Public Health England

Health Protection Report
weekly report

Infection report

Volume 10 Number 19 Published on: **17 June 2016**

Bacteraemia

Voluntary surveillance of bacteraemia caused by *Escherichia coli* in England: 2008-2015

These analyses are based on data relating to diagnoses of bloodstream infections caused by *E. coli*. between 2011 and 2015 in England, extracted on 25 April 2016 from Public Health England's (PHE) voluntary surveillance database Second Generation Surveillance System (SGSS). Data for Wales and Northern Ireland were extracted separately (DataStore on 10 April 2016 and CoSurv on 17 May 2016 resepctively) and are included in the geographical and species analyses only.

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). Compared to CDR's antimicrobial susceptibility data, the AMR module captures more comprehensive antibiogram data (involving all antibiotics tested); however, until the launch of SGSS in 2014 there was lower laboratory coverage to the AMR module. Therefore, antimicrobial non-susceptibility trends cannot currently be undertaken using data from the AMR module but data for 2015 were extracted to assess multi-drug resistance rates.

The data presented here may differ from data in previous publications due to inclusions of late reports.

Rates of bacteraemia laboratory reports were calculated using mid-year resident population estimates for the respective year and geography with the exception of 2015 rates, which were based on 2014 population estimates as population estimates for 2015 were not available at the time of producing this report [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.

The report includes analyses on the trends, age and sex distribution, level of ascertainment, and antibiotic susceptibility of *E. coli* bacteraemia cases in England. In addition, analysis of resistance to more than one antibiotic is based on England's data reported to the AMR module (previously AmSurv) and extracted on 25 April 2016.

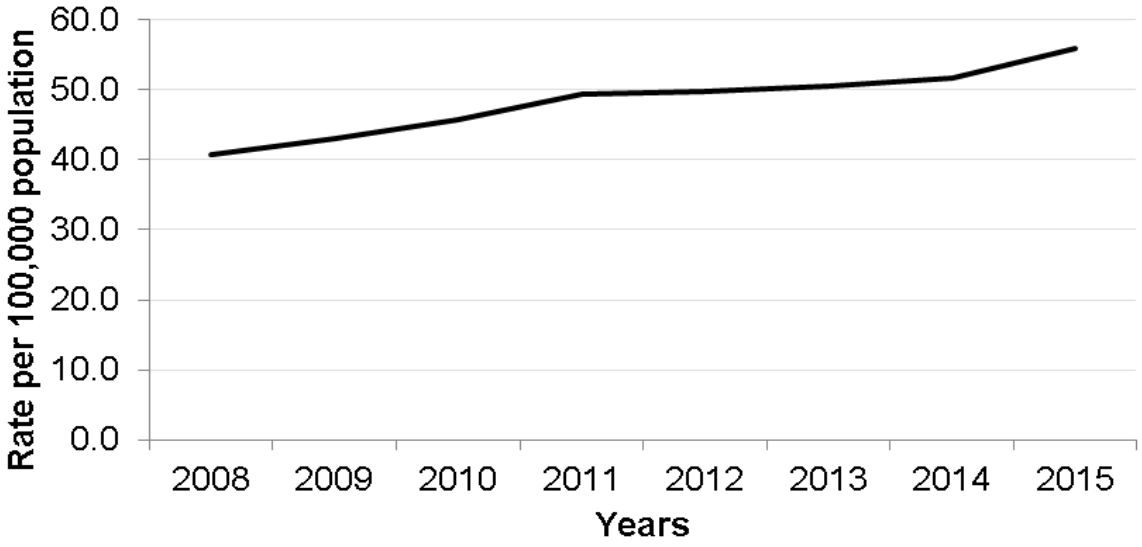
Key points

- There has been a sustained year-on-year increase in the number of *E. coli* bacteraemia.
- In 2015, the rate of *E. coli* bacteraemia per 100,000 population was highest in Northern Ireland (80.7) followed by Wales (74.9) and England (56.0), with an overall rate for England, Wales and Northern Ireland of 57.7 reports per 100,000 population.
- Between 2011 and 2015, the overall rate of *E. coli* bacteraemia in England, Wales and Northern Ireland increased by 14% (50.7 to 57.7 reports per 100,000 population)
- Between 2011 and 2015, England, Wales and Northern Ireland rates increased by 13.5% 11.9% and 30.7% respectively. However between 2014 and 2015 the rates only increased in England and Northern Ireland, while it decreased by 7% in Wales.
- The age group with the highest rates of *E. coli* bacteraemia in England were observed among the elderly (75 years and over) with 402.9 and 313.5 reports per 100,000 population for males and females respectively.
- In 2015, the highest rate of *E. coli* bacteraemia within England was observed in the Devon, Cornwall and Somerset PHE centre (86.0 reports per 100,000 population), while the lowest was observed in Wessex (36.0 reports per 100,000 population)
- The antibiotic non-susceptibility of *E. coli* isolates to selected antimicrobials increased between 2011 and 2015, non-susceptibility to piperacillin/tazobactam and Amoxycillin\clavulanate increased from 8.5% to 11.7% and from 31.5% to 42.2% respectively. However this is due to a change in the Minimum Inhibitory Concentration (MIC) breakpoint within that period (data for England only).
- A total of 3,292 isolates were non–susceptible to third generation cephalosporins. 65.9% (n=2,169) and 37.6% (n=1,237) of these were also non-susceptible to ciprofloxacin and gentamicin respectively.
- Comparison of voluntary reporting with the mandatory surveillance dataset showed a case ascertainment rate of 81.6% in 2015 (data for England only).

Trends in episode numbers and rates: England

There has been an increasing trend in rates of reported *E. coli* bacteraemia in England over the last eight years, with a slight plateau between 2011 to 2013 (figure 1). The overall increase was 37.2% (40.8 to 56.0 reports per 100,000 population).

Figure 1. *E. coli* bacteraemia rate per 100,000 population in England: 2008 to 2015



Geographical distribution: England, Wales and Norther Ireland

The overall rate of reported *E. coli* bacteraemia in England, Wales and Northern Ireland increased by 14.0% (50.7 to 57.7 reports per 100,000 population, table 1) between 2011 and 2015. In the most recent year 2015, compared to the rate in 2014, the rate of *E. coli* bacteraemia increased by 6.9% (54.0 and 57.7 reports per 100,000 population).

Between 2011 and 2015 the rate of *E. coli* bacteraemia in England alone increased by 13.5% (from 49.3 to 56.0 reports per 100,000 population). In Wales, this increase was slightly lower at 11.9% (from 67.0 to 74.9 reports per 100,000 population) while in Northern Ireland, the rate increased by 30.7% (from 61.8 to 80.7 reports per 100,000 population) (table 1). However, between 2014 and 2015, only the rates in England (51.8 to 56.0 reports per 100,000 population) and Northern Ireland (74.9 to 80.7 reports per 100,000 population) increased, while it decreased by 7% in Wales (80.6 to74.9 reports per 100,000 population) (table 1).

The percentage change in rates has varied among PHE centres over time; between 2011 and 2015 only one PHE centre, Greater Manchester, observed a decrease (8.7%; from 65.8 to 60.1 reports per 100,000 population, respectively) in its rate of reported *E. coli* bacteraemia. During the same period, (2011-2015) the highest increases were observed in South Midlands and Hertfordshire (38.6%: 27.4 to 38.0 reports per 100,000 population) and Avon, Gloucestershire and Wiltshire (30.8%: 35.0 to 45.8 reports per 100,000 population) (table 1). Conversely, in recent years (2014-2015) the highest increases were observed in Wessex (22.8%; 29.3 to 36.0 reports per 100,000 population) and Yorkshire and Humber (22.1%; 44.0 to 53.7 reports per 100,000 population) (table 1). However, caution is required when interpreting these increases as we are yet to ascertain if they represent increases of bacteraemia within the area or artefacts of organisational/laboratory restructuring.

Figure 2. Geographical distribution of *E. coli* bacteraemia rates per 100,000 population (England, Wales, and Northern Ireland): 2015

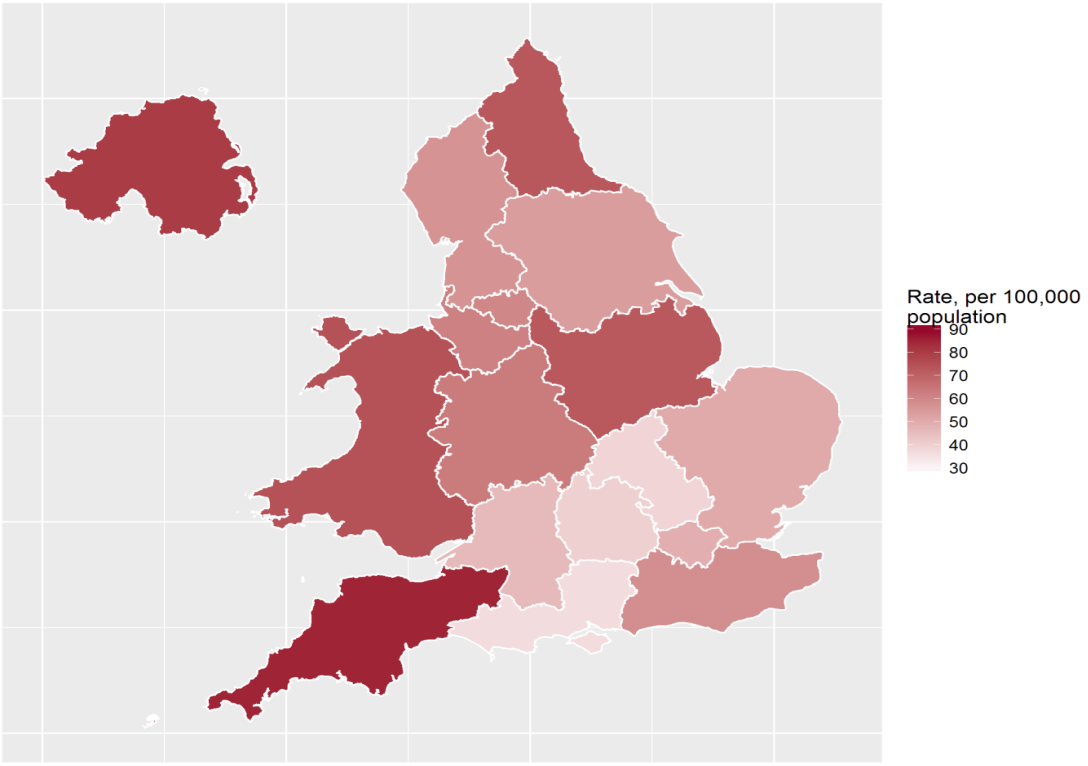


Table 1. *E. coli* bacteraemia rate per 100,000 population by region (England, Wales, and Northern Ireland): 2011to 2015

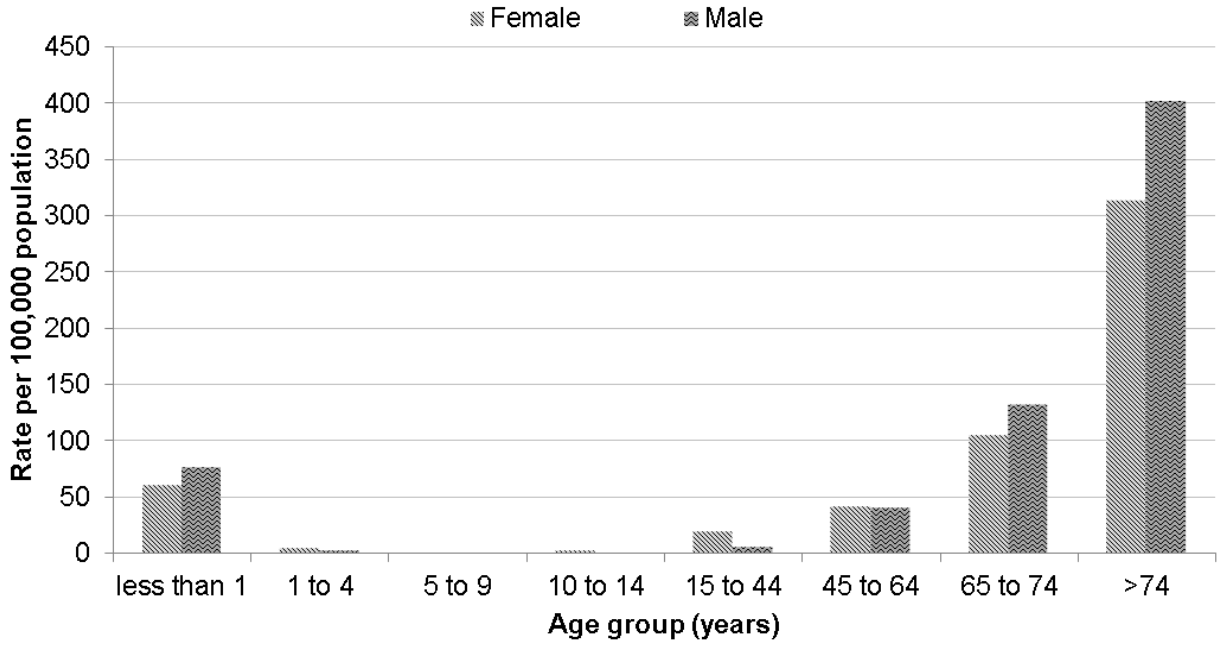
Region		Rate per 100,000				
		2011	**2012**	**2013**	**2014**	**2015**
London	London	44.5	45.0	46.9	46.8	48.9
Midlands	South Midlands and Hertfordshire	27.4	35.7	36.5	40.5	38.0
	East Midlands	62.3	60.8	61.5	65.1	73.1
	Anglia and Essex	47.5	50.0	50.4	50.5	50.0
	West Midlands	54.6	52.3	54.5	58.6	63.6
Northern	Cheshire and Merseyside	57.7	61.1	62.2	62.6	61.8
	Cumbria and Lancashire	50.1	51.5	54.3	56.4	56.6
	Greater Manchester	65.8	61.1	61.7	57.4	60.1
	North East	62.7	66.2	64.9	64.9	73.5
	Yorkshire and Humber	49.9	47.6	43.9	44.0	53.7
Southern	Avon Gloucestershire and Wiltshire	35.0	40.0	35.7	46.8	45.8
	Devon Cornwall and Somerset	69.1	68.6	74.4	78.3	86.0
	Wessex	29.0	28.1	28.0	29.3	36.0
	Kent Surrey and Sussex	47.9	51.1	54.4	50.3	58.2
	Thames Valley	35.7	29.5	32.8	33.7	39.5
England*		**49.3**	**49.8**	**50.6**	**51.8**	**56.0**
Northern Ireland†		**61.6**	**65.0**	**69.0**	**74.9**	**80.7**
Wales¥		**67.0**	**66.2**	**72.9**	**80.6**	**74.9**
England, Wales and Northern Ireland		**50.7**	**51.1**	**52.3**	**54.0**	**57.7**

* Data extracted on 25 April 2016. † Data extracted on 17 May 2016. ¥ Data extracted on 10 April 2016

Age and sex distribution

The highest rates of *E. coli* bacteraemia in England was observed among the elderly (75 years and over) at 402.9 and 313.5 reports per 100,000 population for males and females respectively, followed by older adults (65-74 years) at 132.3 and 104.3 reports per 100,000 population for males and females respectively, and in infants (below 1 year old) at 76.1 and 60.8 reports per 100,000 population for males and females respectively (figure 2).

Figure 3. *E. coli* bacteraemia rates per 100,000 population by age and sex (England): 2015



Antimicrobial susceptibility

Between 2011 and 2015, the antimicrobial non-susceptibility of *E. coli* bacteraemia isolates to selected antimicrobials increased (table 2). The greatest increase in non-susceptibility was for piperacillin/tazobactam, which increased from 8.5% to 11.7%; however, this is due to a change in the Minimum Inhibitory Concentration (MIC) breakpoint within that period (data for England only). More recently, between 2014 and 2015, non-susceptibility to the selected antibiotics have remained relatively stable.

Similarly non-susceptibility to Amoxycillin\clavulanate has also increases steadily from 31.5% in 2011 to 42.2% in 2015. This is due to a change in testing method from a fixed 2:1 ratio of amoxicillin:clavulanate to a fixed 2mg/L clavulanate concentration (as stipulated by current EUCAST guidance). Similar increases due to this switch were also reported by Leverstein-van Hall et al. (2013) [2].

Analysis of resistance to more than one antibiotic (table 3) is based on data extracted from the AMR module of SGSS. As a result figures here may be different from those included in table 4 (analysis of susceptibility to individual antibiotics extracted from the CDR module of SGSS). The data are also limited to isolates from England in 2015.

In 2015 for England, 27,480 isolates were tested against any two combinations of ciprofloxacin, gentamicin and third generation cephalosporins. Of 14,681 isolates tested for ciprofloxacin, gentamicin and third generation cephalosporins, 1,075 (7.3%) were resistant to all three antibiotics. In addition, of the 13,999 isolates tested for ciprofloxacin, gentamicin, third generation cephalosporins and meropenem, only eight (<0.1%) were resistant to all antibiotics.

Strains of *E. coli* with extended spectrum β-lactamases are of a great concern due to their resistance to third generation cephalosporins, and frequent cross-resistance to fluoroquinolones and gentamicin [3]. Table 3 shows that 6.8% of *E. coli* bacteraemias tested for gentamicin and ciprofloxacin were non-susceptible to both, while 8.2% of isolates tested against ciprofloxacin and third generation cephalosporins were non-susceptible to both, while isolates tested against gentamicin and third generation cephalosporins had the highest (14.7%) pair-wise resistance observed.

However, of note, while the percentage of all *E. coli* bacteraemia tested for pair-wise resistance for both a third generation cephalosporin and either gentamicin or ciprofloxacin were relatively low, of the 3,292 isolates which were non–susceptible to third generation cephalosporins, the majority (65.9%, n=2,169) were also non-susceptible to ciprofloxacin and just over a third (37.6%, n=1,237) were non-susceptible to gentamicin.

Table 2. Antibiotic susceptibility† for *E. coli* bacteraemia in England: 2011 to 2015

Antimicrobial	2011		2012		2013		2014		2015	
	No. tested	% Resistant*	No. tested	% Resistant*	No. tested	% Resistant*	No. tested	% Resistant*	No. tested	% Resistant*
Gentamicin	23,345	9.1	24,156	9.3	24,127	9.5	24,384	9.6	27,759	10.1
Ciprofloxacin	21,797	18.7	22,587	18.3	22,893	18.0	22,454	18.6	26,148	18.7
Ceftazidime	18,546	10.4	18,975	9.9	18,231	9.9	18,221	10.8	21,815	11.2
Cefotaxime	13,370	10.9	14,350	10.7	14,185	11.0	13,428	11.8	15,627	12.2
Meropenem	17,538	<0.1	18,896	0.1	19,609	<0.1	20,430	0.1	25,160	0.1
Ertapenem	6,517	0.3	9,419	0.3	11,048	0.3	13,897	0.2	21,436	0.4
Ampicillin\amoxicillin	22,320	63.7	23,044	63.8	22,834	63.4	22,311	63.8	25,991	64.5
Amoxycillin\clavulanate	21,934	31.5	22,889	37.3	23,240	38.8	22,944	42.0	26,166	42.2
Piperacillin\tazobactam	20,651	8.5	22,292	9.6	22,946	10.4	22,446	10.9	26,176	11.7
Total Reports	**25,968**		**26,421**		**27,064**		**27,881**		**30,401**	

† Defined as reduced- or non-susceptible

* Isolates can be tested against multiple antimicrobials

Table 3. Pair-wise antimicrobial testing and resistance summary among *E. coli* isolates causing bacteraemia in England: 2015

Antimicrobial	No. tested	% Resistant
Gentamicin and ciprofloxacin	26,937	6.8
Gentamicin and third generation cephalosporins	14,784	14.7
Ciprofloxacin and 3rd generation cephalosporins*	15,121	8.2

*"3rd generation cephalosporins" includes Cefotaxime, Ceftazidime, Ceftriaxone and Cefpodoxime

Ascertainment: Comparison of voluntary laboratory reported *E. coli* bacteraemia versus *E. coli* bacteraemia from the mandatory surveillance scheme in England

The following data compares *E. coli* bacteraemias reported to the voluntary laboratory surveillance scheme with those reported to the mandatory surveillance scheme. In order for the data to be comparable, the laboratory reports from the voluntary surveillance scheme have been limited to England for June 2011 onwards.

Between 2012 and 2015, the number of *E. coli* reports made to the voluntary surveillance increased by 15.1% (26,421 to 30,401, respectively), similarly, there was a 15.0% (32,405 to 37,275, respectively) increase in the number of reports made to the mandatory surveillance (table 4). However, between 2014 and 2015 the number of *E. coli* bacteraemia reported to the voluntary scheme increased by 9.0% (27,881 to 30,401 reports) compared to the 4.6% increase to the mandatory surveillance scheme (35,647 to 37,275 reports). There has been a slight overall reduction in case ascertainment of *E. coli* bacteraemia between 2011 (82.5%) and 2015 (81.6%), with the lowest percentage ascertainment seen in 2014 (78.2%).

Table 4. Ascertainment of *E. coli* data for the mandatory* and voluntary reporting schemes in England: 2011- 2015**

Year	Voluntary reports	Mandatory reports	% Ascertainment
2011†	15,693	19,019	82.5
2012	26,421	32,405	81.5
2013	27,064	33,497	80.8
2014	27,881	35,647	78.2
2015	30,401	37,275	81.6

* Date extracted 20th April 2016

** Date extracted 25th April 2016

† Data from June to December only

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Acknowledgements

These reports would not be possible without the weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland, as well as colleagues in the regional offices of Public Health England.