Public Health England

Health Protection Report
weekly report

Infection report

Volume 11 Number 18 Published on: **22 May 2017**

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

These analyses are based on volunatry surveillance of diagnoses of bloodstream infections caused by *Klebsiella* spp. reported by laboratories between 2009 and 2016. Data for England were extracted on 7 April 2017 from Public Health England's (PHE) voluntary surveillance database Second Generation Surveillance System (SGSS). Data for Wales and Northern Ireland were extracted on 9 March and 13 April (from DataStore and CoSurv systems), respectively.

SGSS comprises a communicable disease module that includes antimicrobial susceptibility data (CDR; formerly CoSurv/LabBase2) 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 there was a lower laboratory coverage to the AMR module. Therefore, antimicrobial non-susceptibility trends cannot currently be undertaken using data from the AMR module but data for 2015 were extracted to assess multi-drug resistance rates. Only England and Northern Ireland data are included in the antimicrobial susceptibility analyses.

The data presented here for earlier years 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 with the exception of 2016 rates, which were based on 2015 population estimates as population estimates for 2015 were not available at the time of producing this report [1,2]. 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 *Klebsiella* spp. bacteraemia in England, Wales and Northern Ireland. In addition, antimicrobial susceptibility five-year trends for England and Northern Ireland have been included in the report, as has a single year of resistance to more than one antibiotic based on England's data reported to the AMR module (previously AmSurv) and extracted on 7th March 2017. A web appendix is available featuring the findings of this report including only data submitted via SGSS from laboratories in England.

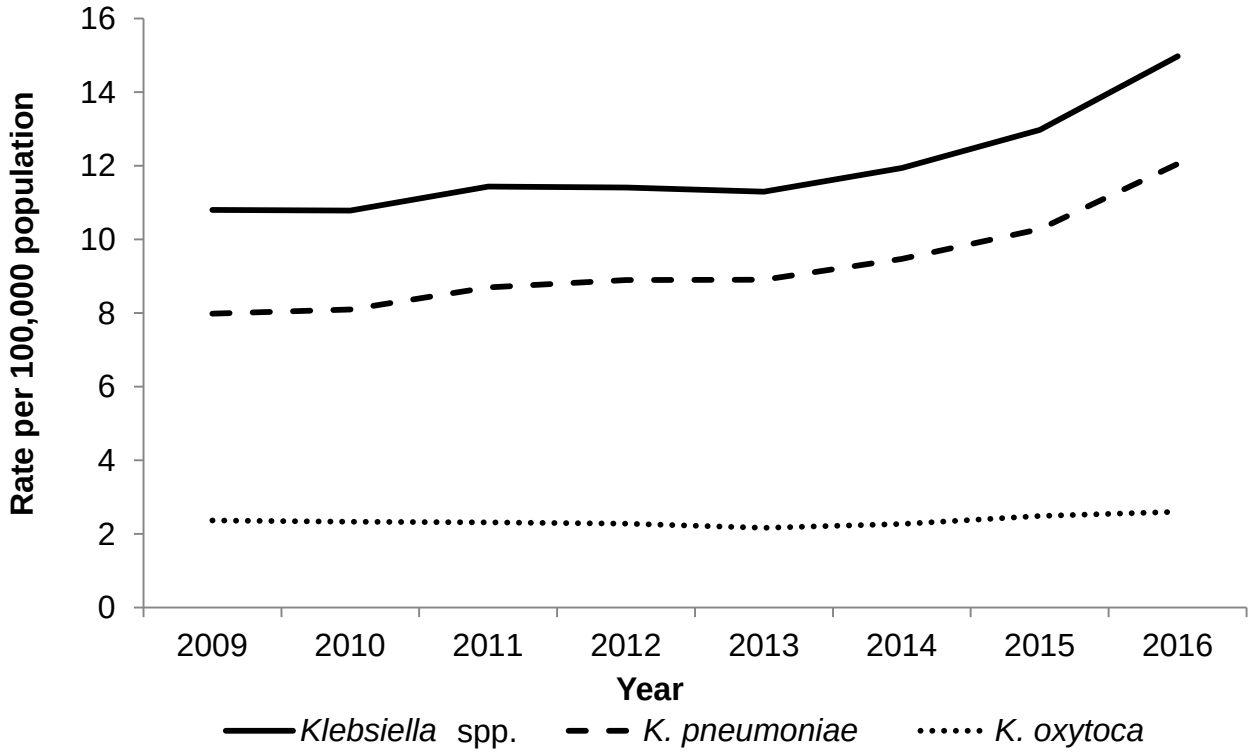
Key points

- between 2015 and 2016 the total number of reports of *Klebsiella* spp. bacteraemia in England, Wales and Northern Ireland increased by 15% (from 7,746 to 8,944 episodes), an increase in population rate from 13.0 to 15.0 per 100,000 population
- the rate of *Klebsiella* spp. bacteraemia reports was generally higher in males than females and among older adults (≥75 years) and infants (<1 year)
- in 2016 the population rates for England, Northern Ireland and Wales were 14.9, 13.9 and 17.1 per 100,000 respectively
- in 2016, the highest rates in England were in the North East PHEC at 18.3 per 100,000 population and East Midlands PHEC (16.3/100,000 population) and the lowest rates were in the Yorkshire and Humber PHEC (11.9/100,000 population)
- antimicrobial susceptibility trends from 2012 to 2016 were examined for five antibiotic classes
    - resistance to cefotaxime and ceftazidime was stable in the study period remaining at 10% for *Klebsiella* spp. in 2016 (12% for *K. pneumoniae*) for each antibiotic; resistance to both agents was lower among *K. oxytoca* isolates although for cefotaxime it decreased from 5% in 2012 to 3% in 2016
    - gradual increases in non-susceptibility to piperacillin/tazobactam occurred for *Klebsiella* spp, reported in 17% of isolates in 2016 (18% for *K. pneumoniae*) up from 13% in 2012 in both analyses; this may reflect the recent switch from CLSI to EUCAST MIC breakpoint from 16 to 8 mg/L for this agent
    - resistance to carbapenems remained low in 2016 (≤2%) at genus and species levels
    - in 2016, 13% of *K. pneumoniae* bacteraemia isolates tested against ciprofloxacin and third-generation cephalosporins were resistant to both antibiotics; only <0.7% of *K. oxytoca* isolates were resistant to gentamicin and ciprofloxacin or gentamicin and third-generation cephalosporins

Trends

Figure 1 shows the trend in the rate of *Klebsiella* spp. bacteraemia laboratory reports between 2009 and 2016 per 100,000 population. The annual rate was relatively stable around 11.0/100,000 population between 2009 and 2013. Increases occurred after this with a 33% increase from 2013 to 2016. Between 2015 and 2016 in particular the rate increased by 15% from 13.0/100,000 population to 15.0/100,000 population, respectively.

Figure 1 Bacteraemia rate for *Klebsiella* spp., *K. pneumoniae* and *K. oxytoca* per 100,000 population (England, Wales and Northern Ireland): 2009- 2016



The trends for the two leading species are also shown. The rate of *K. pneumoniae* bacteraemia was relatively stable at 8-9 cases per /100,000 population *per annum* until 2013. Marginal yet steady increases were observed since then. The rate increased by 35% from 2013 to 2016 and by 17% between 2015 (10.3/100,000 population) and 2016 (12.1/100,000 population) in particular for this species. These trends show that the increases in *Klebsiella* spp. in recent years were largely driven by increases in *K. pneumoniae* laboratory reports.

The rate for *K. oxytoca* (figure 1) was stable for most of the study period at around 2.0/100,000 population *per annum* with the exception of 2016 where the rate increased marginally to 3%.

Geographical distribution

The geographical analyses presented here are not corrected for variation in reporting between geographical areas. Figure 2 is a graphical display of the regional variation in the rates in 2016. Table 2 shows five-year trends by geographical region from 2012 to 2016.

In 2016 the overall rate of laboratory reports of *Klebsiella* spp. bacteraemia for England, Wales and Northern Ireland was 15.0 per 100,000 population. The rates individually by country were 14.9/100,000 population for England, 17.1/100,000 population for Wales and 13.9/100,000 population for Northern Ireland. 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.

Within England, there was variation in the rate between the nine PHE Centres (PHECs). In 2016, the highest rates were in North East at 18.3/100,000 population and East Midlands (16.3/100,000 population). The lowest rates were in Yorkshire and Humber (11.9/100,000 population). Although the highest *Klebsiella* spp. bacteraemia rate was in the North East PHEC, carbapenem-resistant isolates were more frequently reported by laboratories in North West and London (described in the antimicrobial susceptibility section of this report).

Three of nine PHECs experienced a steady year-on-year increase over the five-year period (London, South East and South West (table 1). The lowest rates were observed in Yorkshire and Humber over the last four year of the study period.

The geographical variation may be explained by differences in completeness of reporting between PHECs. Local outbreaks, differences in case-mix and variation in the distribution of specialist care units may also influence these rates.

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

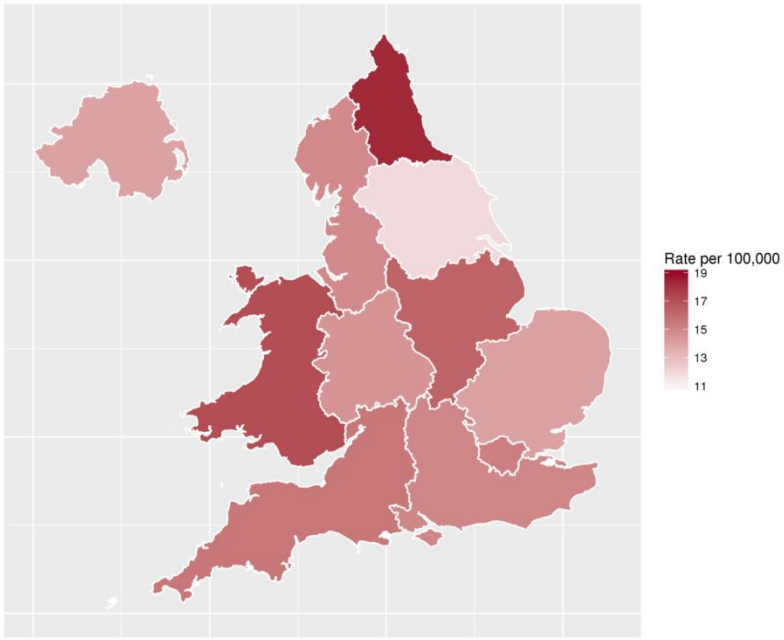


Table 1: Rate of *Klebsiella* spp. bacteraemia reports per 100,000 population by PHE Centre (England, Wales and Northern Ireland): 2012 to 2016

		Rate per 100,000 resident population				
Region	**PHE Centre**	**2012**	**2013**	**2014**	**2015**	**2016**
North of England	North East	12.3	11.9	13.4	14.7	18.3
	Yorkshire and Humber	10.3	7.9	9.4	10.3	11.9
	North West	13.9	13.6	13.5	14.1	14.9
Midlands and East of England	West Midlands	11.5	11.3	12.9	13.9	14.5
	East Midlands	10.1	10.8	10.7	13.7	16.3
	East of England	11.5	10.0	11.3	12.1	14.0
London	London	11.8	12.5	12.9	13.6	15.3
South of England	South West	10.4	10.5	11.7	13.2	15.6
	South East	9.6	10.1	10.4	11.2	15.0
England*		11.2	11.0	11.8	12.8	14.9
Northern Ireland†		11.4	11.5	12.6	13.4	13.9
Wales¥		14.2	15.8	14.6	15.1	17.1
England, Wales and Northern Ireland		11.4	11.3	11.9	13.0	15.0

* Extracted on 7 April 2017; †extracted on 13 April 2017, ¥ extracted on 9 March 2017

Species distribution

In 2016, 98.4% (n=8,804/8,944) of *Klebsiella* spp. blood specimens were identified to species level for combined England, Wales and Northern Ireland data (table 2). This proportion was broadly similar compared to earlier years.

In 2016, the predominant species was typically *K. pneumoniae* accounting for 80% of reports, followed by *K. oxytoca* (17%) although this year a slight increase in the proportion due *to K. pneumoniae* was observed. It should be noted that although *K. aerogenes* is not a valid species, it continues to be reported albeit in substantially reduced numbers (n<5 in 2016). A small number of reports of *K. ornithinolytica* continue to be reported, but these were excluded from all analyses in this report due to the taxonomic change to *Raoultella ornithinolytica* in 2001. *K. variicola* was reported in 2016 (n=41 isolates) which may reflect the use of automated diagnostic technology (MALDI-TOF) which enables laboratories to distinguish more species.

Of the top 10 most frequent organisms involved in monomicrobial and polymicrobial bacteraemia, *K. pneumoniae* was 4th in both rankings. *K. oxytoca* was ranked16th and 12th respectively in these analyses [3].

The total number of *Klebsiella* spp. bacteraemia reports in 2012 and 2013 was stable at around 6,600 *per annum*. However, between 2013 and 2016, these increased by 35% for *Klebsiella* spp. (38% for *K. pneumoniae*). Between 2015 and 2016 in particular there was a 15% increase in *Klebsiella* spp. (from 7,746 to 8,944 episodes) and a 17% increase in *K. pneumoniae* (from 6,138 to 7,199 episodes) (table 2).

Table 2. Reports of *Klebsiella* bacteraemia by species (England, Wales and Northern Ireland): 2012 to 2016

	2012		2013		2014		2015		2016	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
***Klebsiella* spp.**	**6,660**	**100%**	**6,639**	**100%**	**7,070**	**100%**	**7,746**	**100%**	**8,944**	**100%**
K. oxytoca	1,328	19.9%	1,274	19.2%	1,344	19.0%	1,487	19.2%	1,552	17.4%
*K. pneumoniae**	5,191	77.9%	5,231	78.8%	5,608	79.3%	6,138	79.2%	7,199	80.5%
K. variicola	0	0.0%	0	0.0%	0	0.0%	0	0.0%	41	0.5%
Klebsiella spp., other named	10	0.2%	13	0.2%	10	0.1%	11	0.1%	12	0.1%
Klebsiella spp., sp. not recorded	131	2.0%	121	1.8%	108	1.5%	110	1.4%	140	1.6%

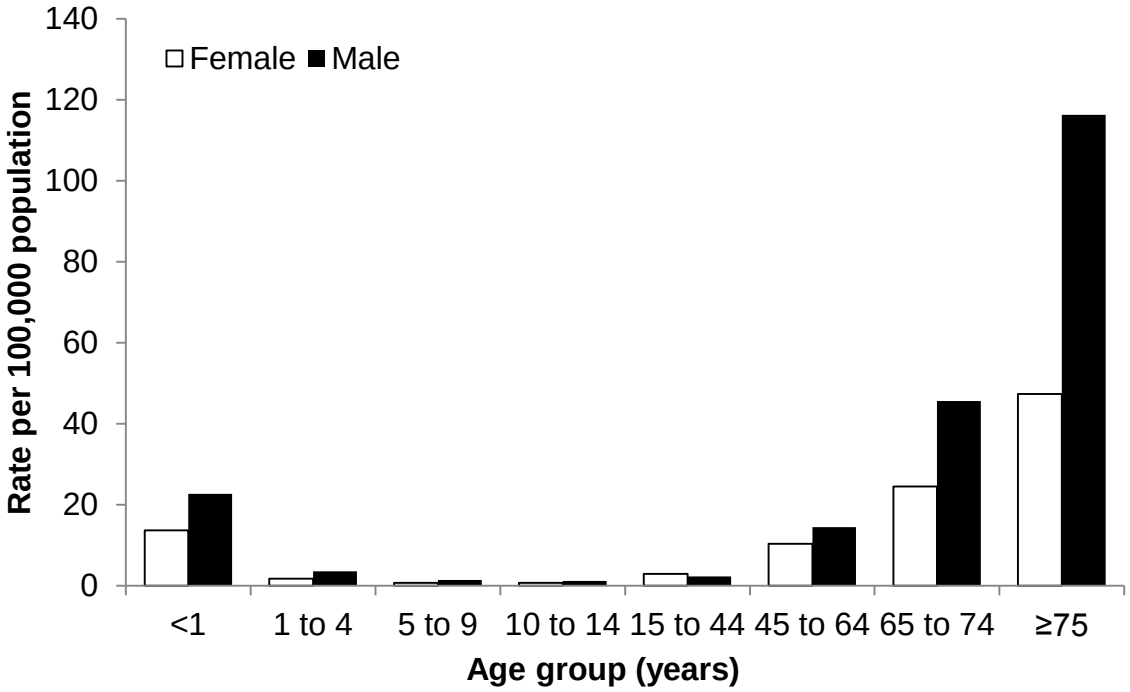
*includes a small number of episodes reported as *K. aerogenes*

Age and sex distribution

Figure 3 shows that the age and sex distribution follows a J-shaped curve as the elderly (≥65 years) and the infant group (<1 year) had higher rates of *Klebsiella* spp. bacteraemia per 100,000 population. Adults aged ≥75 years in particular had the highest rates in both males and females.

The rate was higher among males than females across all age groups except for the age group 15 to 44 years where the rate was slightly higher for females. The largest disparity was in the age group ≥75 years where incidence rate among males was 2.5-fold higher than in females. The second highest disparity was in the age groups 1 to 4 years and 5 to 9 years where the incidence rate among males was two-fold higher than in females in each group.

Figure 3. *Klebsiella* spp. bacteraemia rates by age and sex (England, Wales and Northern Ireland): 2016



Antimicrobial resistance: England and Northern Ireland

Tables 3-5 present antibiotic susceptibility trends from 2012 to 2016 in England and Northern Ireland for blood culture isolates using data from the CDR module of SGSS and CoSurv, respectively. This analysis examines five classes of antibiotics: third-generation cephalosporins (cefotaxime or ceftazidime), carbapenems (meropenem or ertapenem), a fluoroquinolone (ciprofloxacin), a penicillin/beta-lactamase inhibitor combination (piperacillin/tazobactam), and an aminoglycoside (gentamicin).

Table 6 shows multi-drug resistance in 2016 for defined combinations of antimicrobial drugs based on England data from SGSS's AMR module. Trends using data from this module cannot be undertaken at present owing to lower laboratory coverage in previous years.

Among *Klebsiella* spp. the most common mechanism of resistance to third-generation cephalosporins (cefotaxime or ceftazidime) is plasmid-mediated extended-spectrum β-lactamase (ESBL) production. The analysis for *Klebsiella* spp. isolates (all species) showed that resistance to cefotaxime and ceftazidime remained stable between 2012 and 2016, mostly at 10% over the five year period for each agent (table 3). Similarly, for *K. pneumoniae,* resistance to cefotaxime and ceftazidime was stable throughout the five year period remaining at 12% in 2016 for each agent (table 4). *K. oxytoca* showed a lower level of resistance to these agents compared to *K. pneumoniae;* whilst resistance to ceftazidime remained stable between 2012 and 2016 (range 2-3%), resistance to cefotaxime decreased from 5% in 2013 to 3% in 2016 (table 5).

The proportion of isolates reported resistant to piperacillin/tazobactam increased gradually over the five-year period for *Klebsiella* spp. isolates (from 13% in 2012 to 17% in 2016) (table 3). This was similarly reflected in the reports for both *K. pneumoniae (*piperacillin/tazobactam resistance from 13% to18%) and *K. oxytoca* isolates (from 11% to15%) between 2012 and 2016 respectively. These results are likely to reflect laboratories switching from the CLSI MIC breakpoint of 16 mg/L to the EUCAST breakpoint of 8 mg/L for this agent for Enterobacteriaceae introduced in 2011.

A marginal increase in resistance to ciprofloxacin was observed from 8% in 2012 to 10% in 2016 at genus level (table 3). At species level, *K. pneumoniae* tended to have a higher resistance rate to this agent (11% in 2016) compared to *K. oxytoca* (2% in 2016). In both species the proportion of bacteraemia isolates resistant to this agent was stable over the entire five year period (tables 4 and 5).

Resistance to gentamicin increased marginally at genus level (from 6% in 2012 to 8% in 2018) (table 3) and for *K. pneumoniae* (from 7% in 2012 to 9% in 2016) (table 4). However, resistance to this agent remained low for *K. oxytoca* (≤2% throughout the five-year period) (table 5).

Resistance to carbapenems (meropenem and ertapenem) remained low between 2012 and 2016 with ≤2% of isolates reported as resistant.

It should be noted that EUCAST's clinical breakpoint for determining susceptibility to ertapenem is lower than that for meropenem (0.5 mg/L vs 2 mg/L, respectively). However, ertapenem is more prone to resistance due to ESBL production together with porin deficiency arising via mutation. Meropenem resistance is rarer owing to the higher breakpoint and lower vulnerability to

this combination of mechanisms. Consequently resistance to meropenem is more likely to be due to true carbapenemases, hence of public health concern.

In England, the majority of carbapenem-resistant isolates reported between 2012 and 2016 (n=314) were reported from laboratories in North West (n=88) and London (n=83), which combined accounted for 54% (n=171/314) of total carbapenem-resistant isolates.

Klebsiella spp. organisms are the commonest hosts of carbapenemase enzymes which belong to the KPC, OXA-48-like, NDM, VIM or IMP families; other types of carbapenemase, such as GES enzymes, also occur (both in Enterobacteriaceae and non-fermenters such as *Pseudomonas aeruginosa*) and have caused outbreaks in some UK hospitals. Among Enterobacteriaceae in general, resistance to carbapenems may also be mediated by ESBL or AmpC production combined with impermeability (porin loss). However, data on all Enterobacteriaceae isolates from all specimen types referred to PHE's national reference laboratory, the Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit, indicate an increasing trend in carbapenemase-producing Enterobacteriaceae (CPE) from 2008 with sporadic cases reported as far back as 2003. Resistance to the carbapenem class warrants close vigilance given that this class of antibiotics is a powerful last-line treatment for serious infections caused by Gram-negative bacteria. The increases in CPE based on all specimen types observed by PHE's ARMHAI are occurring in the context of the emergence of resistance to these antibiotics among Enterobacteriaceae reported internationally in recent years [4,5].

In recognition of the importance of CPE, PHE issued a toolkit in December 2013 on the identification and management of affected patients in acute healthcare settings [6]. This toolkit includes a risk assessment to identify those individuals who should be screened for colonisation or infection with CPE as part of the routine admission procedure. A toolkit for non-acute settings was issued in June 2015 [7].

As CPE pose significant treatment and public health challenges, PHE launched the electronic reporting system (ERS) for the enhanced surveillance of carbapenem resistance in Gram-negative bacteria in May 2015 to better understand the epidemiology of these organisms. A web-based electronic reporting system (https://cro.phe.nhs.uk/) has been designed to enable laboratories in NHS Trusts in England to capture specimen, demographic, healthcare setting and risk factor details as part of the core and enhanced dataset [8].

Table 3. Antibiotic susceptibility of *Klebsiella* spp. bacteraemia (England and Northern Ireland): 2012-2016

	2012		2013		2014		2015		2016	
Antimicrobial agent	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***
Gentamicin	5,590	6%	5,488	7%	5,720	6%	6,606	7%	7,628	8%
Ciprofloxacin	5,180	8%	5,074	9%	5,251	9%	6,178	9%	7,264	10%
Ceftazidime	4,374	9%	4,126	10%	4,276	10%	5,226	10%	6,087	10%
Cefotaxime	3,217	10%	3,136	10%	3,257	10%	3,618	10%	4,159	10%
Meropenem	4,357	1%	4,478	1%	4,918	1%	5,993	1%	7,099	1%
Ertapenem	2,041	1%	2,450	1%	3,218	2%	4,955	1%	5,980	1%
Piperacillin/Tazobactam	5,291	13%	5,254	15%	5,359	16%	6,250	17%	7,096	17%
Total *Klebsiella* spp. bacteraemeia reports	**6,224**		**6,153**		**6,618**		**7,279**		**8,413**	

***defined as reduced- or non-susceptible

Table 4. Antibiotic susceptibility of *K. pneumoniae* bacteraemia (England and Northern Ireland): 2012-2016

	2012		2013		2014		2015		2016	
Antimicrobial agent	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***
Gentamicin	4,385	7%	4,313	8%	4,547	7%	5,258	9%	6,172	9%
Ciprofloxacin	4,069	10%	3,995	11%	4,197	11%	4,904	11%	5,878	11%
Ceftazidime	3,445	11%	3,283	12%	3,398	12%	4,158	11%	4,922	12%
Cefotaxime	2,563	11%	2,510	11%	2,594	12%	2,916	11%	3,386	12%
Meropenem	3,430	1%	3,525	1%	3,923	1%	4,766	1%	5,745	1%
Ertapenem	1,601	1%	1,941	1%	2,583	2%	3,955	1%	4,836	1%
Piperacillin/Tazobactam	4,151	13%	4,125	16%	4,269	17%	4,969	18%	5,738	18%
Total *K. pneumoniae* bacteraemia reports	**4,858**		**4,850**		**5,264**		**5,793**		**6,805**	

***defined as reduced or non-susceptible

Table 5. Antibiotic susceptibility of *K. oxytoca* bacteraemia (England and Northern Ireland): 2012-2016

	2012		2013		2014		2015		2016	
Antimicrobial agent	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***	**No. tested**	**% resistant***
Gentamicin	1,092	1%	1,063	1%	1,089	2%	1,276	1%	1,324	1%
Ciprofloxacin	1,008	2%	972	2%	975	2%	1,204	2%	1,256	2%
Ceftazidime	858	3%	771	3%	824	2%	1,014	2%	1,077	3%
Cefotaxime	604	5%	579	5%	611	3%	654	3%	714	3%
Meropenem	840	<1%	858	<1%	922	<1%	1,161	<1%	1,239	1%
Ertapenem	399	<1%	470	1%	600	<1%	955	1%	1,035	1%
Piperacillin/Tazobactam	1,026	11%	1,015	13%	1,014	14%	1,213	11%	1,251	15%
Total *K. oxytoca* bacteraemia reports	**1,229**		**1,171**		**1,261**		**1,405**		**1,455**	

***defined as reduced or non-susceptible

Multi-drug resistance testing was based on combinations of two or more different defined antibiotics (tables 6a and 6b). *K. pneumoniae* showed higher levels of multidrug-resistance for all tested antibiotic combinations compared to *K. oxytoca*.

Pair-wise antibiotic resistance testing showed that 13% of *K. pneumoniae* bacteraemia isolates were resistant to ciprofloxacin and third-generation cephalosporins. Only <0.7% of *K. oxytoca* isolates were resistant to gentamicin and ciprofloxacin or gentamicin and third-generation cephalosporins. Resistance to all four antibiotics (gentamicin, ciprofloxacin, third-generation cephalosporins, and meropenem) was uncommon (≤1%) among *K. pneumoniae* (30/3,162) and *K. oxytoca* (2/677) isolates.

Table 6a. Multi-drug antimicrobial testing and resistance summary for *K. pneumoniae* bacteraemia (England): 2016

Antimicrobial combinations	No. tested	% resistant†
Gentamicin and ciprofloxacin	6,105	6%
Gentamicin and third-generation cephalosporin*	5,187	7%
Ciprofloxacin and third-generation cephalosporin*	3,332	13%
Gentamicin, ciprofloxacin, third-generation cephalosporin*and meropenen	3,162	1%

* Any of cefotaxime, ceftazidime, cefpodoxime or ceftriaxone; †defined as reduced or non-susceptible

Table 6b. Multi-drug antimicrobial testing and resistance summary for *K. oxytoca* bacteraemia (England): 2016

Antimicrobial combinations	No. tested	% resistant
Gentamicin and ciprofloxacin	1,353	0.7%
Gentamicin and third-generation cephalosporin*	1,123	0.7%
Ciprofloxacin and third-generation cephalosporin*	715	2.4%
Gentamicin, ciprofloxacin, 3rd generation cephalosporin*and meropenen	677	<1

* Any of cefotaxime, ceftazidime, cefpodoxime or ceftriaxone; †defined as reduced or non-susceptible

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 [9].

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: hcai.amrdepartment@phe.gov.uk

References

1. Office for National Statistics (ONS) mid-year population estimates for England and Wales. Available at: http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2014/stb---mid-2014-uk-population-estimates.html
2. Northern Ireland Statistcs and Research Agency (NISRA) mid-year population esitmates for Northern Ireland. Available at: http://www.nisra.gov.uk/demography/default.asp17.htm
3. Public Health England Polymicrobial bacteraemia and fungaemia in England, Wales and Northern Ireland, 2016. *Health Protection Report*, 2017;11(12): infection report
4. Pitout JD, Laupland KB (2008). Extended-spectrum β-lactamase–producing *Enterobacteriaceae:* an emerging public health concern. *Lancet Infect Dis*. **8**:159–66. Available at: http://www.sciencedirect.com/science/article/pii/S1473309908700410
5. Nordmann P, Naas T, Poirel L (2011). Global spread of carbapenemase-producing Enterobacteriaceae. *Emerg Infect Dis*. **17**(10):1791–8. Available at: http://wwwnc.cdc.gov/eid/article/17/10/11-0655_article.htm
6. PHE (2013). Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae. London: Public Health England. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/329227/Acute_trust_toolkit_for_the_early_detection.pdf
7. PHE (2015). Toolkit managing carbapenemase-producing Enterobacteriaceae in non-acute and community settings. London: Public Health England. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/439801/CPE-Non-AcuteToolkit_CORE.pdf

8. PHE (2015). Electronic reporting system. Enhanced surveillance of of carbapenamase-producing Gram-negative bacteria. NHS Trust and microbiology laboratory user guide. London: Public Health England. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/425502/PHE_ERS_User_Guide_Trust-Micro-Final.pdf

9. Antimicrobial Resistance and Healthcare Associated Infections Reference Unit (AMRHAI): https://www.gov.uk/amrhai-reference-unit-reference-and-diagnostic-services.

PHE publications gateway number: 2017069.