**Surveillance and Outbreak Reports**

*Escherichia coli and Staphylococcus aureus*: bad news and good news from the European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS), 2002 to 2009

C Gagliotti¹, A Balode², F Baquero³, J Degener⁴, H Grundmann⁵, D Gür⁶, V Jarlier⁷, G Kahlmeter⁸, J Monen⁵, D L Monnet¹, G M Rossolini⁹, C Suetens¹⁰, K Weist¹, O Heuer (ole.heuer@ecdc.europa.eu)¹, the EARS-Net Participants (Disease Specific Contact Points for AMR)¹⁰

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**Methods**

Data for *E. coli* and *S. aureus* BSIs were extracted from the EARSS/EARS-Net database for a convenience sample of laboratories reporting susceptibility results continuously during the period from 2002 to 2009 for aminopenicillin, fluoroquinolones, third generation cephalosporins and aminoglycosides in *E. coli* and for oxacillin in *S. aureus* [3]. Countries in which no laboratory participated for the entire period or that had only a small data set (less than 20 isolates per microorganism per year) were not included in the analysis. Only invasive infections has been monitored for a decade by the European Antimicrobial Resistance Surveillance System (EARSS) [1]. Coordination and administration of the EARSS project, previously conducted by the Dutch National Institute of Public Health and the Environment (RIVM), was transferred to the European Centre for Disease Prevention and Control (ECDC) on 1 January 2010, and the network was renamed European Antimicrobial Resistance Surveillance Network (EARS-Net). The first data collection by EARS-Net (antimicrobial susceptibility data referring to 2009) took place during June and July 2010.

Whereas detailed analysis and trends at the national level are available in the EARSS and EARS-Net reports [1,2], the present study describes the trends in susceptibility patterns and number of invasive infections caused by *E. coli* and *S. aureus* in Europe from 2002 to 2009, based on data from laboratories reporting continuously during this period.

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**Introduction**

*Escherichia coli* and *Staphylococcus aureus* are the main causes of bloodstream infections (BSIs) in humans. The antimicrobial resistance of *E. coli* causing BSI is increasing alarmingly across Europe, while meticillin-resistant *S. aureus* (MRSA) is decreasing in several countries [1]. The antimicrobial susceptibility of these microorganisms and other selected bacterial pathogens causing invasive infections has been monitored for a decade by the European Antimicrobial Resistance Surveillance System (EARSS) [1]. Coordination and administration of the EARSS project, previously conducted by the Dutch National Institute of Public Health and the Environment (RIVM), was transferred to the European Centre for Disease Prevention and Control (ECDC) on 1 January 2010, and the network was renamed European Antimicrobial Resistance Surveillance Network (EARS-Net). The first data collection by EARS-Net (antimicrobial susceptibility data referring to 2009) took place during June and July 2010.

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**Methods**

Data for *E. coli* and *S. aureus* BSIs were extracted from the EARSS/EARS-Net database for a convenience sample of laboratories reporting susceptibility results continuously during the period from 2002 to 2009 for aminopenicillin, fluoroquinolones, third generation cephalosporins and aminoglycosides in *E. coli* and for oxacillin in *S. aureus* [3]. Countries in which no laboratory participated for the entire period or that had only a small data set (less than 20 isolates per microorganism per year) were not included in the analysis. Only invasive infections has been monitored for a decade by the European Antimicrobial Resistance Surveillance System (EARSS) [1]. Coordination and administration of the EARSS project, previously conducted by the Dutch National Institute of Public Health and the Environment (RIVM), was transferred to the European Centre for Disease Prevention and Control (ECDC) on 1 January 2010, and the network was renamed European Antimicrobial Resistance Surveillance Network (EARS-Net). The first data collection by EARS-Net (antimicrobial susceptibility data referring to 2009) took place during June and July 2010.

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the first isolate per patient, microorganism and year was included as a representative sample. Sampling and processing of isolates was done in agreement with the EARSS manual 2005 [3]. Resistance (R category of S, I, R) was defined by the guidelines in use in the reporting countries.

The number of BSIs caused by E. coli and S. aureus and the proportions of third-generation cephalosporin-resistant E. coli and of MRSA were recorded for each year from 2002 to 2009. To assess the patterns of combined resistance of E. coli, the following antimicrobial classes were analysed: aminopenicillins (ampicillin and amoxicillin), aminoglycosides (gentamicin, tobramycin and amikacin), third-generation cephalosporins (ceftriaxone, cefotaxime and ceftazidime) and fluoroquinolones (ciprofloxacin, ofloxacin and levofloxacin). Resistance to a class was defined as resistance (R category) to at least one agent in the class. The significance of the temporal linear trends for resistance proportions was evaluated by the Cochran–Armitage test for trend.

Results
A total of 198 laboratories in 22 countries continuously reported data from 2002 to 2009. The number of laboratories per country ranged between one (Iceland and Malta) and 33 (Czech Republic), while the mean number of E. coli and S. aureus isolates reported yearly per country ranged from 96 to 1,973 and from 56 to 1,290, respectively (Table).

Considering the whole group of selected laboratories, the reported number of E. coli BSIs increased by 71% from 10,688 in 2002 to 18,240 in 2009 (Figure 1); most of the rise (38% of 71%) in E. coli BSIs was due to isolates resistant to two or more antimicrobials. During the same period, S. aureus BSIs showed a 34% increase from 7,855 to 10,503 (Figure 1). In the period from 2002 to 2009, if only E. coli susceptible to amoxicillin, third-generation cephalosporins, fluoroquinolones and aminoglycosides are considered, the number of BSIs increased by 39%. Similarly, the BSIs caused by meticillin-susceptible S. aureus showed an increase of 37%.

In the period from 2002 to 2009, the proportion among all E. coli of E. coli resistant to third-generation cephalosporins increased significantly from 1.7% to 8% (p<0.001) and the proportion of MRSA decreased from 21.5% to 19.7% (p<0.001) (Figure 2). Similar trends of resistance proportions as observed for aggregated data of all 198 laboratories were also observed at country level in 18 of 22 countries for E. coli, and in seven of 22 countries for S. aureus.

Table
Mean annual number of Escherichia coli and Staphylococcus aureus isolates per country reported by laboratories (n=198) reporting continuously to EARSS/EARS-Net, 2002–09

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of laboratories</th>
<th>Number of Escherichia coli isolates</th>
<th>Number of Staphylococcus aureus isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>10</td>
<td>802</td>
<td>630</td>
</tr>
<tr>
<td>Belgium</td>
<td>9</td>
<td>646</td>
<td>343</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>7</td>
<td>96</td>
<td>82</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>33</td>
<td>1,837</td>
<td>1,290</td>
</tr>
<tr>
<td>Estonia</td>
<td>5</td>
<td>142</td>
<td>125</td>
</tr>
<tr>
<td>Finland</td>
<td>5</td>
<td>849</td>
<td>381</td>
</tr>
<tr>
<td>France</td>
<td>12</td>
<td>1,583</td>
<td>1,018</td>
</tr>
<tr>
<td>Germany</td>
<td>2</td>
<td>156</td>
<td>121</td>
</tr>
<tr>
<td>Greece</td>
<td>22</td>
<td>829</td>
<td>472</td>
</tr>
<tr>
<td>Hungary</td>
<td>14</td>
<td>446</td>
<td>526</td>
</tr>
<tr>
<td>Iceland</td>
<td>1</td>
<td>97</td>
<td>56</td>
</tr>
<tr>
<td>Ireland</td>
<td>15</td>
<td>1,086</td>
<td>961</td>
</tr>
<tr>
<td>Italy</td>
<td>3</td>
<td>237</td>
<td>166</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>4</td>
<td>176</td>
<td>80</td>
</tr>
<tr>
<td>Malta</td>
<td>1</td>
<td>104</td>
<td>96</td>
</tr>
<tr>
<td>Netherlands</td>
<td>4</td>
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<td>238</td>
</tr>
<tr>
<td>Norway</td>
<td>7</td>
<td>975</td>
<td>467</td>
</tr>
<tr>
<td>Portugal</td>
<td>8</td>
<td>559</td>
<td>574</td>
</tr>
<tr>
<td>Slovenia</td>
<td>9</td>
<td>572</td>
<td>321</td>
</tr>
<tr>
<td>Spain</td>
<td>19</td>
<td>1,973</td>
<td>835</td>
</tr>
<tr>
<td>Sweden</td>
<td>3</td>
<td>578</td>
<td>331</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>5</td>
<td>641</td>
<td>373</td>
</tr>
</tbody>
</table>

Combined resistance in *E. coli* (defined as resistance to two, three or four antimicrobial classes reported to EARS-Net) showed a significant increase (p<0.001) (Figure 3) whereas single resistance diminished from 37.1% in 2002 to 35.8% in 2009 (p<0.001). The proportion of *E. coli* isolates susceptible to all four antimicrobial classes decreased from 51.4% in 2002 to 41.7% in 2009 (p<0.001).

**Discussion**

The increase in antimicrobial resistance in *E. coli* between 2002 and 2009 was evident both in the observed increase of combined resistance and in the reduction of full susceptibility to the antimicrobials included in the analysis. In the same time period and considering the same data source, a significant decrease of meticillin resistance was observed for *S. aureus*. For this species, the number of BSIs increased less (+34%) than for *E. coli* BSI (+71%). Consistently, increasing resistance in *E. coli* and combined resistance of invasive and non-invasive isolates was reported by several European countries [4-8]. At the same time, the proportion of MRSA showed a significant decrease in many European countries [1,2]. The numbers of BSIs caused by MRSA, as reported by the mandatory surveillance system in England, decreased by 56% between 2004 and 2008 [9], and in France a significant decrease in the occurrence of MRSA was reported in 2008 [10]. A similar reduction in the rate of healthcare-associated invasive MRSA infections was observed in the general population in the United States [11].

The sampling approach selected for this study is likely to eliminate a large part of the possible temporal variation in the size of the catchment population behind the numbers. Based on the available surveillance data, it provides the best possible evidence of the increasing burden of disease caused by *E. coli* and *S. aureus* bacteraemia in the European Union. Nevertheless, if the population covered by the participating laboratories became larger during the study period, this may have contributed to the observed increase. Likewise, the sample approach includes laboratories without taking into account the size of the country, and therefore does not allow detailed analysis at national level. The disparity in the BSI trends for *E. coli* and *S. aureus* could partly be explained by ascertainment bias leading to higher reporting of *E. coli* infections. This could be caused by an increase of empirical treatment failures triggering delayed diagnostic procedures (blood culture). A similar upward trend in the number of reported cases of *E. coli* BSIs has been observed by
Resistance trends were monitored using interpretation schemes: susceptible, intermediate or resistant (SIR) [3], since the actual minimum inhibitory concentrations (MIC) were not systematically available from participating laboratories. Reporting MICs rather than SIR interpretations based on clinical breakpoints would improve the dynamic monitoring of subtle, incremental changes in antimicrobial susceptibility. Moreover, the interpretation using SIR categories reported to EARS-Net is based on breakpoints defined in the participating countries’ guidelines over time. Nevertheless, for the combinations of microorganisms and antimicrobials included in this study, the variation in the proportion of resistance caused by using different guidelines is very limited (unpublished data).

Conclusion
This is a serious concern since, if the increasing trend of antimicrobial resistance and the spread of ESBL are not contained, the use of carbapenems will increase favouring the emergence of carbapenemase-producing enterobacteria. This has been already observed for Klebsiella pneumoniae in Greece, Israel and Cyprus [1,2].

At the same time, S. aureus showed a relatively smaller increase in the number of reported BSIs, but a significant decrease in the proportion of MRSA overall in the countries participating in EARS/EARS-Net. This could be the result of public health efforts targeted at the containment of MRSA in several European countries.*

Although an overall decreasing trend for MRSA is evident in Europe, not all countries contribute to this result. Efforts to reduce the occurrence of MRSA should remain a priority irrespective of decreasing trends.

In this context, coordinated international surveillance is particularly important in order to obtain accurate knowledge of the occurrence and spread of antimicrobial resistance and to plan public health interventions.

* Authors’ correction: At the request of the authors, the following correction was made on 18 March 2011: the sentence ‘This could be the result of public health efforts targeted at the containment of MRSA in several European countries.’ was changed to ‘This could be the result of public health efforts targeted at the containment of MRSA in several European countries.’

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EARS-Net Participants (Disease Specific Contact Points for AMR):


References


