

Quarterly laboratory surveillance of acquired carbapenemase-producing Gram-negative bacteria in England: October 2020 to September 2021

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Background

From 1 October 2020, all diagnostic laboratories in England have a duty to notify the following via the UK Health Security Agency (UKHSA)'s Second Generation Surveillance System (SGSS):

- acquired carbapenemase-producing Gram-negative bacteria identified in human samples
- the results of any antimicrobial susceptibility test and any resistance mechanism for any of the causative agents listed in <u>Schedule 2 of the Health Protection</u> (<u>Notifications</u>) <u>Regulations 2010</u>

This requirement was launched in conjunction with the national <u>Framework of actions to contain carbapenemase-producing Enterobacterales (CPE)</u>, which sets out a range of measures, that if implemented well, will help health and social care providers minimise the impact of CPE. These analyses are based on data relating to notifications of confirmed acquired carbapenemase-producing Gram-negative bacteria between October 2020 and September 2021 in England. The data was extracted on 20 October 2021 from both UKHSA's voluntary surveillance database, SGSS, and the <u>Antimicrobial Resistance and Healthcare-Associated Infections (AMRHAI) Reference Unit</u> database.

Rates of acquired carbapenemase-producing Gram-negative bacteria were calculated using mid-year resident population estimates for the respective year and geography. Geographical analyses were based on the patient's residential postcode. Where this information was unknown, the postcode of the patient's General Practitioner was used. Failing that, the postcode of the reporting laboratory was used. Cases in England were further assigned to one of 9 local areas, formed from the administrative local authority boundaries.

As patients may have more than one positive specimen taken, specimens taken from the same patient that yielded growth of the same pathogen and carbapenemase within a 52-week period from the initial positive sterile site specimen, screening site specimen or other specimen type (grouped together), were regarded as comprising the same episode and were de-duplicated. Carbapenemase-producing Gram-negative bacteria referred isolates and local laboratory isolates were combined for this de-duplication process, with resistance mechanism results from the AMRHAI Reference Unit retained preferentially where patient specimen overlap occurred. This method differs slightly from the weekly causative agent notification data, where data is not de-duplicated incorporating specimen type. In addition, the data presented in the weekly notification reports is utilising SGSS reports only.

The following report summarises trends and geographical distribution of carbapenemase mechanisms identified from Gram-negative bacteria in human samples. Species, mechanism,

sample type, and age and sex of patients are also described. For the purposes of this report, quarters are calendar quarters, as such October to December is referred to as 'Q4', January to March is referred to as 'Q1', April to June is referred to as 'Q2' and July to September is referred to as 'Q3', alongside relevant years. When reporting on the combined one-year period, this is referred to as October 2020 to September 2021.

First year of notification data (October 2020 to September 2021)

Between October 2020 and September 2021, there were 2,186 acquired carbapenemase-producing Gram-negative bacteria episodes. The majority were identified in screening samples, accounting for 70.2% of carbapenemase notifications, with only 5.6% reported in sterile site specimens (Table 1).

Table 1. Number and percentage of acquired carbapenemase-producing Gramnegative reports by specimen type (England) October 2020 to September 2021

Specimen type	All re	ports	From AMRHAI ‡			
	Number	Number %		%		
Sterile site samples	122	5.6	65	13.4		
Screening samples	1,535	70.2	228	46.9		
Other samples *	529	24.2	193	39.7		
All samples	2,186	100.0	486	100.0		

^{*} Samples that do not fall into either 'sterile site' or 'screening' samples, for example, urine and lower respiratory tract specimens.

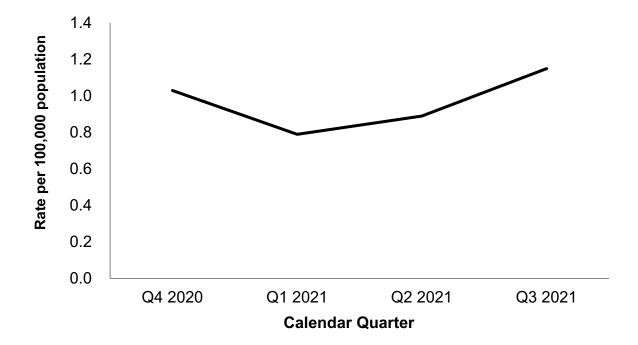
The remaining data summaries in this report consider all samples grouped together.

[‡] The AMRHAI Reference Unit actively encourages submission of sterile site isolates for carbapenemase confirmation; the distribution of specimen type will reflect this.

Trends

The quarterly rate of acquired carbapenemase-producing Gram-negative bacteria reports over the first year of notifiable reporting is shown in Figure 1. The overall rate of reporting between October 2020 and September 2021 was 0.97 per 100,000 population. By quarter, the rate of reporting was higher in Q4 2020 and Q3 2021 (1.03 and 1.15 per 100,000 population) compared to Q1 and Q2 of 2021 (0.79 and 0.89 per 100,000 population respectively). As this is the first year of notification data it is hard to draw any firm conclusions from the quarterly changes. They may be as a result of a seasonal pattern in pathogens or the change could be tied in to the coronavirus (COVID-19) 'waves' seen through 2020 and 2021. Assessing the data over a longer period in future reports will help to shed light on this question.

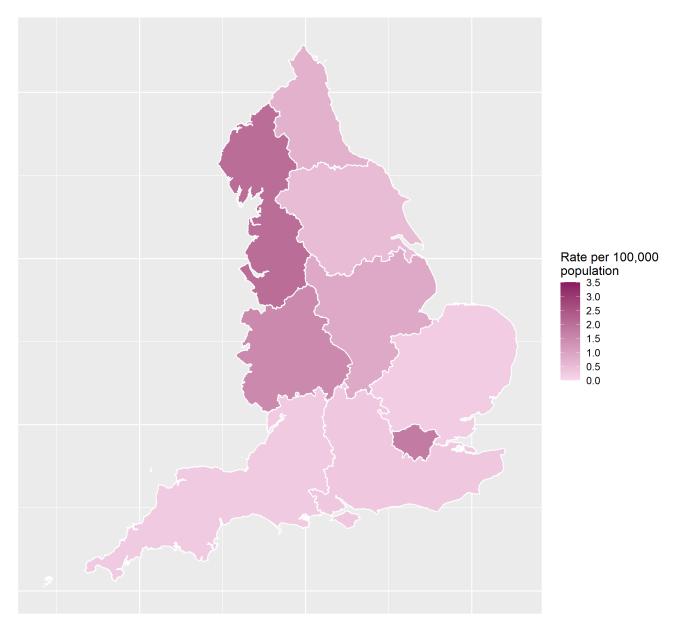
Figure 1. Rate of acquired carbapenemase-producing Gram-negative reports by quarter, October 2020 to September 2021



Geographic distribution

The rate of acquired carbapenemase-producing Gram-negative reports varied by region (Figure 2), with the highest overall rate for all quarters combined being in the North West (2.06 per 100,000 population), followed by the London region (1.77 per 100,000 population). The lowest incidence across the time period was reported in the East of England and South West regions (each 0.22 per 100,000 population).

Figure 2. Geographical distribution of acquired carbapenemase-producing Gramnegative bacteria incidence rates per 100,000 population (England) October 2020 to September 2021



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Comparing the regional case numbers and rates across 4 quarters (<u>Table 2</u>), all regions noted a decrease between Q4 2020 and Q1 2021, with the exception of the North East and Yorkshire and Humber regions, where the rate per 100,000 population increased from 0.34 to 0.75 (9 to 20 reports) and from 0.42 to 0.49 (23 to 27 reports) respectively. Between Q1 and Q2 2021, all regions noted an increase, with the exception of the East of England and West Midlands regions, where the rate per 100,000 population decreased from 0.28 to 0.18 (19 to 12 reports) and from 1.34 to 1.07 (80 to 64 reports), respectively. Between Q2 and Q3 of 2021, case numbers and rates increased or remained fairly stable in the majority of regions. Of note, the number of acquired carbapenemase-producing Gram-negative bacteria reports from the West Midlands more than doubled between Q2 and Q3 2021 (from 64 to 130). This increase likely reflects screening in response to an ongoing investigation, and may not actually represent an increase in prevalence.

While the London region recorded the highest number of acquired carbapenemase-producing Gram-negative bacteria in Q4 2020 and Q1 2021 (183 and 126, respectively), the North West had the highest rate in these quarters (2.23 and 1.60 reports per 100,000 population, respectively). In both Q2 and Q3 2021, the North West recorded both the highest number of acquired carbapenemase-producing Gram-negative bacteria (145 and 181), and the highest rate (1.97 and 2.46 reports per 100,000 population).

Table 2. Number and rate per 100,000 population of acquired carbapenemase-producing Gram-negative reports by region (England) October 2020 to September 2021

		Q4 2	2020	Q1	2021	Q2 :	2021	Q3	2021
	Region	Number of reports	Rate per 100,000 population						
	North East	9	0.34	20	0.75	26	0.97	23	0.86
North of	North West	164	2.23	118	1.60	145	1.97	181	2.46
England	Yorks and Humber	23	0.42	27	0.49	35	0.63	33	0.60
Midlands	East Midlands	47	0.97	32	0.66	41	0.84	54	1.11
and East	East of England	23	0.34	19	0.28	12	0.18	5	0.07
of England	West Midlands	88	1.48	80	1.34	64	1.07	130	2.18
London	London	183	2.03	126	1.40	145	1.61	184	2.04
South of	South East	32	0.36	18	0.20	19	0.21	28	0.31
England	South West	16	0.29	7	0.13	17	0.31	10	0.18
England ov	erall	585	1.03	447	0.79	503	0.88	648	1.15

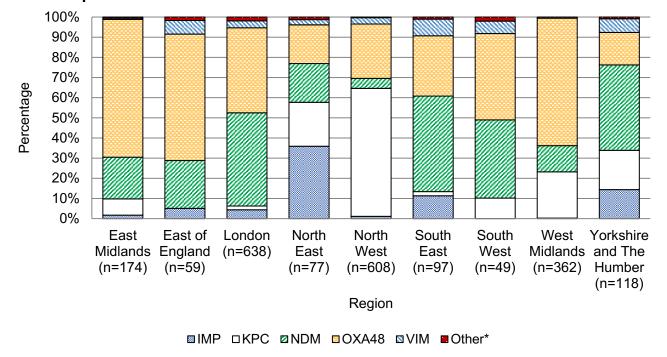
Regional differences in resistance mechanism

Between October 2020 and September 2021, the most common carbapenemase families reported from all regions were OXA-48-like (41%), NDM (25%), and KPC (25%). However, like the incidence variation by region, the carbapenemase families identified also varied regionally (Figure 3).

In the North West, which had the highest incidence rate for the first year of mandatory reporting, the most common carbapenemase families identified were KPC (63%) and OXA-48-like (27%). KPC was not as common in any of the other regions, only accounting for between 0 and 23% of notifications in each region. For example, in London, which also had a high incidence rate, KPC accounted for 2% with NDM and OXA-48-like carbapenemases dominating the reports (46% and 42%, respectively). Another regional difference was observed in the North East, where IMP was the most commonly identified carbapenemase family (36%), only accounting for a small percentage of reports in other regions (up to 14%). However, given the small number of carbapenemases reported in some regions, the diversity of mechanisms reported is likely to strongly impacted by individual outbreaks.

In the 2 regions that had the lowest yearly incidence rates, the most common resistance mechanism was OXA-48-like (63% in the East of England and 43% in the South West).

Figure 3. Regional distribution of reports by resistance mechanism (England) October 2020 to September 2021



^{*} Other resistance mechanisms include GES and IMI.

Distribution of species and resistance mechanism

Across the year, the most frequently isolated Gram-negative bacterial species with a confirmed acquired carbapenemase mechanism was *Klebsiella pneumoniae*, accounting for 32.1% of all specimens. This was followed by *Escherichia coli* and *Enterobacter* spp., which accounted for 25.4% and 21.4% of all specimens, respectively (<u>Table 3</u>).

Across these 3 species, the resistance mechanism most frequently identified was OXA-48-like (47.5%, 34.3% and 44.8% in *K. pneumoniae*, *Enterobacter* spp. and *E. coli*, respectively). In *K. pneumoniae* and *Enterobacter* spp. isolates, this was followed by KPC and NDM resistance mechanisms (28.7% and 21.7% in *K. pneumoniae* and 31.9% and 21.4% in *Enterobacter* spp.), and in *E. coli* this was followed by NDM (33.3%) and KPC (18.9%).

Aside from the 'big 5' carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP), the AMRHAI Reference Unit also screens for rarer carbapenemase families. In England between October 2020 and September 2021, both GES and IMI mechanisms were identified in small numbers (20 total), none being identified from invasive specimens. All IMI mechanisms (12 in total) were identified in *Enterobacter* spp. isolates.

Table 3. Reports of acquired carbapenemase-producing Gram-negative bacteria by species and resistance mechanism (England) October 2020 to September 2021

Resistance mechanism	IN	ИP	K	РС	NI	DM	OXA-	48-like	V	'IM	Oth	ner	Т	otal
Species	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No	%
Acinetobacter spp.	3	13.6	0	0.0	16	72.7	2*	9.1	0	0.0	1	4.5	22	100.0
Citrobacter spp.	6	4.5	34	25.4	31	23.1	57	42.5	5	3.7	1	0.7	134	100.0
Enterobacter spp.	43	9.2	149	31.9	100	21.4	160	34.3	3	0.6	12	2.6	467	100.0
Escherichia coli	11	2.0	105	18.9	185	33.3	249	44.8	5	0.9	1	0.2	556	100.0
Klebsiella oxytoca	7	9.5	24	32.4	4	5.4	36	48.6	3	4.1	0	0.0	74	100.0
Klebsiella pneumoniae	10	1.4	201	28.7	152	21.7	333	47.5	5	0.7	0	0.0	701	100.0
Other Klebsiella spp.	5	6.9	14	19.4	25	34.7	25	34.7	3	4.2	0	0.0	72	100.0
Morganella spp.	0	0.0	0	0.0	4	30.8	9	69.2	0	0.0	0	0.0	13	100.0
Pseudomonas aeruginosa	12	14.3	4*	4.8	24	28.6	3*	3.6	36	42.9	5	6.0	84	100.0
Other Pseudomonas spp.	2	10.0	3*	15.0	4	20.0	2*	10.0	9	45.0	0	0.0	20	100.0
Serratia spp.	0	0.0	0	0.0	4	36.4	7	63.6	0	0.0	0	0.0	11	100.0
Other Gram-negative bacteria‡	1	3.1	8	25.0	4	12.5	19	59.4	0	0.0	0	0.0	32	100.0
Total	1	00	5	42	5	53	9	02	(69	2	0	2,	186

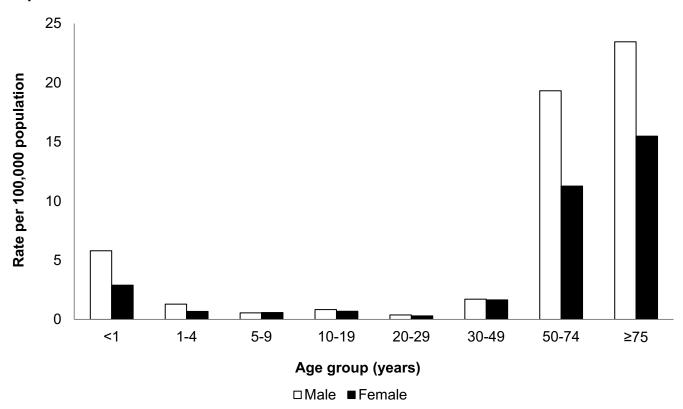
[‡] includes Aeromonas hydrophila, Bacteroides fragilis, coliform, other Escherichia spp., Hafnia spp., Kluyvera spp., Pantoea spp., Phytobacter ursingii, Pluralibacter gergoviae, Proteus mirabilis, and Raoultella spp.

^{*} KPC and OXA-48-like in *Pseudomonas* spp. and OXA-48-like in *Acinetobacter* spp. are extremely rare, and results should be interpreted with caution. The numbers reported here have not been confirmed by the reference laboratory.

Age and sex distribution

The rate of acquired carbapenemase-producing Gram-negative bacteria reports was highest among the oldest and youngest members of the population. A similar age pattern was noted for both sexes, although overall the rate was higher in males compared to females (overall rates of 4.3 and 3.3 reports per 100,000 population, respectively; Figure 4). This aligns with the age group and sex distribution noted in <u>previously published reports</u> on Gram-negative bacteraemia such as *E. coli*, *Klebsiella* spp., *P. aeruginosa* and <u>Enterobacter spp</u>.

Figure 4. Rates of acquired carbapenemase-producing Gram-negative bacteria reports per 100,000 population by age and sex* (England) October 2020 to September 2021



^{*} Information about patient sex is only recorded in 97% of cases.

Figure 4 shows the acquired carbapenemase-producing Gram-negative bacterial incidence rates by age group, with the highest rate reported in those aged 75 years and over (19.1 per 100,000 population) followed by the those aged between 50 to 74 years old (15.5 per 100,000 population). The overall rate of confirmed carbapenemases was 4.9 per 100,000 population in infants less than one year old.

Microbiology services

For reference services, including species identification and confirmation of susceptibility testing results, laboratories should contact UKHSA's <u>Antimicrobial Resistance and Healthcare</u> <u>Associated Infections (AMRHAI) Reference Unit in London.</u>

UKHSA strongly recommends that all diagnostic laboratories should be able to detect the 4 carbapenemase families in bold (the 'big 4') using either PCR or immunochromatographic methods. The following table uses these symbols: ¥ = combinations of mechanism and species would not be considered as exceptional results. A = intrinsic to *A. baumannii* and only expressed when associated with an insertion element; B = almost exclusively reported in *Enterobacter* spp. with less than a handful of reports in other genera; C = reported only in *Serratia marcescens*.

Where an 'exceptional' carbapenemase and species combination result (cells without a ¥ symbol in Table 4) has been identified, or where an unusual organism has been identified with a carbapenemase (that is, any bacterial genera other than a member of the Enterobacterales, *Pseudomonas* spp. or *Acinetobacter* spp.), isolates are requested to be sent to <u>AMRHAI</u> Reference Unit for confirmation.

Table 4. Distribution of carbapenemase genes covered by AMRHAI Reference Unit molecular assay (based on AMRHAI data)

Carbapenemase	Associated with common 'host' organism					
family	Enterobacterales	Pseudomonas spp.	Acinetobacter spp.			
KPC	¥	<10	<10			
OXA-48-like	¥	<10	0			
NDM	¥	¥	¥			
VIM	¥	¥	<10			
IMP	¥	¥	¥			
IMI/NMC-A	B¥	0	0			
GES	¥	¥	0			
FRI	<10	0	0			
SME	<10°¥	0	0			
DIM	0	<10	0			
GIM	<10	0	0			
SIM	0	<10	0			
SPM	0	<10	0			
OXA-23-like	0	0	¥			

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Carbapenemase	Associated with common 'host' organism					
family	Enterobacterales	Pseudomonas spp.	Acinetobacter spp.			
OXA-40-like	0	0	¥			
OXA-51-like ^A	0	0	¥			
OXA-58-like	0	0	¥			

Acknowledgements

These reports would not be possible without the weekly contributions from microbiology colleagues in laboratories across England, without whom there would be no surveillance data. The support from colleagues within the UK Health Security Agency, and the AMRHAI Reference Unit in particular, is valued in the preparation of the report. Feedback and specific queries about this report are welcome via hcai.amrdepartment@phe.gov.uk.

This report covers the first full year of notification reporting of acquired carbapenemase-producing Gram-negative bacteria in England. To influence the future surveillance outputs on acquired carbapenemase-producing Gram-negative bacteria we are seeking the input of interested stakeholders, if you would like to input into this development please indicate your intent by emailing amr@phe.gov.uk before 17 December 2021.

About the UK Health Security Agency

The <u>UK Health Security Agency</u> is an executive agency, sponsored by the <u>Department</u> of Health and Social Care.

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