Public Health England

Voluntary surveillance of *Pseudomonas* spp. and *Stenotrophomonas* spp. causing bacteraemia in England, Wales and Northern Ireland: 2012

These analyses are based on data extracted from the Public Health England[i] (PHE) voluntary surveillance database, LabBase2[ii], on the 20th June 2013 for the period 2008-2012. The data presented here differ in some instances from data in earlier publications due to the inclusion of late reports.

Rates were calculated using 2012 mid-year resident population estimates based on the 2011 census for England, Wales, and Northern Ireland [1][2]. Regional analyses were made based on the residential location of the patient with reference to the Government Office Regions introduced in April 2002[iii].

Geographical analyses within this report break the English reports into Government Office regions rather than the Public Health Centre areas created in April 2013 when Public Health England was established; this is due to the availability of data in this breakdown at the time of producing the report. Future reports will include data presented by PHE Centre.

The report includes analyses on the trends, age and sex distribution, geographical distribution of and the antimicrobial susceptibility data in cases of bacteraemia.

[i] In April 2013 the Health Protection Agency (HPA) was abolished and its functions transferred toPublic Health England.

[ii] LabBase2 is the database that collects laboratory reports of all microorganisms isolated at nearly 400 NHS and other laboratories throughout England and Wales. The database is managed and accessed at the PHE Colindale.

[iii] The algorithm allocates geographical locations based on the available postcode. It looks for a valid postcode of residence first. If this is missing it will then utilise the patient's registered GP postcode, and if this is missing it will then utilise the source laboratory postcode.

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Key Points

- from 2008 to 2012, there was a 6% decrease in the number of *Pseudomonas* spp. bacteraemias reported to PHE (3,987 isolates in 2008 to 3,743 in 2012), compared with 1% decrease for all bacteraemia [3]
- in 2012, 92% of *Pseudomonas* spp. isolates from bacteraemia were identified to species level (3,457 reports), with 91% of these identified as *P. aeruginosa*
- for *S. maltophilia* bacteraemia, there was a 21% decrease in the number of bacteraemias reported to PHE between 2008 and 2012 (453 reports in 2012 compared with 573 in 2008)
- the overall incidence in 2012 for *Pseudomonas* spp. bacteraemia was 6.4 cases/100,000 population in England, Wales and Northern Ireland. As the data were obtained via a voluntary surveillance system, this incidence figure is likely to be an underestimate of the true incidence. The data captured by the mandatory surveillance reporting systems for *S. aureus* bacteraemia in England suggests that the voluntary surveillance system captures ~80% of all reports[iv]. Both mandatory and voluntary systems demonstrated consistent trends in reporting between 2007 and 2011 [4]
- infections were reported significantly more frequently among those aged 75 years and older, especially among male patients with a rate of 52.0/100,000 population compared with19.7/100,000 for female patients among this age group. Reported cases of *Pseudomonas* spp. in children aged <1 year were the second highest group, with a rate of 11.9 and 5.1/100,000 for males and females, respectively
- the proportion of *P. aeruginosa* isolates that were resistant to piperacillin/tazobactam increased by 3% (from 6% to 9%) between 2008 and 2012, whereas resistance to imipenem (13%), meropenem (9%), ceftazidime (6%), ciprofloxacin (9%) and gentamicin (4%) reduced slightly or remained static
- the overall incidence for *S. maltophilia* bacteraemia in England, Wales, and Northern Ireland was 0.8/100,000 population in 2012. *S. maltophilia* was reported most frequently for male patients aged 65 years and above. There was no change in non-susceptibility to co-trimoxazole (4%)
- *Pseudomonas* spp. accounted for 3.6% of monomicrobial bacteraemia in 2011; the eighth most commonly reported monomicrobial bacteraemia-causing organism. In comparison, *Stenotrophomonas* spp. accounted for 0.4%, the 23rd most commonly recorded monomicrobial bacteraemia-causing organism [5]

[iv] Note: Wales and Northern Ireland do not take part in the English mandatory surveillance scheme

Trends

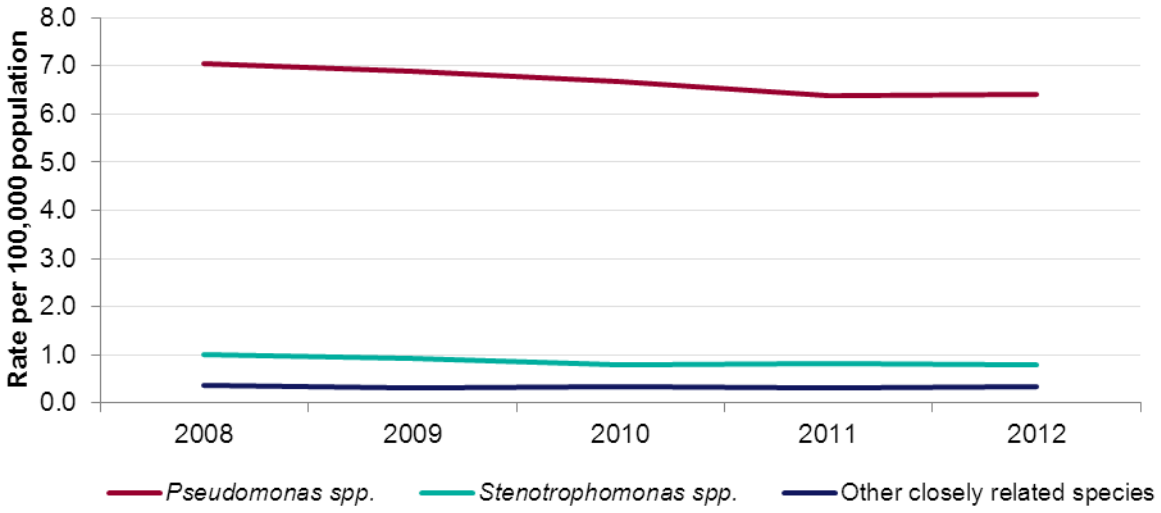
Between 2011 and 2012 there has been a 1% increase in the total bacteraemia reports of *Pseudomonas* spp., *S. maltophilia*, and other closely related genera (4,353 cases and 4,399 cases respectively; table 1). This increase is a slight change from the year on year decrease observed since 2008, but still displays an overall decrease of 8% over the period.

The overall trend differs slightly looking at the organism groups separately (figure 1); a 9% decrease from 2008-2012 is observed in incidence rates of bacteraemia caused by *Pseudomonas* spp. (7.0/100,000 population per year in 2008 to 6.4 in 2012; 1% increase between 2011 and 2012), however rates of reports of bacteraemia caused by *Stenotrophomonas* spp. decreased by 23% over the same period (1.0 to 0.8/100,000; decrease of 5% between 2011 and 2012).

The total reports of bacteraemia for other related species[v] increased 10% between 2011 and 2012, but the 5-yr trend shows a slight decrease of 4% (0.4 to 0.3/100,000 population). Table 1 gives a breakdown of numbers of reports by species between 2008 and 2012.

Reports for 2012 are provisional as of 20th June, the number of reported cases of bacteraemia may increase slightly as late reports are received.

Figure 1. *Pseudomonas* spp. and *Stenotrophomonas* spp. and other related species bacteraemia rates per 100,000 population (England, Wales and Northern Ireland): 2008 to 2012



PHE. Data extracted 20th June 2013

[v] 'Other related species' grouped in figure 1 are: *Brevibacterium* spp., *Brevundimonas* spp., *Burkholderia* spp., *Comamonas* spp., *Ralstonia* spp., *Shewanella* spp., *Sphingomonas* spp.

Table 1. Reports of *Pseudomonas* and *Stenotrophomonas* bacteraemia by species (England, Wales and Northern Ireland): 2008 to 2012

	2008		2009		2010		2011		2012	
	count	**(%)**	**count**	**(%)**	**count**	**(%)**	**count**	**(%)**	**count**	**(%)**
***Pseudomonas* spp.**	**3987**	(100)	**3927**	(100)	**3833**	(100)	**3694**	(100)	**3743**	(100)
P. aeruginosa	3158	(79)	3266	(83)	3212	(84)	3111	(84)	3161	(84)
P. fluorescens	73	(2)	65	(2)	64	(2)	40	(1)	61	(2)
P. putida	75	(2)	56	(1)	66	(2)	69	(2)	68	(2)
P. stutzeri	83	(2)	73	(2)	62	(2)	81	(2)	97	(3)
Pseudomonas spp., other named	81	(2)	62	(2)	54	(1)	72	(2)	70	(2)
Pseudomonas spp., sp not recorded	517	(13)	405	(10)	375	(10)	321	(9)	286	(8)
***Stenotrophomonas* spp.**	**573**	(100)	**522**	(100)	**453**	(100)	**478**	(100)	**456**	(100)
S. maltophilia	571	(100)	519	(99)	453	(100)	473	(99)	453	(99)
Stenotrophomonas spp., sp not recorded	2	(0)	3	(1)	0	(0)	5	(1)	3	(1)
Other closely related genera	**202**	(100)	**173**	(100)	**197**	(100)	**181**	(100)	**200**	(100)
Brevibacterium spp.	16	(8)	15	(9)	21	(11)	21	(12)	36	(18)
Brevundimonas spp.	45	(22)	25	(14)	28	(14)	26	(14)	27	(14)
Burkholderia spp.	29	(14)	35	(20)	45	(23)	45	(25)	46	(23)
Comamonas spp.	10	(5)	9	(5)	10	(5)	15	(8)	7	(4)
Ralstonia spp.	15	(7)	8	(5)	17	(9)	2	(1)	6	(3)
Shewanella spp.	6	(3)	5	(3)	2	(1)	3	(2)	2	(1)
Sphingomonas spp.	81	(40)	76	(44)	74	(38)	69	(38)	76	(38)

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In 2012, 92% of *Pseudomonas* spp. isolates from bacteraemia were identified to species level (3,457 reports), this is an increase on the previous five years where between 87% (in 2008) and 91% (2011) included species level information. Over 90% of *Pseudomonas* spp. reported bacteraemia were identified as *P. aeruginosa*, although the proportion of *P. aeruginosa* amoung isolates identified to species level has decreased each year since 2009 (93% to 91%).

Bacteraemia caused by *P. stutzeri* is the only named *Pseudomonas* spp. to have increased over 5 years, from 83 reports in 2008 to 97 in 2012 (17% increase), although the actual number of reports has fluctuated over that time (table 1).

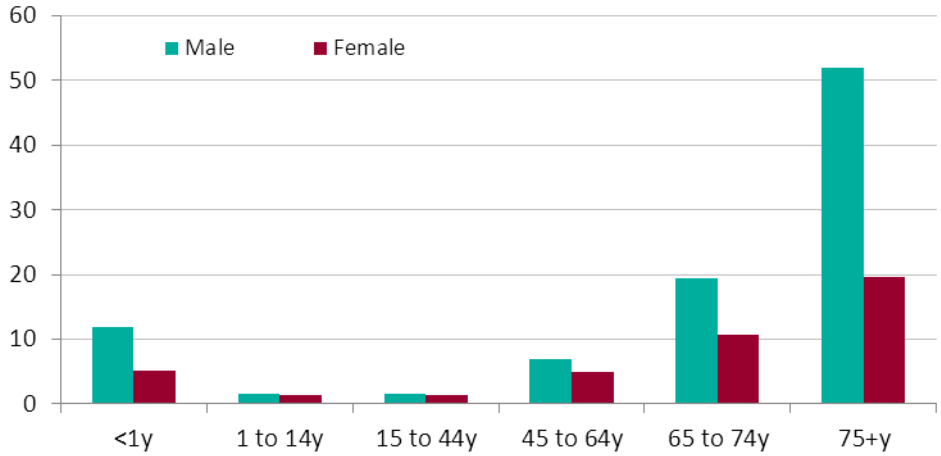
The number of *S. maltophilia* bacteraemia reports decreased by 21% from 573 in 2008 to 456 in 2012; and accounted for 99% of *Stenotrophomonas* spp. bacteraemia reports in 2012.

Of the related genera in 2012, bacteraemia caused by *Sphingomonas spp.* (76 reports) and *Burkholderia spp.* (46 reports) were most frequently reported; both had a slight increase compared with reports in 2011, 2% (45) and 10% (69) respectively.

Age and Sex distribution

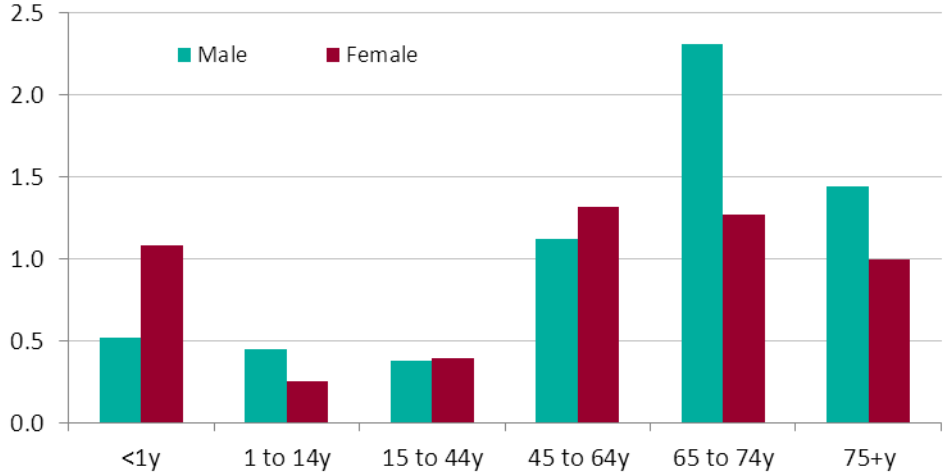
A higher proportion of patients with bacteraemia caused by *Pseudomonas* spp. were male than female, which was reflected across all the age groups; with the highest rates recorded for males aged 75 and over (52.0/100,000 population). The highest rate of infection in females was also in those aged over 75 years where the rate was 19.7/100,000 (figure 2a).

Figure 2a. *Pseudomonas* spp. bacteraemia age and sex rates per 100,000 population (England, Wales and Northern Ireland): 2012



PHE. Data extracted 20th June 2013

Figure 2b. *Stenotrophomonas* spp. bacteraemia age and sex rates per 100,000 population (England, Wales and Northern Ireland): 2012



PHE. Data extracted 20th June 2013

In comparison with *Pseudomonas* spp., bloodstream infection with *Stenotrophomonas* spp. was less common, but was also reported more frequently in male patients aged over 64 years; although the highest rates in males are recorded in the 65 to 74 year age group with 2.3/100,000 (figure 2b). The highest rates in females are seen in the 45 to 64 year age group with 1.3/100,000 population, which is slightly higher than that of the males at 1.1/100,000.

Geographic distribution

In keeping with previous years' reports, regional analyses are made with reference to the Government Office Regions [henceforth called 'region(s)'] based on the residential location of the patient. Figure 3 shows regional distributions of *Pseudomonas* spp. and *Stenotrophomonas* spp. bacteraemia in 2012 and table 2 highlights the regional trend over time. Incidence rates reported for earlier years may differ slightly compared with previous reports due to population estimate amendments made following the 2011 census.

For *Pseudomonas* spp., the overall reported incidence for England, Wales, and Northern Ireland was 6.4 cases/100,000 population. The region with the highest incidence was London (8.4/100,000 population). Low incidences were for Wales and Northern Ireland (both 4.9/100,000) as well as Yorkshire & Humberside (5.0/100,000; figure 3a).

Since 2008 the incidence rate of *Pseudomonas* spp. per 100,000 has decreased in all regions except the North East where a slight increase has been observed (6.1 to 6.8/100,000; table 2a).

For *Stenotrophomonas* spp., the overall reported incidence for England, Wales, and Northern Ireland was 0.8 cases/100,000 population. Regions with high incidence include London (1.0/100,000), the North East (1.1/100,000) and the West Midlands (1.1/100,000). Low incidences were noted for the East Midlands (0.5/100,000) and Northern Ireland (0.5/100,000; figure 3b).

The incidence rate has decreased in most regions since 2008, notable exceptions are the West Midlands (0.7 to 1.1/100,000) and Wales (0.6 to 0.8/100,000; table 2b). When interpreting this data it is important to keep in mind that the numbers involved are small and that there is no indication of a trend over time.

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Figure 3. Geographic distribution of a) *Pseudomonas* spp. and b) *Stenotropomonas* spp. rates per 100,000 population, England, Wales and Northern Ireland: 2012

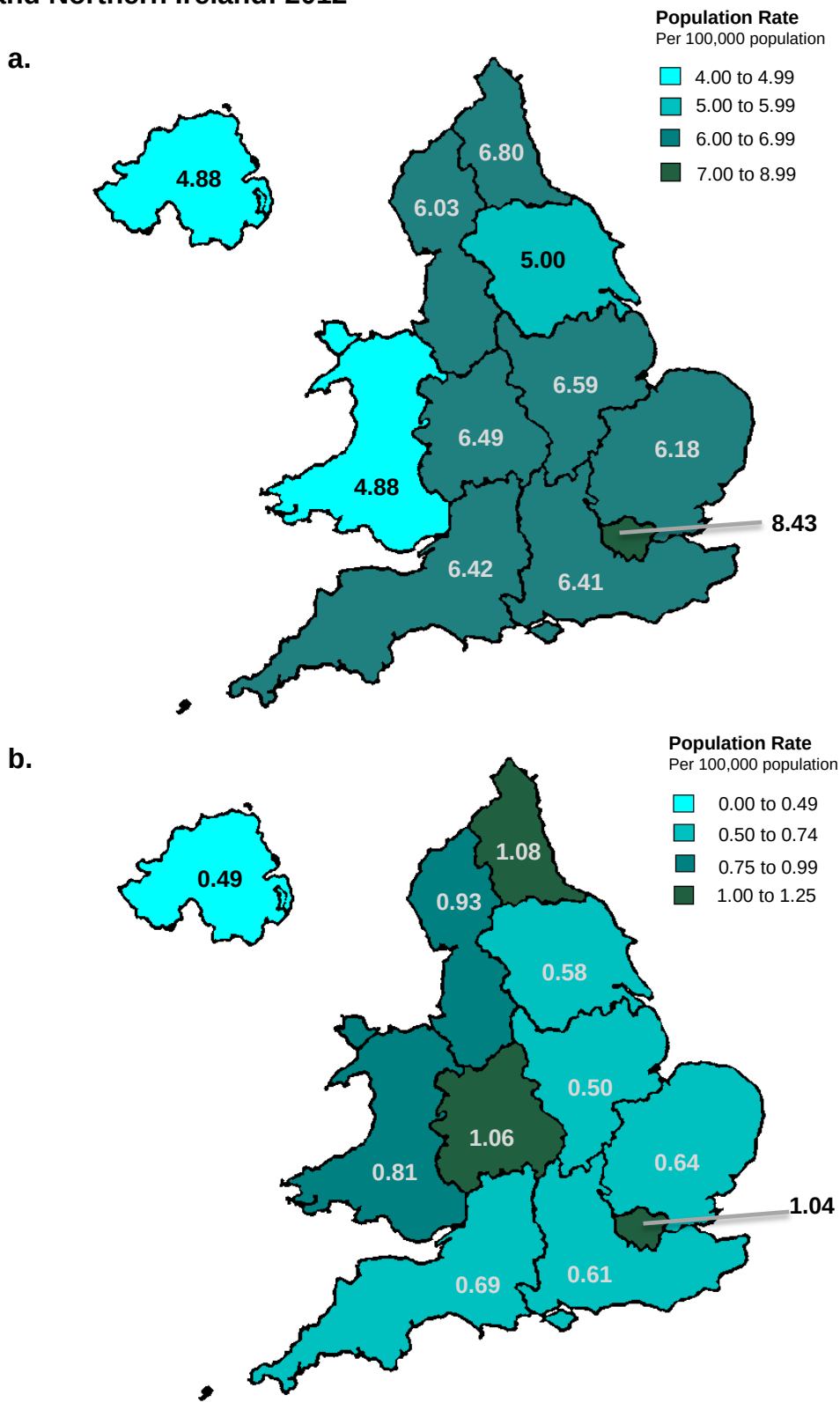

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Table 2a. Rate per 100,000 population *Pseudomonas* spp. bacteraemia reports by Region: 2008 to 2012

Region	Rates per 100,000 population				
	2008	2009	2010	2011	2012
East	6.6	6.8	6.8	5.9	6.2
East Midlands	7.0	7.0	5.9	6.3	6.6
London	9.1	9.3	8.5	8.2	8.4
North East	6.1	6.0	6.0	8.1	6.8
North West	6.3	5.5	6.0	5.7	6.0
South East	7.7	6.5	6.7	6.2	6.4
South West	5.4	6.2	7.1	5.8	6.4
West Midlands	7.8	7.4	6.9	6.5	6.5
Yorkshire and The Humber	8.3	7.8	6.6	5.5	5.0
England	**7.3**	**7.0**	**6.8**	**6.4**	**6.6**
Wales	**3.1**	**5.0**	**4.8**	**5.3**	**4.9**
Northern Ireland (NI)	**6.4**	**5.4**	**5.2**	**6.2**	**4.9**
England, Wales & NI	**7.0**	**6.9**	**6.7**	**6.4**	**6.4**

Table 2b. Rate per 100,000 population *Stenotrophomonas* spp. bacteraemia reports by region: 2008 to 2012

Region	Rates per 100,000 population				
	2008	2009	2010	2011	2012
East	0.8	0.9	0.6	0.7	0.6
East Midlands	0.5	0.6	0.6	0.5	0.5
London	1.2	1.4	0.9	1.3	1.0
North East	1.2	0.9	0.5	1.0	1.1
North West	1.7	1.1	1.1	1.0	0.9
South East	0.9	0.6	0.7	0.6	0.6
South West	0.9	0.9	1.0	0.8	0.7
West Midlands	0.7	0.8	0.6	0.9	1.1
Yorkshire and The Humber	1.2	0.7	0.8	0.6	0.6
England	**1.0**	**0.9**	**0.8**	**0.8**	**0.8**
Wales	**0.6**	**1.0**	**0.8**	**0.7**	**0.8**
Northern Ireland (NI)	**1.1**	**1.1**	**1.1**	**0.6**	**0.5**
England, Wales & NI	**1.0**	**0.9**	**0.8**	**0.8**	**0.8**

Data collection is based on a voluntary reporting system, it is important to note that regional incidence rates are affected by completeness of regional reporting.

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Antimicrobial Susceptibility

Tables 3 and 4 present antibiotic susceptibility data for *P. aeruginosa*, and for *S. maltophilia,* respectively.

The proportion of *P. aeruginosa* isolates that were resistant to piperacillin/tazobactam increased by 3% (from 6% to 9%) between 2008 and 2012. Resistance to all the other antimicrobials listed in table 3 remained stable or reduced slightly during the period 2008-2012; imipenem (13%), meropenem (9%), ceftazidime (6%), ciprofloxacin (9%) and gentamicin (4%).

The number of *P. aeruginosa* bloodstream isolates with susceptibility test results reported has increased for each of the listed antibiotics over this 5 year time period, with the exception of imipenem results where there has been a slight reduction in susceptibility test results reported (28% to 25%). There has been increased meropenem susceptibility result reporting in isolates of *P.aeruginosa*, from 43% of isolates in 2008 to 62% in 2012.

Most imipenem-resistant *P. aeruginosa*, have reduced permeability (specifically, via loss of OprD porin), whereas those with meropenem or doripenem resistance have a combination of reduced permeability and up-regulated efflux, particularly of the MexAB-OprM pump.

However, the PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit receives a steady influx of *P. aeruginosa* and, in smaller numbers, other *Pseudomonas* spp. in which resistance to carbapenems is mediated by carbapenem-hydrolyzing metallo-β-lactamases ('metallo-carbapenemases'; MBLs).

Unlike the mutations that cause porin loss or increased efflux, carbapenemase production involves acquired genes, which may be transferred between strains.

From 2007-2012, AMRHAI confirmed 294 MBL-producing *Pseudomonas* isolates (from any source, not just blood culture); 35 in 2007, 30 in 2008, 41 in 2009, 76 in 2010, 37 in 2011 and 75 in 2012. These included 266 (91%) *P. aeruginosa* isolates.

Most of the carbapenemase-producing *P. aeruginosa* had VIM-type MBLs (247 isolates, 93%), though a minority had IMP-types (18 isolates) and one isolate produced an NDM carbapenemase.

MBL-producing *P. aeruginosa* are a nationally scattered problem although several UK hospitals have had persistent strains causing infections over several years, rather than classic outbreaks.

Table 3. Antibiotic susceptibility for *P. aeruginosa* bacteraemia reports, England, Wales and Northern Ireland: 2008-2012

	2008		2009		2010		2011		2012	
	No. tested	(% resistant)	No. tested	(% resistant)	No. tested	(% resistant)	No. tested	(% resistant)	No. tested	(% resistant)
Piperacillin/Tazobactam	2490	(6)	2509	(8)	2570	(7)	2544	(7)	2654	(9)
Imipenem	1110	(9)	1172	(13)	1038	(12)	926	(14)	947	(13)
Meropenem	1713	(10)	1785	(11)	2017	(9)	2210	(9)	2310	(9)
Ceftazidime	2484	(7)	2461	(8)	2530	(8)	2526	(8)	2595	(6)
Ciprofloxacin	2657	(11)	2709	(11)	2696	(10)	2703	(11)	2728	(9)
Gentamicin	2785	(4)	2778	(4%)	2812	(5)	2810	(6)	2864	(4)
Total *P. aeruginosa* reports	3987		3927		3833		3694		3743	

Table 4. Antibiotic susceptibility for *S. maltophilia* bacteraemia reports, England, Wales and Northern Ireland: 2008-2012

	2008		2009		2010		2011		2012	
	No. tested	(% resistant)	No. tested	(% resistant)	No. tested	(% resistant)	No. tested	(% resistant)	No. tested	(% resistant)
Co-trimoxazole	223	(4)	230	(7)	248	(5)	274	(5)	285	(4)
Total S*. maltophilia* reports	571		619		453		473		453	

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The carbapenemase producers are from a variety of clinical settings though **none of the isolates has been from cystic fibrosis (CF)**, where *P. aeruginosa* with complex mixtures of mutational resistances continue to dominate.

Many of these MBL-producing isolates are resistant to multiple antibiotic classes besides carbapenems, with only colistin remaining active against >90%.

It is difficult to determine the true susceptibility of *S. maltophilia* to aminoglycosides and polymyxins as temperature and medium can influence the results and cause resistant isolates to appear susceptible at 37ºC. However, the favoured treatment option for this species is co-trimoxazole and provides more stable results for interpretation when tested [6].

Although there were no significant changes in non-susceptibility of *S. maltophilia* to co-trimoxazole (4%) between 2008 and 2012, ascertainment of susceptibility results increased from 39% in 2008 to 63% in 2012 (table 4).

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, and the Antimicrobial Resistance and Healthcare Associated Infections (ARMHAI) Reference Unit, in particular, is valued in the preparation of the report. Feedback and specific queries about this report are welcome and can be sent to hcai.amrdepartment@phe.gov.uk.

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