

***Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp. bacteraemia, England, Wales, and Northern Ireland: 2003-2007**

These analyses are based on data extracted from our voluntary surveillance database on the 14th April 2008 for the period 2003-2007. The data presented here differs in some instances from data in earlier publications due to the addition of late reports to the database.

Trend in total reports:

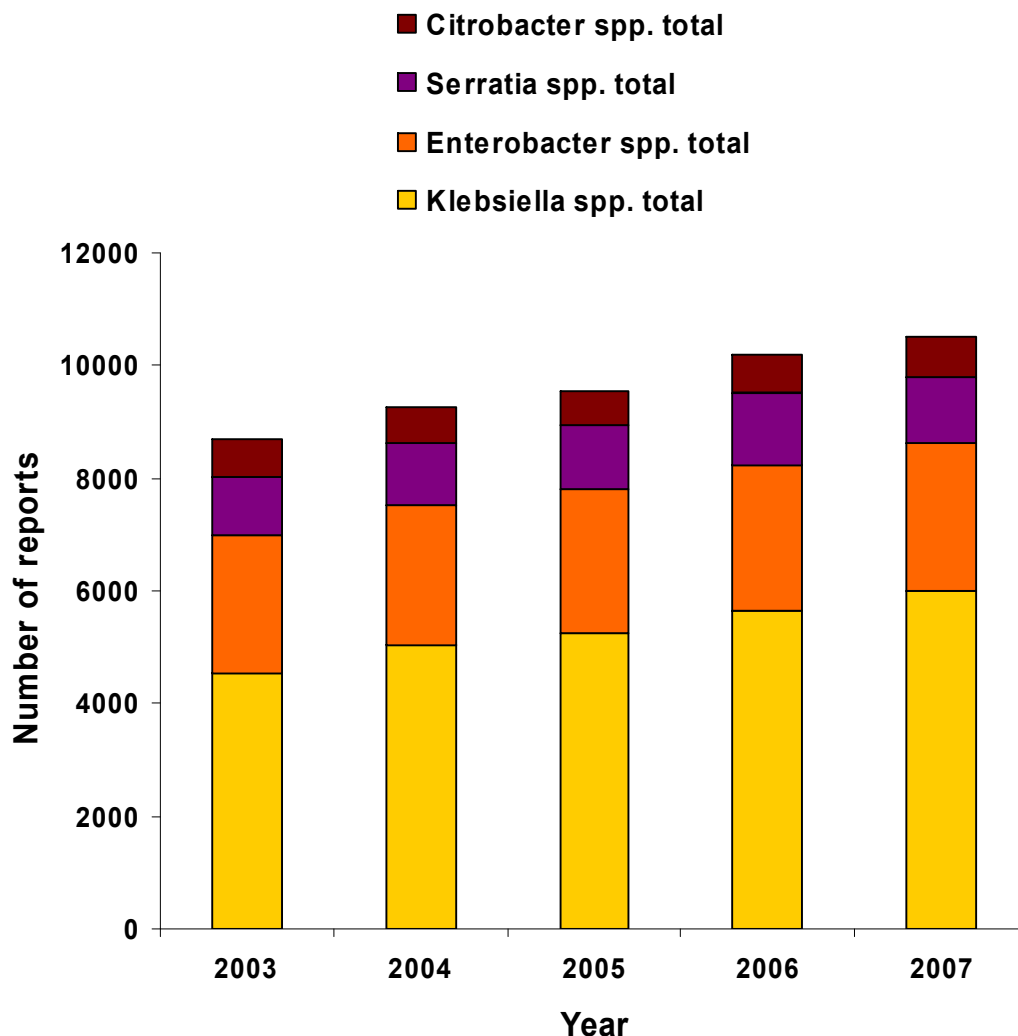
There was a 3.3% increase in the total reports of *Klebsiella* spp, *Enterobacter* spp., *Serratia* spp., and *Citrobacter* spp. bacteraemia reported via the voluntary surveillance scheme in 2007 (10,518 reports), compared to 2006 (10,185 reports) (figure 1). Overall, from 2003 there has been a 21% increase in reports, an increase which is comparable to the 24% increase in reports for all bacteraemia (85,354 to 105,928) via the voluntary surveillance scheme during the same time period (provisional as of 8/Jan/2008). The increases may be due to either increased incidence and/or increased ascertainment. Reports for 2007 are provisional as of 14 April and are expected to increase due to late reporting.

Table 1 *Klebsiella* , *Enterobacter* , *Serratia* , and *Citrobacter* spp. bacteraemia reports 2003-2007*

	2003	2004	2005	2006	2007
Number of reporting laboratories	197	197	195	197	188
Laboratories identifying to species level	100%	100%	99%	99%	99%
Laboratories reporting susceptibility data	83%	83%	89%	91%	93%
Laboratories identifying to species level and reporting susceptibility data	83%	83%	89%	91%	92%

* Data extracted 14th April, 2008

Figure 1 *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp. bacteraemia reports 2003-2007*



* Data extracted 14th April, 2008

Species-specific data

Table 2 gives a breakdown of numbers of reports by species in 2007:

- The majority of bacteraemias due to *Klebsiella* spp. were attributed to *K. pneumonia* (66%), and *K. oxytoca* (21%), 6% were not identified to species level.
- The majority of bacteraemias due to *Enterobacter* spp. were attributed to *E. cloacae* (77%) and *E. aerogenes* (12%), 7% were not identified to species level.
- The majority of bacteraemias due to *Serratia* spp. were attributed to *S. marcescens* (74%) and *S. liquefaciens* (13%), 10% were not identified to species level.
- The majority of bacteraemias due to *Citrobacter* spp. were attributed to *C. freundii* (51%) and *C. koseri (diversus)* (31%), 13% were not identified to species level.

211 reports were attributed to species closely related to the four main genera (*Pantoea*, *Hafnia*, *Kluyvera*, *Edwardsiella*, and *Rahnella* spp.).

Table 2 Laboratory bacteraemia reports of *Klebsiella*, *Enterobacter*, *Serratia*, *Citrobacter* spp. & related species, England, Wales, & Northern Ireland: 2003-2007*

	2003	2004	2005	2006	2007
<i>Klebsiella pneumoniae</i>	2662	2918	3234	3520	3943
<i>Klebsiella oxytoca</i>	921	1002	1028	1154	1265
<i>Klebsiella aerogenes</i>	356	395	355	346	277
<i>Klebsiella</i> spp., other named species	140	169	180	142	115
<i>Klebsiella</i> spp., species not recorded	474	562	474	466	388
<i>Klebsiella</i> spp. total	4553	5046	5271	5628	5988
<i>Enterobacter cloacae</i>	1837	1841	1925	2008	2038
<i>Enterobacter aerogenes</i>	218	270	282	284	321
<i>Enterobacter sakazakii</i>	72	72	52	66	37
<i>Enterobacter</i> spp., other named species	58	47	42	41	57
<i>Enterobacter</i> spp., species not recorded	267	244	221	214	177
<i>Enterobacter</i> spp. total	2452	2474	2522	2613	2630
<i>Serratia marcescens</i>	698	754	846	936	886
<i>Serratia liquefaciens</i>	132	136	134	168	157
<i>Serratia</i> spp., other named species	20	39	32	31	28
<i>Serratia</i> spp., species not recorded	177	179	147	135	125
<i>Serratia</i> spp. total	1027	1108	1159	1270	1196
<i>Citrobacter freundii</i>	374	344	288	325	356
<i>Citrobacter koseri</i> (<i>C. diversus</i>)	157	177	189	212	216
<i>Citrobacter</i> spp., other named species	21	32	34	49	44
<i>Citrobacter</i> spp., species not recorded	107	100	97	88	88
<i>Citrobacter</i> spp. total	659	653	608	674	704
<i>Edwardsiella</i> spp. total	2	0	1	3	1
<i>Hafnia</i> spp. total	34	34	32	31	40
<i>Kluyvera</i> spp. total	23	26	20	24	37
<i>Leclercia</i> spp. total	2	7	3	2	6
<i>Pantoea</i> spp. total	118	135	131	129	124
<i>Rahnella</i> spp. total	1	3	9	2	3

* Data extracted 14th April, 2008

Antibiotic susceptibility data

Tables 3 to 6 present antibiotic susceptibility data for each of the four main genera.

Between 2006 and 2007 decreased resistance to the antibiotic group cephalosporins (e.g. cefotaxime, ceftazidime) was reported for *Klebsiella* spp., *Enterobacter* spp., and *Serratia* spp. (tables 3 – 6). Cephalosporins are the antibiotic group to which the four main genera show the greatest level of resistance compared to all other antibiotics investigated.

Amongst reported specimens of *Klebsiella* spp., *Enterobacter* spp., and *Serratia* spp. resistance to Ciprofloxacin and Gentamicin have decreased significantly ($p < 0.005$ – $p < 0.0001$) from 2003. Resistance to the carbapenems (e.g. imipenem, meropenem) remains low and virtually unchanged at one percent or less for all four genera.

While these low rates are encouraging, it should be noted that for the carbapenem ertapenem (not included in these analyses owing to the small numbers tested by reporting laboratories) researchers have reported resistance rates of 40% amongst *Klebsiella* spp. and *Enterobacter* spp. isolates (N. Woodford et al., Int J Antimicrob. Agents. 2007 Apr 29(4); 456-9). The resistance mechanism is thought to be mediated by a combination of increased cell permeability and Beta-Lactamase production (ESBL and/or AmpC), and while these mechanisms have activity against imipenem or meropenem, they don't entirely confer resistance.

Please note that for some species/years only a small number of reports were provided which may affect the reliability of the percentage-resistant calculations.

Reporting of susceptibility information:

In comparison with previous years there was an increase in the proportion of specimens with susceptibility data for all antibiotics. In comparison with data collected in 2006, there was increased susceptibility reporting for all antibiotics in 2007. In 2007 for the four main genera:

- Gentamicin and ciprofloxacin susceptibility information was provided in approximately 95% of all reports (~90% in 2006).
- Ceftazidime, piperacillin/tazobactam, and imipenem/meropenem susceptibility information was provided in approximately 76% of all reports (~68% in 2006).
- Cefotaxime susceptibility information was provided in about 54% of all reports, this remains the same as 2006 data.

Table 3. Antibiotic susceptibility data for reports of *Enterobacter* spp. bacteraemia, England, Wales, and Northern Ireland: 2003 to 2007*

<i>Klebsiella</i> spp.		2003	2004	2005	2006	2007
Total reports:		4553	5046	5271	5628	5988
Piperacillin/ Tazobactam	% Non-susceptible	13%	16%	14%	15%	14%
	Reports with susceptibility data	1806	2485	2747	3364	4032
Imipenem/ Meropenem	% Non-susceptible	1%	0%	0%	0%	0%
	Reports with susceptibility data	2045	2554	2776	3362	4039
Cefotaxime	% Non-susceptible	12%	17%	16%	15%	14%
	Reports with susceptibility data	1446	1839	2159	2761	2820
Ceftazidime	% Non-susceptible	12%	17%	16%	17%	15%
	Reports with susceptibility data	2102	2563	2736	3282	3891
Ciprofloxacin	% Non-susceptible	12%	17%	15%	18%	15%
	Reports with susceptibility data	3021	3654	3822	4457	4794
Gentamicin	% Non-susceptible	9%	11%	9%	11%	10%
	Reports with susceptibility data	3248	3886	4040	4521	5159

* Data extracted 14th April, 2008

For *Klebsiella* spp., there has been a significant increase in resistance to ciprofloxacin over all five years ($p < 0.005$). However, between 2006 and 2007 ciprofloxacin resistance in *Klebsiella* spp has decreased from 18% to 15%.

Table 4. Antibiotic susceptibility data for reports of *Enterobacter* spp. bacteraemia, England, Wales, and Northern Ireland: 2003 to 2007*

<i>Enterobacter</i> spp.		2003	2004	2005	2006	2007
Total reports:		2452	2474	2522	2613	2630
Piperacillin/ Tazobactam	% Non-susceptible	21%	23%	23%	24%	21%
	Reports with susceptibility data	999	1219	1368	1594	1848
Imipenem/ Meropenem	% Non-susceptible	1%	1%	1%	1%	1%
	Reports with susceptibility data	1283	1386	1506	1732	1956
Cefotaxime	% Non-susceptible	36%	38%	40%	42%	37%
	Reports with susceptibility data	803	932	1040	1213	1247
Ceftazidime	% Non-susceptible	39%	41%	42%	41%	36%
	Reports with susceptibility data	1240	1328	1334	1519	1741
Ciprofloxacin	% Non-susceptible	16%	14%	15%	14%	10%
	Reports with susceptibility data	1631	1804	1860	2092	2201
Gentamicin	% Non-susceptible	13%	13%	12%	11%	9%
	Reports with susceptibility data	1763	1906	1988	2108	2297

* Data extracted 14th April, 2008

For *Enterobacter* spp., there have been significant decreases ($p < 0.0001$) in resistance to ciprofloxacin (from 16% to 10%) and gentamicin (13% to 9%). No other significant changes in resistance were reported.

Table 5. Antibiotic susceptibility data for reports of *Serratia* spp. bacteraemia, England, Wales, and Northern Ireland: 2003 to 2007*

<i>Serratia</i> spp.		2003	2004	2005	2006	2007
Total reports:		1027	1108	1159	1270	1196
Piperacillin/ Tazobactam	% Non-susceptible	23%	18%	20%	20%	16%
	Reports with susceptibility data	436	570	604	774	818
Imipenem/ Meropenem	% Non-susceptible	0%	0%	0%	1%	0%
	Reports with susceptibility data	498	612	642	807	877
Cefotaxime	% Non-susceptible	28%	27%	27%	29%	28%
	Reports with susceptibility data	317	398	426	548	572
Ceftazidime	% Non-susceptible	14%	23%	18%	16%	15%
	Reports with susceptibility data	508	598	549	681	731
Ciprofloxacin	% Non-susceptible	30%	25%	26%	25%	20%
	Reports with susceptibility data	679	808	854	996	995
Gentamicin	% Non-susceptible	4%	3%	3%	2%	1%
	Reports with susceptibility data	713	846	883	1002	1034

* Data extracted 14th April, 2008

For *Serratia* spp., significant decreases in resistance have been observed for piperacillin/tazobactam, ciprofloxacin and gentamicin. Of the three antibiotic groups only gentamicin shows a steady decrease over the whole time period.

Table 6. Antibiotic susceptibility data for reports of *Citrobacter* spp. bacteraemia, England, Wales, and Northern Ireland: 2003 to 2007*

<i>Citrobacter</i> spp.		2003	2004	2005	2006	2007
Total reports:		659	653	608	674	704
Piperacillin/ Tazobactam	% Non-susceptible	13%	10%	6%	9%	9%
	Reports with susceptibility data	238	317	295	348	450
Imipenem/ Meropenem	% Non-susceptible	0%	0%	0%	0%	0%
	Reports with susceptibility data	306	326	320	384	496
Cefotaxime	% Non-susceptible	19%	21%	11%	15%	18%
	Reports with susceptibility data	205	253	245	327	351
Ceftazidime	% Non-susceptible	20%	22%	15%	19%	16%
	Reports with susceptibility data	305	342	321	384	458
Ciprofloxacin	% Non-susceptible	10%	6%	8%	8%	8%
	Reports with susceptibility data	418	469	448	519	571
Gentamicin	% Non-susceptible	7%	5%	4%	6%	5%
	Reports with susceptibility data	478	506	451	509	606

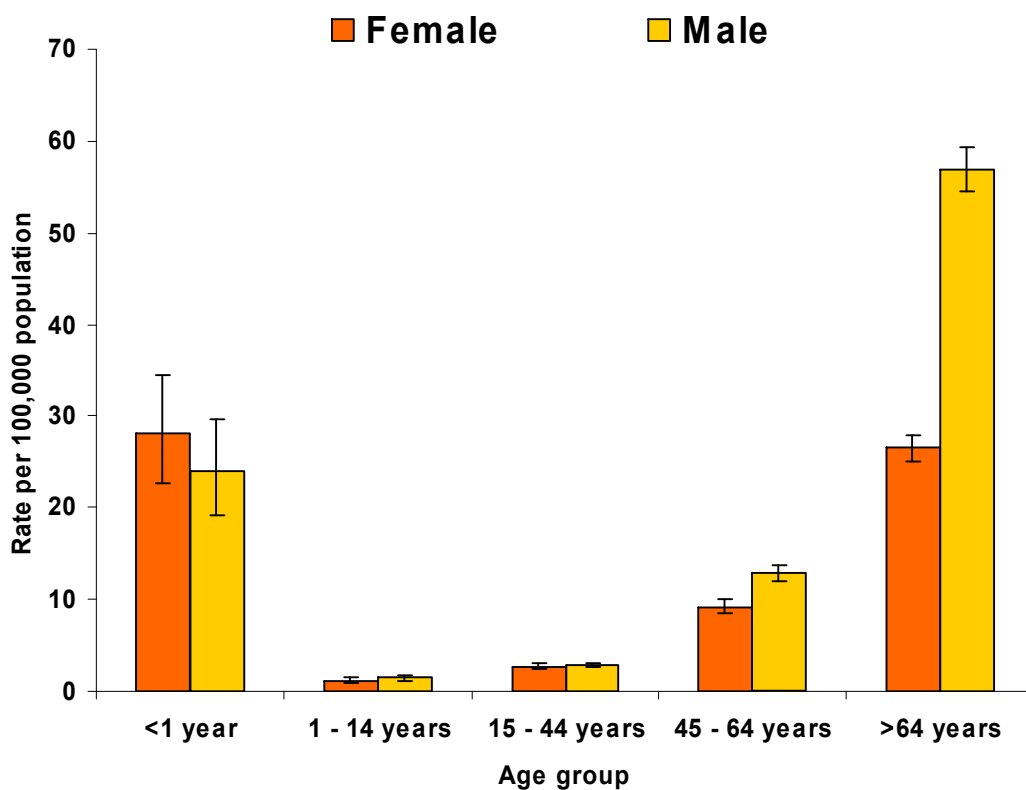
* Data extracted 14th April, 2008

For *Citrobacter* spp., there not have been any statistically significant changes in resistance patterns although slight decreases in resistance have been observed in cefotaxime, ceftazidime and gentamycin between 2006 and 2007. Although many isolates of *Citrobacter* spp. reported to HPA are not identified to species level (around 13%), it is known that cephalosporin resistance in *C. freundii* is mediated by mechanisms similar to those found amongst *Enterobacter* spp. (i.e. AmpC Beta-Lactamases and ESBLs), while in *C. koseri* cephalosporin resistance is mediated by a chromosomal class A Beta-Lactamase.

Age and sex distribution by species

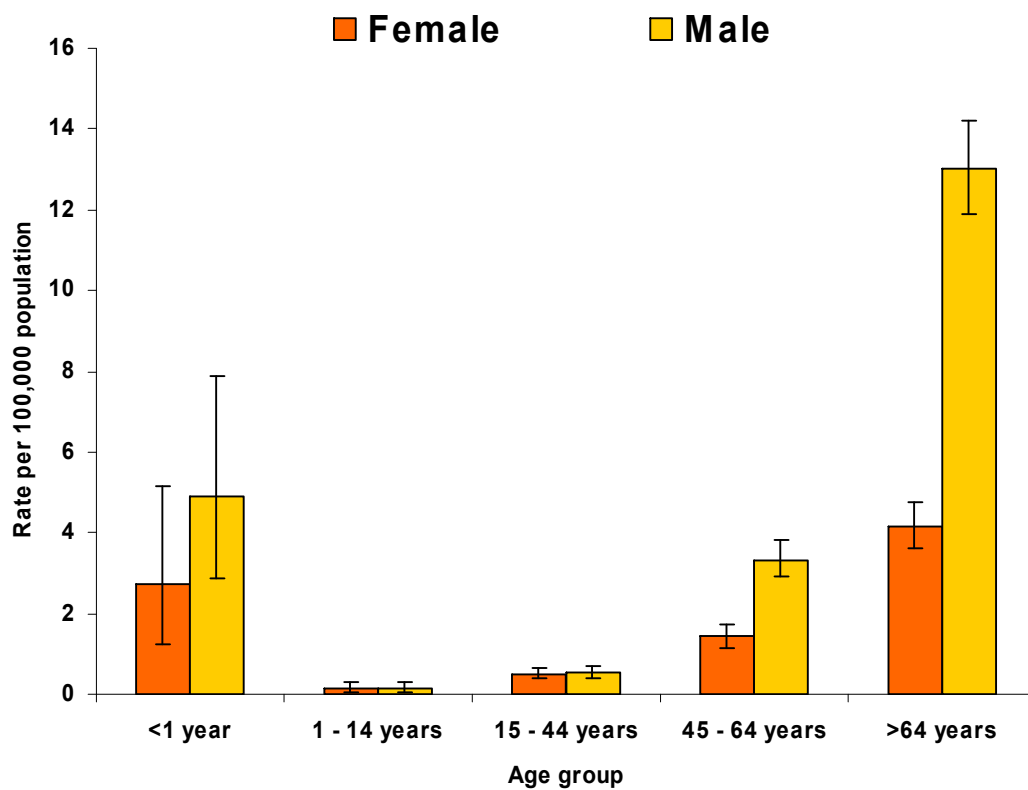
Figures 2 to 5 show the age and sex distribution of bacteraemia reports for *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp. In general, the number of reports for all species was highest in males and prevalence increased with age so that the >65 years age group contained the greatest number of reports.

Figure 2. *Klebsiella* spp. bacteraemia reports in 2007 by age and sex*



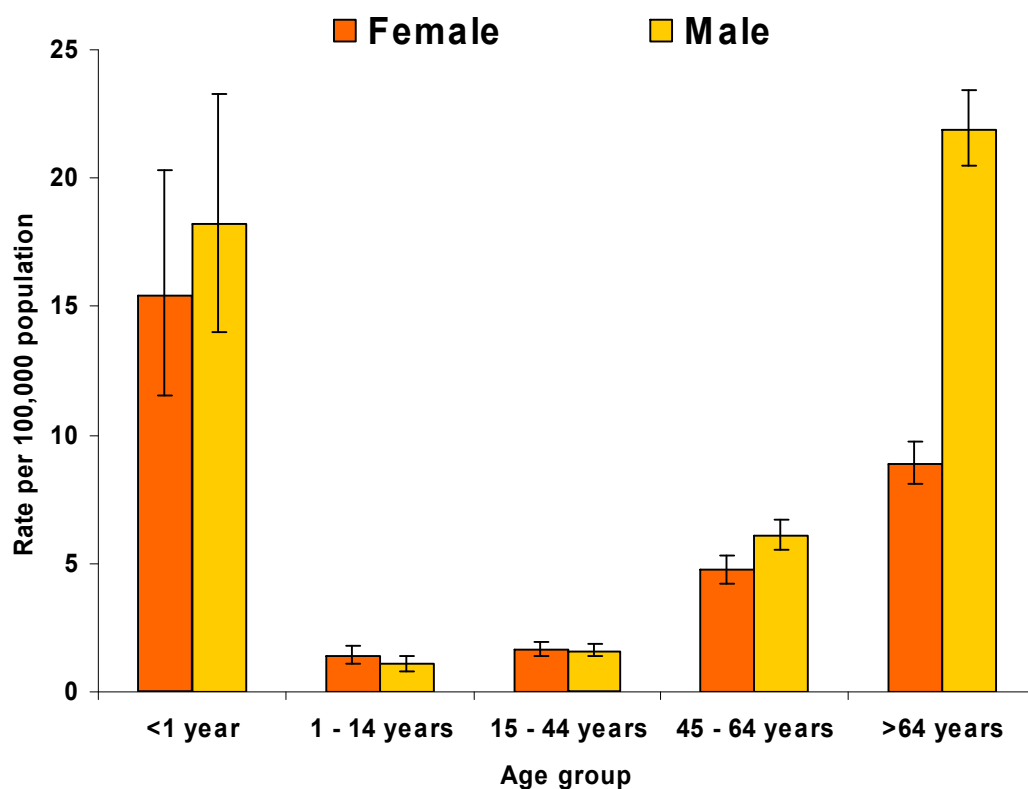
* Data extracted 14th April, 2008

Figure 3. *Enterobacter* spp. bacteraemia reports in 2007 by age and sex*



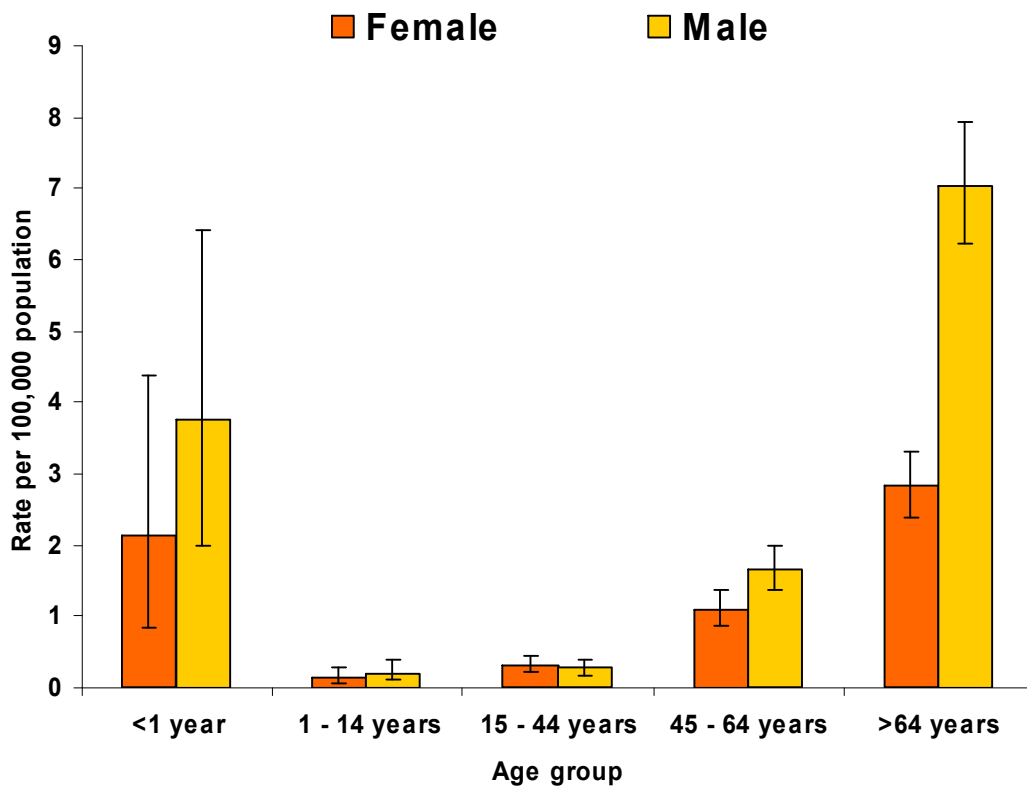
* Data extracted 14th April, 2008

Figure 4. *Serratia* spp. bacteraemia reports in 2007 by age and sex*



* Data extracted 14th April, 2008

Figure 5. *Citrobacter* spp. bacteraemia reports in 2007 by age and sex*

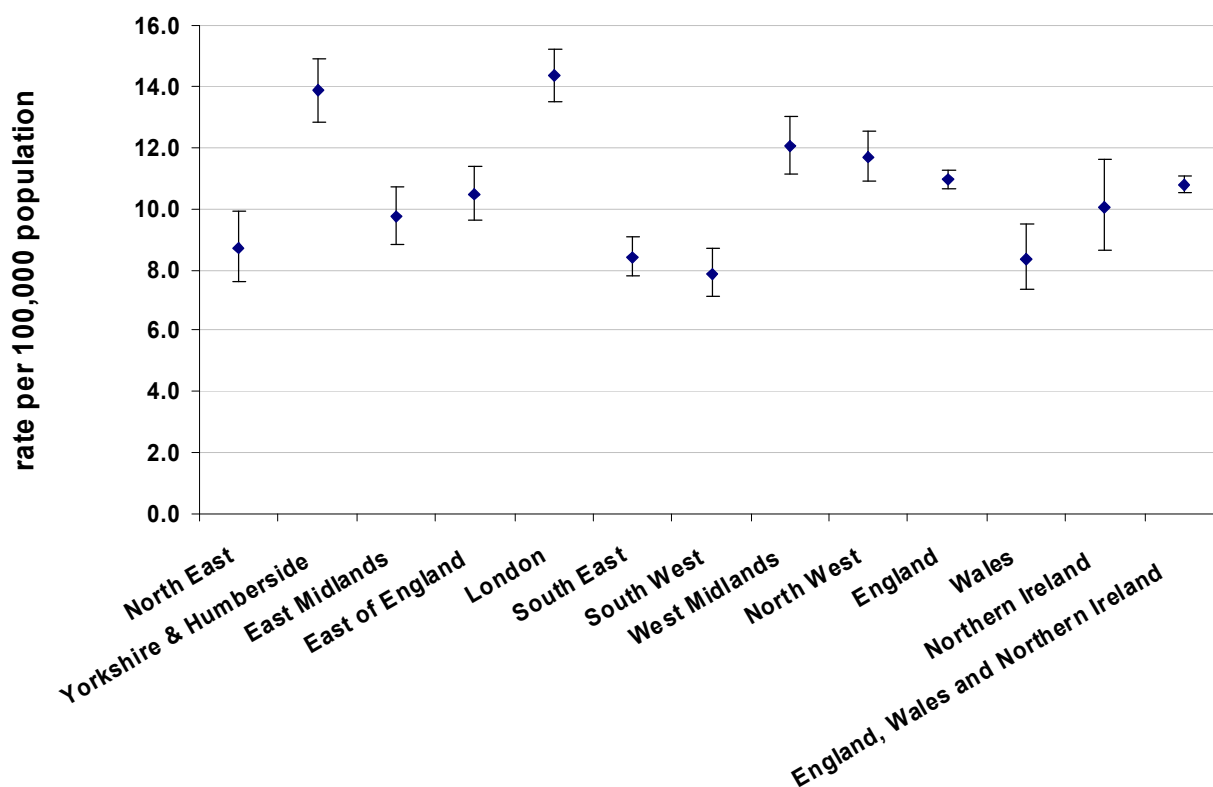


* Data extracted 14th April, 2008

Distribution by region

Figures 6 to 9 show regional distribution of bacteraemia reports for *Klebsiella*, *Enterobacter*, *Serratia*, and *Citrobacter* spp. by region.

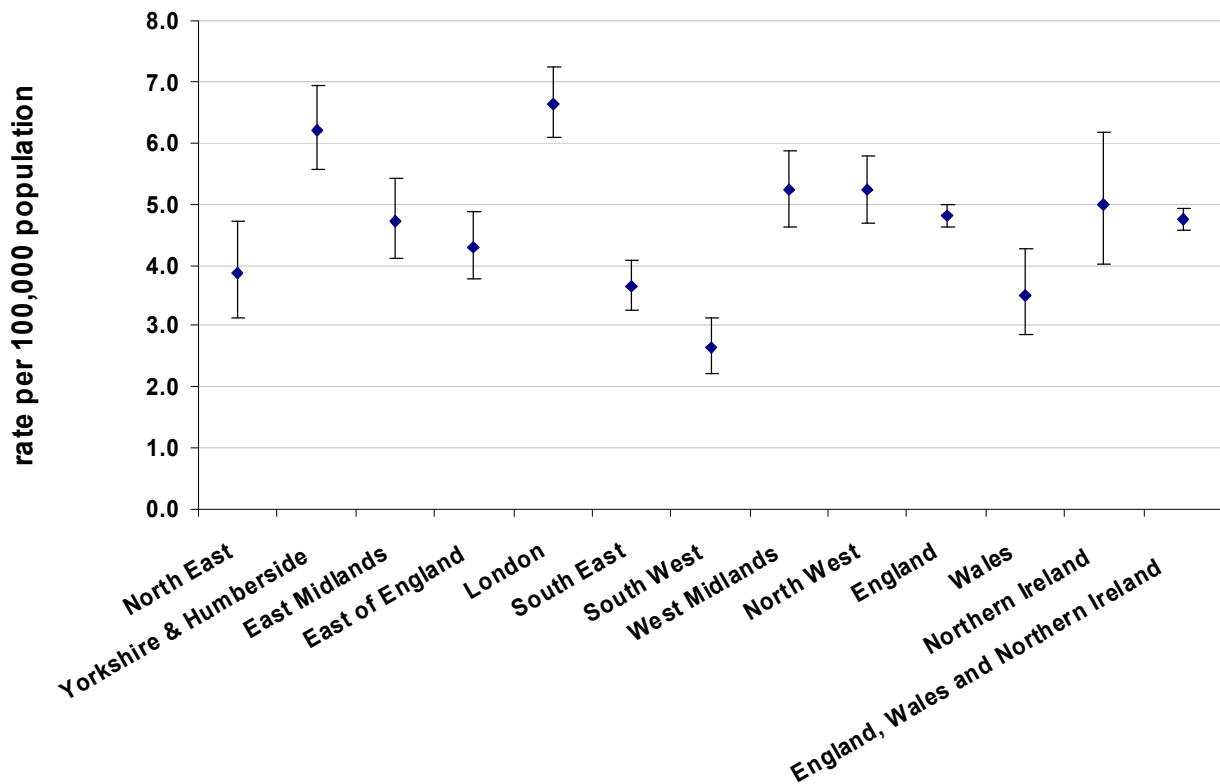
Figure 6. Region-specific rates* of *Klebsiella* spp. bacteraemia: England, Wales, and Northern Ireland, 2007



* Data extracted 14th April, 2008

Regions with high incidence of *Klebsiella* spp. bacteraemia include London (14.35 per 100,000 population) and Yorkshire and Humberside (13.85/100,000). Regions/countries with low incidence include South West (7.86/100,000) and Wales (8.36/100,000). The overall reported incidence for England, Wales, and Northern Ireland is 10.79 per 100,000 population.

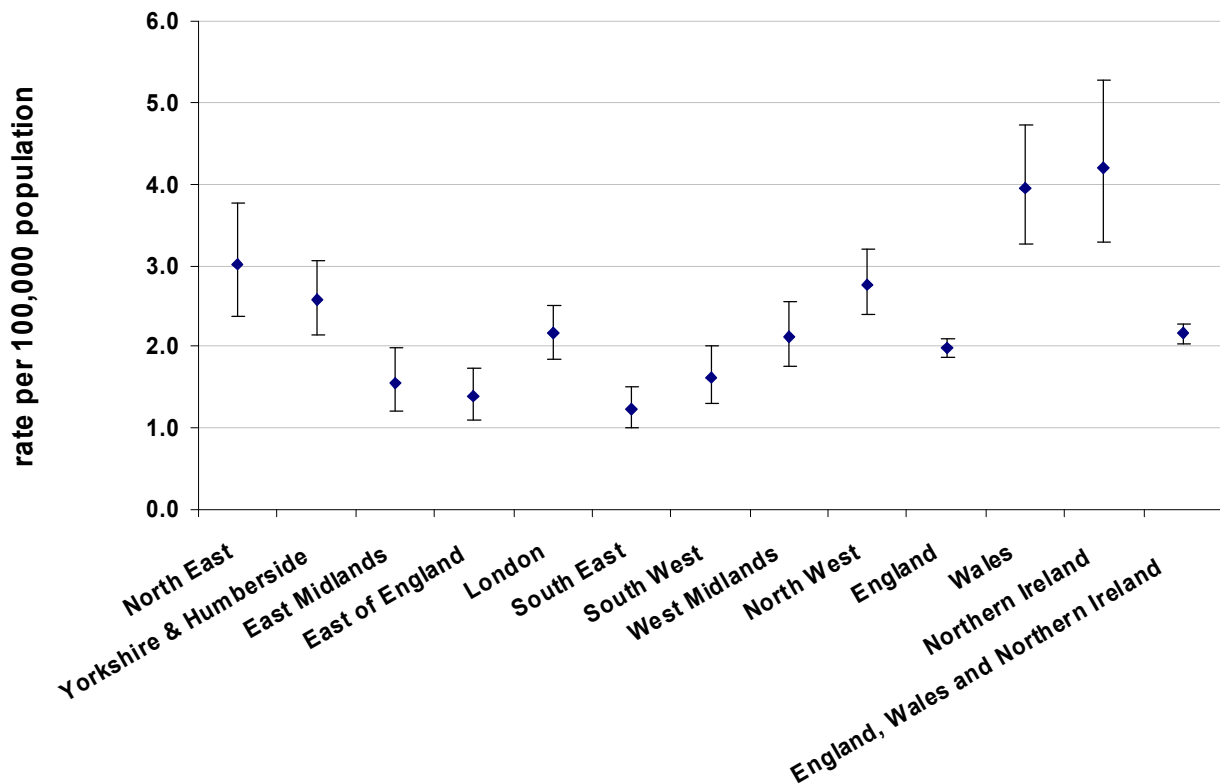
Figure 7. Region-specific rates* of *Enterobacter* spp. bacteraemia: England, Wales, and Northern Ireland, 2007



* Data extracted 14th April, 2008

The highest incidence of *Enterobacter* spp. bacteraemias were reported in London and Yorkshire and the Humber (6.64 and 6.22 per 100,000 population respectively). As with *Klebsiella* spp. reports, the lowest incidence of *Enterobacter* spp. bacteraemia occurs in the South West and Wales (2.65 and 3.51 per 100,000 population respectively). The overall reported incidence for England, Wales, and Northern Ireland is 4.74 per 100,000 population.

Figure 8. Region-specific rates* of *Serratia* spp. bacteraemia: England, Wales, and Northern Ireland, 2007

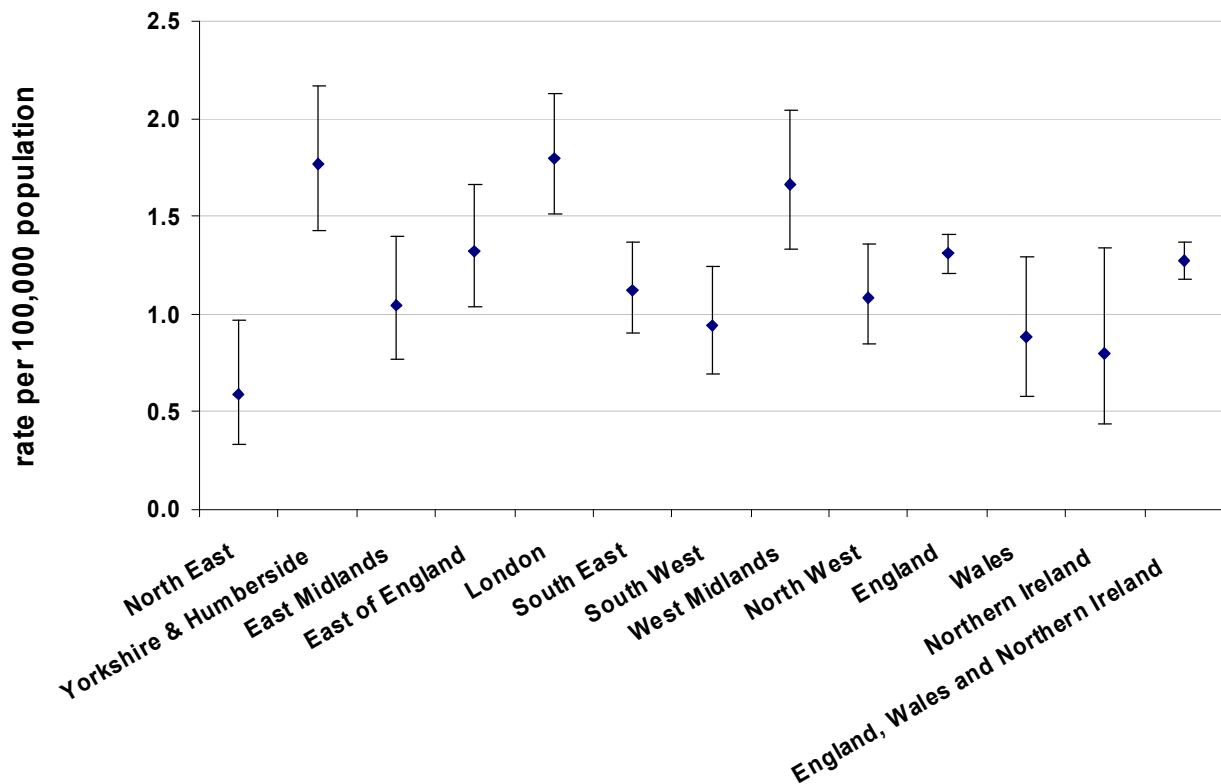


* Data extracted 14th April, 2008

In contrast to regional patterns observed in *Klebsiella* and *Enterobacter* spp. bacteraemias regions with high incidence of *Serratia* spp. bacteraemia include the Wales (3.94 per 100,000 population) and Northern Ireland (4.19/100,000). The high incidence in Northern Ireland may be consistent with impressions that *Serratia* spp. infections are more prevalent in the Republic of Ireland. Historically there are reports of infection via blood transfusion and there is some evidence of a higher than average number of isolations associated with these incidents in the Republic of Ireland a decade ago. However, there have also been a number of outbreaks in Dublin Hospitals that are not linked to blood transfusion.

Regions/countries with low incidence include the South East (1.24 per 100,000 population) and East of England (1.39/100,000). The overall reported incidence for England, Wales, and Northern Ireland is 0.13 per 100,000 population.

Figure 9. Region-specific rates* of *Citrobacter* spp. bacteraemia: England, Wales, and Northern Ireland, 2007



* Data extracted 14th April, 2008

The highest incidence of *Citrobacter* spp. bacteraemias were reported in London and Yorkshire and the Humber (1.80 and 1.77 per 100,000 population respectively). The lowest incidence of *Citrobacter* spp. bacteraemia occurs in the North East and Northern Ireland (0.80 and 0.88 per 100,000 population respectively). The overall reported incidence for England, Wales, and Northern Ireland is 0.10 per 100,000 population.

It is important to note that regional incidence rates are affected by completeness of regional reporting as well as the regional distribution of specialist care units.