

Escherichia coli bacteraemias, England, Wales, and Northern Ireland: 2003

Key points:

- There was an increase in the number of reports of bacteraemias due to *Escherichia coli* in 2003 (16,431) compared to previous years.
- There was a 26% rise in *E. coli* bacteraemia reports made via the voluntary reporting scheme in England, Wales, and Northern Ireland in 2003 compared with reports in 2002. Some of this rise, however, will be due to improved laboratory reporting of isolates, ie, improved data ascertainment.
- Eighty-six per cent of laboratories in England, Wales, and Northern Ireland included susceptibility results to one or more antimicrobials in their reports.
- Of those *E. coli* reports with susceptibility data for amoxycillin/ampicillin more than half (56%) indicated resistance to these antimicrobials.
- Twelve per cent of *E. coli* isolates reported with susceptibility data for ciprofloxacin were resistant. This percentage was 10% for cefuroxime whereas less than 10% of isolates tested were resistant to cefotaxime, ceftazidime, or gentamicin.

This report covers bacteraemias due to *Escherichia coli* reported by laboratories in England, Wales, and Northern Ireland in 2003. All laboratory reports described here concern isolation of this species from blood culture. Rates are calculated using Office for National Statistics (ONS) 2002 mid-year resident population denominators for each corresponding age and region. Regional analyses were made with reference to the English regions introduced in April 2002.

Regional distributions

A total of 16,431 provisional laboratory reports of *Escherichia coli* bacteraemias were received for 2003 from

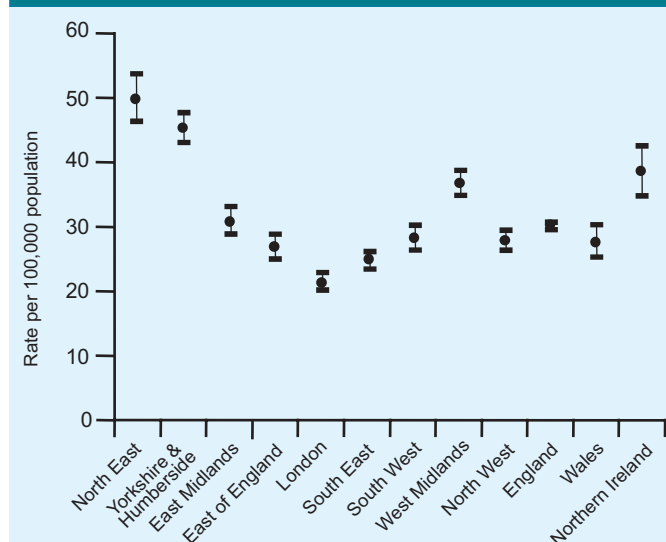
England, Wales, and Northern Ireland, a 26% increase on the equivalent data in 2002 (1). Eighty-six per cent of laboratories in England reported *E. coli* bacteraemias, compared with 79% of laboratories in Wales and 92% of labs in Northern Ireland (table 1). There was considerable regional variation in the reported rates of *E. coli* bacteraemias from England (figure 1): the highest reporting rate was from the North East region (50.1 per 100,000 population) and the highest number of reports was from Yorkshire and Humberside (2201), which had the next highest reporting rate (44.2/100,000). London and the South East had the lowest reporting rates, 21.05/100,000 and 25.1/100,000 respectively. England had an overall reporting rate of 30.2 *E. coli* bacteraemias per 100,000 population, while the rate in Wales was 28.2 per 100,000 population, and the rate was considerably higher in Northern Ireland at 39.1/100,000 population.

Table 1 Laboratory ascertainment data for *E. coli* bacteraemia reports England, Wales, and Northern Ireland: 2003

Region/ Country	Number of laboratories*	No. reporting <i>E. coli</i> bacteraemias	% reporting <i>E. coli</i> bacteraemias	% not reporting <i>E. coli</i> bacteraemias
North East	11	10	91	9
Yorkshire & Humberside	21	20	95	5
East Midlands	11	10	91	9
East of England	18	18	100	—
London	32	22	69	31
South East	29	24	83	17
South West	18	18	100	—
West Midlands	20	20	100	—
North West	31	23	74	26
England	191	165	86	14
Wales	14	11	79	21
Northern Ireland	12	11	92	8

*Provisional data (August 2004).

Figure 1 Region-specific rates* of bacteraemia due to *Escherichia coli*: England, Wales, and Northern Ireland: 2003



*Rates calculated using 2002 mid-year resident population estimates.

Antimicrobial resistance patterns

Eighty-six per cent of laboratories in England, Wales, and Northern Ireland reported susceptibility results for at least one antibiotic (table 2). Eighty-one per cent (13,365/16,431) of *E. coli* bacteraemia reports were accompanied by susceptibility results for one or more antibiotics, a moderate improvement on the percentage of reports with susceptibility information in 2002 (78%). The most commonly reported antimicrobial susceptibility was for gentamicin (12,477) followed by amoxicillin/ampicillin (12,170), ciprofloxacin (11,597), cefuroxime (11,085), ceftazidime (7806), and cefotaxime (4941).

More than half (56%) of *E. coli* reports with amoxicillin/ampicillin susceptibility data indicated resistance to this antibiotic. Resistance to cefuroxime was reported in 10% of reports with susceptibility information and resistance to ciprofloxacin reported in 13% of reports with susceptibility information. Resistance to cefotaxime was reported in 4% of reports, resistance to ceftazidime was reported in 4%, and resistance to gentamicin was reported in 6% of those *E. coli* bacteraemia reports that included susceptibility data for these antimicrobials (table 3).

The proportion of *E. coli* bacteraemia reports containing susceptibility information for ampicillin/amoxicillin varied considerably from 66% in Yorkshire and Humberside to 90% in the East of England region. There was a marked contrast between the proportion of reports with susceptibility results for ampicillin/amoxicillin from Wales (73%) and in Northern Ireland (42%). The percentage of reports with susceptibility data indicating resistance to ampicillin/amoxicillin ranged from 50% in East of England region to 62% in the North East. Fifty-three per cent of *E. coli* reports with susceptibility data were resistant in Wales, while 62% of such reports indicated ampicillin/amoxicillin resistance in Northern Ireland. *E. coli* reports that indicated sensitivity to amoxicillin/ampicillin (5312)

indicated little or no resistance to the other antibiotics listed (figure 2).

There was similar variability in the reporting of susceptibility results for the other antimicrobials reported here.

Reported resistance of *E. coli* bacteraemia isolates to cefuroxime ranged from 5% in Wales and Northern Ireland, and 6% in the North East, to 17% in the South East. The majority of cefuroxime resistant isolates indicated resistance to amoxicillin/ampicillin (82%), with lower proportions of resistance to cefotaxime (16%), ceftazidime (22%), ciprofloxacin (45%), and gentamicin (26%) (figure 3).

Forty-eight percent of *E. coli* reports sensitive to cefuroxime indicated resistance to amoxicillin/ampicillin.

Resistance to cefotaxime in *E. coli* bacteraemia isolates was reported infrequently, ranging from 2% in the East of England and Yorkshire and Humberside regions, 7% in the South East, and 8% in the West Midlands. Resistance to cefotaxime was reported for 2% of *E. coli* isolates reported from Wales and 3% of such reports from Northern Ireland. Resistance to ciprofloxacin and gentamicin was reported in 78% and 48% of cefotaxime-resistant *E. coli* isolates respectively (figure 4).

Resistance to ceftazidime in *E. coli* bacteraemia isolates was also reported infrequently, ranging from 2% in the North East and East of England regions to 7% in London, and 8% in the West Midlands. The reported resistance to ceftazidime of *E. coli* isolates was 1% in Wales and 4% in Northern Ireland. Resistance to ciprofloxacin was reported in 78% of ceftazidime-resistant *E. coli* isolates, while 48% of ceftazidime-resistant *E. coli* isolates were also gentamicin resistant (figure 5).

The percentage of ciprofloxacin resistance in *E. coli*

Table 2 Antimicrobial susceptibility ascertainment for laboratories reporting *E. coli* bacteraemias: England, Wales, and Northern Ireland: 2003

Region/Country	Laboratories reporting <i>E. coli</i> bacteraemias	Laboratories reporting any antimicrobial susceptibility information	(%)
North East	10	10	100
Yorkshire & Humberside	20	16	80
East Midlands	10	8	80
Eastern	18	18	100
London	22	17	77
South East	24	21	88
South West	18	18	100
West Midlands	20	18	90
North West	23	21	91
England	165	147	89
Wales	11	8	73
Northern Ireland	11	6	55

Table 3 Antibiotic susceptibilities for *E. coli* bacteraemia reports England, Wales, and Northern Ireland: 2003

	Sensitive	Resistant (%)*	No information (%)†
Amoxicillin/ampicillin	5312	6858 (56)	4261 (26)
Cefuroxime	9926	1159 (10)	5346 (33)
Cefotaxime	4729	212 (4)	11,490 (70)
Ceftazidime	7513	293 (4)	8625 (52)
Ciprofloxacin	10,149	1448 (12)	4834 (29)
Gentamicin	11,720	757 (6)	3954 (24)
Cefpodoxime	2	2 (50)	16,427 (100)

* As a per cent of reports with susceptibility information.

† As a per cent of total reports.

Figure 2 Ampicillin/amoxycillin susceptibility data for *E. coli* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

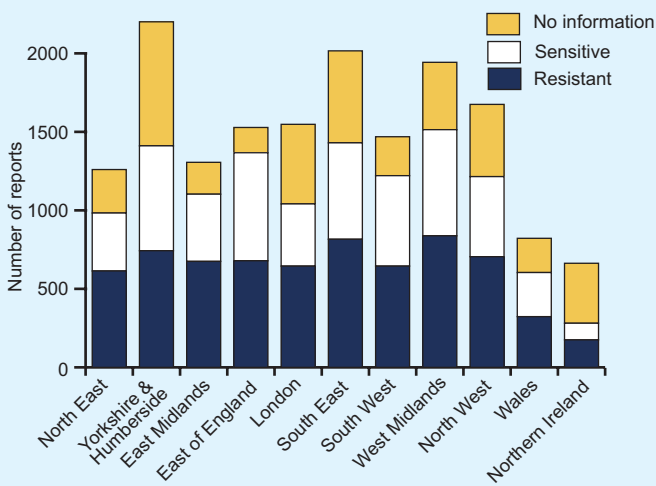


Figure 3 Cefuroxime susceptibility data for *E. coli* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

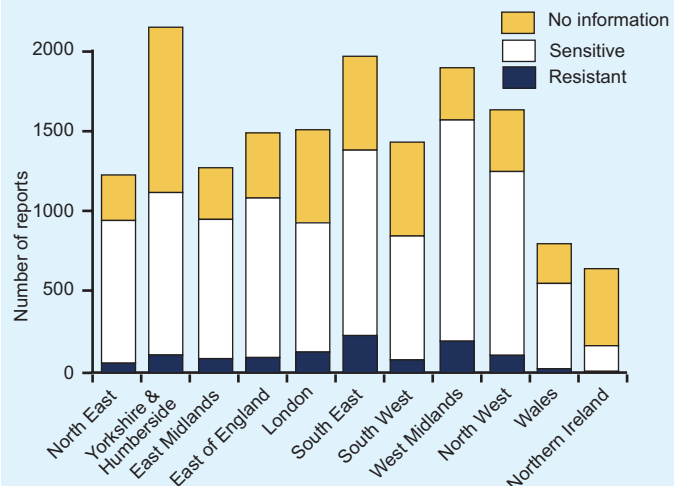


Figure 4 Cefotaxime susceptibility data for *E. coli* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

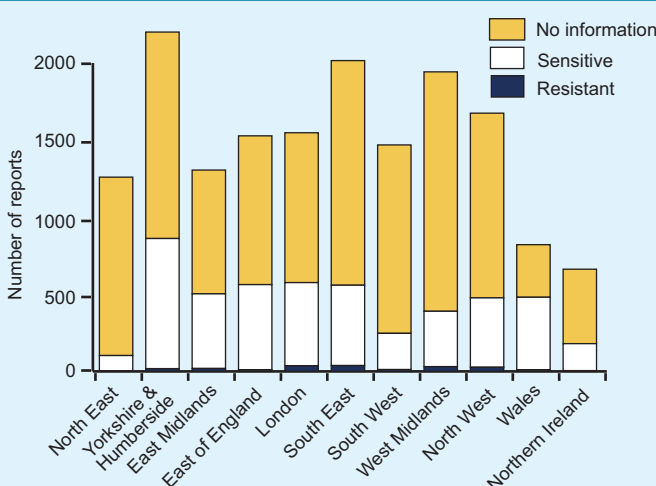


Figure 5 Ceftazidime susceptibility data for *E. coli* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

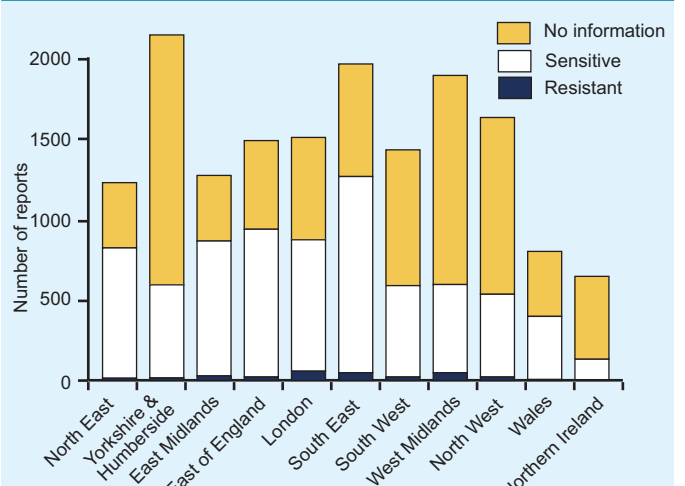


Figure 6 Ciprofloxacin susceptibility data for *E. coli* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

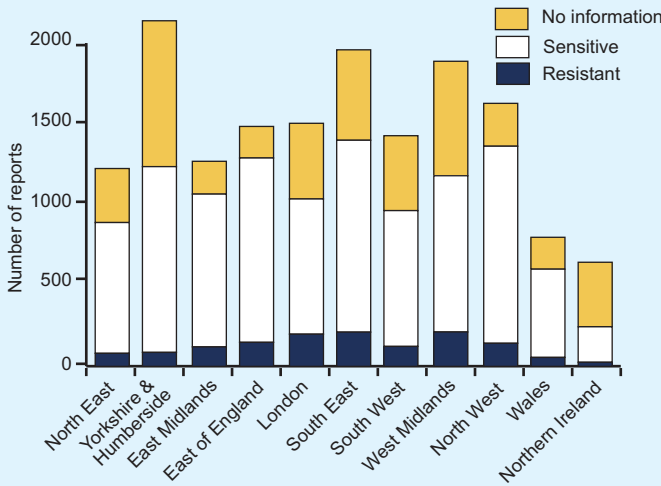
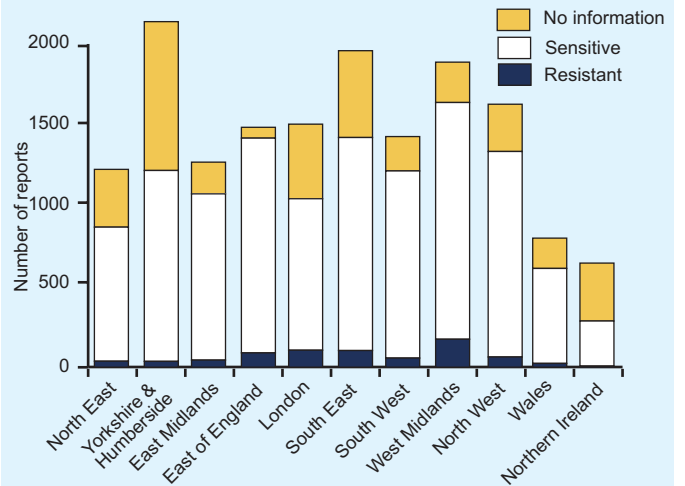


Figure 7 Gentamicin susceptibility data for *E. coli* reported from bacteraemias, England, Wales, and Northern Ireland: 2003



isolates ranged from 7% in Yorkshire and Humberside to 19% in London. Ciprofloxacin resistance was reported in 9% of isolates reported from Wales with susceptibility data and 10% of such isolates reported from Northern Ireland were resistant to ciprofloxacin. The majority of ciprofloxacin resistant *E. coli* isolates (83%) were resistant to amoxicillin/ampicillin, while fewer were resistant to cefuroxime (36%), cefotaxime (11%), ceftazidime (16%), and gentamicin (31%) (figure 6).

The majority of *E. coli* reports from England and Wales included data on gentamicin susceptibility. Northern Ireland, however, reported this information in just 44% of isolates. Reported gentamicin resistance in *E. coli* bacteraemia isolates ranged from 4% in the East Midlands and North East regions to 11% in the West Midlands. Gentamicin resistance was reported in 4% and 2% of *E. coli* bacteraemia reports from Wales and Northern Ireland respectively (figure 7).

Multiple resistance to amoxicillin/ampicillin, cefuroxime, ciprofloxacin, gentamicin, and either or both cefotaxime and ceftazidime was indicated in 59 *E. coli* bacteraemia reports in 2003.

Discussion

Escherichia coli has ranked second only to *Staphylococcus aureus* as the leading cause of bacteraemia in England and Wales in both 2002 and 2003. Of the Gram-negative bacteria, *E. coli* is consistently the most common cause of bacteraemia in England, Wales, and Northern Ireland (2,3).

The number of *E. coli* bacteraemia reports appeared to have stabilised between 11,000 and 12,000 between 1999 and 2001 period (4). This was followed, however, by an increase to more than 12,500 *E. coli* bacteraemia reports in 2002 for England and Wales (13,050 if Northern Ireland is included) (1). Here we report a further increase in *E. coli* bacteraemia reports to 15,768 for England and Wales in 2003 (16,431 including Northern Ireland). This represents an increase of 41% in *E. coli* reports from England and Wales between 1999 and 2003. These data, however, must be interpreted cautiously, as reports of *E. coli* bacteraemias continue to be reported some time after the year-end and the final numbers of reports for both 2002 and 2003 may increase. For example, up until February 2003, 13,050 *E. coli* reports had been made via the voluntary surveillance scheme, but by August 2004, this figure had risen to 14,043, an increase of 7%. Hence, if the provisional number of reports from 2003 are compared with those reported for 2002, there is a 26% increase, but when the 2003 numbers are compared to the latest figures this increase is 17%. In 2003, *E. coli* bacteraemia reports were received from an additional ten laboratories compared to 2002. It is, therefore, difficult to quantify any rise in bacteraemia reports and differentiate this from the contribution of improved data ascertainment.

Reporting information on antimicrobial susceptibilities improved considerably for *E. coli* bacteraemias, from 68% (7796/11,392) in 2001 to 78% in 2002, and 81% in 2003. Resistance to amoxicillin/ampicillin and cefuroxime has remained relatively unchanged since 2001, although 2003 has seen a 2%

increase in cefuroxime resistance between 2002 and 2003 (3, 4). There was an increase in reported resistance of *E. coli* bacteraemia isolates to cefotaxime/ceftazidime (from 2% to 3%) between 2001 and 2002. In 2003, where these antimicrobial resistances have been analysed separately, cefotaxime resistance and ceftazidime resistance have reached 4%. When analysed together, 3% of *E. coli* isolates reported with susceptibility results for cefotaxime/ceftazidime were resistant.

In the period between 2001 and 2003, ciprofloxacin resistance has risen from 6% to 12% and gentamicin resistance from 3% to 6%. The upward trend in ciprofloxacin resistance (from 0.8% in 1990, 3.7% in 1999 (5), 6% in 2001 (4), 8% in 2002 (1), and to 12% in 2003) is striking. These data are in keeping with the disturbing year-on-year rise in ciprofloxacin resistance, reported in late 2003 (6).

Members of the Enterobacteriaceae genus, including *Klebsiella* spp. and *E. coli* are increasingly found to produce extended spectrum beta-lactamases (ESBLs). These enzymes render bacteria resistant to most beta-lactam antibiotics, sparing only the carbapenems and cephamycins.

Recently, outbreaks of *E. coli* producing CTX-M ESBLs have been found in a number of regions in England where some of these infections have resulted in bacteraemias. At present, it is unclear whether these infections are hospital- or community-acquired. Questionnaires were sent to regional leads/regional epidemiologists to establish the extent of investigations and any data ascertainment issues.

Investigations are still ongoing, but an interim analysis of voluntary bacteraemia reports from 2001-2003, using resistance to both ceftazidime and cefotaxime as a crude marker, has identified a further three regions which may have evidence of CTX-M ESBL *E. coli* bacteraemias. It must be noted, however, that the use of these resistances as a marker for ESBL-producing *E. coli* bacteraemias is crude and more detailed investigations will be required at the regional level. Indeed, further investigation of the microbiology and epidemiology of ESBLs is underway in the South East and London regions.

Under laboratory conditions, CTX-M ESBLs confer a clearer resistance to cefotaxime (the best indicator for CTX-M type ESBLs) than to ceftazidime (the best indicator for SHV and TEM ESBLs) and it is strongly advised that all enterobacteriaceae isolates should be screened with both of these antimicrobials, or with cefpodoxime. Isolates resistant to any of these agents should be further investigated for ESBLs using one of the detection methods described in the recent guidance to diagnostic laboratories compiled by the Health Protection Agency's Antibiotic Resistance and Monitoring and Reference Laboratory, available at http://hpa.org.uk/srmd/div/nsi/armrl/ESBL_advice_June_2004.pdf.

Some of the strains identified in the outbreaks mentioned above are also resistant to trimethoprim, fluoroquinolones, and aminoglycosides and some of the more serious infections may require treatment with an intravenous carbapenem (7-9).

Differences in the reporting of antimicrobial

susceptibilities between regions may account for the variation in resistance seen. It is not possible to confirm whether the increases seen in bacteraemias rates due to the species reported here or the increases in antimicrobial resistance are due to enhanced ascertainment of data (reporting of cases), or whether they reflect a real increase in the number of bacteraemias and a real increase in the levels of antimicrobial resistance. Similarly, it is not possible to determine the cause of variation in levels of reported antimicrobial resistance between regions. Indeed, the data reported here are considered provisional as the HPA's Communicable Disease Surveillance Centre continues to receive 2003 bacteraemia reports from regions.

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