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# Laboratory surveillance of *Pseudomonas* spp. and *Stenotrophomonas* spp. bacteraemia in England, Wales and Northern Ireland: 2016

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# Laboratory surveillance of *Pseudomonas* spp. and S*tenotrophomonas* spp. bacteraemia in England, Wales and Northern Ireland: 2016

These analyses are based on data relating to bloodstream infections caused by *Pseudomonas* spp. and *Stenotrophomonas* spp. reported by laboratories between 2009 and 2016. Data for England were extracted on 1 June 2017 from Public Health England's (PHE) voluntary surveillance database, the Second Generation Surveillance System (SGSS). Data for Wales and Northern Ireland were extracted on 9 March 2017 and 26 May 2017 (from DataStore and CoSurv systems), respectively.

SGSS comprises a communicable disease reporting module (CDR; formerly CoSurv/LabBase2) that includes antimicrobial susceptibility data and a separate comprehensive antimicrobial resistance module (AMR; formerly AmSurv). Compared to CDR's antimicrobial susceptibility data, the AMR module captures more comprehensive antibiogram data (involving 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 are not currently undertaken using data from the AMR module. However, data were extracted from the AMR module to assess rates of multi-drug resistance rates in 2015. Only England and Northern Ireland data are included in the antimicrobial susceptibility analyses.

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 laboratory) 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 and geographical distribution of cases of *Pseudomonas* spp. and *Stenotrophomonas* spp. bacteraemia in

England, Wales and Northern Ireland. In addition, antimicrobial susceptibility five-year trends for England and Northern Ireland have been included in this report, as has a single year of resistance to more than one antibiotic, based on data reported to the AMR module of SGSS by laboratories in England. A <u>web appendix is available</u> featuring the findings of this report, including data submitted via SGSS from laboratories in England.

### **Key points**

- the rate of *Pseudomonas* spp. bacteraemia in England, Wales and Northern Ireland increased by 5.4% (from 7.0 to 7.4 reports per 100,000 population) between 2009 and 2016, and by 11.1% (from 6.7 to 7.4 reports per 100,000 population) between 2012 and 2016, respectively
- the combined Stenotrophomonas spp. bacteraemia rate in England, Wales and Northern Ireland remained constant at 0.8 reports per 100,000 population between 2012 and 2016, although the rate in Northern Ireland increased by 140.7% from 0.5 to 1.2 reports per 100,000 during this period
- in England between 2012 and 2016, the highest increases in *Pseudomonas* bacteraemia rate were observed in the South West (29.8%; 6.5 to 8.4 reports per 100,000 population) and the East of England (26.8%; 6.5 to 8.3 reports per 100,000 population) PHE Centres, respectively
- in 2016, the highest rate of *Stenotrophomonas* bacteraemia in England was observed in the London and North West PHE Centres, both at 0.9 reports per 100,000 population
- in 2016, *Pseudomonas aeruginosa* was the most commonly isolated *Pseudomonas* species accounting for approximately 80% of all blood isolates of this genus
- in 2016, the highest *Pseudomonas* bacteraemia rates were observed in patients over the age of 75 years (59.4 and 21.2 reports per 100,000 population in men and women, respectively)
- the highest rate of *Stenotrophomonas* bacteraemia was observed amongst men over the age of 65 years (2.0 reports per 100,000 population) and women between the age of 65 and 74 years (1.6 reports per 100,00 population)
- between 2012 and 2016, the non-susceptibility patterns for *Pseudomonas aeruginosa* for key antimicrobial agents remained broadly stable with small decreases for meropenem (from 9% to 8%) and tobramycin (from 4% to 2%) with the highest non-susceptibility observed for imipenem at 15% and piperacillin/tazobactam at 11%, while it remained stable at 7% for the most reliably active β-lactam ceftazidime

### Trends

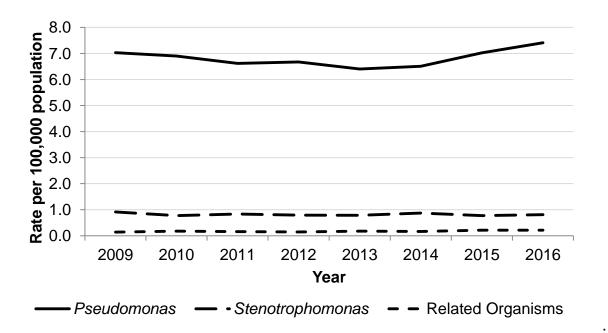
Figure 1 shows the trend in the rate (per 100,000 population) of laboratory-reported bacteraemia in England, Wales and Northern Ireland between 2009 and 2016, due to *Pseudomonas* spp., *Stenotrophomonas* spp. and closely related genera (*Brevudimonas, Burkholderia, Comamonas, Ralstonia and Shewanella*)

There was an overall 5.4% increase in the rate of *Pseudomonas* bacteraemia (from 7.0 to 7.4 reports per 100,000 population) between 2009 and 2016. However, year-to-year fluctuation was seen during this period with the rate decreasing between 2009 and 2013, but increasing year-on-year between 2013 and 2016, with a 5.5% increase between 2015 and 2016 alone (from 7.0 to 7.4 reports per 100,000 population) (figure 1).

There was an overall 11.5% decrease in the rate of *Stenotrophomonas* bacteraemia between 2009 and 2016 (from 0.9 to 0.8 per 100,000 population).

Between 2009 and 2016, the rate of bacteraemia due to other genera closely related to *Pseudomonas* species increased by 53% from 0.14 to 0.18 reports per 100,000 population.





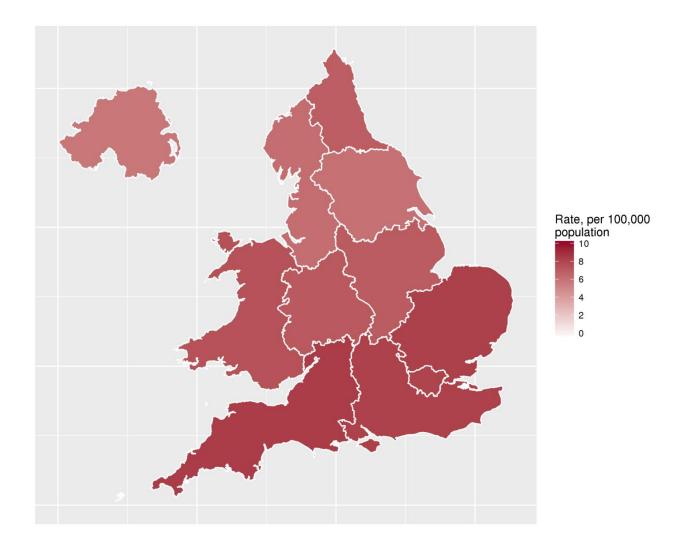
#### Geographic distribution: Pseudomonas

The combined rate of bacteraemia due to *Pseudomonas* spp. in England, Wales and Northern Ireland was 7.4 per 100,000 population in 2016; individually, the rates were 5.7 per 100,000 in Northern Ireland, 7.4 per 100,000 population in Wales and 7.5 per 100,000 population in England. The rate varied in England across PHE centres (PHECs) from 6.0 per 100,000 population in Yorkshire and Humber to 8.4 per 100,000 in South West (figure 2a) (table 1a).

While the rate in England decreased between 2012 and 2013 and increased each year thereafter, the rates of *Pseudomonas* spp. bacteraemia in Northern Ireland and Wales fluctuated considerably with overall increases of 11.6%, 16.0% and 0.1% between 2012 and 2016, respectively (table 1a). The bacteraemia rate decreased by 2.8% from 5.9 to 5.7 reports per 100,000 population in Northern Ireland, while it increased by 5.5% and 9.5% in England (7.1 to 7.5 reports per 100,000) and Wales (6.8 to 7.4 reports per 100,000) between 2015 and 2016, respectively.

While there was an overall increase in rates of *Pseudomonas* spp. bacteraemia observed for England between 2012 and 2016, this was not observed in all PHECs. The bacteraemia rate decreased by 7.7% (7.6 to 7.0 reports per 100,000 population) and 2.1% (6.3 to 6.2 reports per 100,000 population) in East Midlands and North West PHECs between 2012 and 2015, respectively. However, the rates increased by 4.4% and 5.2% in these Centres between 2015 and 2016, respectively. Between 2012 and 2016, the highest increase in *Pseudomonas* spp. bacteraemia rates of 29.8% (6.5 to 8.4 reports per 100,000 population) and 26.8% (6.5 to 8.3 reports per 100,000 population) were observed in South West and East of England PHECs, respectively. Only two PHECs reported a decrease in their rates between 2015 and 2016, namely West Midlands PHEC (8.1% from 7.7 to 7.1 reports per 100,000 population) and Yorkshire and Humber PHEC (4.2% from 6.3 to 6.0 reports per 100,000 population). The rest of the Centres reported increases in their *Pseudomonas* spp. bacteraemia rates between 2015 and 2016, with the highest being observed in South West PHEC (20.4% from 7.0 to 8.4 reports per 100,000 population) and North East PHEC (14.5% from 6.1 to 6.9 reports per 100,000 population).

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



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		R	opulatio	n		
Region	PHE Centre	2012	2013	2014	2015	2016
North of	North East	6.2	5.4	5.4	6.1	6.9
England	Yorkshire and Humber	5.4	5.0	4.7	6.3	6.0
England	North West	6.3	5.9	5.5	5.9	6.2
Midlands	West Midlands	6.4	6.9	7.0	7.7	7.1
and East of	East Midlands	7.6	6.1	6.3	6.7	7.0
England	East of England	6.5	7.0	6.8	8.0	8.3
London	London	7.5	7.1	8.3	7.7	8.1
South of	South West	6.5	6.3	6.6	7.0	8.4
England	South East	7.1	6.7	6.7	7.3	8.2
England*		6.7	6.4	6.5	7.1	7.5
Northern Irela	and <sup>†</sup>	4.9	4.8	5.3	5.9	5.7
Wales <sup>*</sup>		7.4	7.4	6.7	6.8	7.4
England, Wa	ales & Northern Ireland	6.7	6.4	6.5	7.0	7.4

Table 1a: Rate of Pseudomonas spp. bacteraemia reports per 100,000 population by
PHE Centre (England, Wales and Northern Ireland): 2012 to 2016

\* Extracted on 1 June 2017; <sup>†</sup> Extracted on 26 May 2017, <sup>¥</sup> Extracted on 9 March 2017

### Geographic distribution: Stenotrophomonas

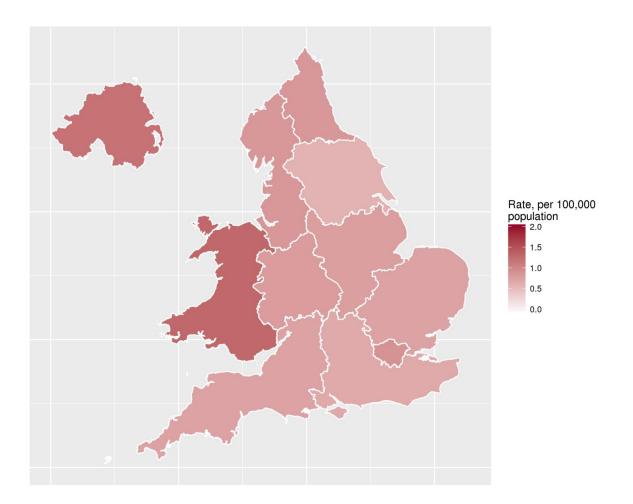
The combined rate of bacteraemia due to *Stenotrophomonas* spp. in England, Wales and Northern Ireland was 0.8 (n=482) reports per 100,000 population in 2016; individually the rates of laboratory-reported bacteraemia were 1.3 per 100,000 population in Wales, 1.2 per 100,000 population in Northern Ireland and 0.8 per 100,000 population in England in 2016. The rate varied in England across PHECs between 0.6 bacteraemia reports per 100,000 population in Yorkshire and Humber PHEC to 0.9 bacteraemia reports per 100,000 population in London and North West PHECs (figure 2b) (table 1b).

Between 2012 and 2016, the highest increase in the bacteraemia rate was observed in Northern Ireland (140.7%; 0.5 to 1.2 reports per 100,000 population), albeit the rate remained stable at 1.2 bacteraemia reports between 2015 and 2016. The bacteraemia rate in Wales increased by 4.4% (from 1.2 to 1.3 reports per 100,000) between 2012 and 2016 while over the same time period the rate remained unchanged at 0.8 reports per 100,000 population in England.

The *Stenotrophomonas* bacteraemia rate increase was observed among four PHECs, of which the highest were in East Midlands (25.6%, 0.6 to 0.8 reports per 100,000 population) and South East (10.9%, 0.6 to 0.7 reports per 100,000 population) PHECs,

with the rest of the Centres reporting decreases in their rates between 2012 and 2016. During this five-year period, the greatest reduction in rates (26.0%) was observed in the West Midlands PHEC (1.1 to 0.8 reports per 100,000); however, between 2015 and 2016, they also experienced the highest increase in rate (64.3%) from 0.5 to 0.8 reports per 100,000 population. The greatest reported reduction between 2015 and 2016 (6.0%) was observed in the East of England PHEC (0.8 to 0.7 reports per 100,000).

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



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		Rate per 100,000 population						
Region	PHE Centre	2012	2013	2014	2015	2016		
North of	North East	0.9	0.9	1.0	0.8	0.8		
North of England	Yorkshire and Humber	0.6	0.5	0.6	0.6	0.6		
	North West	0.9	1.1	1.1	0.9	0.9		
Midlands	West Midlands	1.1	0.7	0.6	0.5	0.8		
and East	East Midlands	0.6	0.7	0.8	0.5	0.8		
of England	East of England	0.7	0.6	0.7	0.8	0.7		
London	London	0.9	0.9	1.3	0.9	0.9		
South of	South West	0.7	0.6	0.7	0.6	0.7		
England	South East	0.6	0.7	0.7	0.7	0.7		
England∗		0.8	0.8	0.9	0.7	0.8		
Northern Ire	land <sup>+</sup>	0.5	1.5	1.1	1.2	1.2		
Wales <sup>*</sup>		1.2	0.7	0.9	1.4	1.3		
England, W	ales & Northern Ireland	0.8	0.8	0.9	0.8	0.8		

# Table 1b: Rate of Strenotrophomonas spp. bacteraemia reports per 100,000 population by PHE Centre (England, Wales and Northern Ireland): 2012 to 2016

\* Extracted on 1 June 2017; † Extracted on 26 May 2017, ¥ Extracted on 9 March 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.

### **Species distribution**

In 2016, 89% (n=3,958 /4,427) of *Pseudomonas* isolates from blood in England, Wales and Northern Ireland were identified to species level, however this is impacted by the limitations of MALDI-ToF analysis, which does not reliably distinguishes between closely related species such as those in the *P. fluorescens* or *P. putida* groups (table 2a). This proportion was broadly similar to previous years. *P. aeruginosa* was the most commonly isolated species in 2016 as in previous years, accounting for approximately 80% of all isolates of this genus. There has been a slight downward trend in these figures with *P. aeruginosa* accounting for 82%, 83%, 82% and 81% of all *Pseudomonas* species bacteraemias in 2012, 2013, 2014 and 2015, respectively. *P. aeruginosa* is the third most common cause of Gram-negative bacteraemia and along with *Escherichia coli* and *Klebsiella* spp. is one of the key pathogens the government is focusing on in its ambition to halve healthcare-associated Gram-negative blood stream infections by financial year 2020/21 [2].

In 2016, the most commonly isolated *Stenotrophomonas* species was *Stenotrophomonas maltophilia* at 99% (n=478/482) in England, Wales and Northern Ireland (table 2b). This is broadly similar to *Stenotrophomonas* species bacteraemia reports in other years with the exception of 2014, when the proportion was 92% (n=472/460) due to a large number of isolates not having species level information recorded. To date, *S. maltophilia* is the only known opportunistic human pathogen in the *Stenotrophomonas* genus, which makes it likely that the small number of isolates with incomplete species data is in fact *S. maltophilia* [3].

*Burkholderia* spp. and *Brevudimonas* spp. were the most commonly reported related organisms\* between 2012 and 2016. In 2016, these accounted for 52% (n=64/124) and 32% (n=40/124) of all closely related organisms, respectively (table 2c).

\* Related organisms include genera where at least one species has previously been classified as *Pseudomonas* spp. or *Stenotrophomonas* spp.

	2012		2013		2014	2014			2016	1
	No.	%	No.	%	No.	%	No.	%	No.	%
Pseudomonas spp.	3,896	100	3,763	100	3,857	100	4,196	100	4,427	100
P. aeruginosa	3,183	82	3,114	83	3,144	82	3,411	81	3,553	80
P. alcaligenes	3	0	2	0	4	0	7	0	8	0
P. chlororaphis	0	0	0	0	0	0	1	0	1	0
P. fluorescens group*	61	2	54	1	56	1	38	1	46	1
P. koreensis	0	0	0	0	1	0	2	0	1	0
P. luteola	2	0	2	0	2	0	3	0	7	0
P. mendocina	0	0	1	0	7	0	4	0	6	0
P. oleovorans	0	0	0	0	0	0	1	0	5	0
P. otitidis	0	0	0	0	1	0	0	0	0	0
P. paucimobilis	70	2	65	2	63	2	56	1	66	1
P. putida group**	77	2	61	2	85	2	94	2	127	3
P. stutzeri	101	3	83	2	94	2	93	2	84	2
P. thomasii	0	0	1	0	0	0	1	0	1	0
Pseudomonas spp.,										
other named	61	2	72	2	79	2	56	1	45	1
Pseudomonas spp., sp.										
not recorded	338	9	308	8	321	8	429	10	469	11

Table 2a. Reports of Pseudomonas spp.	bacteraemia by species (England, W	Vales and Northern Ireland): 2012 to 2016
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\* P. fluorescens and P. tolaasii

\*\* P. putida, P. fulva, P. monteilii, P. mosselii and P. oryzihabitans

#### Table 2b. Reports of Stenotrophomonas spp. bacteraemia by species (England, Wales and Northern Ireland): 2012 to 2016

	2012		2013		2014		2015		2016	
	No.	%								
Stenotrophomonas spp.	463	100	460	100	460	100	460	100	482	100
S. maltophilia	460	99	448	97	472	92	453	98	478	99
Stenotrophomonas spp., species										
not recorded	3	1	12	3	43	8	7	2	4	1

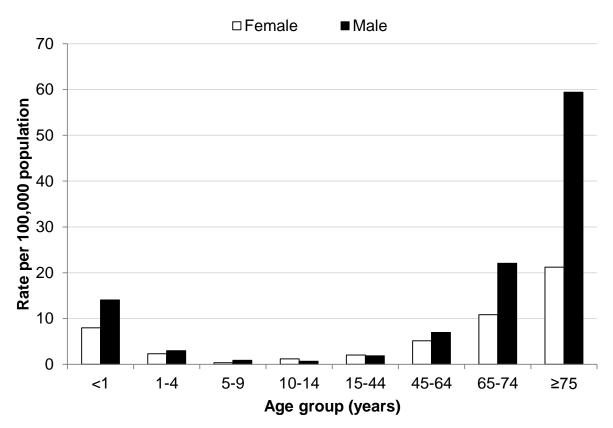
#### Table 2c. Reports of related organisms bacteraemia by genus (England, Wales and Northern Ireland): 2012 to 2016

	2012		2013		2014		2015		2016	
	No.	%								
Related Organisms	82	100	101	100	94	100	123	100	124	100
Brevundimonas spp.	24	29	32	32	40	43	42	34	40	32
<i>Burkholderia</i> spp.	42	51	50	50	31	33	60	49	64	52
Comamonas spp.	9	11	7	7	12	13	13	11	14	11
Ralstonia spp.	5	6	8	8	8	9	4	3	4	3
Shewanella spp.	2	2	4	4	3	3	4	3	2	2

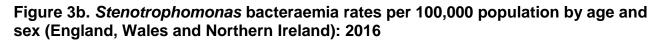
### Age and sex distribution

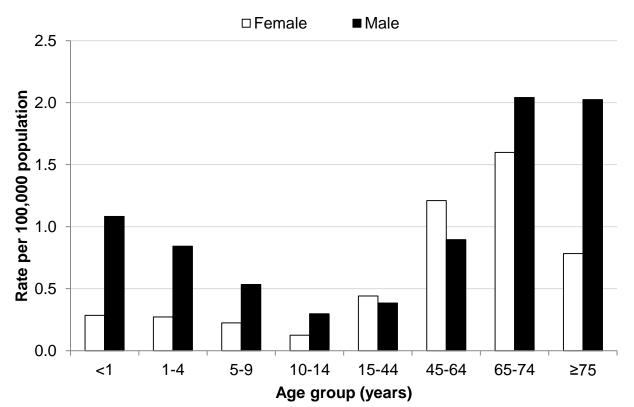
Figure 3a depicts *Pseudomonas* bacteraemia rate per 100,000 population amongst men and women across different age groups in England, Wales and Northern Ireland in 2016. The bacteraemia rate was the highest among older age groups ( $\geq$ 75 years and 65 to 74 years of age) and those below the age of one year. The rate of bacteraemia per 100,000 population in these age groups was markedly higher amongst males in comparison to females ( $\geq$ 75 years: 59.4 vs. 21.2, 65-74 years: 22.1 vs. 10.8 and <1 year: 14.1 vs. 8.0 per 100,000 population). The rate was observed to be higher in females amongst 10-14 years old and 15-44 years old (1.2 vs. 0.7 and 2.0 vs. 1.9 per 100,000 population, respectively). This pattern was broadly similar to previously reported data [4].

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



The rate of Stenotrophomonas bacteraemia in males was the highest amongst those aged 75 years and older, 65-74 years old and those below the age of one year (2.0, 2.0 and 1.1 per 100,000 population). The rate in females was the highest amongst 65-74 years olds and 45-64 years olds and those aged 75 years and over (1.6, 1.2 and 0.8 per 100,000 population, respectively). Generally, the rate was higher amongst men in comparison to women with the exception of 15 to 44 years old and 45 to 64 years old (0.4 vs. 0.4 and 1.2 vs. 0.9 per 100,000 population in women and men, respectively).





### Antimicrobial resistance: England and Northern Ireland

Susceptibility results reported for key antimicrobials for *P. aeruginosa* are presented in table 3a. The susceptibility results for different antimicrobials with the exception of imipenem, tobramycin and amikacin were available for at least 80% of isolates in 2016. Only about 28% of isolates were tested for susceptibility to imipemen, while having the highest non-susceptibility to this agent (15%). Between 2012 and 2016, the non-susceptibility patterns for key antimicrobial agents remained broadly stable with small decreases for meropenem (from 9% to 8%) amikacin (from 4% to 3%) and tobramycin (from 4% to 2%), although the latter needs to be interpreted with caution considering that only about 40% of isolates were tested for this antibiotic, which is surprising given that it is the most active aminoglycoside against the species. The resistance to one of the most reliable active agents – ceftazidime – remained stable at 7% in the five-year period.

The highest percentage of non-susceptibility was observed for imipenem (15%), piperacillin/tazobactam (11%) and ciprofloxacin (10%). These results are in line with *P. aeruginosa* being resistant to a multitude of antibiotics through intrinsic and adaptive mechanisms to these agents [5]. The non-susceptibility patterns to imipemen, meropenem and ciprofloxacin presented in this report indicate the pathogen's ability to develop antibiotic resistance through three main mechanisms- alteration in DNA gyrase by mutation in *gyrA* or *gyrB* genes, decreased drug accumulation by decreased permeability of the cell wall and enhanced efflux [6]. The loss of OprD in *P. aeruginosa* cells affects carbapenem uptake underlying the non-susceptibility to imipenem and meropenem [5,7]. Mutations in *gyrA* and *gyrB* and *parC* and *parE* reducing binding affinity of fluoroquinolones are believed to be involved in resistance to ciprofloxacin [5,6].

The resistance of *P. aeruginosa* in blood samples was shown to be lower in comparison to respiratory isolates according to the British Society for Antimicrobial Chemotherapy Resistance Surveillance Project [8].

*Pseudomonas* species isolates exhibiting increasing drug resistance are of particular concern for patients with weakened immune system. This has resulted in the inclusion of *Pseudomonas* as one of the key groups of pathogens to monitor as part of the UK five-year Antimicrobial Resistance Strategy and the English Surveillance Programme for Antimicrobial Utilisation and Resistance [9,10].

Antibiotic susceptibility results for co-trimoxazole in *Stenotrophomonas* isolates are presented in table 3b. This antimicrobial was selected because it is the drug of choice for treatment of *S. maltophilia* [11,12]. The non-susceptibility to co-trimoxazole mostly remained between 4% and 5% between 2012 and 2016, reaching its highest in 2014 at 7%. The number of *Stenotrophomonas* isolates tested for susceptibility to this agent has steadily increased from 59% to 69% between 2012 and 2016.

Table 4 presents analysis of resistance of *Pseudomonas* species (including *P. aeruginosa*) isolates resistant to more than one antibiotic agent in England in 2016. These figures differ from those presented in table 3a due to a different module of SGSS being used to extract data (3a is based on data from the CDR module and table 4 is based on the AMR module which has more extensive susceptibility data).

In 2016, 3,416 *Pseudomonas* isolates were tested against three or more key antibiotics and 0.7% of these were non-susceptible to all tested agents (n=24/3,416). The highest percentage of non-susceptibility was reported for gentamicin and ciprofloxacin at 3%.

For advice on treatment of antibiotic-resistant infections due to these organisms or for reference services including species identification and confirmation of susceptibility testing results, laboratories should contact PHE's AMRHAI Reference Unit in London [13].

	2012		2	2013		2014		2015		2016	
	No. tested	% resistant*									
Gentamicin	2,714	4	2,653	4	2,587	4	2,931	4	3,038	4	
Ciprofloxacin	2,577	9	2,532	11	2,474	11	2,851	9	2,974	10	
Ceftazidime	2,454	6	2,366	7	2,258	7	2,659	7	2,829	7	
Meropenem	2,241	9	2,283	8	2,307	10	2,739	8	2,872	8	
Imipenem	844	14	763	16	735	19	882	14	1,011	15	
Tobramycin	1,153	4	1,105	4	1,145	3	1,365	3	1,422	2	
Amikacin	1,542	4	1,480	4	1,436	2	1,724	3	1,783	3	
Piperacillin\Tazobactam	2,580	9	2,576	9	2,503	11	2,834	11	2,885	11	
Species total bacteraemia reports		,183	,	5,114	,	,143		s,411	,	,551	

#### Table 3a. Antibiotic susceptibility for *Pseudomonas aeruginosa* bacteraemia in England, Wales and Northern Ireland: 2012 to 2016

\* Defined as reduced- or non-susceptibility

#### Table 3b. Antibiotic susceptibility for Stenotrophomonas bacteraemia in England, Wales and Northern Ireland: 2012 to 2016

		2012		2013	4	2014	2	2015	2	2016
	No. tested	% resistant*								
Co-trimoxazole	274	4	294	5	301	7	303	3	332	5
Total genus bacteraemia reports		463		460		515		460		482

\* Defined as reduced- or non-susceptibility

Antimicrobial combinations	No. tested	% Resistant
Gentamicin and Ciprofloxacin	3,696	3
Gentamicin and Ceftazidime	3,711	1
Ciprofloxacin and Ceftazidime	3,816	2
Gentamicin, Ciprofloxacin and Ceftazidime	3,416	<1

# Table 4. Multi-drug antimicrobial testing and resistance summary for *Pseudomonas* bacteraemia (England): 2016

### Acknowledgements

These reports would not be possible without the weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland, without whom there would be no surveillance data. The support from colleagues within Public Health England, Public Health Wales and Public Health Agency, Northern Ireland and the PHE Reference Unit, in particular, is valued in the preparation of this report. Feedback and specific queries about this report are welcome and can be sent to:

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