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Bacteraemia

Voluntary surveillance of bacteraemia caused by *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. in England, Wales and Northern Ireland: 2010-2014

These analyses are based on data relating to diagnoses of bloodstream infections caused by *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. between 2010 and 2014 in England, Wales and Northern Ireland (EWNI) extracted from Public Health England's (PHE) voluntary surveillance database Second Generation Surveillance System (SGSS).

SGSS comprises a communicable disease module that includes antimicrobial susceptibility data (CDR; formerly CoSurv/LabBase2) and a separate comprehesive antimicrobial resistance module (AMR; formerly AmSurv). Data were extracted on 28 September 2015. The AMR module captures more comprehensive antibiogram data (involving all antibiotics tested), allowing a more robust evaluation of multi-drug resistance rates. However trends cannot be undertaken using AMR data due to lower laboratory coverage in this module in previous years. The data presented here for earlier years will differ in some instances from those in earlier publications partly due to the inclusion of late reports.

Rates of bacteraemia laboratory reports were calculated using mid-year resident population estimates for the respective year and geography[1,2]. Geographical analyses were based on the residential postcode of the patient if known (otherwise the GP postcode if known or failing that the postcode of the laboratory) with cases in England being assigned to one of 15 local PHE centres (PHECs) formed from administrative local authority boundaries.

This report includes analyses of the trends, patient demographic and geographical distribution as well as antimicrobial susceptibility among these bacteraemia episodes.

Key points

- In the context of a large decrease in the rate of bacteraemia due to *Enterobacter* spp. and *Serratia* spp between 2007 and 2014, the rates increased marginally between 2013 and 2014 (by 2% and 6% respectively). This was equivalent to an increase in the rate from 3.27 to 3.34; and from 1.42 to 1.50 respectively per 100,000 population. The rate for *Citrobacter* spp. remained stable from 2007 to 2014 at around 1/100,000 *per annum*

- Of the three genera, *Serratia* spp. had the highest proportion of reports identified to species level (96%) in 2014 representing a continuing improvement in species reporting. Reporting to species level was 93% and 91% for *Enterobacter* spp. and *Citrobacter* spp. respectively in 2014.
- Rates of bacteraemia were generally higher in males than females and among older adults (≥65 years) and infants (<1 year) across the three genera.
- At country level, England had the highest rate of bacteraemia reports across all genera in 2014, 3.39/100,000 for *Enterobacter* spp., 1.52 for *Serratia* spp. and 1.43 for *Citrobacter* spp. These compare to 2.49, 1.46 and 0.94 respectively for Wales and 3.31, 1.09 and 0.49 respectively for Northern Ireland.
- Within England, the rate of bacteraemia varied between PHE centres for each genus. No single geographical area bore the highest burden across all genera.
- Trends in antimicrobial resistance were assessed for five classes of antibiotics from 2010 to 2014.
- There was a decrease in the proportion of isolates reported as resistant to third generation cephalosporins among *Enterobacter* spp. isolates, with 26% reported as resistant to cefotaxime and 28% resistant to ceftazidime by 2014. A decrease was also observed for *Serratia* spp. reaching 14% (for cefotaxime) and 13% for (for ceftazidime) by 2014.
- Resistance to the fluoroquinolone ciprofloxacin decreased for *Serratia* spp. blood culture isolates during the five year period reaching 6% in 2014 whereas the proportion of isolates reported as resistant was stable for the other two genera. Resistance to tobramycin (aminoglycoside) increased markedly among *Serratia* spp. isolates from 9% in 2010 to 19% in 201 but remained stable for the other two genera.
- A slight increase in the proportion of *Enterobacter* spp. and *Citrobacter* spp. isolates reported resistant to piperacillin/tazobactam was observed over the five-year period reaching 21% and 10% respectively in 2014. This may reflect the recent switch from BSAC to EUCAST MIC breakpoint from 16 to 8 mg/L for this agent. In contrast (and despite the breakpoint reduction), a decrease was noted for *Serratia* spp. isolates (reaching 9% in 2014)
- Resistance to meropenen or ertapenem (carbapenems) was uncommon although resistance to ertapenem was relatively higher only for *Enterobacter* spp. (9% of isolates in 2014 and remaining stable). A small but notable increase in ertapenem resistance among *Citrobacter* spp. isolates was identified; from 0% (0/281) in 2013 to 3% (10/369) in 2014 which was in the

context of lower levels resistance to this agent among these isolates in the previous four years (inter-year range 0% - 2%).

- The most common dual resistance was to third generation cephalosporins and gentamicin among *Enterobacer* spp. isolates (5.1%). The least frequent dual resistance was for ciprofloxacin and gentamicin among *Serratia* spp. isolates (0%).

Trends in the number of bacteraemia reports and rates

The proportion of total bacteraemia reports (all causative pathogens) that were *Enterobacter* spp. was low and stable at 2% annually between 2010 (1,992/98,352) and 2014 (1,981/106,708) (data not shown). *Serratia* spp. accounted for 1% of total bacteraemia reports annually in the same five year period with 889 reports in 2014. *Citrobacter* spp. also remained stable at <1% of total bacteraemia reports annually with 799 episodes in 2014.

The number of bacteraemia reports due to *Enterobacter* spp. increased by 3% from 2013 (n=1,920) to 2014 (n=1,981) (Table 1). The number of bacteraemia reports due to *Serratia* spp., increased by 7% over the same period (n=705 and n=749 respectively). *Citrobacter* spp. bacteraemia reports decreased by 6% also over the same two-year period (n=388 and n=366 respectively).

Figure 1 Trends in rates of laboratory reports of *Enterobacter* spp., *Serratia spp.* and *Citrobacter spp.* bacteraemia in England, Wales and Northern Ireland

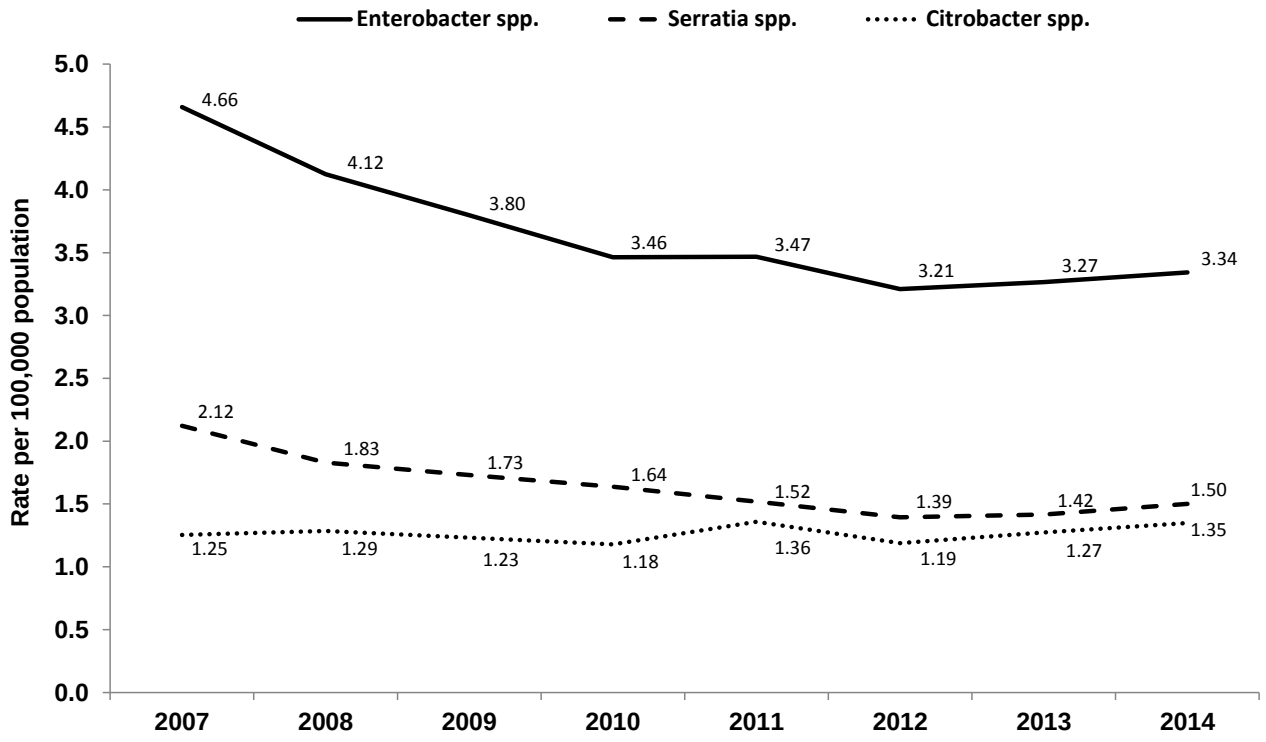


Figure 1 shows trends in the rates of bacteraemia laboratory reports per 100,000 resident population between 2007 and 2014 by genus. Of the three genera, *Enterobacter* spp. had the highest annual rate and *Citrobacter* spp. had the lowest rate. Over the eight year period, the rate of *Enterobacter* spp. bacteraemia decreased by 28% from 4.66/100,000 in 2007 to 3.34/100,000 in 2014; the largest decrease being from 2007 to 2010 and stabilising afterwards. The increase from 2013 to 2014 was 2% but this represented a small fluctuation. The annual rate of bacteraemia due to *Serratia* spp. decreased by 29% from 2.12/100,000 in 2007 to 1.50/100,000 in 2014; the increase from 2013 to 2014 by 6% also represented a small fluctuation. The annual rate of bacteraemia due to *Citrobacter spp.* was relatively stable throughout the study period at around 1/100,000.

Table 1 shows trends in the distribution of species and species identification by genus from 2010 to 2014. In 2014 the great majority of *Enterobacter* spp. reports were reported to species level (93%) but this represented a marginal decrease compared to previous years. In 2014, the predominant species (group) causing *Enterobacter* spp. bacteraemia was *E.* cloacae, accounting for 72% of reports, followed by *E. areogenes* (17%). *E. cloacae* is part of the *Enterobacter cloacae* complex which includes other related species some of which were reported (Table 1). However the distinction between members of the complex is not always reliable. It should be noted that *E. sakazakii* is now classified under the genus *Cronobacter* although the number of reports using the older taxonomy has decreased.

The majority of *Serratia* spp. reports were reported to species level (96%) in 2014, a small improvement compared to previous years. In 2014, the predominant species was *S. marcescens* accounting for 84% of reports, followed by *S. liquefaciens* (9%).

The proportion of *Citrobacter* spp. reported to species level in 2014 (91%) was similar to previous years. This n 2014, the predominant species causing was *C. diversus* accounting for 46% of reports, followed by *C. freundii* (37%). Although these two species are similarly frequent, they differ greatly in susceptibility to antibiotics hence species identification is of great importance.

The expanded list of species being reported for *Enterobacter*/*Citrobacter*/*Serratia* bacteraemia reflects the increased use of automated diagnostic technology (MALDI-TOF) which enables laboratories to distinguish more species.

Table 1. Reports of bacteraemia due to *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. (England, Wales and Northern Ireland): 2010 to 2014

	2010		2011		2012		2013		2014	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
E. cloacae †	1,490	75%	1,501	75%	1,351	72%	1,343	70%	1,422	72%
E. aerogenes	333	17%	334	17%	352	19%	342	18%	338	17%
*E. sakazakii**	27	1%	21	1%	19	1%	28	1%	15	1%
E. amnigenus	6	0%	12	1%	5	0%	7	0%	4	0%
E. gergoviae	6	0%	6	0%	3	0%	7	0%	4	0%
E. intermedius	3	0%	0	0%	1	0%	0	0%	1	0%
E. asburiae †	0	0%	0	0%	0	0%	0	0%	1	0%
E. cancerogenus	0	0%	0	0%	0	0%	0	0%	1	0%
E. kobei †	0	0%	0	0%	0	0%	0	0%	4	0%
Enterobacter spp., other named	36	2%	30	1%	27	1%	48	3%	58	3%
Enterobacter spp, not recorded	91	5%	107	5%	117	6%	145	8%	133	7%
***Enterobacter* spp. total**	**1,992**	**100%**	**2,011**	**100%**	**1,875**	**100%**	**1,920**	**100%**	**1,981**	**100%**
S. marcescens	767	82%	697	79%	670	82%	705	85%	749	84%
S. liquefaciens	103	11%	106	12%	82	10%	71	9%	80	9%
S. fonticola	5	1%	6	1%	8	1%	8	1%	3	0%
S. odorifera	5	1%	7	1%	3	0%	6	1%	2	0%
S. plymuthica	5	1%	2	0%	3	0%	1	0%	0	0%
S. rubidaea	1	0%	1	0%	2	0%	0	0%	1	0%
S. ficaria	0	0%	1	0%	2	0%	1	0%	1	0%
S. proteamaculas	1	0%	1	0%	0	0%	0	0%	0	0%
Serratia spp., other named	0	0%	9	1%	12	1%	10	1%	21	2%
Serratia spp., not recorded	54	6%	51	6%	32	4%	30	4%	32	4%
***Serratia* spp. total**	**941**	**100%**	**881**	**100%**	**814**	**100%**	**832**	**100%**	**889**	**100%**
C. diversus	316	47%	379	48%	322	46%	388	52%	366	46%
C. freundii	250	37%	284	36%	264	38%	236	32%	299	37%
C. amalonaticus	5	1%	3	0%	7	1%	3	0%	4	1%
C. farmeri	0	0%	0	0%	0	0%	0	0%	2	0%
C. youngae	0	0%	0	0%	0	0%	0	0%	1	0%
Citrobacter spp. other named	44	6%	61	8%	45	6%	58	8%	58	7%
Citrobacter spp., not recorded	63	9%	61	8%	56	8%	63	8%	69	9%
***Citrobacter* spp. total**	**678**	**100%**	**788**	**100%**	**694**	**100%**	**748**	**100%**	**799**	**100%**

† Part of the *Enterobacter cloacae* complex

*This species is now recognised under the genus *Cronobacter.* Despite the taxonomic change, laboratories still use the older taxonomic classification. Future HPRs will not include *E. sakazakii*

Age and sex distribution

Figures 2 to 4 show the age and sex-specific rates of bacteraemia reports in EWNI in 2014 per 100,000 resident population. In general, the rates were higher in adults over 75 years and in infants (under one year) of cases. The rate of bacteraemia was substantially higher among males than females across all age groups in general except those aged 5 to 44 years where the rates were similar.

Among the oldest age group (75 years or more), the rate for *Enterobacter* spp. and *Citrobacter spp.* was three to four times higher in males than in females, with incidence rate ratios (IRR) of 3.12 and 4.95 respectively. For *Serratia* spp. the male to female incidence rate ratios was highest in 65 to 74 year-olds (IRR of 2.51).

Figure 2. Age and sex-specific rates of *Enterobacter* spp. bacteraemia reports per 100,000 population (England, Wales and Northern Ireland): 2014

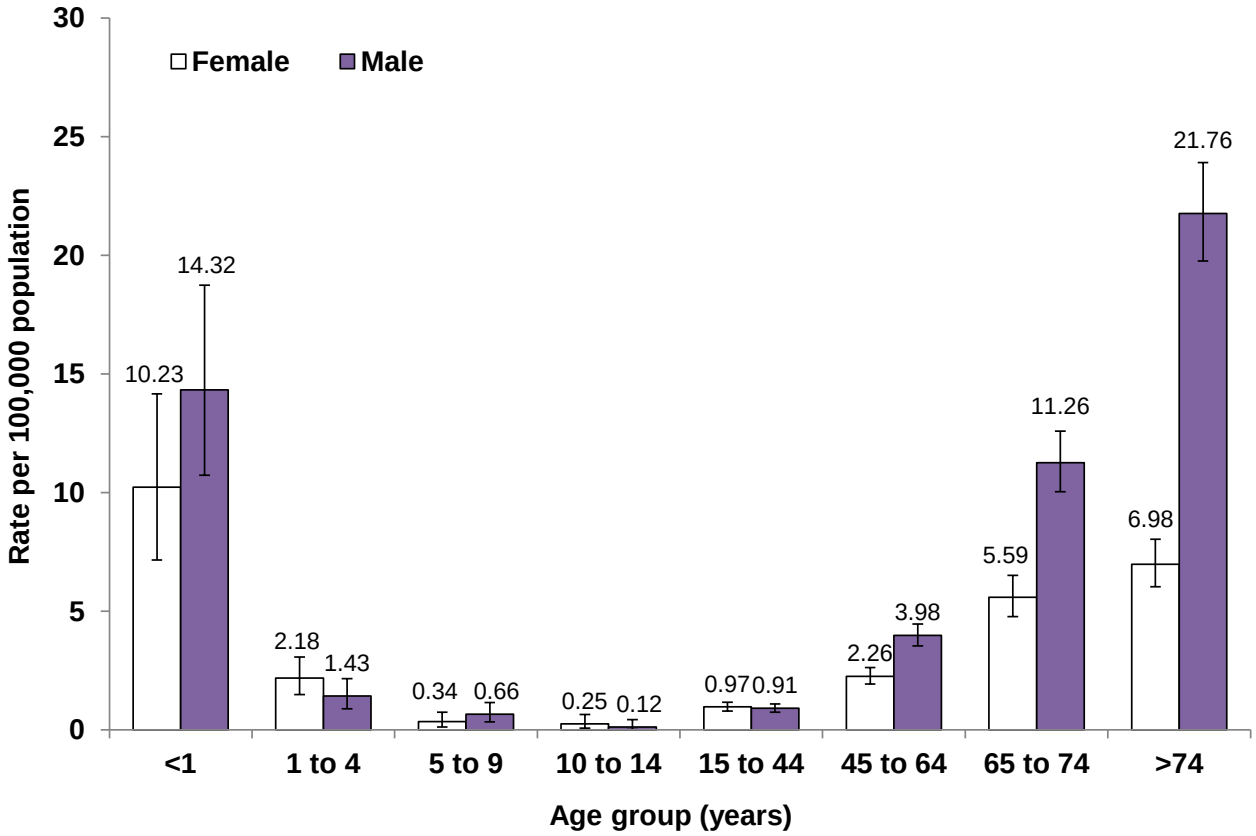


Figure 3. Age and sex-specific rates of *Serratia* bacteraemia reports per 100,000 population (England, Wales and Northern Ireland): 2014

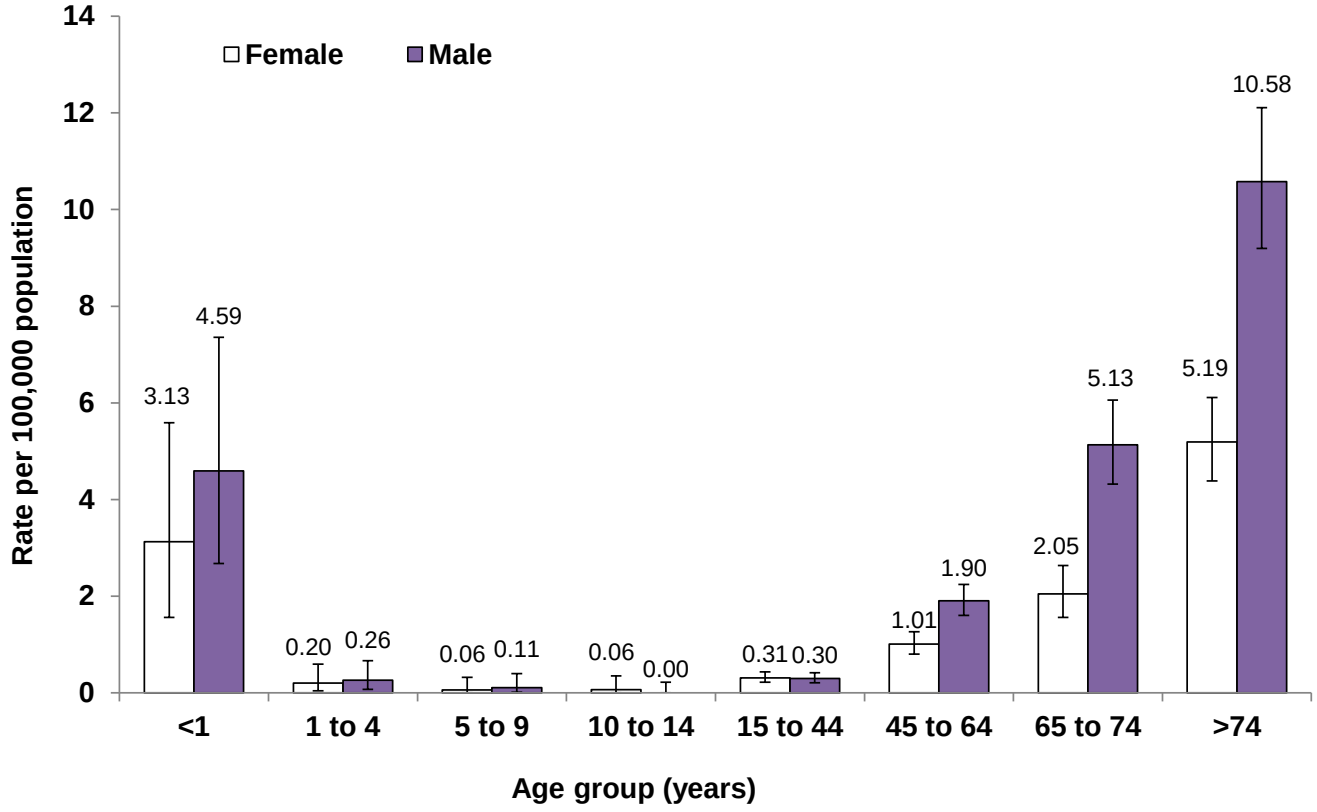
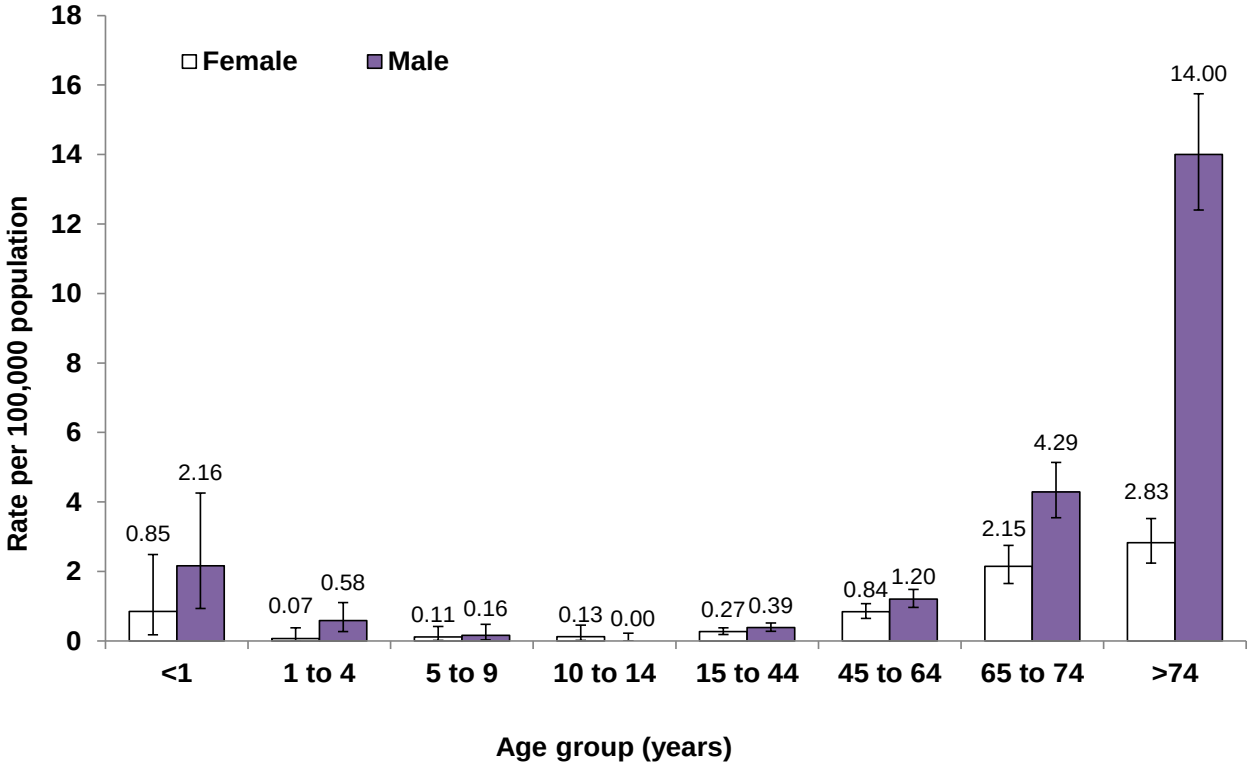


Figure 4. Age and sex-specific rates of *Citrobacter spp.* bacteraemia reports per 100,000 population (England, Wales and Northern Ireland): 2014



Geographical distribution

The geographical analyses presented here are not corrected for variation in reporting between geographical areas. Tables 2-4 show trends by geographical region from 2010 to 2014. Figures 5-7 are graphical displays of the regional variation in 2014.

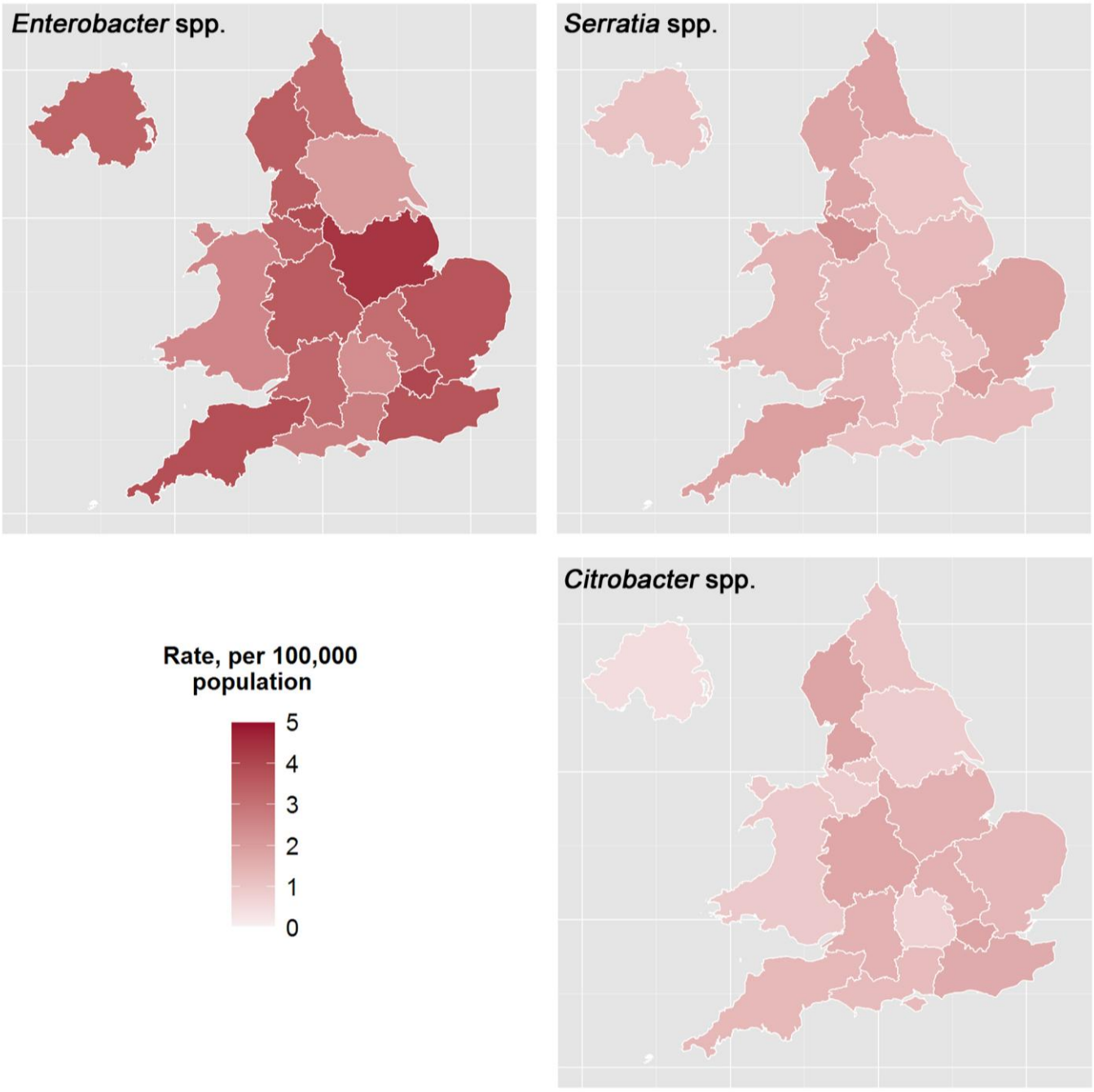
In 2014 the rate of laboratory reports of *Enterobacter* spp. bacteraemia in EWNI was 3.34/100,000; England had the highest rate (3.39) followed by Northern Ireland (3.31) then Wales (2.49). The *Serratia* spp. bacteraemia rate in 2014 was 1.50/100,000 for EWNI with the highest rate was in England (1.52) followed by Wales (1.46) then Northern Ireland (1.09). The *Citrobacter* spp. bacteraemia rate in EWNI was 1.35/100,000 with highest rates again in England (1.43), with rates for Wales and Northern <1 per 100,000 each.

Within England, there was variation in the rate between the 15 PHECs across the three genera. There was no evidence that a single PHE centre bore the greatest burden for all three genera. However Thames Valley tended to have the lowest rate.

For *Enterobacter* spp., the highest rate was in East Midlands in 2014 (4.36) compared to other PHECs except in 2012. The lowest rate in 2014 was in Yorkshire and Humber (1.98) with a steady decline observed in this region since 2010 (3.88). No PHEC experienced a steady year on year increase.

In 2014, the highest rate for *Serratia* spp. was in Cheshire and Merseyside (2.30) and the lowest in Thames Valley (0.91). A general increase in rates in Cheshire and Merseyside and in Cumbria and Lancashire was observed despite small inter-year fluctuations.

Figures 5, 6 and 7. Geographical distribution of the rate of *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. bacteraemia reports, respectively, per 100,000 population (England, Wales and Northern Ireland): 2014



In 2014, the highest rate for *Citrobacter* spp. was in Cumbria and Lancashire and in London (1.78 each) and the lowest in Thames Valley (0.77). From 2010 to 2014 a slow but steady increase in the population rate for this pathogen was observed in Cumbria and Lancashire (0.77 in 2010) and South Midlands and Hertfordshire (from 0.91 to 1.51 respectively). A gradual decrease was observed in Cheshire and Merseyside (from 1.12 to 0.86 respectively).

As comparison, the separate analysis for *Klebsiella* spp. bacteraemia showed that the highest rate was in Greater Manchester in 2014 at 14.11/100,000. The lowest rate was in Thames Valley [3].

Table 2: Rate *Enterobacter* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Wales and Northern Ireland): 2010 to 2014

		Rate per 100,000 resident population				
Region	**PHE centre**	**2010**	**2011**	**2012**	**2013**	**2014**
North of England	Cheshire and Merseyside	2.83	3.69	3.14	3.01	3.37
	Cumbria and Lancashire	2.81	2.75	2.95	4.22	3.45
	Greater Manchester	3.72	4.73	3.52	3.72	3.84
	North East	2.94	3.04	3.11	2.95	3.05
	Yorkshire and Humber	3.88	3.35	2.71	2.64	1.98
Midlands and East of England	Anglia and Essex	3.76	3.37	3.37	3.33	3.65
	East Midlands	4.87	4.63	3.31	4.34	4.36
	South Midlands and Hertfordshire	2.26	1.94	2.22	2.08	3.10
	West Midlands	3.29	2.91	3.62	3.30	3.52
London	London	3.93	3.95	3.90	3.81	3.96
South of England	Avon Gloucestershire and Wiltshire	2.83	2.64	2.66	2.38	3.23
	Devon Cornwall and Somerset	3.74	4.04	3.29	3.23	3.78
	Kent Surrey and Sussex	3.40	3.51	3.08	3.25	3.66
	Thames Valley	2.64	2.72	2.64	2.28	2.31
	Wessex	3.20	3.44	3.08	2.84	2.70
England		**3.49**	**3.46**	**3.22**	**3.25**	**3.39**
Northern Ireland		**3.38**	**3.58**	**2.80**	**4.15**	**3.31**
Wales		**3.05**	**3.59**	**3.35**	**3.11**	**2.49**
England, Wales and Northern Ireland		**3.46**	**3.47**	**3.21**	**3.27**	**3.34**

Table 3: Rate *Serratia* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Wales and Northern Ireland): 2010 to 2014

		Rate per 100,000 resident population				
Region	**PHE centre**	**2010**	**2011**	**2012**	**2013**	**2014**
North of England	Cheshire and Merseyside	1.62	2.03	1.65	2.11	2.30
	Cumbria and Lancashire	1.53	1.63	1.58	1.63	1.78
	Greater Manchester	2.14	1.45	1.89	1.55	1.57
	North East	2.20	2.00	1.58	2.11	1.83
	Yorkshire and Humber	1.71	0.98	1.03	0.88	1.06
Midlands and East of England	Anglia and Essex	1.42	1.58	1.59	1.20	1.87
	East Midlands	1.49	1.90	1.37	1.54	1.27
	South Midlands and Hertfordshire	0.79	0.97	0.55	0.58	1.08
	West Midlands	1.51	1.53	1.06	1.32	1.30
London	London	1.75	1.45	1.54	1.46	1.97
South of England	Avon Gloucestershire and Wiltshire	1.03	0.94	1.22	0.71	1.37
	Devon Cornwall and Somerset	1.74	1.91	2.34	2.11	1.91
	Kent Surrey and Sussex	1.89	1.27	1.13	1.60	1.28
	Thames Valley	0.90	1.19	0.73	0.44	0.91
	Wessex	0.91	1.40	1.39	1.38	1.11
England		**1.56**	**1.46**	**1.35**	**1.36**	**1.52**
Northern Ireland		**2.22**	**2.43**	**1.26**	**2.08**	**1.09**
Wales		**2.59**	**2.02**	**2.18**	**1.95**	**1.46**
England, Wales and Northern Ireland		**1.64**	**1.52**	**1.39**	**1.42**	**1.50**

Table 4: Rate *Citrobacter* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Wales and Northern Ireland): 2010 to 2014

		Rate per 100,000 resident population				
Region	**PHE centre**	**2010**	**2011**	**2012**	**2013**	**2014**
	Cheshire and Merseyside	1.12	1.66	1.53	1.36	0.86
	Cumbria and Lancashire	0.77	0.87	0.97	1.17	1.78
North of England	Greater Manchester	0.83	0.97	1.11	0.85	1.02
	North East	0.77	1.19	0.73	0.96	1.11
	Yorkshire and Humber	1.22	1.30	1.02	0.96	0.86
	Anglia and Essex	1.61	1.62	1.25	1.65	1.37
Midlands and	East Midlands	1.78	2.00	1.34	1.44	1.50
East of England	South Midlands and Hertfordshire	0.91	0.93	0.92	1.06	1.51
	West Midlands	1.24	1.55	1.29	1.69	1.73
London	London	1.15	1.63	1.62	1.57	1.78
	Avon Gloucestershire and Wiltshire	0.99	0.94	1.22	0.88	1.49
	Devon Cornwall and Somerset	1.55	1.18	1.31	1.39	1.33
South of England	Kent Surrey and Sussex	1.60	1.32	1.33	1.41	1.65
	Thames Valley	0.80	0.79	0.59	1.12	0.77
	Wessex	1.03	1.51	1.09	1.27	1.26
England		**1.21**	**1.39**	**1.22**	**1.32**	**1.40**
Northern Ireland		**0.89**	**0.99**	**0.71**	**0.55**	**0.49**
Wales		**0.75**	**1.11**	**0.85**	**0.91**	**0.94**
England, Wales and Northern Ireland		**1.18**	**1.36**	**1.19**	**1.27**	**1.35**

Antimicrobial susceptibility data

Tables 5-7 present antibiotic susceptibility trends from 2010 to 2014 for blood culture isolates by genus. This analysis examines six classes of antibiotics: third-generation cephalosporins (cefotaxime or ceftazidime), carbapenems (meropenem or ertapenem), a fluoroquinolone (ciprofloxacin), a penicillin/beta-lactamase inhibitor combination (piperacillin/tazobactam), and an aminoglycoside (gentamicin, amikacin or tobramycin). Table 8 shows dual resistance in England in 2014 based on a defined combination of antimicrobial drugs using SGSS's AMR data.

In this analysis, the highest level of resistance was found in relation to the cephalosporin class across all three genera. Among *Enterobacter* spp., the mechanism of resistance to third-generation cephalosporins commonly reflects de-repression of chromosomal AmpC β-lactamase. Among *Enterobacter* spp. bacteraemia isolates, a small decline in resistance to both agents was observed between 2010 and 2014, from 32% to 28% for ceftazidime and from 33% to 26% for cefotaxime. Decreasing trends were also found for *Serratia* spp. reaching 13% for ceftazidime and 14% for cefotaxime in 2014. These trends most likely reflect decreased beta-lactam exposure in clinical practice. The level of resistance was comparatively lower among *Citrobacter* spp. with no evidence of change observed. The latter result may reflect the varied AmpC β-lactamase characteristics among *Citrobacter* species (e.g. *C. diversus* does not have

AmpC β-lactamase hence cannot become de-repressed and *C. freundii* behaves like *Enterobacter* spp. with the risk of AmpC β-lactamase de-repression

The proportion of isolates reported as being resistant to gentamicin was lowest among *Serratia* spp. bacteraemia isolates, fluctuating between 1% and 2%. Overall, across all genera, the level of resistance to this agent remained stable over the period. Resistance to amikacin was assessed only for *Enterobacter* spp. and *Citrobacter* spp. This is because *S. marcescens* (which accounts for the majority of *Serratia* spp.) produces a chromosomally encoded AAC(6) enzyme which can become derepressed via mutation, which affects the activity of amikacin [4]. Resistance to amikacin was rare among *Enterobacter* spp. and *Citrobacter* spp. isolates, with no evidence of change from 2010 to 214. Resistance among *Serratia* spp. isolates to tobramycin showed marked increases from 9% of isolates in 2010 to 19% in 2014 whereas for the other two genera resistance levels remained generally stable.

Resistance to piperacillin/tazobactam showed a gradual increase over the five year period for *Enterobacer* spp. (from 18% to 21%) and for *Citrobacter* spp. isolates (from 7% to 10%). This may reflect the recent switch from BSAC to EUCAST MIC breakpoint from 16 to 8 mg/L. However a decrease in resistance was evident for *Serratia* spp., down from 15% in 2010 to 9% in 2014.

Of the two carbapenems, resistance to meropenem remained uncommon in the study period across all genera with 1% or fewer of isolates reported as resistant and with a marginal increase in 2013 for *Enterobacter* spp. isolates not sustained into 2014. Resistance to ertapenem was also uncommon across all genera (1%-2%) except among *Enterobacter* spp. isolates where it was relatively higher (inter-year range between 9% -10% of isolates tested during this period) and remaining at 9% (77/871) in 2014. A small but notable increase in resistance to ertapenem was observed among *Citrobacter* spp. isolates from 0% in 2013 (0/281) to 3% in 2014 (10/369). However the underlying number of isolates resistant to ertapenem was small and it remains to be seen whether this trend will persist given that resistance to this agent was uncommon for *Citrobacter* spp. in the previous four years (inter-year range 0% - 2%).

It should be noted that EUCAST's clinical breakpoint for determining susceptibility to ertapenem is lower than that for meropenem (0.5mg/L vs 2mg/L respectively). However, the ertapenem compound is more prone to resistance due to de-repressed AmpC β-lactamase together with porin deficiency arising via mutation. Meropenem resistance is rarer owing to the higher breakpoint and lower vulnerability to this combination of mechanisms. Consequently resistance to meropenem is more likely to be due to true carbapenemases, hence of public health concern.

Although the increase in resistance to ertapenem was found only for *Citrobacter* spp. this is in the context of an increasing trend in carbapenem resistance among *Klebsiella* spp. bacteraemia isolates reported previously [3]. Despite the small underlying numbers involved for *Citrobacter* spp. (and for *Klebsiella* spp.), the increase among these bacteraemia isolates identified from PHE data is of concern and warrants close vigilance given that this class of antibiotics is a powerful last-line treatment for serious infections caused by Gram-negative bacteria. Moreover these increases are occurring in the context of the emergence of resistance to these antibiotics among Enterobacteriaceae reported internationally in recent years [5,6].

In recognition of the importance of carbapenemase-producing Enterobacteriaceae (CPE), PHE issued a toolkit in December 2013 on the identification and management of affected patients in acute healthcare settings [7]. This toolkit includes a risk assessment to identify those individuals who should be screened for colonisation or infection with CPE as part of the routine admission procedure. A toolkit for non-acute settings is to follow.

Table 5. Antibiotic susceptibility of *Enterobacter* spp. bacteraemia isolates, England, Wales and Northern Ireland: 2010-2014

	2010		2011		2012		2013		2014	
	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant
Gentamicin	1,686	5%	1,767	6%	1,673	6%	1,712	6%	1,676	6%
Ciprofloxacin	1,602	5%	1,652	5%	1,550	5%	1,618	6%	1,567	6%
Ceftazidime	1,339	32%	1,368	30%	1,288	29%	1,265	31%	1,270	28%
Cefotaxime	971	33%	998	29%	973	27%	933	26%	958	26%
Meropenem	1,229	1%	1,351	1%	1,338	1%	1,395	1%	1,457	1%
Ertapenem	248	9%	447	10%	624	9%	735	9%	871	9%
Tobramycin	472	7%	503	9%	508	7%	519	7%	541	10%
Amikacin	969	2%	961	2%	961	1%	990	1%	1,039	1%
Piperacillin/Tazobactam	1,447	18%	1,549	17%	1,467	20%	1,568	20%	1,520	21%
Total *Enterobacter* spp. reports	**1,992**		**2,011**		**1,875**		**1,920**		**1,981**	

Table 6. Antibiotic susceptibility of *Serratia* spp. bacteraemia isolates, England, Wales and Northern Ireland: 2010-2014

	2010		2011		2012		2013		2014	
	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resista	No. Tested	% Resista	No. Tested	% Resistant
Gentamicin	828	2%	817	1%	749	1%	756	2%	759	1%
Ciprofloxacin	786	12%	750	11%	695	9%	721	8%	709	6%
Ceftazidime	672	21%	634	16%	608	14%	571	16%	580	13%
Cefotaxime	492	29%	455	21%	444	20%	440	18%	440	14%
Meropenem	575	1%	627	<1	586	<1%	618	1%	652	<1%
Ertapenem	122	1%	208	1%	271	1%	327	2%	384	1%
Tobramycin	229	9%	222	9%	235	12%	238	20%	209	19%
Piperacillin/Tazobactam	705	15%	702	10%	644	9%	675	12%	690	9%
Total *Serratia* spp. reports	**941**		**881**		**814**		**832**		**889**	

Table 7. Antibiotic susceptibility of *Citrobacter* spp. bacteraemia isolates, England, Wales and Northern Ireland: 2010-2014

	2010		2011		2012		2013		2014	
	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant
Gentamicin	569	4%	683	4%	601	5%	655	4%	683	2%
Ciprofloxacin	533	4%	642	3%	568	2%	608	3%	633	4%
Ceftazidime	459	13%	521	13%	492	12%	491	14%	485	13%
Cefotaxime	313	14%	372	14%	351	11%	373	13%	375	15%
Meropenem	397	0%*	515	0%*	469	0%*	530	<1%	572	<1%
Ertapenem	84	1%	166	2%	196	1%	281	0%*	369	3%
Tobramycin	148	5%	187	6%	182	5%	204	5%	189	3%
Amikacin	303	1%	379	<1%	347	<1%	374	<1%	392	1%
Piperacillin/Tazobactam	498	7%	617	7%	552	8%	610	9%	626	10%
Total *Citrobacter* spp. reports	**678**		**788**		**694**		**748**		**799**	

*0.0% due to 0 cases

The SGSS AMR data for 2014 showed that 98% of total blood culture isolates for the three genera combined had antimicrobial susceptibility data (2,773/2,826). Multi-drug resistance was based on combinations of two different defined antibiotics (Table 8). Of all three genera, *Enterobacter* spp. bacteraemia isolates had the most common dual resistance, with 5.1% of isolates resistant to third generation cephalosporin and gentamicin. The least common dual resistance was found among *Serratia* spp. isolates in relation to ciprofloxacin and gentamicin at 0% of isolates. Resistance to all four agents (third generation cephalosporins, ciprofloxacin, gentamicin and meropenem) was not found in 2014 for these bacteraemia isolates (0%) (data not shown).

Table 8. Dual resistance among isolates of bacteraemia due to *Enterobacter* spp., *Serratia* spp. or *Citrobacter* spp., England, 2014

	3rd-G cephalosporin* and ciprofloxacin		3rd-G cephalosporin* and gentamicin		Ciprofloxacin and gentamicin	
	No. tested	% Resistant	No. tested	% Resistant	No. tested	% Resistant
***Enterobacter* spp.**	1,223	4.9	1,240	5.1	1,395	3.0
***Serratia* spp.**	516	1.7	531	0.8	607	0†
***Citrobacter* spp.**	509	2.0	514	0.8	578	1.6

*cefotaxime or ceftazidime or both; †0.0% due to 0 cases

For advice on treatment of antibiotic-resistant infections due to these organisms or for reference services including species identification and confirmation of sensitivity testing results, laboratories should contact PHE's AMRHAI Reference Unit in London [8].

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