Suomessa. *Moodi* **2008**;5: 190-193.
- Salmenlinna S, Lyytikäinen O, Kanerva M, Vuopio-Varkila J. MRSA:n epidemiologia Suomessa. *Sairaalahygienialehti* **2008**; 6:292-7.
- Kanerva M, Salmenlinna S, Vuopio-Varkila J, Lyytikäinen O. Community-associated methicillin-resistant *Staphylococcus aureus* isolated in Finland in 2004 to 2007. *J Clin Microbiol* **2009**; 47: 2655-7.
- Siira L, Rantala M, Jalava J, Hakanen AJ, Huovinen P, Kajjalainen T, Lyytikäinen O, Virolainen A. Temporal trends of antimicrobial resistance and clonality of invasive *Streptococcus pneumoniae* in Finland, 2002-2006. *Antimicrob Agents Chemother* **2009**; 53: 2066-73.

France

- Anonymous. Recent trends in antimicrobial resistance among *Streptococcus pneumoniae* and *Staphylococcus aureus* isolates: the French experience. *Euro Surveill* **2008**; 13(46): pii=19035.

Italy

- Moro ML, Pantosti A, Boccia D, e il gruppo EARSS-Italia. Sorveglianza dell'antibiotico-resistenza in infezioni invasive da *Streptococcus pneumoniae* e *Staphylococcus aureus*: il progetto EARSS in Italia (Aprile 1999- Aprile 2000). *Ann Ig* **2002**; 14: 361-371.
- Boccia D, Pantosti A, D'Ancona F, Giannitelli S, Monaco M, Salmaso S. Antimicrobial resistance in Italy: preliminary results from the AR-ISS project. *Eurosurveillance* **2002**; 7: 87-93.
- Pantosti A, Boccia D, D'Ambrosio F, Recchia S, Orefici G, Moro ML, National Surveillance of Bacterial Meningitis, and The EARSS-Italia Study. Inferring the potential success of pneumococcal vaccination in Italy: serotypes and antibiotic resistance of *Streptococcus pneumoniae* isolates from invasive diseases. *Microb Drug Resist* **2003**; 9: S61-S68.
- Fokas S, D'Ancona F, Boccia D, Pantosti A, Giannitelli S, Meduri FR, Salmaso S per il gruppo di studio AR-ISS. L'antibioticoresistenza in Italia: il progetto AR-ISS. Risultati del primo anno di attività e prospettive per il futuro. *Not Ist Super Sanità* **2003**; 16: 11-14.
- Boccia D, Spila Alegiani S, Pantosti A, Moro ML, Traversa G. The geographic relationship between the use of antimicrobial drugs and the pattern of resistance for *Streptococcus pneumoniae* in Italy. *Eur J Pharmacol* **2004**; 60: 115-119.
- Stampone L, Del Grosso M, Boccia D, Pantosti A. Clonal spread of a vancomycin-resistant *Enterococcus faecium* strain among bloodstream-infecting isolates in Italy. *J Clin Microbiol* **2005**; 43: 1575-1580.
- Monaco M, Camilli R, D'Ambrosio F, Del Grosso M, Pantosti A. Evolution of erythromycin resistance in *Streptococcus pneumoniae* in Italy. *J Antimicrob Chemother* **2005**; 55: 256-259.
- Boccia D, D'Ancona F, Salmaso S, Monaco M, Del Grosso M, D'Ambrosio F, Giannitelli S, Lana S, Fokas S, Pantosti A e il Gruppo AR-ISS. Antibiotico-resistenza in Italia: un anno di attività del progetto di sorveglianza AR-ISS. *Ann Ig* **2005**; 17: 95-110.

Ireland

- Clarke P, Murchan S, Smyth EG, Humphreys H. Antimicrobial susceptibility of invasive isolates of *Streptococcus pneumoniae* in Ireland. *Clin Microbiol Infect.* **2004**; 10(7): 657-9.
- Murphy OM, Murchan S, Whyte D, Humphreys H, Rossney A, Clarke P, Cunney R, Keane C, Fenelon LE, O'Flanagan D. Impact of the European Antimicrobial Resistance Surveillance System on the development of a national programme to monitor resistance in *Staphylococcus aureus* and *Streptococcus pneumoniae* in Ireland, 1999-2003. *European Journal of Clinical Microbiology and Infectious Diseases* **2005**; 24(7): 480-3.

- Rossney AS, Lawrence MJ, Morgan PM, Fitzgibbon MM, Shore A, Coleman DC, Keane CT, O'Connell B. Epidemiological typing of MRSA isolates from blood cultures taken in Irish hospitals participating in the European Antimicrobial Resistance Surveillance System (1999-2003). *European Journal of Clinical Microbiology and Infectious Diseases* **2006**; 25: 79-89.
- Murchan S, Cunney R; Irish EARSS Steering Group. Rise in antimicrobial resistance in invasive isolates of *Escherichia coli* and *Enterococcus faecium* in Ireland. *Euro Surveill.* **2006** Apr 13; 11(4): E060413.3.

Romania

- Codita I. The global strategy for antimicrobial resistance containment, European Antimicrobial Resistance Surveillance System (EARSS). Preparatory stages for integrating national surveillance of antimicrobial resistance in the European system. *Viata medicala* **2001**; May: 2.
- Chifiriuc Mariana Carmen, Lixandru Mariana, Iordache Carmen, Bleotu Coralia, Larion Cristina, Olguta Dracea, Lazar Veronica, Antohe Felicia, Israil Anca Michaela. Internalization of *Staphylococcus Aureus* and *Pseudomonas Aeruginosa* Bacterial Cells By Non-Phagocytic, Epithelial Human Cells. *Roum. Biotech. Lett.* **2008**; 13 (2), 3651-3658.
- Ani-Ioana Cotar, Sorin Dinu, Mariana-Carmen Balotescu Chifiriuc, Otilia Banu, Carmen Iordache, Cristina Larion, Marcela Bucur, Olguta Dracea, Veronica Lazar. Screening of molecular markers of quorum sensing in *Pseudomonas aeruginosa* strains isolated from clinical infections. *Roum. Biotech. Lett.* **2008**; 13 (3): 3765-3771.
- Ani-Ioana Cotar, Sorin Dinu, Mariana-Carmen Balotescu Chifiriuc, Otilia Banu, Carmen Iordache, Mariana Lixandru, Olguta Dracea, Marcela Bucur, Veronica Lazar. Molecular markers of quorum-sensing and virulence gene regulators in *Staphylococcus aureus* strains isolated from biofilm associated infections. *Roum. Biotech. Lett.* **2008**; 13 (3) 3771-3778.

Slovenia

- Kolman J, Gubina M, Mueller-Premru M, Sočan M, Cyetkovski L, Koren S. Slovenski rezultati občutljivosti bakterij *Staphylococcus aureus* in *Streptococcus pneumoniae* iz hemokultur in likvorjev, zbrani v okviru projekta EARSS. In: Mueller-Premru M, Gubina M, editors. Mikrobi in antibiotiki 2001. Zbornik predavanj Mikrobiološki simpozij z mednarodno udeležbo; 2001 jun 22-23; Ljubljana. Ljubljana: Slovensko zdravniško društvo, Sekcija za klinično mikrobiologijo in hospitalne infekcije, **2001**; 185-92.
- Kolman J, Gubina M, Mueller-Premru M, Lorenčič-Robnik S, Žohar-Čretnik T, Harlander T, Štrumbelj I, Kavčič M, Grmek-Košnik I, Tomič V, Ribič H, Fišer J, Merljak L, Piltaver-Vajdec I. Sodelovanje Slovenije v evropskem projektu EARSS - prikaz rezultatov deleža MRSA - izolatov iz hemokultur. *Isis* **2003**; 12: 30-33.
- Kolman J, Gubina M. Trendi občutljivosti invazivnih izolatov bakterije *Staphylococcus aureus* v Sloveniji in Evropi - rezultati projekta EARSS. *Med Razgl* **2004**; 43: 11-17.
- Kolman J, Gubina M. Sodelovanje Slovenije v projektu EARSS. *Med Razgl* **2006**; 45 (Suppl 2): 3-10.

Spain

- Oteo J, Campos J, Baquero F and the Spanish EARSS Group. Antibiotic resistance in 1962 invasive isolates of *Escherichia coli* in 27 Spanish hospitals participating in the European Antimicrobial Resistance Surveillance System (2001). *J Antimicrob Chemother* **2002**; 50: 945-952.
- Oteo J, Cruchaga S, Campos J, Saez JA, Baquero F, y miembros españoles del grupo "European Antimicrobial Resistance Surveillance System. Antibiotic resistance in blood isolates of *Staphylococcus aureus* in 31 Spanish hospitals participating in the European Antimicrobial Resistance Surveillance System (2000)]. *Medicina Clinica* **2002**; 119: 361-5.
- Oteo J, Cruchaga S, Campos J, Saez JA, Baquero F, y miembros españoles del grupo "European Antimicrobial Resistance Surveillance System. Antibiotic resistance in 622 *Streptococcus pneumoniae* isolated from blood and cerebrospinal fluid in 33 Spanish hospitals participating in the European Antimicrobial Resistance Surveillance System (2000)]. *Enfermedades Infecciosas y Microbiología Clínica* **2003**; 21: 12-9.
- Oteo J, Campos J, Cruchaga S, Baquero G, Lázaro E, Madurga M, de Abajo FJ, Baquero F and the Spanish EARSS Group. Increase of resistance to macrolides in invasive *Streptococcus pneumoniae* in Spain (2000-2001). *Clin Microbiol Infect* **2004**; 12: 851-854.
- Oteo J, Baquero F, Vindel A, Campos J and the Spanish EARSS Group. Antibiotic resistance in 3113 blood isolates of *Staphylococcus aureus* in 40 Spanish hospitals participating in the European Antimicrobial Resistance Surveillance System (2000-2002). *J Antimicrob Chemother* **2004**; 53: 1033-1038.
- Oteo J, Lázaro E, de Abajo FJ, Campos J, and Spanish EARSS Group. Trends in antimicrobial resistance in 1,968 invasive *Streptococcus pneumoniae* strains isolated in Spanish hospitals (2001-2003): Decreasing penicillin-resistance in children's isolates. *J Clin Microbiol* **2004**; 42: 5571-5577.

- Oteo J, Lázaro E, de Abajo FJ, Baquero F, Campos J and the Spanish EARSS Group. Antimicrobial-resistant invasive *Escherichia coli*, Spain. *Emerg Infect Dis* **2005**, 11: 546-553.
- Oteo J, Cuevas O, Navarro C, Aracil B, Campos J; Spanish Group of The European Antimicrobial Resistance Surveillance System (EARSS). Trends in antimicrobial resistance in 3469 enterococci isolated from blood (EARSS experience 2001-06, Spain): increasing ampicillin resistance in *Enterococcus faecium*. *J Antimicrob Chemother.* **2007** 59: 1044-5.
- Oteo J, Campos J, Lázaro E, Cuevas O, et all. Increased Amoxicillin-Clavulanic Acid Resistance in *Escheria coli* Blood Isolates, Spain. *Emerging Infectious Diseases* **2008**; 8: 1259-62.
- Oteo J, Garduño E, Bautista V, Cuevas O, Campos J; Spanish members of European Antimicrobial Resistance Surveillance System. Antibiotic-resistant *Klebsiella pneumoniae* in Spain: analyses of 718 invasive isolates from 35 hospitals and report of one outbreak caused by an SHV-12-producing strain. *J Antimicrob Chemother.* **2008**; 61: 222-4.
- Pérez-Vázquez M, Vindel A, Marcos C, Oteo J, Cuevas O, Trincado P, Bautista V, Grundmann H, Campos J; EARSS Spain spa-typing Group. Spread of invasive Spanish *Staphylococcus aureus* spa-type t067 associated with a high prevalence of the aminoglycoside-modifying enzyme gene ant(4⁺)-Ia and the efflux pump genes msrA/msrB. *J Antimicrob Chemother.* **2009**; 63(1): 21-31. Epub 2008 Oct 23.

United Kingdom

- Johnson AP, Aucken HM, Cavendish S, Ganner M, Wale MC, Warner M et al. Dominance of EMRSA-15 and -16 among MRSA causing nosocomial bacteraemia in the UK: analysis of isolates from the European Antimicrobial Resistance Surveillance System (EARSS). *J Antimicrob Chemother* **2001**; 48: 143-144.
- Johnson AP, Lamagni TL, Wale M, Cavendish S, Bishop L, Alhaddad N et al. Susceptibility to moxifloxacin of pneumococci isolated in English hospitals participating in the European Antimicrobial Resistance Surveillance System (EARSS) in 2003. *Int J Antimicrob Agents* **2005**; 25: 539-541.

Chapter 1. Introduction

Antimicrobial resistance (AMR) threatens the effectiveness of successful treatment of infections and is a public health issue with local, national, and global dimensions. Antimicrobial resistance can result in increased morbidity, disease burden, and mortality. Surveillance of antimicrobial resistance proportions provides data that are needed to raise the awareness to the problem and instigate necessary interventions.

At the ‘Microbial Threat Conference’, held in September 1998 in Denmark, it was concluded that an ‘Effective European surveillance should be in place and must have the agreement and active involvement of all participants’ (‘the Copenhagen Recommendations’ (1)). This conference led to the foundation of the European Antimicrobial Resistance Surveillance System (EARSS), funded by the Directorate General for Health and Consumer Protection (DG SANCO) of the European Commission, the Dutch Ministry of Health, Welfare and Sports and the Dutch National Institute for Public Health and the Environment. Since 1999, it has been the remit of EARSS to maintain a comprehensive surveillance and information system that links national networks by providing comparable and validated data about the prevalence and spread of major invasive bacteria with clinical and epidemiologically relevant AMR in Europe. In 2001, at a follow-up EU conference in Visby, Sweden, it was concluded that all Member States of the European Union (EU) shall join the EARSS initiative as a minimum requirement of national surveillance programmes (‘the Visby recommendations’ (2)) and during the Rome conference convened by the EU Commission Directorate for Research and Development in November 2003, it was made clear that linking antimicrobial resistance with microbial ecology and improving the knowledge about its costs to European societies is essential for the development of effective control strategies (3). From September 2006 onwards, EARSS was co-financed by ECDC from the European Union.

EARSS is coordinated by the Dutch National Institute of Public Health and the Environment (RIVM). Ever since the start of EARSS, the number of participants has increased. By the beginning of 2008, EARSS covers an estimated population of at least 110 million European citizens (20% of the European population; including accession countries and Israel), served by more than 1500 hospitals in 33 countries. The EARSS database contains AMR data on more than 700,000 invasive isolates of *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. It is thus the most comprehensive public health effort that describes and analyses geographic and secular trends in AMR worldwide.

EARSS operates in close collaboration with other EU-financed projects, like the European Surveillance of Antimicrobial Consumption (ESAC). There is a close partnership between the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and two of the society’s sub committees, namely, the European Committee on Antimicrobial Susceptibility Testing (EUCAST), and the ESCMID Study Group for Antimicrobial Resistance Surveillance (ESGARS).

This report presents an overview of activities, innovations and results of the EARSS network in 2008. Chapter 2 summarises the objectives and operational strategy. In chapter 3, the results from the external quality assessment, which was conducted in cooperation with UK NEQUAS, are described. Chapter 4 gives an overview of the results of the laboratory/hospital questionnaire 2008, through

which information was collected on denominators and other relevant determinants of patient care. Chapter 5 provides a descriptive analysis of the situation of AMR in Europe. Chapter 6 presents the overall conclusions and recommendations based on these results. The annexes contain a technical section (annex 1), detailed country summary sheets (annex 2) and overview tables of antibiotic resistance in Europe in 2008 (annex 3). Results are based on data recorded from January 1999 - December 2008, if not otherwise indicated.

References

1. Thamdrup Rosdahl V, Borge Pederson K. Report from the invitational EU Conference on the microbial threat, Copenhagen, Denmark, 9-10 September 1998.
2. Progress Report on Antimicrobial Resistance, Visby, Sweden: Social Styrelsen, the Swedish National Board of Health and Welfare, June 2001. Available at <http://www.sos.se/FULL-TEXT/123/2001-123-68/2001-123-68.pdf>.
3. Report from the European Conference on the Role of Research in Combating Antibiotic Resistance, 2003. *Clin Microbiol Infect* 2004; 10: 473 – 497.

Chapter 2. EARSS objectives and operational strategy

2.1. Objectives

It is the remit of EARSS to maintain a comprehensive surveillance and information system that links national networks by providing comparable and validated data on the prevalence and spread of major invasive bacteria with clinically and epidemiologically relevant antimicrobial resistance in Europe. Thus, EARSS aims to:

- collect comparable and validated AMR data;
- analyse trends in time and place;
- provide timely AMR data that constitute a basis for policy decisions;
- provide feedback to ‘those who need to know’;
- encourage the implementation, maintenance and improvement of national AMR surveillance programmes;
- supports national systems in their efforts to improve diagnostic accuracy at every level of the surveillance chain;
- link AMR data to factors influencing the emergence and spread of AMR, such as antibiotic use data; and
- initiate, foster and complement scientific research in Europe in the field of AMR.

EARSS collects routine antimicrobial susceptibility test (AST) results of invasive (blood culture and CSF) isolates of *Streptococcus pneumoniae*, *Staphylococcus aureus* (both since 1999), *Enterococcus faecalis* and *E. faecium*, *Escherichia coli* (since 2001), *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (both since 2005). These pathogens were selected because they have different epidemiological and ecological backgrounds and serve as markers for clinically and epidemiologically meaningful developments in antibiotic resistance. The decision to collect routine data, preferably according to the internet-accessible EARSS protocols, means that no changes to the regular diagnostic process are needed. In this way, the participation of many laboratories in many countries has become feasible.

2.2. The EARSS network and operational strategy

2.2.1. Organisation of the EARSS network

Each participating country has appointed one or two national representatives. They are medical microbiologists and/or infectious diseases epidemiologists (see table II, page 13). Moreover, each country has a national data manager (see table III, pages 14). The main task of the national representatives is to coordinate the EARSS-specific activities of the participating laboratories in their own country (data collection, reporting, questionnaire completion and EQA strain and results distribution) and to communicate with the EARSS Management Team (EARSS-MT). The national representatives also encourage the laboratories to generate their AST data according to the EARSS protocols, as published in the EARSS Manual 2005 (downloadable from the EARSS website at www.rivm.nl/earss). The main tasks of the national data manager are to collect, approve and forward resistance data each quarter to the international data manager maintaining the EARSS central database and to assist the national representative. Protocols for standardising the data collection have been developed with professional help from the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), the European Committee on Antimicrobial Susceptibility Testing

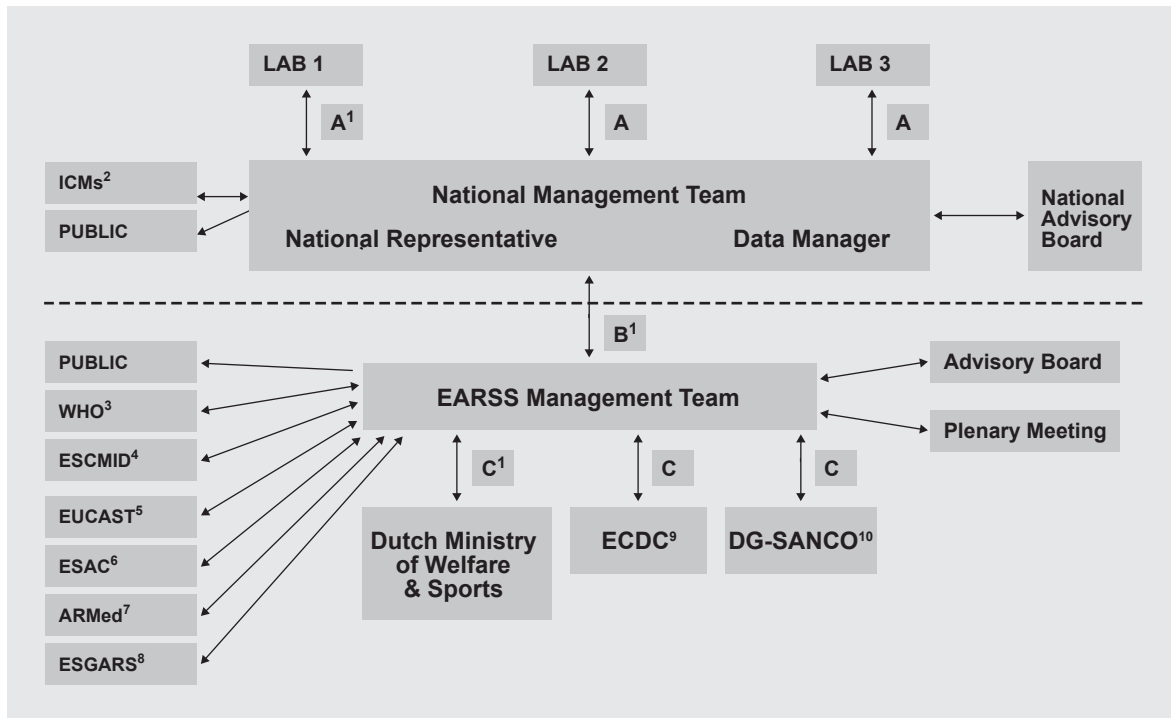


Figure 2.1. Structure of the EARSS network.

¹ Reporting lines are indicated with arrows. The most important reporting lines are further clarified with letters (A-C): A. Participating laboratories collect data and report the data to the national data manager, who checks the data. Messages from the national level and from EARSS-MT, including new protocols, questionnaires and reports, are forwarded by the national representative to the participating laboratories. B. Once checked, the national data manager forwards the data to EARSS-MT, where the data is again checked and a feedback report is produced which is sent to the national representative. EARSS-MT awaits approval of the data by the national representative before the results are added to the EARSS database and thus become visible at the interactive website and published in the annual report. Messages from EARSS-MT, including new protocols, questionnaires and reports, are always directed to the national representatives who shall forward the information to the relevant parties in their own country. (NB: the annual plenary meeting brings together EARSS-MT and all national representatives). C. Official reports are forwarded for final approval to DG-SANCO (until September 2006), respectively ECDC (from September 2006 onwards) and the Dutch Ministry of Welfare and Sports (considering a 45 days term) which are the main sponsor of the EARSS project, before they become official reports of the EARSS network.

² ICMs: Intersectoral Co-operating Mechanisms.

³ WHO: World Health Organisation.

⁴ ESCMID: European Society on Clinical Microbiology and Infectious Diseases.

⁵ EUCAST: European Committee on Antimicrobial Susceptibility Testing.

⁶ ESAC: European Surveillance on Antimicrobial Consumption.

⁷ ARMed: Antibiotic Resistance Surveillance and Control in the Mediterranean Region.

⁸ ESGARS: ESCMID Study Group for Antimicrobial Resistance.

⁹ ECDC: European Centre for Disease Prevention and Control; funding from September 2006 onwards, and prolonged to 31 December 2009.

¹⁰ DG-SANCO: Directorate-General for Health and Consumer Protection; funding until September 2006.

(EUCAST) and WHO microbiology laboratory database software (WHONET). To assess the quality and comparability of AST data, regular EQA exercises are carried out in collaboration with UK-NEQAS. The results of the EQA exercise carried out in 2008 are presented in chapter three.

2.2.2. The national networks

It is the task of the national representatives to select participating laboratories/hospitals that cover at least 20% of the total population and serve various types of institutions (university or tertiary care hospitals, general or district hospitals, rehabilitation centres or nursing homes, and others). Different geographic regions (urban/ rural), and the socio-economic strata should be included in a demographically representative manner.

2.2.3. Collecting and processing antimicrobial susceptibility testing (AST) results

EARSS collects susceptibility test results of invasive isolates and background information about patients. Laboratories are asked to report the first isolate from blood or CSF per reporting quarter, including specific information on the bacterial isolate, host, institution and laboratory that submits the results. Data shall be reported according to the specifications of the EARSS exchange format. AST results are generated and reported as specified by standard EARSS protocols. Furthermore, optional data are collected such as clinical diagnosis, other conditions, and facultative susceptibility data for additional antibiotics. More information about data collection and protocols can be found in the EARSS Manual 2005, which can be downloaded from the official EARSS website at www.rivm.nl/earss.

Laboratories

Participating laboratories can opt for one of two ways of submitting data: electronically or by submitting conventional isolate record forms (on paper). EARSS provides various free software tools for electronic data handling, downloadable from the website at www.rivm.nl/earss: (1) WHONET, the microbiology laboratory software, adapted for EARSS by John Stelling, and (2) Data Entry & Feedback Software (DEFS), which was developed as an exclusive EARSS tool. Laboratories are asked to collect AST data on a routine basis and to forward these to the national representative or data manager quarterly.

Before submission, laboratories are asked to check their data for:

- adherence to the EARSS protocol;
- microbiological consistency/plausibility;
- consistency with clinical breakpoints, sensitive (S), intermediate (I) and resistant (R) breakpoints as defined by the specific guideline used.

National representative and national data manager

At the national level, the national data manager, in consultation with the national representative, processes the data.

This is done in a stepwise fashion:

- recording data from all participating laboratories and manual data entry if isolate record forms are used;
- merging data from all participating laboratories into *one* single file;
- converting data to EARSS exchange format (EARSS Manual 2005);
- revising data with a data check programme, such as DCFP, which is part of the WHONET programme, or DEFS;
- approval of data by the national representative (adherence to EARSS protocol);
- data transfer to EARSS-MT at the end of each quarter (March, June, September and December).

International data manager at EARSS-MT

After receiving the data from the national data manager, the files are examined by the international data manager of EARSS-MT.

This process involves the following steps:

- checking the data format;
- inspection of the contents of the files;
- removing duplicate reports;
- determining resistance proportions;
- identification of unusual or rare results;
- compilation of a feedback report summarizing the results, to be confirmed by the national representative in writing.

After approval by the national representative, data are added to the database, and the results are made public on the EARSS website at www.rivm.nl/earss.

Feedback from EARSS-MT

Once data become available to EARSS-MT, they are processed and returned in a standard feedback report to the national representative in order to obtain confirmation and final approval of validity and completeness of the data. This feedback step also informs the national representatives of the occurrence of resistance patterns with particular public health importance (e.g. MRSA, GISA/VISA, PNSP, and VRE). Subsequently, the national coordinator is asked to confirm the correctness of the results. With his/her approval, the data will be added to the EARSS database and will become immediately available on the interactive EARSS website at www.rivm.nl/earss, where they can be displayed in various downloadable formats, such as tables, figures, and maps. The data from the EARSS database are used to prepare annual reports, newsletters and publications that are disseminated to the participants, the scientific community, policy makers and a broader public.

2.2.4. EARSS meetings

EARSS organizes annual meetings for all national representatives to inform them on the progress of EARSS and discuss future initiatives. The last EARSS plenary meeting in its present form will be held on 20-21 November 2009 at the Medical Faculty of the University of Strassbourg, France. This event in the 'Heart of Europe' will commemorate the tenth anniversary of the EARSS and appropriately coincide with the week of the European Antibiotic Awareness Day on 18 November. An update will be given on the situation of antimicrobial resistance in Europe, and the denominator data and the results of the latest EQA exercise will be discussed. The EARSS annual report 2008 will be presented. And of course, the upcoming transition of EARSS to ECDC will be on the programme.

EARSS also organizes regular training sessions for data managers and reference laboratory personnel, in turns. In June 2009, the workshop for data managers was organized at the RIVM in Bilthoven, the Netherlands. As in previous years, the contents of the workshop concentrated on routine data collection as well as on analysis. However, this time was in the light of the near EARSS transition to ECDC and the data management in this respect, with plenty of opportunities to practically handle own data. For support on WHONET, John Stelling and his assistant Chris Fallon were present. Furthermore, there was an interactive workshop on spatial epidemiology, an application of SRL (Staphylococcus Reference Laboratories). The next data manager workshop will be organized by ECDC in February 2010, which will completely focus on putting the data in The European Surveillance System (TESSy).

In the ongoing EARSS/SeqNet initiative, broad collaboration between 26 European countries was already achieved and clearly spa-typing allowed an easy aggregation of data generated in as many

laboratories. A second cross-sectional study on invasive *S. aureus* shall be carried out in order to determine the dynamics of strain distribution over Europe. On the occasion of the Staphylococcus aureus Reference Laboratories Meeting, which was held 28-29 May 2009, reference laboratories have been introduced into the aims and objectives of the TROCAR project (see 2.2.5), in order to connect both networks and add to the establishment of a strong European AMR-network.

2.2.5 Linkage with other networks

A laboratory protocol on the identification of carbapenemase detection in *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* was devised in cooperation with EUCAST, although not yet implemented.

EARSS and ESAC exchanged their surveillance data for the linking of resistance with the prescription of antimicrobial compounds in Europe. Results have been published in Emerging Infectious Diseases in November 2008 (see EARSS related publications, page 17).

The pilot study resulting from the initiative on ‘Identifying the dominant strains of *Staphylococcus aureus* causing invasive infection in the European region’ was carried out and further expanded in collaboration with the SeqNet.org group. This initiative will be continued, and a new study is in progress. The manuscript from the pilot study is submitted for publication. The TROCAR project (Translational Research on Combating Antimicrobial Resistance) is a research project funded by the Seventh Framework Programme of the European Commission. The driving concept of TROCAR is to investigate the fundamentals of the epidemiology of new highly virulent multiresistant strains. On the occasion of the SRL-meeting, reference laboratories have been introduced into the aims and objectives of this initiative. The EARSS is going to become an important partner in this initiative, and by connecting with European microbiological laboratories, helps to identify strains of potential public health importance that should be further investigated by the excellence centers that participate in this initiative (see also 2.2.4 EARSS meetings).

2.3. EARSS in 2009 and beyond

2.3.1. Collection of antimicrobial susceptibility data

This report includes AST data from the start of EARSS in 1999 up to December 2008; the results are described in Chapter 5 of this report. Data collected in 2009 are included in the interactive EARSS database which is regularly updated and accessible from the EARSS website (see www.rivm.nl/earss). From 2010 on, antimicrobial susceptibility data will be submitted to ECDC, and uploaded in TESSy.

2.3.2. The EARSS network

Since the beginning of EARSS in 1999, the coverage of the network has been extended from 13 countries in 1999, to 33 countries in 2008. In addition to 26 of the 27 Member States, EARSS receives data from 3 of the 4 EEA/EFTA (Norway, Iceland, and Switzerland) and 2 out of 3 candidate countries (Turkey and Croatia), and from Bosnia and Herzegovina and Israel. It is the wish of ECDC that EARSS includes all member states, EEA/EFTA countries and candidate countries. One of the member states, Slovakia, was not able to deliver data since 2006. Liechtenstein and the Republic of Macedonia should still be included.

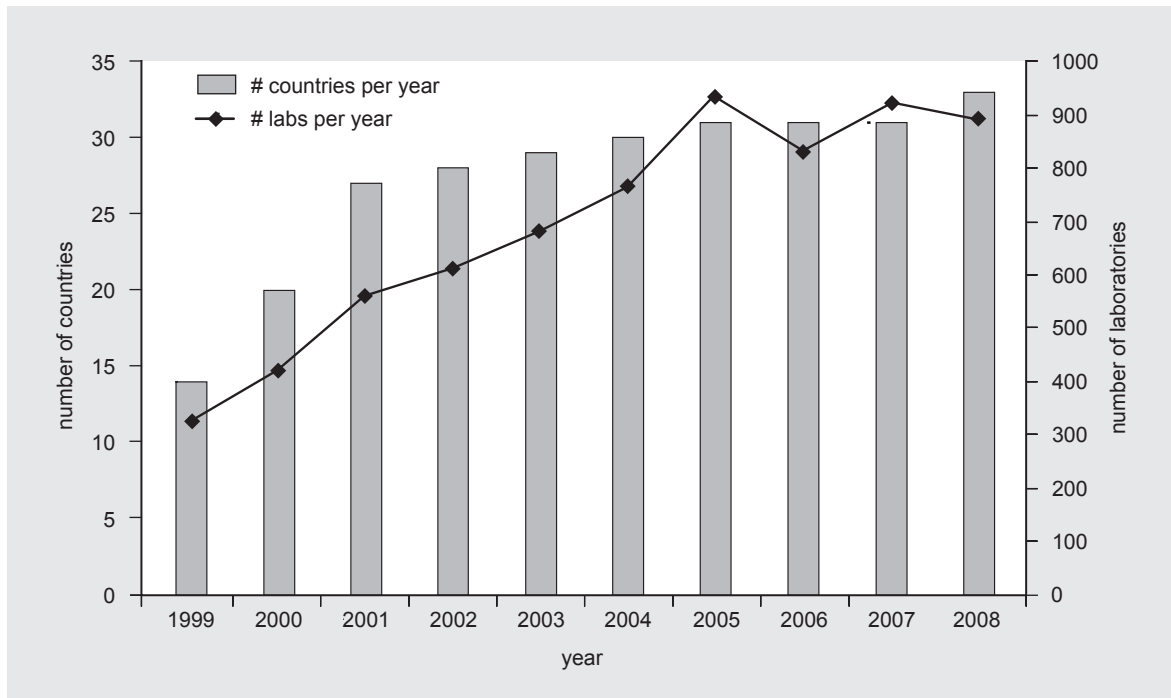


Figure 2.2. Number of laboratories (left axis) and countries (right axis) participating in EARSS by year.

In 2008, we welcomed two new countries starting reporting data to EARSS, Bosnia and Herzegovina and Switzerland. Now that the network is almost complete at country level, the next focus of EARSS will be to assess the national coverage in each country and encourage improvement wherever necessary.

2.3.3. EARSS in 2010

Since November 2007, the Surveillance of antimicrobial resistance in Europe was prolonged by the EARSS-MT at RIVM in Bilthoven, The Netherlands. By 2009, the transition of EARSS to ECDC in Stockholm was prepared by the EARSS-MT in cooperation with the Surveillance Unit of the ECDC. Starting at 1 January 2010, ECDC will completely take over the 'new' EARSS.

Chapter 3. External Quality Assessment Exercise

3.1. Introduction

Since 2000, EARSS has been organizing external quality assessment (EQA) exercises of antibiotic susceptibility testing in collaboration with UK NEQAS (United Kingdom National External Quality Assessment Service). UK NEQAS is based at the Health Protection Agency, Colindale, London (UK) and is a non-profit organization with more than 30 years experience with external quality assessment in different countries (www.ukneqasmicro.org.uk).

The rationale of these EQA exercises is,

- i) to assess the ability of participating laboratories to identify antimicrobial resistance of clinical and public health importance,
- ii) to determine the accuracy of quantitative susceptibility test results reported by individual laboratories and
- iii) to decide on the overall comparability of routinely collected test results between laboratories and countries and thus provide the means for justifying the pooling and comparison of antimicrobial susceptibility test (AST) data across Europe.

The latest EQA held in 2008 consisted of 6 strains provided by UK NEQAS. The strains were characterized and tested by the Addenbrookes Hospital in Cambridge (UK) and the Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL) in London (UK). Both reference laboratories interpreted the results according to different breakpoint criteria of CLSI and BSAC, as indicated in each of the species' chapters.

3.2. Results

UK NEQAS distributed the strains to 913 laboratories participating in EARSS. The laboratories were asked to report the clinical susceptibility categorization (S, I, R) according to the guideline used. Reports were returned by 808 (88%) laboratories, which is 5% higher than in the previous year. This year, for the first time, all countries had to report their results via the UK NEQAS internet website. For some countries this might have been somewhat inconvenient, which could have led to a lower response in these countries. Table 3.1 shows the proportion of participating laboratories returning reports per country.

Results were analyzed and considered 'concordant' if the reported categorization agreed with the interpretation of the reference laboratory.

The majority of laboratories (54-60%) used automated methods for the identification at species level, for *K. pneumoniae*, *E. coli*, *E. faecium* and *P. aeruginosa*. To identify the *S. pneumoniae* strain, mainly conventional methods were used (72%).

In figure 3.1 the adherence to (inter)national guidelines by number of laboratories per country is shown. The majority of laboratories are using CLSI guidelines (72%). Some countries use national guidelines, France (SFM), Germany (DIN), Norway (NWGA), the Netherlands (CRG), Sweden (SRGA), and UK (BSAC). The use of EUCAST guidelines were reported for the first time in 2008 mainly as a result of the incorporation of EUCAST breakpoints in automated systems. At the same

Table 3.1. Proportion of participating laboratories returning reports per country

Country	Number of EQA samples sent	Number of returned reports (%)
Austria	42	41 (98)
Belgium	110	89 (81)
Bulgaria	24	23 (96)
Cyprus	5	5 (100)
Czech Republic	48	46 (96)
Germany	23	18 (78)
Denmark	15	14 (93)
Estonia	11	11 (100)
Spain	40	36 (90)
Finland	14	12 (86)
France	57	57 (100)
Greece	50	36 (72)
Croatia	27	26 (96)
Hungary	27	24 (89)
Ireland	44	40 (91)
Israel	5	4 (80)
Iceland	2	1 (50)
Italy	54	49 (91)
Lithuania	13	12 (92)
Luxembourg	7	6 (86)
Latvia	20	13 (65)
Malta	1	1 (100)
Netherlands	24	21 (88)
Norway	13	10 (77)
Poland	74	73 (99)
Portugal	24	19 (79)
Romania	37	28 (76)
Sweden	22	21 (95)
Slovenia	11	11 (100)
Turkey	16	16 (100)
United Kingdom	53	45 (85)
Total	913	808 (88)

time, harmonisation efforts between the different national guideline committees have accomplished a satisfactory degree of agreement and therefore previous discrepancies between different guidelines have become less significant.

3.2.1. Specimen 9010 *Klebsiella pneumoniae*

The organism was susceptible to piperacillin/tazobactam by agar dilution MIC tests with both BSAC and CLSI guidelines. However, 29% of the participants reported intermediate susceptibility and 25% reported piperacillin/tazobactam resistance. By disc diffusion the organism was borderline susceptible and it is possible that this organism is producing increased amounts of a penicillinase, which could have lead to these divergent results.

By agar dilution MIC tests, the organism (MIC 8 mg/L) had intermediate susceptibility to tobramycin by CLSI breakpoints, but should be reported resistant by other guidelines. Reporting by participants was generally in line with the breakpoint guidelines used. Overall the organism was reported resistant by 37% of participants, intermediate by 48% and susceptible by 15%. The susceptibility profile

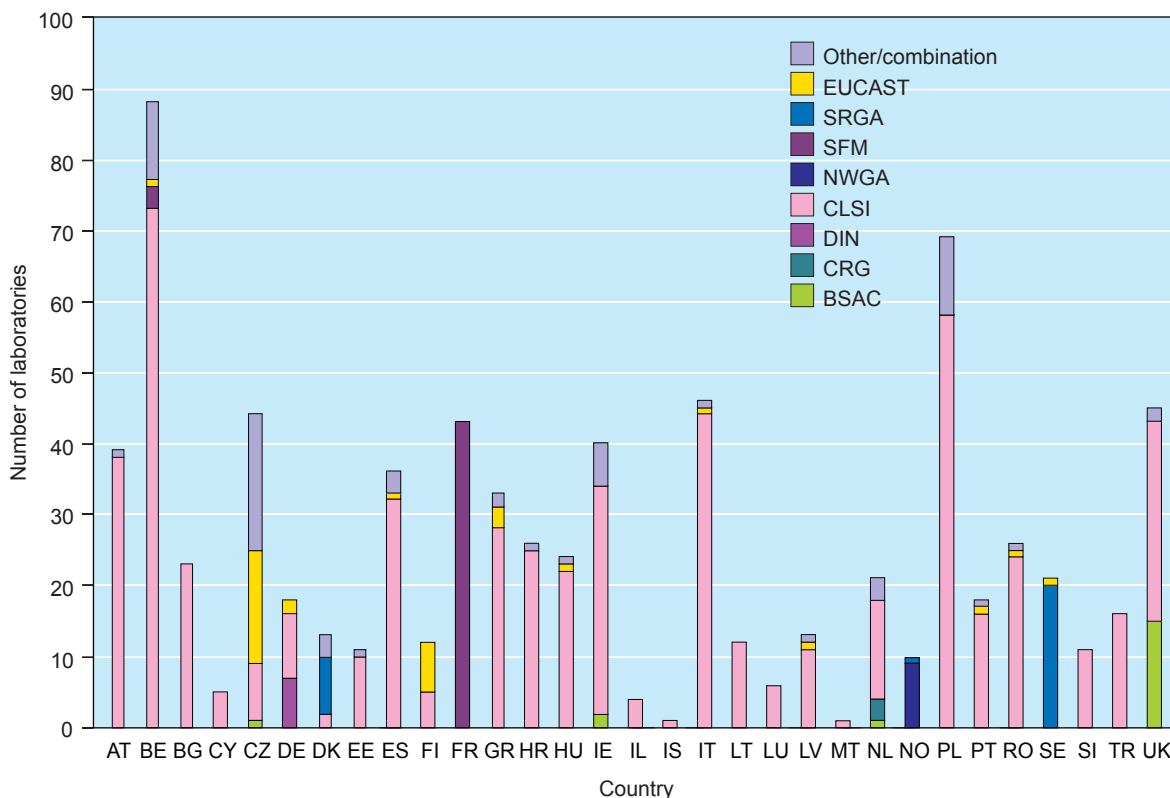


Figure 3.1. Adherence to guidelines*: number of laboratories per country

BSAC, British Society for Antimicrobial Chemotherapy; CRG, Commissie Richtlijnen Gevoeligheidsbepalingen; DIN, Deutsche Industrie Norm; NCCLS/CLSI, (American) Clinical and Laboratory Standards Institute; NWGA, Norwegian Working Group on Antimicrobials; SFM, Comité de l'Antibiogramme de la Société Française de Microbiologie; SRGA, Swedish Reference Group for Antibiotics; EUCAST, European Committee on Antimicrobial Susceptibility Testing.

of intermediate resistance to tobramycin, resistance to gentamicin and susceptibility for amikacin is indicative of low expression of ANT(2'') enzyme and EUCAST expert rules suggest that such isolates should be reported resistant to tobramycin (table 3.2).

Table 3.2. *Klebsiella pneumoniae* (9010): Minimal inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories.

Antibiotic Agent	MIC ref. lab BSAC	MIC ref. lab CLSI	Intended Interpretation BSAC/ CLSI	Overall Concordance (%)
Amikacin	2	2	S	99.1
Amoxicillin	-	-	R	97.6
Ampicillin	>128	>128	R	99.6
Ceftazidime	0.25	0.25	S	98.5
Cefotaxime	0.06	0.06	S	98.6
Ceftriaxone	0.12	0.06	S	97.4
Ciprofloxacin	0.06	0.03	S	99.8
Gentamicin	32	32	R	99.1
Imipenem	0.25	0.25	S	99.3
Meropenem	0.03	0.03	S	99.5
Piperacillin	>128	128	R	96.1
Pip-Tazobactam	4	8	S	45.6
Tobramycin	8	8	R/ I	36.7/ 48.3
ESBL	Negative	Negative	Negative	89.1

Table 3.3. *Escherichia coli* (9011): Minimal inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories.

Antibiotic Agent	MIC ref. lab BSAC	MIC ref. lab CLSI	Intended Interpretation BSAC/ CLSI	Overall Concordance (%)
Amikacin	1	4	S	97.6
Amoxicillin	>128	>128	R	99.2
Ampicillin	>128	>128	R	99.9
Ceftazidime	32	64	R	99.1
Cefotaxime	16	32	R/ I	73.7/ 23.9
Ceftriaxone	32	64	R	85.0
Ciprofloxacin	16	16	R	99.6
Gentamicin	16	64	R	99.4
Imipenem	0.12	0.12	S	99.2
Meropenem	0.016	0.016	S	99.6
Piperacillin	>256	>256	R	86.5
Pip-Tazobactam	4	4	S	67.0
Tobramycin	4	8	I	38.6
ESBL	Negative	Negative	Negative	69.3

3.2.2. Specimen 9011 *Escherichia coli*

This organism produces a plasmid-mediated CIT-type (CMY-like enzymes derived from *C. freundii*) AmpC beta-lactamase. Reduced susceptibility to third-generation cephalosporins was obvious - 100% of the participants reported the isolate intermediately or fully resistant to ceftazidime and 98% intermediately or fully resistant to cefotaxime. Reports of intermediate resistance were substantially more common with cefotaxime (24%) than with ceftazidime (1%). Twenty five percent of participants incorrectly reported that the organism was an ESBL-producer. Synergy between third-generation cephalosporins and clavulanate was not seen in reference tests and some participants may have reported the presence of an ESBL simply because ESBLs are the most common mechanism of resistance to third-generation cephalosporins in *E. coli*. However, AmpC-mediated resistance in *E. coli* is not rare and may reflect either (a) up-regulation of chromosomal AmpC or (b), as here, acquisition of a plasmid-mediated form of the enzyme. Isolates with these mechanisms are typically resistant to third-generation cephalosporins (though this may be borderline with up-regulation of the chromosomal enzyme), cefuroxime, penicillin+clavulanate combinations, and ceftiofuran, but susceptible to cefepime, ceftipime and carbapenems. They are negative in ESBL confirmation tests, but synergy is seen with cephalosporin-boronic acid or cephalosporin-cloxacillin tests.

High discrepancy rates were seen with piperacillin-tazobactam, 67% of participants reporting the organism susceptible, 17% intermediately resistant and 16% fully resistant. In reference MIC tests the organism appeared piperacillin-tazobactam susceptible. In reference disc diffusion tests the organism also appeared piperacillin-tazobactam susceptible, but with a few colonies within the zone close to the zone edge. On retesting of colonies from within the zone the organism appeared more resistant and these colonies may be permeability mutants, leading to variable results in both MIC and disc diffusion tests.

By agar dilution MIC tests, the organism (MIC 4-8 mg/L) had intermediate susceptibility to tobramycin by CLSI breakpoints and should be reported resistant by other guidelines. Overall the organism was reported resistant by 42% of participants, intermediate by 39% and susceptible by 19%. The susceptibility profile of intermediate resistance to tobramycin, resistance to gentamicin and susceptibility for amikacin is indicative of low expression of ANT(2'') enzyme and EUCAST expert rules suggest that such isolates should be reported resistant to tobramycin (table 3.3).

Table 3.4. *Klebsiella pneumoniae* (9012): Minimal inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories.

Antibiotic Agent	MIC ref. lab BSAC	MIC ref. lab CLSI	Intended Interpretation BSAC/ CLSI	Overall Concordance (%)
Amikacin	2	2	S	98.7
Amoxicillin	-	-	R	97.2
Ampicillin	>128	>128	R	99.3
Ceftazidime	64	64	R	93.7
Cefotaxime	8	8	R	89.0
Ceftriaxone	16	8	R	92.4
Ciprofloxacin	0.06	0.06	S	99.6
Gentamicin	0.12	0.25	S	99.5
Imipenem	0.12	0.12	S	100.0
Meropenem	0.03	0.03	S	99.7
Piperacillin	>128	>128	R	93.3
Pip-Tazobactam	2	2	S	74.9
Tobramycin	1	2	S	96.7
ESBL	Positive	Positive	Positive	97.8

3.2.3. Specimen 9012 *Klebsiella pneumoniae*

The organism produces SHV-2 and SHV-5 ESBLs. By MIC testing the strain was resistant to ceftazidime (MIC 64 mg/L), cefotaxime (MIC 8 mg/L) and ceftriaxone (MIC 8-16 mg/L) and a large majority of participants correctly reported the strain resistant to these agents. The organism was susceptible to piperacillin-tazobactam by BSAC and CLSI guidelines and 75% of laboratories reported the organism susceptible. There is insufficient clinical evidence that betalactamase inhibitors have a therapeutic benefit in infections with ESBL-producing strains and carbapenems should be the preferred treatment option.

Overall, 99% of the laboratories testing for ESBL production correctly identified the organism as an ESBL-producer (table 3.4).

3.2.4. Specimen 9013 *Enterococcus faecium*

This organism is high-level resistant to gentamicin and resistant to vancomycin but not to teicoplanin (VanB phenotype). Overall the susceptibility profile of this specimen was correctly identified by the majority of laboratories (table 3.5).

Table 3.5. *Enterococcus faecium* (9013): Minimal inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories.

Antibiotic Agent	MIC ref. lab BSAC	MIC ref. lab CLSI	Intended Interpretation BSAC/ CLSI	Overall Concordance (%)
Amoxicillin	-	-	R	96.3
Ampicillin	64	64	R	99.1
Gentamicin (HLR)	>512	>512	R	81.8
Teicoplanin	0.25	0.5	S	96.6
Vancomycin	32	128	R	96.0

Table 3.6. *Streptococcus pneumoniae* (9014): Minimal inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories.

Antibiotic Agent	MIC ref. lab BSAC	MIC ref. lab CLSI	Intended Interpretation BSAC/ CLSI	Overall Concordance (%)
Cefotaxime	0.004	0.004	S	96.1
Ceftriaxone	0.004	0.004	S	95.5
Oxacillin (screening test)	-	-	R	85.8
Clindamycin	0.12	0.12	S	95.6
Erythromycin	16	16	R	96.8
Penicillin-G Test result			I	74.4
Interpretation: Meningitis	0.25	0.12	R	69.8
Pneumonia			S	55.6
Norfloxacin 10 µg screen disc			R	32.1
Ciprofloxacin 1µg or 5µg			I	23.8

3.2.5. Specimen 9014 *Streptococcus pneumoniae*

The organism has reduced susceptibility to penicillin (MIC 0.12-0.25 mg/L). For wildtype *S. pneumoniae* the MICs for penicillin are ≤ 0.06 mg/L. Published guidelines interpret MICs differently according to anatomical sites of the infection. Strains with intermediate susceptibility still respond to high doses of penicillin as long as meningitis can be excluded. EUCAST has different breakpoints for two categories of specimens, CLSI has different breakpoints for 3 categories of specimens:

EUCAST

meningitis $S \leq 0.06$, $R > 0.06$

other $S \leq 0.06$, $R > 2$

CLSI

meningitis $S \leq 0.06$, $R \geq 0.12$

pneumonia $S \leq 2$, $I = 4$, $R \geq 8$

other $S \leq 0.06$, $I = 0.12-1$, $R \geq 2$

The results for penicillin were assessed on the basis of the phenotypic test result, and on the clinical interpretation for isolates from meningitis (resistant by EUCAST and CLSI) and from pneumonia (susceptible by EUCAST and CLSI).

Overall, 86% participants reported resistance for the oxacillin screening test for penicillin resistance. Although susceptibility was at the low end of the intermediate category there were no problems in detecting reduced susceptibility to oxacillin in reference tests by the BSAC and CLSI methods (zone diameters ≤ 10 mm).

The participants' results for penicillin will include those that only screened for reduced susceptibility with oxacillin discs, those that screened with oxacillin and confirmed with a penicillin MIC, and those that tested with other methods. Overall, 74% reported the isolate as being of intermediate susceptibility to penicillin, with a further 8% reporting the isolate resistant. Susceptibility reported to clinicians indicated that many participants do not interpret test results to suit the clinical situation, as only 70% reported the isolate resistant if the isolate was from a case of meningitis and only 59% susceptible if the isolate was from a case of pneumonia. Significant numbers of participants interpreted the isolate as intermediate in susceptibility to penicillin irrespective of whether the isolate was from meningitis (21% reported intermediate) or from pneumonia (36% reported intermediate). These differences will partly relate to national differences in reporting practices.

The reference laboratory interpreted result for ciprofloxacin by disc susceptibility testing was intermediate. Of the 433 participants testing this agent 23% reported an intermediate result, 73% susceptible and 4% resistant (table 3.6).

From the 808 participating laboratories, 311 used disc diffusion as susceptibility test method to determine the result for ciprofloxacin; 39 used a disc concentration of 1µg and 272 used a 5µg disc. Participants were asked if they would use a norfloxacin screening test with this isolate. 157 laboratories

Table 3.7. *Pseudomonas aeruginosa* (9015): Minimal inhibitory concentration (MIC) and intended results reported by the reference laboratories and the overall concordance of the participating laboratories.

Antibiotic Agent	MIC ref. lab BSAC	MIC ref. lab CLSI	Intended Interpretation BSAC/ CLSI	Overall Concordance (%)
Amikacin	0.5	8	S	99.9
Ceftazidime	16	32	R	93.6
Ciprofloxacin	0.06	0.06	S	99.5
Gentamicin	0.5	0.25	S	99.0
Imipenem	16	32	R	87.1
Meropenem	4	8	I	15.7
Pip-Tazobactam	64	>128	R	92.1
Tobramycin	0.12	0.25	S	99.0

reported use of a 10µg disc, 3 used a 5µg disc and 29 used another unspecified method. The low concordance is simply the result of the default interpretation for *S. pneumoniae* as Ciprofloxacin R in many European countries.

3.2.6. Specimen 9015 *Pseudomonas aeruginosa*

This organism is intermediate in susceptibility to meropenem and resistant to other β-lactams tested. The borderline susceptibility to meropenem was reflected in the variation in susceptibility reported by participants, with 68% reporting susceptible, 16% intermediate and 16% resistant (table 3.7).

3.3. Conclusions

In this seventh EARSS EQA exercise, participation of the laboratories was high. The results show that routinely reported results as collected by EARSS in most instances have sufficient accuracy to provide good estimates of overall resistance prevalences and trends. The overall concordance was high, except in case of intermediate susceptibility, and when various guidelines reveal remaining discrepancies in routine susceptibility testing. More specific differences in interpretation of results were found for Piperacillin-Tazobactam (as frequently noted previously), and the interpretation of betalactam resistance in presence of AmpC expressing plasmids, penicillin susceptibility of *Streptococcus pneumoniae* in relation to the source of the isolate (meningitis vs. pneumonia), and imipenem/ meropenem susceptibility of *Pseudomonas aeruginosa*.

EARSS MT would like to thank UK NEQAS for Microbiology, the reference laboratories, the members of the Advisory Board, the country coordinators for the swift distribution of the strains, and all the participating laboratories for their excellent response rate.

Chapter 4. Results of the EARSS laboratory/hospital questionnaire 2008

4.1. Introduction

For correct interpretation of the EARSS AMR data, timely and accurate background information is indispensable. Therefore, each year, denominator questionnaires are sent to make up-to-date hospital activity data and denominator data available.

The denominator data collected in the questionnaire also enable calculation of incidence rates of antimicrobial resistance instead of proportions, which are generally calculated from the EARSS data. Incidences of antimicrobial resistance are a more direct measure of the impact of antimicrobial resistance in a specific country, provided the data obtained are representative (2).

Apart from denominator data, the questionnaire also collects reference information about the populations for which laboratories provide their services. This information helps to understand the validity, i.e. representativeness and generalisability of the antimicrobial resistance data collected by EARSS. It is crucial for interpretation of the results and helps to understand differences in antimicrobial resistance proportions between countries as reported by EARSS. Antimicrobial resistance proportions may vary due to e.g. differences in blood sampling practices (1, 4), differences in case-mix (which is a determinant of hospital type) or differences in available specialties (3, 5).

4.2. Methods

We sent out the EARSS questionnaires in May of 2009. All EARSS national representatives distributed the digital Excel version or the paper version (translated if needed) to all participating laboratories 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 (both necessary for inclusion), the type of hospital, the bed occupancy and the number of admissions. The national representatives returned completed questionnaires to EARSS-MT in June/July. Details of the inclusion criteria and data-analysis are given in Annex 1. Country-specific results were returned to the national representatives for confirmation and adapted where required. Thereafter, data were processed in Excel and SAS. In this chapter, results of the descriptive analysis are presented. Some of the results can also be found in the country-specific Country Summary Sheets (Table 1 and Figure 1 of Annex 2).

4.3. Results

4.3.1. Participation

In total 29 of the 33 countries reporting AST results returned questionnaires. Almost all questionnaires were returned in digital format. In total, 425 of the 774 laboratories (55%) and 765 of the 1,380 hospitals (56%) reporting AST results over 2008 provided the necessary denominator data (Figure 4.1, Table 4.1, Table 4.4).

The proportion of laboratories responding was a little lower than previous year, although the proportion of hospitals responding was slightly higher than previous year. France failed to report denominator information for laboratories. Denmark did not report any information for the participating hospitals.

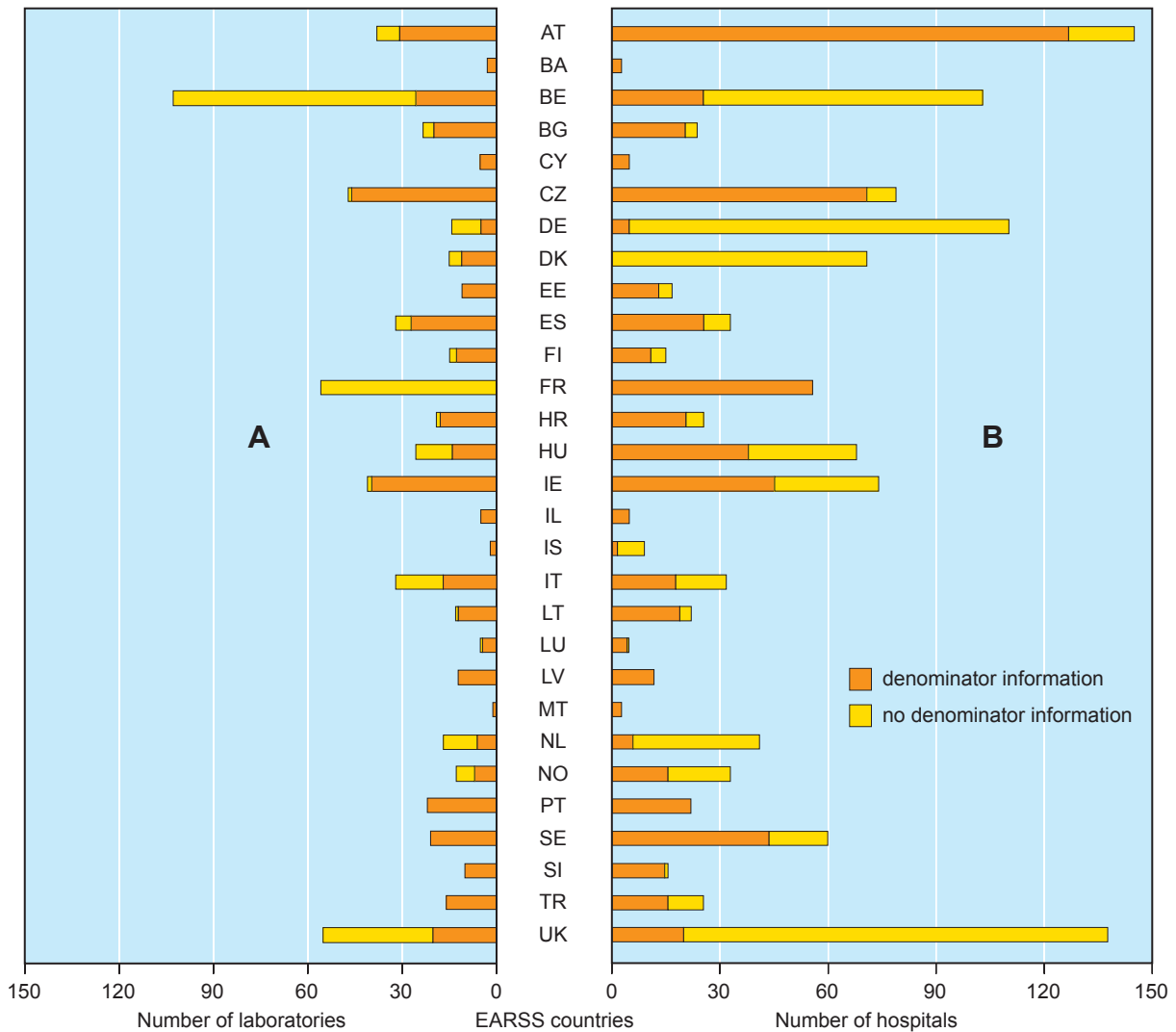


Figure 4.1. Number of laboratories (A) and hospitals (B) reporting AST data in 2008 with and without providing denominator data, per country. *For France only laboratories and hospitals that report on all EARSS pathogens are included. Laboratories and hospitals only reporting to the national pneumococci network are not included.

4.3.2. Population coverage

This year's response suggested that EARSS participating hospitals care for at least 110 million European citizens (20% of the EU population; including accession countries and Israel). This number does not include the catchment population of Germany, Denmark and France, since they were not able to provide this information for their national network. Moreover, the number of inhabitants covered by the EARSS network is an estimate based on the information provided by the participating hospitals. Since the response rate varies greatly between countries (Table 4.1), the total catchment of a 110 million seems to be a conservative estimate. On the other hand, some of the hospital catchment populations overlap, especially in urban areas, which by itself inflates the current estimates to some degree. Estonia, Hungary, Iceland, Luxembourg, and Slovenia reported total national coverage. Austria, Bulgaria, Croatia, Ireland, Lithuania and Malta reported near to complete national coverage (>90%). Spain, Italy, the Netherlands and the United Kingdom had low coverage. For these countries, taking into account the proportion of hospitals responding to the questionnaire, the data still suggest that national coverage was higher than 20%, the preferred lower boundary with respect to national generalisability of EARSS results.

Table 4.1. Hospital denominator data for 2008

Country code	Hospitals providing denominator data/reporting to EARSS	Total number of beds	Proportion of ICU beds (%)	Annual occupancy rate (%)	Median length of stay (days)	IQR length of stay (days)	Proportion of population covered (%)
AT	127/145	48,123	5	70	4.9	4.3-6.1	90
BA	3/3	2,768	6	76	9.2	6.9-11.1	29
BE	26/103	11,161	4	74	7.3	6.6-8.5	40
BG	21/24	10,052	8	79	6.3	5.1-7.0	98
CY	5/5	1,277	10	101	5.7	5.3-7.2	54
CZ	71/79	43,558	9	76	7.2	6.2-8.4	82
DE	5/110	2,443	3	99	15.0	15.0-15.0	na
EE	13/17	5,511	7	76	6.7	5.5-7.1	100
ES	26/33	15,020	4	81	7.5	6.1-8.9	19
FI	11/15	6,290	2	90	4.7	3.4-6	57
FR*	54/56	40,004	5	80	7.2	6.2-8.6	na
HR	21/26	10,081	4	85	6.8	6.3-8.8	90
HU	38/68	23,678	2	74	8.1	7.0-10.8	100
IE	45/74	11,717	3	87	5.6	4.5-8.3	98
IL	5/5	3,946	4	96	3.9	3.8-3.9	33
IS	2/9	988	4	79	6.5	4.8-8.1	100
IT	18/32	12,896	4	81	6.0	5.6-8.4	5
LT	19/22	9,186	4	80	7.3	6.7-7.5	92
LU	4/5	1,637	7	79	6.1	5.1-6.4	100
LV	12/12	6,329	3	76	7.2	6.0-8.0	80
MT	3/3	1,367	2	81	12.4	5.2-49.9	95
NL	6/41	2,952	3	69	5.5	4.9-6.3	6
NO	16/33	4,835	6	70	4.2	2.8-4.4	44
PT	22/22	10,234	5	81	7.3	6.4-8.5	81
SE	44/60	15,392	4	97	5.7	4.7-6.5	73
SI	15/16	7,612	5	73	5.1	4.7-6.6	100
TR	16/26	15,808	10	79	6.7	0.8-8.0	30
UK	20/138	8,245	2	79	3.3	0.4-5.4	5
Total or median[^]	765/1,380	383,889	4[^]	79[^]	6.6[^]		76[^]

ICU = intensive care unit; IQR = Interquartile range; na = not available.

*For France only laboratories and hospitals that report on all EARSS pathogens are included. Laboratories and hospitals only reporting to the national pneumococci network are not included.

The above illustrates how difficult it is to determine the exact coverage of a surveillance network like EARSS and emphasizes the importance of careful interpretation of the coverage figures.

4.3.3. Hospital denominator information

The total number of hospital beds for the hospitals reporting AST results and providing denominator data in the different countries ranged from 988 in Iceland to 40,004 in France, on the one hand representing the size of the country, and on the other hand the high participation rate to EARSS and the high response rate to the questionnaires.

The proportion of ICU beds over total hospital beds per country varied, ranging from 2% to 10%, whereas the absolute number of ICU beds for all participating hospitals in a country ranges from 27 (Malta) to 2,144 (France).

The length of stay differs between European countries; the median length of stay was 6.6 days. Patients in Germany (15.0 days) and Malta (12.4 days) seem to stay longest, whereas patients in

Table 4.2. Hospital characteristics for 2008

Country code	Hospitals providing denominator data/reporting to EARSS	Proportion of hospitals by level of care (%)			
		Tertiary level	Secondary level	Primary level	Other
AT	127/145	6	24	41	28
BA	3/3	100	0	0	0
BE	26/103	27	65	8	0
BG	21/24	48	38	5	10
CY	5/5	20	20	40	20
CZ	71/79	34	37	30	0
DE	5/110	40	0	40	20
EE	13/17	31	46	23	0
ES	26/33	54	42	4	0
FI	11/15	60	40	0	0
FR	54/56	na	na	na	na
HR	21/26	38	48	10	5
HU	38/68	50	37	8	5
IE	45/74	20	47	16	18
IL	5/5	80	20	0	0
IS	2/9	100	0	0	0
IT	18/32	61	33	6	0
LT	19/22	47	37	16	0
LU	4/5	67	33	0	0
LV	12/12	42	42	0	17
MT	3/3	33	0	33	33
NL	6/41	17	83	0	0
NO	16/33	25	50	25	0
PT	22/22	62	24	5	10
SE	44/60	25	43	32	0
SI	15/16	13	47	13	27
TR	16/26	100	0	0	0
UK	20/138	20	45	35	0
Total or median[^]	765/1,380	40[^]	37[^]	8[^]	0[^]

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 ten clinical specialties; bed capacity ranging from 200-800 beds. Tertiary level or central / regional hospital. Highly specialized staff and technical equipment; clinical services are highly differentiated by function; may have teaching activities; bed capacity ranges from 300 to 1,500 beds. Other: hospitals for a specific patient population, like a military hospital, or hospitals with any single specialty, like a burns unit; na = not available.

Austria, Finland, Israel, Norway and the United Kingdom were on average discharged after less than five days. Length of stay may be influenced by several factors, such as case mix, hospital policy, possibility of referral to a long term care facility etc. In theory, increased length of stay may increase the risk of acquiring resistant strains. However, EARSS resistance rates were independent of the median length of stay per country.

For almost all countries the annual occupancy rate exceeded 75%. Only Austria, Belgium, Hungary, the Netherlands, Norway and Slovenia reported an annual occupancy rate below 75%. Cyprus reported the highest annual occupancy rate (101%). From the literature it is known that high bed occupancy, especially significant bed pressure, can increase the incidence of MRSA (6, 7). EARSS data is too highly aggregated to test this hypothesis for European data.

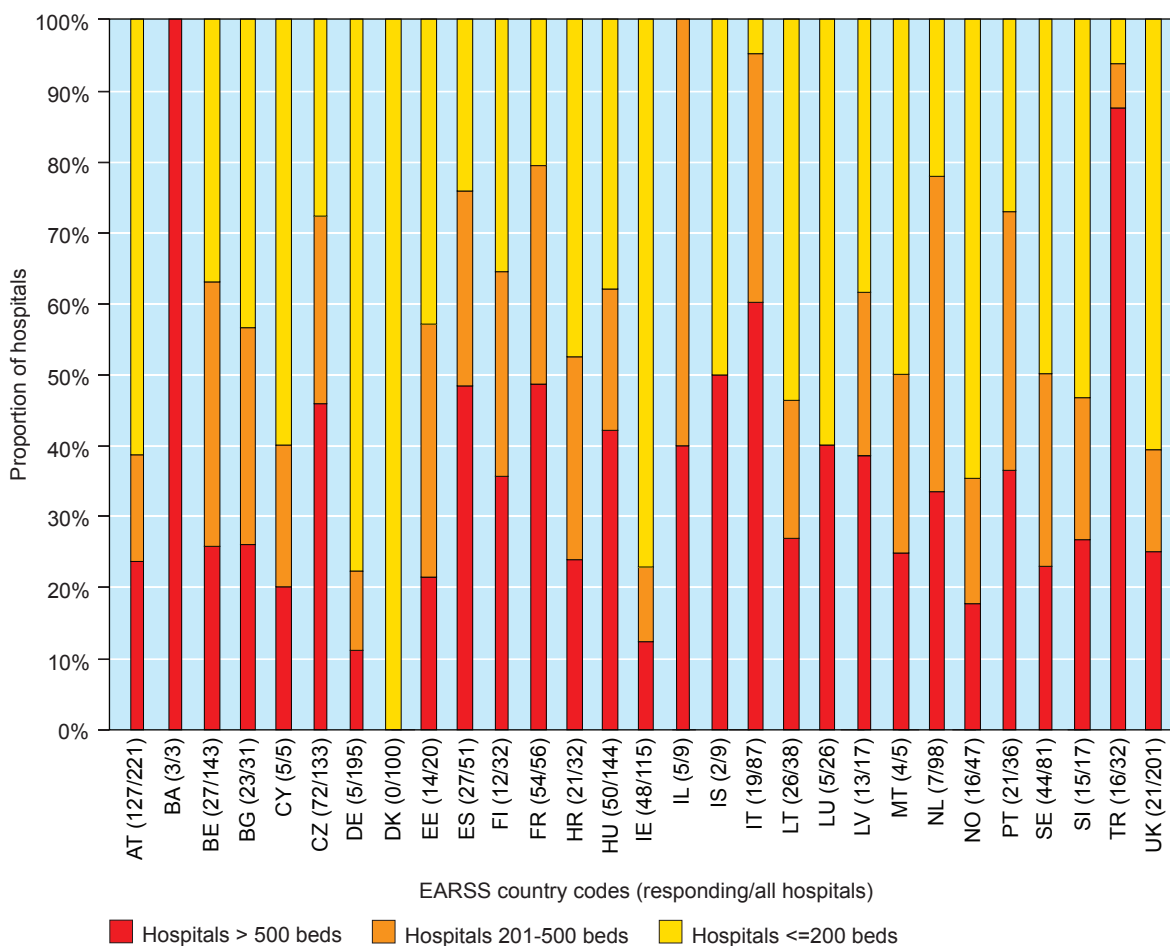


Figure 4.2. The proportion of small, medium and large hospitals per country, based on the (intertertile range of) number of beds, for all hospitals reporting both AST data and denominator data in 2008*.

*For France only laboratories and hospitals that report on all EARSS pathogens are included. Laboratories and hospitals only reporting to the national pneumococci network are not included.

4.3.4. Hospital characteristics

Both the size of a hospital and the level of specialisation can influence the proportion of resistance. As can be seen from Table 4.2 and Figure 4.2, the distribution of size and specialisation level of hospitals was quite different between the participating countries. This diversity can indicate differences in case-mix which may confound comparison of AST results between countries.

Like last years, the total amount of small hospitals (<200 beds) reporting to EARSS is low, compared to medium sized or large hospitals. In general, countries approaching 100% population coverage tend to include relatively more small hospitals than countries with lower population coverage.

The type of hospital and the size of a hospital do not correlate very well. For six countries all of the large hospitals (having more than 500 beds) were also classified as university hospitals, but for fifteen countries (Bulgaria, Germany, Estonia, Spain, Finland, Croatia, Hungary, Ireland, Israel, Iceland, Lithuania, Norway, Portugal, Sweden, Turkey) there were more university hospitals than large hospitals; for the remaining countries (Austria, Czech Republic, Italy, the Netherlands, Slovenia, United Kingdom) there were more large hospitals than university hospitals. Although definitions of care level may differ from country to country, we believe that the WHO definitions that are used by EARSS, including a range of beds and a required number of specialties, clearly distinguish between the different levels of care.

Table 4.3. Laboratory denominator information for 2008

Country code	Labs providing denominator data/reporting to EARSS	Total number of blood culture sets	Number of blood culture sets per 1,000 patient days
AT	31/38	154,481	20.4
BA	3/3	9,011	11.7
BE	26/103	124,142	41.6
BG	20/23	19,553	7.1
CY	5/5	12,032	25.5
CZ	46/47	164,484	12.7
DE	5/14	21,926	4.2
DK	11/15	184,306	na
EE	11/11	20,961	14.0
ES	27/32	219,120	49.2
FI	13/15	185,885	47.4
HR	18/19	57,638	18.7
HU	14/26	45,437	6.0
IE	40/41	183,125	na
IL	5/5	143,397	104.2
IS	2/2	11,830	23.4
IT	17/32	79,295	24.4
LT	12/13	18,526	6.8
LU	4/5	8,393	18.1
LV	12/12	14,584	8.8
MT	1/1	4,161	10.2
NL	6/17	72,527	75.0
NO	7/13	63,824	58.5
PT	22/22	140,514	50.6
SE	21/21	277,465	46.8
SI	10/10	48,730	24.2
TR	16/16	138,513	32.8
UK	20/55	186,046	61.4
Total or median[^]	425/774	2,609,906	23.8[^]

na, not available.

4.3.5. Laboratory denominator information

In 2008, in total, 2,609,906 blood culture sets were processed in the EARSS laboratories responding to the questionnaire. The median culturing frequency was 23.8 blood culture sets per 1,000 patient days in 2008, lower than in 2007 (35.6) (Table 4.3).

In comparison with previous year, the number of blood culture sets taken per 1,000 patient days increased in Austria, Belgium, Czech Republic, Estonia, Spain, Lithuania, The Netherlands, Norway, Portugal, Slovenia and the United Kingdom. In the remaining countries the number of blood culture sets taken per 1,000 patients decreased. Israel still has the highest culturing frequency among the EARSS countries, although decreased from 113.9 per 1,000 patient days in 2007 to 104.2 in 2008 respectively. Low culturing frequency, fewer than 10 per 1,000 patients, are reported in Bulgaria (7.1), Germany (4.2), Hungary (6.0), Lithuania (6.8) and Latvia (8.8).

As described in previous years, Western European countries show higher culturing frequencies compared to Eastern European countries and the Baltic States. Despite these differences in culturing frequencies, no correlation was found between blood culturing rates and resistance proportions.

Table 4.4. Incidence of MRSA per 100,000 patient days in 2008, specified per country

Country code	Incidence of MRSA per 100,000 patient days (95% confidence interval)	Country code	Incidence of MRSA per 100,000 patient days (95% confidence interval)
AT	1.3 (1.1-1.5)	IL	9.9 (8.6-11.3)
BA	1.9 (1.2-3)	IS	0.4 (0.0-2.2)
BE	3.0 (2.3-3.8)	IT	5.7 (5.1-6.3)
BG	1.3 (1.0-1.8)	LT	1.4 (1.0-1.9)
CY	8.9 (6.9-11.0)	LU	1.3 (0.5-2.8)
CZ	2.2 (2.0-2.5)	LV	1 (0.6-1.5)
DE	0.6 (0.0-3.5)	MT	14.7 (12.1-17.3)
DK	na	NL	0.2 (0.0-1.2)
EE	0.5 (0.2-1.0)	NO	0.4 (0.2-1.0)
ES	7.2 (6.5-7.9)	PT	28.3 (26.4-30.2)
FI	0.7 (0.4-1.2)	SE	0.3 (0.2-0.5)
FR	9.0 (8.5-9.5)	SI	1.5 (1.0-2.1)
HR	5.7 (5.0-6.4)	TR	8.9 (8.2-9.6)
HU	2.9 (2.5-3.3)	UK	8.7 (7.5-10.1)
IE	10.6 (9.7-11.5)	Median	4.8

na = not available; the Danish hospitals did not provide the number of patient days.

4.3.6. Incidence rates for MRSA blood stream infections

In contrast to resistance proportions, incidence rates provide patient-based risk estimates for the acquisition of health care-associated MRSA bacteraemia. In the EARSS database, MRSA proportions and MRSA incidence rates correlate very well (Spearman rank correlation coefficient: 0.96, $p < 0.01$). Table 4.4 shows the incidence of MRSA blood stream infections.

The comparability of MRSA proportions and incidence rates indicate that the resistance proportions as reported by EARSS (Chapter 5) are a good approximation of the incidence rates, and comparison of countries thus provides useful information. The median incidence taking the countries' calculated incidences into account was 4.8 MRSA bacteraemias per 100,000 patient days, higher than the incidence reported from 2007, which was 3.5 MRSA bacteraemias per 100,000 patient days. Variation in incidence rates over countries and years of reporting may be the result of real variation in incidence, but various underlying factors, such as changes in blood culturing rate, changes in case-mix (the set of hospitals responding to the questionnaire in a country may vary over years) can also be of influence. Clearly, many other, partly unknown and undetermined factors may play a role in the dynamics of MRSA incidence.

4.4 Conclusions

The response to this year's laboratory/hospital questionnaire per country was comparable to previous year, although for four countries reporting AST results no questionnaires were returned. This year's response suggests that EARSS participating hospitals care for at least 20% of the EU population, accession countries and Israel, which is considered adequate.

The level of care and the size of the reporting hospitals varied between countries. Although assigning unambiguous and comparable levels of care to hospitals in different countries is complicated, this variation could indicate a difference in case mix between countries, which may confound resistance rates.

As reported before, there was large variation in the frequency of blood culturing over the countries. If lower blood culturing frequency is related to the selective sampling of severe cases, this could erroneously lead to higher resistance proportions. However, no correlation was found between blood culture frequency and resistance proportions.

The resistance proportions were highly correlated with the resistance incidence rates. Although resistance incidence rates might be more relevant when comparing countries, we concluded that resistance proportions thus also supply useful information for comparing the resistance problem across Europe.

Although for some countries national generalisability of the EARSS results seems to be low, taking into account the population coverage, we conclude that the resistance proportions provided by EARSS in 2008 seem valid and comparable.

4.5 References

1. Bouza E, Pérez-Molina J, Muñoz P. Report of ESGNI-001 and ESGNI-002 studies. Bloodstream infections in Europe. *Clinical Microbiology and Infections* **1999**; 2S1-2S12.
2. Monnet DL, Fridmott-Møller N. Only percentage within species; neither incidence, nor prevalence: demographic information and representative surveillance data are urgently needed to estimate the burden of antimicrobial resistance. *Int J Antimicrob Agents* **2004**; 24: 622-3; author reply 623-4.
3. NNIS system. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *American Journal of Infection Control* **2004**; 32: 470-485.
4. Tiemersma EW, Bronzwaer SL, Lyytikäinen O, Degener JE, Schrijnemakers P, Bruinsma N et al. Methicillin-resistant *Staphylococcus aureus* in Europe, 1999-2002. *Emerg Infect Dis* **2004**; 10: 1627-34.
5. Voss A, Milatovic D, Wallrauch-Schwarz C, Rosdahl VT, Braveny I. Methicillin-resistant *Staphylococcus aureus* in Europe. *Eur J Clin Microbiol Infect Dis* **1994**; 13: 50-5.
6. Clements A, Halton K, Graves N, Pettitt A, Morton A, Looke D, Whitby M. Overcrowding and understaffing in modern health-care systems: key determinants in methicillin-resistant *Staphylococcus aureus* transmission. *Lancet Infect Dis* **2008**; 8: 427-34.
7. Borg M, Suda D, Scicluna E. Time-series analysis of the impact of bed occupancy rates on the incidence of methicillin-resistant *Staphylococcus aureus* infection in overcrowded general wards. *Infect Control Hosp Epidemiol* **2008**; 29: 496-502.

Chapter 5. Antimicrobial resistance in Europe

5.1. Introduction and methods

This chapter provides an overview of the EARSS data in 2008 and the trends of antimicrobial resistance in Europe. For ten years, EARSS has been collecting antimicrobial susceptibility data of invasive isolates with clinical and epidemiological importance. For each pathogen the clinical and epidemiological relevance, major resistance mechanisms, the data and trends of antimicrobial resistance until 2008 will be described.

This year, to calculate significance in resistance trends, these calculations were performed only over the last four years. We found this to be more informative as it gives a clear view of the recent developments in antimicrobial resistance. For the first time trends are also displayed for *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. To exclude possible biases in the trend analyses, a sensitivity analysis was done, per country, to determine the sensitivity of the trend analysis for using the complete dataset versus a subset from laboratories which consistently reported for all four years (subset of permanent laboratories). If the trends in the subset and the complete dataset were discrepant, these trends were discussed in the text. However, if both datasets indicated the same trend, we indicate

- i) in the text, when significant trends were only identified in the subset,
- ii) in the graphs by an arrow with an asterisk, when significant trends were only identified in the complete dataset,
- iii) in the graphs by an arrow when a significant trend was detected in both the subset and the complete dataset.

More information on the statistical methods and the inclusion criteria for the different analyses and figures can be found in Annex 1.

5.2. *Streptococcus pneumoniae*

5.2.1. 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 invasive blood stream infections and meningitis (1). Since *S. pneumoniae* is the most common cause of pneumonia worldwide, morbidity and mortality are high and annually approximately 3 million people are estimated to die 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 (39). Capsular polysaccharides are highly diverse and play an important role in immune evasion. Around 80 different serotypes have been described. The serotype distribution varies with age, disease and geographical region (16-18). Interestingly, serotypes most frequently involved in pneumococcal disease in infants are also most frequently associated with antimicrobial resistance (36;42).

Resistance mechanisms

Beta-lactam antibiotics bind to cell wall synthesizing 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 results in reduced affinity to this class of antibiotics. Alterations in PBPs occur in a stepwise fashion which causes different degrees of resistance proceeding from reduced susceptibility through low-level clinical resistance – conventionally termed intermediate (I) to full clinical resistance (R). Although intermediately resistant strains are clearly less susceptible than sensitive strains, in absence of meningitis, infections with these strains are often successfully treated with high doses of penicillin or other beta-lactam compounds (10;14).

Macrolide, lincosamine and streptogramin (mls) antibiotics are chemically distinct, but all bind to a ribosomal subunit inhibiting the initiation of mRNA binding and thus act as protein synthesis inhibitors. In *S. pneumoniae* two resistance mechanisms against mls antibiotics have been reported: i) The acquisition of an erythromycin ribosomal methylation gene (*erm*) results in a posttranscriptional 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 macrolide, lincosamines and streptogramin B, termed *mlsB* resistance (40;43). ii) The acquisition of a macrolide efflux system gene (*mefE*) results in the excretion of the antimicrobial, and effectively reduces intracellular erythromycin, azithromycin and clarithromycin to subinhibitory concentrations (24). In contrast to beta-lactam resistance, macrolide resistance via these mechanisms is absolute, and cannot be overcome by increasing the dosages of antibiotics (23). Since *S. pneumoniae* is the most frequent cause of community-acquired pneumonia and can clinically not easily be 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 antimicrobial resistance into account. Habitual prescription of non-beta-lactam compounds is therefore typical in countries where penicillin resistance has been frequently reported. Such reactive prescribing increases the selection pressure for alternative antibiotics such as macrolides and novel fluoroquinolones. It is therefore no surprise to see a dynamic antimicrobial resistance picture emerge in different European countries.

5.2.2. *Streptococcus pneumoniae* resistance trends: 1999-2008

Penicillin

In 2008, 1,152 (10%) of the 11,584 *S. pneumoniae* isolates reported by 32 countries were non-susceptible for penicillin. Penicillin non-susceptible *S. pneumoniae* (PNSP) shows a heterogeneous picture in Europe. For SIR breakpoints see Chapter 3, External Quality Assessment Exercise. Most northern countries had levels of non-susceptibility below 5%, but Finland (11%, n=642), and Ireland (23%, n=441) reported relative high levels. High levels of PNSP, above 25%, were mainly reported from southern and eastern Europe, Cyprus (43%, n=14), France (30%, n=557), Hungary (27%, n=166), Malta (47%, n=17), and Turkey (34%, n=97). Romania (69%, n=13) and Bosnia and Herzegovina (55%, n=11) reported levels of *S. pneumoniae* isolates non-susceptible for penicillin above 50%, but these high percentages were based on a very low number of isolates.

The level of penicillin non-susceptibility in Finland and Ireland has risen significantly from 2005 to 2008. In Croatia, Hungary, Ireland, and Turkey a significant increase was also observed, but only for the percentage of fully resistant isolates (Figure 5.1).

* 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 (From unpublished discussions between CEN and ISO for a new MIC dilution method 2005).

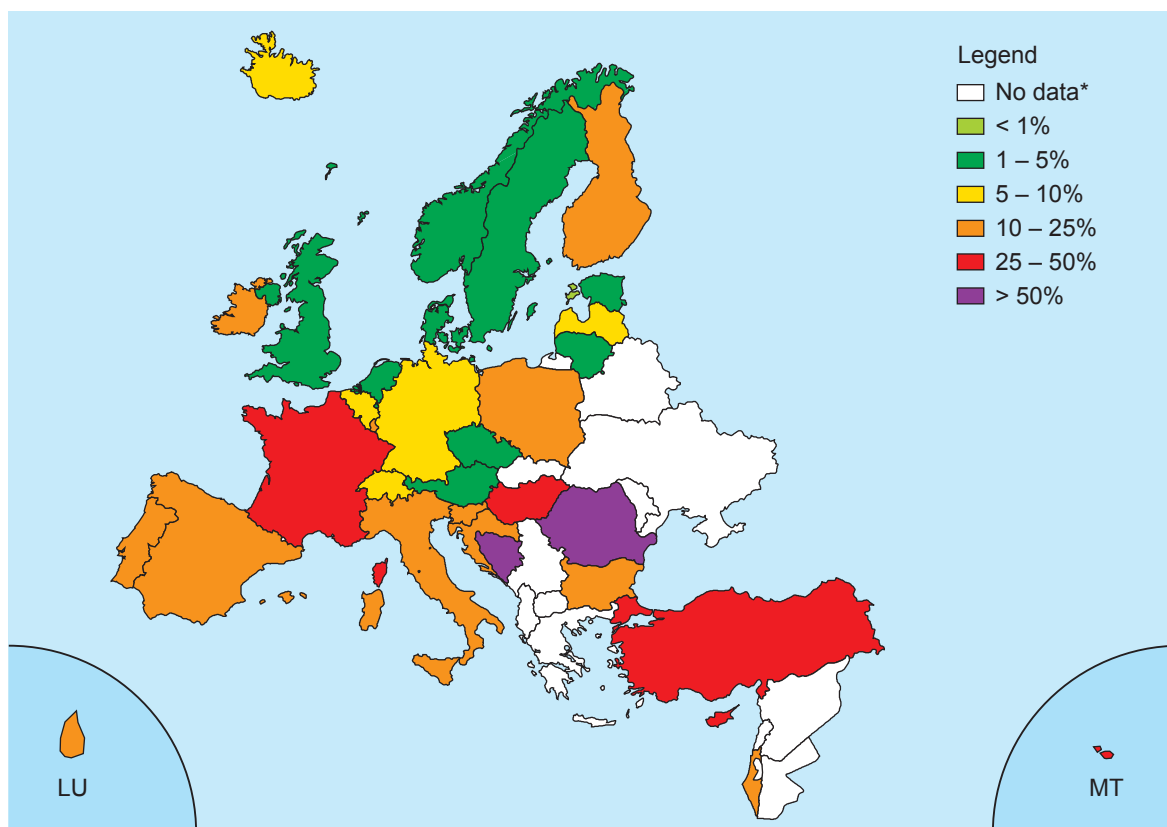


Figure 5.1. *Streptococcus pneumoniae*: proportion of invasive isolates non-susceptible to penicillin (PNSP) in 2008.

* These countries did not report any data or reported less than 10 isolates.

The two countries with the highest levels of PNSP in 2007 (France and Israel) showed significant decreasing rates of PNSP during the past years. Lithuania and Norway (the latter only significantly for the laboratories reporting consistently in the last four years) also showed decreasing trends for PNSP. In Belgium, the proportions PNSP as well as PRSP continued to decrease significantly (Figure 5.1, 5.4, Annex 3.1).

Erythromycin

In the EARSS database 10,982 (95%) *S. pneumoniae* isolates had susceptibility results for erythromycin in 2008. From the 32 countries reporting data, 1,655 (15%) isolates were reported non-susceptible to erythromycin. Latvia (n=11) reported no resistance for erythromycin, and three countries reported erythromycin non-susceptibility below 5% (Czech Republic (n=243), Estonia (n=53) and Bulgaria (n=24)). On the other hand, five countries reported non-susceptibility proportions above 25%, namely Italy (27%, n=154), Turkey (29%, n=97), France (31%, n=557), Hungary (32%, n=158), and Cyprus (29%, n=14).

A very pronounced increase of erythromycin resistance was reported from Turkey (10% in 2005 vs. 29% in 2008) and from Ireland only significant for the selection of laboratories. The proportion of isolates non-susceptible to erythromycin in Belgium, France and the UK continued to decrease, and now also Germany, the Netherlands and Norway reported significant decreasing rates in this respect (Figure 5.2, 5.5, Annex 3.1.)

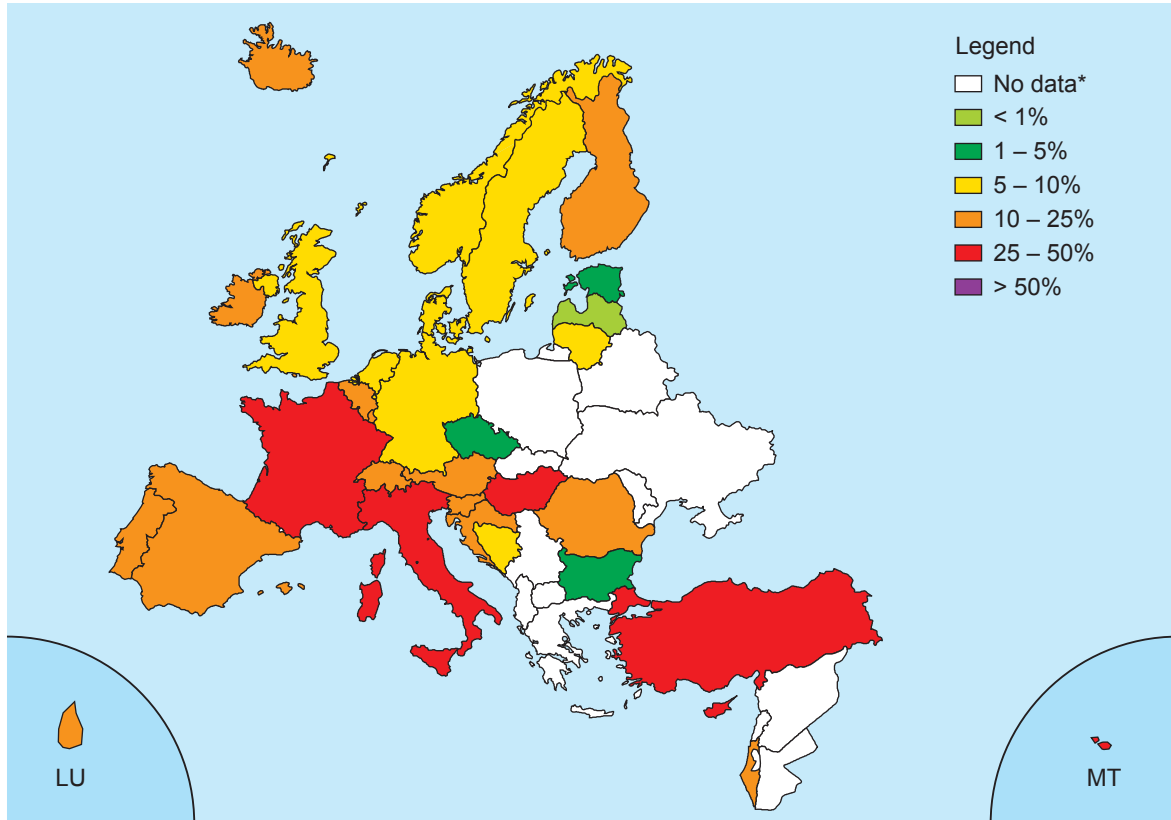


Figure 5.2. *Streptococcus pneumoniae*: proportion of invasive isolates non-susceptible to erythromycin in 2008. * These countries did not report any data or reported less than 10 isolates.

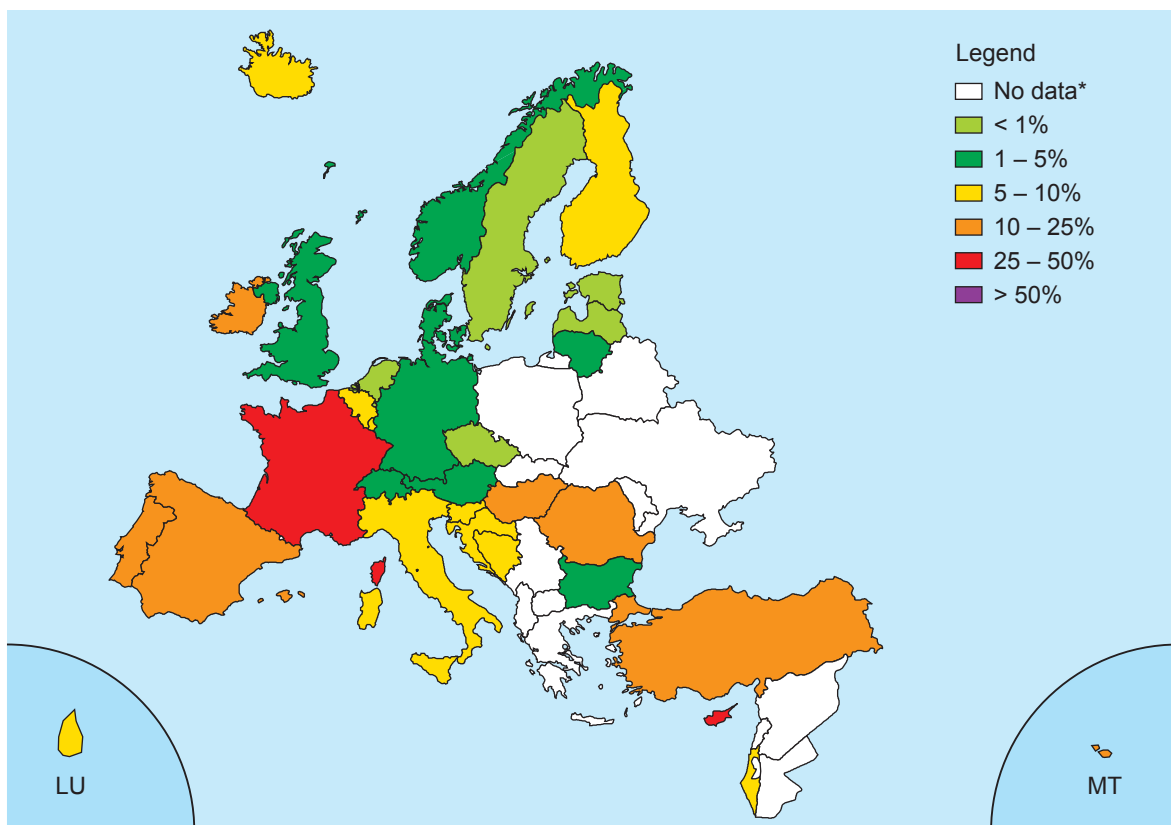


Figure 5.3. *Streptococcus pneumoniae*: proportion of invasive isolates with dual non-susceptibility to erythromycin and penicillin in 2008. * These countries did not report any data or reported less than 10 isolates.

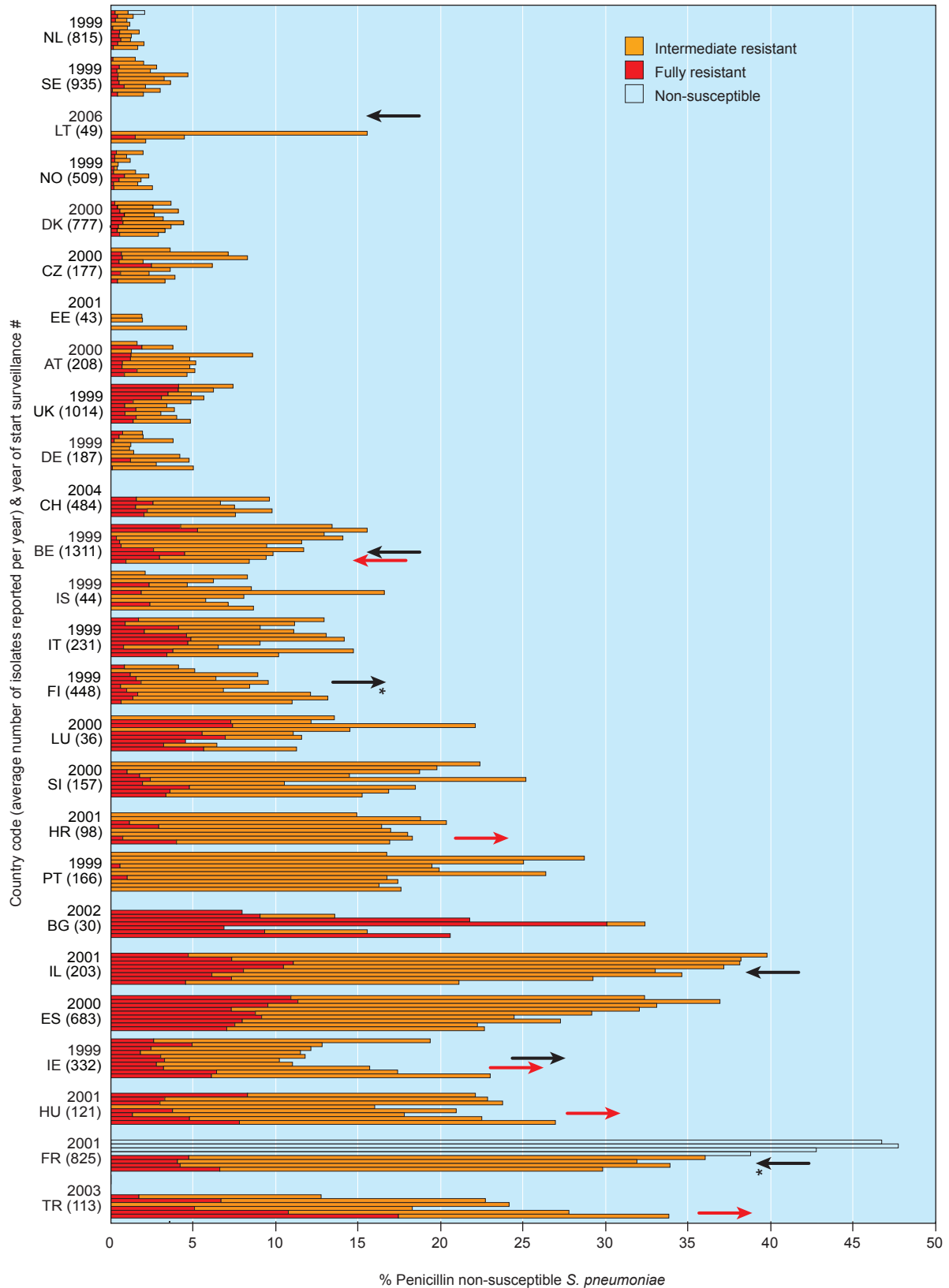


Figure 5.4. *Streptococcus pneumoniae*: trends of penicillin non-susceptibility by country, 1999-2008. Only the countries that reported 20 or more isolates per year for at least four consecutive years were included. The arrows indicate the significant trends in the last four years of surveillance for the proportion of PNSP (black arrows) or full penicillin resistance (red arrows). The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates were reported.

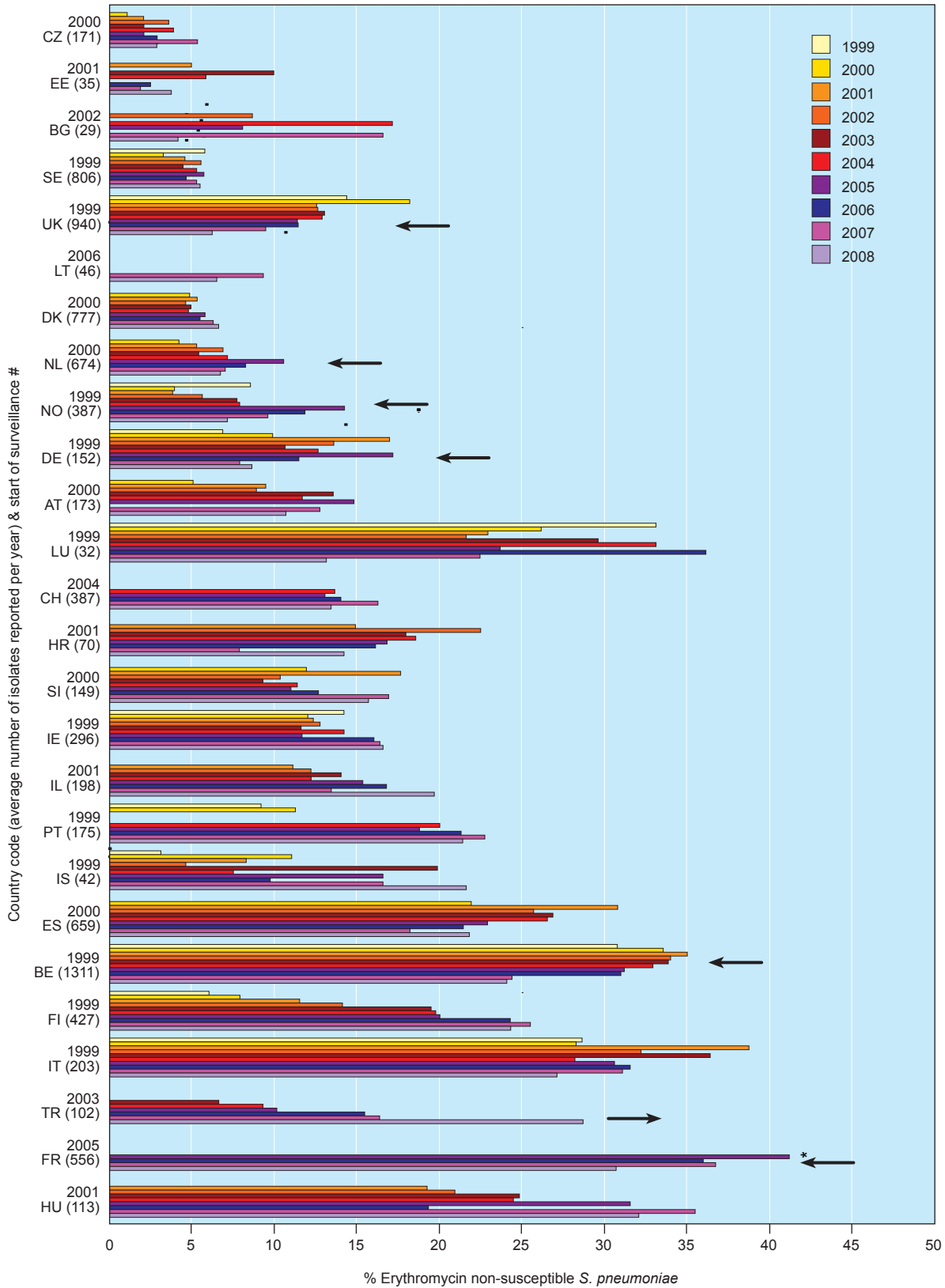


Figure 5.5. *Streptococcus pneumoniae*: trends of erythromycin non-susceptibility by country, 1999-2008. Only the countries that reported 20 or more isolates per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.
 # Either the first year of surveillance or the first year with 20 or more isolates were reported.

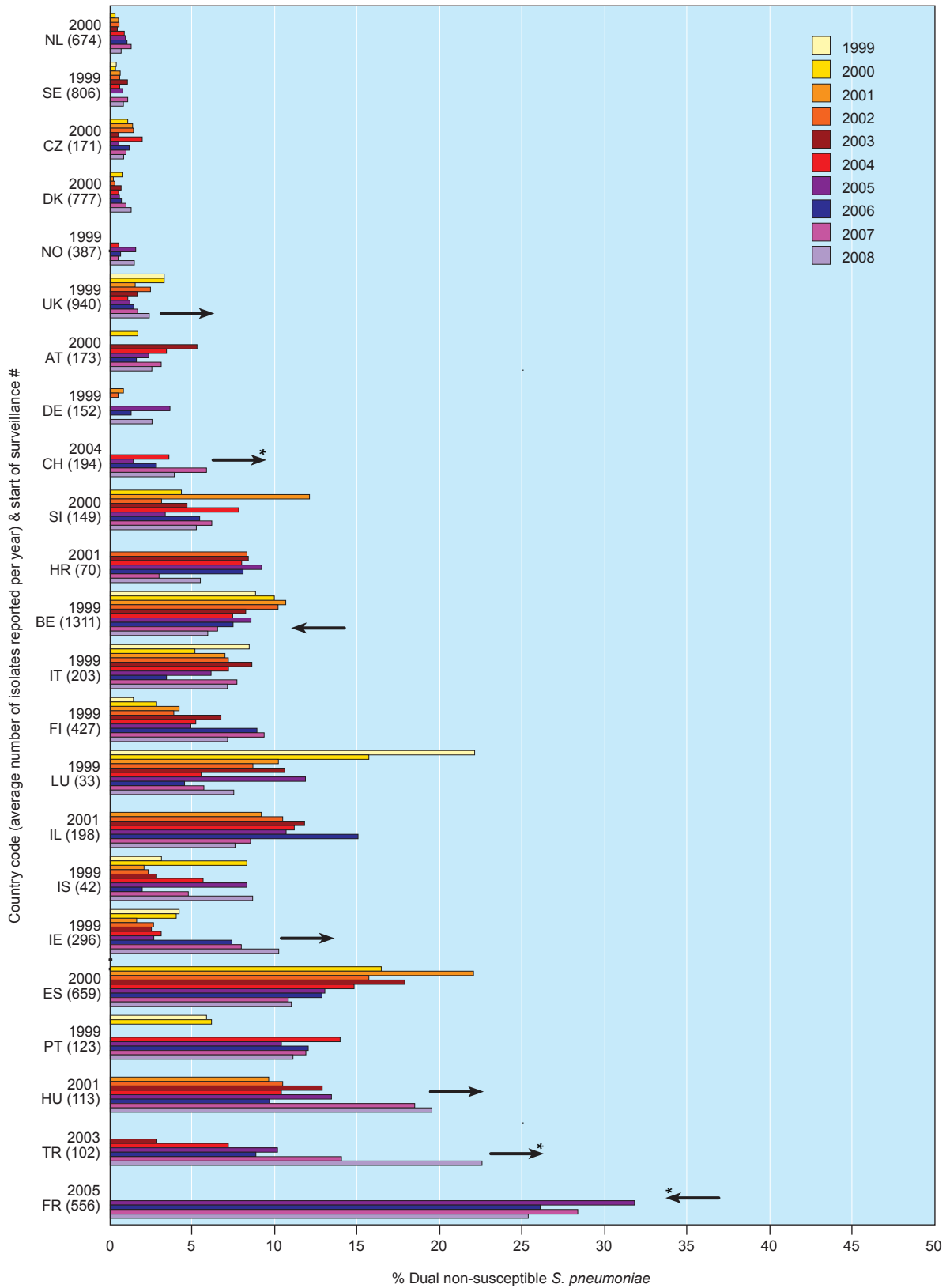


Figure 5.6. *Streptococcus pneumoniae*: trends of dual non-susceptibility to penicillin and erythromycin by country, 1999-2008. Only the countries that reported 20 or more isolates per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years. # Either the first year of surveillance or the first year with 20 or more isolates were reported.

Dual non-susceptibility to penicillin and erythromycin

For 12 of the 32 countries, dual non-susceptibility remained below 5%. For ten countries the level of non-susceptibility ranged between 5%-10% and ten countries reported between 10%-25% in 2008. Among the low-endemic countries, the UK and Switzerland showed a significantly increasing trend. This increase was also observed in Denmark, but only for the laboratories that reported data consistently in the past four years. During the last four years, the level of dual non-susceptibility increased significantly in Ireland (from 3% to 12%), Hungary (from 13% to 21%) and Turkey (from 10% to 23%, not significant for the selected labs). A decrease in the level of dual non-susceptibility was reported from Belgium (from 9% to 6%) and France (from 32% to 25%), although for France this significant trend was not present among the selection of laboratories (Figure 5.3, 5.6 and Annex 3.1).

5.2.3. Serotypes

For five years now, EARSS has collected serogroup information for *S. pneumoniae*. In 2008, twelve countries provided serogroup data. Data from Belgium, Czech Republic, Iceland, and Slovenia had serogroup information for over 95% of all *S. pneumoniae* isolates had serogroup information. For Austria, Ireland and the United Kingdom these proportions were 42%, 84% and 68% respectively. As the serogroup information of these samples were independent from antibiotic-susceptibility, we report these data as well. For The Netherlands and Norway the serogroup information was confined to less than 10%, and Latvia, Cyprus and Germany reported less than 30 isolates; these data are therefore not shown.

Serogroup information was analysed for 3370 isolates from only seven countries, Austria, Belgium, Czech Republic, Ireland, Iceland, Slovenia and the United Kingdom. This does not reflect the serogroup distribution in Europe as a whole, since Belgium and the UK reported together more than 70% and are therefore overrepresented. With this in mind, the distribution of serotypes between countries as well as the resistance within serogroups varied considerably. Compared to 2007, serogroup 1 (13%) and 19 (7%) are still the most prevalent ones, whereas serogroup 7 (8%) and serogroup 3 (15%) became slightly more prevalent. Serogroup 14 (8%) became less prevalent in the population compared to 2007, but was still the most prevalent serogroup in Iceland (20%), Slovenia (17%), and Ireland (12%) (Annex 3.7).

Non susceptibility seemed to be confined to a few serogroups. Penicillin non susceptibility was mainly found among serogroup 9, 14, 19, 23, and to a small degree 6. Erythromycin non susceptibility was mainly found in serogroups 1, 14, and 19, and to a small degree in serogroup 6, 9 and 33. Dual non susceptibility to penicillin and erythromycin was mainly found in serogroups 6, 9, 14, 19 and 23 (Figure 5.7).

The 7-valent conjugate vaccine includes all serogroups with penicillin non susceptibility, but in contrast to the 23-valent vaccine, it does not include serogroup 1 and 33 in which erythromycin non susceptibility is quite common.

5.2.4. Conclusions

The resistance profile of *S. pneumoniae* has a dynamic character. Although penicillin non-susceptibility is increasing in two countries, four countries are on the decrease, among those the high endemic countries Israel and France, strongly decreasing over the past years. Erythromycin non-susceptibility is becoming more prevalent in two countries, but against that, six countries are on the decrease. For dual non-susceptibility, more increasing than decreasing trends were found.

In 2008, again 12 countries have reported serogroup information for *S. pneumoniae* isolates, and data from seven countries were included for analysis. Therefore, this does not reflect the serogroup

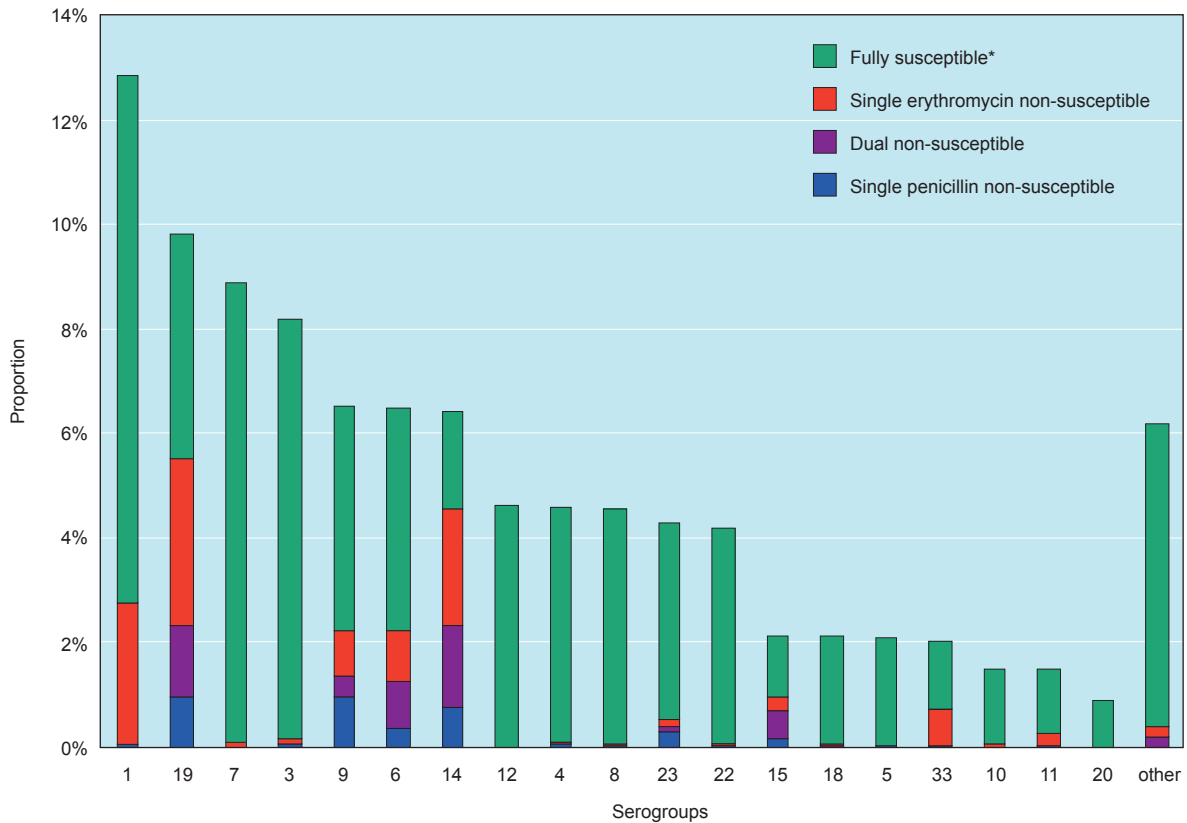


Figure 5.7. The distribution of serogroups and the resistance profile of *S. pneumoniae* isolates per serogroup in 2008. Only countries that reported serogroup information for more than 30 isolates were included in this figure.
*Susceptible to at least penicillin and erythromycin.

distribution in Europe as a whole, and moreover, Belgium and the UK together reported more than 70% of the isolates and are therefore overrepresented. Compared to 2007, changes were small. From the overview of prevalent serotypes, it becomes evident that serogroup 1 and 19 are still the most prevalent ones, whereas serogroup 7 and serogroup 3 became slightly more prevalent, and serogroup 14 became less prevalent in the population.

The highest resistance proportions were identified in serogroups 1, 6, 9, 14, 19, and 33, of which all but 1 and 33 are included in the 7-conjugate vaccine.

5.3. *Staphylococcus aureus*

5.3.1. Clinical and epidemiological importance

Staphylococcus aureus is a gram-positive bacterium that colonizes the skin of about 30% of healthy humans. Although mainly a harmless coloniser, *S. aureus* can cause severe infection. Its oxacillin-resistant form (methicillin-resistant *S. aureus*, MRSA) is the most important cause of antibiotic-resistant health care-associated infections worldwide (26). Since health care-associated MRSA infections add to the number of infections caused by methicillin-susceptible *S. aureus*, a high incidence of MRSA adds to the overall burden of infections caused by this species in hospitals (20). Moreover, infections with MRSA may result in prolonged hospital stay and higher mortality (7). MRSA is currently the most commonly identified antibiotic-resistant pathogen in hospitals in many parts of the world, including Europe, the Americas, North Africa and the Middle and Far-East.

Resistance mechanisms

S. aureus becomes resistant to methicillin and all other beta-lactam antibiotics through the expression of the exogenous *mecA* gene, that codes for a variant penicillin binding protein PBP2' (PBP2a) with low affinity to beta-lactams (21), thus preventing the drug induced inhibition of cell wall synthesis. The level of methicillin resistance (defined by its minimum inhibitory concentration, MIC) depends on the amount of PBP2' production, which is influenced by various genetic factors. Resistance levels of *mecA*-positive strains can thus range from phenotypically susceptible to highly resistant (5). Upon challenge with methicillin, a population of a heterogeneously resistant MRSA strain may quickly be outgrown by a subpopulation of highly resistant variants.

Glycopeptide antibiotics include vancomycin and teicoplanin. Both have unfavourable pharmacological properties which preclude oral uptake and the penetration through lipid membranes. Glycopeptides act on cell wall synthesis of gram-positive bacteria through binding to the terminal amino acid residues (D-alanyl-D-alanine) of the peptide chains in the growing peptidoglycan polymer and inhibit the cross linking essential for cell wall stability. It is estimated that to block cell wall synthesis effectively, the glycopeptide antibiotic has to penetrate about 20 peptidoglycan layers, all with free D-alanyl-D-alanine targets, without being 'trapped', and this together with a poor penetration into infected tissues, limits the therapeutic effects of glycopeptides. Cell wall thickening of *S. aureus* thus increases its ability to resist glycopeptides, and in *S. aureus* most strains with reduced susceptibility have a markedly thicker cell wall (21).

5.3.2. *Staphylococcus aureus* resistance trends: 1999-2008

Beta-lactams

In 2008, 33 countries reported AST results of 31,819 invasive *S. aureus* isolates to EARSS, of which 21% (n=6,648) were identified as MRSA. MRSA proportions varied from less than 1% in the north to over 50% in southern European countries. In the northern part of Europe, MRSA rates were below 5%, except for Lithuania (11%, n=278) and Latvia (13%, n=131). For the first time since eight years, Iceland reported a single case of MRSA bloodstream infection in 2008. Luxembourg showed a significant decrease, from 21% in 2007 (n=105) to 9% in 2008 (n=117). In Slovenia a previously decreasing trend stabilised in 2008 at 7%. In the category of 10-25%, Belgium (21%, n=906), Latvia (13%, n=131), Poland (12%, n=99) and France (24%, n=4,376) showed continuing decreasing trends. Predictably for France the steadily decreasing trend resulted in a change of the map colour from red to orange for the first time since reporting to EARSS in 2000. MRSA proportions however increased in Portugal and Switzerland. Thirteen countries reported MRSA proportions equal or higher than 25%, mostly among the Mediterranean and Balkan countries and the British Isles, except for France, Bosnia and Herzegovina, and Bulgaria. In the UK, the decrease first observed in 2006, persisted and in 2008 was down to 31% (n=3,350). Ireland (33%, n=1,242), Israel (35%, n=386), Italy (34%, n=930) and Romania (33%, n=39) also showed a decrease over the last four years.

Two countries reported MRSA proportions of more than 50%, Malta (56%, n=108) and Portugal (53%, n=1,556), of which Portugal saw proportions rising for already several years. When analysing the trends for only the last four years, nine countries showed a significant decrease in MRSA proportions (Figure 5.8, Figure 5.9, Annex 3.2).

Glycopeptides

Overall, eleven vancomycin-intermediate resistant *S. aureus* (VISA) and two vancomycin-resistant *S. aureus* (VRSA) were reported to the EARSS database in 2008. VISA were reported by Austria (n=8), Hungary (n=2) and the UK (n=1). VRSA was only found in Austria (n=2), whereby the exact

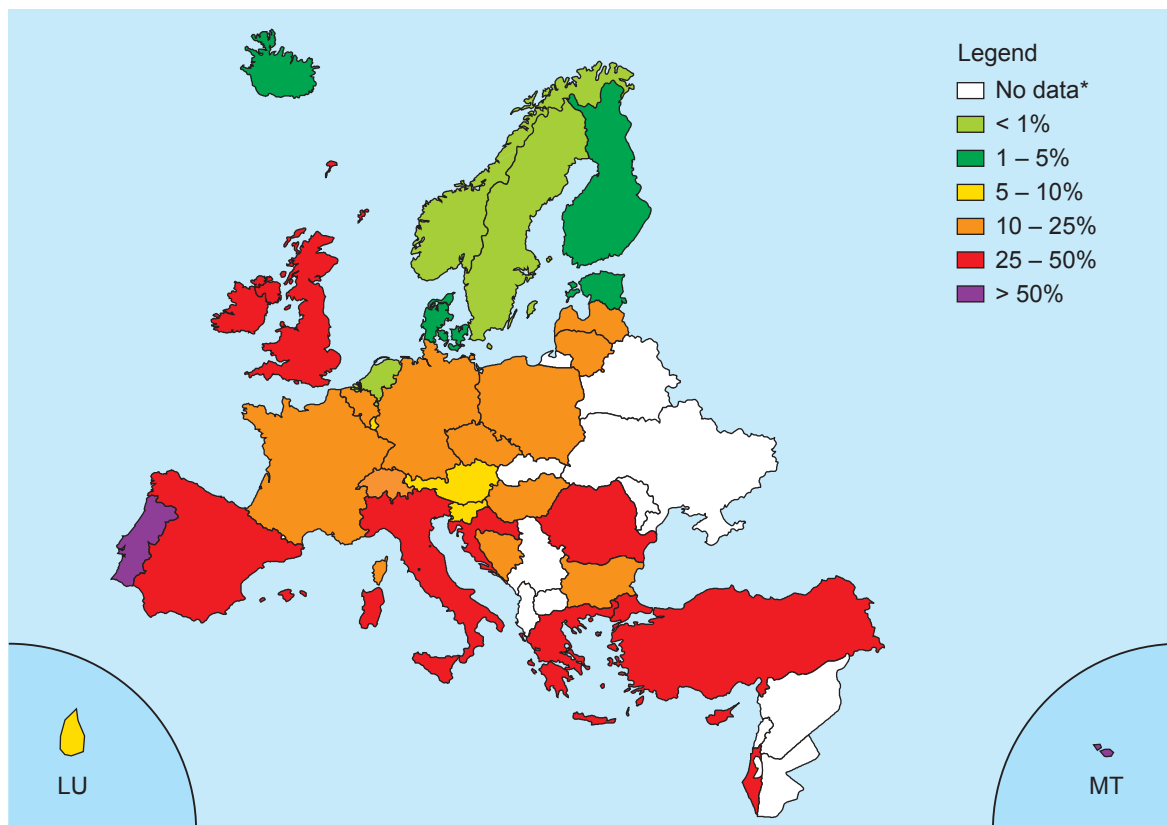


Figure 5.8. *Staphylococcus aureus*: proportion of invasive isolates resistant to oxacillin (MRSA) in 2008.

* These countries did not report any data or reported less than 10 isolates.

resistance mechanism was not reported to the EARSS. In 2007, three countries reported VISA, and VRSA was not reported. Although the absolute numbers of VISA and VRSA have increased, the prevalence of the resistance of *S. aureus* to vancomycin seems very low when judged from the EARSS data.

5.3.3. Conclusions

For the first time, more countries showed decreasing MRSA proportions instead of increasing trends. Although MRSA proportions are still above 10% in 24 countries, and above 25% in 11 countries, the MRSA problem seems to stabilize and even decrease for many European countries. While in previous years low endemic countries showed consistently increasing trends, also for these countries MRSA prevalence seems to have stabilized in 2008. The MRSA problem remains highest in the Mediterranean with Malta and Portugal showing MRSA proportions of over 50%. In contrast to an overall improvement in many European countries there has been a lasting increase of MRSA in Portugal. The most consistent decrease was found in France for a couple of years now. In the UK the decline in MRSA prevalence started only in 2006, but appears sustainable and even gaining momentum in 2008. This is the first time that EARSS is able to report an improvement for MRSA in Europe since for most European countries the proportion of hospital-associated MRSA blood stream infections is stabilizing or even decreasing.

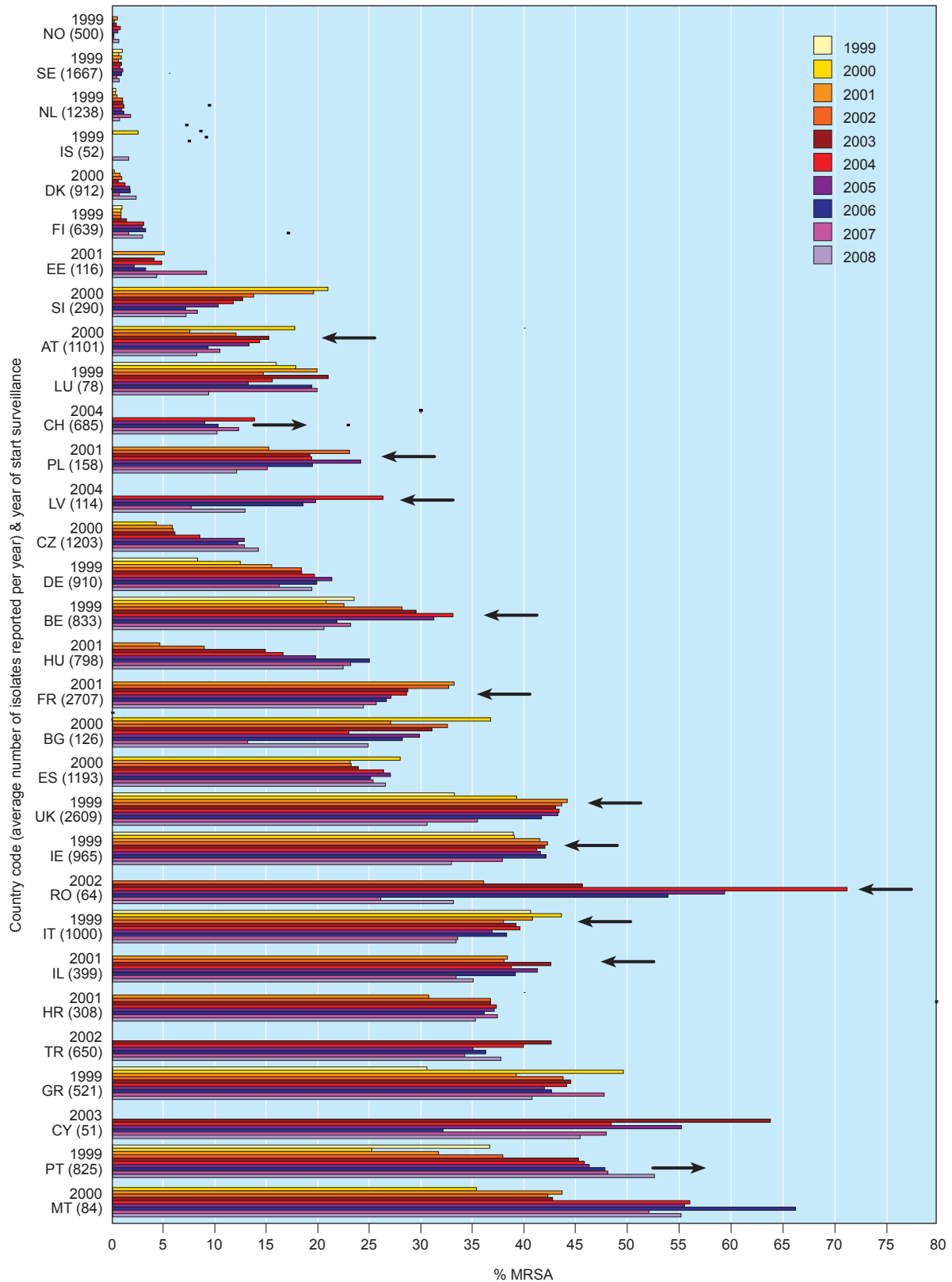


Figure 5.9. *Staphylococcus aureus*: trends of methicillin-resistance by country, 1999-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance.

Either the first year of surveillance or the first year with 20 or more isolates reported.

5.4. *Enterococci*

5.4.1. Clinical and epidemiological importance

Enterococci belong to the resident flora of the gastrointestinal tract of humans, other mammals, birds and reptiles. Under normal circumstances they are harmless commensals, and are even believed to have positive effects on a number of gastrointestinal and systemic conditions (4;13;32). However, when the commensal relationship with the host is disrupted, enterococci can cause invasive diseases (25). Though not as virulent as other Gram-positive organisms, enterococci can cause a variety of clinical syndromes including endocarditis, bacteraemia, meningitis, wound and urinary tract infections and are associated with peritonitis and intra-abdominal abscesses. In the USA, three to four nosocomial bloodstream infections per 10,000 hospital discharges are caused by enterococci (3), and contribute to patient mortality as well as additional hospital stay (27).

The vast majority of clinical enterococcal infections in humans are caused by *Enterococcus faecalis* in around 80% of clinical isolates and *Enterococcus faecium* in most of the remainder (22). Epidemiological data collected over the last two decades have documented the emergence of enterococci, and in particular *E. faecium*, as important nosocomial pathogens, which is seen as the expansion of a major hospital adapted clonal lineage (clonal complex 17, CC17) (47). The emergence of *E. faecalis* and *E. faecium* was paralleled by the increases in glycopeptide and high-level aminoglycoside resistance, both important compounds for the treatment of human infections (42). Besides the fact that infections with these resistant enterococci are difficult to treat, they are highly tenacious and thus disseminate and spread between patients in the hospital setting easily.

Resistance mechanisms

Enterococci are intrinsically resistant to a broad range of antibiotics including cephalosporins, penicillins, sulphonamides and low concentrations of aminoglycosides (15). 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 (33).

Beta-lactam antibiotics. By nature, enterococci have a low susceptibility to beta-lactam antibiotics – a consequence of their low-affinity PBPs. Complete penicillin resistance in *E. faecalis* is currently absent, though two possible mechanisms have been reported; i) the production of beta-lactamase (34) and ii) the overproduction and modification of penicillin-binding proteins (PBPs, particularly PBP5) (12).

Aminoglycosides. In addition to the intrinsic mechanism of low-level resistance, which causes a low uptake of the drug, enterococci have acquired genes conferring high-level resistance to aminoglycosides (42). High-level resistance to streptomycin can be mediated by single mutations within a protein of the 30S ribosomal subunit, the target of aminoglycoside activity (6). In addition, different aminoglycoside-modifying enzymes have been identified, targeting 8 different aminoglycosides (6).

Glycopeptides. Vancomycin resistance in enterococci was first encountered 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 (8). Whereas vancomycin consumption was less pronounced in Europe, a closely related glycopeptide, avoparcin, has been widely utilized in the farming community as growth promoter in animal husbandry from the late-1970s until it was banned in 1998. Glycopeptide resistance is due to the synthesis of modified cell wall precursors that show a decreased affinity for glycopeptides (28). Five phenotypes have been identified of which two have the most clinical relevance; i) VanA with high-level resistance to both vancomycin and teicoplanin, and ii) VanB with a variable level of resistance to only vancomycin. (2;37) The VanA and VanB phenotypes, mostly found among *E. faecalis* and *E. faecium*, may be transferred by plasmids and conjugative transposition.

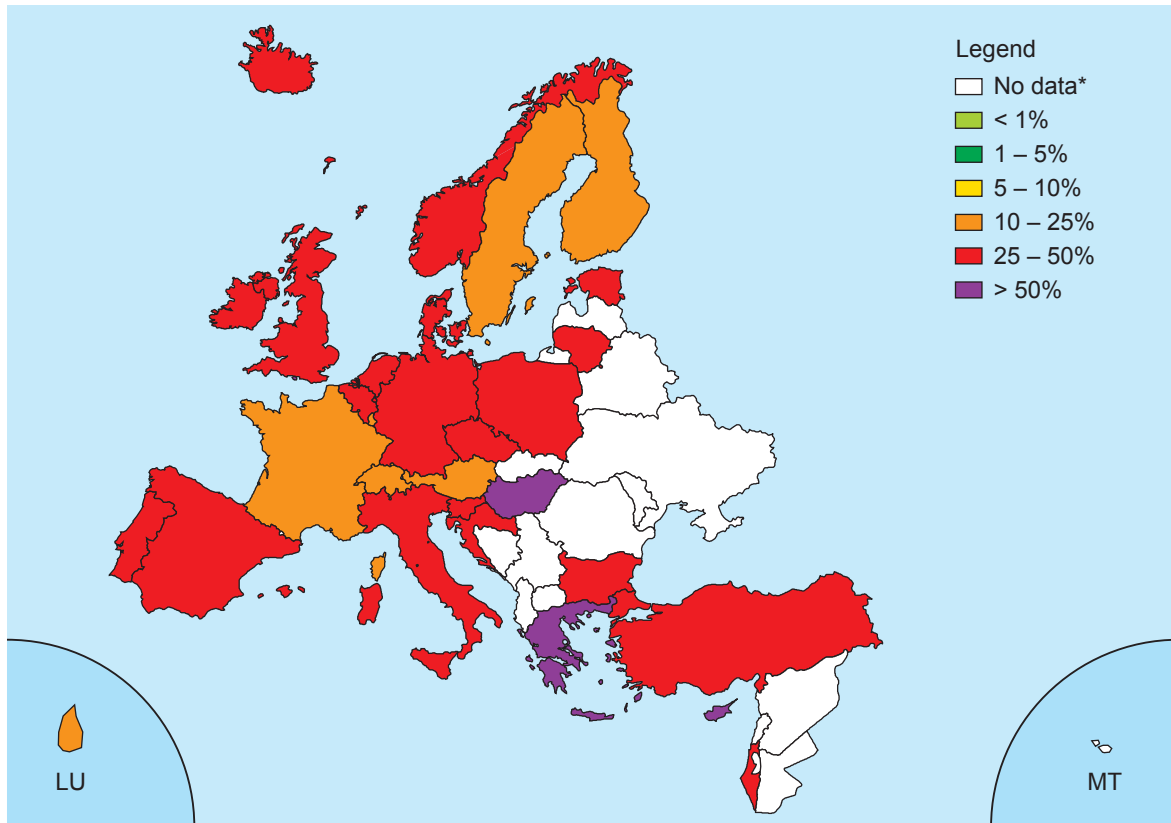


Figure 5.10. *Enterococcus faecalis*: proportion of invasive isolates with high-level resistance to aminoglycosides in 2008.
* These countries did not report any data or reported less than 10 isolates.

5.4.2. *Enterococcus faecalis* resistance trends: 2001-2008

High-level aminoglycosides

In 2008, 31 countries reported AST results for invasive *E. faecalis* isolates (n= 7,282). Only four countries reported less than 20 isolates, namely Iceland (n=10), Latvia (n=9), Poland (n=17) and Romania (n=9) and could therefore not be included in the trend analysis (Annex 3.3). The proportion of high-level aminoglycoside resistance varied between 13% in Finland (n=157) and 65% in Cyprus (n=75). Figure 5.10 shows that Austria (21%, n=289), Switzerland (19%, n=85), France (18%, n=895), Luxembourg (17%, n=36), Romania (22%, n=9, and therefore not shown on the map) and Sweden (20%, n=703) still report resistance levels below 25%. All other countries reported proportions above 25% (Figure 5.10, Annex 3.3). Probably due to the occurrence of outbreaks, the proportions of high-level aminoglycoside resistance can show considerable variation over time. However, a consistent decrease was reported by Estonia (from 50% to 27%), Finland (from 27% to 13%) and Ireland (from 42% to 31%) from 2005 to 2008 (Figure 5.11). In the same period, proportions increased significantly in Spain (from 36% to 41%), Croatia (from 31% to 46%), Hungary (from 43% to 53%) and Italy (from 38% to 47%).

5.4.3. *Enterococcus faecium* resistance trends: 2001-2008

Vancomycin

In general, the total number of invasive *E. faecium* isolates reported by 33 countries was low (n=4,888). Among these countries, six reported less than 20 isolates in 2008; Bosnia and Herzegovina

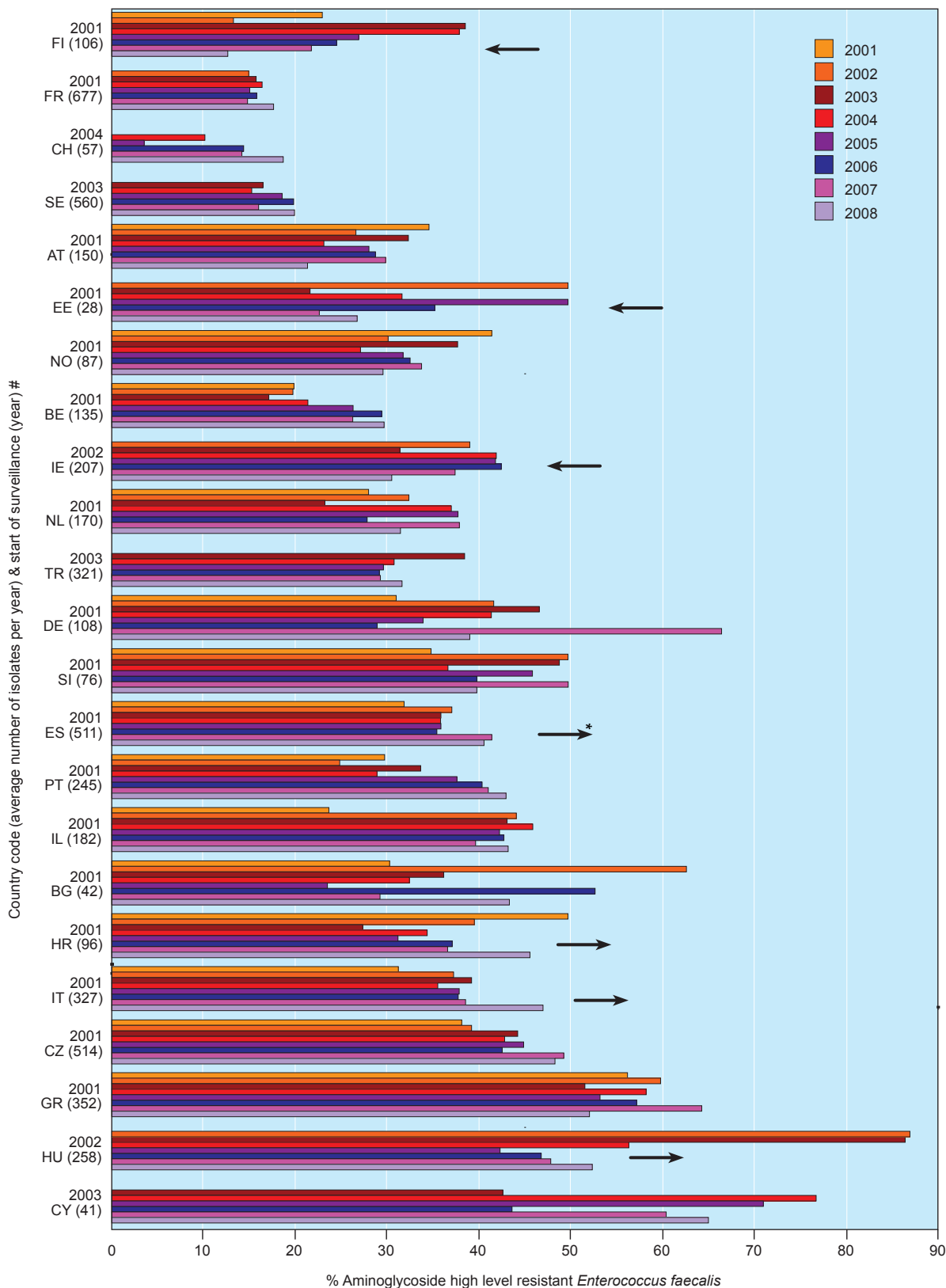


Figure 5.11. *Enterococcus faecalis*: trends of high-level aminoglycoside resistance by country 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

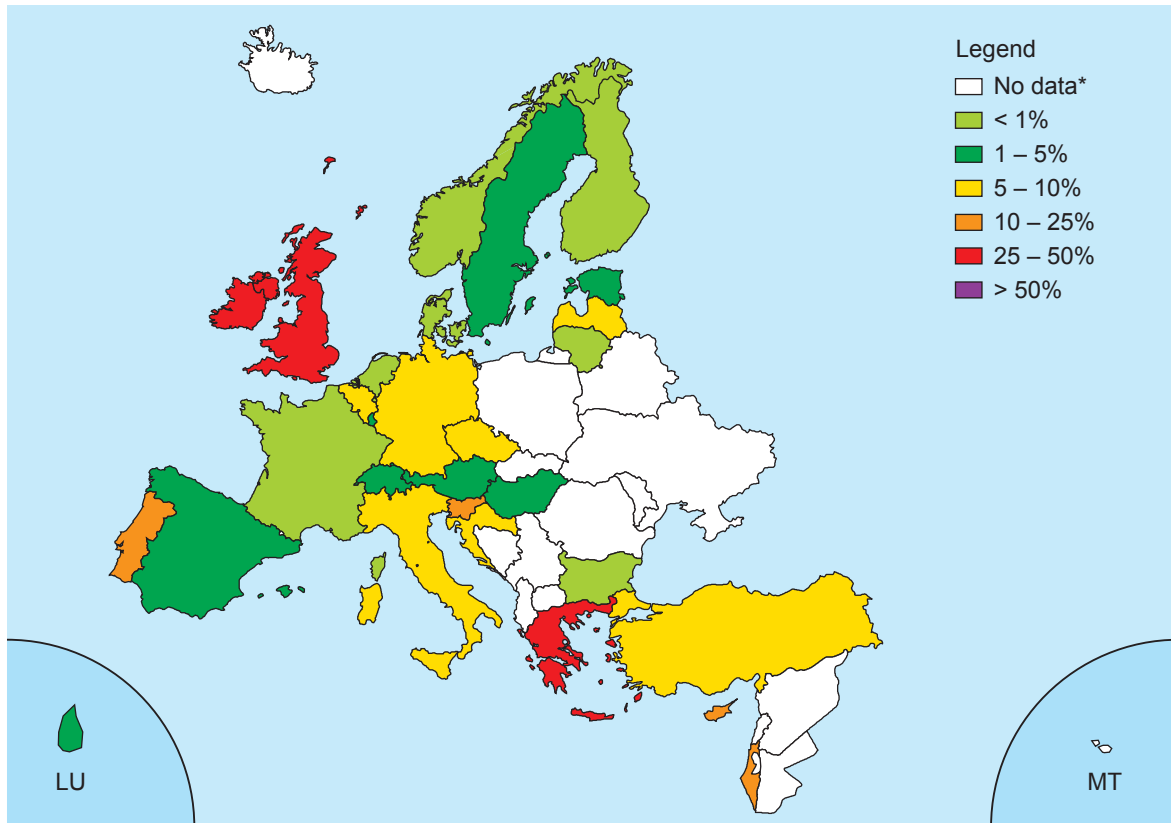


Figure 5.12. *Enterococcus faecium*: proportion of invasive isolates resistant to vancomycin in 2008.

* These countries did not report any data or reported less than 10 isolates.

(n=9), Cyprus (n=10), Iceland (n=7), Malta (n=5), Poland (n=9), and Romania (n=5). Ten countries still reported an absence of vancomycin resistance; Bosnia and Herzegovina (n=9), Bulgaria (n=28), Denmark (n=344), Iceland (n=7), Latvia (n=24), Malta (n=5), the Netherlands (n=165), Norway (n=108) and Romania (n=5). This contrasts to the three countries that reported more than 25% vancomycin-resistant *E. faecium* isolates in 2008, namely Greece (28%, n=368), Ireland (35%, n=390) and the UK (28%, n=88) (Figure 5.12, Annex 3.3). Over the past 4 years, vancomycin resistance only increased significantly in Slovenia, from 0% to 13%. The rapid expansion of *E. faecium* in this country is typically the result of institutional outbreaks, and does not represent the situation for hospitals that have remained unaffected. From 2005 to 2008, a significant decrease in vancomycin resistance was observed in France (from 2% to 0,6%), Greece (from 37% to 28%), Israel (from 46% to 20%) and Italy (from 19% to 6%). Especially the last 3 countries have managed to downsize their very high levels of vancomycin resistance, but still have higher resistance levels than most of the other countries under surveillance (Figure 5.13).

5.4.4. Conclusions

With the ongoing spread of clonal complex 17 in Europe, outbreaks of vancomycin resistant *E. faecium* continues to afflict hospitals in various countries. The spread of these hospital-adapted strains occurs on the background of high-level aminoglycoside resistance. The control of glycopeptide resistant enterococci remains a formidable task for hospital infection control practitioners and it is not difficult to predict that these problematic pathogens will continue to remain a challenge. It will be interesting to examine whether the decrease in resistance that is seen in some countries is the result of specific interventions, for instance in hospital hygiene.

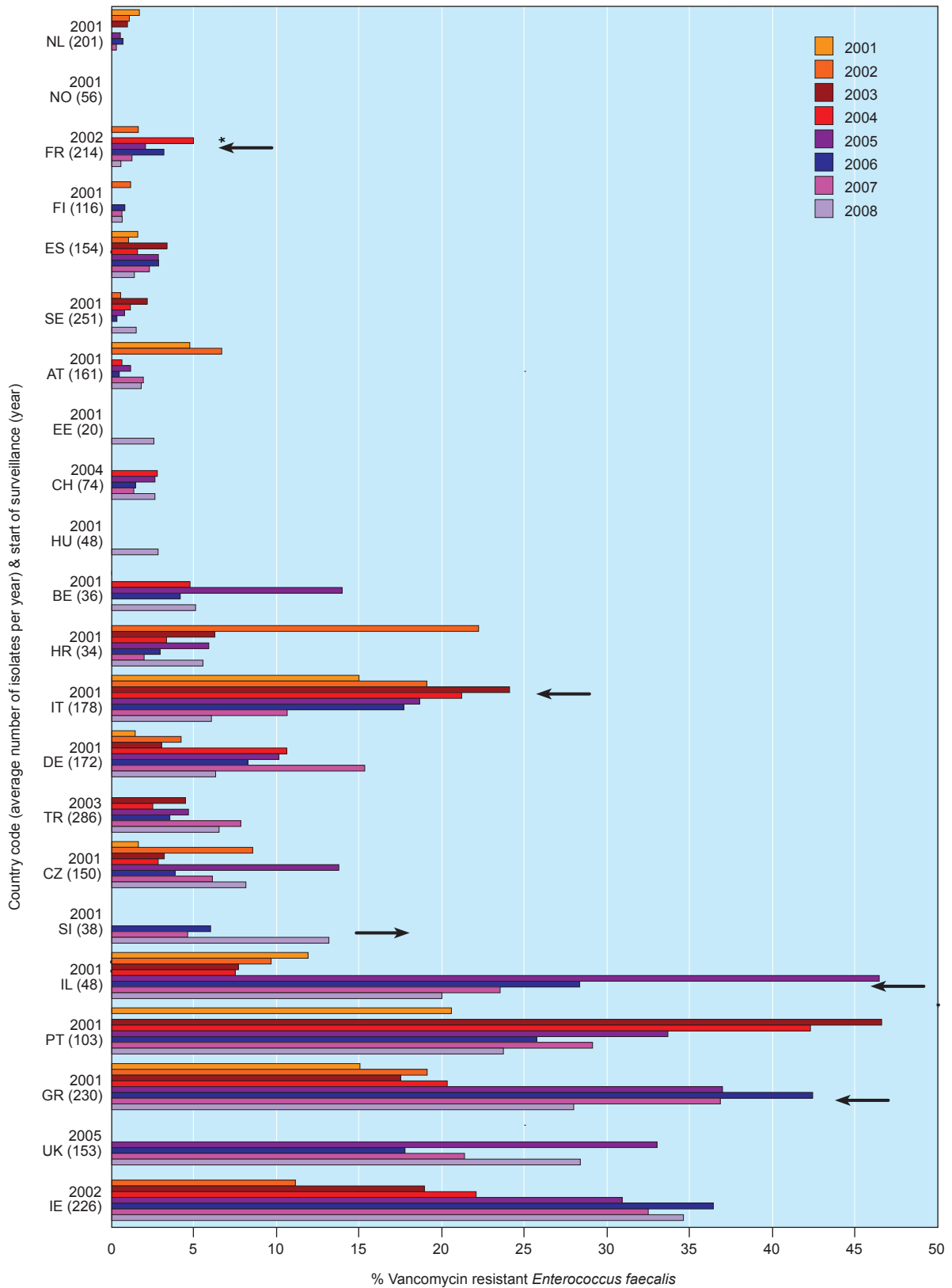


Figure 5.13. *Enterococcus faecium*: trends of vancomycin resistance by country 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

5.5. *Escherichia coli*

5.5.1. Clinical and epidemiological importance

Escherichia coli is the most frequent gram-negative rod isolated from blood cultures in clinical settings. It is the most frequent cause of community and hospital-acquired urinary tract infections, is associated with spontaneous and post-surgical peritonitis, causes neonatal meningitis and polymicrobial wound infections and is one of the most important food-borne pathogens worldwide (9;11;39).

Resistance mechanisms

Beta-lactamases hydrolyse the beta-lactam ring of beta-lactam antibiotics, which is crucial for inhibition of PBPs in bacteria. In *E. coli* resistance to broad-spectrum penicillins such as ampicillin or amoxicillin is usually conferred by plasmid-coded beta-lactamases of the TEM and SHV type, whereby TEM-1 accounts for up to 60% of aminopenicillin resistance. In 1982 the first ESBL was identified during a hospital outbreak of *Klebsiella pneumoniae* in Germany. It was soon understood that single or multiple amino acid substitutions in the basic structure of TEM or SHV enzymes can alter their spectrum of activity and enhance their hydrolyzing ability to include 3rd and 4th generation cephalosporins and monobactams. Many ESBLs can be inhibited by beta-lactamase inhibitors such as clavulanic acid, sulbactam, or tazobactam. More than 300 ESBL variants are known to date. Most of them belong to three enzyme families TEM, SHV, and CTX-M (an overview of identified ESBL types is given on <http://www.lahey.org/studies/>). In *E. coli*, over 90% of ESBL resistance was mediated through TEM variants. In the late 1990's, new ESBLs of the CTX-M family emerged first in South America presumably by transfer of mobile elements from environmental bacteria and soon after attained global importance. In contrast to conventional TEM, and SHV ESBLs, CTX-Ms often display a higher hydrolysing ability against cefotaxime than ceftazidime (hence their name), although variants with enhanced ceftazidimase activity have emerged (e. g. CTX-M-15). Plasmid mediated AmpC-type beta-lactamases (e. g. CMY-2) are still rare in Europe but frequent in North America (43).

Fluoroquinolones interact with DNA gyrase and topoisomerase IV which are enzymes that regulate conformational changes in bacterial DNA during replication and transcription. This leads to irreversible inhibition of DNA strand separation followed by chromosomal fragmentation, and eventually to cell death. Resistance to fluoroquinolones arises through stepwise mutations in the coding regions of the gyrase subunits (*gyrA* and *gyrB*) and DNA topoisomerase IV (*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 membrane porins or from upregulation of efflux pumps, resulting in lower membrane permeability and higher efflux, respectively (19). In recent years, plasmid-mediated quinolone resistance mechanisms have also emerged, including the Qnr proteins, protecting the topoisomerase target from quinolone binding, the AAC(6')-Ib-cr acetylase which can modify some quinolones, and the QepA efflux pump. Although conferring low-level resistance, these mechanisms are of concern because they promote evolution to clinical resistance and are frequently associated with CTX-M and CMY-type enzymes inactivating third generation cephalosporins (40).

Aminoglycosides block protein synthesis by binding to the ribosomes, which are involved in the translation of RNA into proteins, and disrupt the outer membrane of gram-negative rods. Resistance to aminoglycosides is brought about by targeted modification of the large ribosomal subunit which excludes aminoglycoside molecules or by aminoglycoside modifying enzymes that acetylate, adenylate or phosphorylate their target molecules and thereby neutralize the biologic effect of aminoglycosides.

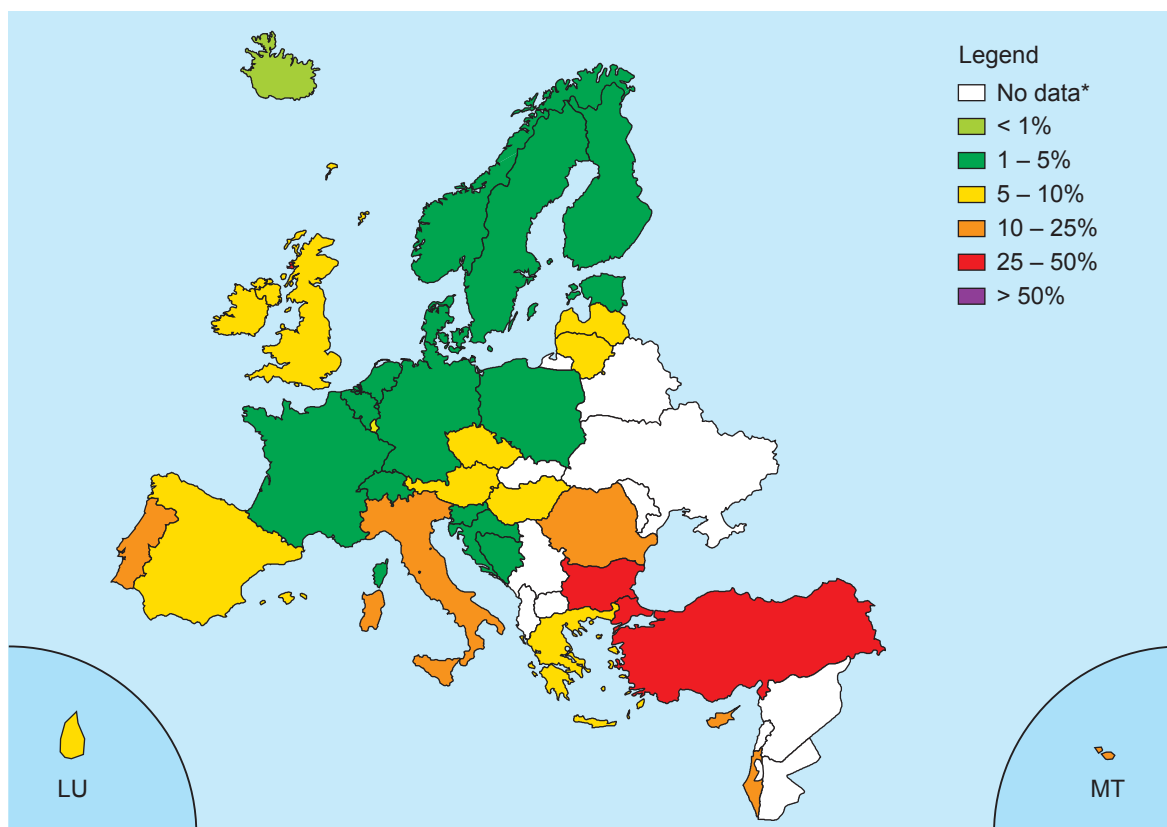


Figure 5.14. *Escherichia coli*: proportion of invasive isolates with resistance to third generation cephalosporins in 2008.

* These countries did not report any data or reported less than 10 isolates.

5.5.2. *Escherichia coli* resistance trends: 2001-2008

EARSS began collecting AST results for invasive *E. coli* in 2001. In 2008, 51,341 isolates were reported from 33 countries.

Aminopenicillins

Aminopenicillin resistance in *E. coli* was highly prevalent in Europe. Most countries reported resistance proportions above 50%, but eight countries reported lower resistance proportions, namely Austria (50%, n=2979), Denmark (43%, n=3287), Estonia (47%, n=252), Finland (35%, n=1,768), The Netherlands (47%, n=2107), Norway (38%, n=1730), Slovenia (49%, n=874) and Sweden (32%, n=2,229). But even in these countries aminopenicillins have lost their position as empirical treatment for *E. coli* infections.

Aminopenicillin resistance, although already high for many years, is still increasing and over the last four years this trend remained significant for 13 countries. Romania was the only country that showed a significant decrease in aminopenicillin resistance. In 2006 the proportion was 85% (n=33), and since then appeared to have decreased to 55% (n=31) in 2008 (Figure 5.17, annex 3.4). Because of the low number of isolates, it is not clear whether this is representative for the whole country.

Third generation cephalosporins

Although less than half of the countries (14 of 33) reported less than 5% resistance against 3rd generation cephalosporins in 2008, the proportion of 3rd generation cephalosporins resistance has been increasing over the last four years in 19 countries (Figure 5.18) and shows the most dynamic expansion of AMR in the entire region. In 2008, two east European countries reported levels higher than 25%, namely Bulgaria (29%, n=147) and Turkey (42%, n= 1,375) (Figure 5.14, 5.18, Annex 3.4).

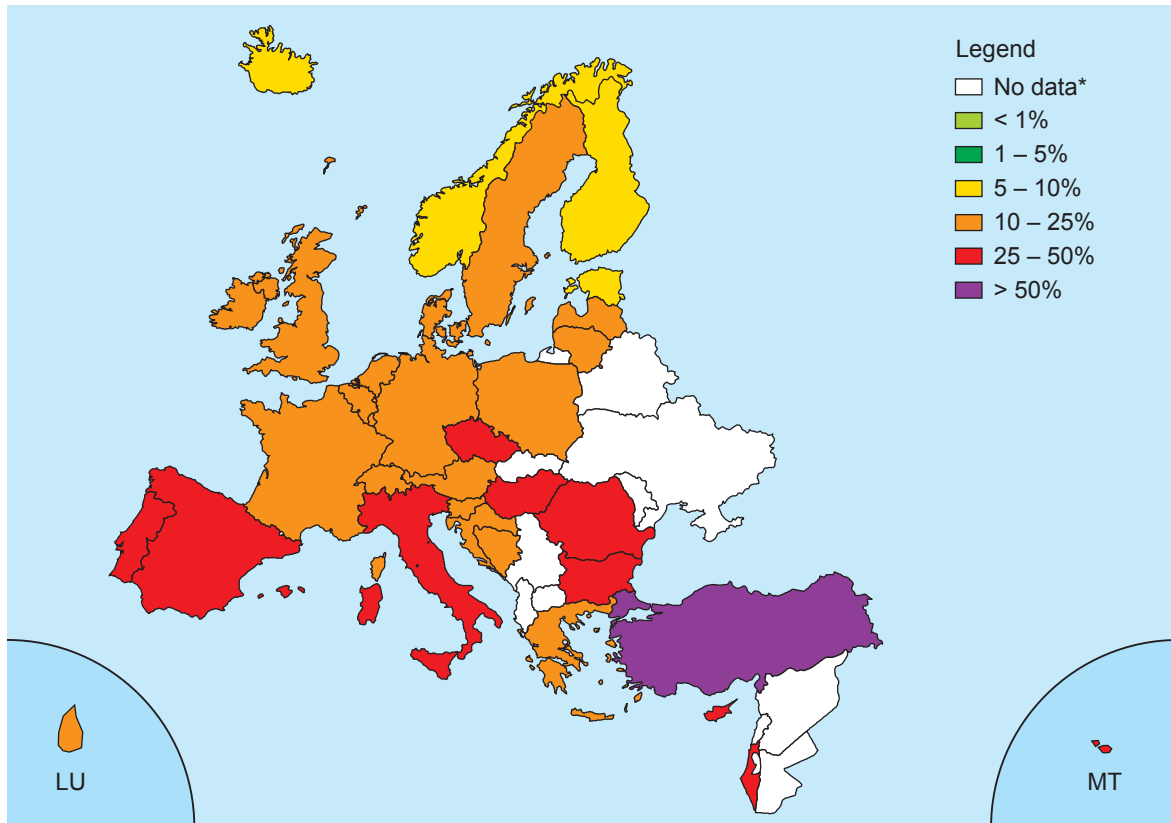


Figure 5.15. *Escherichia coli*: proportion of invasive isolates with resistance to fluoroquinolones in 2008.

* These countries did not report any data or reported less than 10 isolates.

Unfortunately, the EARSS does not receive information that would allow for differential characterisation of resistance mechanisms. It is however expected that the rise in 3rd generation cephalosporin resistance is the result of fast dissemination of ESBLs in hospitals and the communities.

Fluoroquinolones

Fluoroquinolone resistance has consistently and substantially increased over the past seven years all over Europe. In 2005, four countries still had levels of 5% or less, but since that time all countries reported an increase in fluoroquinolone resistance. In 2008 only four countries reported proportions under 10% namely, Iceland (6%, n=115), Estonia (7%, n=252), Norway (7%, n=1719) and Finland (9%, n=2109). At the same time, 10 countries reported fluoroquinolone-resistant *E. coli* in excess of 25%, with three countries reporting resistance proportions above 35%: Italy (38%, n=907), Cyprus (45%, n=116) and Turkey (52%, n=1372) (Figure 5.15, annex 3.4).

In the past four years, fluoroquinolone resistance increased significantly in 19 countries. In Germany (23%, n=1610) and Hungary (26%, n=1045) the increasing trend was only significant in the laboratories that reported all years since 2005, but was not significant for all reported data since 2005. The alarming speed in which fluoroquinolones lose their activity against *E. coli*, which EARSS reported already in 2006 and 2007, unfortunately has not diminished in 2008 (Figure 5.15, 5.19, Annex 3.4).

Aminoglycosides

Only six European countries reported less than 5% resistance against aminoglycosides, namely Sweden (2%, n=4,025), Bosnia and Herzegovina (3%, n=34), Norway (3%, n=1,729), Finland (4%, n=2,057), Denmark (4%, n=3,278) and Belgium (4%, n=1,011). Sixteen countries reported resistance

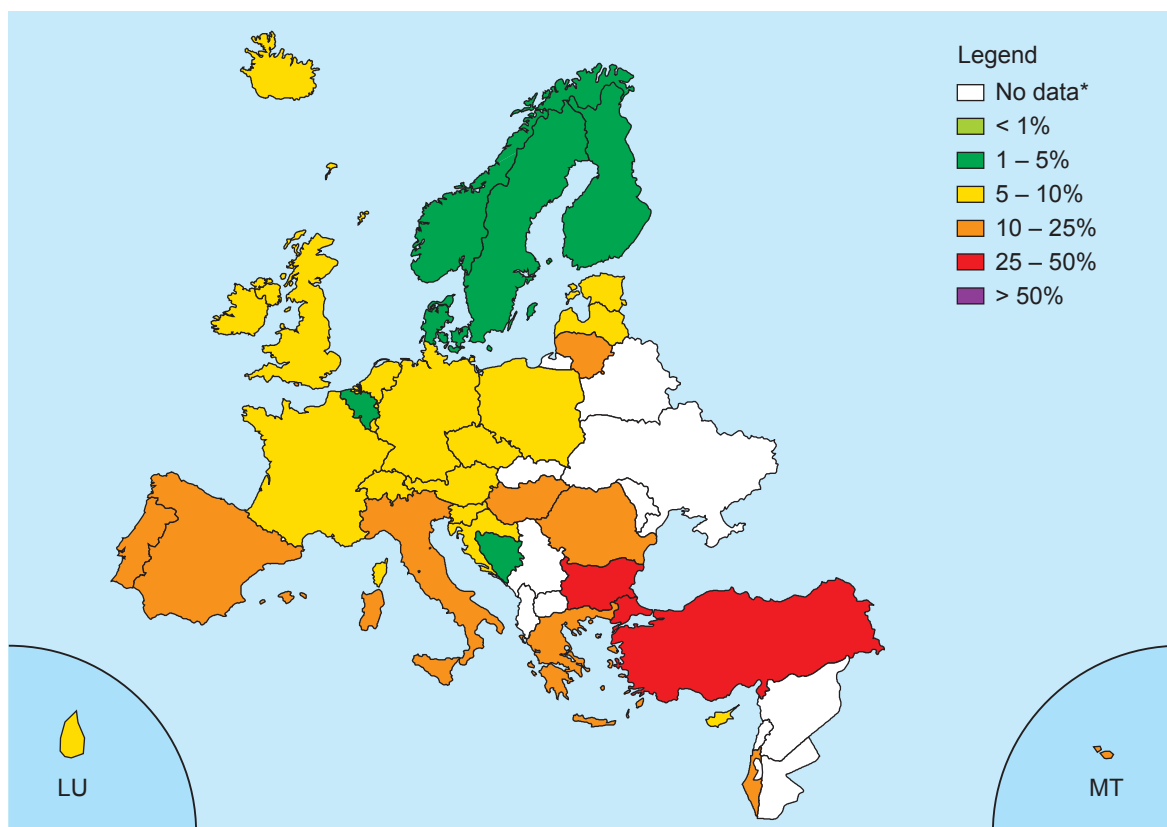


Figure 5.16. *Escherichia coli*: proportion of invasive isolates with resistance to aminoglycosides in 2008.

* These countries did not report any data or reported less than 10 isolates.

between 5% and 10%. In the South and East, most countries reported 10% or more, with the highest percentages reported by Bulgaria (31%, n=147) and Turkey (35%, n=1,377). Consistent with the increase of all other resistance proportions for *E. coli*, aminoglycoside resistance also increased over the last four years in 16 countries (Figure 5.16, 5.20, Annex 3.4).

Combined resistance

It is not surprising that the overall increase of single compound resistance in *E. coli* is paralleled by a concomitant spread of phenotypes with combined resistance. For the first time in 2007, only a minority (47%) of the *Escherichia coli* isolates tested by the laboratories participating in EARSS could be considered wild-type strains, i.e. displayed the original susceptibility to aminopenicillins, fluoroquinolones, 3rd generation cephalosporins, and aminoglycosides. In 2008, the same picture emerged. Combined resistance to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides was still below 2% in twelve countries. Two countries reported a combined resistance above 20%, Bulgaria (20%, n=149) and Turkey (23%, n=921). The majority of countries (19 out of 33) showed a significant increase. A significant increase in combined resistance in Italy was only shown in the selection of laboratories consistently reporting for the last four years. Bulgaria was the only country reporting a significant decrease in combined resistance, although this decrease was only significant in the selection of laboratories reporting consistently over the last four years (Figure 5.21, annex 3.4). Table 5.1 gives an overview of the most common phenotypes (single and combined resistance) based on the overall proportion from all 33 countries in 2008. In *E. coli*, single aminopenicillin resistance was the most frequent phenotype (30.6%), followed by dual resistance to aminopenicillins and fluoroquinolones (8.1%). Importantly, the second most frequent combined resistance was against all 4 antimicrobial classes (3.1%), i.e. aminopenicillins, 3rd generation cephalosporins, fluoroquinolones,

Table 5.1. Overall resistance and resistance combinations among invasive *Escherichia coli* isolates tested against all four classes of drugs (according to the EARSS protocol) (n= 47,746) in Europe, 2008.

Resistance pattern	Number	% of total
fully susceptible	22,396	47,1
Single resistance (to indicated drug classes)		
aminopenicillins only	14,572	30,6
fluoroquinolones only	1,335	2,8
aminoglycosides only	117	0,2
Resistance to two classes of antimicrobial drugs		
aminopenicillins+fluoroquinolones	3,845	8,1
aminopenicillins+3 rd generation cephalosporins	462	1,0
aminopenicillins+aminoglycosides	557	1,2
fluoroquinolones+aminoglycosides	150	0,3
Resistance to three classes of antimicrobial drugs		
aminopenicillins+fluoroquinolones+aminoglycosides	1,422	3,0
aminopenicillins+fluoroquinolones+3 rd generation cephalosporins	1,092	2,3
aminopenicillins+3 rd generation cephalosporins+aminoglycosides	155	0,3
Resistance to four classes of antimicrobial drugs		
aminopenicillins+3 rd generation cephalosporins+fluoroquinolones+aminoglycosides	1,474	3,1

and aminoglycosides, followed by triple resistance to aminopenicillins, fluoroquinolones and aminoglycoside (3.0%) (Figure 5.21, annex 3.4).

NB: Other compounds, including trimethoprim, sulphamethoxazole, nitrofurantoin and tetracyclin, are not taken into account, as reporting of AST results for these substances is not obligatory within EARSS. In the face of the current threat from carbapenemases, EARSS strives to make the reporting of carbapenem-resistance in *E. coli* mandatory. Multi-betalactam-resistant *E.coli* and those with reduced resistance to carbapenems should be screened for carbapenemase production using newly adopted screening guidelines.

5.5.3. Conclusions

The Europe-wide increase of resistance of *Escherichia coli* to all of the antimicrobial classes recorded by EARSS is a disturbing development with seemingly relentless vigor.

The highest resistance proportions have been reported for aminopenicillins ranging between 32 to 78%. Aminopenicillins can therefore no longer be regarded as a useful option for empirical treatment. Irrespective of the high level of resistance, proportions continue to increase in most of the countries, including those with resistance well above 50%. For fluoroquinolones the situation becomes progressively dire. Of the 33 countries providing data, 21 displayed a trend over the last four years that could not be explained by random fluctuations. The speed with which fluoroquinolones lose their activity against *E. coli* is next to no other compound pathogen combination in the EARSS database. Combined resistance is a frequent occurrence, with co-resistance to 4 antimicrobial classes including 3rd generation cephalosporins already among the 4th most common resistance patterns encountered in invasive *E. coli* in Europe and undeniably these resistance traits are on the increase as well.

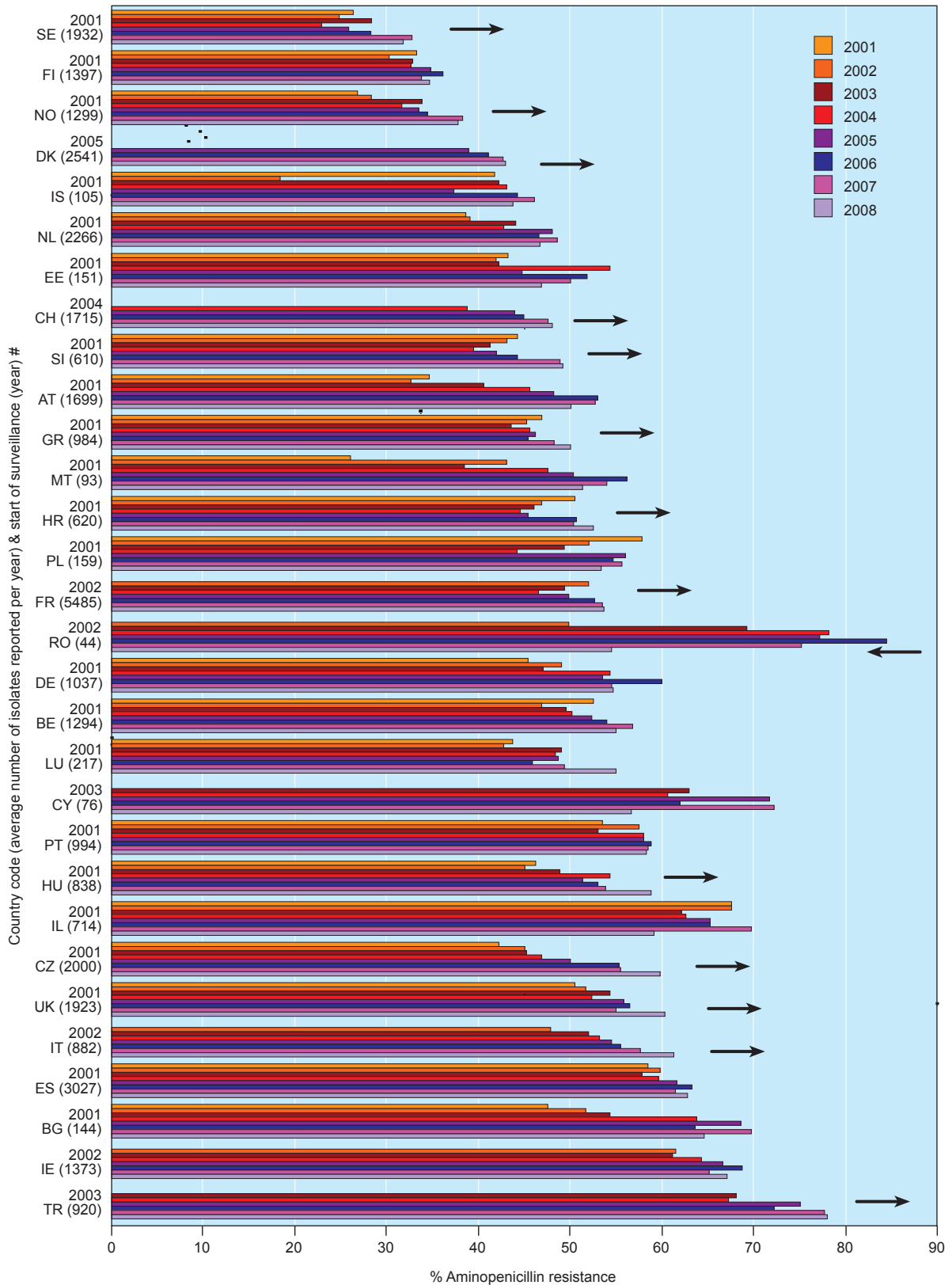


Figure 5.17. *Escherichia coli*: trends of aminopenicillin resistance by country, 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance.

Either the first year of surveillance or the first year with 20 or more isolates reported.

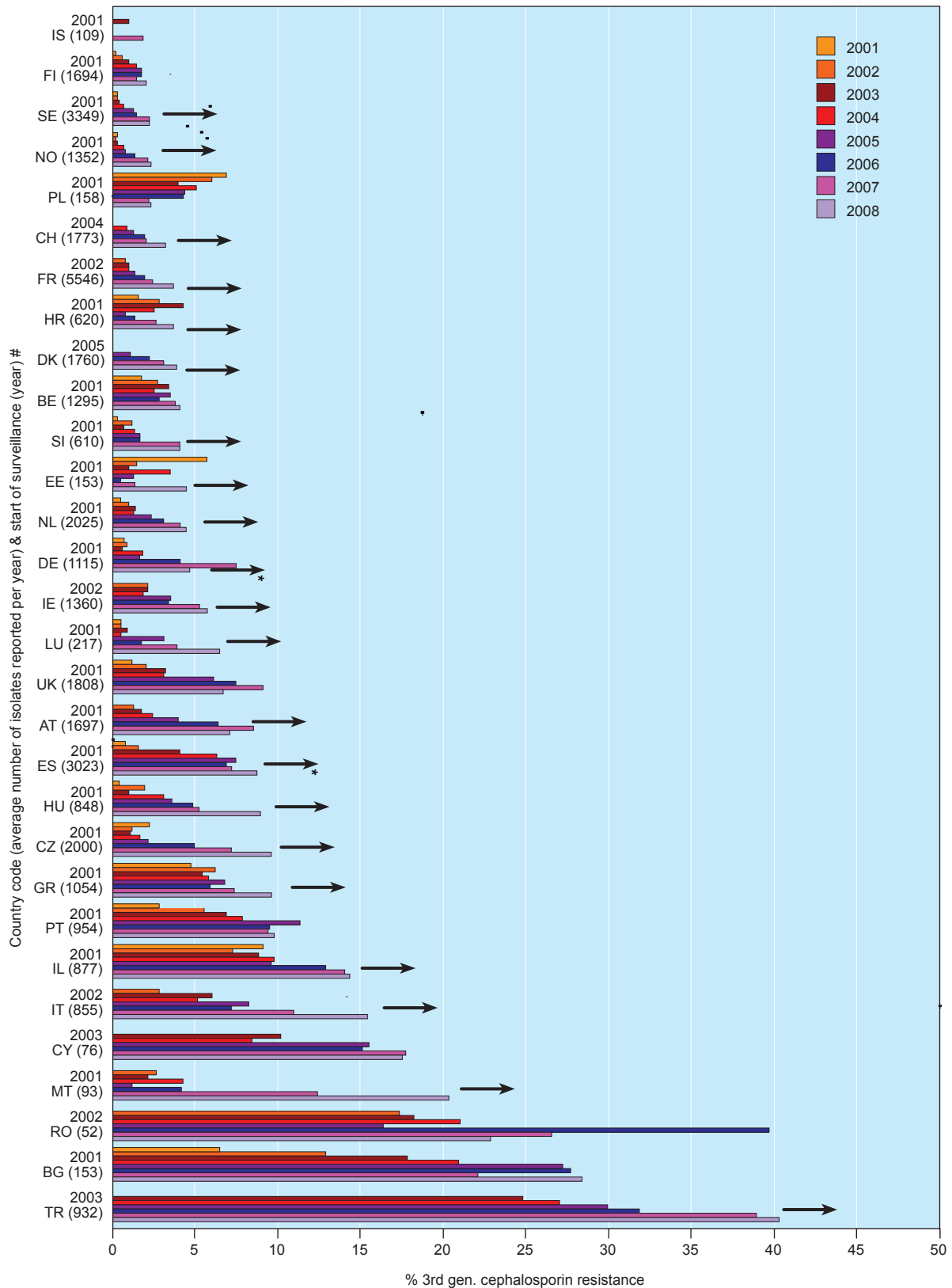


Figure 5.18. *Escherichia coli*: trends of third generation cephalosporin resistance by country, 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

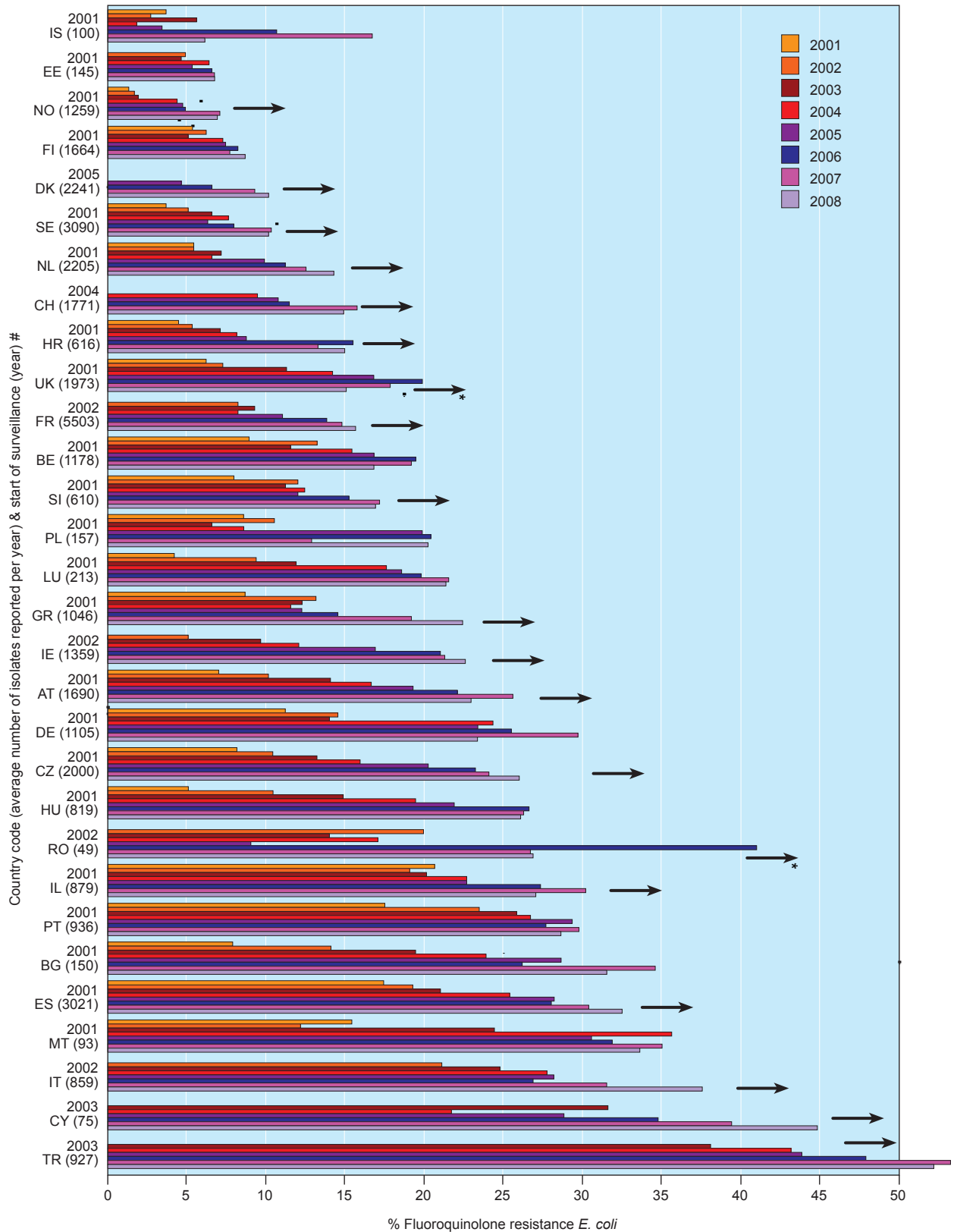


Figure 5.19. *Escherichia coli*: trends of fluoroquinolone resistance by country, 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

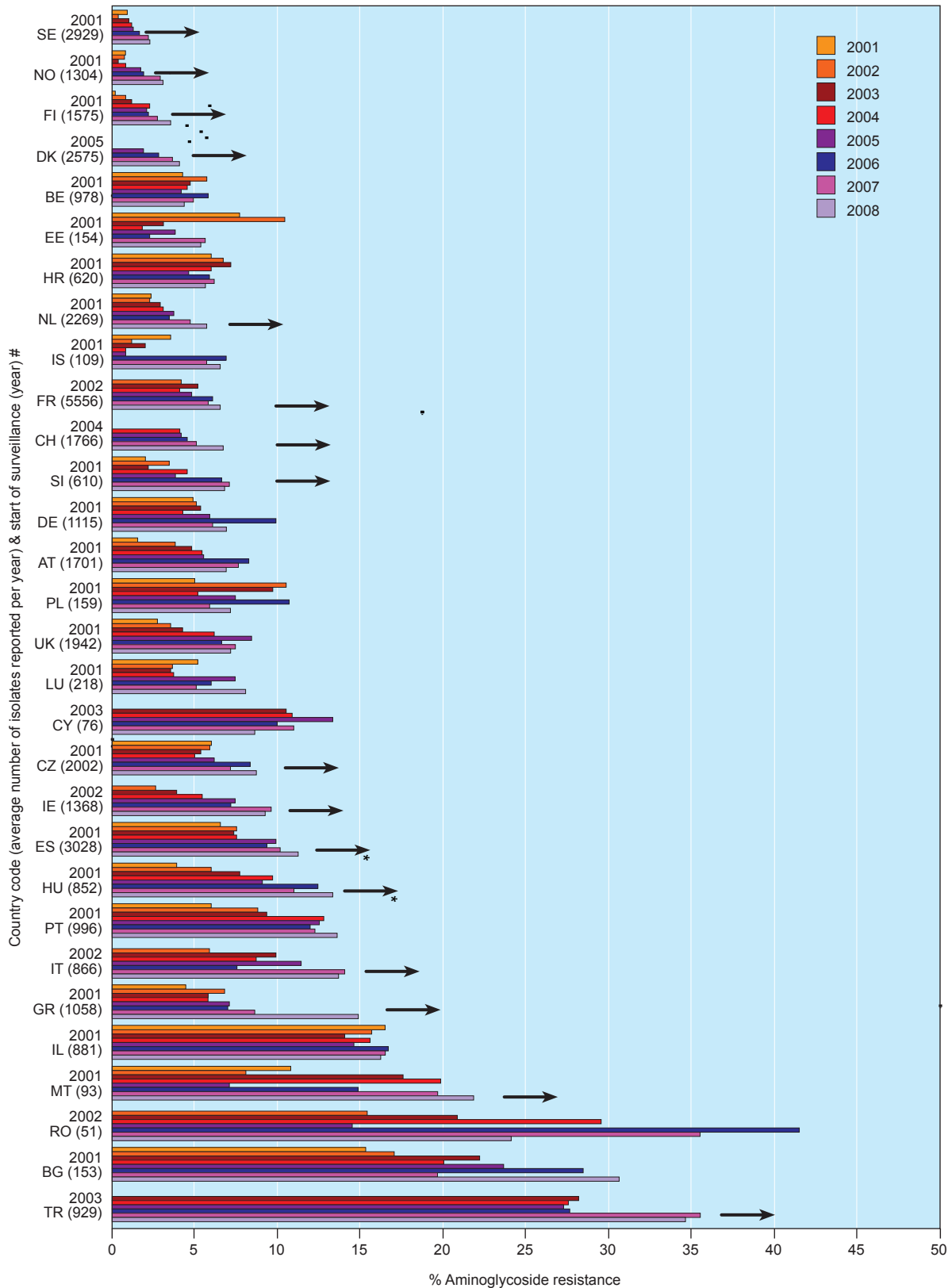


Figure 5.20. *Escherichia coli*: trends of aminoglycoside resistance by country, 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

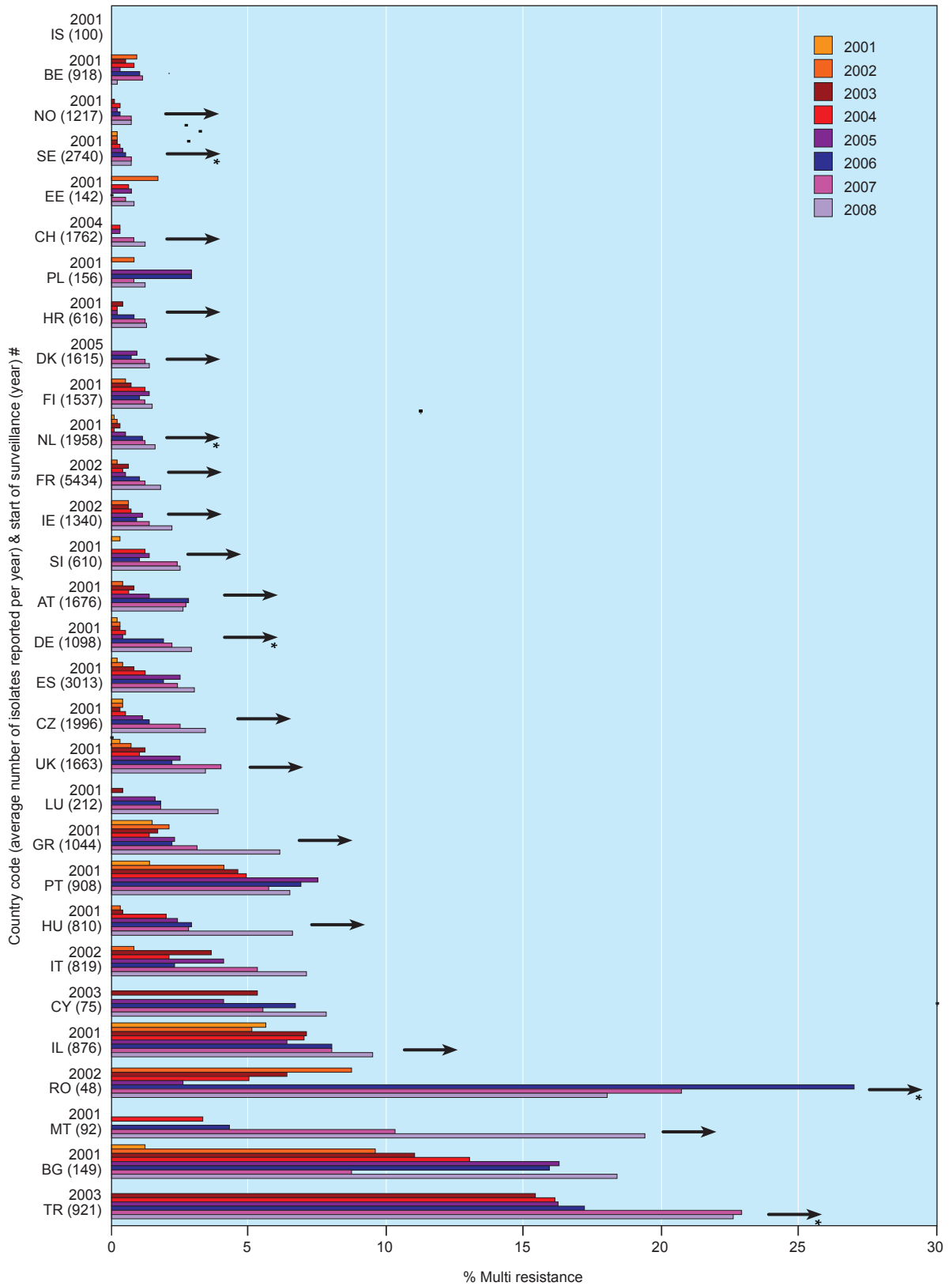


Figure 5.21. *Escherichia coli*: trends of combined resistance (resistant to fluoroquinolones, 3rd gen. cephalosporins and aminoglycosides) by country, 2001-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years. # Either the first year of surveillance or the first year with 20 or more isolates reported.

5.6. *Klebsiella pneumoniae*

5.6.1. Clinical and epidemiological importance

Bacteria of the genus *Klebsiella* are frequent colonizers of the gastrointestinal tract in humans but may also be found on skin, in the oro-pharynx and upper airways in hospitalized individuals. *K. pneumoniae* is frequently associated with opportunistic infections in individuals with impaired natural defences, such as patients with diabetes, alcohol problems, and hospitalized patients with indwelling devices. The most common sites of infection are the urinary and the respiratory tract. Organisms can spread rapidly, from the gastrointestinal tract of patients and via the hands of hospital personnel to other patients, leading to nosocomial outbreaks. *Klebsiella pneumoniae* is the second most frequent cause of gram-negative blood stream infections after *Escherichia coli*. The mortality rates for *Klebsiella pneumoniae* pneumonia depend on the severity of the underlying condition and may be as high as 50%, even when appropriate antibiotic treatment is given.

Resistance mechanisms

Similar to *E. coli*, *K. pneumoniae* can be resistant to multiple antibiotics, 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 against aminopenicillins. Moreover, this organism readily acquires plasmid-mediated resistance determinants. Therefore, many novel ESBL variants were initially identified in *K. pneumoniae* and were only subsequently found in *E. coli*. This central role of Klebsiellae underlines their epidemiological importance as this genus appears to be crucial in the acquisition of novel resistance mechanisms (ESBL-based as well as carbapenemases) and their subsequent dissemination among other enterobacteriaceae. Since resistance mechanisms do not significantly differ from those described for *E. coli*, the reader is referred to paragraph 5.5 for further details (35).

5.6.2. *Klebsiella pneumoniae* resistance trends: 2005-2008

EARSS began collecting AST results for invasive *K. pneumoniae* in 2005. In 2008, 12,227 isolates were reported from 31 countries. This year, for the first time, we were able to calculate trends in time, as results are available now from the past four years. Please keep in mind that the differences in resistance observed between 2005 and 2008 can be due to changes in susceptibility of *K. pneumoniae*, but are also related to the difference in the number of countries reporting (2005: 24, 2006: 30, 2007: 28, 2008: 31), and can be due to an increase of isolates reported per country.

Third generation cephalosporins

In 2008, third generation cephalosporin resistance varied substantially between countries. Nine countries (out of 31) reported resistance levels against 3rd generation cephalosporins less than 10%. Six European countries reported proportions below 5% namely, Switzerland (3%, n=448), Finland (2%, n=288), Iceland (4%, n=24), Malta (0%, n=36), Norway (2%, n=341), Sweden (2%, n=825). Eleven countries reported between 25% and 50%, Bosnia and Herzegovina (44%, n=39), Cyprus (35%, n=62), Czech Republic (48%, n=1493), Hungary (35%, n=369), Israel (38%, n=351), Italy (38%, n=351), Lithuania (36%, n=53), Poland (37%, n=19), Portugal (26%, n=533), Slovenia (26%, n=157), and Turkey (45%, n=711). Four countries reported 50% or more: Bulgaria (73%, n=49), Greece (66%, n=1080), Croatia (54%, n=330) and Latvia (58%, n=31) (Figure 5.22, Annex 3.5).

A significant increase in third generation cephalosporin resistance was found in many of the countries reporting high levels of resistance, Bulgaria, Greece, Croatia, Czech Republic, Italy and Hungary. A significant increase over the last four years was also seen in France and the Netherlands (Figure 5.26).

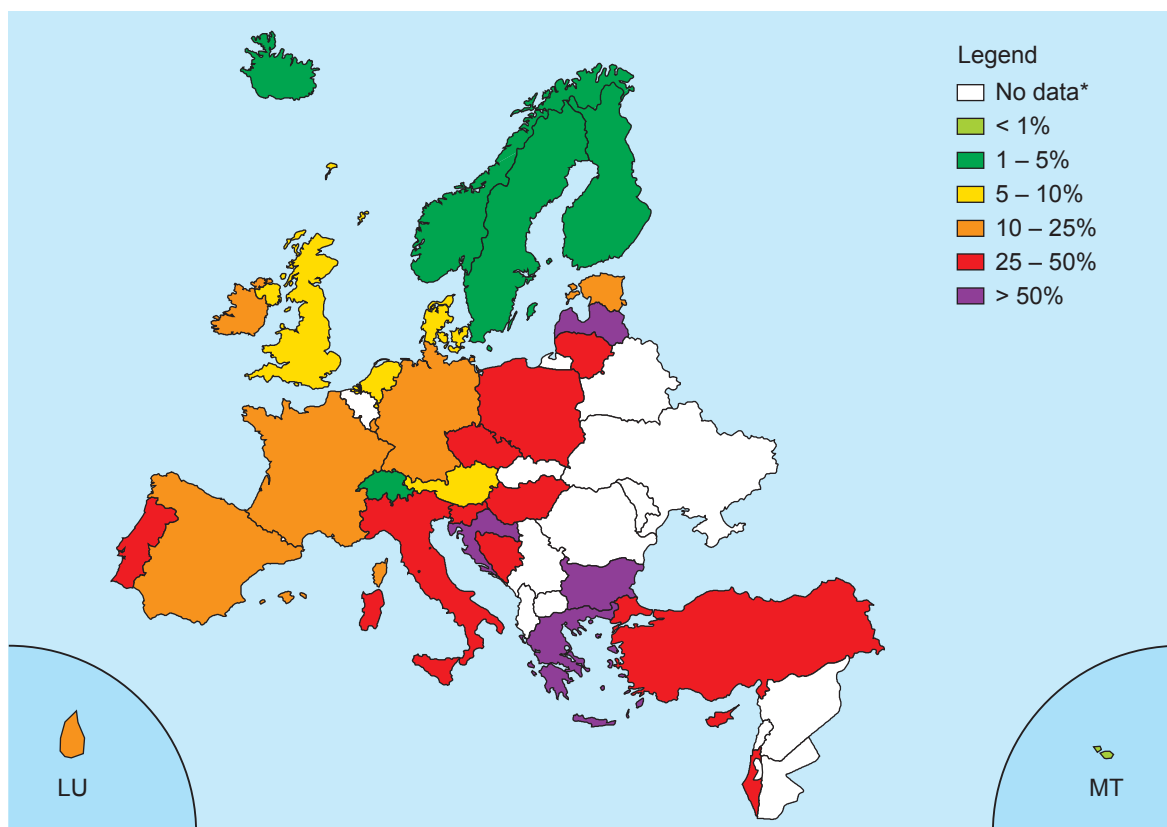


Figure 5.22. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to 3rd generation cephalosporins in 2008.

* These countries did not report any data or reported less than 10 isolates.

Fluoroquinolones

In 2008, fluoroquinolone resistance among *K. pneumoniae* in Europe was rather heterogeneous; three countries recorded resistance against fluoroquinolones below 5%: Switzerland (3%, n=448), Finland (2%, n=287), and Norway (4%, n=340), while other countries report more than 50%, Czech Republic (52%, n=1,492), Bulgaria (52%, n=48) and Greece (64%, n=1,067).

Significant increases over the last four years were seen in all countries reporting high levels of resistance. Resistance levels from the UK decreased significantly over the last four years (Figure 5.23, 5.27, Annex 3.5).

Aminoglycosides

Low resistance proportions were found in the northern part of Europe. Resistance proportions were 2% or less in Norway (1%, n=340), Finland (2%, n=281) and Sweden (1%, n=825). Proportions above 50% were found in Bulgaria (59%, n=49), Greece (55%, n=1075), Croatia (51%, n=333), and Latvia (55%, n=31).

A significant increase over the last four years was seen in Czech Republic, France, Croatia, Hungary, Italy and the Netherlands (Figure 5.24, 5.28, Annex 3.5).

Carbapenems

Although reporting of AST results for carbapenems has not been obligatory in EARSS until now, all countries reported carbapenem susceptibility. In 2008, data were available for 84% of all isolates. Carbapenem resistance is still absent in most countries. Seven countries reported from 1% to 5% resistance, Bosnia and Herzegovina (3%, n=36), Italy (2%, n=309), Latvia (3%, n=31), Norway (1%, n=289), Portugal (1%, n=138), Turkey (3%, n=633) and the UK (1%, n=242). In three countries

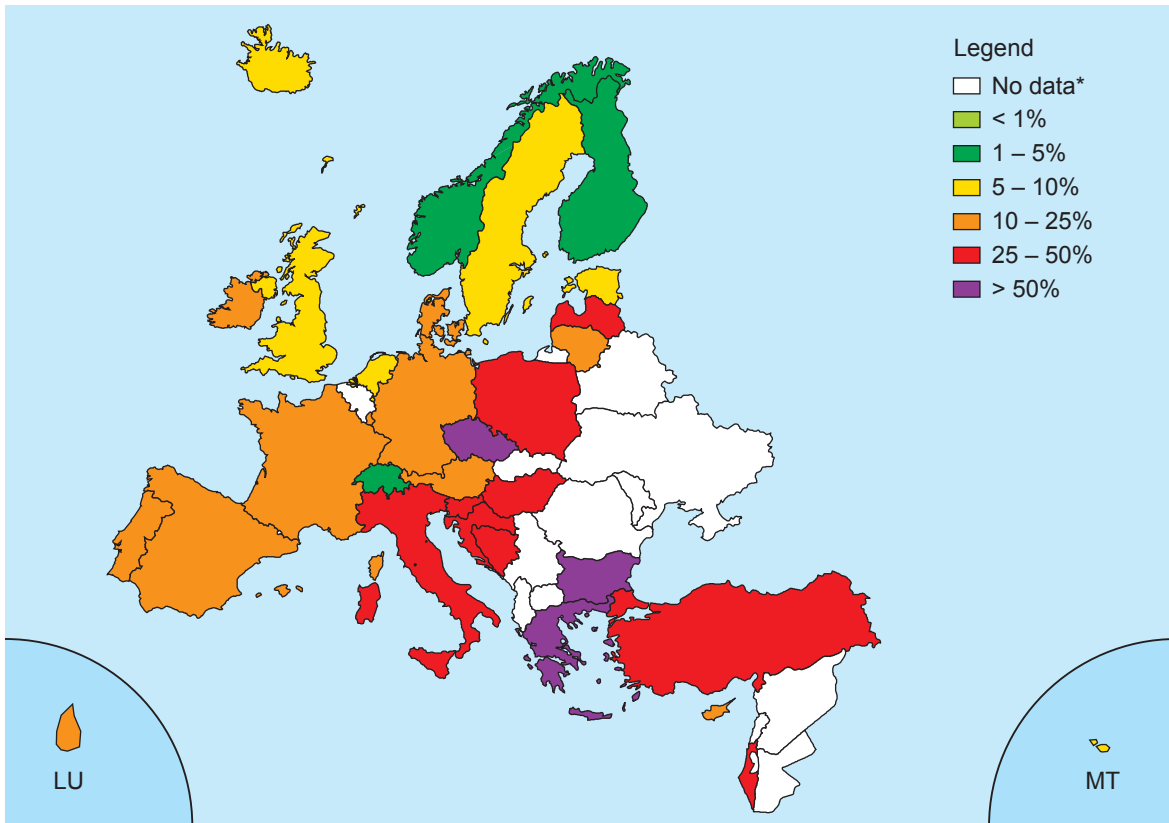


Figure 5.23. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to fluoroquinolones in 2008.

* These countries did not report any data or reported less than 10 isolates.

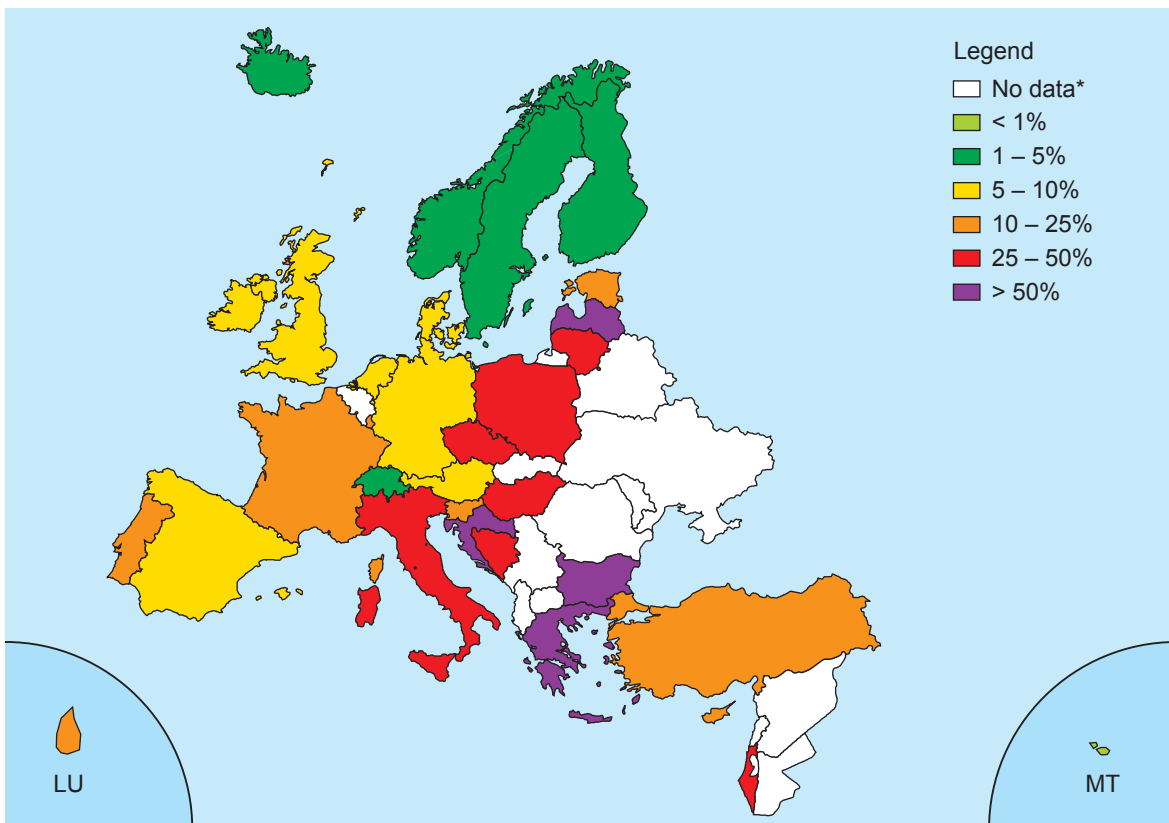


Figure 5.24. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to aminoglycosides in 2008.

* These countries did not report any data or reported less than 10 isolates.

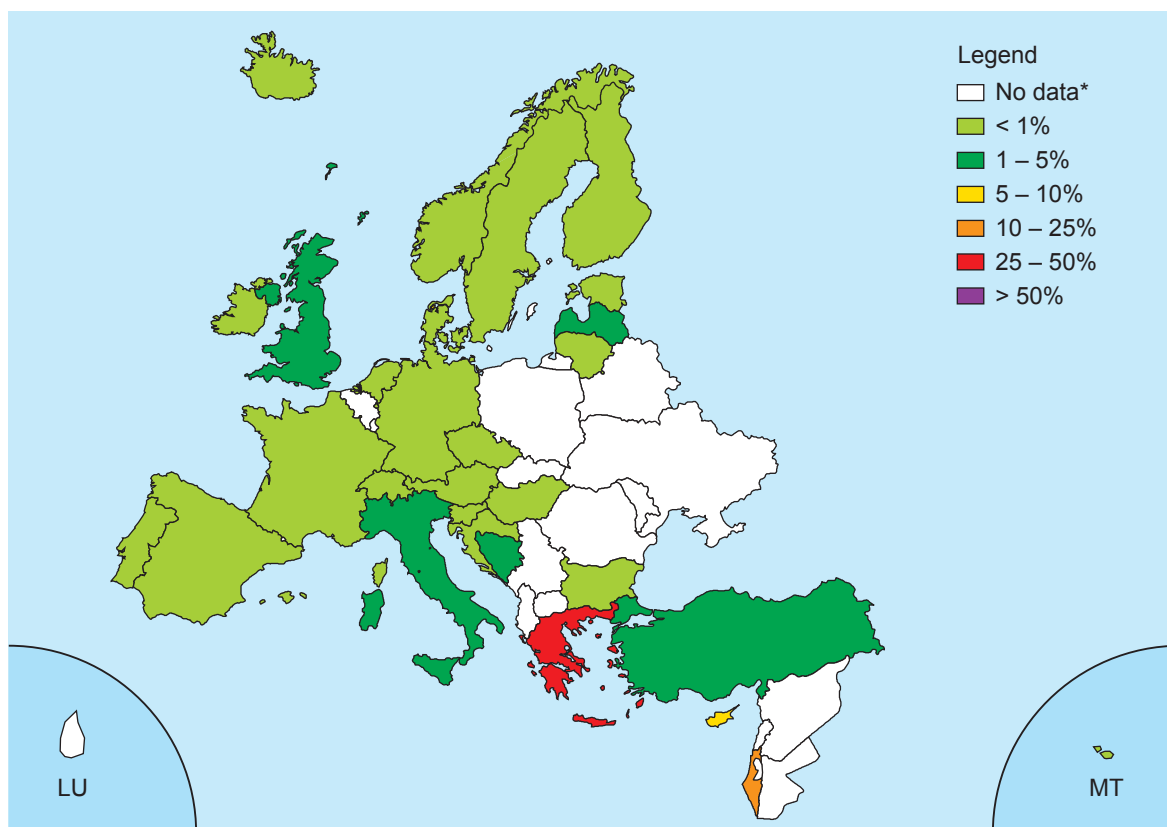


Figure 5.25. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2008.

* These countries did not report any data or reported less than 10 isolates.

carbapenem resistance is considerably higher: Cyprus (10%, n=62), Greece (37%, n=1,074) and Israel (19%, n=350) (29;44).

Since carbapenems are regarded as reserve antibiotics with life-saving potential when isolates show resistance to other antibiotics (36), it is important to monitor the susceptibility of this group of antibiotics (Figure 5.25, Annex 3.5).

Combined resistance

In 2008, 66% of the *Klebsiella pneumoniae* isolates displayed susceptibility to fluoroquinolones, 3rd generation cephalosporins, and aminoglycosides. All other isolates were resistant to at least one of the other antibiotic classes. As shown in Table 5.3, single resistance was rather rare (8%), and the most frequent pattern was combined resistance against all three classes (14%). Ten countries reported combined resistance of more than 20%, namely Bosnia and Herzegovina (26%, n=38), Bulgaria (44%, n=48), Czech Republic (32%, n=1,484), Greece (51%, n=1,063), Croatia (38%, n=320), Hungary (27%, n=365), Israel (28%, n=351), Italy (22%, n=278), Latvia (29%, n=31) and Poland (21%, n=19) (Annex 3.5). The combined resistance levels of nine countries showed a significant increase over the last four years: Bulgaria (from 21% to 44%), Czech Republic (from 17% to 32%), Spain (from 4% in 2005, 1% in 2006, to 4% in 2008), France (from 2% to 13%), Greece (from 46% to 51%), Croatia (from 15% to 38%), Hungary (from 22% to 27%), Italy (from 3% to 22%), and the Netherlands (from 2% to 4%) (Figure 5.29). In Ireland the trend (increase) was only significant for the laboratories reporting for the whole period, but not when data from all laboratories were included.

Table 5.2. Overall resistance and resistance combinations among invasive *Klebsiella pneumoniae* isolates tested against all three classes of drugs (according to the EARSS protocol*) (n= 9480) in Europe, 2008. Intrinsic resistance against aminopenicillins is excluded; therefore results for only 3 classes are illustrated.

***Reporting of carbapenems susceptibility was not obligatory within EARSS in 2008.**

Resistance pattern	Number	% of total
fully susceptible	6,568	69.3
Single resistance (to indicated drug classes)		
fluoroquinolones only	379	4.0
3 rd generation cephalosporins only	246	2.6
aminoglycosides only	125	1.3
Resistance to two classes of antimicrobial drugs		
fluoroquinolones+aminoglycosides	140	1.5
3 rd generation cephalosporins+fluoroquinolones	405	4.3
3 rd generation cephalosporins+aminoglycosides	294	3.1
Resistance to three classes of antimicrobial drugs		
3 rd generation cephalosporins+fluoroquinolones+aminoglycosides	1,323	14.0

5.6.3. Conclusions

In *K. pneumoniae* a high prevalence of resistant strains to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides becomes evident in central and south-eastern Europe. Many of these strains have combined resistance and the most frequent phenotype shows resistance to all three antimicrobial classes recorded by EARSS. Although carbapenems are still effective in most countries, the rapid emergence and dissemination of strains with carbapenemase production are threatening the effectiveness of this last line therapeutic option. It is thus necessary to closely monitor the effectiveness of carbapenems and be aware that carbapenemase-positive isolates may not be detected by automated systems. EARSS therefore recommends to further scrutinise all isolates with MIC \geq 0.5 mg/l.

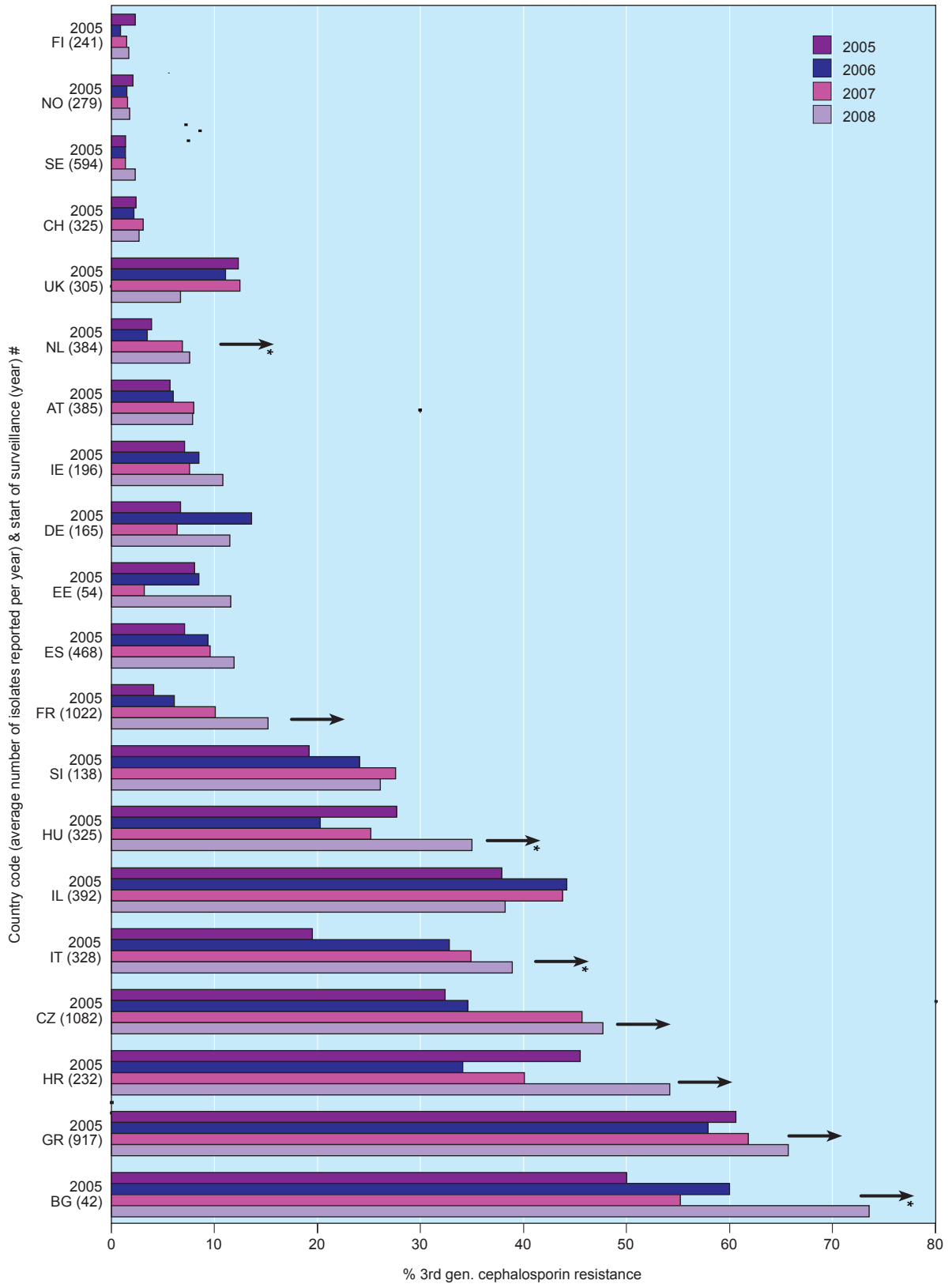


Figure 5.26. *Klebsiella pneumoniae*: trends of third generation cephalosporin resistance by country, 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting for all four years.
 # Either the first year of surveillance or the first year with 20 or more isolates reported.

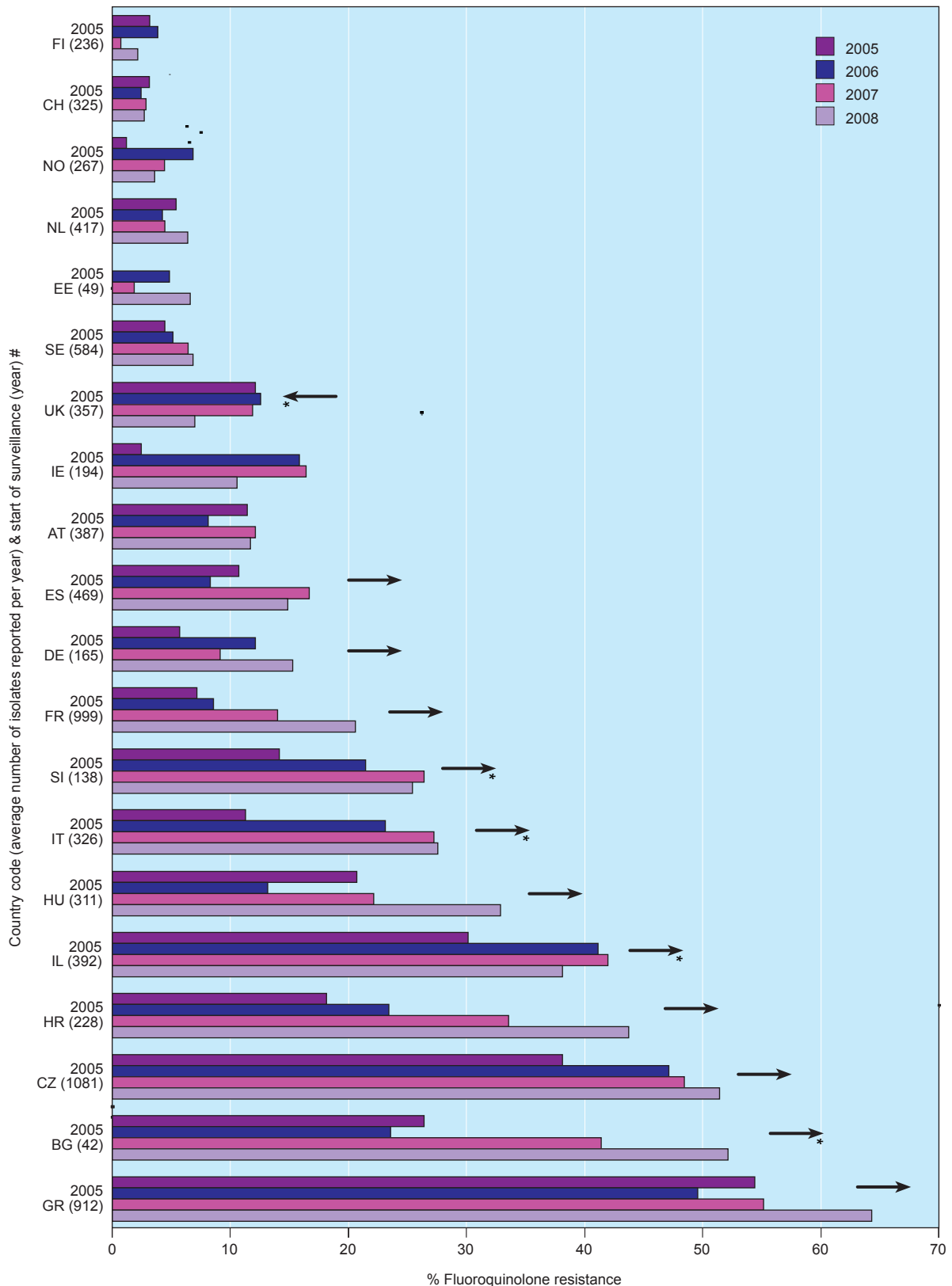


Figure 5.27. *Klebsiella pneumoniae*: trends of fluoroquinolone resistance by country, 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting for all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

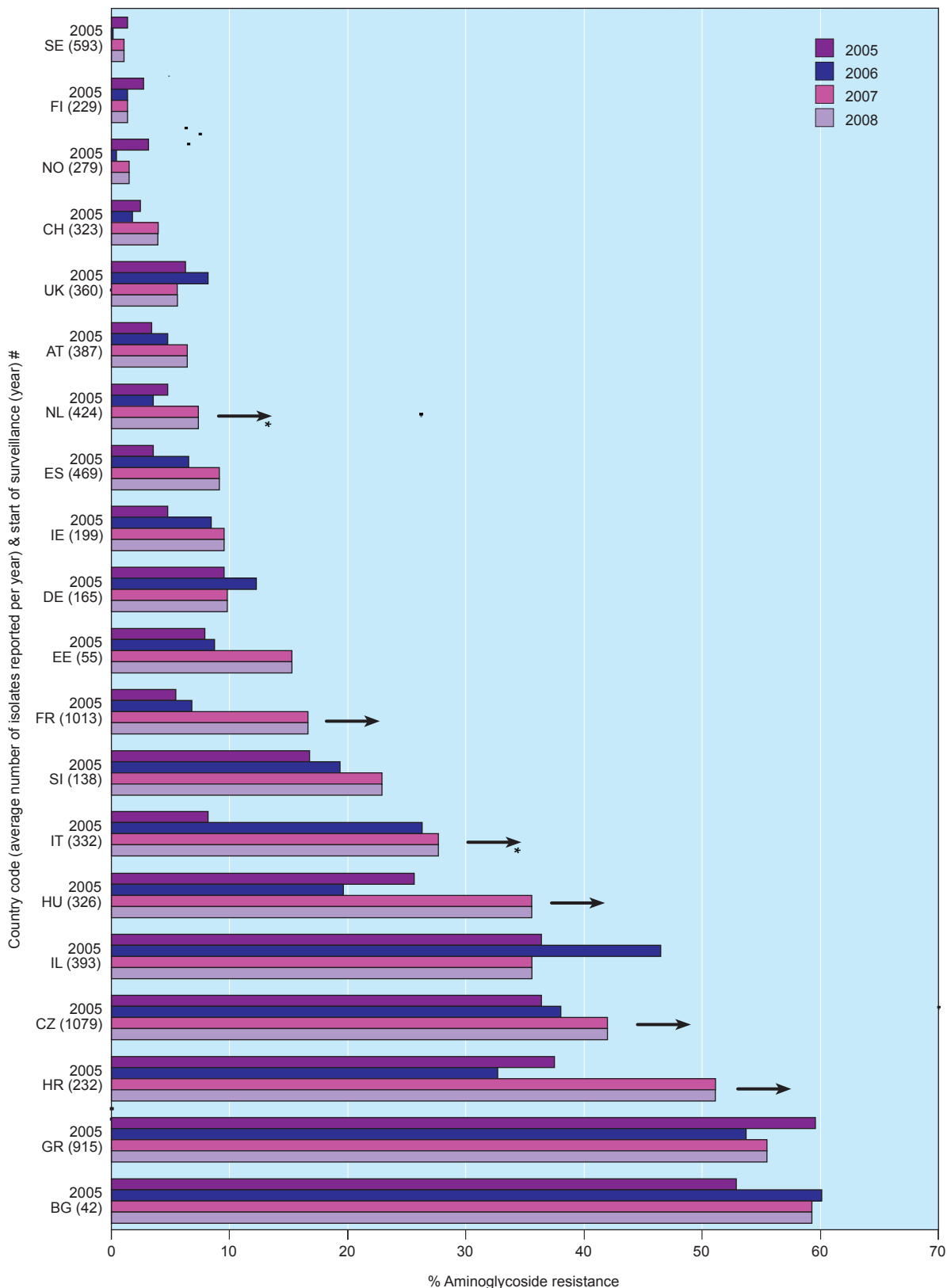


Figure 5.28. *Klebsiella pneumoniae*: trends of aminoglycoside resistance by country, 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting for all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

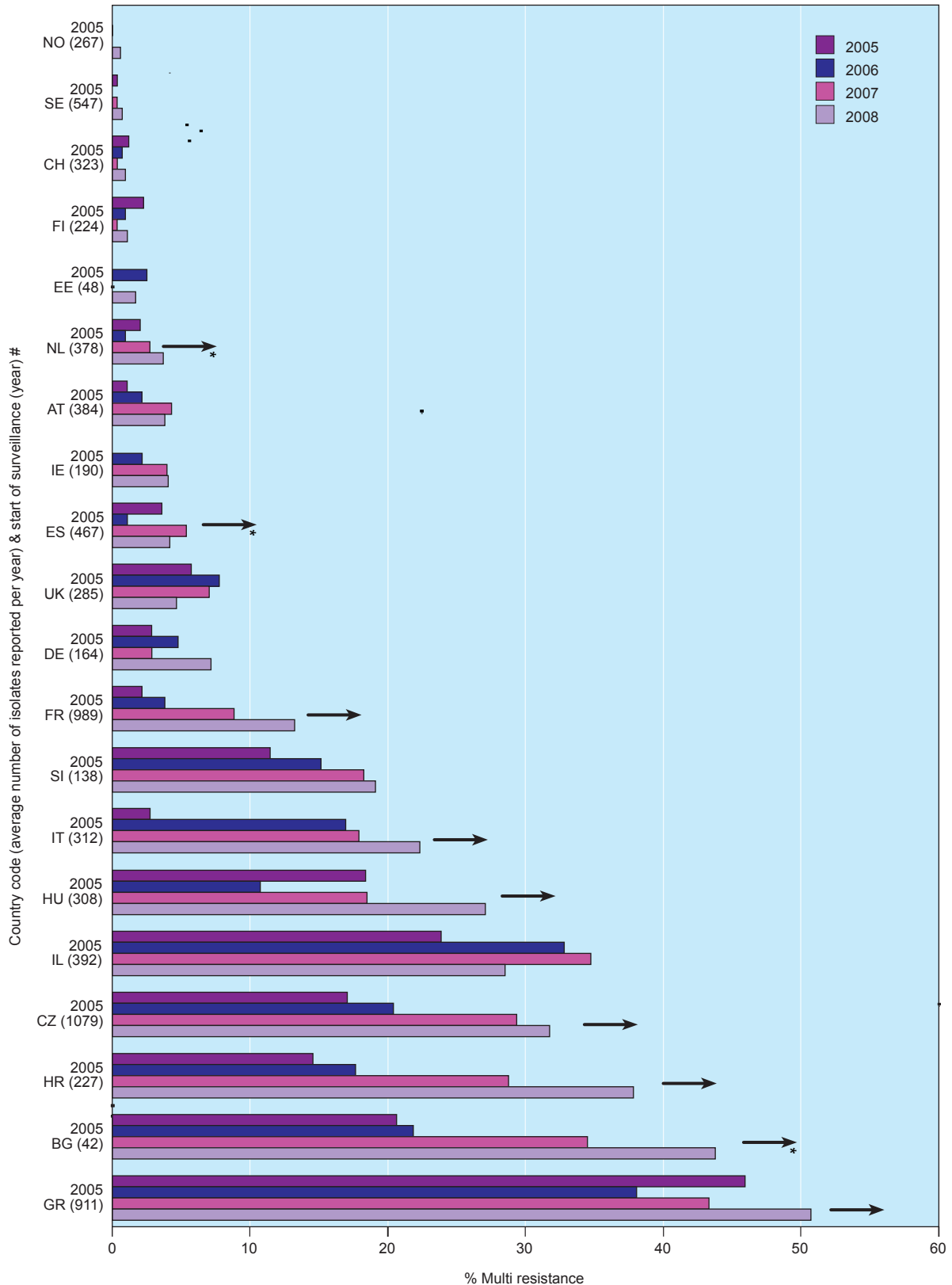


Figure 5.29. *Klebsiella pneumoniae*: trends of combined resistance (resistant to fluoroquinolones, 3rd gen. cephalosporins and aminoglycosides) by country, 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance.

The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting for all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

5.7. *Pseudomonas aeruginosa*

5.7.1. Clinical and epidemiological importance

Pseudomonas aeruginosa is a non-fermenting gram-negative bacterium that is ubiquitously present in aquatic environments in nature. It is an opportunistic pathogen for plants, animals and humans, and is a major and dreaded cause of infection among nosocomial patients. Because of its ubiquitous presence, its enormous versatility and intrinsic tolerance to many detergents, disinfectants and antimicrobial compounds is difficult to control *P. aeruginosa* in hospitals and institutional environments. Moreover, *P. aeruginosa* is a frequent cause for skin infections such as folliculitis and otitis externa in recreational and competitive swimmers. It causes the most important bacterial complication in patients with cystic fibrosis leading to chronic colonization and intermittent exacerbations ranging from bronchiolitis to acute lung syndrome. Finally, *P. aeruginosa* is a common pathogen found in burns units and in these locations almost impossible to eradicate by classical infection control procedures.

Resistance mechanisms

P. aeruginosa is intrinsically resistant to the majority of antimicrobial compounds due to its ability to exclude various molecules from penetrating its outer membrane and/or to efflux them via several efflux systems. Acquired resistance in *P. aeruginosa* is caused by one or more of five mechanisms: i) mutational modification of antibiotic target sites such as gyrase, topoisomerase or ribosomal proteins which confer resistance to fluoroquinolones or aminoglycosides, ii) constitutional or inducible derepression of chromosomally coded AmpC beta-lactamase, iii) mutational loss of outer membrane proteins preventing the uptake of antimicrobial substances such as carbapenems, iv) efficient efflux systems, that can confer resistance to beta-lactams, fluoroquinolones, tetracycline, chloramphenicol, trimethoprim and aminoglycosides, and v) plasmid-mediated expression of various beta-lactamases and aminoglycoside modifying enzymes that can confer resistance to antipseudomonas cephalosporins (ESBLs), carbapenems (metallo-beta-lactamases) and aminoglycosides (31;38).

5.7.2. *Pseudomonas aeruginosa* resistance trends: 2005-2008

EARSS began collecting AST results for invasive *P. aeruginosa* in 2005, and 3,887 isolates were reported from 23 countries in this first year alone. In 2008, 8,252 isolates were reported by 32 countries. This year, for the first time, we were able to calculate trends over the past four years.

Piperacillin and Piperacillin/ Tazobactam

In the EARSS database, the proportion of piperacillin resistance was higher than that for the piperacillin-tazobactam combination owing to the fact that the beta-lactamase inhibitor (tazobactam), although not effective against the AmpC beta-lactamase, has some residual inhibitory effect on additional plasmid mediated betalactamases frequently present in *P. aeruginosa*. All countries reported susceptibility to piperacillin-tazobactam with or without susceptibility results for piperacillin for the vast majority of *P. aeruginosa* isolates, except for Bosnia and Herzegovina, which reported piperacillin only for a selection of isolates. In 14 countries resistance rates did not exceed 10%. Resistance proportions of 25% and more were reported from Bosnia and Herzegovina (25%, n=8), Bulgaria (48%, n=23), the Czech Republic (27%, n=568), Greece (34%, n=915), Croatia (34%, n=220), Latvia (43%, n=7), Malta (45%, n=31), Poland (32%, n=22), and Romania (25%, n=8). For a number of countries, these resistance rates should be considered with in mind the low number of isolates reported.

The only significant change in the past four years was seen in Germany (n=167), where resistance rates decreased from 18% in 2005 to 9% in 2008 (Figure 5.30, 5.35, Annex 3.6). However, due to low level of participation and changes in hospitals from one year to the next, this may reflect a real change or could be attributed to a change in the composition of the hospital subset.

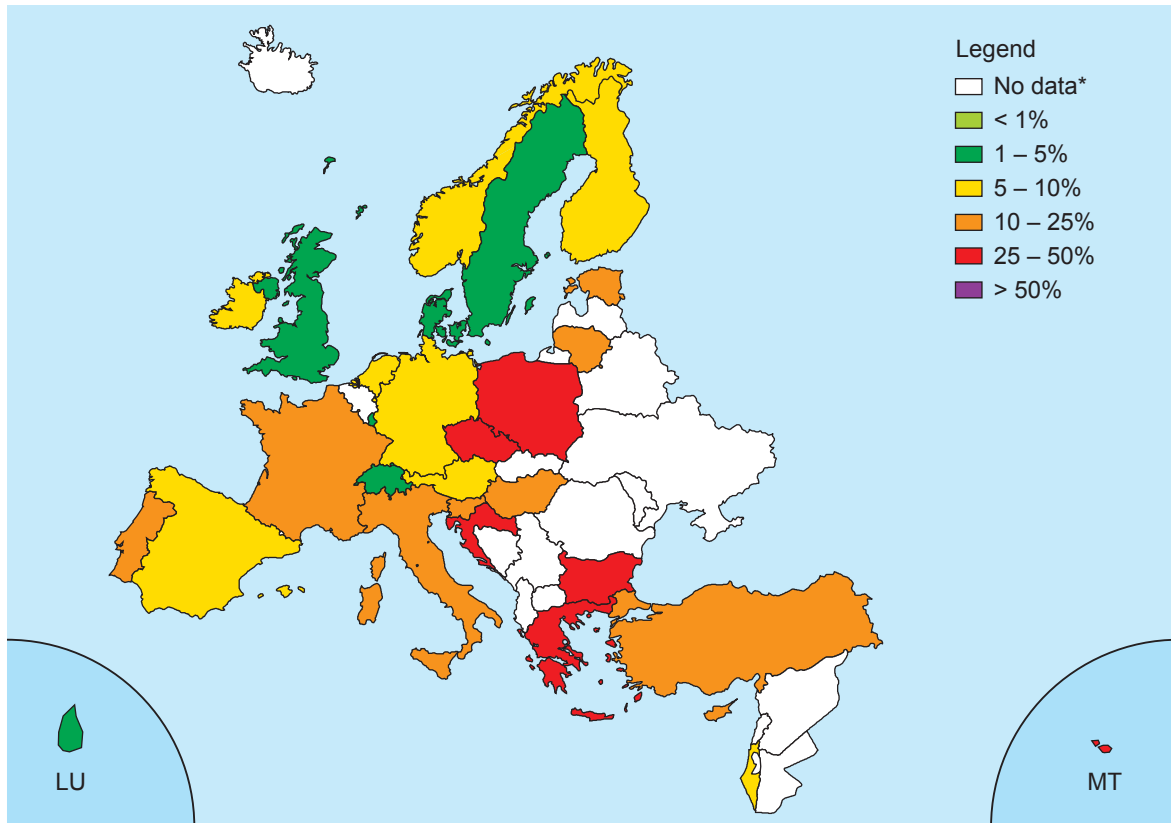


Figure 5.30. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to piperacillins in 2008.

* These countries did not report any data or reported less than 10 isolates.

Ceftazidime

A line can be drawn from Northeast to Southwest Europe, between countries with ceftazidime resistance below and over 10% respectively. Eight countries, mostly situated in the northern part of Europe still reported resistance proportions below 5%, namely Switzerland (n=278), Denmark (n=398), Finland (n=175), Ireland (n=187), Israel (n=7), Luxembourg (n=3), Norway (n=4), and the United Kingdom (n=283). In seven countries ceftazidime resistance was 25% or more, namely Bosnia and Herzegovina (47%, n=15), Bulgaria (55%, n=22), Czech Republic (44%, n=568), Greece (37%, n=915), Latvia (50%, n=8), Malta (45%, n=30), and Poland (27%, n=22).

Israel showed a significant decrease in ceftazidime resistance, from 17% in 2005 to 6% in 2008. Greece reported a significant increase from 27% in 2005 to 37% in 2008. A significant increase was also seen in Spain, although not confirmed in the selection of laboratories (Figure 5.31, 5.36, Annex 3.6).

Fluoroquinolones

Low fluoroquinolone resistance levels (<5%) for invasive *P. aeruginosa* isolates were only found in Denmark (n=349), Iceland (n=7), and Norway (n=147). Most countries (25 of 32) reported 10% or more fluoroquinolone resistance, of which nine more than 25%, coloured orange or red respectively on the map (Figure 5.32).

The trends over the last four years show two upward and two downward trends, in Malta (from 44% to 19%) and France (from 27% to 22%) fluoroquinolone resistance decreased, but Greece (from 39% to 48%) and Spain (from 14% to 23%) showed an increase; in Spain this was not significant for the selected laboratories (Figure 5.37, Annex 3.6).

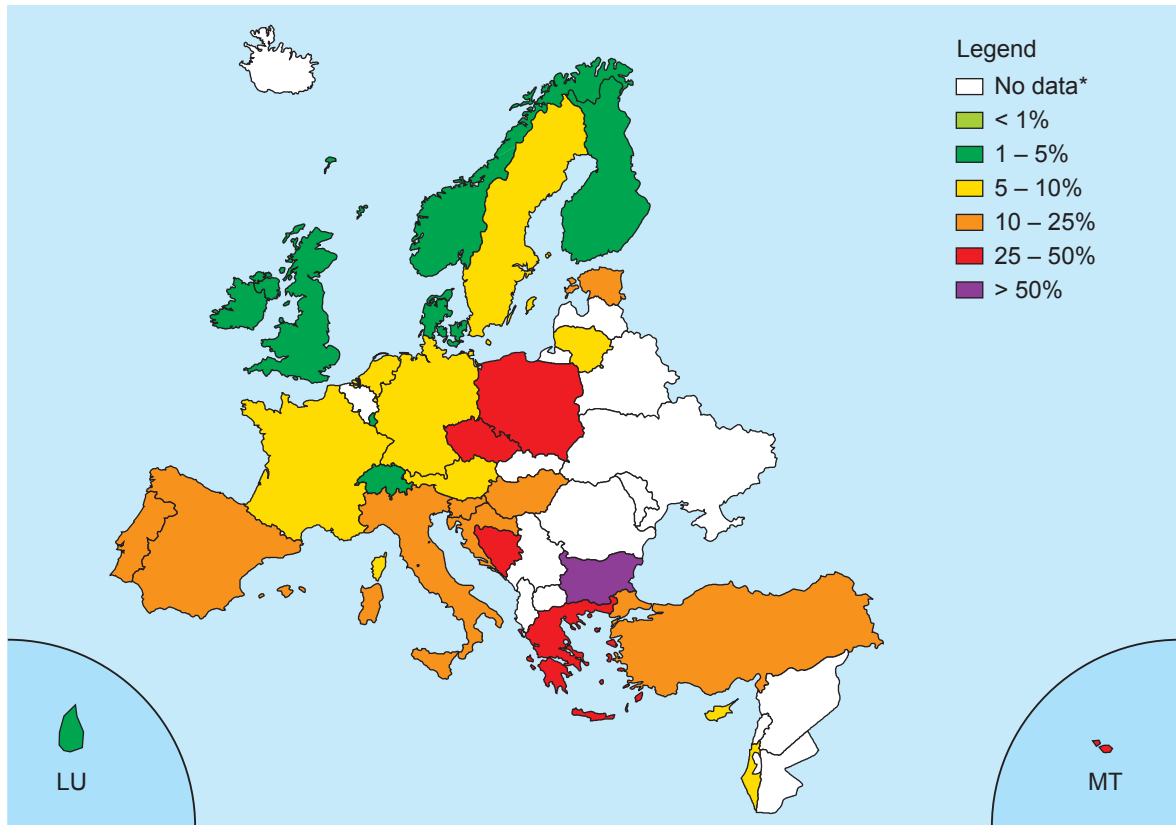


Figure 5.31. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to ceftazidime in 2008.

* These countries did not report any data or reported less than 10 isolates.

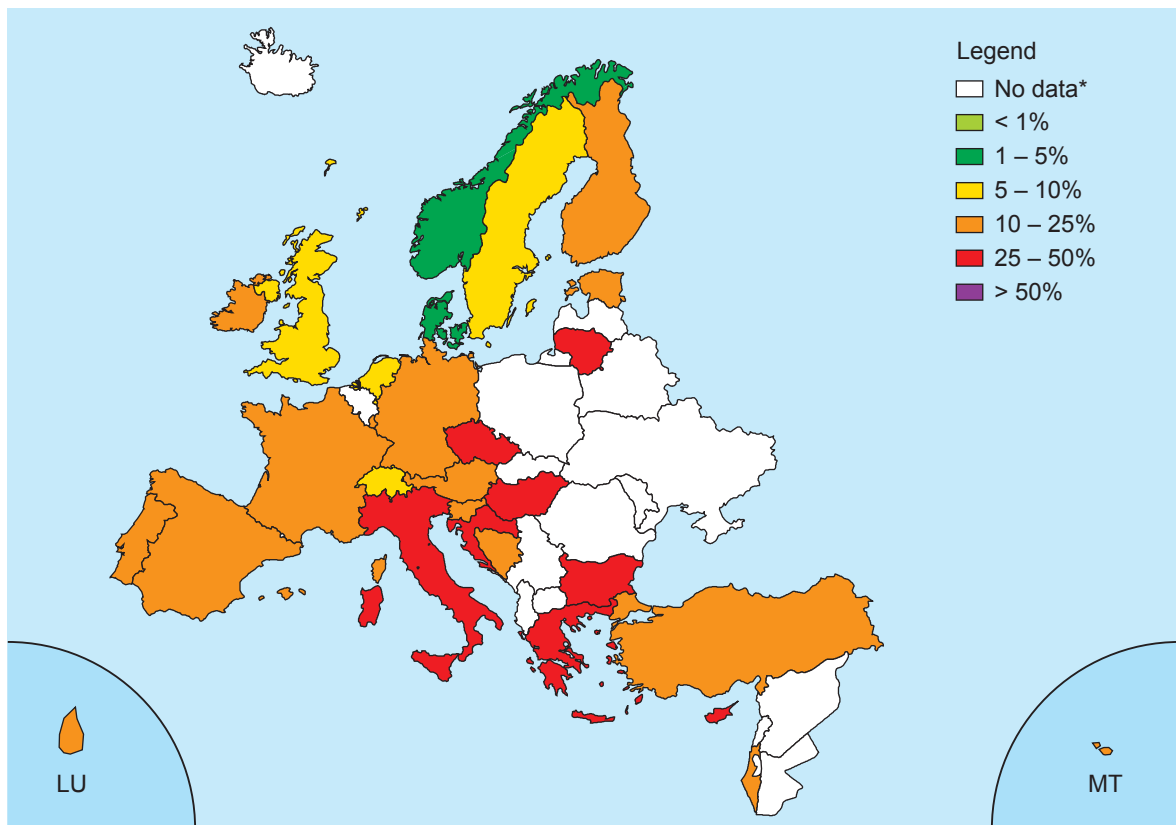


Figure 5.32. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to fluoroquinolones in 2008.

* These countries did not report any data or reported less than 10 isolates.

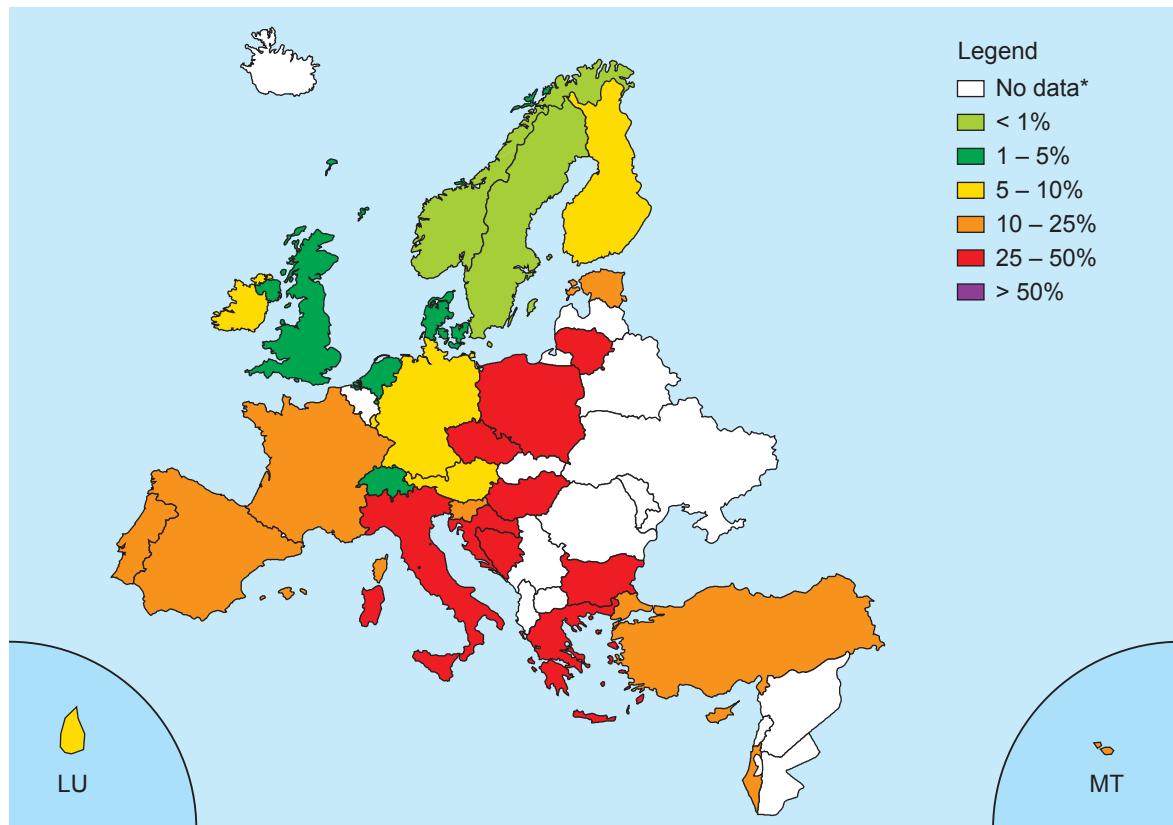


Figure 5.33. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to aminoglycosides in 2006.

* These countries did not report any data or reported less than 10 isolates.

Aminoglycosides

Eleven of 32 countries reported aminoglycoside resistance over 25%. Especially in the southeastern European countries proportions were high, up to 48% in Bulgaria (n=23) and Greece (n=903). Most northern European countries report resistance levels of less than 5%, Denmark (n=420), Iceland (n=7), The Netherlands (n=345), Norway (n=147), Sweden (n=314), Switzerland (n=277), and the United Kingdom (n=311).

Resistance trend figures show three upward arrows and three downward arrows. A significant decrease in resistance proportions over the last four years was seen in France (from 22% to 15%), Israel (from 23% to 18%), and Poland (from 56% to 27%); and in Hungary (from 32% to 26%) only in a selection of laboratories. The Czech Republic (from 28% to 45%), Greece (from 40% to 48%), and Spain (from 4% to 18%) showed a significant increase, although for the latter not confirmed in the selection of laboratories. From Austria (from 6% to 8%) a significant increase was reported only from the selection of laboratories reporting consistently in the last four years (Figure 5.33, 5.38, Annex 3.6).

Carbapenems

Countries differ in the reporting routine for carbapenems. Some hardly or never test for meropenem (France, Malta, Spain, Sweden), whereas others hardly test for imipenem susceptibility (Denmark, Czech Republic, Finland, Iceland, Ireland). We took a pragmatic approach and combined the AST results for both drugs. With this restriction in mind, we were able to draw up the overall distribution of carbapenem resistance without losing too much valuable data (Figure 5.34).

Pseudomonas aeruginosa resistance proportions to carbapenems appear to be rather high all over Europe, as almost three quarters of countries (23 of 32) reported more than 10% carbapenem resist-

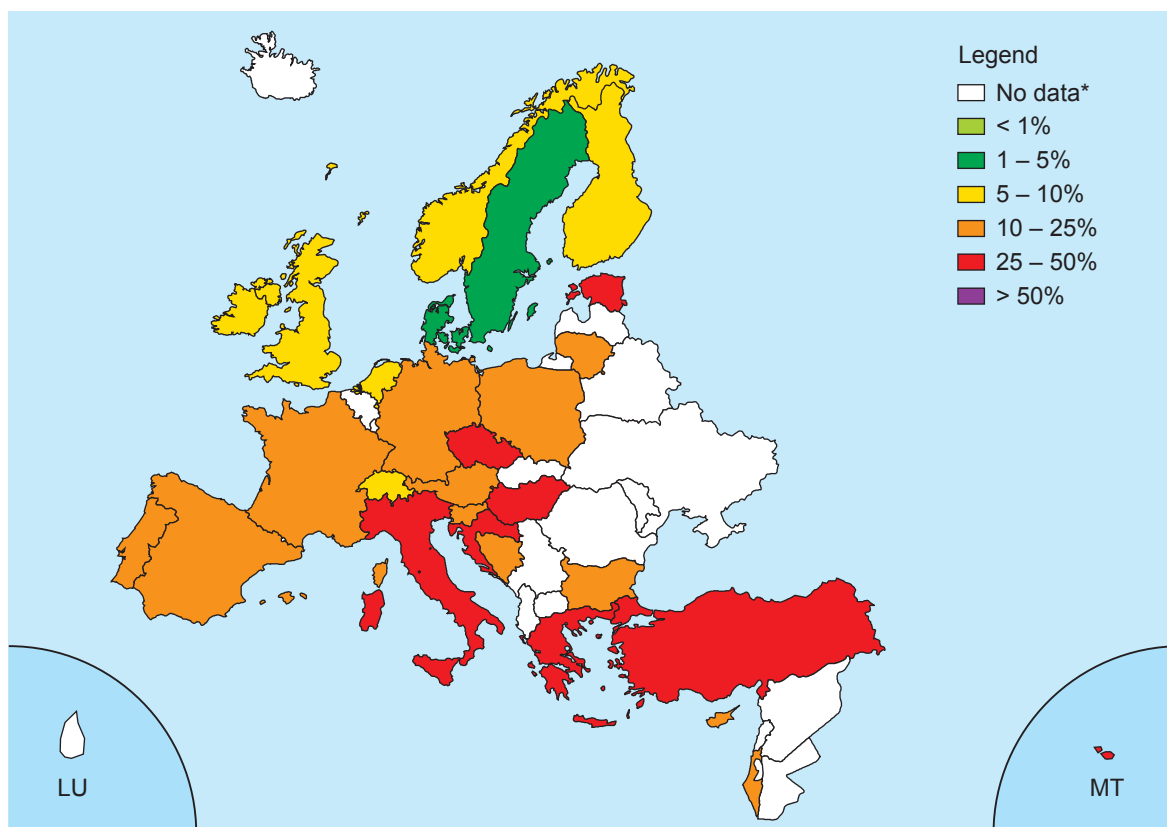


Figure 5.34. *Pseudomonas aeruginosa*: proportion of invasive isolates resistant to carbapenems in 2008.

* These countries did not report any data or reported less than 10 isolates.

ance, displayed in orange or red on the map (Figure 5.34). The highest proportions of resistance were reported by Greece (49%, n=916), Italy (33%, n=161), and Latvia (57%, n=7). All northern European countries still reported resistance below 10%; Finland (6%, n=175), Ireland (6%, n=175), The Netherlands (6%, n=345), Norway (7%, n=145), Switzerland (7%, n=277), United Kingdom (6%, n=251), of which Denmark (1%, n=340), Iceland (0%, n=7), and Sweden (4%, n=279) below 5%. Sweden, Finland and Germany, which all had relatively high resistance rates in 2005, now all showed a significant decrease, for Sweden this was from 18% to 4%, for Germany from 24% to 11%, and for Finland from 15% to 6% respectively. A significant increase was reported from Hungary, from 17% to 26%, and Greece, from 39% to 49% (Figure 5.34, 5.39, Annex 3.6).

Combined resistance

P. aeruginosa isolates were often found to be multi-resistant (17%), i.e. being resistant to three or more antibiotics from the EARSS protocol. What is very striking is that the most dominant phenotype in the EARSS database in 2008 was combined resistance to all the five classes of antimicrobials recorded by EARSS (6%). The second and third most common pattern consisted of single resistance to fluoroquinolones (4%), and dual resistance to fluoroquinolones/ aminoglycosides (3%). The derepressed AmpC phenotype with both piperacillin and ceftazidime resistance could be ascertained in only 1.4% of all resistant isolates.

Trends over the past four years for combined resistance in *Pseudomonas aeruginosa* showed a decline in Finland, Germany, and Turkey. In Finland, and Turkey this was not confirmed in the selection of laboratories reporting consistently in the last four years. In Turkey, resistance rates fell from 40% in 2005 to 21% in 2008. In Germany the decrease was mainly ascribed to a strong decline in 2008 compared to 2007, from 17% to 6% respectively. In Estonia (from 24% to 10%) and The Netherlands

(from 6% to 5%) a significant decrease was only observed for the selection of laboratories reporting consistently in the last four years. In contrast, in Spain (from 5% to 11%) and Greece (from 38% to 46%) an increase in combined resistance was obvious, although in Spain this was not confirmed in the selection of laboratories reporting consistently in the last four years, and in Greece resistance in 2008 was slightly lower compared to 2007 (Fig 5.40, Table 5.3, Annex 3.6).

5.7.3. Conclusions

Combined resistance is the dominant threat imposed by invasive *P. aeruginosa* on Europe. Since resistance in *P. aeruginosa* emerges readily during antibiotic treatment, the time when blood cultures are taken is crucial as any isolate collected after prolonged exposure with antimicrobial chemotherapy will predictably be a multi-resistant phenotype. Assuming the diagnostic habits in Europe are comparable, the picture that our data suggest is that the geographical gradient observed for all other gram-negative pathogens, namely lower resistance in the Northwest and increasing resistance towards the Southeast also holds for *P. aeruginosa*.

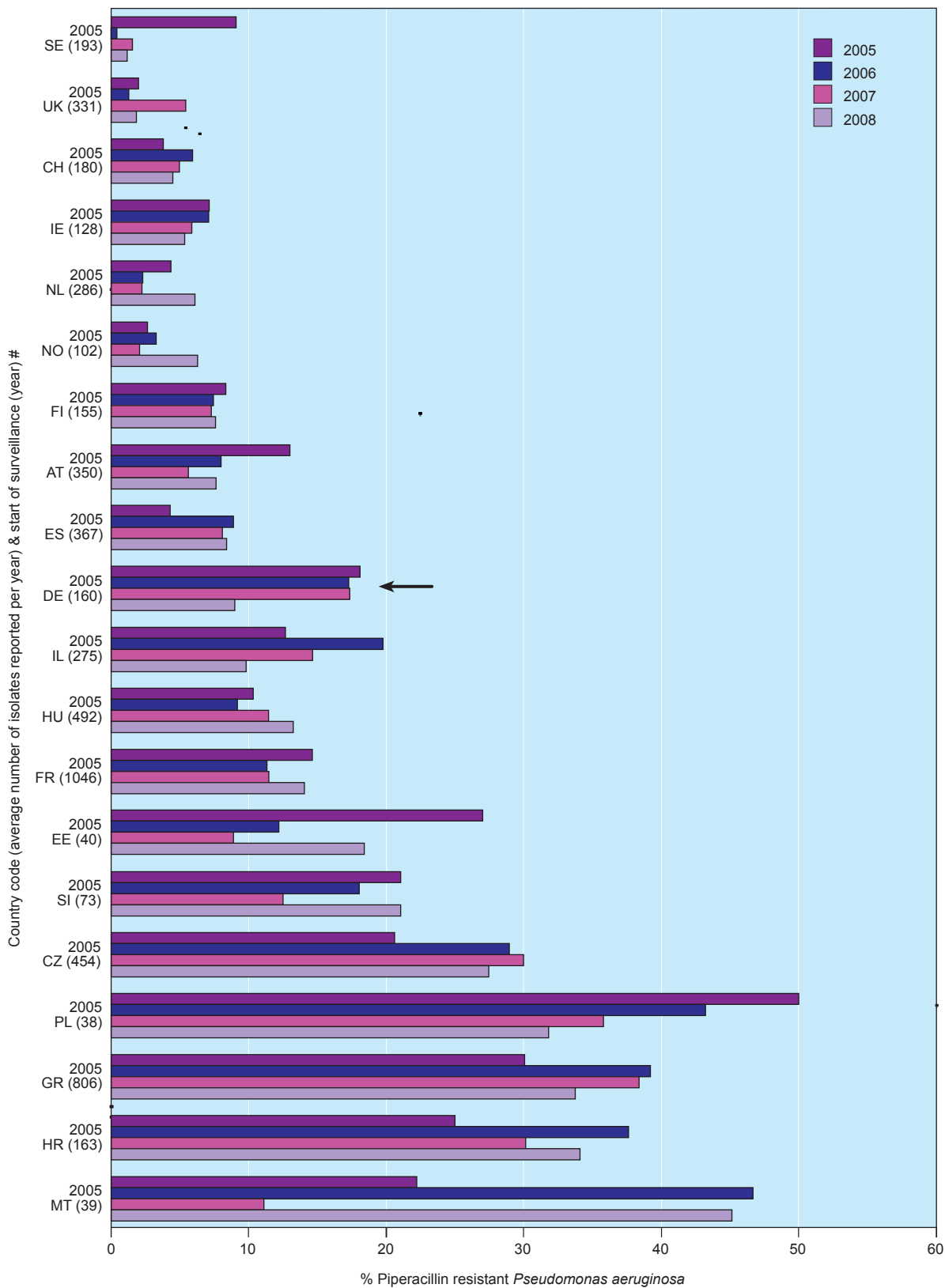


Figure 5.35. *Pseudomonas aeruginosa*: trends of piperacillin resistance by country 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance.

Either the first year of surveillance or the first year with 20 or more isolates reported.

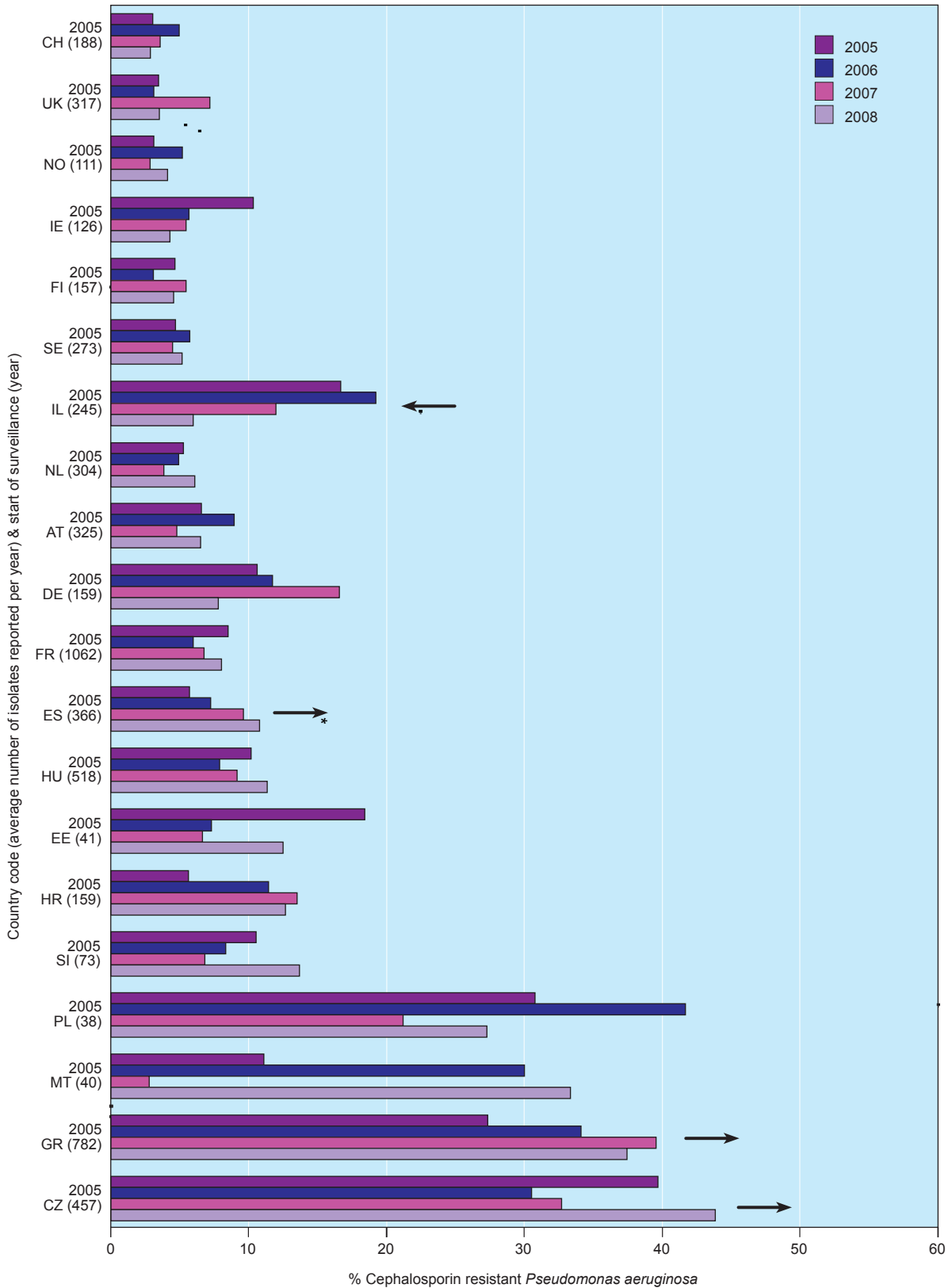


Figure 5.36. *Pseudomonas aeruginosa*: trends of ceftazidime resistance by country 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

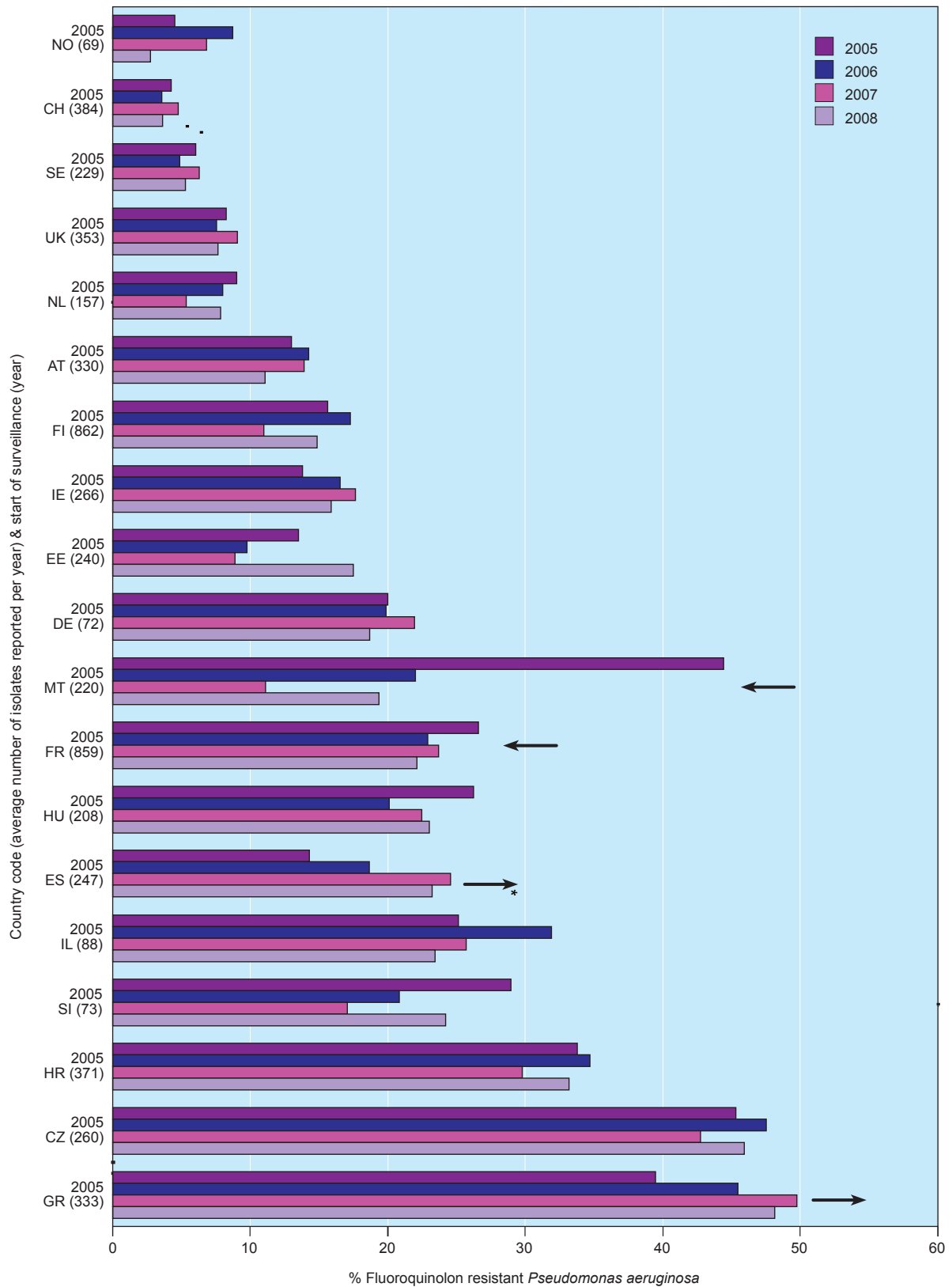


Figure 5.37. *Pseudomonas aeruginosa*: trends of fluoroquinolone resistance by country 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

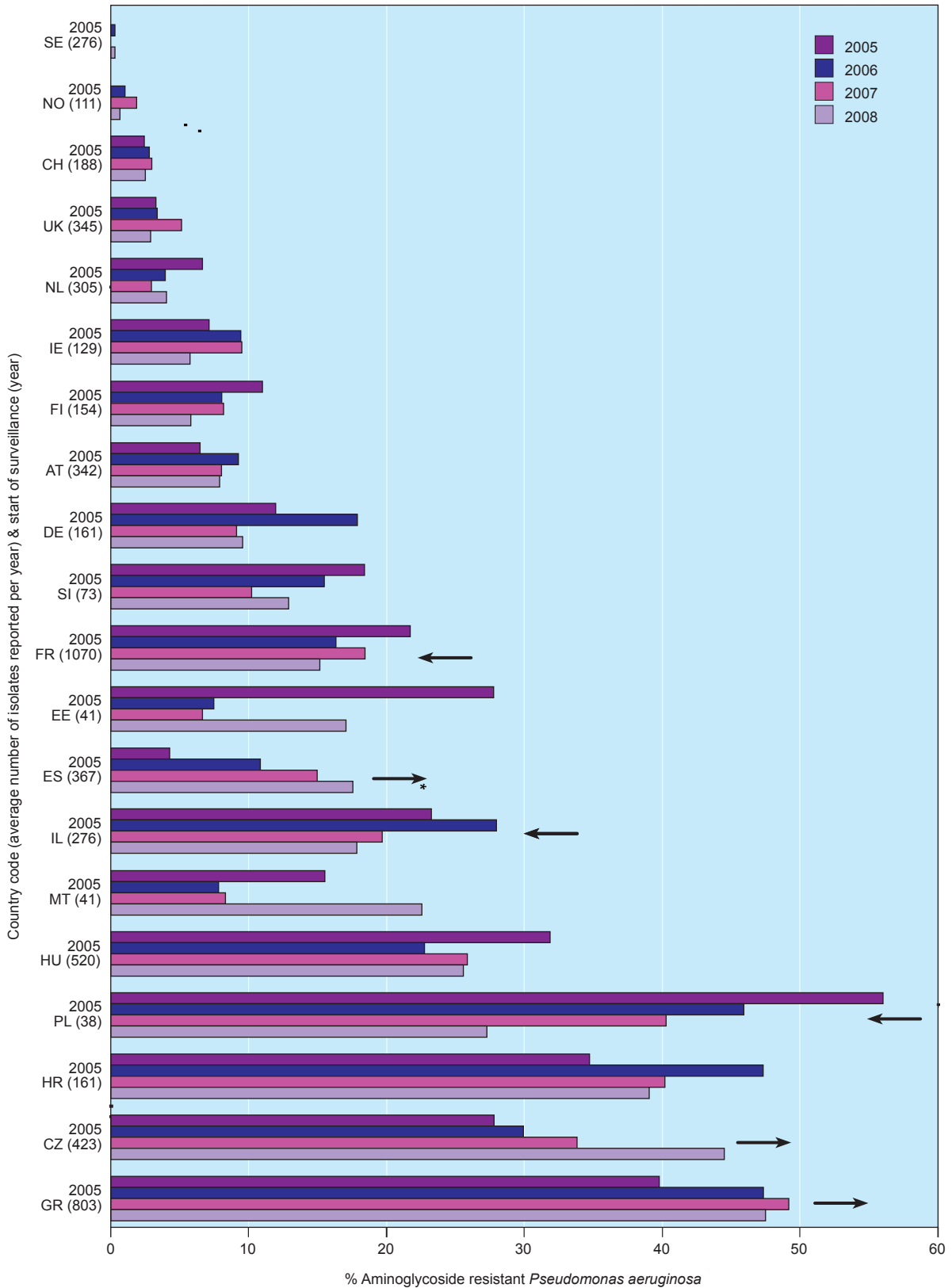


Figure 5.38. *Pseudomonas aeruginosa*: trends of aminoglycoside resistance by country 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.
Either the first year of surveillance or the first year with 20 or more isolates reported.

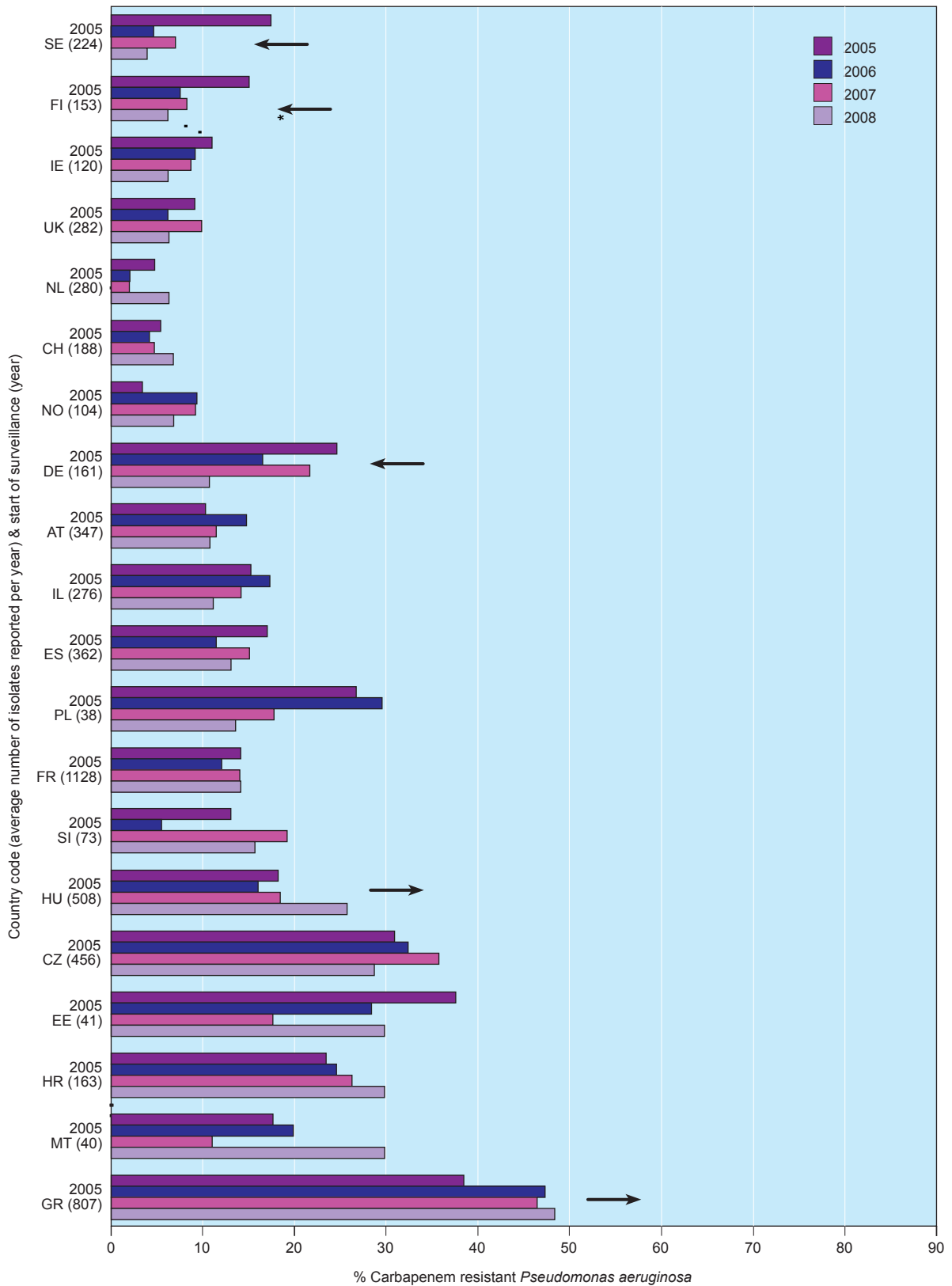


Figure 5.39. *Pseudomonas aeruginosa*: trends of carbapenem resistance by country 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

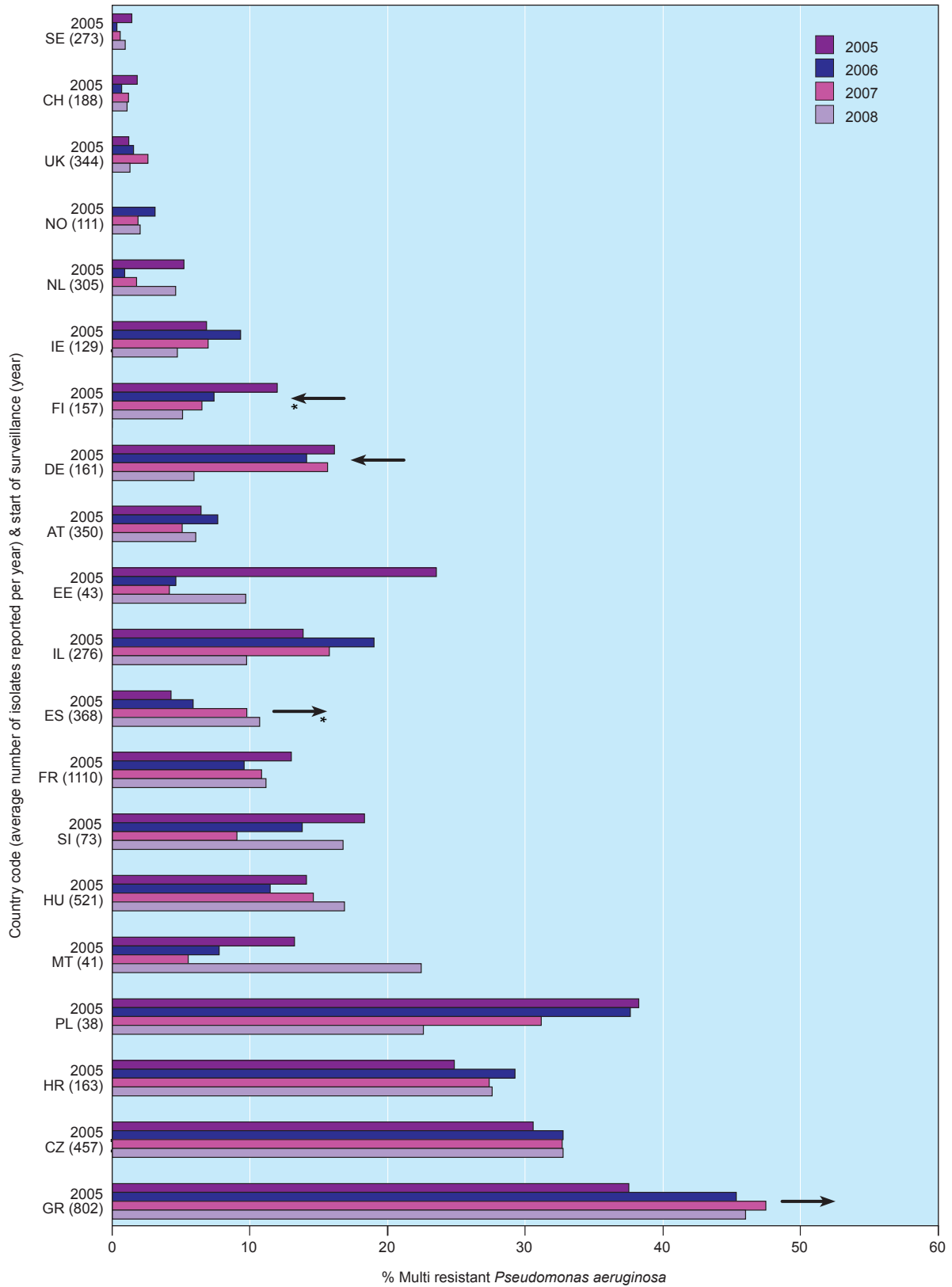


Figure 5.40. *Pseudomonas aeruginosa*: trends of combined resistance by country 2005-2008. Only the countries that reported 20 isolates or more per year for at least four consecutive years were included. The arrows indicate significant trends in the last four years of surveillance. The asterisks indicate significant trends in the overall national data that were not supported by data from laboratories consistently reporting all four years.

Either the first year of surveillance or the first year with 20 or more isolates reported.

5.8. References

1. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* **1997**;46:1-24.
2. Arthur M, Molinas C, Depardieu F, Courvalin P. Characterization of Tn1546, a Tn3-related transposon conferring glycopeptide resistance by synthesis of depsipeptide peptidoglycan precursors in *Enterococcus faecium* BM4147. *J Bacteriol* **1993**;175:117-27.
3. Banerjee SN, Emori TG, Culver DH, Gaynes RP, Jarvis WR, Horan T et al. Secular trends in nosocomial primary bloodstream infections in the United States, 1980-1989. National Nosocomial Infections Surveillance System. *Am J Med* **1991**;91:86S-9S.
4. Benyacoub J, Czarnecki-Maulden GL, Cavadini C, Sauthier T, Anderson RE, Schiffrin EJ et al. Supplementation of food with *Enterococcus faecium* (SF68) stimulates immune functions in young dogs. *J Nutr* **2003**;133:1158-62.
5. Berger-Bachi B, Rohrer S. Factors influencing methicillin resistance in staphylococci. *Arch Microbiol* **2002**;178:165-71.
6. Chow JW. Aminoglycoside resistance in enterococci. *Clin Infect Dis* **2000**;31:586-9.
7. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis* **2003**;36:53-9.
8. DiazGranados CA, Jernigan JA. Impact of vancomycin resistance on mortality among patients with neutropenia and enterococcal bloodstream infection. *J Infect Dis* **2005**;191:588-95.
9. Diekema DJ, Pfaller MA, Schmitz FJ, Smayevsky J, Bell J, Jones RN et al. Survey of infections due to *Staphylococcus* species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997-1999. *Clin Infect Dis* **2001**;32 Suppl 2:S114-32.
10. Evans AS BP. Bacterial infections of Humans, epidemiology and control. New York, US: Plenum Medical Book Company; 1991. p. 525-46.
11. Fluit AC, Jones ME, Schmitz FJ, Acar J, Gupta R, Verhoef J. Antimicrobial susceptibility and frequency of occurrence of clinical blood isolates in Europe from the SENTRY antimicrobial surveillance program, 1997 and 1998. *Clinical Infectious Diseases* **2000**;30:454-60.
12. Fontana R, Ligozzi M, Pittaluga F, Satta G. Intrinsic penicillin resistance in enterococci. *Microb Drug Resist* **1996**;2:209-13.
13. Franz CM, Holzapfel WH, Stiles ME. Enterococci at the crossroads of food safety? *Int J Food Microbiol* **1999**;47:1-24.
14. Garau J. Role of beta-lactam agents in the treatment of community-acquired pneumonia. *Eur J Clin Microbiol Infect Dis* **2005**;24:83-99.
15. Gold HS, Moellering RC Jr. Antimicrobial-drug resistance. *N Engl J Med* **1996**;335:1445-53.
16. Hausdorff WP, Bryant J, Kloek C, Paradiso PR, Siber GR. The contribution of specific pneumococcal serogroups to different disease manifestations: implications for conjugate vaccine formulation and use, part II. *Clin Infect Dis* **2000**;30:122-40.
17. Hausdorff WP, Bryant J, Paradiso PR, Siber GR. Which pneumococcal serogroups cause the most invasive disease: implications for conjugate vaccine formulation and use, part I. *Clin Infect Dis* **2000**;30:100-21.
18. Hausdorff WP, Siber G, Paradiso PR. Geographical differences in invasive pneumococcal disease rates and serotype frequency in young children. *Lancet* **2001**;357:950-2.
19. Hawkey PM. Mechanisms of quinolone action and microbial response. *J Antimicrob Chemother* **2003**;51 Suppl 1:29-35.

20. Herwaldt LA. Control of methicillin-resistant *Staphylococcus aureus* in the hospital setting. *Am J Med* **1999**;106:11S-8S; discussion 48S-52S.
21. Hiramatsu K, Cui L, Kuroda M, Ito T. The emergence and evolution of methicillin-resistant *Staphylococcus aureus*. *Trends Microbiol* **2001**;9:486-93.
22. Huycke MM, Sahm DF, Gilmore MS. Multiple-drug resistant enterococci: the nature of the problem and an agenda for the future. *Emerg Infect Dis* **1998**;4:239-49.
23. Jacobs MR. In vivo veritas: in vitro macrolide resistance in systemic *Streptococcus pneumoniae* infections does result in clinical failure. *Clin Infect Dis* **2002**;35:565-9.
24. Jacobs MR. Worldwide trends in antimicrobial resistance among common respiratory tract pathogens in children. *Pediatr Infect Dis J* **2003**;22(8 Suppl):S109-19.
25. Jett BD, Huycke MM, Gilmore MS. Virulence of enterococci. *Clin Microbiol Rev* **1994**;7:462-78.
26. Karchmer AW. Nosocomial bloodstream infections: organisms, risk factors, and implications. *Clin Infect Dis* **2000**;31 Suppl 4:S139-43.
27. Landry SL, Kaiser DL, Wenzel RP. Hospital stay and mortality attributed to nosocomial enterococcal bacteremia: a controlled study. *Am J Infect Control* **1989**;17:323-9.
28. Leclercq R, Courvalin P. Resistance to glycopeptides in enterococci. *Clin Infect Dis* **1997**;24:545-54; quiz 555-6.
29. Marchaim D, Navon-Venezia S, Schwaber MJ, and Carmeli Y. Isolation of Imipenem-Resistant Enterobacter Species: Emergence of KPC-2 Carbapenemase, Molecular Characterization, Epidemiology, and Outcomes. *Antimicrob Agents Chemother* 2008;52(4): 1413–18. Published online 2008 January 28. doi: 10.1128/AAC.01103-07.
30. McCormick AW, Whitney CG, Farley MM, Lynfield R, Harrison LH, Bennett NM et al. Geographic diversity and temporal trends of antimicrobial resistance in *Streptococcus pneumoniae* in the United States. *Nat Med* **2003**;9:424-30.
31. McGowan JE. Resistance in nonfermenting gram-negative bacteria: multidrug resistance to the maximum. *Am J Infect Control* **2006**;34(5 Suppl 1).
32. Mitra AK, Rabbani GH. A double-blind, controlled trial of bioflorin (*Streptococcus faecium* SF68) in adults with acute diarrhea due to *Vibrio cholerae* and enterotoxigenic *Escherichia coli*. *Gastroenterology* **1990**;99:1149-52.
33. Mundy LM, Sahm DF, Gilmore M. Relationships between enterococcal virulence and antimicrobial resistance. *Clin Microbiol Rev* **2000**;13:513-22.
34. Murray BE. Beta-lactamase-producing enterococci. *Antimicrob Agents Chemother* **1992**;36:2355-9.
35. Paterson DL. Resistance in gram-negative bacteria: Enterobacteriaceae. *Am J Infect Control* **2006**;34(5 Suppl 1).
36. Paterson DL, Ko WC, Von Gottberg A, Mohapatra S, Casellas JM, Goossens H et al. International prospective study of *Klebsiella pneumoniae* bacteremia: implications of extended-spectrum beta-lactamase production in nosocomial infections. *Ann Intern Med* **2004**;140:26-32.
37. Perichon B, Reynolds P, Courvalin P. VanD-type glycopeptide-resistant *Enterococcus faecium* BM4339. *Antimicrob Agents Chemother* **1997**;41:2016-8.
38. Peterson LR. Squeezing the antibiotic balloon: the impact of antimicrobial classes on emerging resistance. *Clin Microbiol Infect* **2005**;11 Suppl 5.
39. Reacher, M. H., Shah, A., Livermore, D. M., Wale, M. C., Graham, C., Johnson, A. P., Heine, H., Monnickendam, M. A., Barker, K. F., James, D., and George, R. C. Bacteraemia and antibiotic resistance of its pathogens reported in England and Wales between 1990 and 1998: trend analysis. *BMJ* **2000**;320, 213-6.

40. Rodriguez-Martinez JM, Poirel L, Pascual A, Nordmann P. Plasmid-mediated quinolone resistance in Australia. *Microb Drug Resist* **2006**;12:99-102.
41. Schmitt HJ. Pneumococcal conjugate vaccines in Europe, Berlin, Germany, 23-25 August 2000. Report of a European advisory board meeting. *Vaccine* **2001**;19:3347-54.
42. Shepard BD, Gilmore MS. Antibiotic-resistant enterococci: the mechanisms and dynamics of drug introduction and resistance. *Microbes Infect* **2002**;4:215-24.
43. Sturenburg E, Mack D. Extended-spectrum beta-lactamases: implications for the clinical microbiology laboratory, therapy, and infection control. *J Infect* **2003**;47:273-95.
44. Vatopoulos A. High rates of metallo-beta-lactamase-producing *Klebsiella pneumoniae* in Greece—a review of the current evidence. *Euro surveillance* **2008**; 13(4)
45. Watson DA, Musher DM. A brief history of the pneumococcus in biomedical research. *Semin Respir Infect* **1999**;14:198-208.
46. Weisblum B. Insights into erythromycin action from studies of its activity as inducer of resistance. *Antimicrob Agents Chemother* **1995**;39:797-805.
47. Willems RJ, Top J, van Santen M, Robinson DA, Coque TM, Baquero F et al. Global spread of vancomycin-resistant *Enterococcus faecium* from distinct nosocomial genetic complex. *Emerg Infect Dis* **2005**;11:821-8.
48. Wuorimaa T, Kayhty H. Current state of pneumococcal vaccines. *Scand J Immunol* **2002**;56:111-29.
49. Zhong P, Cao Z, Hammond R, Chen Y, Beyer J, Shortridge VD et al. Induction of ribosome methylation in MLS-resistant *Streptococcus pneumoniae* by macrolides and ketolides. *Microb Drug Resist* **1999**;5:183-8.

Chapter 6. Conclusions and Recommendations

Based on the denominator data reported through the laboratory/hospital questionnaire, the overall hospital catchment population of the EARSS network is estimated to include at least 20% of the EU population, including accession countries and Israel. Most countries covered between 20-100%, which is considered to be adequate. The comparability of MRSA incidence rates and proportions indicate that the resistance proportions, as reported by EARSS, are a good approximation of the incidence rates, when comparing the occurrence of resistance across Europe.

The resistance profile of *S. pneumoniae* has a dynamic character. Although penicillin non-susceptibility is increasing in two countries, four countries are on the decrease, among those the high endemic countries Israel and France, strongly decreasing over the past years. Erythromycin non-susceptibility has become more prevalent in two countries, while, six countries showed a decrease. For dual non-susceptibility more countries showed increasing trends compared to decreasing trends. In 2008, again 12 countries have reported serogroup information for *S. pneumoniae* isolates, and data from seven countries were included for analysis. Compared to 2007, changes were small. Serogroup 1 and 19 were still the most prevalent ones, whereas serogroup 7 and serogroup 3 became slightly more prevalent, and serogroup 14 became less prevalent in the population.

For the first time, more countries showed decreasing MRSA proportions instead of increasing trends, so the MRSA problem seems to stabilize and even decrease for most European countries. Nevertheless, MRSA proportions are still above 25% in one third of all countries. The highest rates were reported from the Mediterranean, with Malta and Portugal showing MRSA proportions of over 50%.

With the ongoing spread of clonal complex 17 in Europe, outbreaks of vancomycin resistant *E. faecium* continues to afflict hospitals in various countries. The spread of these hospital-adapted strains occurs on the background of high-level aminoglycoside resistance. The control of glycopeptide resistant enterococci is a formidable task and these problematic pathogens will continue to remain a challenge for hospital infection control practitioners.

The Europe-wide increase of resistance of *Escherichia coli* to all of the antimicrobial classes recorded by EARSS seems to be a relentless development. For fluoroquinolones the situation becomes progressively critical. Invasive *E. coli* isolates are losing susceptibility to fluoroquinolones with exceptional speed. Next to that, combined resistance is a frequent occurrence, with co-resistance to 4 antimicrobial classes including 3rd generation cephalosporins already among the 4th most common resistance patterns encountered in invasive *E. coli* in Europe, and undeniably these resistance traits are on the increase as well.

In *K. pneumoniae* a high prevalence of resistant strains to 3rd generation cephalosporins, fluoroquinolones and aminoglycosides becomes evident in central and southeastern Europe. Many of these strains have combined resistance and the most frequent phenotype shows resistance to all three antimicrobial classes recorded by EARSS. Although carbapenems are still effective in most countries, the rapid emergence and dissemination of strains with carbapenemase production are threatening the effectiveness of this last line therapeutic option. It is thus necessary to closely monitor the effectiveness of carbapenems and be aware that carbapenemase-positive isolates may not be detected by automated systems. EARSS therefore recommends to further scrutinise all isolates with MIC ≥ 0.5 mg/l.

Combined resistance is the dominant threat imposed by invasive *P. aeruginosa* on Europe. Since resistance in *P. aeruginosa* emerges readily during antibiotic treatment, the time when blood cultures are taken is crucial as any isolate sampled after prolonged exposure with antimicrobial chemotherapy will predictably be a multi-resistant phenotype. Assuming the diagnostic habits in Europe are comparable, the picture that our data suggest is that the geographical gradient observed for all other gram-negative pathogens, namely lower resistance in the Northwest and increasing resistance towards the Southeast also holds for *P. aeruginosa*.

In conclusion, the data that EARSS has gathered over the years bring an unpleasant, but important truth: the loss of effective antimicrobial therapy increasingly threatens the delivery of crucial health services in hospitals and in the community.

Annex 1. Technical Notes

1.1. Technical Notes for table 1 of the Country Summary Sheets

Inclusion criteria

To be included in the analyses presented in table 1 of the country summary sheets (annex 2), countries, laboratories and hospitals had to provide both denominator data and AST results in 2008. Necessary details for inclusion were information on blood culture frequencies for laboratories and the number of beds for hospitals.

Cumulative variables

Number of blood culture sets, number of hospital beds (total and ICU beds), number of patient-days, catchment population, and type of hospitals were added up by country.

Number of blood culture sets

The Total number of blood culture sets was defined as the number of blood samples, not the number of patients sampled.

Patient-days

If patient-days were not available at hospital level, these were calculated by:

$$\text{Number of beds} * (\text{Annual occupancy} / 100) * 365$$

Catchment population & Percentage of the total population covered

The total catchment population was the sum of the catchment populations of primary, secondary and tertiary level care hospitals. Hospitals providing only a specific type of care (classified as 4=other, e.g. oncology or psychiatric hospitals) were not included as we considered this population as probably overlapping with the catchment populations of the other hospitals.

The percentage of population covered was then calculated by dividing the total catchment population by the estimated national population, which we derived from the CIA factbook available from <https://www.cia.gov/library/publications/the-world-factbook/index.html>. Some NRs were able to provide the national catchment population for all EARSS hospitals, in that case this number was used instead of the number derived from the questionnaire data.

If the percentage of population covered exceeded 100%, this was reduced to 100%.

Type of hospitals

Since hospital categorisation was always intricate, we now supplied more specific definitions from WHO that hopefully made categorising the hospitals easier.

Primary level, often referred to as a district hospital or first-level referral: A hospital has few specialities, mainly internal medicine, obstetrics-gynecology, pediatrics, and general surgery, or only general practice; limited laboratory services are available for general, but not for specialized pathological analysis; the bed capacity ranges from 30 to 200 beds.

Secondary level, often referred to as provincial hospital: A hospital highly differentiated by function with five to ten clinical specialities; bed capacity ranging from 200-800 beds.

Tertiary level, often referred to as central, regional or tertiary-level hospital: A hospital with highly specialized staff and technical equipment, e.g., cardiology, ICU and specialized imaging units; clinical services are highly differentiated by function; the hospital may have teaching activities; bed

capacity ranges from 300 to 1,500 beds.
A fourth category was for hospitals with a single specialty.

Averaged variables

Annual occupancy rate and length of stay were averaged per country. In these totals only laboratory/hospital questionnaires were included that provided information on all variables needed for the specific formula.

Annual occupancy rate

The average annual occupancy per country was calculated as :

$$[\sum(\text{Annual occupancy} / 100 * \text{Number of beds}) / \sum(\text{Number of beds})] * 100$$

Length of stay

The median length of stay per country was determined, since the values of the hospital-specific lengths of stay had a skewed distribution for most countries.

1.2 Technical Notes for the MRSA incidence calculations in chapter 4

In the case of linking of AST results with denominator information only AST results from those hospitals that also provided denominator information were included.

1.3. Technical Notes for chapter 5

Resistance trend analysis

This year, resistance trends were calculated for the last four years, as we think this is more informative compared to calculating them over all years, as we used to do. To determine significant trends over time, the Cochran Armitage test was used, excluding countries reporting less than 20 isolates per year. In addition, at least 3 years of data had to be reported by country to be included in the analysis. To exclude possible biases in the trend analyses, a sensitivity analysis was done, per country, to determine the sensitivity of the trend analysis for using the complete dataset versus a subset from laboratories reporting all four years. If the trends in the subset and the complete dataset were contradictive, these trends were discussed in the text. However, if both datasets indicated a similar trend, we included this;

- i) in the text, when significant trends were only identified in the subset of data,
- ii) in the graphs by an arrow with asterisk, when significant trends were only identified in the complete dataset,
- iii) in the graphs by an arrow when a significant trend was detected in both the subset and the complete dataset.

European maps with resistance levels

To be included in the maps of Europe displaying the resistance proportions per country, for all drug-bug combinations under surveillance by EARSS, a country had to report AST results for at least 10 isolates.

Annex 2. Country Summary Sheets

In the following appendix, country-specific resistance information is presented together with denominator data and the characteristics of the participating laboratories and hospitals.

Explanation to the country summary sheets

General information about EARSS participating laboratories and hospitals

Table 1 and 2 and figure 1 give an indication of the sample size and the representativeness of the country-specific resistance data available to EARSS.

Table 1 displays results of the laboratories and hospitals that provided denominator data in 2008 (i.e. that responded to the questionnaire) and thus only includes the *laboratories* that 1) reported AST results to EARSS in 2008, and 2) provided blood culture information; and the *hospitals* that 1) reported AST results to EARSS in 2008, and 2) provided their number of hospital beds. For details about the calculation of the average annual occupancy rate, the estimated catchment population and the percentage of the total population covered, we refer to the technical notes (annex 1). If data were not available this is stated as “na”.

Table 2 gives the number of laboratories and isolates reported by year and by pathogen under EARSS surveillance for the period 2001 to 2008.

Figure 1 shows the geographic location of the laboratories reporting in 2008. The size of the dots in the maps represents the number of laboratories in that area:

Dot	•	●	●	●
Number of labs	1	5	10	15

Antibiotic resistance 2001-2008

Table 3 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 protocols. When interpreting table 3 always check the number of isolates the proportions are based on given in table 2.

Demographic characteristics

Table 4 gives the proportional distribution of the isolates reported by source, gender, age, and hospital department, and the proportion of resistance within the different groups, for the period 2007-2008. The abbreviations used in this table stand for; PNSP = penicillin non-susceptible *S. pneumoniae*, MRSA = methicillin resistant *S. aureus*, FREC = fluoroquinolone resistant *E. coli*, VRE = vancomycin resistant *E. faecalis* or *E. faecium*, CRKP = 3rd 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 0 and the % resistance is not shown.

PNSP at laboratory level / MRSA at hospital level

Figures 2 and 3 show the local variation in the proportions of PNSP and MRSA by laboratory and by hospital, respectively. Both figures are based on data from 2007 and 2008, only including the laboratories and hospitals that reported at least 5 isolates in these 2 years. The total number of laboratories or hospitals, the minimum, maximum, median, 1st and 3rd quartile of the proportion of resistance is displayed in a box in the figures. If an ‘X’ is displayed at the end of a hospital code this means that the hospital code is not provided; consequently, this can compass one or more unknown hospitals.

Austria

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	31/38
Hosps providing denom.data/ reporting data to EARSS	127/145
Number of blood culture sets	154,481
Number of hospital beds	48,123
Patient-days	12,347,311
Average occupancy rate (%)	70%
Median length of stay (days)	5
Estimated catchment population	na
% total population covered	90%
Type of participating hospitals	
Regional/Tertiary	6%
Provincial/Secondary	24%
District/Primary	41%

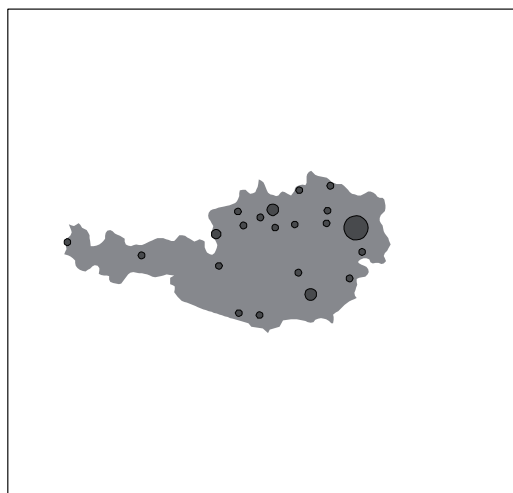


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	8	53	9	278	8	260	6	67	0	0	0	0
2002	10	80	11	455	10	479	10	181	0	0	0	0
2003	19	162	20	871	21	985	19	327	0	0	0	0
2004	27	250	30	1420	31	1862	28	604	0	0	0	0
2005	30	290	32	1472	33	2059	30	568	7	89	8	77
2006	32	291	33	1637	33	2483	33	699	30	434	31	405
2007	34	313	34	1503	34	2545	33	688	33	445	33	411
2008	37	367	38	1894	38	2985	38	864	38	583	38	510

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	2	<1	1	1	<1	<1	2	<1
	Penicillin I+R	4	1	9	5	5	5	5	5
	Macrolides I+R	10	9	14	12	15	12	13	11
<i>S. aureus</i>	Oxacillin/Methicillin R	8	12	15	14	13	9	9	8
<i>E. coli</i>	Aminopenicillins R	35	33	41	46	48	53	53	50
	Aminoglycosides R	2	4	5	5	5	8	8	7
	Fluoroquinolones R	7	10	14	17	19	22	26	23
	3rd gen. Cephalosporins R	<1	1	2	3	4	7	9	7
<i>E. faecalis</i>	Aminopenicillins I+R	13	3	1	<1	1	2	2	2
	HL Aminoglycosides R	35	27	33	23	28	29	30	21
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	86	84	85	85	84	89	82	90
	HL Aminoglycosides R	13	21	22	22	28	21	28	19
	Glycopeptides R	5	7	<1	<1	1	<1	2	2
<i>K. pneumoniae</i>	Aminoglycosides R	3	5	5	6
	Fluoroquinolones R	11	8	12	12
	3rd gen. Cephalosporins R	6	6	8	8
<i>P. aeruginosa</i>	Piperacillin R	13	8	6	8
	Ceftazidime R	7	9	5	6
	Carbapenems R	10	15	12	11
	Aminoglycosides R	6	9	8	8
	Fluoroquinolones R	14	15	15	12

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=680		<i>S. aureus</i> n=3397		<i>E. coli</i> n=5506		<i>E. faecalis</i> n=914		<i>E. faecium</i> n=593		<i>K. pneumo.</i> n=1019		<i>P. aeruginosa</i> n=915	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	97	5	100	9	100	24	100	0	100	2	100	8	100	11
CSF	3	14	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	55	6	58	10	41	27	62	1	58	2	55	10	57	13
Female	44	4	41	9	58	22	37	0	41	2	44	5	42	9
Unknown	1	0	1	17	1	26	1	0	1	0	1	43	1	14
Age (years)														
0-4	6	9	1	4	1	5	5	0	1	0	3	15	1	8
5-19	4	0	2	3	1	29	1	0	1	0	0	.	1	14
20-64	38	6	34	8	26	25	31	1	40	3	34	11	35	15
65 and over	52	4	62	10	72	24	64	0	57	1	63	6	63	9
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	15	8	11	13	7	29	16	1	28	1	12	15	17	19
Internal Med.	46	5	48	9	54	23	41	0	32	2	40	6	34	9
Surgery	2	15	11	13	8	22	12	0	11	2	14	7	10	6
Other	31	4	28	7	28	26	27	0	25	3	31	8	36	12
Unknown	5	0	2	13	3	27	3	0	3	5	3	0	3	0

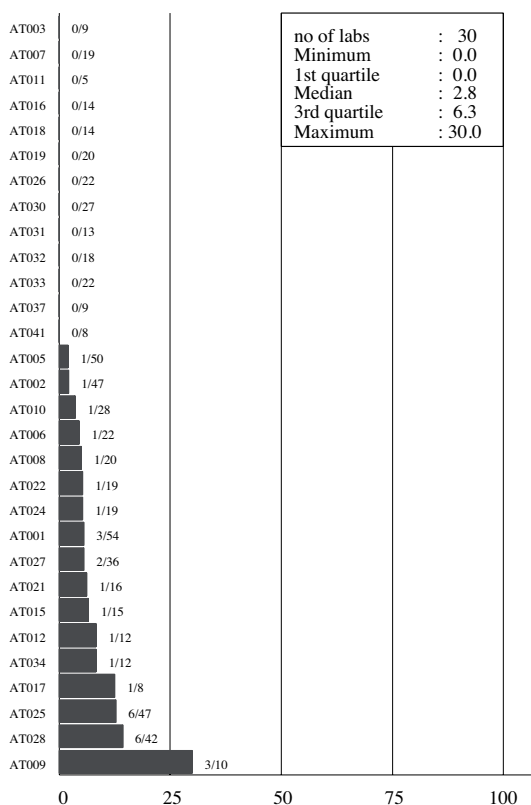
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
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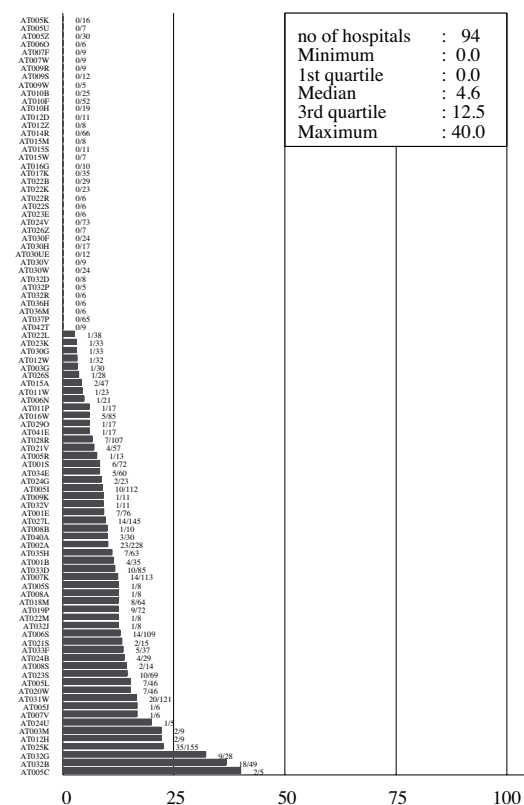
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=11		<i>S. aureus</i> n=71		<i>E. coli</i> n=34		<i>E. faecalis</i> n=15		<i>E. faecium</i> n=9		<i>K. pneumo.</i> n=39		<i>P. aeruginosa</i> n=15	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	91	50	100	21	100	15	100	0	100	0	100	44	100	20
CSF	9	100	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	82	67	59	17	47	19	53	0	67	0	49	47	60	22
Female	18	0	41	28	53	11	47	0	33	0	51	40	40	17
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	0	.	0	.	0	.	0	.	0	.	0	.	0	.
5-19	0	.	0	.	0	.	0	.	0	.	0	.	0	.
20-64	0	.	0	.	0	.	0	.	0	.	0	.	0	.
65 and over	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Unknown	100	55	100	21	100	15	100	0	100	0	100	44	100	20
Hospital dep.														
ICU	0	.	0	.	3	100	20	0	22	0	8	100	20	0
Internal Med.	0	.	18	15	18	0	7	0	0	.	13	20	7	0
Surgery	0	.	4	100	0	.	13	0	11	0	10	100	20	33
Other	45	40	32	22	47	19	27	0	0	.	56	36	33	40
Unknown	55	67	45	16	32	9	33	0	67	0	13	20	20	0

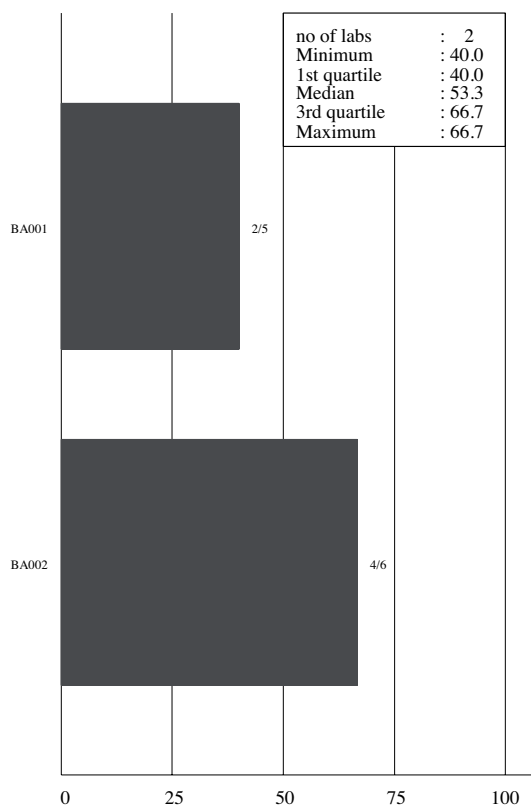
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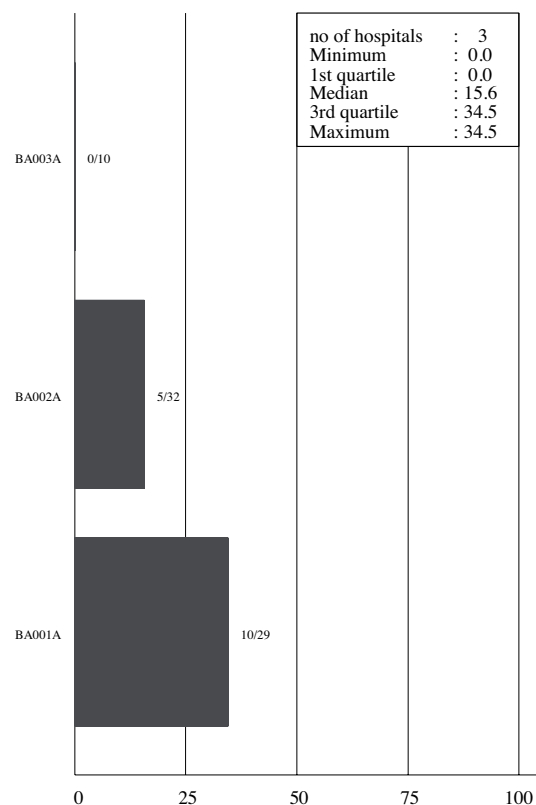
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=3158		<i>S. aureus</i> n=1761		<i>E. coli</i> n=2717		<i>E. faecalis</i> n=374		<i>E. faecium</i> n=101		<i>K. pneumo.</i> n=0		<i>P. aeruginosa</i> n=0	
	%tot	%PNSP	%tot	%MRSA	%tot	%FRECC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	96	9	100	22	100	18	100	1	100	3
CSF	4	10	0	.	0	.	0	.	0
Gender														
Male	54	9	59	22	45	21	65	0	58	3
Female	45	9	39	22	55	16	33	1	38	3
Unknown	1	7	1	17	0	.	2	0	4	0
Age (years)														
0-4	16	9	4	5	2	4	3	0	3	0
5-19	5	3	2	17	1	17	1	0	0
20-64	35	7	36	16	28	15	27	1	36	3
65 and over	43	12	56	27	69	20	68	0	61	3
Unknown	0	.	2	30	0	.	0	.	0
Hospital dep.														
ICU	14	11	15	30	0	.	24	0	22	5
Internal Med.	38	9	40	21	2	37	38	1	37	3
Surgery	2	16	11	26	1	29	9	0	12	0
Other	27	8	26	18	2	25	24	0	24	4
Unknown	19	8	9	19	95	17	6	5	6	0

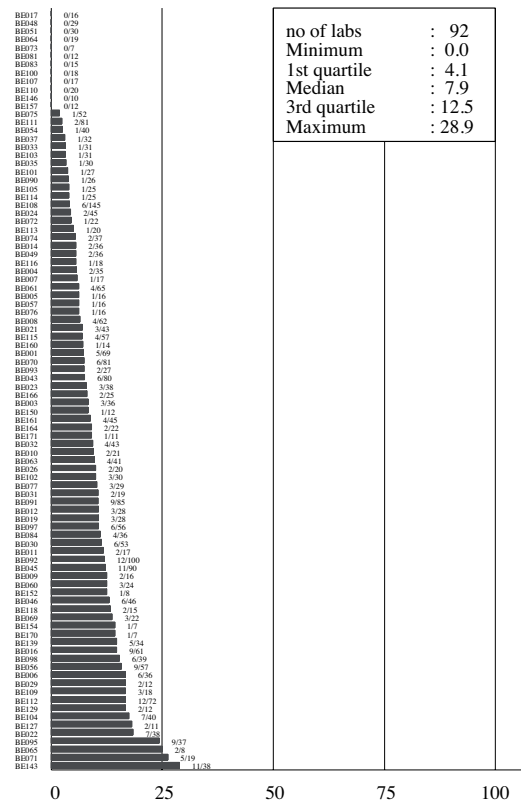
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VRE = Vancomycin Resistant Enterococcus

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FRECC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

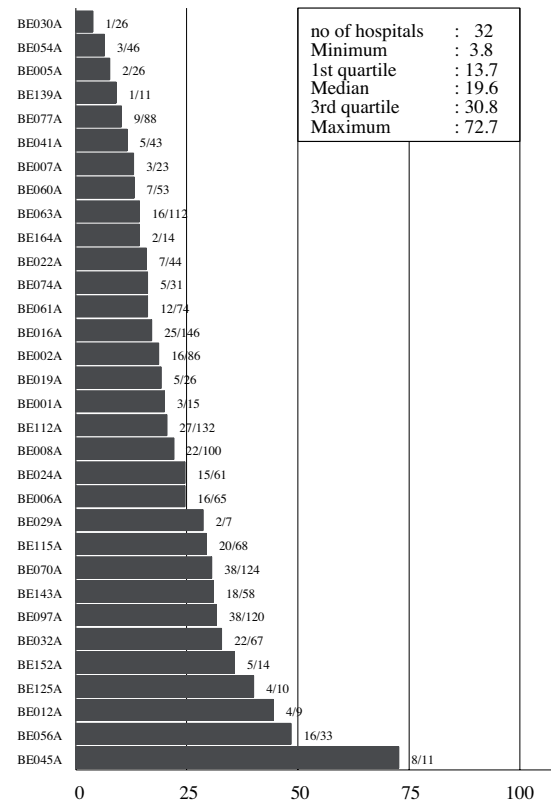
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Bulgaria

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	20/23
Hosps providing denom.data/ reporting data to EARSS	21/24
Number of blood culture sets	19,553
Number of hospital beds	10,052
Patient-days	2,748,047
Average occupancy rate (%)	79%
Median length of stay (days)	6
Estimated catchment population	7,090,203
% total population covered	98%
Type of participating hospitals	
Regional/Tertiary	48%
Provincial/Secondary	38%
District/Primary	5%

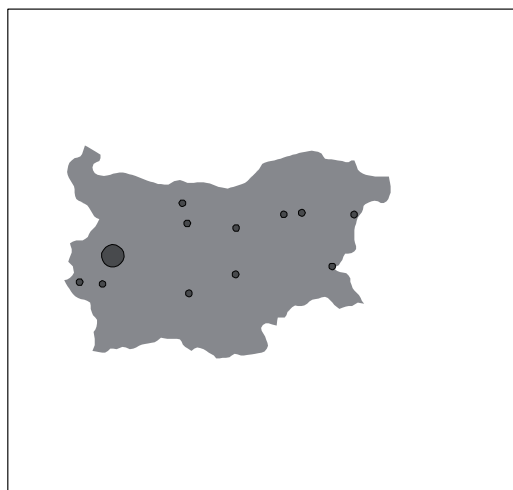


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	8	16	17	103	15	98	11	30	0	0	0	0
2002	11	25	21	116	20	135	16	42	0	0	0	0
2003	13	22	20	157	20	158	16	49	0	0	0	0
2004	13	32	22	169	20	167	16	75	0	0	0	0
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

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	6	8	9	22	30	7	9	21
	Penicillin I+R	6	8	14	22	33	7	16	21
	Macrolides I+R	9	9	11	17	8	16	17	4
<i>S. aureus</i>	Oxacillin/Methicillin R	27	33	31	24	31	28	13	25
<i>E. coli</i>	Aminopenicillins R	48	52	54	64	69	64	70	65
	Aminoglycosides R	15	17	22	20	24	28	20	31
	Fluoroquinolones R	8	14	19	24	29	26	35	32
	3rd gen. Cephalosporins R	7	13	18	22	28	29	23	29
<i>E. faecalis</i>	Aminopenicillins I+R	5	26	7	15	8	31	13	8
	HL Aminoglycosides R	30	63	36	33	24	53	29	44
	Glycopeptides R	<1	<1	<1	2	<1	2	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	50	71	60	59	96	97	100	93
	HL Aminoglycosides R	33	83	60	62	56	79	75	84
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	53	60	59	59
	Fluoroquinolones R	26	24	41	52
	3rd gen. Cephalosporins R	50	60	55	73
<i>P. aeruginosa</i>	Piperacillin R	50	33	14	48
	Ceftazidime R	45	13	21	55
	Carbapenems R	38	14	7	17
	Aminoglycosides R	53	42	29	48
	Fluoroquinolones R	47	17	14	36

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=61		<i>S. aureus</i> n=281		<i>E. coli</i> n=273		<i>E. faecalis</i> n=90		<i>E. faecium</i> n=40		<i>K. pneumo.</i> n=78		<i>P. aeruginosa</i> n=37	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	74	18	100	20	99	33	100	0	100	0	100	67	100	14
CSF	26	19	0	.	1	25	0	.	0	.	0	.	0	.
Gender														
Male	61	14	58	22	48	37	69	0	43	0	63	69	70	8
Female	39	25	42	17	52	29	31	0	58	0	37	62	30	27
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	18	36	9	25	5	15	10	0	20	0	13	60	19	29
5-19	8	20	6	19	3	13	4	0	0	.	5	75	3	0
20-64	61	8	58	19	53	38	49	0	45	0	46	81	41	7
65 and over	13	38	27	21	40	31	37	0	35	0	36	50	38	14
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	10	17	13	42	9	38	24	0	30	0	19	73	30	18
Internal Med.	28	18	38	13	52	31	31	0	18	0	28	55	22	0
Surgery	0	.	9	38	11	35	9	0	18	0	15	58	8	33
Other	62	18	40	15	28	34	36	0	35	0	37	76	41	13
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

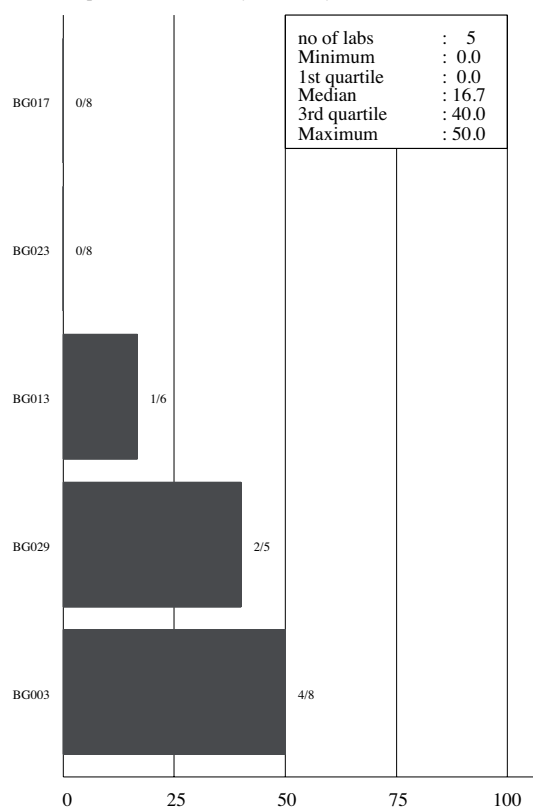
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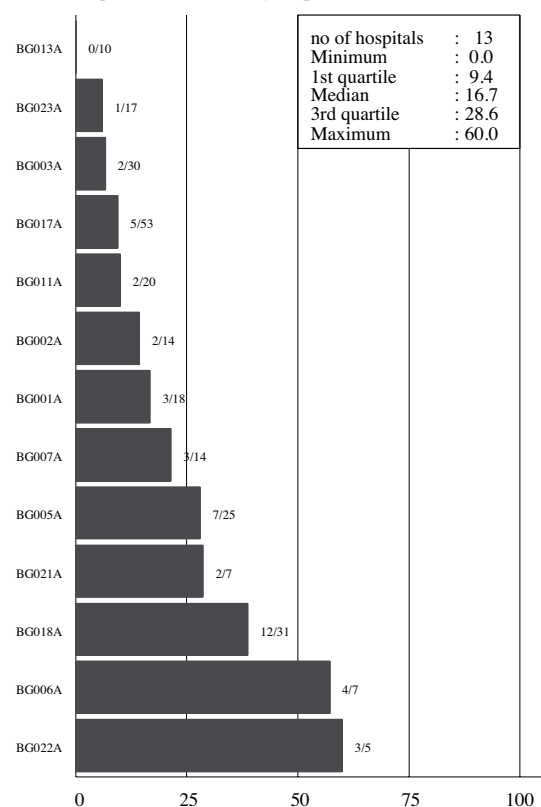
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Croatia

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	18/19
Hosps providing denom.data/ reporting data to EARSS	21/26
Number of blood culture sets	57,638
Number of hospital beds	10,081
Patient-days	3,163,238
Average occupancy rate (%)	85%
Median length of stay (days)	7
Estimated catchment population	4,500,000
% total population covered	90%
Type of participating hospitals	
Regional/Tertiary	38%
Provincial/Secondary	48%
District/Primary	10%



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	10	20	14	149	13	182	7	33	0	0	0	0
2002	14	90	14	279	15	490	13	96	0	0	0	0
2003	12	88	14	360	16	570	11	101	0	0	0	0
2004	12	103	13	392	14	535	11	115	0	0	0	0
2005	15	129	17	354	16	638	11	120	14	112	10	72
2006	14	116	17	391	17	780	16	178	15	205	15	170
2007	15	136	15	375	17	852	13	174	17	279	16	189
2008	13	100	18	474	17	915	16	232	17	333	14	221

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	1	3	<1	<1	<1	4
	Penicillin I+R	15	19	20	17	17	18	18	17
	Macrolides I+R	15	23	18	19	17	16	8	14
<i>S. aureus</i>	Oxacillin/Methicillin R	32	37	37	38	37	36	38	35
<i>E. coli</i>	Aminopenicillins R	51	47	46	45	46	51	51	53
	Aminoglycosides R	6	7	7	6	5	6	6	6
	Fluoroquinolones R	5	5	7	8	9	15	13	15
	3rd gen. Cephalosporins R	2	3	4	3	<1	1	3	4
<i>E. faecalis</i>	Aminopenicillins I+R	13	5	4	5	6	3	2	5
	HL Aminoglycosides R	50	40	28	35	31	37	37	46
	Glycopeptides R	3	<1	<1	<1	1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	100	56	47	69	82	69	78	79
	HL Aminoglycosides R	100	67	41	63	62	59	59	65
	Glycopeptides R	<1	22	6	3	6	3	2	6
<i>K. pneumoniae</i>	Aminoglycosides R	38	33	38	51
	Fluoroquinolones R	18	23	34	44
	3rd gen. Cephalosporins R	46	34	40	54
<i>P. aeruginosa</i>	Piperacillin R	25	38	30	34
	Ceftazidime R	6	11	14	13
	Carbapenems R	24	25	26	30
	Aminoglycosides R	35	47	40	39
	Fluoroquinolones R	34	35	30	33

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=236		<i>S. aureus</i> n=849		<i>E. coli</i> n=1767		<i>E. faecalis</i> n=283		<i>E. faecium</i> n=123		<i>K. pneumo.</i> n=609		<i>P. aeruginosa</i> n=409	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	93	19	100	36	100	14	100	0	100	4	100	48	100	28
CSF	7	6	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	63	15	62	36	42	16	68	1	62	5	61	52	62	29
Female	37	23	37	37	58	13	32	0	38	2	39	41	38	28
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	32	21	3	7	7	2	13	0	8	0	11	70	5	47
5-19	6	0	3	17	1	15	2	0	2	0	2	71	2	44
20-64	43	16	47	36	35	15	38	1	45	7	39	42	51	35
65 and over	19	22	46	40	58	15	48	0	45	2	48	46	42	18
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	11	26	15	70	6	22	13	0	23	0	18	56	24	26
Internal Med.	17	23	41	29	39	17	33	0	38	0	29	31	27	20
Surgery	0	.	13	66	4	16	10	0	7	13	13	65	16	28
Other	72	15	32	19	51	11	44	1	33	10	40	50	33	38
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

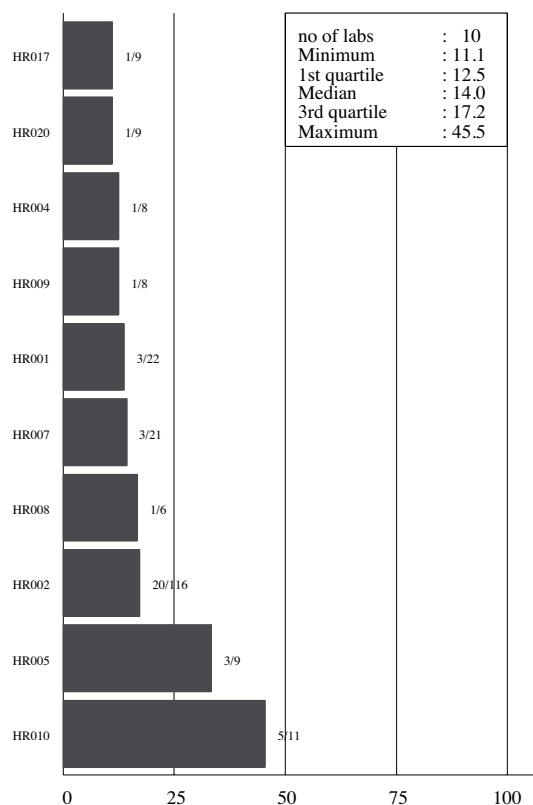
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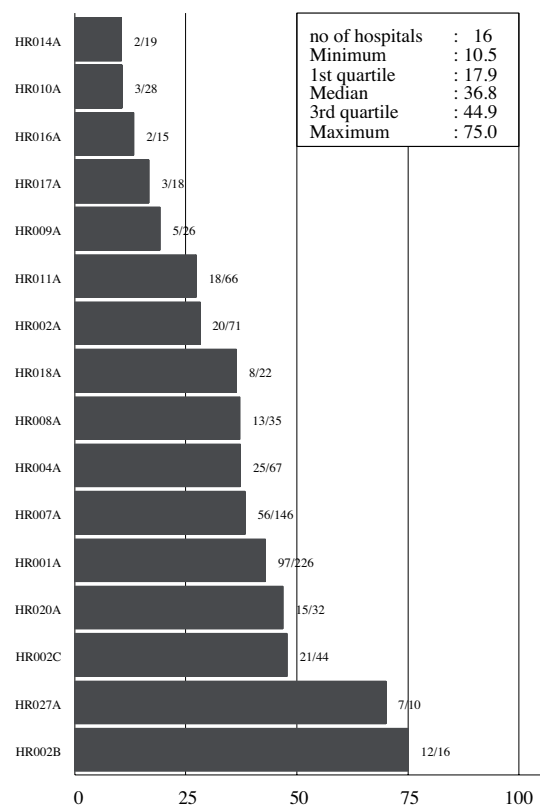
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Cyprus

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	5/5
Hosps providing denom.data/ reporting data to EARSS	5/5
Number of blood culture sets	12,032
Number of hospital beds	1,277
Patient-days	471,767
Average occupancy rate (%)	101%
Median length of stay (days)	6
Estimated catchment population	428,921
% total population covered	54%
Type of participating hospitals	
Regional/Tertiary	20%
Provincial/Secondary	20%
District/Primary	40%

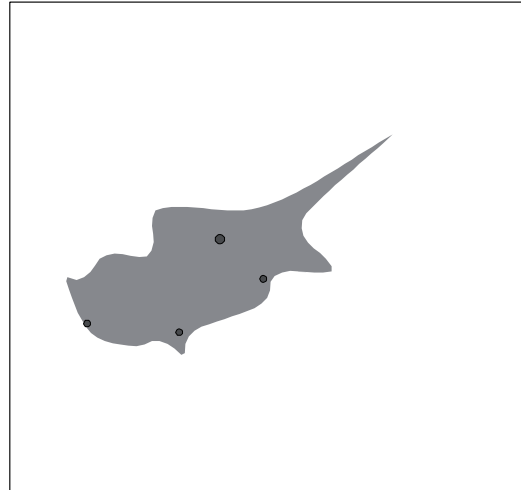


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	0	0	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0	0	0	0	0
2003	1	3	1	28	1	19	1	28	0	0	0	0
2004	1	7	3	39	4	46	3	38	0	0	0	0
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	38	3	52
2008	4	14	5	92	4	116	5	85	5	62	5	43

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	.	.	<1	<1	<1	31	7	21
	Penicillin I+R	.	.	<1	14	19	38	33	43
	Macrolides I+R	.	.	33	<1	13	31	27	29
<i>S. aureus</i>	Oxacillin/Methicillin R	.	.	64	49	56	32	48	46
<i>E. coli</i>	Aminopenicillins R	.	.	63	61	72	62	72	57
	Aminoglycosides R	.	.	11	11	13	10	11	9
	Fluoroquinolones R	.	.	32	22	29	35	39	45
	3rd gen. Cephalosporins R	.	.	11	9	16	16	18	18
<i>E. faecalis</i>	Aminopenicillins I+R	.	.	<1	3	3	5	2	16
	HL Aminoglycosides R	.	.	43	77	71	44	61	65
	Glycopeptides R	.	.	<1	3	<1	<1	<1	1
<i>E. faecium</i>	Aminopenicillins I+R	.	.	100	100	80	43	92	60
	HL Aminoglycosides R	.	.	.	33	<1	14	33	10
	Glycopeptides R	.	.	<1	33	40	14	25	20
<i>K. pneumoniae</i>	Aminoglycosides R	11	12	13	21
	Fluoroquinolones R	22	12	24	23
	3rd gen. Cephalosporins R	33	27	32	35
<i>P. aeruginosa</i>	Piperacillin R	13	27	29	23
	Ceftazidime R	38	24	13	9
	Carbapenems R	13	11	19	19
	Aminoglycosides R	13	11	23	21
	Fluoroquinolones R	13	27	21	38

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=29		<i>S. aureus</i> n=177		<i>E. coli</i> n=225		<i>E. faecalis</i> n=126		<i>E. faecium</i> n=22		<i>K. pneumo.</i> n=100		<i>P. aeruginosa</i> n=95	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	97	39	100	47	100	42	100	1	100	23	100	34	100	19
CSF	3	0	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	62	33	66	45	52	39	70	0	73	13	59	37	72	21
Female	38	45	33	51	47	46	29	3	27	50	35	23	25	17
Unknown	0	.	1	0	1	50	1	0	0	.	6	67	3	0
Age (years)														
0-4	17	20	1	0	1	0	0	.	5	0	5	80	4	0
5-19	3	0	3	40	2	40	1	0	5	0	2	0	0	.
20-64	24	14	21	32	11	48	24	0	18	25	25	44	27	12
65 and over	14	75	27	60	29	55	31	3	32	14	24	29	23	14
Unknown	41	50	49	48	56	35	44	0	41	33	44	27	45	28
Hospital dep.														
ICU	10	33	19	41	10	27	40	0	45	20	34	56	52	24
Internal Med.	59	41	37	50	52	38	27	0	18	25	26	15	19	17
Surgery	0	.	10	61	9	52	12	0	14	33	5	40	8	38
Other	31	33	33	41	29	52	21	4	23	20	35	26	20	0
Unknown	0	.	1	100	0	.	0	.	0	.	0	.	1	0

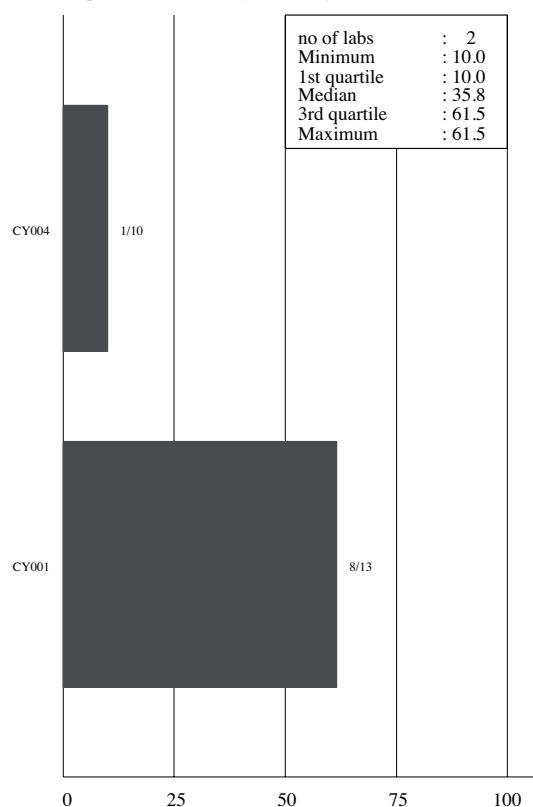
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

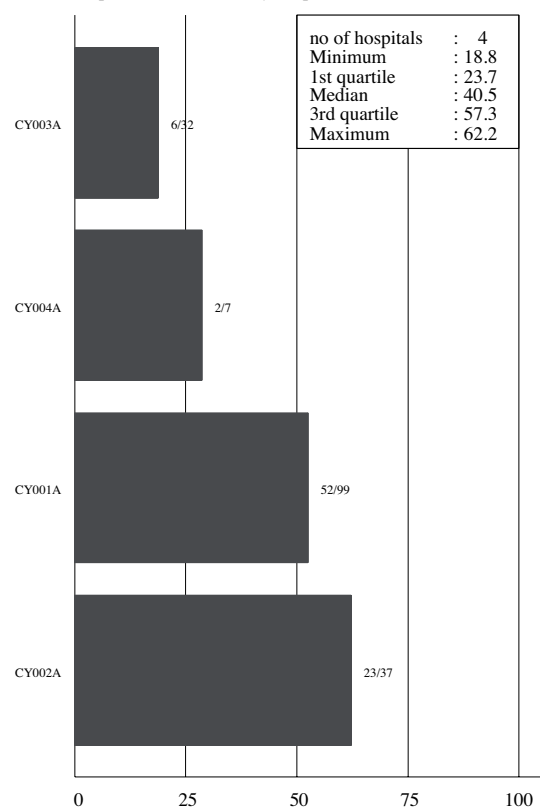
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Czech Republic

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	46/47
Hosps providing denom.data/ reporting data to EARSS	71/79
Number of blood culture sets	164,484
Number of hospital beds	43,558
Patient-days	11,170,547
Average occupancy rate (%)	76%
Median length of stay (days)	7
Estimated catchment population	8,379,721
% total population covered	82%
Type of participating hospitals	
Regional/Tertiary	34%
Provincial/Secondary	37%
District/Primary	30%

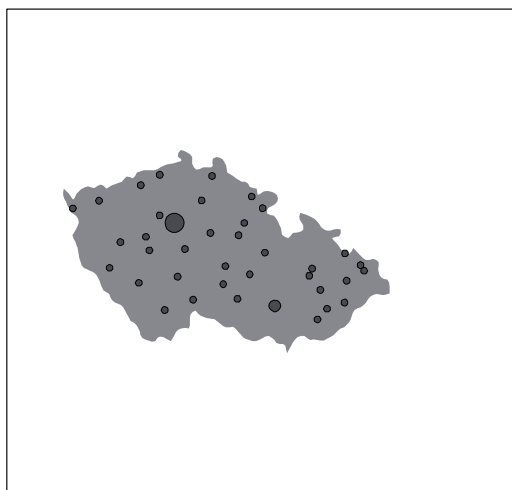


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	32	154	39	1074	36	1176	34	461	0	0	0	0
2002	34	144	41	1168	40	1587	39	587	0	0	0	0
2003	32	204	45	1387	43	1766	44	630	0	0	0	0
2004	37	162	45	1444	44	1966	41	660	0	0	0	0
2005	39	194	47	1553	47	2234	45	758	37	478	36	257
2006	39	172	47	1520	47	2165	45	695	45	1125	43	486
2007	41	205	47	1652	48	2407	47	816	48	1231	41	517
2008	40	243	47	1715	46	2738	44	883	45	1493	42	568

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	<1	2	<1	<1	<1	<1
	Penicillin I+R	7	8	2	6	4	2	4	3
	Macrolides I+R	2	4	2	4	2	3	5	3
<i>S. aureus</i>	Oxacillin/Methicillin R	6	6	6	9	13	12	13	14
<i>E. coli</i>	Aminopenicillins R	42	45	45	47	50	56	56	60
	Aminoglycosides R	6	6	5	5	6	8	7	9
	Fluoroquinolones R	8	10	13	16	20	23	24	26
	3rd gen. Cephalosporins R	2	1	1	2	2	5	7	10
<i>E. faecalis</i>	Aminopenicillins I+R	3	2	4	<1	<1	2	3	2
	HL Aminoglycosides R	38	39	44	43	45	43	49	49
	Glycopeptides R	2	<1	<1	<1	<1	<1	1	<1
<i>E. faecium</i>	Aminopenicillins I+R	67	73	80	81	92	90	91	94
	HL Aminoglycosides R	33	35	48	43	69	74	79	75
	Glycopeptides R	2	9	3	3	14	4	6	8
<i>K. pneumoniae</i>	Aminoglycosides R	36	38	43	42
	Fluoroquinolones R	38	47	48	52
	3rd gen. Cephalosporins R	32	35	46	48
<i>P. aeruginosa</i>	Piperacillin R	21	29	30	27
	Ceftazidime R	40	31	33	44
	Carbapenems R	31	33	36	29
	Aminoglycosides R	28	30	34	45
	Fluoroquinolones R	45	48	43	46

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=448		<i>S. aureus</i> n=3367		<i>E. coli</i> n=5142		<i>E. faecalis</i> n=1235		<i>E. faecium</i> n=463		<i>K. pneumo.</i> n=2723		<i>P. aeruginosa</i> n=1081	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	87	3	100	14	100	25	100	1	100	7	100	47	99	32
CSF	13	7	0	.	0	.	0	.	0	.	0	.	1	56
Gender														
Male	59	4	61	14	43	27	63	1	58	8	59	50	64	33
Female	41	3	39	14	57	24	37	1	42	6	41	42	36	31
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	13	10	4	2	2	12	4	2	1	0	3	31	2	24
5-19	6	4	2	3	1	10	0	.	0	.	1	34	2	25
20-64	46	3	42	13	32	23	43	1	52	10	41	51	41	40
65 and over	35	1	51	16	65	27	52	1	47	5	55	45	54	27
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	20	4	24	17	20	25	44	1	49	5	39	53	41	39
Internal Med.	40	2	45	13	49	23	29	1	21	3	33	40	27	27
Surgery	1	0	10	14	7	23	8	1	4	0	10	48	8	24
Other	36	6	20	11	24	29	19	0	26	16	18	46	24	29
Unknown	2	0	1	13	0	.	0	.	0	.	0	.	0	.

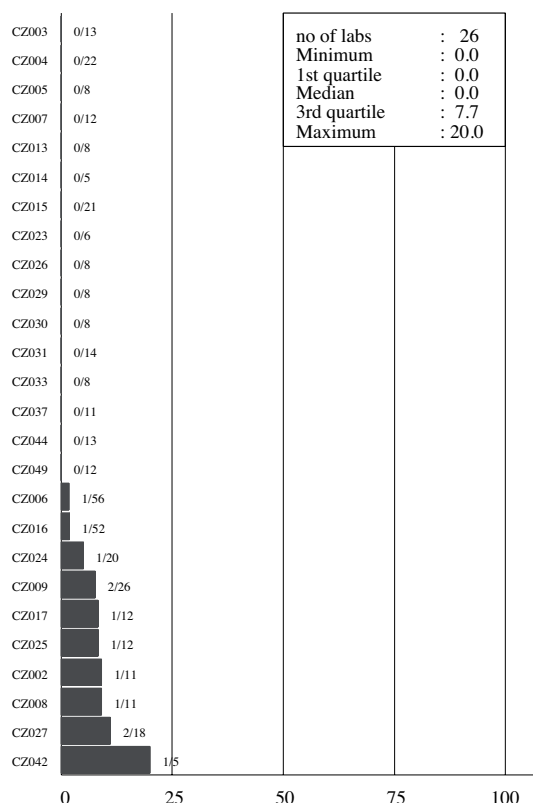
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

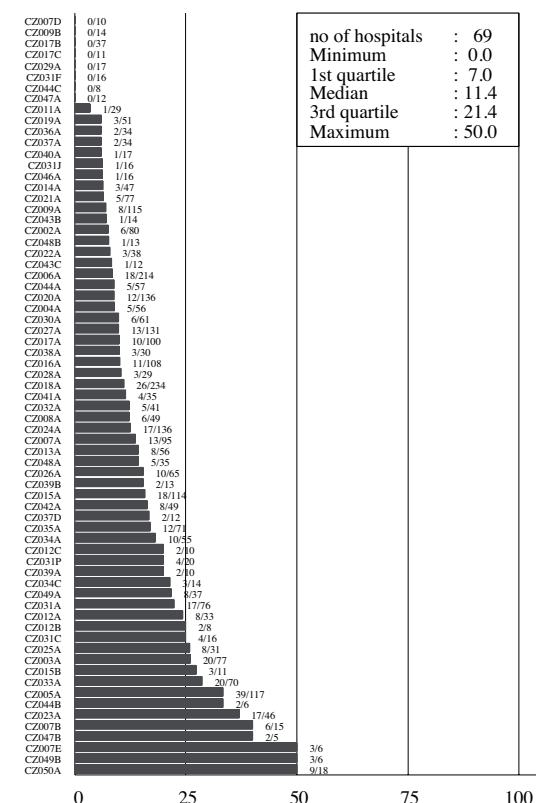
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=1964		<i>S. aureus</i> n=2610		<i>E. coli</i> n=5836		<i>E. faecalis</i> n=808		<i>E. faecium</i> n=678		<i>K. pneumo.</i> n=1112		<i>P. aeruginosa</i> n=649	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	93	3	100	1	100	10	100	0	100	0	100	10	100	2
CSF	7	3	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	50	3	62	2	47	12	67	1	57	0	58	12	62	1
Female	50	3	38	1	53	8	33	0	43	1	42	6	38	2
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	7	7	4	0	1	4	2	0	1	0	2	0	2	0
5-19	2	3	2	2	1	5	1	0	2	0	1	10	3	6
20-64	37	3	40	1	28	11	36	1	43	0	33	11	30	3
65 and over	54	3	54	2	70	9	61	0	54	1	64	9	65	1
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	0	.	1	6	3	17	13	0	34	0	5	12	8	8
Internal Med.	0	.	3	0	43	10	42	0	23	1	46	11	29	0
Surgery	0	.	1	12	16	6	20	0	15	0	21	9	14	3
Other	0	.	2	0	19	11	22	2	18	1	23	9	31	1
Unknown	100	3	94	1	19	10	3	0	10	0	5	4	18	2

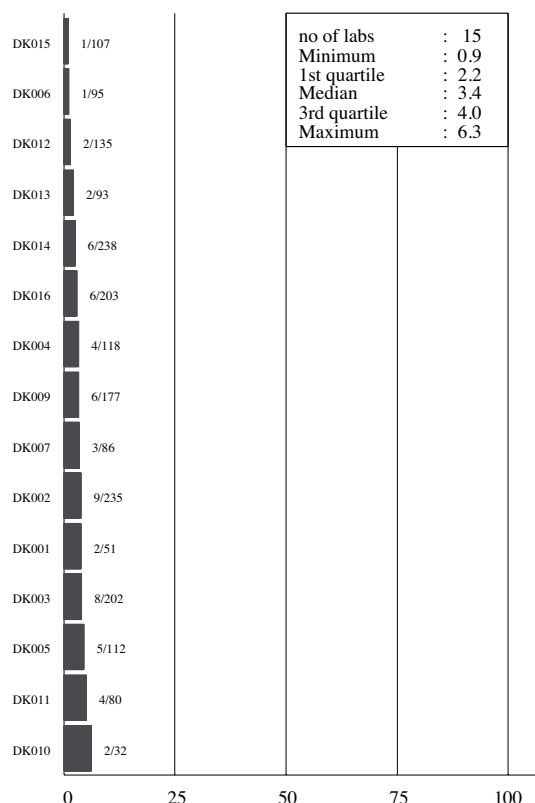
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
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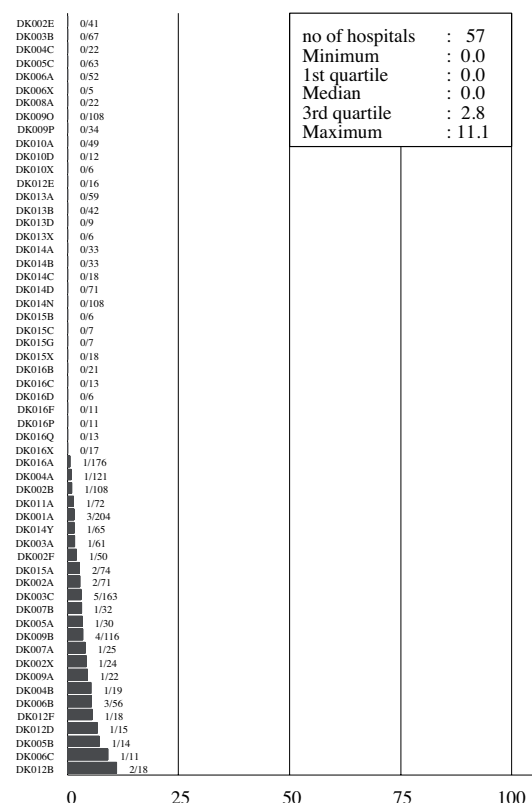
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Estonia

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	11/11
Hosps providing denom.data/ reporting data to EARSS	13/17
Number of blood culture sets	20,961
Number of hospital beds	5,511
Patient-days	1,531,284
Average occupancy rate (%)	76%
Median length of stay (days)	7
Estimated catchment population	1,300,000
% total population covered	100%
Type of participating hospitals	
Regional/Tertiary	31%
Provincial/Secondary	46%
District/Primary	23%

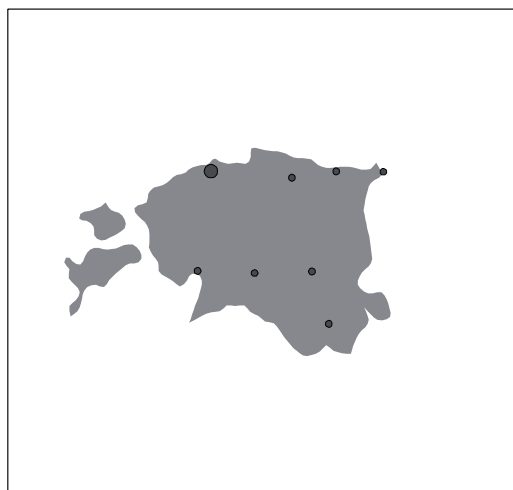


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	5	20	6	79	4	52	4	21	0	0	0	0
2002	5	21	8	81	6	67	3	13	0	0	0	0
2003	8	26	9	98	9	98	6	27	0	0	0	0
2004	6	40	9	104	10	167	5	63	0	0	0	0
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	65	11	185	11	267	11	86	10	72	8	41

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1
	Penicillin I+R	<1	<1	<1	<1	2	2	<1	5
	Macrolides I+R	5	<1	10	6	<1	3	2	4
<i>S. aureus</i>	Oxacillin/Methicillin R	5	1	4	5	2	3	9	4
	<i>E. coli</i>								
<i>E. coli</i>	Aminopenicillins R	43	42	42	55	45	52	50	47
	Aminoglycosides R	8	10	3	2	4	2	6	5
	Fluoroquinolones R	<1	5	5	6	5	7	7	7
	3rd gen. Cephalosporins R	6	2	1	4	1	<1	1	5
<i>E. faecalis</i>	Aminopenicillins I+R	8	10	4	14	14	9	<1	9
	HL Aminoglycosides R	<1	50	22	32	50	35	23	27
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	63	33	75	79	83	84	94	85
	HL Aminoglycosides R	63	67	50	79	74	78	89	75
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	3
<i>K. pneumoniae</i>	Aminoglycosides R	8	9	2	15
	Fluoroquinolones R	<1	5	2	7
	3rd gen. Cephalosporins R	8	9	3	12
<i>P. aeruginosa</i>	Piperacillin R	27	12	9	18
	Ceftazidime R	18	7	7	13
	Carbapenems R	38	29	18	30
	Aminoglycosides R	28	8	7	17
	Fluoroquinolones R	14	10	9	18

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=129		<i>S. aureus</i> n=391		<i>E. coli</i> n=460		<i>E. faecalis</i> n=77		<i>E. faecium</i> n=70		<i>K. pneumo.</i> n=132		<i>P. aeruginosa</i> n=85	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	84	3	100	7	99	7	100	0	100	1	100	8	100	24
CSF	16	0	0	.	1	0	0	.	0	.	0	.	0	.
Gender														
Male	60	3	59	7	40	10	62	0	54	0	64	7	58	22
Female	40	2	39	5	59	4	38	0	41	3	36	8	42	25
Unknown	0	.	1	60	2	0	0	.	4	0	0	.	0	.
Age (years)														
0-4	5	0	12	9	3	0	9	0	9	0	16	0	5	25
5-19	2	0	3	8	3	0	0	.	0	.	2	0	4	33
20-64	64	1	50	6	41	9	32	0	40	4	38	8	44	19
65 and over	29	3	34	8	51	6	55	0	50	0	42	11	48	27
Unknown	1	100	2	0	3	0	4	0	1	0	2	0	0	.
Hospital dep.														
ICU	43	0	22	11	15	6	25	0	36	0	36	15	54	26
Internal Med.	29	5	35	1	47	4	42	0	23	0	26	9	14	25
Surgery	1	0	10	5	5	22	8	0	7	0	5	0	6	0
Other	27	3	33	11	33	9	26	0	34	4	33	0	26	23
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

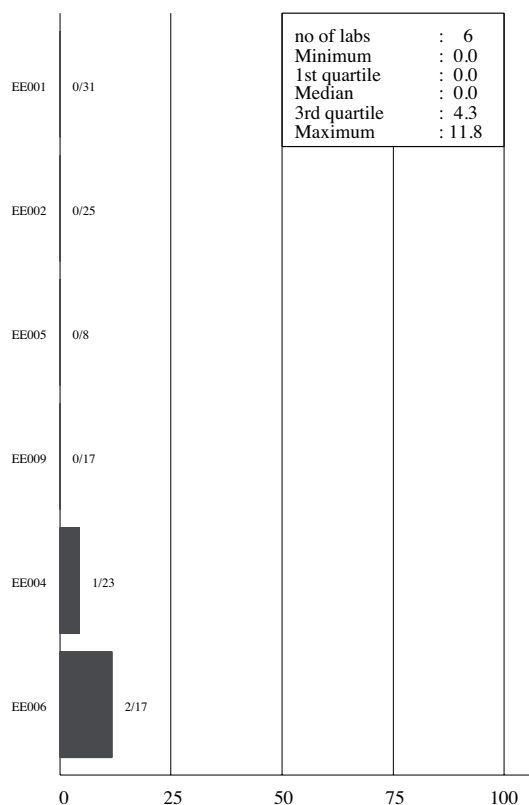
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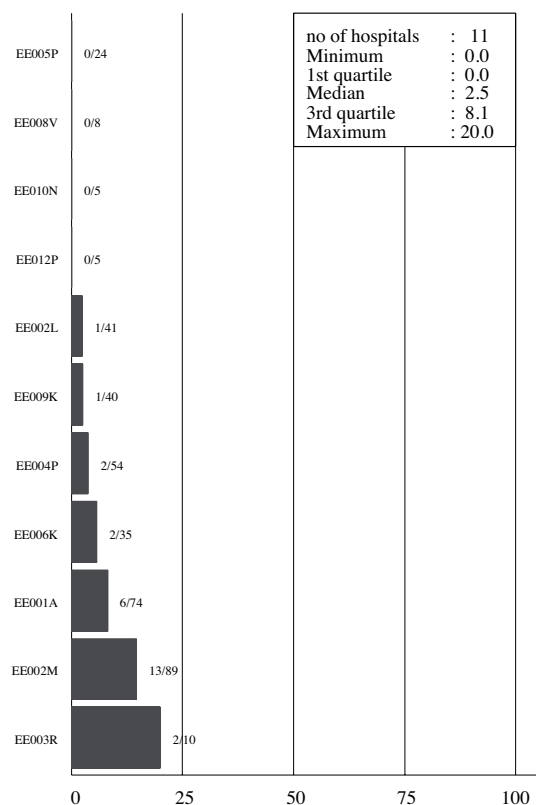
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Finland

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	13/15
Hosps providing denom.data/ reporting data to EARSS	11/15
Number of blood culture sets	185,885
Number of hospital beds	6,290
Patient-days	1,943,098
Average occupancy rate (%)	90%
Median length of stay (days)	5
Estimated catchment population	2,964,958
% total population covered	57%
Type of participating hospitals	
Regional/Tertiary	60%
Provincial/Secondary	40%
District/Primary	0%

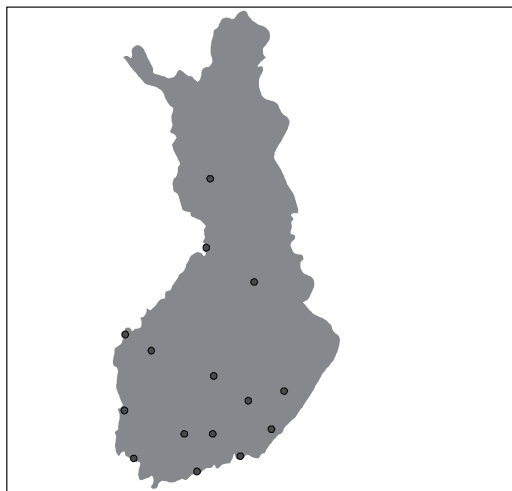


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	13	425	13	606	14	1284	13	274	0	0	0	0
2002	15	453	15	721	15	1330	14	278	0	0	0	0
2003	16	490	16	727	15	1450	15	266	0	0	0	0
2004	17	508	17	882	17	1749	17	336	0	0	0	0
2005	16	525	17	790	17	1924	17	341	14	175	13	108
2006	15	493	15	891	15	1875	15	348	14	228	14	163
2007	16	522	16	814	16	1949	16	400	15	273	14	183
2008	15	642	15	921	15	2111	15	382	12	288	12	175

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	1	2	2	<1	<1	2	1	<1
	Penicillin I+R	9	6	10	8	7	12	13	11
	Macrolides I+R	12	14	20	20	20	24	26	24
<i>S. aureus</i>	Oxacillin/Methicillin R	<1	<1	1	3	3	3	2	3
<i>E. coli</i>	Aminopenicillins R	33	30	33	33	35	36	34	35
	Aminoglycosides R	<1	<1	1	2	2	2	3	4
	Fluoroquinolones R	5	6	5	7	7	8	8	9
	3rd gen. Cephalosporins R	<1	<1	<1	2	2	2	2	2
<i>E. faecalis</i>	Aminopenicillins I+R	1	2	<1	<1	<1	<1	2	<1
	HL Aminoglycosides R	23	13	39	38	27	25	22	13
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	66	80	79	69	78	80	87	87
	HL Aminoglycosides R	<1	<1	4	12	1	16	19	15
	Glycopeptides R	<1	1	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	3	1	<1	1
	Fluoroquinolones R	3	4	<1	2
	3rd gen. Cephalosporins R	2	<1	1	2
<i>P. aeruginosa</i>	Piperacillin R	8	7	7	8
	Ceftazidime R	5	3	5	5
	Carbapenems R	15	8	8	6
	Aminoglycosides R	11	8	8	6
	Fluoroquinolones R	16	17	11	15

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=1164		<i>S. aureus</i> n=1735		<i>E. coli</i> n=4058		<i>E. faecalis</i> n=445		<i>E. faecium</i> n=318		<i>K. pneumo.</i> n=560		<i>P. aeruginosa</i> n=355	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	97	12	100	2	100	8	100	0	100	1	100	2	97	7
CSF	3	6	0	.	0	.	0	.	0	.	0	.	3	11
Gender														
Male	59	12	62	3	35	9	67	0	58	1	54	2	64	6
Female	41	12	38	2	65	8	33	0	42	0	46	1	36	9
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	14	19	3	0	2	5	3	0	1	0	2	20	0	.
5-19	3	5	4	3	1	6	1	0	1	0	0	.	2	0
20-64	49	11	43	2	30	8	29	0	38	1	33	3	26	9
65 and over	34	12	51	2	67	8	67	0	61	1	65	1	72	7
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	1	13	1	4	1	5	3	0	6	0	2	0	3	8
Internal Med.	9	7	12	1	8	7	9	0	12	0	9	4	7	0
Surgery	1	14	4	1	3	5	6	0	10	0	4	4	6	5
Other	32	10	20	2	25	8	14	0	10	0	22	2	17	8
Unknown	58	14	62	3	63	9	67	0	61	1	63	1	66	8

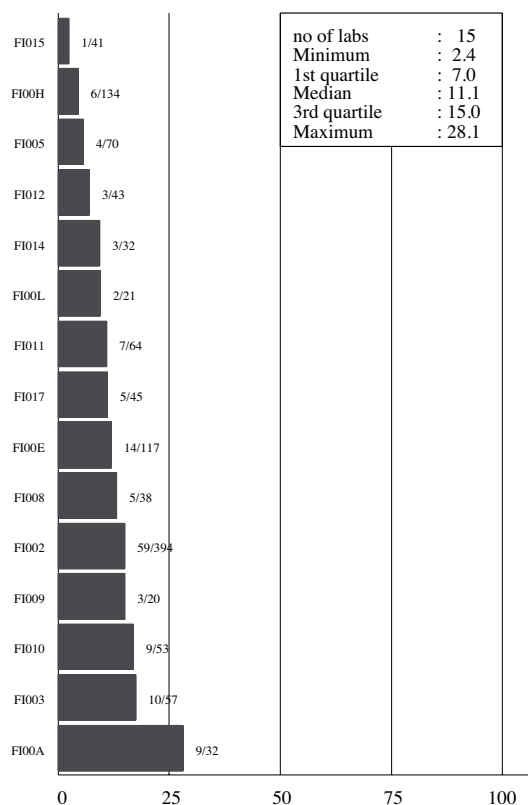
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

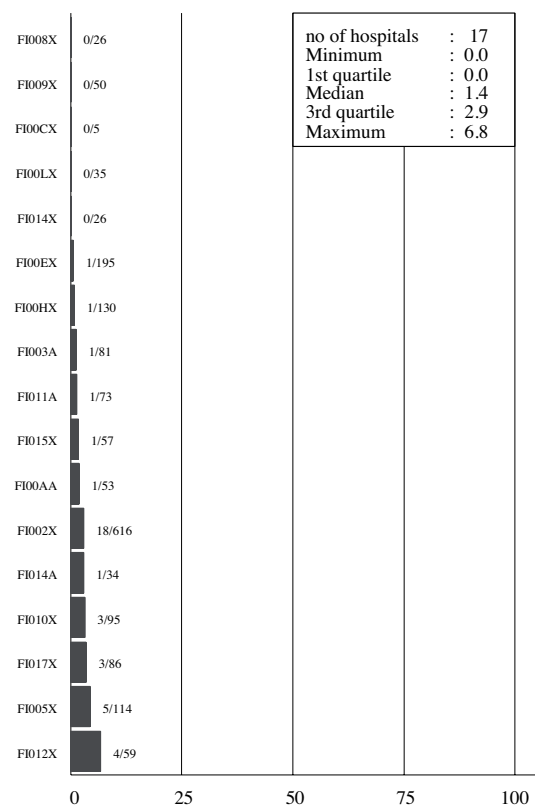
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



France

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data*

	Total
Labs providing denom.data/ reporting data to EARSS	0/56
Hosps providing denom.data/ reporting data to EARSS	54/56
Number of blood culture sets	na
Number of hospital beds	40,004
Patient-days	11,921,546
Average occupancy rate (%)	80%
Median length of stay (days)	7
Estimated catchment population	na
% total population covered	na
Type of participating hospitals	
Regional/Tertiary	na
Provincial/Secondary	na
District/Primary	na

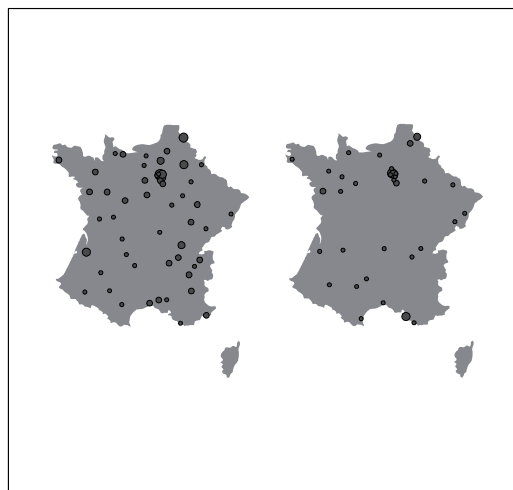


Figure 1. Geographic distribution of laboratories in 2008 (left: reporting on *S. pneumoniae*, right: reporting on all other pathogens)

* Denominator data from one surveillance network, reporting all pathogens except *S. pneumoniae*

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i> *		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	21	1714	0	0	0	0	0	0	0	0
2002	0	0	21	1663	21	2495	21	467	0	0	0	0
2003	0	0	21	1708	21	2267	21	483	0	0	0	0
2004	0	0	50	3347	50	5678	47	882	0	0	0	0
2005	195	632	50	3483	50	6056	47	1023	49	839	48	993
2006	97	371	50	3818	50	6718	50	1154	50	963	47	1006
2007	168	663	57	4250	57	8115	56	1552	56	1194	56	1314
2008	127	557	56	4376	56	7996	54	1556	54	1138	54	1227

* Data from the first half of each year

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	5	4	4	7
	Penicillin I+R	36	32	34	30
	Macrolides I+R	41	36	37	31
<i>S. aureus</i>	Oxacillin/Methicillin R	33	33	29	29	27	27	26	24
<i>E. coli</i>	Aminopenicillins R	.	52	50	47	50	53	54	54
	Aminoglycosides R	.	4	5	4	5	6	6	7
	Fluoroquinolones R	.	8	9	8	11	14	15	16
	3rd gen. Cephalosporins R	.	<1	<1	<1	1	2	2	4
<i>E. faecalis</i>	Aminopenicillins I+R	.	5	3	1	<1	1	1	<1
	HL Aminoglycosides R	.	15	16	17	15	16	15	18
	Glycopeptides R	.	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	.	34	30	56	64	69	67	68
	HL Aminoglycosides R	.	10	23	21	24	30	30	30
	Glycopeptides R	.	2	<1	5	2	3	1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	5	7	11	17
	Fluoroquinolones R	7	9	14	21
	3rd gen. Cephalosporins R	4	6	10	15
<i>P. aeruginosa</i>	Piperacillin R	15	11	11	14
	Ceftazidime R	9	6	7	8
	Carbapenems R	14	12	14	14
	Aminoglycosides R	22	16	18	15
	Fluoroquinolones R	27	23	24	22

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=1220		<i>S. aureus</i> n=8626		<i>E. coli</i> n=15469		<i>E. faecalis</i> n=2282		<i>E. faecium</i> n=675		<i>K. pneumo.</i> n=2299		<i>P. aeruginosa</i> n=2525	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	70	32	100	25	100	15	100	0	100	1	100	13	100	14
CSF	30	32	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	57	29	62	25	46	18	63	0	59	1	57	14	63	14
Female	42	36	36	25	52	13	35	0	39	0	42	11	35	14
Unknown	0	.	2	17	2	15	2	0	3	6	1	3	2	13
Age (years)														
0-4	20	34	4	13	2	6	4	0	2	0	2	12	2	2
5-19	10	18	3	7	1	8	1	0	1	0	1	24	2	9
20-64	33	27	40	18	34	15	39	0	43	2	45	13	47	18
65 and over	38	40	52	33	63	16	56	0	54	0	51	12	49	12
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	0	.	15	25	8	16	24	0	23	1	17	26	30	23
Internal Med.	100	32	34	28	28	16	27	0	28	0	29	10	23	11
Surgery	0	.	15	23	11	16	17	0	16	0	16	18	11	13
Other	0	.	34	23	51	14	31	0	32	2	37	7	35	9
Unknown	0	.	1	29	2	17	1	0	1	0	1	9	1	4

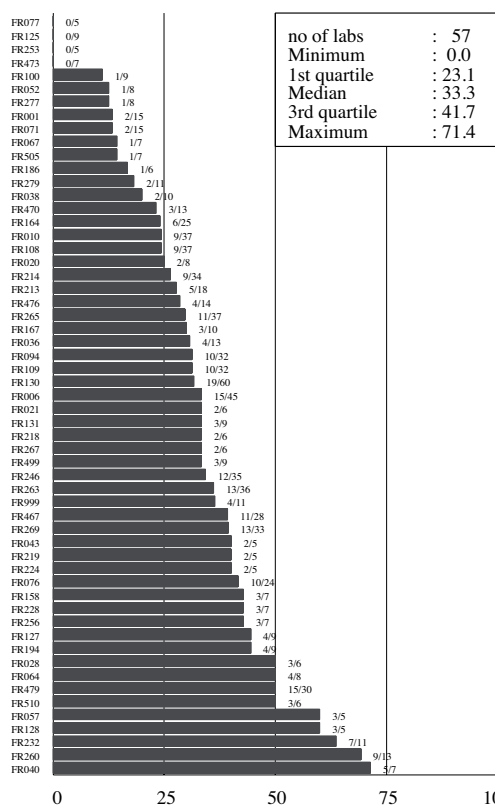
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VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

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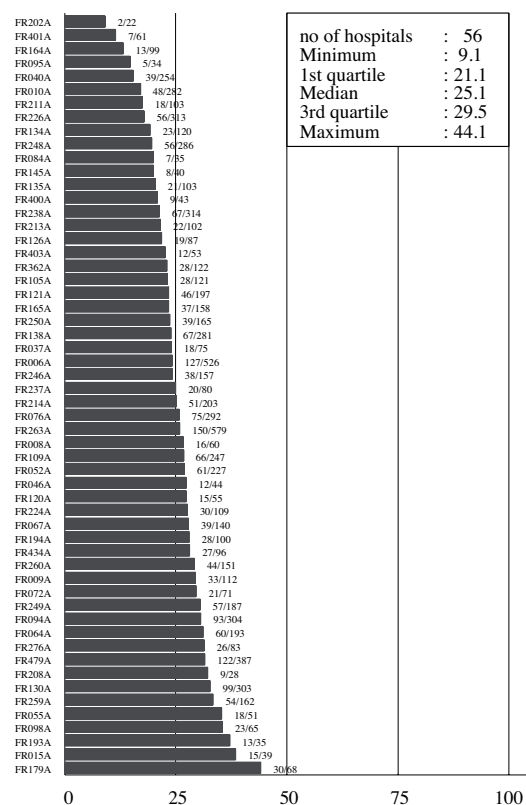
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Germany

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	5/14
Hosps providing denom.data/ reporting data to EARSS	5/110
Number of blood culture sets	21,926
Number of hospital beds	2,443
Patient-days	156,465
Average occupancy rate (%)	99%
Median length of stay (days)	15
Estimated catchment population	na
% total population covered	na
Type of participating hospitals	
Regional/Tertiary	40%
Provincial/Secondary	0%
District/Primary	40%

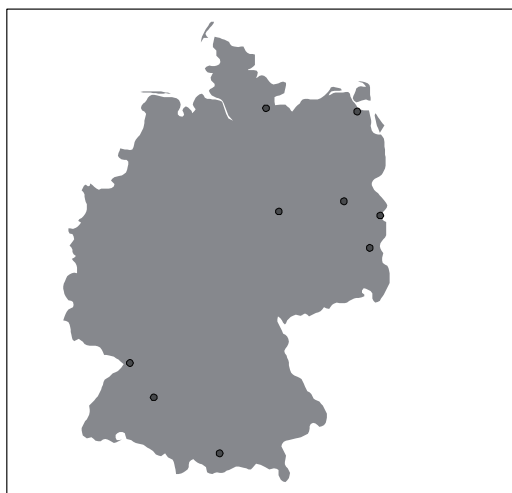


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	21	211	22	1220	21	1269	20	294	0	0	0	0
2002	17	248	18	1067	16	1068	14	290	0	0	0	0
2003	17	175	20	920	19	997	17	347	0	0	0	0
2004	16	144	22	1106	22	1217	22	607	0	0	1	1
2005	15	119	17	826	17	961	17	569	12	105	12	117
2006	14	84	18	796	18	851	16	529	14	148	12	162
2007	10	72	12	853	12	977	12	648	10	173	11	198
2008	11	199	14	1089	14	1615	13	451	11	235	11	167

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	1	<1	<1	<1	<1	1	<1	<1
	Penicillin I+R	4	1	1	1	4	5	3	5
	Macrolides I+R	17	14	11	13	17	12	8	9
<i>S. aureus</i>	Oxacillin/Methicillin R	16	18	18	20	21	20	16	19
<i>E. coli</i>	Aminopenicillins R	46	49	47	55	54	60	55	55
	Aminoglycosides R	5	5	5	4	6	10	6	7
	Fluoroquinolones R	11	15	14	24	23	29	30	23
	3rd gen. Cephalosporins R	<1	<1	<1	2	2	4	8	5
<i>E. faecalis</i>	Aminopenicillins I+R	8	10	7	7	3	3	6	<1
	HL Aminoglycosides R	31	42	47	42	34	29	67	39
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	79	80	78	93	96	94	95	95
	HL Aminoglycosides R	43	68	47	61	52	38	73	35
	Glycopeptides R	1	4	3	11	10	8	15	6
<i>K. pneumoniae</i>	Aminoglycosides R	10	12	6	10
	Fluoroquinolones R	6	12	9	15
	3rd gen. Cephalosporins R	7	14	6	11
<i>P. aeruginosa</i>	Piperacillin R	.	.	.	<1	18	17	17	9
	Ceftazidime R	.	.	.	<1	11	12	17	8
	Carbapenems R	.	.	.	<1	25	17	22	11
	Aminoglycosides R	.	.	.	<1	12	18	9	10
	Fluoroquinolones R	.	.	.	<1	23	28	28	22

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=271		<i>S. aureus</i> n=1942		<i>E. coli</i> n=2582		<i>E. faecalis</i> n=647		<i>E. faecium</i> n=449		<i>K. pneumo.</i> n=408		<i>P. aeruginosa</i> n=364	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	95	4	100	18	100	26	100	1	100	12	100	9	99	17
CSF	5	7	0	.	0	.	0	.	0	.	0	.	1	33
Gender														
Male	46	4	55	18	38	30	61	1	54	12	50	8	53	18
Female	37	5	31	17	45	23	27	0	35	13	33	7	34	14
Unknown	18	4	14	21	17	23	12	0	11	6	17	18	14	18
Age (years)														
0-4	10	11	2	7	2	2	2	0	3	0	5	5	1	20
5-19	5	15	2	8	0	.	1	0	1	25	0	.	1	40
20-64	34	3	31	14	24	29	33	0	41	13	29	13	32	18
65 and over	51	3	65	21	74	25	64	1	55	11	65	8	65	15
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	18	4	16	20	12	24	16	3	21	4	19	8	17	15
Internal Med.	49	4	41	17	51	23	35	0	27	15	36	7	28	13
Surgery	4	0	15	21	10	30	17	0	20	7	13	6	15	13
Other	26	7	26	15	25	30	30	0	31	18	30	13	38	23
Unknown	3	0	2	35	2	23	2	0	0	.	2	22	2	11

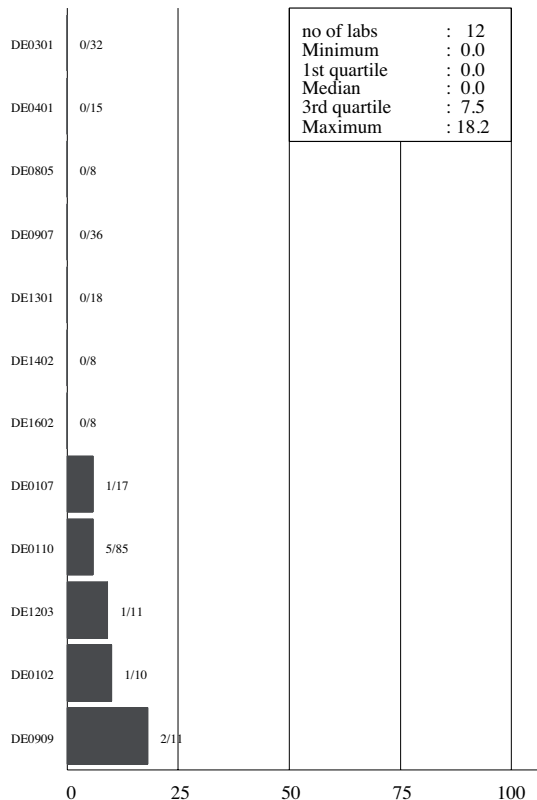
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MRSA = Methicillin Resistant *S. aureus*
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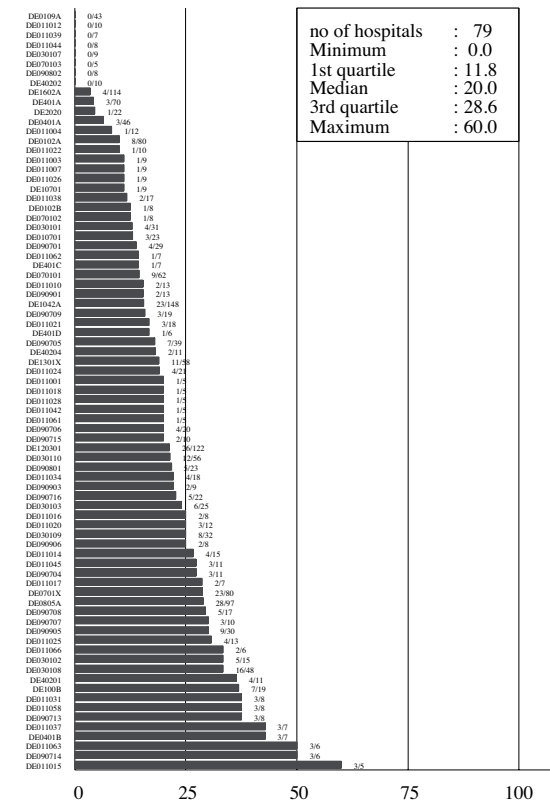
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Greece

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	na
Hosps providing denom.data/ reporting data to EARSS	na
Number of blood culture sets	na
Number of hospital beds	na
Patient-days	na
Average occupancy rate (%)	na
Median length of stay (days)	na
Estimated catchment population	na
% total population covered	na
Type of participating hospitals	
Regional/Tertiary	na
Provincial/Secondary	na
District/Primary	na



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	25	360	26	619	25	304	0	0	0	0
2002	0	0	33	368	35	588	28	293	0	0	0	0
2003	0	0	34	666	35	1076	32	623	0	0	0	0
2004	0	0	35	609	39	1131	34	566	0	0	0	0
2005	0	0	35	681	35	1140	34	737	33	774	33	699
2006	0	0	42	826	41	1253	39	948	38	841	38	818
2007	0	0	41	806	43	1234	39	999	38	972	37	802
2008	0	0	46	859	44	1467	42	996	41	1099	42	920

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R
	Penicillin I+R
	Macrolides I+R
<i>S. aureus</i>	Oxacillin/Methicillin R	39	44	45	44	42	43	48	41
	<i>E. coli</i>								
<i>E. coli</i>	Aminopenicillins R	47	45	44	46	46	46	48	50
	Aminoglycosides R	4	7	6	6	7	7	9	15
	Fluoroquinolones R	9	13	12	12	12	14	19	22
	3rd gen. Cephalosporins R	5	6	6	6	7	6	8	10
<i>E. faecalis</i>	Aminopenicillins I+R	8	4	4	4	3	5	4	3
	HL Aminoglycosides R	57	60	52	59	54	58	65	52
	Glycopeptides R	7	13	7	4	4	5	7	7
<i>E. faecium</i>	Aminopenicillins I+R	86	75	89	84	85	88	91	85
	HL Aminoglycosides R	45	52	40	52	34	35	44	52
	Glycopeptides R	15	19	18	20	37	42	37	28
<i>K. pneumoniae</i>	Aminoglycosides R	60	54	54	55
	Fluoroquinolones R	54	50	55	64
	3rd gen. Cephalosporins R	61	58	62	66
<i>P. aeruginosa</i>	Piperacillin R	30	39	38	34
	Ceftazidime R	27	34	40	37
	Carbapenems R	39	48	47	49
	Aminoglycosides R	40	47	49	48
	Fluoroquinolones R	39	45	50	48

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=0		<i>S. aureus</i> n=1665		<i>E. coli</i> n=2673		<i>E. faecalis</i> n=1227		<i>E. faecium</i> n=756		<i>K. pneumo.</i> n=2052		<i>P. aeruginosa</i> n=1714	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	.	.	100	44	99	21	100	7	100	33	97	63	96	47
CSF	.	.	0	.	1	6	0	.	0	.	3	80	4	73
Gender														
Male	.	.	9	47	6	20	7	7	8	41	7	55	6	29
Female	.	.	6	39	9	19	5	6	6	31	5	63	3	36
Unknown	.	.	86	45	85	21	88	7	85	32	88	65	90	50
Age (years)														
0-4	.	.	4	38	5	20	5	10	6	51	4	64	5	59
5-19	.	.	0	.	0	.	0	.	0	.	0	.	0	.
20-64	.	.	2	31	2	11	1	13	3	65	2	55	1	36
65 and over	.	.	2	59	2	24	3	13	2	24	2	63	2	15
Unknown	.	.	92	45	91	21	91	6	89	30	92	64	92	48
Hospital dep.														
ICU	.	.	15	64	4	24	33	10	33	34	45	87	43	62
Internal Med.	.	.	64	38	77	20	50	5	47	33	37	38	38	35
Surgery	.	.	13	60	11	28	14	4	15	27	13	64	16	47
Other	.	.	3	41	3	2	1	0	1	29	2	31	1	15
Unknown	.	.	5	33	5	21	2	14	4	33	2	39	3	32

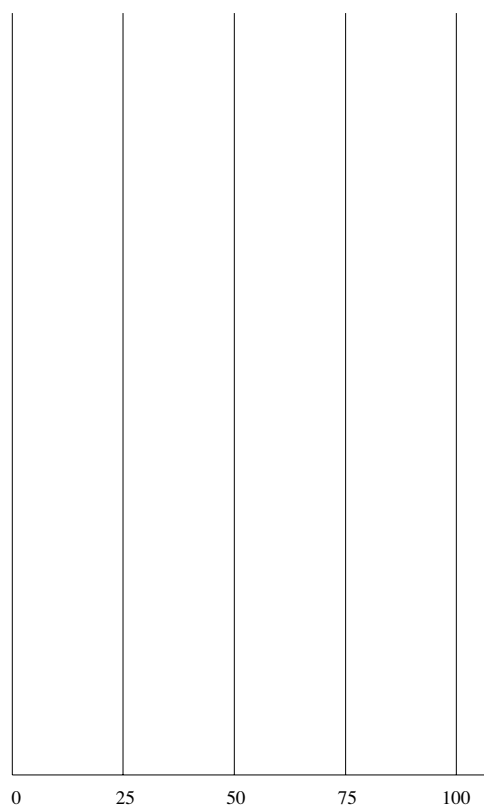
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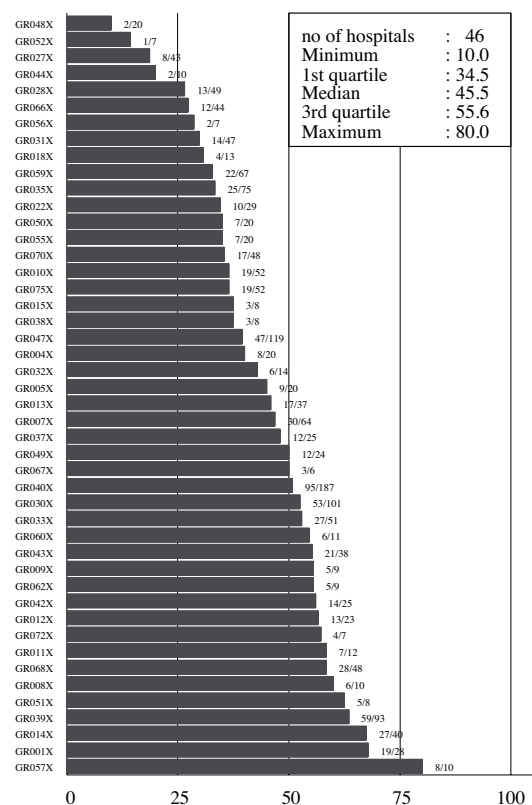
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Hungary

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	14/26
Hosps providing denom.data/ reporting data to EARSS	38/68
Number of blood culture sets	45,437
Number of hospital beds	23,678
Patient-days	6,342,602
Average occupancy rate (%)	74%
Median length of stay (days)	8
Estimated catchment population	9,900,000
% total population covered	100%
Type of participating hospitals	
Regional/Tertiary	50%
Provincial/Secondary	37%
District/Primary	8%

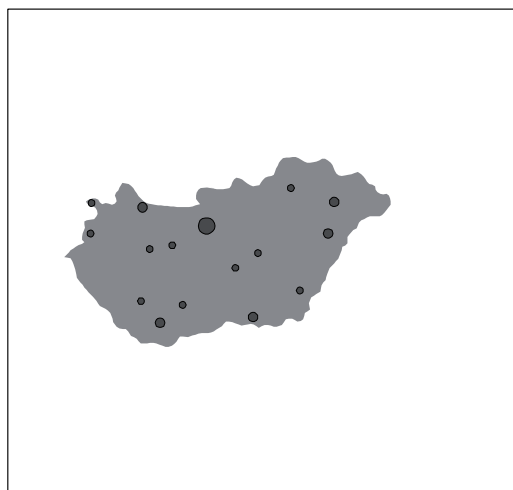


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	14	36	18	301	18	264	17	121	0	0	0	0
2002	17	61	24	413	24	354	23	169	0	0	0	0
2003	20	134	27	858	27	842	25	279	0	0	0	0
2004	26	143	30	1020	28	967	26	366	0	0	0	0
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

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	8	3	3	<1	4	1	5	8
	Penicillin I+R	22	23	24	16	21	18	23	27
	Macrolides I+R	19	21	25	25	32	19	36	32
<i>S. aureus</i>	Oxacillin/Methicillin R	5	9	15	17	20	25	23	23
<i>E. coli</i>	Aminopenicillins R	46	45	49	55	51	53	54	59
	Aminoglycosides R	4	6	8	10	9	12	11	13
	Fluoroquinolones R	5	10	15	19	22	27	26	26
	3rd gen. Cephalosporins R	<1	2	<1	3	4	5	5	9
<i>E. faecalis</i>	Aminopenicillins I+R	5	2	<1	2	1	3	2	3
	HL Aminoglycosides R	.	100	87	57	43	47	48	53
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	100	89	91	95	91	88	88	96
	HL Aminoglycosides R	.	100	96	80	64	67	53	62
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	3
<i>K. pneumoniae</i>	Aminoglycosides R	26	20	29	36
	Fluoroquinolones R	21	13	22	33
	3rd gen. Cephalosporins R	28	20	25	35
<i>P. aeruginosa</i>	Piperacillin R	10	9	11	13
	Ceftazidime R	10	8	9	11
	Carbapenems R	18	16	19	26
	Aminoglycosides R	32	23	26	26
	Fluoroquinolones R	28	21	24	26

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=312		<i>S. aureus</i> n=2380		<i>E. coli</i> n=2212		<i>E. faecalis</i> n=680		<i>E. faecium</i> n=130		<i>K. pneumo.</i> n=686		<i>P. aeruginosa</i> n=1001	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	68	28	100	23	100	26	100	0	100	2	99	30	98	22
CSF	32	19	0	.	0	.	0	.	0	.	1	44	2	29
Gender														
Male	80	26	84	23	79	28	88	0	86	1	85	32	85	22
Female	19	20	16	24	21	21	12	0	14	6	15	23	15	25
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	13	45	2	5	3	11	3	0	5	0	11	24	5	14
5-19	5	27	1	3	2	31	1	0	2	0	2	27	2	32
20-64	53	21	48	23	42	25	49	0	51	3	41	36	50	27
65 and over	29	23	48	24	53	28	47	0	43	0	45	27	43	17
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	30	26	19	29	13	20	32	0	45	0	26	39	37	28
Internal Med.	12	16	26	24	25	23	18	0	11	0	17	23	13	12
Surgery	3	38	12	27	7	29	13	0	7	0	12	34	13	21
Other	50	27	38	17	48	28	32	0	34	5	36	23	29	22
Unknown	5	19	6	24	6	32	5	0	4	0	8	45	8	14

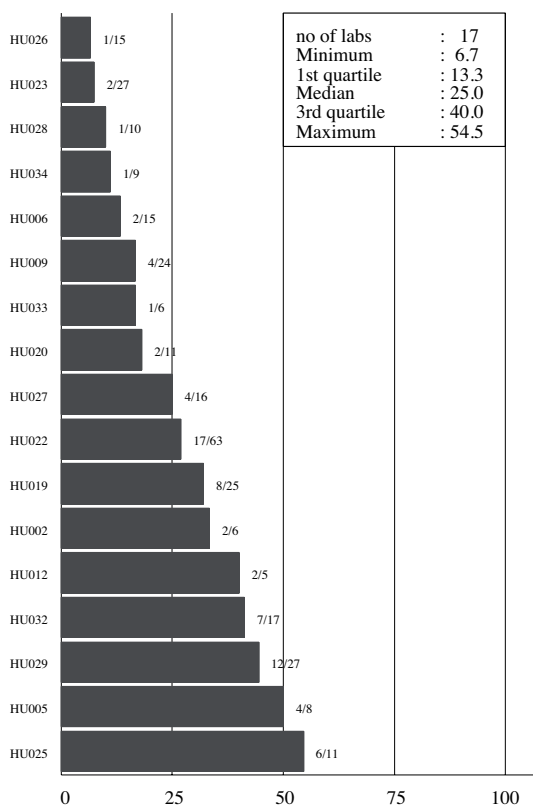
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

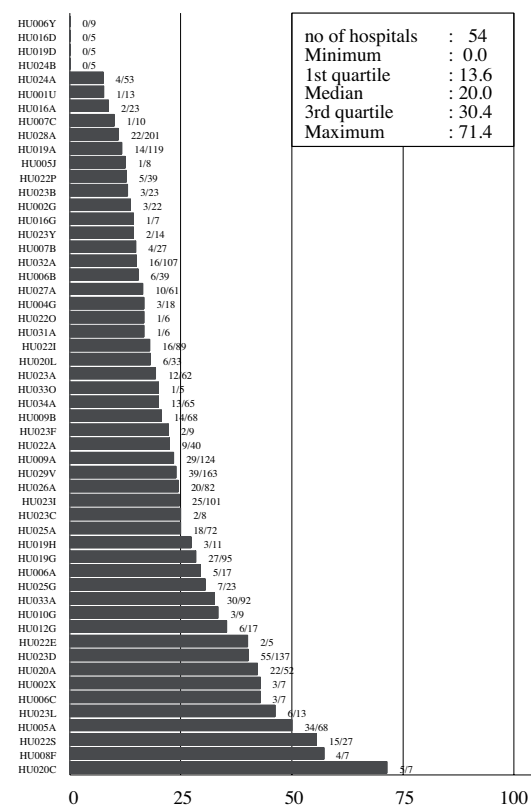
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Iceland

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	2/2
Hosps providing denom.data/ reporting data to EARSS	2/9
Number of blood culture sets	11,830
Number of hospital beds	988
Patient-days	274,410
Average occupancy rate (%)	79%
Median length of stay (days)	7
Estimated catchment population	300,000
% total population covered	100%
Type of participating hospitals	
Regional/Tertiary	100%
Provincial/Secondary	0%
District/Primary	0%

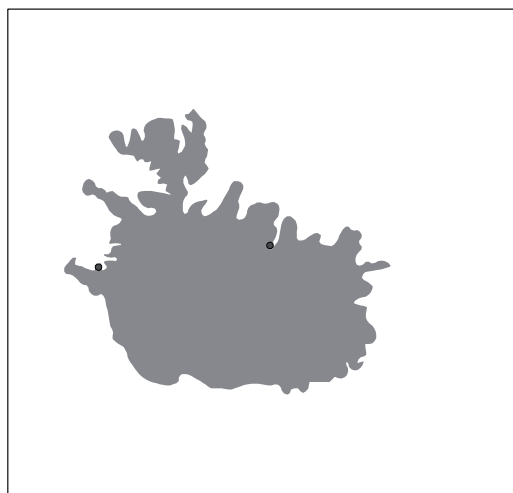


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	2	48	2	63	2	86	2	18	0	0	0	0
2002	2	43	2	60	2	83	2	25	0	0	0	0
2003	2	35	2	64	2	100	2	22	0	0	0	0
2004	2	54	2	55	2	119	1	27	0	0	0	0
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

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	2	<1	2	<1	<1	2	<1
	Penicillin I+R	6	5	9	17	8	6	7	9
	Macrolides I+R	8	5	20	8	17	10	17	22
<i>S. aureus</i>	Oxacillin/Methicillin R	<1	<1	<1	<1	<1	<1	<1	2
<i>E. coli</i>	Aminopenicillins R	42	19	42	43	38	45	46	44
	Aminoglycosides R	4	1	2	<1	<1	7	6	7
	Fluoroquinolones R	4	3	6	2	3	11	17	6
	3rd gen. Cephalosporins R	<1	<1	1	<1	<1	<1	2	<1
<i>E. faecalis</i>	Aminopenicillins I+R	<1	<1	<1	<1	<1	7	<1	<1
	HL Aminoglycosides R	8	6	<1	5	<1	3	13	30
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	40	29	57	63	80	56	57	43
	HL Aminoglycosides R	<1	<1	<1	13	<1	14	14	43
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	<1	<1	<1	4
	Fluoroquinolones R	<1	<1	<1	8
	3rd gen. Cephalosporins R	<1	<1	<1	4
<i>P. aeruginosa</i>	Piperacillin R	8	<1	<1	<1
	Ceftazidime R	8	<1	<1	<1
	Carbapenems R	8	<1	<1	<1
	Aminoglycosides R	<1	<1	<1	<1
	Fluoroquinolones R	<1	<1	<1	<1

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=88		<i>S. aureus</i> n=128		<i>E. coli</i> n=205		<i>E. faecalis</i> n=25		<i>E. faecium</i> n=21		<i>K. pneumo.</i> n=51		<i>P. aeruginosa</i> n=18	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	93	9	100	1	100	11	100	0	100	0	100	2	94	0
CSF	7	0	0	.	0	.	0	.	0	.	0	.	6	0
Gender														
Male	59	8	55	1	43	13	68	0	62	0	49	0	72	0
Female	41	8	45	0	57	9	32	0	38	0	51	4	28	0
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	22	11	5	0	5	0	4	0	0	.	0	.	6	0
5-19	5	0	8	0	0	.	0	.	0	.	0	.	0	.
20-64	41	8	40	2	30	13	28	0	33	0	35	6	50	0
65 and over	33	7	48	0	64	11	68	0	67	0	65	0	44	0
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	3	0	2	0	2	0	4	0	14	0	2	0	11	0
Internal Med.	8	0	20	0	12	0	16	0	10	0	20	0	28	0
Surgery	0	.	4	0	4	38	16	0	10	0	10	0	0	.
Other	84	8	68	1	73	13	56	0	62	0	65	3	61	0
Unknown	5	25	5	0	9	0	8	0	5	0	4	0	0	.

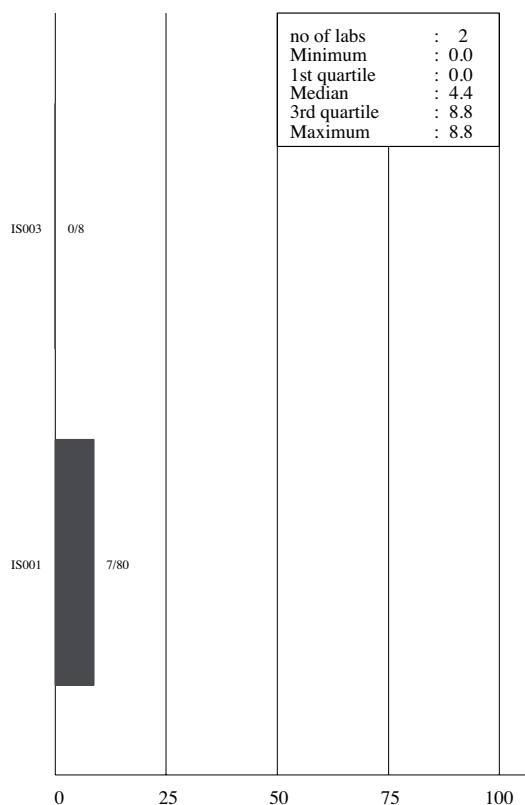
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VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

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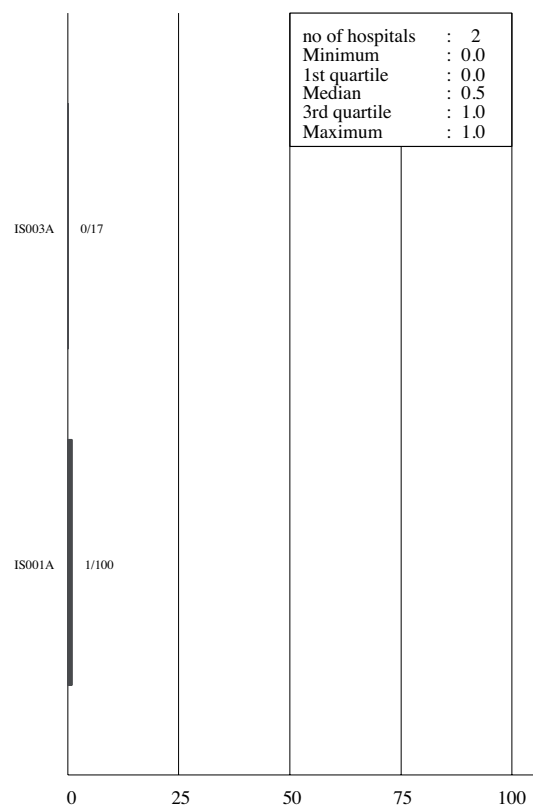
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Ireland

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	40/41
Hosps providing denom.data/ reporting data to EARSS	45/74
Number of blood culture sets	183,125
Number of hospital beds	11,717
Patient-days	374729833
Average occupancy rate (%)	87%
Median length of stay (days)	.0
Estimated catchment population	4,116,600
% total population covered	98%
Type of participating hospitals	
Regional/Tertiary	20%
Provincial/Secondary	47%
District/Primary	16%

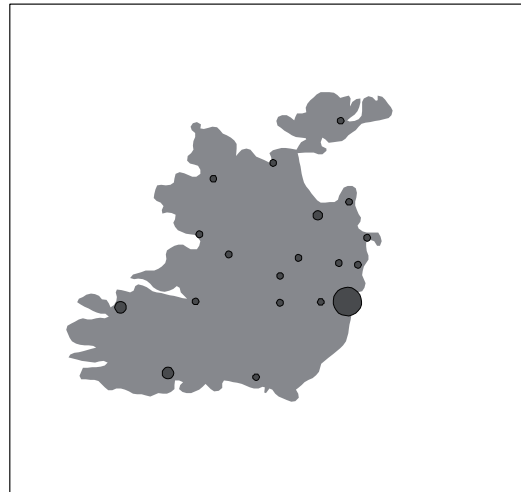


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	21	246	19	798	0	0	0	0	0	0	0	0
2002	20	277	22	998	20	736	15	250	0	0	0	0
2003	24	363	26	1108	26	978	21	348	0	0	0	0
2004	28	399	38	1286	37	1235	29	418	0	0	0	0
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	441	38	1242	41	1875	37	685	33	307	29	191

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	2	2	3	3	3	3	6	6
	Penicillin I+R	12	12	12	10	11	16	17	23
	Macrolides I+R	12	13	12	14	12	16	17	17
<i>S. aureus</i>	Oxacillin/Methicillin R	42	42	42	41	42	42	38	33
<i>E. coli</i>	Aminopenicillins R	.	62	61	65	67	69	65	67
	Aminoglycosides R	.	3	4	5	7	7	10	9
	Fluoroquinolones R	.	5	10	12	17	21	21	23
	3rd gen. Cephalosporins R	.	2	2	2	4	4	5	6
<i>E. faecalis</i>	Aminopenicillins I+R	.	8	5	<1	4	5	2	<1
	HL Aminoglycosides R	.	39	32	42	42	43	38	31
	Glycopeptides R	.	2	<1	1	3	3	3	3
<i>E. faecium</i>	Aminopenicillins I+R	.	89	91	96	93	94	93	95
	HL Aminoglycosides R	.	17	54	56	52	44	36	27
	Glycopeptides R	.	11	19	22	31	36	33	35
<i>K. pneumoniae</i>	Aminoglycosides R	5	9	10	9
	Fluoroquinolones R	3	16	17	11
	3rd gen. Cephalosporins R	7	9	8	11
<i>P. aeruginosa</i>	Piperacillin R	7	7	6	5
	Ceftazidime R	10	6	5	4
	Carbapenems R	11	9	9	6
	Aminoglycosides R	7	9	10	6
	Fluoroquinolones R	14	17	18	16

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=876		<i>S. aureus</i> n=2574		<i>E. coli</i> n=3597		<i>E. faecalis</i> n=569		<i>E. faecium</i> n=713		<i>K. pneumo.</i> n=541		<i>P. aeruginosa</i> n=335	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	96	20	100	36	100	22	100	3	100	34	100	9	99	8
CSF	4	31	0	.	0	.	0	.	0	.	0	.	1	0
Gender														
Male	57	21	63	34	45	27	59	3	58	33	60	9	63	7
Female	42	20	37	39	55	18	41	3	42	35	40	11	37	9
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	15	24	6	12	3	3	8	0	3	9	5	7	6	0
5-19	2	10	4	10	1	2	1	0	2	8	1	25	2	29
20-64	39	18	40	26	31	20	37	3	44	42	42	12	36	8
65 and over	43	22	50	48	64	24	53	3	51	29	52	8	56	7
Unknown	0	.	0	.	0	.	0	.	0	.	1	33	0	.
Hospital dep.														
ICU	3	25	4	51	3	24	6	0	10	41	4	15	7	4
Internal Med.	16	22	12	40	14	22	11	2	6	29	9	4	10	17
Surgery	2	39	7	50	7	26	7	5	7	22	10	0	6	5
Other	29	21	19	28	22	15	15	0	10	29	20	8	16	7
Unknown	50	18	58	35	55	24	62	4	67	35	57	12	60	6

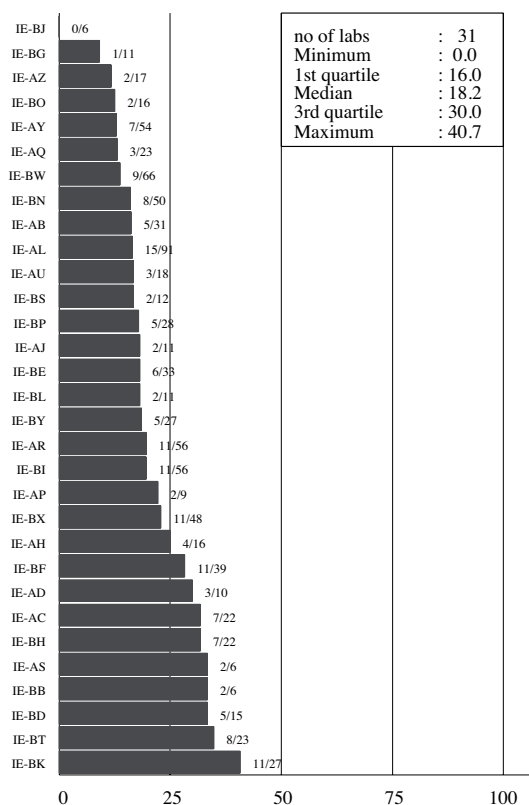
PNSP = Penicillin Non-Susceptible *S. pneumonia*
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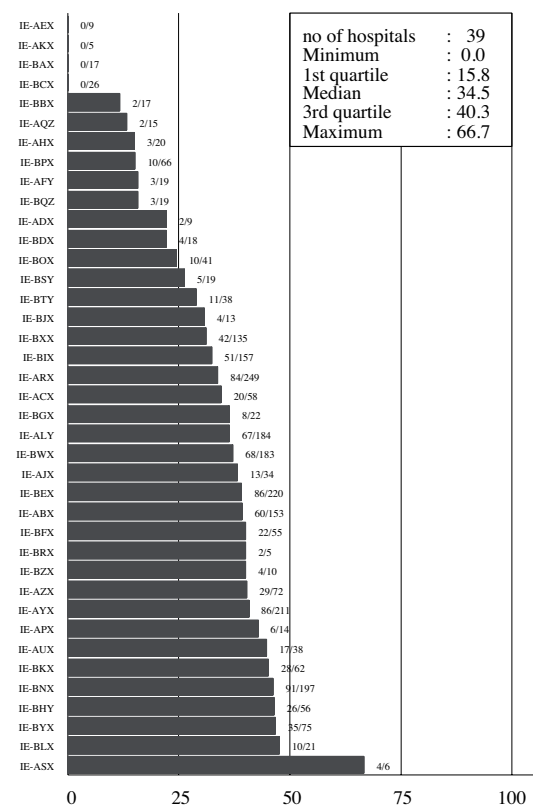
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Israel

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	5/5
Hosps providing denom.data/ reporting data to EARSS	5/5
Number of blood culture sets	143,397
Number of hospital beds	3,946
Patient-days	1,376,692
Average occupancy rate (%)	96%
Median length of stay (days)	4
Estimated catchment population	2,400,000
% total population covered	33%
Type of participating hospitals	
Regional/Tertiary	80%
Provincial/Secondary	20%
District/Primary	0%



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	5	170	5	381	5	741	5	184	0	0	0	0
2002	5	177	5	468	5	865	5	254	0	0	0	0
2003	5	180	5	369	5	774	5	244	0	0	0	0
2004	5	190	5	475	5	917	5	288	0	0	0	0
2005	5	235	5	547	5	943	5	296	4	331	4	215
2006	5	227	5	513	5	955	5	289	5	434	5	350
2007	5	246	5	456	5	1041	5	275	5	454	5	315
2008	5	198	5	386	5	813	5	228	5	351	5	224

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	5	7	11	11	8	6	7	5
	Penicillin I+R	40	38	38	37	33	35	29	21
	Macrolides I+R	11	12	14	12	15	17	13	20
<i>S. aureus</i>	Oxacillin/Methicillin R	39	38	43	39	41	39	34	35
<i>E. coli</i>	Aminopenicillins R	68	68	62	63	66	66	70	59
	Aminoglycosides R	16	16	14	16	15	17	17	16
	Fluoroquinolones R	21	19	20	23	23	27	30	27
	3rd gen. Cephalosporins R	9	8	9	10	10	13	14	15
<i>E. faecalis</i>	Aminopenicillins I+R	<1	4	2	3	1	1	1	3
	HL Aminoglycosides R	24	44	43	46	43	43	40	43
	Glycopeptides R	<1	2	<1	1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	46	50	48	65	87	82	84	80
	HL Aminoglycosides R	33	42	38	18	20	20	17	13
	Glycopeptides R	12	10	8	8	46	28	24	20
<i>K. pneumoniae</i>	Aminoglycosides R	36	47	46	36
	Fluoroquinolones R	30	41	42	38
	3rd gen. Cephalosporins R	38	44	44	38
<i>P. aeruginosa</i>	Piperacillin R	13	20	15	10
	Ceftazidime R	17	19	12	6
	Carbapenems R	15	17	14	11
	Aminoglycosides R	23	28	20	18
	Fluoroquinolones R	25	32	26	23

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=444		<i>S. aureus</i> n=842		<i>E. coli</i> n=1851		<i>E. faecalis</i> n=396		<i>E. faecium</i> n=106		<i>K. pneumo.</i> n=805		<i>P. aeruginosa</i> n=538	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	100	26	100	34	100	29	100	0	100	22	100	41	100	13
CSF	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	55	23	60	35	41	36	58	0	55	9	56	45	59	16
Female	42	30	39	34	58	24	40	0	44	36	42	36	41	9
Unknown	3	25	1	40	1	40	2	0	1	100	2	62	1	0
Age (years)														
0-4	30	38	7	14	5	16	9	0	7	0	11	27	7	3
5-19	13	12	5	15	4	33	2	0	8	13	3	43	4	10
20-64	24	24	37	26	28	28	23	0	32	12	34	38	38	17
65 and over	31	21	51	45	62	30	66	0	54	32	52	46	49	12
Unknown	2	25	1	50	1	32	0	.	0	.	1	71	2	22
Hospital dep.														
ICU	4	17	7	57	3	34	12	0	18	37	12	69	17	22
Internal Med.	43	23	53	38	53	26	54	0	42	27	41	46	33	13
Surgery	1	17	8	30	11	39	7	0	10	18	14	32	11	12
Other	51	30	32	25	33	30	27	0	30	6	33	29	39	10
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

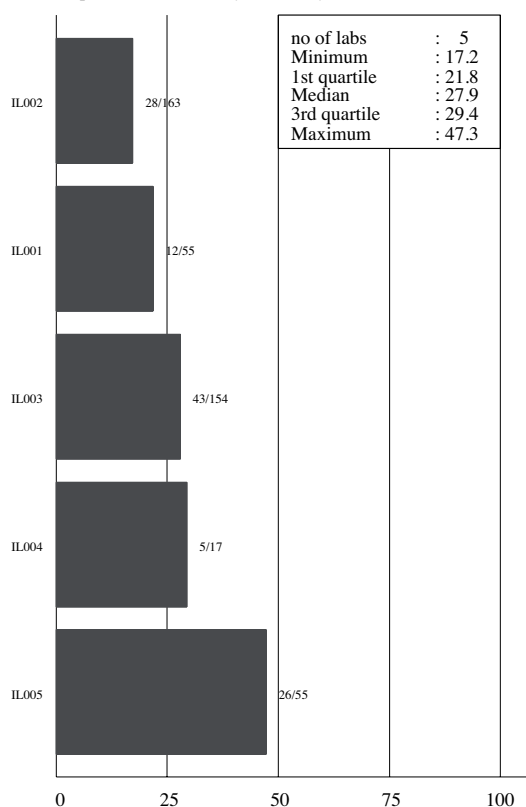
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CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

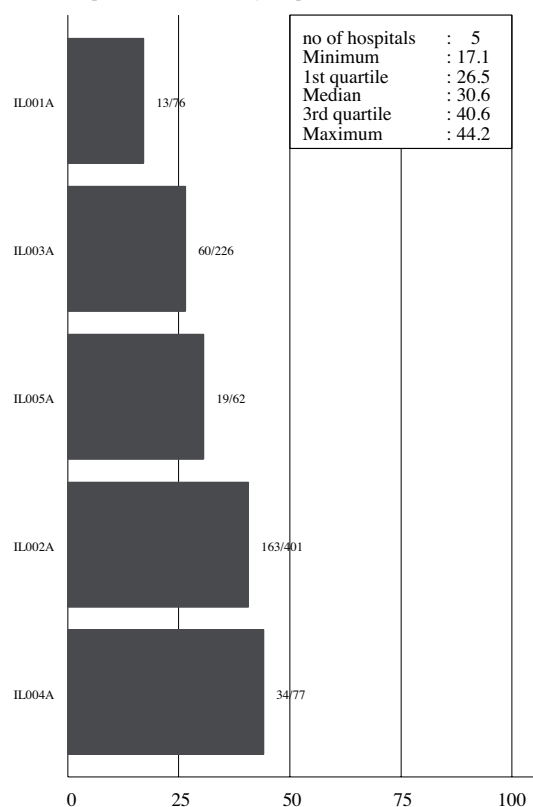
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Italy

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	17/32
Hosps providing denom.data/ reporting data to EARSS	18/32
Number of blood culture sets	79,295
Number of hospital beds	12,896
Patient-days	3,902,052
Average occupancy rate (%)	81%
Median length of stay (days)	6
Estimated catchment population	2,750,328
% total population covered	5%
Type of participating hospitals	
Regional/Tertiary	61%
Provincial/Secondary	33%
District/Primary	6%



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	39	121	53	839	0	0	42	297	0	0	0	0
2002	50	296	53	1343	17	618	49	602	0	0	0	0
2003	43	282	46	1465	17	923	44	634	0	0	0	0
2004	37	267	42	1219	14	645	40	576	0	0	0	0
2005	37	319	41	1431	16	1195	40	714	38	344	0	0
2006	33	260	37	1104	13	910	35	650	32	321	12	183
2007	34	291	37	1059	14	1052	36	656	37	391	10	185
2008	26	176	30	930	14	957	31	624	27	332	12	172

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	4	2	5	5	5	<1	4	3
	Penicillin I+R	9	11	13	14	9	7	15	10
	Macrolides I+R	39	32	37	28	31	32	31	27
<i>S. aureus</i>	Oxacillin/Methicillin R	41	38	39	40	37	38	34	34
<i>E. coli</i>	Aminopenicillins R	.	48	52	53	55	56	58	62
	Aminoglycosides R	.	6	10	9	11	8	14	14
	Fluoroquinolones R	.	21	25	28	28	27	32	38
	3rd gen. Cephalosporins R	.	3	6	5	8	7	11	16
<i>E. faecalis</i>	Aminopenicillins I+R	3	6	4	4	4	4	4	13
	HL Aminoglycosides R	31	38	39	36	38	38	39	47
	Glycopeptides R	1	<1	2	2	3	3	2	2
<i>E. faecium</i>	Aminopenicillins I+R	69	79	80	78	77	86	73	64
	HL Aminoglycosides R	18	37	44	39	36	48	53	49
	Glycopeptides R	15	19	24	21	19	18	11	6
<i>K. pneumoniae</i>	Aminoglycosides R	8	26	25	28
	Fluoroquinolones R	11	23	27	28
	3rd gen. Cephalosporins R	20	33	35	39
<i>P. aeruginosa</i>	Piperacillin R	23	20	19
	Ceftazidime R	20	25	24
	Carbapenems R	21	27	33
	Aminoglycosides R	30	27	30
	Fluoroquinolones R	36	35	36

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=467		<i>S. aureus</i> n=1989		<i>E. coli</i> n=1884		<i>E. faecalis</i> n=738		<i>E. faecium</i> n=469		<i>K. pneumo.</i> n=647		<i>P. aeruginosa</i> n=345	
	%tot	%PNSP	%tot	%MRSA	%tot	%FRECC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	86	12	100	34	100	34	100	2	100	9	100	37	99	30
CSF	14	19	0	.	0	.	0	.	0	.	0	.	1	0
Gender														
Male	38	12	43	36	30	39	49	3	44	10	45	45	29	40
Female	24	17	27	35	32	28	31	1	35	8	26	27	20	26
Unknown	38	12	30	29	38	37	19	1	22	6	30	33	51	25
Age (years)														
0-4	7	13	2	17	1	15	3	0	2	10	3	64	1	0
5-19	3	15	1	35	0	.	1	0	0	.	1	33	2	0
20-64	27	14	24	24	15	34	22	3	20	10	27	40	23	45
65 and over	39	9	46	40	29	30	49	1	41	7	42	28	33	24
Unknown	24	18	27	33	55	37	26	4	37	10	26	44	41	28
Hospital dep.														
ICU	7	9	8	45	4	38	18	2	16	8	12	63	19	38
Internal Med.	22	12	29	36	28	30	25	2	26	6	25	33	11	21
Surgery	0	.	5	40	6	30	8	2	8	8	9	42	4	40
Other	23	12	14	24	12	38	13	0	10	13	16	39	6	27
Unknown	48	15	44	32	51	36	35	3	40	10	37	28	59	28

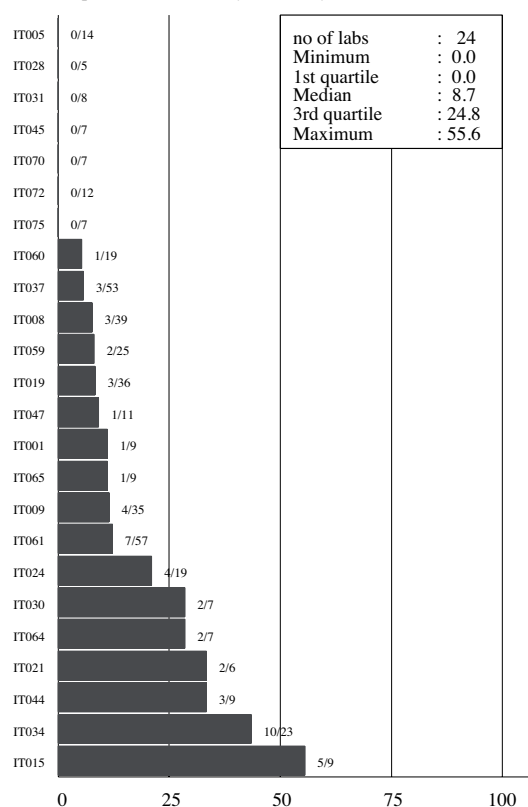
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FRECC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

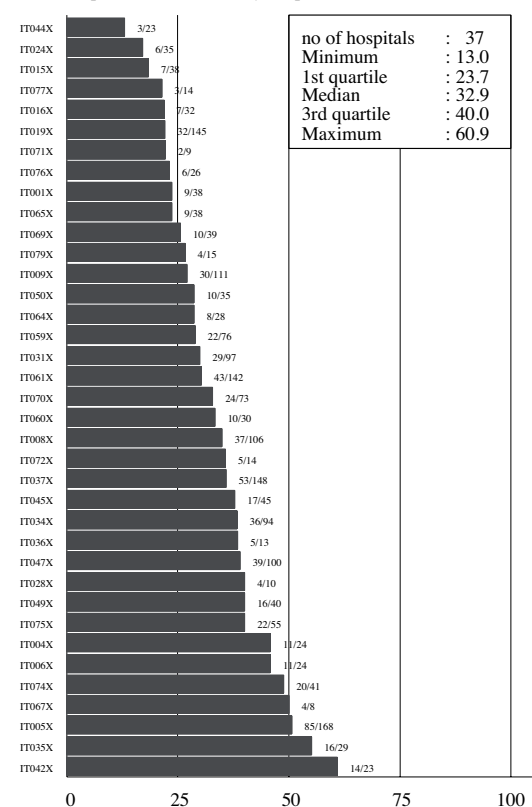
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Latvia

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	12/12
Hosps providing denom.data/ reporting data to EARSS	12/12
Number of blood culture sets	14,584
Number of hospital beds	6,329
Patient-days	1,746,084
Average occupancy rate (%)	76%
Median length of stay (days)	7
Estimated catchment population	1,710
% total population covered	80%
Type of participating hospitals	
Regional/Tertiary	42%
Provincial/Secondary	42%
District/Primary	0%

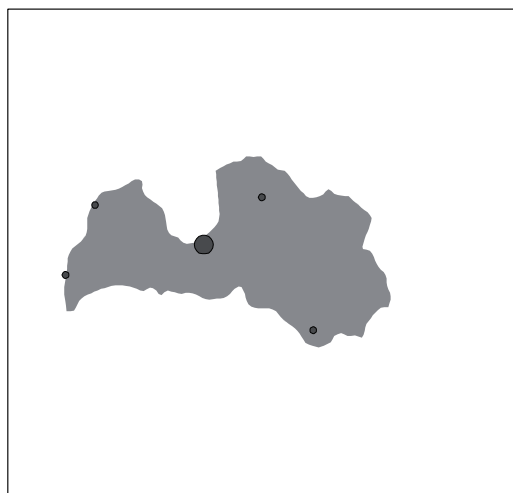


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	0	0	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0	0	0	0	0
2004	4	17	7	87	0	0	0	0	0	0	0	0
2005	5	36	7	126	0	0	0	0	0	0	0	0
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	11	12	131	9	66	9	43	11	31	6	8

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	.	.	.	<1	<1	<1	<1	9
	Penicillin I+R	.	.	.	<1	<1	<1	<1	9
	Macrolides I+R	.	.	.	7	3	3	<1	<1
<i>S. aureus</i>	Oxacillin/Methicillin R	.	.	.	25	20	18	8	14
<i>E. coli</i>	Aminopenicillins R	44	43	52
	Aminoglycosides R	5	14	9
	Fluoroquinolones R	10	17	12
	3rd gen. Cephalosporins R	6	14	9
<i>E. faecalis</i>	Aminopenicillins I+R	9	30	6
	HL Aminoglycosides R	50	.	33
	Glycopeptides R	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	94	77	92
	HL Aminoglycosides R	73	<1	75
	Glycopeptides R	<1	<1	8
<i>K. pneumoniae</i>	Aminoglycosides R	25	22	55
	Fluoroquinolones R	26	27	42
	3rd gen. Cephalosporins R	36	44	58
<i>P. aeruginosa</i>	Piperacillin R	17	31	43
	Ceftazidime R	29	13	50
	Carbapenems R	13	6	57
	Aminoglycosides R	47	31	43
	Fluoroquinolones R	33	13	38

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=42		<i>S. aureus</i> n=300		<i>E. coli</i> n=142		<i>E. faecalis</i> n=43		<i>E. faecium</i> n=55		<i>K. pneumo.</i> n=58		<i>P. aeruginosa</i> n=23	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	95	3	100	10	100	15	100	0	100	4	100	52	100	22
CSF	5	0	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	57	4	53	11	35	8	63	0	53	3	57	48	61	36
Female	43	0	44	10	65	18	35	0	44	4	43	56	39	0
Unknown	0	.	3	0	0	.	2	0	4	0	0	.	0	.
Age (years)														
0-4	5	50	10	3	11	0	12	0	11	0	21	58	30	0
5-19	2	0	4	8	3	0	2	0	0	.	2	0	0	.
20-64	79	0	55	10	50	17	56	0	38	0	45	46	39	33
65 and over	14	0	27	15	33	19	26	0	44	8	28	56	30	29
Unknown	0	.	3	0	3	0	5	0	7	0	5	67	0	.
Hospital dep.														
ICU	45	0	21	5	18	36	28	0	58	6	31	61	39	22
Internal Med.	10	0	25	7	19	15	16	0	7	0	12	14	17	0
Surgery	0	.	8	13	6	13	5	0	5	0	9	80	0	.
Other	45	5	46	14	57	9	47	0	27	0	47	52	43	30
Unknown	0	.	1	0	1	0	5	0	2	0	2	0	0	.

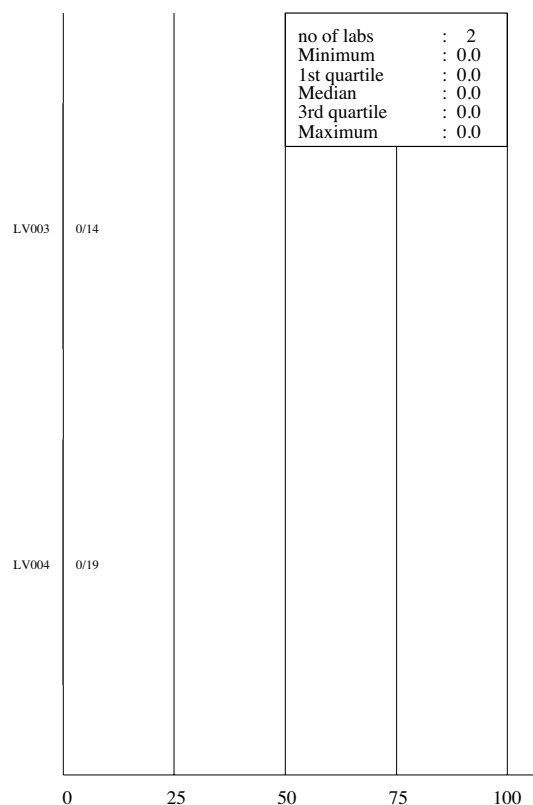
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

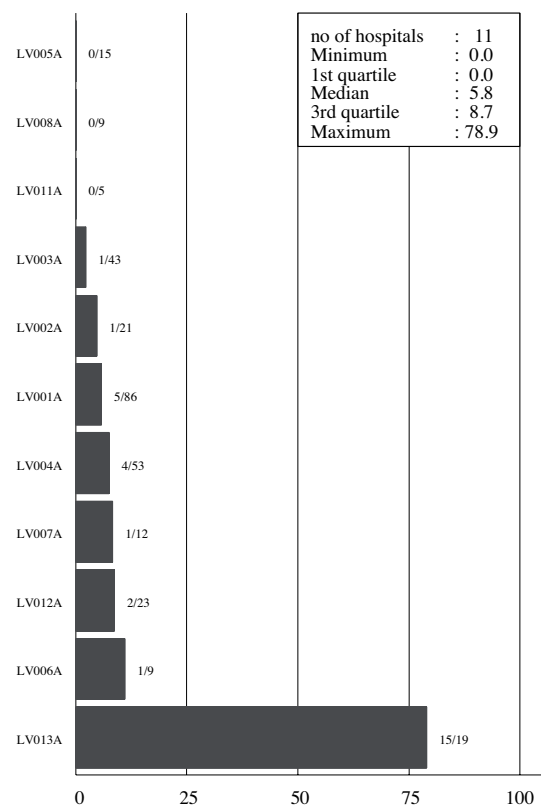
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Lithuania

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	12/13
Hosps providing denom.data/ reporting data to EARSS	19/22
Number of blood culture sets	18,526
Number of hospital beds	9,186
Patient-days	2,578,412
Average occupancy rate (%)	80%
Median length of stay (days)	7
Estimated catchment population	3,306,550
% total population covered	92%
Type of participating hospitals	
Regional/Tertiary	47%
Provincial/Secondary	37%
District/Primary	16%

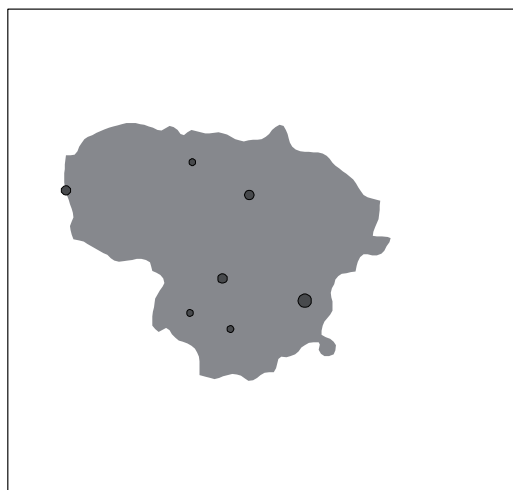


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	0	0	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0	0	0	0	0
2006	9	32	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	47	12	278	12	304	10	67	11	54	7	21

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	1	<1
	Penicillin I+R	16	4	2
	Macrolides I+R	<1	9	7
<i>S. aureus</i>	Oxacillin/Methicillin R	12	9	11
<i>E. coli</i>	Aminopenicillins R	55	50	54
	Aminoglycosides R	15	12	12
	Fluoroquinolones R	12	9	14
	3rd gen. Cephalosporins R	5	7	6
<i>E. faecalis</i>	Aminopenicillins I+R	5	3	5
	HL Aminoglycosides R	50	41	33
	Glycopeptides R	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	75	100	88
	HL Aminoglycosides R	75	81	78
	Glycopeptides R	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	26	37	41
	Fluoroquinolones R	3	8	23
	3rd gen. Cephalosporins R	23	27	36
<i>P. aeruginosa</i>	Piperacillin R	21	5	14
	Ceftazidime R	31	<1	10
	Carbapenems R	21	30	24
	Aminoglycosides R	29	33	38
	Fluoroquinolones R	46	38	35

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=114		<i>S. aureus</i> n=518		<i>E. coli</i> n=536		<i>E. faecalis</i> n=81		<i>E. faecium</i> n=42		<i>K. pneumo.</i> n=94		<i>P. aeruginosa</i> n=41	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	87	3	100	10	99	12	100	0	100	0	95	29	100	27
CSF	13	7	0	.	1	25	0	.	0	.	5	80	0	.
Gender														
Male	73	4	56	9	39	18	69	0	60	0	53	42	54	27
Female	27	3	43	12	61	8	30	0	40	0	45	21	46	26
Unknown	0	.	1	0	0	.	1	0	0	.	2	0	0	.
Age (years)														
0-4	13	7	4	0	3	7	7	0	10	0	3	67	5	0
5-19	5	0	6	3	2	9	1	0	5	0	5	40	5	50
20-64	59	3	49	8	40	12	47	0	50	0	40	29	54	32
65 and over	21	4	40	16	54	13	44	0	36	0	49	33	37	20
Unknown	2	0	2	0	1	0	0	.	0	.	2	0	0	.
Hospital dep.														
ICU	40	4	22	12	20	7	32	0	38	0	37	40	34	14
Internal Med.	32	3	36	11	34	9	36	0	31	0	28	0	20	25
Surgery	2	50	11	14	5	12	11	0	2	0	10	56	5	50
Other	25	0	30	7	39	17	21	0	29	0	26	46	41	35
Unknown	1	0	1	0	2	11	0	.	0	.	0	.	0	.

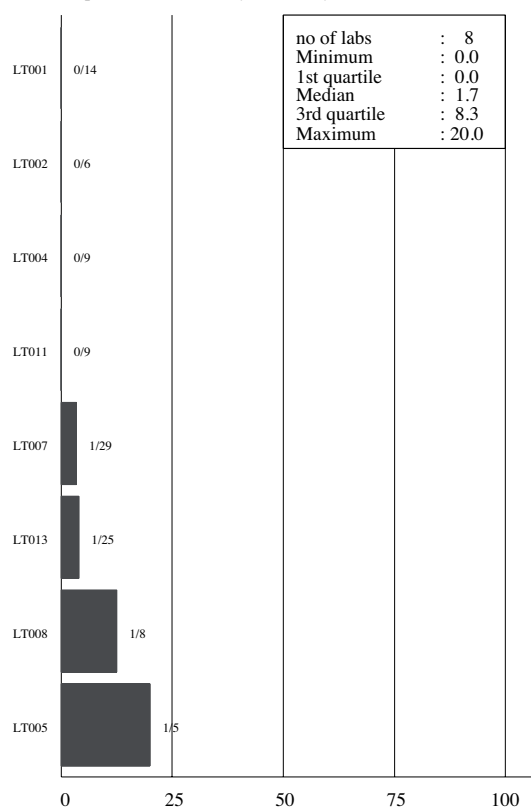
PNSP = Penicillin Non-Susceptible *S. pneumonia*
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MRSA = Methicillin Resistant *S. aureus*
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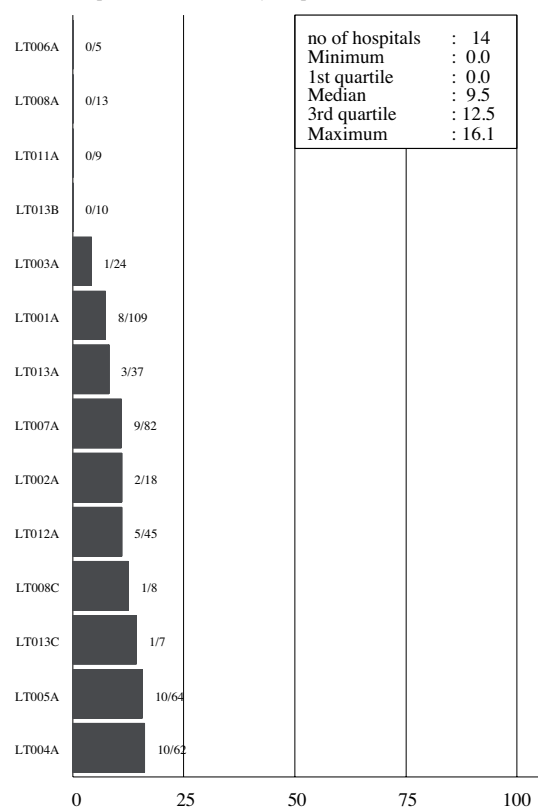
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Luxembourg

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	4/5
Hosps providing denom.data/ reporting data to EARSS	4/5
Number of blood culture sets	8,393
Number of hospital beds	1,637
Patient-days	464,154
Average occupancy rate (%)	79%
Median length of stay (days)	6
Estimated catchment population	500,000
% total population covered	100%
Type of participating hospitals	
Regional/Tertiary	67%
Provincial/Secondary	33%
District/Primary	0%

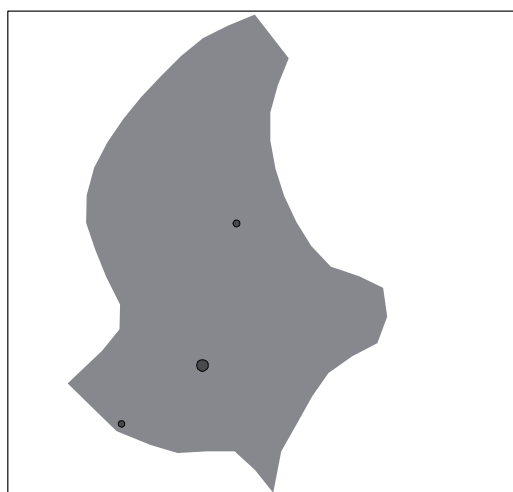


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	8	41	8	85	8	193	7	31	0	0	0	0
2002	7	27	9	95	9	193	8	30	0	0	0	0
2003	7	48	8	95	8	227	7	41	0	0	0	0
2004	6	36	7	96	7	216	5	28	0	0	0	0
2005	5	43	5	83	5	188	5	31	0	0	1	1
2006	4	22	5	77	5	167	4	42	4	21	4	23
2007	5	35	6	115	6	275	5	37	6	52	5	36
2008	5	53	5	117	5	285	5	61	5	50	4	33

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	7	7	<1	6	7	5	3	6
	Penicillin I+R	12	22	15	11	12	5	6	11
	Macrolides I+R	23	22	30	33	24	36	23	13
<i>S. aureus</i>	Oxacillin/Methicillin R	20	15	21	16	13	19	20	9
<i>E. coli</i>	Aminopenicillins R	44	43	49	49	49	46	49	55
	Aminoglycosides R	5	4	4	4	7	6	5	8
	Fluoroquinolones R	4	9	12	18	19	20	21	21
	3rd gen. Cephalosporins R	<1	<1	<1	<1	3	2	4	7
<i>E. faecalis</i>	Aminopenicillins I+R	<1	<1	5	<1	<1	<1	<1	3
	HL Aminoglycosides R	13	17	32	18	24	32	44	17
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	3
<i>E. faecium</i>	Aminopenicillins I+R	<1	60	100	50	36	75	67	76
	HL Aminoglycosides R	.	14	<1	<1	23	30	10	21
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	5
<i>K. pneumoniae</i>	Aminoglycosides R	<1	4	12
	Fluoroquinolones R	6	12	12
	3rd gen. Cephalosporins R	10	2	20
<i>P. aeruginosa</i>	Piperacillin R	<1	9	15	3
	Ceftazidime R	<1	10	11	3
	Carbapenems R	<1	7	20	25
	Aminoglycosides R	<1	4	22	6
	Fluoroquinolones R	<1	10	36	15

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=88		<i>S. aureus</i> n=232		<i>E. coli</i> n=560		<i>E. faecalis</i> n=54		<i>E. faecium</i> n=34		<i>K. pneumo.</i> n=101		<i>P. aeruginosa</i> n=18	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	95	10	100	15	100	21	100	2	100	3	100	11	100	22
CSF	5	0	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	49	0	47	12	28	21	35	5	24	0	30	13	28	20
Female	36	19	25	25	41	20	30	0	18	17	44	11	61	27
Unknown	15	15	29	10	31	23	35	0	59	0	27	7	11	0
Age (years)														
0-4	13	0	2	0	1	13	2	0	0	.	1	0	0	.
5-19	5	0	3	25	0	.	0	.	0	.	0	.	0	.
20-64	40	9	37	10	26	17	33	0	41	7	34	24	39	29
65 and over	34	13	43	14	59	24	54	3	56	0	51	6	56	20
Unknown	9	13	15	26	14	21	11	0	3	0	14	0	6	0
Hospital dep.														
ICU	7	17	8	17	3	32	24	0	21	14	12	25	17	67
Internal Med.	5	25	3	0	7	20	6	0	0	.	4	0	11	0
Surgery	2	0	1	33	3	29	0	.	0	.	3	0	0	.
Other	48	7	30	11	29	23	24	0	32	0	25	28	28	20
Unknown	39	9	58	16	58	20	46	4	47	0	56	2	44	13

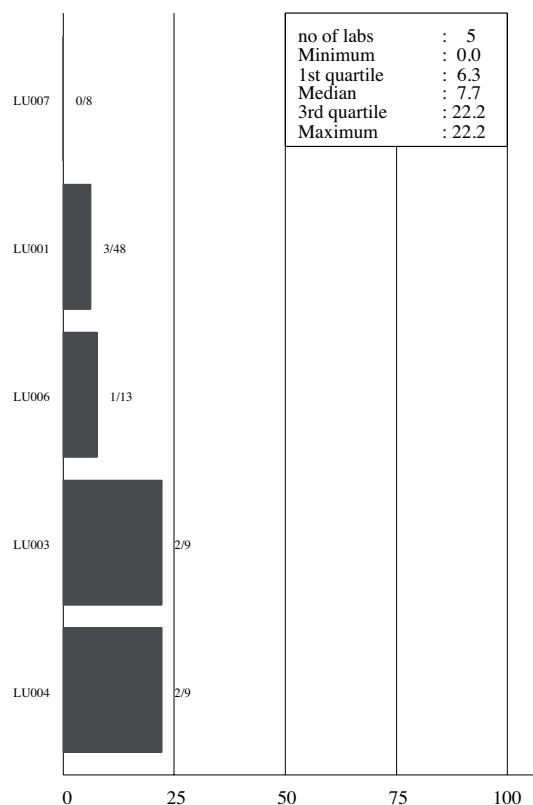
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
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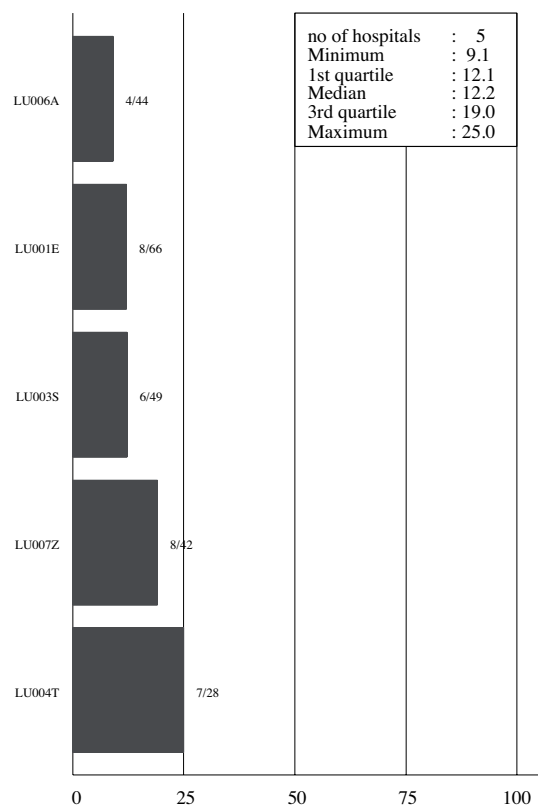
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Malta

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	1/1
Hosps providing denom.data/ reporting data to EARSS	3/3
Number of blood culture sets	4,161
Number of hospital beds	1,367
Patient-days	406,793
Average occupancy rate (%)	81%
Median length of stay (days)	12
Estimated catchment population	380,000
% total population covered	95%
Type of participating hospitals	
Regional/Tertiary	33%
Provincial/Secondary	0%
District/Primary	33%



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	1	12	1	82	1	65	1	12	0	0	0	0
2002	1	12	1	87	1	74	1	33	0	0	0	0
2003	1	9	1	121	1	91	1	26	0	0	0	0
2004	1	18	1	94	1	91	1	41	0	0	0	0
2005	1	13	1	77	1	85	1	38	1	18	1	45
2006	1	30	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

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	<1	<1	8	3	<1	24
	Penicillin I+R	8	<1	<1	<1	15	7	<1	47
	Macrolides I+R	18	25	38	25	46	47	8	35
<i>S. aureus</i>	Oxacillin/Methicillin R	54	43	43	56	56	67	52	52
<i>E. coli</i>	Aminopenicillins R	26	43	39	48	51	56	54	52
	Aminoglycosides R	11	8	18	20	7	15	20	22
	Fluoroquinolones R	15	12	24	36	31	32	35	34
	3rd gen. Cephalosporins R	<1	3	2	4	1	4	13	21
<i>E. faecalis</i>	Aminopenicillins I+R	9	<1	5	<1	3	2	3	<1
	HL Aminoglycosides R	9	17	29	44	32	.	.	.
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	100	33	33	43	25	14	40	60
	HL Aminoglycosides R	<1	<1	50	<1	<1	.	.	.
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	17	6	<1	<1
	Fluoroquinolones R	11	6	11	8
	3rd gen. Cephalosporins R	6	6	7	<1
<i>P. aeruginosa</i>	Piperacillin R	22	47	11	45
	Ceftazidime R	11	30	3	33
	Carbapenems R	18	20	11	30
	Aminoglycosides R	16	8	8	23
	Fluoroquinolones R	44	24	11	19

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=30		<i>S. aureus</i> n=213		<i>E. coli</i> n=245		<i>E. faecalis</i> n=58		<i>E. faecium</i> n=11		<i>K. pneumo.</i> n=64		<i>P. aeruginosa</i> n=66	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	93	29	100	54	100	34	100	0	100	0	100	3	98	20
CSF	7	0	0	.	0	.	0	.	0	.	0	.	2	0
Gender														
Male	40	17	66	55	43	37	67	0	45	0	52	3	53	26
Female	60	33	33	53	57	32	28	0	55	0	47	3	47	13
Unknown	0	.	1	0	0	.	5	0	0	.	2	0	0	.
Age (years)														
0-4	17	20	6	54	1	0	19	0	0	.	11	29	5	0
5-19	10	33	4	63	2	17	3	0	0	.	2	0	6	0
20-64	17	20	41	48	28	23	38	0	73	0	42	0	38	24
65 and over	57	29	48	60	68	40	40	0	27	0	44	0	52	21
Unknown	0	.	1	0	0	.	0	.	0	.	2	0	0	.
Hospital dep.														
ICU	23	14	12	65	11	29	52	0	55	0	22	14	50	24
Internal Med.	27	25	47	48	42	37	19	0	18	0	45	0	20	15
Surgery	10	33	18	58	22	32	19	0	18	0	22	0	17	18
Other	37	27	14	60	9	30	7	0	0	.	9	0	11	14
Unknown	3	100	9	53	16	37	3	0	9	0	2	0	3	0

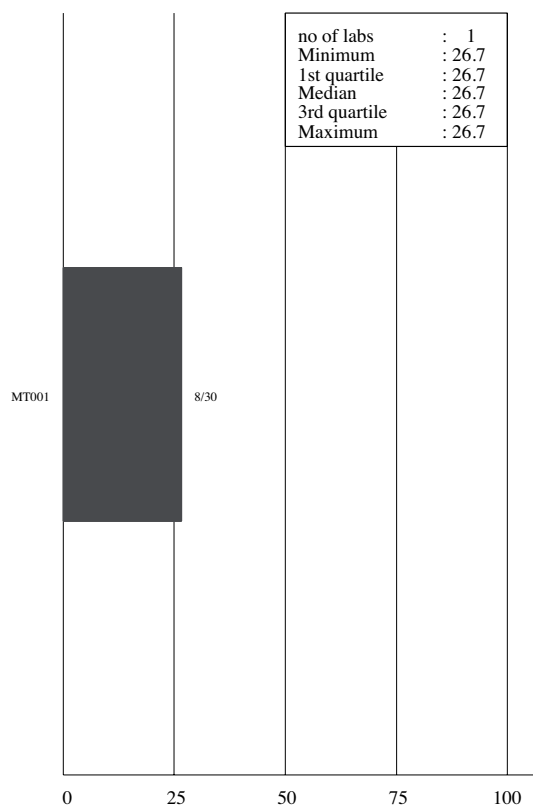
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MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
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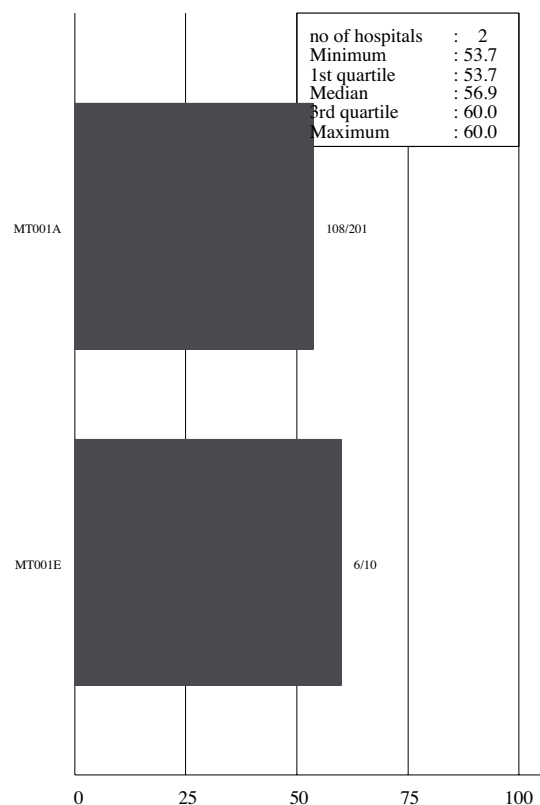
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Netherlands

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	6/17
Hosps providing denom.data/ reporting data to EARSS	6/41
Number of blood culture sets	72,527
Number of hospital beds	2,952
Patient-days	520,127
Average occupancy rate (%)	69%
Median length of stay (days)	6
Estimated catchment population	1,020,735
% total population covered	6%
Type of participating hospitals	
Regional/Tertiary	17%
Provincial/Secondary	83%
District/Primary	0%



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	20	723	21	1290	20	1864	14	275	0	0	0	0
2002	23	860	22	1502	22	2427	22	536	0	0	0	0
2003	24	886	22	1363	23	2143	23	482	0	0	0	0
2004	22	755	22	1336	21	2112	22	455	0	0	0	0
2005	23	802	23	1408	23	2203	23	566	16	301	16	210
2006	22	1005	23	1633	22	2910	23	778	18	459	19	330
2007	21	939	21	1469	21	2806	21	832	19	497	19	338
2008	16	674	15	1004	15	2116	16	603	15	463	15	345

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1
	Penicillin I+R	<1	1	1	2	1	1	2	2
	Macrolides I+R	5	7	5	7	11	8	7	7
<i>S. aureus</i>	Oxacillin/Methicillin R	<1	<1	1	1	<1	1	1	<1
<i>E. coli</i>	Aminopenicillins R	39	39	44	43	48	47	49	47
	Aminoglycosides R	2	2	3	3	4	3	5	6
	Fluoroquinolones R	5	5	7	7	10	11	13	14
	3rd gen. Cephalosporins R	<1	<1	1	1	2	3	4	5
<i>E. faecalis</i>	Aminopenicillins I+R	2	3	4	3	3	5	5	<1
	HL Aminoglycosides R	28	33	23	37	38	28	38	32
	Glycopeptides R	<1	<1	1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	64	23	30	42	61	73	83	86
	HL Aminoglycosides R	4	11	19	20	40	50	62	53
	Glycopeptides R	2	1	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	5	4	5	7
	Fluoroquinolones R	6	4	4	7
	3rd gen. Cephalosporins R	4	4	7	8
<i>P. aeruginosa</i>	Piperacillin R	4	2	2	6
	Ceftazidime R	5	5	4	6
	Carbapenems R	5	2	2	6
	Aminoglycosides R	7	4	3	4
	Fluoroquinolones R	9	9	5	8

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=1613		<i>S. aureus</i> n=2473		<i>E. coli</i> n=4795		<i>E. faecalis</i> n=519		<i>E. faecium</i> n=493		<i>K. pneumo.</i> n=884		<i>P. aeruginosa</i> n=643	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	93	2	100	1	100	13	100	0	100	0	99	7	99	4
CSF	7	1	0	.	0	.	0	.	0	.	1	0	1	11
Gender														
Male	51	2	58	1	48	16	65	0	56	0	52	8	62	5
Female	47	2	39	1	50	11	30	1	37	0	45	6	36	4
Unknown	2	0	3	1	2	10	4	0	7	0	3	4	2	8
Age (years)														
0-4	5	4	9	1	3	5	7	3	5	0	4	10	3	6
5-19	2	3	4	2	1	18	1	0	4	0	2	31	2	8
20-64	40	2	33	1	31	14	39	0	46	0	37	9	35	6
65 and over	53	2	55	2	65	13	51	0	42	0	57	5	60	3
Unknown	0	.	0	.	0	.	3	0	2	0	1	0	0	.
Hospital dep.														
ICU	5	2	7	1	6	15	22	0	32	0	9	11	13	7
Internal Med.	31	2	25	1	29	13	13	0	11	0	26	4	24	5
Surgery	4	2	11	2	9	10	8	0	5	0	10	10	13	6
Other	18	3	23	1	20	17	24	0	26	0	21	10	19	5
Unknown	42	1	35	2	37	12	34	1	25	1	34	6	31	2

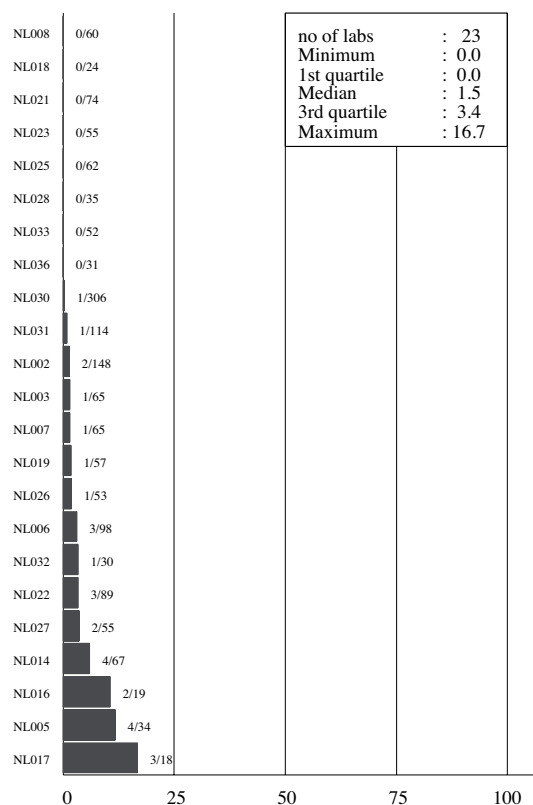
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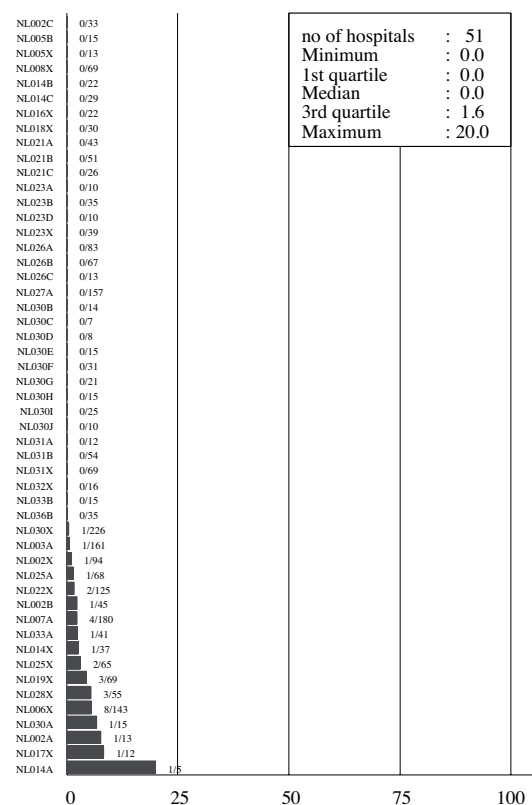
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Norway

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	7/13
Hosps providing denom.data/ reporting data to EARSS	16/33
Number of blood culture sets	63,824
Number of hospital beds	4,835
Patient-days	1,195,571
Average occupancy rate (%)	70%
Median length of stay (days)	4
Estimated catchment population	4,700,000
% total population covered	44%
Type of participating hospitals	
Regional/Tertiary	25%
Provincial/Secondary	50%
District/Primary	25%

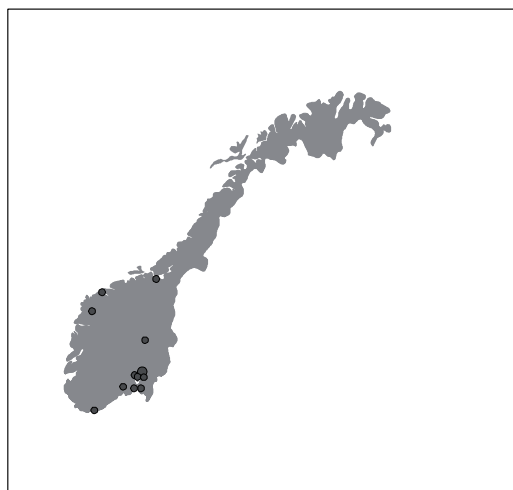


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	11	425	11	411	11	966	11	155	4	26	4	20
2002	11	451	11	502	11	1119	11	177	4	29	4	27
2003	11	512	11	503	11	1179	11	192	4	46	4	25
2004	11	598	11	514	11	1212	11	235	4	51	4	27
2005	11	606	11	551	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	790	13	1713	13	416	13	320	13	105
2008	13	554	13	810	13	1731	13	388	13	341	13	147

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1
	Penicillin I+R	1	<1	<1	2	2	2	2	3
	Macrolides I+R	4	6	8	8	14	12	10	7
<i>S. aureus</i>	Oxacillin/Methicillin R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. coli</i>	Aminopenicillins R	27	29	34	32	34	35	38	38
	Aminoglycosides R	<1	<1	<1	<1	2	2	3	3
	Fluoroquinolones R	1	2	2	4	5	5	7	7
	3rd gen. Cephalosporins R	<1	<1	<1	<1	<1	1	2	2
<i>E. faecalis</i>	Aminopenicillins I+R	3	4	4	<1	3	3	2	1
	HL Aminoglycosides R	42	30	38	27	32	33	34	30
	Glycopeptides R	1	3	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	28	49	43	80	72	75	81	77
	HL Aminoglycosides R	40	14	14	25	44	45	52	53
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	<1	<1	<1	2	3	<1	<1	1
	Fluoroquinolones R	<1	<1	<1	<1	1	7	5	4
	3rd gen. Cephalosporins R	<1	<1	<1	<1	2	2	2	2
<i>P. aeruginosa</i>	Piperacillin R	.	<1	<1	13	3	3	2	6
	Ceftazidime R	15	<1	<1	<1	3	5	3	4
	Carbapenems R	7	<1	<1	4	3	9	9	7
	Aminoglycosides R	<1	<1	<1	4	<1	1	2	<1
	Fluoroquinolones R	9	<1	4	5	4	9	7	3

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=1170		<i>S. aureus</i> n=1600		<i>E. coli</i> n=3370		<i>E. faecalis</i> n=559		<i>E. faecium</i> n=205		<i>K. pneumo.</i> n=661		<i>P. aeruginosa</i> n=242	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	96	2	100	0	100	7	100	0	100	0	100	2	100	8
CSF	4	2	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	48	1	60	0	45	9	74	0	55	0	58	2	67	8
Female	50	3	38	0	54	6	25	0	44	0	41	1	31	7
Unknown	2	4	2	0	1	13	1	0	1	0	2	0	2	25
Age (years)														
0-4	4	0	5	0	2	2	2	0	0	.	1	0	1	33
5-19	2	0	3	0	1	6	1	0	0	.	1	11	2	25
20-64	42	2	34	0	25	8	24	0	32	0	27	2	27	12
65 and over	52	2	59	0	72	7	73	0	68	0	70	2	70	5
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	11	3	9	0	5	9	11	0	17	0	9	5	12	20
Internal Med.	55	1	43	0	48	6	37	0	36	0	43	1	47	6
Surgery	4	8	17	1	15	9	21	0	19	0	19	1	11	4
Other	28	2	30	0	30	7	30	0	27	0	27	2	28	6
Unknown	2	0	2	0	2	4	1	0	1	0	2	0	2	20

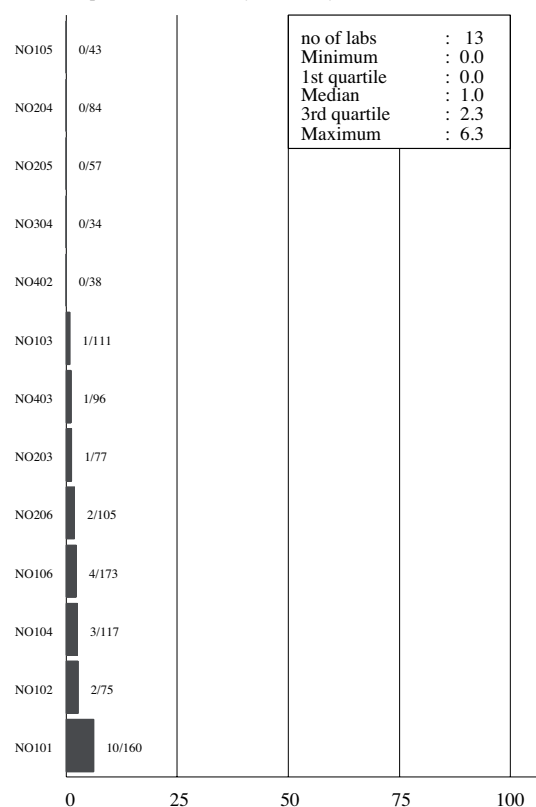
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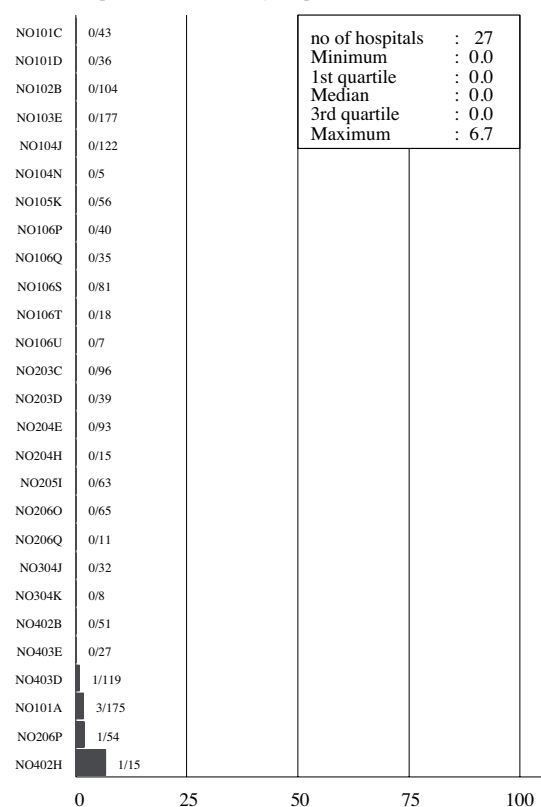
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Poland

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	na
Hosps providing denom.data/ reporting data to EARSS	na
Number of blood culture sets	na
Number of hospital beds	na
Patient-days	na
Average occupancy rate (%)	na
Median length of stay (days)	na
Estimated catchment population	na
% total population covered	na
Type of participating hospitals	
Regional/Tertiary	na
Provincial/Secondary	na
District/Primary	na

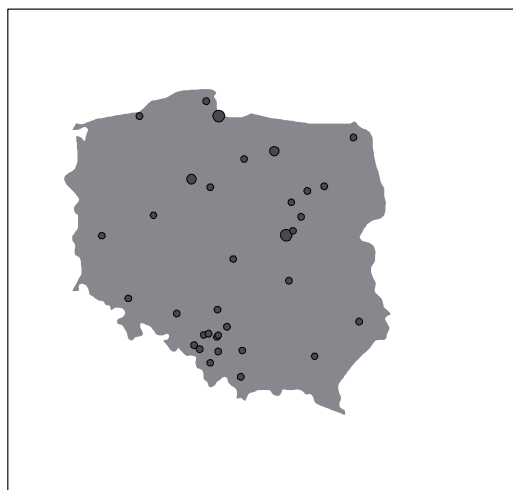


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	4	6	19	151	20	103	16	57	0	0	0	0
2002	7	10	21	186	22	135	19	56	0	0	0	0
2003	11	16	24	166	25	124	16	64	0	0	0	0
2004	11	16	30	262	29	192	23	52	0	0	0	0
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	21	24	185	27	256	20	71	18	32	23	67
2008	34	84	15	99	14	84	11	26	11	19	8	22

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	30	19	<1	17	<1	10	12
	Penicillin I+R	<1	30	19	<1	33	<1	29	13
	Macrolides I+R	<1	67	14	19	33	11	.	50
<i>S. aureus</i>	Oxacillin/Methicillin R	15	23	19	19	24	20	15	12
<i>E. coli</i>	Aminopenicillins R	58	52	50	45	56	55	56	54
	Aminoglycosides R	5	11	10	5	7	11	6	7
	Fluoroquinolones R	9	11	7	9	20	20	13	20
	3rd gen. Cephalosporins R	7	6	4	5	5	4	2	2
<i>E. faecalis</i>	Aminopenicillins I+R	5	12	<1	2	9	2	4	6
	HL Aminoglycosides R	43	41	48	33	48	50	46	29
	Glycopeptides R	<1	<1	<1	<1	<1	<1	2	<1
<i>E. faecium</i>	Aminopenicillins I+R	77	80	91	86	95	95	88	78
	HL Aminoglycosides R	73	73	55	100	62	85	84	67
	Glycopeptides R	<1	<1	<1	<1	5	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	57	36	31	26
	Fluoroquinolones R	34	29	3	32
	3rd gen. Cephalosporins R	66	38	34	37
<i>P. aeruginosa</i>	Piperacillin R	50	43	36	32
	Ceftazidime R	31	42	21	27
	Carbapenems R	27	30	18	14
	Aminoglycosides R	56	46	40	27
	Fluoroquinolones R	31	41	37	13

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=105		<i>S. aureus</i> n=284		<i>E. coli</i> n=340		<i>E. faecalis</i> n=63		<i>E. faecium</i> n=34		<i>K. pneumo.</i> n=51		<i>P. aeruginosa</i> n=89	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	72	13	100	14	100	15	100	2	100	0	100	35	100	17
CSF	28	24	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	53	18	57	17	38	22	48	3	53	0	55	29	65	16
Female	47	14	42	10	62	10	51	0	47	0	45	43	34	20
Unknown	0	.	1	0	0	.	2	0	0	.	0	.	1	0
Age (years)														
0-4	16	24	10	24	4	7	5	0	3	0	24	42	4	25
5-19	10	10	1	0	0	.	0	.	0	.	0	.	3	0
20-64	50	21	47	13	37	14	46	3	38	0	39	30	57	18
65 and over	25	4	42	13	59	16	49	0	59	0	37	37	35	16
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	9	11	8	17	8	11	19	0	26	0	10	40	47	19
Internal Med.	54	14	61	9	73	16	52	3	38	0	41	33	27	13
Surgery	0	.	12	35	5	19	19	0	21	0	10	60	15	31
Other	37	21	19	15	14	10	10	0	15	0	39	30	11	0
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

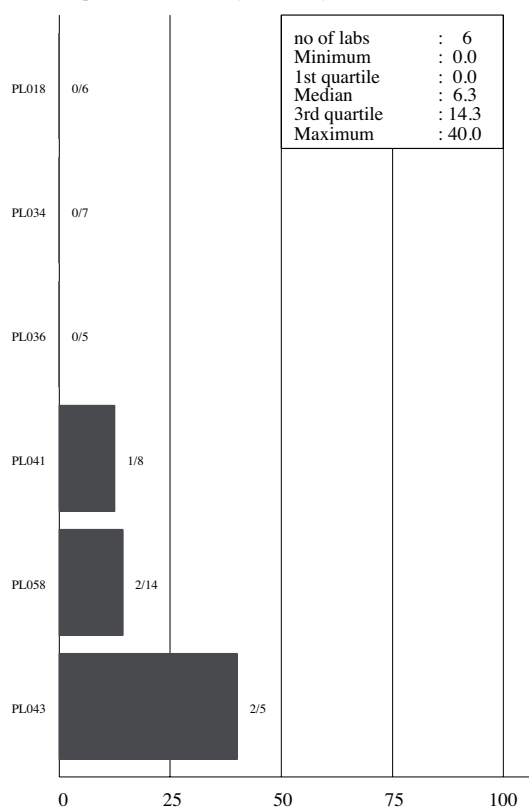
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
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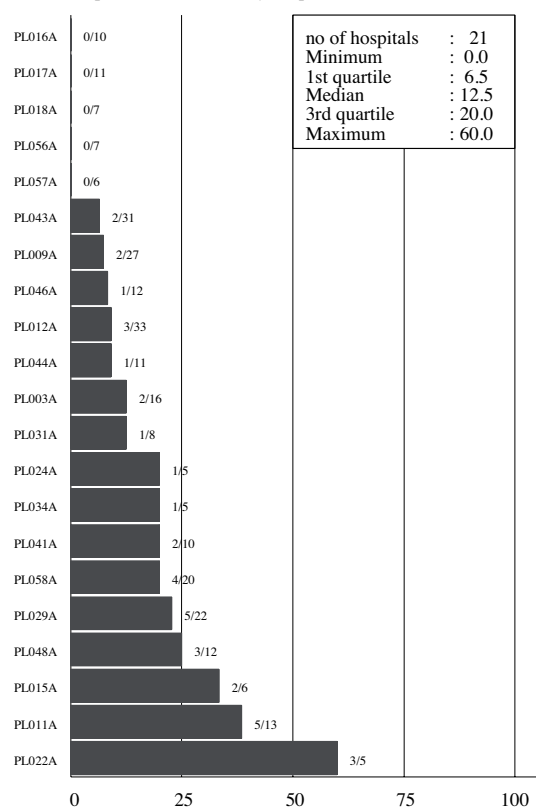
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Portugal

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	22/22
Hosps providing denom.data/ reporting data to EARSS	22/22
Number of blood culture sets	140,514
Number of hospital beds	10,234
Patient-days	2,995,771
Average occupancy rate (%)	81%
Median length of stay (days)	7
Estimated catchment population	8,622,873
% total population covered	81%
Type of participating hospitals	
Regional/Tertiary	62%
Provincial/Secondary	24%
District/Primary	5%



Figure 1. Geographic distribution of laboratories in 2008 (One laboratory on Madeira is not shown)

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	16	155	16	521	13	418	12	185	0	0	0	0
2002	14	184	16	543	17	444	13	101	0	0	0	0
2003	12	95	22	1033	21	792	18	398	0	0	0	0
2004	14	166	23	1063	19	761	19	410	0	0	0	0
2005	13	202	19	1153	19	1171	17	405	1	1	0	0
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	1556	21	1625	20	588	21	543	19	467

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	<1	<1	<1	<1	<1	<1
	Penicillin I+R	25	20	20	27	17	17	16	18
	Macrolides I+R	.	<1	.	20	19	21	23	22
<i>S. aureus</i>	Oxacillin/Methicillin R	32	38	45	46	47	48	48	53
<i>E. coli</i>	Aminopenicillins R	54	58	53	58	58	59	59	58
	Aminoglycosides R	6	9	9	13	12	12	12	14
	Fluoroquinolones R	18	23	26	27	29	28	30	29
	3rd gen. Cephalosporins R	3	6	7	8	12	10	10	10
<i>E. faecalis</i>	Aminopenicillins I+R	5	2	4	5	<1	2	4	4
	HL Aminoglycosides R	30	25	34	29	38	41	41	43
	Glycopeptides R	5	6	3	6	5	5	4	4
<i>E. faecium</i>	Aminopenicillins I+R	76	79	88	83	92	76	93	86
	HL Aminoglycosides R	23	33	55	66	68	53	49	28
	Glycopeptides R	21	.*	47	42	34	26	29	24
<i>K. pneumoniae</i>	Aminoglycosides R	<1	13	11	19
	Fluoroquinolones R	<1	20	18	22
	3rd gen. Cephalosporins R	21	17	26
<i>P. aeruginosa</i>	Piperacillin R	15	14	17
	Ceftazidime R	19	16	16
	Carbapenems R	21	15	18
	Aminoglycosides R	17	16	11
	Fluoroquinolones R	21	19	23

* Proportion not given, due to a very low number of isolates.

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=462		<i>S. aureus</i> n=2939		<i>E. coli</i> n=2964		<i>E. faecalis</i> n=739		<i>E. faecium</i> n=335		<i>K. pneumo.</i> n=878		<i>P. aeruginosa</i> n=753	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	91	18	100	51	100	29	100	4	100	26	100	22	99	17
CSF	9	12	0	.	0	.	0	.	0	.	0	.	1	11
Gender														
Male	55	15	62	51	49	34	57	3	56	26	59	25	59	18
Female	45	20	38	51	51	24	43	5	44	27	40	18	41	15
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	5	14	2	15	1	0	2	0	1	0	1	36	2	0
5-19	5	10	2	16	1	14	1	0	0	.	2	27	2	0
20-64	45	13	29	40	29	26	24	5	39	25	33	23	37	19
65 and over	40	22	47	60	54	33	53	3	44	24	47	21	45	17
Unknown	6	22	20	52	15	25	21	6	17	36	17	22	15	13
Hospital dep.														
ICU	6	29	11	60	5	31	14	2	14	19	12	32	17	27
Internal Med.	12	24	22	59	18	30	19	6	20	29	19	29	14	10
Surgery	0	.	8	70	5	36	11	0	12	15	11	14	9	21
Other	81	16	55	43	66	28	52	5	48	28	53	20	54	13
Unknown	1	0	5	55	6	33	5	3	5	44	5	15	6	22

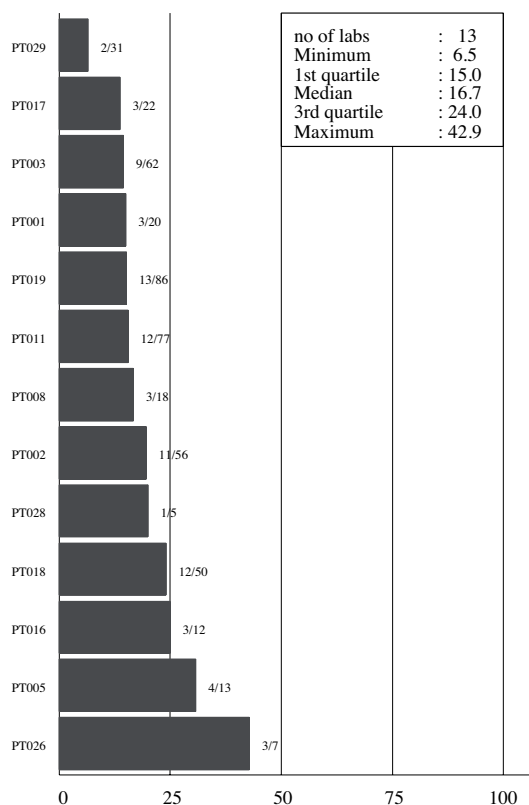
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CRPA = Carbapenem Resistant *P. aeruginosa*

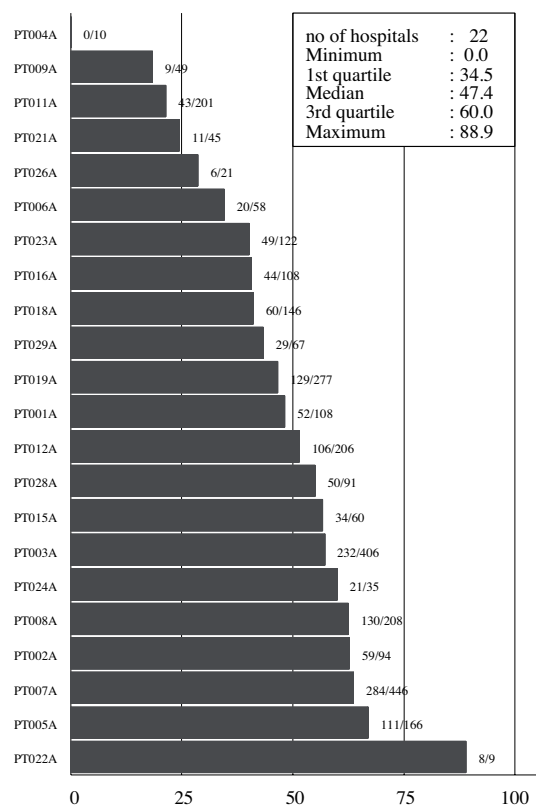
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Romania

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	na
Hosps providing denom.data/ reporting data to EARSS	na
Number of blood culture sets	na
Number of hospital beds	na
Patient-days	na
Average occupancy rate (%)	na
Median length of stay (days)	na
Estimated catchment population	na
% total population covered	na
Type of participating hospitals	
Regional/Tertiary	na
Provincial/Secondary	na
District/Primary	na



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	0	0	0	0	0	0	0	0	0	0
2002	6	10	10	80	8	28	4	11	0	0	0	0
2003	4	22	9	85	9	50	5	12	0	0	0	0
2004	4	9	15	92	12	46	4	9	0	0	0	0
2005	5	18	13	92	13	83	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	13	5	39	4	58	4	15	3	6	3	8

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	.	10	23	11	22	10	22	54
	Penicillin I+R	.	50	36	11	39	28	33	69
	Macrolides I+R	.	10	27	<1	31	25	19	20
<i>S. aureus</i>	Oxacillin/Methicillin R	.	36	46	72	60	54	26	33
<i>E. coli</i>	Aminopenicillins R	.	50	70	79	78	85	76	55
	Aminoglycosides R	.	15	21	30	14	41	35	24
	Fluoroquinolones R	.	20	14	17	9	41	27	27
	3rd gen. Cephalosporins R	.	18	19	22	17	41	27	24
<i>E. faecalis</i>	Aminopenicillins I+R	.	<1	<1	29	<1	<1	25	10
	HL Aminoglycosides R	.	40	25	<1	50	15	50	22
	Glycopeptides R	.	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	.	100	86	100	100	100	100	100
	HL Aminoglycosides R	.	80	63	100	70	80	67	67
	Glycopeptides R	.	17	<1	<1	<1	<1	<1	<1
<i>K. pneumoniae</i>	Aminoglycosides R	100	91	80	60
	Fluoroquinolones R	33	34	23	20
	3rd gen. Cephalosporins R	100	94	80	50
<i>P. aeruginosa</i>	Piperacillin R	61	33	25	25
	Ceftazidime R	52	<1	<1	13
	Carbapenems R	61	<1	<1	13
	Aminoglycosides R	64	33	25	38
	Fluoroquinolones R	64	33	25	25

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=40		<i>S. aureus</i> n=81		<i>E. coli</i> n=112		<i>E. faecalis</i> n=14		<i>E. faecium</i> n=14		<i>K. pneumo.</i> n=34		<i>P. aeruginosa</i> n=12	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	58	48	100	30	98	26	100	0	100	0	100	76	100	8
CSF	43	41	0	.	2	50	0	.	0	.	0	.	0	.
Gender														
Male	73	45	32	23	52	24	57	0	64	0	53	94	67	13
Female	28	45	17	36	48	30	43	0	36	0	47	56	8	0
Unknown	0	.	51	32	0	.	0	.	0	.	0	.	25	0
Age (years)														
0-4	20	88	7	17	23	23	29	0	21	0	53	100	17	0
5-19	8	0	5	0	7	25	0	.	14	0	9	33	0	.
20-64	58	39	27	27	34	32	50	0	36	0	29	60	0	.
65 and over	15	33	11	44	36	25	14	0	21	0	9	33	8	0
Unknown	0	.	49	33	0	.	7	0	7	0	0	.	75	11
Hospital dep.														
ICU	0	.	11	33	0	.	0	.	0	.	0	.	0	.
Internal Med.	13	0	5	75	35	28	57	0	64	0	41	57	0	.
Surgery	0	.	10	13	0	.	0	.	0	.	0	.	0	.
Other	88	51	10	38	65	26	43	0	36	0	59	90	75	0
Unknown	0	.	64	27	0	.	0	.	0	.	0	.	25	33

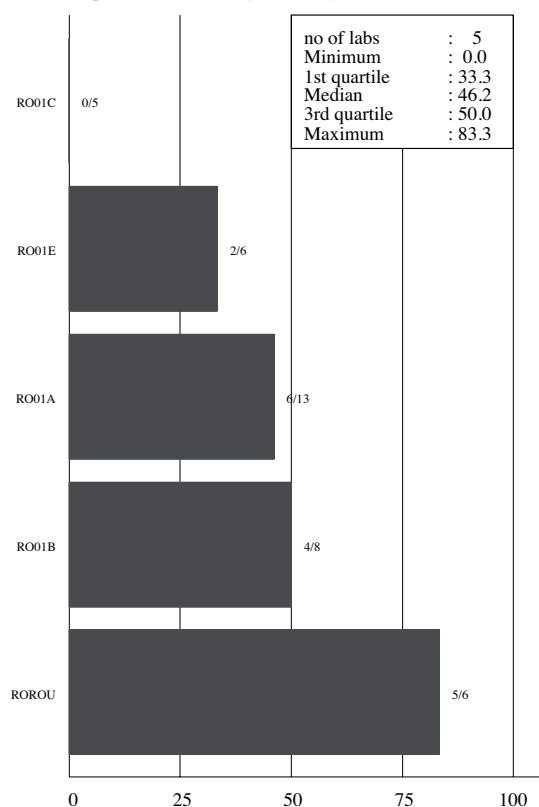
PNSP = Penicillin Non-Susceptible *S. pneumonia*
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FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

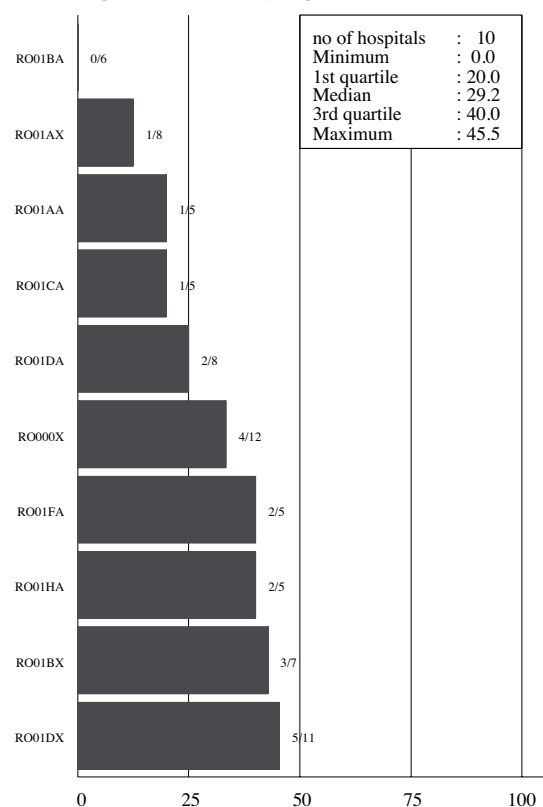
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Slovenia

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	10/10
Hosps providing denom.data/ reporting data to EARSS	15/16
Number of blood culture sets	48,730
Number of hospital beds	7,612
Patient-days	2,016,643
Average occupancy rate (%)	73%
Median length of stay (days)	5
Estimated catchment population	1,923,085
% total population covered	100%
Type of participating hospitals	
Regional/Tertiary	13%
Provincial/Secondary	47%
District/Primary	13%

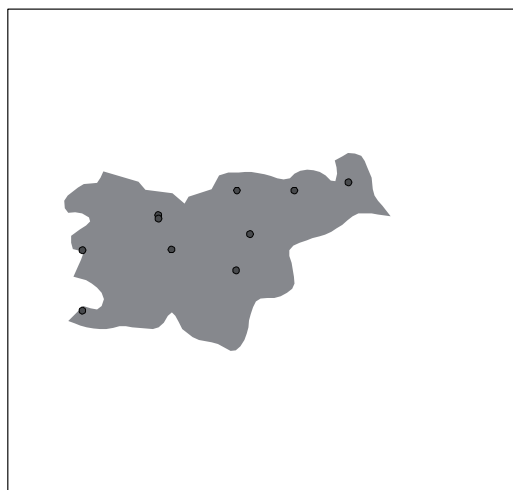


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	10	156	10	270	10	398	10	54	0	0	0	0
2002	11	101	11	276	11	409	9	45	0	0	0	0
2003	11	172	11	299	11	401	10	76	0	0	0	0
2004	10	166	11	347	11	573	9	91	0	0	0	0
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

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	<1	<1	2	2	2	5	4	3
	Penicillin I+R	20	19	15	25	11	19	17	15
	Macrolides I+R	18	10	9	11	11	13	17	16
<i>S. aureus</i>	Oxacillin/Methicillin R	20	14	13	12	10	7	8	7
<i>E. coli</i>	Aminopenicillins R	44	43	41	40	42	44	49	49
	Aminoglycosides R	2	3	2	5	4	7	7	7
	Fluoroquinolones R	8	12	11	12	12	15	17	17
	3rd gen. Cephalosporins R	<1	1	<1	1	2	2	4	4
<i>E. faecalis</i>	Aminopenicillins I+R	<1	<1	<1	<1	1	1	<1	<1
	HL Aminoglycosides R	35	50	49	37	46	40	50	40
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	64	69	83	76	93	86	92	96
	HL Aminoglycosides R	50	62	82	56	47	54	63	57
	Glycopeptides R	<1	<1	<1	<1	<1	6	5	13
<i>K. pneumoniae</i>	Aminoglycosides R	17	19	24	23
	Fluoroquinolones R	14	21	26	25
	3rd gen. Cephalosporins R	19	24	28	26
<i>P. aeruginosa</i>	Piperacillin R	21	18	13	21
	Ceftazidime R	11	8	7	14
	Carbapenems R	13	6	19	16
	Aminoglycosides R	18	15	10	13
	Fluoroquinolones R	29	21	17	24

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=404		<i>S. aureus</i> n=840		<i>E. coli</i> n=1725		<i>E. faecalis</i> n=238		<i>E. faecium</i> n=141		<i>K. pneumo.</i> n=327		<i>P. aeruginosa</i> n=183	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	94	15	100	8	100	17	100	0	100	9	100	27	98	17
CSF	6	29	0	.	0	.	0	.	0	.	0	.	2	33
Gender														
Male	55	17	63	8	39	19	61	0	55	12	54	34	60	20
Female	45	15	37	6	61	16	39	0	45	6	46	19	40	14
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	26	29	4	0	2	3	6	0	2	0	2	13	1	0
5-19	5	10	3	0	1	7	0	.	0	.	0	.	3	20
20-64	31	13	37	7	28	18	29	0	36	18	33	30	38	27
65 and over	38	11	56	9	70	17	64	0	62	5	65	26	58	11
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	5	14	8	11	6	16	15	0	25	0	15	43	13	42
Internal Med.	40	9	47	6	53	16	34	0	25	3	40	17	36	12
Surgery	1	0	10	14	7	16	12	0	12	0	14	39	17	16
Other	53	22	35	8	34	19	38	0	38	22	31	27	34	15
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

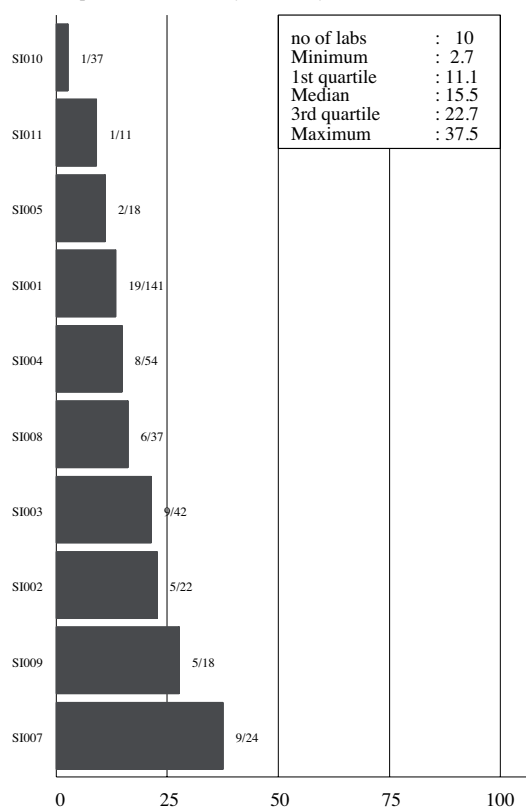
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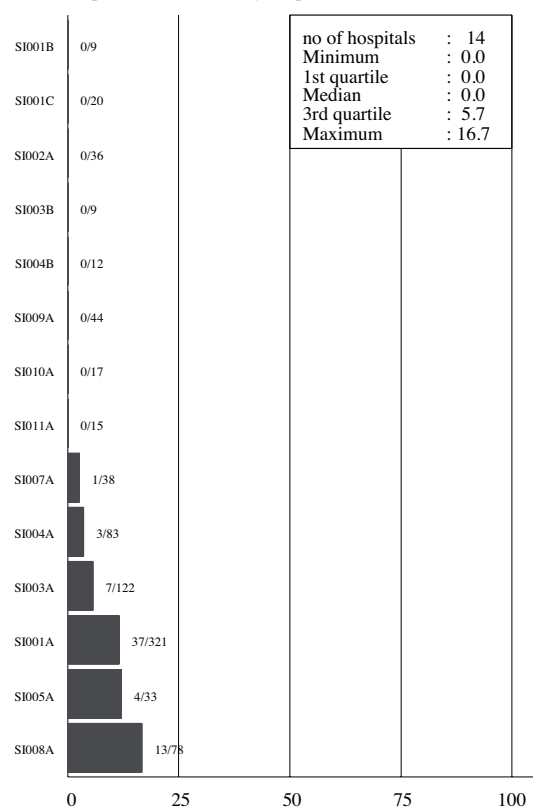
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Spain

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	27/32
Hosps providing denom.data/ reporting data to EARSS	26/33
Number of blood culture sets	219,120
Number of hospital beds	15,020
Patient-days	4,393,174
Average occupancy rate (%)	81%
Median length of stay (days)	8
Estimated catchment population	7,646,720
% total population covered	19%
Type of participating hospitals	
Regional/Tertiary	54%
Provincial/Secondary	42%
District/Primary	4%

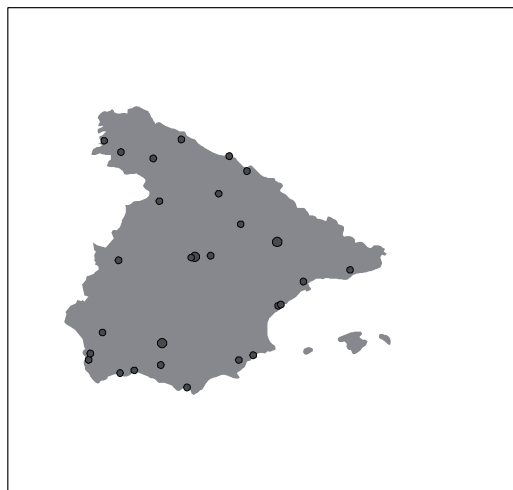


Figure 1. Geographic distribution of laboratories in 2008 (One laboratory on the Canary Islands is not shown)

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	36	649	35	1013	27	1967	26	371	0	0	0	0
2002	35	658	36	1196	29	2484	35	566	0	0	0	0
2003	35	655	36	1391	29	2650	36	608	0	0	0	0
2004	36	682	36	1526	36	3471	36	710	0	0	0	0
2005	34	740	34	1337	34	2997	35	623	14	56	13	70
2006	35	624	35	1483	35	3364	34	755	33	564	32	405
2007	35	860	35	1642	35	3678	35	885	33	618	35	448
2008	31	694	32	1505	32	3626	32	1002	30	639	32	548

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	11	10	7	9	9	8	8	7
	Penicillin I+R	37	33	32	29	25	27	22	23
	Macrolides I+R	31	26	27	27	23	22	18	22
<i>S. aureus</i>	Oxacillin/Methicillin R	23	23	24	26	27	25	25	27
<i>E. coli</i>	Aminopenicillins R	59	60	58	60	62	64	62	63
	Aminoglycosides R	7	8	7	7	10	9	10	11
	Fluoroquinolones R	17	19	21	25	28	28	30	33
	3rd gen. Cephalosporins R	<1	2	4	7	8	7	7	9
<i>E. faecalis</i>	Aminopenicillins I+R	3	2	1	2	<1	2	1	3
	HL Aminoglycosides R	32	37	36	36	36	36	42	41
	Glycopeptides R	<1	<1	<1	<1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	49	59	64	66	67	73	79	79
	HL Aminoglycosides R	15	16	11	17	16	21	40	35
	Glycopeptides R	2	1	3	2	3	3	2	1
<i>K. pneumoniae</i>	Aminoglycosides R	4	7	9	9
	Fluoroquinolones R	11	8	17	15
	3rd gen. Cephalosporins R	7	9	10	12
<i>P. aeruginosa</i>	Piperacillin R	4	9	8	8
	Ceftazidime R	6	7	10	11
	Carbapenems R	17	12	15	13
	Aminoglycosides R	4	11	15	18
	Fluoroquinolones R	14	19	25	23

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=1554		<i>S. aureus</i> n=3147		<i>E. coli</i> n=7269		<i>E. faecalis</i> n=1380		<i>E. faecium</i> n=507		<i>K. pneumo.</i> n=1252		<i>P. aeruginosa</i> n=988	
	%tot	%PNSP	%tot	%MRSA	%tot	%FRECC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	96	22	100	26	100	31	100	0	100	2	100	11	100	14
CSF	4	31	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	61	22	65	26	52	36	65	0	65	1	60	12	69	14
Female	39	24	35	27	48	27	34	0	35	3	39	10	31	14
Unknown	0	.	0	.	0	.	1	0	0	.	0	.	0	.
Age (years)														
0-4	13	26	4	8	3	10	7	0	4	0	5	26	3	4
5-19	5	7	2	9	1	19	1	0	1	0	1	22	1	14
20-64	40	18	34	19	27	27	31	0	36	2	34	9	35	19
65 and over	39	29	57	32	67	34	57	0	58	2	57	11	59	12
Unknown	3	16	2	24	2	25	4	0	1	0	3	5	3	7
Hospital dep.														
ICU	7	22	12	28	6	32	21	0	17	2	12	12	22	28
Internal Med.	17	24	30	30	22	36	22	0	23	4	24	7	21	11
Surgery	1	56	8	31	6	34	11	1	14	0	9	15	7	25
Other	73	22	48	22	65	30	45	0	46	1	52	12	47	8
Unknown	2	27	2	28	1	36	1	0	1	0	2	5	2	6

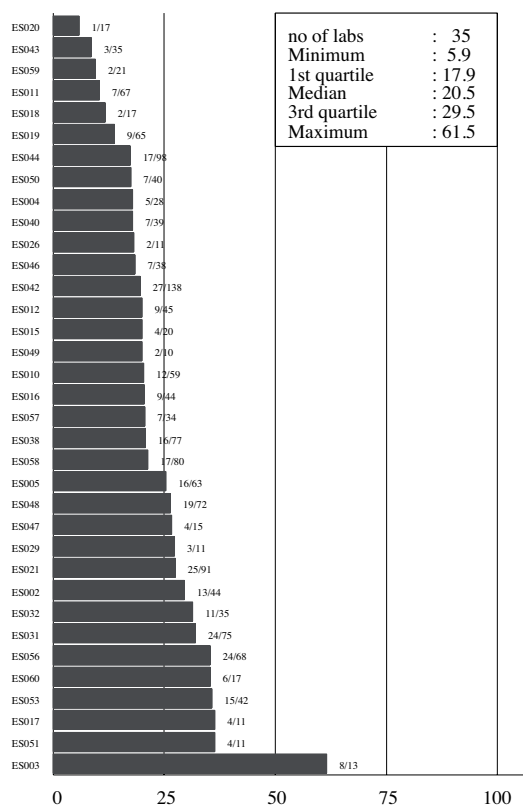
PNSP = Penicillin Non-Susceptible *S. pneumoniae*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FRECC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

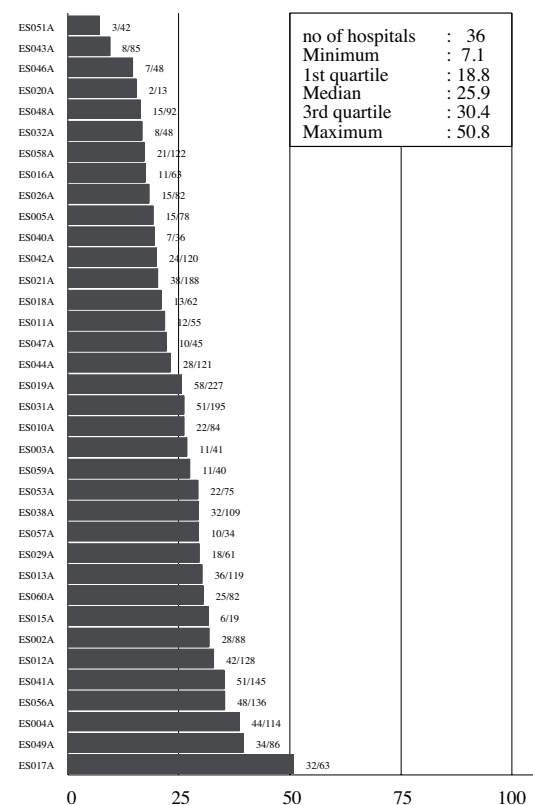
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=2241		<i>S. aureus</i> n=4571		<i>E. coli</i> n=7297		<i>E. faecalis</i> n=1371		<i>E. faecium</i> n=612		<i>K. pneumo.</i> n=1474		<i>P. aeruginosa</i> n=603	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	98	2	100	1	100	10	100	0	100	1	100	2	100	6
CSF	2	4	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	49	2	62	0	46	13	71	0	55	1	58	2	66	5
Female	51	2	38	1	54	8	29	0	45	1	42	2	34	7
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Age (years)														
0-4	4	3	4	2	1	2	5	0	3	0	1	5	2	7
5-19	2	3	4	0	1	12	1	0	1	0	1	0	2	7
20-64	41	2	31	1	25	12	25	0	31	2	24	2	26	9
65 and over	53	3	61	0	73	10	70	0	66	0	74	2	69	4
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.
Hospital dep.														
ICU	7	2	6	0	3	12	6	0	12	3	5	3	8	6
Internal Med.	47	3	41	0	41	9	34	0	35	0	39	2	44	6
Surgery	5	5	16	0	20	11	24	0	26	1	25	1	15	9
Other	41	2	37	1	35	12	35	0	27	1	31	3	32	4
Unknown	0	.	0	.	0	.	0	.	0	.	0	.	0	.

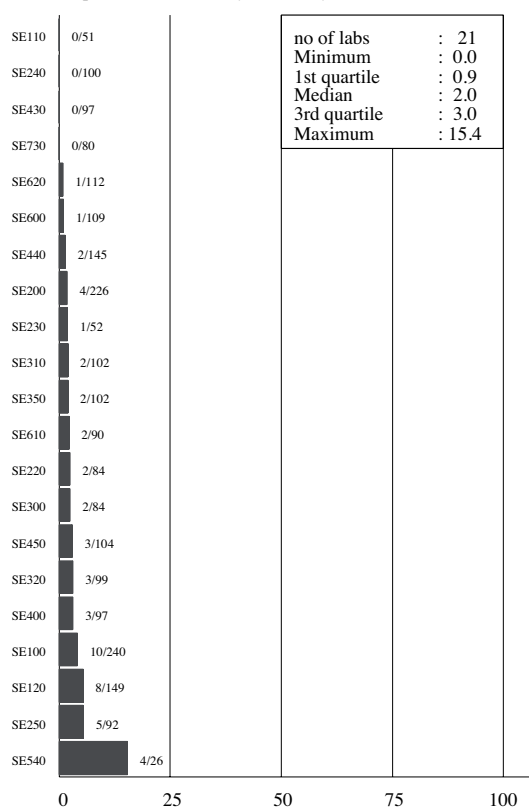
PNSP = Penicillin Non-Susceptible *S. pneumonia*
VRE = Vancomycin Resistant Enterococcus

MRSA = Methicillin Resistant *S. aureus*
CRKP = 3rd gen. Cephalosporine Resistant *K. pneumoniae*

FREC = Fluoroquinolone Resistant *E. coli*
CRPA = Carbapenem Resistant *P. aeruginosa*

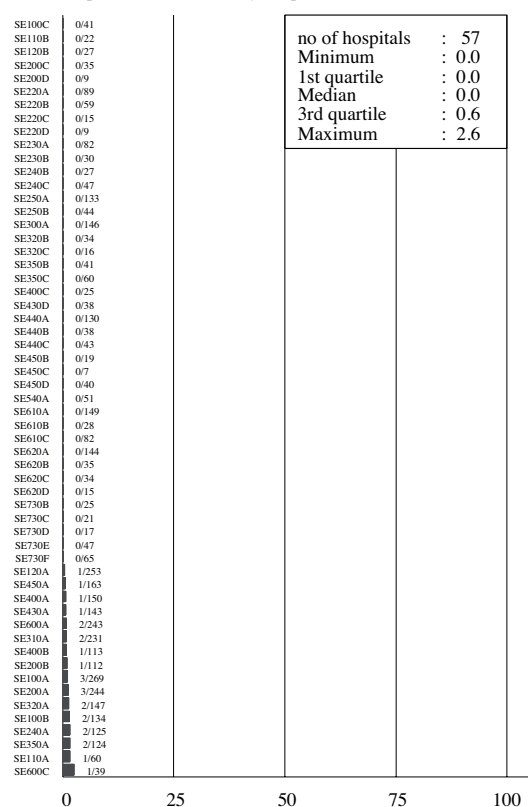
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Turkey

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	16/16
Hosps providing denom.data/ reporting data to EARSS	16/26
Number of blood culture sets	138,513
Number of hospital beds	15,808
Patient-days	4,365,778
Average occupancy rate (%)	79%
Median length of stay (days)	7
Estimated catchment population	23,383,271
% total population covered	30%
Type of participating hospitals	
Regional/Tertiary	100%
Provincial/Secondary	0%
District/Primary	0%



Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	0	0	0	0	0	0	0	0	0	0	0	0
2002	0	0	1	1	0	0	0	0	0	0	0	0
2003	11	117	11	749	12	719	10	370	0	0	0	0
2004	11	149	11	703	11	765	11	476	0	0	0	0
2005	10	103	10	761	10	782	10	551	3	13	2	5
2006	12	98	14	796	14	889	14	583	14	456	13	313
2007	11	111	16	1128	16	1076	16	778	16	639	15	420
2008	13	97	16	1060	16	1377	16	1030	16	711	15	468

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	.	.	2	7	<1	5	11	18
	Penicillin I+R	.	.	13	23	24	18	28	34
	Macrolides I+R	.	.	7	9	10	16	16	29
<i>S. aureus</i>	Oxacillin/Methicillin R	.	<1	43	40	35	36	34	38
<i>E. coli</i>	Aminopenicillins R	.	.	68	68	75	72	78	78
	Aminoglycosides R	.	.	28	27	27	28	35	35
	Fluoroquinolones R	.	.	38	43	44	48	53	52
	3rd gen. Cephalosporins R	.	.	26	28	31	33	40	42
<i>E. faecalis</i>	Aminopenicillins I+R	.	.	10	23	8	10	8	12
	HL Aminoglycosides R	.	.	39	31	30	29	29	32
	Glycopeptides R	.	.	1	1	<1	<1	<1	<1
<i>E. faecium</i>	Aminopenicillins I+R	.	.	75	81	87	87	91	92
	HL Aminoglycosides R	.	.	55	58	60	70	69	70
	Glycopeptides R	.	.	4	3	5	4	8	7
<i>K. pneumoniae</i>	Aminoglycosides R	15	28	26	22
	Fluoroquinolones R	46	23	23	26
	3rd gen. Cephalosporins R	46	43	44	45
<i>P. aeruginosa</i>	Piperacillin R	40	28	24	19
	Ceftazidime R	50	24	23	21
	Carbapenems R	40	33	28	30
	Aminoglycosides R	50	33	24	21
	Fluoroquinolones R	40	30	26	25

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=208		<i>S. aureus</i> n=2188		<i>E. coli</i> n=2435		<i>E. faecalis</i> n=933		<i>E. faecium</i> n=863		<i>K. pneumo.</i> n=1350		<i>P. aeruginosa</i> n=888	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	78	26	100	36	100	53	100	0	100	7	100	45	100	29
CSF	22	47	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	72	31	61	39	55	55	51	0	53	6	58	46	61	28
Female	27	32	38	32	44	50	48	0	46	9	41	42	39	30
Unknown	1	0	1	23	0	.	1	0	1	10	1	58	0	.
Age (years)														
0-4	22	42	10	25	6	23	10	0	12	8	19	54	14	30
5-19	17	22	8	29	4	39	3	3	3	4	6	39	5	22
20-64	39	31	52	36	50	55	46	0	46	8	47	42	48	31
65 and over	22	24	30	41	39	55	41	0	39	6	27	45	33	27
Unknown	0	.	0	.	0	.	0	.	0	.	1	29	0	.
Hospital dep.														
ICU	4	33	19	62	11	56	36	0	33	8	21	60	26	38
Internal Med.	12	33	21	22	19	56	13	0	18	9	15	31	16	24
Surgery	3	50	12	58	14	58	13	0	14	5	12	51	15	36
Other	79	30	47	27	55	49	37	1	35	6	51	41	43	23
Unknown	2	20	1	22	1	52	0	.	0	.	1	13	1	0

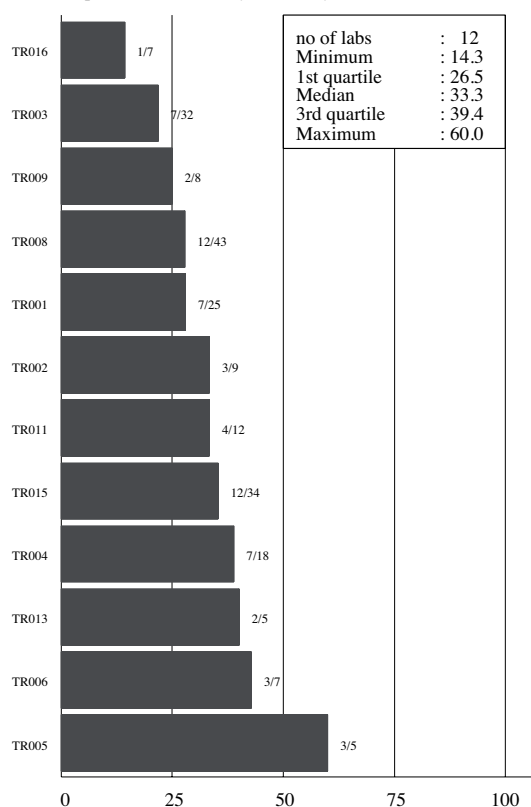
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MRSA = Methicillin Resistant *S. aureus*
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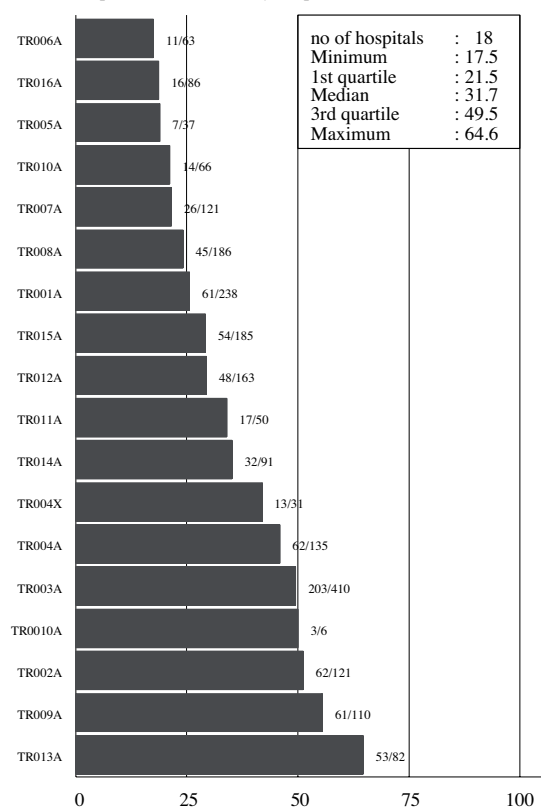
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



United Kingdom

General Information about EARSS participating laboratories and hospitals

Table 1. Reference data of 2008, based on laboratories/hospitals providing denominator data

	Total
Labs providing denom.data/ reporting data to EARSS	20/55
Hosps providing denom.data/ reporting data to EARSS	20/138
Number of blood culture sets	186,046
Number of hospital beds	8,245
Patient-days	1,503,035
Average occupancy rate (%)	79%
Median length of stay (days)	3
Estimated catchment population	3,075,569
% total population covered	5%
Type of participating hospitals	
Regional/Tertiary	20%
Provincial/Secondary	45%
District/Primary	35%

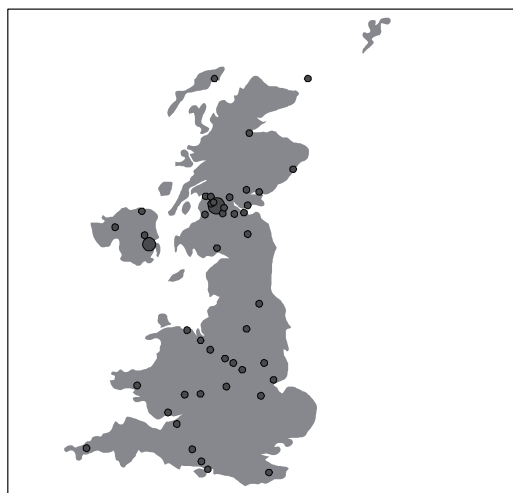


Figure 1. Geographic distribution of laboratories in 2008

Table 2. Number of laboratories and number of isolates reported for the period 2001-2008

Year	<i>S. pneumoniae</i>		<i>S. aureus</i>		<i>E. coli</i>		Enterococci		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
2001	26	573	25	1517	20	1424	0	0	0	0	0	0
2002	23	617	21	1703	20	1958	0	0	0	0	0	0
2003	50	1334	51	3639	19	2253	0	0	0	0	0	0
2004	54	1058	54	3560	20	2091	0	0	0	0	0	0
2005	53	1373	58	3967	23	2359	27	598	23	425	25	438
2006	51	1510	55	4000	26	2444	22	547	22	410	24	353
2007	50	1744	55	4811	20	2393	18	435	18	394	19	370
2008	50	1177	55	3350	15	2493	14	274	15	356	14	345

Antibiotic resistance from 2001 to 2008

Table 3. Proportion of antibiotic non-susceptible isolates in percent

Pathogen	Antimicrobial classes	2001	2002	2003	2004	2005	2006	2007	2008
<i>S. pneumoniae</i>	Penicillin R	3	3	1	<1	2	<1	2	1
	Penicillin I+R	5	6	5	3	4	3	4	5
	Macrolides I+R	13	13	13	13	11	12	10	6
<i>S. aureus</i>	Oxacillin/Methicillin R	44	44	43	44	44	42	36	31
<i>E. coli</i>	Aminopenicillins R	51	52	55	53	56	57	55	61
	Aminoglycosides R	3	3	4	6	8	7	7	7
	Fluoroquinolones R	6	7	11	14	17	20	18	15
	3rd gen. Cephalosporins R	1	2	3	3	6	8	9	7
<i>E. faecalis</i>	Aminopenicillins I+R	2	3	4	2
	HL Aminoglycosides R	47	52	31	42
	Glycopeptides R	2	1	2	4
<i>E. faecium</i>	Aminopenicillins I+R	84	78	82	83
	HL Aminoglycosides R	53	18	35	7
	Glycopeptides R	33	18	21	28
<i>K. pneumoniae</i>	Aminoglycosides R	6	8	9	6
	Fluoroquinolones R	12	13	12	7
	3rd gen. Cephalosporins R	12	11	13	7
<i>P. aeruginosa</i>	Piperacillin R	2	1	5	2
	Ceftazidime R	3	3	7	4
	Carbapenems R	9	6	10	6
	Aminoglycosides R	3	3	5	3
	Fluoroquinolones R	8	8	9	8

Demographic characteristics

Table 4. Selected details on invasive isolates from the reporting period 2007 and 2008

Characteristic	<i>S. pneumo.</i> n=2921		<i>S. aureus</i> n=8161		<i>E. coli</i> n=4509		<i>E. faecalis</i> n=447		<i>E. faecium</i> n=219		<i>K. pneumo.</i> n=625		<i>P. aeruginosa</i> n=512	
	%tot	%PNSP	%tot	%MRSA	%tot	%FREC	%tot	%VRE	%tot	%VRE	%tot	%CRKP	%tot	%CRPA
Isolate source														
Blood	98	4	100	34	100	16	100	3	100	24	100	10	100	8
CSF	2	7	0	.	0	.	0	.	0	.	0	.	0	.
Gender														
Male	50	4	62	36	47	19	64	3	61	23	61	11	67	8
Female	48	5	38	30	53	14	35	3	39	26	39	9	33	8
Unknown	2	8	1	17	0	.	0	.	0	.	1	0	0	.
Age (years)														
0-4	7	6	5	13	2	9	7	0	5	25	4	4	3	7
5-19	4	3	2	12	1	10	2	0	4	25	1	11	3	23
20-64	44	3	39	26	25	16	31	5	39	30	29	8	30	14
65 and over	45	5	54	42	72	17	60	2	52	19	65	11	64	5
Unknown	0	.	0	.	0	.	0	.	0	.	1	0	0	.
Hospital dep.														
ICU	5	1	7	44	0	.	0	.	0	.	0	.	0	.
Internal Med.	26	4	24	34	0	.	0	.	0	.	0	.	0	.
Surgery	2	4	7	42	0	.	0	.	0	.	0	.	0	.
Other	41	4	38	29	0	.	0	.	0	.	0	.	0	.
Unknown	26	5	24	36	100	16	100	3	100	24	100	10	100	8

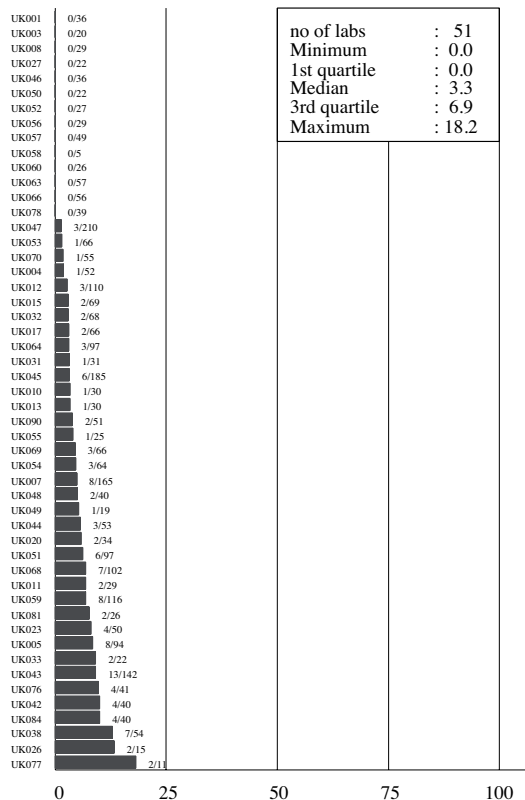
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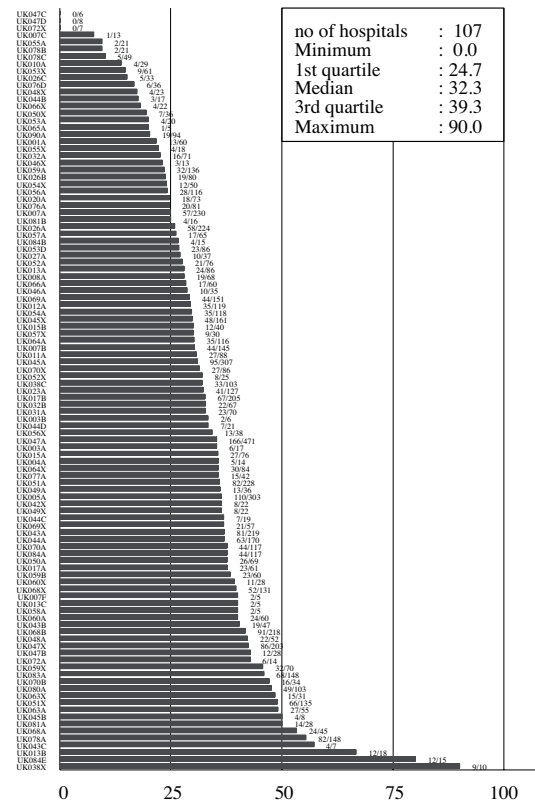
PNSP at laboratory level

Figure 2. Proportion (%) PNSP by laboratory (2007 & 2008)



MRSA at hospital level

Figure 3. Proportion (%) MRSA by hospital (2007 & 2008)



Annex 3. Overview of antibiotic resistance in Europe, 2008

Annex 3.1. The number (No) of invasive *S. pneumoniae* (SPN) isolates, and the proportion penicillin non-susceptible (PNSP), penicillin resistant (PRSP), erythromycin non-susceptible (ENSP), single penicillin (PEN), single erythromycin (ERY) and dual non-susceptible isolates, including 95% confidence intervals (95CI) reported per country in 2008.

Country	No SPN isolates tested for PEN/ERY	%PNSP (95CI)	%PRSP (95CI)	%ENSP (95CI)	%single PEN (95CI)	%single ERY (95CI)	%DUAL (95CI)
AT	367/316	5 (3-7)	1 (0-3)	11 (8-15)	2 (1-5)	8 (6-12)	3 (2-6)
BA	11/11	55 (25-82)	45 (18-75)	9 (0-43)	45 (18-75)	0 (0-32)	9 (0-43)
BE	1,647/1,647	8 (7-10)	1 (1-2)	24 (22-26)	2 (2-3)	18 (16-20)	6 (5-7)
BG	29/24	21 (9-40)	21 (9-40)	4 (0-23)	21 (8-43)	0 (0-17)	4 (0-23)
CH	646/511	8 (6-10)	2 (1-4)	14 (11-17)	4 (2-6)	10 (7-13)	6 (4-8)
CY	14/14	43 (19-70)	21 (6-51)	29 (10-58)	14 (3-44)	0 (0-27)	29 (10-58)
CZ	243/243	3 (2-7)	0 (0-3)	3 (1-6)	2 (1-6)	2 (1-5)	1 (0-3)
DE	199/196	5 (3-9)	0 (0-2)	9 (5-14)	3 (1-6)	6 (3-11)	3 (1-6)
DK	934/934	3 (2-4)	1 (0-1)	7 (5-8)	2 (1-3)	5 (4-7)	1 (1-2)
EE	65/53	5 (1-14)	0 (0-7)	4 (1-14)	6 (1-17)	4 (1-14)	0 (0-8)
ES	694/679	23 (20-26)	7 (5-9)	22 (19-25)	12 (10-15)	11 (9-14)	11 (9-14)
FI	642/642	11 (9-14)	1 (0-2)	24 (21-28)	4 (3-6)	17 (14-20)	7 (5-10)
FR	557/557	30 (26-34)	7 (5-9)	31 (27-35)	4 (3-7)	5 (4-8)	25 (22-29)
HR	100/91	17 (10-26)	4 (1-11)	14 (8-24)	12 (6-21)	9 (4-17)	7 (3-14)
HU	166/158	27 (21-35)	8 (4-13)	32 (25-40)	8 (4-13)	13 (8-19)	21 (15-28)
IE	441/408	23 (19-27)	6 (4-9)	17 (13-21)	13 (10-17)	6 (4-9)	12 (9-15)
IL	198/197	21 (16-28)	5 (2-9)	20 (15-26)	14 (9-19)	12 (8-18)	8 (4-12)
IS	46/46	9 (3-22)	0 (0-10)	22 (11-37)	0 (0-10)	13 (5-27)	9 (3-22)
IT	176/154	10 (6-16)	3 (1-8)	27 (21-35)	5 (2-10)	20 (14-28)	7 (4-13)
LT	47/46	2 (0-13)	0 (0-9)	7 (2-19)	0 (0-10)	4 (1-16)	2 (0-13)
LU	53/53	11 (5-24)	6 (1-17)	13 (6-26)	4 (1-14)	6 (1-17)	8 (2-19)
LV	11/11	9 (0-43)	9 (0-43)	0 (0-32)	9 (0-43)	0 (0-32)	0 (0-32)
MT	17/17	47 (24-71)	24 (8-50)	35 (15-61)	29 (11-56)	18 (5-44)	18 (5-44)
NL	674/592	2 (1-3)	0 (0-1)	7 (5-9)	1 (0-2)	6 (4-8)	1 (1-3)
NO	554/543	3 (1-4)	0 (0-1)	7 (5-10)	1 (0-2)	6 (4-8)	2 (1-3)
PL	84/6	13 (7-23)	12 (6-21)	50 (14-86)	0 (0-48)	17 (1-64)	73 (45-91)
PT	260/260	18 (13-23)	0 (0-2)	22 (17-27)	7 (4-10)	10 (7-15)	11 (8-16)
RO	13/10	69 (39-90)	54 (26-80)	20 (4-56)	50 (20-80)	0 (0-34)	33 (11-65)
SE	1,213/1,123	2 (1-3)	0 (0-1)	6 (4-7)	1 (1-2)	5 (4-6)	1 (1-2)
SI	209/209	15 (11-21)	3 (1-7)	16 (11-22)	10 (6-15)	11 (7-16)	5 (3-9)
TR	97/97	34 (25-44)	18 (11-27)	29 (20-39)	11 (6-20)	6 (3-14)	23 (15-33)
UK	1,177/1,134	5 (4-6)	1 (1-2)	6 (5-8)	2 (2-3)	4 (3-5)	3 (2-4)
Total	11,584/10,982	10	2	15	4	9	6

Annex 3.2. The number (No) of invasive *S. aureus* (SAU) isolates, and the proportion resistant to methicillin (MRSA) including 95% confidence intervals (95CI) reported per country in 2008.

Country	SAU isolates No	% MRSA (95CI)
AT	1,894	8 (7-10)
BA	71	21 (13-33)
BE	906	21 (18-23)
BG	160	25 (19-33)
CH	1,097	10 (9-12)
CY	92	46 (35-56)
CZ	1,715	14 (13-16)
DE	1,089	19 (17-22)
DK	1,295	2 (2-3)
EE	185	4 (2-9)
ES	1,505	27 (24-29)
FI	921	3 (2-4)
FR	4,376	24 2(3-26)
GR	859	41 (38-44)
HR	474	35 (31-40)
HU	1,181	23 (20-25)
IE	1,242	33 (30-36)
IL	386	35 (31-40)
IS	63	2 (0-10)
IT	930	34 (31-37)
LT	278	11 (8-16)
LU	117	9 (5-17)
LV	131	13 (8-20)
MT	108	56 (46-65)
NL	1,004	1 (0-1)
NO	810	1 (0-2)
PL	99	12 (7-21)
PT	1,556	53 (50-55)
RO	39	33 (20-50)
SE	2,408	1 (0-1)
SI	418	7 (5-10)
TR	1,060	38 (35-41)
UK	3,350	31 (29-32)
Total	31,819	23

Annex 3.3. The number (No) of invasive *E. faecalis* and *E. faecium* isolates, and the proportion high level aminoglycoside resistant *E. faecalis*, and vancomycin resistant *E. faecium* (%R) including 95% confidence intervals (95CI) reported per country in 2008.

Country	High level aminoglycoside resistant <i>E. faecalis</i>		Vancomycin resistant <i>E. faecium</i>	
	No	%R (95CI)	No	%R (95CI)
AT	289	21 (17-27)	334	2 (1-4)
BA	–	–	9	0 (0-37)
BE	144	30 (23-38)	59	5 (1-15)
BG	39	44 (28-60)	28	0 (0-15)
CH	85	19 (11-29)	152	3 (1-7)
CY	75	65 (53-76)	10	20 (4-56)
CZ	644	49 (45-53)	234	8 (5-13)
DE	191	39 (32-47)	175	6 (3-11)
DK	49	37 (24-52)	344	0 (0-2)
EE	26	27 (12-48)	39	3 (0-15)
ES	694	41 (37-45)	289	1 (0-4)
FI	157	13 (8-19)	155	1 (0-4)
FR	895	18 (15-20)	353	1 (0-2)
GR	590	52 (48-56)	368	28 (24-33)
HR	157	46 (38-54)	72	6 (2-14)
HU	357	53 (47-58)	71	3 (0-11)
IE	277	31 (25-37)	390	35 (30-40)
IL	168	43 (36-51)	55	20 (11-33)
IS	10	30 (8-65)	7	0 (0-44)
IT	254	47 (41-54)	215	6 (3-10)
LT	42	33 (20-50)	24	0 (0-17)
LU	36	17 (7-33)	22	5 (0-25)
LV	9	33 (9-69)	25	8 (1-28)
MT	–	–	5	0 (0-54)
NL	161	32 (25-40)	165	0 (0-3)
NO	185	30 (23-37)	108	0 (0-4)
PL	17	29 (11-56)	9	0 (0-37)
PT	345	43 (38-49)	177	24 (18-31)
RO	9	22 (4-60)	5	0 (0-54)
SE	703	20 (17-23)	333	2 (1-4)
SI	120	40 (31-49)	76	13 (7-23)
TR	506	32 (28-36)	492	7 (5-9)
UK	48	42 (28-57)	88	28 (20-39)
Total	7,282	35	4,888	9

Annex 3.4. The number of invasive *E. coli* isolates (No), and the proportion aminopenicillins, third generation cephalosporins, fluoroquinolones, aminoglycosides and multi-resistance (%R) including 95% confidence intervals (95CI) reported per country in 2008.

Country	Aminopenicillins		Fluoroquinolones		Third gen. Cephalosporines		Aminoglycosides		Multi-resistance*	
	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)
AT	2,979	50 (49-52)	2,975	23 (21-24)	2,968	7 (6-8)	2,985	7 (6-8)	2,958	3 (2-3)
BA	34	62 (44-77)	34	15 (6-32)	34	3 (0-17)	34	3 (0-17)	34	0 (0-13)
BE	1,425	55 (53-58)	1,324	17 (15-19)	1,409	4 (3-5)	1,011	4 (3-6)	988	0 (0-1)
BG	128	65 (56-73)	146	32 (24-40)	147	29 (22-37)	147	31 (23-39)	146	20 (14-27)
CH	2,519	48 (46-50)	2,615	15 (14-16)	2,613	3 (3-4)	2,614	7 (6-8)	2,612	1 (1-2)
CY	116	57 (47-66)	116	45 (36-54)	116	18 (12-27)	116	9 (4-16)	116	8 (4-15)
CZ	2,738	60 (58-62)	2,736	26 (24-28)	2,738	10 (9-11)	2,738	9 (8-10)	2,736	3 (3-4)
DE	1,000	55 (52-58)	1,610	23 (21-26)	1,613	5 (4-6)	1,615	7 (6-8)	1,608	3 (2-4)
DK	3,282	43 (41-45)	3,018	10 (9-11)	2,489	4 (3-5)	3,278	4 (3-5)	2,453	1 (1-2)
EE	266	47 (41-53)	252	7 (4-11)	262	5 (2-8)	262	5 (3-9)	242	1 (0-3)
ES	3,621	63 (61-65)	3,610	33 (31-34)	3,626	9 (8-10)	3,622	11 (10-12)	3,607	3 (2-4)
FI	1,768	35 (33-37)	2,109	9 (8-10)	2,087	2 (2-3)	2,057	4 (3-4)	2,035	2 (1-2)
FR	7,979	54 (53-55)	7,485	16 (15-17)	7,990	4 (3-4)	7,609	7 (6-7)	7,483	2 (1-2)
GR	1,428	50 (48-53)	1,446	22 (20-25)	1,460	10 (8-12)	1,451	15 (13-17)	1,446	6 (5-7)
HR	915	53 (49-56)	915	15 (13-17)	915	4 (3-5)	915	6 (4-7)	915	1 (1-2)
HU	1,043	59 (56-62)	1,045	26 (24-29)	1,057	9 (8-11)	1,054	13 (11-16)	1,043	7 (5-8)
IE	1,869	67 (65-69)	1,856	23 (21-25)	1,859	6 (5-7)	1,869	9 (8-11)	1,837	2 (2-3)
IL	522	59 (55-64)	811	27 (24-30)	812	15 (12-17)	813	16 (14-19)	810	10 (8-12)
IS	123	44 (35-53)	115	6 (3-13)	123	0 (0-4)	123	7 (3-13)	115	0 (0-4)
IT	943	62 (58-65)	907	38 (34-41)	767	16 (13-19)	956	14 (12-16)	765	7 (5-9)
LT	228	54 (47-61)	304	14 (10-18)	304	6 (3-9)	302	12 (9-17)	302	3 (1-6)
LU	284	55 (49-61)	285	21 (17-27)	285	7 (4-10)	285	8 (5-12)	285	4 (2-7)
LV	66	52 (39-64)	66	12 (6-23)	66	9 (4-19)	66	9 (4-19)	66	8 (3-18)
MT	128	52 (43-60)	128	34 (26-43)	124	21 (14-29)	128	22 (15-30)	124	19 (13-28)
NL	2,107	47 (45-49)	2,070	14 (13-16)	2,107	5 (4-6)	2,113	6 (5-7)	2,058	2 (1-2)
NO	1,730	38 (36-40)	1,719	7 (6-8)	1,731	2 (2-3)	1,729	3 (2-4)	1,717	1 (0-1)
PL	84	54 (42-64)	84	20 (13-31)	84	2 (0-9)	84	7 (3-15)	84	1 (0-7)
PT	1,620	58 (56-61)	1,577	29 (26-31)	1,584	10 (9-12)	1,624	14 (12-15)	1,555	6 (5-8)
RO	31	55 (36-72)	52	27 (16-41)	55	24 (14-37)	54	24 (14-38)	50	18 (9-32)
SE	2,229	32 (30-34)	3,577	10 (9-11)	4,028	2 (2-3)	4,025	2 (2-3)	3,574	1 (0-1)
SI	874	49 (46-53)	874	17 (15-20)	874	4 (3-6)	874	7 (5-9)	874	3 (2-4)
TR	1,375	78 (76-80)	1,372	52 (50-55)	1,375	42 (39-44)	1,377	35 (32-37)	1,370	23 (20-25)
UK	1,763	61 (58-63)	2,369	15 (14-17)	2,193	7 (6-8)	1,923	7 (6-8)	1,738	3 (3-4)
Total	47,217	53	49,602	20	49,895	7	49,853	8	47,746	3

* Multi-resistance was defined as being resistant to fluoroquinolones, third generation cephalosporins, and aminoglycosides, irrespective of aminopenicillin susceptibility

Annex 3.5. The number of invasive *K. pneumoniae* isolates (No), and the proportion aminopenicillins, third generation cephalosporins, fluoroquinolones, aminoglycosides and multi-resistance (%R) including 95% confidence intervals (95CI) reported per country in 2008.

Country	Aminopenicillins		Fluoroquinolones		Third gen. Cephalosporins		Aminoglycosides		Carbapenem		Multi-resistance*	
	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)
AT	579	97 (95-98)	581	12 (9-15)	579	8 (6-11)	581	6 (5-9)	397	0 (0-1)	579	4 (2-6)
BA	39	92 (78-98)	39	33 (20-50)	39	44 (28-60)	38	39 (24-57)	36	3 (0-16)	38	26 (14-43)
BG	47	100 (91-100)	48	52 (37-66)	49	73 (59-85)	49	59 (44-73)	45	0 (0-10)	48	44 (30-59)
CH	438	100 (99-100)	448	3 (1-5)	448	3 (1-5)	448	4 (2-6)	400	0 (0-1)	448	1 (0-2)
CY	62	100 (93-100)	62	23 (13-35)	62	35 (24-49)	62	21 (12-34)	62	10 (4-21)	62	16 (8-28)
CZ	1,492	98 (97-98)	1,492	52 (49-54)	1,493	48 (45-50)	1,485	42 (39-45)	1,260	0 (0-1)	1,484	32 (29-34)
DE	161	99 (95-100)	235	15 (11-21)	235	11 (8-16)	235	10 (6-15)	231	0 (0-2)	235	7 (4-12)
DK	543	100 (99-100)	739	16 (13-19)	620	9 (7-12)	793	7 (5-9)	523	0 (0-1)	615	5 (3-7)
EE	71	94 (85-98)	61	7 (2-17)	69	12 (5-22)	72	15 (8-26)	62	0 (0-7)	58	2 (0-10)
ES	639	94 (92-96)	639	15 (12-18)	639	12 (10-15)	638	9 (7-12)	586	0 (0-1)	638	4 (3-6)
FI	240	93 (89-96)	287	2 (1-5)	288	2 (1-4)	281	1 (0-4)	280	0 (0-2)	280	1 (0-3)
FR	1,136	99 (98-100)	1,045	21 (18-23)	1,138	15 (13-17)	1,064	17 (14-19)	1,021	0 (0-0)	1,045	13 (11-16)
GR	1,001	93 (91-95)	1,067	64 (61-67)	1,080	66 (63-69)	1,075	55 (52-58)	1,074	37 (34-40)	1,063	51 (48-54)
HR	329	100 (98-100)	323	44 (38-49)	330	54 (49-60)	333	51 (46-57)	320	0 (0-1)	320	38 (33-43)
HU	362	100 (99-100)	365	33 (28-38)	369	35 (30-40)	369	36 (31-41)	360	0 (0-1)	365	27 (23-32)
IE	305	97 (94-98)	302	11 (7-15)	305	11 (8-15)	306	9 (7-13)	230	0 (0-2)	299	4 (2-7)
IL	260	84 (79-88)	351	38 (33-44)	351	38 (33-44)	351	36 (31-41)	350	19 (15-23)	351	28 (24-34)
IS	24	100 (83-100)	24	8 (1-28)	24	4 (0-23)	24	4 (0-23)	24	0 (0-17)	24	4 (0-23)
IT	322	93 (89-95)	309	28 (23-33)	280	39 (33-45)	330	28 (23-33)	309	2 (1-4)	278	22 (18-28)
LT	52	98 (88-100)	52	23 (13-37)	53	36 (23-50)	54	41 (28-55)	53	0 (0-8)	51	18 (9-31)
LU	50	100 (91-100)	49	12 (5-25)	50	20 (11-34)	50	12 (5-25)	2	0 (5-80)	49	4 (1-15)
LV	30	97 (81-100)	31	42 (25-61)	31	58 (39-75)	31	55 (36-72)	31	3 (0-19)	31	29 (15-48)
MT	36	97 (84-100)	36	8 (2-24)	36	0 (0-12)	36	0 (0-12)	36	0 (0-12)	36	0 (0-12)
NL	460	90 (87-93)	459	7 (5-9)	462	8 (5-10)	463	7 (5-10)	420	0 (0-1)	458	4 (2-6)
NO	341	100 (99-100)	340	4 (2-6)	341	2 (1-4)	340	1 (1-4)	289	1 (0-3)	339	1 (0-2)
PL	19	95 (72-100)	19	32 (14-57)	19	37 (17-61)	19	26 (10-51)	8	0 (1-40)	19	21 (7-46)
PT	537	98 (96-99)	528	22 (18-26)	533	26 (22-30)	543	19 (16-23)	138	1 (0-5)	526	9 (7-12)
SE	465	79 (75-83)	724	7 (5-9)	825	2 (1-4)	825	1 (1-2)	639	0 (0-1)	722	1 (0-2)
SI	157	99 (95-100)	157	25 (19-33)	157	26 (20-34)	157	23 (17-30)	157	0 (0-3)	157	19 (13-26)
TR	709	98 (96-99)	707	26 (22-29)	711	45 (41-49)	711	22 (19-25)	633	3 (2-5)	707	10 (8-12)
UK	264	96 (93-98)	328	7 (5-10)	298	7 (4-10)	301	6 (3-9)	242	1 (0-4)	263	5 (2-8)
Total	11,170	96	11,847	26	11,914	26	12,064	22	10,218	5	11,588	16

* Multi-resistance was defined as being resistant to fluoroquinolones, third generation cephalosporins, and aminoglycosides, irrespective of aminopenicillin susceptibility

Annex 3.6. The number of invasive *Pseudomonas aeruginosa* isolates (No), and the proportion piperacillin (+/- tazobactam), ceftazidime, carbapenems, fluoroquinolones, aminoglycosides, and multi-resistance (%R) including 95% confidence intervals (95CI) reported per country in 2008.

Country	Piperacillin +/-		Fluoroquinolones		Third gen. Cephalosporins		Aminoglycosides		Carbapenem		Multi-resistance*	
	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)	No	%R (95CI)
AT	510	8 (6-10)	477	6 (5-9)	507	11 (8-14)	506	12 (9-15)	506	8 (6-11)	509	6 (4-9)
BA	8	25 (4-64)	15	47 (22-73)	15	20 (5-49)	13	15 (3-46)	14	43 (19-70)	15	13 (2-42)
BG	23	48 (27-69)	22	55 (33-75)	23	17 (6-40)	22	36 (18-59)	23	48 (27-69)	23	43 (24-65)
CH	267	4 (2-8)	278	3 (1-6)	277	7 (4-11)	278	5 (3-8)	277	3 (1-5)	278	1 (0-3)
CY	43	23 (12-39)	43	9 (3-23)	43	19 (9-34)	42	38 (24-54)	43	21 (11-36)	43	26 (14-41)
CZ	568	27 (24-31)	568	44 (40-48)	564	29 (25-33)	568	46 (42-50)	539	45 (40-49)	568	33 (29-37)
DE	167	9 (5-15)	167	8 (4-13)	167	11 (7-17)	166	22 (16-30)	167	10 (6-15)	167	6 (3-11)
DK	349	2 (1-4)	398	3 (2-5)	340	1 (0-3)	414	3 (2-6)	420	1 (0-3)	398	1 (0-3)
EE	38	18 (8-35)	40	13 (5-28)	40	30 (17-47)	40	18 (8-33)	41	17 (8-33)	41	10 (3-24)
ES	548	8 (6-11)	546	11 (8-14)	547	13 (11-16)	547	23 (20-27)	546	18 (15-21)	548	11 (8-14)
FI	171	8 (4-13)	175	5 (2-9)	175	6 (3-11)	175	15 (11-22)	172	6 (3-11)	175	5 (3-10)
FR	1144	14 (12-16)	1134	8 (7-10)	1223	14 (12-16)	1131	22 (20-25)	1080	15 (13-17)	1138	11 (10-13)
GR	915	34 (31-37)	884	37 (34-41)	916	49 (45-52)	901	48 (45-51)	903	48 (44-51)	899	46 (43-50)
HR	220	34 (28-41)	213	13 (9-18)	220	30 (24-37)	214	33 (27-40)	215	39 (33-46)	220	28 (22-34)
HU	484	13 (10-17)	511	11 (9-15)	494	26 (22-30)	508	26 (23-30)	512	26 (22-30)	513	17 (14-21)
IE	187	5 (3-10)	187	4 (2-9)	175	6 (3-11)	189	16 (11-22)	191	6 (3-10)	189	5 (2-9)
IL	224	10 (6-15)	217	6 (3-10)	223	11 (8-16)	222	23 (18-30)	224	18 (13-24)	224	10 (6-15)
IS	7	0 (0-44)	7	0 (0-44)	7	0 (0-44)	7	0 (0-44)	7	0 (0-44)	7	0 (0-44)
IT	167	19 (14-26)	153	24 (18-32)	161	33 (26-41)	165	36 (29-44)	166	30 (23-38)	166	30 (23-37)
LT	21	14 (4-37)	21	10 (2-32)	21	24 (9-48)	20	35 (16-59)	21	38 (19-61)	21	24 (9-48)
LU	32	3 (0-18)	33	3 (0-18)	8	25 (4-64)	33	15 (6-33)	33	6 (1-22)	33	6 (1-22)
LV	7	43 (12-80)	8	50 (17-83)	7	57 (20-88)	8	38 (10-74)	7	43 (12-80)	8	38 (10-74)
MT	31	45 (28-64)	30	33 (18-53)	30	30 (15-50)	31	19 (8-38)	31	23 (10-42)	31	23 (10-42)
NL	344	6 (4-9)	345	6 (4-9)	345	6 (4-10)	345	8 (6-12)	345	4 (2-7)	345	5 (3-8)
NO	143	6 (3-12)	146	4 (2-9)	145	7 (4-13)	147	3 (1-7)	147	1 (0-4)	147	2 (1-6)
PL	22	32 (15-55)	22	27 (12-50)	22	14 (4-36)	8	13 (1-53)	22	27 (12-50)	22	23 (9-46)
PT	461	17 (14-21)	464	16 (13-20)	430	18 (14-22)	458	23 (19-27)	460	11 (8-14)	467	13 (11-17)
RO	8	25 (4-64)	8	13 (1-53)	8	13 (1-53)	8	25 (4-64)	8	38 (10-74)	8	25 (4-64)
SE	252	1 (0-4)	309	5 (3-8)	279	4 (2-7)	266	5 (3-9)	314	0 (0-2)	315	1 (0-3)
SI	95	21 (14-31)	95	14 (8-23)	95	16 (9-25)	95	24 (16-34)	93	13 (7-22)	95	17 (10-26)
TR	466	19 (16-23)	466	21 (18-25)	468	30 (26-34)	465	25 (21-29)	409	21 (17-25)	468	21 (18-25)
UK	330	2 (1-4)	283	4 (2-7)	251	6 (4-10)	314	8 (5-11)	311	3 (1-6)	307	1 (0-4)
Total	8,252	15	8,265	15	8,226	19	8,306	23	8,247	19	8,388	16

* Multi-resistance was defined as being resistant to at least three groups of piperacillin +/- tazobactam, ceftazidime, carbapenems, fluoroquinolones, or aminoglycosides.

Annex 3.7. Distribution of single penicillin, single erythromycin and dual penicillin-erythromycin non-susceptibility among the most common serogroups reported to EARSS per country in 2008. Only countries reporting more than 30 isolates were presented.

Serogroups	Austria			Belgium			Czech republic			Ireland			Iceland			Slovenia			United Kingdom						
	Number	% PNSP	% dual	Number	% PNSP	% dual	Number	% PNSP	% dual	Number	% PNSP	% dual	Number	% PNSP	% dual	Number	% PNSP	% dual	Number	% PNSP	% dual				
1	18	0	0	269	0	34	0	33	0	0	0	0	3	0	0	10	0	0	20	0	0	80	1	0	0
3	20	0	0	130	0	2	0	30	0	0	0	0	4	0	0	14	0	0	23	0	4	58	3	2	0
4	7	0	0	37	0	0	0	26	0	0	0	0	9	3	0	32	0	0	15	0	0	35	3	3	0
5	0	0	0	70	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
6	6	0	17	78	8	27	9	21	5	5	5	3	45	31	0	33	12	8	17	17	17	68	3	9	7
7	11	0	0	158	0	1	0	14	0	0	0	0	7	0	0	24	0	33	0	12	0	77	0	0	0
8	5	0	0	53	0	0	0	5	0	0	0	0	6	0	0	19	0	0	3	0	0	69	1	0	1
9	14	14	0	74	5	31	3	22	5	9	0	11	51	3	15	39	0	0	21	19	0	46	4	2	11
10	0	0	0	34	0	6	0	4	0	0	0	0	0	0	0	1	0	0	3	0	0	8	0	0	0
11	4	0	0	29	0	28	0	1	0	0	0	2	17	0	0	6	0	0	0	0	0	10	0	0	0
12	3	0	0	111	0	0	0	1	0	0	0	2	0	0	0	8	0	0	0	0	0	32	0	0	0
14	11	0	45	9	70	6	26	54	20	5	0	12	30	38	10	40	0	56	11	34	21	32	6	53	0
15	6	17	0	38	13	18	32	7	0	0	14	1	0	0	50	4	0	0	3	0	0	14	0	21	14
18	0	0	0	24	0	4	0	5	0	0	0	4	0	0	7	14	0	0	7	0	0	20	0	0	0
19	10	10	10	191	8	50	16	13	15	8	0	8	7	10	34	29	0	0	29	11	45	70	9	4	4
20	1	0	0	5	0	0	0	1	0	0	0	2	0	0	0	6	0	0	0	0	0	17	0	0	0
22	6	0	0	68	0	1	0	2	0	0	0	3	0	0	0	9	0	0	11	0	0	43	2	0	0
23	7	14	29	0	48	6	4	6	15	0	7	13	0	0	24	0	0	0	12	25	0	35	0	0	0
33	2	0	0	35	0	63	0	1	0	0	0	4	0	8	0	12	0	0	3	33	0	13	0	8	0
other	3	0	0	120	2	3	4	15	0	0	0	6	10	0	10	20	0	0	10	0	20	44	0	2	0
Total/average	134	4	8	2 1642	2	18	6	236	2	2	1	100	13	6	11	342	0	14	9	200	11	6 772	2	4	2



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