EARSS Annual Report 2003

- The European Antimicrobial Resistance Surveillance System (EARSS) is funded by DG SANCO of the European Commission and the Dutch Ministry of Health, Welfare and Sports. The project is co-ordinated by the National Institute of Public Health and the Environment (RIVM) of the Netherlands.

- 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.

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

- By December 2003, 791 microbiological laboratories serving approximately 1300 hospitals from 28 countries had provided susceptibility data for over 178,000 bacterial isolates.

- An interactive Website where regularly updated details can be found on resistance levels for important groups of antibiotics is available at http://www.earss.rivm.nl.

Period of data collection: January 1999 – December 2003

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the Dutch Ministry of Health, Welfare and Sports
for their financial support.

Contents

Why EARSS?

When in the last decades of the nineteenth century, pioneering microbiologists crushed what was known as the miasma theory (toxic vapours as the origin of epidemic diseases), one of the most revealing explanatory models in contemporary science had won the day. The imprint that the discoveries by Pasteur, Koch and others had on mankind and it's understanding was probably only equalled by Darwin's and Wallace's theory of natural selection. It was also quickly understood that combating infectious diseases could be accomplished by chemical substances targeted at the causative organisms themselves and Paul Ehrlich's dream of 'magic bullets' became a surprising reality by the successive discovery of sulpha drugs and Fleming's, Florey's and Chain's work on penicillin. An apparently endless stream of newly identified antimicrobial compounds in the three decades that followed the first successful treatment with penicillin left the impression that humanity had once and for all, established superiority over the microbial kingdom. And indeed achievements were impressive. Before the availability of antimicrobial chemotherapy over 50% of the overall burden of disease was still caused by infectious diseases in Europe and the US alike. With the advent of antibiotics and its congeners, epidemic infections seemed to melt away like ice in the sunshine. A few evolutionary biologists and social scientists remained however sceptical on the sustainability of the antimicrobial miracle. The former argued that with growing availability of antibiotic compounds, large scale emergence of resistance would only be a matter of time and the latter pointed to the fact that demographic transition as well as changes in lifestyles that shaped the societies in advanced market communities after World War II, was equally if not more important than all vaccination, disinfection and antibiotic chemotherapy in reducing infectious diseases; and that a reversal of these social improvements would rapidly translate into re-emergence of major epidemics.

Forty years on, we are confronted with a 22-year-old AIDS pandemic that has killed more people than any single epidemic in history. We see MDR-TB, multidrug-resistant malaria (*P. falciparum*), quinolone- and beta-lactam-resistant *Shigella* and *Salmonella*, community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), the first reports of glycopeptide high-level resistant hospital MRSA and next to complete antibiotic resistance in *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. At the same time the once copious supply with new or improved anti-infective compounds has worn thin, as drug developers invest in more lucrative markets. With this hindsight, it is not surprising that 21st century infectious diseases consultants and public health specialist have become more modest in their claims to combat infectious diseases, as they witness the relentless upwards move of antimicrobial resistance on the public health agenda.

EARSS has been devised as the first publicly funded monitoring tool for antimicrobial resistance in the European Region and indeed worldwide, able to provide official, validated and comparable resistance data for five major indicator bacteria. Designed as a surveillance network, it does not by itself control antimicrobial resistance but it provides the transparency and trend analysis needed for the public awareness to a problem that could reverse some of the major accomplishments in modern medicine.

The EARSS Management Team is thankful to all laboratories that continuously provide their routine susceptibility data to the EARSS network for their joint effort, which shows their commitment to contribute to the sustainability of the antimicrobial miracle.

I also wish to thank UK-NEQAS for its major role in preparing and organising the essential external quality assurance (EQA) exercises in close cooperation with the members of the EARSS EQA committee. I would like to express my gratitude to all members of the EARSS Advisory Board and the European Society for Clinical Microbiology and Infectious Diseases for sharing their expertise, for their contribution to this report and also for making the activities organised within EARSS successful during the past year. Furthermore, I would like to thank John Stelling for visiting many participating countries to give WHONET support for EARSS.

Finally, I would like to thank the funding bodies, The European Commission and the Dutch Ministry of Welfare and Sports for their support of this professional collaborative effort and the well-functioning network, which in 2004 includes almost 800 laboratories in 28 countries. I look forward to continuing this fruitful cooperation for many years to come.

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Summary

The European Antimicrobial Resistance Surveillance System (EARSS) is an international network funded by the Directorate General for Health and Consumer Protection (DG SANCO) of the European Commission and the Dutch Ministry of Health, Welfare and Sports. 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 is co-ordinated by the Dutch National Institute of Public Health and the Environment (RIVM), and since it's beginning in 1999, it has steadily drawn in new participants from all over Europe. By December 2003, 791 laboratories serving almost 1300 hospitals in 28 European countries took part in this initiative. Together, they provide health care for an estimated population of more than 100 million inhabitants. The EARSS database contains AMR data on approximately 178,000 invasive isolates of five pathogens (*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, and *Enterococcus faecium*). It is thus the most comprehensive public health effort that describes and analyses geographic and secular trends in AMR and the only publicly funded initiative of this kind worldwide. Since 2000, EARSS has been organising external quality assessment (EQA) exercises of antibiotic susceptibility testing in collaboration with UK NEQAS (United Kingdom National External Quality Assessment Scheme), Centre National de Référence des Antibiotiques (CRAB) and the members of the EQA committee. In 2003 this exercise could again demonstrated that, countries participating in EARSS are capable of delivering susceptibility data of satisfactory quality illustrating that routinely reported results as collected by EARSS have sufficient accuracy to provide good estimates of overall resistance prevalences and trends.

The high proportion of erythromycin resistance (18%) among invasive *S. pneumoniae* isolates of which (35%) was due to dual resistance with penicillin is remarkable. At the same time there are early indications that penicillin resistance in invasive *S. pneumoniae* declines in some of the countries that previously reported high rates. MRSA (methicillin-resistant *S. aureus*) rates vary largely over Europe. Trends are consistent with those reported in previous EARSS annual reports, indicating a steady rise in most countries including those with hitherto low overall resistance rates, whereas in the United Kingdom and Ireland the increase of MRSA reported during 1999-2001 seems to even out. For the majority of countries the proportion of vancomycin-resistant *E. faecium* isolates remained ≤ 5%, but 4 countries reported resistance above 15%. A widespread development of declining effectiveness of fluoroquinolones in *E. coli* at times when fluoroquinolones have become one of the most frequently prescribed antibiotic class has been recorded. This development becomes accentuated by the finding of increasing resistance against 3rd generation cephalosporins. Certainly, infections with *E. coli* are becoming increasingly difficult to treat with the spectre of serious therapeutic limitations in the future.

The EARSS 2003 annual report would not have been possible without the financial support of DG SANCO of the European Commission Agreement Number - 2003212 and the Dutch Ministry of Health, Welfare and Sports.

List of abbreviations and acronyms

AMR	Antimicrobial resistance
ARMed	Antibiotic resistance surveillance and control in the Mediterranean region
AST	Antimicrobial susceptibility testing
BSAC	British Society for Antimicrobial Chemotherapy
BSI	Blood stream infection
CA-SFM	Comité de l'Ántibiogramme de la Société Française de Microbiologie
CRAB	Centre National de Référence des Antibiotiques
CRG	Commissie Richtlijnen Gevoeligheidsbepalingen
CZECH	Czech Republic antimicrobial susceptibility guideline
CSF	Cerebrospinal fluid
DCFP	Data check and feedback program
DEFS	Data Entry & Feedback Software
DG SANCO	Directorate General for Health and Consumer Protection
DIN	Deutsche Industrie Norm
EARSS	European Antimicrobial Resistance Surveillance System
EARSS-MT	EARSS Management Team
ENSP	Erythromycin non-susceptible *Streptococcus pneumoniae*
EQA	External quality assurance
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
FIRE	Finnish study group for Antimicrobial Resistance
FREC	Fluoroquinolone-resistant *Escherichia coli*
GISA	Glycopeptide intermediate resistant *Staphylococcus aureus*
HLR	High-level resistance
ICU	Intensive care unit
MENSURA	Mesa Espanola de Normalización de la Sensibilidad y Resistencia a los Antimicrobianos
MIC	Minimal inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
NCCLS	(American) National Committee for Clinical Laboratory Standards
NWGA	Norwegian Working Group on Antibiotics
PNSP	Penicillin non-susceptible *Streptococcus pneumoniae*
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment)
SAR	Self-medication with antibiotics and resistance
SRGA	Swedish Reference Group for Antibiotics
UK-NEQAS	United Kingdom National External Quality Assessment Scheme for Microbiology
VRE	Vancomycin-resistant enterococci
WHO	World Health Organization
WHONET	WHO microbiology laboratory database software

The EARSS Network in 2003

Countries participating in EARSS in 2003

Austria	AT	Israel	IL
Belgium	BE	Italy	IT
Bulgaria	BG	Luxembourg	LU
Croatia	HR	Malta	MT
Czech Republic	CZ	Netherlands	NL
Denmark	DK	Norway	NO
Estonia	EE	Poland	PL
Finland	FI	Portugal	PT
France	FR	Romania	RO
Germany	DE	Slovakia	SK
Greece	GR	Slovenia	SI
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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. In subsistence economies such as developing countries, resistance frequently occurs in microorganisms that are very likely to cause disease even when healthy individuals become infected (so called obligate pathogens, such as the causative agents of dysentery, typhoid fever, tuberculosis and malaria). As a result of antimicrobial resistance, patients infected with such organisms do not improve in response to conventional chemotherapy and are left with an equivocal prognosis unless alternative treatment options are available. Conversely, in more advanced market communities, antibiotic resistance has until now remained mainly confined to opportunistic pathogens with moderate to low disease causing potential. These organisms are usually part of the normal bacterial flora of humans and only cause disease when introduced into body sites that are normally free from bacterial colonisation e.g. when anatomical barriers are breached due to trauma or medical/surgical interventions or in patients with immature or defective immune systems. For this reason, problems with resistant organism in Europe, the US, Australia, the Middle East, North Africa, South America, China and Japan are mainly seen in infants or in elderly, frail patients or those with complicating underlying illness and the highest proportions of resistant bacteria are encountered in hospitals. Predicting the future of antimicrobial resistance in these countries is difficult. In the best-case, increasing antimicrobial resistance will limit the ability of modern medicine to deliver complicated or live saving interventions such as advanced surgery, organ transplantation, intensive care and cancer therapy. In its worst outlook, pathogens with higher virulence may become resistant or resistant pathogens may develop higher virulence, posing a real threat to the healthy non-hospitalised segments of the population. On numerous scientific meetings these consequences have been addressed and it has become clear that monitoring trends in antimicrobial resistance is needed to identify the health threats imposed by antimicrobial resistance.

During 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 and the Dutch Ministry of Health, Welfare and Sports. 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, is was made clear that linking antimicrobial resistance with microbial ecology and improving the knowledge about it’s costs to European societies is essential for the development of effective control strategies [3].

EARSS is co-ordinated by the Dutch National Institute of Public Health and the Environment (RIVM), and since it’s beginning in 1999, it has steadily drawn in new participants from the European countries. At present, 791 laboratories serving approximately 1300 hospitals in 28

European countries participate. Thus EARSS receives data from of an estimated population of 100 million inhabitants served by the participating hospitals. The EARSS database contains AMR data on approximately 180 000 invasive isolates of five species of indicator bacteria (*Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium*, and *Escherichia coli*). It is thus the most comprehensive public health effort that describes and analyses geographic and secular trends in AMR worldwide.

EARSS has encouraged and helped sustain national surveillance efforts and the network is the perfect basis for an integrated public health approach for AMR containment in Europe. To this end, EARSS operates in close collaboration with other EU-financed projects: European Surveillance of Antimicrobial Consumption (ESAC), Self-medication with Antibiotics and Resistance (SAR) and Antibiotic Resistance Surveillance and Control in the Mediterranean region (ARMed). 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 2003. Chapter 2 summarises the objectives and operational strategy. Chapter 3 presents the results of the annual external quality assurance (EQA) exercise for the year 2003. Chapter 4 provides a descriptive analysis of the situation of AMR in the European region. Chapter 5 summarises the overall conclusions based on these results. The appendixes contain detailed country summary sheets (appendix A) and a technical section (appendix B). Results are based on data recorded from January 1999 - December 2003, if not otherwise indicated.

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Chapter 2. The EARSS objectives and operational strategy

Objectives

It is the public health purpose of EARSS to assist in the control of AMR; therefore, the following objectives have been defined:

- To collect comparable and validated AMR data
- To analyse trends in time and place (among various European countries)
- To provide official national AMR data that constitute a basis for policy decisions
- To provide feedback to 'those who need to know'
- To provide information about clinically and epidemiologically relevant AMR and to evaluate interventions.

Furthermore, EARSS aims are:

- To encourage the implementation, maintenance and improvement of national AMR surveillance programmes to provide timely information for national policy decisions
- To link AMR data to factors influencing the emergence and spread of AMR, particularly to antibiotic use data, in close cooperation with the European Surveillance of Antimicrobial Consumption (ESAC)
- To initiate, foster and complement scientific research in Europe in the field of AMR.

At the start of the project, EARSS identified two bacterial species (*S. aureus* and *S. pneumoniae*) for which routinely generated antimicrobial susceptibility test (AST) results were collected. The pathogens that subsequently became objects of surveillance were selected according to epidemiological (community versus hospital acquisition) and ecological (transmission versus selection) paradigms. At the same time, the occurrence of clinically and epidemiologically meaningful antibiotic resistance traits was determined for international comparison. The decision to collect routine data meant that no changes to the regular diagnostic process were needed. Therefore, the participation of many laboratories has become feasible, and this has facilitated the probing of a substantial part of the population in the participating countries. Sampling of the pathogens was and is restricted to invasive (blood culture and CSF) isolates, which are routinely tested for antimicrobial susceptibility in most laboratories. Data collection started in 1999 for *S. pneumoniae* and *S. aureus* after a preparatory phase in 1998. In 2001, the surveillance was extended to *E. coli* and enterococci (*E. faecalis* and *E. faecium*).

Operational strategy

Organisation of the EARSS network

Each participating country has appointed one or two national representatives. They are medical microbiologists and/or infectious diseases epidemiologists. Moreover, each country has a national data manager. The main task of the national representatives is to coordinate the EARSS-specific activities of the participating laboratories (data collection, reporting, questionnaire completion and EQA strain and results distribution) and to communicate with the EARSS central database, which is maintained and updated by the EARSS Management Team (EARSS-MT). The national representatives also ensure that the laboratories generate their AST data according to the EARSS

protocols, as published in the EARSS manual 2004 (downloadable in pdf format from the official EARSS website at www.earss.rivm.nl).

The main task of the national data manager is to collect, approve and forward resistance data each quarter 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) and WHO microbiology laboratory database software (WHONET). To assess the quality and comparability of AST data, an EQA exercise is carried out every year in collaboration with the UK-NEQAS, the Centre National de Référence des Antibiotiques (CRAB), and members of the EARSS-EQA committee (for more details, see Chapter 3). EARSS also contributes to the global strategy established by the World Health Organization (WHO) for worldwide surveillance of drug resistance (Figure 2.1).

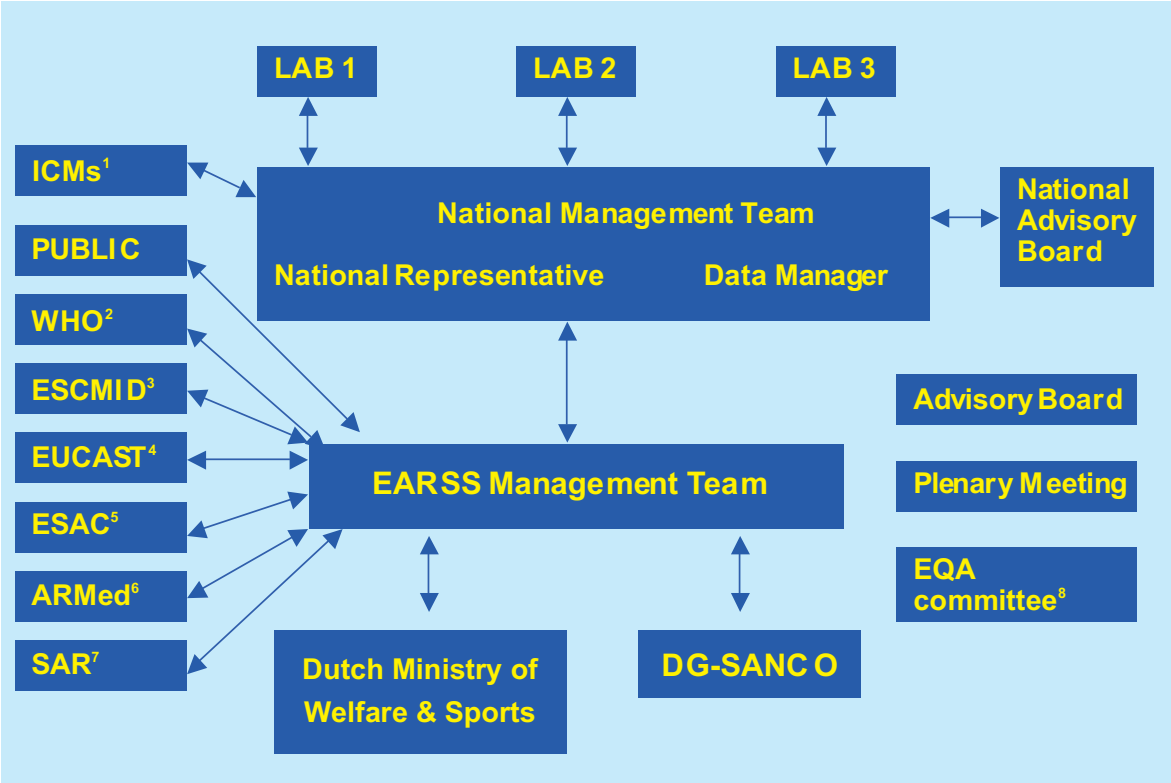

Figure 2.1 Structure of the EARSS network

[1] Intersectoral co-ordinating mechanisms, [2] World Health Organisation, [3] European Society for Clinical Microbiology and Infectious Diseases, [4] European Committee on Antimicrobial Susceptibility Testing, [5] European Surveillance of Antimicrobial Consumption, [6] Antibiotic Resistance Surveillance & Control in the Mediterranean countries, [7] Self-medication of antimicrobial and resistance levels in Europe, [8] Committee on External Quality Assurance.

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 represented in an optimal manner.

Collecting and processing antimicrobial susceptibility test (AST) results

EARSS routinely collects susceptibility test results of invasive isolates and background information about patients. Laboratories are asked only to report the first isolate from blood or cerebrospinal fluid (CSF) per patient per reporting quarter. For optimal data collection EARSS requires specific information on the bacterial isolate, host, institution and laboratory that submits the results according to the specifications of the EARSS exchange format (EARSS manual 2004). AST results are generated and reported as specified by standard EARSS protocols. Furthermore, optional data are collected; they include clinical diagnosis, other conditions, and facultative susceptibility data for additional antibiotics. The EARSS manual 2004 can be downloaded in pdf format from the official EARSS website at www.earss.rivm.nl.

Laboratories

Participating laboratories can opt for one of two ways of submitting data: electronically or by sending in conventional isolate record forms (on paper). EARSS provides various free software tools for electronic data handling, downloadable from the Website at www.earss.rivm.nl:
(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 them 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 (Each guideline is subject to revision by national guideline committees, see Chapter 3).

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.
- 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 2004).
- Revising data with the Data Check and Feedback Programme (DCFP).
- Approval of data by the national representative (adherence to EARSS protocol, check for microbiological consistency, and check whether the S, I and R interpretations agree with the minimal inhibitory concentrations (MICs) reported.
- 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
- Compiling of a feedback report summarizing the results
- After approval by National Representative: data are added to the database, and the results are made public on the EARSS website at www.earss.rivm.nl

Feedback from EARSS-MT

Accurate and timely feedback is important for surveillance systems. 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 (MRSA, PNSP, VRE, GISA and ESBLs). Subsequently, the national co-ordinator 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.earss.rivm.nl, where they can be displayed in various downloadable formats, such as tables, figures, and maps.

Furthermore, 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.

Chapter 3. Quality and comparability of antimicrobial susceptibility test results: The EARSS external quality assurance exercise 2003

Introduction

Methods of antimicrobial susceptibility testing (AST) and differences in national guidelines between European laboratories may affect the comparability of interpretative results based on clinical breakpoints in various ways. In order to validate the usefulness and comparability of highly aggregated data it is therefore indispensable that laboratories participate in EQA schemes. Since 2000, EARSS has been organising external quality assessment (EQA) exercises of antibiotic susceptibility testing in collaboration with UK NEQAS (United Kingdom National External Quality Assessment Scheme), Centre National de Référence des Antibiotiques (CRAB), under the professional guidance of the members of the EQA committee. The rationale of these EQA exercises is, i) to assess the ability of participating laboratories to identify AMR 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 AST data across Europe.

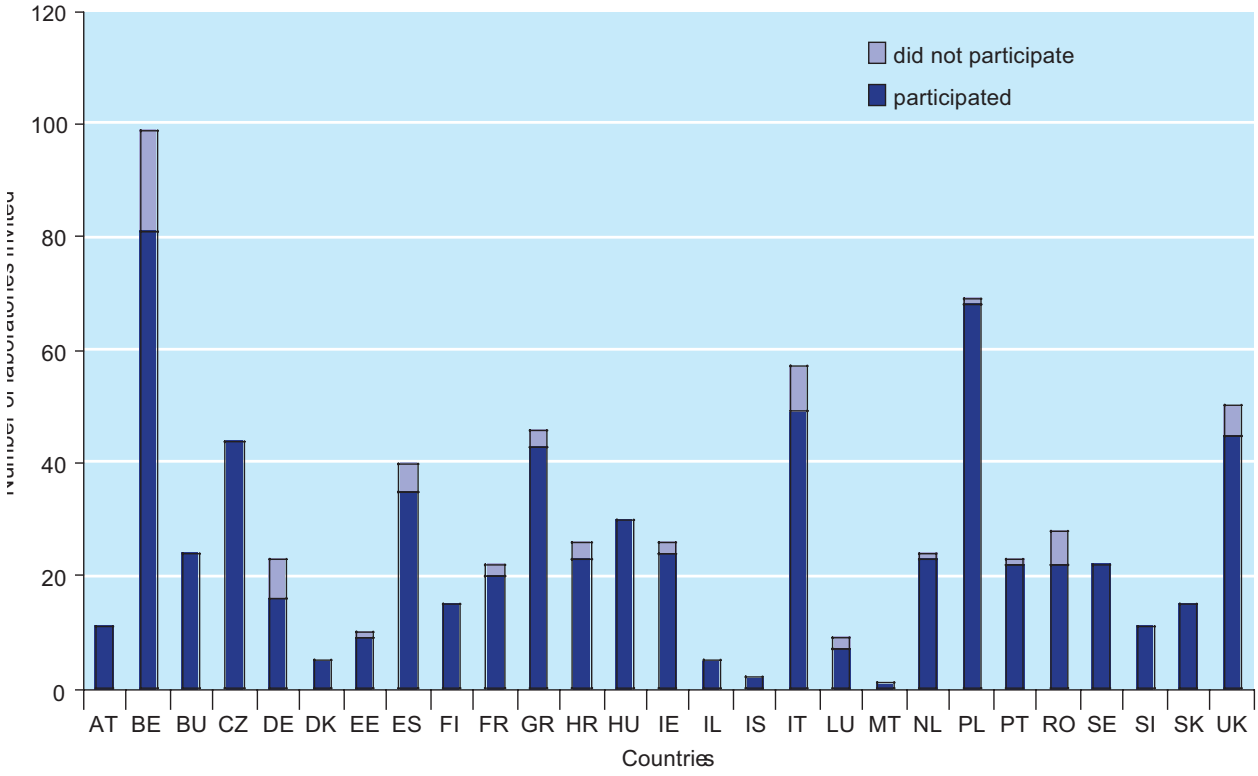

Figure 3.1 Participation in the 2003 external quality assurance (EQA) exercise.

Methods

In September 2003, UK-NEQAS distributed a set of six strains to the laboratories participating in EARSS that were provided by the 'French Reference Centre for Antibiotics-Institut Pasteur' and the Canisius Wilhelmina Hospital, Nijmegen, The Netherlands (Table 3.1). The strains were characterised and tested by the two reference laboratories in France and The Netherlands and additionally by two laboratories in the United Kingdom appointed by UK-NEQAS. Each reference laboratory identified the minimal inhibitory concentrations and provided results according to breakpoints recommended by different national guidelines such as: CA-SFM, CRG/NCCLS, and BSAC (see list of abbreviations and acronyms on page 8). The reference laboratories agreed on a reference interpretation as an acceptable test result of each compound-pathogen combination (Table 3.1). The strains were distributed by UK-NEQAS to 737 laboratories participating in EARSS, and the laboratories were asked to report species identification, methods and guidelines used, and clinical susceptibility results (S, I, R) according to their routine laboratory procedures. Results were considered 'concordant' if the susceptibility results agreed with the designated reference interpretation.

Results and Discussion

In Figure 3.1 the number of participating laboratories returning reports specified per country is shown. As in the previous years, the overall response rate was extremely satisfactory (91%). The adherence to guidelines, by number of laboratories per country is shown in Table 3.2. The majority (72%) of laboratories used NCCLS guidelines. Most laboratories used E-test for the determination of MICs (86%). Of the laboratories that used automated laboratory systems (n = 197), VITEK systems were most frequently utilised (59%).

Table 3.1 Reference laboratory results: MICs, susceptibility as determined by the reference laboratories (reference interpretation), and overall concordance

	Reference laboratory range (MICs in mg/L)	Reference interpretation	Overall concordance (%)
Specimen U2A 166 *S. aureus*			
Species identification			99
Oxacillin	0.25 - 0.5	S	99
Gentamicin	≤ 0.5	S	99
Erythromycin	0.25 - 0.5	S	98
Tetracycline	0.25 - 0.5	S	99
Rifampicin	< 0.016	S	99
Vancomycin	1 - 2	S	100
Teicoplanin	0.25 - 1	S	100
Penicillin	0.016 - 0.064	S	96
Ciprofloxacin	1	S	85
Cefoxitin	1 - 2	S	99
Specimen U2A 1786 *S. aureus* (*mecA* positive)			
Species identification			100
Oxacillin	2 - 4	R	81
Gentamicin	0.12 -0.5	S	98
Erythromycin	> 128	R	99
Tetracycline	0.25 - 1	S	99
Rifampicin	≤ 0.016	S	100
Vancomycin	1 - 2	S	99
Teicoplanin	0.25 - 2	S	99
Penicillin	8 - 64	R	98
Ciprofloxacin	≥ 16	R	94
Cefoxitin	4 - 16	R	78
Specimen U2A 961 *S. pneumoniae*			
Species identification			98
Oxacillin	0.064	S	97
Penicillin-G	≤ 0.016	S	98
Ceftriaxone	0.016	S	98
Cefotaxime	0.016	S	99
Ciprofloxacin	1	S/I*	84
Erythromycin	8 - 16	R	96
Clindamycin	0.125 - 0.5	S	95

Table continues on next page

	Reference laboratory range (MICs in mg/L)	Reference interpretation	Overall concordance (%)
Specimen U2A 1787 *S. pneumoniae*			
Species identificatio			99
Oxacillin	2	I/R*	86
Penicillin-G	0.25	I	77
Ceftriaxone	0.064 - 0.125	S	98
Cefotaxime	0.016 - 0.064	S	96
Ciprofloxacin	0.5 - 1	S/I*	88
Erythromycin	0.064 - 0.125	S	98
Clindamycin	0.125 - 0.5	S	99
Specimen U2A 1789 *E. coli*			
Species identification			99
Ampicillin	> 256	R	97
Gentamicin	1	S	99
Tobramycin	16	R	80
Ciprofloxacin	0.008-0.016	S	99
Cefotaxime	≥16	I/R*	91
Ceftriaxone	≥16	I/R*	90
Ceftazidime	>256	R	91
Piperacillin	>256	R	93
Piperacillin/Tazobactam	2	S	76
ESBL		positive	94
Specimen U2A 604 *E. gallinarum* (*vanC* positive)			
Species identification			51
Amoxicillin	NT	S	97
Ampicillin	0.5-2	S	99
Vancomycin	16	I/R*	58
Gentamicin	8	Non-HLR**	97
Teicoplanin	0.5-1	S	98

* Depending on the guideline used

** Investigated for high-level resistance to aminoglycosides.

Table 3.2 Guidelines used by laboratories

	Guideline*												
Country	**BSAC**	**CA-SFM**	**CRG**	**CZECH**	**DIN**	**FIRE**	**MENSURA**	**NCCLS**	**SRGA**	**> 1**	**Other****	**Missing**	**Total**
AT								11					11
BE		1						72		4	3	19	99
BU								21				3	24
CZ		1		8				5		28		2	44
DE					8			4		3	1	7	23
DK									3		2		5
EE								9				1	10
ES							2	29		2		7	40
FI						2		9		4			15
FR		20										2	22
GR							1	40				5	46
HR								23				3	26
HU								29				1	30
IE	2							14			7	3	26
IL								5					5
IS								2					2
IT								48		1	8		57
LU								6		1	2		9
MT								1					1
NL			5					14		3	2		24
PL								52		6	1	10	69
PT								18		2		3	23
RO		1						17		1	2	7	28
SE									22				22
SI								11					11
SK								11				4	15
UK	22							9		2	11	6	50
Total	**25**	**22**	**5**	**8**	**8**	**2**	**3**	**460**	**25**	**57**	**27**	**95**	**737**

* For explanation of acronyms, see page 8

** Including Stokes method

For the *S. aureus* strain U2A166, the overall concordance was > 95% for all antibiotic compounds tested, except for ciprofloxacin (85%, Table 3.1). The *S. aureus* strain U2A1786 was *mecA* positive and heterogeneously expressing this resistance determinant. This MRSA strain (sequence type 45 or Berlin strain) has caused hospital outbreaks in The Netherlands and Germany due to this 'stealth' resistance behaviour. Only 81% of the laboratories identified the oxacillin-resistance of this MRSA strain correctly. Another rare feature of this strain was the low specificity of the cefoxitin test, otherwise known to be a good screening test for MRSA [1]. These results underline the importance of a high degree of suspicion where quinolone-resistance and/or erythromycin resistance is identified in what *prima vista* appears to be a MSSA isolate. Strains of this nature are difficult to

detect, which partly explains their success as epidemic clones in hospitals. The concordance for gentamicin, vancomycin, teicoplanin, penicillin and ciprofloxacin was ≥ 94% (Table 3.1).

S. pneumoniae strain U2A961 was characterised by an erythromycin efflux mechanism. This trait was correctly detected by 94% of laboratories (Table 3.1). *S. pneumoniae* strain U2A1787 was intermediately resistant to penicillin, which was correctly detected by only 77% of the laboratories (Table 3.1). Instead of identifying penicillin intermediate susceptibility correctly, 12% of the laboratories called this strain penicillin-resistant. This feature may lead to an overprescription of alternative antibiotics, such as macrolides and may lead to a further increase in resistance to this antibiotic class as currently observed in many European countries. The ESBL expressed by the *E. coli* strain U2A1789 was correctly identified by 94% of the laboratories (Table 3.1). However, 10% of the laboratories failed to detect cefotaxime/ceftriaxone resistance associated with ESBL-production. This type of ESBL (SHV-5) has become very prevalent in Europe in the past 15 years and is mostly encountered in *Klebsiella pneumoniae*, rendering host cells highly resistant to ceftazidime. Rather unexpectedly, 20% of the laboratories also missed the tobramycin resistance in the same *E. coli* strain.

Specimen U2A604 was an *Enterococcus gallinarum* with a *vanC* resistance. The identification of enterococci by automated systems is notoriously unreliable, as pigment production and motility are not identified by these instruments. Sadly, only 51% of the laboratories were able to identify the species correctly. Most laboratories (90%) identified reduced susceptibility to vancomycin (I = 58%/ R = 32%) and susceptibility to teicoplanin, which is typical for *vanC* resistance (Table 3.1).

Conclusions

The fourth EARSS external quality assessment showed that laboratories participating in EARSS are in general capable of delivering susceptibility data of good quality. However, 19% of laboratories failed to detect an epidemic MRSA known to cause outbreaks in hospitals. The strain is difficult to detect due to the fact that the resistance phenotype is heterogeneously expressed. However, laboratories should take this opportunity to re-evaluate the methodology used for the detection of MRSA.

Twenty-three per cent of laboratories failed to correctly categorize penicillin non-susceptibility in *S. pneumoniae*. In the *E. coli* strain 20% missed overt tobramycin resistance and although 94% identified the ESBL phenotype, 10% missed the cefotaxime/ceftriaxone resistance. The results show that there is room for re-evaluation, calibration and improvement of methodology. At the same time they illustrate that routinely reported results as collected by EARSS in most instances have sufficient accuracy to provide good estimates of overall resistance prevalences and trends.

References

1 Skov, R., Smyth, R., Clausen, M. *et a*l. (2003). Evaluation of a cefoxitin 30 µg disc on Iso-Sensitest agar for detection of methicillin-resistant *Staphylococcus aureus*, Journal of *Antimicrobial Chemotherapy* 52, 204-207

Chapter 4. The antimicrobial resistance situation in Europe in 2003

Introduction

European countries are characterised by a high degree of diversity, be it cultural, economic, or social. The heterogeneity of values and administrative strategies is reflected by different health care seeking behaviour and fundamentally different health care systems; all of which influence the emergence, dissemination, and introduction of infectious diseases caused by antibiotic-resistant organisms in a complex manner.

During the past five years (1999-2003), EARSS has collected antimicrobial susceptibility test (AST) results of invasive isolates of five bacterial species that serve as indicators for the development of AMR in Europe. The species included are *S. pneumoniae*, *S. aureus*, *E. coli*, *E. faecalis*, and *E. faecium*. At the end of 2003, the EARSS database contained information on 178,040 isolates from 791 laboratories serving 1300 hospitals in 28 countries. This chapter will discuss the current dimension and pertinent trends of antimicrobial resistance that became visible by the end of 2003. We also report the demographic characteristics of patients for whom antibiotic-resistant indicator organisms were reported to EARSS.

Methods

In table 4.1 clinically and epidemiologically relevant antibiotic compound-pathogen combinations required for EARSS reporting are listed. For all five pathogens, laboratories determined and interpreted their susceptibility results according to national or international guidelines as S (sensitive), I (intermediately resistant), and R (resistant), using routine procedures. AST breakpoints from the different guidelines used by participating laboratories can be found on the EARSS website at www.earss.rivm.nl.

Table 4.1. Pathogens and antibiotic compounds

Pathogen	**Antimicrobial susceptibility**
*S. pneumonia*e	Penicillin non-susceptibility, defined as Pen I or Pen R
	Erythromycin resistance
S. aureus	Methicillin resistance
E. faecalis/ E. faecium	Vancomycin non-susceptibility
	Aminoglycoside high-level resistance (HLR)
E. coli	Ampicillin resistance
	3rd generation cephalosporin (cefotaxime, ceftriaxone and ceftazidime) resistance
	Fluoroquinolone (ofloxacin or ciprofloxacin) resistance
	Aminoglycoside (gentamicin or tobramycin) resistance

Data analysis of AST results reported and approved by the National Representatives and Data Managers was carried out using SAS software (SAS Institute Inc, Cary, NC, USA, release 8.02).

The countries represented in the maps had to report at least 10 isolates of a specific pathogen in 2003. For trend analysis a Cochran-Armitage trend test was used, considering only the laboratories that permanently provided data from 2000 through 2003 for *S. aureus* and *S. pneumoniae* and from 2001 through 2003 for *E. coli*, *E. faecalis* and *E. faecium*. In addition, at least 20 isolates per year had to be reported per country to be included into the analysis for trend.

Results and discussion

Streptococcus pneumoniae

Streptococcus pneumoniae is the single most important cause of community-acquired pneumonia and acute otitis media and is one of the most important pathogens leading to bloodstream infections and meningitis in children and adults. Increasing prevalence of resistant strains in the past 15 years is now threatening the successful treatment of these infections [1, 2]. Country-specific resistance proportions were shown to be associated with antibiotic prescription habits [3], which emphasises the importance of judicious antibiotic use and the possible need for alternative control strategies such as vaccination.

Penicillin non-susceptibility

Between 1999-2003, 653 laboratories from 26 countries reported susceptibility results for 30,374 invasive *S. pneumoniae* isolates to EARSS, of which 93% were recovered from blood cultures.

The average proportion of penicillin non-susceptibility was 10% for all isolates reported in 2003. In Figure 4.1 the proportions for penicillin non-susceptible *S. pneumoniae* (PNSP) in 2003 by country are illustrated in a map format with different colours indicating various levels of resistance. The highest proportions of penicillin non-susceptibility were observed in the Mediterranean countries (Figure 4.1). Most of the penicillin non-susceptible invasive *S. pneumonia*e isolates (79%) showed intermediate resistance to penicillin. Infections caused by these strains can still be treated with appropriately dosed beta-lactams. The ratio between penicillin intermediate (I) and full resistance (R) differed largely between countries. Countries that reported the highest proportions of full resistance were Romania (19%), Poland (19%), Bulgaria (11%), and Spain (10%, Figure 4.2).

From 2000 to 2003, an increase of penicillin non-susceptibility was observed in Sweden (from 2% to 5%) and in Austria (from 2% to 11%). Austria reported low numbers of isolates each year (when considering only the laboratories that permanently provided data from 2000 through 2003 for trend analysis). This limitation in sample size warrants caution when interpreting the results for the whole country. A decrease in the proportion of fully penicillin-resistant isolates from 2000 to 2003 was observed in Belgium (from 5% to 1%), Ireland (from 4% to 2%), Spain (from 11% to 8%), and the UK (from 5% to 3%).

Even though this decreasing trend was only significant for Belgium, it is unlikely that this simultaneous development has happened by chance alone.

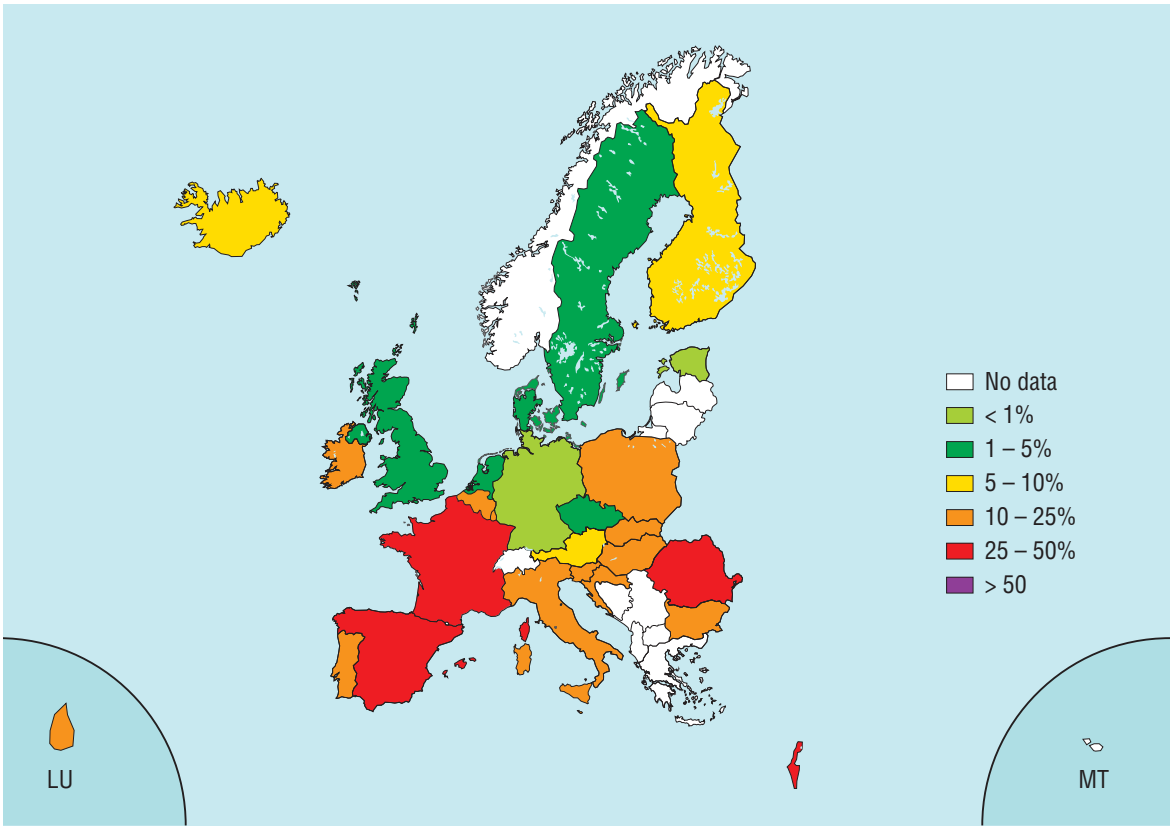

Figure 4.1 *Streptococcus pneumoniae*: invasive isolates non-susceptible to penicillin (PNSP) in 2003.

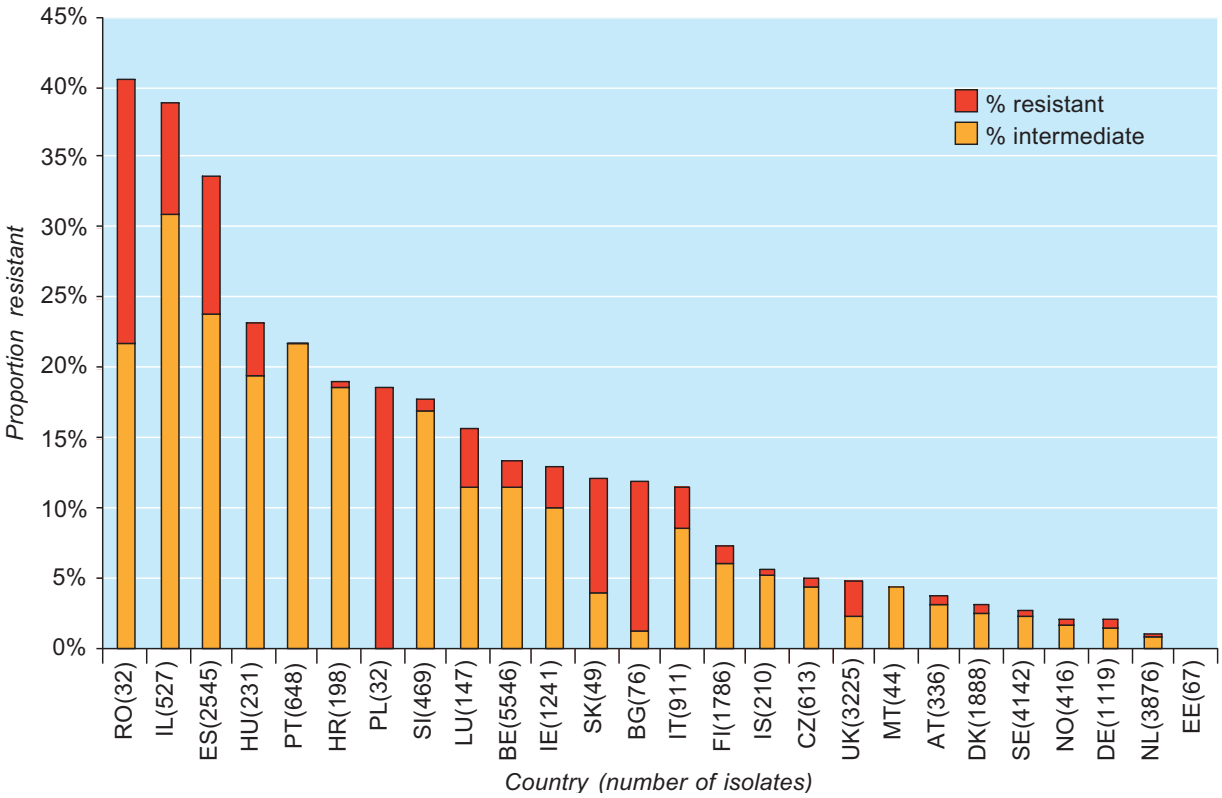

Figure 4.2 *Streptococcus pneumoniae*: invasive isolates with intermediate and full resistance to penicillin reported for the entire EARSS observation period (all isolates with reported penicillin susceptibility were included).

Erythromycin resistance

AST results for erythromycin were reported for 24,980 of the isolates (82%).

Erythromycin resistance is more frequent (18%) than penicillin non-susceptibility (10%) and follows the same geographical pattern in Europe (Figure 4.3). Significant changes were remarkable for Finland, which showed an increase in erythromycin resistance from 9% to 18%. This trend is known and was already reported in 2002 by the Finnish surveillance system FINRES [4] but remained unabated in 2003. Austria also witnessed a similar trend from 4% to 16% which tallies with the increase penicillin-non-susceptibility in laboratories that reported for the entire observation period to EARSS. The predominance of erythromycin resistance in most European countries indicates that either selective constraints due to the amount of macrolide consumption favours the emergence and spread of this phenotype or the fact that acquisition of macrolide resistance determinants are less costly to the ecological fitness than target modification of penicillin binding protein that result from DNA recombination events.

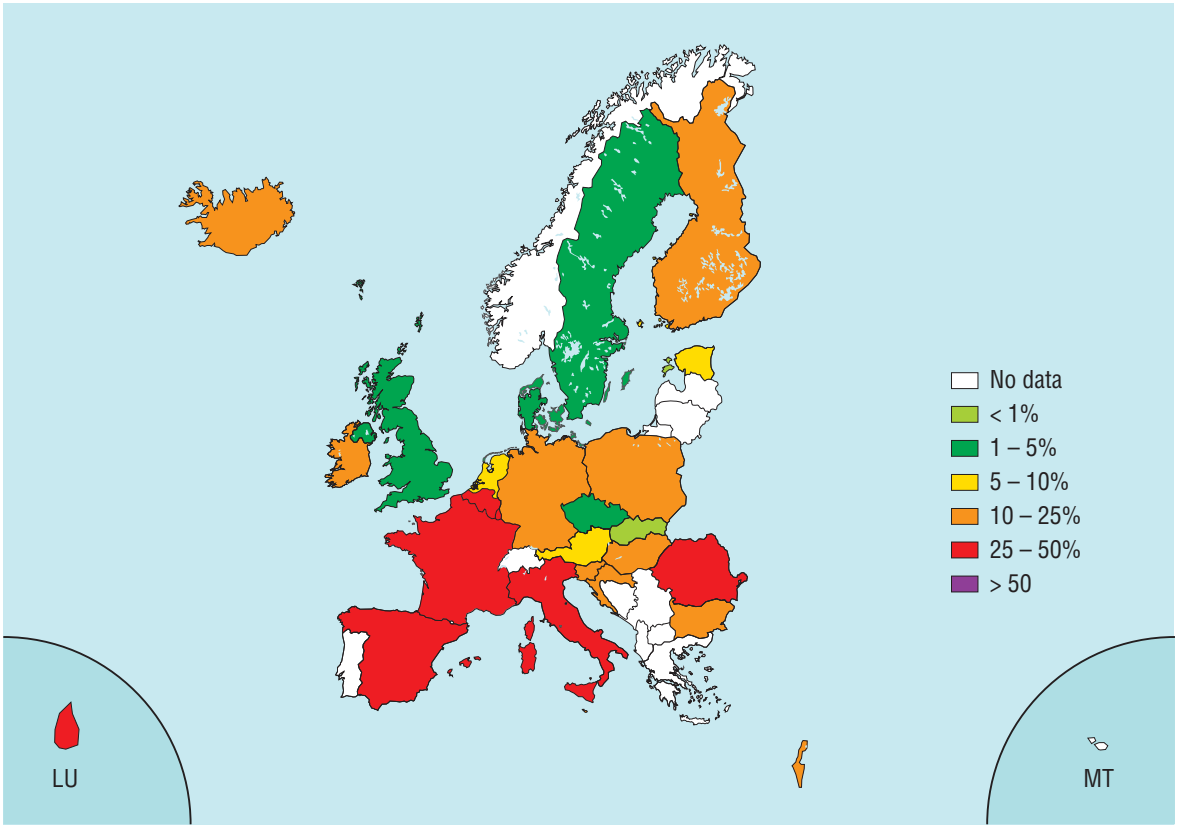

Figure 4.3 *Streptococcus pneumoniae*: invasive isolates resistant to erythromycin (ENSP) in 2003.

Single and dual resistance to penicillin and erythromycin

In 2003, the proportion of single non-susceptibility to penicillin among isolates collected from all participating laboratories in Europe was 5%, whereas erythromycin single resistance was 12%. Dual resistance to both erythromycin and penicillin (I+R) was 6%. Figure 4.4 shows the proportion of penicillin and/or erythromycin resistance by country for the aggregated 1999-2003 data set. The highest proportions of dual resistance were found in Spain (18%; CI_{95} 17-20%), Luxembourg (12%; CI_{95} 7-18%), Hungary (12%; CI_{95} 8-17%), Israel (11%; CI_{95} 8-14%), and Belgium (10%; CI_{95} 9-11%). High proportions were also found in Romania (16%; CI_{95} 5-36%) and Poland (18%; CI_{95} 6-

37%), but the low numbers of isolates resulted in wide confidence intervals and render conclusions difficult (Figure 4.4).

On the basis of the recorded resistance developments (until 2002), EARSS used a nominal regression model to extrapolate the pertinent trends and concluded that single non-susceptibility to penicillin will further decrease, while erythromycin resistance and dual resistance will increase if the ecological forces that shape the current population structure will remain unchanged [5].

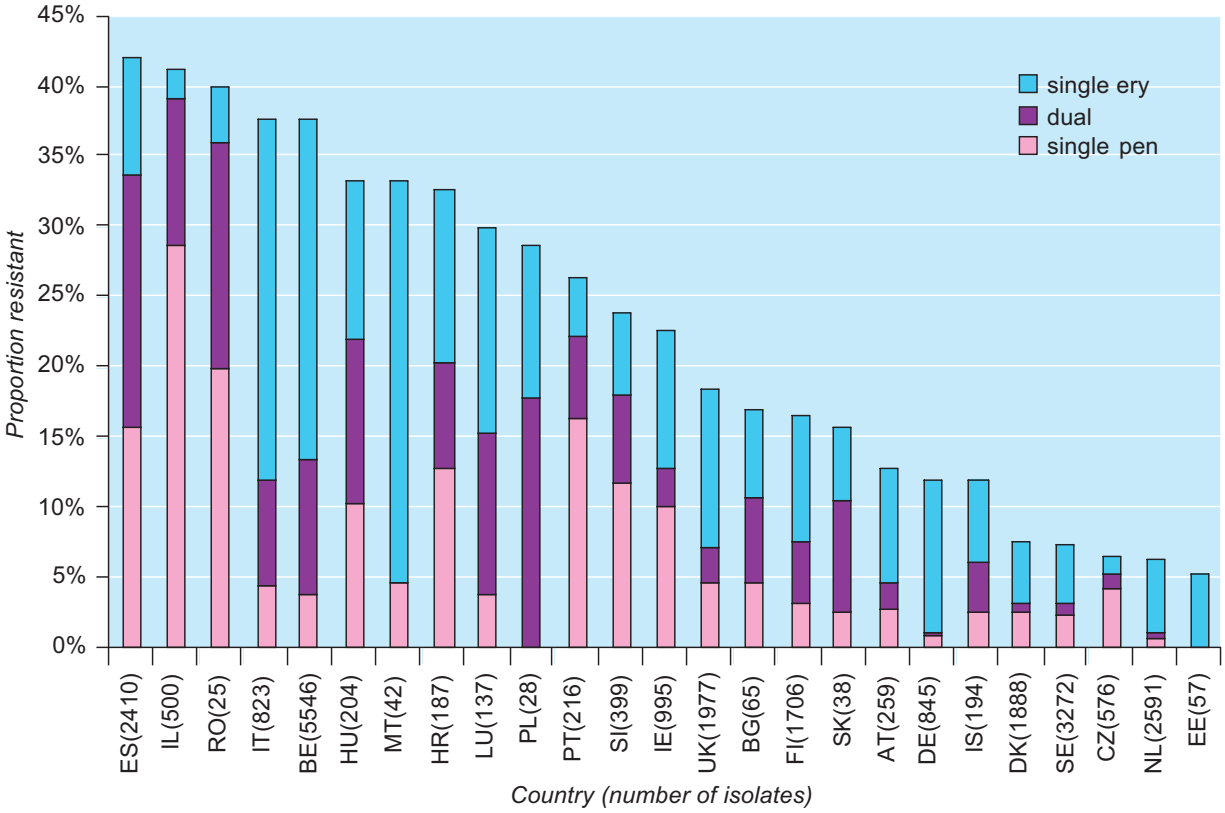

Figure 4.4 *Streptococcus pneumoniae*: invasive isolates with dual resistance to penicillin and erythromycin and single resistance to erythromycin and penicillin reported for the entire EARSS observation period (penicillin-resistant isolates include both intermediate and fully resistant isolates).

Demographic characteristics

Similar proportions of single and dual resistance were observed between male and female patients for identical age groups. The highest proportions of single resistance (both substances) and dual resistance to penicillin (I+R) and erythromycin has been recorded for the age group less than five years of age (Figure 4.5). It is known that the paediatric age group is most vulnerable to pneumococcal infections [2, 6, 7], which is substantiated by the highest relative number of *S. pneumoniae* isolates reported to EARSS in the under five-years-olds. It appears that this age group represents the reservoir for antibiotic-resistant pneumococci, and thus extra benefit might be expected, if it could be shown that protein conjugate vaccine is able to reduce carriage in young children.

Figures 4.6 A and B show the relative proportions of single and dual resistance by age group and country. The illustration also shows that the highest percentage of erythromycin resistance (both single erythromycin and dual resistance) was consistently reported for the youngest age groups by most of the countries. This may be a consequence of common prescribing of oral paediatric erythromycin formulation.

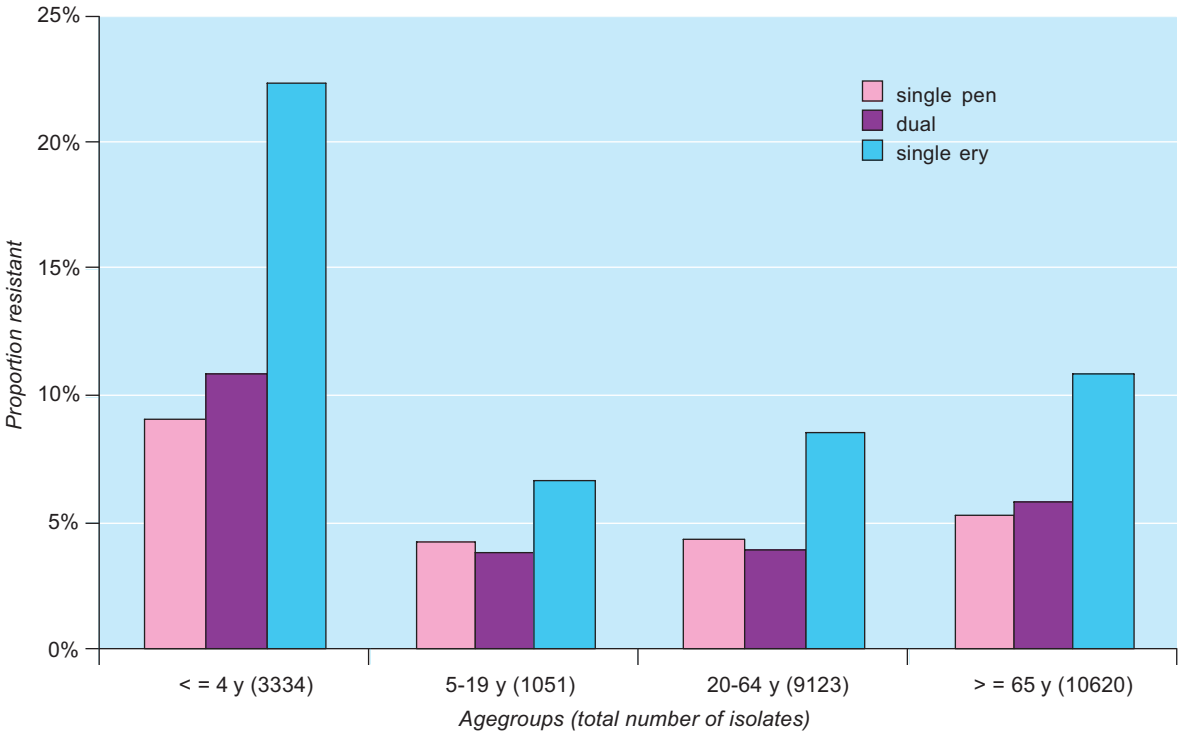

Figure 4.5 *Streptococcus pneumoniae*: Proportion single and dual resistance to penicillin (I+R) and erythromycin by age groups for the period 1999-2003.

Conclusions

Non-susceptibility to penicillins, with or without concomitant resistance to erythromycin, is still high in many European countries. In Germany, Czech Republic, Estonia, the UK, the Netherlands and most Scandinavian countries it is below 5% and for some hitherto unexplained reason the rates in full penicillin resistance have been declining for several countries. However, the high overall erythromycin resistance, 18%, is remarkable (single erythromycin resistance 12% and dual penicillin and erythromycin resistance 6%). The marked differences in the distribution of single and dual penicillin and macrolide resistance between countries is noteworthy, but not yet understood.

Conservative use of macrolides is especially important in situations where penicillin and erythromycin resistance is common and appropriately dosed beta-lactams should remain the preferred empirical treatment. Vaccination, especially of young children may affect antibiotic resistance in pneumococcal disease in Europe. Whether vaccine use will slow the expansion of resistant pneumococci, or whether resistant strains not included in the vaccine will replace vaccine serotypes, remains to be explored.

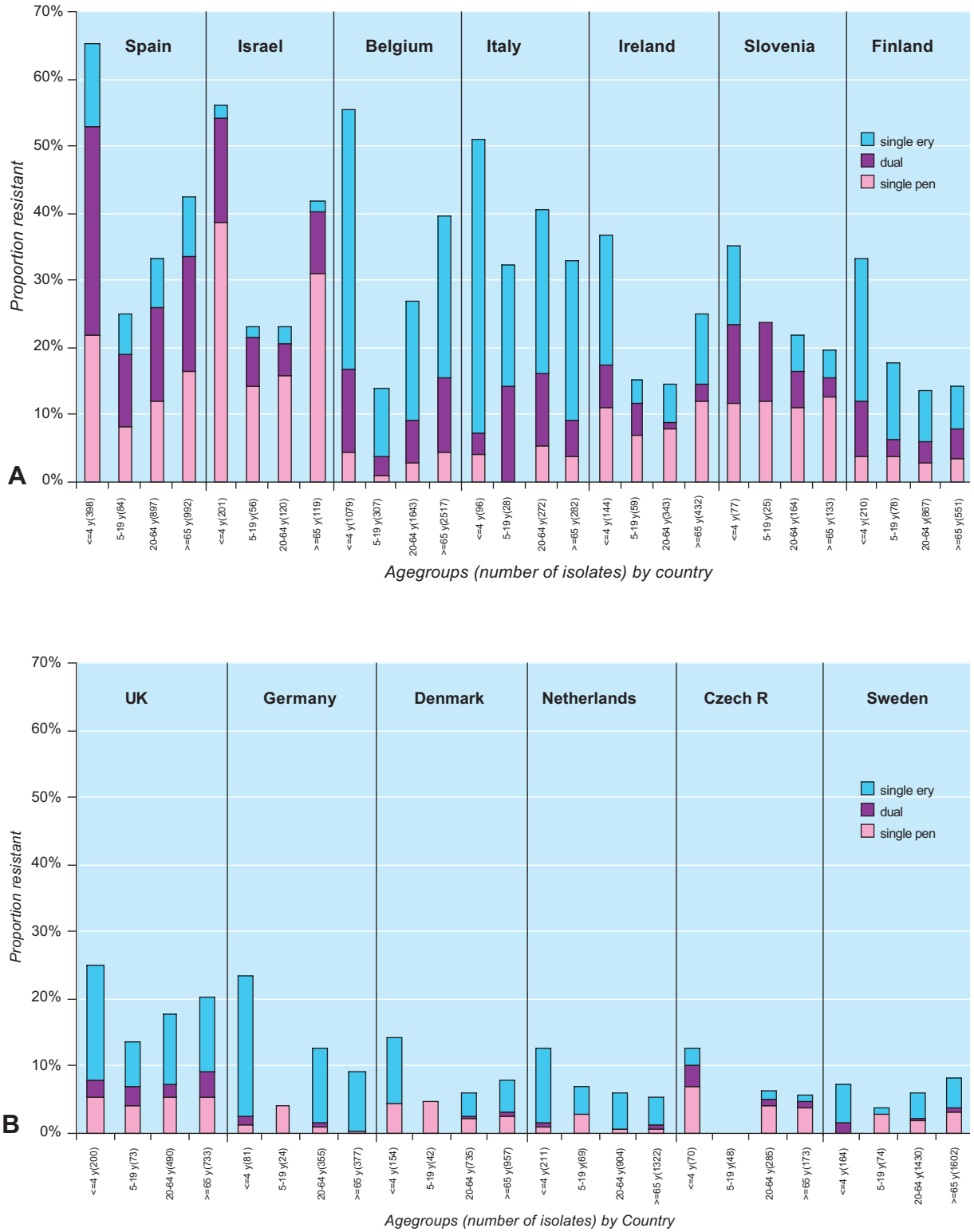

Figure 4.6 A/B *Streptococcus pneumoniae*: Proportion single and dual resistance to penicillin (I+R) and erythromycin by age group per country for the period 1999-2003. Countries are displayed in descending order of resistance. (Only the countries with at least 20 isolates in each age groups were included).

Staphylococcus aureus

Staphylococcus aureus is the main cause of bone, joint and soft-tissue infections acquired in hospital and in the community. It also causes blood stream infections and endocarditis, and it is a frequent cause of food poisoning. *S. aureus* resistant to penicillinase-fast beta-lactam antibiotics such as methicillin, oxacillin, cloxacillin, flucloxacillin, nafcillin and cephalosporins is conventionally termed MRSA (for methicillin-resistant *S. aureus*) and is genetically determined by the presence and expression of the *mecA* gene located within a staphylococcal cassette chromosome SCC*mec* that inserts at a specific recombination site in the bacterial chromosome. MRSA has become a notorious cause of hospital-acquired infections and thrives in hospitals worldwide [8, 9]. Recently, novel MRSA clones have been described that cause infections in the community. These are mainly skin and soft tissue infections caused by strains that express a particular virulence marker termed Panton-Valentin Leukocidin.

Methicillin resistance

Between 1999-2003, 702 laboratories from 27 countries reported susceptibility results for 73,609 *S. aureus* blood isolates to EARSS. PCR detection of the mecA gene or MIC-values for oxacillin as a confirmation of oxacillin-resistance were available for 68% of the reported isolates (n = 15,537). The geographical variation of MRSA in 2003 is shown in Figure 4.7. It demonstrates a north-south gradient, with the lowest MRSA prevalence in northern Europe and highest in southern Europe and Israel, but also in the United Kingdom and Ireland. MRSA proportions varied almost 100-fold, with the lowest proportion in Iceland (< 1%) and the highest proportion in Greece (51%).

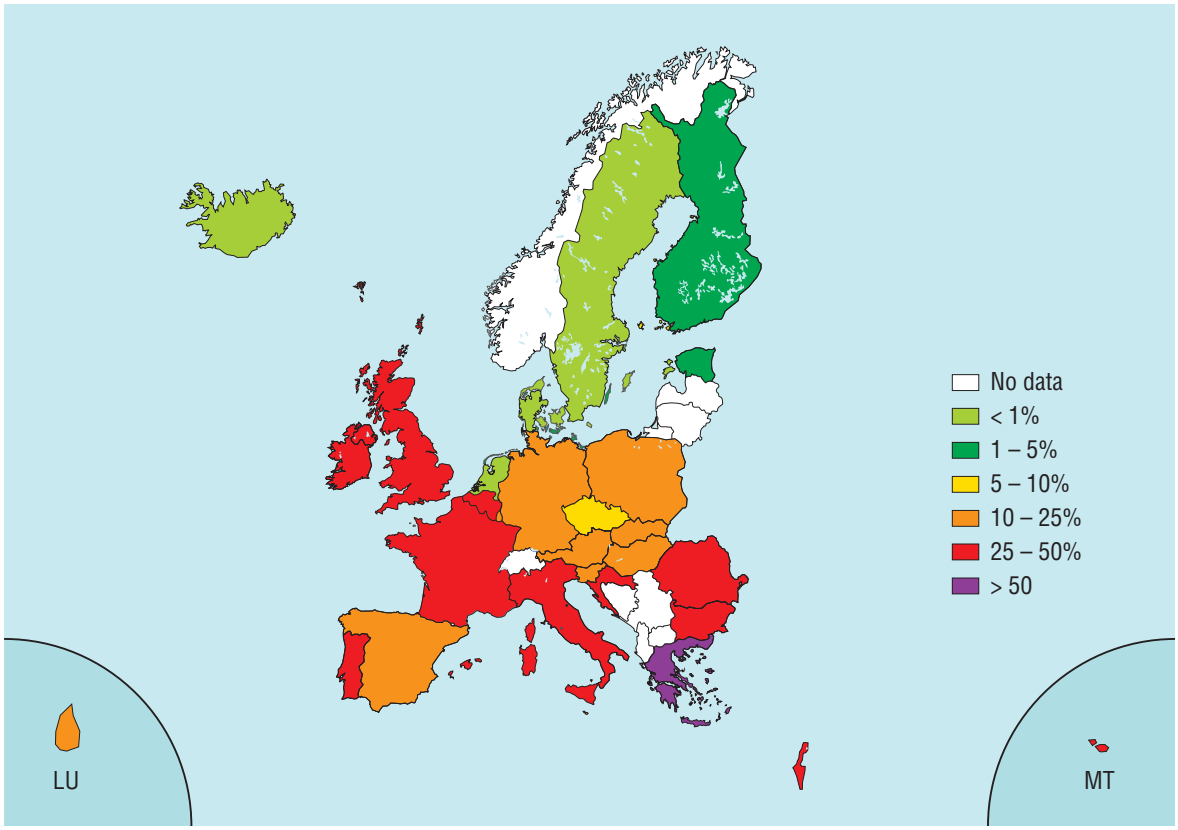

Figure 4.7 *Staphylococcus aureus*: invasive isolates resistant to methicillin (MRSA) in 2003.

For the observation period 2000-2003, a significant increase in the proportions of MRSA was observed in Belgium, Germany, The Netherlands, Portugal and The United Kingdom. The increase reported by the Scandinavian countries is at a much lower level but the trend must be taken seriously since a low threshold for 'losing control' may exist but is not well defined. For the British Isles the relentless increase of MRSA proportions among bloodstream infections that occurred between 1992 and 2000 seems to have petered out and consistent with the mandatory *Staphylococcus aureus* bacteraemia surveillance scheme in England and Wales, EARSS data show no further increase in the last three years (Figure 4.8).

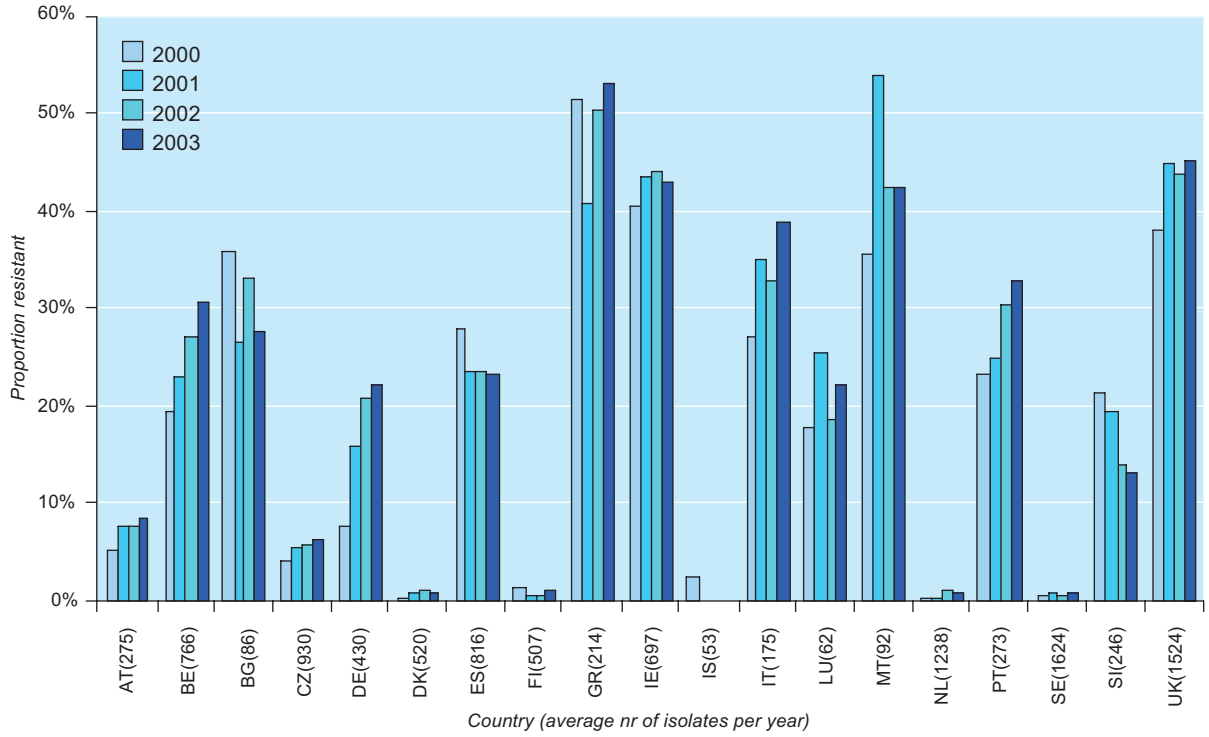

Figure 4.8 *Staphylococcus aureus*: invasive isolates resistant to methicillin (MRSA) from 2000 to 2003.

The proportion of outpatient samples increased from 7% in 2000 to 12% in 2003 (only considering the laboratories participating for the full period) (p trend < 0.0001), specifically in Northern countries (Sweden, Denmark and the Netherlands) and Ireland and Belgium. Presently, the EARSS database does not distinguish between certain clones or the expression of certain virulence markers and therefore it is impossible to decide whether this increase is due to the dissemination of hospital MRSA among returning patients who are sampled in outpatient settings or due to an increase in genuine community-acquired MRSA.

Conclusions

Rates of MRSA in invasive infections vary between < 1% and 50% over Europe. The trends are consistent with those reported in previous EARSS annual reports. The persistent increase, although at a low and much envied level, is worrying to the Scandinavian countries. The proportion of MRSA reported per year seems to have stabilised in the United Kingdom and Ireland, which might be the result of increased efforts in these countries to contain the MRSA epidemic, or a saturation effect as a result of fitness thresholds that limit the spread of typically hospital-acquired MRSA outside

hospitals. Slovenia still shows decreasing MRSA proportions, which indicate that the interventions implemented in the last years still produce effects.

Enterococci

Among all EARSS indicator organisms, enterococci are regarded as the least virulent pathogens and are a constitutive part of the natural gut flora of vertebrates. When causing infections, enterococci are mainly involved in urinary tract infection and contribute to abdominal infections such as abscess-forming peritonitis. Despite their mainly benign habits, some lineages exist that have accumulated a genetic repertoire that make them particularly successful in the hospital environment and may cause serious infections in debilitated patients. They can cause severe forms of endocarditis as well as blood stream or bone infections and occasionally meningitis. Their opportunistic behaviour is complemented by an extreme ability to survive environmental stress such as desiccation, temperatures up to 65°C, and they show some degree of tolerance to disinfectants. By nature, enterococci are also resistant to many antibiotic compounds and they were the first gram-positive bacteria for which the acquisition of resistance to third-line glycopeptide antibiotics (vancomycin and teicoplanin) was described. Ever since, vancomycin-resistant enterococci (VRE) have served as the paradigm for the post-anti-microbial era [10].

Vancomycin non-susceptible Enterococcus faecium

Between 2001-2003, 495 laboratories from 25 countries reported susceptibility results from 3931 *E. faecium* blood isolates to EARSS. The highest proportions of vancomycin non-susceptible *E. faecium* in 2003 were reported by Portugal (50%; n = 103), Italy (25%; n = 112), Greece (23%; n = 93), and Ireland (19%; n = 134) (Figure 4.9). As the number of *E. faecium* isolates reported is small, trend analyses of the proportion of vancomycin non-susceptibility do not yield reliable conclusions.

High-level aminoglycoside-resistant Enterococcus faecalis

AST results for high-level aminoglycoside were reported by 495 laboratories from 25 countries of 12,065 *E. faecalis* blood isolates between 2001-2003. In 2003, the highest proportions of aminoglycoside high-level resistance among *E. faecalis* isolates were observed for Hungary (87%; total number of isolates n = 69) and Greece (57%; n = 81) (Figure 4.10). From Iceland no high-level resistance to aminoglycosides was reported, but this was only based on a total of 15 isolates.

Among the 10 countries that reported ≥ 20 *E. faecalis* isolates per year (after considering only the laboratories that permanently provided data from 2001 through 2003), the Czech Republic observed a significant trend of increased high-level aminoglycoside resistance from 38% (n = 388) in 2001 to 45% (n = 472) in 2003. A significant increase was also observed in Finland, 23% in 2001 (n = 26) to 39% in 2003 (n = 72), and Israel, 24% in 2001 (n = 63) to 43% in 2003 (n = 196). On the other hand, a significant decrease was observed for Croatia, 48% in 2001 (n = 31) to 26% in 2003 (n = 57). However, due to the low number of isolates leading to wide confidence intervals, conclusions should be drawn with caution.

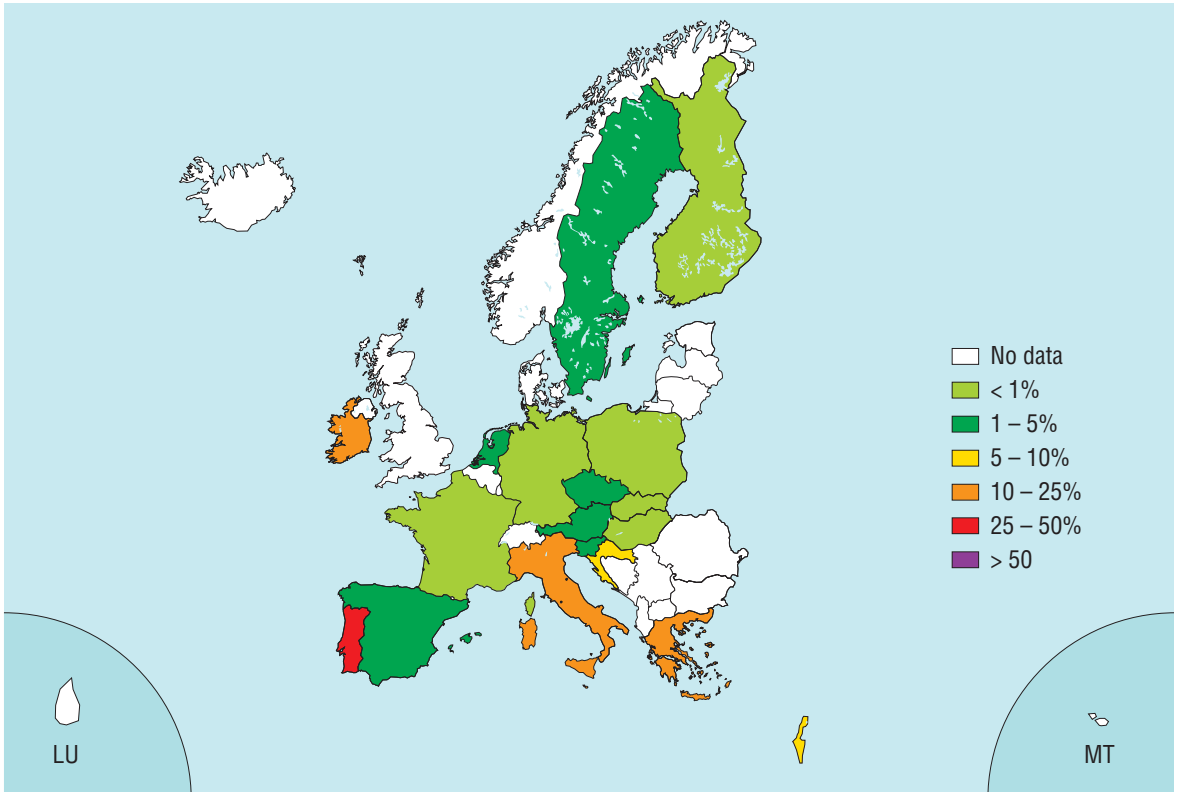

Figure 4.9 *Enterococcus faecium*: invasive isolates non-susceptible to vancomycin in 2003*.

* Vancomycin non-susceptibility in *E. faecalis* is not displayed in the map as proportion for the majority of countries did not exceed 1%.

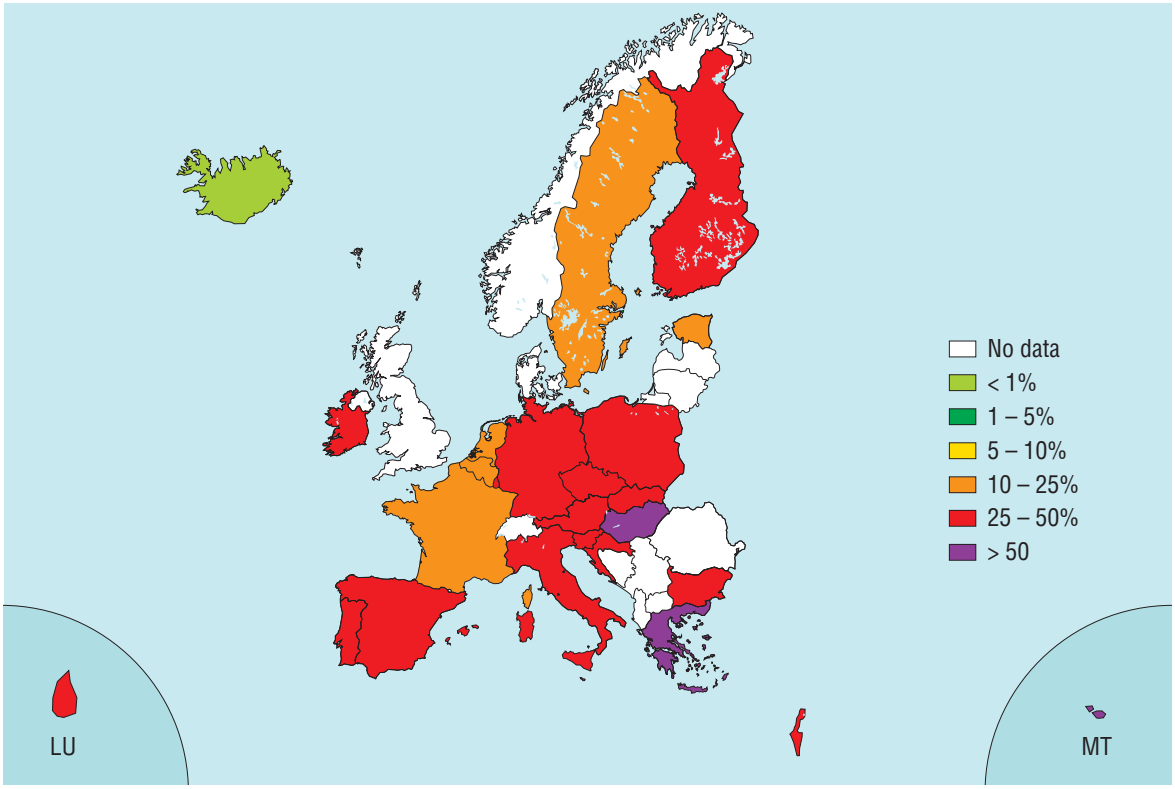

Figure 4.10 *Enterococcus faecalis*: invasive isolates resistant to high-level aminoglycoside (gentamicin) in 2003.

Demographic characteristics

Enterococci were more frequently isolated from male patients (Table 4.2). The AMR proportions did not differ by gender. Only in young females (ageband 5-19 years) VRE and high-level aminoglycoside-resistant enterococci were more frequently isolated than in males of the same age which may reflect the higher proportion of bacteraemias originating from ascending urinary tract infections in young females compared to males of the same age band.

Conclusions

Vancomycin resistance appears to be still rare in *E. faecali*s and below 5% in *E. faecium* in most countries that contribute to the EARSS database. A complete picture for Europe can however not been provided as data from Bulgaria, Denmark, England, Norway, Northern Ireland, and Scotland were still not available in 2003. Nevertheless, four countries reported resistance proportions above 15%. It appears that countries reporting high levels of VRE, are witnessing outbreaks of *E. faecium* in several care facilities. The overall low number of isolates reported to EARSS does not yet permit a country-specific trend analysis. High-level aminoglycoside resistance has become common among *E. faecalis* in all countries, the majority reporting levels between 25 and 50%.

Table 4.2 Proportion of antibiotic resistance by gender and age group.

	Vancomycin non-susceptible *E. faecium*				**Aminoglycoside HL resistant *E. faecalis***			
Age group	♂		♀		♂		♀	
	N	**%R**	**N**	**%R**	**N**	**%R**	**N**	**%R**
≤ 4 y	117	4%	88	1%	295	14%	238	15%
5-19 y	35	6%	35	11%	66	27%	41	37%
20-64 y	803	7%	545	8%	1687	38%	944	33%
≥ 65 y	1024	5%	738	7%	2330	33%	1394	36%
Total	**1979**	**6%**	**1406**	**7%**	**4378**	**34%**	**2617**	**33%**

Escherichia coli

Escherichia coli is the most frequently gram-negative bacterium isolated from blood cultures in clinical settings. It is the most frequent cause of community and hospital-acquired urinary tract infections. It is associated with spontaneous and surgical peritonitis, it causes synergistic wound infections and it is one of the most important food-borne pathogens. Broad-spectrum penicillins such as ampicillin and amoxicillin were the treatment of choice before plasmid-coded TEM1 beta-lactamases became an almost ubiquitous component of genetic equipment of this species, and aminopenicillin resistance has exceeded 40% in most European countries. Since the early 90's fluoroquinolones have been widely used for therapy of invasive enteric pathogens. For years fluoroquinolones have been effective in the treatment of infections caused by *Escherichia coli*, but recently resistance has been spreading in several European countries, including countries with overall low resistance levels [11-14].

Between 2001-2003, 502 laboratories from 25 countries reported susceptibility results for 58,061 invasive *E. coli* isolates to EARSS. Susceptibility test results for aminopenicillin, 3rd generation cephalosporins, fluoroquinolones, and aminoglycosides, were reported for 53,126 (92%), 55,086 (95%), 52,899 (91%), and 56,501 (97%) respectively.

Aminopenicillin resistance

The overall proportion of aminopenicillin resistance in Europe among invasive *E. coli* in Europe has reached 47% in 2003. Sweden reported the lowest proportion of this type of resistance (28%), whereas Romania, Ireland and Israel reported > 60% (Figure 4.11). In the last three years (2001-2003), aminopenicillin resistance has remained relatively stable. Only in Germany a significant increase was observed from 43% in 2001 to 48% in 2003 ($p < 0.05$).

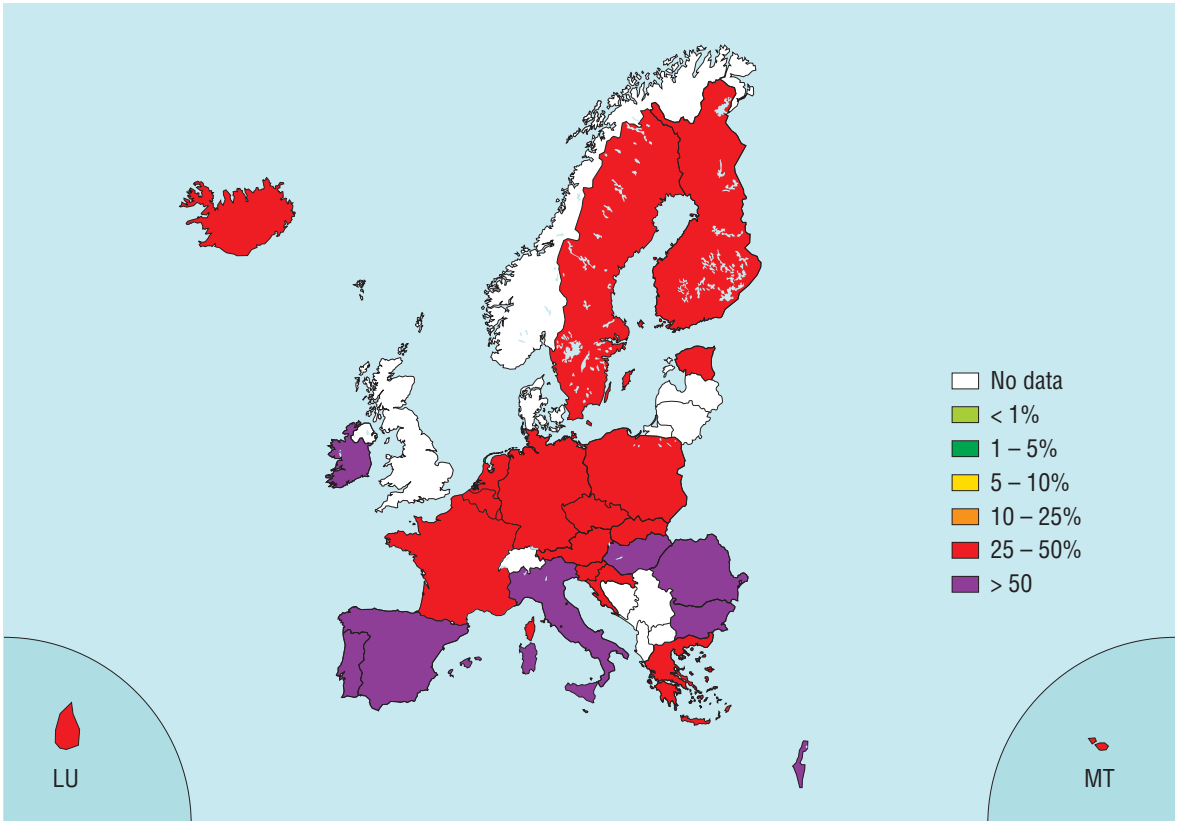

Figure 4.11 *Escherichia coli*: invasive isolates resistant to aminopenicillin in 2003

3rd generation Cephalosporin resistance

Among the four antibiotic groups under EARSS surveillance for *E. coli*, the lowest overall proportion of resistance was reported for 3rd gen. cephalosporins (3%). Nevertheless, high frequencies were observed in Bulgaria (18%) and Romania (19%) (Figure 4.12). Furthermore, seven countries (AT, BG, CZ, DE, ES, HU and SE) witnessed a significant increase from 2001 to 2003 (Figure 4.13). The overall spread of 3rd gen. cephalosporin resistance coincides with numerous reports of CTX-M ESBL in *E. coli*, and should serve as an early warning.

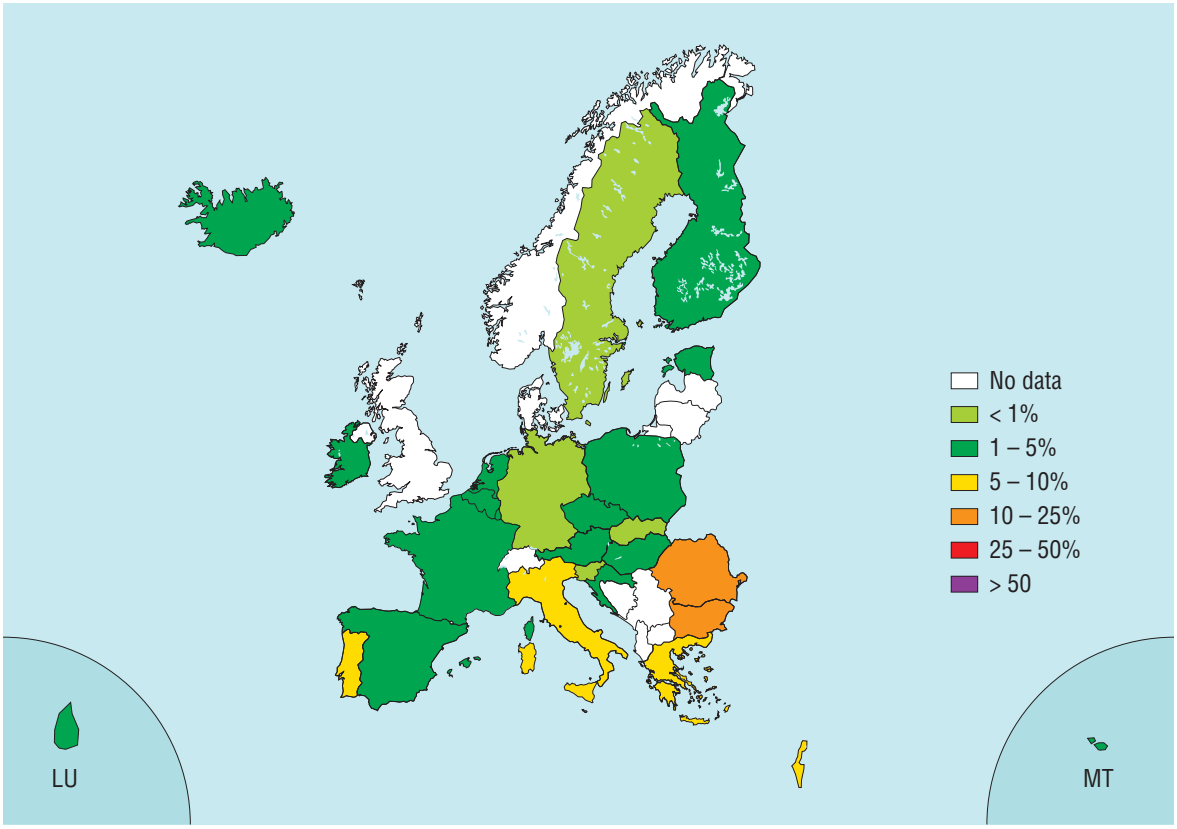

Figure 4.12 *Escherichia coli*: invasive isolates resistant to 3rd generation cephalosporins in 2003

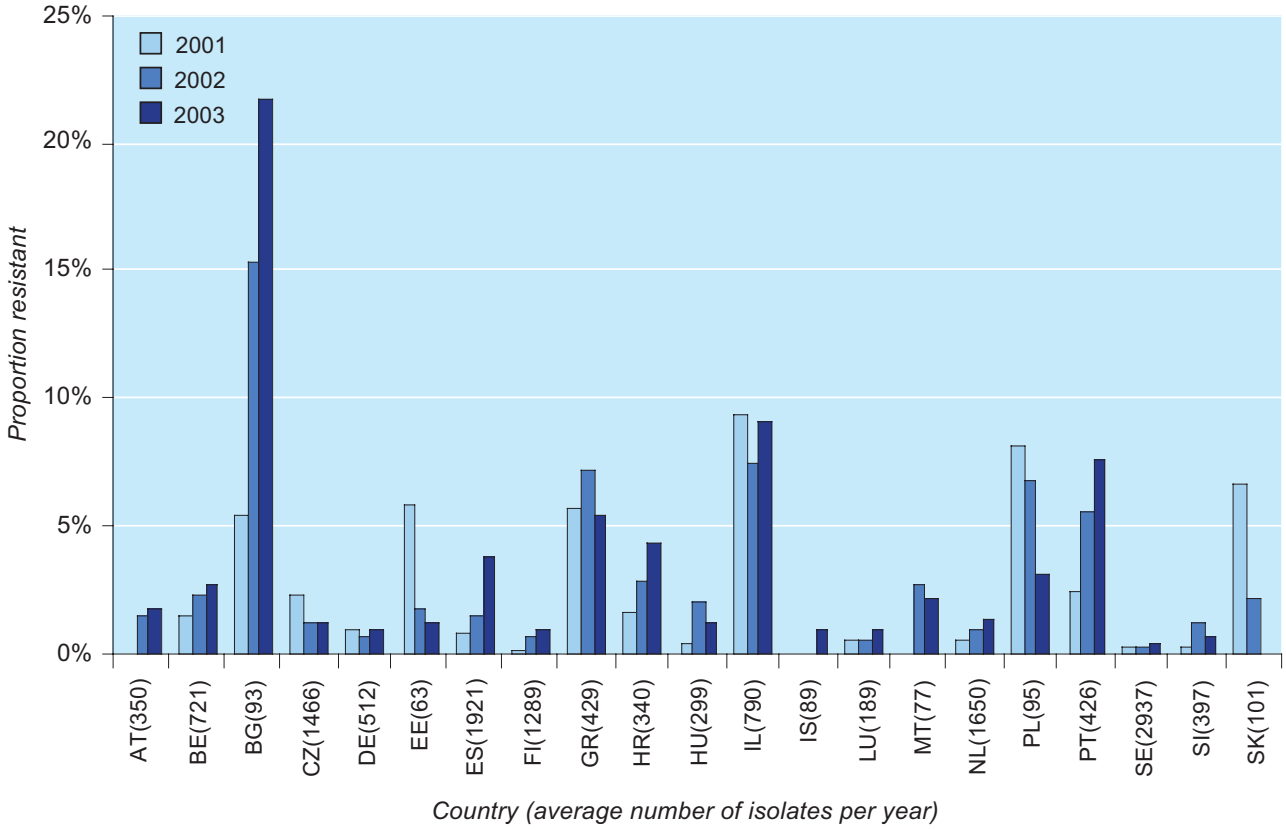

Figure 4.13 *Escherichia coli*: invasive isolates resistant to 3rd gen. cephalosporins from 2001 to 2003.

Fluoroquinolone resistance

In 2003, Fluoroquinolone resistance was the second most prevalent phenotype after aminopenicillin resistance, reaching an average of 12.5% overall. Israel, Italy, Malta, Portugal, Spain and Slovakia reported fluoroquinolone resistance proportions of ≥ 20%. The lowest proportions were reported from Finland and Estonia (5%) (Figure 4.14). This trend already observed from 2001 to 2002, continued in 2003 and was statistically significant in seven countries (AT, BG, CZ, DE, ES, HU, SE). At the same time it seems unlikely that sampling error could account for the statistically non-significant but consistent increase in eight other countries (Figure 4.15).

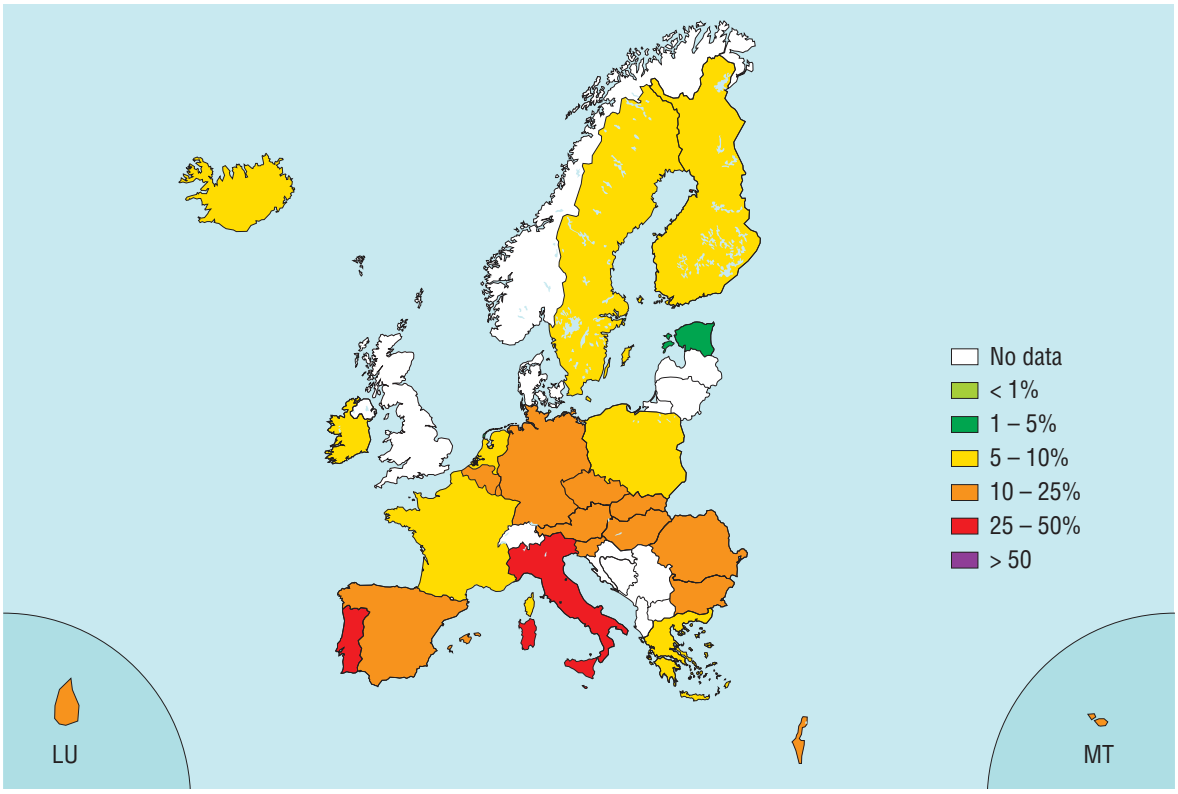

Figure 4.14 *Escherichia coli*: invasive isolates resistant to fluoroquinolones in 2003

Aminoglycoside resistance

Aminoglycoside resistance is rare as a single resistance trait in *E. coli*. The proportion of aminoglycoside-resistant *E. coli* in Europe is still quite low, with an average of 5%, but has reached more than 10% in Israel, Bulgaria, Romania, and Malta (Figure 4.16). In the last three years (2001-2003), aminoglycoside resistance has remained relatively stable. Only Finland witnessed an increase, albeit at low levels from 0.2% in 2001 to 1.2% in 2003 ($p < 0.05$).

Combined resistance

In total 46,948 of the 58,061 invasive *E. coli* isolates (81%) reported to EARSS were tested for all 4 antibiotic classes included in the EARSS protocol. Overall 4% of these isolates were resistant to ≥ 3 antibiotics reported to EARSS. Resistance to aminopenicillin + fluoroquinolone + aminoglycoside occurred in 2.5% of the *E.coli*. Approximately 1% of all isolates were resistant to all 4 antibiotics reported to EARSS. (Table 4.3).

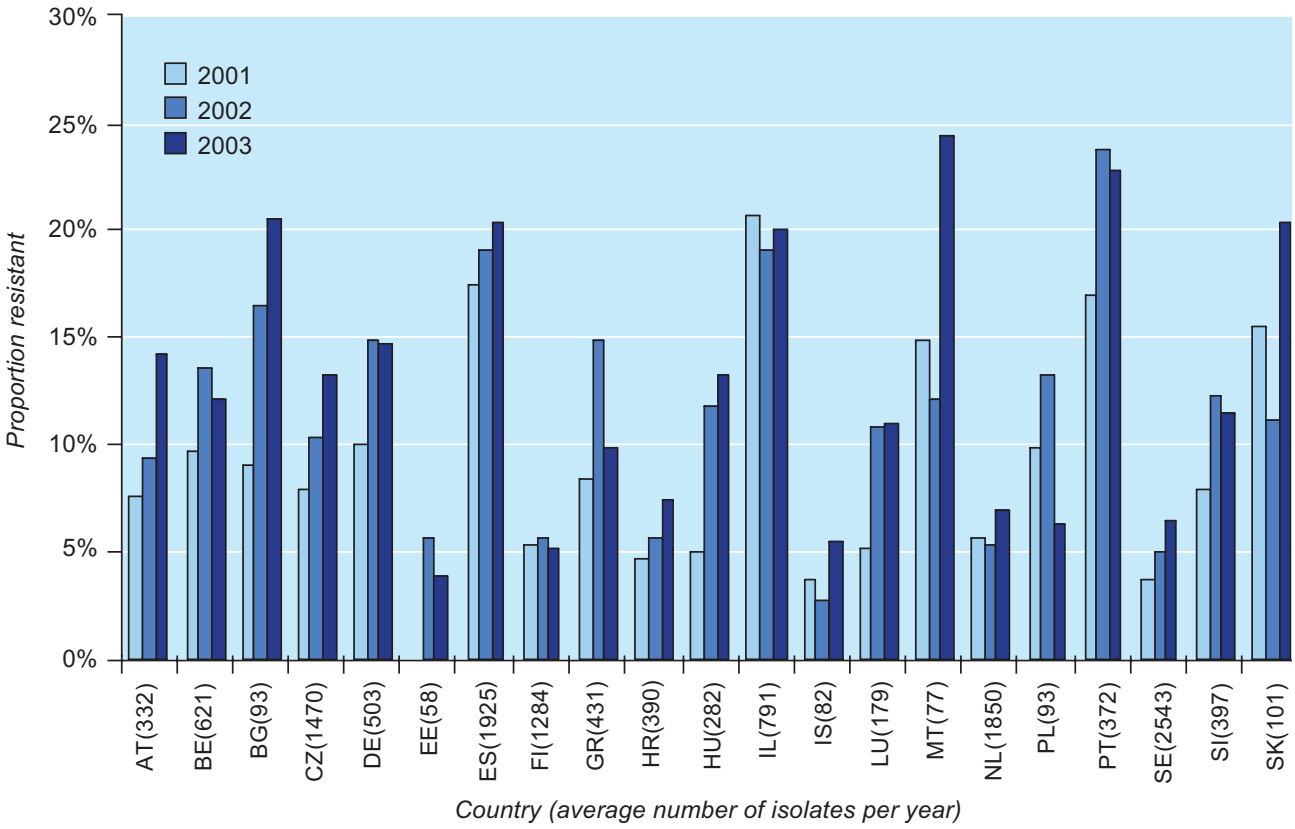

Figure 4.15. *Escherichia coli*: invasive isolates resistant to fluoroquinolones from 2001 to 2003.

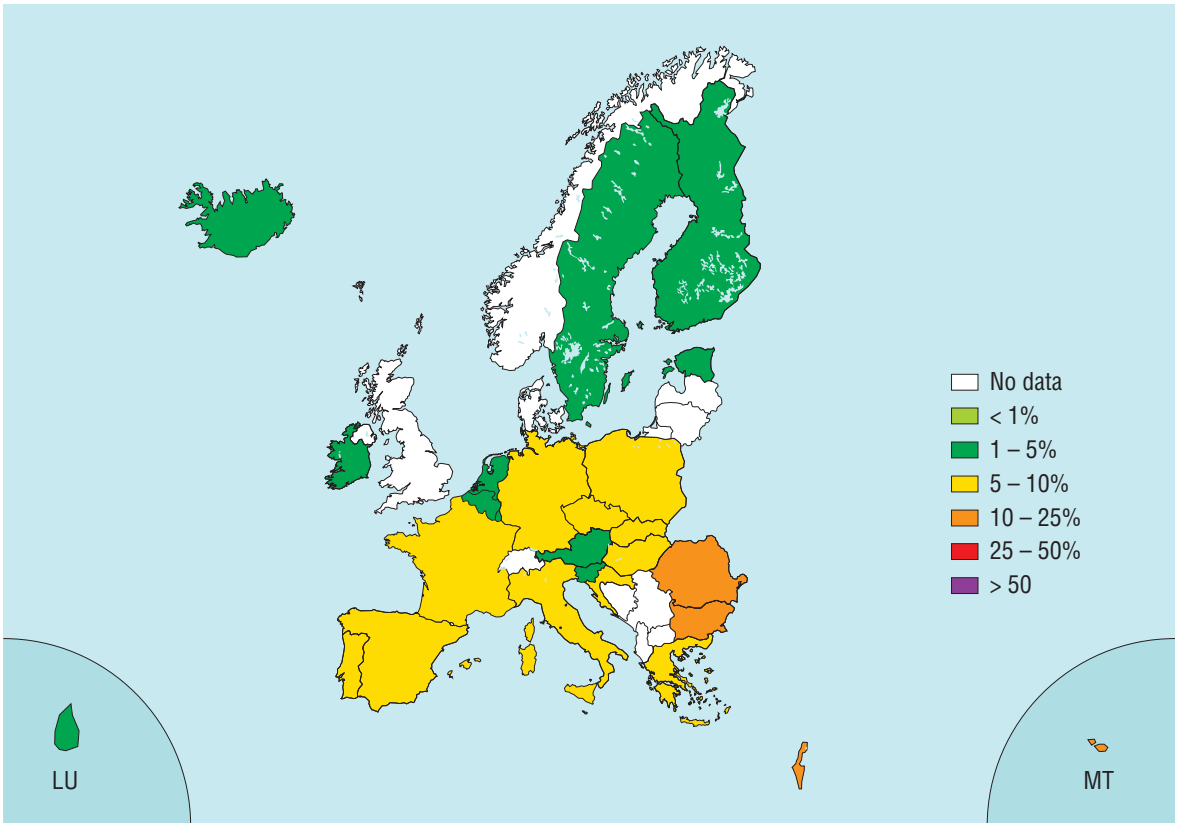

Figure 4.16 *Escherichia coli*: invasive isolates resistant to aminoglycosides in 2003

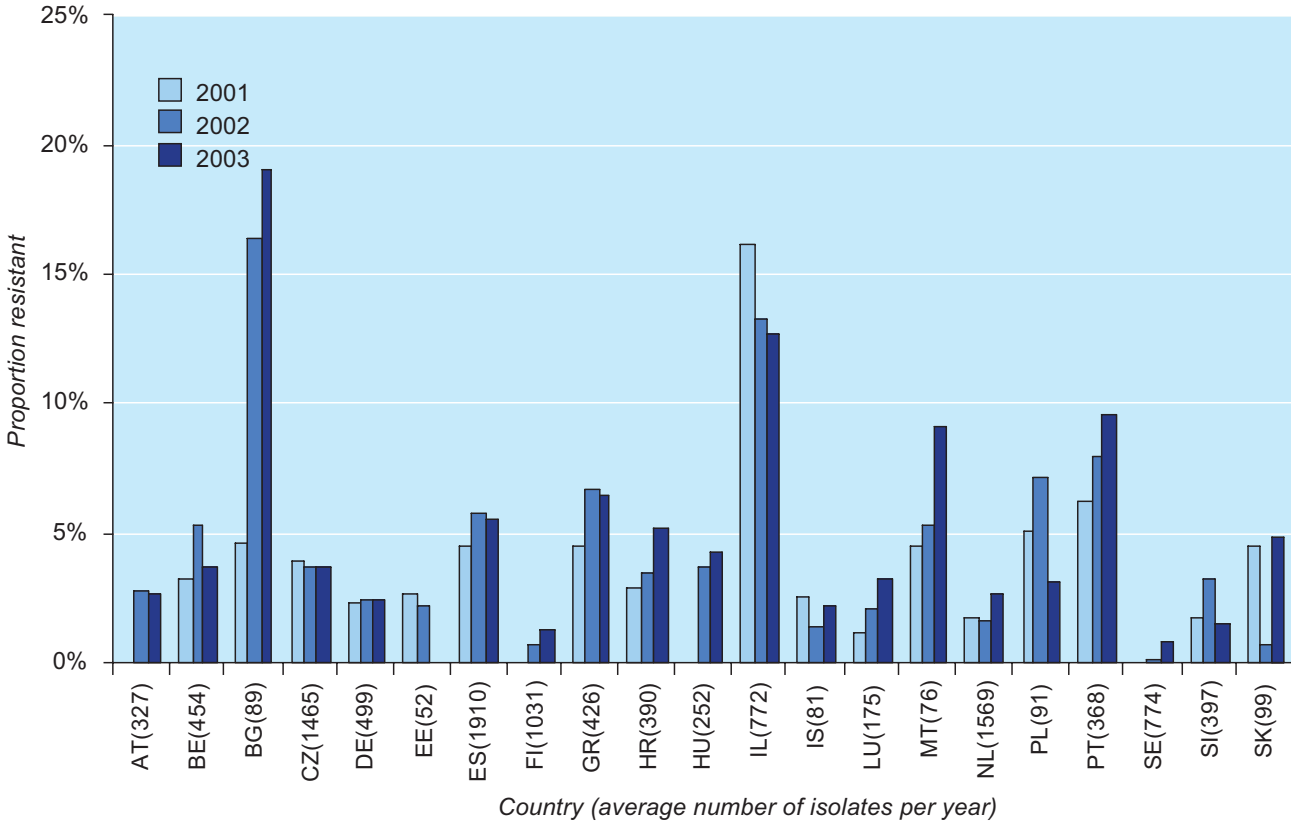

Figure 4.17 *Escherichia coli*: invasive isolates with multiresistance (≥ 3 antibiotic groups) reported from 2001 to 2003. Only the isolates with reported data for all 4 antibiotic groups were included.

Fifty per cent of the invasive *E.coli* isolates were susceptible to the four drugs recorded in the EARSS database. A recent study on *E.coli* in urinary tract infections in Europe came to very similar conclusions. Just over half the isolates were susceptible to 12 antibiotic substances included in that investigation [14]. However, figures suggested in the current analysis for single aminopenicillin resistance have to be used with caution as resistance to aminopenicillins is frequently coupled with resistance to trimethoprim and/or sulphonamide which is not reported by EARSS network [15].

Even though the prevalence of combined resistance to three or all four of the antibiotics reported to EARSS is still low in Europe (4%), five countries witnessed an increase over the last three years (BG, FI, HU, NL, and SE). Several countries that did not observe resistance to three or more antibiotics in 2001, reported multiple combined resistance in the following two years (AT, FI, HU, and SE) (Figure 4.17). The countries with the highest proportions of combined resistance are Bulgaria and Israel (> 15%). In Bulgaria the reporting is still increasing, whereas Israel reported decreasing figures in the past three years.

Table 4.3 Single resistance and resistance combinations among invasive Escherichia coli isolates for the period 2001-2003 in Europe (n = 46,948).

Single resistance and resistance combinations	Number	(% of total)
Fully susceptible	**23,653**	**(50.38)**
Aminopenicillin	16,445	(35.03)
Fluoroquinolones	732	(1.56)
3rd gen. Cephalosporins	14	(0.03)
Aminoglycosides	172	(0.37)
Aminopenicillin + Fluoroquinolones	3,014	(6.42)
Aminopenicillin + 3rd gen. Cephalosporins	289	(0.62)
Aminopenicillin + Aminoglycosides	577	(1.23)
Fluoroquinolones + 3rd gen. Cephalosporins	1	(0.00)
Fluoroquinolones + Aminoglycosides	94	(0.20)
3rd gen. Cephalosporins + Aminoglycosides	2	(0.00)
Aminopenicillin + Fluoroquinolones + Aminoglycosides	1,181	(2.52)
Aminopenicillin + Fluoroquinolones + 3rd gen. Cephalosporins	231	(0.49)
Aminopenicillin + Aminoglycosides + 3rd gen. Cephalosporins	121	(0.26)
Aminopenicillin + Fluoroquinolones + Aminoglycosides + 3rd gen. Cephalosporins	422	(0.90)
Total	**46,948**	**(100)**

Demographic characteristics

Both the patient's age and gender was available for 53,887 (93%) of all 58,061 *E. coli* isolates reported to EARSS respectively. The overall age distribution of invasive *E. coli* isolates reported, clearly indicates that most *E. coli* blood strain infections are found among the elderly (≥ 65 years). Overall the *E. coli* isolates were more frequently isolated from female patients (56%) especially among adults and elderly. In addition, women develop urinary tract infections more frequently than men, which will have a bearing on the occurrence of blood stream infections. Conversely, in the under five-years-old, male patients were more frequent, indicating that at this age boys are more likely to develop an invasive *E. coli* infection.

The proportion of aminopenicillin, aminoglycoside, and 3rd gen cephalosporin resistance was comparable between age groups and gender, whereas in the under five-year-olds fluoroquinolone resistance was significantly lower compared to the older patients independent of gender (Table 4.4). In addition, above the age of five, fluoroquinolone resistance among males was significantly lower compared to females (Table 4.4). The low resistance rates in those aged under five years confirms recently published findings [16] and could be explained by the restricted fluoroquinolone use in infants.

Table 4.4 Proportion of antibiotic resistance by age group.

	Aminopenicillin		Fluoroquinolones*		Aminoglycosides		3rd gen. Ceph	
Age group	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
≤ 4 y	1701	49	1696	4	1694	7	1757	4
5-19 y	673	58	676	9	671	7	705	4
20-64 y	15881	49	16367	11	15960	5	16794	2
≥ 65 y	32066	44	33563	11	31807	5	34444	2

* For fluoroquinolones there was a small but significant difference (≤ 4%) between males and females. For the other investigated drugs there were no differences between males and females.

Conclusion

E. coli is rapidly becoming a 'difficult-to-treat' organism in many countries. Aminopenicillin resistance is so high that it renders the drug useless for empirical therapy unless combined with an aminoglycoside. Resistance rates to fluoroquinolones and to 3rd generation cephalosporins are also increasing and threaten to jeopardize the usefulness of these drugs too. A further disquieting trend is the increased finding of strains with co-resistance to several drugs.

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Chapter 5. Conclusions

The geographic diversity in antimicrobial resistance across Europe is evident and appears to follow time worn cultural boundaries. Although national borders are drawn along historical lines of political and military disposition, they may indeed circumscribe country-specific values including beliefs shared by patients and their doctors concerning the treatment of disease. Undeniably, European countries have different health care-, administration-, and reimbursement systems. These influence prescription and antimicrobial consumption patterns as well as infection control policies in the community and health care facilities in various ways. Results illustrated in map formats as displayed by EARSS undoubtedly oversimplify the occurrence of antimicrobial resistance in Europe and are vulnerable to several types of bias. Thus the selection of hospitals varies between participating national networks, as does the number of laboratories, which if small, may not be representative for the country as a whole. Moreover, differences exist in antimicrobial susceptibility testing methodology and antimicrobial breakpoints between countries and laboratories, affecting the consistency with which resistance is ascertained. Finally, diagnostic habits influence the reporting of resistance. Hospitals in which microbiological investigations are performed only after the initial empirical treatment has failed are bound to report higher resistance rates as institutions that conventionally sample patients before the administration of antimicrobial chemotherapy.

Despite these differences between and within countries a credible overall picture emerges. The number of participating laboratories is convincing and the fact that the number of countries and laboratories continue to increase adds to the value of EARSS. Over 90% of all laboratories repeatedly participate in the EARSS programs for external quality assessment. It is indisputable that this commitment to quality will continuously improve the accuracy and usefulness of this surveillance initiative. The fourth EARSS external quality assessment showed that laboratories participating in EARSS are in general capable of delivering susceptibility data of good quality (over 90% concordance between laboratories). However, when challenged with a difficult MRSA, 19% of the laboratories failed to detect an epidemic MRSA which had caused outbreaks in Dutch and German hospitals. The strain is notorious in that it is easily misclassified due to the fact that the resistance phenotype is heterogeneously expressed and this has probably contributed to its dissemination in hospitals. All laboratories should take this opportunity to re-evaluate the methodology used for the detection of MRSA. Twenty-three per cent of laboratories either over- or understated penicillin resistance in a penicillin non-susceptibility in *S. pneumoniae*. In the *E. coli* strain 20% missed overt tobramycin resistance and although 94% identified the ESBL phenotype, 10% missed the cefotaxime/ceftriaxone resistance. The results show that there is room for re-evaluation, calibration and improvement of methodology. At the same time they illustrate that routinely reported results as collected by EARSS in most instances have sufficient accuracy to provide good estimates of overall resistance prevalences and trends and that pooling of reported resistance data as done by EARSS is justified. Especially trend analyses for a stable and representative set of laboratories within each country provide a reliable indication for resistance developments since diagnostic habits, methods and standards usually remain unchanged; and with a continuously growing database, EARSS is able to report trends with increasing confidence.

In 2003 non-susceptibility to penicillins in ***S. pneumoniae*** with or without concomitant resistance to erythromycin, was still high in many European countries. In Germany, Czech Republic, Estonia, the UK, the Netherlands and most Scandinavian countries the rate was still below 5%, and for some

hitherto unexplained reason penicillin resistance has been declining for several countries. However, the high overall erythromycin resistance remains remarkable (single erythromycin resistance 12% and dual Pen+Ery resistance 6%). The pronounced differences in the ratios of penicillin to macrolide resistance between countries are noteworthy, but not yet understood. Conservative use of macrolides is especially important in situations where penicillin and erythromycin resistance is common and appropriately dosed beta-lactams should remain the preferred empirical treatment. Vaccination, especially of young children may affect antibiotic resistance in pneumococcal disease in Europe. Whether vaccine use will slow the expansion of resistant pneumococci, or whether resistant strains not covered by the vaccine will replace vaccine serotypes, remains to be explored.

For ***S. aureus*** rates of MRSA in invasive infections varied between < 1% and 50% in 2003. The trends are consistent with those reported in previous EARSS annual reports. The relentless increase, although at a low and much envied level, is reason for concern to the Scandinavian countries. The proportion of MRSA reported per year seems to have stabilised in the United Kingdom and Ireland, which might be the result of increased efforts in these countries to contain the hospital MRSA epidemic, or a saturation effect as a result of fitness thresholds that limit the spread of MRSA outside hospitals. Slovenia still shows decreasing MRSA proportions, which indicate that the interventions implemented in the last years still produce effects.

In contrast to MRSA, which has become established at various endemic levels in many European hospitals, epidemiology of vancomycin resistance was still unstable. In ***E. faecalis*** vancomycin resistance is low and it remained below 5% in ***E. faecium*** in most countries although 4 countries reported resistance above 15%. Six countries that regularly provide AST data for *S. pneumoniae* and *S. aureus* were still unable to report data for enterococci by 2003 and conclusions drawn by EARSS remain incomplete for this important indicator organism. It appears that in countries reporting higher levels of VRE, these were likely due to outbreaks of *E. faecium* in care facilities. The low number of reports did not permit far-reaching statistical conclusions. High-level aminoglycoside resistance has become frequent among *E. faecalis* in all countries, the majority reporting levels between 25 and 50%.

E. coli is rapidly becoming a 'difficult-to-treat' organism in many countries. Aminopenicillin resistance has become so high that it renders the drug useless for empirical therapy unless combined with an aminoglycoside. Resistance rates to fluoroquinolones and to 3rd generation cephalosporins continued to increase in 2003. The usefulness of these drugs in the empirical treatment of severe infections is thus increasingly threatened. A further disquieting trend was the increased finding of strains with co-resistance to several drugs. Since *E. coli* is an important pathogen responsible for many hospital as well as community-acquired infections the steady increase of multiple-resistant strains warrants a watchful eye.

Appendix A. 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:

Table 1 and 2 and Figures 1 and 2 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 2002 (i.e. that responded to the questionnaire) and thus only includes the laboratories that reported AST results to EARSS in 2002, and provided blood culture information and the hospitals that reported AST results to EARSS in 2002, and 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 (Appendix B). If data were not available this is stated as 'na'.
Figure 1 gives and indication about the degree of specialisation of the participating hospitals, and Figure 2 shows the geographic location of the laboratories reporting in 2003. The size of the dots in the maps represents the number of laboratories in that area:

Antibiotic resistance 1999-2003. Table 3 provides information on the proportion of invasive bacterial isolates not susceptible to the antibiotic classes mentioned in the EARSS protocols. From the majority of all non susceptible *S. pneumoniae* and *S. aureus* isolates we received the corresponding MIC or Etest result, according to the EARSS protocols, however for some of the non susceptible isolates this information is missing. Resistance proportions in Table 3 are based on the reported number of isolates given in Table 2.
Table 4 gives details about the origin of the isolate (patient, source and hospital department). The abbreviations used in this table stand for; PNSP = pencillin non-susceptible *S. pneumoniae* MRSA = methicillin-resistant *S. aureus*, FREQ = fluoroquinolone-resistant *E. coli*, and VRE = vancomycin-resistant (I+R) *E. faecalis* or *E. faecium*. If the number of isolates in a certain category accounts for less than 0.5% of the total number of isolates, the percentage total is set at 0 and the percentage resistance is not shown.

Local variation. Figures 3 and 4 show local variation in the proportions of PNSP and MRSA by displaying these by laboratory and by hospital, respectively.
For both Figures, a minimum of 5 isolates and at least 2 years of participation in EARSS for each laboratory or hospital was required, before being included in the figure. The total number of laboratories or hospitals (included in the figure), 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 encompass one or more unknown hospitals.

Countries

Austria

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	10/46
Labs/Hosps providing denom.data *	10/33
Number of blood culture sets *	29000
Number of hospital beds *	21772
Average annual occupancy rate *	na
Estimated catchment population *	3500000
% total population covered *	43%

*** Based on labs/hospitals providing denominator data**

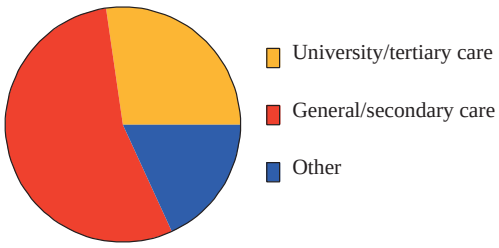


Figure 1. Type of hospitals in 2002

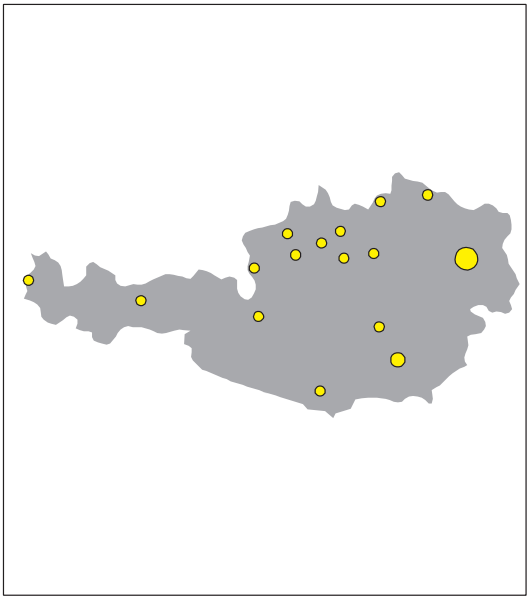


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	9	53	9	156	0	0	0	0
2001	9	63	9	277	9	269	8	74
2002	9	71	10	404	9	417	9	166
2003	18	149	19	773	20	930	18	293

Antibiotic resistance in 1999-2003

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

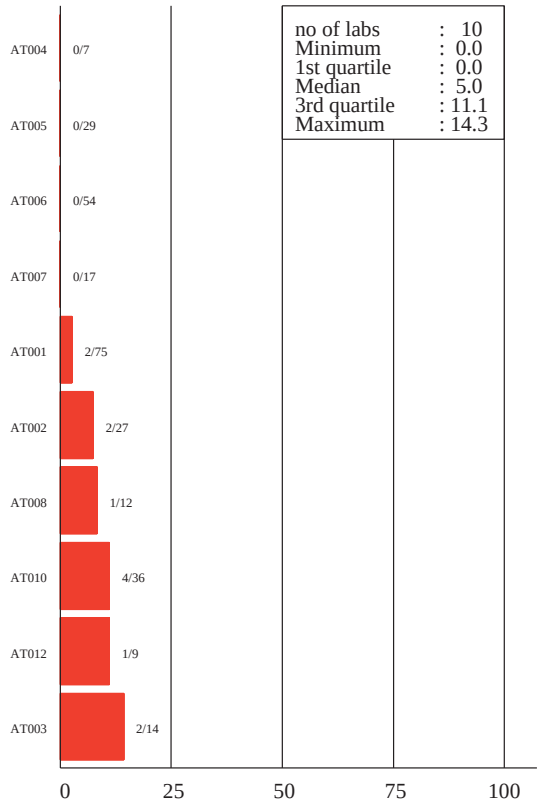
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	<1	<1	<1	1
	Penicillin I+R	.	2	3	1	6
	Macrolides I+R	.	4	10	10	13
S. aureus	Oxacillin/Methicillin R	.	5	8	11	14
E. coli	Aminopenicillins R	.	.	35	33	40
	Aminoglycosides R	.	.	1	4	5
	Fluoroquinolones R	.	.	8	10	14
	3rd gen. Cephalosporins R	.	.	<1	1	2
E. faecalis	Aminopenicillins I+R	.	.	10	3	<1
	Aminoglycosides (high-level resistance)	.	.	35	17	35
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	86	83	87
	Aminoglycosides (high-level resistance)	.	.	13	20	23
	Glycopeptides I+R	.	.	5	8	1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=336		*S. aureus* n=1610		*E. coli* n=1550		*E. faecalis* n=395		*E. faecium* n=133	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	89	4	100	11	100	12	100	1	100	4
CSF	11	3	0	.	0	.	0	.	0	.
Sex										
Male	59	5	60	12	37	12	59	1	57	1
Female	40	2	39	10	62	11	38	0	40	6
Unknown	1	0	1	0	1	29	3	0	3	25
Age (years)										
0-4	9	3	3	2	2	5	5	0	5	0
5-19	5	0	3	0	1	9	1	0	2	0
20-64	43	3	38	11	33	12	44	0	56	7
65 and over	44	5	56	13	63	12	49	1	38	0
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	14	6	13	24	7	13	25	2	33	7
Internal Medicine	50	3	43	8	54	11	34	0	28	3
Surgery	2	0	12	17	9	9	12	0	13	0
Other	29	4	29	9	27	14	28	0	26	3
Unknown	4	8	2	3	2	6	2	0	1	0

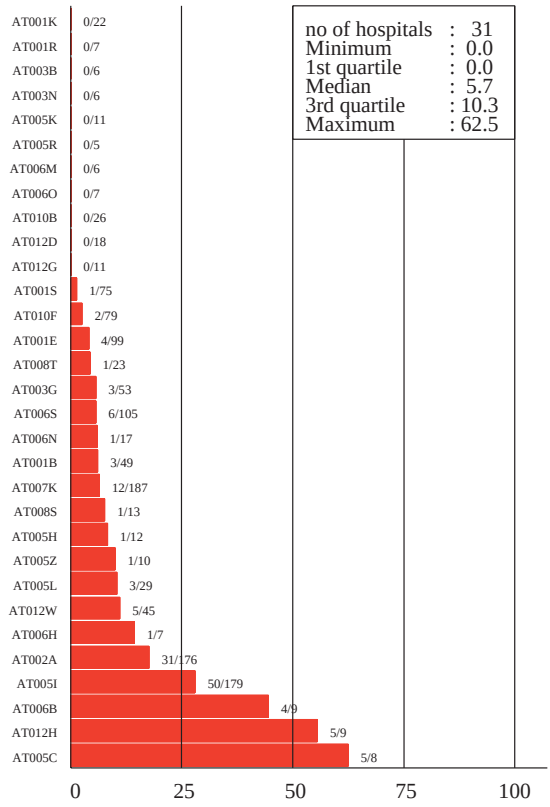
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Belgium

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	102/102
Labs/Hosps providing denom.data *	0/0
Number of blood culture sets *	na
Number of hospital beds *	na
Average annual occupancy rate *	na
Estimated catchment population *	na
% total population covered *	na

*** Based on labs/hospitals providing denominator data**

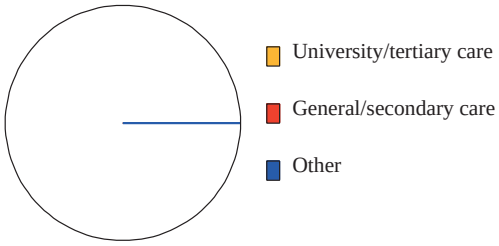


Figure 1. Type of hospitals in 2002

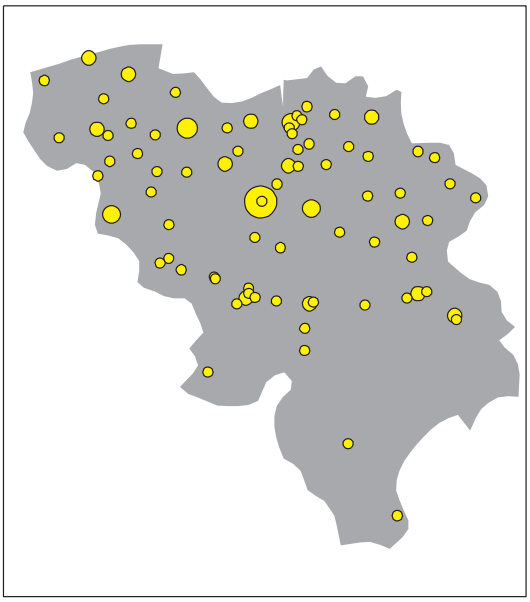


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	92	846	47	442	0	0	0	0
2000	90	909	42	657	0	0	0	0
2001	89	1093	47	941	23	226	19	42
2002	98	1210	48	1092	27	1184	23	205
2003	107	1488	47	1133	24	1326	16	146

Antibiotic resistance in 1999-2003

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

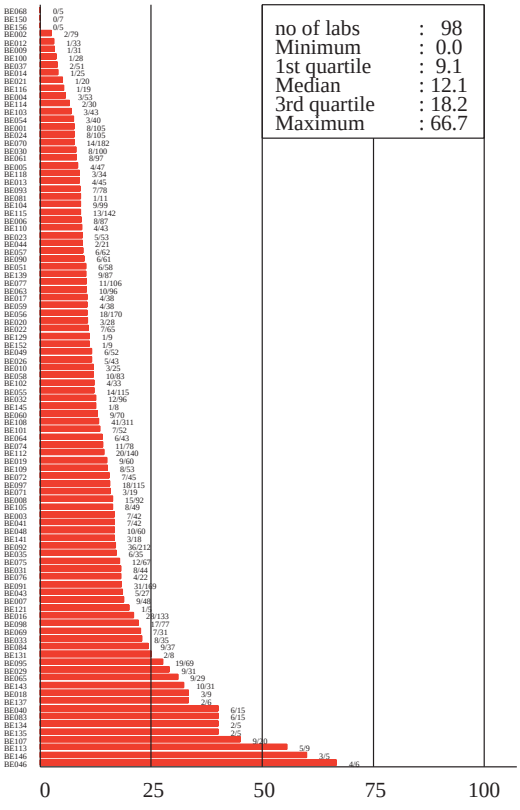
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	4	5	<1	<1	<1
	Penicillin I+R	13	16	13	14	12
	Macrolides I+R	31	34	35	34	34
S. aureus	Oxacillin/Methicillin R	23	21	23	28	29
E. coli	Aminopenicillins R	.	.	53	47	50
	Aminoglycosides R	.	.	4	6	5
	Fluoroquinolones R	.	.	9	13	12
	3rd gen. Cephalosporins R	.	.	2	3	3
E. faecalis	Aminopenicillins I+R	.	.	<1	<1	1
	Aminoglycosides (high-level resistance)	.	.	20	20	17
	Glycopeptides I+R	.	.	<1	3	1
E. faecium	Aminopenicillins I+R	.	.	60	56	78
	Aminoglycosides (high-level resistance)	.	.	<1	5	<1
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=5546		*S. aureus* n=4265		*E. coli* n=2362		*E. faecalis* n=330		*E. faecium* n=54	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	94	14	100	26	100	12	100	2	100	0
CSF	6	10	0	.	0	.	0	.	0	.
Sex										
Male	56	13	59	26	44	13	62	2	54	0
Female	43	14	40	25	55	11	36	1	43	0
Unknown	1	13	1	21	1	18	2	13	4	0
Age (years)										
0-4	19	17	4	8	3	1	4	8	4	0
5-19	6	4	3	6	1	0	1	0	0	.
20-64	30	9	33	20	28	12	28	0	39	0
65 and over	45	16	59	31	68	13	67	3	57	0
Unknown	0	.	2	20	0	.	0	.	0	.
Hospital department										
ICU	13	13	16	35	9	9	24	4	33	0
Internal Medicine	34	13	33	19	32	12	38	2	28	0
Surgery	2	16	11	27	6	8	11	0	7	0
Other	27	13	25	29	52	13	25	1	28	0
Unknown	23	14	16	22	1	9	2	0	4	0

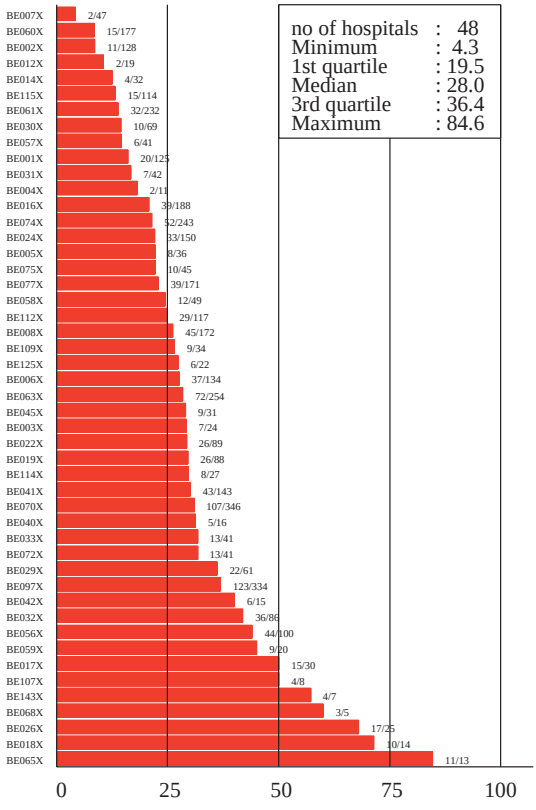
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Bulgaria

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	22/22
Labs/Hosps providing denom.data *	19/18
Number of blood culture sets *	15549
Number of hospital beds *	9168
Average annual occupancy rate *	76%
Estimated catchment population *	7621000
% total population covered *	100%

*** Based on labs/hospitals providing denominator data**

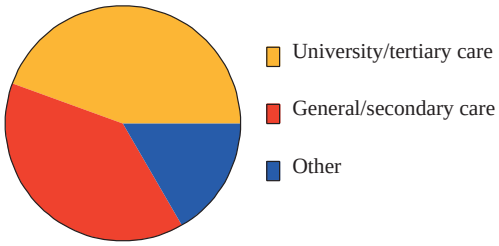


Figure 1. Type of hospitals in 2002

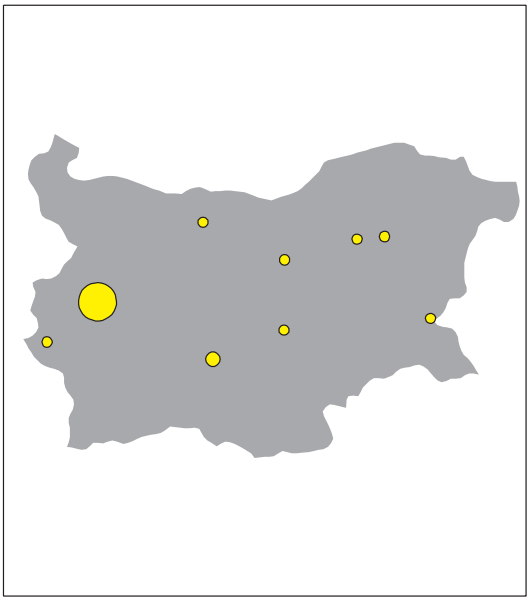


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	8	13	16	111	0	0	0	0
2001	8	16	17	103	15	98	11	30
2002	11	25	21	116	20	135	16	42
2003	13	22	20	157	20	158	16	49

Antibiotic resistance in 1999-2003

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

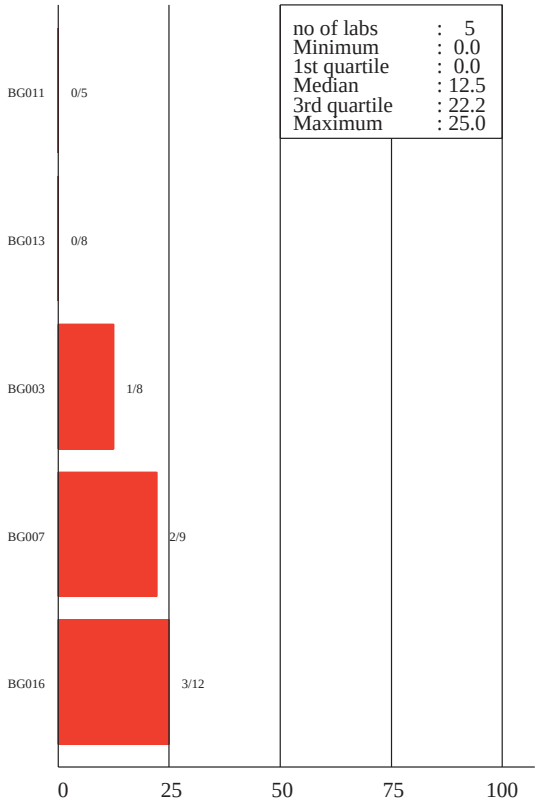
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	23	6	8	9
	Penicillin I+R	.	23	6	8	14
	Macrolides I+R	.	25	9	9	11
S. aureus	Oxacillin/Methicillin R	.	37	27	33	31
E. coli	Aminopenicillins R	.	.	48	52	56
	Aminoglycosides R	.	.	16	17	22
	Fluoroquinolones R	.	.	8	14	19
	3rd gen. Cephalosporins R	.	.	7	13	18
E. faecalis	Aminopenicillins I+R	.	.	5	26	7
	Aminoglycosides (high-level resistance)	.	.	30	63	36
	Glycopeptides I+R	.	.	<1	4	<1
E. faecium	Aminopenicillins I+R	.	.	50	71	60
	Aminoglycosides (high-level resistance)	.	.	33	83	60
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=76		*S. aureus* n=487		*E. coli* n=379		*E. faecalis* n=97		*E. faecium* n=24	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	50	8	100	32	98	15	100	1	100	0
CSF	50	16	0	.	2	0	0	.	0	.
Sex										
Male	67	16	61	31	47	22	66	2	58	0
Female	32	4	39	33	53	9	34	0	42	0
Unknown	1	0	0	.	0	.	0	.	0	.
Age (years)										
0-4	13	40	13	48	12	11	10	0	8	0
5-19	14	18	7	19	4	20	1	0	0	.
20-64	51	3	55	31	48	13	48	2	67	0
65 and over	16	17	22	27	35	17	37	0	13	0
Unknown	5	0	4	40	1	40	3	0	13	0
Hospital department										
ICU	12	0	17	51	9	14	21	0	46	0
Internal Medicine	43	12	37	22	45	8	42	0	21	0
Surgery	8	0	15	34	16	24	14	7	13	0
Other	37	18	32	33	30	20	23	0	21	0
Unknown	0	.	0	.	0	.	0	.	0	.

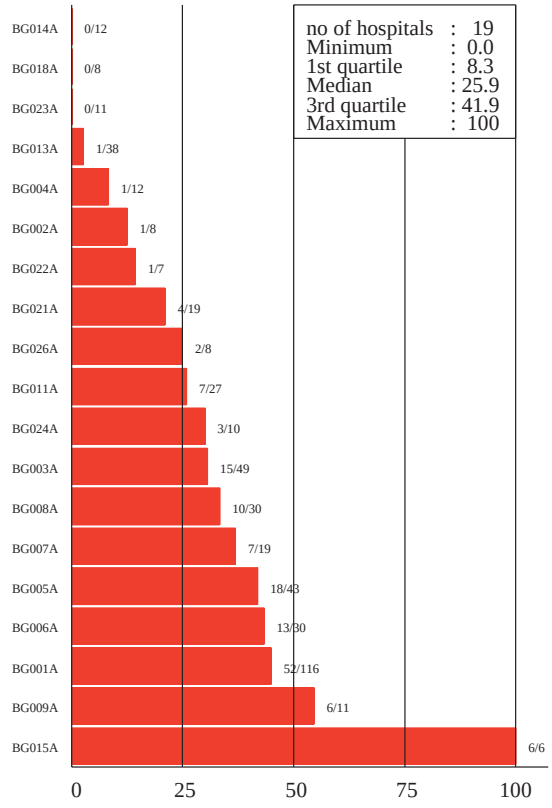
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Croatia

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	15/15
Labs/Hosps providing denom.data *	15/15
Number of blood culture sets *	34742
Number of hospital beds *	8533
Average annual occupancy rate *	91%
Estimated catchment population *	3775000
% total population covered *	86%

*** Based on labs/hospitals providing denominator data**

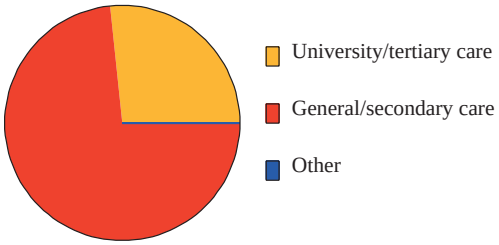


Figure 1. Type of hospitals in 2002

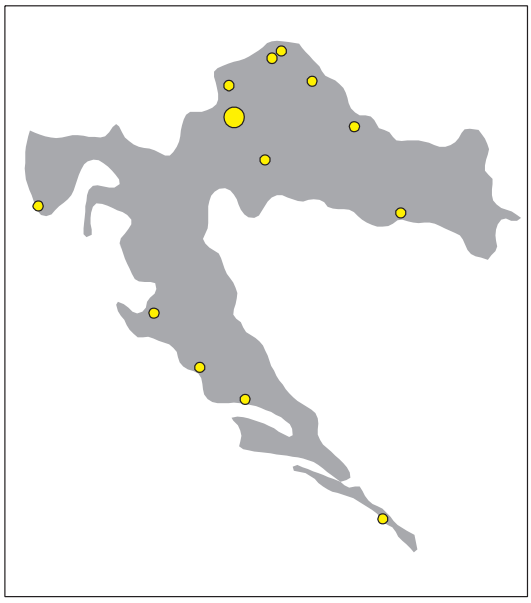


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	10	20	14	149	13	182	7	33
2002	14	90	14	279	15	490	13	96
2003	12	88	14	360	16	570	11	101

Antibiotic resistance in 1999-2003

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

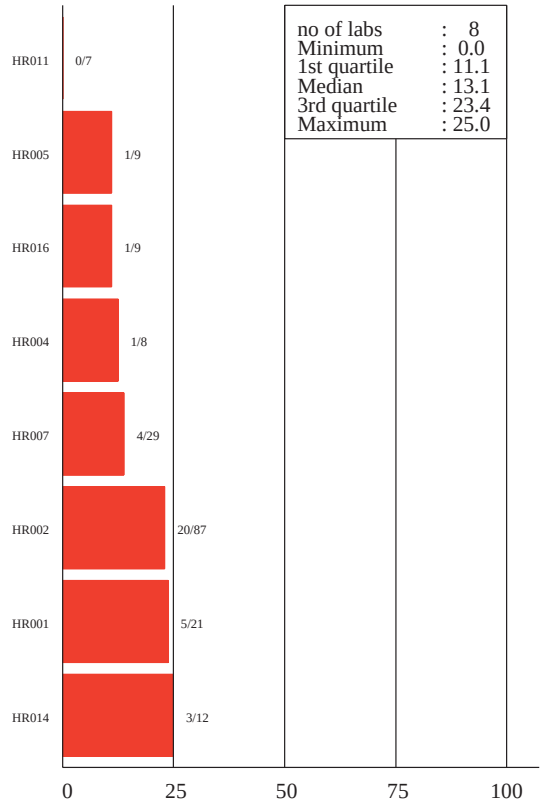
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	<1	<1	1
	Penicillin I+R	.	.	15	19	20
	Macrolides I+R	.	.	15	23	18
S. aureus	Oxacillin/Methicillin R	.	.	32	37	37
E. coli	Aminopenicillins R	.	.	51	47	47
	Aminoglycosides R	.	.	6	7	7
	Fluoroquinolones R	.	.	5	5	7
	3rd gen. Cephalosporins R	.	.	2	3	4
E. faecalis	Aminopenicillins I+R	.	.	13	5	4
	Aminoglycosides (high-level resistance)	.	.	50	40	28
	Glycopeptides I+R	.	.	3	<1	<1
E. faecium	Aminopenicillins I+R	.	.	100	56	47
	Aminoglycosides (high-level resistance)	.	.	100	67	41
	Glycopeptides I+R	.	.	<1	22	6

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=198		n=788		n=1214		n=179		n=51	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	86	19	100	36	100	6	100	1	100	12
CSF	14	18	0	.	0	.	0	.	0	.
Sex										
Male	63	21	65	35	40	8	65	0	61	13
Female	37	16	35	37	59	5	35	2	39	10
Unknown	0	.	0	.	1	13	0	.	0	.
Age (years)										
0-4	31	23	3	12	7	0	11	0	10	20
5-19	8	27	3	12	2	15	2	0	4	50
20-64	37	16	48	35	34	6	34	0	37	11
65 and over	23	15	46	40	57	7	53	1	49	8
Unknown	1	100	0	.	0	.	0	.	0	.
Hospital department										
ICU	16	19	16	64	7	6	17	0	14	0
Internal Medicine	22	16	41	26	41	5	33	0	47	13
Surgery	1	100	12	68	3	5	9	0	4	0
Other	62	20	30	21	49	7	41	1	35	17
Unknown	0	.	0	.	0	.	0	.	0	.

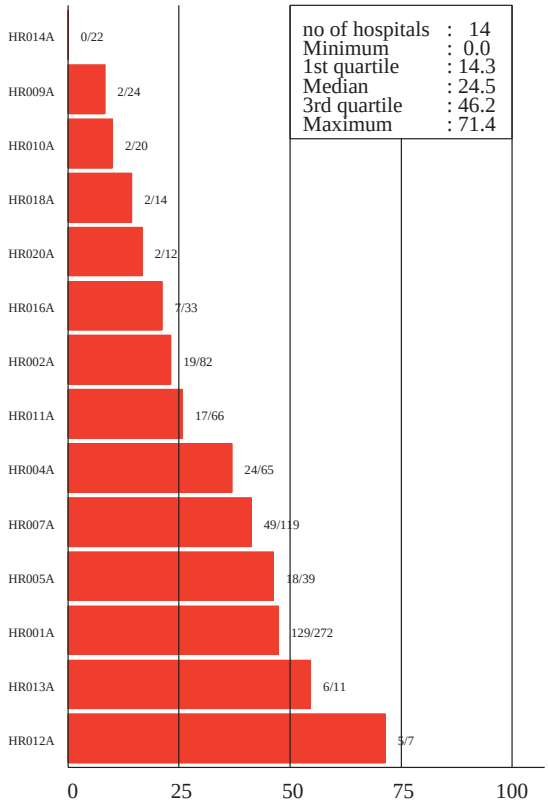
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Czech Republic

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	42/95
Labs/Hosps providing denom.data *	42/82
Number of blood culture sets *	76188
Number of hospital beds *	44322
Average annual occupancy rate *	78%
Estimated catchment population *	8283000
% total population covered *	81%

*** Based on labs/hospitals providing denominator data**

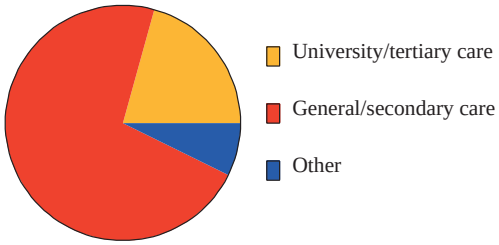


Figure 1. Type of hospitals in 2002

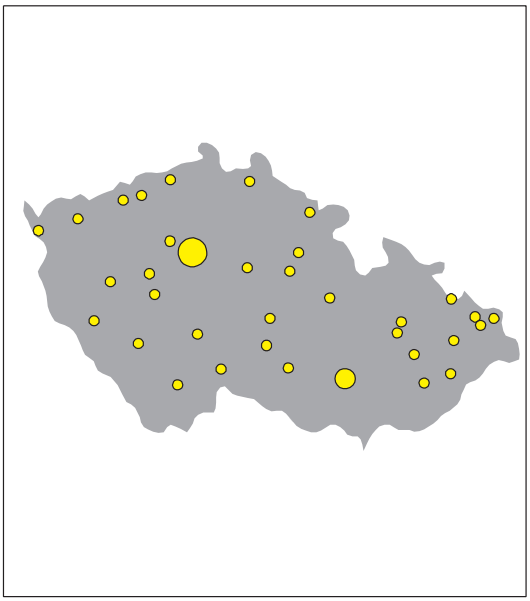


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	26	111	31	515	0	0	0	0
2001	32	154	39	1074	36	1176	34	461
2002	34	144	41	1168	40	1587	39	587
2003	32	204	45	1387	43	1766	44	630

Antibiotic resistance in 1999-2003

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

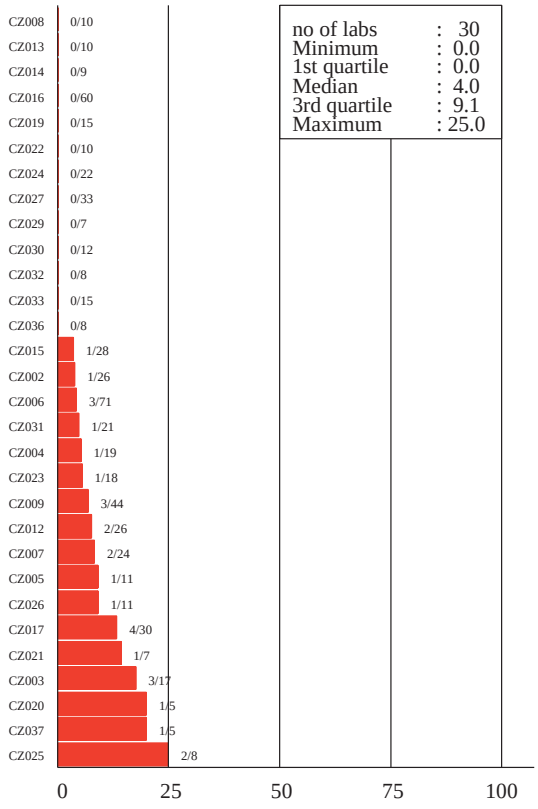
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	<1	<1	<1	<1
	Penicillin I+R	.	4	7	8	2
	Macrolides I+R	.	1	2	4	2
S. aureus	Oxacillin/Methicillin R	.	4	6	6	6
E. coli	Aminopenicillins R	.	.	42	45	45
	Aminoglycosides R	.	.	6	6	5
	Fluoroquinolones R	.	.	8	10	13
	3rd gen. Cephalosporins R	.	.	2	1	1
E. faecalis	Aminopenicillins I+R	.	.	3	2	4
	Aminoglycosides (high-level resistance)	.	.	38	39	44
	Glycopeptides I+R	.	.	2	<1	<1
E. faecium	Aminopenicillins I+R	.	.	67	73	80
	Aminoglycosides (high-level resistance)	.	.	33	35	48
	Glycopeptides I+R	.	.	2	9	3

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=613		n=4144		n=4524		n=1428		n=238	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	72	6	100	6	100	11	100	1	100	5
CSF	28	4	0	.	0	.	0	.	0	.
Sex										
Male	62	5	59	6	42	12	62	1	59	4
Female	38	6	41	5	58	10	38	0	41	5
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	12	10	4	4	5	3	6	0	5	0
5-19	8	0	3	5	1	6	1	0	3	0
20-64	50	5	45	6	34	12	46	1	49	6
65 and over	30	5	47	6	61	11	47	1	44	4
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	18	4	15	10	10	11	28	0	30	3
Internal Medicine	40	6	49	4	54	11	32	1	31	3
Surgery	2	15	13	8	10	11	15	1	9	5
Other	39	4	22	5	25	10	25	1	29	7
Unknown	0	.	0	.	0	.	0	.	0	.

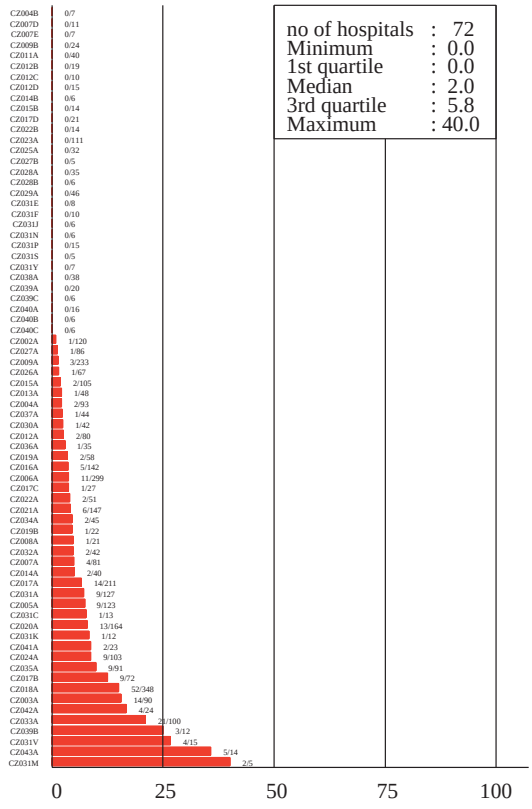
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Denmark

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	5/35
Labs/Hosps providing denom.data *	0/35
Number of blood culture sets *	na
Number of hospital beds *	na
Average annual occupancy rate *	na
Estimated catchment population *	2490000
% total population covered *	46%

*** Based on labs/hospitals providing denominator data**

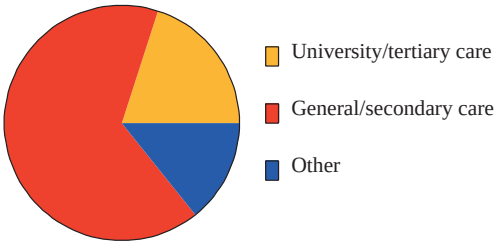


Figure 1. Type of hospitals in 2002

Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	5	718	0	0	0	0
2000	5	410	4	501	0	0	0	0
2001	5	506	4	520	0	0	0	0
2002	5	366	5	752	0	0	0	0
2003	5	606	5	671	0	0	0	0

Antibiotic resistance in 1999-2003

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

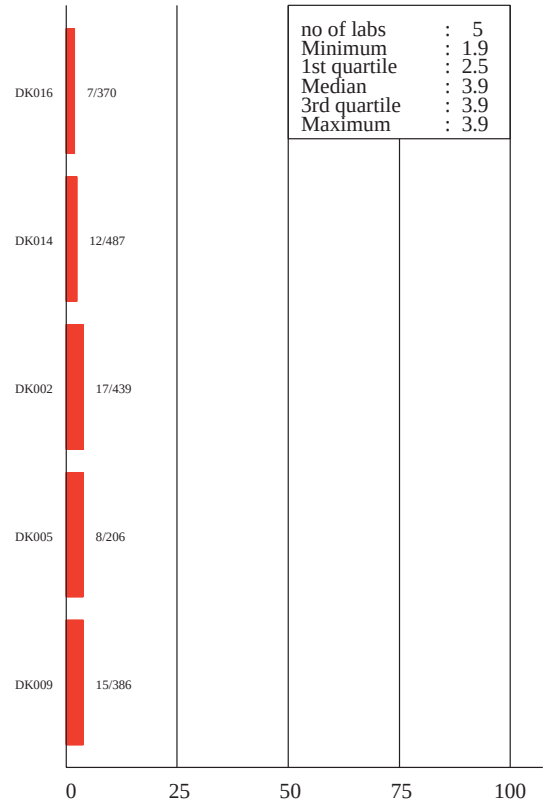
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	<1	<1	<1	<1
	Penicillin I+R	.	4	3	4	3
	Macrolides I+R	.	5	5	5	5
S. aureus	Oxacillin/Methicillin R	< 1	<1	<1	<1	<1
E. coli	Aminopenicillins R	.	.	.	.	.
	Aminoglycosides R	.	.	.	.	.
	Fluoroquinolones R	.	.	.	.	.
	3rd gen. Cephalosporins R	.	.	.	.	.
E. faecalis	Aminopenicillins I+R	.	.	.	.	.
	Aminoglycosides (high-level resistance)	.	.	.	.	.
	Glycopeptides I+R	.	.	.	.	.
E. faecium	Aminopenicillins I+R	.	.	.	.	.
	Aminoglycosides (high-level resistance)	.	.	.	.	.
	Glycopeptides I+R	.	.	.	.	.

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=1888		n=3162		n=0		n=0		n=0	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	91	3	100	1	.	.	.	.	.	.
CSF	9	2	0	.	.	.	.	.	.	.
Sex										
Male	49	3	58	1	.	.	.	.	.	.
Female	51	3	39	0	.	.	.	.	.	.
Unknown	0	.	2	1	.	.	.	.	.	.
Age (years)										
0-4	8	5	1	0	.	.	.	.	.	.
5-19	2	5	3	1	.	.	.	.	.	.
20-64	39	3	41	1	.	.	.	.	.	.
65 and over	51	3	54	1	.	.	.	.	.	.
Unknown	0	.	0	.	.	.	.	.	.	.
Hospital department										
ICU	0	.	5	0	.	.	.	.	.	.
Internal Medicine	0	.	49	1	.	.	.	.	.	.
Surgery	0	.	18	0	.	.	.	.	.	.
Other	0	.	16	1	.	.	.	.	.	.
Unknown	100	3	11	1	.	.	.	.	.	.

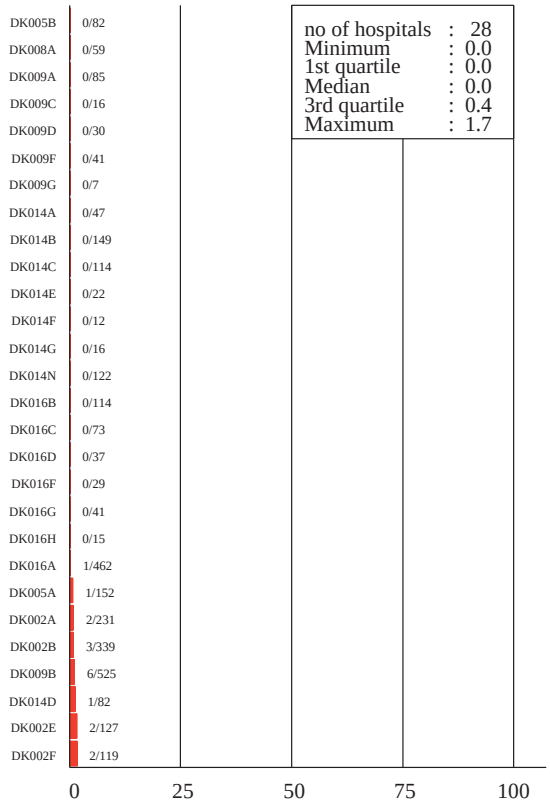
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Estonia

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	8/12
Labs/Hosps providing denom.data *	7/7
Number of blood culture sets *	4217
Number of hospital beds *	3021
Average annual occupancy rate *	75%
Estimated catchment population *	1416000
% total population covered *	100%

*** Based on labs/hospitals providing denominator data**

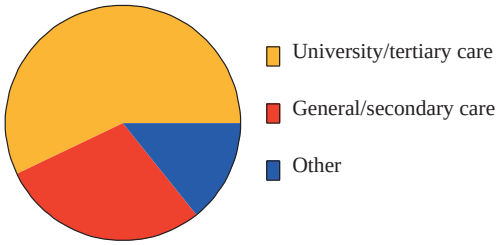


Figure 1. Type of hospitals in 2002

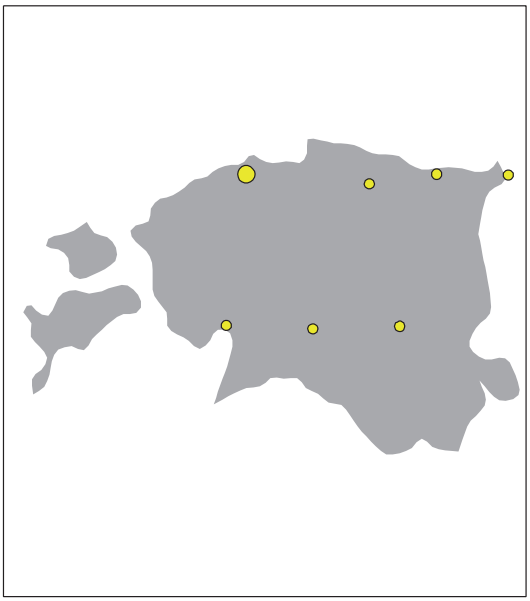


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	5	20	6	79	4	52	4	21
2002	5	21	8	81	6	67	3	13
2003	8	26	9	98	9	98	6	27

Antibiotic resistance in 1999-2003

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

Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	<1	<1	<1
	Penicillin I+R	.	.	<1	<1	<1
	Macrolides I+R	.	.	5	<1	10
S. aureus	Oxacillin/Methicillin R	.	.	5	1	4
E. coli	Aminopenicillins R	.	.	43	42	42
	Aminoglycosides R	.	.	8	10	3
	Fluoroquinolones R	.	.	<1	5	5
	3rd gen. Cephalosporins R	.	.	6	2	1
E. faecalis	Aminopenicillins I+R	.	.	8	10	4
	Aminoglycosides (high-level resistance)	.	.	<1	50	22
	Glycopeptides I+R	.	.	<1	<1	5
E. faecium	Aminopenicillins I+R	.	.	63	33	75
	Aminoglycosides (high-level resistance)	.	.	63	67	50
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

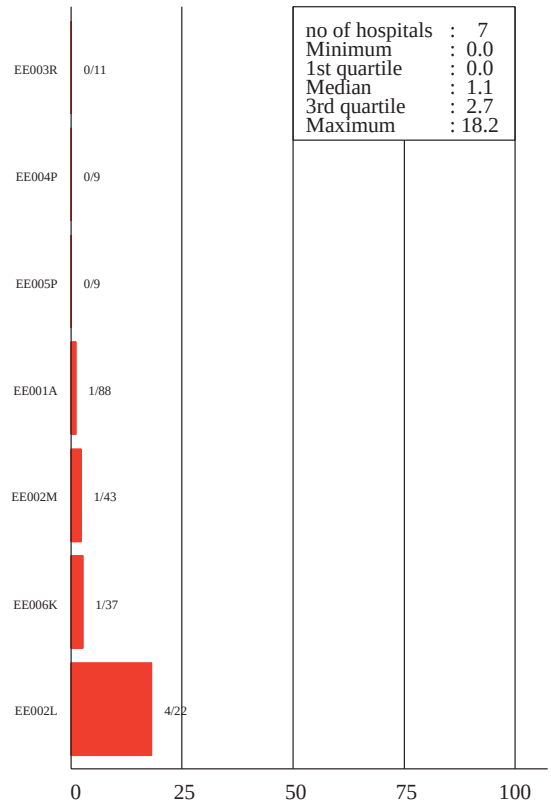
Characteristic	*S. pneumoniae* n=67		*S. aureus* n=258		*E. coli* n=193		*E. faecalis* n=45		*E. faecium* n=15	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	48	0	100	3	99	4	100	2	100	0
CSF	52	0	0	.	1	0	0	.	0	.
Sex										
Male	69	0	56	6	34	5	49	5	73	0
Female	28	0	38	1	64	3	44	0	27	0
Unknown	3	0	6	0	2	0	7	0	0	.
Age (years)										
0-4	6	0	10	11	5	0	29	8	13	0
5-19	9	0	7	6	2	0	0	.	7	0
20-64	34	0	35	1	33	2	16	0	27	0
65 and over	4	0	11	4	31	5	24	0	40	0
Unknown	46	0	37	3	29	5	31	0	13	0
Hospital department										
ICU	36	0	18	2	20	8	18	0	33	0
Internal Medicine	13	0	29	1	27	2	9	0	7	0
Surgery	3	0	16	5	10	5	16	0	13	0
Other	48	0	37	5	41	3	58	4	47	0
Unknown	0	.	0	.	2	0	0	.	0	.

PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)

MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Finland

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	16/16
Labs/Hosps providing denom.data *	13/12
Number of blood culture sets *	121484
Number of hospital beds *	8880
Average annual occupancy rate *	86%
Estimated catchment population *	4242000
% total population covered *	82%

*** Based on labs/hospitals providing denominator data**

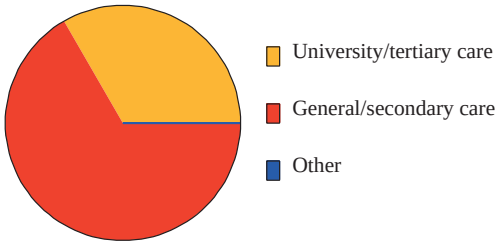


Figure 1. Type of hospitals in 2002

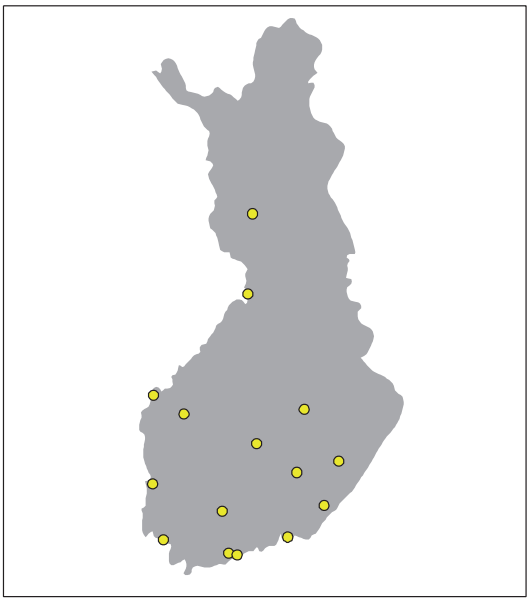


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	14	242	13	316	0	0	0	0
2000	9	176	12	362	0	0	0	0
2001	13	425	13	606	14	1284	13	274
2002	15	453	15	721	15	1330	14	278
2003	16	490	16	727	15	1450	15	266

Antibiotic resistance in 1999-2003

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

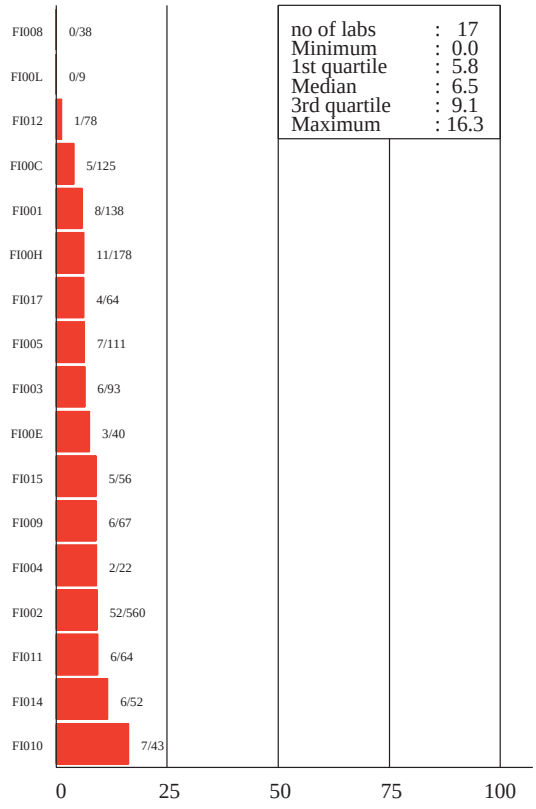
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	< 1	<1	1	2	2
	Penicillin I+R	4	5	9	6	10
	Macrolides I+R	6	8	12	14	20
S. aureus	Oxacillin/Methicillin R	< 1	1	<1	<1	1
E. coli	Aminopenicillins R	.	.	33	30	33
	Aminoglycosides R	.	.	<1	<1	1
	Fluoroquinolones R	.	.	5	6	5
	3rd gen. Cephalosporins R	.	.	<1	<1	<1
E. faecalis	Aminopenicillins I+R	.	.	1	2	<1
	Aminoglycosides (high-level resistance)	.	.	23	13	39
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	66	80	79
	Aminoglycosides (high-level resistance)	.	.	<1	<1	4
	Glycopeptides I+R	.	.	<1	1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=1786		n=2732		n=3984		n=539		n=278	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	95	8	100	1	100	6	100	0	100	0
CSF	5	6	0	.	0	.	0	.	0	.
Sex										
Male	56	6	61	1	35	5	63	0	61	0
Female	44	10	39	1	65	6	37	1	39	1
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	13	12	3	0	3	0	6	0	2	0
5-19	5	6	6	1	1	4	1	0	2	0
20-64	50	6	44	1	31	3	33	1	45	0
65 and over	32	8	46	1	65	7	60	0	51	1
Unknown	0	.	1	10	0	.	0	.	0	.
Hospital department										
ICU	2	9	2	0	0	.	0	.	2	0
Internal Medicine	15	5	17	1	10	6	13	3	17	0
Surgery	4	4	11	1	10	8	11	0	8	0
Other	40	7	30	1	34	5	32	0	31	0
Unknown	38	9	40	1	46	6	44	0	42	1

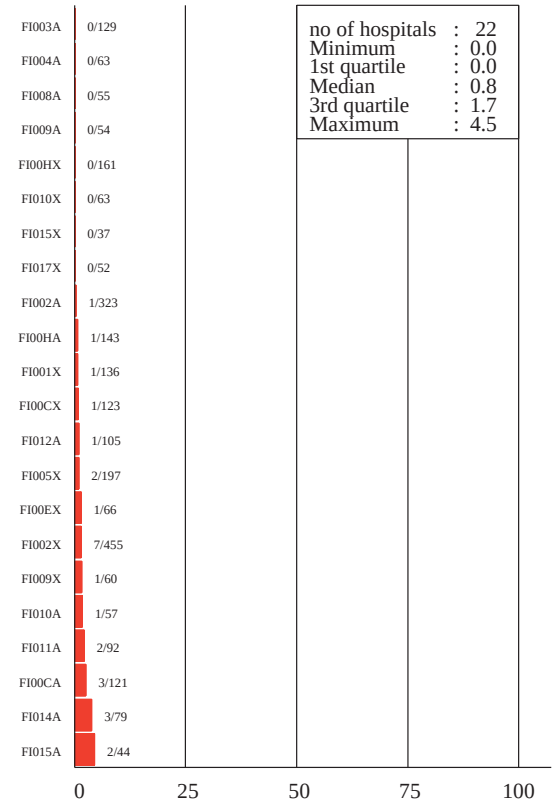
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



France

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	21/21
Labs/Hosps providing denom.data *	21/21
Number of blood culture sets *	242938
Number of hospital beds *	18804
Average annual occupancy rate *	84%
Estimated catchment population *	na
% total population covered *	na

*** Based on labs/hospitals providing denominator data**

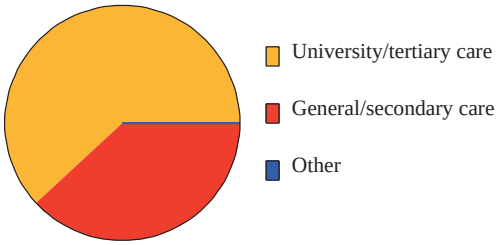


Figure 1. Type of hospitals in 2002

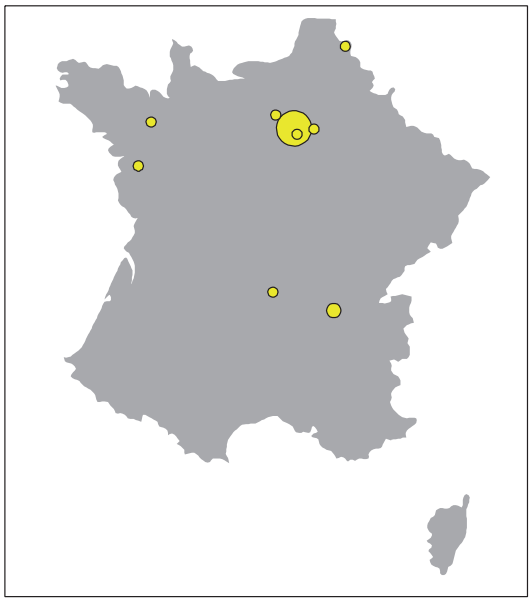


Figure 2. Geographic distribution of laboratories in 2003

The Observatoires Regionaux du Pneumocoque (ORP) and the NRC involved in invasive pneumococcal infections survey are nationwide distributed.

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae* *		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	329	1337	21	1714	0	0	0	0
2002	296	1132	21	1663	21	2495	21	467
2003	298	547 **	21	1708	21	2267	21	483

*** aggregated data** **** Two first quarters of 2003**

Antibiotic resistance in 1999-2003

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

Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	11	8	8*
	Penicillin I+R	.	.	47	48	41*
	Macrolides I+R	.	.	49	53	48*
S. aureus	Oxacillin/Methicillin R	.	.	33	33	29
E. coli	Aminopenicillins R	.	.	.	52	48
	Aminoglycosides R	.	.	.	4	5
	Fluoroquinolones R	.	.	.	8	9
	3rd gen. Cephalosporins R	.	.	.	<1	<1
E. faecalis	Aminopenicillins I+R	.	.	.	5	3
	Aminoglycosides (high-level resistance)	.	.	.	15	16
	Glycopeptides I+R	.	.	.	<1	1
E. faecium	Aminopenicillins I+R	.	.	.	34	30
	Aminoglycosides (high-level resistance)	.	.	.	10	23
	Glycopeptides I+R	.	.	.	2	<1

*** Two first quarters of 2003**

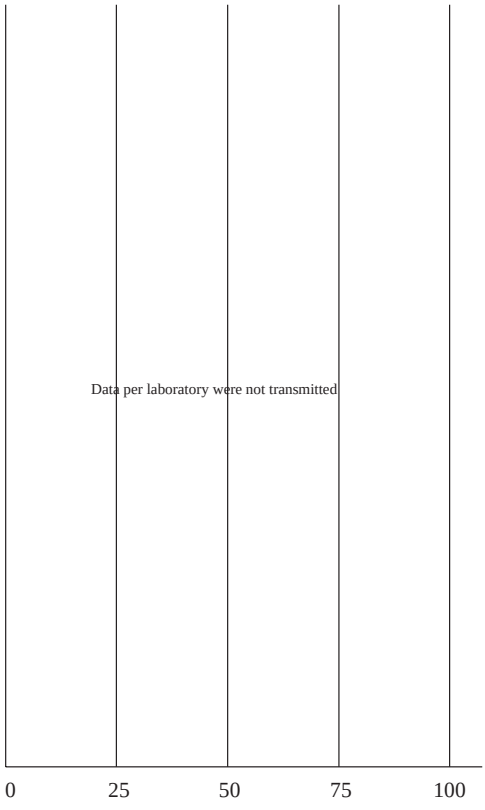
Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=2469 **		*S. aureus* n=5085		*E. coli* n=4754		*E. faecalis* n=671		*E. faecium* n=246	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	77	48	100	32	100	9	100	1	100	1
CSF	23	46	0	.	0	.	0	.	0	.
Sex										
Male	.	.	59	31	40	10	61	1	56	0
Female	.	.	32	33	48	7	30	0	39	2
Unknown	.	.	10	35	12	10	9	3	5	0
Age (years)										
0-4	29	60	3	10	2	6	4	0	4	0
5-19	6	26	3	9	1	5	1	0	2	0
20-64	30	37	44	26	41	9	42	0	47	2
65 and over	34	49	50	39	55	9	52	1	46	0
Unknown	1	90	0	.	0	.	0	.	0	.
Hospital department										
ICU	.	.	23	37	13	9	29	0	20	0
Internal Medicine	.	.	31	34	31	9	19	2	22	0
Surgery	.	.	20	32	14	11	24	1	26	2
Other	.	.	26	25	42	8	28	2	32	1
Unknown	.	.	0	.	0	.	0	.	1	0

** for 2001 and 2002

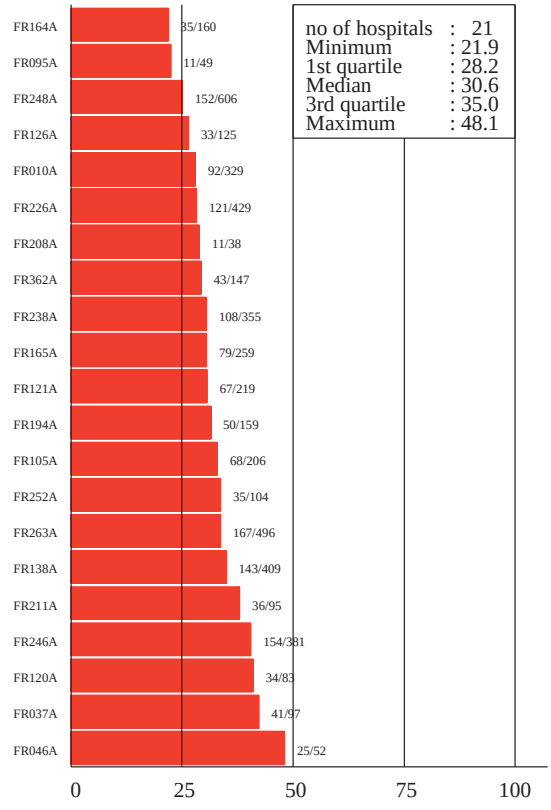
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Germany

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	19/19
Labs/Hosps providing denom.data *	2/0
Number of blood culture sets *	10317
Number of hospital beds *	na
Average annual occupancy rate *	na
Estimated catchment population *	na
% total population covered *	na

*** Based on labs/hospitals providing denominator data**

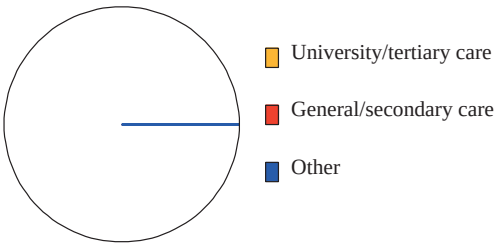


Figure 1. Type of hospitals in 2002

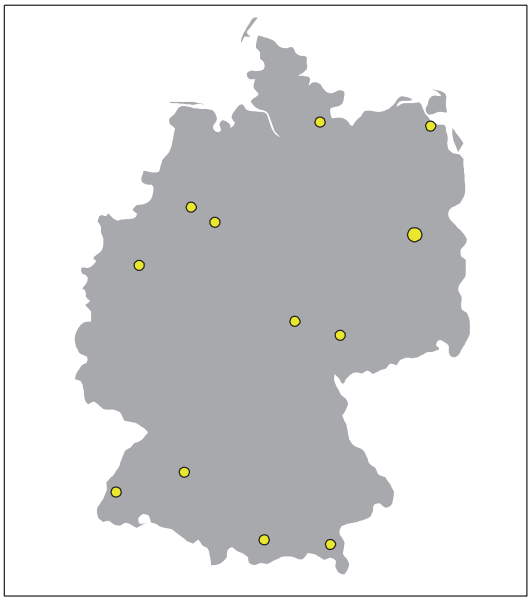


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	23	417	25	1239	0	0	0	0
2000	18	204	19	890	0	0	0	0
2001	21	211	22	1220	21	1269	20	295
2002	16	232	18	1039	16	1026	13	282
2003	9	55	12	225	12	221	8	84

Antibiotic resistance in 1999-2003

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

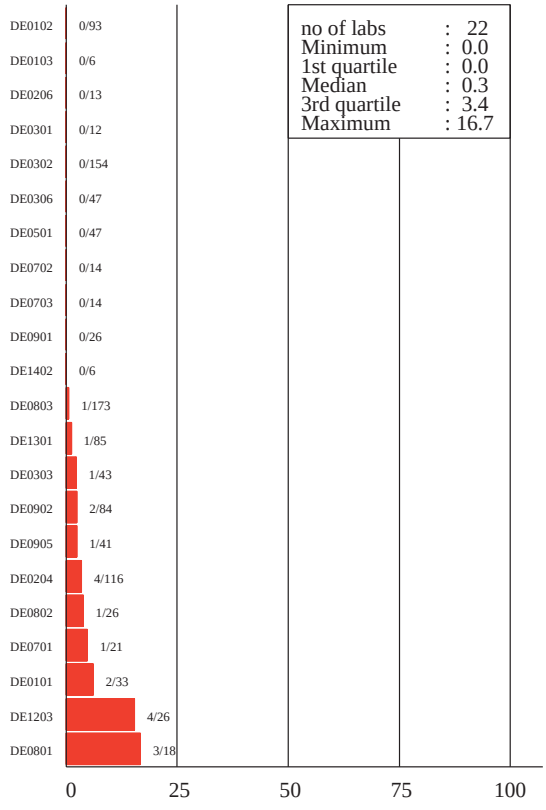
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R <	1	<1	1	<1	<1
	Penicillin I+R	2	2	4	1	<1
	Macrolides I+R	7	10	17	14	13
S. aureus	Oxacillin/Methicillin R	8	12	16	19	18
E. coli	Aminopenicillins R	.	.	46	50	47
	Aminoglycosides R	.	.	5	5	5
	Fluoroquinolones R	.	.	11	15	15
	3rd gen. Cephalosporins R	.	.	<1	<1	<1
E. faecalis	Aminopenicillins I+R	.	.	8	9	7
	Aminoglycosides (high-level resistance)	.	.	31	42	38
	Glycopeptides I+R	.	.	<1	1	<1
E. faecium	Aminopenicillins I+R	.	.	79	79	69
	Aminoglycosides (high-level resistance)	.	.	43	68	38
	Glycopeptides I+R	.	.	1	6	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=1119		*S. aureus* n=4613		*E. coli* n=2470		*E. faecalis* n=479		*E. faecium* n=164	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	93	2	100	14	100	13	100	1	100	3
CSF	7	3	0	.	0	.	0	.	0	.
Sex										
Male	50	3	52	16	37	14	60	1	58	3
Female	38	2	35	13	50	13	33	1	40	3
Unknown	13	1	13	7	13	12	7	0	2	0
Age (years)										
0-4	9	4	3	7	2	0	2	0	4	0
5-19	3	7	2	8	1	13	0	.	1	0
20-64	43	3	39	13	27	14	38	2	43	1
65 and over	44	1	55	15	70	13	59	0	52	5
Unknown	1	0	1	15	0	.	1	0	1	0
Hospital department										
ICU	17	4	19	26	12	13	26	0	30	6
Internal Medicine	48	1	44	10	53	11	38	1	31	2
Surgery	2	0	9	12	6	14	8	3	10	0
Other	22	2	18	12	22	17	23	1	26	0
Unknown	12	1	10	10	8	15	5	0	3	20

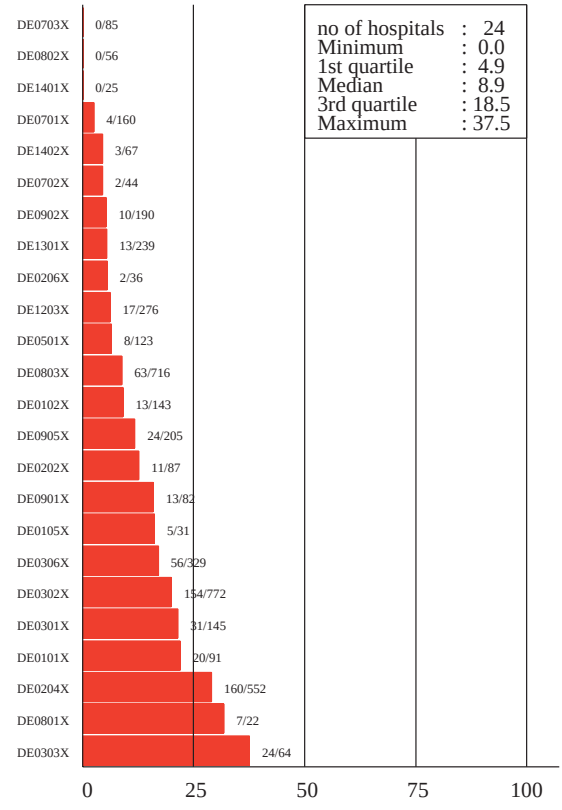
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Greece

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	36/36
Labs/Hosps providing denom.data *	0/0
Number of blood culture sets *	na
Number of hospital beds *	na
Average annual occupancy rate *	na
Estimated catchment population *	na
% total population covered *	na

*** Based on labs/hospitals providing denominator data**

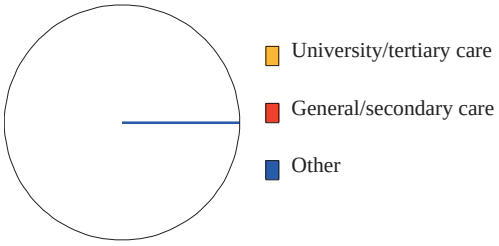


Figure 1. Type of hospitals in 2002

Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	19	192	0	0	0	0
2000	0	0	15	356	0	0	0	0
2001	0	0	25	358	26	619	25	304
2002	0	0	33	368	35	588	28	293
2003	0	0	30	321	30	507	30	320

Antibiotic resistance in 1999-2003

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

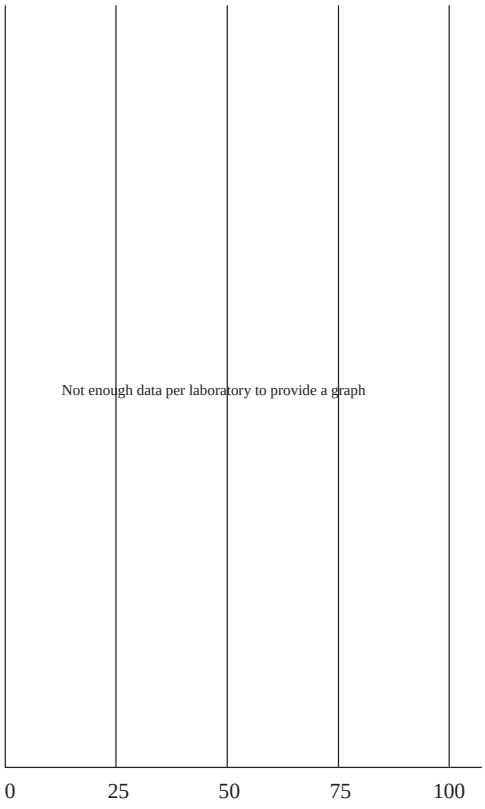
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	.	.	.
	Penicillin I+R	.	.	.	.	.
	Macrolides I+R	.	.	.	.	.
S. aureus	Oxacillin/Methicillin R	31	51	40	44	51
E. coli	Aminopenicillins R	.	.	46	46	43
	Aminoglycosides R	.	.	5	7	7
	Fluoroquinolones R	.	.	8	13	10
	3rd gen. Cephalosporins R	.	.	5	6	5
E. faecalis	Aminopenicillins I+R	.	.	8	4	3
	Aminoglycosides (high-level resistance)	.	.	57	60	57
	Glycopeptides I+R	.	.	10	15	9
E. faecium	Aminopenicillins I+R	.	.	86	75	88
	Aminoglycosides (high-level resistance)	.	.	45	52	38
	Glycopeptides I+R	.	.	18	19	23

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=0		n=1595		n=1662		n=633		n=254	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	.	.	100	44	100	11	100	11	100	20
CSF	.	.	0	.	0	.	0	.	0	.
Sex										
Male	.	.	16	39	12	11	15	11	18	27
Female	.	.	11	42	19	7	13	12	11	33
Unknown	.	.	73	46	69	11	72	11	72	16
Age (years)										
0-4	.	.	0	.	0	.	0	.	0	.
5-19	.	.	1	0	0	.	0	.	0	.
20-64	.	.	1	42	2	13	1	0	1	33
65 and over	.	.	1	48	2	17	3	5	2	33
Unknown	.	.	97	45	96	10	96	12	96	20
Hospital department										
ICU	.	.	17	70	3	16	42	18	39	23
Internal Medicine	.	.	59	37	78	10	39	4	44	15
Surgery	.	.	11	55	10	14	12	13	8	19
Other	.	.	5	21	2	4	1	0	1	50
Unknown	.	.	7	45	7	16	5	7	8	30

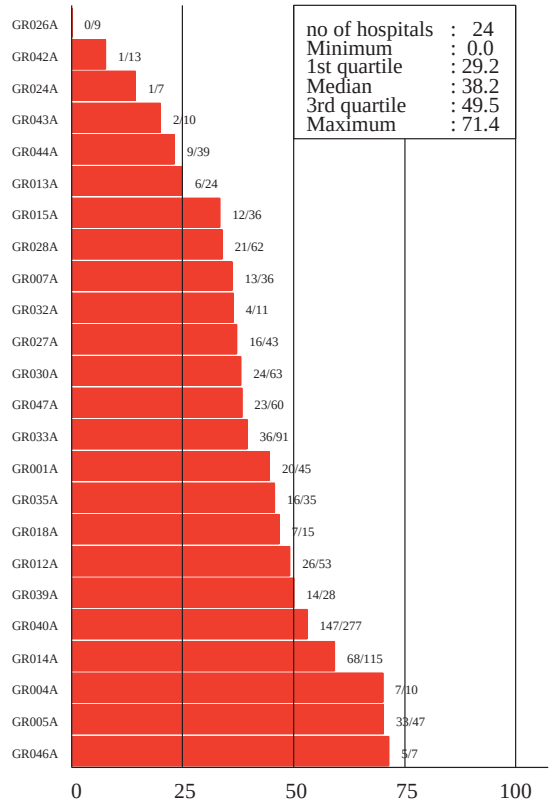
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Hungary

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	26/69
Labs/Hosps providing denom.data *	26/56
Number of blood culture sets *	19656
Number of hospital beds *	34569
Average annual occupancy rate *	78%
Estimated catchment population *	9312000
% total population covered *	92%

*** Based on labs/hospitals providing denominator data**

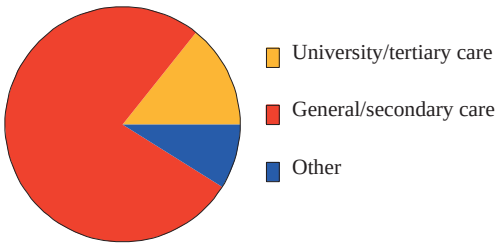


Figure 1. Type of hospitals in 2002

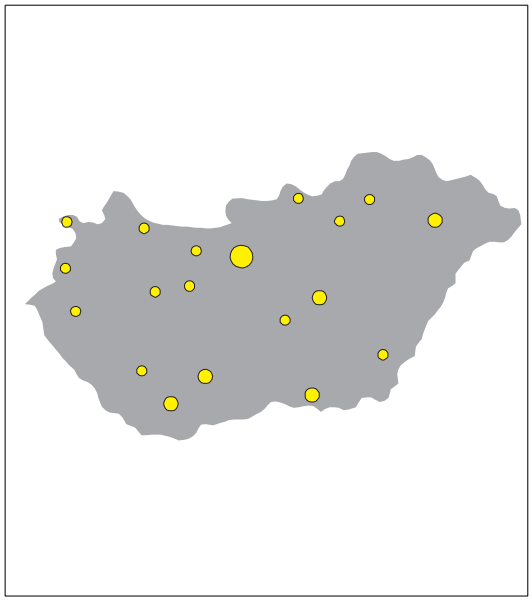


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	14	36	18	301	18	264	17	121
2002	17	61	24	413	24	354	23	169
2003	20	134	27	858	27	842	25	279

Antibiotic resistance in 1999-2003

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

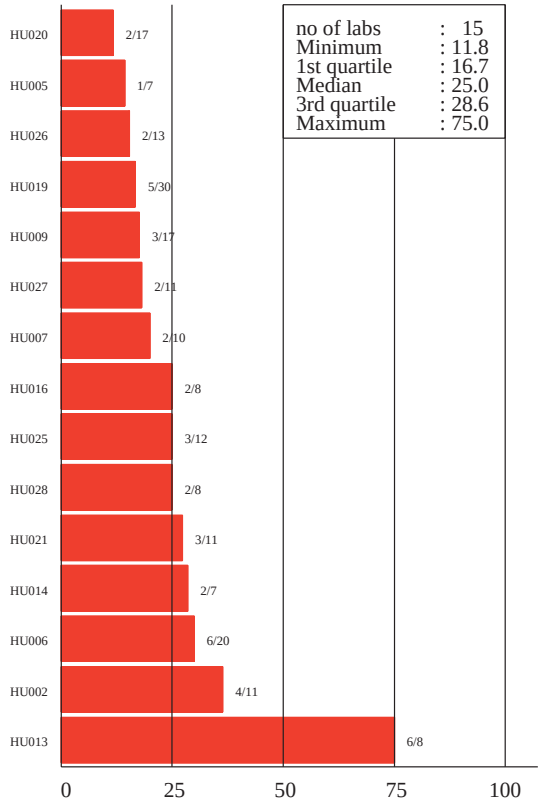
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	8	3	3
	Penicillin I+R	.	.	22	23	24
	Macrolides I+R	.	.	19	21	25
S. aureus	Oxacillin/Methicillin R	.	.	5	9	15
E. coli	Aminopenicillins R	.	.	47	45	49
	Aminoglycosides R	.	.	4	6	8
	Fluoroquinolones R	.	.	5	10	15
	3rd gen. Cephalosporins R	.	.	<1	2	<1
E. faecalis	Aminopenicillins I+R	.	.	5	2	<1
	Aminoglycosides (high-level resistance)	.	.	.	100	87
	Glycopeptides I+R	.	.	<1	3	<1
E. faecium	Aminopenicillins I+R	.	.	100	89	91
	Aminoglycosides (high-level resistance)	.	.	.	100	96
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=231		*S. aureus* n=1572		*E. coli* n=1397		*E. faecalis* n=481		*E. faecium* n=77	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	67	26	100	11	98	12	100	1	100	0
CSF	33	18	0	.	2	0	0	.	0	.
Sex										
Male	66	24	61	12	53	14	56	1	53	0
Female	33	24	37	11	46	10	44	2	47	0
Unknown	1	0	1	6	1	0	1	0	0	.
Age (years)										
0-4	13	39	2	9	3	0	2	0	9	0
5-19	5	8	2	11	1	12	2	0	1	0
20-64	55	21	50	11	41	12	50	1	42	0
65 and over	27	24	45	12	55	13	45	2	48	0
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	17	15	15	29	10	12	25	0	35	0
Internal Medicine	29	25	37	6	42	11	28	2	14	0
Surgery	2	20	12	17	7	12	9	2	18	0
Other	41	23	19	8	29	14	22	0	27	0
Unknown	11	32	17	8	12	11	16	3	5	0

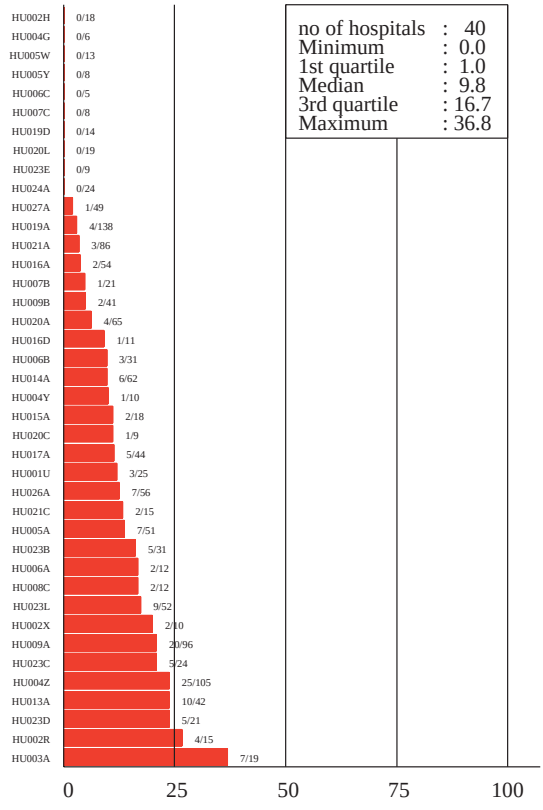
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Iceland

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	2/2
Labs/Hosps providing denom.data *	2/2
Number of blood culture sets *	8647
Number of hospital beds *	1139
Average annual occupancy rate *	92%
Estimated catchment population *	279000
% total population covered *	100%

*** Based on labs/hospitals providing denominator data**

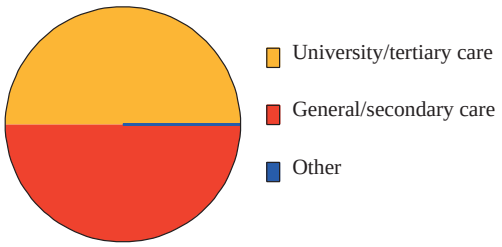


Figure 1. Type of hospitals in 2002

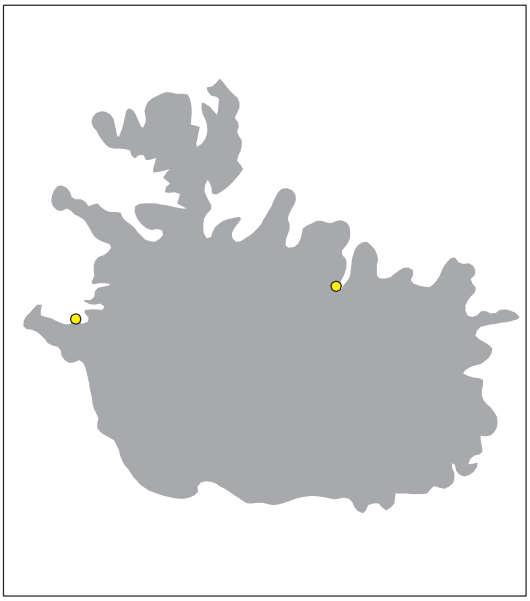


Figure 2. Geographic distribution of laboratories in 2003

Iceland counts 9 hospitals that all report AST-results to EARSS. However, only 2 of these are relevant to EARSS with respect to denominator information, because these are the main hospitals to provide acute and general care.

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	1	48	1	32	0	0	0	0
2000	1	36	1	40	0	0	0	0
2001	2	48	2	63	2	86	2	18
2002	2	43	2	60	2	83	2	25
2003	2	35	2	64	2	100	2	22

Antibiotic resistance in 1999-2003

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

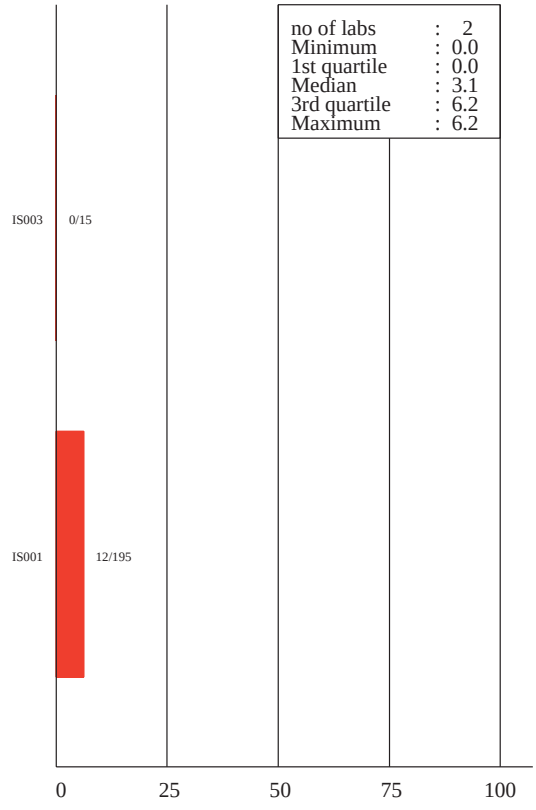
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	< 1	<1	<1	2	<1
	Penicillin I+R	2	8	6	5	9
	Macrolides I+R	3	11	8	5	20
S. aureus	Oxacillin/Methicillin R	< 1	3	<1	<1	<1
E. coli	Aminopenicillins R	.	.	42	33	42
	Aminoglycosides R	.	.	4	1	2
	Fluoroquinolones R	.	.	4	3	6
	3rd gen. Cephalosporins R	.	.	<1	<1	1
E. faecalis	Aminopenicillins I+R	.	.	<1	<1	<1
	Aminoglycosides (high-level resistance)	.	.	8	6	<1
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	40	29	57
	Aminoglycosides (high-level resistance)	.	.	<1	<1	<1
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=210		*S. aureus* n=259		*E. coli* n=245		*E. faecalis* n=46		*E. faecium* n=19	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	95	6	100	0	100	4	100	0	100	0
CSF	5	9	0	.	0	.	0	.	0	.
Sex										
Male	50	5	60	1	42	6	63	0	47	0
Female	50	7	40	0	58	3	37	0	53	0
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	22	6	9	0	2	0	4	0	5	0
5-19	3	0	12	0	2	0	2	0	0	.
20-64	38	5	38	0	31	5	15	0	11	0
65 and over	37	6	41	1	66	4	78	0	84	0
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	4	11	2	0	0	.	0	.	0	.
Internal Medicine	7	0	9	0	6	7	4	0	5	0
Surgery	0	.	3	0	3	14	7	0	0	.
Other	22	7	15	3	3	0	4	0	5	0
Unknown	67	6	71	0	88	4	85	0	89	0

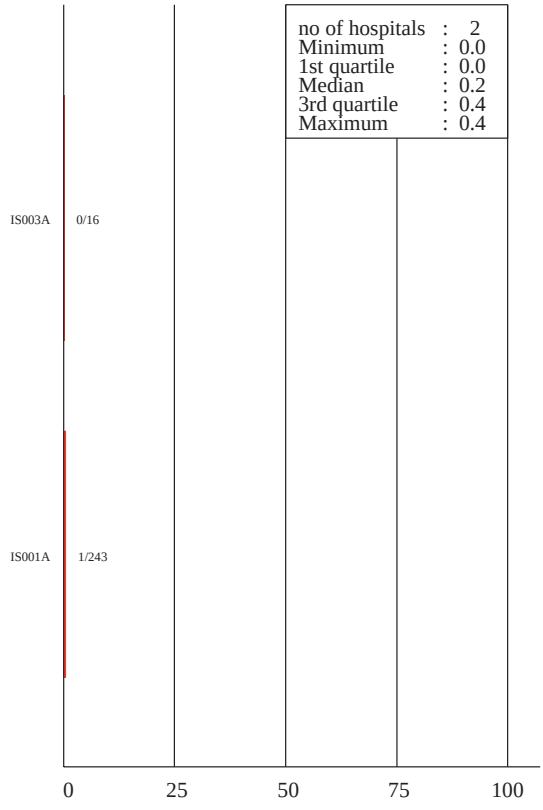
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Ireland

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	22/22
Labs/Hosps providing denom.data *	21/43
Number of blood culture sets *	na
Number of hospital beds *	9643
Average annual occupancy rate *	85%
Estimated catchment population *	3500000
% total population covered *	90%

*** Based on labs/hospitals providing denominator data**

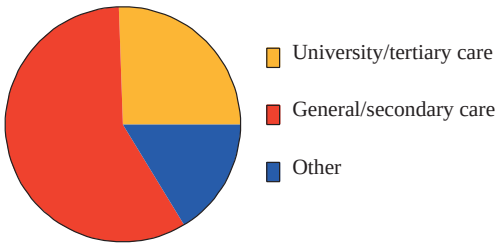


Figure 1. Type of hospitals in 2002

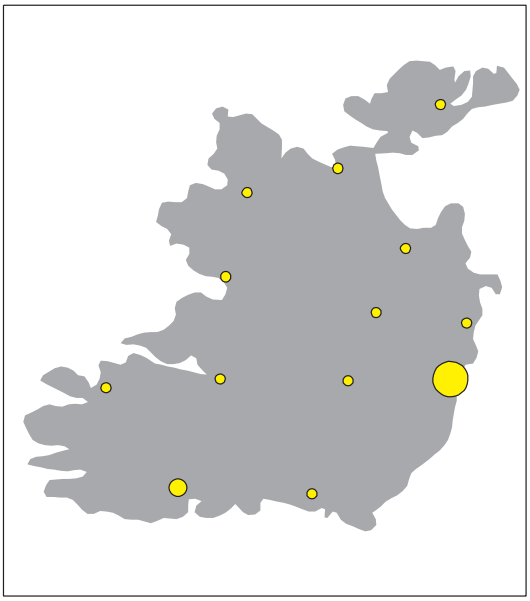


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	10	154	11	511	0	0	0	0
2000	18	202	18	632	0	0	0	0
2001	21	246	19	798	0	0	0	0
2002	20	277	22	998	20	736	15	250
2003	23	362	25	1109	25	976	21	348

Antibiotic resistance in 1999-2003

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

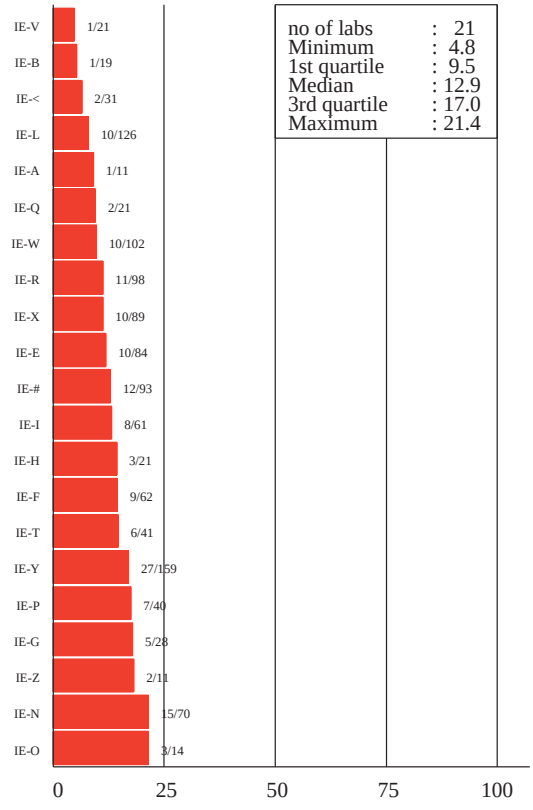
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	3	5	2	2	3
	Penicillin I+R	19	13	12	12	12
	Macrolides I+R	14	12	12	13	12
S. aureus	Oxacillin/Methicillin R	39	39	42	42	42
E. coli	Aminopenicillins R	.	.	.	62	61
	Aminoglycosides R	.	.	.	3	4
	Fluoroquinolones R	.	.	.	5	10
	3rd gen. Cephalosporins R	.	.	.	2	2
E. faecalis	Aminopenicillins I+R	.	.	.	8	6
	Aminoglycosides (high-level resistance)	.	.	.	39	35
	Glycopeptides I+R	.	.	.	2	1
E. faecium	Aminopenicillins I+R	.	.	.	89	89
	Aminoglycosides (high-level resistance)	.	.	.	17	54
	Glycopeptides I+R	.	.	.	11	19

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=1241		*S. aureus* n=4048		*E. coli* n=1671		*E. faecalis* n=375		*E. faecium* n=215	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	98	13	100	41	100	8	100	2	100	16
CSF	2	24	0	.	0	.	0	.	0	.
Sex										
Male	54	13	61	43	42	9	66	2	57	12
Female	44	13	36	40	57	7	33	2	42	20
Unknown	2	8	3	32	1	0	1	0	1	33
Age (years)										
0-4	15	16	5	17	3	5	6	4	3	0
5-19	6	10	4	14	1	4	1	0	1	33
20-64	36	9	40	36	33	8	42	3	47	16
65 and over	42	15	48	52	61	8	50	1	48	16
Unknown	2	15	2	28	1	0	0	.	1	0
Hospital department										
ICU	5	13	8	60	3	8	9	0	16	15
Internal Medicine	36	14	27	43	19	5	21	0	9	37
Surgery	2	14	12	54	6	8	10	3	6	8
Other	29	11	22	28	22	3	14	6	7	7
Unknown	27	13	32	40	49	11	47	2	63	15

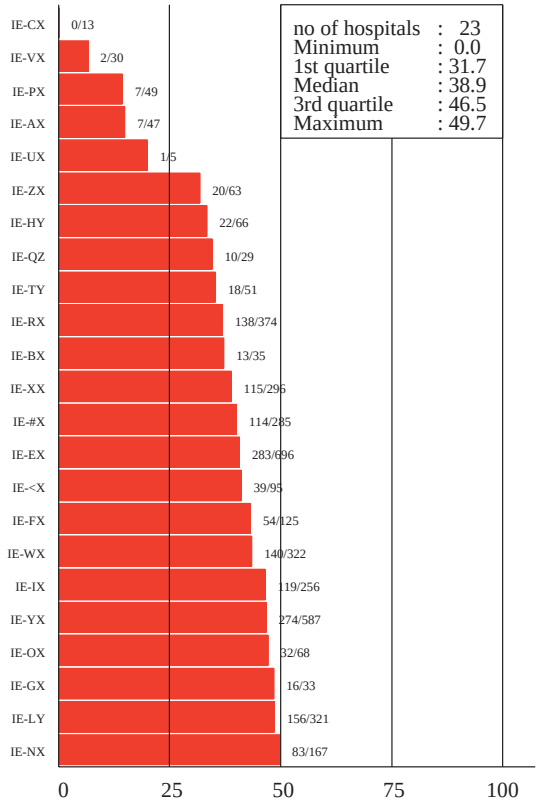
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Israel

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	5/5
Labs/Hosps providing denom.data *	5/5
Number of blood culture sets *	118289
Number of hospital beds *	4409
Average annual occupancy rate *	97%
Estimated catchment population *	2430000
% total population covered *	40%

*** Based on labs/hospitals providing denominator data**

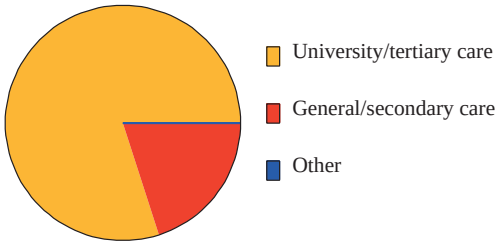


Figure 1. Type of hospitals in 2002

Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	5	170	5	381	5	741	5	184
2002	5	177	5	468	5	865	5	254
2003	5	180	5	368	5	774	5	244

Antibiotic resistance in 1999-2003

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

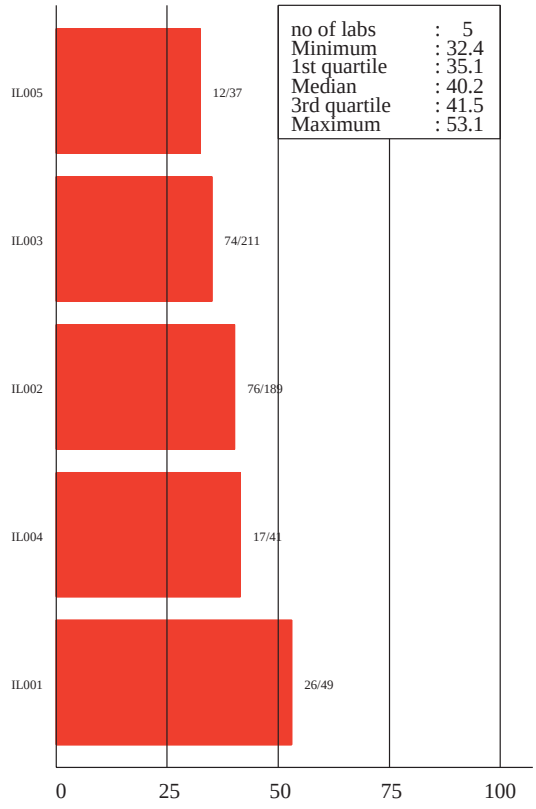
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	5	7	11
	Penicillin I+R	.	.	40	38	38
	Macrolides I+R	.	.	11	12	14
S. aureus	Oxacillin/Methicillin R	.	.	39	38	43
E. coli	Aminopenicillins R	.	.	66	62	62
	Aminoglycosides R	.	.	17	16	14
	Fluoroquinolones R	.	.	21	19	20
	3rd gen. Cephalosporins R	.	.	9	8	9
E. faecalis	Aminopenicillins I+R	.	.	<1	4	2
	Aminoglycosides (high-level resistance)	.	.	24	44	43
	Glycopeptides I+R	.	.	1	2	<1
E. faecium	Aminopenicillins I+R	.	.	46	50	48
	Aminoglycosides (high-level resistance)	.	.	33	42	38
	Glycopeptides I+R	.	.	12	10	8

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=527		n=1217		n=2373		n=567		n=99	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	100	39	100	40	100	20	100	1	100	10
CSF	0	.	0	.	0	.	0	.	0	.
Sex										
Male	57	36	60	41	41	24	57	1	55	7
Female	43	42	40	38	59	17	43	2	45	13
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	40	54	10	27	5	4	13	0	12	8
5-19	11	22	6	16	2	23	2	0	9	22
20-64	24	20	33	37	26	18	27	3	21	5
65 and over	25	41	51	46	66	22	58	1	58	11
Unknown	1	50	0	.	0	.	0	.	0	.
Hospital department										
ICU	5	32	10	45	6	26	16	1	21	10
Internal Medicine	38	31	44	40	58	19	42	1	19	11
Surgery	2	10	14	45	10	28	10	0	14	0
Other	55	46	32	35	26	19	33	2	45	13
Unknown	0	.	0	.	0	.	0	.	0	.

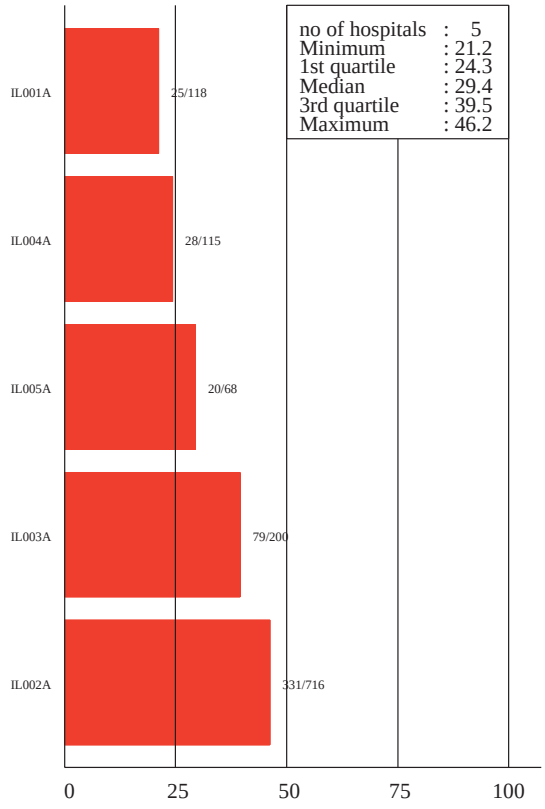
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Italy

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	56/56
Labs/Hosps providing denom.data *	0/0
Number of blood culture sets *	na
Number of hospital beds *	na
Average annual occupancy rate *	na
Estimated catchment population *	na
% total population covered *	na

*** Based on labs/hospitals providing denominator data**

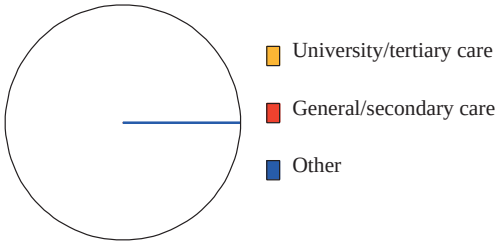


Figure 1. Type of hospitals in 2002

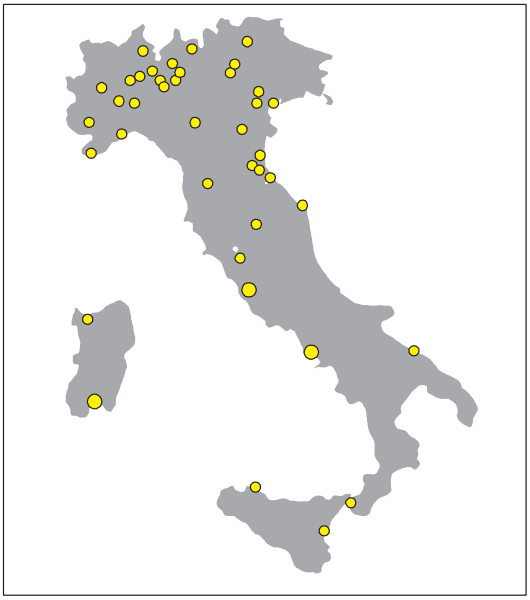


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	41	177	56	1158	0	0	0	0
2000	36	116	48	456	0	0	0	0
2001	39	121	53	839	0	0	42	297
2002	50	296	53	1343	17	618	49	602
2003	38	201	19	394	16	669	38	425

Antibiotic resistance in 1999-2003

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

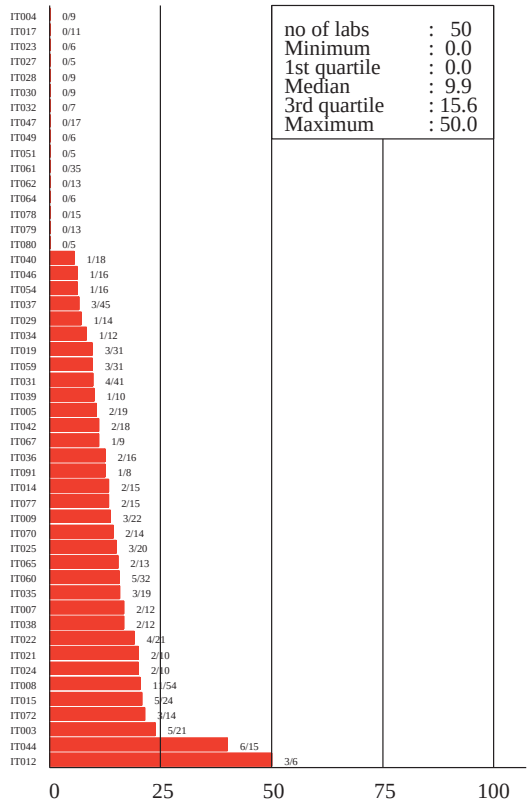
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	2	<1	4	2	5
	Penicillin I+R	13	11	9	11	12
	Macrolides I+R	29	28	39	32	38
S. aureus	Oxacillin/Methicillin R	41	44	41	38	38
E. coli	Aminopenicillins R	.	.	.	48	51
	Aminoglycosides R	.	.	.	6	7
	Fluoroquinolones R	.	.	.	21	25
	3rd gen. Cephalosporins R	.	.	.	3	6
E. faecalis	Aminopenicillins I+R	.	.	3	6	3
	Aminoglycosides (high-level resistance)	.	.	31	38	36
	Glycopeptides I+R	.	.	2	<1	2
E. faecium	Aminopenicillins I+R	.	.	69	79	75
	Aminoglycosides (high-level resistance)	.	.	18	37	38
	Glycopeptides I+R	.	.	19	21	25

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=911		*S. aureus* n=4190		*E. coli* n=1286		*E. faecalis* n=944		*E. faecium* n=370	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	81	11	100	40	100	23	100	1	100	22
CSF	19	15	0	.	0	.	0	.	0	.
Sex										
Male	53	13	55	41	24	22	49	1	51	19
Female	39	8	35	37	29	22	29	1	34	22
Unknown	9	16	11	44	47	24	22	1	15	30
Age (years)										
0-4	12	6	2	16	1	0	4	0	4	6
5-19	3	14	2	14	0	.	1	0	1	0
20-64	35	15	31	33	14	22	23	0	27	22
65 and over	34	9	44	43	35	22	41	2	42	17
Unknown	16	12	21	49	49	25	32	1	25	32
Hospital department										
ICU	8	17	13	59	3	19	19	2	16	22
Internal Medicine	33	8	34	35	42	20	33	1	35	17
Surgery	2	16	11	50	6	26	11	3	16	17
Other	42	13	31	33	14	23	16	1	16	22
Unknown	14	13	11	40	36	27	21	0	18	33

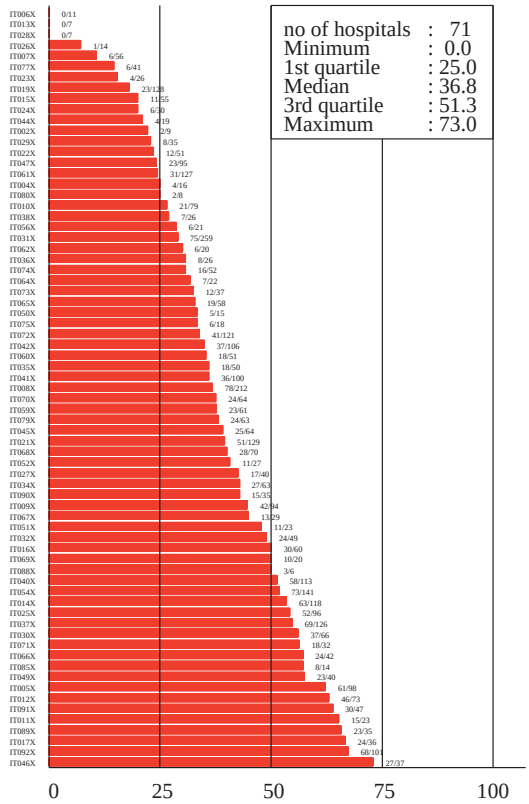
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Luxembourg

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	9/14
Labs/Hosps providing denom.data *	7/6
Number of blood culture sets *	10083
Number of hospital beds *	1693
Average annual occupancy rate *	76%
Estimated catchment population *	449000
% total population covered *	100%

*** Based on labs/hospitals providing denominator data**

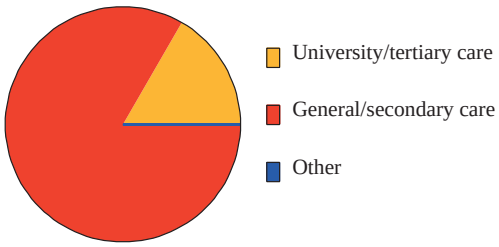


Figure 1. Type of hospitals in 2002

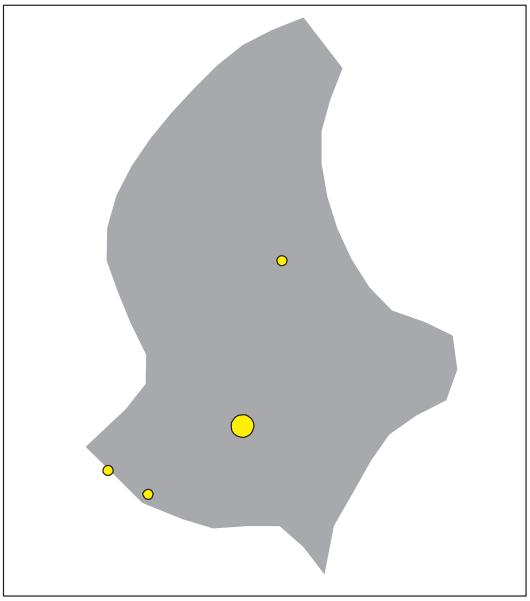


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	1	9	1	25	0	0	0	0
2000	5	22	4	67	0	0	0	0
2001	8	41	8	85	8	193	7	31
2002	7	27	9	95	9	193	8	30
2003	7	48	8	95	8	227	7	41

Antibiotic resistance in 1999-2003

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

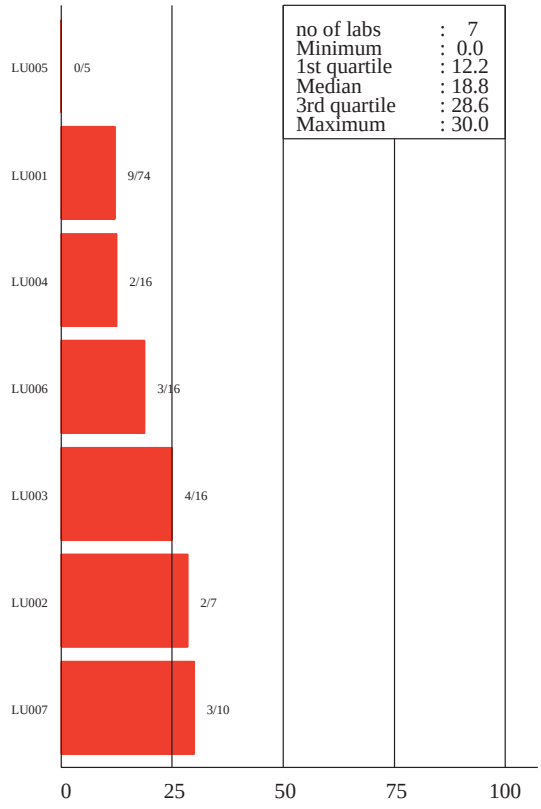
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	11	<1	7	7	<1
	Penicillin I+R	22	14	12	22	15
	Macrolides I+R	33	26	23	22	30
S. aureus	Oxacillin/Methicillin R	16	18	20	15	21
E. coli	Aminopenicillins R	.	.	44	43	49
	Aminoglycosides R	.	.	5	4	4
	Fluoroquinolones R	.	.	5	10	12
	3rd gen. Cephalosporins R	.	.	<1	<1	<1
E. faecalis	Aminopenicillins I+R	.	.	<1	<1	5
	Aminoglycosides (high-level resistance)	.	.	13	17	32
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	<1	60	100
	Aminoglycosides (high-level resistance)	.	.	.	14	<1
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=147		n=367		n=574		n=75		n=12	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	88	16	100	18	100	9	100	0	100	0
CSF	12	11	0	.	0	.	0	.	0	.
Sex										
Male	56	18	56	16	38	10	55	0	33	0
Female	44	12	40	22	53	7	43	0	58	0
Unknown	0	.	4	19	9	17	3	0	8	0
Age (years)										
0-4	13	16	8	20	3	0	3	0	8	0
5-19	3	40	3	9	1	0	1	0	0	.
20-64	41	10	39	14	26	1	37	0	8	0
65 and over	42	19	46	22	62	12	56	0	75	0
Unknown	0	.	4	20	9	17	3	0	8	0
Hospital department										
ICU	16	8	11	23	10	4	40	0	33	0
Internal Medicine	27	21	26	21	36	12	17	0	17	0
Surgery	3	0	10	29	4	8	8	0	0	.
Other	24	14	19	17	20	6	17	0	25	0
Unknown	30	18	34	13	30	10	17	0	25	0

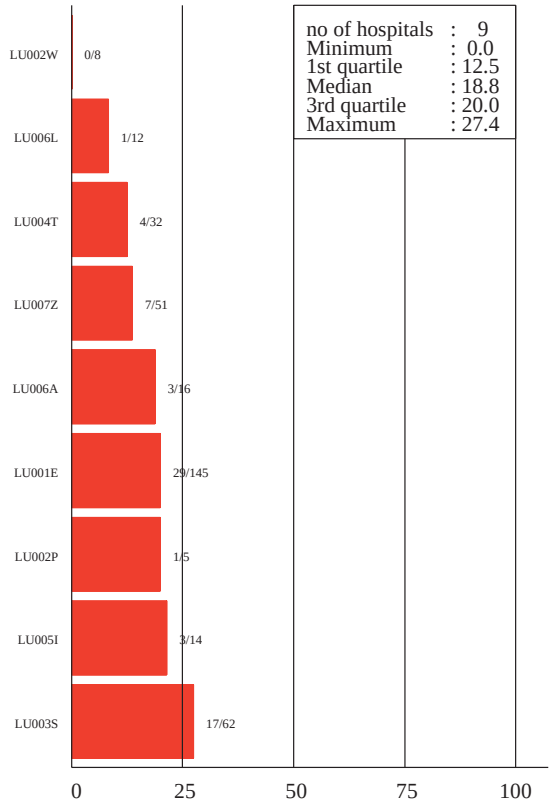
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Malta

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	1/1
Labs/Hosps providing denom.data *	1/1
Number of blood culture sets *	2863
Number of hospital beds *	846
Average annual occupancy rate *	83%
Estimated catchment population *	370000
% total population covered *	93%

*** Based on labs/hospitals providing denominator data**

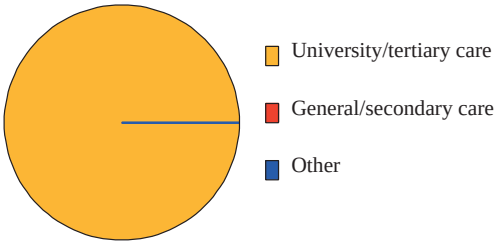


Figure 1. Type of hospitals in 2002

Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	1	11	1	76	0	0	0	0
2001	1	12	1	83	1	67	1	13
2002	1	12	1	87	1	74	1	33
2003	1	9	1	122	1	91	1	26

Antibiotic resistance in 1999-2003

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

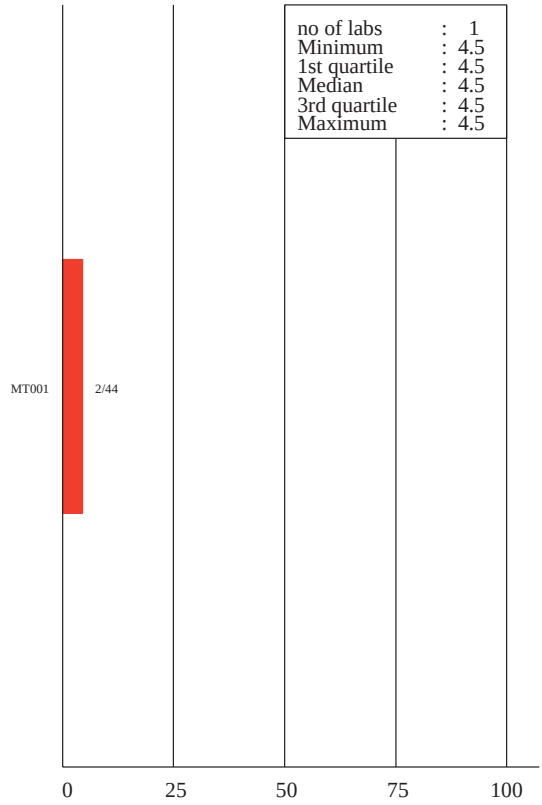
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	<1	<1	<1	<1
	Penicillin I+R	.	9	8	<1	<1
	Macrolides I+R	.	36	18	25	38
S. aureus	Oxacillin/Methicillin R	.	36	54	43	43
E. coli	Aminopenicillins R	.	.	27	43	39
	Aminoglycosides R	.	.	10	8	18
	Fluoroquinolones R	.	.	15	12	24
	3rd gen. Cephalosporins R	.	.	<1	3	2
E. faecalis	Aminopenicillins I+R	.	.	8	<1	5
	Aminoglycosides (high-level resistance)	.	.	8	17	29
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	100	33	33
	Aminoglycosides (high-level resistance)	.	.	<1	<1	50
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=44		*S. aureus* n=368		*E. coli* n=231		*E. faecalis* n=62		*E. faecium* n=10	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	91	3	100	44	100	18	100	0	100	0
CSF	9	25	0	.	0	.	0	.	0	.
Sex										
Male	70	3	57	45	45	26	61	0	30	0
Female	30	8	43	42	55	11	39	0	70	0
Unknown	0	.	1	0	0	.	0	.	0	.
Age (years)										
0-4	34	0	8	18	6	13	8	0	10	0
5-19	5	0	7	15	2	20	0	.	10	0
20-64	30	8	42	40	24	18	42	0	40	0
65 and over	32	7	43	57	67	18	50	0	40	0
Unknown	0	.	0	.	1	0	0	.	0	.
Hospital department										
ICU	23	10	17	55	10	0	63	0	70	0
Internal Medicine	30	8	43	37	49	21	16	0	20	0
Surgery	0	.	19	52	21	24	13	0	10	0
Other	39	0	13	27	6	7	3	0	0	.
Unknown	9	0	8	65	14	13	5	0	0	.

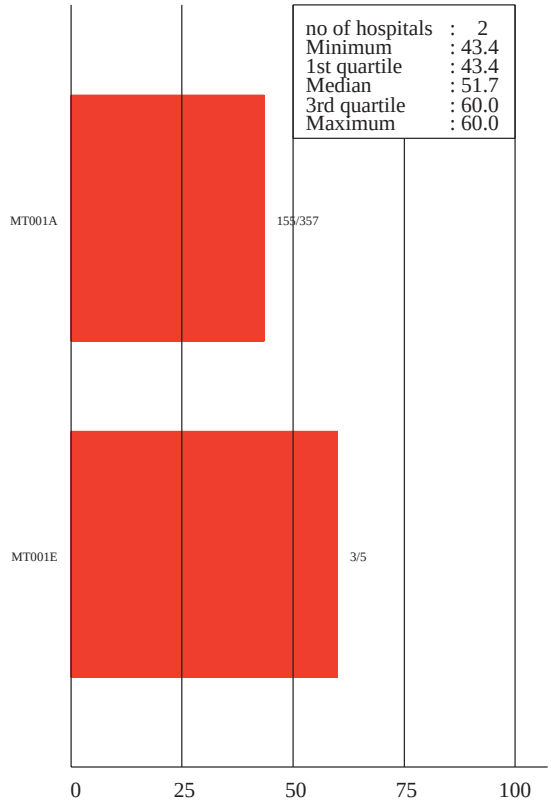
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Netherlands

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	23/39
Labs/Hosps providing denom.data *	16/22
Number of blood culture sets *	113149
Number of hospital beds *	13093
Average annual occupancy rate *	65%
Estimated catchment population *	5989000
% total population covered *	37%

*** Based on labs/hospitals providing denominator data**

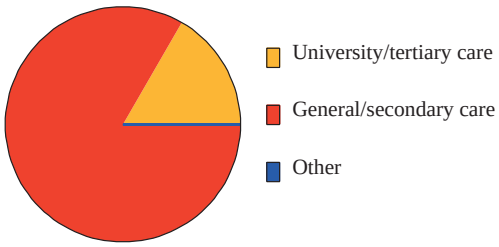


Figure 1. Type of hospitals in 2002

Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	21	762	20	1224	0	0	0	0
2000	23	740	24	1388	0	0	0	0
2001	20	723	21	1290	20	1864	14	275
2002	23	860	22	1502	22	2427	22	536
2003	21	791	20	1175	21	1915	21	419

Antibiotic resistance in 1999-2003

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

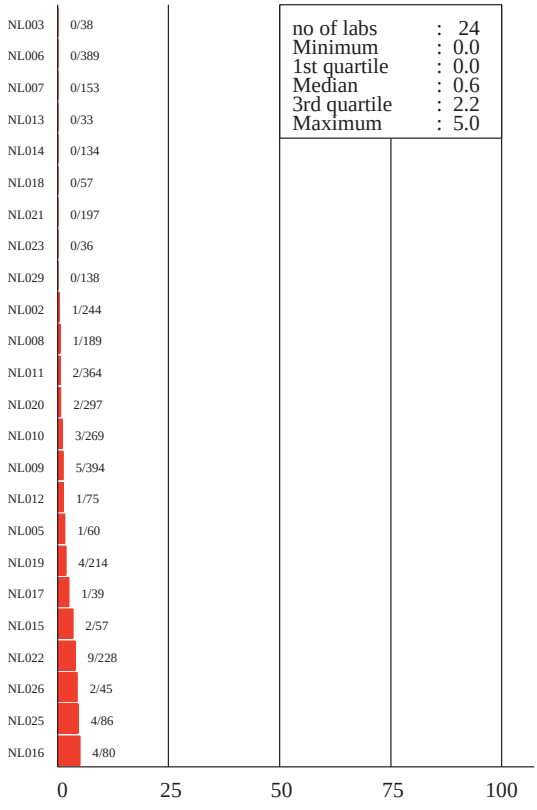
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	< 1	<1	<1	<1	<1
	Penicillin I+R	1	1	<1	1	<1
	Macrolides I+R	.	4	5	7	5
S. aureus	Oxacillin/Methicillin R	< 1	<1	<1	<1	<1
E. coli	Aminopenicillins R	.	.	39	39	42
	Aminoglycosides R	.	.	2	2	3
	Fluoroquinolones R	.	.	6	5	7
	3rd gen. Cephalosporins R	.	.	<1	<1	1
E. faecalis	Aminopenicillins I+R	.	.	2	3	5
	Aminoglycosides (high-level resistance)	.	.	28	33	22
	Glycopeptides I+R	.	.	<1	1	2
E. faecium	Aminopenicillins I+R	.	.	64	23	25
	Aminoglycosides (high-level resistance)	.	.	4	11	18
	Glycopeptides I+R	.	.	5	2	4

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=3876		*S. aureus* n=6579		*E. coli* n=5773		*E. faecalis* n=764		*E. faecium* n=427	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	90	1	100	1	99	6	100	1	100	3
CSF	10	1	0	.	1	2	0	.	0	.
Sex										
Male	54	1	57	1	46	7	61	1	62	2
Female	45	1	42	1	54	5	38	2	37	5
Unknown	1	3	1	0	0	.	1	0	1	0
Age (years)										
0-4	8	2	9	1	4	1	10	0	7	0
5-19	3	2	4	0	1	5	2	0	2	0
20-64	35	1	35	1	29	8	41	2	36	3
65 and over	51	1	50	1	62	5	46	1	49	4
Unknown	2	0	2	1	4	9	1	0	5	0
Hospital department										
ICU	5	2	6	1	4	10	18	1	10	0
Internal Medicine	11	1	12	0	13	6	13	1	6	8
Surgery	2	0	7	1	6	6	10	1	2	10
Other	19	2	20	0	12	6	16	1	11	0
Unknown	63	1	55	1	65	6	43	2	71	3

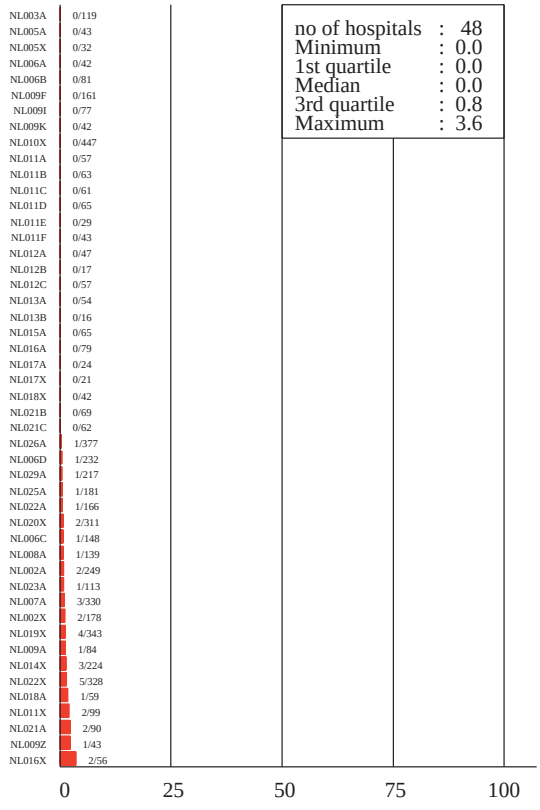
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Norway

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	24/24
Labs/Hosps providing denom.data *	0/0
Number of blood culture sets *	na
Number of hospital beds *	na
Average annual occupancy rate *	na
Estimated catchment population *	4552000
% total population covered *	100%

*** Based on labs/hospitals providing denominator data**

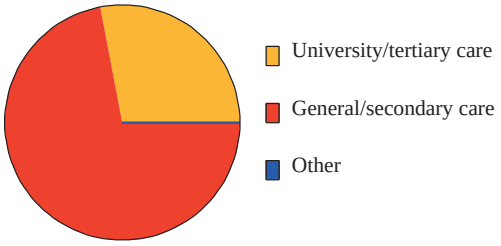


Figure 1. Type of hospitals in 2002

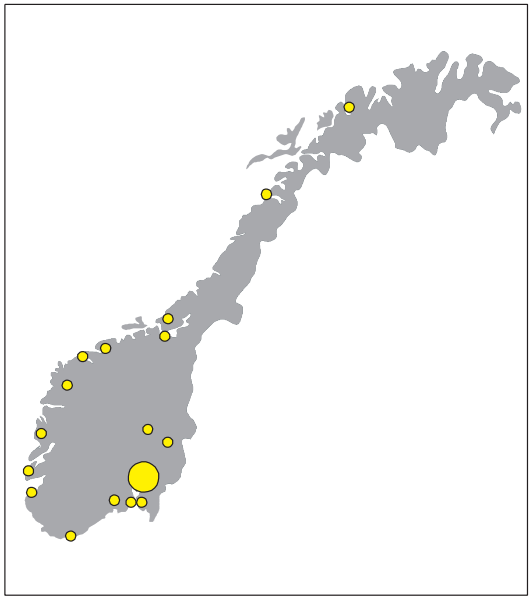


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	1	28	0	0	0	0	0	0
2000	1	388	0	0	0	0	0	0
2001	0	0	0	0	0	0	0	0
2002	25	538	25	726	25	973	25	235
2003	24	514	24	637	24	966	24	252

Antibiotic resistance in 1999-2003

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

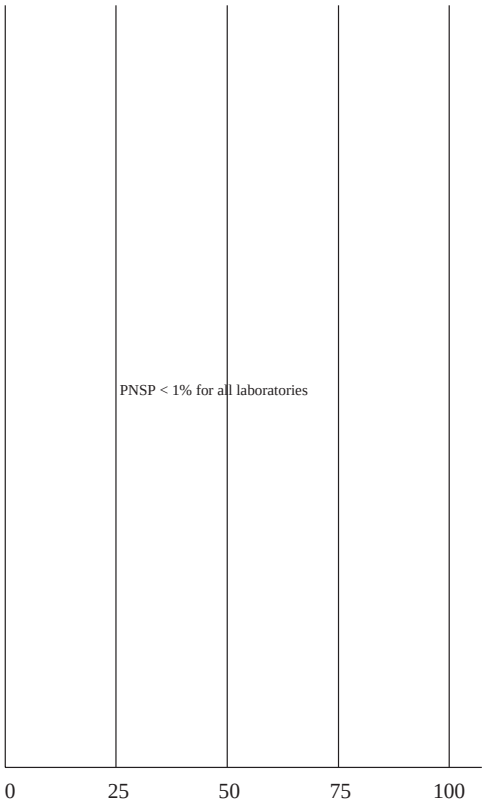
Pathogen	Antimicrobial classes		1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	<	1	<1	.	<1	<1
	Penicillin I+R		<1	2	.	<1	<1
	Macrolides I+R		.	.	.	5	6
S. aureus	Oxacillin/Methicillin R		.	.	.	<1	<1
E. coli	Aminopenicillins R		.	.	.	27	30
	Aminoglycosides R		.	.	.	1	<1
	Fluoroquinolones R		.	.	.	2	2
	3rd gen. Cephalosporins R		.	.	.	<1	<1
E. faecalis	Aminopenicillins I+R		.	.	.	1	<1
	Aminoglycosides (high-level resistance)		.	.	.	10	14
	Glycopeptides I+R		.	.	.	<1	<1
E. faecium	Aminopenicillins I+R		.	.	.	62	63
	Aminoglycosides (high-level resistance)		.	.	.	4	3
	Glycopeptides I+R		.	.	.	<1	3

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=954		n=726		n=973		n=188		n=47	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	98	2	100	0	100	2	100	1	100	0
CSF	2	0	0	.	0	.	0	.	0	.
Sex										
Male	47	3	.	.	.	.	.	.	.	.
Female	52	1	.	.	.	.	.	.	.	.
Unknown	1	20	.	.	.	.	.	.	.	.
Age (years)										
0-4	5	5	.	.	.	.	.	.	.	.
5-19	2	0	.	.	.	.	.	.	.	.
20-64	44	3	.	.	.	.	.	.	.	.
65 and over	48	2	.	.	.	.	.	.	.	.
Unknown	0	.	.	.	.	.	.	.	.	.
Hospital department										
ICU	0	.	.	.	.	.	.	.	.	.
Internal Medicine	0	.	.	.	.	.	.	.	.	.
Surgery	0	.	.	.	.	.	.	.	.	.
Other	0	.	.	.	.	.	.	.	.	.
Unknown	100	2	.	.	.	.	.	.	.	.

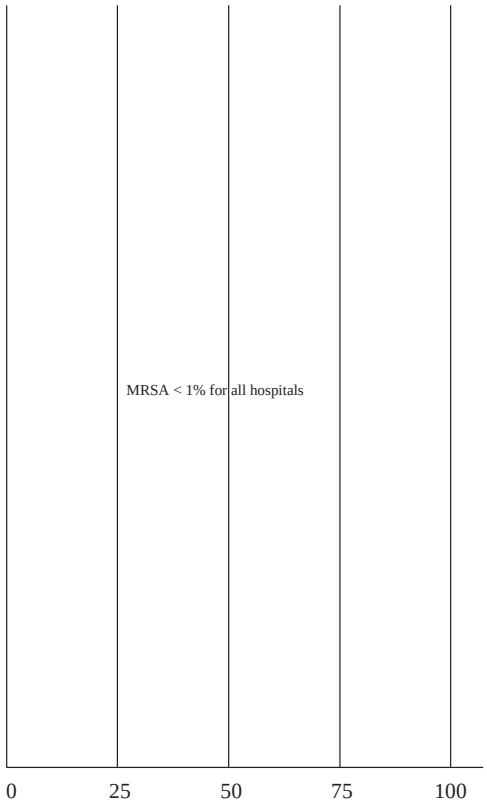
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Poland

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	24/24
Labs/Hosps providing denom.data *	24/24
Number of blood culture sets *	33634
Number of hospital beds *	14706
Average annual occupancy rate *	77%
Estimated catchment population *	8508000
% total population covered *	22%

*** Based on labs/hospitals providing denominator data**

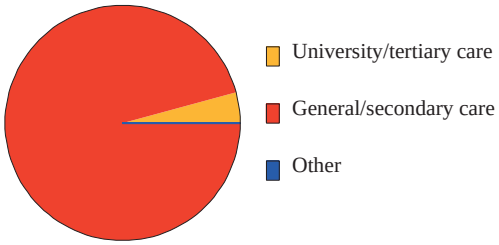


Figure 1. Type of hospitals in 2002

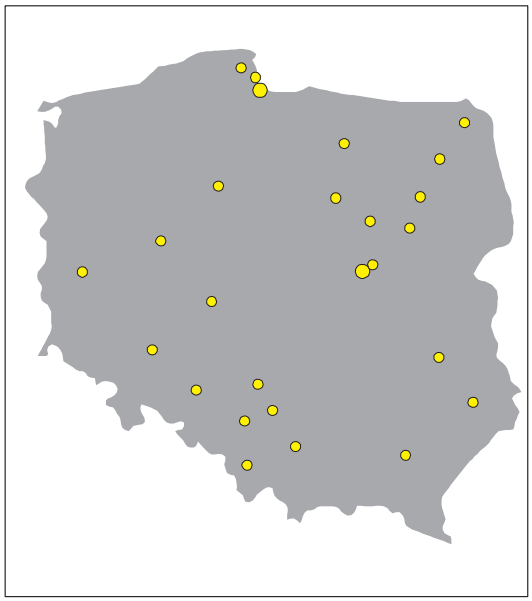


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	4	6	19	151	20	103	16	57
2002	7	10	21	186	22	135	19	56
2003	11	16	24	166	25	123	16	64

Antibiotic resistance in 1999-2003

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

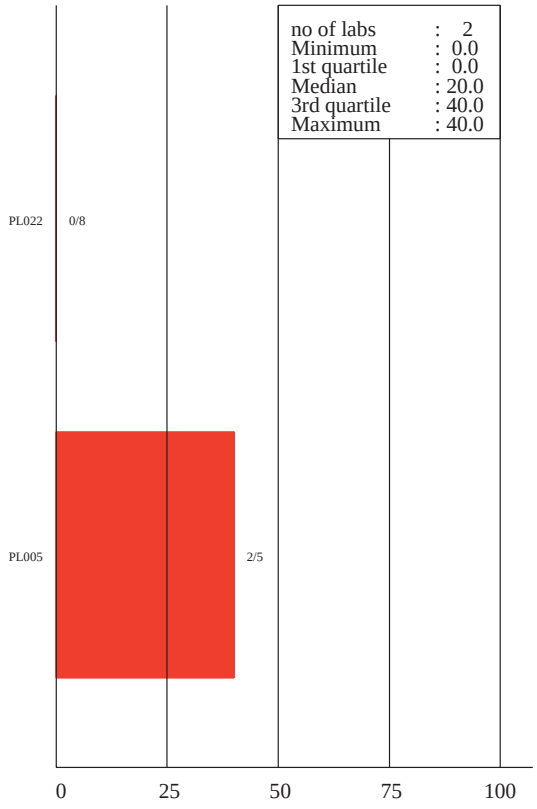
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	<1	30	19
	Penicillin I+R	.	.	<1	30	19
	Macrolides I+R	.	.	<1	67	14
S. aureus	Oxacillin/Methicillin R	.	.	15	23	19
E. coli	Aminopenicillins R	.	.	58	52	49
	Aminoglycosides R	.	.	5	11	10
	Fluoroquinolones R	.	.	9	11	7
	3rd gen. Cephalosporins R	.	.	7	6	4
E. faecalis	Aminopenicillins I+R	.	.	5	12	<1
	Aminoglycosides (high-level resistance)	.	.	43	41	48
	Glycopeptides I+R	.	.	<1	<1	2
E. faecium	Aminopenicillins I+R	.	.	77	80	91
	Aminoglycosides (high-level resistance)	.	.	73	73	55
	Glycopeptides I+R	.	.	7	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=32		n=503		n=346		n=125		n=52	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	84	19	100	19	99	9	100	1	100	2
CSF	16	20	0	.	1	0	0	.	0	.
Sex										
Male	53	6	61	23	42	10	62	0	46	0
Female	47	33	39	14	57	8	38	2	54	4
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	16	20	14	17	11	0	9	0	19	0
5-19	9	67	3	36	2	14	3	0	2	0
20-64	56	11	53	22	43	13	38	0	58	3
65 and over	19	17	30	15	44	7	50	2	21	0
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	13	0	14	37	10	12	15	0	29	0
Internal Medicine	47	20	50	16	51	9	42	0	23	8
Surgery	3	100	16	23	17	12	26	3	25	0
Other	38	17	20	14	22	4	17	0	23	0
Unknown	0	.	0	.	0	.	0	.	0	.

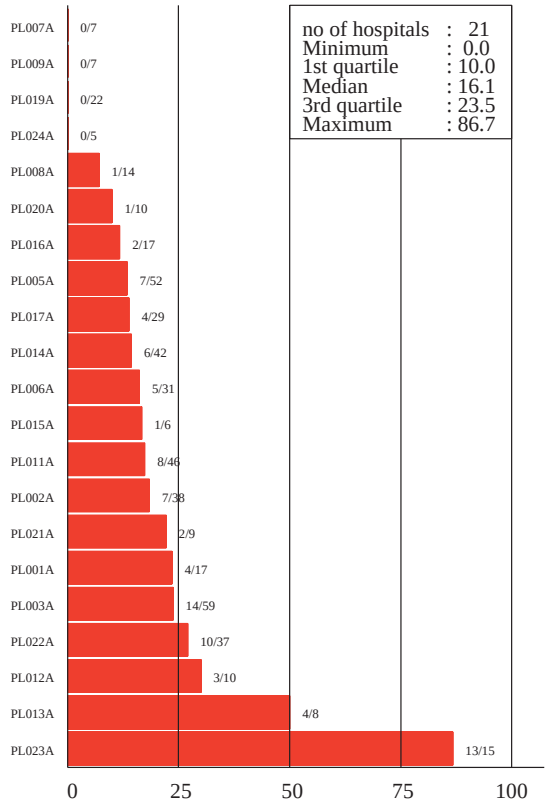
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Portugal

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	18/18
Labs/Hosps providing denom.data *	15/15
Number of blood culture sets *	36481
Number of hospital beds *	6577
Average annual occupancy rate *	78%
Estimated catchment population *	2305000
% total population covered *	23%

*** Based on labs/hospitals providing denominator data**

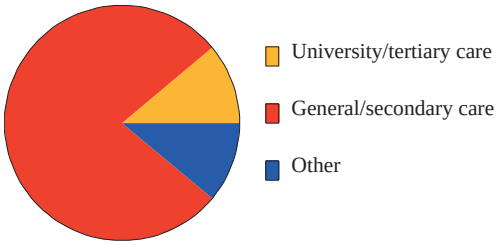


Figure 1. Type of hospitals in 2002

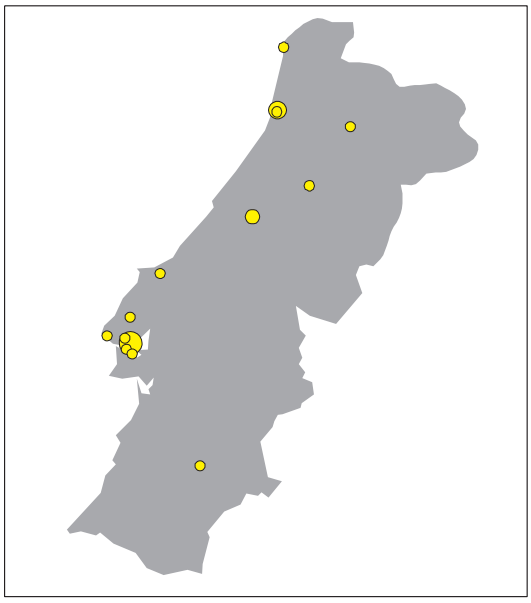


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	12	119	13	369	0	0	0	0
2000	11	97	8	150	0	0	0	0
2001	16	155	16	521	13	418	12	185
2002	14	182	16	543	17	444	13	101
2003	12	95	22	1033	21	792	18	398

Antibiotic resistance in 1999-2003

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

Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R <	1	<1	<1	<1	<1
	Penicillin I+R	17	29	25	20	20
	Macrolides I+R	9	11	.	.	.
S. aureus	Oxacillin/Methicillin R	37	25	32	38	45
E. coli	Aminopenicillins R	.	.	54	58	53
	Aminoglycosides R	.	.	6	9	9
	Fluoroquinolones R	.	.	18	23	26
	3rd gen. Cephalosporins R	.	.	3	6	7
E. faecalis	Aminopenicillins I+R	.	.	5	2	4
	Aminoglycosides (high-level resistance)	.	.	30	25	34
	Glycopeptides I+R	.	.	7	6	6
E. faecium	Aminopenicillins I+R	.	.	76	79	88
	Aminoglycosides (high-level resistance)	.	.	23	33	55
	Glycopeptides I+R	.	.	24	.*	50

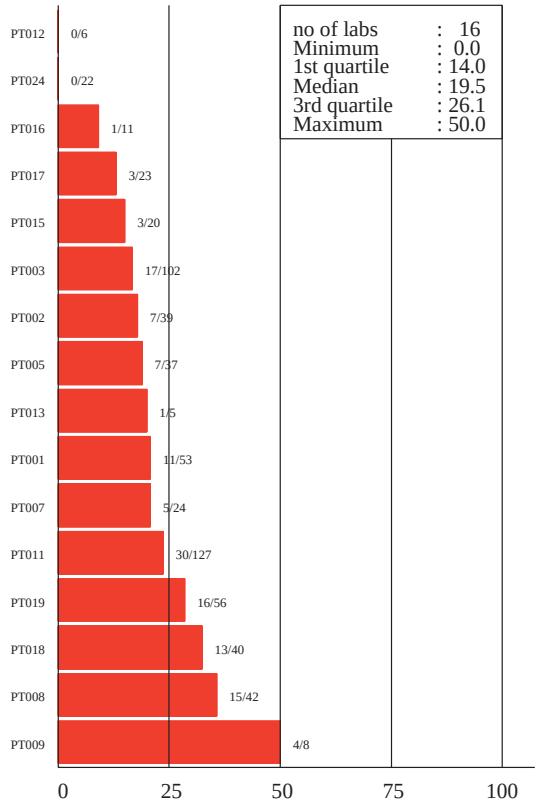
*** Proportion not given, due to very low numbers of isolates.**

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=648		n=2616		n=1430		n=532		n=150	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	80	22	100	39	99	23	100	6	100	39
CSF	20	22	0	.	1	25	0	.	0	.
Sex										
Male	60	20	63	39	46	28	58	6	55	41
Female	38	24	37	39	54	20	41	7	45	37
Unknown	2	30	0	.	0	.	0	.	0	.
Age (years)										
0-4	14	47	3	10	1	10	2	0	3	40
5-19	5	11	3	29	2	13	1	14	1	50
20-64	42	16	43	34	38	23	35	5	47	45
65 and over	27	16	42	49	51	27	52	8	37	38
Unknown	12	33	9	28	8	11	10	2	11	18
Hospital department										
ICU	7	20	12	57	6	34	16	4	19	36
Internal Medicine	20	17	27	43	30	25	24	9	15	48
Surgery	0	.	8	55	7	20	11	2	13	30
Other	68	24	53	31	56	22	49	7	52	41
Unknown	5	21	1	26	1	21	0	.	1	0

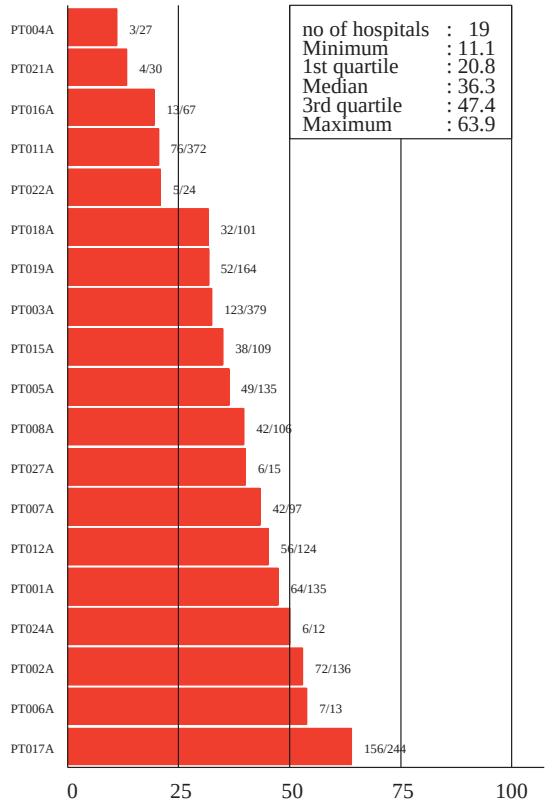
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Romania

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	12/11
Labs/Hosps providing denom.data *	8/8
Number of blood culture sets *	10515
Number of hospital beds *	6201
Average annual occupancy rate *	87%
Estimated catchment population *	10243000
% total population covered *	46%

*** Based on labs/hospitals providing denominator data**

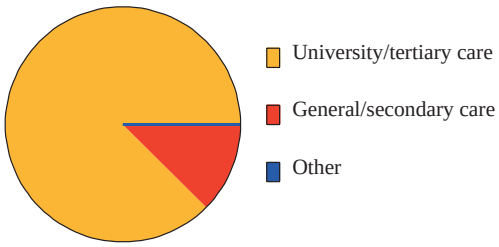


Figure 1. Type of hospitals in 2002

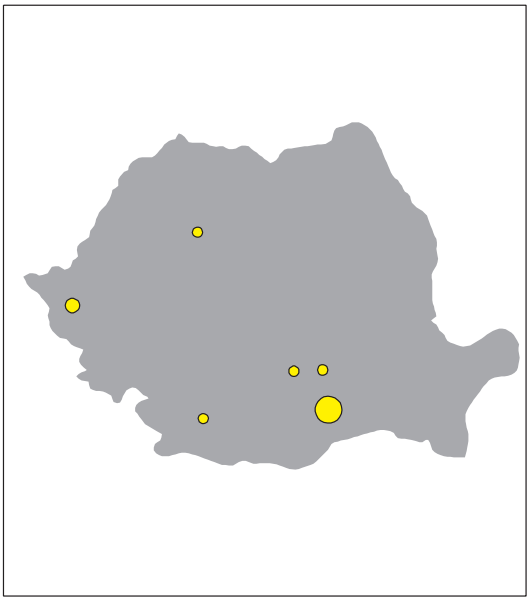


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	0	0	0	0	0	0	0	0
2002	6	10	11	81	8	28	4	11
2003	4	22	9	85	9	50	5	12

Antibiotic resistance in 1999-2003

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

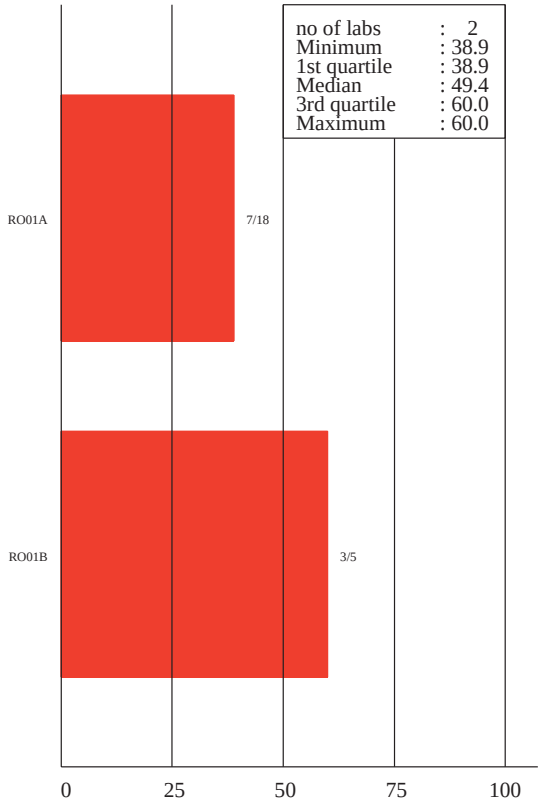
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	.	10	23
	Penicillin I+R	.	.	.	50	36
	Macrolides I+R	.	.	.	10	27
S. aureus	Oxacillin/Methicillin R	.	.	.	36	46
E. coli	Aminopenicillins R	.	.	.	64	66
	Aminoglycosides R	.	.	.	19	21
	Fluoroquinolones R	.	.	.	21	14
	3rd gen. Cephalosporins R	.	.	.	18	19
E. faecalis	Aminopenicillins I+R	.	.	.	<1	<1
	Aminoglycosides (high-level resistance)	.	.	.	40	25
	Glycopeptides I+R	.	.	.	<1	<1
E. faecium	Aminopenicillins I+R	.	.	.	100	86
	Aminoglycosides (high-level resistance)	.	.	.	80	63
	Glycopeptides I+R	.	.	.	17	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=32		*S. aureus* n=166		*E. coli* n=78		*E. faecalis* n=9		*E. faecium* n=14	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	78	28	100	41	99	17	100	0	100	7
CSF	22	86	0	.	1	0	0	.	0	.
Sex										
Male	63	30	65	40	58	24	33	0	21	33
Female	38	58	35	43	41	6	67	0	79	0
Unknown	0	.	0	.	1	0	0	.	0	.
Age (years)										
0-4	28	67	26	49	15	17	22	0	50	0
5-19	16	0	17	17	14	55	11	0	21	0
20-64	41	46	39	45	37	7	22	0	7	100
65 and over	16	20	9	33	29	13	44	0	7	0
Unknown	0	.	8	57	4	0	0	.	14	0
Hospital department										
ICU	0	.	4	100	1	0	0	.	0	.
Internal Medicine	0	.	6	20	5	0	0	.	0	.
Surgery	0	.	2	100	1	0	0	.	0	.
Other	69	36	39	36	81	17	56	0	36	0
Unknown	31	50	49	40	12	22	44	0	64	11

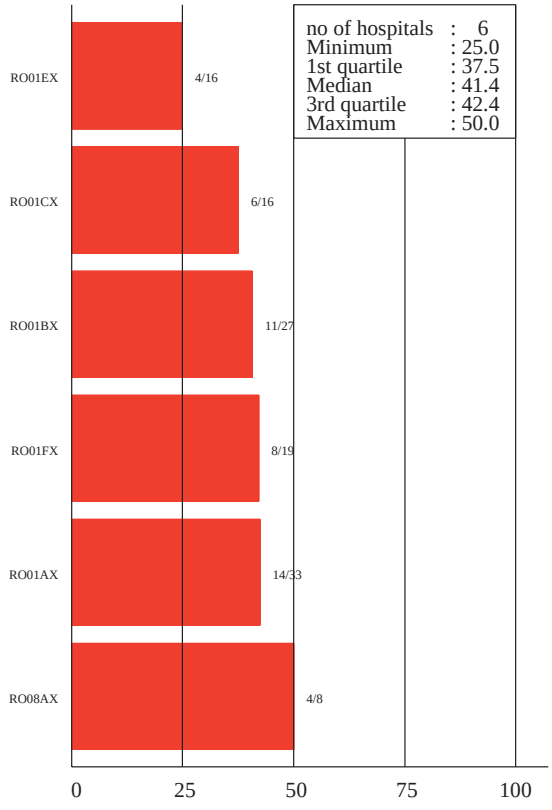
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Slovakia

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	14/14
Labs/Hosps providing denom.data *	14/14
Number of blood culture sets *	15207
Number of hospital beds *	11502
Average annual occupancy rate *	67%
Estimated catchment population *	5117000
% total population covered *	94%

*** Based on labs/hospitals providing denominator data**

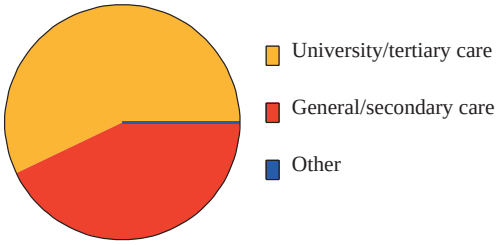


Figure 1. Type of hospitals in 2002

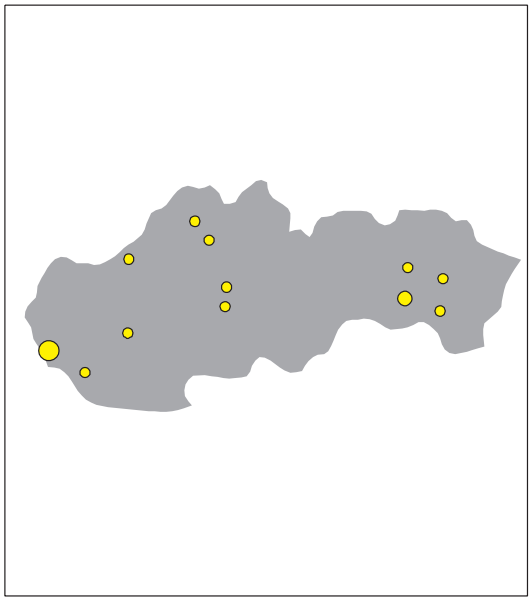


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	4	6	7	37	8	45	6	17
2002	9	16	14	259	14	215	12	79
2003	14	27	16	267	16	239	10	75

Antibiotic resistance in 1999-2003

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

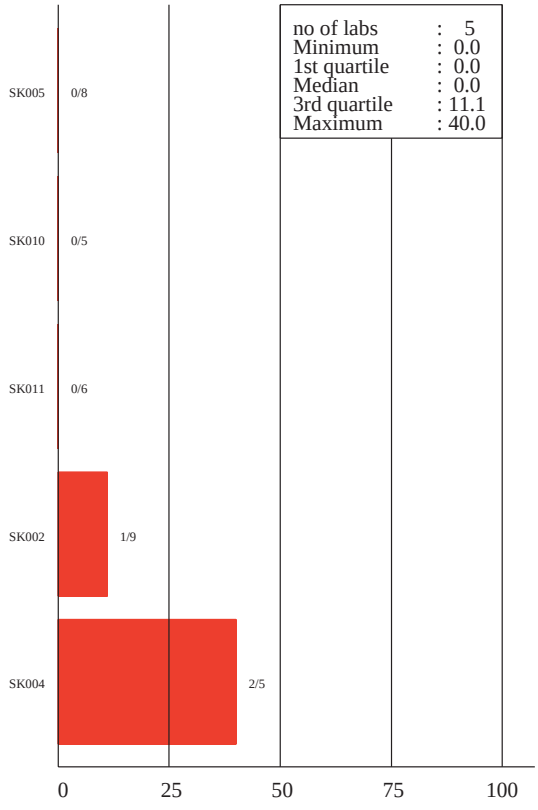
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	.	<1	19	4
	Penicillin I+R	.	.	<1	19	11
	Macrolides I+R	.	.	20	29	<1
S. aureus	Oxacillin/Methicillin R	.	.	5	8	12
E. coli	Aminopenicillins R	.	.	36	51	54
	Aminoglycosides R	.	.	2	4	6
	Fluoroquinolones R	.	.	16	14	20
	3rd gen. Cephalosporins R	.	.	7	2	<1
E. faecalis	Aminopenicillins I+R	.	.	<1	4	<1
	Aminoglycosides (high-level resistance)	.	.	58	34	35
	Glycopeptides I+R	.	.	<1	3	<1
E. faecium	Aminopenicillins I+R	.	.	67	75	92
	Aminoglycosides (high-level resistance)	.	.	50	75	60
	Glycopeptides I+R	.	.	<1	<1	<1

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=49		*S. aureus* n=563		*E. coli* n=497		*E. faecalis* n=151		*E. faecium* n=19	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	69	15	100	10	100	17	100	1	100	0
CSF	31	7	0	.	0	.	0	.	0	.
Sex										
Male	55	11	60	11	43	17	55	1	53	0
Female	45	14	40	8	57	17	45	1	47	0
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	22	27	5	19	4	5	5	0	11	0
5-19	10	0	3	12	1	0	6	0	5	0
20-64	47	4	49	8	38	19	48	3	53	0
65 and over	20	20	43	11	57	17	40	0	32	0
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	10	0	11	13	8	18	18	4	16	0
Internal Medicine	24	17	48	9	45	18	32	0	21	0
Surgery	2	0	11	10	13	15	13	0	16	0
Other	63	13	29	11	34	17	36	2	47	0
Unknown	0	.	0	.	0	.	0	.	0	.

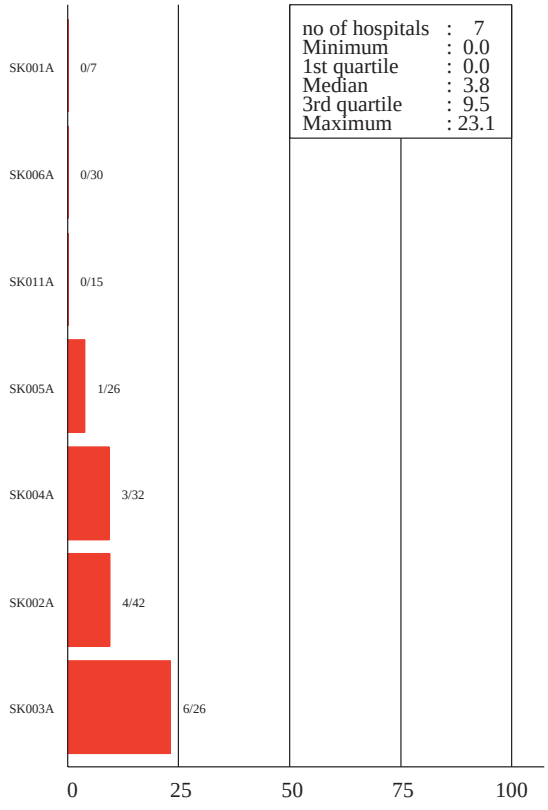
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Slovenia

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	11/15
Labs/Hosps providing denom.data *	11/15
Number of blood culture sets *	28092
Number of hospital beds *	7960
Average annual occupancy rate *	73%
Estimated catchment population *	1933000
% total population covered *	100%

*** Based on labs/hospitals providing denominator data**

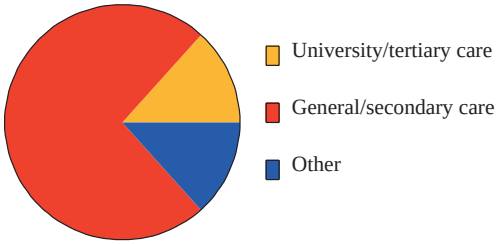


Figure 1. Type of hospitals in 2002

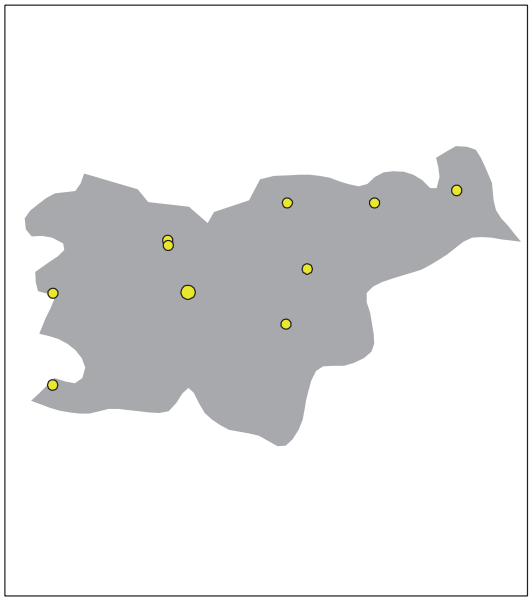


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	7	40	10	154	0	0	0	0
2001	10	156	10	270	10	398	10	54
2002	11	101	11	276	11	409	9	45
2003	11	172	11	299	11	401	10	76

Antibiotic resistance in 1999-2003

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

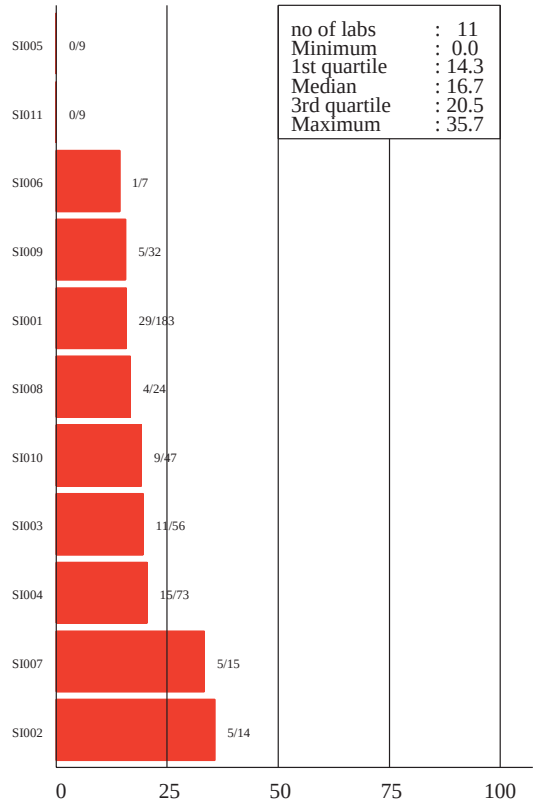
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	<1	<1	<1	2
	Penicillin I+R	.	23	20	19	15
	Macrolides I+R	.	12	18	10	9
S. aureus	Oxacillin/Methicillin R	.	21	20	14	13
E. coli	Aminopenicillins R	.	.	44	43	41
	Aminoglycosides R	.	.	2	3	2
	Fluoroquinolones R	.	.	8	12	11
	3rd gen. Cephalosporins R	.	.	<1	1	<1
E. faecalis	Aminopenicillins I+R	.	.	<1	<1	<1
	Aminoglycosides (high-level resistance)	.	.	35	50	49
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	64	69	83
	Aminoglycosides (high-level resistance)	.	.	50	62	82
	Glycopeptides I+R	.	.	<1	<1	4

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=469		n=999		n=1208		n=125		n=50	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	92	18	100	16	100	10	100	0	100	2
CSF	8	16	0	.	0	.	0	.	0	.
Sex										
Male	65	17	58	18	39	12	58	0	58	0
Female	35	19	42	13	61	9	42	0	42	5
Unknown	0	.	0	.	0	.	0	.	0	.
Age (years)										
0-4	21	26	4	0	4	2	17	0	2	0
5-19	6	20	4	5	2	13	1	0	0	.
20-64	40	15	39	14	33	11	28	0	42	0
65 and over	32	16	52	20	62	11	54	0	56	4
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	13	13	14	33	9	17	12	0	22	0
Internal Medicine	36	19	48	12	54	10	35	0	44	5
Surgery	1	0	13	31	6	10	11	0	4	0
Other	50	19	25	6	32	9	42	0	30	0
Unknown	0	.	0	.	0	.	0	.	0	.

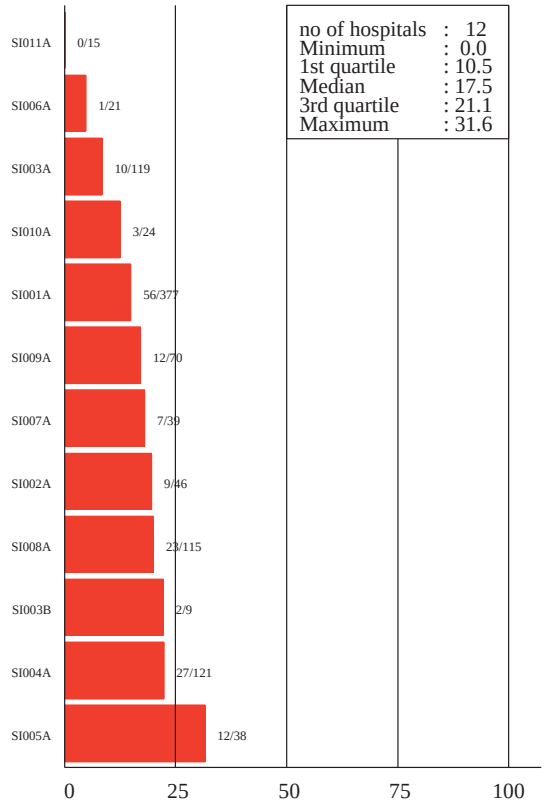
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Spain

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	37/37
Labs/Hosps providing denom.data *	28/28
Number of blood culture sets *	136260
Number of hospital beds *	14043
Average annual occupancy rate *	82%
Estimated catchment population *	7714000
% total population covered *	19%

*** Based on labs/hospitals providing denominator data**

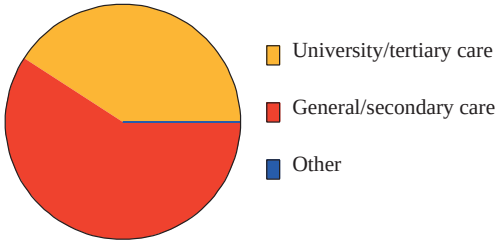


Figure 1. Type of hospitals in 2002

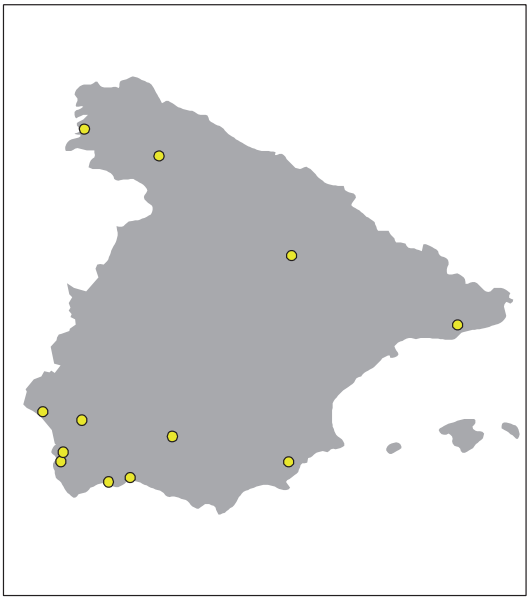


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	0	0	0	0	0	0	0	0
2000	33	584	30	836	0	0	0	0
2001	36	649	35	1013	27	1967	26	371
2002	35	658	36	1196	28	2483	35	566
2003	37	654	39	1391	32	2651	38	608

Antibiotic resistance in 1999-2003

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

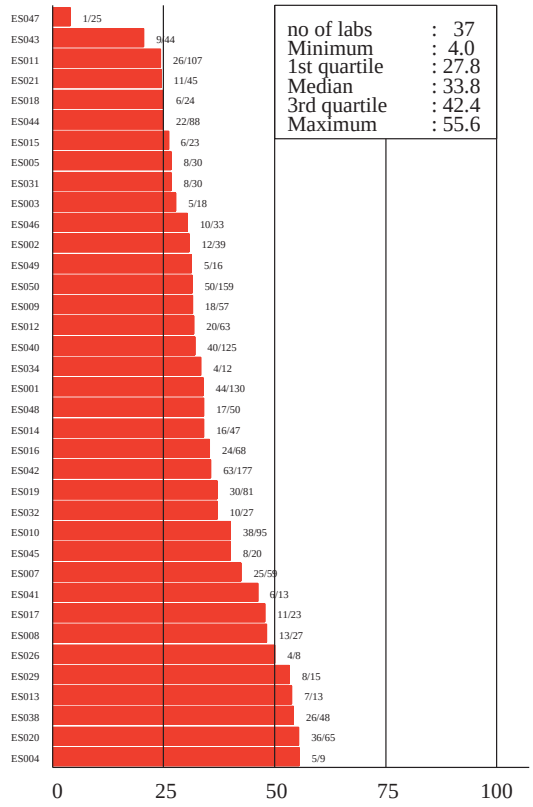
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	.	11	11	10	7
	Penicillin I+R	.	33	37	33	32
	Macrolides I+R	.	22	31	26	27
S. aureus	Oxacillin/Methicillin R	.	28	23	23	24
E. coli	Aminopenicillins R	.	.	59	60	58
	Aminoglycosides R	.	.	7	8	7
	Fluoroquinolones R	.	.	17	19	21
	3rd gen. Cephalosporins R	.	.	<1	2	4
E. faecalis	Aminopenicillins I+R	.	.	3	2	1
	Aminoglycosides (high-level resistance)	.	.	32	37	36
	Glycopeptides I+R	.	.	2	<1	<1
E. faecium	Aminopenicillins I+R	.	.	49	59	64
	Aminoglycosides (high-level resistance)	.	.	15	16	11
	Glycopeptides I+R	.	.	2	4	4

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=2545		n=4436		n=7079		n=1264		n=279	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	94	34	100	24	100	19	100	1	100	4
CSF	6	37	0	.	0	.	0	.	0	.
Sex										
Male	63	32	64	25	49	22	63	1	58	4
Female	37	36	35	23	50	16	37	0	41	4
Unknown	0	.	1	55	0	.	0	.	1	0
Age (years)										
0-4	17	53	4	8	3	9	10	0	14	3
5-19	4	22	4	10	2	11	2	0	3	14
20-64	37	26	39	22	29	17	32	1	33	3
65 and over	41	34	52	29	65	21	55	1	50	4
Unknown	2	38	1	19	1	16	0	.	0	.
Hospital department										
ICU	7	28	13	36	4	22	24	1	16	2
Internal Medicine	32	32	33	26	34	20	25	1	21	2
Surgery	1	13	11	30	8	16	8	1	14	3
Other	58	36	41	18	53	19	42	1	48	5
Unknown	2	32	2	26	1	15	1	0	2	0

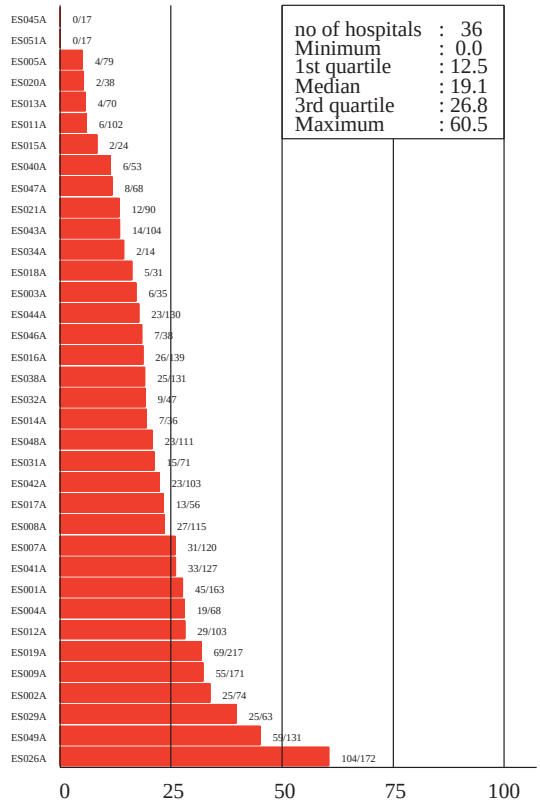
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Sweden

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	21/63
Labs/Hosps providing denom.data *	20/57
Number of blood culture sets *	176079
Number of hospital beds *	18447
Average annual occupancy rate *	88%
Estimated catchment population *	6276000
% total population covered *	71%

*** Based on labs/hospitals providing denominator data**

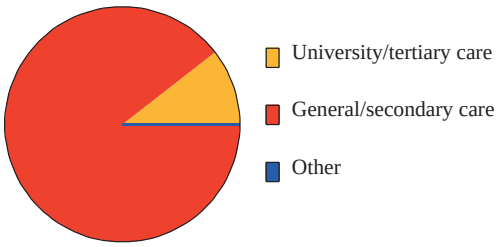


Figure 1. Type of hospitals in 2002

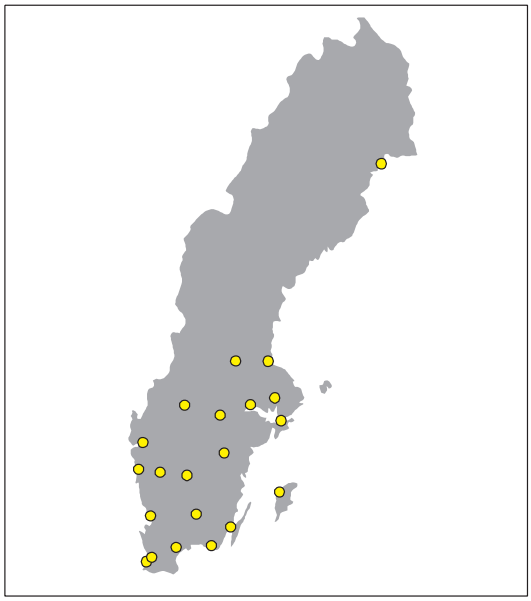


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	24	805	24	1320	0	0	0	0
2000	19	803	19	1478	0	0	0	0
2001	20	788	21	1633	20	2800	20	671
2002	21	830	21	1836	21	3066	21	696
2003	21	916	21	1854	22	3349	21	850

Antibiotic resistance in 1999-2003

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

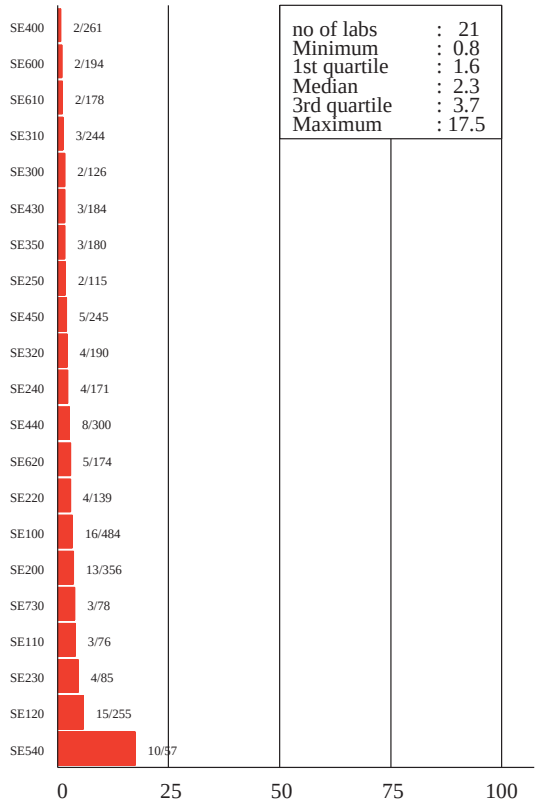
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	< 1	<1	<1	<1	<1
	Penicillin I+R	1	2	3	2	5
	Macrolides I+R	6	3	5	6	4
S. aureus	Oxacillin/Methicillin R	< 1	<1	<1	<1	<1
E. coli	Aminopenicillins R	.	.	27	25	28
	Aminoglycosides R	.	.	<1	<1	1
	Fluoroquinolones R	.	.	4	5	7
	3rd gen. Cephalosporins R	.	.	<1	<1	<1
E. faecalis	Aminopenicillins I+R	.	.	<1	1	<1
	Aminoglycosides (high-level resistance)	.	.	.	.	17
	Glycopeptides I+R	.	.	<1	<1	<1
E. faecium	Aminopenicillins I+R	.	.	75	75	77
	Aminoglycosides (high-level resistance)	.	.	.	.	11
	Glycopeptides I+R	.	.	<1	<1	2

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae*		*S. aureus*		*E. coli*		*E. faecalis*		*E. faecium*	
	n=4142		n=8121		n=7807		n=1418		n=581	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	97	3	100	1	100	5	100	0	100	1
CSF	3	4	0	.	0	.	0	.	0	.
Sex										
Male	50	3	59	1	45	6	66	0	57	2
Female	48	3	38	1	52	5	30	0	40	0
Unknown	2	2	3	0	3	2	4	0	3	0
Age (years)										
0-4	5	2	4	1	1	1	6	0	3	0
5-19	2	2	4	0	1	3	1	0	1	0
20-64	43	2	34	1	24	7	24	0	30	2
65 and over	50	3	58	1	73	5	69	0	65	1
Unknown	0	.	0	.	0	.	0	.	0	.
Hospital department										
ICU	9	3	7	1	4	4	8	0	10	0
Internal Medicine	42	3	44	0	40	5	32	0	38	1
Surgery	4	1	15	1	20	4	26	0	28	1
Other	44	3	34	1	35	6	34	0	24	1
Unknown	1	0	1	0	0	.	0	.	0	.

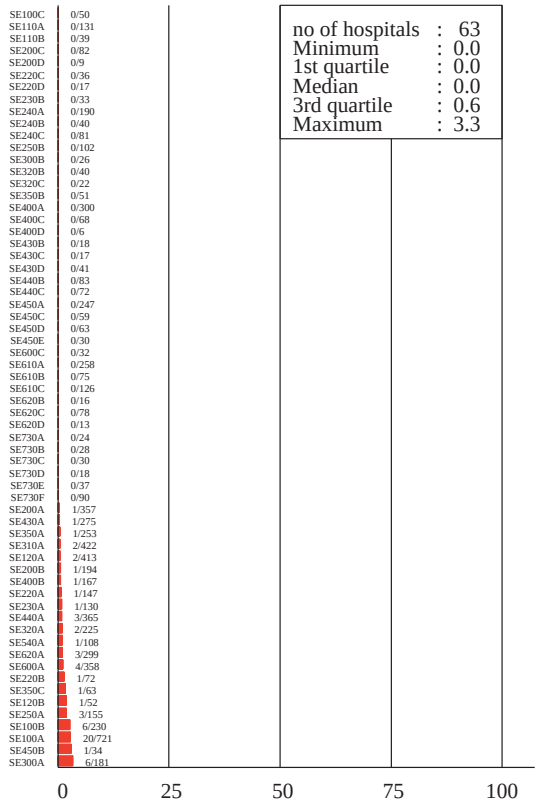
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



United Kingdom

Denominators

Table 1. Reference data of 2002

	Total
Labs/Hosps reporting to EARSS	23/26
Labs/Hosps providing denom.data *	18/18
Number of blood culture sets *	141543
Number of hospital beds *	13664
Average annual occupancy rate *	82%
Estimated catchment population *	9685000
% total population covered *	16%

*** Based on labs/hospitals providing denominator data**

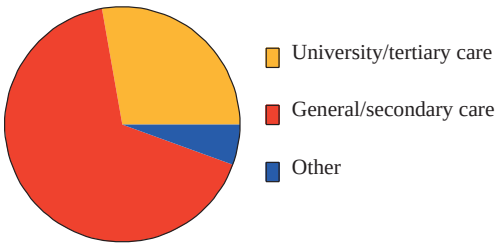


Figure 1. Type of hospitals in 2002

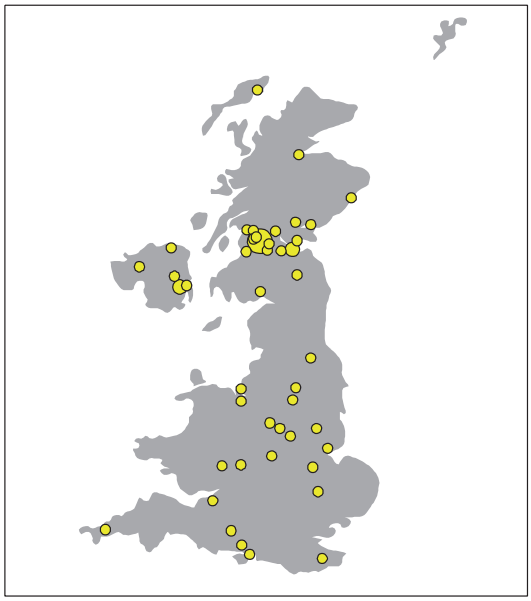


Figure 2. Geographic distribution of laboratories in 2003

Table 2. Number of laboratories and number of isolates reported for the period 1999-2003

Year	*S. pneumoniae*		*S. aureus*		*E. coli*		Enterococci	
	Labs	Isolates	Labs	Isolates	Labs	Isolates	Labs	Isolates
1999	22	240	23	653	0	0	0	0
2000	28	503	27	1495	0	0	0	0
2001	26	569	25	1518	0	0	0	0
2002	23	615	21	1706	0	0	0	0
2003	50	1298	51	3493	0	0	0	0

Antibiotic resistance in 1999-2003

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

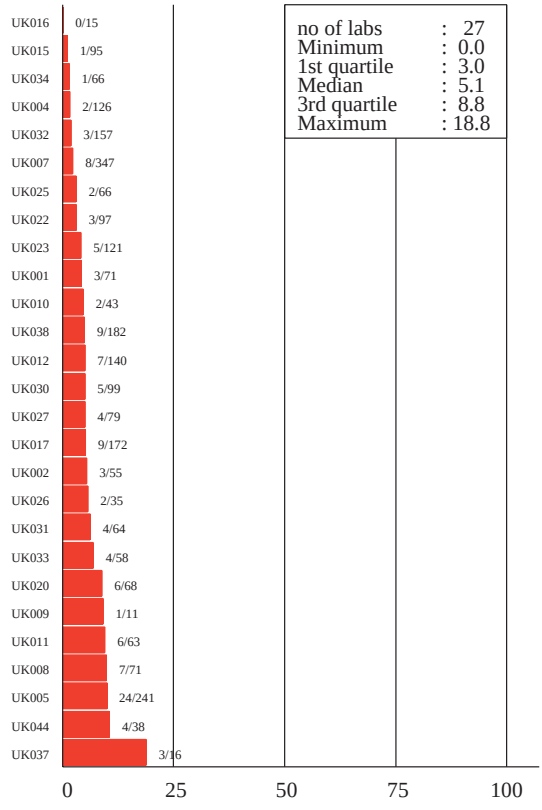
Pathogen	Antimicrobial classes	1999	2000	2001	2002	2003
S. pneumoniae	Penicillin R	4	4	3	3	1
	Penicillin I+R	7	6	4	5	4
	Macrolides I+R	15	18	13	13	13
S. aureus	Oxacillin/Methicillin R	33	40	44	44	43
E. coli	Aminopenicillins R	.	.	.	.	.
	Aminoglycosides R	.	.	.	.	.
	Fluoroquinolones R	.	.	.	.	.
	3rd gen. Cephalosporins R	.	.	.	.	.
E. faecalis	Aminopenicillins I+R	.	.	.	.	.
	Aminoglycosides (high-level resistance)	.	.	.	.	.
	Glycopeptides I+R	.	.	.	.	.
E. faecium	Aminopenicillins I+R	.	.	.	.	.
	Aminoglycosides (high-level resistance)	.	.	.	.	.
	Glycopeptides I+R	.	.	.	.	.

Table 4. Details on the origin of invasive isolates in the reporting period

Characteristic	*S. pneumoniae* n=3225		*S. aureus* n=8865		*E. coli* n=0		*E. faecalis* n=0		*E. faecium* n=0	
	%total	%PNSP	%total	%MRSA	%total	%FREC	%total	%VRE	%total	%VRE
Isolate source										
Blood	97	5	100	42	.	.	.	.	.	.
CSF	3	6	0	.	.	.	.	.	.	.
Sex										
Male	45	5	58	44	.	.	.	.	.	.
Female	41	5	35	40	.	.	.	.	.	.
Unknown	14	4	6	42	.	.	.	.	.	.
Age (years)										
0-4	11	6	4	8	.	.	.	.	.	.
5-19	4	4	3	14	.	.	.	.	.	.
20-64	27	5	34	36	.	.	.	.	.	.
65 and over	42	5	51	51	.	.	.	.	.	.
Unknown	16	4	8	39	.	.	.	.	.	.
Hospital department										
ICU	5	5	8	66	.	.	.	.	.	.
Internal Medicine	33	5	40	41	.	.	.	.	.	.
Surgery	2	5	11	56	.	.	.	.	.	.
Other	38	5	33	33	.	.	.	.	.	.
Unknown	22	5	8	43	.	.	.	.	.	.

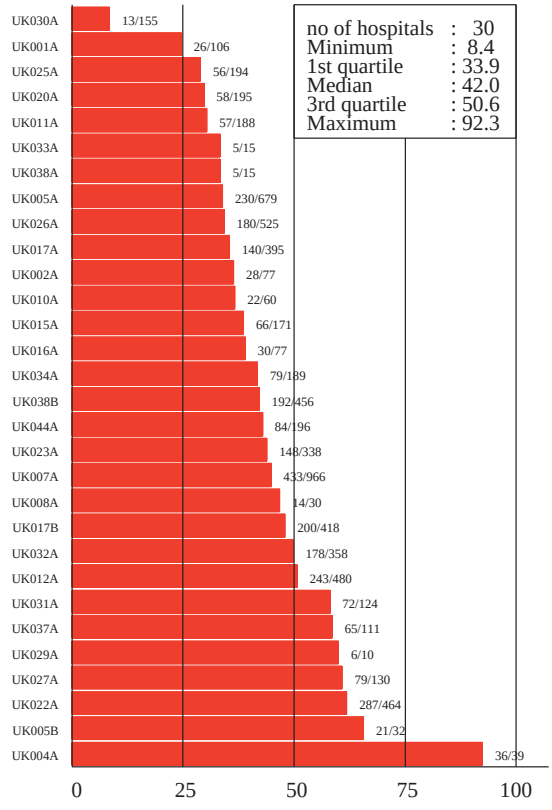
PNSP at laboratory level

Figure 3. Proportion (%) PNSP by laboratory (1999-2003)



MRSA at hospital level

Figure 4. Proportion (%) MRSA by hospital (1999-2003)



Appendix B Technical Notes

Notes to Country Summary Sheets (Appendix A)

Inclusion criteria.
To be included in the analyses presented in Table 1 of the country summary sheets (Appendix A), countries, laboratories and hospitals had to provide both denominator data and AST results in 2002. Also, a laboratory had to indicate blood culture frequencies and the number of hospital beds for each hospital served.

Presentation of variables per country.
Catchment population, number of beds, and number of blood culture sets were aggregated by country. If ranges were given for catchment population, occupancy rate, or number of blood culture bottles per set, means were used instead (e.g. 1 to 3 = 2).

Formulas.
From each hospital, either hospital occupancy rate or the number of patient-days was required. Occupancy rates could then be derived from patient-days, and *vice versa*.
Hospital occupancy rate was calculated if not provided or if the occupancy was considered implausible (i.e. less than 25% or more than 125%). The following formula was used:

$$\text{no. of patient-days} / (\text{no. of beds} \times 365).$$

The average occupancy rate per country was calculated as follows:

$$[\sum (\text{occupancy rate} \times \text{no. of beds}) / \sum (\text{no. of beds})]$$

For calculation of the total catchment population, hospitals providing only a specific (superregional) type of care (classified as other, e.g. oncology or psychiatric hospitals) were not included because we considered this population as probably overlapping with the catchment populations of the hospitals providing general care.

Population coverage per country was calculated using the following formula:

$$\sum (\text{hospital catchment population}) / \text{total population}$$

The total population of mid 2002 was obtained from the CIA World Fact book.