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Introduction

The following analysis is based on voluntary surveillance of diagnoses of bloodstream infections caused by *Enterococcus* spp. reported by laboratories between 2011 and 2020 in England. Voluntary surveillance data for England were extracted on 27 September 2021 from both the communicable disease reporting (CDR) and antimicrobial resistance (AMR) modules of the UK Health Security Agency's (UKHSA, formerly Public Health England) Second Generation Surveillance System (SGSS).

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 were further assigned to 1 of 9 of the then PHE local centres, formed from the administrative local authority boundaries [2].

The following report will look at the trends and geographical distribution of *Enterococcus* spp. bacteraemia cases in England. Cases are further broken down by species, age and sex. Antimicrobial susceptibility trends are based on SGSS AMR data, and reported for the period 2016 to 2020.

A web appendix is available featuring the data behind the findings of this report.

It should be noted that the data presented here for earlier years may differ from those in previous publications due to the inclusion of late reports.

Main points

Principal conclusions of this report are that:

- the overall rate of *Enterococcus* spp. bacteraemia in England was 14.1 per 100,000 population in 2020, a slight increase from 2019 (13.5 per 100,000), continuing a year-on-year increasing trend since 2014 (9.8 per 100,000 population)
- the rate of *Enterococcus* spp. bacteraemia in England increased from 2019 to 2020, unlike other pathogens such as *Escherichia coli* and Meticillin-susceptible *Staphylcoccus aureus* [3]
- within England, *Enterococcus* spp. bacteraemia rates ranged from 12.1 per 100,000 population in the East of England to 16.2 in the South West in 2020
- the highest rates of *Enterococcus* spp. bacteraemia were seen in the elderly (≥75 years; males: 98 per 100,000 population and females: 38 per 100,000 population)
- the majority of isolates from enterococcal bacteraemia episodes (89%) were identified to species level in 2020
- in 2020, the two most frequently identified *Enterococcus* spp. from blood were *E. faecalis* (43%) and *E. faecium* (42%)
- antibiotic resistance in *E. faecalis* was generally low in 2020, with resistance to glycopeptides at 2%
- resistance of *E. faecium* to glycopeptides decreased from 21% in 2019 to 19% in 2020 and decreased for linezolid from 2% in 2019 to 1% in 2020
- the COVID-19 pandemic affected the general case-mix of hospital patients during much of 2020, this has likely impacted the data for 2020

Trends

The rate of bacteraemia caused by *Enterococcus* spp. in England has been increasing year-onyear since 2014 (Figure 1), from 9.8 per 100,000 population in 2014 to 14.1 per 100,000 population in 2020 (an increase of 43.8%).

Figure 1. Rates of *Enterococcus* spp. bacteraemia per 100,000 population in England: 2011 to 2020



The observed increase in *Enterococcus* spp. bacteraemia since 2014 may partially be due to increased reporting following the launch of UKHSA's Second Generation Surveillance System (SGSS) in 2014.

Of note, there was an increase in the incidence of *Enterococcus* spp. bactereamia between 2019 and 2020, unlike other key pathogens such as *E. coli* which decreased in 2020 [3]. This may be due to an increased number of patients being admitted to intensive care units (ICUs) in 2020, as a result of the COVID-19 pandemic, receiving prophylactic antibiotic treatment targeting prevention of Gram-negative bacterial infections (*Enterococcus* spp. are intrinsically resistant to cephalosporins) [4,5]. Patients on ICUs are at higher risk for bacteraemia as the setting allows the opportunistic pathogen to become invasive, with many risk factors for *Enterococcus* spp. bacteraemia overlapping with characteristics of patients on ICUs [6]. These are possible reasons for the increasing incidence; however the increase is likely to be multifactorial.

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Geographic distribution

In 2020, the rate of *Enterococcus* spp. bacteraemia across England was 14.1 per 100,000 population, which represents an increase of 15.8% since 2016 and an increase of 4.4% from 2019 (Table 1).

		Rate per 100,000 population									
Region	PHE Centre	2016	2017	2018	2019	2020					
	North East	11.8	11.3	12.4	12.7	12.3					
North of England	North West	13.8	12.8	11.9	15.2	15.9					
North of England	Yorkshire and Humber	9.1	9.2	13.2	12.1	12.9					
Midlands and East of England	East Midlands	13.1	13.2	13.8	13.8	14.2					
	East of England	12.1	12.7	11.2	11.8	12.1					
	West Midlands	12.8	14.2	14.5	12.8	14.3					
London	London	11.2	11.7	11.0	12.8	13.2					
South of England	South East	11.7	12.3	12.8	14.6	16.0					
	South West	14.8	14.9	16.1	16.8	16.2					
England		12.2	12.5	12.8	13.5	14.1					

Table 1. <i>Enterococcus</i> sp	p. bacteraemia per 100,	000 population by	region (England):
2016 to 2020	-		

From a public health perspective, England is split into constituent geographical areas: 4 Regions and 9 Centres. In 2020, all geographical areas had similar or higher rates of *Enterococcus* spp. bacteraemia compared to 2016. Similarly, rates increased in all regions between 2019 and 2020, except for the North East and South West centres where slight decreases were noted. The increase was most marked in the West Midlands, from 12.8 per 100,000 population in 2019 to 14.3 per 100,000 population in 2020.

The centre with the highest rate of *Enterococcus* spp. bacteraemia in 2020 was the South West (16.2 per 100,000) (Figure 2). The lowest recorded rate continued to be in the East of England (12.1 per 100,000), consistent with the past 3 years.

Differences between geographical areas may account for the variation observed. These include completeness of reporting, local outbreaks, as well as differences in the resident populations and distribution of specialist care units.

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Figure 2. Geographical distribution of *Enterococcus* spp. bacteraemia rates per 100,000 population (England): 2020



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Species distribution

Eighty-nine per cent of isolates from *Enterococcus* spp. bacteraemia episodes reported in 2020 were identified to species level in England, a similar figure to previous years (Table 2). The most frequently identified species in 2020 was *E. faecalis* (3,389 reports, 43%), similar to previous years.

The second most commonly reported *Enterococcus* species in England in 2020 was *E. faecium* (42%). The percentage of *Enterococcus* species due to *E. faecium* has been increasing slightly year-on-year, from 37.3 % in 2017 (2,588 reports) to 42.2% in 2020 (3,364 reports).

E. faecium was identified in 1.8 % of mono-microbial (bacterial and fungal) bloodstream infections (BSI; ranked seventh) and 3.2% of poly-microbial BSI in 2020 (ranked seventh) in England. *E. faecalis* was identified in 1.6% of mono-microbial (bacterial and fungal) BSI (ranked eighth) and 4.1% of poly-microbial BSI in 2020 (ranked fifth) in England.

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	2016		201	7	201	8	2019		2020	
	No	(%)								
Enterococcus spp.	6,751	(100)	6,947	(100)	7,174	(100)	7,622	(100)	7,963	(100)
E. avium	48	(<1)	64	(<1)	74	(1.0)	60	(<1)	72	(<1)
E. casseliflavus	61	(<1)	60	(<1)	73	(1.0)	77	(1.0)	80	(1.0)
E. durans	16	(<1)	27	(0.4)	15	(0.2)	16	(<1)	19	(<1)
E. faecalis	2,826	(41.9)	3,031	(43.6)	3,137	(43.7)	3,290	(43.2)	3,389	(42.6)
E. faecium	2,569	(38.1)	2,588	(37.3)	2,795	(39.0)	3,152	(41.4)	3,364	(42.2)
E. gallinarum	93	(1.4)	90	(1.3)	117	(1.6)	97	(1.3)	86	(1.1)
E. raffinosus	40	(<1)	59	(0.8)	55	(<1)	73	(1.0)	72	(<1)
Enterococcus spp., other named+	39	(0.5)	51	(<1)	49	(<1)	37	(<1)	30	(<1)
Enterococcus spp., sp. not recorded	1,059	(16)	977	(14)	859	(12)	820	(11)	851	(11)

	Table 2. Reports of Enterococcus spp.	bacteraemia by spe	ecies (England)	: 2016 to 2020
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+ including E. cecorum, E. columbae, E. gilvus, E. hirae, E. italicus, E. maldoratus, E. mundtii, E. pnoeniculicola, E. saccharolyticus and E. thailandicus

Age and sex distribution

As in previous years, enterococcal bacteraemia continues to be the most prevalent in the youngest and oldest members of the population (Figure 3) [7].





Children under one year of age had an overall rate of 48 per 100,000 population in 2020. This was higher in males than females (53 vs 37 per 100,000 population), and considerably higher than for older children (Figure 3). The rate of *Enterococcus* spp. bacteraemia per 100,000 population in the 1 to 4 year, 5 to 9 year and 10 to 14 year age groups was 4, 2 and 1 per 100,000 population, respectively.

The highest overall rate of bacteraemia caused by enterococci was seen in persons 75 years old and over (63 per 100,000 population). This is consistent with findings in previous years [7]. Sex differences were more significant in older age groups; in persons aged 75 years and over, more men (per 100,000 population) had *Enterococcus* spp. bacteraemia in 2020 than women (males: 98 per 100,000 and females: 38 per 100,000) (Figure 3).

Antimicrobial resistance: England

Resistance of *Enterococcus* spp. to glycopeptides (vancomycin or teicoplanin) is monitored in the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) annual report [8], as it is one of the key drug/bug combinations identified by the Department of Health and Social Care Advisory Committee for Antimicrobial Prescribing, Resistance and Healthcare Associated Infections (APRHAI) [9].

In 2020, antimicrobial resistance in *E. faecalis* bacteraemia remained rare, at around 2% resistant to several antimicrobial agents (ampicillin/amoxicillins*, vancomycin, teicoplanin) and one per cent to linezolid, and has remained largely unchanged (Table 3a).

The percentage of *E. faecium* bacteraemia episodes reported as resistant to glycopeptides has decreased from 2016 to 2020 (Table 3b), from 23% to 19% for vancomycin and 24% to 19% for teicoplanin. The percentage of isolates that were resistant to linezolid remained low, at around one per cent resistant in 2020.

It is important to identify enterococcal bacteraemia episodes to species level and perform all relevant antimicrobial susceptibility tests; this knowledge is especially important for infection control and limitation of potential outbreaks [5]. Referral to the reference lab for molecular testing is needed where transferable resistance may be suspected, the concern being that acquired resistance is transferrable between organisms. Patients yielding linezolid-resistant enterococci should be isolated, as a precaution, to prevent onward transmission as enterococci possessing one of the transferable genes conferring linezolid resistance are of greater public health concern than isolates that are resistant to linezolid due to chromosomal mutation(s).

^{*} *E. faecalis* samples resistant to ampicillin/amoxicillin are unlikely to be correctly identified as ampicillin/amoxicillin resistance in this species is rare.

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Table 3a. Antimicrobial susceptibility for *E. faecalis* bacteraemia isolates (England): 2016 to 2020

Key

S = susceptible; I = intermediate (susceptible dose-dependent); R = resistant

		2016		2017			2018			2019			2020		
Antimicrobial agent	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)
Ampicillin/Amoxicillin	98	<1	2	98	<1	2	98	<1	2	98	<1	2	98	<1	2
Vancomycin	99	0	1	99	0	1	98	0	2	98	0	2	98	0	2
Teicoplanin	98	0	2	98	0	2	98	0	2	98	0	2	98	0	2
Linezolid	100	0	<1	100	<1	<1	99	0	<1	100	0	<1	100	0	1

Table 3b. Antimicrobial susceptibility for *E. faecium* bacteraemia isolates (England): 2016 to 2020

Key

S = susceptible; I = intermediate (susceptible dose-dependent); R = resistant

		2016		2017			2018			2019			2020		
Antimicrobial agent	S (%)	l (%)	R (%)	S (%)	ا (%)	R (%)									
Ampicillin/Amoxicillin	9	0	91	9	0	91	9	<1	91	9	<1	91	8	<1	92
Vancomycin	77	0	23	79	0	21	78	0	22	79	0	21	81	0	19
Teicoplanin	76	0	24	78	0	22	77	0	23	79	0	21	81	0	19
Linezolid	99	0	1	99	0	<1	99	0	1	98	0	2	99	0	1

Microbiology services

In 2020, the percentage of reports of enterococcal bacteraemia in which the organism was not fully identified decreased to 11% from 16% in 2016. Precise species identification of isolates would improve the monitoring of trends in emerging enterococci, in addition to assisting with instigating appropriate treatment and control mechanisms locally [10].

Laboratories are requested to send any enterococcal isolates with suspected linezolid or tigecycline resistance and isolates that show resistance to teicoplanin but not vancomycin to UKHSA's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit for further investigation (amrhai@phe.gov.uk) [10]. AMRHAI will also examine isolates with suspected high-level daptomycin MICs (a daptomycin MIC for *E. faecium* >4mg/L and for *E. faecalis* >2mg/L), although it should be noted that there are no EUCAST clinical breakpoints. For advice on treatment of antibiotic-resistant infections due to these opportunistic pathogens, laboratories should contact the Medical Microbiologists at UKHSA's Bacteriology Reference Department at Colindale on colindalemedmicro@phe.gov.uk.

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