



RIJKSINSTITUUT VOOR VOLKSGEZONDHEID EN MILIEU
NATIONAL INSTITUTE OF PUBLIC HEALTH AND THE ENVIRONMENT

RIVM report 218621001

EARSS:

European Antimicrobial Resistance Surveillance System; data from the Netherlands (1999)

Incidence and resistance rates for *Streptococcus pneumoniae* and *Staphylococcus aureus*

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June 2001

¹for participating laboratories see page 3

This investigation has been performed by order and for the account of the European Union, DGV, within the framework of project EARSS (V/218621/10/AR).

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Abstract

In a prospective prevalence and incidence survey in the Netherlands in 1999 antimicrobial susceptibility data on invasive *Streptococcus pneumoniae* and *Staphylococcus aureus* infections were collected within the framework of European Antimicrobial Resistance Surveillance System (EARSS). Data on the catchment population and the hospital coverage (in patient-days) indicated that the EARSS project covered approximately 40% of the Dutch population (extramural) and 40% of the total number of patient-days (intramural). Susceptibility data on 767 invasive *S. pneumoniae* isolates and 1259 invasive *S. aureus* isolates were collected from 21 laboratories. Penicillin resistance in *S. pneumoniae* was minimal; only 9 of 767 (1.2%) isolates were non-susceptible. These strains all had MICs between 0.12 and 1 mg/l. Resistance to other antibiotics in *S. pneumoniae* was also low. Resistance to oxacillin in *S. aureus* was low, only 4 (0.3%) isolates were MRSA (*mecA* positive). Resistance to other antibiotics in *S. aureus* was also low. The incidence of invasive *S. pneumoniae* was 117 cases/1,000,000 person-years; the incidence of invasive penicillin non-susceptible *S. pneumoniae* was 1 case/1,000,000 person-years. The incidence of invasive *S. aureus* infections was 0.25 cases/1000 patient-days; the incidence of invasive MRSA infections was 0.0006 cases/1000 patient-days. EARSS can be concluded to contribute added value to national antimicrobial surveillance in Netherlands, since not only data on susceptibility testing were collected and compared, but also data on susceptibility testing methods, and hospital and community coverage. Integration of these different information sources has led to more insight into the comparability of susceptibility data and the public health relevance of antimicrobial resistance.

Preface

Antimicrobial resistance is an emerging problem across the Member States of the European Union (EU). In order to compare differences in antibiotic resistance in the Member States an European Antimicrobial Resistance Surveillance System (EARSS) was started in the beginning of 1998. This project is funded by the European Commission, DG Sanco, (DG responsible for Health) and accumulates antimicrobial resistance surveillance data from the different Member States as well from Iceland and Norway. EARSS is based on national surveillance systems. Data from these national surveillance systems are collected, aggregated and analysed at the Dutch National Institute of Public Health and the Environment. In this report we present the start up of the Dutch National Part of the EARSS surveillance and the results of one year EARSS surveillance in the Netherlands.

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Samenvatting

Doel: Het verzamelen en analyseren van gevoeligheidsgegevens van invasieve *Streptococcus pneumoniae* and *Staphylococcus aureus* isolaten in Nederland binnen het kader van het European Antimicrobial Resistance Surveillance System (EARSS).

Opzet: Prospectief prevalentie en incidentie onderzoek in de medische microbiologische laboratoria in Nederland in 1999.

Methode: Gegevens over de dekkinggraad in de open bevolking van het EARSS project werden geschat met behulp van adherentiegegevens van ziekenhuizen, die door de EARSS laboratoria werden bediend. Gegevens over de dekkinggraad van EARSS over alle Nederlandse ziekenhuizen (in patiëntdagen) werden ontvangen uit de gegevens van het Nederlandse instituut Prismant. Daarnaast werden gegevens over de gebruikte gevoeligheidsbepalingen verzameld om deze te vergelijken met de resultaten van de gevoeligheidsbepalingen. Tenslotte werden de gevoeligheidsgegevens met betrekking tot *S. pneumoniae* and *S. aureus* elektronisch elk kwartaal van de deelnemende laboratoria verzameld.

Resultaten: EARSS had een dekkinggraad van ongeveer 40% (zowel over de ziekenhuizen als over de open populatie). Gegevens uit de vragenlijsten over de gebruikte testmethoden gaven aan dat de meeste (16/20) Nederlandse laboratoria voor *S. pneumoniae* het EARSS protocol volgden. Daarentegen werd voor *S. aureus* slechts door een aantal laboratoria (10/19) het EARSS protocol gevolgd. Gevoeligheidsgegevens werden verzameld over 767 invasieve *S. pneumoniae* isolaten en 1259 invasieve *S. aureus* isolaten van 21 laboratoria. Penicilline resistentie in *S. pneumoniae* was minimaal; slechts 9 van 767 (1.2%) isolates waren niet gevoelig. Deze stammen hadden allen MICs tussen de 0.12 en 1 mg/l. Resistentie in *S. pneumoniae* tegen andere antibiotica was ook laag. Resistentie tegen oxacilline in *S. aureus* was laag, slechts 4 (0.3%) isolaten waren MRSA (*mecA* positief). Ook was de resistentie tegen andere antibiotica in *S. aureus* laag. De incidentie van invasieve *S. pneumoniae* was 117 cases/1.000.000 bewoners; de incidentie van invasieve penicilline niet gevoelige *S. pneumoniae* was 1 case/1.000.000 bewoners. De incidentie van invasieve *S. aureus* infecties was 0.25 cases/1000 patiëntdagen; de incidentie van invasieve MRSA infecties was 0.0006 cases/1000 patiëntdagen.

Conclusies: EARSS heeft een toegevoegde waarde voor de nationale surveillance van antimicrobiële resistentie omdat in deze surveillance niet alleen gevoeligheidsgegevens, maar ook gegevens over de gebruikte gevoeligheidstesten en gegevens over de dekkinggraad van de surveillance worden verzameld. Integratie van deze informatiebronnen heeft geleid tot meer inzicht in de vergelijkbaarheid van de gevoeligheidsdata en in public health relevantie van antibioticumresistentie.

Summary

Objective: The collection and analysis of susceptibility data on invasive *S. pneumoniae* and *S. aureus* isolates in the Netherlands in the framework of the European Antimicrobial Resistance Surveillance System (EARSS).

Design: Prospective prevalence and incidence survey in medical microbiological laboratories in the Netherlands in 1999.

Methods: Data on the catchment population were estimated using adherence population data from hospitals served by the EARSS. Data on the hospital coverage (in patient-days) were derived from Prismant. Laboratories were interviewed for the methods and the interpretative criteria that were used locally for susceptibility testing. Subsequently, test results were compared with the methods and criteria in order to be able to explain discrepancies between laboratories. Finally, susceptibility data on *S. pneumoniae* and *S. aureus* were electronically extracted from local laboratories on a quarterly basis.

Results: Approximately 40% of the Dutch population participated in the EARSS project and 40% of the total number of patient-days were used. Data from the questionnaire on susceptibility methods indicated that most laboratories had followed the EARSS protocol for susceptibility testing for *S. pneumoniae*. However, only a few laboratories strictly followed the EARSS protocol for *S. aureus*. In 1999, susceptibility data on 1259 invasive *S. aureus* isolates and 767 invasive *S. pneumoniae* isolates were collected from 21 laboratories. Penicillin resistance in *S. pneumoniae* was minimal; only 9 out of 767 (1.2%) isolates were non-susceptible. These strains all had MICs between 0.12 mg/l and 1 mg/l. Resistance of *S. pneumoniae* to other antibiotics was also low. Resistance of *S. aureus* to oxacillin was low; only 4 (0.3%) isolates were MRSA (mecA positive). Resistance to other antibiotics in *S. aureus* was also low. Invasive *S. pneumoniae* showed an incidence of 117 cases/1,000,000 inhabitants; the incidence of invasive penicillin non-susceptible *S. pneumoniae* was one case/1,000,000 inhabitants. The incidence of invasive *S. aureus* infections was 0.25 cases/1000 patient-days; the incidence of invasive MRSA infections was 0.0006 cases/1000 patient-days.

Conclusions: EARSS contributes added value to national antimicrobial surveillance in Netherlands, since not only data on susceptibility testing were collected and compared, but also data on susceptibility testing methods, and hospital and community coverage. Integration of these different information sources has led to more insight into the comparability of susceptibility data and the public health relevance of antimicrobial resistance.

1. Introduction

Antimicrobial resistance is an emerging problem across the Member States of the European Union (EU). In order to compare differences in antibiotic resistance in the Member States an European Antimicrobial Resistance Surveillance System (EARSS) started in the beginning of 1998. This project is funded by the European Commission (DG V) and accumulates antimicrobial resistance surveillance data from the different Member States and Iceland and Norway. EARSS is based on national surveillance systems. Data from these national surveillance systems are collected, aggregated and analysed at the Dutch National Institute of Public Health and the Environment.

In most participating countries the EARSS surveillance was set up or based on an already present surveillance system for antimicrobial resistance. In the Netherlands two major surveillance systems were already present: the Infectious Diseases Surveillance Information System (ISIS; www.isis.rivm.nl) and the National Public Health Laboratory Resistance Surveillance System. We used those two surveillance systems to start up the EARSS surveillance for *S. pneumoniae* and *S. aureus*. Additionally, a number of other laboratories also participated in EARSS in order to increase the coverage of EARSS in the Netherlands.

In this report, we want to describe the experiences with one year of EARSS surveillance (1999) in the Netherlands. We will give special attention to:

1. How to use different data sets and formats for surveillance?
2. What are the techniques used for antimicrobial susceptibility testing?
3. How can we calculate coverage for hospital- and community-acquired pathogens?
4. Do we find resistance to the most important antibiotics in invasive *S. pneumoniae* and *S. aureus* infections?
5. What is the value of the EARSS network in addition to the existing antimicrobial susceptibility surveillance networks?

2. Material and Methods

2.1 Selection of laboratories

Laboratories were selected on basis of a number of criteria:

- a. Coverage of all participating laboratories had to be at least 20% of the Dutch population (for *S. pneumoniae*) and 20% of the total number of patient-days in 1999 in the Netherlands (for *S. aureus*)
- b. Coverage had to be nation-wide, no important regions can be missed.
- c. All different kinds of hospitals had to be covered; academic and non-academic hospitals
- d. Participation in an already existing electronic surveillance network, such as ISIS surveillance network or the Public Health Laboratory Resistance Network (PHLRN). This is not mandatory, laboratories which were not participating in these two projects were also included in the EARSS

2.2 Calculation of the coverage

2.2.1 Hospital coverage

In order to calculate hospital coverage, data on the number of patient-days were derived from a Dutch National Institute, called Prismant, which collects basic data on a yearly basis from all Dutch hospitals¹. However, in some cases the laboratories did not identify the hospital for every single isolate. So, we were only able to calculate the total hospital coverage for a laboratory, knowing which hospitals were served by an individual EARSS participating laboratory.

2.2.2 Coverage of the community

Data on the catchment population (or coverage) of laboratories were often not present. For that reason we tried to estimate the catchment population of the Dutch laboratories on basis of adherence of the hospitals which were served by these laboratories. Data on the number of admissions from all hospitals in the Netherlands were available for every individual municipality for the year 1996 at the National Institute of Public Health². We assumed that there was a linear relation between the number of admissions and microbiological workload for a laboratory. This seemed a reasonable assumption in case of invasive infections, where the microbiological sample is taken in the hospital where the patient stays. Using this information it was possible to calculate a percentage of laboratory coverage for every municipality (see table 1). Using the percentages, and the number of people living in the municipalities, we could calculate a catchment population for every laboratory (for an example, see table 1). For some laboratories the catchment population, calculated on basis of the adherence of hospitals, could be compared with the catchment population calculated on the basis of geographical background information on the isolates tested by these laboratories. This indicated that the catchment population, calculated on basis of the adherence of the hospital, gave a good indication of the catchment of a laboratory³.

Table 1. Example of a calculation of catchment population on basis of the adherence of the hospitals in the different municipalities

| Name of lab | Location of lab | Municipality | Number of admissions | Total number of admissions | % ¹ | Number of citizens | Catchment ² |
|-------------------|-----------------|--------------|----------------------|----------------------------|----------------|--------------------|------------------------|
| St. Jans Gasthuis | Weert | WEERT | 4137 | 5052 | 82 | 40695 | 33324 |
| St. Jans Gasthuis | Weert | NEDERWEERT | 1349 | 1672 | 81 | 15506 | 12511 |
| St. Jans Gasthuis | Weert | STRAMPROY | 435 | 552 | 79 | 4961 | 3909 |
| St. Jans Gasthuis | Weert | BUDEL | 858 | 1375 | 62 | 12025 | 7504 |
| St. Jans Gasthuis | Weert | HUNSEL | 379 | 610 | 62 | 5762 | 3580 |
| St. Jans Gasthuis | Weert | HEYTHUYSEN | 471 | 1179 | 40 | 11300 | 4514 |
| St. Jans Gasthuis | Weert | THORN | 122 | 364 | 34 | 2645 | 887 |
| St. Jans Gasthuis | Weert | MAARHEEZE | 320 | 1011 | 32 | 8925 | 2825 |
| St. Jans Gasthuis | Weert | MEIJEL | 106 | 543 | 20 | 5348 | 1044 |
| St. Jans Gasthuis | Weert | HEEL | 125 | 865 | 14 | 8320 | 1202 |
| | | TOTAL | | | | | 71300 |

¹=percentage of admissions covered by this laboratory

²=catchment is a product of the percentage coverage and the number of citizens

2.3 Collection of data on laboratory testing methods

A questionnaire (annex 2) was developed in order to get information on:

- the participating laboratory
- the hospitals which were served by this laboratory
- laboratory methods which were used to determine *S. pneumoniae* and *S. aureus*
- testing methods which were used to assess the susceptibility of these two micro-organisms (see annex 2). These testing methods were compared to the official EARSS protocol as was defined in the EARSS manual (annex 6).

This questionnaire was sent out to all laboratories. Additionally, some laboratories which were part from ISIS or PHLRN got a similar, but somewhat different, questionnaire.

2.4 Data check of susceptibility testing results from the laboratories

Data from ISIS and PHLRN surveillance were converted into EARSS format (see annex 3) using SAS software, version 6.12 (SAS Institute, Cary, NC, USA). Data from laboratories that did not participate in these two surveillance systems, were mostly received in ASCII format and were converted in EARSS format using SAS software. Data were validated using SAS software; records without any information on the month or year of birth were deleted. Month and year of birth, gender, type of pathogen and laboratory-code were used to specify an unique patient-identifier in order to remove duplicates in every quarter. Validated data were used for the analysis of susceptibility of *S. pneumoniae* and *S. aureus*.

3. Results

3.1 Basic characteristics of participating laboratories

We collected data from 21 laboratories (annex 4). Most of the laboratories were public health laboratories (13), but also general (5) and university hospitals (3) were included. Most regions of the Netherlands were represented in the EARSS surveillance (figure 1).

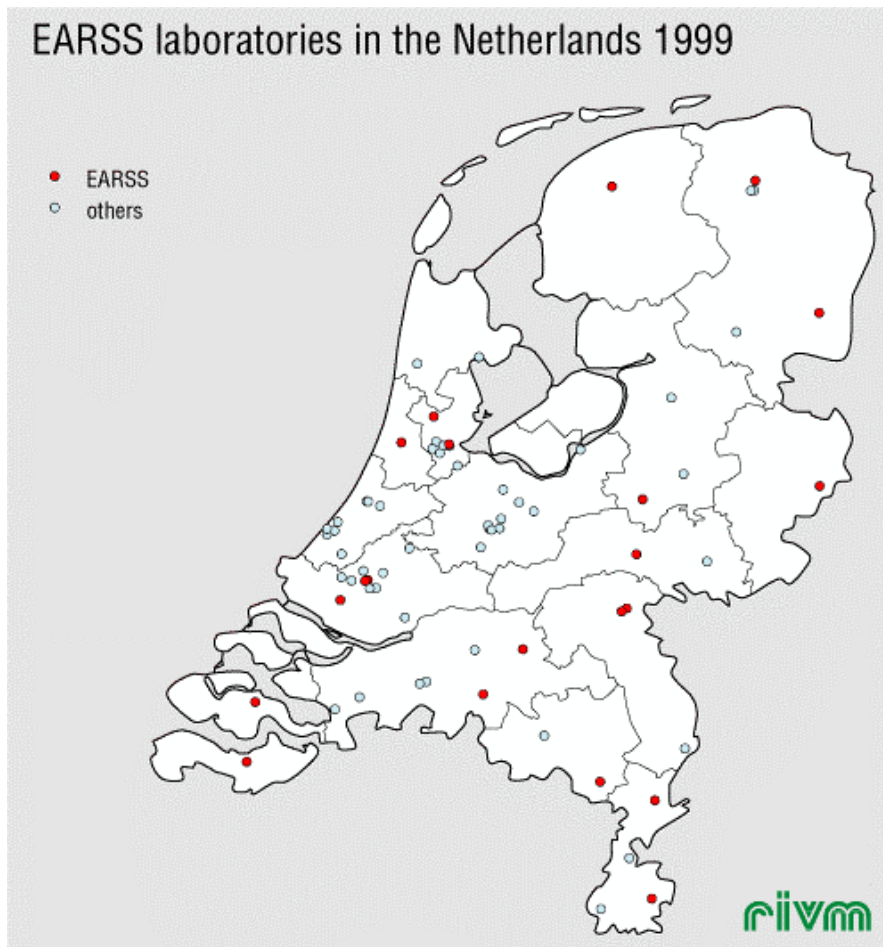


Figure 1. EARSS laboratories in the Netherlands in 1999

3.2 Coverage of EARSS in the Netherlands

Calculation of the hospital catchment indicated that the laboratories covered approximately 40% of the total number patient-days in the Netherlands in 1999 (annex 4).

Calculation of the community catchment based on the admission data of the hospital indicated a coverage of EARSS of approximately 40% of the Dutch population. The catchment data on individual hospitals demonstrated a large variation in coverage (annex 4).

3.3 Methods of antibiotic susceptibility testing

3.3.1 Type of antibiotics tested

We collected information on testing methods from 20 laboratories on *S. pneumoniae* and 19 laboratories on *S. aureus*. A large number of antibiotics was tested by the different laboratories. Table 2 summarises the most important antibiotics tested with *S. pneumoniae* and *S. aureus*. Most antibiotics tested for both pathogens were oxacillin and erythromycin. For *S. pneumoniae* oxacillin was mostly tested in combination with penicillin; when the *S. pneumoniae* strain was non-susceptible after the first oxacillin disk test, the MIC was measured using an E-test (15/20). Other antibiotics, as defined by the EARSS protocol (annex 6), were not tested very frequently, cefotaxime (7/20), ceftriaxone (7/20) and ciprofloxacin (5/20) were only tested in some laboratories. However, in some cases these antibiotics were only tested in the case of a suspected MRSA. For *S. aureus*, mostly oxacillin is used for MRSA testing, additionally sometimes methicillin is used. Also vancomycin is often tested, not only on methicillin resistant *S. aureus* (MRSA) but also on methicillin susceptible *S. aureus* (MSSA).

Table 2. Antibiotics tested for *S. aureus* and *S. pneumoniae*

| | | <i>S. pneumoniae</i> | | <i>S. aureus</i> | |
|-------------------------|------------------------------|----------------------|------------------------|------------------|------------------------|
| | | always | resistant ¹ | always | resistant ² |
| Penicillins | Oxacillin | 18/20 | 1/20 | 15/19 | 1/19 |
| | Methicillin | -- | -- | 5/19 | 3/19 |
| | Flucloxacilline | -- | -- | 1/19 | 0/19 |
| | Penicillin | 9/20 | 8/20 | 8/19 | 0/19 |
| | Amoxicillin | 6/20 | 0/20 | 5/19 | 0/19 |
| | Amoxicillin/clavulanic acid | 4/20 | 0/20 | 3/19 | 1/19 |
| Cefalosporins | Cefotaxime | 5/20 | 2/20 | 1/19 | 0/19 |
| | Cefuroxime | 6/20 | 0/20 | 3/19 | 0/19 |
| | Ceftriaxone | 1/20 | 6/20 | -- | -- |
| Macrolides | Erythromycin | 19/20 | 0/20 | 16/19 | 0/19 |
| | Clarithromycin | 3/20 | 0/20 | 1/19 | 0/19 |
| Tetracyclines | Tetracycline | 15/20 | 0/20 | 7/19 | 1/19 |
| | Doxycycline | 3/20 | 0/20 | 1/19 | 0/19 |
| Aminoglycosides | Gentamicin | 2/20 | 0/20 | 11/19 | 2/19 |
| | Tobramycin | 1/20 | 0/20 | 3/19 | 3/19 |
| Fluoroquinolones | Ciprofloxacin | 3/20 | 2/20 | 5/19 | 4/19 |
| | Ofloxacin | 3/20 | 0/20 | 5/19 | 1/19 |
| Others | Clindamycin | 3/20 | 0/20 | 9/19 | 0/19 |
| | Trimethoprim/sulfamethoxazol | 7/20 | 1/20 | 7/19 | 2/19 |
| | Vancomycin | 10/20 | 6/20 | 14/19 | 3/19 |
| | Rifampin | -- | -- | 3/19 | 2/19 |
| | Fusidic acid | -- | -- | 0/19 | 3/19 |
| | Mupirocin | -- | -- | 2/19 | 2/19 |

¹resistant=only tested when penicillin non-susceptible *S. pneumoniae* is suspected.

²resistant=only tested when methicillin resistant *S. aureus* is suspected

Additionally, we compared data from the questionnaire with real susceptibility data in order to verify whether strains were tested for the antibiotics indicated in the questionnaire. Table 3 indicated that there were large discrepancies between the information from questionnaire and the real data. For instance, oxacillin test results for *S. pneumoniae* and *S. aureus* seemed to be far less common than suggested from the data from the questionnaire. This will be reviewed in more detail in the discussion.

Table 3. Percentage of isolates tested for antibiotics as indicated 'always tested' in the questionnaire

| <i>S. pneumoniae</i> | never | <25% | 26-50% | 51-75% | >75% | always |
|----------------------|-------|------|--------|--------|------|--------|
| Oxacillin | 11/18 | 2/18 | 1/18 | 1/18 | 0/18 | 3/18 |
| Penicillin | 0/9 | 0/9 | 1/9 | 0/9 | 0/9 | 8/9 |
| Ceftotaxime | 0/5 | 1/5 | 1/5 | 1/5 | 1/5 | 1/5 |
| Erythromycin | 1/19 | 0/19 | 0/19 | 1/19 | 1/19 | 16/19 |
| Tetracycline | 3/15 | 1/15 | 0/15 | 3/15 | 5/15 | 3/15 |
| Ciprofloxacin | 0/3 | 1/3 | 0/3 | 0/3 | 0/3 | 2/3 |

| <i>S. aureus</i> | never | <25% | 26-50% | 51-75% | >75% | always |
|------------------|-------|------|--------|--------|------|--------|
| Oxacillin | 6/15 | 1/15 | 0/15 | 1/15 | 0/15 | 6/15 |
| Methicillin | 2/5 | 1/5 | 0/5 | 0/5 | 0/5 | 2/5 |
| Penicillin | 0/8 | 0/8 | 0/8 | 0/8 | 1/8 | 7/8 |
| Erythromycin | 1/16 | 1/16 | 0/16 | 0/16 | 3/16 | 11/16 |
| Gentamicin | 0/11 | 1/11 | 0/11 | 1/11 | 4/11 | 5/11 |
| Vancomycin | 0/14 | 1/14 | 0/14 | 1/14 | 2/14 | 10/14 |

3.3.2 Type of methods used for antibiotic testing

We analysed the techniques used to perform antimicrobial susceptibility testing; mainly three techniques were used; screen- disk and MIC testing. Data indicated that there was large variation between the techniques used in the different laboratories. For *S. pneumoniae* disks were often used for susceptibility testing. Mostly, Rosco tablets were used, sometimes also Oxoid disks were used (annex 5). Additionally, when a MIC-test was used, mostly E-tests were used, for example for testing penicillin resistance (annex 5). For *S. aureus* MIC testing was more common (annex 5). However, this could be partly attributed to the use of an automated machine, such as the VITEK (annex 5), which does not measure a real MIC, but calculates a MIC on basis of the growth curve of bacteria in media supplemented with antibiotics.

3.3.3 Comparison between susceptibility testing methods as indicated in the questionnaire and the EARSS protocol

We compared the techniques used by the different laboratories with the EARSS protocol (annex 6) at different levels (table 4). For *S. pneumoniae*, it was clear that most laboratories tested the bacteria for oxacillin, using a 1 µg oxacillin disk. In case of a non-susceptible strain additionally a MIC for penicillin was determined (table 4). The agreement with the EARSS protocol was lower when breakpoint were added to comparison (table 4A). For *S. aureus*, the compatibility with the EARSS protocol was low (table 4). When breakpoint were included in the comparison only a few laboratories strictly followed the EARSS protocol

Table 4. Comparison of methods used for antibiotic susceptibility testing for *S. aureus* and *S. pneumoniae* and the EARSS protocols.

| <i>S. pneumoniae</i> | | |
|-----------------------------|---|---|
| Method | | Result |
| 1. | Oxacillin disk | 18/20 |
| 2. | 1 µg or 5 µg oxacillin disk | 18/20 |
| 3. | 1 µg (20 mm S breakpoint) or 5 µg (26 mm S breakpoint) oxacillin disk | 13/20 |
| 4. | MIC for penicillin | 18/20 |
| 5. | Combination of 1 and 4 | } 16/20 |
| 6. | Combination of 2 and 4 | }> adherence to EARSS protocol 16/20 |
| 7. | Combination of 3 and 4 | } 11/20 |

| <i>S. aureus</i> | | |
|-------------------------|--|---|
| Method | | Result |
| 1. | Oxacillin disk or oxacillin screen plate | 12/19 |
| 2. | 1 µg or 5 µg oxacillin disk or 6 µg oxacillin screen plate | 11/19 |
| 3. | 1 µg (10 mm S breakpoint) or 5 µg (19 mm S breakpoint) oxacillin disk or 6 µg oxacillin screen plate | 3/19 |
| 4. | MIC for oxacillin | 5/19 |
| 5. | PCR <i>mecA</i> test (local or at reference laboratory) | 10/19 |
| 6. | Combination of 1 and 4 and 5 | } 10/19 |
| 7. | Combination of 2 and 4 and 5 | }> adherence to EARSS protocol 10/19 |
| 8. | Combination of 3 and 4 and 5 | } 2/19 |

3.4 Susceptibility results

3.4.1 Basic characteristics of the data

Data were collected electronically. Five laboratories delivered the data using the ISIS system; eight laboratories used the format of the PHLRN; seven laboratories delivered data in EARSS format and one laboratory sent on paper. Most of the data, obtained from those laboratories were qualitative data; that means interpretations (S, I, R). In some cases, also data from MIC, E-tests and zone diameters were delivered.

3.4.2 Basic characteristics of the patients and isolates

Susceptibility test results from 767 invasive *S. pneumoniae* and 1259 *S. aureus* isolates were collected from 21 laboratories. Basis statistics on the patients are summarised in annex 7. Information on clinical diagnosis and other conditions was rare. Information on hospital department was reported in approximately 50% of the isolates. Information on the origin of the patient showed that most patients with both infections were admitted (>80% of the 'known' patients). There was a slight overrepresentation of male patients (55-60%) and nearly 50% of the patients was 66 years or older. Most isolates were from blood, only 10% of the strains were isolated from cerebrospinal fluid in case of *S. pneumoniae* infections.

3.4.3 Results from ATCC quality control

Of all participating laboratories four laboratories regularly sent data on the testing of the four quality control ATCC strains. This response was low. Results of these four labs indicated that their testing results were similar to the testing results of the Dutch Reference Laboratory for EARSS (National Institute of Public Health and the Environment).

3.4.4 Antibiotic susceptibility in *S. pneumoniae*

On a total of 767 isolates we found 9 isolates, which were scored as non-susceptible. Eight of those had MICs for penicillin, which were all intermediate (annex 8). Most of these were susceptible for other antibiotics. Overall, in all *S. pneumoniae* isolates resistance to the most antibiotics was low (figure 2A). Only resistance to ciprofloxacin/ofloxacin seemed to be high. This was probably due to the low intrinsic activity of this generation of fluoroquinolones for *S. pneumoniae*. Results for the individual laboratories are presented in annex 9.

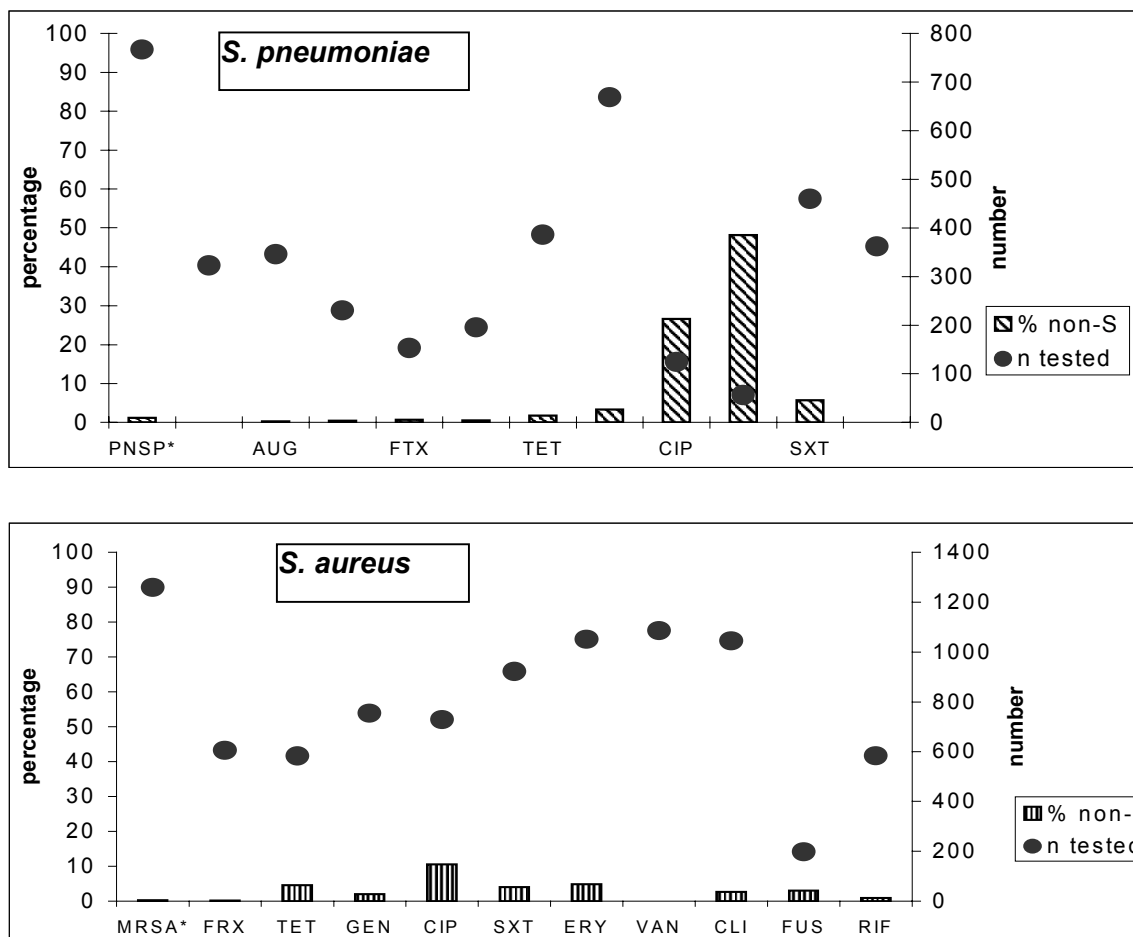


Figure 2. Resistance to most important antibiotics and number of isolates tested in *S. pneumoniae* and *S. aureus*. PNSP* (penicillin non susceptible *S. pneumoniae*) is determined by testing of susceptibility for oxacillin in combination with penicillin. MRSA* (methicillin resistant *S. aureus*) is determined by testing of susceptibility for oxacillin or methicillin.

3.4.5 Antibiotic susceptibility in *S. aureus*

On a total of 1259 invasive *S. aureus* isolates 4 MRSA were found. All four strains were PCR Meca positive and had high MICs for flucloxacillin and methicillin (annex 8). The strains were susceptible for vancomycin, gentamicin (3/4 tested), cotrimoxazole (3/4 tested). When all *S. aureus* strains were studied, the percentage of non-susceptible strains was low; for most antibiotics the percentage of non-susceptible strains was below 5%. Results for the individual laboratories were presented in annex 9.

3.4.6 Incidence of *S. pneumoniae* and *S. aureus*

Incidences were calculated for invasive *S. pneumoniae* and *S. aureus* infections using the hospital and community coverage data. Data are presented for the individual laboratories in figure 3. Incidence of invasive *S. pneumoniae* infections varied between 0.07 and 0.3 cases per 1000 nursing days and varied between 7 and 20 cases per 100000 person-years. Incidence of invasive *S. aureus* infections varied between 0.1 and 0.5 cases per 1000 nursing days and varied between 10 and 40 cases per 100000 person-years. Incidence of PRP and MRSA was low; only a few hospitals reported 1 or 2 invasive PRP and MRSA infections.

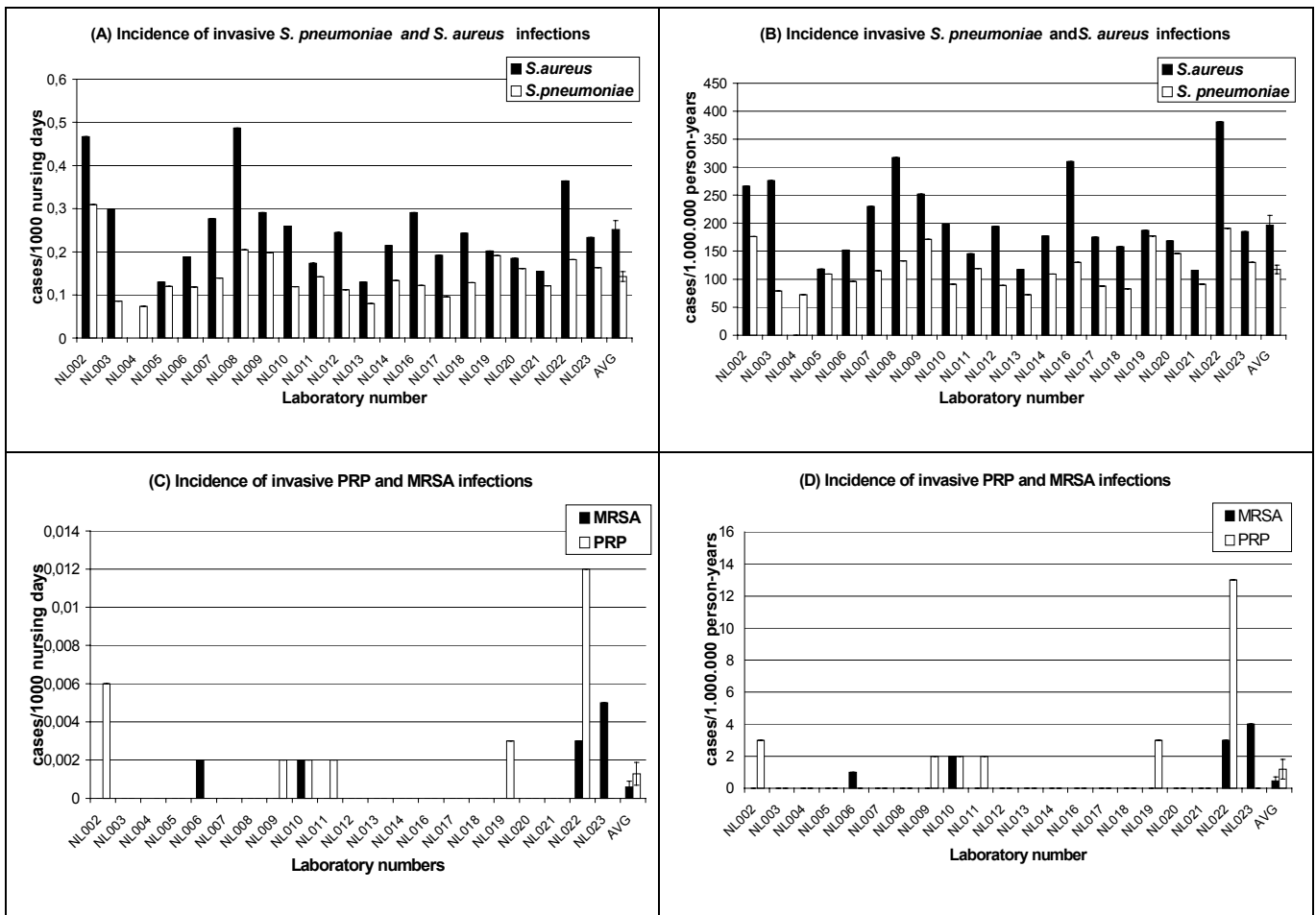


Figure 3. Incidence of invasive S. pneumoniae and S. aureus and in the hospital (A) and community (B) and incidence of invasive PRP and MRSA in the hospital (C) and community (D). AVG=average, which is presented as average of all laboratories + standard error of the mean (SEM).

4. Discussion

The results of 1999 EARSS data collection indicated that it is possible to get data on susceptibility of different pathogens together with information on the testing methods of the participating laboratories. This information is necessary when the validity of a comparison of surveillance data from different laboratories is estimated.

The data on the coverage indicated that EARSS in the Netherlands covered a reasonable number of laboratories, which served 40% of the community and the hospitals. In the EARSS surveillance different kinds of laboratories were included; not only public health laboratories but also laboratories affiliated to general hospitals and large university hospitals were included. We also demonstrated in figure 1 that EARSS covered all regions of the Netherlands. So, we believe that EARSS gave a representative picture of the Netherlands, concerning the antibiotic susceptibility of invasive *S. pneumoniae* and *S. aureus* infections. However, we decided in 2000 to expand the EARSS system in the Netherlands, because we believe that it is important to involve a larger number of (university) hospitals in order to increase the support for this surveillance system.

A comparison of the information on the testing methods used (as we got from the questionnaire) and the susceptibility results showed some interesting differences. While most laboratories indicated in the questionnaire that they tested oxacillin as a first screening method for *S. pneumoniae* and *S. aureus*, the laboratories often reported results on penicillin (*S. pneumoniae*), methicillin (*S. aureus*) and flucloxacillin (*S. aureus*). The reason for this difference is obvious; results from antibiotic susceptibility testing must guide the clinicians in the hospitals in their choice of therapy. Thus, medical microbiologists will report on penicillin (*S. pneumoniae*) and flucloxacillin (*S. aureus*) which are the first choice for the clinician when the strains are susceptible, but not on oxacillin which is not used for clinical therapy. This result, however, underlines the importance of information on the susceptibility testing methods; on basis of the test data only it could be wrongly assumed that only a few Dutch laboratories use oxacillin as a first screening for PRP and MRSA.

More detailed information on the methods used for susceptibility testing indicated a large variety of different methods used. For penicillin susceptibility testing of *S. pneumoniae*, there was a large agreement in testing method. The use of a 1 µg oxacillin disk, followed by a penicillin E-test, for penicillin susceptibility testing is common and accepted around the world. So, for this pathogen the EARSS protocol was followed by most participating laboratories. However, it must be emphasised that the second step in the EARSS protocol was only partly followed; additional E-test testing for ceftriaxone or cefotaxime and ciprofloxacin were rarely performed (less than 25% of the participating laboratories).

A large variety of methods was used for MRSA testing. In addition to the widely accepted 6 µg oxacillin screen test, 1 and 5 µg oxacillin and methicillin disks were used for MRSA testing. Furthermore, also the VITEK was used often for the susceptibility testing of *S. aureus*. Thus, the EARSS protocol was only utilised by a limited number of participating laboratories (10/19). Results of the external QA can be used in order to estimate whether the use of different testing methods will lead to different test results.

A first analysis of the quality of the testing results indicated that it is difficult for most laboratories to get additional clinical information. Not only information on the clinical diagnosis but also information on the condition of the patient was difficult to obtain. The standard set of data from the susceptibility testing of isolates, which derived from a laboratory information system (LIS), had only limited information on the patient. However, this problem was not limited to the Dutch laboratories, in general in EARSS participating laboratories had no or limited clinical information⁴.

Another problem was the availability of quantitative MIC data. Especially MICs on ceftriaxone for *S. pneumoniae* and on vancomycin for *S. aureus* were difficult to obtain. We believe that it is important to collect this information, because it gives additional valuable insight in the susceptibility pattern of non-susceptible *S. pneumoniae* and *S. aureus*.

In the beginning of 1999 we asked the participating laboratories to regularly test 4 ATCC strains in order to get some insight in the comparability of the data. However, only a limited number of laboratories regularly tested these 4 ATCC strains. Contacts with laboratories indicated that, although the workload of monthly testing of the four ATCC strains was not high, incorporation of this protocol within the regular daily testing was difficult. Also in other countries there were problems with incorporation of these QA strains in the daily practice. For that reason, we decided to (temporarily) stop this internal QA with strains with known susceptibility pattern. Instead, an external QA protocol was initialised in co-operation with the NEQAS and executed in September 2000. Participation in this protocol was more than 90% in the Netherlands, but also in average within the whole EARSS program. The results of this QA will be reported in a later stage.

Antibiotic resistance in *S. aureus* and *S. pneumoniae* was low. Penicillin resistance in *S. pneumoniae* was minimal ($\approx 1\%$). This result was comparable to other results from the Netherlands, which also reported low resistance to penicillin in invasive and non-invasive *S. pneumoniae* strains.^{5,6} When compared to other countries in the EARSS, it was clear that this resistance percentage is one of the lowest in the EU (figure 4).^{4,7} Resistance to other antibiotics, such as the cephalosporins, tetracycline, erythromycin and cotrimoxazole was also below 6%.

Oxacillin resistance in *S. aureus* was under 1%, which was in line with other results previously reported from the Netherlands^{8,9,10}. In comparison to the other EARSS participating countries, the resistance percentage was low (figure 4)⁷. Only four invasive MRSA infections were found, which were mostly susceptible for gentamicin and cotrimoxazole. Nevertheless, the EARSS surveillance for these two pathogens is only representative for invasive infections and resistance percentage in other compartments might be higher⁹.

Incidence rates are important in order to estimate the public health relevance of antimicrobial resistance. For that reason, we tried to calculate the incidence of susceptible and resistant *S. aureus* and *S. pneumoniae* infections in two different ways. Firstly, we calculated the number of (resistant) strains in relation to the number of patient-days in order to estimate the public health relevance of resistance for the hospital. Secondly, we also calculated the number of (resistant) strains in relation to the community coverage in order to estimate the public health relevance of resistance for the community. Our data gave an indication on the incidence of invasive *S. aureus* and *S. pneumoniae* infections in the

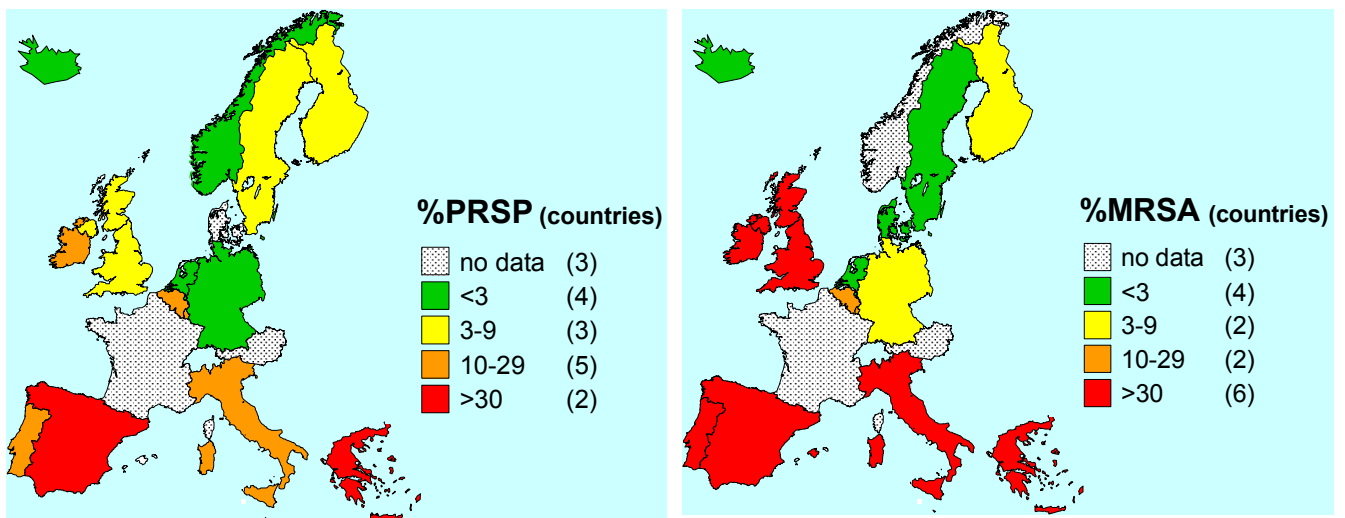


Figure 4. Percentages of invasive PRSP (penicillin resistant *S. pneumoniae*) and MRSA (methicillin resistant *S. aureus*) in the different EU countries participating in EARSS (1999)

different hospitals or in the community For *S. pneumoniae* these results were comparable to previous results reported by our institute¹¹. These data were difficult to compare to data on specific diagnoses¹², because the information on clinical diagnosis was rarely present in the EARSS database. Nevertheless, the information becomes relevant when it is compared to other countries. In comparison with Swedish data, it is evident that the incidence of invasive PRSP infections in the Netherlands is lower (1 case/1.000.000 pyrs (NL) versus 6 cases/1.000.000 pyrs (SE)). However, in most countries catchment data are still not available, which makes a comparison difficult. We believe that incidence data are important in order to investigate the public health relevance of resistant pathogens and to evaluate the effect of new intervention strategies or control policies directed to decrease the antimicrobial resistance. For that reason, it is important to find methods to calculate the catchment populations for the local laboratories in the different countries. EARSS must be committed to support its participating countries to develop these methods.

In conclusion, we believe that the EARSS surveillance in the Netherlands has an added value to already existing national surveillance systems. Firstly, we collected data in a format which was used in more than 15 countries, which made it easy to compare our national data to data from other countries. Secondly, in addition to SIR interpretations, we also collected quantitative data, which gave us more insight in the susceptibility of non-susceptible *S. aureus* and *S. pneumoniae* strains. Thirdly, by comparing the testing results to the data from the questionnaire it was possible to explain certain differences in testing methods by the different laboratories. However, external QA, as was already performed in September 2000, is essential to estimate whether the use of different techniques can be ignored or is relevant for the interpretation of the test results. Finally, we believe that the calculation of incidences of resistant pathogens will become more common in the near future; the EARSS network in the Netherlands is on the forefront in determining catchment populations in the order to estimate these incidences.

5. Acknowledgements

This study was impossible without the help of the medical microbiologists, laboratory personal and system administrators of the participating laboratories. Additionally, we want to thank Prof dr. J. Degener, dr. U. Buchholz and P. Schrijnemakers from the RIVM for reviewing this report.

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Annex 1 Mailing list

| | |
|---------|---|
| 1 | Ministerie van VWS, Directeur-Generaal |
| 2 | Hoofdinspecteur voor de Gezondheidszorg |
| 3-4 | Ministerie van VWS, Directie Gezondheidsbeleid |
| 5-6 | Inspectie voor de Gezondheidszorg |
| 7-11 | Earss Management Team |
| 12-112 | Contactpersonen EARSS project |
| 113 | Stichting Zorgonderzoek Nederland |
| 114 | Gezondheidsraad |
| 115 | Nederlandse Vereniging voor Medische Microbiologie |
| 116 | Landelijk Coördinatiestructuur Infectieziektenbestrijding |
| 117 | Vereniging voor Infectieziekten |
| 118 | Drs. M. Esveld |
| 119 | Drs. L. Koole |
| 120 | Prof. dr. J. Huisman |
| 121 | Prof. dr. J. van der Noordaa |
| 122 | Prof. dr. H. Verbrugh |
| 123 | Prof. dr. C.M.J.E. Vandenbroucke-Grauls |
| 124 | Prof. dr. J. Dankert |
| 125 | Prof. dr. J. Verhoef |
| 126 | Prof. dr. J.A.A. Hoogkamp-Korstanje |
| 127 | Dr. E. Stobberingh |
| 126-186 | Nationale coördinatoren EARSS |
| 187 | Depot Nederlandse Publicaties en Nederlandse bibliografie |
| 188 | Directie RIVM |
| 189 | Prof. dr. ir. D. Kromhout, RIVM |
| 190 | Hoofd CIE, RIVM |
| 191 | Drs. W.J. van Leeuwen, RIVM |
| 192 | Dr. J.F.P. Schellekens, RIVM |
| 193 | VPR |
| 194 | Bureau Rapporten registratie |
| 195-215 | Rapportenbeheer |
| 216 | Bibliotheek RIVM |
| 217-400 | Reserve |

ANNEX 2 Questionnaire on susceptibility testing

Questionnaire on *S. pneumoniae* and *S. aureus* susceptibility testing

Introduction

This survey is part of the pilot phase of EARSS (European Antimicrobial Resistance Surveillance System), funded by the EC/DG V and co-ordinated by the RIVM (National Institute of Public Health and Environment) in Bilthoven, the Netherlands.

Comparison of resistance in the different countries of the EU is biased by differences in the antimicrobial agents tested, the samples chosen for testing, the susceptibility test systems used, and the breakpoints adopted. EARSS is an international network of national surveillance systems, which aims to aggregate comparable and reliable antimicrobial resistance data for public health purposes, in Europe.

Taking into account laboratory methods as well as epidemiological principles, EARSS will act as an early warning system, analyse regional differences, assess risk factors, and provide electronic feedback. For the feasibility study of 18 months, microbiologists and epidemiologists, from all western European countries, decided to collect quantitative resistance data on *Streptococcus pneumoniae* and *Staphylococcus aureus*.

In order to come to proper comparisons and have denominator data we ask the laboratories that will participate in the EARSS project to fill out this questionnaire. See the EARSS Manual, for more information. You can also consult the EARSS web-site: www.earss.rivm.nl

Instructions for filling out the questionnaire

Fill out the questionnaire by typing or writing in capital letters in the appropriate space, or ticking the box corresponding to your answer. You may tick several boxes for the same question, except for 'yes/no' questions. This questionnaire consists of three parts:

Part 1: *Questions concerning the participating laboratory in general*

Part 2: *S. pneumoniae* susceptibility testing procedures

Part 3: *S. aureus* susceptibility testing procedures

If you will not forward resistance data on one of the above mentioned pathogens, it is not necessary to fill out the part of the questionnaire concerning that pathogen.

Contact addresses

Any clarifications regarding the questionnaire can be requested from the contact persons listed below; a copy of the questionnaire in **electronic format** can also be acquired from these persons.

Your national co-ordinator

To be filled out by the national coordinator

Project co-ordinator EARSS

Stef Bronzwaer
National Institute of Public Health and
Environment (RIVM), the Netherlands
Antonie van Leeuwenhoeklaan 9
PO Box 1, 3720 BA Bilthoven
the Netherlands
Tel. +31(30)274 3911
Fax +31(30)274 4409
e-mail info.earss@rivm.nl

Thank you very much for your very precious collaboration. It will provide you with access to most up-to-date information on resistance in Europe. Please send the completed copy, to your national co-ordinator (see above), by courier, express mail, or electronic mail, before **18 December 1998**.

'Neither the European Commission nor any person acting on its behalf is liable for any use made of this information'.

Part I: Questions concerning laboratory in general

I. 1) Information on laboratory

Name of laboratory:

Address:

City:

Country:

Contact person laboratory:

Tel: Fax: E-mail:

Laboratory Code (*to be filled out by national co-ordinator*):

I.2) Which person and institution/ laboratory is to be acknowledged if data of your laboratory will be used for publication?

Title / Name

Name Institution/laboratory

I. 3) What is the catchment population of your laboratory (coverage)?

The catchment population of my laboratory is (coverage):

Comments:

I. 4a) Do you have an automated laboratory information system in which you save isolate information?

Yes

No

If yes, what data-entry program do you use?

WHONET (DOS)

Other:

I. 4b) Will you forward EARSS resistance data electronically (on diskette) to your national co-ordinator?

Yes

No

If yes, in what format?

ASCII

DBase

Part III: S. aureus susceptibility testing procedures(Fill out only if you will forward data on *S. aureus*)**III. 1 If your laboratory is serving more hospitals please copy this page as many times as needed and fill out, as completely as possible, questions III. 1 – III.4 for every hospital:**

Name of hospital:

Hospital address:

Postal Code and Town:

Contact person in hospital:

Name/ Title

Tel: Fax: E-mail:

Hospital Code (see *EARSS Manual*):

III. 2 How is the hospital best classifiable?

- Nursing home
- General hospital
- Tertiary (academic) hospital

III. 3 Please fill out the following table

| Denominator data in 1997 | 1997 |
|--|------|
| Total number of admissions | |
| Total number of beds | |
| Average annual bed occupancy rate | |
| Number of intensive care units (ICU) beds (adult, pediatric, neonatal) | |
| ICU, total number of admissions | |
| ICU, total number of patient-days | |

III. 4 Is the hospital offering one of the following facilities

- Dialysis / CAPD
- Transplantation unit (renal, cardiac, liver)
- Cardiac surgery
- Infectious diseases (e.g. AIDS) department
- Chemotherapy (immunosuppressive treatments)
- Vascular surgery

ANNEX 3 Isolate Record Forms and data exchange format

Isolate Record Form - *Staphylococcus aureus* - Blood isolates

(Please send data on resistant and on susceptible strains; use one form per isolate!)

TO BE FILLED OUT BY LABORATORY

Case definition: Resistance data on the first isolate only of each strain from the **blood** of each patient with a hospital acquired *S. aureus* infection, confirmed by a coagulase test.

Laboratory Data

Current date dd/mm/yyyy ___ / ___ / _____
 Laboratory Code * CC000 _____

Isolate Data

Isolate sample number (lab) max. 12 characters _____
 Date of sample collection dd/mm/yyyy ___ / ___ / _____

Patient Data

Patient ID / Code § max. 12 characters _____
 Sex tick box Male Female Unknown
 Month + Year of birth mm/yyyy ___ / _____
 Clinical diagnosis § free text

Hospital Data

Name/code of hospital free text
 Origin of patient tick box Admitted Outpatient Unknown
 Hospital Department tick box Surgery (Internal) Medicine Infectious diseases (AIDS)
 Ob/Gyn ICU Emergency
 Pediatrics Pediatric ICU Other: _____

Antibiotic susceptibility testing

| | S / R (fill in S or R) | Zone diameter (mm) | MIC (in mg/l) |
|--------------|---|--------------------------|---|
| Oxacillin | S/R, zone and/or MIC | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Vancomycin | S/R, zone and/or MIC | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| PCR mec-gene | <input type="checkbox"/> Positive <input type="checkbox"/> Negative | | |

Optional

| | S/R, zone and/or MIC | | |
|---------------|----------------------|--------------------------|---|
| Streptomycin | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Tetracycline | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Gentamicin | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Erythromycin | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Ciprofloxacin | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Rifampin | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Other: | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Other: | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |
| Other: | | <input type="checkbox"/> | <input type="checkbox"/> <input type="checkbox"/> |

* The national co-ordinator will provide a laboratory code, that consists of the ISO-Country Code (CC) followed by 3 numbers.
 § Optional information

| |
|--|
| Send this form to: (name national co-ordinator) (name Institute) |
| Address: Tel: Fax: E-mail: |

Data exchange format EARSS

Pilot phase

On the following pages you find a description of the data exchange format between national databases and the central database at the RIVM. The format can be ASCII fixed format or tab separated. We worked out a brief description in a table and an extensive description in which we explain the variables more in detail, and specify the codification.

Motivation

Choosing a format to exchange data is quite complex, because many factors should be considered. The most important factors in this matter for the EARSS project are:

1. Many parties are involved.
2. The parties may not always have easy access to the necessary programming skills.
3. Many computing platforms are involved.
4. The amount of work to produce the data should be minimal and equally distributed between the parties.
5. The data must be easily accessible (so that it can be reviewed/checked).
6. The data infrastructure around it must be maintainable.
7. The format should be unambiguous.

Therefore the format should be as simple as possible, but should allow some flexibility to extend the collection of data (i.e., more antibiotics can be added).

Looking at the choices made:

1. ASCII was chosen in favour of other formats like Dbase, because those formats are usually generated by various tools. Very often the exact Dbase format can not be controlled and it is very hard to write custom made routines to do so.
2. The most simple format is to put everything into columns and thus to reserve columns for every type of antibiotic. Doing so, the lines will get too long (above 254 characters). Many editors and other tools have problems handling very long lines. Therefore every antibiotic gets its own line (instead of a column).
3. Patient, sample and other data are repeated in every line. This is the main drawback. It uses a lot of disk memory (if not compressed). To counter this problem one could introduce some simple database structures, but the integrity of the data is easily compromised.
4. The format is fixed length or tab-separated. Tab-separated data is usually easier to produce. A disadvantage is that the length of the lines is harder to control, but because codes are used this should be no problem.

We ask you to send the files every 3 months to the RIVM on diskette. The name of the file will be composed of 10 characters, as follows: CCQYYYY.txt

CC = Country Code (ISO country code as proposed by EARSS, see also Manual – Annex 4)

Q = number of quarter (i.e. 1, 2, 3, or 4)

YYYY = year (4 characters, e.g., 1999)

The file may be zipped using “pkzip” or a compatible program.

Each line contains test-results for one antibiotic.

Laboratory, Isolate, Patient, Hospital, and Pathogen data are repeated every line.

| | |
|-------------------------|--|
| Field Name: | Name of the variable |
| Field Length: | The field length is the total number of characters allowed for that field. |
| Mandatory Field: | All mandatory fields must be entered. In order not to 'lose' isolates for data analysis very few fields are obligatory. Fill out as many fields as possible. |
| Description: | Description/explanation for a field, and in some cases the codification. |

In case of fixed format

| | |
|------------------------|---|
| Field Type: | A = Alphanumeric (spaces if unknown) (tabs / special ASCII characters not allowed) N = Numeric (all numbers, dots, and comma's allowed) (spaces if unknown) D = Date format: YYYYMMDD (spaces if unknown) |
| Initial column: | The number of the first column where the field starts. It is very important to follow exactly this format since it is a 'fixed format'. |

In case of tab separated format

| | |
|--------------------|--|
| Field Type: | A = Alphanumeric (tabs or special characters not allowed) N = Numeric (all numbers, dots, and comma's allowed) D = Date format: YYYYMMDD - No trailing spaces in fields allowed - In case a field can not be filled out, one can go to the next column using a tab - In case the last fields of the line do not have to be filled out records may be truncated to omit trailing tabs. Records are terminated with a carriage return, line feed. |
|--------------------|--|

Remarks

Regarding susceptibility testing results:

- On the Isolate Record Forms there is space to fill out S (susceptible) or R (resistant). In the database also the test result I (intermediate) is allowed.
- For both pathogens the test results for Oxacillin will always be filled out. In case of a *S. pneumoniae* isolate, also the test results for penicillin will always be mentioned.
- Fill out the following test results in the following fields:
 - The result of the Oxacillin screen plate (and disk) will be mentioned in the S/I/R field, and in case of the Oxacillin disk, possibly the zone diameter will be filled out (e.g., <= 19 mm).
 - Disk diffusion test results in the Zone fields.
 - MIC methods (agar, (micro-)broth, automated) in the MIC fields.
 - Etest results in the Etest fields (Because some EARSS participating labs will perform next to "conventional" MIC methods also Etests to compare both results, it was necessary to add two fields for the Etest result.)

Clinical diagnosis: To be able to code and store varying answers in the free text space on the Isolate Record Forms, we worked out two fields for this variable. The field "Clinical diagnosis" contains infectious disease diagnosis, and the field "Other conditions" contains mainly immuno-compromising factors. The codification is specified under the extensive description.

Laboratory Code: The laboratory code consists of the ISO-country Code (CC) followed by 3 numbers. The National Co-ordinator assigns a specific number to every EARSS participating laboratory (starting from 001, 002, etc.)

Hospital code: Because one laboratory may serve more hospitals it is very important to specify in which hospital the isolate was taken. The national co-ordinator assigns a letter to all the hospitals that are served by

one laboratory. The code consists in 4 characters (000X). The first 3 characters are the number-code of the laboratory, and the 4th character is the letter assigned to a hospital (starting from A, B, etc.)

Antibiotic coding: The coding for antibiotics in EARSS is the same as in WHONET4 (DOS version). See table Antibiotic coding EARSS. (*With regards to R. Williams and J. Stelling of WHO/EMC. In WHONET 5 (Windows version), a number of the antibiotic codes will be changed to better conform to existing official WHO codes and to standard codes of diagnostic manufacturers where sufficient consensus exists*).

Duplicates: Exclude duplicate isolates of the same strain (species) from the same patient, and send information only on the first isolate of each strain from each patient.

For comments and questions you can contact:

Stef LAM Bronzwaer

Project co-ordinator EARSS

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National Institute of Public Health and the Environment,

PO Box 1, 3720 BA Bilthoven, The Netherlands

Tel: +31(30)2743911

Fax: +31(30)2744409

E-mail: info.earss@rivm.nl

Brief description data exchange format EARSS

| Field Name | Field type | Initial column | Field length | Mandatory Field |
|---|------------|----------------|--------------|-----------------|
| Current date | D | 1 | 8 | |
| Laboratory code | A | 9 | 5 | Yes |
| Isolate sample number (lab) | A | 14 | 12 | |
| Isolate source | A | 26 | 2 | |
| Date of sample collection | D | 28 | 8 | |
| Patient ID / Code | A | 36 | 12 | |
| Sex | N | 48 | 1 | |
| Month of birth | N | 49 | 2 | |
| Year of birth | N | 51 | 4 | |
| Clinical diagnosis | A | 55 | 3 | |
| Other conditions | A | 58 | 3 | |
| Hospital code | A | 61 | 4 | |
| Origin of patient | N | 65 | 1 | |
| Hospital department | A | 66 | 3 | |
| Pathogen code | A | 69 | 3 | Yes |
| PCR mec-gene | N | 72 | 1 | |
| <i>Antibiotic susceptibility testing</i> | | | | |
| Antibiotic code | A | 73 | 3 | Yes |
| S/I/R | A | 76 | 1 | |
| Zone (> < =) | A | 77 | 2 | |
| Zone (Value in mm) | N | 79 | 2 | |
| MIC (> < =) | A | 81 | 2 | |
| MIC (Value in mg/l) | N | 83 | 5 | |
| Etest (> < =) | A | 88 | 2 | |
| Etest (Value in mg/l) | N | 90 | 5 | |

Extensive description data exchange format EARSS

Columns: 1-8
 Field Length: 8 [D] YYYYMMDD
 Field Name: Current date
 Description: The date that the Isolate Record Form was filled in.

Columns: 9-13, Mandatory
 Field Length: 5 [A] CC000
 Field Name: Laboratory code
 Description: The laboratory code consists of the ISO-country Code (CC) followed by 3 numbers. The National Co-ordinator assigns a specific number to every EARSS participating laboratory (starting from 001, 002, etc.)

Columns: 14-25
 Field Length: max. 12 [A]
 Field Name: Isolate sample number (lab)
 Description: Number in use in lab to specify isolate

Columns: 26-27
 Field Length: 2 [A]
 Field Name: Isolate source
 Description: The source of the isolate, coded as follows:
 bl = Blood sf = CSF ot = other source xx = Unknown

Columns: 28-35
 Field Length: 8 [D] YYYYMMDD
 Field Name: Date of sample collection
 Description: Date when sample was taken

Columns: 36-47
 Field Length: max. 12 [A]
 Field Name: Patient ID / Code
 Description: Patient ID / Code

Columns: 48
 Field Length: 1 [N]
 Field Name: Sex
 Description: Coded as follows: 1 = Male 2 = Female 9 = Unknown

Columns: 49-50
 Field Length: 2 [N] MM
 Field Name: Month of birth
 Description: Month of birth of the patient

Columns: 51-54
 Field Length: 4 [N] YYYY
 Field Name: Year of birth
 Description: Year of birth of the patient

To be able to code and store varying answers in the free text space on the Isolate Record Forms, we worked out two fields for the variable “Clinical diagnosis”.

Columns: 55-57

Field Length: 3 [A]

Field Name: Clinical diagnosis

Description: The information regarding clinical diagnosis may vary. You will have to choose the most appropriate code for the infectious disease diagnosis:

1 = Pneumoniae, 2 = Meningitis, 3 = Arthritis, 4 = Endocarditis, 5 = Primary Peritonitis, 6 = Sepsis without focus in children, 7 = Complicated Otitis Media, 8 = Complicated Sinusitis, 9 = Osteomyelitis, 10 = Empyema, 11 = Skin lesion (11a = Furuncle, 11b = Carbuncle), 12 = Abscess (12a = breast, 12b = cerebral, 12c = lung, 12d = renal, 12e = subcutaneous/intramuscular), ot = other, xx = Unknown

Columns: 58-60

Field Length: 3 [A]

Field Name: Other conditions

Description: The information regarding other conditions may vary. You will have to choose the most appropriate code:

1 = Immunocompromised, 2 = Following splenectomy, 3 = Infected burn wounds, 4 = Postoperative woundinfection, 5 = Drug abuse, 6 = Intravascular procedures (6a = Intravenous catheters, 6b = Intravascular prosthetic devices, 6c = Dialysis), ot = other, xx = Unknown

Columns: 61-64

Field Length: 4 [A] 000X

Field Name: Hospital code

Description: The code consists in 4 characters. The first 3 characters are the number-code of the lab, and the 4th character is the letter assigned to a hospital (starting from A, B, etc.)

Columns: 65

Field Length: 1 [N]

Field Name: Origin of patient

Description: Is the patient at the moment the isolate is taken admitted in a hospital (inpatient), or not. This is coded as follows:

1 = Admitted 2 = Outpatient 8 = Other (e.g., emergency room) 9 = Unknown

Columns: 66-68

Field Length: 3 [A]

Field Name: Hospital department

Description: The variable permits the general classification of locations by service, as follows:

| | | | |
|----------------------|---------------------|---------------------------|------------------|
| med = Medicine | ped = Pediatrics | pic = Ped. Intensive Care | in = Inpatient |
| sur = Surgery | neo = Neonates | mix = Mixed | out = Outpatient |
| icu = Intensive Care | eme = Emergency | obg = Obstet./Gynec. | com = Community |
| oth = Other | xxx = Not specified | | |

Columns: 69-71, Mandatory

Field Length: 3 [A]

Field Name: Pathogen code

Description: This is coded as follows: spn = *S. pneumoniae* sau = *S. aureus*

Columns: 72

Field Length: 1 [N]

Field Name: PCR mec-gene

Description: The outcome of this test is coded as follows: 1 = positive 2 = negative 9 = Unknown

Antibiotic susceptibility testing

Specify the antibiotic in the field “Antibiotic code”, making use of the Table Antibiotic coding EARSS (see below). For both pathogens the test results for Oxacillin will always be filled out. In case of a *S. pneumoniae* isolate, also the test results for Penicillin will always be mentioned.

Columns: 73-75

Field Length: 3 [A]

Field Name: Antibiotic code

Description: Coded as follows:

Table Antibiotic coding EARSS Part 1: Most commonly used antibiotics in EARSS

| Code | Antibiotic |
|------|---------------------------------|
| FTX | CEFOTAXIME |
| CRO | CEFTRIAZONE |
| CIP | CIPROFLOXACIN (NCCLS-5ug) |
| CI1 | CIPROFLOXACIN (SWEDISH-10ug) |
| CLI | CLINDAMYCIN (NCCLS,SFM-2ug) |
| CL1 | CLINDAMYCIN (SFM ana,SWE-15ug) |
| ERY | ERYTHROMYCIN |
| GEN | GENTAMICIN (NCCLS-10ug) |
| GE1 | GENTAMICIN (SFM-15ug) |
| GE3 | GENTAMICIN (SWEDISH-30ug) |
| GEH | GENTAMICIN-HIGH (NCCLS-120ug) |
| GE5 | GENTAMICIN-HIGH (SFM-500ug) |
| OXA | OXACILLIN (NCCLS,SFM spn-1ug) |
| OX5 | OXACILLIN (SFM-5ug) |
| PEN | PENICILLIN G |
| RIF | RIFAMPIN (NCCLS-5ug) |
| RI3 | RIFAMPIN (SFM-30ug) |
| STR | STREPTOMYCIN |
| STH | STREPTOMYCIN-HIGH (NCCLS-300ug) |
| ST5 | STREPTOMYCIN-HIGH (SFM-500ug) |
| TET | TETRACYCLINE |
| VAN | VANCOMYCIN |

(See also Table Antibiotic coding EARSS Part 2)

Columns: 76

Field Length: 1 [A] (S, I, or R)

Field Name: S/I/R

Description: Result of susceptibility testing, differentiating susceptible (S), intermediate (I), and resistant (R)

Columns: 77-78

Field Length: 2 [A] (> <=)

Field Name: Zone (> <=)

Description: This field can indicate if a value of the zone is “greater than” (>); “equal to or greater than” (>=); “less than” (<); or “equal to or less than” (<=) the value indicated in the following field

Columns: 79-80

Field Length: 2 [N]

Field Name: Zone (Value in mm)

Description: Zone diameter in millimetres

Columns: 81-82

Field Length: 2 [A] (> < =)

Field Name: MIC (> < =)

Description: This field can indicate if a value of the MIC is “greater than” (>); “equal to or greater than” (>=); “less than” (<); or “equal to or less than” (<=) the value indicated in the following field

Columns: 83-87

Field Length: 5 [N]

Field Name: MIC (Value in mg/l)

Description: The value of the MIC test result that can vary from 0.002 to 1024

Columns: 88-89

Field Length: 2 [A] (> < =)

Field Name: Etest (> < =)

Description: This field can indicate if a value of the Etest is “greater than” (>); “equal to or greater than” (>=); “less than” (<); or “equal to or less than” (<=) the value indicated in the following field

Columns: 90-94

Field Length: 5 [N]

Field Name: Etest (Value in mg/l)

Description: The value of the Etest test result that can vary from 0.002 to 1024

Other antibiotic test results of the same isolate will be mentioned as a new line.

Table Antibiotic coding EARSS

Part 2: Other antibiotics

| Code | Antibiotic | Code | Antibiotic |
|------|--------------------------------|------|--------------------------------|
| ACM | ACETYLMIDECAMYCIN | CI3 | CINOXACIN (SWEDISH-30ug) |
| ASP | ACETYLSPIRAMYCIN | CLA | CLARITHROMYCIN |
| AMD | AMDINOCILLIN | CLN | CLINAFOXACIN |
| AMK | AMIKACIN | CLO | CLOTRIMAZOLE |
| AMX | AMOXICILLIN | CLX | CLOXACILLIN |
| AUG | AMOXICILLIN/CLAVULANIC ACID | COL | COLISTIN (NCCLS-10ug) |
| AXS | AMOXICILLIN/SULBACTAM | CO5 | COLISTIN (SFM-50ug) |
| AMB | AMPHOTERICIN B | CCL | CYCLACILLIN |
| AMP | AMPICILLIN | CYC | CYCLOSERINE |
| AMS | AMPICILLIN/SULBACTAM | DEM | DEMECLOCYCLINE |
| APA | APALCILLIN | DIB | DIBEKACIN |
| APR | APRAMYCIN | DIC | DICLOXACILLIN |
| AST | ASTROMICIN | DIR | DIRITHROMYCIN |
| AZI | AZITHROMYCINE | DOX | DOXYCYCLINE |
| AZL | AZLOCILLIN | ENX | ENOXACIN |
| ATM | AZTREONAM | ENR | ENROFLOXACIN |
| BAM | BACAMPICILLIN | ETH | ETHAMBUTOL |
| BAC | BACITRACIN | ETI | ETHIONAMIDE |
| CAP | CAPREOMYCIN | FLE | FLEROXACIN |
| CAR | CARBENICILLIN | FLO | FLOMOXEF |
| CAM | CARUMONAM | FLC | FLUCLOXACILLIN |
| FAC | CEFACETRILE | FLU | FLUCONAZOL |
| CFC | CEFACTOR (NCCLS-30ug) | FLM | FLUMEQUINE |
| CF1 | CEFACTOR (SFM-10ug) | FOS | FOSFOMYCIN |
| DRX | CEFADROXIL | FRM | FRAMYCETIN |
| RID | CEFALORIDIN | FUS | FUSIDIC ACID (SFM-10ug) |
| MAN | CEFAMANDOLE | FU5 | FUSIDIC ACID (SWEDISH-50ug) |
| FAP | CEFAPIRINE | GRE | GREPAFLOXACIN |
| FAT | CEFATRIZINE | IMP | IMPENEM |
| CFZ | CEFAZOLIN | ISE | ISEPAMICIN |
| CEP | CEFCAPENE | ISO | ISOCONAZOLE |
| DIN | CEFDINIR | INH | ISONIAZID |
| DIT | CEFDITOREN | ITR | ITRACONAZOLE |
| FEP | CEFEPIME | JOS | JOSAMYCIN |
| FET | CEFETAMET | KAN | KANAMYCIN |
| FIX | CEFIXIME (NCCLS-5ug) | KAH | KANAMYCIN-HIGH |
| F11 | CEFIXIME (SFM-10ug) | KET | KETOCONAZOLE |
| MEN | CEFMENOXIME | KIT | KITASAMYCIN |
| CMZ | CEFMETAZOLE | LEV | LEVOFLOXACIN |
| DIZ | CEFODIZIME | LIN | LINCOMYCIN |
| CID | CEFONICID | LOM | LOMEFLOXACIN |
| CFP | CEFOPERAZONE (NCCLS-75ug) | LOR | LORACARBEF |
| CF3 | CEFOPERAZONE (SFM-30ug) | MEC | MECILLINAM |
| CFS | CEFOPERAZONE/SULBACTAM | MEL | MELEUMYCIN |
| CTN | CEFOTETAN | MER | MEROPENEM |
| FOT | CEFOTIAM | MET | METHICILLIN |
| FOX | CEFOXITIN | MTR | METRONIDAZOLE (SFM-4ug) |
| PIR | CEFPIROME | ME1 | METRONIDAZOLE (SWEDISH-10ug) |
| POD | CEFPODOXIME (NCCLS-10ug) | MEZ | MEZLOCILLIN |
| PO3 | CEFPODOXIME (SWEDISH-30ug) | MID | MIDECAMYCINE |
| PRO | CEFPROZIL | MIN | MINOCYCLINE |
| SLD | CEFSULODIN | MOX | MOXALACTAM (LATAMOXEF) |
| CAZ | CEFTAZIDIME | MUP | MUPIROCI |
| BUT | CEFTIBUTEN (NCCLS-30ug) | NAF | NAFCILLIN |
| BU1 | CEFTIBUTEN (SFM-10ug) | NAL | NALIDIXIC ACID |
| TIO | CEFTIOFUR | NEO | NEOMYCIN |
| ZOX | CEFTIZOXIME | NET | NETILMICIN |
| FRA | CEFUROXIME AXETIL (NCCLS-30ug) | FUR | NITROFURANTOIN (NCCLS-300ug) |
| FR1 | CEFUROXIME AXETIL (SFM-10ug) | FU1 | NITROFURANTOIN (SWEDISH-100ug) |
| FRX | CEFUROXIME SODIUM | NIF | NITROFUZAZONE |
| ZON | CEFUZONAM | NIT | NITROXOLINE |
| ZOP | CEFUZOPRAN | NOR | NORFLOXACIN (NCCLS-10ug) |
| LEX | CEPHALEXIN | NO5 | NORFLOXACIN (SFM-5ug) |
| KEF | CEPHALOTHIN | NVA | NORVANCOMYCIN |
| RAD | CEPHRADINE | NOV | NOVOBIOCIN |
| CHL | CHLORAMPHENICOL | OFL | OFLOXACIN (NCCLS-5ug) |
| CTE | CHLORTETRACYCLINE | OF1 | OFLOXACIN (SWEDISH-10ug) |
| CIN | CINOXACIN (NCCLS-100ug) | OLE | OLEANDOMYCIN |
| | | OPT | OPTOCHIN |
| | | ORN | ORNIDAZOLE |
| | | OXO | OXOLINIC ACID |
| | | OXY | OXYTETRACYCLINE |
| | | PAS | P-AMINOSALICYLIC ACID |
| | | PAN | PANIPENEM |
| | | PEF | PEFLOXACIN |

| | |
|-----|--|
| PNV | PENICILLIN V |
| PNO | PENICILLIN/NOVOBIOCIN |
| PPA | PIPEMIDIC ACID |
| PIP | PIPERACILLIN (NCCLS-100ug) |
| PI7 | PIPERACILLIN (SFM-75ug) |
| PI3 | PIPERACILLIN (SWEDISH-30ug) |
| PTA | PIPERACILLIN/TAZOBACTAM (NCCLS-100/10ug) |
| PT7 | PIPERACILLIN/TAZOBACTAM (SFM-75ug/6ug) |
| PT3 | PIPERACILLIN/TAZOBACTAM (SWEDISH-30/6ug) |
| PIL | PIRLIMYCIN |
| POL | POLYMXIN B |
| PRI | PRISTINAMYCIN |
| PRP | PROPICILLIN |
| PRT | PROTHIONAMIDE |
| PZA | PYRAZINAMIDE |
| QUI | QUINUPRISTIN/DALFOPRISTIN |
| RIB | RIFABUTIN |
| ROS | ROSOXACINE |
| ROX | ROXITROMICIN |
| SIS | SISOMICIN |
| SPA | SPARFLOXACIN |
| SPE | SPECTINOMYCIN |
| SPI | SPIRAMYCINE |
| SLB | SULBENICILLIN |
| SUL | SULFONAMIDES |
| TEI | TEICOPLANIN |
| TEM | TEMAFLOXACIN |
| THA | THIACETAZONE |
| THI | THIAMPHENICOL |
| TIA | TIAMULIN |
| TIC | TICARCILLIN |
| TIM | TICARCILLIN/CLAVULANIC ACID |
| TIL | TILMICOSIN |
| TIN | TINIDAZOLE |
| TOB | TOBRAMYCIN (NCCLS-10ug) |
| TO3 | TOBRAMYCIN (SWEDISH-30ug) |
| TMP | TRIMETHOPRIM |
| SXT | TRIMETHOPRIM/SULFAMETHOXAZOLE |
| TRL | TROLEANDOMYCIN |
| TRO | TROSPECTOMYCIN |
| TRV | TROVAFLOXACIN |
| VIO | VIOMYCIN |
| VIR | VIRGINIAMYCINE |

ANNEX 4. Characterisation of the EARSS participating laboratories

| Code of lab | Catchment population | Patient-days |
|--------------------|-----------------------------|---------------------|
| NL002 | 290000 | 164914 |
| NL003 | 290000 | 267510 |
| NL004 | 180000 | 174999 |
| NL005 | 110000 | 99651 |
| NL006 | 670000 | 541964 |
| NL007 | 270000 | 223685 |
| NL008 | 300000 | 195203 |
| NL009 | 480000 | 415153 |
| NL010 | 650000 | 496064 |
| NL011 | 580000 | 484280 |
| NL012 | 180000 | 142577 |
| NL013 | 180000 | 161928 |
| NL014 | 220000 | 180982 |
| NL016 | 100000 | 106627 |
| NL017 | 80000 | 72994 |
| NL018 | 120000 | 78139 |
| NL019 | 310000 | 287230 |
| NL020 | 410000 | 372251 |
| NL021 | 320000 | 239332 |
| NL022 | 320000 | 335146 |
| NL023 | 270000 | 214975 |
| TOTAL | 6330000 | 5255604 |
| NL | 15700000 | 12890235 |
| % coverage | 40,1 | 40,8 |

ANNEX 5 Methods used for antibiotic susceptibility testing for *S. aureus* and *S. pneumoniae*.

A. Differentiation between MIC, disk and screen test

| | <i>S. pneumoniae</i> | | <i>S. aureus</i> | | |
|---------------|----------------------|-------|------------------|-------|-------|
| | MIC | disk | screen | MIC | disk |
| Oxacillin | 4/19 | 18/19 | 6/19 | 11/19 | 10/19 |
| Methicillin | -- | -- | 3/7 | 6/7 | 3/7 |
| Penicillin | 18/19 | 5/19 | -- | 3/8 | 5/8 |
| Cefotaxime | 3/7 | 5/7 | -- | 1/1 | -- |
| Erythromycin | 5/19 | 16/19 | 1/16 | 7/16 | 10/16 |
| Tetracycline | 4/15 | 13/15 | 1/8 | 4/8 | 4/8 |
| Gentamicin | -- | 2/2 | 2/13 | 6/13 | 8/13 |
| Ciprofloxacin | 4/5 | 2/5 | 1/9 | 4/9 | 5/9 |
| Vancomycin | 6/16 | 14/16 | 1/17 | 8/17 | 10/17 |

B. Manufacturer of disk tests

| | <i>S. pneumoniae</i> | | <i>S. aureus</i> | |
|---------------|----------------------|-------|------------------|-------|
| | Rosco | Oxoid | Rosco | Oxoid |
| Oxacillin | 8/12 | 4/12 | 7/9 | 2/9 |
| Methicillin | -- | -- | 1/3 | 2/3 |
| Penicillin | 4/4 | -- | 4/5 | 1/5 |
| Cefotaxime | 3/3 | -- | -- | -- |
| Erythromycin | 7/11 | 4/11 | 8/10 | 2/10 |
| Tetracycline | 7/11 | 4/11 | 3/4 | 1/4 |
| Gentamicin | 1/2 | 1/2 | 6/8 | 2/8 |
| Ciprofloxacin | 2/2 | -- | 5/5 | -- |
| Vancomycin | 7/10 | 3/10 | 8/10 | 2/10 |

C. Types of MIC testing

| | <i>S. pneumoniae</i> | | | | <i>S. aureus</i> | | | |
|---------------|----------------------|-------|--------|--------|------------------|-------|--------|--------|
| | agar | broth | e-test | Vitek* | agar | broth | e-test | Vitek* |
| Oxacillin | 1/3 | -- | 2/3 | -- | 1/11 | 2/11 | 5/11 | 3/11 |
| Methicillin | -- | -- | -- | -- | -- | 1/6 | 4/6 | 1/6 |
| Penicillin | 2/18 | 1/18 | 15/18 | -- | -- | 2/3 | -- | 1/3 |
| Cefotaxime | -- | 1/3 | 2/3 | -- | -- | 1/1 | -- | -- |
| Erythromycin | 1/5 | 2/5 | 2/5 | -- | 1/7 | 2/7 | 1/7 | 3/7 |
| Tetracycline | 1/4 | 1/4 | 2/4 | -- | 1/4 | 1/4 | 1/4 | 1/4 |
| Gentamicin | -- | -- | -- | -- | -- | 1/6 | 2/6 | 3/6 |
| Ciprofloxacin | 1/4 | 2/4 | 1/4 | -- | -- | 1/4 | 1/4 | 2/4 |
| Vancomycin | 1/6 | 2/6 | 3/6 | -- | 1/8 | 3/8 | 1/8 | 3/8 |

*=automated method which delivers an interpreted MIC

ANNEX 6 Protocols for susceptibility testing

Protocol *Staphylococcus aureus* testing

Objective:

To study the (methicillin)-resistance of *S. aureus*, in blood isolates in hospitals in Europe.

Case definition

Resistance data on the first isolate only of each strain from the blood of each patient with a hospital acquired *S. aureus* infection (confirmed by a coagulase test).

Indicators

- Proportion of oxacillin (=methicillin) resistant strains (MRSA) divided by total number of *S. aureus* cases in a specific lab/hospital.
- Quarterly incidence of MRSA cases per 100 patients admitted during the period of the study.
- Quarterly incidence of MRSA cases per 1,000 patient-days (and bed-days) during the period of the study.

Test procedure:¹

Oxacillin screen **plate** (6 µg/ml according to NCCLS or other national boards) or oxacillin **disk**² (1 µg³ or 5 µg⁴) will be used.

Output from participating labs: Zone diameter, if possible⁵

Please exclude duplicate isolates of the same strain from the same patient, and send information only on the first isolate, of each strain, from each patient (“patient-isolate”).

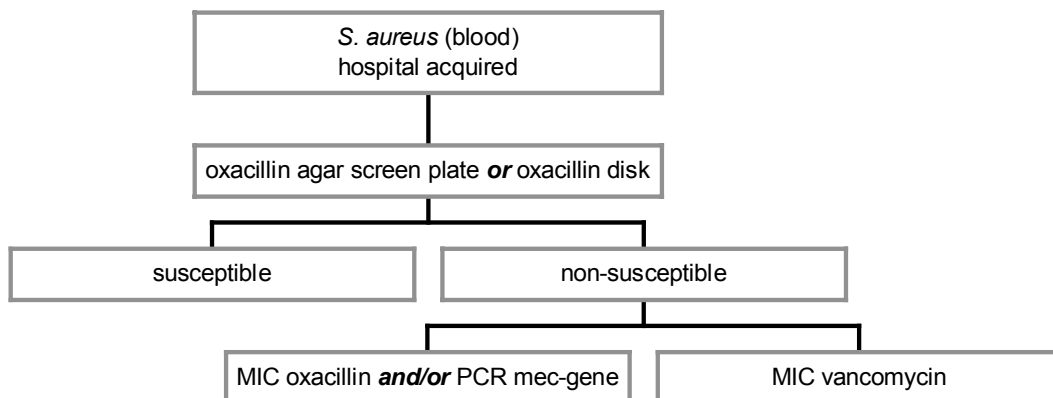
Oxacillin susceptible and non-susceptible, according to standards in use in your lab:

- register, when possible, the inhibition zone (in case of the disk method). No other tests required.

Oxacillin non-susceptible:⁶

- determine MIC of oxacillin,⁷ specifying the method used: microdilution, agardilution or E-test (range of dilutions: 0,016 - 256).⁸
- determine MIC of vancomycin,⁹ specifying the method used: microdilution, agardilution or E-test (range of dilutions: 0,016 - 256).

Protocol for testing *S.aureus*



Considerations *S. aureus*

1. For a reliable comparison of resistance against oxacillin in *S. aureus* (SA) the advantage of the use of oxacillin agar screen plates is indisputable. However, results from the questionnaire to the national co-ordinators illustrate that agar screen plates are only used in a few countries. Because one of the key features of EARSS is easy accessibility, the protocol will also accept data from the oxacillin disk diffusion test.
2. Testing of resistance to oxacillin in SA, using disk diffusion tests, may not always lead to comparable results, because of differences in inoculum, medium, time of incubation and temperature, and use of CO₂. Thus, it is important to know what are the test procedures in each individual participating laboratory, in order to check for these differences and to relate these to possible differences in the outcome of resistance testing. An inventory of the test methods in use will be done by means of a questionnaire that will be sent to participating laboratories. As discussed elsewhere (QA), the regular use (monthly) of quality control strains is also necessary to check for the validity of the resistance data from the participating laboratories.
3. If using a disk with a load of 1 µg oxacillin (NCCLS) for oxacillin susceptibility testing, non-susceptibles are strains with a zone size of 10 mm or less (≤ 10 mm).
4. If using a disk with a load of 5 µg oxacillin (e.g. SFM) for oxacillin susceptibility testing, non-susceptibles are strains with a zone size of 19 mm or less (≤ 19 mm).
5. The collection of zone diameters has an additional value. Firstly, zone diameters will give more insight in the distribution of SA strains with different susceptibilities to oxacillin, e.g. high resistance versus intermediate resistance. Secondly, the distribution of zone diameters may be used to study the quality of resistance data from the different participating laboratories. It is acknowledged that laboratories in some participating countries are not able to collect zone diameters.
6. A participating country can decide whether the local laboratory will perform the second step of the protocol or that a 'reference' laboratory will collect the non-susceptible strains and perform the MIC for oxacillin (or the PCR for the *mec*-gene) and vancomycin.
7. The golden standard for confirmation of a MRSA is testing for the presence of a *mec*-gene. However, when a participating laboratory is not able to perform a PCR, determination of a MIC for oxacillin is important to confirm that a MRSA is not a false positive.
8. It is possible to perform a MIC for oxacillin and vancomycin in one plate using two E-test strips (inoculum is 0.5 McFarland). Regarding the test conditions (medium), discussions are not finalised yet.
9. Testing of MRSA for resistance against vancomycin is very relevant but under debate. Vancomycin-Intermediate SA (VISA) strains, which were first reported in Japan, are often heterogeneously resistant, only a very limited percentage of total population of isolated bacteria is intermediate resistant. The presence of these VISA can be missed measuring a MIC under standard conditions. At this moment there is not an established protocol to test for the VISA. In addition, the relevance of this intermediate resistance to vancomycin for vancomycin therapy of MRSA can be disputed. For that reason, we test the MRSA for vancomycin using the E-test, with a standardised protocol (inoculum is 0.5 McFarland) which is also used testing the oxacillin MIC, realising that some intermediate VISA strains might be missed. The determination of the vancomycin MIC will preferably be done at a central 'reference' lab in each country. In case of finding a VISA strain arrangements will be made for further analysis (e.g., sequence analysis).

Protocol *Streptococcus pneumoniae* testing

Objective:

To study the penicillin-resistance of *S. pneumoniae* blood- and CSF-isolates in Europe.

Case definition

Resistance data on the first isolate only, of each strain from the blood or CSF of each patient with a community acquired *S. pneumoniae* infection (confirmed by an optochin test).

Indicators

- Prevalence of oxacillin (penicillin) resistance of *S. pneumoniae* blood and CSF-isolates.
- Quarterly incidence of PRP cases per 1,000,000 persons during the period of study.

Test procedure¹

Oxacillin disk² (1 µg³ or 5 µg⁴) will be used.

Output from participating labs: Zone diameters, if possible⁵

Please exclude duplicate isolates of the same strain from the same patient, and send information only on the first isolate, of each strain, from each patient (“patient-isolate”).

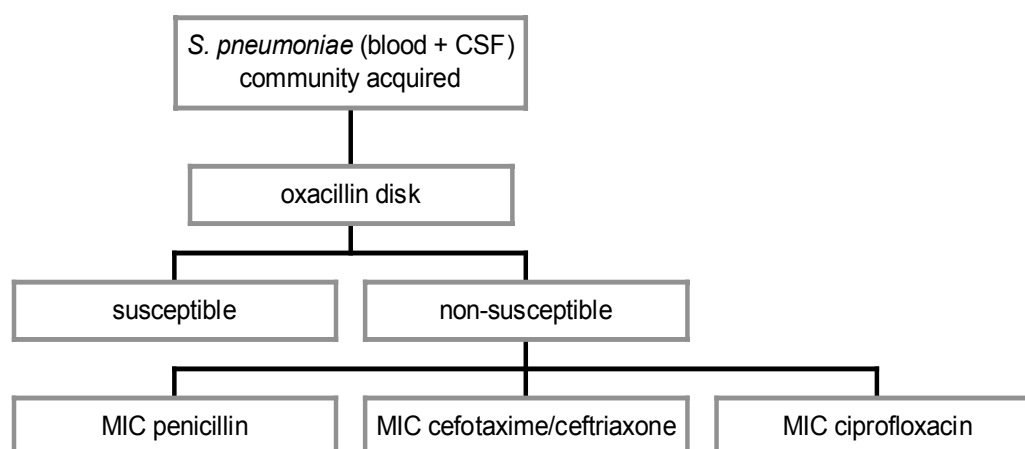
Oxacillin susceptible and non-susceptible, according to standards in use in your lab:

- register, when possible, the inhibition zone (in case of the disk method). No other tests required.

Oxacillin non-susceptible:⁶

- determine MIC of penicillin, specifying the method used: agardilution, microdilution or E-test (range of dilutions: 0,016 - 256).
- determine MIC cefotaxime or ceftriaxone, specifying the method used: agardilution, microdilution or E-test (range of dilutions: 0,002 - 32).
- determine MIC ciprofloxacin, specifying the method used: agardilution, microdilution or E-test (range of dilutions: 0,002 - 32)⁷.

Protocol for testing *S. pneumoniae*



Considerations *S. pneumoniae*

- ¹. In this version of the protocol, testing of ciprofloxacin resistance for all strains was not continued, because it was clear from the questionnaires that laboratories in most countries do not perform this testing on a routine basis. In addition, testing for susceptibility of fluoroquinolones in *S. pneumoniae* may be an unwanted incentive. Results from this testing may demonstrate that this pathogen is susceptible for fluoroquinolones, which may lead to unnecessary use of fluoroquinolones for therapy of *S. pneumoniae* infections. For this reason we ask to test for ciprofloxacin resistance only on strains that are non-susceptible to oxacillin.
- ². Testing of resistance to oxacillin in *S. pneumoniae* (SP) using a disk diffusion test may not always lead to comparable results, because of differences in inoculum, medium, time of incubation and use of CO₂. Thus, it is important to know what are the test procedures in each individual participating laboratory, in order to check for these differences and to relate these to possible differences in the outcome of resistance testing. An inventory of the test methods in use will be done by means of a questionnaire that will be sent to participating laboratories. As discussed elsewhere (QA), the regular use (monthly) of quality control strains is also necessary to check for the validity of the resistance data from the participating laboratories.
- ³. Most used in oxacillin susceptibility testing is a disk with a load of 1 µg oxacillin (NCCLS). Non-susceptible penicillin resistant *S. pneumoniae* are strains with a zone size of 20 mm or less (≤ 20 mm).
- ⁴. An alternative in oxacillin susceptibility testing is a disk with a load of 5 µg oxacillin (e.g. SFM). Non-susceptible penicillin resistant *S. pneumoniae* are strains with a zone size of 26 mm or less (< 26 mm).
- ⁵. It is recognised that the laboratories in some participating countries are not able or willing to collect the zone diameters. However, we believe that the collection of zone diameters has additional value. Firstly, zone diameters will give more insight in the distribution of SP strains with different susceptibilities to oxacillin, e.g. highly resistant versus intermediate resistant. Secondly, the distribution of zone diameters may be used to study the comparability of resistance data from the different participating laboratories.
- ⁶. A participating country can decide whether the local laboratory will perform the second step of the protocol or that a 'reference' laboratory will collect the non-susceptible strains and perform the MIC for penicillin, cefotaxime/ceftriaxone and ciprofloxacin.
- ⁷. In case of finding a *S. pneumoniae* strain non-susceptible to ciprofloxacin (the breakpoint will still be defined), arrangements will be made for further analysis.

ANNEX 7 Characteristics of the patients with *S. pneumoniae* and *S. aureus* infections

| 5.1 | 5.2 | <i>S. pneumoniae</i> | | <i>S. aureus</i> | |
|-----------------------|----------------------------------|----------------------|------|------------------|------|
| | | freq | % | freq | % |
| isolate source | blood | 695 | 90,6 | 1252 | 99,4 |
| | CSF | 72 | 9,4 | 7 | 0,6 |
| age | 0-4 y | 74 | 9,6 | 85 | 6,8 |
| | 5-40 y | 114 | 14,9 | 173 | 13,7 |
| | 41-65y | 218 | 28,4 | 361 | 28,7 |
| | >65 y | 361 | 47,1 | 640 | 50,8 |
| sex | male | 431 | 56,2 | 733 | 58,2 |
| | female | 336 | 43,8 | 526 | 41,8 |
| diagnosis | pneumoniae | 43 | 5,6 | 6 | 0,5 |
| | meningitis | 12 | 1,6 | 1 | 0,1 |
| | arthritis | | | 6 | 0,5 |
| | endocarditis | | | 3 | 0,2 |
| | sepsis without focus in children | | | 12 | 1,0 |
| | osteomyelitis | | | 2 | 0,2 |
| | empyema | | | 1 | 0,1 |
| | skin lesion | | | 8 | 0,6 |
| | primary peritonitis | 1 | 0,1 | | |
| | abcess | 1 | 0,1 | 17 | 1,4 |
| | other | 31 | 4,0 | 87 | 6,9 |
| | unknown | 679 | 88,5 | 1116 | 88,6 |
| condition | immunocompromised | 6 | 0,8 | 5 | 0,4 |
| | postoperative woundinfection | 1 | 0,1 | 4 | 0,3 |
| | drug abuse | 1 | 0,1 | 2 | 0,2 |
| | intravascular procedures | 1 | 0,1 | 16 | 1,3 |
| | other conditions | 2 | 0,3 | 22 | 1,7 |
| | unknown | 756 | 98,6 | 1210 | 96,1 |
| origin patient | admitted | 514 | 67,0 | 845 | 67,1 |
| | outpatient | 86 | 11,2 | 103 | 8,2 |
| | other | 10 | 1,3 | 7 | 0,6 |
| | unknown | 157 | 20,5 | 304 | 24,1 |
| department | (internal) medicine | 72 | 9,4 | 133 | 10,6 |
| | pediatrics | 23 | 3,0 | 40 | 3,2 |
| | ped. intensive care | 8 | 1,0 | 8 | 0,6 |
| | inpatient | 28 | 3,7 | 39 | 3,1 |
| | surgery | 16 | 2,1 | 93 | 7,4 |
| | neonates | | | 14 | 1,1 |
| | mixed | 27 | 3,5 | 51 | 4,1 |
| | outpatients | 11 | 1,4 | 11 | 0,9 |
| | intensive care | 25 | 3,3 | 73 | 5,8 |
| | emergency | 19 | 2,5 | 12 | 1,0 |
| | obstet/gyneacology | 1 | 0,1 | 6 | 0,5 |
| | other | 131 | 17,1 | 158 | 12,5 |
| | unknown | 404 | 52,8 | 621 | 49,3 |

ANNEX 8. Characterization of resistant *S. pneumoniae* and *S. aureus*

A. *S. pneumoniae*

| <i>Nr</i> | <i>sex</i> | <i>source</i> | <i>age</i> | <i>PEN</i> | <i>CTX</i> | <i>CRO</i> | <i>ERY</i> | <i>TET</i> | <i>SXT</i> | <i>VAN</i> |
|-----------|------------|---------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 1 | m | bl | 72 | -- | | | S | S | S | S |
| 2 | m | bl | 60 | 0,5 | | S | | | R | |
| 3 | m | bl | 71 | 1,0 | | | | S | R | |
| 4 | m | bl | 78 | 0,25 | | | S | S | S | S |
| 5 | m | bl | 71 | 1 | 0,125 | 0,125 | S | S | R | S |
| 6 | m | bl | 0 | 0,5 | S | S | S | S | R | S |
| 7 | f | bl | 44 | 0,25 | | | S | S | S | S |
| 8 | m | bl | 61 | 0,25 | | | S | S | | S |
| 9 | f | sf | 86 | 0,5 | 0,125 | | S | S | | S |

B. *S. aureus*

| <i>Nr</i> | <i>sex</i> | <i>age</i> | <i>MecA</i> | <i>MET</i> | <i>FLC</i> | <i>VAN</i> | <i>ERY</i> | <i>GEN</i> | <i>SXT</i> | <i>CLI</i> |
|-----------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|
| 1 | m | 72 | + | | 64 | S | R | S | S | S |
| 2 | m | 60 | + | | | 0,5 | 0,5 | S | S | S |
| 3 | f | 71 | + | 256 | | 1,5 | | S | | |
| 4 | m | 78 | + | 256 | | | R | | S | R |

ANNEX 9 Individual susceptibility results of the laboratories

Invasieve Streptococcus pneumoniae infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

----- LA_CODE=NL002 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|----------------|-----------|----------------|----------|
| penicilline | 1 | 51 | 2.0 |
| cefuroxime | 0 | 51 | 0.0 |
| ceftriaxon | 0 | 2 | 0.0 |
| amoxicilline | 0 | 51 | 0.0 |
| augmentin | 0 | 51 | 0.0 |
| tetracycline | 1 | 50 | 2.0 |
| ciprofloxacin | 23 | 51 | 45.1 |
| cotrimoxazol | 2 | 51 | 3.9 |
| erythromycine | 0 | 51 | 0.0 |
| vancomycine | 0 | 51 | 0.0 |
| chloramfenicol | 0 | 2 | 0.0 |
| rifampicine | 0 | 3 | 0.0 |
| Tobramycine | 34 | 51 | 66.7 |

----- LA_CODE=NL003 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| oxacilline | 0 | 15 | 0.0 |
| penicilline | 0 | 23 | 0.0 |
| tetracycline | 1 | 23 | 4.3 |
| ciprofloxacin | 1 | 1 | 100.0 |
| erythromycine | 1 | 23 | 4.3 |
| vancomycine | 0 | 23 | 0.0 |
| cefpimizole | 6 | 23 | 26.1 |

----- LA_CODE=NL004 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| penicilline | 0 | 13 | 0.0 |
| cefotaxim | 0 | 8 | 0.0 |
| amoxicilline | 0 | 1 | 0.0 |
| augmentin | 0 | 2 | 0.0 |
| cefazidime | 0 | 1 | 0.0 |
| tetracycline | 0 | 12 | 0.0 |
| gentamicine | 1 | 2 | 50.0 |
| cotrimoxazol | 0 | 2 | 0.0 |
| erythromycine | 1 | 13 | 7.7 |
| vancomycine | 0 | 1 | 0.0 |

----- LA_CODE=NL005 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| penicilline | 0 | 12 | 0.0 |
| amoxicilline | 0 | 12 | 0.0 |
| augmentin | 0 | 12 | 0.0 |
| doxycycline | 1 | 12 | 8.3 |
| erythromycine | 3 | 12 | 25.0 |
| cefpimizole | 0 | 2 | 0.0 |

----- LA_CODE=NL006 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| oxacilline | 0 | 7 | 0.0 |
| penicilline | 0 | 64 | 0.0 |
| amoxicilline | 0 | 64 | 0.0 |
| augmentin | 0 | 7 | 0.0 |
| cefazidime | 0 | 57 | 0.0 |
| tetracycline | 0 | 57 | 0.0 |
| doxycycline | 0 | 7 | 0.0 |
| ciprofloxacin | 1 | 7 | 14.3 |
| cotrimoxazol | 0 | 64 | 0.0 |
| erythromycine | 3 | 64 | 4.7 |
| vancomycine | 0 | 7 | 0.0 |
| cefpimizole | 0 | 57 | 0.0 |

----- LA_CODE=NL007 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|----------------|-----------|----------------|----------|
| antibioticum | 0 | 31 | 0.0 |
| penicilline | 0 | 30 | 0.0 |
| tetracycline | 0 | 4 | 0.0 |
| ciprofloxacin | 0 | 3 | 0.0 |
| cotrimoxazol | 0 | 31 | 0.0 |
| erythromycine | 0 | 5 | 0.0 |
| vancomycine | 1 | 30 | 3.3 |
| chloramfenicol | 0 | 8 | 0.0 |
| rifampicine | 0 | | |

Invasieve Streptococcus pneumoniae infecties
Resistente tegen meerdere antibiotica
Resultaten per laboratorium

| LA_CODE=NL008 | | | | LA_CODE=NL013 | | | | LA_CODE=NL014 | | | |
|---------------------------|-----------|-------------------|----------|-----------------|-----------|-------------------|----------|----------------|-----------|-------------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 0 | 40 | 0 | oxacilline | 0 | 13 | 0.0 | antibioticum | 0 | 1 | 0 |
| cefotaxim | 0 | 40 | 0 | penicilline | 0 | 5 | 0.0 | oxacilline | 0 | 24 | 0.0 |
| cefuroxime | 0 | 40 | 0 | cefotaxim | 1 | 13 | 7.7 | penicilline | 0 | 1 | 0.0 |
| amoxicilline | 0 | 40 | 0.0 | ceftriaxon | 0 | 13 | 0.0 | cefotaxim | 0 | 4 | 0.0 |
| augmentin | 0 | 40 | 0.0 | tetracycline | 0 | 10 | 0.0 | ceftriaxon | 0 | 22 | 0.0 |
| doxycycline | 2 | 40 | 5.0 | ciprofloxacine | 1 | 13 | 7.7 | amoxicilline | 0 | 24 | 0.0 |
| ciprofloxacine | 6 | 40 | 15.0 | erythromycine | 0 | 13 | 0.0 | augmentin | 0 | 4 | 0.0 |
| cotrimoxazol | 1 | 40 | 2.5 | vancomycine | 0 | 13 | 0.0 | cefazidime | 0 | 4 | 0.0 |
| erythromycine | 1 | 40 | 2.5 | | | | | ciprofloxacine | 0 | 4 | 0.0 |
| vancomycine | 0 | 40 | 0.0 | | | | | cotrimoxazol | 0 | 24 | 0.0 |
| clindamycine | 1 | 40 | 2.5 | | | | | erythromycine | 1 | 24 | 4.2 |
| flucoxacilline | 0 | 39 | 0.0 | | | | | clindamycine | 0 | 24 | 0.0 |
| meticilline | 0 | 1 | 0.0 | | | | | cefpimizole | 0 | 24 | 0.0 |
| cefpimizole | 0 | 40 | 0.0 | | | | | Tobramycine | 2 | 4 | 50.0 |
| chlooramfenicol | 0 | 40 | 0.0 | | | | | | | | |
| Tobramycine | 40 | 40 | 100.0 | | | | | | | | |
| ----- LA_CODE=NL009 ----- | | | | | | | | | | | |
| antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 1 | 82 | 1.2 | penicilline | 0 | 82 | 0.0 | antibioticum | 0 | 1 | 0 |
| cefuroxime | 0 | 82 | 0.0 | cefuroxime | 0 | 79 | 0.0 | penicilline | 0 | 24 | 0.0 |
| ceftriaxon | 0 | 82 | 0.0 | ceftriaxon | 0 | 82 | 0.0 | cefotaxim | 0 | 4 | 0.0 |
| amoxicilline | 0 | 82 | 0.0 | amoxicilline | 0 | 82 | 0.0 | ceftriaxon | 0 | 22 | 0.0 |
| augmentin | 0 | 82 | 0.0 | augmentin | 0 | 82 | 0.0 | augmentin | 0 | 24 | 0.0 |
| cefazidime | 0 | 82 | 0.0 | cefazidime | 0 | 82 | 0.0 | cefazidime | 0 | 4 | 0.0 |
| tetracycline | 0 | 1 | 0.0 | tetracycline | 0 | 1 | 0.0 | ciprofloxacine | 0 | 4 | 0.0 |
| ciprofloxacine | 1 | 1 | 100.0 | ciprofloxacine | 1 | 1 | 100.0 | cotrimoxazol | 0 | 24 | 0.0 |
| cotrimoxazol | 6 | 81 | 7.4 | cotrimoxazol | 6 | 81 | 7.4 | erythromycine | 0 | 24 | 0.0 |
| erythromycine | 2 | 80 | 2.5 | erythromycine | 2 | 80 | 2.5 | clindamycine | 0 | 24 | 0.0 |
| chlooramfenicol | 0 | 79 | 0.0 | chlooramfenicol | 0 | 79 | 0.0 | Tobramycine | 2 | 4 | 50.0 |
| ----- LA_CODE=NL010 ----- | | | | | | | | | | | |
| antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 1 | 59 | 1.7 | penicilline | 1 | 59 | 1.7 | antibioticum | 1 | 69 | 1.4 |
| cefotaxim | 0 | 5 | 0.0 | cefotaxim | 0 | 5 | 0.0 | penicilline | 0 | 52 | 0.0 |
| cefuroxime | 1 | 44 | 2.3 | cefuroxime | 1 | 44 | 2.3 | tetracycline | 1 | 17 | 5.9 |
| ceftriaxon | 0 | 15 | 0.0 | ceftriaxon | 0 | 15 | 0.0 | doxycycline | 0 | 5 | 0.0 |
| amoxicilline | 0 | 17 | 0.0 | amoxicilline | 0 | 17 | 0.0 | cotrimoxazol | 2 | 69 | 2.9 |
| augmentin | 0 | 42 | 0.0 | augmentin | 0 | 42 | 0.0 | erythromycine | 0 | 5 | 0.0 |
| cefazidime | 0 | 18 | 0.0 | cefazidime | 0 | 18 | 0.0 | vancomycine | 0 | 5 | 0.0 |
| tetracycline | 0 | 1 | 0.0 | tetracycline | 0 | 1 | 0.0 | | | | |
| gentamicine | 2 | 2 | 100.0 | gentamicine | 2 | 2 | 100.0 | | | | |
| cotrimoxazol | 4 | 44 | 9.1 | cotrimoxazol | 4 | 44 | 9.1 | | | | |
| erythromycine | 0 | 1 | 0.0 | erythromycine | 0 | 1 | 0.0 | | | | |
| ofloxacine | 0 | 1 | 0 | ofloxacine | 0 | 1 | 0 | | | | |
| chlooramfenicol | 0 | 17 | 0 | chlooramfenicol | 0 | 17 | 0 | | | | |
| ----- LA_CODE=NL011 ----- | | | | | | | | | | | |
| antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 1 | 69 | 1.4 | penicilline | 1 | 69 | 1.4 | antibioticum | 1 | 69 | 1.4 |
| tetracycline | 0 | 52 | 0.0 | tetracycline | 0 | 52 | 0.0 | penicilline | 0 | 52 | 0.0 |
| doxycycline | 1 | 17 | 5.9 | doxycycline | 1 | 17 | 5.9 | tetracycline | 1 | 17 | 5.9 |
| cotrimoxazol | 2 | 69 | 2.9 | cotrimoxazol | 2 | 69 | 2.9 | doxycycline | 0 | 5 | 0.0 |
| erythromycine | 0 | 5 | 0.0 | erythromycine | 0 | 5 | 0.0 | cotrimoxazol | 2 | 69 | 2.9 |
| vancomycine | 0 | 5 | 0.0 | vancomycine | 0 | 5 | 0.0 | erythromycine | 0 | 5 | 0.0 |
| ----- LA_CODE=NL012 ----- | | | | | | | | | | | |

Invasieve Streptococcus pneumoniae infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

| ----- LA_CODE=NL016 ----- | | | | ----- LA_CODE=NL017 ----- | | | | ----- LA_CODE=NL018 ----- | | | | ----- LA_CODE=NL019 ----- | | | |
|---------------------------|-----------|-------------------|----------|---------------------------|-----------|-------------------|----------|---------------------------|-----------|-------------------|----------|---------------------------|-----------|-------------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 0 | 13 | 0.0 | penicilline | 0 | 7 | 0.0 | oxacilline | 0 | 3 | 0.0 | antibioticum | 1 | 55 | 1.8 |
| ceftriaxon | 0 | 13 | 0.0 | ceftriaxon | 0 | 7 | 0.0 | penicilline | 0 | 10 | 0.0 | cefotaxim | 0 | 54 | 0.0 |
| tetracycline | 1 | 9 | 11.1 | amoxicilline | 0 | 5 | 0.0 | cefotaxim | 0 | 10 | 0.0 | augmentin | 1 | 55 | 1.8 |
| doxycycline | 0 | 13 | 0.0 | augmentin | 0 | 1 | 0.0 | ceftriaxon | 0 | 9 | 0.0 | tetracycline | 0 | 51 | 0.0 |
| erythromycine | 0 | 13 | 0.0 | tetracycline | 1 | 7 | 14.3 | augmentin | 0 | 1 | 0.0 | doxycycline | 0 | 4 | 0.0 |
| vancomycine | 0 | 13 | 0.0 | cotrimoxazol | 1 | 7 | 14.3 | tetracycline | 0 | 6 | 0.0 | cotrimoxazol | 2 | 55 | 3.6 |
| clindamycine | 0 | 13 | 0.0 | erythromycine | 1 | 7 | 14.3 | doxycycline | 0 | 4 | 0.0 | erythromycine | 0 | 55 | 0.0 |
| | | | | vancomycine | 0 | 7 | 0.0 | gentamicine | 1 | 4 | 25.0 | vancomycine | 0 | 53 | 0.0 |
| | | | | clindamycine | 1 | 7 | 14.3 | ciprofloxacine | 0 | 1 | 0.0 | clindamycine | 0 | 53 | 0.0 |
| | | | | chlooramfenicol | 0 | 2 | 0.0 | erythromycine | 1 | 7 | 14.3 | rifampicine | 0 | 27 | 49.1 |
| | | | | | | | | vancomycine | 0 | 9 | 0.0 | | | | |
| | | | | | | | | clindamycine | 0 | 9 | 0.0 | | | | |
| | | | | | | | | rifampicine | 0 | 1 | 0.0 | | | | |

clindamycine 0 55 0.0
rifampicine 0 1 0.0

----- LA_CODE=NL020 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|-------------------|----------|
| penicilline | 0 | 60 | 0.0 |
| cefotaxim | 0 | 5 | 0.0 |
| ceftriaxon | 0 | 13 | 0.0 |
| erythromycine | 2 | 60 | 3.3 |
| vancomycine | 0 | 46 | 0.0 |
| clindamycine | 0 | 5 | 0.0 |
| cefpimizole | 0 | 8 | 0.0 |

----- LA_CODE=NL021 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|-----------------|-----------|-------------------|----------|
| antibioticum | 0 | 29 | 0.0 |
| penicilline | 0 | 14 | 0.0 |
| cefotaxim | 1 | 16 | 6.3 |
| amoxicilline | 0 | 29 | 0.0 |
| augmentin | 0 | 29 | 0.0 |
| gentamicine | 29 | 29 | 100.0 |
| ciprofloxacine | 0 | 1 | 0.0 |
| cotrimoxazol | 0 | 29 | 0.0 |
| erythromycine | 1 | 29 | 3.4 |
| vancomycine | 0 | 29 | 0.0 |
| clindamycine | 0 | 17 | 0.0 |
| chlooramfenicol | 0 | 29 | 0.0 |

----- LA_CODE=NL022 -----

| antibioticum | resistent | antal_ getest | res_perc |
|---------------|-----------|---------------|----------|
| penicilline | 4 | 61 | 6.6 |
| cefotaxim | 0 | 3 | 0.0 |
| ceftriaxon | 0 | 3 | 0.0 |
| tetracycline | 3 | 61 | 4.9 |
| cotrimoxazol | 10 | 55 | 18.2 |
| erythromycine | 2 | 61 | 3.3 |
| vancomycine | 0 | 61 | 0.0 |

----- LA_CODE=NL023 -----

| antibioticum | resistent | antal_ getest | res_perc |
|--------------|-----------|---------------|----------|
| oxacilline | 0 | 35 | 0 |
| penicilline | 0 | 1 | 0 |

Invasieve Staphylococcus aureus infecties
Resistente tegen meerdere antibiotica
Resultaten per laboratorium

----- LA_CODE=NL002 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc |
| cefuroxime | 0 | 77 | 0.0 |
| amoxicilline | 55 | 76 | 72.4 |
| augmentin | 0 | 77 | 0.0 |
| cotrimoxazol | 0 | 77 | 0.0 |
| erythromycine | 0 | 1 | 0.0 |
| vancomycine | 0 | 77 | 0.0 |
| clindamycine | 2 | 76 | 2.6 |
| meticilline | 0 | 77 | 0.0 |
| rifampicine | 0 | 77 | 0.0 |
| tobramycine | 0 | 77 | 0.0 |

----- LA_CODE=NL003 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc |
| oxacilline | 0 | 80 | 0.0 |
| penicilline | 68 | 79 | 86.1 |
| augmentin | 0 | 78 | 0.0 |
| tetracycline | 5 | 79 | 6.3 |
| gentamicine | 3 | 78 | 3.8 |
| cotrimoxazol | 4 | 79 | 5.1 |
| erythromycine | 0 | 80 | 0.0 |
| vancomycine | 0 | 80 | 0.0 |
| cefpimizole | 0 | 80 | 0.0 |
| rifampicine | 1 | 77 | 1.3 |
| tobramycine | 0 | 1 | 0.0 |

----- LA_CODE=NL005 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|----------------|-----------|----------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 10 | 13 | 76.9 |
| ceftriaxon | 0 | 7 | 0.0 |
| augmentin | 0 | 13 | 0.0 |
| ciprofloxacin | 1 | 7 | 14.3 |
| cotrimoxazol | 0 | 12 | 0.0 |
| erythromycine | 2 | 13 | 15.4 |
| vancomycine | 0 | 7 | 0.0 |
| clindamycine | 0 | 13 | 0.0 |
| flucoxacilline | 0 | 13 | 0.0 |
| cefpimizole | 0 | 2 | 0.0 |
| tobramycine | 0 | 7 | 0.0 |

----- LA_CODE=NL006 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc |
| oxacilline | 0 | 9 | 0.0 |
| penicilline | 83 | 94 | 88.3 |
| amoxicilline | 78 | 94 | 83.0 |
| augmentin | 1 | 102 | 1.0 |
| ceftazidime | 87 | 94 | 92.6 |
| tetracycline | 3 | 94 | 3.2 |
| doxycycline | 0 | 9 | 0.0 |
| gentamicine | 0 | 9 | 0.0 |
| Ciprofloxacin | 7 | 102 | 6.9 |
| cotrimoxazol | 1 | 94 | 1.1 |
| erythromycine | 11 | 94 | 11.7 |

| | | | |
|--------------|----|-----|------|
| vancomycine | 0 | 9 | 0.0 |
| clindamycine | 6 | 102 | 5.9 |
| meticilline | 1 | 94 | 1.1 |
| cefpimizole | 1 | 94 | 1.1 |
| tobramycine | 94 | 102 | 92.2 |

----- LA_CODE=NL007 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|-----------------|-----------|----------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 58 | 62 | 93.5 |
| cefuroxime | 0 | 62 | 0.0 |
| tetracycline | 0 | 61 | 0.0 |
| gentamicine | 1 | 61 | 1.6 |
| ciprofloxacin | 3 | 62 | 4.8 |
| cotrimoxazol | 0 | 2 | 0.0 |
| erythromycine | 0 | 2 | 0.0 |
| vancomycine | 0 | 62 | 0.0 |
| clindamycine | 1 | 61 | 1.6 |
| fusidinezuur | 0 | 1 | 0.0 |
| meticilline | 0 | 62 | 0.0 |
| chlooramfenicol | 0 | 1 | 0.0 |
| rifampicine | 0 | 61 | 0.0 |

----- LA_CODE=NL008 -----

| antibioticum | resistent | aantal_ getest | res_perc |
|---------------|-----------|----------------|----------|
| antibioticum | resistent | aantal_ getest | res_perc |
| penicilline | 74 | 95 | 77.9 |
| cefotaxim | 0 | 95 | 0.0 |
| cefuroxime | 0 | 95 | 0.0 |
| amoxicilline | 74 | 95 | 77.9 |
| augmentin | 0 | 95 | 0.0 |
| doxycycline | 2 | 95 | 2.1 |
| Ciprofloxacin | 20 | 95 | 21.1 |

Invasieve Staphylococcus aureus infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

| LA_CODE=NL008 | | | | LA_CODE=NL012 | | | |
|---------------------------|-----------|-------------------|----------|---------------------------|-----------|-------------------|----------|
| (Continued) | | | | | | | |
| antibioticum | resistent | aantal_ getest | res_perc | antibioticum | resistent | aantal_ getest | res_perc |
| cotrimoxazol | 6 | 95 | 6.3 | antibioticum | 0 | 84 | 0.0 |
| erythromycine | 5 | 95 | 5.3 | oxacilline | 30 | 35 | 85.7 |
| vancomycine | 0 | 95 | 0.0 | penicilline | 2 | 35 | 5.7 |
| clindamycine | 2 | 95 | 2.1 | tetracycline | 1 | 35 | 2.9 |
| fluoxacilline | 0 | 95 | 0.0 | ciprofloxacine | 0 | 34 | 2.9 |
| meticilline | 0 | 95 | 0.0 | erythromycine | 0 | 35 | 0.0 |
| cefpimizole | 0 | 95 | 0.0 | vancomycine | 0 | 35 | 0.0 |
| chloramfenicol | 4 | 95 | 4.2 | ----- LA_CODE=NL013 ----- | | | |
| rifampicine | 0 | 2 | 0.0 | antibioticum | 0 | 21 | 0.0 |
| tobramycine | 12 | 95 | 12.6 | oxacilline | 13 | 13 | 100.0 |
| ----- LA_CODE=NL009 ----- | | | | penicilline | 13 | 13 | 100.0 |
| antibioticum | resistent | aantal_ getest | res_perc | cefotaxim | 0 | 13 | 0.0 |
| penicilline | 98 | 121 | 81.0 | cefuroxime | 1 | 21 | 4.8 |
| cefuroxime | 0 | 121 | 0.0 | gentamicine | 0 | 12 | 0.0 |
| amoxicilline | 98 | 121 | 81.0 | ciprofloxacine | 1 | 21 | 4.8 |
| augmentin | 0 | 121 | 0.0 | erythromycine | 0 | 21 | 0.0 |
| tetracycline | 7 | 121 | 5.8 | vancomycine | 0 | 21 | 0.0 |
| gentamicine | 0 | 121 | 0.0 | tobramycine | 0 | 13 | 0 |
| ciprofloxacine | 4 | 121 | 3.3 | ----- LA_CODE=NL010 ----- | | | |
| cotrimoxazol | 4 | 121 | 3.3 | antibioticum | resistent | aantal_ getest | res_perc |
| erythromycine | 5 | 121 | 4.1 | penicilline | 102 | 129 | 79.1 |
| vancomycine | 0 | 120 | 0.0 | cefotaxim | 0 | 4 | 0.0 |
| ofloxacine | 3 | 120 | 2.5 | cefuroxime | 0 | 1 | 0.0 |
| clindamycine | 2 | 121 | 1.7 | augmentin | 0 | 129 | 0.0 |
| meticilline | 0 | 121 | 0.0 | gentamicine | 5 | 129 | 3.9 |
| cefpimizole | 0 | 121 | 0.0 | ciprofloxacine | 1 | 2 | 50.0 |
| rifampicine | 0 | 120 | 0.0 | cotrimoxazol | 2 | 129 | 1.6 |
| ----- LA_CODE=NL011 ----- | | | | erythromycine | 10 | 129 | 7.8 |
| antibioticum | resistent | aantal_ getest | res_perc | vancomycine | 0 | 129 | 0.0 |
| penicilline | 102 | 129 | 79.1 | ofloxacine | 9 | 129 | 7.0 |
| cefotaxim | 0 | 4 | 0.0 | clindamycine | 2 | 129 | 1.6 |
| cefuroxime | 0 | 1 | 0.0 | fluoxacilline | 1 | 129 | 0.8 |
| augmentin | 0 | 129 | 0.0 | ----- LA_CODE=NL011 ----- | | | |
| gentamicine | 5 | 129 | 3.9 | antibioticum | resistent | aantal_ getest | res_perc |
| ciprofloxacine | 1 | 2 | 50.0 | penicilline | 67 | 84 | 79.8 |
| cotrimoxazol | 2 | 129 | 1.6 | cefuroxime | 0 | 72 | 0.0 |
| erythromycine | 10 | 129 | 7.8 | amoxicilline | 57 | 72 | 79.2 |
| vancomycine | 0 | 129 | 0.0 | gentamicine | 1 | 72 | 1.4 |
| ofloxacine | 9 | 129 | 7.0 | cotrimoxazol | 0 | 12 | 0.0 |
| clindamycine | 2 | 129 | 1.6 | erythromycine | 0 | 72 | 0.0 |
| fluoxacilline | 1 | 129 | 0.8 | vancomycine | 0 | 83 | 0.0 |

Invasieve Staphylococcus aureus infecties
Resistente tegen meerdere antibiotica
Resultaten per laboratorium

----- LA_CODE=NL014 -----

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| oxacilline | 0 | 39 | 0.0 |
| penicilline | 28 | 39 | 71.8 |
| ceftriaxon | 0 | 39 | 0.0 |
| augmentin | 0 | 38 | 0.0 |
| cefprozidime | 1 | 39 | 2.6 |
| ciprofloxacin | 3 | 39 | 7.7 |
| cotrimoxazol | 1 | 39 | 2.6 |
| erythromycine | 0 | 39 | 0.0 |
| vancomycine | 0 | 38 | 0.0 |
| clindamycine | 0 | 39 | 0.0 |
| ceftimizole | 0 | 39 | 0.0 |
| tobramycine | 0 | 39 | 0.0 |

----- LA_CODE=NL016 -----

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| penicilline | 26 | 31 | 83.9 |
| cefuroxime | 0 | 31 | 0.0 |
| ceftriaxon | 0 | 31 | 0.0 |
| augmentin | 0 | 31 | 0.0 |
| ciprofloxacin | 0 | 31 | 0.0 |
| cotrimoxazol | 0 | 31 | 0.0 |
| erythromycine | 2 | 31 | 6.5 |
| vancomycine | 0 | 31 | 0.0 |
| clindamycine | 1 | 31 | 3.2 |
| fusidinezuur | 2 | 31 | 6.5 |
| fluoxacilline | 0 | 31 | 0.0 |
| rifampicine | 0 | 31 | 0.0 |

----- LA_CODE=NL017 -----

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| penicilline | 13 | 14 | 92.9 |
| cefuroxime | 0 | 14 | 0.0 |
| ceftriaxon | 0 | 2 | 0.0 |
| augmentin | 0 | 14 | 0.0 |
| doxycycline | 1 | 14 | 7.1 |
| ciprofloxacin | 1 | 14 | 7.1 |
| cotrimoxazol | 1 | 14 | 7.1 |
| erythromycine | 1 | 14 | 7.1 |
| vancomycine | 0 | 2 | 0.0 |
| clindamycine | 1 | 14 | 7.1 |
| fusidinezuur | 1 | 2 | 0.0 |
| fluoxacilline | 0 | 14 | 0.0 |
| rifampicine | 1 | 2 | 50.0 |

----- LA_CODE=NL018 -----

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| oxacilline | 0 | 19 | 0.0 |
| penicilline | 8 | 13 | 61.5 |
| cefotaxim | 0 | 1 | 0.0 |
| ceftriaxon | 0 | 1 | 0.0 |
| tetracycline | 2 | 15 | 13.3 |
| gentamicine | 0 | 19 | 0.0 |
| ciprofloxacin | 0 | 2 | 0.0 |
| cotrimoxazol | 0 | 2 | 0.0 |
| erythromycine | 2 | 20 | 10.0 |
| vancomycine | 0 | 12 | 0.0 |

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| clindamycine | 1 | 1 | 100.0 |
| fluoxacilline | 0 | 5 | 0.0 |
| meticilline | 0 | 2 | 0.0 |
| rifampicine | 1 | 5 | 20.0 |

----- LA_CODE=NL019 -----

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| penicilline | 47 | 58 | 81.0 |
| cefotaxim | 0 | 1 | 0.0 |
| amoxicilline | 1 | 3 | 33.3 |
| augmentin | 0 | 5 | 0.0 |
| tetracycline | 1 | 57 | 1.8 |
| gentamicine | 1 | 58 | 1.7 |
| ciprofloxacin | 0 | 51 | 0.0 |
| cotrimoxazol | 0 | 58 | 0.0 |
| erythromycine | 0 | 58 | 0.0 |
| ofloxacin | 0 | 58 | 0.0 |
| clindamycine | 0 | 58 | 0.0 |
| fluoxacilline | 0 | 8 | 0.0 |
| rifampicine | 0 | 6 | 0.0 |

----- LA_CODE=NL020 -----

| antibioticum | resistent | aantal_ | res_perc |
|---------------|-----------|---------|----------|
| | | getest | |
| penicilline | 59 | 69 | 85.5 |
| augmentin | 0 | 1 | 0.0 |
| erythromycine | 2 | 69 | 2.9 |
| vancomycine | 0 | 66 | 0.0 |
| clindamycine | 0 | 69 | 0.0 |
| fusidinezuur | 1 | 66 | 1.5 |
| fluoxacilline | 0 | 69 | 0.0 |
| ceftimizole | 0 | 69 | 0.0 |
| rifampicine | 1 | 66 | 1.5 |

Invasieve Staphylococcus aureus infecties
Resistente tegen meerdere antibiotica
Resultaten per laboratorium

----- LA_CODE=NL021 -----

| antibioticum | resistent | antal_ getest | res_perc |
|-----------------|-----------|------------------|----------|
| oxacilline | 0 | 24 | 0.0 |
| penicilline | 32 | 37 | 86.5 |
| ceftriaxon | 0 | 27 | 0.0 |
| amoxicilline | 32 | 37 | 86.5 |
| augmentin | 0 | 37 | 0.0 |
| gentamicine | 3 | 37 | 8.1 |
| ciprofloxacine | 2 | 27 | 7.4 |
| cotrimoxazol | 0 | 37 | 0.0 |
| erythromycine | 0 | 37 | 0.0 |
| vancomycine | 0 | 37 | 0.0 |
| clindamycine | 0 | 31 | 0.0 |
| meticilline | 0 | 13 | 0.0 |
| chlooramfenicol | 4 | 37 | 10.8 |

----- LA_CODE=NL022 -----

| antibioticum | resistent | antal_ getest | res_perc |
|----------------|-----------|------------------|----------|
| oxacilline | 1 | 122 | 0.8 |
| penicilline | 101 | 121 | 83.5 |
| cefuroxime | 1 | 119 | 0.8 |
| tetracycline | 6 | 100 | 6.0 |
| gentamicine | 0 | 122 | 0.0 |
| ciprofloxacine | 33 | 120 | 27.5 |
| cotrimoxazol | 19 | 120 | 15.8 |
| erythromycine | 12 | 120 | 10.0 |
| vancomycine | 0 | 122 | 0.0 |
| clindamycine | 9 | 120 | 7.5 |
| fusidinezuur | 3 | 98 | 3.1 |
| rifampicine | 1 | 122 | 0.8 |

----- LA_CODE=NL023 -----

| antibioticum | resistent | antal_ getest | res_perc |
|--------------|-----------|------------------|----------|
| oxacilline | 1 | 50 | 2 |
| gentamicine | 0 | 1 | 0 |
| vancomycine | 0 | 1 | 0 |