

# *Pseudomonas* spp and *Stenotrophomonas maltophilia* bacteraemia: England, Wales, and Northern Ireland: 2002

## Key points:

- 2597 reports of *Pseudomonas* spp bacteraemias were received from laboratories in England, Wales, and Northern Ireland in 2002.
- There was an 8% increase in the number of *Pseudomonas* spp reports from England and Wales since 2001.
- Seventy-nine per cent of *Pseudomonas* spp reports for England, Wales, and Northern Ireland concerned *Pseudomonas aeruginosa*.
- The comprehensiveness of susceptibility reporting provided for *Pseudomonas* spp varied according to the species, region, and antimicrobial.
- There was an 18% increase in the number of reports of *Stenotrophomonas maltophilia* bacteraemias from England and Wales between 2001 and 2002.
- There was a considerable (17%) decrease in the number of isolates of *S. maltophilia* with antimicrobial susceptibility data. There was, however, an increase in the number of *S. maltophilia* isolates with antibiotic susceptibility for co-trimoxazole, the first-line antimicrobial used to treat *S. maltophilia* infection.

This report details bacteraemia due to *Pseudomonas* spp, *Stenotrophomonas maltophilia*, and related species diagnosed from specimens collected during 2002. The bacteria were isolated from blood by laboratories across England, Wales, and Northern Ireland. As data from Northern Ireland have only been available since 2001, this is the first report on bacteraemias due to *Pseudomonas* and related species to include these data. The data do not distinguish between healthcare-associated and community acquired bacteraemias.

Rates were calculated using the Office for National Statistics 2001 resident population denominators for each region or age group. Regional analyses were carried out according to the English regional boundaries established in April 2002.

The majority of reported bacteraemias due to *Pseudomonas* and related species were due to *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* (table 1). Of the isolates from species other than *Pseudomonas* spp and *Stenotrophomonas* spp, the majority (37%) were due to *Comamonas* spp. Due to the small number of such cases, these data are not examined further in this report.

## *Pseudomonas* spp

There were 2597 reports of *Pseudomonas* spp bacteraemia made in 2002 (table 1), placing *Pseudomonas* spp among the top ten causes of bacteraemias in 2002 (1). The majority (2050; 79%) of reports were due to *P. aeruginosa*, although 413 (16%) of reports did not identify further than the genus.

There has been an 8% increase in reports of *P. aeruginosa* in England and Wales since 2001 and a 30% increase since 1999. This may be due, in part, to an increase in the number of *Pseudomonas* isolates that are fully identified to the species level, but may also reflect

**Table 1** Bacteraemia laboratory reports of *Pseudomonas*, *Stenotrophomonas* and related species, England, Wales and Northern Ireland: 2002

	Number of reports
<i>P. aeruginosa</i>	2050
<i>P. alcaligenes</i>	3
<i>P. fluorescens</i>	54
<i>P. putida</i>	47
<i>P. stutzeri</i>	30
<i>Pseudomonas</i> not fully identified	413
<b>Total</b>	<b>2597</b>
<i>S. maltophilia</i>	606
<i>Stenotrophomonas</i> not fully identified	1
<b>Total</b>	<b>607</b>
<i>Burkholderia cepacia</i>	45
<i>B. pseudomallei</i>	–
<i>Brevibacterium</i> not fully identified	11
<i>Brevundimonas diminuta</i>	6
<i>B. vesicularis</i>	12
<i>Brevundimonas</i> not fully identified	–
<i>Comamonas acidovorans</i>	29
<i>C. testosteroni</i>	3
<i>Comamonas</i> not fully identified	37
<i>Shewanella putrefaciens</i>	3
<i>Sphingomonas paucimobilis</i>	23
<i>Sphingomonas</i> not fully identified	1
<i>Ralstonia pickettii</i>	9
<b>Total</b>	<b>179</b>

increased reporting of isolates.

### Regional distribution

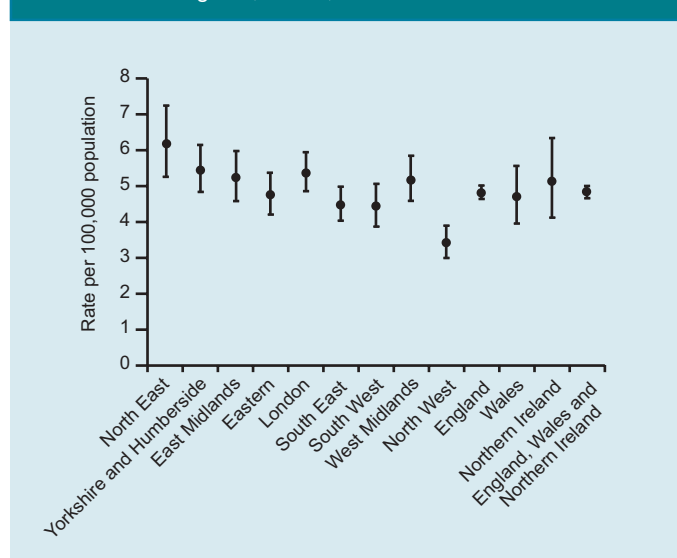
A number of regions changed their boundaries in April 2002, but of those that did not change, London region provided the largest increase (43%) in the number of reports of *Pseudomonas* spp compared with 2001 (table 2).

*P. aeruginosa* reports from Wales and the South West region also reported increased numbers of *Pseudomonas* spp bacteraemias compared with 2001 (20% and 1% respectively), whereas Eastern and West Midlands regions had 12% and 7% fewer reports respectively. The overall reporting rate for *Pseudomonas* spp bacteraemias in England, Wales, and Northern Ireland in 2002 was 4.83 per 100,000 population (figure 1).

The overall reporting rate for *Pseudomonas* spp bacteraemias in England was 4.83/100,000, was 4.72/100,000 in Wales and 5.15/100,000 in Northern Ireland. The region-specific rates within England

	<i>Pseudomonas</i> spp no (%)	<i>S.maltophilia</i> no (%)
North East	156 (6)	21 (3)
Yorkshire & Humberside	271 (10)	35 (6)
East Midlands	219 (8)	50 (8)
Eastern	257 (10)	57 (9)
London	387 (15)	79 (13)
South East	360 (14)	59 (10)
South West	219 (8)	54 (9)
West Midlands	273 (11)	91 (15)
North West	231 (9)	104 (17)
Wales	137 (5)	31 (5)
Northern Ireland	87 (3)	25 (4)
<b>England, Wales and Northern Ireland</b>	<b>2597 (100)</b>	<b>606 (100)</b>

**Figure 1** Region-specific rates\* of *Pseudomonas* spp bacteraemia with 95% confidence intervals, England, Wales, and Northern Ireland: 2002



\* rates calculated using 2001 mid-year resident population estimates

ranged from 3.43/100,000 in the North West to 6.20/100,000 in the North East.

### Antimicrobial susceptibility

Seventy-three per cent (1501/2050) of *P. aeruginosa* bacteraemia reports included susceptibility test results for at least one antimicrobial agent. Of these, 109 reports included data on susceptibility to all of the following antimicrobial agents: gentamicin, ciprofloxacin, imipenem, ceftazidime, and piperacillin/tazobactam. In comparison, only 52% of the other and incompletely identified *Pseudomonas* spp were accompanied by susceptibility results. This, however, is a considerable increase on the susceptibility testing reports from 2001, which included susceptibility data for only 32% of other and incompletely identified *Pseudomonas* species.

Gentamicin was the antimicrobial for which information on susceptibility was most often given for both *P. aeruginosa* (73%) and for the incompletely identified and other *Pseudomonas* spp, followed by ciprofloxacin, ceftazidime, and imipenem (table 3).

A higher percentage of isolates of *Pseudomonas* species other than *P. aeruginosa* were reported as antibiotic resistant, compared to isolates identified as *P. aeruginosa*. Of particular note were the susceptibility reports for

	resistant	(%*)	sensitive	no information	(% of total)
<b><i>Pseudomonas aeruginosa</i> (n=2050)</b>					
Gentamicin	115	(8)	1386	549	(27)
Ciprofloxacin	170	(12)	1273	607	(30)
Imipenem	52	(8)	611	1387	(68)
Ceftazidime	57	(4)	1271	722	(35)
Meropenem	20	(6)	293	1737	(85)
Piperacillin/tazobactam	27	(4)	588	1435	(70)
<b>Not fully identified and other <i>Pseudomonas</i> spp (n=547)</b>					
Gentamicin	31	(11)	253	263	(48)
Ciprofloxacin	53	(20)	211	283	(52)
Imipenem	12	(15)	67	468	(86)
Ceftazidime	21	(9)	213	313	(57)
Meropenem	12	(18)	55	480	(88)
Piperacillin/tazobactam	12	(9)	129	406	(74)
<b><i>Stenotrophomonas maltophilia</i> (n=606)</b>					
Gentamicin	167	(46)	198	241	(40)
Ciprofloxacin	225	(62)	136	245	(40)
Imipenem	193	(89)	25	388	(64)
Ceftazidime	33	(11)	273	300	(50)
Meropenem	61	(59)	43	502	(83)
Piperacillin/tazobactam	18	(10)	160	428	(71)

\* as a percentage of reports with susceptibility information

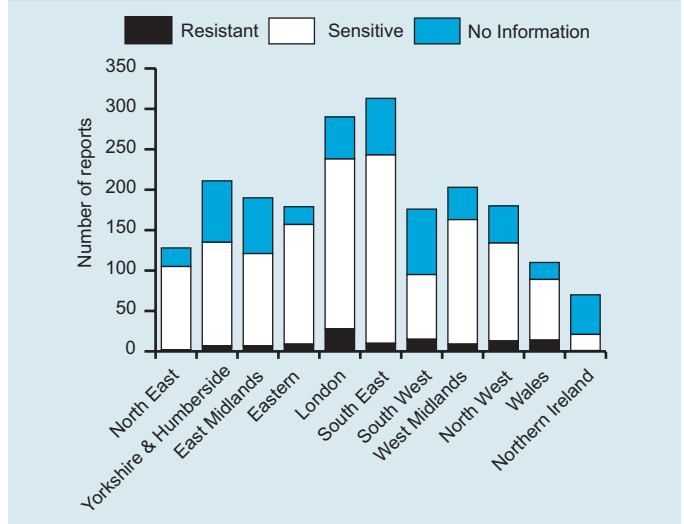
ciprofloxacin, imipenem, and meropenem, of which 20%, 15%, and 18% respectively indicated resistance compared to 12%, 8%, and 6% for *P. aeruginosa* (table 3).

The most common resistance reported for *P. aeruginosa* and isolates of other and not fully identified *Pseudomonas* species was to ciprofloxacin, which were 12% and 20% respectively.

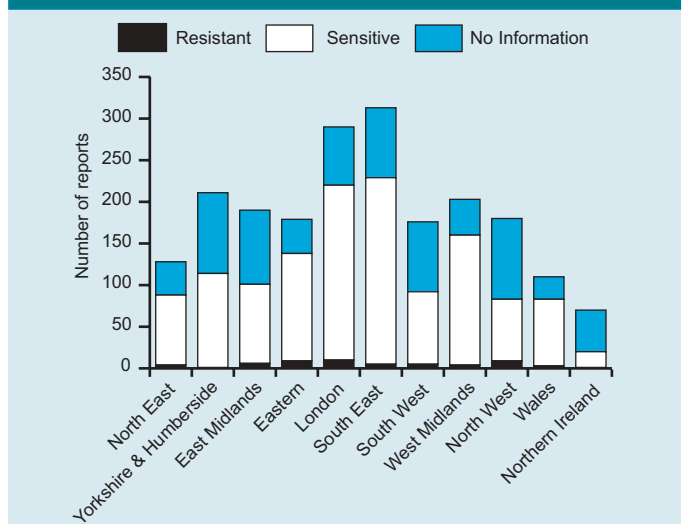
Regional breakdowns of antimicrobial susceptibility reporting are shown in figures 2 to 6. The proportion of isolates without information on antimicrobial susceptibility varied by region and across different antimicrobials. For example, Northern Ireland had the highest proportion of isolates with no reported susceptibility information (70% to 90%) for every antimicrobial, followed by the South West (45% to 82%).

Antimicrobial resistance reported for *P. aeruginosa* bacteraemia isolates also varied between the regions, with resistance in the West Midlands, Yorkshire and Humberside, and Northern Ireland being generally lower than the average for England, Wales, and

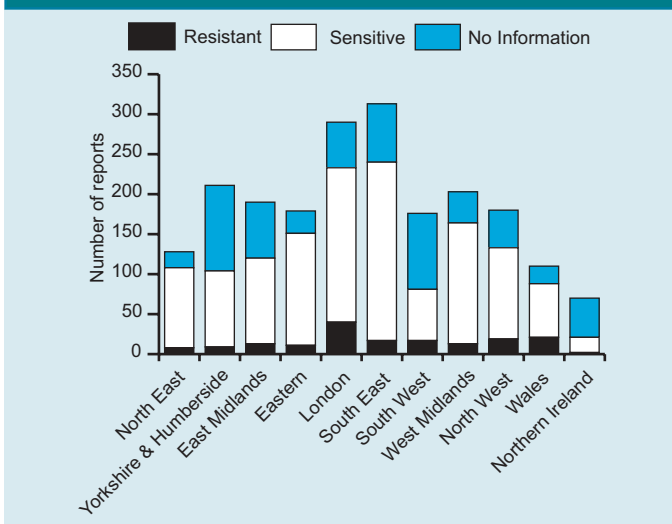
**Figure 2** Gentamicin susceptibility data for *P. aeruginosa* bacteraemia laboratory reports, England, Wales, and Northern Ireland 2002



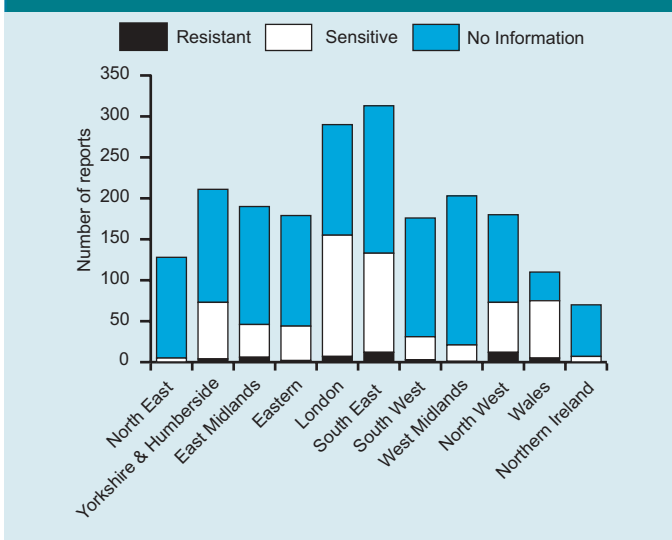
**Figure 4** Ceftazidime susceptibility data for *P. aeruginosa* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



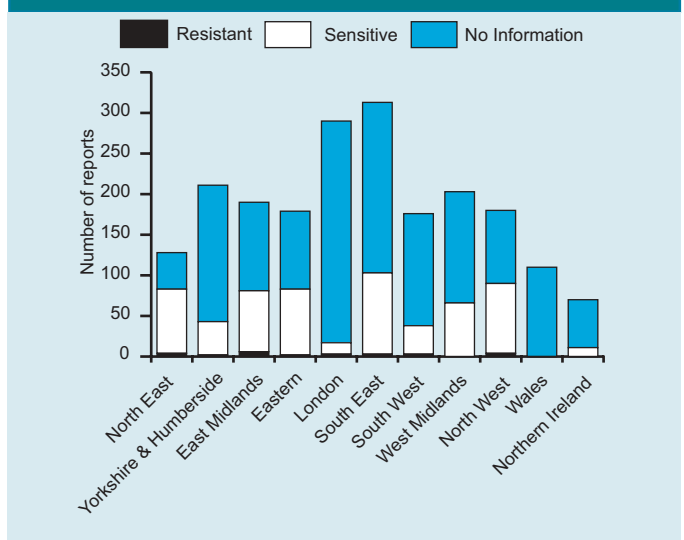
**Figure 3** Ciprofloxacin susceptibility data for *P. aeruginosa* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



**Figure 5** Imipenem susceptibility data for *P. aeruginosa* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



**Figure 6** Piperacillin/tazobactam susceptibility data for *P. aeruginosa* bacteraemia laboratory reports, England, Wales, and Northern Ireland 2002



**Table 4** Multiple antibiotic resistance patterns for *Pseudomonas aeruginosa* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002

		Gentamicin				Ciprofloxacin				Imipenem				Ceftazidime				Piperacillin/tazobactam				mr*	
		resistant %†	sensitive	no Info		resistant %†	sensitive	no Info		resistant %†	sensitive	no Info		resistant %†	sensitive	no Info		resistant %†	sensitive	no Info		%†	resistant
Gentamicin	resistant (n=115) sensitive (n=1386)					63 (61)	41	11		15 (25)	44	56		21 (21)	79	15		11 (26)	31	73		(-)	0/3
						10 (8)	1183	102		35 (6)	552	799		31 (3)	1152	203		14 (3)	543	829			
Ciprofloxacin	resistant (n=170) sensitive (n=1273)	63 (38)	101	6						19 (23)	65	86		20 (13)	132	18		12 (22)	42	116		(-)	0/7
		41 (1)	1183	49						27 (5)	496	750		28 (3)	1062	183		12 (2)	502	759			
Imipenem	resistant (n=50) sensitive (n=611)	15 (30)	35	-		19 (41)	27	4						7 (16)	37	6		4 (19)	17	29		(-)	0/13
		44 (7)	552	15		65 (12)	496	50						16 (3)	523	72		2 (1)	151	458			
Ceftazidime	resistant (n=57) sensitive (n=1271)	21 (40)	31	5		20 (42)	28	9		7 (30)	16	34						18 (72)	7	32		(-)	0/5
		79 (6)	1152	40		132 (11)	1062	77		37 (7)	523	711						3 (1)	454	814			
Piperacillin/tazobactam	resistant (n=27) sensitive (n=588)	11 (44)	14	2		12 (50)	12	3		4 (67)	2	21		18 (86)	3	6						(-)	0/4
		31 (5)	543	14		42 (8)	502	44		17 (10)	151	420		7 (2)	454	127							

mr = multiple resistance; \* resistant to gentamicin, ciprofloxacin, imipenem, ceftazidime, and piperacillin/tazobactam

† as a percentage of reports with susceptibility information

Northern Ireland for all antimicrobials. London and the North West regions had consistently higher than average rates of resistance. These figures, however, should be viewed with caution, given the variation in reporting susceptibility information between different regions.

Resistance to gentamicin was reported in 16% of isolates in Wales and the South West, compared with only 2% in the North East. These regional differences, however, may be due to differential use of the British Society for Antimicrobial Chemotherapy (BSAC) breakpoints. Those regions, where a majority of laboratories use the BSAC guidelines, may report higher rates of resistance, as the BSAC definitions are more conservative than would be expected from interpretation of Stokes' plates, as previously used by most laboratories.

Resistance to ciprofloxacin among *P. aeruginosa* was particularly high in Wales (24%), one out of four isolates being reported as resistant, while ciprofloxacin resistance was lowest in Northern Ireland (2%). No resistance was reported to imipenem in the North East or Northern Ireland, although few isolates (5/128 and 7/70 respectively) included susceptibility information for imipenem in these areas. The North West recorded the highest level of resistance in *P. aeruginosa* isolates to imipenem at 16%.

Resistance to ceftazidime ranged from 11% in the North West to 1% in the Yorkshire and Humberside region. None of the reports of *P. aeruginosa* from Wales contained information on susceptibility to meropenem. All tested isolates from Yorkshire and Humberside, Eastern, and Northern Ireland were reported as being sensitive to meropenem, although there were few isolates reported with susceptibility information from Yorkshire and Humberside region. It should be noted that cross-resistance between imipenem and meropenem is not complete for *Pseudomonas aeruginosa*,

and that the species has subtly different behaviour to these antibiotics (2).

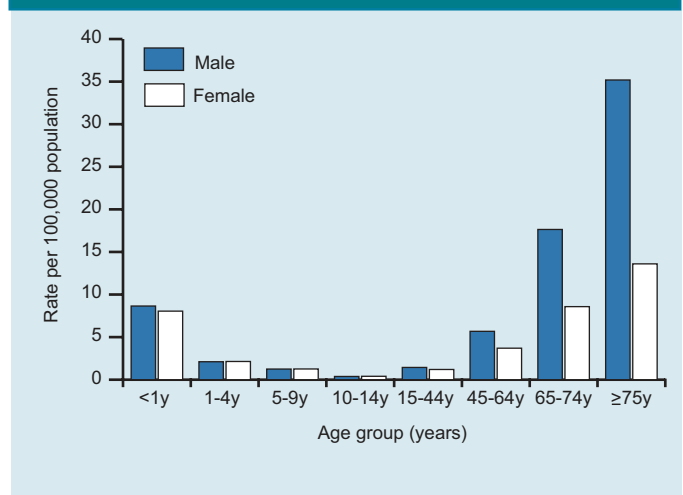
No *P. aeruginosa* bacteraemia isolates were reported as resistant to piperacillin/tazobactam in the West Midlands, Wales, or Northern Ireland, although 18% were reported as resistant in London. All other regions reported 2% to 6% of isolates as resistant to this antimicrobial.

No *P. aeruginosa* bacteraemia isolates were reported as resistant to all of gentamicin, ciprofloxacin, imipenem, ceftazidime, and piperacillin/tazobactam (table 4).

### Age distributions

The highest age-specific rate of *Pseudomonas* spp bacteraemia was in patients aged over 75 years (figure 7), followed by those aged between 65 and 74 years,

**Figure 7** Age-specific rates of *Pseudomonas* spp bacteraemia per 100,000 population, England, Wales, and Northern Ireland: 2002



**Table 5** Multiple antibiotic resistance patterns for *S. maltophilia* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002

			Gentamicin				Ciprofloxacin				Imipenem				Ceftazidime				Piperacillin/tazobactam				mr*	
			resistant	%†	sensitive	no Info	resistant	%†	sensitive	no Info	resistant	%†	sensitive	no Info	resistant	%†	sensitive	no Info	resistant	%†	sensitive	no Info	%†	resistant
Gentamicin	resistant	(n=166)					111 (69)	49	6	93 (95)	5	68	21 (17)	105	40	9 (10)	77	80	(12)	2/17				
	sensitive	(n=198)					102 (57)	78	18	88 (82)	19	91	11 (27)	149	38	9 (11)	74	115						
Ciprofloxacin	resistant	(n=225)	111 (52)	102	12					128 (95)	7	90	25 (15)	145	55	13 (12)	96	116	(6)	2/34				
	sensitive	(n=136)	49 (39)	78	9					47 (73)	17	72	6 (5)	105	25	4 (6)	60	72						
Imipenem	resistant	(n=193)	93 (51)	88	12	128 (73)	47	18					22 (15)	123	48	11 (14)	66	116	(5)	2/43				
	sensitive	(n=25)	5 (21)	19	1	7 (29)	17	1					2 (10)	19	4	1 (20)	4	20						
Ceftazidime	resistant	(n=33)	21 (66)	11	1	25 (81)	6	2	22 (92)	2	9				6 (67)	3	24	(50)	2/4					
	sensitive	(n=273)	105 (41)	149	19	145 (58)	105	23	123 (87)	19	131				7 (6)	112	154							
Piperacillin/tazobactam	resistant	(n=18)	9 (50)	9	–	13 (76)	4	1	11 (92)	1	6	6 (46)	7	5				(33)	2/6					
	sensitive	(n=160)	77 (51)	74	9	96 (62)	60	4	66 (94)	4	90	3 (3)	112	45										

mr = multiple resistance; \* resistant to gentamicin, ciprofloxacin, imipenem, ceftazidime, and piperacillin/tazobactam

† as a percentage of reports with susceptibility information

and then the under-one year olds. The rates were higher in males than females except in the 10 to 14 year age group where the age-specific rate for each sex was equal.

### *Stenotrophomonas maltophilia*

#### Regional distribution

There were 606 reports made of *Stenotrophomonas maltophilia* bacteraemia for England, Wales, and Northern Ireland in 2002 (table 1). In comparison to the 2001 figures, there has been an 18% increase in reports for this organism in England and Wales. The reporting rate for England, Wales, and Northern Ireland overall in 2002 was 1.13/100,000 population (figure 8), 1.12 /100,000 in England, 1.07 /100,000 in Wales and 1.48 /100,000 in Northern Ireland. As in 2001,

the highest rate of *S. maltophilia* bacteraemia reports was from the West Midlands (1.73 /100,000). The region with the lowest rate was Yorkshire and Humberside (0.70 /100,000), closely followed by the South East (0.74 /100,000).

#### Antimicrobial susceptibility

Overall, 60% of *S. maltophilia* bacteraemia isolates had information on susceptibility for at least one antimicrobial. This is a marked decrease on the number of isolates with susceptibility data in 2001 (72%).

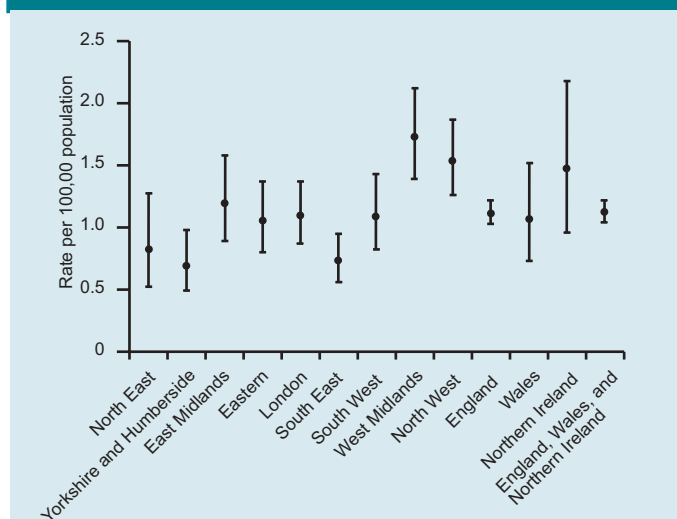
Antimicrobial susceptibility information was given most commonly for gentamicin and ciprofloxacin (60% of reports contained this information), followed by ceftazidime, imipenem, and piperacillin/tazobactam (table 3).

Eight per cent of *S. maltophilia* reports included susceptibility data for co-trimoxazole, an improvement on the previous year, when three per cent of reports included this information.

A high percentage (89%) of *S. maltophilia* bacteraemia isolates were resistant to imipenem. This is not unexpected, as *S. maltophilia* has a carbapenemase making it inherently resistant to imipenem. Apart from imipenem, resistance among *S. maltophilia* isolates was highest for ciprofloxacin (62%), meropenem (59%), and gentamicin (46%). Eleven per cent of isolates were reported as resistant to ceftazidime and 10% were reported as resistant to piperacillin/tazobactam (figures 9-12).

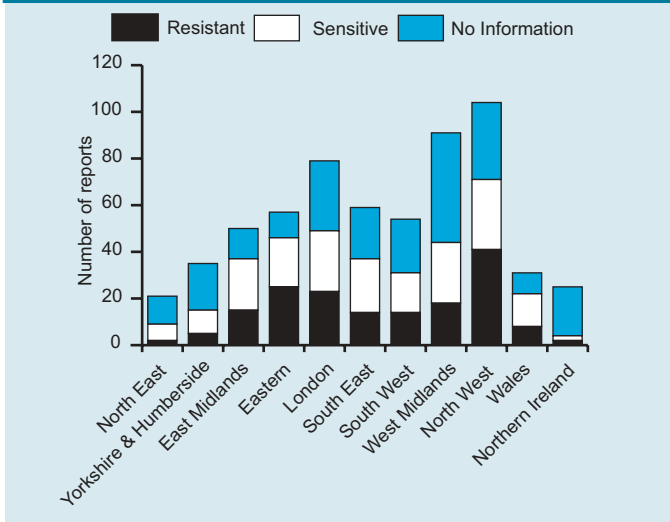
Of the isolates tested for antimicrobial susceptibility, two isolates were reported as resistant to gentamicin, ciprofloxacin, imipenem, ceftazidime, and piperacillin/tazobactam. Both of these isolates were reported from the West Midlands region (table 5).

**Figure 8** Region-specific rates\* of *S. maltophilia* bacteraemia with 95% confidence intervals, England, Wales, and Northern Ireland: 2002

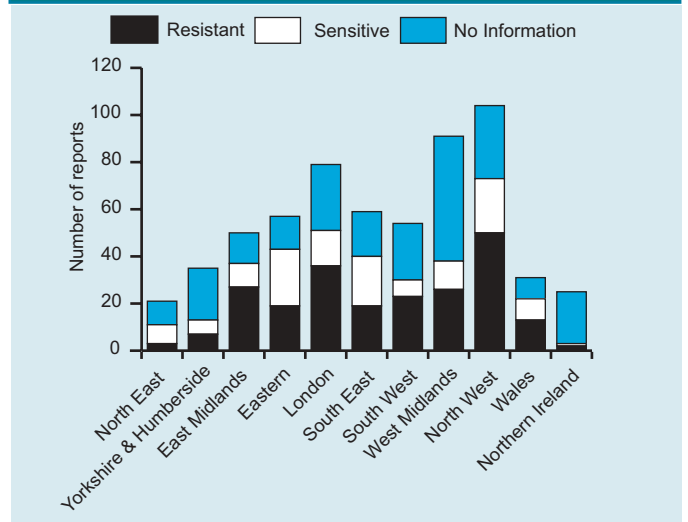


\* rates calculated using 2001 mid-year resident population estimates

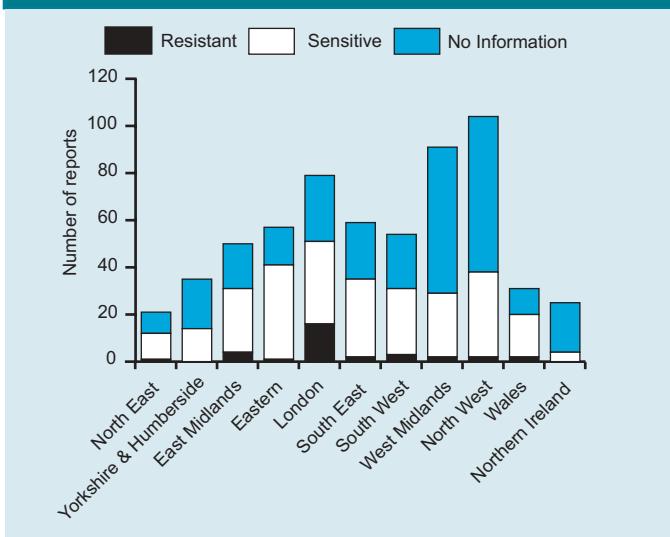
**Figure 9** Gentamicin susceptibility data for *S. maltophilia* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



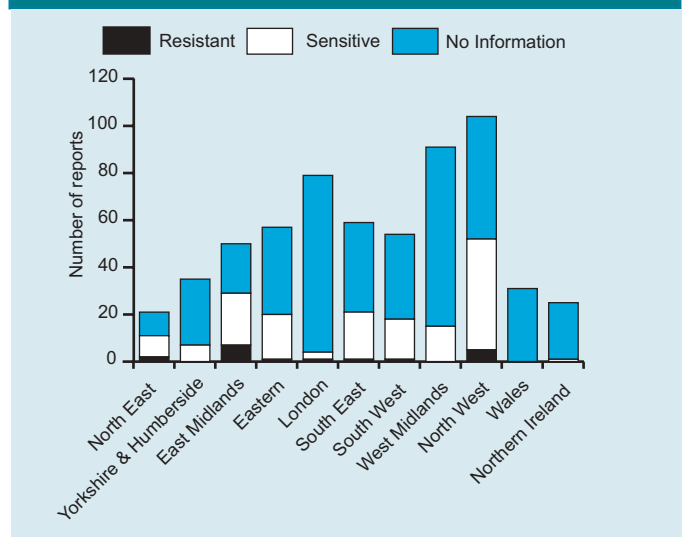
**Figure 10** Ciprofloxacin susceptibility data for *S. maltophilia* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



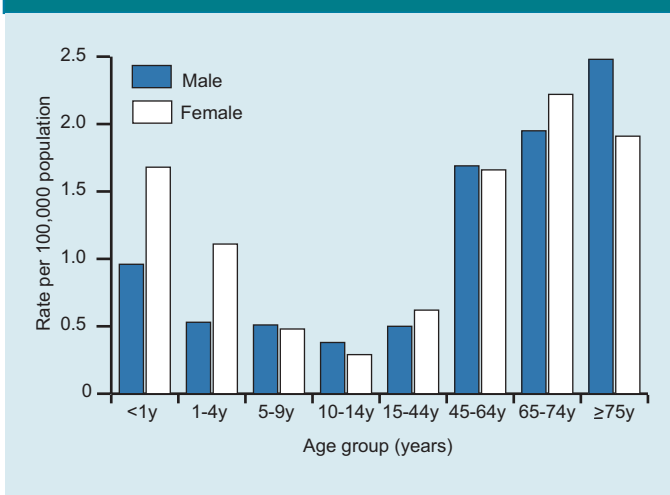
**Figure 11** Ceftazidime susceptibility data for *S. maltophilia* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



**Figure 12** Piperacillin/tazobactam susceptibility data for *S. maltophilia* bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2002



**Figure 13** Age-specific rates of *S. maltophilia* bacteraemia per 100,000 population, England, Wales, and Northern Ireland: 2002



**Age distributions**

For males, *S. maltophilia* bacteraemia rates were highest in those aged over 75 years, but in the 65 to 74 year age group, the higher rate was in females with 2.22 per 100,000 in the female population compared to 1.95 per 100,000 in the male population (figure 13). The absolute number of reports was low, however, and caution should be applied in the interpretation of these data.

In contrast to 2001, when there were no reports of bacteraemias due to *S. maltophilia* received for females aged less than one year, five such isolates were reported in females under one year in 2002.

**Discussion**

There was an increase in the number of reports of both *Pseudomonas* spp and *S. maltophilia* bacteraemias in England and Wales in 2002, compared with 2001 (3). It is not clear how much this reflects improved reporting or indicates a real increase. For example, there was a 43% rise in reports of *Pseudomonas* spp from the London

region, but this may just reflect an increase in bacteraemia reporting from the London region. When expressed as a percentage of the total bacteraemia reports, the number of *Pseudomonas* reports has only varied by 0.2% since 1999.

The number of reports identifying *P. aeruginosa* increased by 8%, and the proportion of *Pseudomonas* spp that were *P. aeruginosa* also increased from 77% in 2001 to 79% in 2002, reflecting a decrease in the proportion of incompletely identified *Pseudomonas* spp, from 17% to 16% between 2000 and 2001. The number of *S. maltophilia* reports also increased by 18% in England and Wales compared with 2001.

Although the proportion of reports with antimicrobial susceptibility information had increased slightly for *P. aeruginosa* (from 67% in 2001 to 73% in 2002), almost a third of *P. aeruginosa* isolates still did not include information on susceptibility to any antimicrobial. Furthermore, the percentage of *S. maltophilia* isolates reported with antimicrobial susceptibility data for at least one antimicrobial agent has actually decreased from 72% in 2001 to 60% in 2002.

Certain regions were consistently better at reporting antimicrobial susceptibilities. For example, Eastern and South East regions were among the better reporters for gentamicin, ciprofloxacin, and ceftazidime susceptibility in *P. aeruginosa* isolates and Eastern and East Midlands regions were consistently among the better reporters for the same susceptibilities in *S. maltophilia* isolates. A higher number of *S. maltophilia* isolates assayed for susceptibility to co-trimoxazole were reported from the North West, London, and Eastern regions.

The proportion of *Pseudomonas* spp and *S. maltophilia* isolates that were reported as resistant to the various antimicrobials increased in 2002 compared with 2001, although it is difficult to say whether this represents a true increase or reflects the improvement in susceptibility reporting, and the inclusion of reports from new laboratories. Rates of resistance were higher in the incompletely identified and other *Pseudomonas* spp than *P. aeruginosa*. It is unclear why this should be the case, but it is probably confounded by the fact that many of the isolates not identified to the species level are likely to be *P. aeruginosa*. Of particular note were the susceptibility reports for ciprofloxacin, imipenem, and meropenem, of which 20%, 15%, and 18% respectively indicated resistance compared to 12%, 8%, and 6% for *P. aeruginosa* (table 3). The reliability of these results is, however, undermined by the scarcity of susceptibility information among the other *Pseudomonas* spp, and the small numbers involved.

It was surprising that no *P. aeruginosa* isolates resistant to all of gentamicin, ciprofloxacin, imipenem, ceftazidime and piperacillin/tazobactam were reported in 2002, given its resistance to many drug classes and ability to acquire resistance through mutation (4). This finding may be due to the small number of isolates that were tested against all five antibiotics. For example, only three of the isolates resistant to gentamicin were also tested for resistance to the other four agents (table 4). In contrast, Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL) regularly receives

multiply-resistant *P. aeruginosa* isolates. These are mostly from cystic fibrosis patients, although a few are from burns and other sources, occasionally including bacteraemias.

When compared to the data produced by the BSAC, the routine laboratory reporting data demonstrates similar levels of resistance in *P. aeruginosa* isolates. The utility of these data are limited, as both analyses are based on a small number of isolates (5).

*S. maltophilia* is inherently resistant to imipenem, so the 25 reports of isolates sensitive to this antimicrobial are unlikely. The more commonly reported antimicrobials are generally less reliable against this species. The type of susceptibility test used influences the result, as does the temperature at which susceptibility testing is carried out. It should be noted that the activity of ceftazidime and piperacillin/tazobactam varies with the test medium and that the provenance for their clinical efficacy is much less than for co-trimoxazole against this species.

As previously reported, co-trimoxazole is the main antimicrobial agent used in the treatment of *S. maltophilia* infections (3). In 2001, 3% of isolates included susceptibility results for this antimicrobial. In 2002, 50 isolates (8%) were reported with susceptibility results against this antimicrobial. Although this is an improvement, it compares poorly with the reporting of other, less relevant antimicrobials.

## Acknowledgments

These reports would not be possible without the enduring weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland, without which there would be no surveillance data. This is your data, so please tell us what you would like done with it. We are always pleased to hear your views. Please send your comments/feedback to [georgia.duckworth@hpa.org.uk](mailto:georgia.duckworth@hpa.org.uk). In addition, the support from colleagues within the Health Protection Agency, Specialist and Reference Microbiology Division in particular, is valued in the preparation of the reports. These contributions are greatly appreciated.

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