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Laboratory surveillance of *Escherichia coli* bacteraemia in England, Wales and Northern Ireland: 2016

These analyses are based on data relating to diagnoses of bloodstream infections caused by *E. coli* between 2009 and 2016 in England, extracted on 3 April 2017 from Public Health England's (PHE) voluntary surveillance database, the Second Generation Surveillance System (SGSS). Data for Wales and Northern Ireland were extracted separately (from DataStore on 9 March 2017 and from CoSurv on 4 April 2017, respectively).

SGSS comprises a communicable disease module that includes antimicrobial susceptibility data (CDR; formerly CoSurv/LabBase2) and a separate comprehensive antimicrobial resistance module (AMR; formerly AmSurv). Compared with CDR's antimicrobial susceptibility data, the AMR module captures more comprehensive antibiogram data (for all antibiotics tested); however, until the launch of SGSS in 2014 fewer laboratories used the AMR module. Therefore, antimicrobial non-susceptibility trends cannot currently be undertaken using data from the AMR module, but data for 2016 were extracted to assess multidrug-resistance rates.

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

Rates of laboratory reported bacteraemia were calculated using mid-year resident population estimates for the respective year and geography with the exception of 2016 rates, which were based on 2015 population estimates as population estimates for 2016 were not available at the time of producing this report [1]. 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 reporting laboratory) with cases in England being assigned to one of nine local PHE centres (PHECs) formed from administrative local authority boundaries.

*** Data in table 3 (and text related to table 3 data) were corrected prior to republication on 9 June 2017.**

The report includes analyses on the trends, age and sex distribution, geographical distribution of cases of *E. coli* bacteraemia cases in England, Wales and Northern Ireland. In addition, antimicrobial susceptibility five-year trends for England and Northern Ireland have been included in the report, as has a single year of resistance to more than one antibiotic based on England's data reported to the AMR module (previously AmSurv) and extracted on 3 April 2017. A web appendix is available featuring the findings of this report including only data submitted via SGSS from laboratories in England.

Key points

- there has been a sustained year-on-year increase in the number of *E. coli* bacteraemia cases.
- the overall rate of *E. coli* bacteraemia in England, Wales and Northern Ireland increased by 45% (44.8 to 64.9 cases per 100,000 population) between 2009 and 2016 and 25% (52.0 to 64.9 cases per 100,000 population) between 2012 and 2016
- in 2016, the rate of *E. coli* bacteraemia per 100,000 population was 63.6 for England, 79.6 for Northern Ireland and 79.9 for Wales, with an overall rate for England, Wales and Northern Ireland of 64.9 cases per 100,000 population.
- in England, the highest rate each year was observed in the North East PHEC with a rate of 86.2 cases per 100,000 population in 2016. In contrast, London had lowest rate in 2016 (55.4 cases per 100,000 population)
- the highest rates are observed in males and females 75 years or older (457.4 cases per 100,000 population and 364.0 cases per 100,000 population, respectively)
- between 2012 and 2016, there was no change in the antibiotic resistance of *E. coli* isolates to selected antimicrobials, except for resistance to piperacillin/tazobactam and amoxicillin/clavulanate which increased from 10% to 12% and from 37% to 41%, respectively. However these probably are largely due to a change in the Minimum Inhibitory Concentration (MIC) breakpoint for piperacillin/tazobactam within that period and a change in testing for amoxicillin/clavulanate - from a fixed 2:1 ratio of amoxicillin:clavulanate to a fixed 2mg/L clavulanate concentration
- in 2016 for England, resistance to gentamicin, ciprofloxacin, third-generation cephalosporins, piperacillin/tazobactam and amoxicillin/clavulanate were 10% (3,417/32,603), 19% (6,122/32,304), 12% (3,954/32,336), 12% (3,610/31,148) and 41% (12,929/31,839), respectively
- in 2016 for England, 4% (1,319/ 31,197) of isolates tested against ciprofloxacin, gentamicin and third-generation cephalosporins were resistant, 3% (820/ 29,585) tested against piperacillin/tazobactam, amoxicillin/clavulanate and gentamicin were

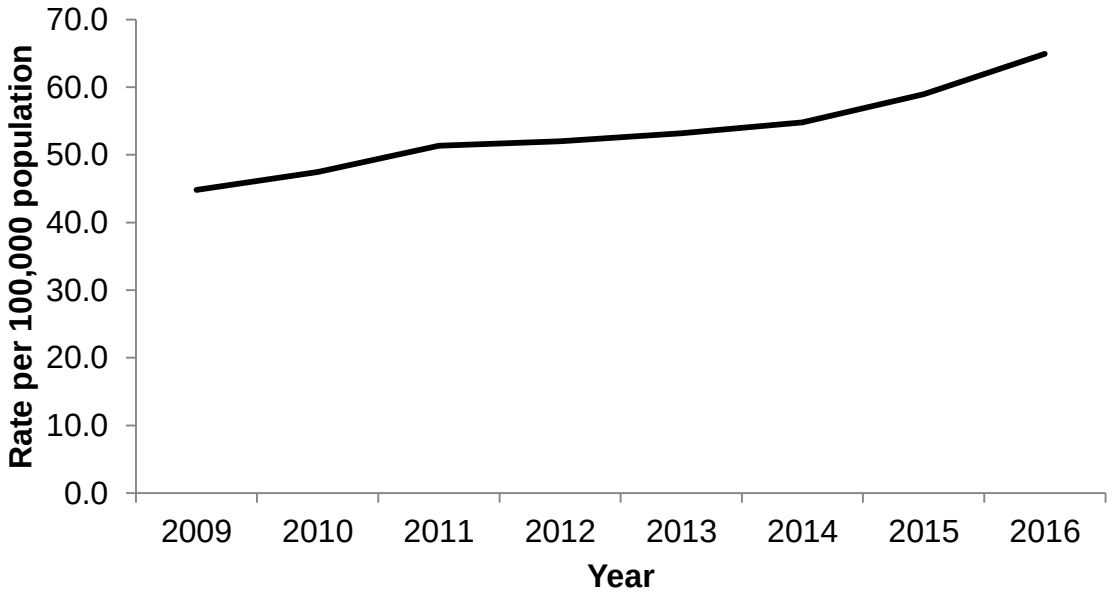
resistant and 5% (1,403/ 29,303) tested against piperacillin/tazobactam, amoxicillin/clavulanate and ciprofloxacin were resistant.

- comparison of voluntary reporting with the mandatory surveillance dataset showed a case ascertainment rate of 93% in 2016 (data for England only)

Trends

In England, Northern Ireland and Wales, the overall rates of *E.coli* bacteraemia increased consecutively each year between 2009 and 2016. The counts and rates of *E. coli* bacteraemia increased by 45% from 44.8 to 64.9 cases per 100,000 population (n=25,544 to n=38,791 cases) (figure 1) over this period, with a relatively steep increase (19%) between 2014 and 2016 (54.8 to 64.9 cases per 100,000 population; n=32,457 to n=38,791 cases).The steep increase in reports (beginning in 2015) is not observed in reports made to the mandatory surveillance scheme within the same period [2] as such is possibly due to the change in reporting database from LabBase2 to the current SGSS.

Figure 1. *E. coli* bacteraemias per 100,000 population (England, Wales and Northern Ireland): 2009-2016



Geographic distribution

The combined rate of reported *E. coli* bacteraemia in England, Wales and Northern Ireland increased by 25% (52.0 to 64.9 cases per 100,000 population, table 1) between 2012 and 2016. Similarly, increases in the individual rates for England, Wales and Northern Ireland were observed over the same period.

Between 2012 and 2016, the rate of *E. coli* bacteraemia in England increased by 26% (from 50.6 to 63.6 cases per 100,000 population, table 1). During this same period, the rate in Northern Ireland increased by 24%, from 64.1 to 79.6 cases per 100,000 population and in Wales the rate increased by 17%, from 68.4 to 79.9 cases per 100,000 population.

It is of note that in England and Northern Ireland, there are links from the different laboratory information systems that report clinically significant isolates to SGSS/CoSurv. Data from Wales are collected by extraction from a single laboratory information system used by all microbiology laboratories, where all positive blood cultures are extracted from all laboratories, including those not thought to be clinically significant. Therefore the rates in Wales will be relatively higher compared to that in England and Northern Ireland.

The increasing trend in reports in England between 2012 and 2016 is also observed in all Public Health England Centres (PHEC); however, the increase in rates varied among PHECs over time. Between 2012 and 2016, the highest increase was observed in the South West and South East PHECs, both increased by 41% (from 47.0 to 66.4 cases per 100,000 population and from 43.8 to 61.8 cases per 100,000 population respectively). However, the highest rate each year was observed in the North East PHEC with a rate of 86.2 cases per 100,000 population in 2016 – this is also observed in the mandatory surveillance scheme with the highest rates of *E. coli* bacteraemia over the same period reported in the North East PHEC. In contrast, the London PHEC had the lowest rate in 2016 (55.4 cases per 100,000 population).

Figure 2. Geographical distribution of pathogen *E. coli* bacteraemia per 100,000 population (England, Wales and Northern Ireland): 2016

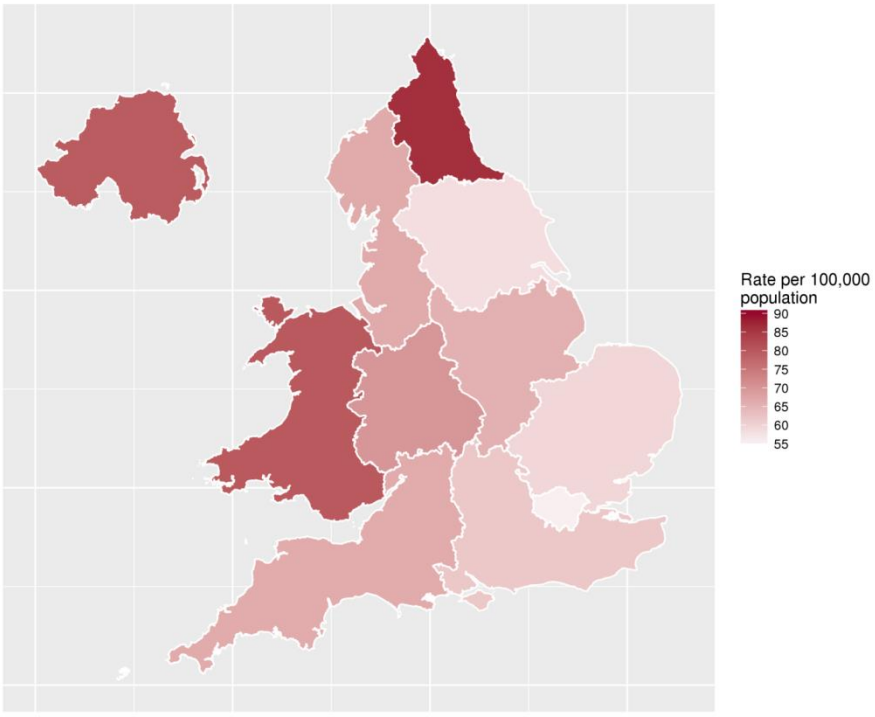


Table 1. *E.coli* bacteraemia per 100,000 population by region (England, Wales and Northern Ireland): 2012 to 2016

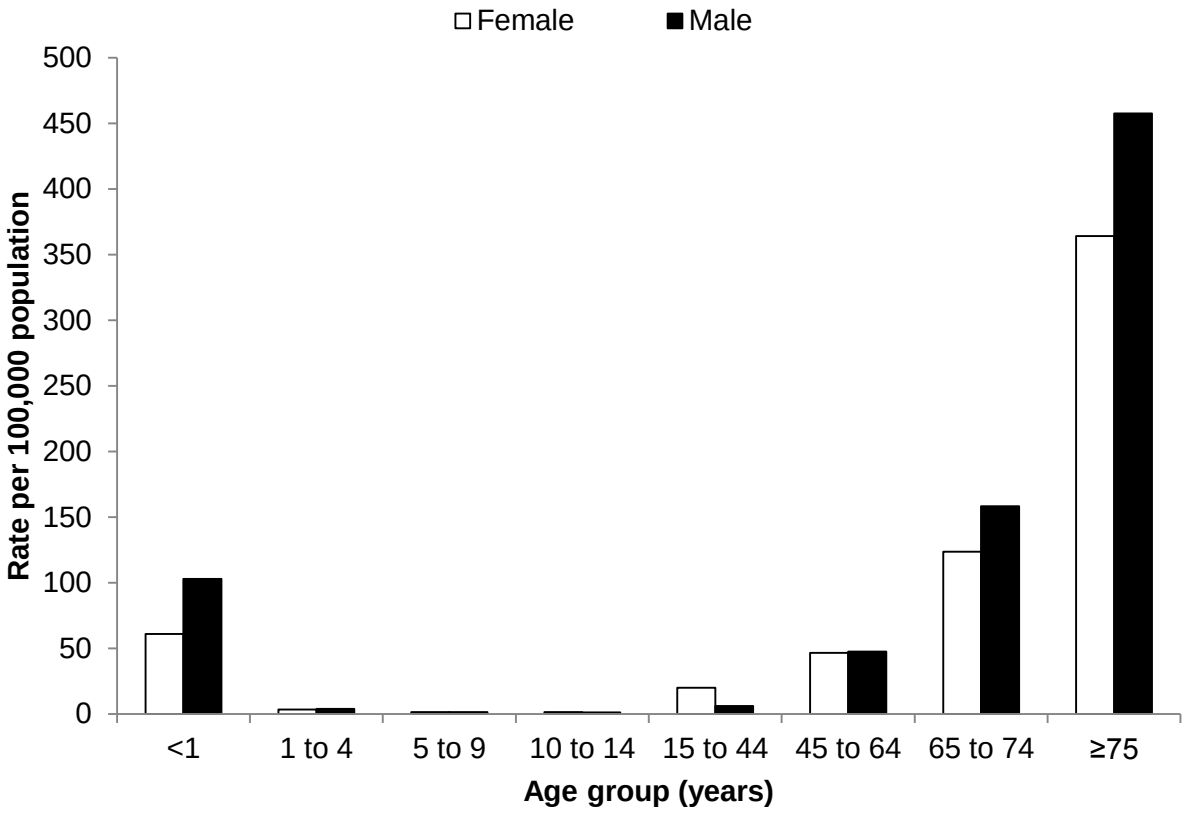
		Rate per 100,000 population				
Region	**PHE Centre**	**2012**	**2013**	**2014**	**2015**	**2016**
North of England	North East	67.3	66.1	66.0	75.0	86.2
	Yorkshire and Humber	49.3	45.0	45.2	55.0	58.2
	North West	59.7	60.9	60.1	61.8	66.6
Midlands and East of England	West Midlands	53.3	55.7	60.1	65.4	70.1
	East Midlands	52.6	53.0	56.5	63.7	65.5
	East of England	50.2	50.9	52.2	51.3	59.3
London	London	45.4	47.5	47.4	49.7	55.4
South of England	South West	47.0	47.4	53.8	57.0	66.4
	South East	43.8	46.5	44.7	52.7	61.8
England*		50.6	51.5	52.6	57.3	63.6
Northern Ireland†		64.1	68.2	73.7	79.2	79.6
Wales¥		68.4	73.9	81.4	77.1	79.9
England, Wales and Northern Ireland		**52.0**	**53.2**	**54.8**	**59.0**	**64.9**

* Data extracted on 3 April 2017. † Data extracted on 4 April 2017. ¥ Data extracted on 9 March 2017

Age and sex distribution

In England, Wales and Northern Ireland, the rate of reported *E. coli* bacteraemia increases with age in patients aged 1 year and older. The highest rates are observed in males and females 75 years or older (457.4 cases per 100,000 population and 364.0 cases per 100,000 population, respectively, figure 3). Relatively high rates are observed in infants (<1 year old); 103.0 and 61.0 cases per 100,000 population in males and females, respectively. This trend is similar to what was reported in 2015 [3].

Figure 3. *E. coli* bacteraemia rates per 100,000 population by age and sex (England, Wales and Northern Ireland): 2016



Antimicrobial resistance: England and Northern Ireland

Between 2012 and 2016 in England and Northern Ireland, the percentage of antimicrobial resistant *E. coli* bacteraemia remained relatively stable (table 2) except for percentage resistance to piperacillin/tazobactam and amoxicillin/clavulanate. Resistance to piperacillin/tazobactam increased from 10% to 12% over this period (2012 to 2016); however, this was confounded by a change in the Minimum Inhibitory Concentration (MIC) breakpoint (data for England only) within that period and by laboratories' moves from

BSAC to EUCAST disc testing, with zone breakpoints for the latter predicated on the reduced MIC breakpoint. Percentage resistance to amoxicillin/clavulanate also increased from 37% in 2012 to 41% in 2016. This again may be largely due to changes in testing methodology, from a fixed 2:1 ratio of amoxicillin/clavulanate to a fixed 2 mg/L clavulanate concentration (as stipulated by current EUCAST guidance)[4] and by moves to EUCAST disc testing, with the disc breakpoints based on the latter criterion. More recently, between 2015 and 2016, resistance to these two antibiotics remained relatively stable.

Analysis of resistance to more than one antimicrobial (table 3) is based on data extracted from the AMR module of SGSS for England only in 2016. As a result, figures here are different from those included in table 2 (analysis of susceptibility to individual antimicrobials extracted from the CDR module of SGSS for England and CoSurv for Northern Ireland).

Resistance to third-generation cephalosporins is a broad (but not specific) indicator of extended spectrum β-lactamases (ESBL) producers. Strains of *E. coli* with ESBL are of great concern due to this and also frequent cross-resistance to fluoroquinolones and gentamicin [5]. In 2016 for England, 33,153 isolates were tested against any two of ciprofloxacin, gentamicin, third-generation cephalosporins, piperacillin/tazobactam and amoxicillin/clavulanate. Table 3 shows that 7% of bloodstream *E. coli* tested for gentamicin and ciprofloxacin were resistant to both agent, while 15% of isolates tested against ciprofloxacin and third-generation cephalosporins were resistant to both, 8% of isolates tested against gentamicin and third-generation cephalosporins were resistant to both antibiotics. 7% of isolates tested against third generation cephalosporins and piperacillin/tazobactam were also resistant to both antibiotics.

Of 31,197 isolates tested for ciprofloxacin, gentamicin and third-generation cephalosporins in 2016, 1,319 (4%) were resistant to all these three antibiotics. Of 29,585 isolates tested against piperacillin/tazobactam, amoxicillin/clavulanate and gentamicin, 3% (n=820) were resistant to all three antibiotics, while 5% (n=1,403) of 29,303 tested against piperacillin/tazobactam, amoxicillin/clavulanate and ciprofloxacin were resistant to all three antibiotics.

Less than 1% of the isolates tested for meropenem were resistant to the antibiotic agent.

Table 2. Antimicrobial susceptibility for *E. coli* bacteraemia (England and Northern Ireland): 2012 to 2016

	2012		2013		2014		2015		2016	
Antimicrobial agent	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***
Gentamicin	25,831	9	25,903	9	26,297	10	30,097	10	33,106	10
Ciprofloxacin	24,059	18	24,446	18	24,052	19	28,203	19	31,437	18
Ceftazidime	20,167	10	19,419	10	19,309	11	23,174	11	25,580	11
Cefotaxime	15,338	10	15,188	11	14,429	12	16,993	12	18,123	12
Meropenem	20,300	<1	21,123	<1	21,995	<1	27,159	<1	30,546	<1
Ertapenem	9,628	<1	11,323	<1	14,286	<1	22,156	<1	25,554	<1
Tobramycin	7,624	16	7,637	16	7,477	13	9,493	14	11,240	14
Ampicillin/Amoxicillin	24,697	64	24,577	63	24,169	64	28,185	64	31,407	63
Amikacin	13,749	3	14,511	3	14,643	3	16,787	3	19,459	3
Piperacillin/ Tazobactam	23,881	10	24,693	11	24,310	11	28,449	12	30,786	12
Amoxicillin/ Clavulanate	24,509	37	24,956	38	24,794	42	28,447	42	31,125	41
Total *E. coli* bacteraemia reports	**28,261**		**28,974**		**29,940**		**32,833**		**36,315**	

*defined as reduced- or non-susceptibility

Table 3. Multi-drug antimicrobial testing and resistance summary for *E. coli* bacteraemia (England): 2016¥

Antimicrobial combinations	No. tested	% resistant
Gentamicin and Ciprofloxacin	31,759	7
Gentamicin and third-generation Cephalosporin*	31,788	5
Gentamicin and Piperacillin/Tazobactam	30,753	3
Gentamicin and Amoxicillin/Clavulanate	31,296	8
Ciprofloxacin and third-generation Cephalosporin*	31,695	9
Ciprofloxacin and Piperacillin/Tazobactam	30,411	5
Ciprofloxacin and Amoxicillin/Clavulanate	31,064	13
Third-generation Cephalosporin* and Piperacillin/Tazobactam	30,545	4
Piperacillin/Tazobactam and Amoxicillin/Clavulanate	29,939	11
Ciprofloxacin, Gentamicin and third-generation Cephalosporins*	31,197	4
Piperacillin/Tazobactam, Amoxicillin/Clavulanate and Gentamicin	29,585	3
Piperacillin/Tazobactam, Amoxicillin/Clavulanate and Ciprofloxacin	29,303	5
Ciprofloxacin, Gentamicin, third-generation Cephalosporins* and Meropenem	30,124	<1

* Cefotaxime or Ceftazidime or Ceftriaxone or Cefpodoxime

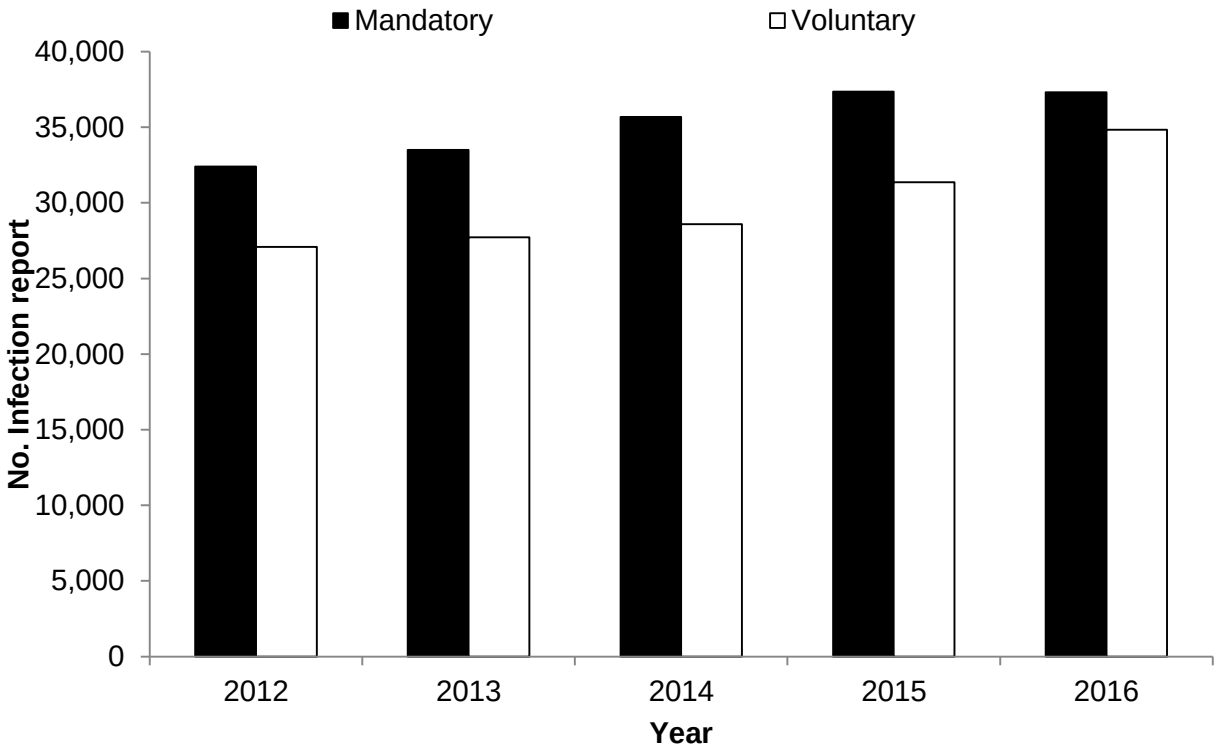
¥ Data corrected prior to republication on 9 June 2017

Ascertainment: England

The following data compares *E. coli bacteraemia* reported to the voluntary laboratory surveillance scheme with those reported to the mandatory surveillance scheme. Between 2012 and 2016, the number of *E. coli* reports made to the voluntary surveillance increased by 29% (n=27,092 to n=34,841 cases, respectively). In addition, the number of reports to the mandatory surveillance scheme also increased, albeit at a lower rate of 15% over the same time period (n=32,405 to n=37,308 cases, respectively, table 4). Between 2014 and 2016 there was a steeper increase in the number of *E. coli* bacteraemia reported to the voluntary scheme (21%; n=27,888 to n=33,844 cases, respectively) compared to the mandatory surveillance scheme (5%; n=35,673 to n=37,308 cases, respectively) leading to an increase in ascertainment between those period from 80% to 93%. We therefore take the view that the greater increase in voluntary reports over this period is a reflection of the change of reporting database from its predecessor (LabBase2) to the current SGSS as this steep increase is

not observed in the mandatory reports. The highest case ascertainment between 2012 and 2016 was observed in 2016 (93%).

Figure 4. Ascertainment of E. coli bacteraemia data for the mandatory* and voluntary reporting schemes in England: 2012- 2016



*Data extracted 3 April 2017

Acknowledgements

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