



A decade of *Campylobacter* and *Campylobacter* bacteraemias in a district general hospital and the surrounding London and South East region, England



Alice Graham^a, Lois Hawkins^b, Sooria Balasegaram^a, Subha Narasimhan^b, John Wain^{c,d}, John Clarke^{a,b,c,d}, Rohini Manuel^{a,b,*}

^a Field Service London and South East, UK Health Security Agency, Nobel House, London, United Kingdom

^b Department of Infection, Epsom and St Heliers' University Hospitals, Carshalton, United Kingdom

^c Quadram Institute Bioscience, Norwich Research Park, Norwich, United Kingdom

^d Norwich Medical School, University of East Anglia (UEA), Norwich, United Kingdom

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SUMMARY

Background: *Campylobacter* bacteraemia is a rare complication of the most common bacterial gastrointestinal infection but is associated with significant morbidity and mortality. There is limited data describing current trends in surveillance and antimicrobial resistance for the *Campylobacter* strains involved. At the Epsom and St Helier's University Hospital (ESTH), we noted a marked increase in *Campylobacter* bacteraemia infections in 2021.

Methods: We extracted *Campylobacter* reports using the UK Health Security Agency's (UKHSA) Second Generation Surveillance System (laboratory reporting system) between 1st January 2012 and 31st December 2021. We reviewed patient records of patients with *Campylobacter* bacteraemia for details including presentation, past medical history, duration of hospital stay, and antibiotic use.

Results: Between 2012 and 2021, ESTH reported a total of 34 cases of *Campylobacter* bacteraemia. In 2021, the estimated incidence was 6.8 cases per 100,000 population and in the surrounding area, the incidence was 0.4 per 100,000 population. The incidence rate of *Campylobacter* bacteraemia in London and the South East region was significantly lower than ESTH (RR = 0.17, $p < 0.0001$). *Campylobacter* bacteraemia cases at ESTH reported a high number of co-morbidities (average number of comorbidities = 2.3) and had a duration of stay in hospital of a median of 7 days (IQR = 4–10 days). *Campylobacter jejuni* was the most commonly reported species for stool and blood *Campylobacter* in ESTH, London, and South East England.

Conclusion: *Campylobacter* bacteraemia reports at ESTH were significantly ($p < 0.001$) higher than the surrounding London and South East region. While no common cause for the exceedance of *Campylobacter* bacteraemia has been identified, common risk factors for *Campylobacter* bacteraemia infection include underlying health conditions, being older, and male.

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Introduction

Bacteria belonging to the genus *Campylobacter* are the leading cause of bacterial diarrhoeal infections in humans. In England and Wales, approximately 60,000 cases of campylobacteriosis are reported annually,¹ although this number is likely an underestimate by as much as 10-fold.² *Campylobacter* infections primarily occur

through consumption of contaminated raw or undercooked poultry products,³ although unpasteurised milk, raw red meat, fruit, and vegetables can also be contaminated with *Campylobacter*.⁴ Patients with *Campylobacter* infections, most commonly with *C. jejuni* and *C. coli*, typically present with self-limiting gastrointestinal symptoms, yet a broad range of clinical symptoms have been described including acute watery or bloody diarrhoea, fever, abdominal pain, pneumonia, endocarditis, and post-infectious complications such as Guillain-Barré Syndrome and reactive arthritis.⁵

Campylobacter detected in stool can spread viable bacteria into the blood circulation (*Campylobacter* bacteraemia).⁶ *Campylobacter* bacteraemias are rare and incidence rates have been estimated

* Corresponding author at: Field Service London and South East, UK Health Security Agency, Nobel House, London, United Kingdom.

E-mail address: Rohini.Manuel@ukhsa.gov.uk (R. Manuel).

between 0.20 and 1.00 cases per 100,000 population,⁶ this however, is likely to be an underestimate. *Campylobacter jejuni*, *Campylobacter coli*, and *Campylobacter fetus* are the species most frequently isolated from blood and faecal specimens.^{4,7} Underlying conditions known to predispose individuals to *Campylobacter* bacteraemia include liver diseases, malignancy, and HIV infection.^{8,9} Whilst the elderly and immunocompromised patients are prone to *Campylobacter* bacteraemia infections, some studies have shown that these infections can occur in younger patients without any significant underlying health conditions.⁷ *Campylobacter* infections can be severe or even fatal, owing to a high-risk of complications or the exacerbation of underlying co-morbidities.^{8,10} A 10-year surveillance study in Finland showed the risk of death was higher in patients that did not receive the appropriate antimicrobial therapy,¹¹ emphasising the importance of diagnosis and antimicrobial resistance testing. Whilst published literature on antimicrobial susceptibility of *Campylobacter* bacteraemias is scarce, some studies have indicated that resistance to fluoroquinolones is common, but in general resistance patterns reflect that of faecal isolates. In 2021, we noted a marked increase in *Campylobacter* bacteraemia reported by Epsom and St Helier University Hospitals (ESTH). Consequently, we systematically looked, over a 10-year period, at the hospital and the surrounding catchment regions (London and South East) for *Campylobacter* cases to improve our understanding of the epidemiology and management of this infection.

Methods

Study design

We conducted a retrospective analysis of *Campylobacter* surveillance data, in London and South East England regions, between January 2012 to December 2021, focusing on ESTH. In 2021, the population of London was 8,796,628 and the population of the South East was 9,278,065, which is the catchment population for the approximately, 900,000 patients that are treated at ESTH each year. The majority of ESTH patients are residents of the local authority boroughs Sutton, Epsom, Ewell, and Merton, which are located in London and South East England. The samples processed by the ESTH laboratory were from a combination of both patients admitted to ESTH and local general practices.

Case definition

We included laboratory confirmed *Campylobacter* cases of residents in London and South East England. Individuals with missing National Health Service (NHS) numbers and personally identifiable information (forename, surname, date of birth, and postcode) in the database were excluded. Additionally, samples with missing specimen dates were excluded.

Data collection

As *Campylobacter* is a notifiable organism, samples positive for *Campylobacter* must be reported by all UK laboratories.¹² Laboratories detect *Campylobacter* by inoculation onto selective agar in a microaerophilic environment and subsequent identification of colonies using MALDI-TOF. The mechanism for reporting is through the UKHSA laboratory reporting system, Second Generation Surveillance System (SGSS). SGSS systemically collects notifiable positive laboratory reports, which include samples collected from primary, secondary, and tertiary care centres. Data was extracted using from SGSS between 1st January 2012 and 31st December 2021 from residents in the London and South East region, reported by 76 different

laboratories. Extracted data was de-duplicated, by grouping samples by NHS number and repeat positive samples within 21 days were removed. If a patient's NHS number was not available, individuals were de-duplicated using forename, surname, date of birth and postcode. Patient notes, obtained from ESTH, were reviewed and details including symptoms, past medical history and length of antimicrobial treatment were documented for each patient presenting with *Campylobacter* bacteraemia. Susceptibility of *Campylobacter* was determined using EUCAST standardised disc diffusion methods (Muller-Hinton blood agar and incubated at 41+/-1 °C). ESTH antimicrobial guidance states that first line microbial susceptibility testing should be performed initially on ciprofloxacin and erythromycin and if resistance to both first line antibiotics is detected, then doxycycline is tested.

Data analysis and methods

Descriptive statistics were used to summarise the exceedance at ESTH. Comparisons were also made with ESTH and the surrounding London and South East England region. Results were reported as percentages for categorical outcomes and mean with standard deviations for continuous outcomes. All quantitative analyses were performed using R studio.

Results

Campylobacter infections detected in stool

Between 1 January 2012 and 31 December 2021, ESTH reported *Campylobacter* in 6547 stool samples to UKHSA (previously Public Health England (PHE)), from 6349 individuals (male: 3502, 53%, median age, inter quartile range: 43 years, 23–62 years), with an incidence ranging between 91 and 158.7 per 100,000 population per annum. During the same period, 142,290 reports of *Campylobacter* detected in stool were made to UKHSA across the London and South East England region, reported in 138,614 individuals (male: 54%, median age, inter quartile range: 45 years, 24–63 years), with an incidence ranging between 67.1 and 90.3 per 100,000 population per annum (Fig. 1). Stool *Campylobacter* detected by ESTH reference laboratory ranged from a minimum prevalence of 3.6% (512/14,287), in 2012, to a maximum prevalence of 7.0% (968/13,850), in 2014, of all samples in reported in London and South East England.

Campylobacter bacteraemias

Between 2012 and 2021, ESTH had a total of 34 laboratory reports (male: 21/34, 62%, median age, inter quartile range: 75 years, 53 – 80 years) of *Campylobacter* bacteraemia, with an overall proportion of 1 report per 200 of stool *Campylobacter* (Fig. 2). Only, 1 (3%) positive *Campylobacter* bacteraemia report had a previous (1–21 days) positive stool sample. The number of *Campylobacter* bacteraemia reports increased from 0 cases in 2012–11 reports in 2021 (Fig. 3). In 2021, there was limited evidence of clustering or seasonality in the occurrence of reports, and the estimated incidence was 6.8 cases per 100,000 population, which was substantially (RR = 4.75, $p < 0.00001$) higher than the previous 9 years. Between 2012 and 2021, in the surrounding London and South East region, a total of 723 *Campylobacter* bacteraemia samples were reported (male: 439/723, 61%, median age, inter quartile range: 58 years, 28 – 76 years), giving a proportion of 1 bacteraemia report per 200 of stool *Campylobacter*. A low frequency (13/723, 1.7%) of positive *Campylobacter* bacteraemia reports had a previous (1–21 days) positive *Campylobacter* in stool. In London and South East, the number of *Campylobacter* bacteraemia reports increased by 7 times between 2012 and 2020, and in 2021, the number of reports reduced by

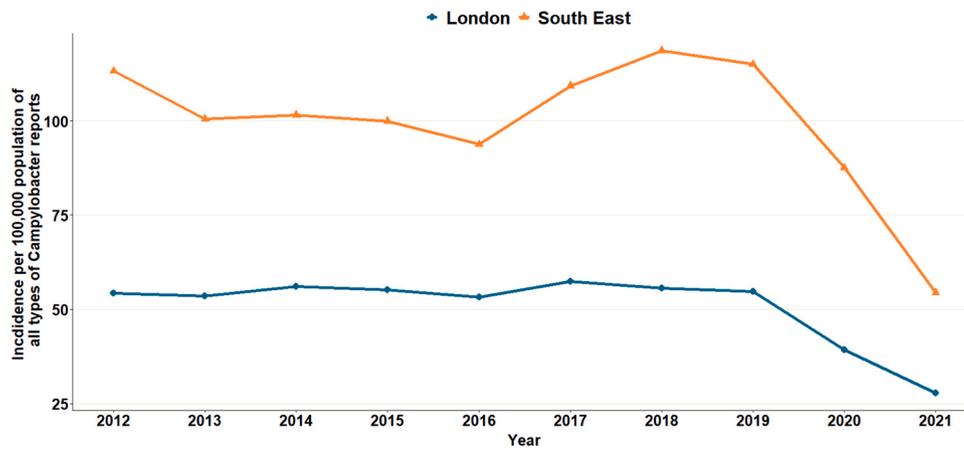


Fig. 1. The number of all specimen types of *Campylobacter* reports, by year, made to the UK Health Security Agency's (previously the Health Protection Agency and Public Health England) Second Generation Surveillance System (SGSS) in the South East and London region, between 2012 and 2021. Data was de-duplicated if records are within 21 days of each other.

72% giving an incidence 0.4 per 100,000 population. In 2021, the incidence rate for *Campylobacter* bacteraemia in London and South East region was significantly ($p < 0.0001$) lower than the incidence rate at ESTH (RR = 0.17, 95% CI: 0.08–0.32).

Summary of the Campylobacter species reported at ESTH and London and South East

Over the 10-year study period, 28 (28/34, 82%) *Campylobacter* bacteraemia species of *C. jejuni* (24/28, 86%), *C. fetus* (2/28, 7%), *C. coli* (2/28, 7%) were reported by ESTH. Over the same period, ESTH reported 2010 (2010/6548, 31%) stool *Campylobacter* species of *C. jejuni* (n = 1832, 91%) and *C. coli* (n = 178, 9%) (Table 1). From the laboratory reports of *Campylobacter* bacteraemia 27 had a corresponding stool sample (79.4%, 27/34) and *C. jejuni* was the only species detected among the matching stool and blood samples. Between 2012 and 2015, ESTH did not speciate isolates of *Campylobacter*. From 2015–2021, speciation increased to 96% of all *Campylobacter* isolates.

In South East and London, a total of 393 *Campylobacter* bacteraemia isolates were identified over the study period, which included *C. coli* (38/393, 10%), *C. fetus* (46/393, 12%), *C. jejuni* (279/393, 71%) and *C. spp* (30/393, 8%). Over the same period, a high proportion of stool *Campylobacter* samples were not speciated (121,123/142,290, 85%). Among the 21,167 speciated samples *Campylobacter* detected in stool samples *C. coli* (8.9%), *C. fetus* (0.01%), *C. jejuni* (90.6%) and *C. spp* (0.5%) were reported in London and South East. The number of *Campylobacter* stool samples speciated ranged from a minimum of 6% in 2012, to a maximum of 28%, in 2016.

Summary of patients' clinical notes with Campylobacter bacteraemia at ESTH

Of the 34 laboratory reports of *Campylobacter* bacteraemia at ESTH, between 2012 and 2022, one case had persistent bacteraemia beyond 21 days, and therefore, based on de-duplication methods, the case was included twice in the previous analysis. The clinical



Fig. 2. A heat map to show the 10 laboratories with the highest absolute numbers of blood *Campylobacter*, and the absolute number of blood *Campylobacter* / stool *Campylobacter* infections in brackets, between 2012 and 2021. Second Generation Surveillance System (SGSS).

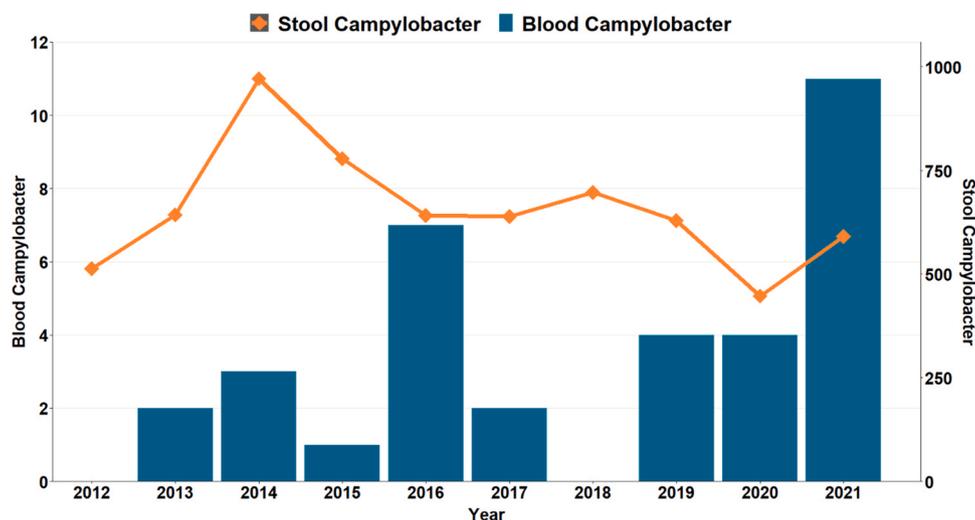


Fig. 3. Number of stool and blood *Campylobacter* isolates recorded at Epsom and St Helier University Hospitals between 2012 and 2021.

Table 1

Epsom and St Helier University Hospital recorded cases of *Campylobacter* by sample type, between 2012 and 2021.

Second Generation Surveillance System (SGSS).

Variable	Overall, n (%) N = 6582	Sample Type	
		Blood, n (%) N = 34	Stool, n (%) N = 6548
Organism Species			
<i>Campylobacter coli</i> [†]	180 (3)	2 (6)	178 (3)
<i>Campylobacter fetus</i> [†]	2 (<0.1)	2 (6)	0
<i>Campylobacter jejuni</i> [†]	1856 (28)	24 (71)	1832 (28)
<i>Campylobacter sp</i> [†]	4544 (69)	6 (18)	4538 (69)
Age			
Median (IQR)	43 (23 – 62)	75 (53 – 80)	43 (23–61)
Patient Sex			
Female	3079 (47)	13 (38)	3066 (47)
Male	3502 (53)	21 (62)	3481 (53)
Unknown	1 (<0.1)	0	1 (<0.1)

IQR: Interquartile range

notes, however, were obtained from 33 individuals. Patients reported symptoms of diarrhoea (n = 22, 67%), vomiting (n = 13, 39%), fever (n = 12, 36%) and abdominal pain (n = 12, 36%). Symptoms persisted for a median of 1.5 days (interquartile range: 1–3 days) before presentation to hospital. Initially, 15 (46.8%) of these individuals were diagnosed with gastroenteritis and 20 (65%) had a subsequent stool sample taken. Most individuals had existing comorbidities (average number of comorbidities = 2.3) that cause immunosuppression, including diabetes (n = 7, 21%), cancer (total n = 8, 24%; prostate cancer n = 3, lung cancer n = 1, myeloma n = 1, ovarian n = 1, lymphoma n = 1, Basal Cell Carcinoma (BCC) n = 1) and other conditions that cause immune suppression (n = 2, 6%). Other patients had comorbidities including heart disease (n = 11, 33%), dementia (n = 4, 12%) and lung disease (n = 6, 18%) (Table 2).

Individuals had a median duration of 7 days in hospital (IQR = 4–10 days), 15 (45%) individuals spent more than 9 days in hospital, and there was one recorded death (mortality rate: 3%). Antibiotics used to treat *Campylobacter* bacteraemia (median number of different antibiotics = 2, interquartile range=1–2), include clarithromycin (n = 17, 53.1%), meropenem (n = 13, 41%), gentamicin (n = 6, 19%) and azithromycin (n = 6, 19%). The median duration of

antibiotic treatment was 13 days (interquartile range: 10–14 days). Antimicrobial therapy was given successively, apart from 6 patients who received gentamicin as adjunct therapy. Ciprofloxacin resistance was identified in 14 (45%) *Campylobacter* samples (*C. jejuni* 11/14, 79% and *Campylobacter spp.* 3/14, 21%) and no erythromycin resistance was identified.

Discussion

Campylobacter bacteraemia rates at ESTH increased significantly (p < 0.0001) in 2021 compared to the surrounding South East and London region, with an estimated incidence of 6.8 per 100,000 population, which is approximately 17 times higher than the incidence in the surrounding area. As shown in Fig. 1, laboratory reports of *Campylobacter* bacteraemia decreased during the pandemic period in ESTH and the surrounding London and South East area, however, in 2021 ESTH reported an increase in *Campylobacter* bacteraemia, whilst the surrounding area continued to have a fall in the number of *Campylobacter* bacteraemia reports. A low frequency (3%) of *campylobacter* bacteraemia cases had a previous positive stool sample and patients reported symptoms for a short period of time before presentation to the hospital (median: 1.5 days IQR: 1–3 days).

In this study, the most common *Campylobacter* bacteraemia species was *C. jejuni* (71%), which is the most common among the speciated causes of bacterial gastroenteritis worldwide.¹³ A clinical study found milder symptoms associated with *C. jejuni* and *C. coli* infection compared to other species.¹⁴ Patients at ESTH with *Campylobacter* bacteraemia infection had an average of 3 symptoms, with a high frequency of diarrhoea, vomiting, abdominal pain, and fever. While symptoms usually lasted for a short duration of time, a high frequency of patients (n = 15, 45%) spent more than 15 days in hospital, which may be explained by the high number of comorbidities (average number: 2.3) among the study population. *Campylobacter* bacteraemia is well recognised amongst individuals with underlying health conditions,¹⁵ which correlates with the findings of our study where 97% of patients had an underlying health condition.

In line with other UK studies, our study found ciprofloxacin resistance was to be common (45%).^{16,17} We therefore recommend routine laboratory susceptibility testing of isolates if ciprofloxacin is used as a first line treatment for *Campylobacter* cases. Among the

Table 2

Characteristics of individuals testing positive for blood *Campylobacter* at Epton and St Heliers Hospital (ESTH) between 2012 and 2021, n = 33.

ESTH clinical notes.

	Variable	N (%)	
Ethnicity	White	28 (84.8)	
	Black	1 (3.0)	
	Mixed race–White and Black	2 (6.1)	
	Other	2 (6.17)	
Average number of co-morbidities	Mean	2.3	
Co-morbidities	None	3 (9.1)	
	Diabetes	7 (21.2)	
	Cancer	8 (24.2)	
	Heart disease/circulation conditions (e.g., AF, DVT, hypertension)	11 (33.3)	
	Lung disease (e.g., COPD, emphysema)	6 (18.1)	
	Dementia / Parkinson's	4 (12)	
	Arthritis	2 (6.1)	
	Crohns disease	3 (9.1)	
	Other conditions that cause immune suppression	2 (6.1)	
	Other GI conditions: IBS and diverticulitis	5 (15.1)	
	Other long term conditions (e.g. Paget's bone disease, asthma)	7 (21.2)	
	Symptoms	Diarrhoea	22 (66.7)
		Vomiting	13 (39.3)
Abdominal pain		12 (36.4)	
Fever		12 (36.4)	
Back pain		2 (9.5)	
Confusion		2 (9.5)	
Urinary frequency		2 (9.5)	
Other		10 (30.3)	
Duration of symptoms before presentation to hospital		Median (IQR) days	1.5 (1–3)
		1 day	11 (45.8)
		2–4 days	8 (33.3)
	5–7 days	2 (8.3)	
	8–14 days	1 (4.2)	
	15–21 days	1 (4.2)	
	More than 21 days	1 (4.2)	
Initial diagnosis	Missing	9	
	Gastroenteritis	15 (45.5)	
	Sepsis (urosepsis and neutropenic sepsis)	7 (21.2)	
	UTI	4 (12.1)	
Stool culture	Other	3 (9.1)	
	Not available	1 (3.0)	
	Positive	11 (36.7)	
	Negative	8 (26.7)	
	No sample	11 (36.7)	
Duration of stay in hospital	Not available	1	
	0 days	4 (12.5)	
	1 day	1 (3.1)	
	2–4 days	5 (15.6)	
	5–8 days	7 (21.9)	
	9–10 days	8 (25.0)	
	10+ days	6 (18.8)	
	Not admitted	1 (3.3)	
Abx Tx	Not available	1	
	Meropenem	13 (40.6)	
	Gentamicin	6 (18.8)	
	Erythromycin	1 (3.1)	
	Clarithromycin	17 (53.1)	
	Azithromycin	6 (18.8)	
	Piperacillin-tazobactam	3 (9.4)	
	Ciprofloxacin	4 (12.5)	
	Flucloxacillin	1 (3.1)	
	Phenoxymethylpenicillin	1 (3.1)	
	Amoxicillin	1 (3.1)	
	Not available	1	
	Duration of antibiotic treatment	Median (IQR)	13 (10–14)
Not available		7	
Ciprofloxacin	Resistant	14 (45.2)	
	Susceptible	17 (54.8)	
	Not available	2	

Table 2 (continued)

	Variable	N (%)
Erythromycin	Susceptible	31 (100)
	Not available	2

IQR: Interquartile range

AF: Atrial Fibrillation

DVT: Deep Vein Thrombosis

COPD: Chronic Obstructive Pulmonary Disease

IBS: Irritable Bowel Syndrome

ciprofloxacin resistance isolates speciated in our study all were *C. jejuni*. In line with this, a study speciating ciprofloxacin resistant isolates in meat, showed 54% (237/437) *C. jejuni* and 48% (52/108) *C. coli*.¹⁷ Previous studies have shown that ciprofloxacin resistant *Campylobacter* increases duration of symptoms,¹⁸ however, individuals with ciprofloxacin resistance did not have a longer duration of stay in the hospital in comparison to those whose isolate was sensitive to ciprofloxacin. The one deceased individual in this study (where no tests for antimicrobial resistance were performed) was treated with six different antibiotics, suggesting possible links to antibiotic resistance. While studies have shown erythromycin resistance to be increasing in recent years, resistance is still rare. A Food Standard Agency project on UK meat samples estimated resistance to be approximately 3%,¹⁸ in line with this our study showed no resistance to erythromycin.

The main limitation of this study was the small number of *Campylobacter* bacteraemia infections at ESTH reducing the power of the study and consequently reducing the ability to determine the cause of the exceedance of *Campylobacter* bacteraemia in 2021. So far, in March 2022, 5 cases of *Campylobacter* bacteraemia have been detected at ESTH (0.98 *Campylobacter* bacteraemia cases per 100 cases of stool *Campylobacter*), following a similarly high trend to the previous year, giving scope for further investigation into the underlying causes of these exceedances. Another limitation is the limited risk factor data available from routine laboratory requests making it difficult to preclude any meaningful investigation between *Campylobacter* bacteraemia and gastroenteritis.

Overall, this study adds to the limited body of published evidence describing *Campylobacter* bacteraemias infections in the UK. While no common cause for the exceedance of *Campylobacter* bacteraemia has been identified, common risk factors for *Campylobacter* bacteraemias include underlying health conditions and older males. The early diagnosis of *Campylobacter* bacteraemia, may be reflected in the low mortality rate identified in this study, reinforcing the importance of enhanced surveillance and testing. So far in March 2022, trends of *Campylobacter* bacteraemia are following the same trajectory in ESTH compared with the previous year, therefore, further research is warranted to identify risk factors associated with this increase and the apparent emergence of *C. jejuni* blood stream infections.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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