Antimicrobial Resistance in Ireland, 2003

Key Points

In 2003,

- 1140 invasive isolates of *Staphylococcus aureus* were reported. The proportion of isolates that were methicillin-resistant *S. aureus* (MRSA) was 42.1%, which remains one of the highest in countries reporting to EARSS
- 364 invasive isolates of *Streptococcus pneumoniae* were reported. The proportion that was penicillin-non-susceptible *S. pneumoniae* (PNSP) was 11.8%, which is moderately high compared to other European countries. Of the 43 PNSP isolates identified, eight were found to be high-level resistant [minimum inhibitory concentration (MIC) >2 mg/L] and 32 were determined to have intermediate levels of resistance (MIC 0.12–1.0 mg/L). No MICs were available for three isolates
- 991 invasive isolates of *Escherichia coli* were reported. The proportions of isolates that were resistant to third-generation cephalosporins, fluoroquinolones and aminoglycosides were 2.4%, 9.5% and 3.9%, respectively. These figures are low compared with other European countries
- 218 invasive isolates of *Enterococcus faecalis* were reported. The proportion of isolates that were vancomycin-resistant was 1.4%. Although this figure is low, it is still slightly higher than observed in most other European countries (<1%)
- 135 invasive isolates of *Enterococcus faecium* were reported. The proportion of isolates that were vancomycin-resistant was 19.4%, which is moderately high compared with most other European countries

Introduction

The European Antimicrobial Resistance Surveillance System (EARSS) was established in 1998 and is funded by DG SANCO of the European Commission. It is an international network of national surveillance systems, encompassing over 600 laboratories in 28 countries, which aims to collect comparable and reliable antimicrobial resistance data on invasive infections of *Staphylococcus aureus,*

Streptococcus pneumoniae, Escherichia coli, and *Enterococcus faecium/faecalis* for public health action.

EARSS in Ireland started in 1999 with the surveillance of *S. aureus* and *S. pneumoniae* and expanded in 2002 to include three further pathogens, *E. coli* and the enterococci, *E. faecalis* and *E. faecium*. Five additional laboratories joined the program in 2003 bringing the total number of participating laboratories to 28. The method for determining the percentage population coverage has been revised from a very rough estimate of the catchment populations reported by each participating hospital laboratory in previous years to a calculation based on acute public hospital activity data obtained from DoHC. This revised calculation gives an estimated population coverage approaching 90%, which represents an increase from the revised 80% coverage in 2002.

Protocol

Data are collected on the first invasive isolate per patient per quarter of *S. aureus* and the enterococci (from blood only) and *S. pneumoniae* and *E. coli* [from blood and cerebrospinal fluid (CSF)]. Laboratories report routinely generated qualitative disc diffusion data on:

- oxacillin/methicillin for *S. aureus*
- oxacillin/penicillin and erythromycin for *S. pneumoniae*
- ampicillin, cetotaxime/ceftriaxone and/or ceftazidime [third-generation cephalosporins (3GCs)], ciprofloxacin/ofloxacin (fluoroquinolones) and gentamicin/tobramycin (aminoglycosides) for *E. coli*. Laboratories are also asked to specifically test for the presence of extended-spectrum beta-lactamases (ESBLs)
- ampicillin, high-level gentamicin and vancomycin for enterococci

All methicillin-resistant *S. aureus* (MRSA) isolates are submitted to the National MRSA Reference laboratory (NMRSARL) at St James's Hospital, where minimum inhibitory concentrations (MICs) are determined for oxacillin and vancomycin. Laboratories are requested to submit data on MICs or Etests performed in-house for

penicillin and cefotaxime or ceftriaxone on all penicillin-non-susceptible *S. pneumoniae* (PNSP) isolates.

Results

Staphylococcus aureus

In 2003, 1140 reports of *S. aureus* isolates from bacteraemia were received from 26 laboratories, of which 480 (42.1%) were resistant to methicillin. By comparison, the proportion of *S. aureus* isolates that were methicillin-resistant in 2002 was 42.7%. In 2003, there was a peak in Q2 when the proportion of MRSA was 46.5% compared with the other three quarters of the year when the proportion ranged from 40.3-41.4% (see figure 1). A similar pattern was seen in 2002.

Data from the NMRSARL showed that gentamicin resistance among MRSA isolates decreased from 33.9% in 2001 (and an initial high of 58.4% in 1999) to 24.0% in 2002 and again in 2003 to 13.1% (see figure 2). This continues to reflect the growing trend throughout Europe in which epidemic strains of MRSA that are less multi-resistant to antibiotics are becoming more prevalent.

The overall annual proportion of MRSA observed in Ireland remains high and is comparable with proportions observed in the UK, France and most Southern European countries (see figure 3). For the first time since EARSS commenced in 1999, a country (Greece) has reported a proportion of MRSA that is over 50%. Increases have also been observed in Finland and parts of Central Europe (Hungary and Slovakia). The Scandinavian countries and The Netherlands report the lowest proportions of MRSA.

Streptococcus pneumoniae

In 2003, 364 reports of *S. pneumoniae* isolates from bacteraemia/meningitis were received from 24 laboratories. The majority of isolates (n = 359) were from blood but five were from CSF. Forty-three isolates (11.8%) were PNSP. By comparison, the proportion of *S. pneumoniae* isolates that were penicillin-non-susceptible in 2002 was 11.5%.

As in previous years, a seasonal variation was seen in the numbers of *S. pneumoniae* isolates reported with a trough in Q3, reflecting the quieter summer period (see figure 4).

Of the 43 PNSP isolates reported, MIC data for penicillin and cefotaxime were available for 40 and 24 isolates, respectively. Eight isolates were found to be high-level penicillin resistant (MIC ≥2 mg/L) and the remaining 32 isolates of the 40 tested were determined to have intermediate levels of resistance (MIC 0.12–1.0 mg/L). No MICs were available for three PNSP isolates. One isolate was intermediately resistant to cefotaxime (MIC 2 mg/L according to NCCLS non-meningitis breakpoints) in addition to being high-level resistant to penicillin (MIC 2 mg/L). The remaining 23 isolates of the 24 tested were susceptible to cefotaxime (MIC ≤1 mg/L).

Two additional isolates were reported that were oxacillin-resistant on screening by disc diffusion but were subsequently found to be penicillin-susceptible on MIC testing. This highlights the importance of MIC testing on all isolates that appear to be non-susceptible on the initial screening test.

Data on susceptibility to erythromycin or clarithromycin were available for 344 isolates. Forty (11.6%) were reported to be resistant.

Of the five CSF isolates reported in 2003, one (from a two-year old child) was intermediately resistant to penicillin (MIC 1 mg/L) but susceptible to cefotaxime (MIC 0.5 mg/L, interpreted using NCCLS meningitis breakpoints). The other four isolates (from three children under 4 years and one adult aged 48 years) were susceptible to penicillin.

Based on the total population of 3,917,203 in the Republic of Ireland as determined in the 2002 census and approximately 90% coverage of the population by the EARSS surveillance system, the crude incidence of invasive pneumococcal disease in Ireland is estimated to be 10.4 per 100,000 population. This represents an increase on the 8.8 per 100,000 population in 2002 (previously reported as 7.8 per 100,000 population but this figure has been revised based on acute public hospital activity data, which is considered to give a better estimate of population coverage). The corresponding

revised figures for 1999, 2000 and 2001 are 8.2, 7.8 and 8.1 per 100,000 population, respectively. By comparison, the rates of invasive pneumococcal disease reported in England and Wales in 1999 and 2000 were 8.6 and 8.9 per 100,000 population, respectively.[1,2] In Scotland, a recent study reported that the overall incidence of IPD between 1999 and 2001 was 11 per 100,000.[3]

The overall annual proportion of PNSP observed in Ireland remains moderately high (see figure 5) compared to the UK, Scandinavia and some Central European countries, such as Germany, which are generally associated with lower PNSP proportions. Higher proportions of PNSP are observed in Belgium, Southern Europe and some countries of the former Eastern Bloc.

Escherichia coli

In 2003, 991 reports of *E. coli* isolates from bacteraemia/meningitis were received from 27 laboratories. The majority of isolates (n = 989) were from blood but two were from CSF.

The proportions of isolates reported to be resistant to ampicillin, 3GCs, ciprofloxacin/ofloxacin (fluoroquinolones) and gentamicin were 61.9%, 2.4%, 9.5% and 3.9%, respectively, compared with 62.2%, 3.0%, 5.4% and 2.7%, respectively, reported in 2002.

The total numbers of *E. coli* isolates and proportion of resistance reported by quarter for 3GCs, fluoroquinolones and gentamicin are shown in figure 6.

Thirty-three isolates were identified as multi-drug resistant [defined as resistance to three or more of the mandatory antibiotics (ampicillin, 3GCs, fluoroquinolones and gentamicin)]:

- six isolates were resistant to ampicillin, 3GCs, fluoroquinolones and gentamicin - ESBL data were reported on five of these, all of which were positive
- eighteen were resistant to ampicillin, fluoroquinolones and gentamicin
- eight were resistant to ampicillin, 3GCs and fluoroquinolones. Four of these were ESBL-positive

- one was resistant to ampicillin, 3GCs and gentamicin

In total, 576 (58%) of the 991 isolates were examined for the presence of ESBLs. ESBLs were detected in 11 (1.9%) of these.

The two CSF isolates, both from newborns aged 11 and 16 days, respectively, were susceptible to 3GCs, fluoroquinolones and aminoglycosides. One of these isolates was resistant to ampicillin while the other was susceptible.

The proportion of ampicillin resistance reported in participating countries in Europe in 2003 was generally categorised as moderately high (25-50%) to high (>50%). The proportion in Ireland was high (61.9%) and was comparable with proportions seen in Italy, Spain and Portugal. The proportion of resistance to 3GCs, fluoroquinolones and gentamicin observed in Ireland in 2003 was low compared with most other European countries (see figures 7-9). The lowest proportions of resistance were observed in the Scandinavian countries while the highest proportions were seen in Southern and Eastern Europe.

Enterococcus faecalis

In 2003, 218 reports of *E. faecalis* isolates from bacteraemia were received from 19 laboratories.

The total numbers of *E. faecalis* isolates and proportion of resistance reported by quarter for ampicillin, high-level gentamicin and vancomycin are shown in figure 10.

Eleven isolates (5.1%) were reported to be ampicillin-resistant. Ampicillin resistance in *E. faecalis* is unusual and further investigation of these isolates is warranted to confirm their identity as it is generally acknowledged that speciation of enterococci can be problematic.

Sixty-one isolates (34%) of the 179 tested were reported to be high-level gentamicin resistant, of which 10 were confirmed by MIC determination. By comparison, 39% of isolates were reported to be high-level gentamicin resistant in 2002. The proportion of isolates tested for susceptibility to high-level gentamicin increased from 30% in

2002 to 82% in 2003, indicating increased awareness of this susceptibility testing issue and greater concordance with the protocol.

Three isolates (1.4%) were reported to be vancomycin resistant. Two of these were also resistant to teicoplanin. The other isolate was intermediately resistant to vancomycin (MIC 8 mg/L) and susceptible to teicoplanin, which would merit confirmation of the species identification. By comparison, 2.4% of isolates were vancomycin-resistant in 2002.

No isolates were resistant to ampicillin, high-level gentamicin and vancomycin. However, one isolate was resistant to high-level gentamicin and vancomycin and susceptible to ampicillin.

In 2003, the proportion of resistance to high-level gentamicin observed in Ireland, as well as in most other European countries (see figure 11), was generally high (≥25%). The majority of countries reported proportions of <1% for vancomycin resistance (see figure 12). The proportion of vancomycin resistance in Ireland was slightly higher and was comparable with France, Italy, the Netherlands and Poland.

Enterococcus faecium

In 2003, 135 reports of *E. faecium* isolates from bacteraemia were received from 17 laboratories.

The total numbers of *E. faecium* isolates and proportion of resistance reported by quarter for ampicillin, high-level gentamicin and vancomycin are shown in figure 13.

One hundred and twenty-one (91%) of the 133 isolates for which ampicillin susceptibility data were available were reported to be ampicillin-resistant, which is not unexpected as most *E. faecium* are resistant to this antibiotic.

Fifty-eight (54.7%) of 106 isolates tested were reported to be high-level gentamicin resistant, which is a substantial increase on 2002 when 16.7% of isolates tested were reported to be resistant. Twenty-two of the 58 isolates were confirmed by MIC determination. The proportion of isolates tested for susceptibility to high-level

gentamicin increased from 35% in 2002 to 79% in 2003, which is similar to the situation observed with *E. faecalis* isolates.

Twenty-six isolates (19.4%) were reported to be vancomycin resistant (16 confirmed by MICs). This represents an increase on 2002 when 11.1% of isolates were vancomycin-resistant.

Twelve isolates were resistant to ampicillin, high-level gentamicin (six confirmed by MICs) and vancomycin (seven confirmed by MICs).

In 2003, the proportion of resistance to high-level gentamicin in Ireland was one of the highest observed across Europe (see figure 14). The majority of countries reported proportions of <5% for vancomycin resistance (see figure 15). The proportion in Ireland was moderately high (10-25%) and together with Italy and Greece was one of the highest observed in Europe.

Additional information

The quarterly EARSS Newsletters produced by NDSC can be accessed on the NDSC website:
http://www.ndsc.ie/Publications/AntimicrobialResistance-EARSSReports/

Antimicrobial resistance data, including the most up-to-date maps (in full colour) showing the distributions of resistance, for all five pathogens surveyed in the 28 countries participating in this surveillance system can be obtained from the interactive database available on the EARSS website:
http://www.earss.rivm.nl/PAGINA/interwebsite/home_earss.html

The Future

The recent change in the Infectious Diseases legislation has made reporting on the EARSS pathogens mandatory for all Irish laboratories. It is anticipated that coverage of the Irish population by EARSS will reach 100% in 2004 as the remaining Irish laboratories join the surveillance system.

Using the acute public hospital activity data from DoHC, it is planned to produce both national and regional rates of invasive infections for the EARSS pathogens, which

will be useful for SARI local and regional committees. Collection of enhanced clinical data has also commenced in a number of laboratories and analysis of this data is currently being undertaken.

Acknowledgements

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- John Stelling, for help with WHONET; and
- Paul Schrijnemakers, Jos Monen and the EARSS Management Team in the Netherlands, for their support, feedback and assistance.

References

1. CDSC. Invasive Pneumococcal Infection: England and Wales, 1999. *CDR Weekly* 2001; **11** (21). Available at http://www.hpa.org.uk/cdr/PDFfiles/2001/cdr2101.pdf

2. CDSC. Invasive Pneumococcal Infection: England and Wales, 2000. *CDR Weekly* 2003; **13** (21). Available at http://www.hpa.org.uk/cdr/PDFfiles/2003/cdr2103.pdf

3. Kyaw MH, Christie P, Clarke S, Mooney JD, Ahmed S, Jones IG, Campbell H. Invasive pneumococcal disease in Scotland, 1999–2001: use of record linkage to explore associations between patients and disease in relation to future vaccination policy. *Clin Inf Dis* 2003; **37**: 1283–1291.

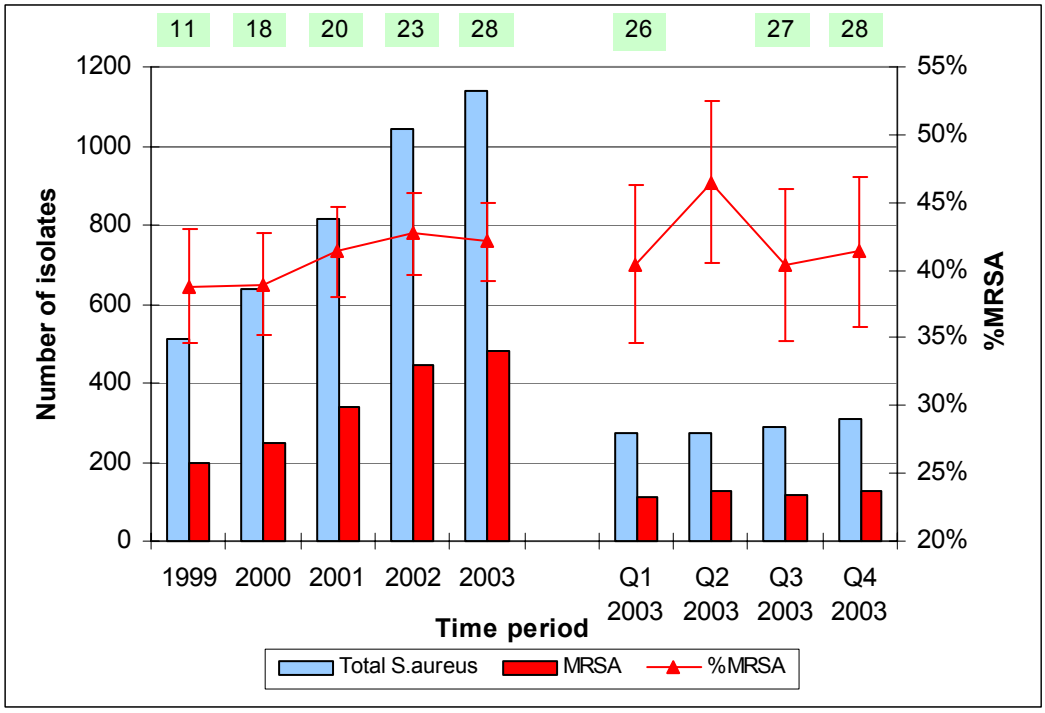

Figure 1. Trends for S. aureus *by time period: by year for 1999-2003 and by quarter for 2003 (Q1-Q4) – total numbers of* S. aureus*/MRSA and percentage MRSA with 95% confidence intervals. Changes in the numbers of laboratories participating in the surveillance system by year-end are indicated above the chart*

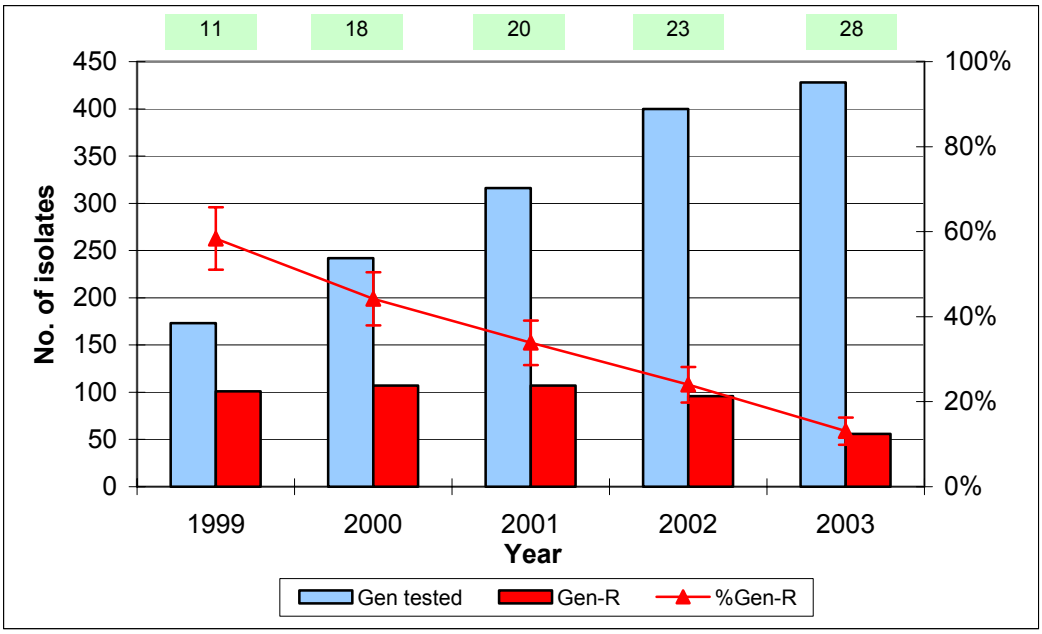

Figure 2. Trend in gentamicin resistance among MRSA isolates referred to NMRSARL between 1999 and 2003 - total numbers of MRSA isolates tested and *gentamicin-resistant MRSA isolates identified and percentage gentamicin-resistant MRSA with 95% confidence intervals. Changes in the numbers of laboratories participating in the surveillance system by year-end are indicated above the chart*

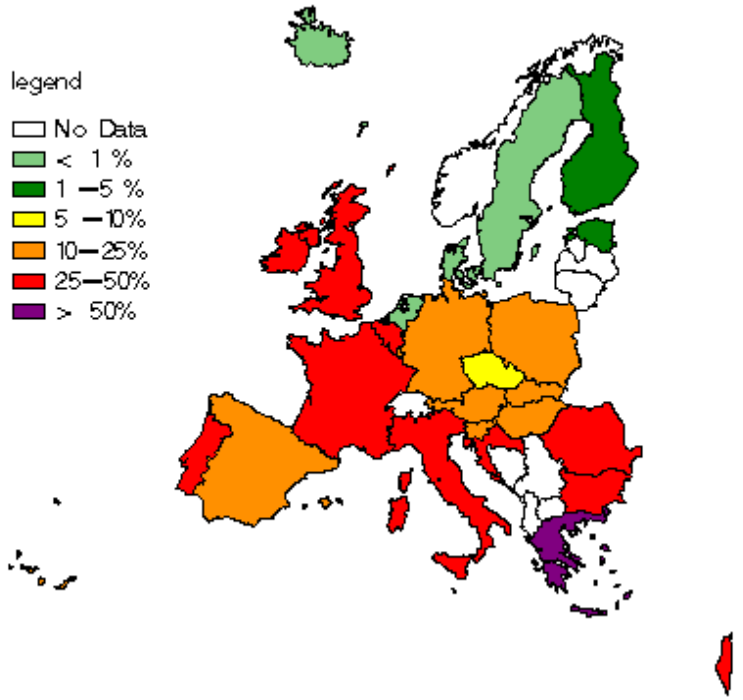

Figure 3. Map illustrating the distribution of MRSA in EARSS countries in 2003

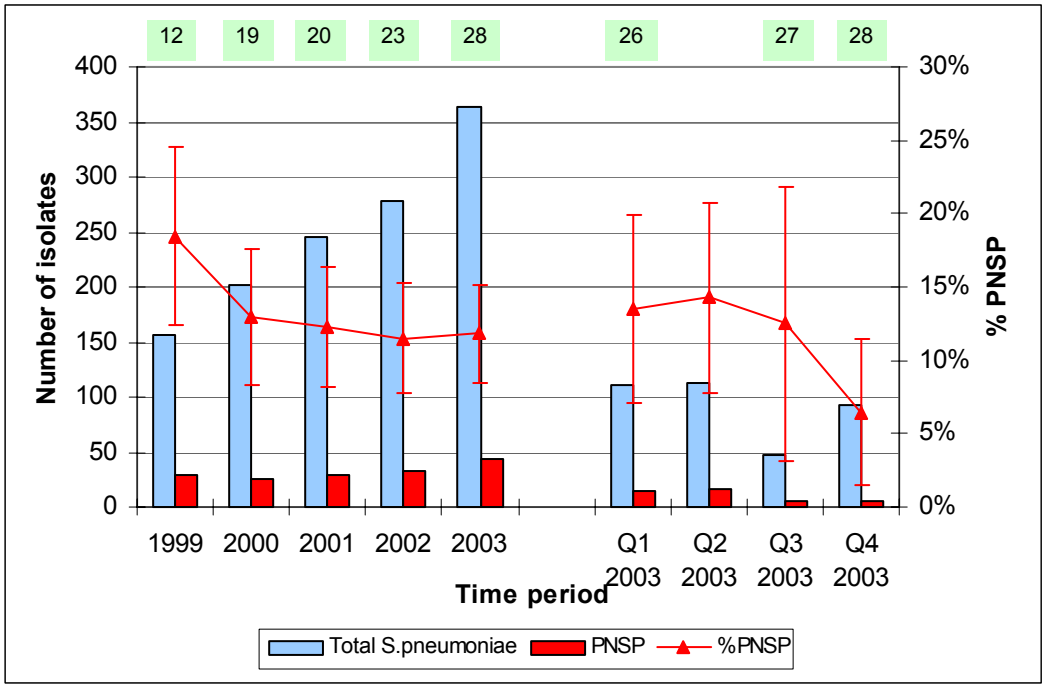

Figure 4. Trends for S. pneumoniae *by time period: by year for 1999-2003 and by quarter for 2003 (Q1-Q4) – total numbers of S. pneumoniae/PNSP and percentage PNSP with 95% confidence intervals. Changes in the numbers of laboratories participating in the surveillance system by year-end are indicated above the chart*

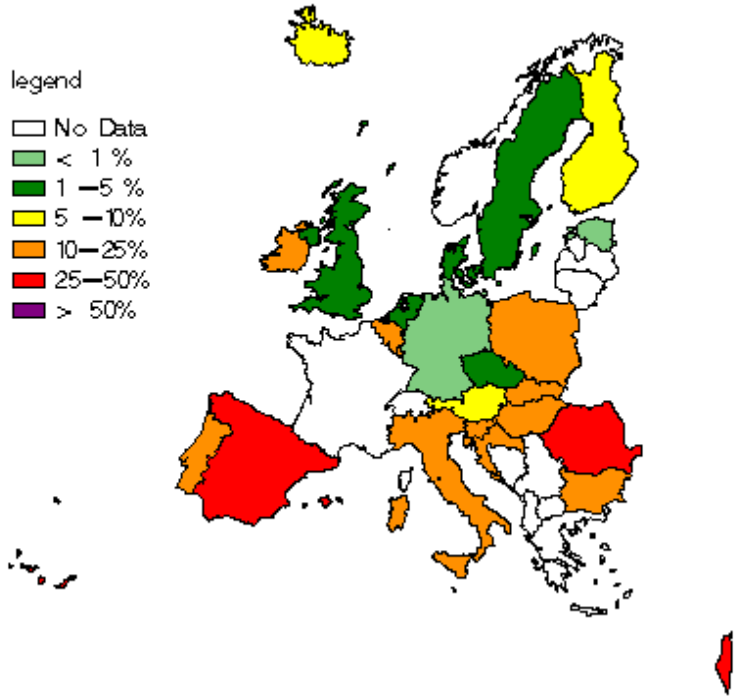

Figure 5. Map illustrating the distribution of PNSP in EARSS countries in 2003

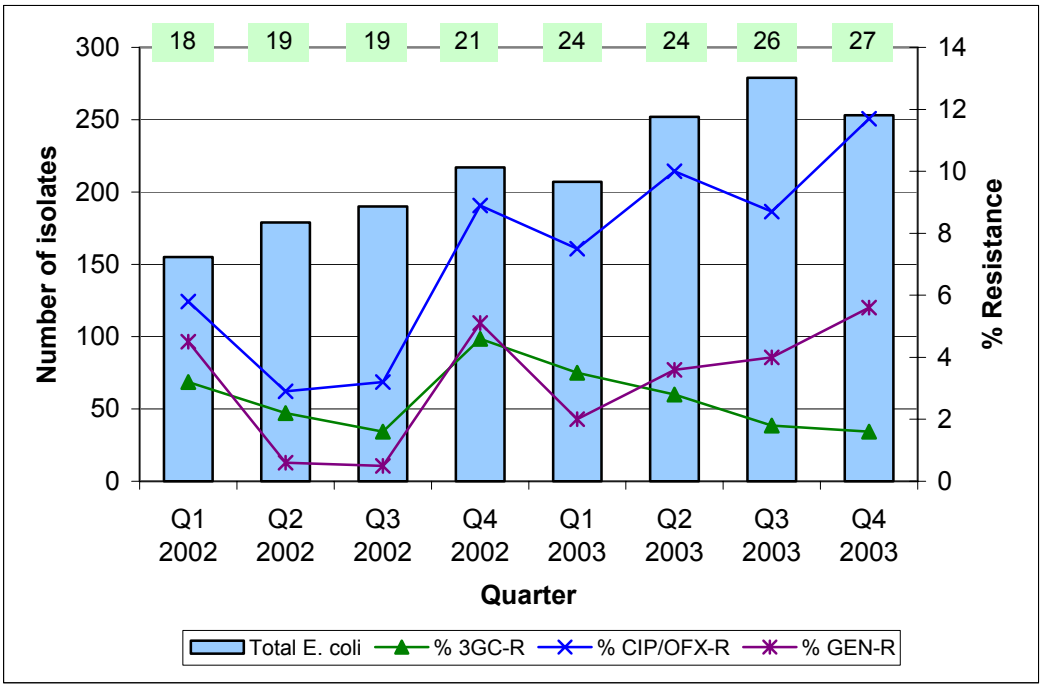

Figure 6. Trends for E. coli *by quarter for 2003 – total numbers of* E. coli *and percentage resistance to 3GCs, ciprofloxacin/ofloxacin (CIP/OFX) and gentamicin (GEN). Number of participating laboratories is indicated for each quarter*

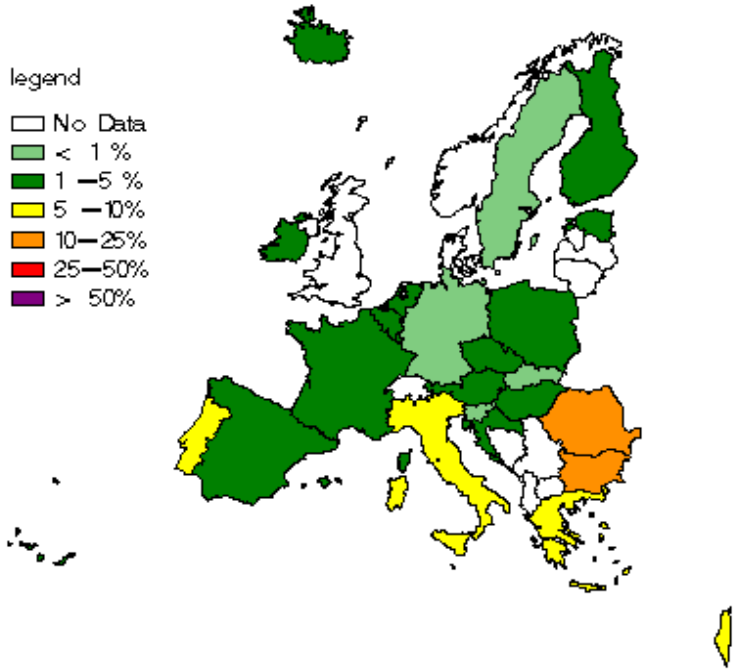

Figure 7. Map illustrating the distribution of resistance to 3GCs among E. coli *in EARSS countries in 2003*

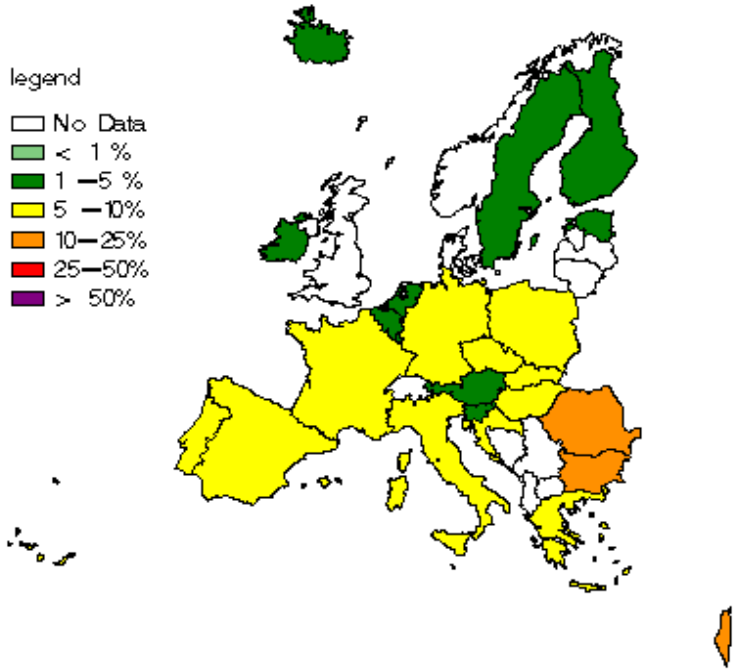

Figure 8. Map illustrating the distribution of resistance to aminoglycosides among E. coli *in EARSS countries in 2003*

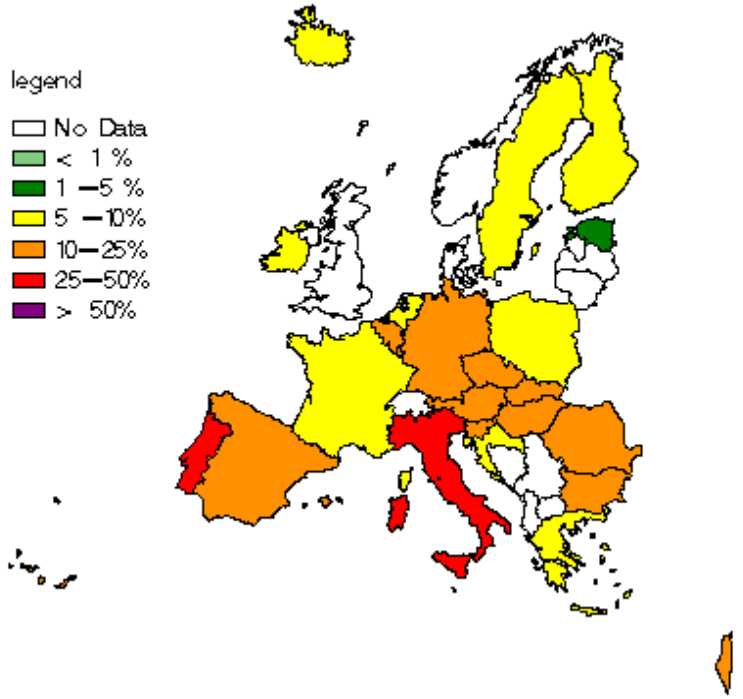

Figure 9. Map illustrating the distribution of resistance to fluoroquinolones among E. coli *in EARSS countries in 2003*

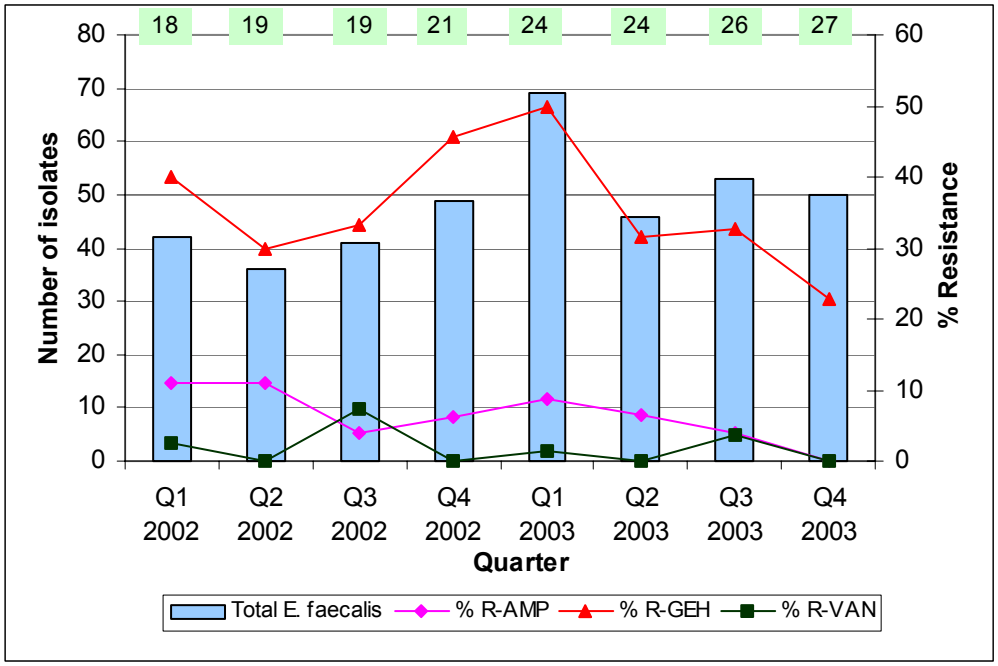

Figure 10. Trends for E. faecalis *by quarter for 2003 – total numbers of* E. faecalis *and percentage resistance to ampicillin (AMP), high-level gentamicin (GEH) and vancomycin (VAN). Number of participating laboratories is indicated for each quarter*

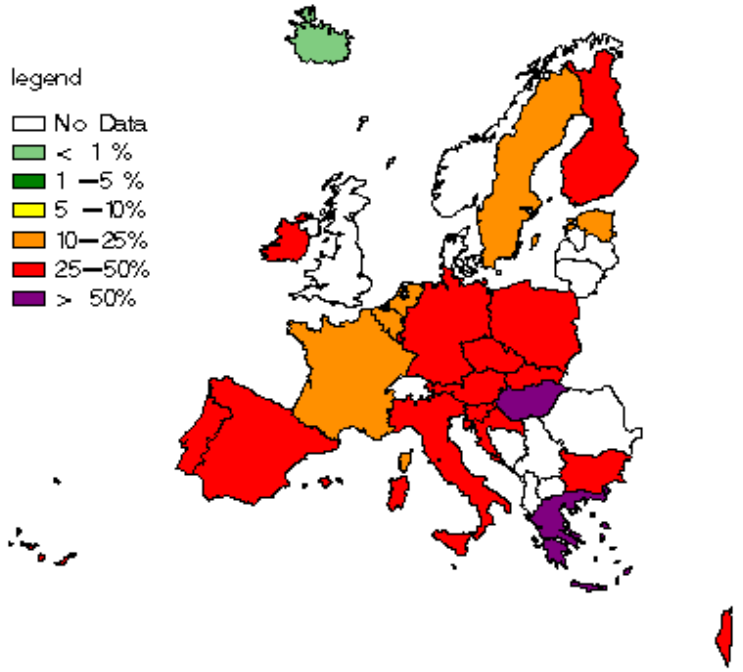

Figure 11. Map illustrating the distribution of high-level resistance to aminoglycosides among E. faecalis *in EARSS countries in 2003*

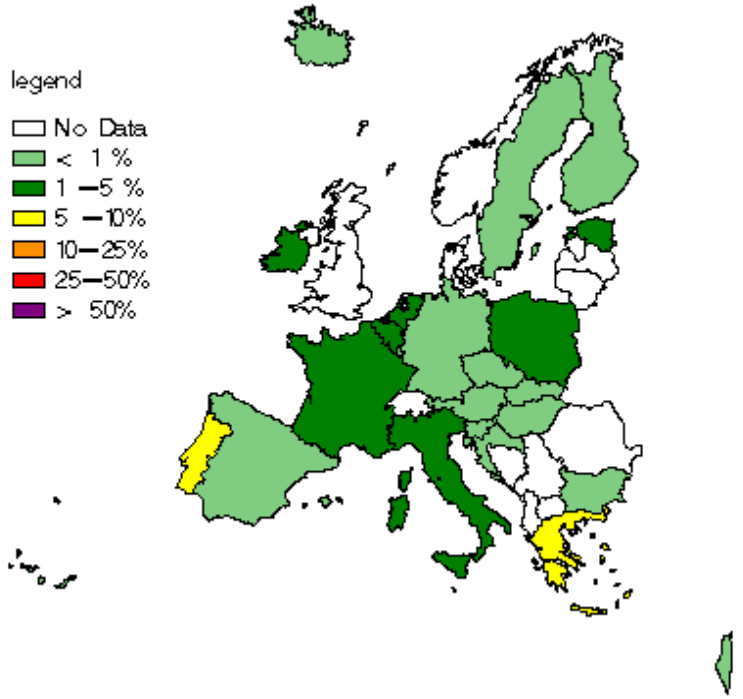

Figure 12. Map illustrating the distribution of resistance to glycopeptides among E. faecalis *in EARSS countries in 2003*

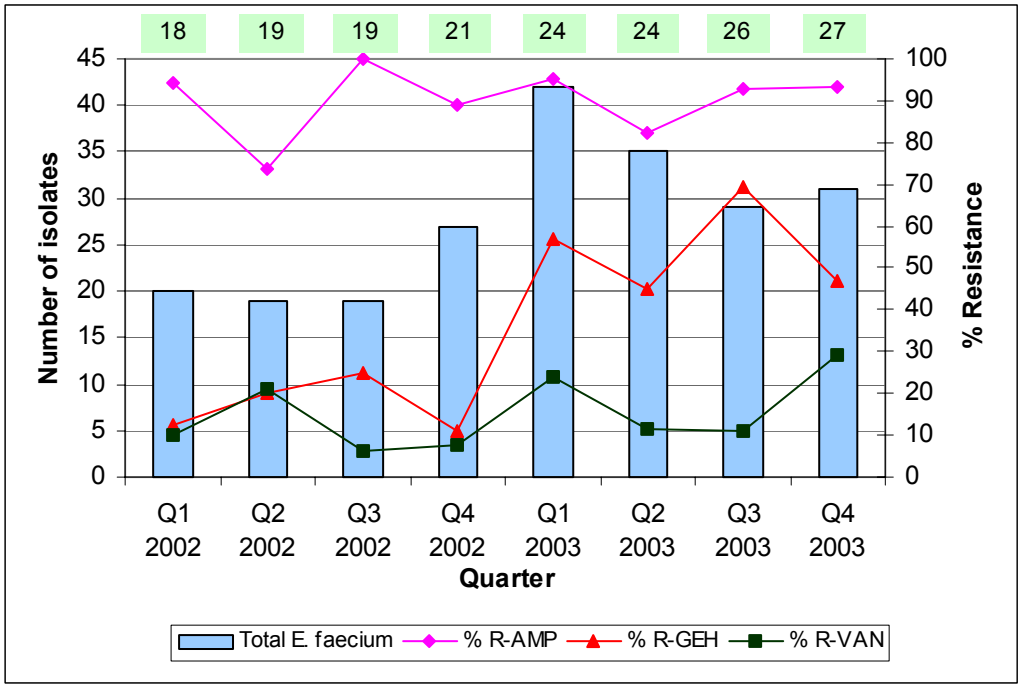

Figure 13. Trends for E. faecium *by quarter for 2003 – total numbers of* E. faecium *and percentage resistance to ampicillin (AMP), high-level gentamicin (GEH) and vancomycin (VAN). Number of participating laboratories is indicated for each quarter*

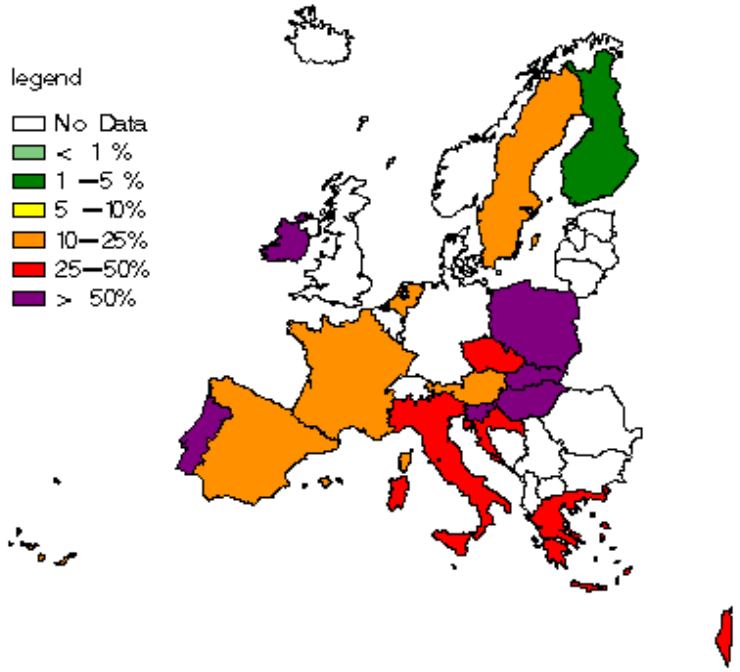

Figure 14. Map illustrating the distribution of high-level resistance to aminoglycosides among E. faecium *in EARSS countries in 2003*

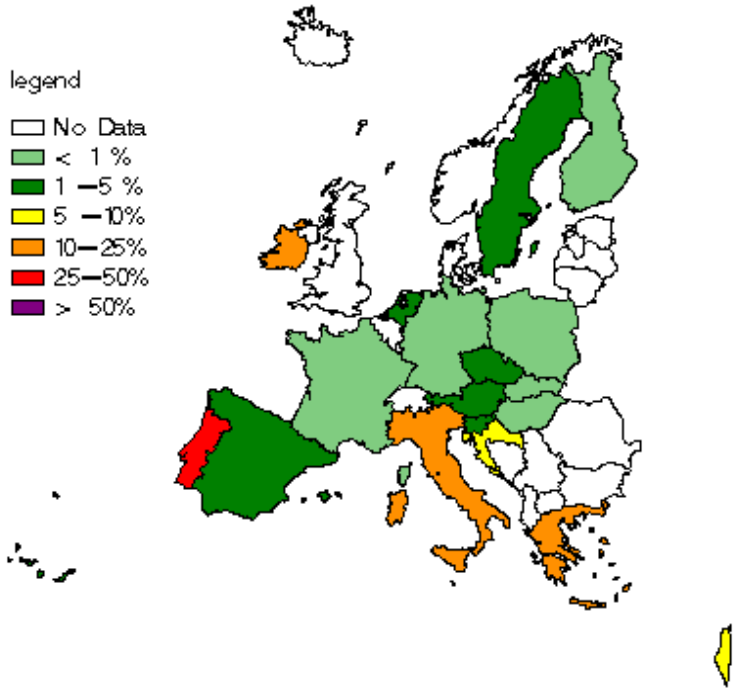

Figure 15. Map illustrating the distribution of resistance to glycopeptides among E. faecium *in EARSS countries in 2003*