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Surveillance of *Pseudomonas* and *Stenotrophomonas* species causing bacteraemia in England, Wales and Northern Ireland: 2014

These analyses are based on data relating to diagnoses of *Pseudomonas* spp. and *Stenotrophomonas* spp. bloodstream infections during 2007 – 2014 in England, Wales and Northern Ireland (E, W & NI) extracted from Public Health England's (PHE) voluntary surveillance database Second Generation Surveillance System (SGSS).

SGSS comprises a communicable disease module (CDR; formerly CoSurv/LabBase2) and an antimicrobial resistance module (AMR; formerly AmSurv). Most analyses presented here are based on data extracted from the CDR module of SGSS data on 30 June 2015, except for the evaluation of multi-drug resistance data from the AMR module of SGSS. This module captures more comprehensive antibiogram data allowing more robust evaluation of multi-resistance rates. However these data cannot be used for the trend analysis due to the addition of this data collection being relatively recent and therefore a lower laboratory coverage in previous years.

The data presented here will differ in some instances from those in earlier publications partly due to the inclusion of late reports.

Rates of bacteraemia laboratory reports were calculated using mid-year resident population estimates for the respective year and geography [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 the catchment area of one of 15 local PHE centres (PHECs) formed from administrative local authority boundaries.

This report includes analyses of the trends, patient demographic and geographical distribution as well as antimicrobial susceptibility among these bacteraemia episodes.

Key points

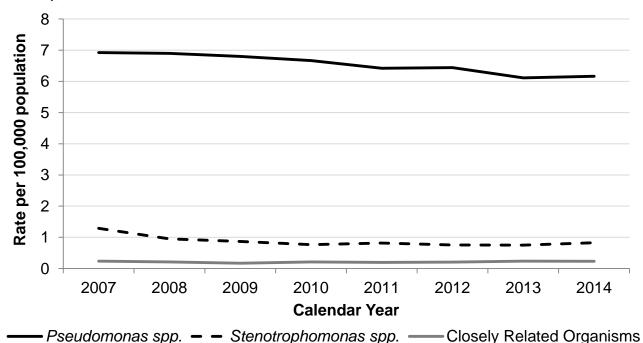
- the overall rate of *Pseudomonas* spp. bacteraemia in England, Wales and Northern Ireland was 6.2 per 100,000 population in 2014, an 11% decrease from 6.9/100,000 observed in 2007;
- the rate of *Stenotrophomonas* spp. was 0.8/100,000 in 2014, representing a decline of 36% since 2007 (1.3/100,000);
- the geographical distribution of *Pseudomonas* spp. bacteraemia varied widely in 2014,
 from 3.1/100,000 population in Wales to 8.0/100,000 in the London region of England;
- each country reported infection rates of below 1.0/ 100,000 population of Stenotrophomonas spp. bacteraemia in 2014;
- the most frequently identified *Pseudomonas* species in blood isolates in 2014 was *Pseudomonas aeruginosa* (81%);
- of the closely related organisms reported here, in 2014 Brevibacterium spp. and Brevundimonas spp. were the most commonly identified;
- the highest rates of *Pseudomonas* spp. bacteraemia were observed in those aged 75 years or older (31.5/100,000 population), and in males in the majority of age groups;
- the age distribution of *Stenotrophomonas* spp. bacteraemia showed higher rates in those aged between 65 and 74 years and in those aged less than one year (both 1.9/100,000 population);
- the proportion of *Pseudomonas* spp. bacteraemia reports which were reported as
 resistant (defined as reduced- or non-susceptible) to one of the key antimicrobials in
 2014 remained steady or increased slightly compared to 2013;
- a steady increase in reported resistance of *Pseudomonas* spp. isolates to the penicillin and β-lactamase inhibitor combination 'piperacillin/tazobactam' has been seen between 2010 and 2014;
- no clear pattern in the proportion of Stenotrophomonas spp. bacteraemia test results reported as resistant to co-trimoxazole between 2010 and 2014;
- in England, dual resistance to ciprofloxacin and ceftazidime was reported in 2%
 Pseudomonas spp. bacteraemia; 1% were reported resistant to ciprofloxacin,
 ceftazidime and piperacillim/tazobactam.

Trends

The overall rate of *Pseudomonas* spp. bacteraemia in England, Wales and Northern Ireland was 6.2 per 100,000 population in 2014, a slight decrease from 6.9/100,000 observed in 2007 (11% decrease; figure 1). England had the highest reported incidence rate of *Pseudomonas* spp. with 6.4/100,000 followed by Northern Ireland (4.1) and Wales (3.1). A much steeper decrease in *Pseudomonas* spp. bacteraemia incidence rate has been seen in Wales (36% decrease) and Northern Ireland (26% decrease) compared to England over the past five years (6% decrease; 2010 to 2014; table 1a).

The rate of *Stenotrophomonas* spp. was 0.8/100,000 in 2014, representing a decline of 36% since 2007 (1.3/100,000) but a slight increase on that observed in 2013 (0.7; figure 1). Reporting of closely related species has remained steady, at less than 0.25/100,000 population, over the time period (including *Brevibacterium* spp.*, *Brevundimonas* spp., *Burkholderia* spp., *Comamonas* spp., *Ralstonia* spp. and *Shewanella* spp.).

Figure 1. Eight year trend in *Pseudomonas* spp., *Stenotrophomonas* spp. and closely related species bacteraemia reports per 100,000 population (England Wales and Northern Ireland); 2007 to 2014



Pseudomonas spp. accounted for 3.1% of mono-microbial bloodstream infections (BSI; all reported bacteraemia and/or fungaemia) in 2014; making them the eighth most commonly reported mono-microbial BSI causing organisms. In contrast, *Stenotrophomonas* spp.

^{*} Closely related organisms include genera where at least one species has previously been classified as *Pseudomonas* spp. or *Stenotrophomonas* spp.

accounted for 0.4% mono-microbial BSI in 2014 (ranked 24th) [2]. *Pseudomonas* spp. and *Stenotrophomonas* spp. were identified in 8.2% and 1.8% of poly-microbial BSI respectively in 2014.

Between 2013 and 2014 there was a 2% increase in *Pseudomonas* spp. bacteraemia reports (3593 and 3652 reports respectively; table 2a); a slight contrast to a 3% increase observed in all bacteraemia reported (to SGSS CDR) between 2013 and 2014 (103,808 and 106,708 respectively [2]).

Geographic distribution

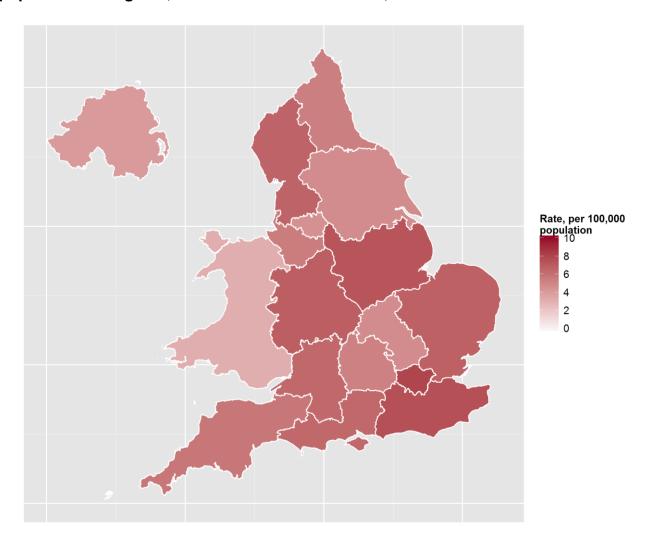
In England, Wales and Northern Ireland the geographical distribution of *Pseudomonas* spp. bacteraemia varied widely in 2014, from 3.1/100,000 population in Wales (95% CI 2.5 to 3.8) to 8.0/100,000 seen in the London region of England (95% CI 7.4 to 8.6; figure 2a).

Table 1a. Five year PHE Centre Pseudomonas spp. bacteraemia per 100,000 population (England, Wales and Northern Ireland); 2010 to 2014

Region		Rate per 100,000 population				
		2010	2011	2012	2013	2014
London	London	7.8	7.5	7.4	6.8	8.0
	South Midlands and Hertfordshire	4.8	3.6	4.3	4.9	4.7
	East Midlands	7.6	7.9	8.8	6.9	7.3
	Anglia and Essex	7.4	6.5	6.7	7.0	6.8
Midlands	West Midlands	6.8	6.5	6.3	6.8	6.9
	Cheshire and Merseyside	7.5	6.1	7.1	7.1	5.5
	Cumbria and Lancashire	5.3	6.0	5.9	5.8	6.7
	Greater Manchester	6.0	5.4	5.8	4.5	4.5
	North East	5.4	7.5	6.1	5.4	5.4
Northern	Yorkshire and Humber	6.6	5.9	5.2	4.9	4.8
	Avon Gloucestershire and Wiltshire	6.0	5.0	6.0	5.4	6.5
	Devon Cornwall and Somerset	7.4	6.3	6.2	6.4	5.7
	Wessex	8.3	7.0	7.2	7.0	6.4
	Kent Surrey and Sussex	6.9	7.5	8.0	7.6	7.5
Southern	Thames Valley	4.9	4.8	4.6	4.6	5.3
England	England	6.8	6.5	6.6	6.3	6.4
Northern Ireland	Northern Ireland	5.5	6.5	5.0	4.8	4.1
Wales	Wales	4.9	5.2	5.1	4.5	3.1
England, Wales a	6.7	6.4	6.4	6.1	6.2	

The rate of *Pseudomonas* spp. bacteraemia has varied over the five years between 2010 and 2014 within the English PHECs, however, no area has continuously reported the highest (or lowest) rates across the period (table 1a).

Figure 2a. Geographical distribution of Pseudomonas spp. bacteraemia per 100,000 population in England, Wales and Northern Ireland; 2014



The geographical distribution of *Stenotrophomonas* spp. bacteraemia varied in 2014, with each country reporting infection rates of below 1.0/100,000 population (table 1b), slightly more variation was observed within England, where rates ranged from 0.4/100,000 in Avon, Gloucestershire and Wiltshire (95% CI 0.2 to 0.8) and Thames Valley (95% CI 0.2 to 0.8) areas to 1.5/100,000 in the Cumbria and Lancashire area (95% CI 1.0 to 2.1; figure 2b). The numbers of reported *Stenotrophomonas* spp. bacteraemia have remained low across the recent five years (2010 to 2014; table 2b), leading to seemingly large fluctuations in the rates being reported. None of the increases or decreases seen in each of the areas between 2010 and 2014 were statistically significant.

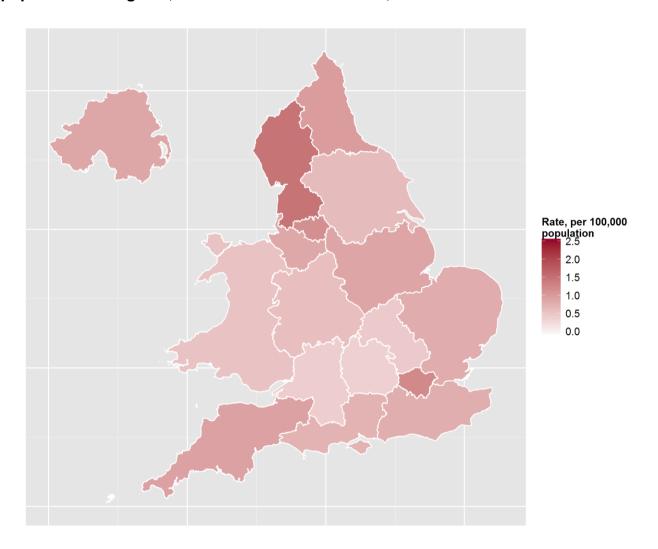
Table 1b. Five year PHE Centre Stenotrophomonas spp. bacteraemia per 100,000

population (England, Wales and Northern Ireland); 2010 to 2014

Region		Rate per 100,000 population				
		2010	2011	2012	2013	2014
London	London	8.0	1.2	0.9	0.9	1.2
	South Midlands and Hertfordshire	0.6	0.6	0.3	0.2	0.5
	East Midlands	8.0	0.7	0.7	8.0	0.9
	Anglia and Essex	0.6	0.7	8.0	8.0	8.0
Midlands	West Midlands	0.7	0.9	1.0	0.7	0.6
	Cheshire and Merseyside	0.6	8.0	0.4	0.4	0.9
	Cumbria and Lancashire	0.9	0.5	0.7	1.2	1.5
	Greater Manchester	1.6	1.5	1.4	1.6	1.1
	North East	0.4	8.0	0.9	0.9	1.0
Northern	Yorkshire and Humber	0.7	0.7	0.6	0.5	0.6
	Avon Gloucestershire and Wiltshire	8.0	0.3	0.7	0.7	0.4
	Devon Cornwall and Somerset	1.1	1.0	0.7	0.7	0.9
	Wessex	0.7	0.9	0.9	0.6	0.7
	Kent Surrey and Sussex	0.7	0.6	0.6	8.0	8.0
Southern	Thames Valley	0.4	0.7	0.2	0.4	0.4
England	England	8.0	8.0	8.0	0.7	8.0
Northern Ireland	Northern Ireland	1.1	0.7	0.5	1.3	0.9
Wales	Wales	8.0	8.0	8.0	0.5	0.5
England, Wales a	nd Northern Ireland	8.0	8.0	8.0	0.7	8.0

Reports of the closely related genera were distributed evenly across England, Wales and Northern Ireland, with no area reporting incidence of greater than 0.4 per 100,000 population in 2014. With reported numbers being so small any fluctuation in trend at the regional level are likely to be artefacts and insignificant. Further details on geographical distribution of these other genera are not presented within this report.

Figure 2b. Geographical distribution of Stenotrophomonas spp. bacteraemia per 100,000 population in England, Wales and Northern Ireland; 2014



Species distribution

The most frequently identified *Pseudomonas* species in blood isolates in 2014 was *Pseudomonas aeruginosa* (81%; table 2a). Ninety-two per cent of *Pseudomonas* bacteraemia cases were identified to species level in 2014, demonstrating an improving trend from the 89% reported to species level in 2010.

As expected *Stenotrophomonas maltophilia* is the most commonly isolated *Stenotrophomonas* species between 2010 and 2014, with between 91% and 100% isolated identified at this level (table 2b). Of note in 2014, 9% of *Stenotrophomonas* species bacteraemia have not been identified further, as *S. maltophilia* is the only known opportunistic human pathogen in the *Stenotrophomonas* genera it is likely that further investigation will yield these as *S. maltophilia* [3]. Further investigation is required to understand this change in reporting practice.

Table 2a. Distribution of Pseudomonas species identified in blood specimens

(England, Wales and Northern Ireland); 2010 to 2014

	2010	2011	2012	2013	2014
	Count %	Count %	Count %	Count %	Count %
P. aeruginosa	3104 81%	3014 81%	3059 81%	2953 82%	2970 81%
P. alcaligenes	1 0%	4 0%	3 0%	2 0%	4 0%
P. fluorescens	64 2%	40 1%	61 2%	52 1%	53 1%
P. koreensis	0 0%	0 0%	0 0%	0 0%	1 0%
P. mendocina	0 0%	0 0%	0 0%	0 0%	2 0%
P. mosselii	0 0%	0 0%	0 0%	1 0%	0 0%
P. oleovorans	0 0%	0 0%	0 0%	1 0%	0 0%
P. oryzihabitans	5 0%	4 0%	6 0%	3 0%	13 0%
P. otitidis	0 0%	0 0%	0 0%	0 0%	1 0%
P. paucimobilis	72 2%	68 2%	72 2%	70 2%	65 2%
P. putida	67 2%	68 2%	68 2%	54 2%	69 2%
P. stutzeri	61 2%	80 2%	96 3%	82 2%	91 2%
P. thomasii	0 0%	0 0%	0 0%	1 0%	0 0%
P. tolaasii	0 0%	0 0%	0 0%	0 0%	1 0%
Pseudomonas spp., other named	48 1%	63 2%	61 2%	70 2%	79 2%
Pseudomonas spp., sp. not recorded	411 11%	383 10%	336 9%	304 8%	303 8%
Genus Total	3833 100%	3724 100%	3762 100%	3593 100%	3652 100%

Table 2b. Distribution of Stenotrophomonas species identified in blood specimens (England, Wales and Northern Ireland); 2010 to 2014

	2010	2011	2012	2013	2014
	Count %				
S. maltophilia	439 100%	469 99%	438 99%	428 97%	446 91%
Stenotrophomonas spp., sp. not recorded	0 0%	5 1%	3 1%	12 3%	43 9%
Genus Total	439 100%	474 100%	441 100%	440 100%	489 100%

Of the closely related organisms reported here, Brevibacterium spp.* and Brevundimonas spp. were the most commonly identified in 2014, identified in 41 bacteraemia episodes each (table 2c). Due to small numbers the trends in these species fluctuate dramatically and will not be discussed further here.

^{*} Closely related organisms include genera where at least one species has previously been classified as Pseudomonas spp. or Stenotrophomonas spp.

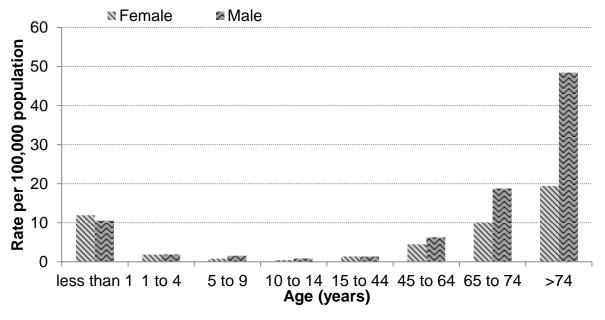
Table 2c. Distribution of the 'closely related organisms' identified in blood specimens (England, Wales and Northern Ireland); 2010 to 2014

,	2010	2011	2012	2013	2014
	Count %	Count %	Count %	Count %	Count %
Brevibacterium spp.	21 17%	21 19%	36 30%	41 29%	41 30%
Brevundimonas spp.	28 23%	26 23%	27 23%	30 21%	41 30%
Burkholderia spp.	44 36%	45 40%	41 34%	50 36%	31 23%
Comamonas spp.	10 8%	15 13%	7 6%	6 4%	13 9%
Ralstonia spp.	17 14%	2 2%	6 5%	8 6%	9 7%
Shewanella spp.	2 2%	3 3%	2 2%	5 4%	2 1%
Closely Related Organisms Total	122 100%	112 100%	119 100%	140 100%	137 100%

Age and Sex distribution

The age distribution of *Pseudomonas* spp. bacteraemia for 2014 is presented in figure 3a. The highest rates of *Pseudomonas* spp. bacteraemia were observed in those aged 75 years or older (31.5/100,000 population), followed by those aged between 65 and 74 years (14.3/100,000). *Pseudomonas* bacteraemia rates were also high in those aged less than one year (11.4/100,000). This is similar to the pattern observed in previous years [4].

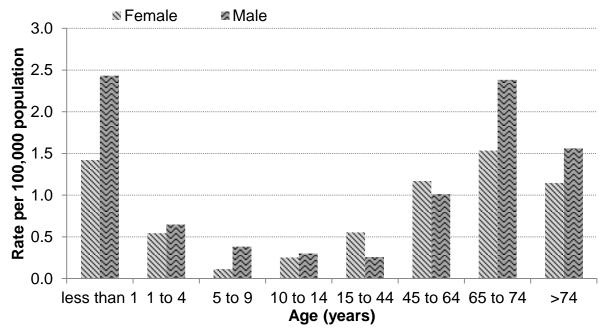
Figure 3a. Rate per 100,000 population Pseudomonas by age and sex (England, Wales and Northern Ireland); 2014



Variation of *Pseudomonas* spp. bacteraemia rates were also observed by gender, with higher rates noted in males in the majority of age groups (figure 3a). The most striking differences were noted in those aged 75 years and over (males: 48.4/100,000; females: 19.4/100,000) and those aged between 65 and 74 years (males: 18.8; females: 10.1).

The age distribution of *Stenotrophomonas* spp. bacteraemia showed higher rates in those aged between 65 and 74 years and in those aged less than one year (both 1.9/100,000 population; figure 3b). Rates were highest in males in all age groups except those aged between 15 and 64 years where higher bacteraemia rates were reported in females.

Figure 3b. Population rate by age group for bacteraemia caused by Stenotrophomonas spp. (England, Wales and Northern Ireland); 2014



Antimicrobial Resistance

The proportion of *Pseudomonas* spp. isolates with susceptibility test results reported was >70% for each of the key antimicrobials except imipenem, where 24% of reports included a result in 2014 (table 3a). Either carbapenem (meropenem or imipenem) had a susceptibility test result reported in 74% of cases.

Table 3a. Antimicrobial susceptibility for *Pseudomonas* spp. bacteraemia (England, Wales and Northern Ireland); 2010 to 2014

	2010		2	2011	2012		2013		2014	
	No. Tested	% Resistant								
Gentamicin	3277	5%	3313	6%	3360	4%	3194	4%	3095	4%
Ciprofloxacin	3125	10%	3164	11%	3192	10%	3059	10%	2964	11%
Ceftazidime	2935	9%	2962	9%	3030	7%	2849	7%	2704	7%
Meropenem	2358	9%	2611	10%	2695	9%	2643	8%	2711	10%
Imipenem	1156	10%	1018	13%	1019	12%	905	13%	873	16%
Piperacillin/Tazobactam	2978	7%	2997	7%	3117	9%	3017	9%	2933	10%
Total Reports	3	8833	3	3724	3	3762	3	593	3	3652

Table 3b. Antimicrobial susceptibility for *Stenotrophomonas* spp. bacteraemia (England, Wales and Northern Ireland); 2010 to 2014

	2010		2011 2012		2013		2014			
	No. Tested	% Resistant								
Co-Trimoxazole	240	5%	272	5%	271	3%	289	6%	296	7%
Total Reports		439		474		441		440		489

Overall the proportion of *Pseudomonas* spp. bacteraemia reports that were reported as resistant (defined as reduced- or non-susceptible) to an antimicrobial in 2014 remained steady or increased slightly compared to 2013 (table 3a). Imipenem resistance increased the most from 13% of isolates in 2013 to 16% isolates in 2014; however, as previously mentioned, the level of imipenem susceptibility test reporting remained low and may not be a true reflection of what is observed in all *Pseudomonas* isolates.

In 2014 the proportion of resistant *Pseudomonas* spp. bacteraemia isolates reported was piperacillin/tazobactam (10%), ciprofloxacin (11%), ceftazidime (7%), meropenem (10%), imipenem (16%) and gentamicin (4%).

It should be noted that there has been a steady increase reported resistance to the penicillin and β-lactamase inhibitor combination 'piperacillin/tazobactam' between 2010 (7% resistant) and 2014 (10% resistant).

There is a growing concern regarding the shift towards increased numbers of more drug-resistant organisms, this is a particular concern in *Pseudomonas* spp. bacteria which are known to affect patients with weakened immune systems. This ongoing concern has led to *Pseudomonas* spp. inclusion as one of the key pathogens to monitor as part of the UK 5-year Antimicrobial Resistance Strategy as well as the English surveillance programme for antimicrobial utilisation on resistance [5][6].

In 2014 the proportion of *S. maltophilia* isolates with a reported susceptibility test result to the favoured treatment option, co-trimoxazole, was 61% (table 3b), an increase on the 55% reported in 2010. There has been a slight fluctuation in the proportion of test results reported as resistant to co-trimoxazole between 2010 (5%) and 2014 (7%).

A one-year snapshot of multi-resistance, based on combinations of two different defined antibiotics, using the SGSS AMR data showed that 89% reported *Pseudomonas* spp. bacteraemia in England (2301/2589) had susceptibility results reported for both ceftazidime and ciprofloxacin; of those 2% were resistant (45 isolates; table 4). Seventy-one per cent of isolates resistant to both ciprofloxacin and ceftazidime were also resistant to piperacillin/tazobactam (32 isolates; 2196 tested for all 3 antibiotics).

For advice on treatment of antibiotic-resistant infections due to these opportunistic pathogens or for reference services including species identification and confirmation of

Table 4. Pair-Wise antimicrobial testing and resistance summary (England); 2014

	Ceft	azidime	Cipro	ofloxacin	Gentamicin		
	No.	%	No.	%	No.	%	
	tested	Resistant	tested	Resistant	tested	Resistant	
Ceftazidime							
Ciprofloxacin	2301	2%					
Gentamicin	2333	1%	2471	2%			

sensitivity testing results, laboratories should contact the Medical Microbiologists at PHE's Bacteriology Reference Department at Colindale on

<u>mailto:colindalemedmicro@phe.gov.uk</u> and PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit in London [7].

Acknowledgements

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