



Volume 8 Number 19 Published on: 16 May 2014

Current News

Group A streptococcal infections: fifth update on seasonal activity, 2013/14

PHE, Department of Health and NHS England announce HPV vaccination programme schedule change

Public Health England heatwave plan 2014

Travel

Ebola virus disease in West Africa: an update

Infection Reports

Bacteraemia

Voluntary surveillance of *Klebsiella* spp. bacteraemia (EW&NI, 2009-2013)

Voluntary surveillance of *Escherichia coli* bacteraemia in (EW&NI, 2009-2013)

Group A streptococcal infections: fifth update on seasonal activity, 2013/14

PHE Surveillance of scarlet fever continues to show elevated levels of notified cases in England although substantially reduced compared to the first half of April 2014 [1]. GP consultations for pharyngitis/scarlet fever via the GP sentinel (syndromic) surveillance have similarly dropped [2]. Routine laboratory reports and isolate referrals of invasive group A streptococcal (iGAS) disease remain at usual seasonal levels.

Microbiological analysis of scarlet fever isolates submitted from across the country is underway as a means to identify possible reasons for the widespread upsurge seen this year.

Due to rare but potentially severe complications associated with GAS infections, continued vigilance is recommended.

Scarlet fever

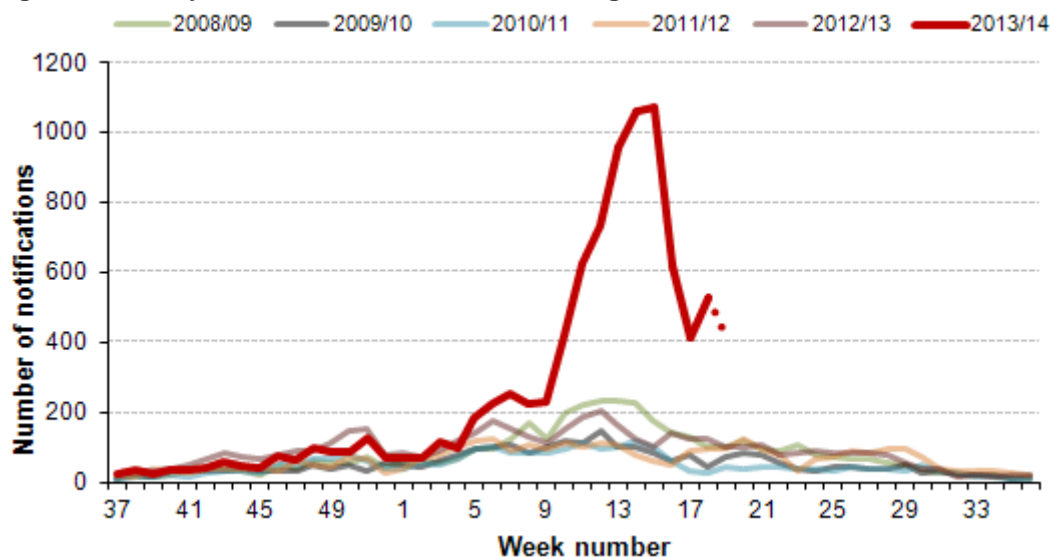
A total of 9228 notifications of scarlet fever have been made so far this season (week 37 2013 to week 19 2014) in England. Scarlet fever notifications peaked in weeks 14 and 15 of 2014 with just over 1000 notifications made each week (figure 1). Numbers of notifications fell between week 15 and 17 and have fluctuated since then, with 404 received to date in week 19.

The total number of cases already notified for 2014, 9030 for England and Wales (8322 for England), represents the highest number of cases reported in a single calendar year since 1980 when 11,118 notifications were made for England and Wales.

All areas in England reported higher scarlet fever levels for the last four weeks (week 16 to 19) than for the same period last year, from 2 to 12 times as high. The highest cumulative rates of notification so far this season were seen in the East Midlands (37.9), Avon, Gloucestershire and Wiltshire (30.1), Thames Valley (23.8), North East (22.6), and Cumbria and Lancashire (20.4)(figure 2).

Eighty seven per cent of notifications received this season have been in children aged less than 10 years, the median age remaining at 4 years (range <1y to 90y). The sex ratio of notifications remains similar with 49% being in males overall.

Figure 1. Weekly scarlet fever notifications in England, 2008/09 onwards*



* Dashed line indicates that numbers may increase as further notifications expected.

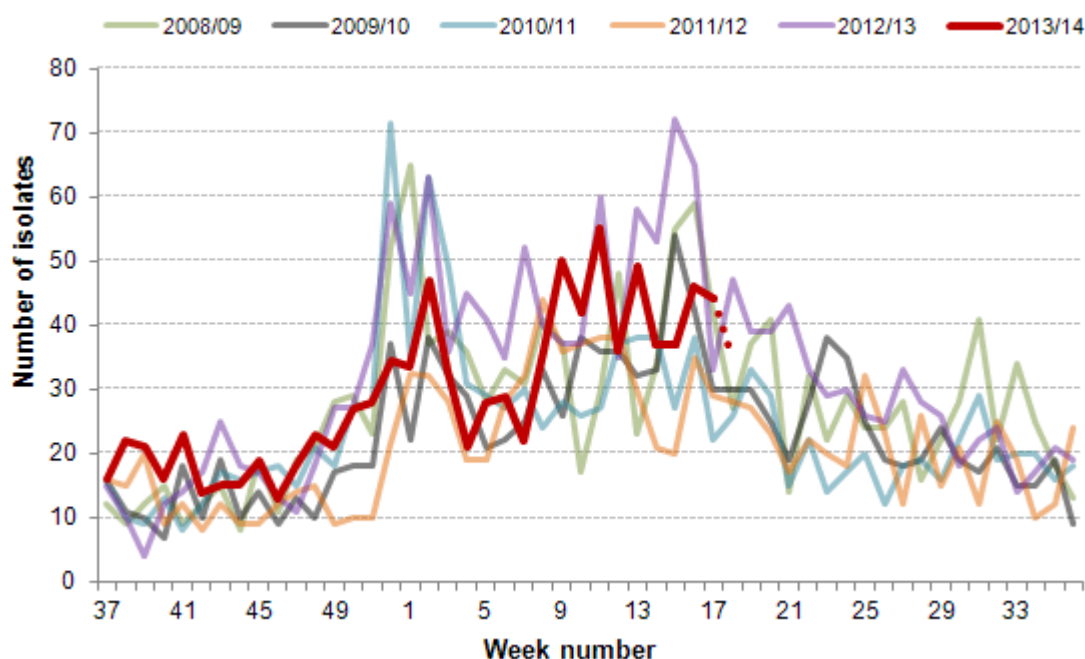
Invasive Group A Streptococcus

The number of iGAS isolate referrals, defined as isolation of GAS from a normally sterile site, to the Respiratory and Vaccine Preventable Bacteria Reference Unit at Colindale PHE from laboratories in England, Wales and Northern Ireland continues to remain within normal levels this season, with 1006 isolates referred for specimens taken between week 37 of 2013 to week 19 of 2014 (figure 3). This compares to a range of 775 to 1217 for the same period in the previous 5 years.

Analysis of iGAS *emm* strain diversity remains similar to what is normally seen with *emm1* and *emm3* the most common types identified between January and April 2014, with *emm3* marginally dominant in April accounting for 26% of strains typed.

No changes have been identified in iGAS isolate antimicrobial susceptibility patterns from routine laboratory reporting this year (weeks 1-19), with 6% non-susceptible to erythromycin, 8% tetracycline and 4% clindamycin, similar to previous years [3]. There have been no reports of penicillin resistance in iGAS isolates in England to date.

Figure 2. Weekly count of sterile site GAS isolates referred to the national reference laboratory, England, 2008/09 onwards*



* Dashed line indicates that numbers may increase as further isolates expected.

Whilst the continuation of the drop in scarlet fever incidence bodes well for a sustained decrease, the levels of incidence still remain strongly elevated compared to recent years, with little change over the past three weeks. As such, continued close monitoring and rapid and decisive response to potential outbreaks remains essential. Clinicians, microbiologists and HPTs should continue to be mindful of potential increases in invasive disease and maintain a high index of suspicion in relevant patients as early recognition and prompt initiation of specific and supportive therapy for patients with iGAS infection can be life-saving. Invasive disease isolates and those from suspected clusters or outbreaks should be submitted to the Respiratory and Vaccine Preventable Bacteria Reference Unit at Public Health England, 61 Colindale Avenue, London NW9 5HT.

Relevant guidelines/FAQs are available on the PHE health protection website, as follows:

- ▶ Guidelines on infection control in schools and other childcare settings, including recommended exclusion periods for scarlet fever and new guidelines on management of scarlet fever outbreaks: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/SchoolsGuidanceOnInfectionControl/>
- ▶ FAQs on scarlet fever at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ScarletFever/>
- ▶ Guidelines for the management of close community contacts of invasive GAS cases and prevention and control of GAS transmission in acute healthcare and maternity settings at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/StreptococcalInfections/Guidelines>.

References

1. PHE. Group A streptococcal infections: fourth update on seasonal activity, 2013/14. *HPR* 8(17): news.
2. PHE. GP In Hours Syndromic Surveillance System Weekly Bulletin 2014 week 18. PHE health protection website: [Syndromic Systems and Bulletin Archive](#).
3. PHE. [Voluntary surveillance of pyogenic and non-pyogenic streptococcal bacteraemia in England, Wales and Northern Ireland: 2012](#).

PHE, Department of Health and NHS England announce HPV vaccination programme schedule change

A tri-partite letter from Public Health England, Department of Health and NHS England announced earlier this week the forthcoming changes to the human papillomavirus (HPV) vaccine programme.

Following a recommendation from the Joint Committee on Vaccination and Immunisation earlier this year, the schedule will change from three to two doses from September 2014. The HPV vaccine is currently routinely offered to girls aged 12 to 13 in school year 8. Recent research shows that antibody response to the two dose schedule in adolescent girls is equivalent to the response that correlated with protection against persistent infection and precancerous lesions in the initial vaccine trials.

Since the routine vaccination programme was introduced in 2008/09, uptake has been consistently high – with 86% of 12-13 year old girls completing the course in 2012/13. Recent data indicate that the HPV vaccination programme has successfully reduced vaccine-type HPV infections in sexually active young women in England [1]. It is hoped the new dosage schedule will build upon this success.

Unlike the current schedule, the two doses of the new schedule must be given at least six months and not more than 24 months apart. The [complete letter](#) should be consulted for detailed guidance on the recommended gaps between the two doses.

Importantly, girls who have received two HPV vaccine doses under the 2013-14 programme should still receive their third dose, to complete their course. An updated Q & A for health professionals and revised information leaflet will be available from mid-June.

Related information for health professionals and immunisation practitioners is available at: <https://www.gov.uk/government/collections/immunisation>.

References

1. Mesher D, Soldan K, Howell-Jones R, Panwar K, Manyenga P, Jit M, *et al* (2013). Reduction in HPV 16/18 prevalence in sexually active young women following the introduction of HPV immunisation in England. *Vaccine* **32**(1): 26-32.

Public Health England heatwave plan 2014

The Heatwave Plan for England has been released for operation. Its objective is to protect the population from heat-related harm to health, by raising awareness of the negative health effects of severe heat and enabling services and the public to prepare and respond appropriately. It is an important component of long term and emergency planning which will become increasingly relevant in adapting to the impacts of climate change [1].

Information newly released comprises:

- ▶ the Heatwave Plan for England 2014;
- ▶ Making the Case, a companion document giving further information on a range of topics related to the Heatwave Plan; and
- ▶ three information pamphlets containing action cards based on the plan for easy use by organisations, staff and the public.

The plan sets out a series of clear actions to minimise the effects of severe heat on health, to be taken by:

- ▶ the NHS, social care and other public agencies;
- ▶ professionals working with vulnerable people; and
- ▶ individuals and local communities.

The Plan continues to be underpinned by the Heat-Health Watch service. The Met Office will issue Heatwave Alerts from 1 June 2014 to 15 September 2014.

Following consultation with stakeholders, no significant or immediate changes were considered essential this year. Therefore, the only changes to content have been the removal of specific dates relevant only to 2013.

The plan has been jointly agreed between Public Health England, the Department of Health, NHS England, the Local Government Association and other stakeholders. It continues to be underpinned by the Heat-Health Watch service, developed with the Met Office to alert key stakeholders to the likelihood of severe hot weather in different parts of the country, so they can take appropriate action.

Reference

Public Health England (2014) "[Heatwave plan for England - protecting health and reducing harm from sever heat and heatwaves](#)" 13 May.

Travel

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Ebola virus disease in West Africa: an update

The outbreak of Ebola virus disease in West Africa continues, although it appears to be slowing. However, a period of 42 days (two incubation periods) is required without detection of new cases before the outbreak can be declared over. The most recent cases were isolated on 11 May.

By 12 May, Guinea had reported 248 clinically compatible cases including 171 deaths [1]. One hundred and thirty-eight cases have been confirmed by PCR and serological testing is planned for clinical cases who tested negative by PCR, thus final case numbers may yet increase. Cases have occurred in several regions across the country [2].

Ebola has also been confirmed in neighbouring Liberia. Initial cases had been exposed in Guinea, with secondary cases occurring from local transmission. By 10 May, there had been 12 clinically compatible cases, of which six have been confirmed.

In Sierra Leone initial suspected cases were not confirmed, and suspected cases in other nearby countries have thus far also proven negative.

The risk for tourists, visitors or UK expatriates remains very low. Anyone returning from affected areas who has a sudden onset of symptoms such as fever, headache, sore throat and general malaise within three weeks of their return should seek rapid medical attention and mention their recent travel.

In the event of a symptomatic person with a relevant travel history presenting to health care, the PHE Imported Fever Service (0844 7788990) should be contacted by infectious disease clinicians or microbiologists in order to discuss testing.

References

1. WHO update 15 May 2014: http://www.who.int/csr/don/2014_05_15_ebola/en/.
2. Further information and maps
http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1254510365073.



Infection report

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Bacteraemia

Voluntary surveillance of *Klebsiella* spp. bacteraemia in England, Wales and Northern Ireland: 2009-2013

These analyses are based on data relating to diagnoses of *Klebsiella* spp. bloodstream infections during 2009 – 2013 in England, Wales and Northern Ireland (E,W & NI) that were extracted from Public Health England's (PHE) voluntary surveillance database (LabBase2) on 10 April 2014. The data presented here differ in some instances from those in earlier publications due to the inclusion of late reports. Analyses by main species are also included in this report.

As the mid-year resident population estimates for 2013 were not available at the time of producing this report, rates of bacteraemia were calculated using 2012 mid-year resident population estimates based on the 2011 census for England, Wales, and Northern Ireland [1,2]. Geographical analyses were based on the residential postcode of the patient if known (otherwise the GP postcode was used if known or failing that the postcode of the laboratory was used) 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

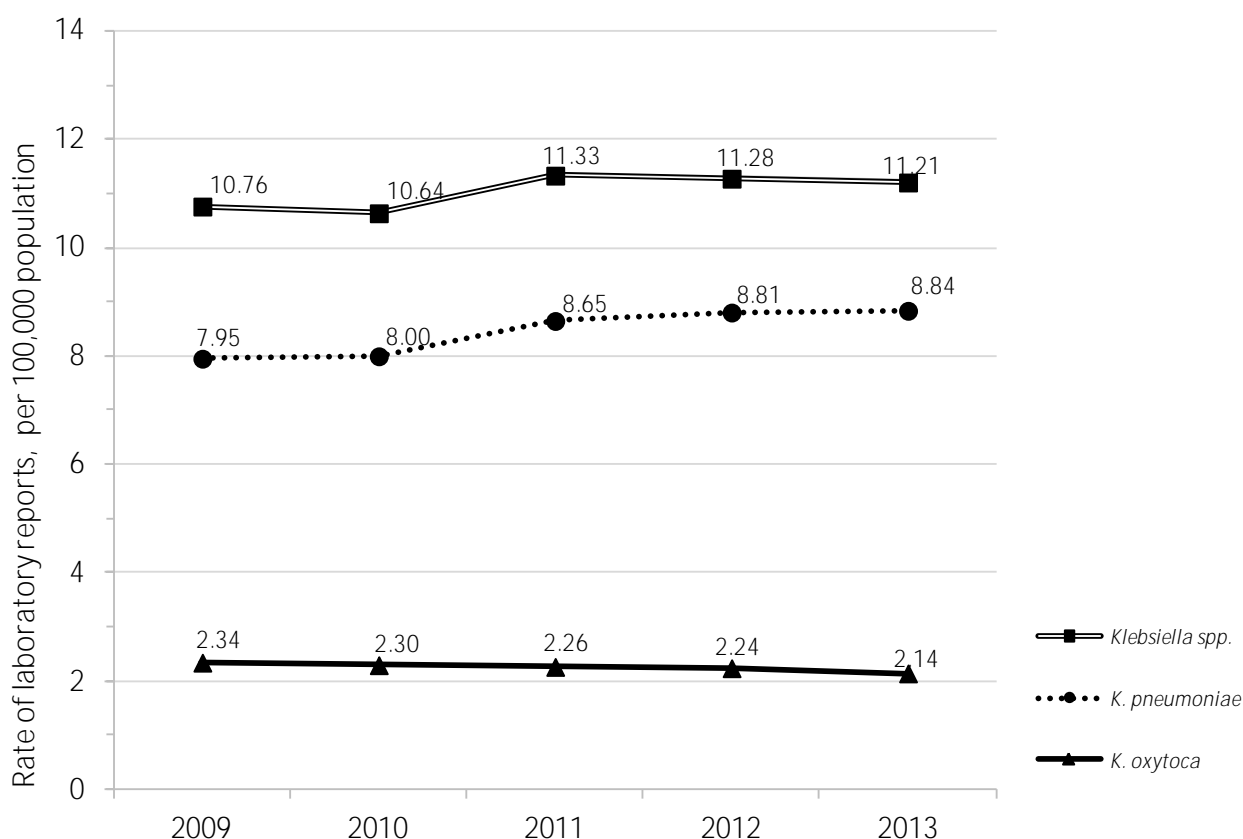
- Between 2012 and 2013 the total number of reports of *Klebsiella* spp. bacteraemia in E,W & NI decreased marginally by 0.6% (from 6,585 to 6,544 episodes respectively).
- The rate of reported *Klebsiella* spp. bacteraemias per 100,000 resident population in E,W & NI was initially stable in 2009 (10.76/100,000) and in 2010 (10.64/100,000). The rate increased by 7% between 2010 and 2011 (11.33/100,000) and remained at this level in 2012 and 2013.
- The rate of bacteraemia due to *K. pneumoniae* was also initially stable in 2009 and 2010 but increased by 8% from 8.00/100,000 in 2010 to 8.65/100,000 in 2011 and remained at this level for the remaining period.
- In 2013, 98% of bacteraemia reports of *Klebsiella* spp. were identified to species level. This represented a continuing improvement in species identification compared with previous years.
- The rate of *Klebsiella* spp. was higher among infants (<1 year) and the elderly than in other age groups. The rate was higher among males and particularly among patients aged ≥75 years.
- At country level, N. Ireland had the highest rate of *Klebsiella* spp. bacteraemia (11.95/100,000) followed by England (11.23/100,000) with Wales having the lowest rate (10.34/100,000).
- Within England, Cheshire and Merseyside had the highest rate of *Klebsiella* spp. bacteraemia at 14.98/100,000 followed by Greater Manchester (14.73/100,000). London had the third highest rate at 13.11/100,000. The lowest rate was in Thames Valley (6.75/100,000). This may reflect variation in reporting or case-mix or a combination of both.
- Antimicrobial susceptibility trends from 2009 to 2013 were examined for five classes of antibiotics with results for *Klebsiella* spp. (all species), *K. pneumoniae* and *K. oxytoca*. In general, an increase in resistance was observed across most antibiotic classes except for the fluoroquinolone (ciprofloxacin) where strong evidence of a decrease was observed over the five year period among *K. oxytoca* isolates (from 3% in 2009 to 2% in 2013).
- Of two third-generation cephalosporins examined (cefotaxime and ceftazidime), a significant increase in resistance to cefotaxime was observed (from 8% in 2009 to 10% in 2013). No evidence of change in resistance was found in relation to gentamicin.
- No evidence of change in resistance was found in relation to gentamicin.
- Resistance to piperacillin/tazobactam increased significantly for *Klebsiella* spp. (from 10% in 2009 to 15% in 2013) which may reflect a reduction in the MIC breakpoint from 16 to 8 mg/L for this agent.
- Resistance to the carbapenems remained uncommon, but nonetheless increased significantly over the five-year period with 14 of 4,420 (0.3%) isolates reported resistant in 2009 compared to 42 of 4,941 (0.9%) isolates in 2013.

Trends in the number of reports and rates

Between 2012 and 2013, the total number of bacteraemia reports of *Klebsiella* spp. in E,W & NI decreased by 0.6% (from 6,585 to 6,544 respectively) (table 1). In the context of the five year-period under study, the total number of *Klebsiella* spp. bacteraemia reports increased by 7% from 6,138 in 2009 to 6,572 in 2011 and continued to exceed 6,500 for the remaining period. The increase in total *Klebsiella* spp. from 2009 to 2011 was largely accounted for by the increase in *K. pneumoniae* (by 11%) over the corresponding time period. The number of *K. pneumoniae* reports exceeded 5,000 in 2011 and continued at this level into 2012 and 2013.

Figure 1 shows trends in the incidence of bacteraemia for all *Klebsiella* species and by two main named species in E,W & NI between 2009 and 2013. The rate of *Klebsiella* spp. bacteraemia was initially stable in 2009 and 2010 at (10.76/100,000 and 10.64/100,000 respectively). But this increased by 7% from 10.64/100,000 in 2010 to 11.33/100,000 in 2011 and remained at this level for the rest of study period. The rate of bacteraemia due to *K. pneumoniae* was also initially stable in 2009 and 2010 but increased by 8% from 8.00/100,000 in 2010 to 8.65/100,000 in 2011 and remained at this level for the remaining period. The rate for *K. oxytoca* was stable throughout the study period.

Figure 1: Rate of laboratory bacteraemia reports of *Klebsiella* spp. (all species), *K. pneumoniae* and *K. oxytoca* in England, Wales and Northern Ireland per 100,000 resident population, 2009-2013*



* Data extracted 10 April 2014

Table 1 gives a breakdown of the number of reports by species between 2009 and 2013. In 2013, the majority of isolates from blood were identified to species level (98%). The level of species identification in 2013 represents a slight, but continuing improvement over previous years (96% in 2009). It should be noted that the analysis for 'other named species' in Table 1 includes data for the option '*Klebsiella* other named' available in LabBase2 if selected by the reporting laboratory.

In 2013, the predominant *Klebsiella* species causing bacteraemia was *K. pneumoniae* (79%) followed by *K. oxytoca* (19%). Inspection of the other named species revealed that all were reported under the option '*Klebsiella* other named' with no further detail – this group consisted of very small number of reports over the five-year period.

Table 1. Reports of bacteraemia due to *Klebsiella* spp. (England, Wales and Northern Ireland): 2009 to 2013*

	2009		2010		2011		2012		2013	
	No.	%	No.	%	No.	%	No.	%	No.	%
<i>Klebsiella</i> spp.	6,138	100%	6,117	100%	6,572	100%	6,585	100%	6,544	100%
<i>Klebsiella pneumoniae</i>	4,536	74%	4,599	75%	5,016	76%	5,142	78%	5,161	79%
<i>Klebsiella oxytoca</i>	1,336	22%	1,320	22%	1,313	20%	1,308	20%	1,252	19%
<i>Klebsiella</i> , other named species	3	0%	0	0%	9	0%	10	0%	13	0%
<i>Klebsiella</i> , species not recorded	263	4.3%	198	3.2%	234	3.6%	125	1.9%	118	1.8%

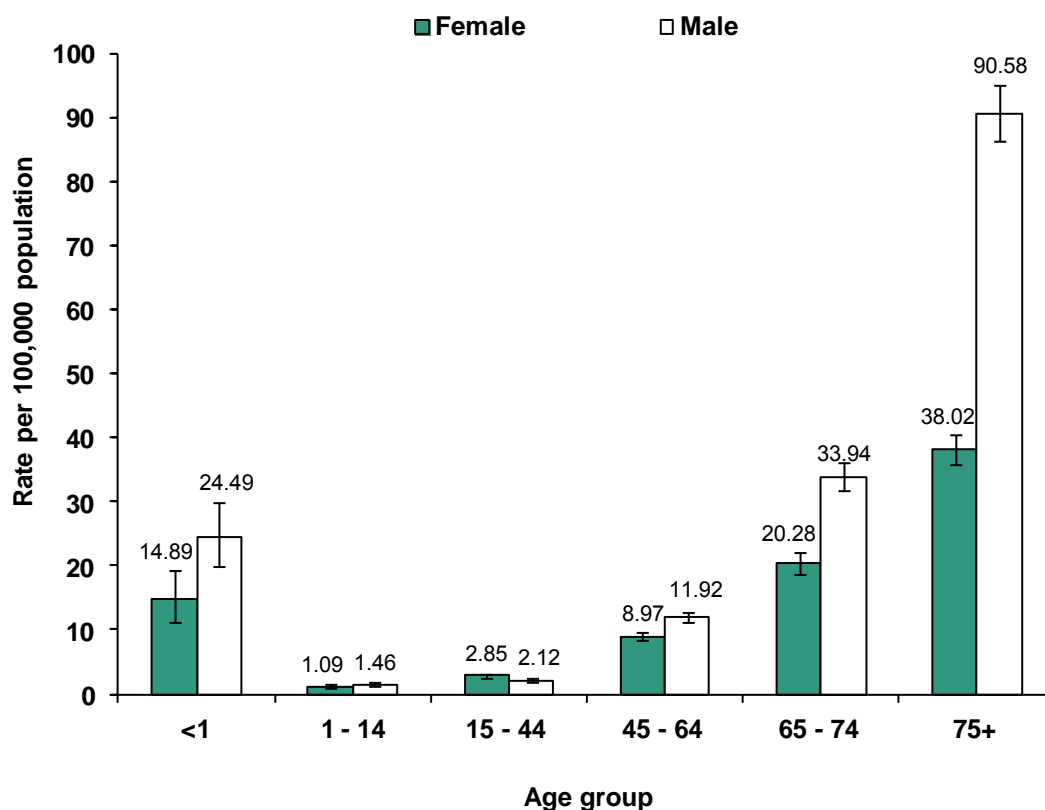
* Data extracted 10 April 2014

Age and sex distribution

Figures 2 to 4 show the age and sex-specific rate of bacteraemia reports in E,W & NI in 2013 per 100,000 resident population for *Klebsiella* spp. and three main *Klebsiella* species. In general, the rate was higher in the infant group (under one year) and in the elderly groups although the rate in the infant group was based on a relatively smaller sample (150 *Klebsiella* spp. reports, of which 101 concerned *K. pneumoniae* and 47 *K. oxytoca*). Across all analyses, the highest rate was among patients aged 75 years or more. The rate of bacteraemia was higher among male patients across all age groups except among those aged 15-44 years where it was higher among female patients.

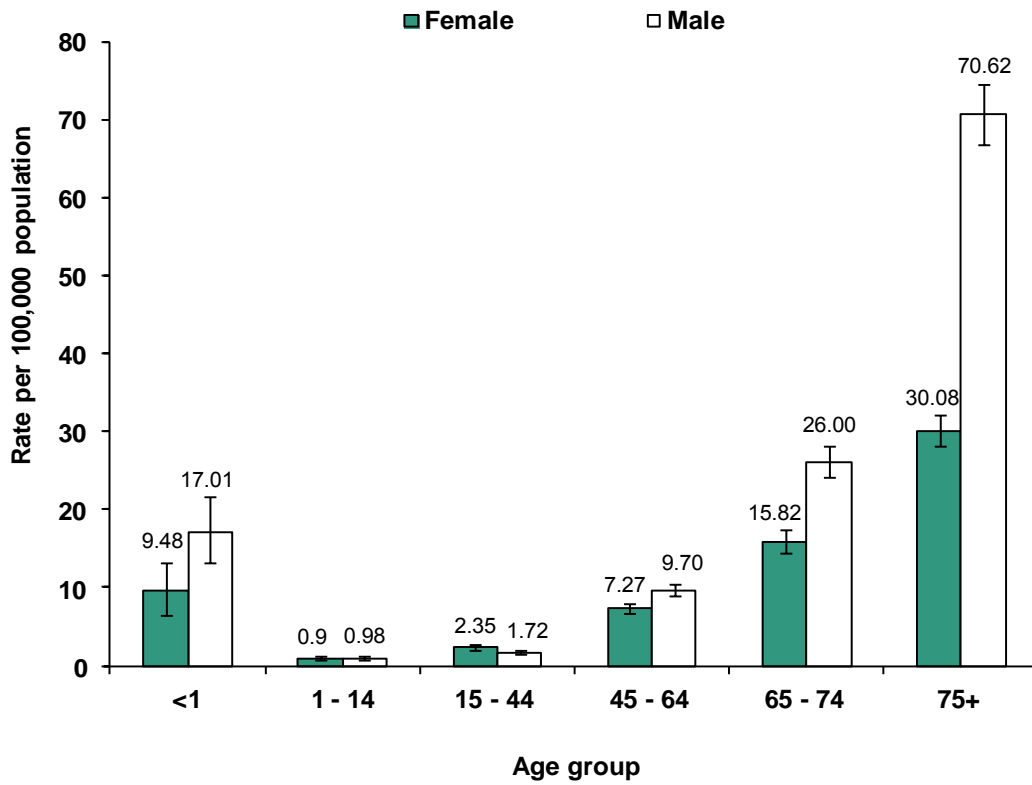
Among the oldest age group (75 years or more), the rate was found to be more than twice as high in males than females. In this age group, the male to female incidence rate ratio was 2.38; 2.35 and 2.44 for *Klebsiella* spp.(all species), *K. pneumoniae* and *K. oxytoca* respectively. Among patients aged 15-44 years the male to female rate ratio was 0.74 for *Klebsiella* spp. (all species); 0.73 for *K. pneumoniae* and 0.72 for *K. oxytoca*.

Figure 2. Age and sex-specific rates of bacteraemia reports of *Klebsiella* spp. per 100,000 resident population (England, Wales and Northern Ireland): 2013*



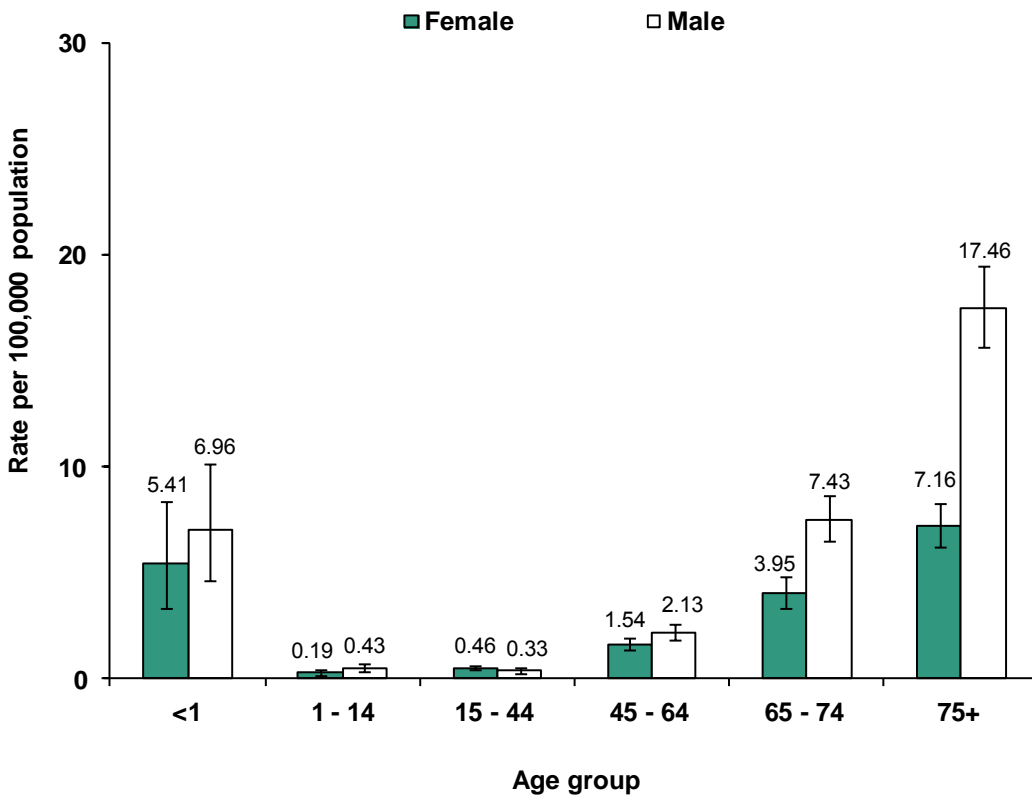
* Data extracted 10 April 2014

Figure 3. Age and sex-specific rates of bacteraemia reports of *K. pneumoniae* per 100,000 resident population (England, Wales and Northern Ireland): 2013*



* Data extracted 10 April 2014

Figure 4. Age and sex-specific rates of bacteraemia reports of *K. oxytoca* per resident 100,000 population (England, Wales and Northern Ireland): 2013*



* Data extracted 10 April 2014

Geographic distribution

Figure 5 shows the reporting rate of bacteraemia based on *Klebsiella* spp. (all reports) reports per 100,000 resident population at country level and at English regional level (Public Health England Centres). This analysis is not corrected for variation in reporting between geographical areas.

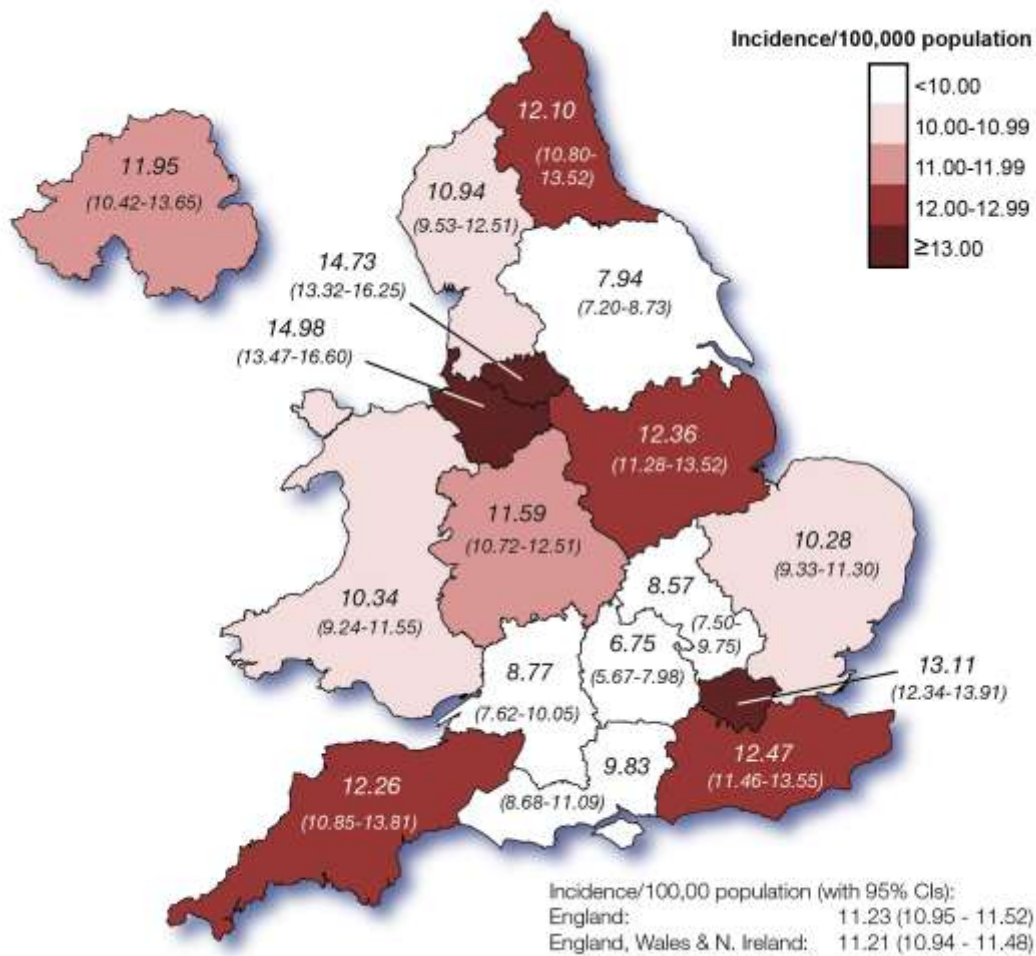
The reported bacteraemia rate for E,W, & NI was 11.21/100,000. Between countries, Northern Ireland had the highest rate at 11.95/100,000 followed by England at 11.23/100,000 then Wales at 10.34/100,000.

In England, variation in the rate between the 15 Public Health Centres (PHECs) was observed. Cheshire and Merseyside was identified as having the highest rate at 14.98/100,000 population, followed by Greater Manchester at 14.73/100,000. Both these PHECs are located in the North West, a region observed to have the highest *Klebsiella* spp bacteraemia rate in previous years [3][4][5].

London was found to have the next highest rate in 2013 at 13.11/100,000. The lowest rate was in Thames Valley at 6.75/100,000.

The geographical variation may be explained by differences in completeness of reporting between PHECs. Other factors include case-mix, accounted for by variation in the distribution of specialist care units. Further work will be undertaken to assess completeness of reporting in order to interpret these variations more robustly in future reports.

Figure 5: Geographic distribution of the rate of bacteraemia reports of *Klebsiella* spp. per 100,000 resident population (England, Wales and Northern Ireland): 2013*



* Data extracted 10 April 2014

Antimicrobial susceptibility data

Tables 2 to 4 present antibiotic susceptibility data for *Klebsiella* spp. blood culture isolates (all species combined), *K. pneumoniae* and *K. oxytoca*. This analysis examines five classes of antibiotics: third-generation cephalosporins (cefotaxime or ceftazidime), carbapenems (imipenem/meropenem), a fluoroquinolone (ciprofloxacin), a penicillin/beta-lactamase inhibitor combination (piperacillin/tazobactam) and an aminoglycoside (gentamicin).

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. For the analysis based on *Klebsiella* spp. isolates (all species), resistance to cefotaxime increased significantly albeit slowly from 8% in 2009 to 10% in 2013 ($p < 0.05$). By comparison, there was no evidence that the increase in resistance to ceftazidime was significant ($p = 0.240$). A similar result was found for *K. pneumoniae*, where a significant increase was observed for cefotaxime from 9% in '09 to 12% in '13 ($p < 0.05$), but with no evidence of change for ceftazidime ($p = 0.487$). The analysis for *K. oxytoca*, showed no evidence of change in resistance to either cefotaxime or ceftazidime ($p = 0.815$ and $p = 0.817$, respectively). The different susceptibility trends observed for cefotaxime and ceftazidime among *Klebsiella* spp. isolates is worrying given that the same ESBL enzymes are expected to affect both cephalosporin compounds in the same way. The different results are more likely to be due to artefact (e.g. differences between laboratories in testing one agent over the other or susceptibility testing errors) rather than a genuine increase in specific ESBLs among *Klebsiella* spp. that predominantly attack cefotaxime but are weak against ceftazidime.

Table 2: Antibiotic susceptibility data on all *Klebsiella* spp. bacteraemia isolates, England, Wales and Northern Ireland: 2009-2013

	2009		2010		2011		2012		2013	
	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant
Piperacillin/ Tazobactam	4,482	10%	4,635	11%	5,217	12%	5,430	13%	5,427	15%
Imipenem/ Meropenem**†	4,420	<1%	4,407	<1%	4,851	<1%	4,975	<1%	4,941	<1%
Cefotaxime	3,130	8%	3,061	9%	3,393	9%	3,487	10%	3,373	10%
Ceftazidime	4,007	9%	4,195	9%	4,618	9%	4,651	10%	4,420	10%
Ciprofloxacin	4,741	9%	4,897	8%	5,374	8%	5,526	8%	5,440	9%
Gentamicin	5,195	6%	5,276	6%	5,859	6%	5,934	6%	5,859	7%
Total <i>Klebsiella</i> spp. reports	6,138		6,117		6,572		6,585		6,544	

*0.3% in 2009; 0.4% in 2010; 0.8% in 2011; 0.7% in 2012; 0.9% in 2013

† Ertapenem not included due to the small number of test results reported

Table 3: Antibiotic susceptibility data on *K pneumoniae* bacteraemia isolates, England, Wales and Northern

	2009		2010		2011		2012		2013	
	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant
Piperacillin/ Tazobactam	3,319	10%	3,433	10%	3,941	13%	4,223	13%	4,232	16%
Imipenem/ Meropenem**†	3,237	<1%	3,292	<1%	3,675	1.0%	3,849	<1%	3,857	<1%
Cefotaxime	2,341	9%	2,323	10%	2,617	10%	2,730	11%	2,669	12%
Ceftazidime	2,916	10%	3,126	11%	3,514	11%	3,621	11%	3,484	12%
Ciprofloxacin	3,461	10%	3,641	10%	4,064	10%	4,285	10%	4,248	11%
Gentamicin	3,832	6%	3,944	7%	4,442	7%	4,599	7%	4,569	8%
Total <i>K. pneumoniae</i> reports	4,536		4,599		5,016		5,142		5,161	

*0.4% in 2009; 0.5% in 2010; 0.8% in 2012; 0.9% in 2013

† Ertapenem not included due to the small number of test results reported

Table 4: Antibiotic susceptibility data on *K oxytoca* bacteraemia isolates, England, Wales and Northern Ireland: 2009-2013

	2009		2010		2011		2012		2013	
	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant	No. tested	% resistant
Piperacillin/ Tazobactam	1,009	12%	1,015	12%	1,029	12%	1,046	11%	1,038	13%
Imipenem/ Meropenem*†	950	<1%	932	<1%	953	<1%	984	<1%	951	<1%
Cefotaxime	650	6%	638	4%	651	4%	661	5%	625	5%
Ceftazidime	872	4%	887	2%	881	3%	910	3%	826	4%
Ciprofloxacin	1,039	3%	1,056	2%	1,058	2%	1,080	2%	1,038	2%
Gentamicin	1,106	2%	1,123	2%	1,156	1%	1,161	2%	1,129	1%
Total <i>K. oxytoca</i> reports	1,336		1,320		1,313		1,308		1,252	

*0.1% in 2009; 0.0% in 2010 due to 0 cases; 0.1% in 2011; 0.4% in 2012; 0.5% in 2013

† Ertapenem not included due to the small number of test results reported

Source: PHE, 2014

The proportion of isolates reported resistant to piperacillin/tazobactam increased significantly over the five-year period based on all *Klebsiella* isolates (from 10% in 2009 to 15% in 2013) ($p < 0.001$). The analysis for *K. pneumoniae* also showed a significant increase from 10% in 2009 to 16% in 2013 ($p < 0.001$). These results may reflect the revised MIC breakpoint from 16 to 8 mg/L for this agent with regards to Enterobacteriaceae. However there was no evidence of change in resistance in relation to this antibiotic among *K. oxytoca* isolates ($p = 0.929$).

In terms of ciprofloxacin, no trend in resistance was found between 2009 and 2013 for either *Klebsiella* spp. (all species) or for *K. pneumoniae* ($p = 0.539$; $p = 0.366$, respectively). However, the analysis for *K. oxytoca* indicated that resistance to this antibiotic decreased year on year over the five-year period from 3% in 2009 to 2% in 2013 with strong evidence that this decreasing trend was significant ($p < 0.01$).

No evidence of change in resistance to gentamicin was found based on all *Klebsiella* spp. isolates ($p = 0.067$). At species level, no evidence of change was found for either *K. pneumoniae* ($p = 0.058$) or for *K. oxytoca* ($p = 0.225$).

Resistance to carbapenems was uncommon in the five-year period at less than 1% of isolates (except for *K. pneumoniae* where it reached 1%). However, despite the small underlying numbers, a slow but steady increase in the proportion of isolates resistant to this class of antibiotic was observed between 2009 and 2013. This increase was significant across the three analyses: $p < 0.001$ for *Klebsiella* spp. (all species); $p < 0.001$ for *K. pneumoniae* and $p = 0.025$ for *K. oxytoca*.

The increase in resistance to carbapenems based on *Klebsiella* spp. (all species) was first identified using data available up to 2011 where the year on year increase observed from 2009 to 2011 was found to be significant [4]. Resistance to carbapenems was observed prior to 2009 among isolates of all specimen types referred to PHE's national reference laboratory. Despite the small underlying numbers the increase among bacteraemia isolates also raised concerns given that this class of antibiotic is a powerful last-line treatment for serious infections. The trend in E,W & NI occurred in the context of the recent emergence of resistance to this antibiotic reported internationally [6][7]. In this report, the data for E,W & NI indicated a further but small increase in 2013 ($n = 42$). Further analysis of these resistant isolates showed that 51% (75/146) were reported by laboratories from London, Greater Manchester and Cheshire and Merseyside. The patient sex breakdown showed a higher proportion among males at 65% (78/120) compared to 35% among females (42/120). The additional breakdown by age showed that among females the 45-64 year age group was the most affected (38%; 16/42) whilst for males the oldest groups (65-74 years and ≥ 75 years) were the most affected (23%; 18/78 per group).

Despite the small overall number of carbapenem-resistant isolates involved, the trend in carbapenem-resistant *Klebsiella* spp. warrants close vigilance. Although carbapenem resistance in *Klebsiella* spp. may be mediated by ESBL production combined with impermeability (porin loss), a growing number of isolates referred to PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit produce carbapenemases belonging to the KPC, OXA-48-like, NDM, VIM and IMP families. *Klebsiella* spp. is the commonest hosts of these enzymes. However approximately only 10% of confirmed carbapenemase producers are isolated from bacteraemias.

In recognition of the importance of carbapenemase-producing Enterobacteriaceae (CPE), PHE issued a Toolkit in December 2013 on the identification and management of affected patients in acute healthcare settings [8]. 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 is to follow.

For advice on treatment of antibiotic resistant infections due to these organisms or for reference services including species identification and confirmation of sensitivity testing results, laboratories should contact PHE's AMRHAI Reference Unit in London [9].

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Infection report

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Bacteraemia

Voluntary surveillance of *Escherichia coli* bacteraemia in England, Wales and Northern Ireland: 2009-2013

This report covers voluntary reports of bacteraemia caused by *Escherichia coli*, made to Public Health England (PHE) between 2009 and 2013 from participating laboratories in England, Wales and Northern Ireland. Only *E. coli* bacteraemia isolates identified by culture were included in the analysis. Data were extracted on 2nd April 2014 and are provisional as the number of reports for 2013 may increase due to late reporting.

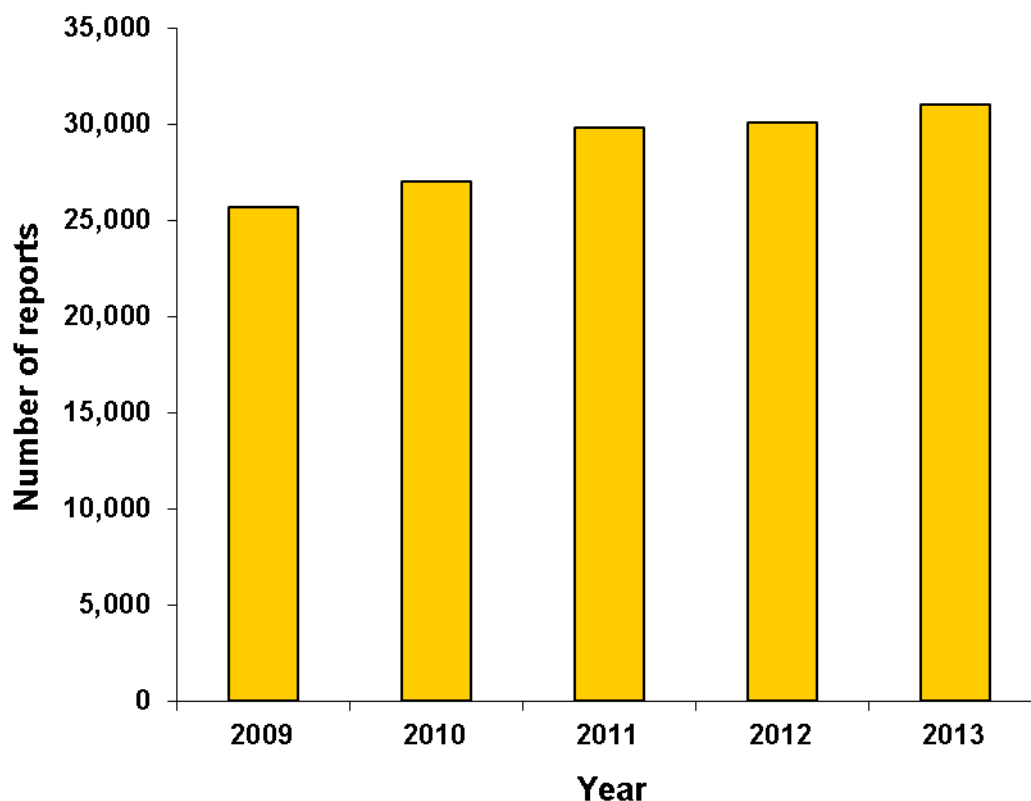
Key Points

- There have been year-on-year increases in the number of *E. coli* bacteraemia reports.
- In 2013 there were 31,023 reports for *E. coli*, which was a slight increase (3.0%), compared to 2012 (30,101) (Figure 1). In the same period, the total number of bacteraemia reports via LabBase2 increased by 2% from 96,469 in 2012 to 98,473 in 2013.
- By 2013 *E. coli* accounted for just under a third (31.5%) of all bacteraemia reports, compared with 27.2% in 2009.
- The rates per 100,000 population of *E. coli* bacteraemia were highest in patients aged 65 years and over and in those under 1 year of age (Figure 2). In both of these groups the rates were generally higher for males. Among those aged 1-14 and 15-44 years, the rates were higher among females.
- The overall incidence rate of infection of *E. coli* bacteraemia in 2013 was 53.1 per 100,000 population (Figure 3).
- There was very little change in the rates of non-susceptibility to 3rd generation cephalosporins and gentamicin from 2009-2013 (Table 2).
- The percentages of isolates non-susceptible to ciprofloxacin and gentamicin in 2013 remain very similar to 2012, at 18% (19% in 2012) and 10% (10% in 2012). Non-susceptibility to ciprofloxacin decreased early in the 2009-13 period, but the decline has since levelled off.
- The percentage of isolates testing non-susceptible to the 3rd generation cephalosporins ceftazidime and cefotaxime remains stable at 10-11% in 2012 and 2013.
- Most isolates tested against either imipenem or meropenem were reported susceptible. A small but growing number of *E. coli* resistant to carbapenems are referred to PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit, but are largely from samples other than blood.

Trends in reports

E. coli has been the most common cause of bacteraemia in England, Wales and Northern Ireland, for most years since 1990, apart from 2000 and 2003 when reports of MRSA bacteraemia peaked [1]. Since 1990 the number of *E. coli* bacteraemia reports has continued to increase. In 2013 there were 31,023 voluntary reports concerning *E. coli* bacteraemia to PHE (Figure 1). This is a 3% increase compared with 2012 (30,101 reports). In comparison, the total numbers of all bacteraemia reports irrespective of pathogen have also increased slightly by 0.3% over this time period. *E. coli* reports for 2013 are provisional as of 2nd April 2014 and the number of reported cases may increase slightly as late reports are received.

Figure 1. *E. coli* bacteraemia reports, England, Wales and Northern Ireland: 2009 to 2013*



* Data extracted 2 April 2014

Completeness of laboratory reports

The number of laboratories voluntarily reporting data for *E. coli* bacteraemia has decreased from 184 in 2009 to 163 in 2013 probably due to consolidation into fewer, larger units serving multiple hospitals. The percentage of laboratories reporting drug susceptibility data decreased from 98% in 2009 to 96% in 2013.

Table 1. Laboratories reporting *E. coli* bacteraemia, England, Wales and Northern Ireland: 2009-2013*

	2009	2010	2011	2012	2013
No of <i>E. coli</i> bacteraemia reports	25,662	27,045	29,851	30,101	31,023
Number of reporting laboratories	184	180	180	172	163
Laboratories reporting susceptibility data	98%	98%	98%	97%	96%

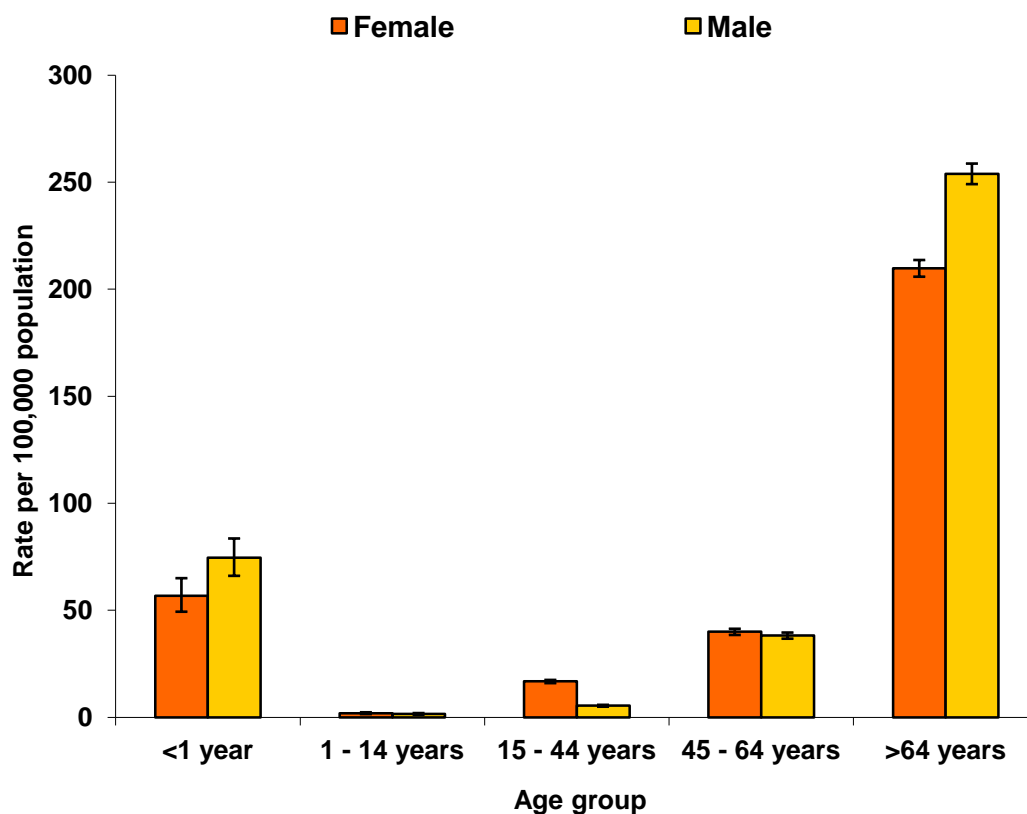
* Data extracted 2 April 2014

Age and sex distribution

Figure 2 shows the age and sex distribution for patients with *E. coli* bacteraemia reported in 2013 as rates per 100,000 population. The distribution between the sexes differs by age group; reports were more frequent for males than females in those aged under one year or aged 64 years and over; while the infection was more frequent among females in the 1-14 and 15-44 years age groups. The rates of bacteraemia for females and males were similar for those aged 45-64 years.

The rate for males aged less than 1 year has decreased from 79.8/100,000 in 2012 to 74.5/100,000 in 2013, whilst the rate for female infants increased slightly from 51.2/100,000 in 2012 to 56.8/100,000 in 2013. The rate of *E. coli* bacteraemia in females and males aged over 64 remained stable between 2012 and 2013.

Figure 2. *E. coli* bacteraemia reports in 2013, England, Wales and Northern Ireland by age and sex*



Data extracted 2 April 2014

Distribution by region

Figure 3 shows the reporting rate of bacteraemia based on the total of *E. coli* bacteraemia at country level and at English regional level (Public Health England Centres (PHECs)) in 2013. Geographical analyses were based on the residential location of the patient, derived from their postcode if known (otherwise the GP postcode was used if known, or failing that the postcode of the laboratory was used) with cases in England being assigned to the catchment area of one of the 15 local PHE centres (PHECs) formed from administrative local authority boundaries. Rates for 2013 were calculated using 2012 mid-year population estimates as mid-year population data for 2013 was not available at the time of publication.

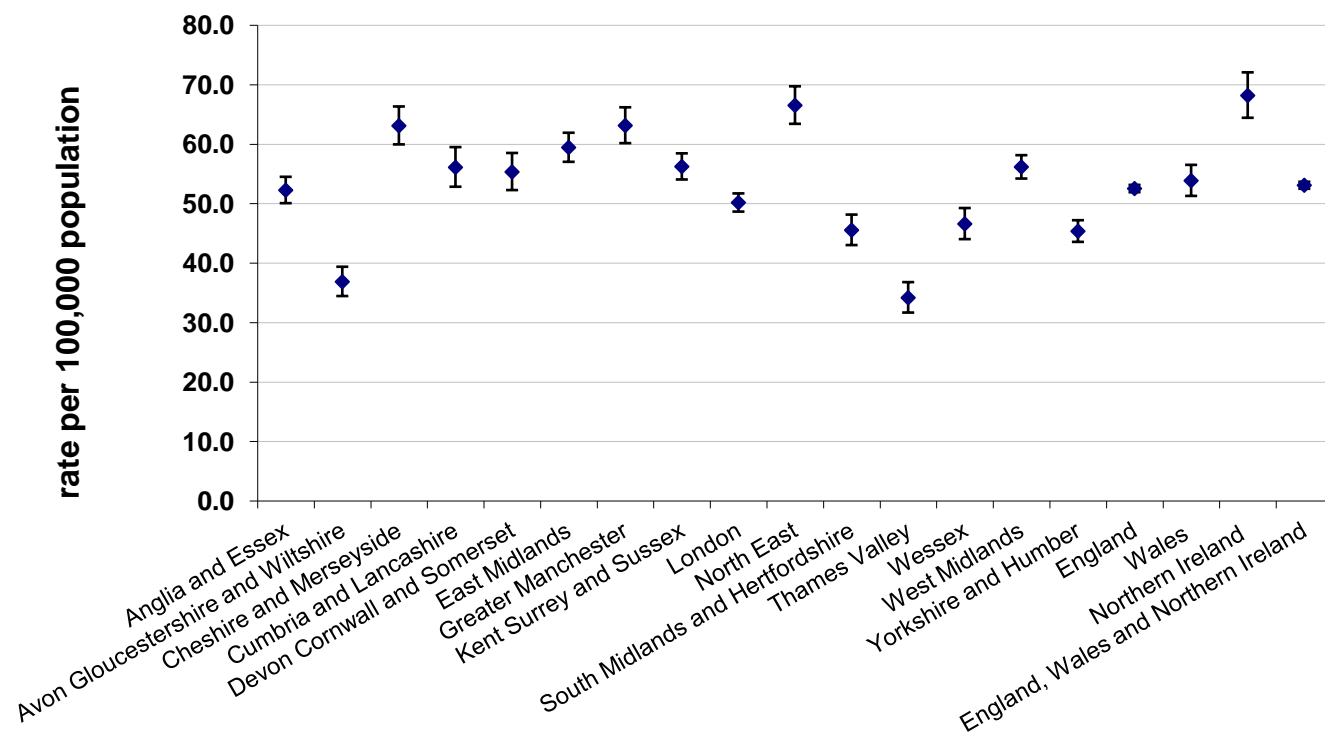
Figure 4 is a spatial representation of region-specific bacteraemia rates.

Based on voluntary reporting, the overall rate of *E. coli* bacteraemia in England, Wales and Northern Ireland was 53.1 per 100,000 population. Regions with high rates of infection include the North East (66.6/100,000), Greater Manchester and Cheshire and Merseyside (63.1/100,000). The country with the highest rate of infection was Northern Ireland (68.2 per 100,000). The region with the lowest incidence was Thames Valley (34.2/100,000).

England's rate increased from 45.2/100,000 in 2009 to 52.6/100,000 in 2013. For England as a whole, comparison of voluntary and mandatory surveillance showed that the voluntary system had 84% case ascertainment. The rates of infection for Wales and Northern Ireland increased from 44.0/100,000 and 55.6/100,000 in 2009 to 53.9/100,000 and 68.2/100,000 in 2013, respectively. The overall rate of *E. coli* bacteraemia for England, Wales and Northern Ireland has increased from 41.6/100,000 in 2009 to 53.1/100,000 in 2013.

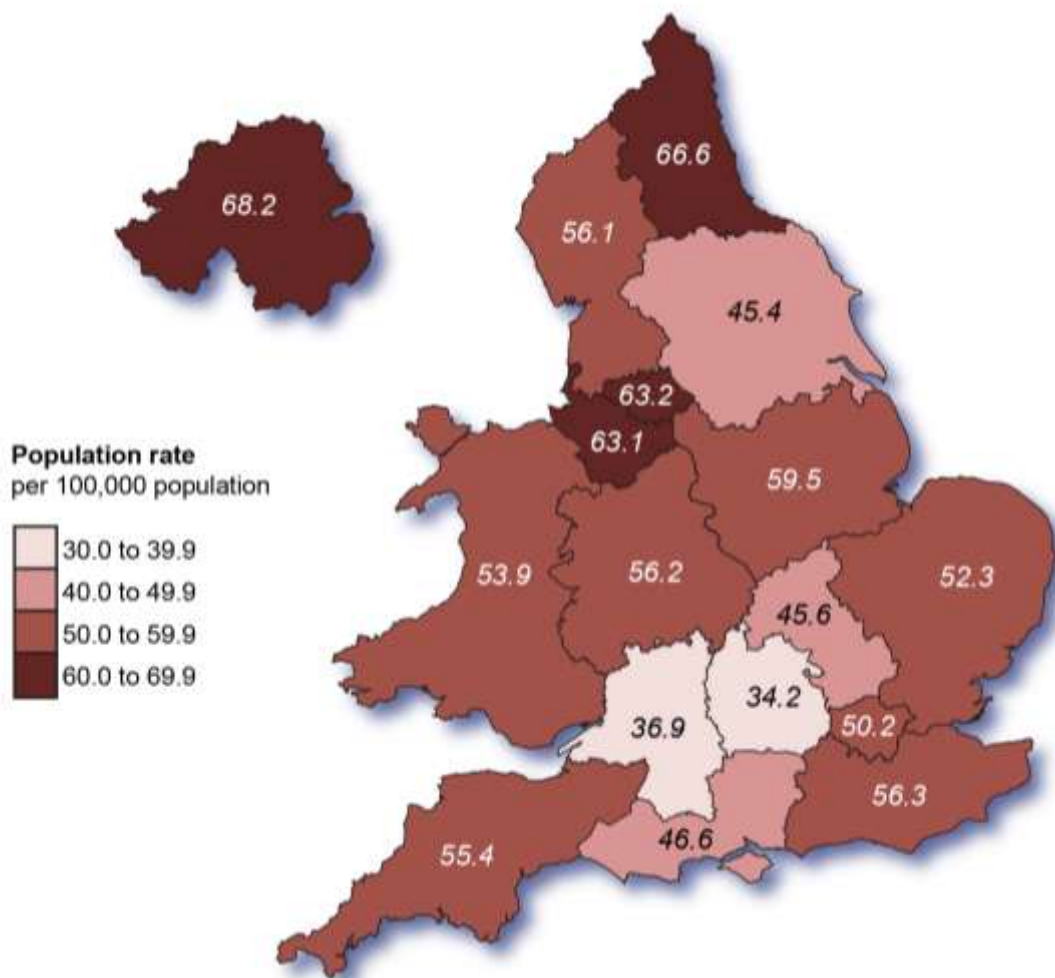
As data-collection is based on a voluntary reporting system, it is important to note that variation in regional rates of infection may reflect regional differences in reporting rather than genuine differences.

Figure 3: Region-specific rates of *E. coli* bacteraemia: England, Wales and Northern Ireland, 2013*



* Data extracted 2 April 2014

Figure 4: Region-specific rates of *E. coli* bacteraemia: England, Wales and Northern Ireland, 2013*



* Data extracted 2 April 2014

Antimicrobial susceptibility

Trends in non-susceptibility to key antimicrobials are presented in Table 2. The percentages of *E. coli* isolates showing non-susceptibility to 3rd generation cephalosporins and gentamicin were stable between 2009 and 2013; changes were within 2%. Specifically, non-susceptibility rates for cefotaxime and ceftazidime were 10-11% in both 2012 and 2013 whereas, rates for ciprofloxacin and gentamicin also remained similar at 18-19% and 9-10%, respectively.

These stable rates contrasted with the significant increases in the number of *E. coli* non-susceptible to cephalosporins from 2001 to 2006 [2], which largely reflected the emergence and spread of strains producing extended-spectrum β -lactamases (ESBLs), particularly cefotaxime-Munich- β -lactamase enzyme type 15 (CTX-M-15), which has become the dominant ESBL in the species [3, 4]. Ciprofloxacin resistance decreased from 20% in 2009 to 19% resistance in 2012 ($p < 0.0001$). This trend is not in agreement with that of the Bacteraemia Surveillance Programme of the British Society for Antimicrobial Chemotherapy (BSAC) data, which has a different sampling scheme to LabBase2 and includes data from Scotland and the Irish Republic (<http://www.bsacsurv.org>), which showed a decrease in resistance from 26% in 2006 to 18% in 2008, but increased from 14% in 2009 to 22% in 2012. Susceptibility of isolates tested against 3rd generation cephalosporins (cefotaxime & ceftazidime) showed that rates of resistance remained largely stable between 2009 and 2012 (10-11% of isolates were resistant). BSAC also showed that the resistance to cephalosporins between 2009 and 2012 remained broadly stable, ranging from 7% to 11% for cefotaxime and from 6% to 8% for ceftazidime respectively.

The BSAC data for 2013 have not been released at the time of publication. Nevertheless the pictures from the two surveillance schemes are broadly consistent.

Most isolates tested against either imipenem or meropenem remained fully susceptible. The numbers of isolates reported resistant to imipenem were 7 out of 4,938 in 2012 and 5 out of 4,378 in 2013. The numbers resistant to meropenem were 26 out of 20,826 in 2012 and 12 out of 21,742 in 2013. There was a significant increase in meropenem resistant isolates between 2009 and 2013 ($p < 0.025$). A growing number of *E. coli* isolates (and substantially more *Klebsiella pneumoniae*) with acquired carbapenemases are confirmed by PHE's AMRHA1 Reference Unit and variously produce New Delhi Metallo β -lactamase-1 (NDM-1), which is epidemiologically often linked to India and Pakistan [6].

Table 2. Antibiotic susceptibility data for reports of *E. coli* bacteraemia, England, Wales and Northern Ireland: 2009-2013*

<i>E. coli</i>		2009	2010	2011	2012	2013
Total reports:		25,662	27,045	29,851	30,101	31,023
Cefotaxime	% Non-susceptible	10%	10%	11%	11%	11%
	Reports with susceptibility data	12,850	13,487	15,393	16,323	16,165
Ceftazidime	% Non-susceptible	10%	10%	11%	10%	10%
	Reports with susceptibility data	16,507	18,437	20,798	21,201	20,608
Ciprofloxacin	% Non-susceptible	20%	19%	19%	19%	18%
	Reports with susceptibility data	20,063	21,817	24,796	25,505	26,029
Gentamicin	% Non-susceptible	8%	9%	9%	10%	10%
	Reports with susceptibility data	22,106	23,632	26,711	27,402	27,619
Imipenem	% Non-susceptible	0.1%	0.0%	0.1%	0.1%	0.1%
	Reports with susceptibility data	7,220	6,456	5,755	4,938	4,378
Meropenem	% Non-susceptible	0.1%	0.1%	0.1%	0.1%	0.1%
	Reports with susceptibility data	13,524	15,434	19,296	20,826	21,742

* Data extracted 2 April 2014

Concluding remarks

The data presented in this report show that the number of laboratory reports of *E. coli* bacteraemia continues to rise year-on-year [7], with a 27% increase in bacteraemia reports since 2009 and a 3.0% increase from 2012 to 2013. In addition, there are continuing concerns about antimicrobial resistance in this species [2,3,4].

Compared to 2012, the rate of *E. coli* bacteraemia laboratory reports per 100,000 population in 2013 have remained stable in England, Wales and Northern Ireland (51.9/100,000 in 2012 to 53.1/100,000 in 2013).

Trends in non-susceptibility to key antimicrobials (3rd generation cephalosporins, quinolones and gentamicin) showed that there was a decrease in *E. coli* resistance to ciprofloxacin (from 20% in 2009 to 18% in 2013) while resistance to 3rd generation cephalosporins and gentamicin remained stable. The percentages of *E. coli* resistant to ciprofloxacin, 3rd generation cephalosporins and gentamicin in 2013 were 18%, 10-11% and 10%, respectively.

The increase in the number of laboratory reports across England, Wales and Northern Ireland, coupled with the public health impact of *E. coli* confirms that it should remain a priority. There is also a need for continued surveillance and interventions to prevent the spread of *E. coli* producing ESBLs, particularly CTX-M types and emergent carbapenem-resistant strains (e.g. with NDM-1, VIM, OXA-48 and KPC enzymes) which are frequently associated with multiple antibiotic resistance.

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