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Voluntary surveillance of *Escherichia coli* bacteraemia in England, Wales and Northern Ireland: 2008-2014

This report is based on data extracted from the Public Health England (PHE) voluntary surveillance database, Second Generation Surveillance System (SGSS), on the 14th April 2015 for bacteraemias caused by *Escherichia coli* (*E. coli*) between 2010 and 2014 in England, Wales and Northern Ireland. The data presented here may differ from data in previous publications due to inclusions of late reports and the change in surveillance systems.

Most analyses presented here are based on data extracted from the CDR module (previously CoSurv/LabBase2) of SGSS, except for the analysis of resistance to more than one antibiotic, which is based on data reported to the AMR module (previously AmSurv).

The report includes analyses on the trends, age and sex distribution, geographical distribution, level of ascertainment, and antibiotic susceptibility of *E. coli* bacteraemia cases in England, Wales and Northern Ireland.

Rates were calculated using mid-2013 year resident population estimates based on the 2011 census for England, Wales, and Northern Ireland [1,2]. Geographical analyses were made based on the residential location of the patient with reference to the Public Health England Centres.

Key points

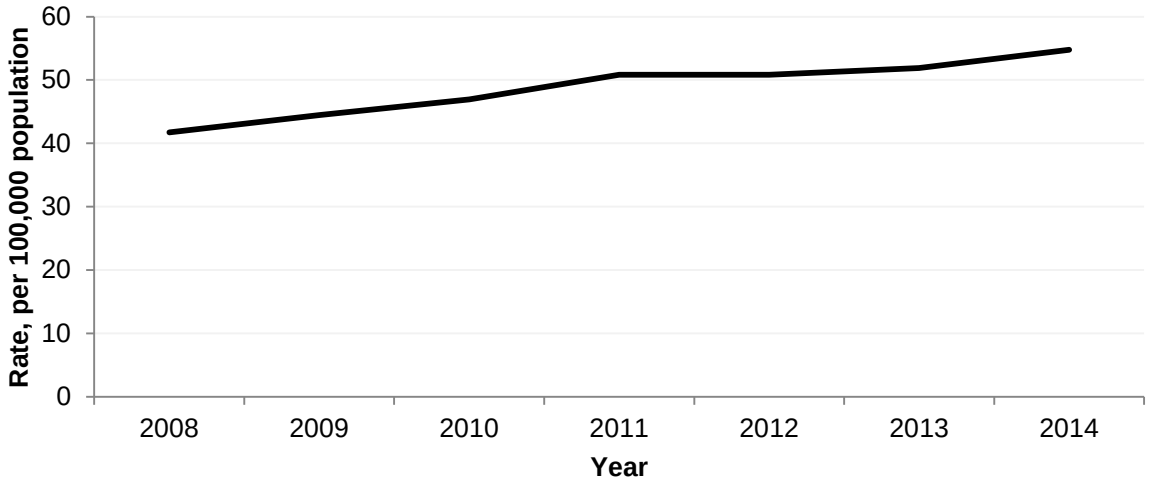
- There was a year-on-year increase in the number of *E. coli* bacteraemia reports across the period reviewed.
- The incidence rate of *E. coli* bacteraemia per 100,000 population increased by 16.7% between 2010 and 2014.
- In 2014, the rates per 100, 000 population were highest amongst elderly (>75 years). Men had higher bacteraemia rates than women in older age groups (>65 years) and in those below one year.
- In 2014, the rate of *E. coli* bacteraemia per 100,000 population was highest in England (55.3), followed by Northern Ireland (53.3) and Wales (46.4).
- Within England, the highest incidence rate of *E. coli* bacteraemia was observed in the North East (67.8 per 100,000 population), followed by Cheshire and Merseyside (67.6 per 100,000 population), and Devon, Cornwall and Somerset (66.0 per 100,000 population).

- Comparison of voluntary reporting with the mandatory surveillance dataset showed a case ascertainment rate of 83.7% in 2014.
- Percentage of non-susceptibility for *E. coli* isolates to tested antibiotics changed very little with the exception of amoxicillin/clavulanate, where it increased from 25.2% in 2010 to 40.9% in 2014.

Trends in episode numbers and rates

The rate of *E. coli* bacteraemia per 100,000 population in England, Wales and Northern Ireland increased between 2008 and 2010, levelled off in 2011 and 2012, then resumed its increase (figure 1). The rate of reports per 100,000 population has increased by 31.2% since 2008, and 5.6% since 2013.

Figure 1. *E. coli* bacteraemia rates per 100,000 population (England, Wales, and Northern Ireland): 2008-2014*

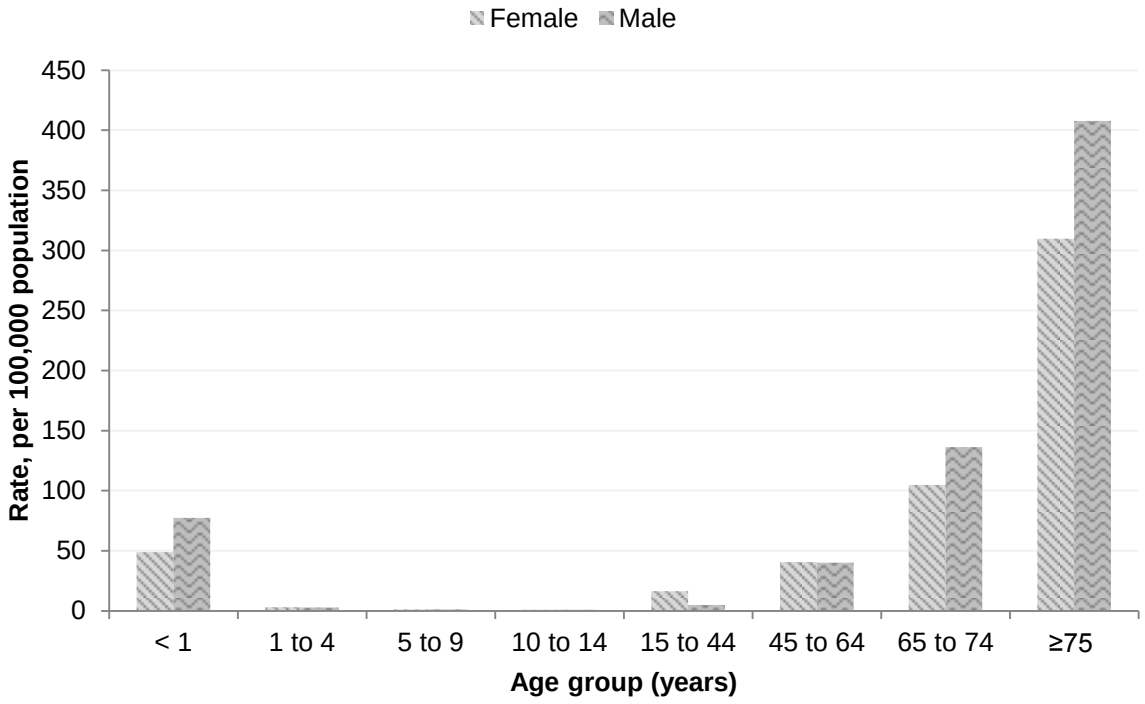


* Data extracted on 14 April 2015

Age and sex distribution

The highest incidence rate of *E. coli* bacteraemia per 100,000 population was in those aged 75 and over (combined rate of 350.4 per 100,000 population), followed by those aged between 65-74 years (combined rate of 120.1 per 100,000 population), and in infants below one year old (combined rate of 61.7 per 100,000 population) (figure 2). Gender differences were observed between younger and older age groups, with rates being higher in older males (65 years and over) and those below one year old (309.8/100,000 and 407.9/100,000 in ≥75 year-olds, 104.8/100,000 and 136.4/100,000 in 65-74 year-olds, and 48.9/100,000 and 77.4/100,000 in <1 year old in females and males, respectively). The percentage differences in infection rates between sexes were larger for age groups with higher male *E. coli* bacteraemia rates (<1, 65-74, and ≥ 75 year-olds; 58.3%, 30.2%, and 31.2%, respectively).

Figure 2. *E. coli* rates† by age and sex per 100,000 population (England, Wales and Northern Ireland): 2014*



† Rates are calculated using 2013 ONS mid-year population estimates

* Data extracted on 14 April 2015

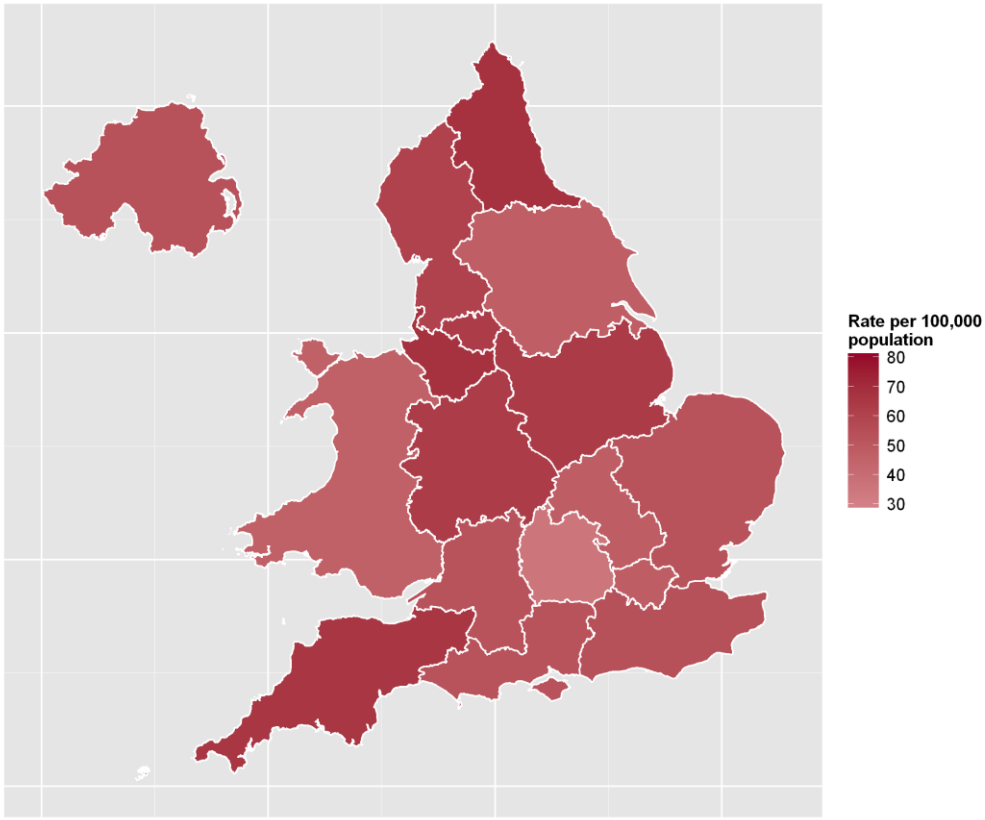
Geographical distribution

The overall *E. coli* bacteraemia rate in England, Wales and Northern Ireland in 2014 was 54.8 per 100,000 population (table 1). This was a 16.7% increase since 2010 (47.0 per 100,000 population) and 5.5% increase since 2013 (51.9 per 100,000 population) (table 1). The total number of bacteraemia reports has been also increasing since 2010, with *E. coli* being the most frequently reported pathogen in monomicrobial infections, in 31.5% of cases in 2013 [3]. While there was a steady year-on-year *E. coli* bacteraemia rate increase in England between 2010 and 2014, the rates in Wales and Northern Ireland peaked in 2011 and 2013, respectively, and decreased thereafter.

England had the highest incidence of *E. coli* bacteraemia of 55.3 per 100,000 population in 2014, followed by Northern Ireland (53.3/100,000) and Wales (46.4/ 100,000). The rate in England increased by 18.9% since 2010 (46.5/100,000) and by 7.9% since 2013 (51.3/100,000). The rate of *E. coli* bacteraemia in Northern Ireland decreased by 2.4% since 2010 (54.6/100,000) and by 21.4% since 2013 (67.8/ 100,000). Similarly, the incidence rate in Wales decreased by 7.2% since 2010 (49.9/100,000) and by 13.4% since 2013 (53.6/100,000).

Regions with the highest infection rate per 100,000 population in 2014 included the North East (67.8), Cheshire and Merseyside (67.6) and Devon, Cornwall and Somerset (66.0) (figure 3) (table 1). Conversely, the region with lowest rate in 2014 was the Thames Valley (36.0). The incidence rate of *E. coli* bacteraemia in Avon, Gloucestershire and Wiltshire increased by 90.4% between 2010 and 2014 (27.9/100,000 vs 53/100,000, respectively).

Figure 3. *E. coli* bacteraemia rates per 100,000 population by PHE Centres in England, Wales, and Northern Ireland: 2014*



* Data extracted on 14 April 2015

Table 1. *E. coli* bacteraemia rate per 100,000 population by PHE Centre (England, Wales, and Northern Ireland): 2010-2014*

PHE Centre	2010	2011	2012	2013	2014
London	41.2	44.2	44.8	46.5	48.1
South Midlands and Hertfordshire	35.5	34.0	42.2	44.5	47.8
East Midlands	57.1	59.9	57.4	56.8	63.7
Anglia and Essex	45.2	48.2	50.6	51.4	52.8
West Midlands	50.6	55.3	53.3	55.6	62.9
Cheshire and Merseyside	53.8	57.9	62.3	62.9	67.6
Cumbria and Lancashire	43.0	51.8	52.6	55.8	60.5
Greater Manchester	59.5	66.6	62.3	62.7	63.2
North East	51.9	63.6	67.2	65.8	67.8
Yorkshire and Humber	52.3	50.8	49.2	45.2	47.3
Avon Gloucestershire and Wiltshire	27.9	33.7	39.4	35.4	53.0
Devon Cornwall and Somerset	52.3	51.7	49.5	54.9	66.0
Wessex	42.1	45.1	45.1	46.2	52.5
Kent Surrey and Sussex	45.5	48.2	51.6	55.4	53.7
Thames Valley	32.6	36.8	30.4	33.6	36.0
England	**46.5**	**49.9**	**50.4**	**51.3**	**55.3**
Northern Ireland (NI)	**54.6**	**61.9**	**64.9**	**67.8**	**53.3**
Wales	**49.9**	**60.9**	**50.3**	**53.6**	**46.4**
England, Wales & NI	**47.0**	**50.8**	**50.8**	**51.9**	**54.8**

* Data extracted on 14 April 2015

Antimicrobial susceptibility

The antibiotic non-susceptibility of E. coli isolates to selected antimicrobials remained broadly stable or increased slightly with the exception of amoxicillin/clavulanate between 2010 and 2014 (table 2).

There was a small increase in the number of isolates non-susceptible to imipenem or meropenem from six out of 18,125 in 2010 to 23 out of 19,759 in 2014, albeit these fluctuated over this period, translating into a rate of 0.1%.

Non-susceptibility to third generation cephalosporins and piperacillin/tazobactam increased by 2.1% (9.7% to 11.8%) and 2.7% (8.1% to 10.8%) between 2010 and 2014, respectively. Ciprofloxacin and gentamicin non-susceptibility remained fairly stable at around 18-19% and 9%, respectively.

The highest increase in non-susceptibility was observed for amoxicillin/clavulanate from 25.2% in 2010 to 40.9% in 2014. Leverstein-van Hall and colleagues reported that switching from a fixed 2:1 ratio of amoxicillin:clavulanate in susceptibility testing to a fixed 2mg/L clavulanate concentration (as stipulated by current EUCAST guidance) causes an increase from 19% to 31% from one year to another [4]. The same shift in MIC breakpoints has been gradually adopted in the UK, doubtless with similar effects.

Data presented here are broadly consistent with those of the Bacteraemia Surveillance Programme of the British Society for Antimicrobial Chemotherapy (BSAC) with the exception of amoxicillin/clavulanate between 2010 and 2013 (BSAC data for 2014 has not been published at the time of publication) [5]. BSAC reported resistance rates for amoxicillin/clavulanate considerably lower than those presented here (26.9% in 2010, 28% in 2011, 29.8% in 2012, and 27.8% in 2013). BSAC used fixed 2:1 ration for amoxicillin:clavulanate testing up to 2013, and this strengthens the hypothesis that the sharp increase observed in SGSS CDR data reflects methodological rather than biological changes. However, Hall et al. found that the new EUCAST method correlated better with clinical efficacy than the ratio based, in-vitro testing, thus even if the increases in non-susceptibility in recent years is in question the resulting prevalence is more likely to represent actual clinical experience.

Table 2. Antibiotic susceptibility for E. coli bacteraemia in England, Wales and Northern Ireland: 2010-2014*

		2010	2011	2012	2013	2014
Total reports		26,998	29,477	29,685	30,513	32,196
Meropenem/imipenem	**% non-susceptible**	**0.0**	**0.1**	**0.1**	**0.1**	**0.1**
	Reports with susceptibility data	18,125	20,505	21,208	21,248	19,759
Cefotaxime/ceftazidime	**% non-susceptible**	**9.7**	**10.4**	**10.2**	**10.1**	**11.8**
	Reports with susceptibility data	18,045	20,350	21,147	20,593	18,467
Ciprofloxacin	**% non-susceptible**	**18.1**	**18.7**	**18.5**	**17.9**	**18.7**
	Reports with susceptibility data	20,437	22,997	23,667	23,873	21,220
Gentamicin	**% non-susceptible**	**8.7**	**8.7**	**9.2**	**9.4**	**9.3**
	Reports with susceptibility data	22,055	24,759	25,435	25,359	23,298
Amoxicillin/clavulanate	**% non-susceptible**	**25.2**	**31.0**	**36.6**	**37.9**	**40.9**
	Reports with susceptibility data	20,518	23,343	24,090	24,416	21,905
Piperacillin/tazobactam	**% non-susceptible**	**8.1**	**8.1**	**9.5**	**10.2**	**10.8**
	Reports with susceptibility data	18,713	20,962	22,712	23,396	20,877

* Data extracted on 14 April 2015

Analyses of resistance to more than one antibiotic were based on data extracted from the AMR module of SGSS. The data are limited to isolates from England in 2014.

There were 20,560 isolates of E. coli causing bacteraemia tested for susceptibility to ciprofloxacin, imipenem or meropenem, cefotaxime or ceftazidime, gentamicin, piperacillin/tazobactam, and amoxicillin/clavulanate extracted from the AMR module of SGSS. Forty-seven percent (9,622) of these were non-susceptible to at least one antibiotic. Non-susceptibility to the combination of any two antibiotics was observed in 21% (4,373) of cases. Two isolates tested were non-susceptible 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 [6]. Table 3 shows that 8.2% of E. coli from bacteraemias tested non-susceptible to both cefotaxime or ceftazidime and ciprofloxacin, while 4.6% isolates were non-susceptible to cefotaxime or ceftazidime and gentamicin. This is most likely due to isolates with CTX-M-group 1 ESBLs (the commonest type now in the UK) that also often carry an inhibitor-resistant penicillinase OXA-1 and the AAC(6')-1b-cr aminoglycoside acetyltransferase enzyme, which also augments ciprofloxacin resistance [7]. Note, fluoroquinolone resistance has been on increase even in isolates lacking ESBLs [8], a point exemplified by co-non-susceptibility to ciprofloxacin and amoxicillin/clavulanate (13.4%) being higher than that seen for third generation cephalosporin and fluoroquinolone non-susceptibility (8.2%).

Some CTX-M ESBLs producing E. coli strains contain plasmids carrying genes that code for resistance to aminoglycosides and fluoroquinolones [7], and 4.2% (650/15650) of isolates exhibited this pattern of non-susceptibility.

Non-susceptibility of isolates to carbapenems and other antibiotics remained low at less than 1%.

Table 3. Pair-wise comparison of antimicrobial resistance among E. coli isolates causing bacteraemia in England: 2014*

	Cefotaxime/ ceftazidime		Ciprofloxacin		Gentamicin		Imipenem/ meropenem		Piperacillin/ tazobactam		Amoxicillin/ clavulanate	
	tested	% resistant	tested	% resistant	tested	% resistant	tested	% resistant	tested	% resistant	tested	% resistant
Cefotaxime/ ceftazidime												
Ciprofloxacin	15,851	8.2										
Gentamicin	16,051	4.6	17,994	7.0								
Imipenem/ meropenem	15,586	0.1	17,200	0.1	17,485	<0.1						
Piperacillin/ tazobactam	15,449	4.2	17,211	5.2	17,728	2.9	16,801	0.1				
Amoxicillin/ clavulanate	15,848	9.3	17,694	13.4	18,118	7.8	17,172	0.0	17,344	11.3		

*Data extracted on 14 April 2015

Ascertainment: Comparison of *E. coli* positive specimens from the voluntary laboratory reporting scheme versus E. coli infections from the mandatory surveillance scheme in England

The following data compare E. coli bacteraemias reported to the voluntary laboratory surveillance scheme with E. coli bacteraemia reports 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 and June 2011 onwards.

Between 2013 and 2014, the number of E. coli reports made to the voluntary surveillance increased by 7.9% (27,621 to 29,791, respectively) in comparison to a 6.2% (33,497 to 35,589, respectively) increase in the number of reports made to the mandatory surveillance (table 4). Percentage increases in E. coli bacteraemia reports for the voluntary and mandatory schemes from 2012 to 2014 were 10.5% and 9.8%, respectively; comparison to 2011 is not included because testing did not include the full calendar year. The case ascertainment of E. coli reported to the voluntary scheme has fluctuated between 2011 (84.1%) and 2014 (83.7%), with the highest ascertainment obtained in 2011 (84.1%).

Table 4. Ascertainment of E. coli data for the mandatory and voluntary reporting schemes in England: 2011- 2014*

Year	Voluntary reports	Mandatory reports	% Ascertainment
2011†	16,000	19,019	84.1
2012	26,954	32,405	83.2
2013	27,621	33,497	82.5
2014	29,791	35,589	83.7

* Data extracted on 14 April 2015

† Data from June to December only

Concluding remarks

The data presented here indicate year-on-year increase in the number of laboratory reports of E. coli bacteraemia with 27% increase since 2008 and 3% increase from 2013 to 2014, correlating with the increase in total number of bacteraemia reports [3].

The rate of E. coli bacteraemia per 100,000 population in England, Wales and Northern Ireland increased by 5.5% between 2013 and 2014.

Trends in non-susceptibility to key antibiotics (3rd generation cephalosporins, quinolones and gentamicin) indicated an increase in resistance to cefotaxime or ceftazidime (9.7% in 2010 to 11.8% in 2014), while resistance to ciprofloxacin and gentamicin remained stable (18.1% and 8.7% in 2010, and 18.7% and 9.3% in 2014, respectively).

The increase in the number of laboratory reports across England, Wales and Northern Ireland in conjunction with the public health impact of E. coli confirms that it should remain a priority. There is also a need for continued surveillance and interventions to prevent the spread of E. coli producing ESBLs, in particular CTX-M types and emergent carbapenem-resistant strains, such as those producing NDM-1, VIM, OXA-48, and KPC enzymes, which are frequently associated with multiple antibiotic resistance.

References

1. Office for National Statistics (ONS) mid-year population estimates for England and Wales.

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5. BSAC, Resistance surveillance website (bacteraemia data).

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Acknowledgements

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