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Laboratory surveillance of *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. bacteraemia in England, Wales and Northern Ireland: 2018

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Laboratory surveillance of *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. bacteraemia in England, Wales and Northern Ireland: 2018

These analyses are based on data relating to diagnoses of bloodstream infections caused by *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. between 2009 and 2018 in England, Wales and Northern Ireland. The data were extracted on 29 July 2019 from Public Health England's voluntary surveillance database, the Second Generation Surveillance System (SGSS). Data for Wales and Northern Ireland were extracted separately (DataStore on 30 April 2019 and CoSurv on 18 June 2019, respectively).

Rates of laboratory reported bacteraemia were calculated using mid-year resident population estimates for the respective year and geography [1]. Geographical analyses were based on the patient's residential postcode. Where this information was unknown, the postcode of the patient's General Practitioner was used. Failing that, the postcode of the reporting laboratory was used. Cases in England were further assigned to one of nine local PHE Centres (PHECs), formed from the administrative local authority boundaries [2].

The following report summarises trends and geographical distribution of *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. bacteraemia. Single-agent antimicrobial susceptibility trends are reported for England and Northern Ireland, based on SGSS AMR and CoSurv data, respectively. Multi-drug resistance trends are reported for England only. A web appendix is available featuring additional findings including data submitted to SGSS from laboratories in England.

Data presented here for earlier years may differ from those in previous publications due to the inclusion of late reports.

Key points

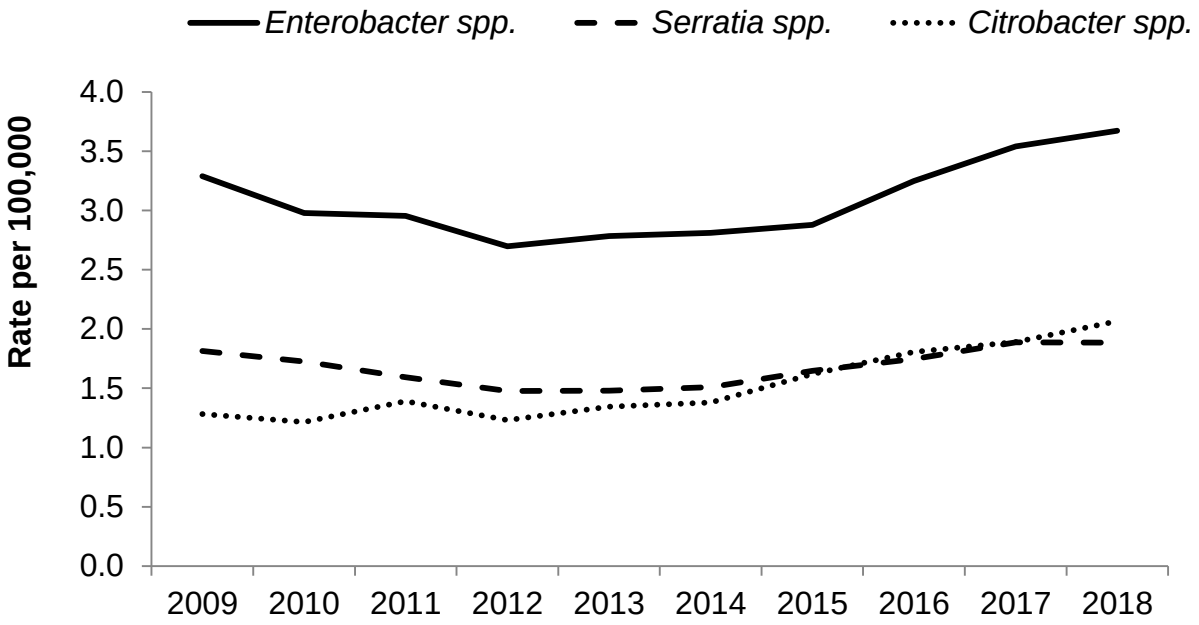
- the overall rate of *Enterobacter* spp. bacteraemia in England, Northern Ireland and Wales was 3.7 per 100,000 population (n=2,240) in 2018, a 4% increase from 2017 (3.5 per 100,000 population)
- the overall rate of *Serratia* spp. bacteraemia in England, Northern Ireland and Wales was 1.9 per 100,000 population (n=1,149) in 2018, unchanged from the rate observed in 2017
- the overall rate of *Citrobacter* spp. bacteraemia in England, Northern Ireland and Wales was 2.1 per 100,000 population (n=1,260) in 2018, a 9% increase from 2017 (1.9 per 100,000 population)
- the North East had the highest reported *Enterobacter* spp. and *Serratia* spp. bacteraemia rate in England in 2018, 4.1 and 2.3 per 100,000 population, respectively
- the North West had the lowest *Enterobacter* spp. and *Citrobacter* spp. bacteraemia rate in England in 2018, 3.0 and 1.6 per 100,000 population, respectively
- rates of *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. bacteraemia were higher in the elderly (aged ≥75 years) and infants (<1 year) than other age groups and higher for males compared to females overall, but particularly in the elderly
- across all three genera the proportion of isolates resistant to the third-generation cephalosporins remains highest when assessing antimicrobial susceptibility to single agents (12-26% resistance depending on genus)
- among the single-agent carbapenems tested, the highest non-susceptibility observed was to ertapenem in *Enterobacter* spp. isolates (6% in 2018)
- *Enterobacter* spp. isolates exhibited the highest frequency of multi-drug resistance, with 6% resistance to the combination of gentamicin and third-generation cephalosporins
- multi-drug resistance to all four classes of antibiotics remains rare (<1%) for all three genera

Trends

Figure 1 shows ten-year trends in the annual rate (per 100,000 population) of laboratory-reported bacteraemia by genus for England, Northern Ireland and Wales.

Since 2013 there has been a year-on-year increase in bacteraemia rates across all three genera, until 2018 when the *Serratia* spp. bacteraemia rate stabilized at 1.9 per 100,000 population. For *Serratia* and *Citrobacter* spp., the biggest increase was observed between 2014 and 2015 (9% and 17%, respectively) whereas for *Enterobacter* spp., the most pronounced increase was between 2015 and 2016. Assessing recent changes from 2017 to 2018 across all three genera, the greatest annual increase was seen in the *Citrobacter* spp. bacteraemia rate (1.9 per 100,000 to 2.1 per 100,000). The *Enterobacter* spp. bacteraemia rate has shown the steepest incline in trend overall. While the rate continued to increase from 3.5 per 100,000 in 2017 to 3.7 per 100,000 in 2018; this annual increase was smaller than that observed in the previous year (4% vs 9%).

Figure 1. *Enterobacter* spp., *Serratia* spp., and *Citrobacter* spp. bacteraemia rate per 100,000 population (England, Northern Ireland and Wales): 2009 to 2018



Geographic distribution

In 2018, the combined rate of reported *Enterobacter* spp. bacteraemia for England, Northern Ireland and Wales was 3.7 per 100,000 population, an increase of 4% from 2017 (see table 1a). The *Enterobacter* spp. bacteraemia rate in England has increased steadily since 2015. Northern Ireland saw the greatest percentage increase in 2018 compared to 2017 (22%), returning to the bacteraemia rate of 3.8/100,000 reported in 2015. Wales remained relatively stable between 2017 and 2018 (3.8/ 100,000 in 2018) after a prior decline in 2017.

Within England, there was variation among the nine PHECs. All PHECs had higher rates of *Enterobacter* bacteraemia in 2018 compared to 2014. The relative increase from 2017 to 2018 was greatest for Yorkshire and Humber (2.7 to 3.6 per 100,000). While in 2017 the region had reported the lowest rate of *Enterobacter* spp. bacteraemia, in 2018 the lowest rate was seen in the North West (3.0/100,000). The highest rate of *Enterobacter* spp. bacteraemia in 2018 was in the North East (4.1/100,000) (see figure 2a).

Table 1a. Rate of *Enterobacter* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Northern Ireland and Wales): 2014 to 2018

		Rate per 100,000				
Region	**PHE Centre**	**2014**	**2015**	**2016**	**2017**	**2018**
North of England	North East	2.6	2.9	3.6	4.2	4.1
	North West	2.8	2.8	2.9	3.0	3.0
	Yorkshire and Humber	1.7	2.3	2.6	2.7	3.6
Midlands and East of England	East of England	2.8	2.9	3.4	3.7	3.8
	East Midlands	3.0	3.7	3.7	4.1	4.0
	West Midlands	2.9	2.6	2.9	3.3	3.7
London	London	2.8	2.9	3.3	4.0	3.9
South of England	South East	2.7	2.9	3.3	3.7	3.6
	South West	2.8	2.7	3.2	3.5	3.5
England		2.7	2.8	3.2	3.5	3.7
Northern Ireland		3.9	3.1	3.8	3.1	3.8
Wales		4.0	3.7	4.0	3.7	3.8
England, Northern Ireland and Wales		**2.8**	**2.9**	**3.3**	**3.5**	**3.7**

Figure 2a. Geographical distribution of *Enterobacter* spp. bacteraemia rates per 100,000 population (England, Northern Ireland and Wales): 2018

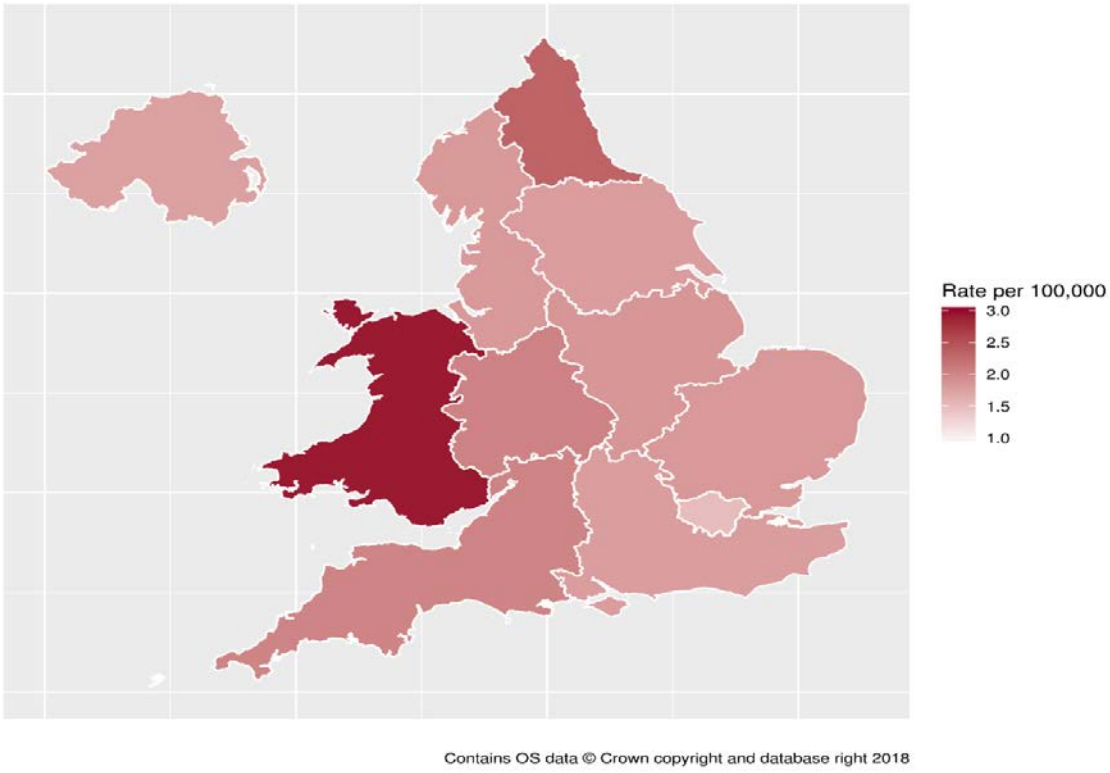
The combined rate of reported *Serratia* spp. bacteraemia for England, Northern Ireland and Wales was 1.9 per 100,000 population, the same as reported in 2017 (see table 1b). The bacteraemia rate in England remained stable between 2017 and 2018 at 1.8/100,000. Northern Ireland saw the greatest annual increase from 1.1 to 1.8/100,000. Rates in Wales remained above those in England and Northern Ireland although a 10% decrease was see from 2017 to 2018 (3.3 to 2.9 per 100,000).

Across the regions in England, the North East reported the highest bacteraemia rate in 2018 (2.3/100,000), while London reported the lowest (1.5/100,000) (see figure 2b). The percentage increase from 2017 was greatest for Yorkshire and Humber (1.3 to 1.8 per 100,000). London had the greatest decrease compared to 2017 (2.0 to 1.5 per 100,000).

Table 1b. Rate of *Serratia* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Northern Ireland and Wales): 2014 to 2018

		Rate per 100,000				
Region	**PHE Centre**	**2014**	**2015**	**2016**	**2017**	**2018**
North of England	North East	1.8	2.2	1.9	2.4	2.3
	North West	1.8	1.7	2.0	1.8	1.8
	Yorkshire and Humber	1.0	1.1	1.5	1.3	1.8
Midlands and East of England	East of England	1.7	1.4	1.5	1.9	1.8
	East Midlands	1.1	1.4	1.4	2.0	1.9
	West Midlands	1.3	1.3	1.8	2.0	2.0
London	London	1.8	1.8	1.7	2.0	1.5
South of England	South East	1.1	1.6	1.6	1.6	1.8
	South West	1.5	1.5	1.7	1.9	2.0
England		1.5	1.5	1.7	1.8	1.8
Northern Ireland		1.4	1.9	1.8	1.1	1.8
Wales		2.5	3.4	2.7	3.3	2.9
England, Northern Ireland and Wales		**1.5**	**1.6**	**1.7**	**1.9**	**1.9**

Figure 2b. Geographical distribution of *Serratia* spp. bacteraemia rates per 100,000 population (England, Northern Ireland and Wales): 2018



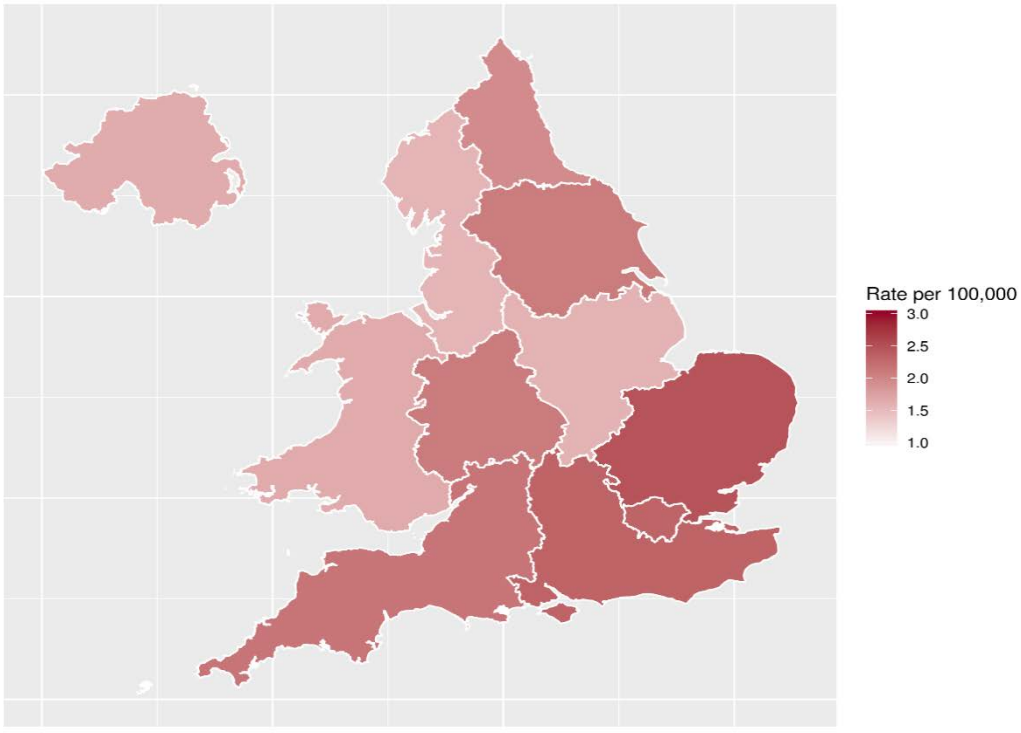
The combined rate of reported *Citrobacter* spp. bacteraemia for England, Northern Ireland and Wales was 2.1 per 100,000 population, an increase of 9% since 2017. Individually, bacteraemia rates in 2018 increased across all countries compared to 2017. The greatest annual increase was seen in Northern Ireland, from 1.2 to 1.6/100,000.

Across the regions in England, East of England reported the highest bacteraemia rate in 2018 (2.5/100,000), while East Midlands and North West reported the lowest (both 1.6 per 100,000). The North West reported the lowest *Citrobacter* spp. bacteraemia rates since 2015. The percentage increase from 2017 was greatest in the North East (1.4 to 2.0 per 100,000).

Table 1c. Rate of *Citrobacter* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Northern Ireland and Wales): 2014 to 2018

		Rate per 100,000				
Region	**PHE Centre**	**2014**	**2015**	**2016**	**2017**	**2018**
North of England	North East	1.1	1.8	1.5	1.4	2.0
	North West	1.2	1.2	1.3	1.2	1.6
	Yorkshire and Humber	0.9	1.7	1.3	1.6	2.1
Midlands and East of England	East of England	1.6	1.7	1.9	2.2	2.5
	East Midlands	1.3	1.6	1.6	1.7	1.6
	West Midlands	1.7	1.7	1.8	1.9	2.1
London	London	1.7	1.8	2.2	2.4	2.3
South of England	South East	1.3	1.6	2.2	2.4	2.3
	South West	1.5	1.9	2.0	1.8	2.2
England		1.4	1.6	1.8	1.9	2.1
Northern Ireland		0.8	1.1	1.2	1.2	1.6
Wales		1.6	1.5	1.9	1.5	1.7
England, Northern Ireland and Wales		**1.4**	**1.6**	**1.8**	**1.9**	**2.1**

Figure 2c. Geographical distribution of *Citrobacter* spp. bacteraemia rates per 100,000 population (England, Northern Ireland and Wales): 2018



It is important to note differences in the way data are collected between the three countries. In England and Northern Ireland, microbiology laboratories electronically report clinically significant isolates to SGSS or CoSurv, respectively. In Wales, data are collected by extraction from a single laboratory information system used by all the microbiology laboratories. The system extracts all positive blood cultures, including those not thought to be clinically significant.

Other factors may account for the variation observed between regions. These include completeness of reporting, local outbreaks, as well as different resident populations and distribution of specialist care units.

Species distribution

The total number of *Enterobacter* spp. bacteraemia reports increased by 4% from 2017 to 2018 (2,145 to 2,240 isolates). Due to the reclassification of *Enterobacter aerogenes* as *Klebsiella aerogenes,* overall isolate numbers for *Enterobacter* spp. are lower to those previously reported. As in previous years, approximately 90% of reported *Enterobacter* spp. bacteraemia isolates were identified to species level (see table 2a). The most predominant species remains *E. cloacae,* presented here as part of the *E. cloacae* complex (88.6%).

Table 2a. Reports of *Enterobacter* spp. bacteraemia by species (England, Northern Ireland and Wales): 2014 to 2018

	2014		2015		2016		2017		2018	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
***Enterobacter* spp.**	**1,665**	**100**	**1,718**	**100**	**1,954**	**100**	**2,145**	**100**	**2,240**	**100**
E. amnigenus	4	0.2	11	0.6	5	0.3	1	0.1	0	0.0
E. cloacae complex*	1,439	86.4	1,510	87.9	1,722	88.1	1,902	88.7	1,985	88.6
E. gergoviae	4	0.2	7	0.4	5	0.3	4	0.2	8	0.4
E. intermedius	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
E. sakazakii	13	0.8	6	0.3	2	0.1	3	0.1	2	0.1
Enterobacter spp., other named	56	3.4	24	1.4	26	1.3	26	1.2	26	1.2
Enterobacter spp., species not recorded	148	8.9	160	9.3	194	9.9	208	9.7	219	9.8

*****Species of the *Enterobacter cloacae* complex reported: *E. absuriae*, *E. cancerogenus, E. cloacae* (predominant), *E. hormaechei, E. kobei,* and *E. ludwigii*

Of the 1,149 isolates of *Serratia* spp. bacteraemia reported in 2018, 95% were identified to species level. While overall species identification remains very high for this genus, the *per cent* of species not recorded in 2018 did increase from previous years (4.7% compared to 2.8% in 2017). The most predominant species remains *S. marcescens* (87.0%) (see table 2b).

Table 2b. Reports of *Serratia* spp. bacteraemia by species (England, Northern Ireland and Wales): 2014 to 2018

	2014		2015		2016		2017		2018	
	No.	%	No.	%	No.	%	No.	%	No.	%
***Serratia* spp.**	**894**	100	**984**	100	**1,052**	100	**1,144**	100	**1,149**	100
S. ficaria	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
S. fonticola	3	0.3	2	0.2	7	0.7	5	0.4	1	0.1
S. liquefaciens	74	8.3	86	8.7	87	8.3	86	7.5	72	6.3
S. marcescens	760	85.0	838	85.2	920	87.4	1,009	88.2	1,000	87.0
S. odorifera	2	0.2	7	0.7	4	0.4	7	0.6	4	0.3
S. plymuthica	0	0.0	2	0.2	0	0.0	0	0.0	3	0.3
S. proteamaculas	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
S. rubidaea	1	0.1	5	0.5	1	0.1	3	0.3	3	0.3
S. ureilytica	0	0.0	0	0.0	3	0.3	1	0.1	8	0.7
Serratia spp., other named	20	2.2	2	0.2	0	0.0	1	0.1	4	0.3
Serratia spp., species not recorded	33	3.7	41	4.2	30	2.8	32	2.8	54	4.7

The total number of *Citrobacter* spp. bacteraemia reports increased by 10% from 2017 to 2018 (1,146 to 1,260 isolates). 94% of reported *Citrobacter* spp. bacteraemia isolates were identified to species level in 2018, as in the previous year. The predominant species remain *C. koseri (*formerly *C. diversus),* which accounted for 53.5% of identified species in 2018 and *C. freundii,* which accounted for 34.4% of identified species in 2018 (see table 2c).

Table 2c. Reports of *Citrobacter* spp. bacteraemia by species (England, Northern Ireland and Wales): 2014 to 2018

	2014		2015		2016		2017		2018	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
***Citrobacter* spp.**	**818**	**100**	**968**	**100**	**1,088**	**100**	**1,146**	**100**	**1,260**	**100**
C. amalonaticus	4	0.5	5	0.5	5	0.5	3	0.3	10	0.8
C. braakii	4	0.5	28	2.9	30	2.8	34	3.0	38	3.0
C. farmeri	2	0.2	4	0.4	4	0.4	1	0.1	4	0.3
C. freundii	303	37.0	336	34.7	355	32.6	377	32.9	434	34.4
C. gillenii	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
*C. koseri (*formerly *C. diversus)*	374	45.7	484	50.0	569	52.3	633	55.2	674	53.5
C. sedlakii	0	0.0	1	0.1	1	0.1	2	0.2	2	0.2
C. werkmanii	0	0.0	4	0.4	1	0.1	1	0.1	1	0.1
C. youngae	1	0.1	3	0.3	7	0.6	9	0.8	7	0.6
Citrobacter spp., other named	54	6.6	37	3.8	40	3.7	16	1.4	14	1.1
Citrobacter spp., species not recorded	76	9.3	66	6.8	76	7.0	70	6.1	75	6.0

In 2018, one report of *C. gillenii* was made. While the increased use of automated diagnostic technology (MALDI-TOF) has enhanced the capability of laboratories to distinguish species over time, the identification of *Citrobacter* species remains challenging as the species of this genus have very similar patterns [3].

Of the most frequently reported causes of bacteraemia/fungaemia in England, Northern Ireland, and Wales in 2017, *Enterobacter cloacae* complex featured as the 13th most commonly reported (accounting for only 0.9% of monomicrobial infections) and *Serratia marcescens* as the 17th most reported pathogen (0.6% of monomicrobial infections) [4].

Age and sex distribution

Figures 3a-c show age and sex-specific bacteraemia rates of *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. in 2018. As in previous years, *Serratia* spp. and *Citrobacter* spp. bacteraemia rates were highest for the older age groups (≥65 years), particularly in the elderly (aged ≥75 years). Bar charts show a j-shaped curve as higher rates were also seen amongst the youngest age group (<1 year). The *Enterobacter* spp. bacteraemia rate was also high from middle to older age groups, but the highest reported rate was in the <1 year age group.

Across all genera, the overall rate of infection was higher among males than females. This difference was most pronounced in persons aged 75 years and older; the male bacteraemia rate was threefold higher than the female rate for *Enterobacter* spp., twofold higher for *Serratia* spp. and fourfold higher for *Citrobacter* spp.

Figure 3a. *Enterobacter* spp. bacteraemia rates by age and sex (England, Northern Ireland and Wales): 2018

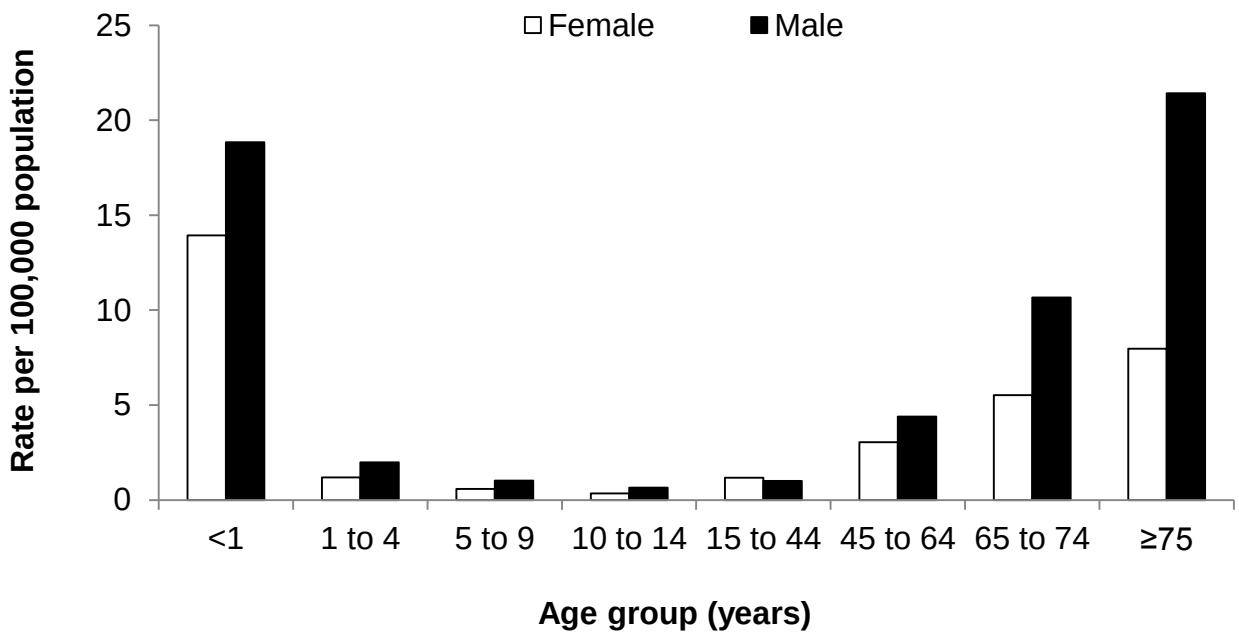


Figure 3b. *Serratia* spp. bacteraemia rates by age and sex (England, Northern Ireland and Wales): 2018

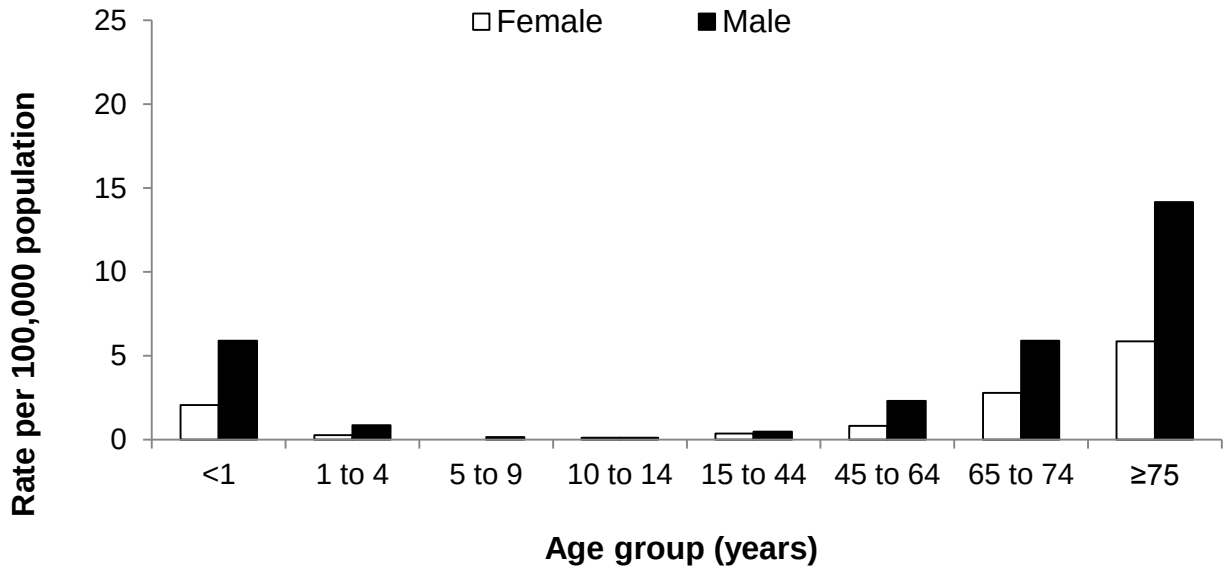
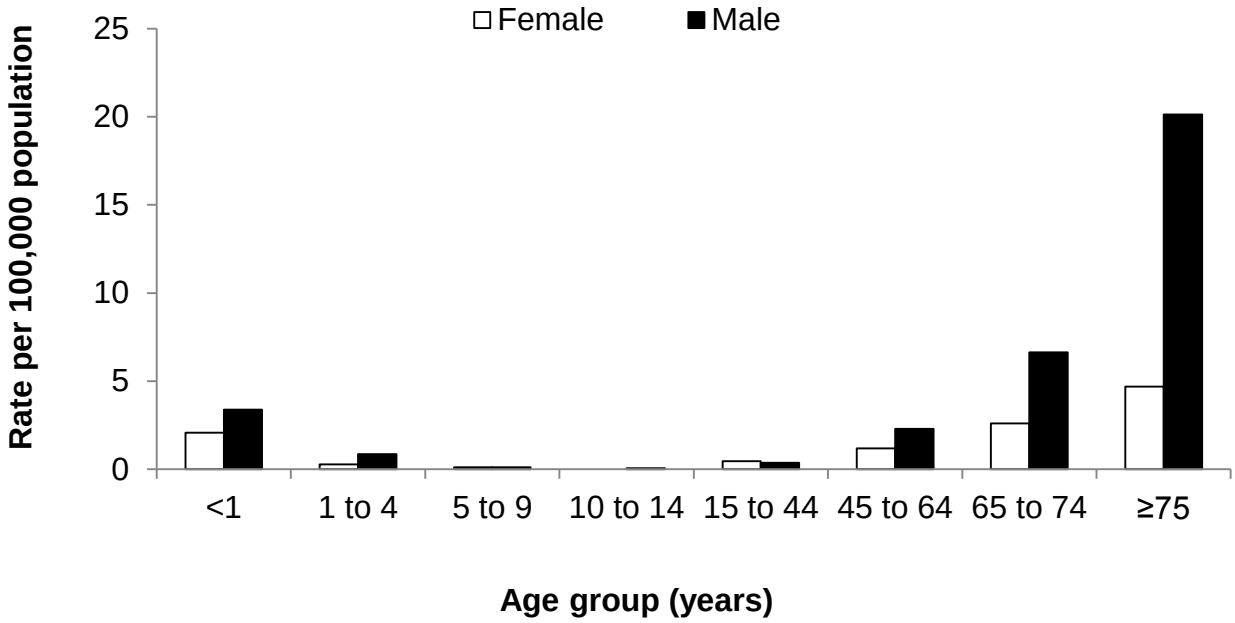


Figure 3c. *Citrobacter* spp. bacteraemia rates by age and sex (England, Northern Ireland and Wales): 2018



Antimicrobial resistance: England and Northern Ireland

Tables 3a-c present reported antibiotic susceptibility trends for *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. isolates from 2015 to 2018 for England and Northern Ireland. In 2018, the proportion of *Enterobacter* spp. isolates with reported susceptibility test results ranged from 45% for tobramycin to 98% for gentamicin. The percentage of resistant *Enterobacter* spp. isolates was highest for cefotaxime (26%), ceftazidime (25%) and piperacillin/tazobactam (15%) (see table 3a). While the prevalence of cefotaxime resistance had increased markedly in 2017, a decrease was seen in 2018 (31% to 26%). Similarly, reported ceftazidime resistance was lower in 2018 compared to 2017 (28% to 25%). IMI carbapenemases, named based on their ability to hydrolyse the antibiotic imipenem, have been sporadically identified in Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) submissions since 2010 for *Enterobacter* spp. isolates, particularly in those species within the *Enterobacter cloacae* complex. In 2016, AMRHAI identified an *E. cloacae* complex strain that produced a plasmid encoded FRI carbapenemase, which was only the second report globally of this family of carbapenemase. To date however, these reports are from patients who have been colonised with these carbapenemase-producing strains, rather than infected. IMI and FRI represent rarer class A carbapenemases outside of the 'big 5' families. As most commercial and in-house molecular assays will tend to focus on the detection of the 'big 5' families however, these other carbapenemase families have the potential to pose a problem for infection prevention and control [5-6]. The *per cent* of isolates reported as non-susceptible to carbapenems in 2018 remains low, particularly for meropenem. From 2017 to 2018 however, reported meropenem resistance increased from 1% to 2% while ertapenem resistance remained stable at 6%.

In 2018, the proportion of *Serratia* spp. isolates with reported susceptibility test results ranged from 43% for tobramycin to 95% for gentamicin and meropenem. The percentage of resistant *Serratia* spp. isolates was highest for cefotaxime (16%), ceftazidime (13%) and tobramycin (10%) (see table 3b). Resistance to the third-generation cephalosporins remained relatively stable from 2017 to 2018 (ceftazidime: 14% to 13% and cefotaxime: 17% to 16%). Reported tobramycin resistance continued to decrease from 2016 (18% to 14% to 10%); results however, should be interpreted with caution as less than half of isolates had susceptibility test results reported for this agent. Resistance to gentamicin, an

aminoglycoside preferred for treatment for *Serratia* species, was uncommon at 1%. Carbapenemase-producing *S. marcescens* isolates were reported to be circulating at very low levels in the UK as of 2015, however only one of these was isolated from a bloodstream infection [5, 7]. In 2018, reported non-susceptibility to meropenem and ertapenem remained relatively rare (<1%).

In 2018, the proportion of *Citrobacter* spp. isolates with reported susceptibility test results ranged from 42% for tobramycin to 95% for gentamicin. The percentage of resistant *Citrobacter* spp. isolates was highest for cefotaxime and ceftazidime (both 12%), as well as piperacillin/tazobactam (7%) (see table 3c). Single-agent antimicrobial resistance rates have remained relatively stable among reported *Citrobacter* spp. isolates since 2015 (varying only by 1-2%). Overall resistance across all presented agents remains lower in comparison to the other two genera, particularly for tobramycin (3% resistance in 2018).

Table 3a. Antibiotic susceptibility* for *Enterobacter* spp. bacteraemia in England and Northern Ireland: 2015 to 2018

	2015			2016			2017			2018		
Antimicrobial agent	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**
Gentamicin	94	0	6	94	0	5	95	0	5	93	1	7
Ciprofloxacin	94	1	5	94	1	5	94	2	5	93	1	6
Ceftazidime	75	1	23	73	1	25	70	2	28	73	2	25
Cefotaxime	77	1	22	75	1	24	68	2	31	73	1	26
Meropenem	99	1	1	99	1	0	98	1	1	98	1	2
Ertapenem	92	4	5	91	4	5	91	3	6	91	3	6
Tobramycin	90	1	10	91	1	7	94	0	6	91	0	9
Amikacin	99	1	1	99	1	0	98	1	0	98	1	1
Piperacillin/tazobactam	82	2	16	81	2	16	80	2	18	83	2	15

*__S__ = susceptible; __I__ = intermediate (reduced susceptibility); __R__ = resistant

Table 3b. Antibiotic susceptibility* for *Serratia* spp. bacteraemia in England and Northern Ireland: 2015 to 2018

	2015			2016			2017			2018		
Antimicrobial agent	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**
Gentamicin	98	1	1	98	1	2	98	0	2	99	0	1
Ciprofloxacin	94	2	4	95	2	3	94	2	4	94	1	4
Ceftazidime	88	1	11	88	2	9	85	1	14	87	0	13
Cefotaxime	85	2	13	84	1	15	81	2	17	83	1	16
Meropenem	99	0	0	100	0	0	100	0	0	100	0	0
Ertapenem	99	0	1	99	0	1	99	0	1	99	0	1
Tobramycin	75	11	15	70	12	18	75	11	14	80	10	10
Amikacin	92	4	4	88	8	5	86	10	4	94	5	1
Piperacillin/tazobactam	91	1	8	91	1	8	90	1	9	91	0	8

* __S__ = susceptible; __I__ = intermediate (reduced susceptibility); __R__ = resistant

Table 3c. Antibiotic susceptibility* for *Citrobacter* spp. bacteraemia in England and Northern Ireland: 2015 to 2018

	2015			2016			2017			2018		
Antimicrobial agent	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**	**S (%)**	**I (%)**	**R (%)**
Gentamicin	96	0	3	97	0	3	96	0	3	97	0	2
Ciprofloxacin	97	0	3	97	1	2	97	0	3	97	1	2
Ceftazidime	86	0	14	89	2	10	88	1	10	87	1	12
Cefotaxime	88	2	11	90	1	9	87	0	13	87	1	12
Meropenem	100	0	0	100	0	0	100	0	0	99	0	0
Ertapenem	99	1	1	100	0	0	100	0	0	99	0	1
Tobramycin	95	0	5	96	0	4	93	1	5	97	0	3
Amikacin	99	1	0	99	0	0	98	1	1	99	0	1
Piperacillin/tazobactam	90	1	8	91	1	8	92	2	6	90	3	7

* **S** = susceptible; **I** = intermediate (reduced susceptibility); **R** = resistant

Tables 4a-c show multi-drug resistance testing results for *Enterobacter* spp.*, Citrobacter* spp. and *Serratia* spp. for England from 2015 to 2018. This analysis examined combinations for four classes of antibiotics: third-generation cephalosporins (any of cefotaxime, ceftazidime, ceftriaxone or cefpodoxime), a fluoroquinolone (ciprofloxacin), carbapenems (meropenem) and an aminoglycoside (gentamicin).

Multi-drug resistance to a combination of all four classes of antibiotics remains rare (<1%) across all three genera. *Enterobacter* spp. exhibited the highest frequency of multi-drug resistance for all tested antibiotic combinations compared to the other two genera. The proportion of resistant *Enterobacter* spp. isolates was highest for the combination of gentamicin and third-generation cephalosporins (6%). The *per cent* resistant has increased from 2017 when it was 4% of reported results. The second highest reported resistance was for the combination of ciprofloxacin and third-generation cephalosporins, although this has remained stable at 4% since 2015. Reported resistance of *Serratia* spp. and *Citrobacter* spp. isolates to the antimicrobial combinations analysed remained low in 2018 (<3%).

Table 4a. Multi-drug antimicrobial testing and resistance summary* for *Enterobacter* spp. bacteraemia (England): 2015 to 2018

	2015		2016		2017		2018	
Antimicrobial combinations	**No. tested**	**R (%)**	**No. tested**	**R (%)**	**No. tested**	**R (%)**	**No. tested**	**R (%)**
Gentamicin and ciprofloxacin	1,418	3	1,710	2	1,957	2	1,998	3
Gentamicin and 3rd gen cephalosporin†	1,424	5	1,710	4	1,969	4	2,023	6
Gentamicin and meropenem	1,404	0	1,686	0	1,941	0	2,008	1
Ciprofloxacin and 3rd gen cephalosporin†	1,400	4	1,698	4	1,961	4	2,020	4
Ciprofloxacin and meropenem	1,378	0	1,675	0	1,928	0	2,004	1
3rd gen cephalosporin† and meropenem	1,385	1	1,683	0	1,947	1	2,037	2
Gentamicin, ciprofloxacin, 3rd gen cephalosporin† and meropenem	1,359	0	1,635	0	1,861	0	1,920	1

† cefotaxime, ceftazidime, ceftriaxone, cefpodoxime

Table 4b. Multi-drug antimicrobial testing and resistance summary* for *Serratia* spp. bacteraemia (England): 2015 to 2018

	2015		2016		2017		2018	
Antimicrobial combinations	**No. tested**	**R (%)**	**No. tested**	**R (%)**	**No. tested**	**R (%)**	**No. tested**	**R (%)**
Gentamicin and ciprofloxacin	762	0	890	1	969	0	959	0
Gentamicin and 3rd gen cephalosporin†	769	1	887	1	978	1	986	1
Gentamicin and meropenem	760	0	879	0	953	0	983	0
Ciprofloxacin and 3rd gen cephalosporin†	759	2	885	2	979	3	969	2
Ciprofloxacin and meropenem	746	0	874	0	952	0	963	0
3rd gen cephalosporin† and meropenem	753	0	872	0	968	0	988	0
Gentamicin, ciprofloxacin, 3rd gen cephalosporin† and meropenem	728	0	850	0	920	0	923	0

† cefotaxime, ceftazidime, ceftriaxone, cefpodoxime

Table 4c. Multi-drug antimicrobial testing and resistance summary* for *Citrobacter* spp. bacteraemia (England): 2015 to 2018

	2015		2016		2017		2018	
Antimicrobial combinations	**No. tested**	**R (%)**	**No. tested**	**R (%)**	**No. tested**	**R (%)**	**No. tested**	**R (%)**
Gentamicin and ciprofloxacin	841	1	986	1	1,021	1	1,086	1
Gentamicin and 3rd gen cephalosporin†	850	2	993	1	1,026	1	1,098	1
Gentamicin and meropenem	826	0	961	0	998	0	1,073	0
Ciprofloxacin and 3rd gen cephalosporin†	832	2	975	1	1,022	1	1,086	1
Ciprofloxacin and meropenem	809	0	941	0	991	0	1,052	0
3rd gen cephalosporin† and meropenem	821	0	955	0	1,010	0	1,079	0
Gentamicin, ciprofloxacin, 3rd gen cephalosporin† and meropenem	801	0	926	0	950	0	1,024	0

† cefotaxime, ceftazidime, ceftriaxone, cefpodoxime

Microbiology services

For advice on treatment of antibiotic-resistant infections caused by these opportunistic pathogens, laboratories should contact the Medical Microbiologists at PHE's Bacteriology Reference Department in Colindale (colindalemedmicro@phe.gov.uk). 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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