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Laboratory surveillance of Staphylococcus aureus bacteraemia in England, Wales and Northern Ireland: 2016

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Laboratory surveillance of *Staphylococcus aureus* bacteraemia in England, Wales and Northern Ireland: 2016

These analyses are based on data relating to bloodstream infections caused by *Staphylococcus aureus* (*S. aureus*) reported by laboratories between 2009 and 2016. Data for England were extracted on 19 July 2017 from Public Health England's (PHE) voluntary surveillance database, the Second Generation Surveillance System (SGSS). Data for Northern Ireland and Wales were extracted on 14 June 2017 and 1 August 2017 (CoSurv and DataStore systems), respectively.

SGSS comprises a communicable disease reporting module (CDR; formerly CoSurv/LabBase2) that includes antimicrobial susceptibility and other data and a separate antimicrobial resistance module (AMR; formerly AmSurv) that captures more comprehensive antibiogram data (including all antibiotics tested). However, until the launch of SGSS in 2014, AmSurv had lower laboratory coverage than CoSurv/LabBase2. Therefore, analysis of trends in antimicrobial susceptibility is not currently undertaken using data from the AMR module.

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 [1]. Geographical analyses were based on the residential postcode of the patient if known (otherwise the GP postcode if known, or the postcode of the laboratory in this order) with cases in England being assigned to one of nine local PHE centres (PHECs) formed from administrative local authority boundaries.

The report includes analyses on the trends, age and sex distribution, geographical distribution of cases of *S. aureus* bacteraemia in England, Wales and Northern Ireland. In addition, antimicrobial susceptibility five-year trend data for England and Northern Ireland have been included in this report. Finally, the level of ascertainment by laboratories in England as compared to the mandatory surveillance of MRSA and MSSA bacteraemia has been included. A web appendix is available featuring the findings of this report, including data submitted via SGSS from laboratories in England.

Data from six laboratories (two in London, one in the South East, one in the North East, one in the North West and one in Yorkshire and Humber) were excluded from the analyses due to concerns about the quality of data submitted to SGSS.

Key Points

- The overall *Staphylococcus aureus* bacteraemia rate in England, Wales and Northern Ireland decreased by 16.8% between 2009 (17.7/100,000) and 2012 (14.7/100,000) and increased thereafter reaching 18.2 reports per 100,000 population in 2016
- between 2009 and 2016, the rate of MRSA bacteraemia decreased by 61.0%, the rate of MSSA bacteraemia increased by 14.2% and the rate of untested *S. aureus* bacteraemia increased by 37.9% in England, Wales and Northern Ireland
- in 2016, the combined MRSA bacteraemia rate in England, Wales and Northern Ireland was 1.3 per 100,000 population, while the MSSA bacteraemia rate per 100,000 population was 14.7
- in England in 2016, the highest MRSA bacteraemia rate was observed in North East, North West and East of England PHE Centres (PHECs) (1.4/100,000 population), while North East, West Midlands and South West PHECs reported the highest MSSA bacteraemia rates (22.3/100,000, 17.5/100,000 and 17.5/100,000, respectively)
- the MRSA bacteraemia rates per 100,000 population were the highest amongst the elderly (≥75 years: 8.3/100,000 in men and 3.7/100,000 in women) in England, Wales and Northern Ireland in 2016. Males had higher MRSA bacteraemia rates than females in all age groups except for 10-14 years old
- the MSSA bacteraemia rates were the highest amongst the elderly and the very young (≥75 years: 86.3/100,000 in men and 40.3/100,000 in women, <1 year: 46.9/100,000 in males and 28.5/100,000 in females), with rates being higher in males in all age groups in England, Wales and Northern Ireland in 2016
- between 2012 and 2016, the non-susceptibility of MRSA isolates to ciprofloxacin and erythromycin decreased by 20% (88% to 68%) and 10% (65% to 55%), respectively,
- the non-susceptibility of MRSA isolates to fusidic acid increased by 5% (16% to 21%) between 2012 and 2016
- during the five-year period, the non-susceptibility of MSSA isolates to erythromycin and fusidic acid increased by 4% (12% to 16%) and 2% (12% to 14%), respectively

Trends

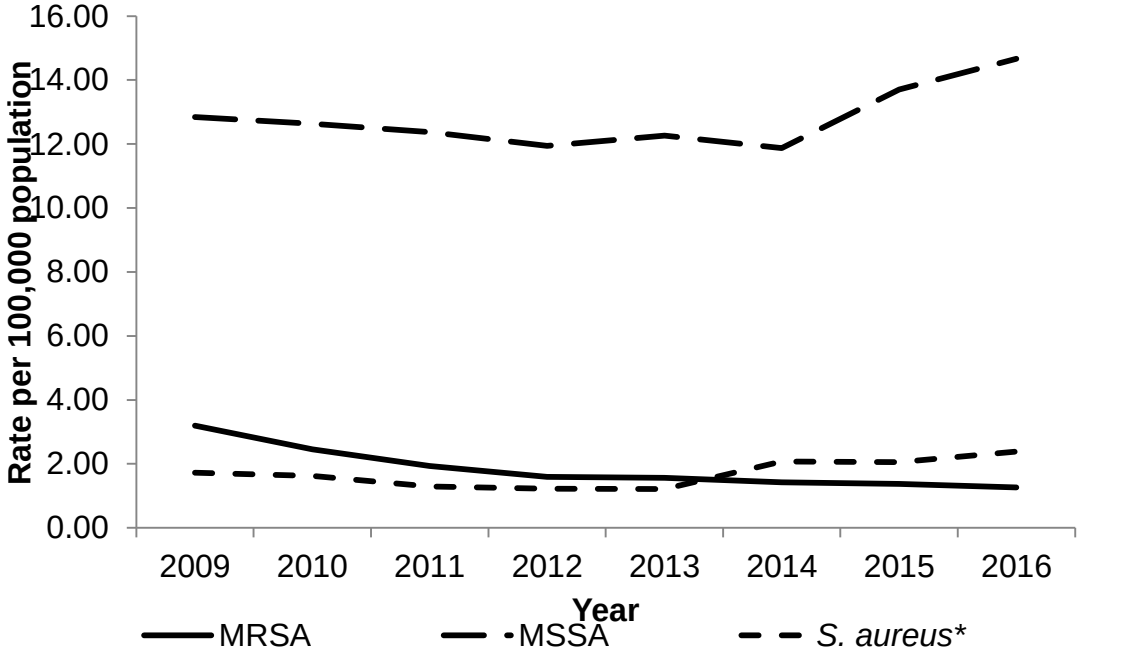
Figure 1 shows the trend in the rate (per 100,000 population) of laboratory-reported MRSA (non-susceptibility to meticillin, oxacillin, cloxacillin and/or cefoxitin in England and Northern Ireland, and cefoxitin in Wales), MSSA and untested *S. aureus* bacteraemia in England, Wales and Northern Ireland between 2009 and 2016.

Between 2009 and 2016, the bacteraemia rate of MRSA decreased by 61.0% in England, Wales and Northern Ireland, with the largest reductions of 23.1%, 21.3% and 17.4% observed between 2009 and 2010, 2010 and 2011, and 2011 and 2012, after which it continued to decrease year-on-year, albeit by a much smaller percentage.

There was an overall increase of 14.2% in the rate of MSSA bacteraemia between 2009 and 2016. The rate of MSSA bacteraemia per 100,000 population decreased between 2009 and 2012 but increased thereafter.

Caution should be used when interpreting these figures as there was a 37.9% increase in bacteraemia rate of *S. aureus* without susceptibility data between 2009 and 2016. The bacteraemia rate of unspecified *S. aureus* has exceeded the rate MRSA since 2014.

Figure 1. Rates of bacteraemia per 100,000 population (England, Wales and Northern Ireland) caused by MRSA, MSSA and *S. aureus* where susceptibility to methicillin was not reported: 2009 to 2016



**S. aureus* where susceptibility to methicillin was not reported*

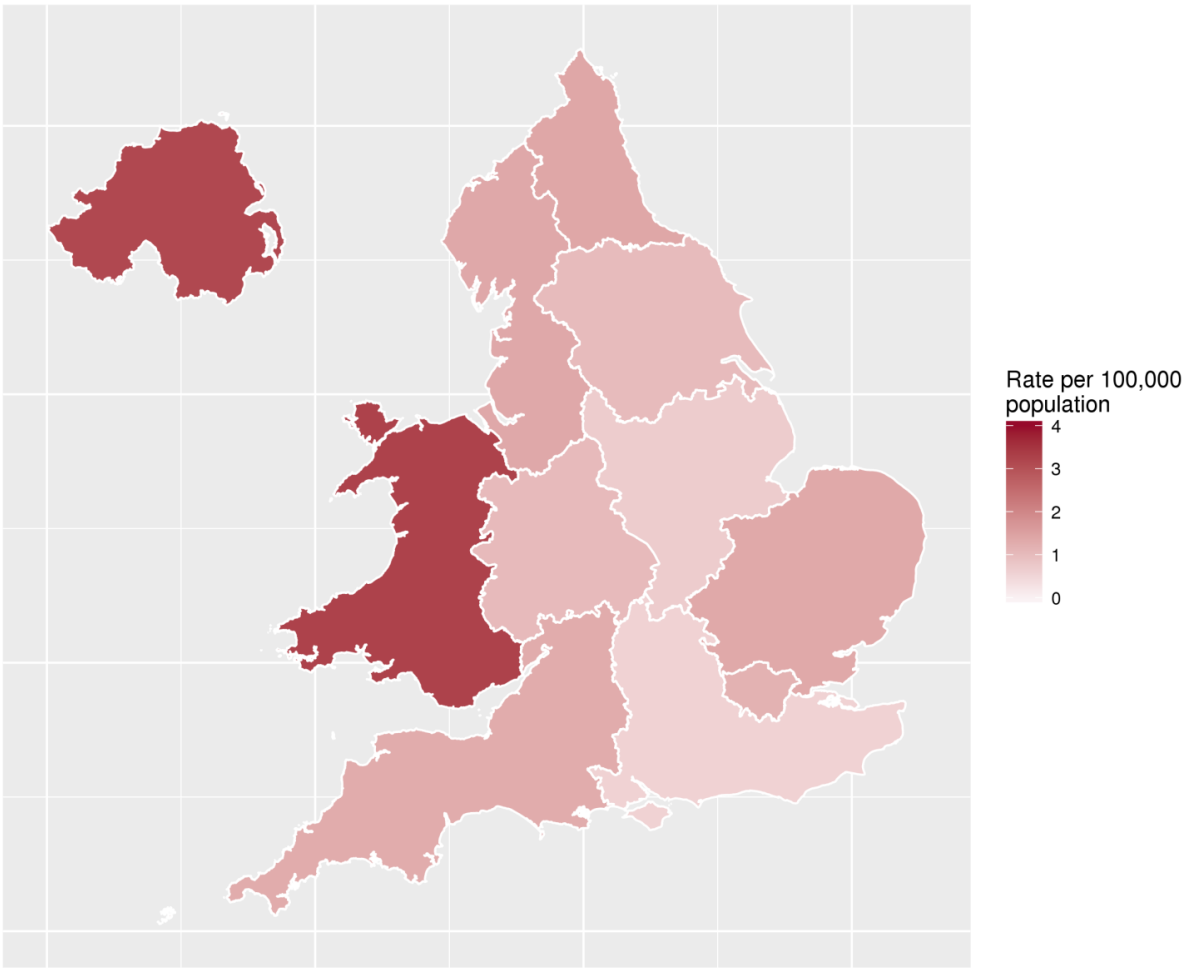
Geographic distribution: MRSA

The combined rate of bacteraemia due to MRSA in England, Wales and Northern Ireland was 1.3 per 100,000 population in 2016; individually, the rates were 1.1, 3.3 and 3.2 reports per 100,000 population in England, Wales and Northern Ireland, respectively. The rate varied in England across PHE centres (PHECs) from 0.6 reports per 100,000 population in South East PHEC to 1.4 per 100,000 in North East, North West and East of England PHECs (Figure 2a) (Table 1a).

While the rate of MRSA in England and Wales decreased by 14.1% (1.3 to 1.1 reports per 100,000 population) and 43.7% (5.8 to 3.3 reports per 100,000 population) between 2012 and 2016, respectively, the rate of MRSA bacteraemia in Northern Ireland fluctuated considerably over the same time period, with the overall percentage change being 23.0% from 4.1 to 3.2 reports per 100,000 population between 2012 and 2016 (Table 1a). The MRSA bacteraemia rate decreased by 4.7% (1.14 to 1.10 reports per 100,000 population), 12.5% (3.7 to 3.3 reports per 100,000 population) and 26.7% (4.3 to 3.2 reports per 100,000) in England, Wales and Northern Ireland between 2015 and 2016, respectively.

While there was an overall decrease in rates of MRSA bacteraemia observed for England between 2012 and 2016, this wasn't observed in all PHECs. The bacteraemia rate increased by 13.2% (1.2 to 1.4 reports per 100,000 population) and 0.1% (1.36 to 1.37 reports per 100,000 population) in East of England and North West PHECs between 2012 and 2016, respectively. The largest decreases in MRSA bacteraemia rates of 42.7% (1.1 to 0.6 reports per 100,000 population) and 28.6% (2.0 to 1.4 reports per 100,000 population) were observed in South East and North East PHECs during the five-year period. While more recently, between 2015 and 2016, five PHECs, namely North East, Yorkshire and Humber, North West, London and South West reported increases in their MRSA bacteraemia rate, the highest of which was observed in North East (22.8%; 1.1 to 1.4 reports per 100,000 population). The largest decrease in the bacteraemia rate of 40.6% (1.2 to 0.7 reports per 100,000 population) and 36.7% (1.6 to 1.0 reports per 100,000 population) was observed in East Midlands and West Midlands PHECs between 2015 and 2016, respectively.

Figure 2a. Geographical distribution of MRSA bacteraemia rates per 100,000 population (England, Wales and Northern Ireland): 2016*



* Data extracted on 19 July 2017.

Table 1a: Rate of MRSA bacteraemia reports per 100,000 population by PHE Centre (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	2.0	1.3	0.7	1.1	1.4
	Yorkshire and Humber	1.1	1.0	0.7	1.0	1.0
	North West	1.4	1.5	1.1	1.2	1.4
Midlands and East of England	West Midlands	1.3	1.3	1.3	1.6	1.0
	East Midlands	0.8	1.1	1.1	1.2	0.7
	East of England	1.2	1.2	1.8	1.4	1.4
London	London	1.5	1.4	1.1	1.0	1.2
South of England	South West	1.6	1.0	1.4	1.2	1.3
	South East	1.0	1.4	1.0	0.8	0.6
England*		1.3	1.3	1.2	1.1	1.1
Wales[¥]		5.8	5.3	5.1	3.7	3.3
Northern Ireland[†]		4.1	3.9	2.9	4.3	3.2
England, Wales & Northern Ireland		1.6	1.6	1.4	1.4	1.3

* Extracted on 19 July 2017; [¥] extracted on 1 August 2017, [†]extracted on 14 June 2017

Geographic distribution: MSSA

The combined rate of bacteraemia due to MSSA in England, Wales and Northern Ireland was 14.7 reports per 100,000 population in 2016; individually the rates of laboratory-reported bacteraemia were 14.1, 23.0 and 18.8 per 100,000 population in England, Wales and Northern Ireland,. The rate varied in England across PHECs between 8.1 to 22.3 bacteraemia reports per 100,000 population in London and North East PHECs respectively (Figure 2b) (Table 1b),.

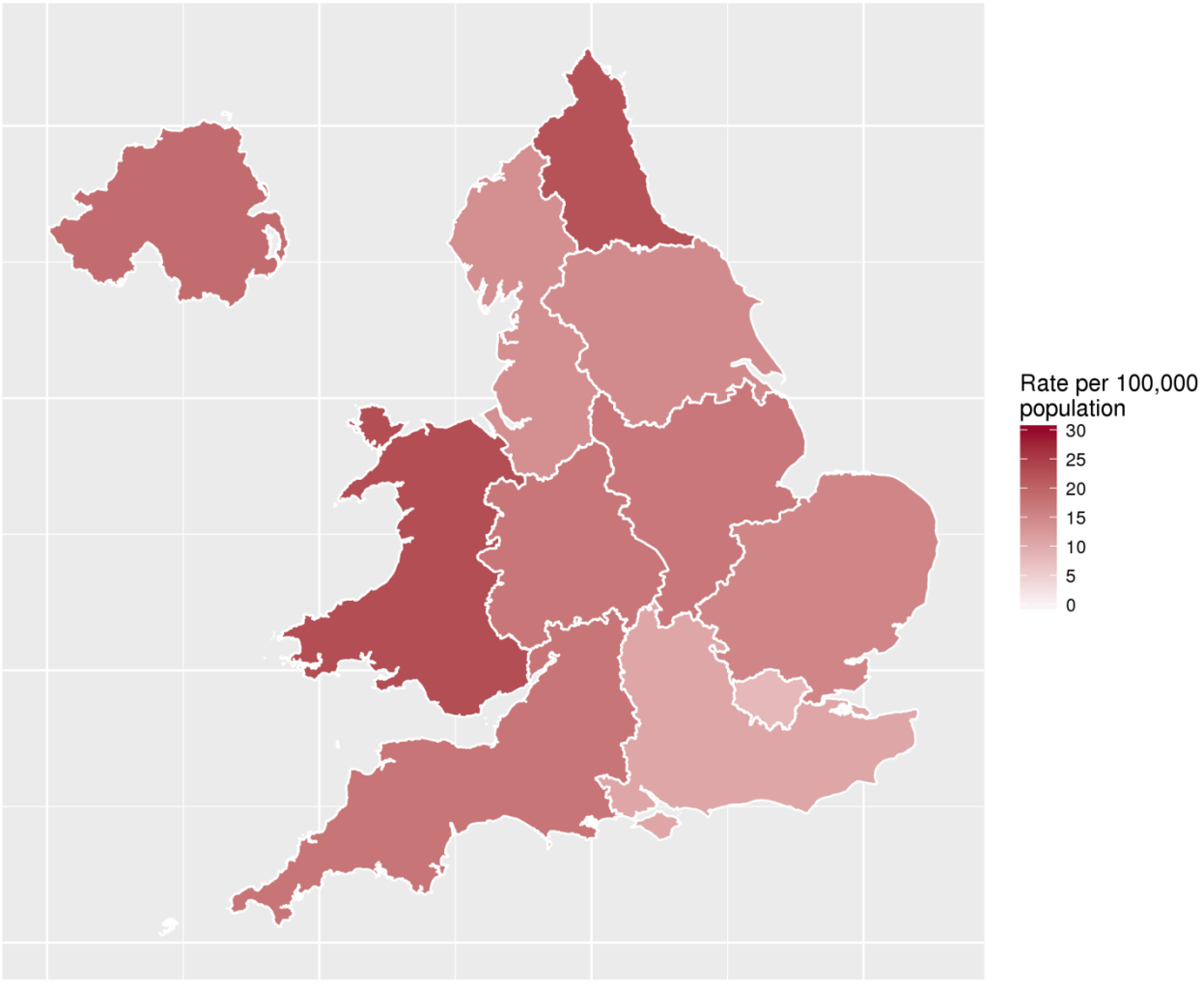
Between 2012 and 2016, the MSSA bacteraemia rate increased by 25.7% (11.2 to 14.1 reports per 100,000 population), 1.1% (22.7 to 23.0 reports per 100,000 population) and 17.3% (16.1 to 18.8 reports per 100,000 population) in England, Wales and Northern Ireland, respectively. While the bacteraemia rate increased by 8.8% (12.9 to 14.1 reports per 100,000 population) and 13.7% (16.6 to 18.8 reports per 100,000 population) in England and Northern Ireland between 2015 and 2016, respectively, the rate decreased by 11.0% (25.8 to 23.0 reports per 100,000 population) in Wales during the same period.

The MSSA bacteraemia rate increase was observed among all PHECs, except for London, of which the highest were in Yorkshire and Humber (71.0%; 8.4 to 14.4 reports per 100,000 population) and South West (54.5%; 11.3 to 17.5 reports per 100,000 population)

PHECs, between 2012 and 2016. During this period, the bacteraemia rate in London PHEC decreased by 17.7% (9.8 to 8.1 reports per 100,000 population).

More recently, between 2015 and 2016, only three PHECs (London, Yorkshire and Humber and North West PHECs) reported reductions in their MSSA bacteraemia rates of 1.2% (8.2 to 8.1 reports per 100,000 population), 0.5% (14.5 to 14.4 reports per 100,000 population) and 0.2% (13.88 to 13.85 reports per 100,000 population), respectively.

Figure 2b. Geographical distribution of MSSA bacteraemia rates per 100,000 population (England, Wales and Northern Ireland): 2016*



* Data extracted on 19 July 2017.

Table 1b: Rate of MSSA bacteraemia reports per 100,000 population by PHE Centre (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	16.7	15.3	13.5	19.8	22.3
	Yorkshire and Humber	8.4	8.7	9.4	14.5	14.4
	North West	12.9	12.6	11.4	13.9	13.9
Midlands and East of England	West Midlands	12.0	14.0	13.8	15.2	17.5
	East Midlands	11.9	11.1	11.4	15.9	17.2
	East of England	11.8	11.6	12.5	13.9	15.1
London	London	9.8	9.6	7.9	8.2	8.1
South of England	South West	11.3	13.2	13.7	14.9	17.5
	South East	9.9	10.1	9.6	8.7	10.6
England*		11.2	11.5	11.1	12.9	14.1
Wales[¥]		22.7	24.6	23.8	25.8	23.0
Northern Ireland[†]		16.1	15.4	15.3	16.6	18.8
England, Wales & Northern Ireland		11.9	12.3	11.9	13.7	14.7

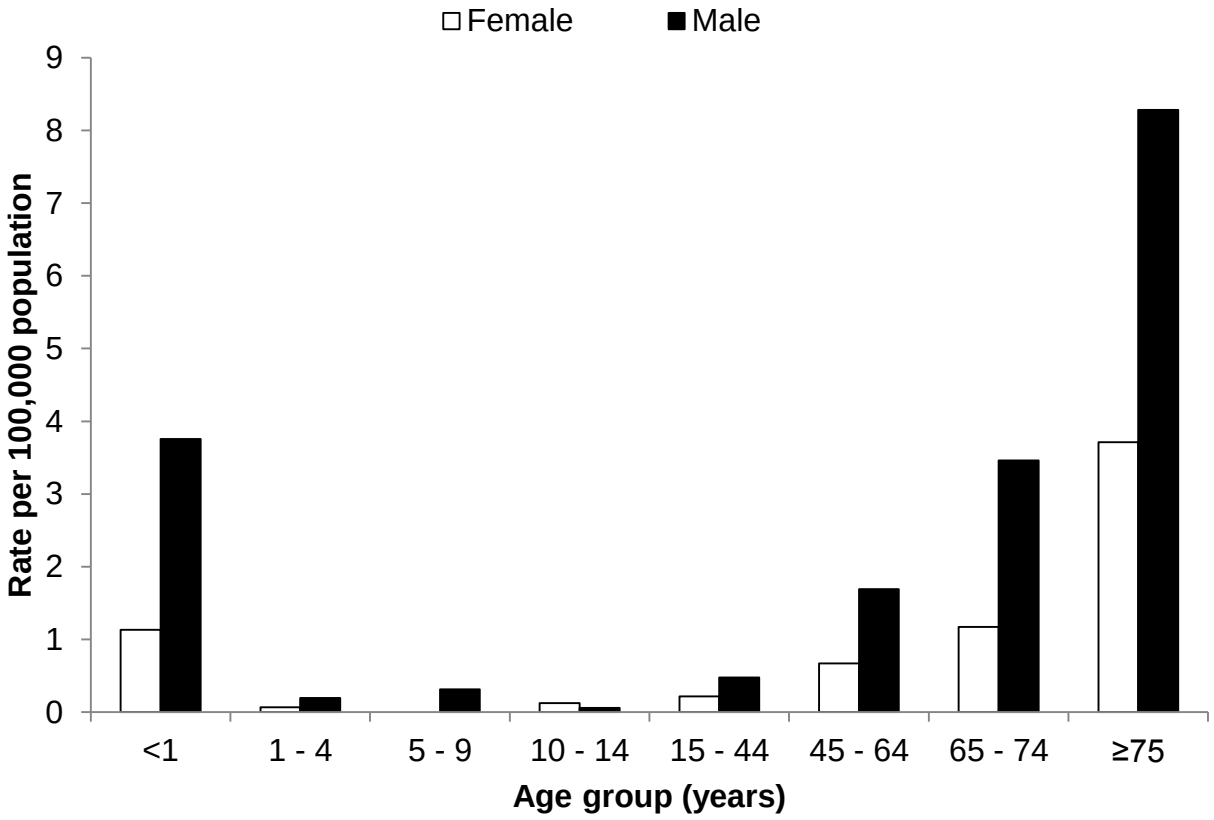
* Extracted on 19 July 2017; [¥] extracted on 1 August 2017; [†] extracted on 14 June 2017

It is of note that in England and Northern Ireland, there are links from the different laboratories to SGSS/CoSurv that report clinically significant isolates. Data from Wales is 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.

Age and sex distribution: MRSA

Figure 3a depicts MRSA bacteraemia rate per 100,000 population amongst men and women across different age groups in England, Wales and Northern Ireland in 2016. The bacteraemia rate was the highest among ≥75 years old, those below the age of one year and 65-74 years old. The rate of bacteraemia per 100,000 population in these age groups was markedly higher amongst males in comparison to females (≥75 years: 8.3 vs. 3.7, <1 year: 3.8 vs. 1.1 and 65-74 years: 3.5 vs 1.2 per 100,000 population). The rate was observed to be higher in females only amongst 10-14 years old (0.12 vs. 0.06 per 100,000 population in females and males, respectively). This pattern was broadly similar to previously reported data [2].

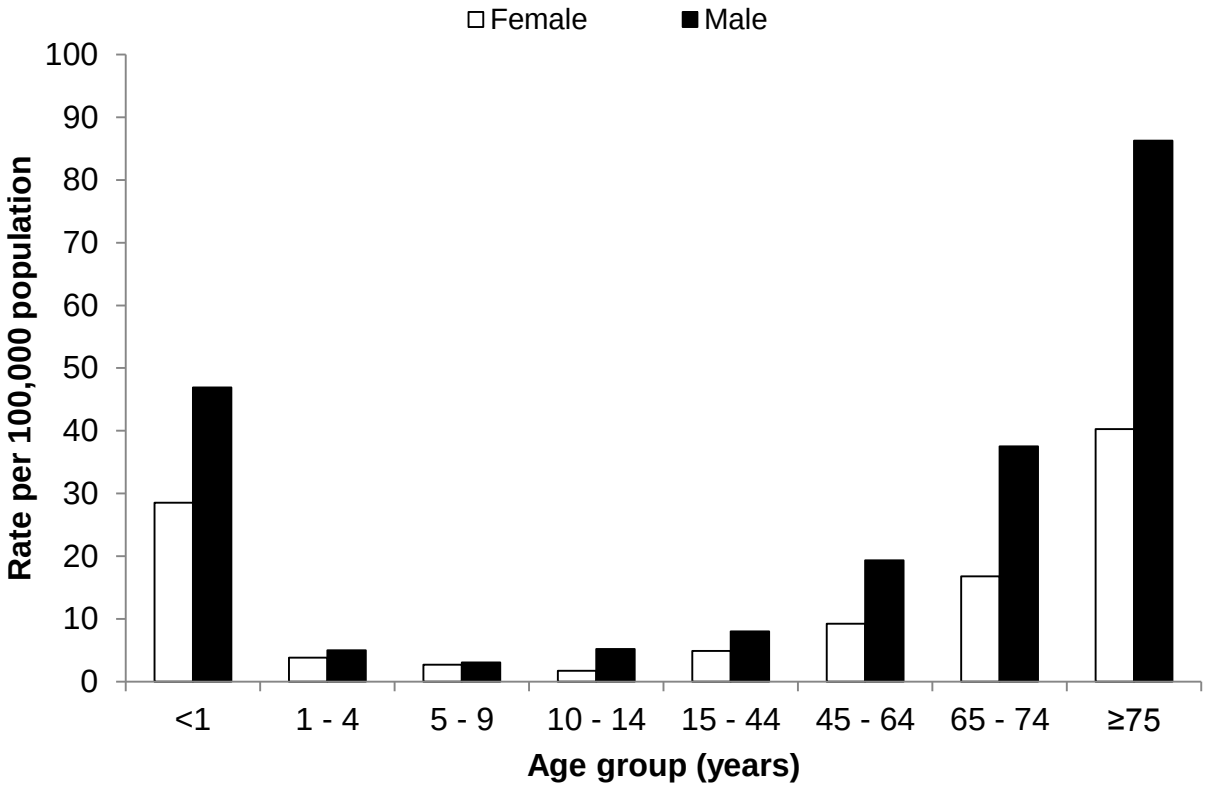
Figure 3a. MRSA bacteraemia rates per 100,000 population by age and sex (England and Northern Ireland): 2016



Age and sex distribution: MSSA

Figure 3b shows that the rate of MSSA bacteraemia had similar distribution patterns across age and sex as MRSA bacteraemia (Figure 3a). The highest combined bacteraemia rate was observed in those 75 years old and over (60.0 reports per 100,000 population), those below the age of one (38.7 reports per 100,000 population) and in 65-74 year olds (26.8 reports per 100,000 population). The bacteraemia rate was higher in males in comparison to females across all age groups, and males over 75 years and 65-74 years old had double the rate of females in these age groups (86.3 vs. 40.3 and 37.5 vs. 16.8 per 100,000 population, respectively).

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



Antimicrobial resistance: England and Northern Ireland

Tables 2a and 2b show trends in non-susceptibility to key antibiotic agents for MRSA and MSSA between 2012 and 2016.

MRSA bacteraemia isolates had a high proportion (>80%) of susceptibility test results reported for the majority of key antibiotics, except for glycopeptides (vancomycin (78%), teicoplanin (69%)) and linezolid (78%) in 2016. Similar patterns were observed for MSSA with at least 70% susceptibility test results available for key antimicrobials with the exception of glycopeptides (vancomycin (64%) and teicoplanin (57%)).

Ciprofloxacin resistance rates decreased in MRSA isolates by 20% between 2012 (88%) and 2016 (68%), but remained stable at 7% in MSSA isolates during the five- year period. Fluoroquinolone resistance is relatively stable in the dominant healthcare associated MRSA (HA-MRSA) clone in the UK (EMRSA-15; CC22-SCC*mec*IVh) thus these changes in prevalence may be due to penetration by different clones [3].

Non-susceptibility to macrolides decreased in MRSA isolates by 10% between 2012 (65%) and 2016 (55%) in comparison to MSSA isolates, where the macrolide resistance increased by 4% since 2012 (12% vs.16% in 2016).

Mupirocin resistance rates in MRSA decreased between 2012 (8%) and 2016 (6%), while the resistance in MSSA isolates remained stable at around 1% during the same period.

Resistance to fusidic acid in MRSA and MSSA increased by 5% (16% to 21%) and 2% (12% to 14%) between 2012 and 2016, respectively.

Non-susceptibility to rifampicin in MRSA as well as MSSA remained stable between 2012 and 2016, being broadly around 2-5% and 2%, respectively.

Laboratories are asked to send any isolates suspected to have intermediate or full glycopeptide resistance, or resistance to newer agents used to treat staphylococcal infections (daptomycin, linezolid, tigecycline and ceftaroline) to PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit, Colindale [4] for characterisation, including exploring the emergence and spread of new clones. Furthermore, between April 2017 and March 2019, AMRHAI is undertaking enhanced surveillance of MRSA bacteraemia cases in England. As part of this initiative, laboratories are invited to refer MRSA isolates from each episode of MRSA bacteraemia for analysis by whole-genome sequencing [5].

In 2016, non-susceptibility to vancomycin (not high level vanA-mediated resistance), teicoplanin and linezolid remained low at 1% or less in MRSA and MSSA, though it is notable that AMRHAI observes small numbers of isolates where mutational resistance to linezolid or daptomycin has been selected during therapy, and occasional isolates with the *cfr* gene, a transferable element conferring resistance to linezolid.

Historically, the two most common HA-MRSA clones in the UK were the epidemic strains EMRSA-15 (CC22-SCC*mec*IVh) and EMRSA-16 (CC30-SCC*mec*II), which are usually resistant to ciprofloxacin and erythromycin [6]. Analysis of data from the British Society for Antimicrobial Chemotherapy Survey shows that the proportion of EMRSA-16 decreased among all MRSA, while the proportion of EMRSA-15 increased between 2001 and 2007 [7,8]. A molecular epidemiological study of MRSA bacteraemia in England has shown that EMRSA-15 (CC22-SCC*mec*IVh), albeit still predominant, is declining and this has been associated with an increase in clonal diversity. Furthermore, CC5 has replaced EMRSA-16 as the second most frequent lineage [9].

Table 2a. Antibiotic susceptibility for MRSA bacteraemia isolates in England and Northern Ireland: 2012 to 2016

	2012		2013		2014		2015		2016	
	No. tested	% resistant*	No. tested	% resistant*	No. tested	% resistant*	No. tested	% resistant*	No. tested	% resistant*
Gentamicin	622	10	650	10	568	13	626	11	613	10
Ciprofloxacin	599	88	597	82	525	75	568	74	562	68
Vancomycin**	567	<1	566	<1	503	<1	558	<1	516	1
Teicoplanin	491	<1	503	1	473	<1	493	<1	456	<1
Linezolid	427	<1	436	<1	341	<1	453	<1	512	<1
Erythromycin	557	65	514	64	399	61	515	58	531	55
Rifampicin	586	2	591	5	519	4	572	5	573	3
Mupiricin	592	8	583	8	529	7	563	7	577	6
Fusidic Acid	645	16	664	20	570	20	630	20	615	21
Total MRSA bacteraemia reports	**750**		**755**		**683**		**703**		**658**	

*defined as reduced- or non-susceptibility
** not high level vanA-mediated resistance

Table 2b. Antibiotic susceptibility for MSSA bacteraemia in England and Northern Ireland: 2012 to 2016

	2012		2013		2014		2015		2016	
	No. tested	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***
Gentamicin	5,496	1	5,598	1	5,385	1	6,426	1	7,311	1
Ciprofloxacin	4,660	7	4,737	7	4,567	6	5,507	7	6,381	7
Vancomycin**	4,247	<1	4,070	<1	3,899	<1	5,031	<1	5,233	<1
Teicoplanin	3,559	<1	3,504	<1	3,434	<1	4,153	<1	4,701	<1
Linezolid	3,604	<1	3,972	<1	3,873	<1	4,972	<1	5,875	<1
Erythromycin	4,852	12	4,940	12	4,614	14	5,464	15	6,447	16
Rifampicin	4,954	2	5,160	2	4,971	2	6,255	2	7,061	2
Mupirocin	4,529	1	4,668	1	4,550	1	5,813	1	6,689	1
Fusidic Acid	5,660	12	5,725	14	5,547	13	6,492	14	7,184	14
Total MSSA bacteraemia reports	**6,275**		**6,450**		**6,300**		**7,383**		**8,120**	

*defined as reduced- or non-susceptibility
**not high level vanA-mediated resistance

Ascertainment: Comparison of MRSA and MSSA positive specimens from the voluntary laboratory reporting scheme versus MRSA and MSSA infections from the mandatory surveillance scheme in England

The following data compare MRSA and MSSA bacteraemias reported to the voluntary laboratory surveillance scheme with those reported to the mandatory surveillance scheme. All voluntary bacteraemia reports were limited to those from England only (Wales and Northern Ireland do not take part in the English mandatory surveillance scheme); data from several laboratories were excluded due to data issues (page 2).

The number of MRSA bacteraemia reports under voluntary and mandatory reporting schemes shows a broadly similar decreasing trend (Figure 4a), albeit there was a dip in the numbers of MRSA reported to the mandatory scheme in 2014, which wasn't observed in the voluntary scheme. The numbers of MRSA infection reports to the mandatory surveillance decreased by 14.9% between 2012 and 2016, compared with 11.3% under the voluntary scheme.

Unlike the declines observed for MRSA bacteraemia reports in both surveillance schemes, the number of MSSA bacteraemia reports increased in both the mandatory and voluntary surveillance schemes between 2012 and 2016 by approximately 29% over the five-year time period.

The case ascertainment of MRSA bacteraemia reports to the voluntary scheme fluctuated between 2012 and 2016, reaching its highest at 80.2% in 2014 and decreasing thereafter. The case ascertainment of MRSA bacteraemia reports was 75.4% in 2016. The case ascertainment of MSSA reported to the voluntary scheme was stable at approximately 69% between 2012 and 2016, with the exception of 2014, when it decreased to 61.8%. These numbers need to be interpreted with caution given the data exclusions mentioned above, which decreased the case ascertainment to the voluntary scheme versus the mandatory scheme.

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

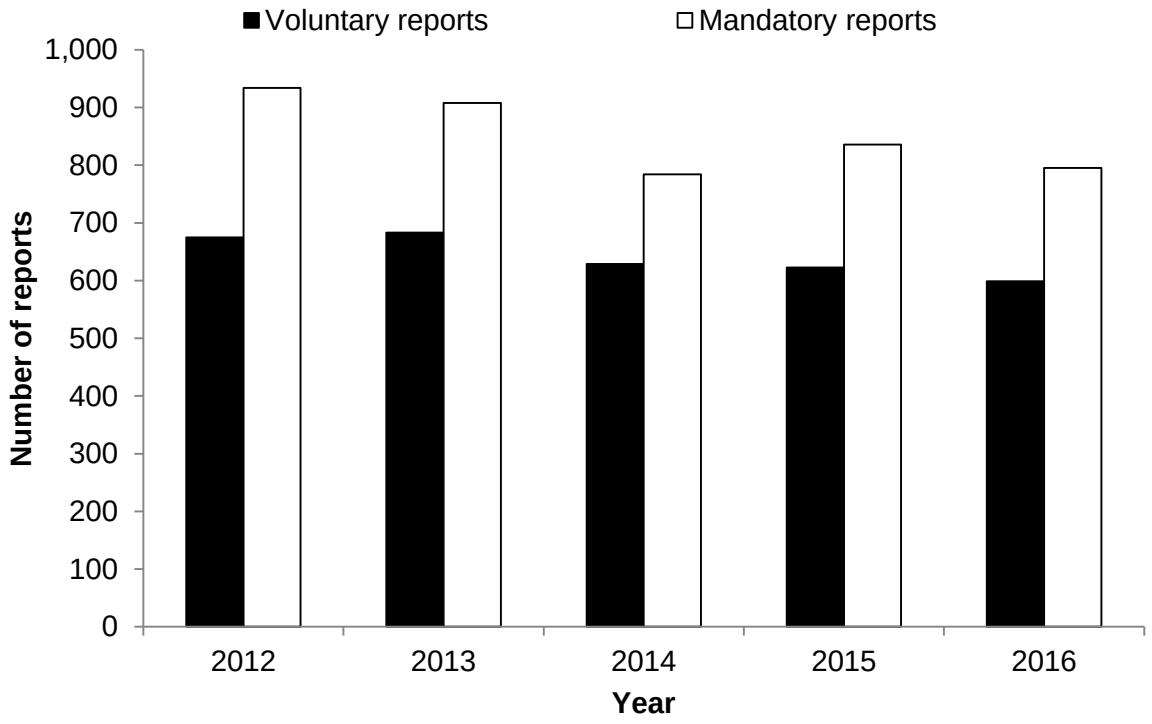
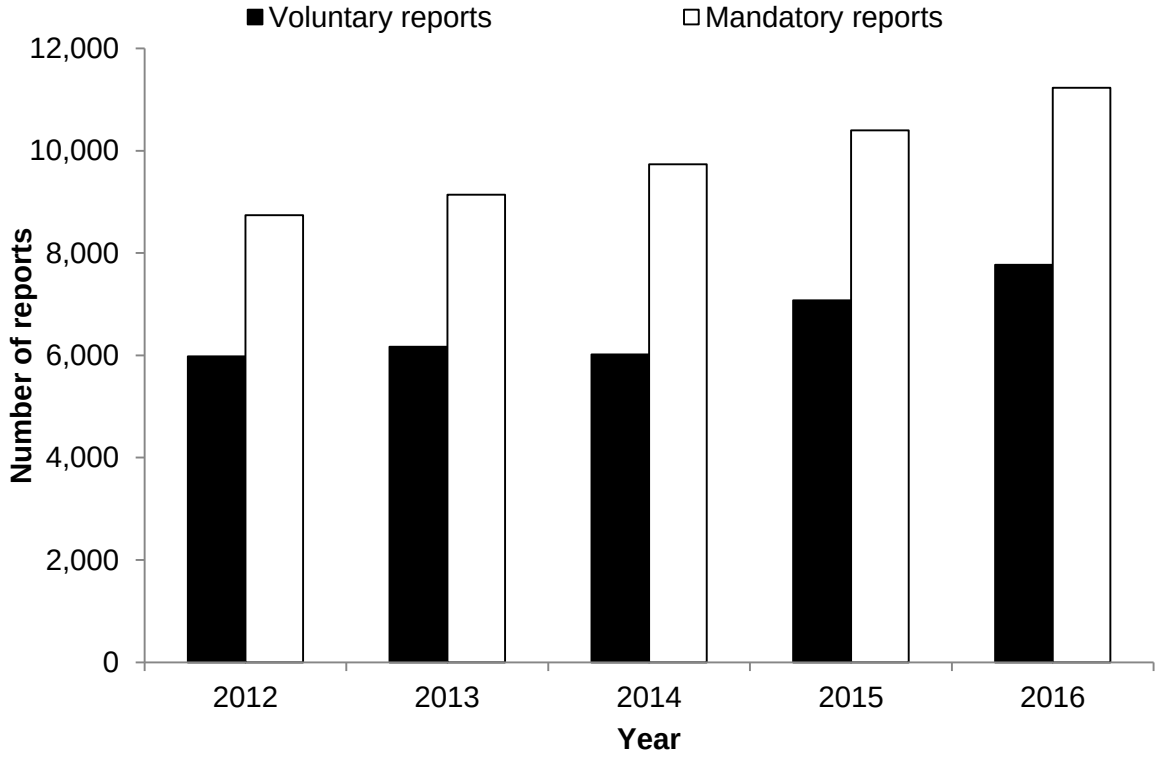


Figure 4b. Ascertainment of MSSA bacteraemia data for the mandatory and voluntary reporting schemes in England: 2012-2016



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