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Surveillance of *Enterococcus* spp. causing bacteraemia in England, Wales and Northern Ireland: 2015

These analyses are based on data extracted from the voluntary surveillance databases, SGSS (Second Generation Surveillance System; for cases within England), CoSurv (for cases within Northern Ireland) and Datastore (for cases within Wales). Data were extracted on 8 March 2016 for England, 17 May 2016 for Northern Ireland and 10 April 2015 for Wales. The data presented here may differ in some instances from data in earlier publications due to inclusion of late reports.

Rates were calculated using 2014 mid-year resident population estimates based on the 2011 census for England, Wales, and Northern Ireland [1]. Rates of bacteraemia in infants were calculated using 2014 live birth denominators [2]. Geographical analyses were based on the residential location of the patient with cases in England being assigned to 15 local region catchments formed from administrative local authority boundaries (formerly PHE Centres).

This report includes analyses of the trends, patient demographic and geographical distribution, antimicrobial susceptibility among the isolates from enterococcal bacteraemia episodes as well asdetails of relevant recent antimicobial resistance alerts and microbiological services guidance concerning enterococcal isolates.

Key Points

- The overall incidence rate of *Enterococcus* spp. bacteraemia in England, Wales and Northern Ireland was 11.2 per 100,000 population in 2015
- in 2015, the *Enterococcus* spp. bacteraemia rates in England, Northern Ireland and Wales were 10.9, 13.6 and 14.8 per 100,000 population, respectively
- between 2014 and 2015, the rates of bacteraemia caused by *Enterococcus* spp. increased by 8.4% in England, 3.1% in Northern Ireland and 3.3% in Wales
- within England, the Devon, Cornwall & Somerset area reported the highest rate (15.1/100,000) of *Enterococcus* spp. bacteraemia and Thames Valley the lowest (7.8) in 2015; all areas reported an increase between 2011 and 2015 with the exception of Anglia & Essex
- in England, 82% of enterococcal bacteraemia isolates were reported to species level in 2015, an increase from the 77% identified to species level in 2011
- the two most frequently isolated species within the genus in 2015 were *Enterococcus faecalis*, and *Enterococcus faecium*, representing 41% and 37% of reported enterococcal bacteraemia respectively; the primacy of each varied by Country
- the incidence rate of *Enterococcus* spp. bacteraemia was highest among the elderly (≥75 years; 47.4/100,000) and infants (<1 year old; 35.7) and higher among males than females in 2015 in England
- a differing age distribution was noted between the two most frequently identified enterococcal bacteraemia species in England; there was a relatively low rate of *E. faecium* bacteraemia in infants (aged <1 year) compared with *E. faecalis* bacteraemia (3.0 compared with 27.7/100,000)
- half of infant enterococcal bacteraemias occurred in the first four weeks of life, with 86% caused by *E. faecalis*
- in 2015 the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates in England with antimicrobial susceptibility test results reported for at least one key antimicrobial was 88%
- among *E. faecalis* and *E. faecium* isolates in England, the proportions resistant to vancomycin in 2015 were 1.5% and 23.9% respectively

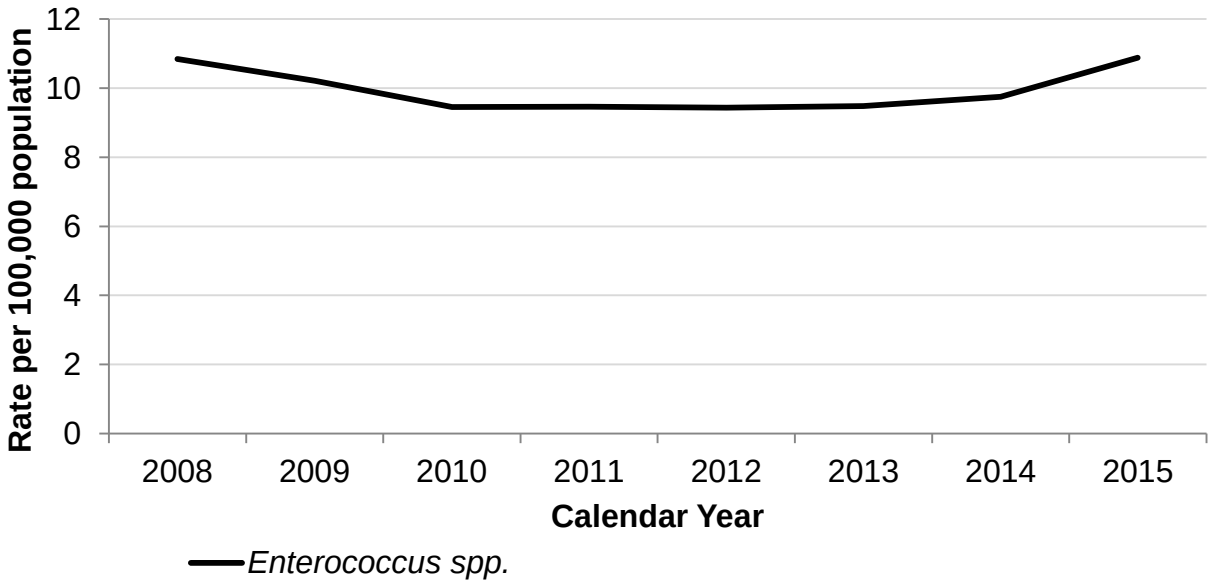
Trends

Between 2008 and 2015 there was no overall change in incidence rate of bacteraemia caused by *Enterococcus* spp., remaining around 10.8 per 100,000 (figure 1). However, the incidence rate by year has not remained steady, with a decrease in the incidence rate seen between 2008 and 2010, followed by a relatively stable period (around ~9.5/100,000) until 2014. Between 2014 and 2015 an increase of 8.4% in the rate of enterococcal bacteraemia infection was reported (9.8/100,000 to 10.9 respectively).

A note of caution should be taken when interpreting these results. At the end of 2014 the system of laboratory reporting to PHE changed; this may partly explain the increase in *Enterococcus* spp. bacteraemia reports observed in 2015 due to improved accessibility to reporting within England.

Enterococcus spp. were the seventh most commonly identified organism in reported mono-microbial bloodstream infection in 2014, comprising 4.2% of such infections), and the third most common organism in poly-microbial bloodstream infections (22.3% of such infections) [3].

Figure 1. *Enterococcus* spp. bacteraemia per 100,000 population (England); 2008 to 2015

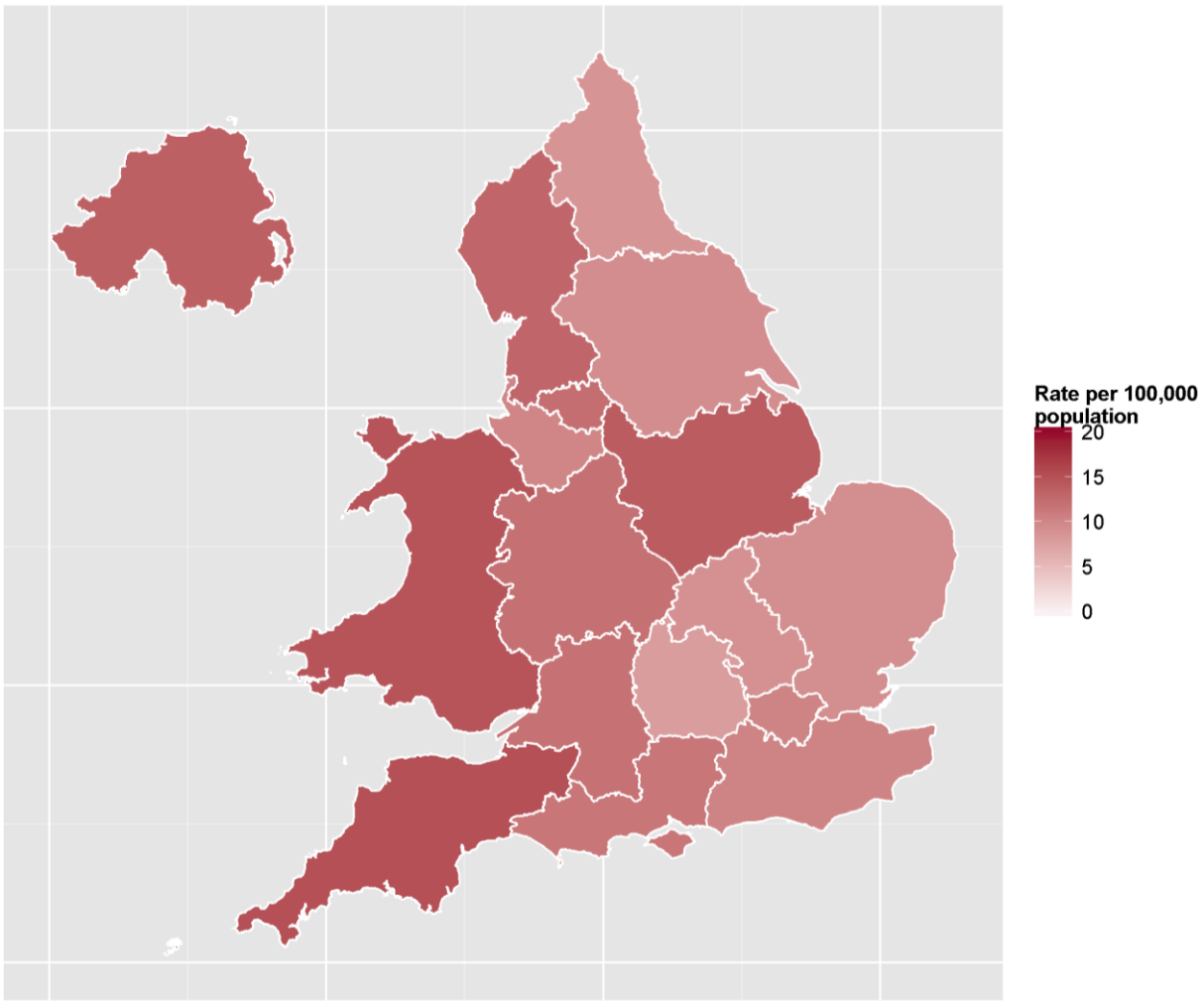


In line with this series of reports, all analyses presented hereafter, focus on the most recent five years (2011-2015), or latest year of data.

Geographic distribution

The overall rate of *Enterococcus* spp. bacteraemia in England, Wales and Northern Ireland in 2015 was 10.9, 13.6 and 14.8 per 100,000 population per year respectively (figure 2).

Figure 2. Geographical distribution of *Enterococcus* spp. bacteraemia per 100,000 population (England, Wales and Northern Ireland); 2015



Across the five year period, 2011-2015, the reported *Enterococcus* spp. bacteraemia rates increased by 15% in England (9.5 to 10.9/100,000; table 1), 11% in Northern Ireland (12.2 to 13.6), and a 2% increase reported in Wales (14.6 to 14.8).

Within England, incidence rates of *Enterococcus* spp. bacteraemia varied greatly in 2015, from 7.8 per 100,000 population in the Thames Valley region to 15.1/100,000 in the Devon, Cornwall & Somerset region (table 1).

All local regions in England reported an increase in rates of *Enterococcus* spp. bacteraemia between 2011 and 2015, with the exception of the Anglia & Essex region where a 9% decrease was noted. No single region in England has continuously reported the highest (or lowest) rates.

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

		Rate per 100,000 population				
Region	**Local Region**	**2011**	**2012**	**2013**	**2014**	**2015**
London	London	10.1	10.2	9.8	10.3	10.3
Midlands and East of England	South Midlands & Hertfordshire	6.9	5.6	6.9	7.8	9.1
	East Midlands	12.0	11.1	11.0	10.6	14.0
	Anglia & Essex	10.3	10.4	8.7	9.7	9.3
	West Midlands	10.1	9.8	11.8	12.1	12.2
North of England	Cheshire & Merseyside	9.8	10.7	11.9	10.8	10.0
	Cumbria & Lancashire	8.6	9.0	9.5	11.3	13.0
	Greater Manchester	11.9	13.1	13.0	12.5	12.3
	North East	8.4	6.5	8.6	8.0	8.7
	Yorkshire & Humber	8.4	7.5	6.4	6.7	9.4
South of England	Avon, Gloucestershire & Wiltshire	7.3	9.6	9.1	9.8	11.9
	Devon, Cornwall & Somerset	10.2	11.3	10.4	10.8	15.1
	Wessex	9.6	9.8	10.9	10.6	11.6
	Kent, Surrey & Sussex	9.1	9.4	9.0	8.5	10.3
	Thames Valley	6.0	5.7	4.6	6.3	7.8
England		**9.5**	**9.4**	**9.5**	**9.8**	**10.9**
Northern Ireland		**12.2**	**13.2**	**14.2**	**13.2**	**13.6**
Wales		**14.6**	**14.9**	**15.9**	**14.3**	**14.8**
England, Wales & Northern Ireland		**9.8**	**9.8**	**10.0**	**10.1**	**11.2**

Species distribution

The number of *Enterococcus* spp. bacteraemia reports, between 2011 and 2015, in England, Northern Ireland and Wales increased by 19%, 14% and 2% respectively (table 2). Comparably, in England, the total number of bacteraemia (any genus) reported to SGSS increased by 30% between 2011 and 2015 (92,905 to 121,220 reports)[1].

In 2015, 83% of *Enterococcus* spp. bacteraemia reports were identified to species level in England, Wales and Northern Ireland, a 25% increase on the 78% reported to species level in 2011. There was variation by country with 82%, 94% and 98% *Enterococcus* spp. bacteraemia reports identified to species level in England, Wales and Northern Ireland in 2015 respectively (table 2).

In 2015, 41% of *Enterococcus* spp. bacteraemia reports were identified as *E. faecalis* in England (2412/5910), 50% in Wales (228/457) and 42% in Northern Ireland (105/251). *E. faecium* was the second most frequently identified *Enterococcus* spp. in England and Wales (36% and 41% respectively), but the most frequently identified species in Northern Ireland (52%; 130/251).

Over the past five years, the proportion of *Enterococcus* spp. bacteraemia caused by *E. faecium* has increased from 29% in 2011 to 37% in 2015, reflecting a 48% increase in the number of reports (1657 to 2445 reports respectively). This increase is greater than that of the improvement in the proportion of isolates undergoing speciation, suggesting that there is an increasing dominance of *E. faecium* compared with other enterococci.

Of the other enterococcal bacteraemia species, only in *E. raffinosus* reports had a greater observed percentage increase compared with *E. faecium*, with the number of reports increasing by 185% from 13 in 2011 to 37 in 2015 in England; however, the number of actual reports in bacteraemia remained low. Of note, there was a sustained decrease in the number of *E. gallinarum* bacteraemia reports in England, from 125 in 2011 to 83 in 2015 (a decrease of 34%).

The changes in distribution of less common species of *Enterococcus* may in part be due to the increasing use of MALDI-ToF analysis in hospitals, which allows for better species identification and also a greater reporting of minor species not previously recognised in most clinical laboratories.

[1]The number of reported blood cultures positive for distinct bacterial genera

Table 2. Reports of *Enterococcus* spp. bacteraemia by species (England, Wales and Northern Ireland); 2011 to 2015

	2011		2012		2013		2014		2015	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
England										
E. avium	52	1	49	1	45	1	46	1	60	1
E. casseliflavus	30	1	32	1	38	1	51	1	49	1
E. durans	26	1	23	0	18	0	19	0	19	0
E. faecalis	2068	41	2069	41	2084	41	2129	41	2412	41
E. faecium	1446	29	1684	34	1759	35	1922	37	2128	36
E. gallinarum	125	3	120	2	106	2	84	2	83	1
E. hirae	3	0	4	0	0	0	4	0	4	0
E. raffinosus	13	0	19	0	33	1	27	1	37	1
Enterococcus spp., other named	81	2	60	1	39	1	54	1	36	1
Enterococcus spp., sp. not recorded	1140	23	953	19	953	19	916	17	1082	18
***Enterococcus* spp.**	**4984**	100	**5013**	100	**5075**	100	**5252**	100	**5910**	100
Wales										
E. avium	0	0	0	0	4	1	6	1	4	1
E. casseliflavus	0	0	2	0	3	1	4	1	2	0
E. durans	0	0	1	0	1	0	1	0	0	0
E. faecalis	226	51	220	48	216	44	210	48	228	50
E. faecium	102	23	155	34	205	42	179	41	187	41
E. gallinarum	1	0	2	0	2	0	0	0	2	0
E. hirae	1	0	0	0	1	0	1	0	1	0
E. raffinosus	1	0	3	1	4	1	4	1	7	2
Enterococcus spp., other named	0	0	0	0	0	0	0	0	0	0

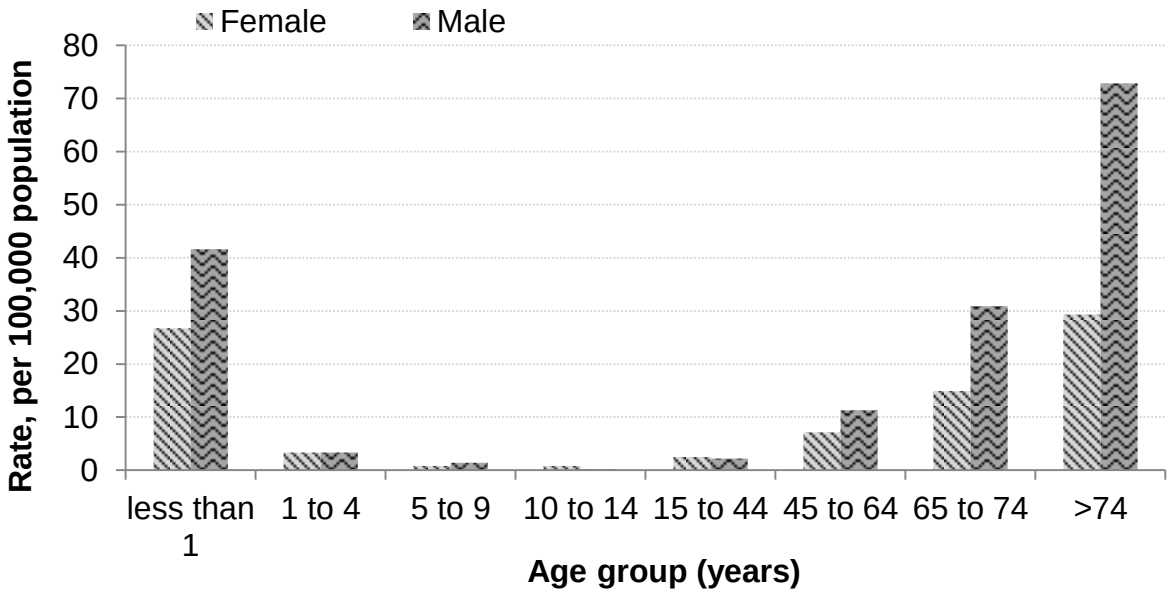
	Enterococcus spp., sp. not recorded	113	25	72	16	54	11	36	8	26	6
	***Enterococcus* spp.**	**444**	**100**	**455**	**100**	**490**	**100**	**441**	**100**	**457**	**100**
Northern Ireland											
	E. avium	2	1	6	3	1	0	2	1	1	0
	E. casseliflavus	6	3	0	0	2	1	1	0	2	1
	E. durans	1	0	1	0	3	1	0	0	1	0
	E. faecalis	95	43	107	45	123	47	99	41	105	42
	E. faecium	109	49	117	49	118	46	132	55	130	52
	E. gallinarum	3	1	6	3	3	1	2	1	3	1
	E. hirae	0	0	0	0	0	0	0	0	0	0
	E. raffinosus	0	0	1	0	5	2	4	2	5	2
	Enterococcus spp., other named	0	0	0	0	0	0	0	0	0	0
	Enterococcus spp., sp. not recorded	5	2	2	1	4	2	2	1	4	2
	***Enterococcus* spp.**	**221**	**100**	**240**	**100**	**259**	**100**	**242**	**100**	**251**	**100**

Age and Sex distribution

In line with previous reports, the highest rates of *Enterococcus* spp. bacteraemia in England in 2015 were observed in those aged 75 years or older (47.4 /100,000 population) and those aged less than one year (35.7/100,000) [4].

Variation in rates were also observed by gender, with higher rates noted in men for the majority of age groups in 2015, the exceptions being for those aged between 10 and 44 years (figure 3a). The most striking differences were noted in those aged 75 years and over (males: 72.8; females: 29.3) and to a lesser extent in those aged between 65 and 74 years (males: 30.9; females: 14.9).

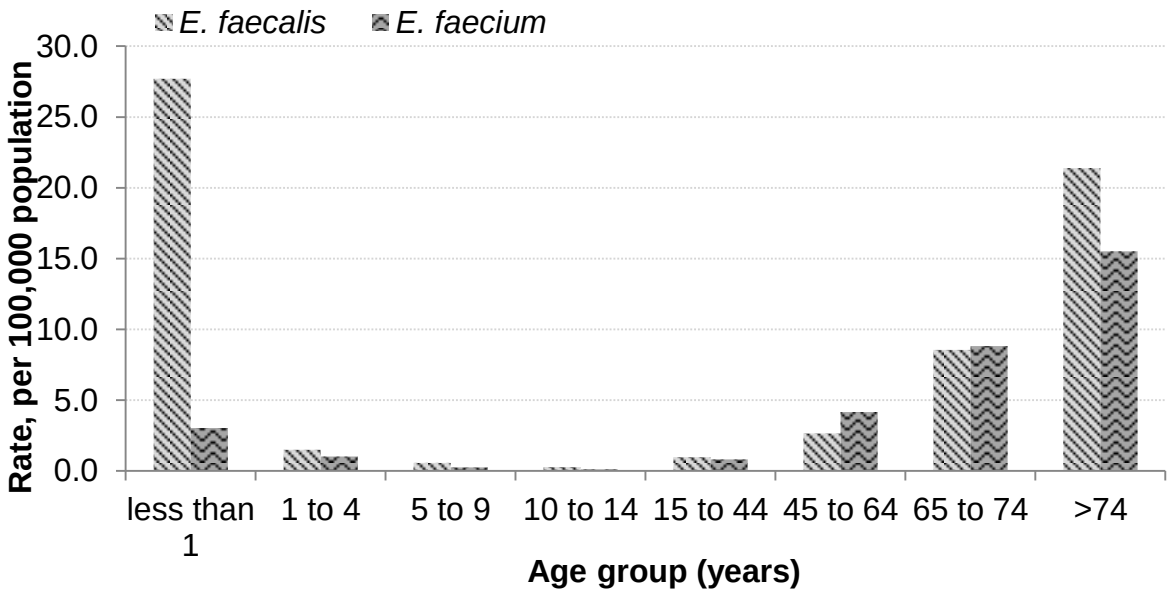
Figure 3a. *Enterococcus* spp. bacteraemia rates per 100,000 population by age and sex (England); 2015



Of the Enterococcal bacteraemia reported in infants less than 1 year, 78% are identified as *E. faecalis* (205/263) and 8% as *E. faecium* (22/263). The relative age distribution between the two most frequently reported *Enterococcus* spp. bacteraemia species, *E. faecalis* and *E. faecium*, differed in 2015 in England. Reviewed by species the rate of infection in infants less than 1 year was the highest incidence of *E. faecalis* (27.7/100,000 population), followed by those aged 75 years and over (21.4/100,000; figure 3b), differing from bacteraemia caused by *E. faecium* which was much less likely to be in infants (3.0/100,000).

The rate of *Enterococcus* spp. bacteraemia in neonates (<29 days old) in England was 0.20/1000 live births in 2015. Neonatal reports accounted for 50% of Enterococcal bacteraemia in infants (<1 year; 131/263), and 86% of those were reported as *E. faecalis* (113/131). Neonatal incidence of *E. faecalis* (<29 days) was 0.17/1000 live births, with early onset disease (<3 days old) occurring less often than late onset disease (3-28 days old) in 2015 (0.04 compared with 0.13/1000 live births).

Figure 3b. Age and sex population rate per 100,000 population for *E. faecalis* and *E. faecium* bacteraemia (England); 2015



Antimicrobial Resistance

Antimicrobial resistance of *Enterococcus* spp. to a glycopeptide (vancomycin/teicoplanin) has been identified by the Department of Health expert advisory committee for antimicrobial resistance and healthcare associated infections (ARHAI) as a key drug-bug combination and features in the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) annual report [5][6].

The proportion of isolates showing vancomycin resistance among all *Enterococcus* spp. from bacteraemia in England increased each year from 10% in 2011 to 17% in 2015.

Focussing on the most commonly reported enterococci causing bacteraemia, (*E. faecalis* and *E. faecium*), the proportion of isolates for which antimicrobial susceptibility test results were reported for at least one of ampicillin/amoxicillin, vancomycin, teicoplanin or linezolid, was 88% in 2015 (2133/2412 and 1870/2128 respectively; tables 3a and 3b). A 2016 UK public health resistance alert has recommended that laboratories perform linezolid

susceptibility tests on all *Enterococcus* spp. isolates from blood (and other sterile sites); the level of test reporting in 2015 was 61%, and represents a 28% increase in linezolid susceptibility test reporting from 2011, when only 47% enterococcal bacteraemia episodes had a linezolid result reported.

Reported resistance among *E. faecalis* isolates was low in 2015, comprising ≤2% for each of ampicillin/amoxicillin, vancomycin, teicoplanin and linezolid (table 3a). The proportion of *E. faecalis* bacteraemia isolates that were resistant to each of the reported antimicrobials decreased between 2011 and 2015, most notably for reported resistance to ampicillin/amoxicillin from 4.8% in 2011 to 2.0% in 2015. The decline in reported ampicillin/amoxicillin resistance is likely to be as a result of the overall improved species identification within *Enterococcus* spp; resistance to ampicillin/amoxicillin is not expected in *E. faecalis* isolates and this fact is commonly used as a distinguishing characteristic to differentiate between *E. faecalis* and *E. faecium* species.

The proportion of isolates of *E. faecium* resistant to each antibiotic was higher than the corresponding proportion seen with *E. faecalis* In 2015 the proportion of susceptibility tested *E. faecium* bacteraemia specimens resistant to ampicillin/amoxicillin was 92% (1673/1817), vancomycin 24% (423/1770), teicoplanin 25% (368/1452) and linezolid 1% (18/1374; table 3b).

Resistance to ampicillin/amoxicillin and linezolid identified in *E. faecium* specimens has remained stable over the 5 year period (2011 to 2015), with only slight fluctuations observed. However, a steady increase in the proportion of *E. faecium* bacteraemia isolates resistant to glycopeptides over the same period was reported. In 2015, the proportion of *E. faecium* isolates resistant to glycopeptides (vancomycin or teicoplanin) was 27%.

The most prevalent glycopeptide resistance genes (*vanA* and *vanB*) confer resistance to vancomycin and teicoplanin (v*anA*) or to vancomycin without resistance to teicoplanin (v*anB*). The apparent higher proportion of isolates resistant to teicoplanin (table 3b) may reflect differential local testing and reporting preferences for one or other glycopeptide.

Table 3a. Antimicrobial susceptibility for *E. faecalis* bacteraemia (England); 2011 to 2015**

	2011		2012		2013		2014		2015	
	No. Tested	% Resistant*	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant
Ampicillin/Amoxicillin	1805	5	1847	4	1844	3	1758	3	1986	2
Vancomycin	1710	3	1777	1	1761	1	1711	2	1969	1
Teicoplanin	1292	3	1365	2	1360	1	1366	2	1551	2
Linezolid	1018	<1	1123	<1	1240	<1	1201	<1	1422	<1
Total Reports	**2068**		**2069**		**2084**		**2129**		**2412**	

***** defined as reduced- or non-susceptible
** isolates can be tested against multiple drugs

Table 3b. Antimicrobial susceptibility for *E. faecium* bacteraemia (England); 2011 to 2015**

	2011		2012		2013		2014		2015	
	No. Tested	% Resistant*	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant	No. Tested	% Resistant
Ampicillin/Amoxicillin	1279	89	1501	92	1560	92	1540	91	1710	92
Vancomycin	1269	17	1499	19	1558	23	1570	22	1770	24
Teicoplanin	1020	16	1239	19	1260	22	1278	23	1452	25
Linezolid	839	<1	1095	<1	1203	1	1191	2	1374	1
Total Reports	**1446**		**1684**		**1759**		**1922**		**2128**	

***** defined as reduced- or non-susceptible
** isolates can be tested against multiple drugs

Caution is needed in the interpretation of vancomycin resistance in all enterococci rather than by particular species. A number of enterococci have low lying intrinsic vancomycin resistance mechanism genes (*vanC;* such as *E. gallinarum* and *E. casseliflavus*), while others can acquire resistance (*vanA* or *vanB*; such as *E. faecalis* and *E. faecium*) [7].

It is important to identify enterococcal bacteraemia episodes to species level and perform all relevant antimicrobial relevant susceptibility tests; this knowledge would be especially important for infection control and the limitation of potential outbreaks, the concern being that acquired resistance is transferable between organisms [8]. Patients yielding linezolid-resistant enterococci should be isolated, as a precaution, to prevent onward transmission.

Microbiology services

In 2015, the proportion of reports of enterococcal bacteraemia in which the organism was not fully identified remained around 18%. Precise species identification of isolates would improve the monitoring of trends in emerging enterococci in particular, in addition to assisting with instigating appropriate treatment and control mechanisms locally [9].

A UK Public Health Resistance Alert was cascaded in June 2016; highlighting that potentially transferable oxadolidinone (linezolid and tedizolid) resistance mediated by the *optrA* gene has been detected in *Enterococcus faecalis* in the UK. Laboratories are recommended to screen enterococci and staphylococci from sterile sites or where oxazolidinone treatment is a viable option for resistance to linezolid. Any isolates classified as linezolid-resistant (using the EUCAST criteria[2]) should be referred to PHE's Antimicrobial Resistance and Healthcare Associated Infections Reference Unit (AMRHAI) for confirmation [10]. Welsh laboratories should refer any linezolid-resistant isolates to the Specialist Antimicrobial Chemotherapy Unit (SACU), which will confirm resistance to linezolid before referring on to PHE's AMRHAI [11].

Laboratories are requested to send any enterococcal isolates with suspected linezolid, daptomycin or tigecycline resistance, as well as isolates which show resistance to teicoplanin but not vancomycin to AMRHAI for further investigation [12].For advice on treatment of antibiotic-resistant infections due to these opportunistic pathogens laboratories should contact the Medical Microbiologists at PHE's Bacteriology Reference Department at Colindale on colindalemedmicro@phe.gov.uk.

[2] European Committee on Antimicrobial Susceptibility Testing: resistant by disc (<19 mm) or by MIC (>4mg/l)

Acknowledgements

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