

***Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp bacteraemia, England, Wales, and Northern Ireland: 2003**

Key points:

- In 2003 there were 8369 laboratory reports of bacteraemias due to *Klebsiella* (4389), *Enterobacter* (2354), *Serratia* (992), and *Citrobacter* (634) spp.
- There has been an increase in the number of reports on 2002 for each genera; *Klebsiella* (19%), *Enterobacter* (18%), *Serratia* (26%), and *Citrobacter* (26%). Whether these increases are due to increased prevalence or ascertainment is under investigation.
- Information on antibiotic susceptibility was not provided in approximately two thirds of reports for cefotaxime, half of reports for ceftazidime and carbapenems, and one third of reports for gentamicin and ciprofloxacin.
- There appears to be no significant increases in levels of antimicrobial resistance discernable from the information available.

Introduction

This report contains data from *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp bacteraemia reports made in 2003, with brief comparative details on the two 2002 and 2001 data for the less common Enterobacteriaceae. These data are derived from routine laboratory reports submitted voluntarily to the Health Protection Agency's Communicable Disease Surveillance Centre (CDSC) via regional offices indicating isolations of these bacterial species from blood specimens. Analysis of ascertainment of reports from each region has been undertaken. Rates were calculated using 2002 mid-year population denominators, and according to the geographical boundaries introduced in April 2002. The data on bacteraemias attributed to other members of the Enterobacteriaceae family have been published in a previous issue of the *CDR Weekly* (1).

Reports of *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp

In 2003 there were 8369 reports of bacteraemias due to *Klebsiella*, *Enterobacter*, *Serratia*, or *Citrobacter* spp, of which 4389 reports were due to *Klebsiella* spp (table 1). The majority of bacteraemias due to Klebsiellae were attributed to *Klebsiella pneumoniae* (66%; 2915/4389) (table 1). *Klebsiella oxytoca* was the next most common species within this genus, accounting for 20% (881/4389) and 460 Klebsiellae (10%) were not speciated.

There were 2354 reports of *Enterobacter* spp and 992 reports of *Serratia* spp. Seventy-five per cent of reports of bacteraemia due to *Enterobacter* spp were attributed to *E. cloacae* followed by *E. aerogenes* (9%) and *E. sakazakii* (3%), while 13% were not speciated. The two most common *Serratia* species were *S. marcescens* (67%) and *S. liquefaciens* (13%), while 175 reports (18%) of *Serratia* isolates were not speciated.

There were 634 bacteraemia reports of *Citrobacter* spp. Over half (56%) of these reports were attributed to *C. freundii* followed by *C. koseri (diversus)* with 24%. One hundred and twenty-five reports (20%) of *Citrobacter* isolates were not speciated. Of the 171 reports of species closely related to the four main genera, 110 reports were attributed to *Pantoea* spp, 34 were attributed to *Hafnia* spp, and 22 were attributed to *Kluyvera* spp. There were two reports of both *Edwardsiella* spp and *Leclercia adecarboxylata* and one report of *Rahnella* spp.

The rate of *Klebsiella* spp bacteraemia reporting in England, Wales, and Northern Ireland was 8.1 per 100,000 population. Regional offices in England accounted for the majority of these reports (4009) followed by Wales (214), and Northern Ireland (166). Within the English regions, rates varied from 6.25 per 100,000 population in the South East to 13.33 per 100,000 in the North East (table 2).

The rate of *Enterobacter* spp bacteraemia reporting in England, Wales, and Northern Ireland was 4.35/100,000. Regional offices in England received the majority of these reports (2160) followed by Wales, (116) and Northern Ireland (78). Within the English regions, rates varied from 3.41/100,000 in the North West to 7.36/100,000 in the North East (table 2).

Rates of *Serratia* spp bacteraemia were substantially higher in Northern Ireland compared with other regions (5.07/100,000; 86 reports), the North East of England (5.01/100,000; 126 reports), and Wales (3.32/100,000; 97 reports). The average rate in England was 1.63/100,000, with rates for all regions except the North East varying between 0.98/100,000 and 1.96/100,000.

The rate of *Citrobacter* spp bacteraemia in England, Wales, and Northern Ireland was (1.17/100,000). Reports submitted to regional offices in England accounted for the majority of these reports (572)

Table 1 Laboratory reports of *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp and related species bacteraemia, England, Wales, and Northern Ireland: 2001 to 2003

	2001	2002	2003
<i>Klebsiella pneumoniae</i>	2116	2418	2915
<i>Klebsiella oxytoca</i>	667	753	881
<i>Klebsiella terrigena</i>	41	53	80
<i>Klebsiella ornithinolytica</i>	18	26	34
<i>Klebsiella ozenae</i>	8	12	16
<i>Klebsiella planticola</i>	–	–	2
<i>Klebsiella edwardsii</i>	–	–	1
<i>Klebsiella rhinoscleromatis</i>	–	2	–
<i>Klebsiella</i> spp total*	3219	3695	4389
<i>Enterobacter cloacae</i>	1207	1438	1762
<i>Enterobacter aerogenes</i>	187	224	210
<i>Enterobacter sakazakii</i>	53	53	67
<i>Enterobacter amnigenus</i>	3	9	8
<i>Enterobacter intermedium</i>	3	4	3
<i>Enterobacter gergoviae</i>	2	7	1
<i>Enterobacter asburiae</i>	3	–	–
<i>Enterobacter</i> spp total*	1736	1998	2354
<i>Serratia marcescens</i>	414	526	669
<i>Serratia liquefaciens</i>	96	112	128
<i>Serratia fonticola</i>	2	9	8
<i>Serratia odorifera</i>	5	8	7
<i>Serratia ficaria</i>	1	2	2
<i>Serratia plymuthica</i>	7	4	1
<i>Serratia proteamaculans</i>	2	1	1
<i>Serratia rubidaea</i>	2	4	1
<i>Serratia</i> spp total*	643	786	992
<i>Citrobacter freundii</i>	242	261	357
<i>Citrobacter koseri</i> (diversus)	104	135	150
<i>Citrobacter amalonaticus</i>	4	4	2
<i>Citrobacter braakii</i>	3	–	–
<i>Citrobacter youngae</i>	1	–	–
<i>Citrobacter</i> spp total*	456	505	634
<i>Pantoea agglomerans</i> (<i>Erwinia herbicola</i>)	46	31	19
<i>Pantoea</i> spp total*	74	93	110
<i>Hafnia alvei</i>	40	19	32
<i>Hafnia</i> spp total*	42	19	34
<i>Kluyvera</i> spp	20	21	22
<i>Edwardsiella</i> spp	1	–	2
<i>Leclercia adecarboxylata</i>	1	1	2
<i>Rahnella</i> spp	3	7	1
Grand Total	6195	7125	8540

*Includes unspiciated reports.

followed by Wales (36), and Northern Ireland (26). Within the English regions, rates varied from 0.67/100,000 in the North West to 1.89/100,000 in Yorkshire and Humberside (table 2).

The number of laboratories reporting in each region (table 3) should be taken into account when analyses of these reporting rates are undertaken. The increases in total numbers of reports between 2001 and 2003 (table

1) are being investigated in light of the ascertainment increases seen over a 14 year period (figure 1).

Age distributions

For all four genera the general distribution of reports was highest in the very young and the elderly. Reporting rates in the over 75 years age group were more than double in males than in females. Gender differences were more marked in the elderly age groups compared to the under one year age group (figure 2).

Antibiotic susceptibility

For all four genera, reviewed, gentamicin and ciprofloxacin susceptibility information was not provided in approximately one third of all reports. Ceftazidime and carbapenem susceptibility information was not provided in approximately half of reports and cefotaxime and piperacillin/tazobactam susceptibility information was not provided in 57% to 69% of reports depending on antibiotic and genera (table 4). The number of reports including susceptibility information in 2003 improved marginally on 2002, although an investigation is underway to determine whether this is a true increase or due to ascertainment.

Among *Klebsiella* spp bacteraemias, the most commonly reported resistance was to piperacillin/tazobactam (13%, of reports that included susceptibility information for that antibiotic), however, it has been reported that routine disc tests overestimate resistance to this drug in the Enterobacteriaceae (2,3). Rates of resistance to ciprofloxacin, ceftazidime, cefotaxime, and gentamicin were 12%, 11%, 11%, and 9% respectively (table 4). Six *Klebsiella* spp isolates were reported as showing resistance to imipenem and/or meropenem, although these unusual resistance reports remain unconfirmed and are under investigation. Out of the 1044 reports containing susceptibility information on ceftazidime and cefotaxime, 114 isolates (11%) were resistant to both.

Resistance to either ceftazidime or cefotaxime was indicated in over a third (39% and 36% respectively) of the *Enterobacter* spp bacteraemia reports including susceptibility information for those antibiotics. This is unsurprising as *Enterobacter* spp are prone to derepression of their chromosomal AmpC beta-lactamase genes (*ie*, hyper-production of AmpC beta-lactamases), which results in cephalosporin resistance. Piperacillin/tazobactam resistance was indicated in 22% of reports followed by resistance to ciprofloxacin (17%) and gentamicin (13%) (table 4). Imipenem and/or meropenem resistance was reported in 14 isolates, although these remain unconfirmed. Out of the 578 reports containing susceptibility information on ceftazidime and cefotaxime, 184 isolates (32%) were resistant to both.

Resistance to ciprofloxacin was indicated in 30% of *Serratia* spp reports containing ciprofloxacin susceptibility information. Rates of resistance to cefotaxime, piperacillin/tazobactam, ceftazidime, and

Table 2 *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp bacteraemia laboratory reports and rates* (per 100,000 population): England, Wales and Northern Ireland: 2003

	<i>Klebsiella</i> spp			<i>Enterobacter</i> spp			<i>Serratia</i> spp			<i>Citrobacter</i> spp		
	Reports	Rate	95% CI†	Reports	Rate	95% CI†	Reports	Rate	95% CI†	Reports	Rate	95% CI†
North East	335	13.33	(11.9-14.8)	185	7.36	(6.3-8.5)	126	5.01	(4.1-6)	35	1.39	(1-1.9)
Yorkshire & Humberside	595	11.94	(11-12.9)	326	6.54	(5.8-7.3)	79	1.59	(1.3-2)	94	1.89	(1.5-2.3)
East Midlands	313	7.42	(6.6-8.3)	179	4.25	(3.6-4.9)	55	1.30	(1-1.7)	42	1.00	(0.7-1.3)
Eastern	379	6.99	(6.3-7.7)	196	3.62	(3.1-4.2)	59	1.09	(0.8-1.4)	71	1.31	(1-1.7)
London	567	7.71	(7.1-8.4)	356	4.84	(4.3-5.4)	95	1.29	(1-1.6)	76	1.03	(0.8-1.3)
South East	502	6.25	(5.7-6.8)	223	2.77	(2.4-3.2)	79	0.98	(0.8-1.2)	66	0.82	(0.6-1)
South West	323	6.51	(5.8-7.3)	170	3.43	(2.9-4)	80	1.61	(1.3-2)	55	1.11	(0.8-1.4)
West Midlands	540	10.18	(9.3-11.1)	295	5.56	(4.9-6.2)	104	1.96	(1.6-2.4)	88	1.66	(1.3-2)
North West	455	6.74	(6.1-7.4)	230	3.41	(3-3.9)	132	1.96	(1.6-2.3)	45	0.67	(0.5-0.9)
England	4009	8.0	(7.8-8.3)	2160	4.36	(4.2-4.5)	809	1.63	(1.5-1.7)	572	1.15	(1.1-1.3)
Wales	214	7.33	(6.3-8.4)	116	3.97	(3.3-4.8)	97	3.32	(2.7-4.1)	36	1.23	(0.9-1.7)
Northern Ireland	166	9.78	(8.3-11.4)	78	4.60	(3.6-5.7)	86	5.07	(4.1-6.3)	26	1.53	(1-2.2)
England, Wales, and Northern Ireland	4389	8.10	(7.9-8.3)	2354	4.35	(4.2-4.5)	992	1.83	(1.7-1.9)	634	1.17	(1.1-1.3)

*Rates were calculated using mid-year 2002 resident population estimates for England, Wales and Northern Ireland. Regional analyses were performed using the English regional boundaries introduced in 2002. †CI= Confidence interval.

Table 3 Ascertainment: laboratories reporting *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp bacteraemias as a percentage of total laboratories: 2003

	Number of laboratories	<i>Klebsiella</i> spp	<i>Enterobacter</i>	<i>Serratia</i> spp	<i>Citrobacter</i> spp
North East	12	12 (100%)	11 (92%)	11 (92%)	8 (67%)
Yorkshire & Humberside	22	21 (95%)	19 (86%)	17 (77%)	16 (73%)
East Midlands	11	10 (91%)	10 (91%)	10 (91%)	8 (73%)
Eastern	18	18 (100%)	18 (100%)	15 (83%)	17 (94%)
London	36	22 (61%)	21 (58%)	18 (50%)	20 (56%)
South East	33	23 (70%)	22 (67%)	22 (67%)	20 (61%)
South West	18	18 (100%)	18 (100%)	17 (94%)	15 (83%)
West Midlands	20	20 (100%)	20 (100%)	17 (85%)	16 (80%)
North West	31	23 (74%)	21 (68%)	19 (61%)	15 (48%)
England	201	167 (83%)	160 (80%)	146 (73%)	135 (67%)
Wales	15	12 (80%)	12 (80%)	10 (67%)	11 (73%)
Northern Ireland	14	11 (79%)	12 (86%)	10 (71%)	10 (71%)

*provisional data

Figure 1 Comparison of annual reports of *Klebsiella* spp, *Enterobacter* spp, *Serratia* spp, and *Citrobacter* spp. 1990-2003

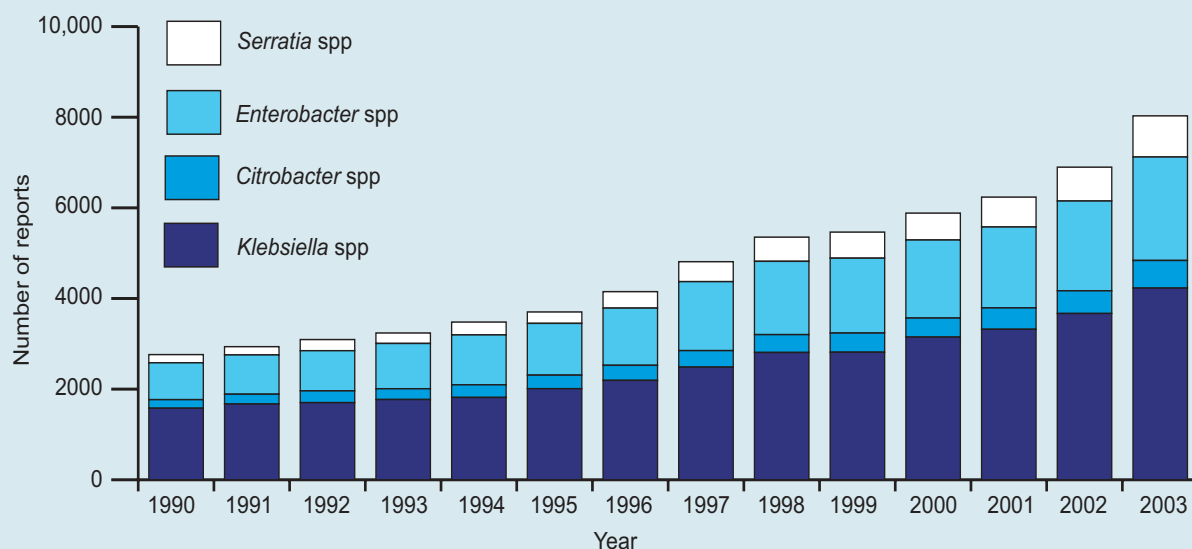


Table 4 Antibiotic susceptibility data for *Klebsiella, Enterobacter, Serratia, and Citrobacter* spp bacteraemia reports: England, Wales, and Northern Ireland:: 2001-2003*

	2001			2002			2003		
	Number with susceptibility data	Resistant (%)†	No Information (%‡)	Number with susceptibility data	Resistant (%)†	No Information (%‡)	Number with susceptibility data	Resistant (%)†	No Information (%‡)
<i>Klebsiella</i> spp									
gentamicin	2051	93 (5)	1168 (36)	2567	176 (7)	1128 (31)	3155	279 (9)	1234 (28)
ciprofloxacin	1872	164 (9)	1347 (42)	2319	248 (11)	1376 (37)	2937	341 (12)	1452 (33)
ceftazidime	1345	106 (8)	1874 (58)	1692	174 (10)	2003 (54)	2036	234 (11)	2353 (54)
cefotaxime	971	58 (6)	2248 (70)	1004	77 (8)	2691 (73)	1385	157 (11)	3004 (68)
carbapenem§	1060	3 (0.3)	2159 (67)	1581	6 (0.4)	2114 (57)	1986	6 (0.3)	2403 (55)
piperacillin/tazobactam	–	–	–	–	–	–	1759	226 (13)	2630 (60)
<i>Enterobacter</i> spp									
gentamicin	1125	104 (9)	611 (35)	1387	147 (11)	611 (31)	1704	224 (13)	650 (28)
ciprofloxacin	1028	153 (15)	708 (41)	1228	175 (14)	770 (39)	1580	266 (17)	774 (33)
ceftazidime	787	254 (32)	949 (55)	960	329 (34)	1038 (52)	1203	471 (39)	1151 (49)
cefotaxime	574	186 (32)	1162 (67)	555	186 (34)	1443 (72)	775	281 (36)	1579 (67)
carbapenem§	644	11 (2)	1092 (63)	951	12 (1)	1047 (52)	1247	14 (1)	1107 (47)
piperacillin/tazobactam	–	–	–	–	–	–	972	211 (22)	1382 (59)
<i>Serratia</i> spp									
gentamicin	413	11 (3)	230 (36)	541	19 (4)	245 (31)	697	24 (3)	295 (30)
ciprofloxacin	384	104 (27)	259 (40)	484	117 (24)	302 (38)	663	196 (30)	329 (33)
ceftazidime	282	11 (4)	361 (56)	382	33 (9)	404 (51)	495	70 (14)	497 (50)
cefotaxime	221	44 (20)	422 (66)	202	54 (27)	584 (74)	307	87 (28)	685 (69)
carbapenem§	262	1 (0.4)	381 (59)	344	2 (1)	442 (56)	484	2 (0.4)	508 (51)
piperacillin/tazobactam	–	–	–	–	–	–	427	99 (23)	565 (57)
<i>Citrobacter</i> spp									
gentamicin	288	9 (3)	168 (37)	356	13 (4)	149 (30)	464	31 (7)	170 (27)
ciprofloxacin	270	21 (8)	186 (41)	326	27 (8)	179 (35)	408	42 (10)	226 (36)
ceftazidime	204	33 (16)	252 (55)	232	42 (18)	273 (54)	297	59 (20)	337 (53)
cefotaxime	141	23 (16)	315 (69)	145	30 (21)	360 (71)	199	36 (18)	435 (69)
carbapenem§	168	1 (1)	288 (63)	212	1 (0.5)	293 (58)	297	– (–)	337 (53)
piperacillin/tazobactam	–	–	–	–	–	–	230	31 (13)	404 (64)

*Provisional data. †Calculated as a proportion of isolates with susceptibility data provided. ‡ Calculated as a percentage of total reports. §Imipenem and/or meropenem.

gentamicin were 28%, 23%, 14%, and 3% respectively (table 4). Two isolates were reported as resistant to imipenem and/or meropenem although these remain unconfirmed.

Among *Citrobacter* spp bacteraemias, the most commonly reported resistances were to ceftazidime (20%) and cefotaxime (18%). As with *Enterobacter* spp, *C. freundii* are prone to AmpC derepression; all cephalosporin resistance noted here was reported in *C. freundii*. Rates of resistance to piperacillin/tazobactam, ciprofloxacin, and gentamicin were 13%, 10%, and 7% respectively (table 4). No isolates were reported as being resistant to imipenem or meropenem.

The ascertainment of antimicrobial susceptibility data is shown in table 5.

Discussion

An increase in the number of reports of the genera presented here was noted in 2002 and this trend would

appear to have continued (4); *Klebsiella* spp increased by 19%, *Enterobacter* spp by 18%, *Serratia* spp by 26%, and *Citrobacter* spp by 26%. The proportion of this increase due to increased ascertainment is under investigation

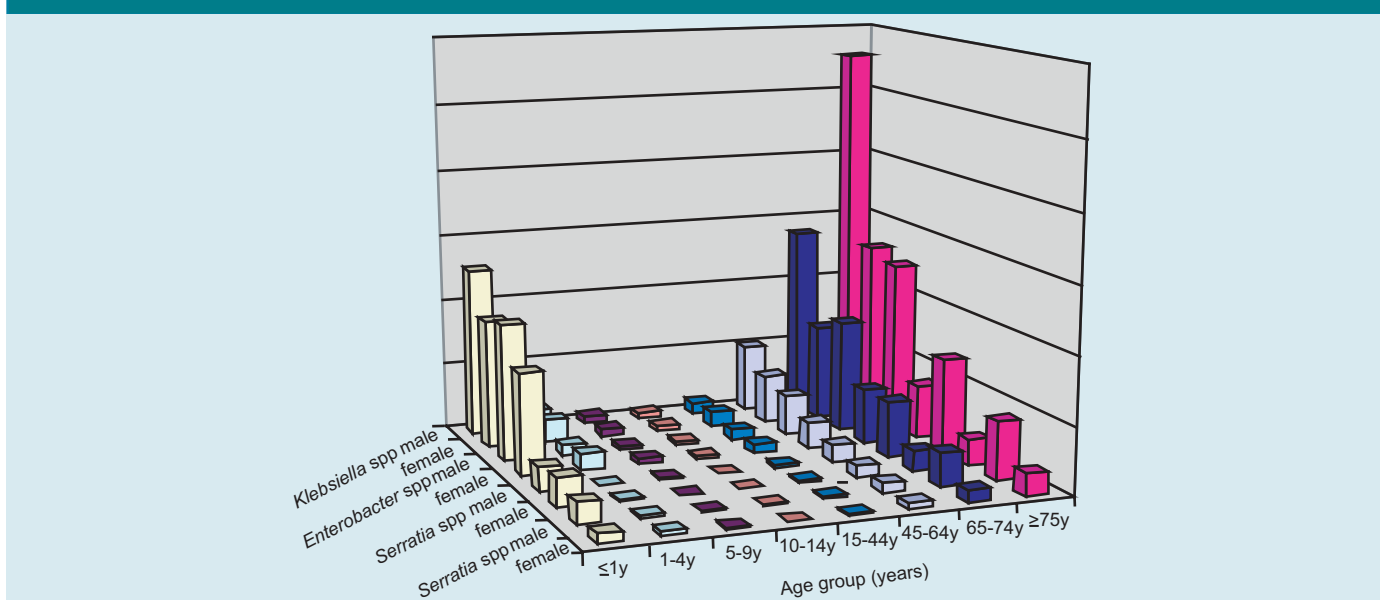
The highest reporting rate for all four genera was in Northern Ireland followed by England in the *Klebsiella* and *Enterobacter* spp, and Wales in the *Serratia* and *Citrobacter* spp bacteraemias. Of the English regions, the North East had the highest rate for *Klebsiella, Enterobacter, and Serratia* spp bacteraemias. These results should be interpreted in light of the data in table 3, which demonstrates considerable variation in data ascertainment. An investigation is underway to determine levels of ascertainment in each region and this will aid further interpretation of the reported rates of bacteraemias associated with these organisms.

Age-specific rates of the four genera increased between 2002 and 2003, although the age group and sex breakdowns were similar. Rates were much higher

Table 5 Ascertainment: laboratories submitting antimicrobial susceptibility information as a percentage of laboratories reporting *Klebsiella, Enterobacter, Serratia, and Citrobacter* spp bacteraemias: 2003

	<i>Klebsiella</i> spp	<i>Enterobacter</i>	<i>Serratia</i> spp	<i>Citrobacter</i> spp
North East	10/12 (83%)	10/11 (91%)	10/11 (91%)	8/8 (100%)
Yorkshire & Humberside	16/21 (76%)	14/19 (74%)	13/17 (76%)	13/16 (81%)
East Midlands	7/10 (70%)	7/10 (70%)	7/10 (70%)	6/8 (75%)
Eastern	18/18 (100%)	18/18 (100%)	16/16 (100%)	18/18 (100%)
London	19/22 (86%)	18/21 (86%)	14/18 (78%)	15/20 (75%)
South East	19/23 (83%)	18/22 (82%)	16/22 (73%)	16/20 (80%)
South West	14/18 (78%)	13/18 (72%)	9/17 (53%)	9/15 (60%)
West Midlands	18/20 (90%)	16/20 (80%)	13/17 (76%)	12/16 (75%)
North West	20/23 (87%)	18/21 (86%)	14/19 (74%)	13/15 (87%)
England	142/170 (84%)	133/162 (82%)	112/148 (76%)	110/136 (81%)
Wales	9/12 (75%)	8/12 (67%)	7/10 (70%)	5/11 (45%)
Northern Ireland	4/11 (36%)	4/12 (33%)	5/10 (50%)	5/10 (50%)

Figure 2 Age-specific rates* of *Klebsiella, Enterobacter, Serratia, and Citrobacter* spp bacteraemia reports: England, Wales, and Northern Ireland: 2003



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

in males compared to females, and in those aged over 65 years and aged under 1 year.

The ascertainment of antimicrobial susceptibility information (table 5) should be taken into account when considering resistance rates for each antibiotic. Some laboratories reporting *Klebsiella, Enterobacter, Serratia, or Citrobacter* spp isolates provide no information on antibiotic susceptibilities. Nevertheless, with the exception of piperacillin/tazobactam, the rates of resistance found here are in good agreement with those from susceptibility testing under the ambit of the British Society for Antimicrobial Chemotherapy (BSAC) Bacteraemia Resistance Surveillance Programme (5,6). More meaningful interpretations would be possible with an increase in ascertainment of susceptibility data.

Please submit any isolates of these genera found to be resistant to carbapenems including ertapenem as well as imipenem and meropenem, to the Health Protection Agency's Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL), Colindale, London.

Acknowledgements

These reports would not be possible without the enduring weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland. This is your data, so please tell us what you would like done with it. We are always pleased to hear your views. Please send your comments/feedback to Andrew Pearson <andrew.pearson@hpa.org.uk> or Allison Lee <allison.lee@hpa.org.uk>. In addition, the support from colleagues within the Health Protection Agency's Specialist and Reference Microbiology Division and Local and Regional Services is valued in the preparation of the reports.

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