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Socioeconomic and ethnic inequalities in incidence and severity of enteric fever in England 2015–2019: analysis of a national enhanced surveillance system

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Abstract

There is limited research on whether inequalities exist among individuals from different ethnicities and deprivation status among enteric fever cases. The aim of the study was to investigate the association between the enteric fever incidence rates, ethnicity and deprivation for enteric fever cases in England. Additionally, it was assessed if ethnicity and deprivation were associated with symptom severity, hospital admission and absence from school/work using logistic regression models. Incidence rates were higher in the two most deprived index of multiple deprivation quintiles and those of Pakistani ethnicity (9.89, 95% CI 9.08–10.75) followed by Indian (7.81, 95% CI 7.18–8.49) and Bangladeshi (5.68, 95% CI 4.74–6.76) groups: the incidence rate in the White group was 0.07 (95% CI 0.06–0.08). Individuals representing Pakistani (3.00, 95% CI 1.66–5.43), Indian (2.05, 95% CI 1.18–3.54) and Other/Other Asian (3.51, 95% CI 1.52–8.14) ethnicities had significantly higher odds of hospital admission than individuals representing White (British/Other) ethnicity, although all three groups had statistically significantly lower symptom severity scores. Our results show that there are significant ethnic and socioeconomic inequalities in enteric fever incidence that should inform prevention and treatment strategies. Targeted, community-specific public health interventions are needed to impact on overall burden.

Background

Typhoid and paratyphoid, also known collectively as enteric fever, are bacterial infections caused by *Salmonella enterica* subgroup *enterica* serovar Typhi and *Salmonella enterica* subgroup *enterica* serovar Paratyphi, which has three serotypes A, B and C. Humans are the only host for typhoidal salmonellae [1] and transmission usually occurs via ingestion of food or water contaminated with human faeces [2]. There are approximately 11–21 million cases and 128 000–161 000 typhoid-related deaths each year globally [2]. Diagnosis is challenging as symptoms are non-specific and often overlap with those of other febrile illnesses, such as dengue [3].

The infection is characterised by fever, headache, abdominal pain, nausea, loss of appetite, constipation and diarrhoea. Symptoms of typhoid usually start within week of the exposure (range 3–60 days) and within 3–7 days for paratyphoid [4]. Asymptomatic shedding of the bacteria in the faeces can occur prior to symptomatic disease [5]. Following recovery, 1–3% of patients will become long-term carriers and a proportion of patients may excrete *Salmonella* Typhi for more than a year [6]. Most cases in the UK are caused by travelling to typhoid endemic countries, which may have areas with higher prevalence, poor sanitation, poor hygiene, poor access to clean drinking water and a limited public health infrastructure to support health education and vaccination programmes [3]. Endemic countries include parts of Asia (especially India, Pakistan and Bangladesh), Africa, the Caribbean, Central and South America and the Middle East. Indeed, typhoid has been reported as the most common bacterial cause of fever in travellers from those areas [3]. Paratyphoid is mostly present in parts of South Asia and China [3].

Although foodborne illnesses, such as typhoid, are not typically tracked by ethnicity or income, a literature review from 2013 [7] states that analyses of reported cases found increased rates of other foodborne infections among ethnic minorities. For certain pathogens, such as listeria and yersinia, increased rates are due to unique food consumption patterns, while for

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others, notably salmonella, shigella and campylobacter, it is unclear why this health disparity exists [7]. Despite some evidence of the relationship between deprivation and the incidence of enteric fever, there are very limited data regarding the social and economic burden of enteric fever: most of the studies conducted so far have showed that higher deprivation might be associated with increased risk of typhoid [8–10]. However, those studies have been done in low- and middle-income areas and on small populations, and therefore the results may not be representative of high-income countries such as England.

The aims of the study were to investigate the differences in enteric fever incidence across different ethnicities and index of multiple deprivation (IMD) quintiles in England. Additionally, it was assessed how ethnicity and IMD affected the severity of symptoms, admission to the hospital and absence from school/work.

Methods

Dataset

Salmonella Typhi and *Salmonella* Paratyphi are statutorily notifiable in England: local health protection teams are routinely requested to complete enhanced surveillance questionnaires of all notified cases for local management and national reporting. Surveillance system includes individuals who present to primary care/hospital and have a sample taken (blood or stool) which results in a positive *Salmonella* Typhi/Paratyphi culture. Responses to the Enhanced Surveillance of Enteric Fever Questionnaire (Supplementary Questionnaire) were extracted from data held in the enhanced typhoid and paratyphoid surveillance database for all cases in England for 2015–2019 and were merged to achieve an adequate sample size. The questionnaire is a self-administered online survey. Once a case completes it, the questionnaire is automatically sent to the local Health Protection Team and the UKHSA Travel Health and International Health Regulations Team. The gap between a positive *Salmonella* Typhi/Paratyphi culture and form administration is 24 h. The study dataset covers fields such as ethnicity, travel history, symptoms, antibiotic administration or vaccination history, absence from school and work as well as history of hospital admission. Responders who did not provide a valid UK postcode in the questionnaire were excluded from the analyses as IMD and relevant population denominators could not have been estimated. Duplicate cases were excluded. Chronic cases were also excluded as date of onset of the infection could not be estimated. Cases who had data missing from sex, ethnicity, symptom severity, hospital admission, travel abroad and organism variables were also excluded. Tabulations with basic confounders (sex and age) were undertaken for excluded cases who had data missing to assess whether the missing values were present at random.

Explanatory variables

The main explanatory variables were ethnicity and IMD quintile, which was based on the IMD 2019, a measure that aggregates data on deprivation by lower super output area (LSOA) in seven domains: income, employment, education, health, crime, housing and living environment [11]. IMD quintiles were derived using respondent's UK home postcode, with first quintile being the most deprived and fifth quintile being the least deprived. Some ethnicities were combined so that every category had a sufficient number of cases included. Six ethnicity categories were created: Bangladeshi, Indian, Pakistani, White (British/Other), Other/Mixed and Black (African/Caribbean). Individuals who had data on ethnicity missing but were born in a non-European country had been assigned their ethnicity based on the most prevalent ethnicity in their country of birth.

Outcome variables

The outcome for aim 1 was the incidence rate of enteric fever calculated as number of enteric fever cases per 100 000 person-years of the total population in England. For aim 2, the first outcome was the symptom severity. 'Other, please state' free-text field was split into eight specific symptoms (fatigue, pain in the muscles/joints, urinary tract infection, other, no appetite/weight loss, confusion, infection of ear/throat and nausea), based on descriptions given by the cases. Together with nine direct questions from the questionnaire (fever, abdominal pain, diarrhoea, constipation, vomiting, headache, rigors, cough, rash), 17 symptoms were present in total. Symptoms for each respondent were added together to create overall sum of symptoms. Each symptom was multiplied by 1, 2 or 3, depending on how serious the symptom was. This scoring system was previously used in other papers on gastrointestinal (GI) infections [12]. A symptom severity variable was created by converting sum of symptoms' scores into terciles so that three approximately sized groups were created (mild: score 0–5, moderate: score 6–9, severe: score 10+). The second and third outcomes of interest were two binary variables: absence from school/work and hospital admission. Those outcomes were chosen as they were previously suggested to be correlated with increased deprivation [12, 13].

Control variables

Several control variables were included in multivariable regression models based on the existing literature [1, 2, 6, 8]: sex (male/female), age (age groups 0–4, 5–9, 10–14, 15–24, 25–44, 45–65 and 65+), rurality/urbanicity, travel abroad status (yes/no), organism identified (*Salmonella* Typhi, Paratyphi A and Paratyphi B) and antibiotic administration (yes/no). Antibiotic administration was included as a control variable as it can reduce the severity of symptoms [1]. Urbanicity–rurality data were obtained through LSOA codes classification from Office for National Statistics (ONS) Geography [14].

Data analysis

Descriptive statistics and visualisations were produced to summarise data and identify key trends. The χ^2 test was used to assess the associations between the explanatory variables and ethnicity and deprivation quintiles at $P < 0.05$ significance level. Incidence rates of reported enteric fever cases were calculated and compared by ethnicity and IMD per 100 000 person-years. The results were further stratified by sex and age group for both ethnicity and IMD (separately). For incidence rate calculations by IMD, sex and age, 2017 mid-year population estimates by LSOA in England [15] were used. For incidence rate calculations by ethnicity, sex and age, 2011 Census population estimates in England and Wales were used [16]. Although the dataset included data on populations in both England and Wales, Welsh total population is considerably smaller compared to English population (5.8% of English population in 2011), therefore its effect was likely to be

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small. For incidence rate calculations by ethnicity and IMD, the dataset from the Ministry of Housing, Communities and Local Government was used [17]. The dataset combined population estimates from the 2011 Census and The English Indices of Deprivation 2019 (IMD 2019). Those specific datasets were used as they were the most up-to-date estimates of population in England which included data on the variables necessary for each of the calculations. Confidence intervals (95% CI) were calculated with open-source collection of epidemiological calculators, OpenEpi, using Byar's method [18] for each incidence rate. Following that, negative binomial regression model was fit to assess the association between ethnicity, IMD quintile and incidence rates. In the model, number of cases for each ethnicity-IMD group was used as an outcome, IMD and ethnicity were used as explanatory variables and person-years for each ethnicity-IMD group were used as an offset. Person-years were calculated for each ethnicity-IMD group using previously mentioned data from the Ministry of Housing, Communities and Local Government [17]. A second model was fit which included an additional variable: interaction between ethnicity and IMD. Incidence risk ratios, 95% CIs and *P*-value at significance level <0.05 were presented for both analyses. Proportions of ethnic groups in each of the IMD quintiles were calculated.

Time series charts using monthly time period were produced to visually assess whether there was a specific pattern connected to, for example, summer holidays or national celebrations. The travel patterns were observed for total number of travellers as well as Pakistani and Indian travellers (both ethnicities represented approximately a third of all cases respectively) and White (British/Other) travellers for a reference. Reasons for travelling abroad and whether pre-travel health advice was sought were described for total, Pakistani, Indian and White (British/Other) travellers, as well as for travellers from each IMD quintile.

Following that, ordinal logistic regression was used to assess the association between ethnicity, IMD quintile and severity of symptoms. Binary logistic regression was used to calculate the correlation between ethnicity, IMD quintile and hospital admission as well as absence from school/work. For the ordinal logistic regression model, the proportional odds assumption was checked. Models were fitted in a hierarchical manner: first, model with only an outcome and explanatory variables (IMD and ethnicity) was fitted (unadjusted model). Second, baseline models for each of the three outcomes (severity of symptoms, hospital admission, absence from school/work) were fit with age and sex as independent variables (model 1). Age group 25–44-years-old was chosen as a reference group as this group represented the highest proportion of the cases. Then, ethnicity and IMD quintile were added to model 1 as additional explanatory variables (model 2). Finally, other control variables (rurality/urbanicity, travel abroad status, organism identified and antibiotic administration) were added to model 2 in order to obtain fully adjusted model 3. All models which had absence from work/school as the main outcome had an additional 391 cases removed due to high proportion of unknown/missing values of absence from work/school variable. Odds ratios, 95% CIs and *P*-value at significance level <0.05 were presented for each analysis. Interaction terms between IMD and rurality/urbanicity, ethnicity and travel abroad status and IMD and ethnicity were tested. The significance of the interactions across analyses was assessed using the Wald's test at $P <$ 0.05 significance level. All data cleaning, manipulation and analyses were done in Stata 15.0 and R version 4.2.1.

Sensitivity analysis

The analysis was repeated using a revised symptom severity variable, which did not include multiplicators of how serious the symptom was: symptom severity scale suggested in Methods section was based on methods used in previous studies, but was not an official guideline. The analysis was also repeated only for cases who travelled abroad as very few cases acquired the infection in England and they are likely to be secondary cases of the travel cases [19]: this allowed additional confounders, such as reason for travelling, whether health advice was sought, and presumed region of infection, to be assessed.

Results

Descriptive analysis

The dataset contained 1811 respondents. There was one duplicate case and eight chronic cases. One case had data missing from sex variable and 109 cases had data missing from ethnicity variable. Twenty-two cases did not have valid postcode data. Cases had data missing from the travel abroad ($n = 24$), antibiotic administration ($n = 98$) and hospital admission ($n = 11$) variables.

Analysis was conducted based on 1412 individuals (Table 1). The second most deprived IMD quintile was the most prevalent quintile in the dataset (30.52%, $n = 431/1412$). Most patients identified as being Pakistani or Indian (35.98%, $n = 508/1412$ and 35.84%, $n = 506/1412$, respectively). Most cases from each ethnic group were admitted to hospital with Other/Other Asian ethnicity having the highest proportion of cases admitted (90.7%, $n = 88/97$). Severe symptoms were most reported by patients identifying as White (British/Other) (41.3%, $n = 57/138$), whereas in all other ethnic groups most patients reported moderate symptoms. The majority of cases reported being absent from work/school (56.73%, $n = 801/1412$) (Table 1). Overall, the most prevalent age group was 25–44-year-olds (37.89%, $n = 535/1412$), just over half of the cases were male (51.13%, $n = 722/1412$), and a high proportion (96.10%, $n = 1357/1412$) lived in urban areas. The majority of cases had travelled abroad in the recent 28 days (95.18%, $n = 1344/1412$).

Incidence rates analysis

The overall annual incidence rate of enteric fever in England was approximately 0.57 (95% CI 0.54–60) per 100 000 person-years between 2015 and 2019. When looking at the incidence rates stratified by ethnicity, sex and age (Fig. 1a and 1b), the incidence rate was highest in those of Pakistani ethnicity for the total population (9.89, 95% CI 9.08–10.75), for women (9.70, 95% CI 8.57–10.94) and for men (10.07, 95% CI 8.94–11.29): these figures were statistically much higher than any other ethnic group for the total and male populations and significantly higher than all except the Indian group for women (Fig. 1a, Supplementary Table S1). The incidence rates in Indian and Bangladeshi groups were also statistically higher than in other non-Asian groups for both sexes, while the White (British/Other) group had the lowest incidence rate. The incidence rate was the highest among cases of Pakistani ethnicity for all age groups except 5–9 and 65+-year-olds, where the incidence rate was the highest in patients of Indian ethnicity (Fig. 1b, Supplementary Table S1). Each of the three South Asian ethnic groups (Indian, Pakistani and Bangladeshi) had statistically significantly higher rates than

Table 1. Predictors and confounding variables described by their total frequency, the frequency of hospital admission, absence from school/work and symptom severity

Variable	Total $n = 1412$ (%)	Admission to the hospital $n = 1412$ (%)			Absence from school/work $n = 1020$ (%)			Symptom Severity $n = 1412$ (%)			
		No	Yes	*P*-value	No	Yes	*P*-value	Mild	Moderate	Severe	*P*-value
IMD quintile				0.097			0.224				0.399
1 (most deprived)	420 (29.8)	49 (11.7)	371 (88.3)		60 (20.6)	232 (79.5)		107 (25.5)	192 (45.7)	121 (28.8)	
2	431 (30.52)	74 (17.2)	357 (82.8)		62 (19.4)	258 (80.6)		118 (27.4)	196 (45.5)	117 (27.2)	
3	244 (17.28)	37 (15.2)	207 (84.8)		34 (20.1)	135 (79.9)		73 (29.9)	91 (37.3)	80 (32.8)	
4	162 (11.47)	20 (12.4)	142 (87.7)		35 (29.2)	85 (70.8)		37 (22.8)	72 (44.4)	53 (32.7)	
5 (least deprived)	155 (11.0)	29 (18.7)	126 (81.3)		28 (23.5)	91 (76.5)		38 (24.5)	74 (47.7)	43 (27.7)	
Ethnicity				<0.001***			0.444				0.040*
White (British/Other)	138 (9.8)	39 (28.3)	99 (71.7)		28 (26.7)	77 (73.3)		25 (18.1)	56 (40.6)	57 (41.3)	
Bangladeshi	115 (8.1)	20 (17.4)	95 (82.6)		13 (16.9)	64 (83.1)		23 (20.0)	61 (53.0)	31 (27.0)	
Pakistani	508 (36.0)	53 (10.4)	455 (89.6)		86 (23.2)	284 (76.8)		149 (29.3)	215 (42.3)	144 (28.4)	
Indian	506 (35.8)	79 (15.6)	427 (84.4)		74 (20.3)	291 (79.7)		138 (27.3)	225 (44.5)	143 (28.3)	
Black (African/ Caribbean)	48 (3.4)	9 (18.8)	39 (81.3)		6 (20.0)	24 (80.0)		15 (31.3)	20 (41.7)	13 (27.1)	
Other/Other Asian	97 (6.9)	9 (9.3)	88 (90.7)		12 (16.4)	61 (83.6)		23 (23.7)	48 (49.5)	26 (26.8)	
Sex				0.465			0.012*				0.105
Male	722 (51.1)	102 (14.1)	620 (85.9)		103 (18.5)	453 (81.5)		201 (27.8)	327 (45.3)	194 (26.9)	
Female	690 (48.9)	107 (15.5)	583 (84.9)		116 (25.0)	348 (75.0)		172 (24.9)	298 (43.2)	220 (31.9)	
Age				0.001**			<0.001***				<0.001***
0–4	108 (7.7)	15 (13.9)	93 (86.1)		27 (44.3)	34 (55.7)		45 (41.7)	47 (43.5)	16 (14.8)	
5–9	157 (11.1)	23 (14.7)	134 (85.4)		11 (7.8)	131 (92.3)		40 (25.5)	67 (42.7)	50 (31.9)	
10–14	100 (7.1)	13 (13.0)	87 (87.0)		8 (9.6)	75 (90.4)		28 (28.0)	47 (47.0)	25 (25.0)	
15–24	277 (19.6)	27 (9.8)	250 (90.3)		54 (27.6)	142 (72.5)		59 (21.3)	120 (43.3)	98 (35.4)	
25–44	535 (37.9)	74 (13.8)	461 (86.2)		74 (18.3)	330 (81.7)		121 (22.6)	241 (45.1)	173 (32.3)	
45–64	197 (14.0)	48 (24.4)	149 (75.6)		32 (27.1)	86 (72.9)		64 (32.5)	88 (44.7)	45 (22.8)	
65+	38 (2.7)	9 (23.7)	29 (76.3)		13 (81.3)	3 (18.8)		16 (42.1)	15 (39.5)	7 (18.4)	
Residence				0.471			0.995				0.018*
Urban	1357 (96.1)	199 (14.7)	1158 (85.3)		210 (21.5)	768 (78.5)		366 (27.0)	601 (44.3)	390 (28.7)	
Rural	55 (3.9)	10 (18.2)	45 (81.8)		9 (21.4)	33 (78.6)		7 (12.7)	24 (43.6)	24 (43.6)	

Travel abroad				0.982			0.385				0.242
Yes	1344 (95.2)	199 (14.8)	1145 (85.2)		207 (21.2)	768 (78.8)		350 (26.0)	601 (44.7)	393 (29.2)	
No	68 (4.8)	10 (14.7)	58 (85.3)		12 (26.7)	33 (73.3)		23 (33.8)	24 (35.3)	21 (30.9)	
Antibiotic administration				<0.001***			0.171				0.403
Yes	1369 (97.0)	180 (13.2)	1189 (86.9)		209 (21.2)	779 (78.9)		358 (26.2)	607 (44.3)	404 (29.5)	
No	43 (3.1)	29 (67.4)	14 (32.6)		10 (31.3)	22 (68.8)		15 (34.9)	18 (41.9)	10 (23.3)	
Organism				<0.001***			0.275				0.045*
Salmonella Typhi	829 (58.7)	93 (11.2)	736 (88.8)		120 (20.0)	480 (80.0)		195 (23.5)	383 (46.2)	251 (30.3)	
Salmonella Paratyphi A	529 (37.5)	103 (19.5)	426 (80.5)		88 (23.0)	294 (77.0)		164 (31.0)	220 (41.6)	145 (27.4)	
Salmonella Paratyphi B	54 (3.8)	13 (24.1)	41 (75.9)		11 (29.0)	27 (71.1)		14 (25.9)	22 (40.7)	18 (33.3)	

χ^2 test at a significance level $P < 0.05$.
$^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

other groups in each age group except those aged 65+; the White group had the lowest rate in each age group.

When looking at the incidence rates stratified by IMD, sex and age (Fig. 2a and 2b), the incidence rates were significantly higher in each of the two most deprived IMD quintiles than in the any of the other three IMD quintiles for the total population and for each sex individually (Fig. 2a, Supplementary Table S2). A broadly similar pattern was seen for each age group, but these differences did not reach statistical significance in these (smaller sized) aged-based subgroups, except for the 25–44 group (Fig. 2b, Supplementary Table S2).

When looking at the incidence rates stratified by ethnicity and IMD (Fig. 3a and 3b), the incidence rates were significantly higher in all three South Asian ethnicities than in White (British/Other) or Black (African/Caribbean) ethnicities in each of the five IMD quintiles (Fig. 3a, Supplementary Table S3). There is limited evidence of the excess incidence in two most deprived quintiles when each ethnic group was analysed separately (Fig. 3a, Supplementary Table S3).

The negative binomial regression model results (Supplementary Table S4) were broadly similar: individuals from all three South Asian ethnicities had significantly higher incidence risk than individuals from White (British/Other), Black (African/Caribbean) or Other/Other Asian ethnicities, even after IMD was considered. Individuals from Black (African/Caribbean) and Other/Other Asian ethnicities both had higher incidence risk than individuals from White (British/Other) ethnicity. There is little evidence of a pattern in incidence by IMD quintile, once ethnicity was considered, except for the individuals from the second most deprived and the least deprived quintiles who had significantly higher incidence risk than individuals from the most deprived quintile. The interaction between ethnicity and IMD was found not to be statistically significant. All ethnicities, apart from White (British/Other) ethnicity, had the highest proportion of cases across three most deprived IMD quintiles, while White (British/Other) ethnicity had the highest proportion of cases across two least deprived IMD quintiles (Supplementary Table S5).

Travelling patterns

Most individuals of Indian or Pakistani ethnicity travelled during summer (July–September), whereas travel patterns for those reporting as White (British/Other) were consistent throughout the year (Fig. 4a and 4b). For total cases, the main purpose of travel was to visit family and relatives (VFR) ($n = 1135/1412$, 76%). Among individuals from Indian and Pakistani ethnicities, VFR was also the main reason to go abroad, while going on holiday was the main reason for individuals from White (British/Other) ethnicity (Supplementary Fig. S1a and S1b). Exact travel destinations by ethnicity have been previously described by UKHSA [20]. Before travelling abroad, 25.0% ($n = 395/1412$) individuals sought health advice, 19.7% ($n = 312/1412$) did not report whether they sought advice, and 55.3% ($n = 875/1412$) of individuals did not seek health advice (Supplementary Fig. 2a and 2b). Majority of individuals of Indian and Pakistani ethnicities did not seek health advice (57.5%, $n = 291/506$ and 62.6%, $n = 318/508$), while majority of individuals of White (British/Other) ethnicity did seek health advice pre-travel (51.4%, $n = 71/138$). The majority of travellers from all IMD quintiles mostly travelled to VFR. The proportion of individuals who did not seek health advice was greater in more deprived quintiles than in less deprived ones.

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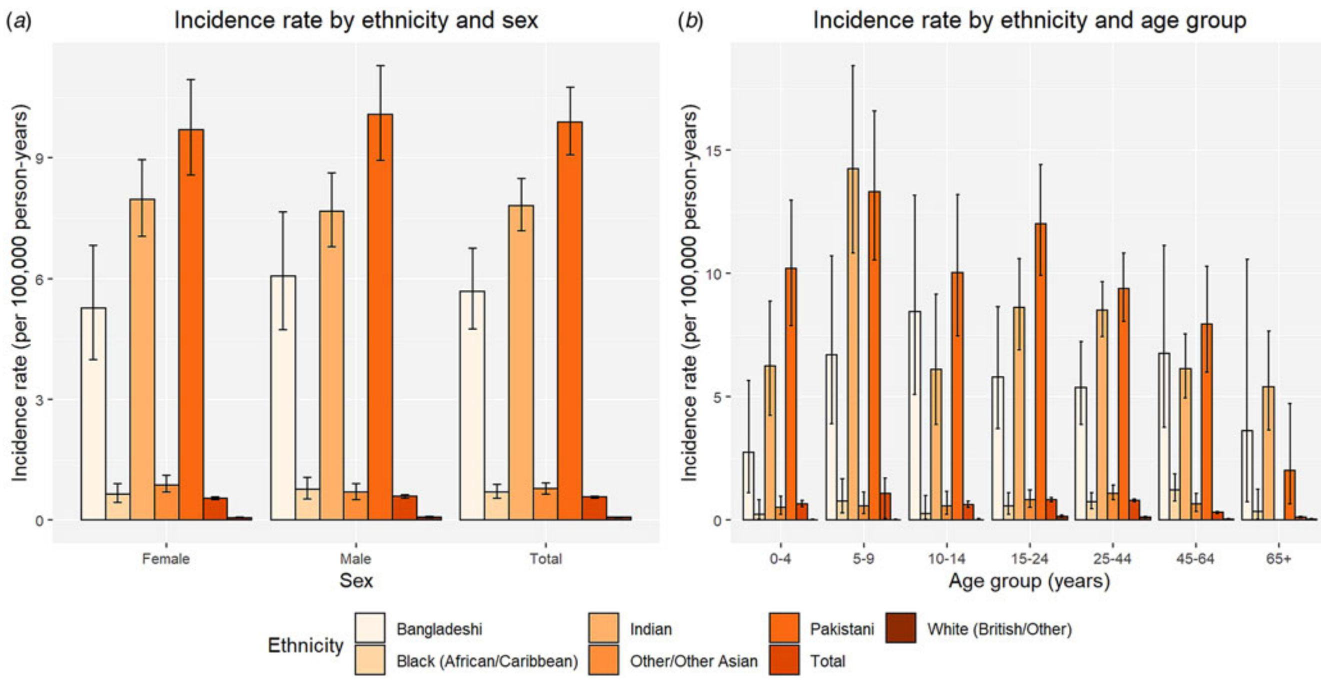

Fig. 1. Enteric fever incidence rates per 100 000 person-years described by ethnicity and sex (a) and ethnicity and age group (b) with 95% CIs calculated using Byar's method.

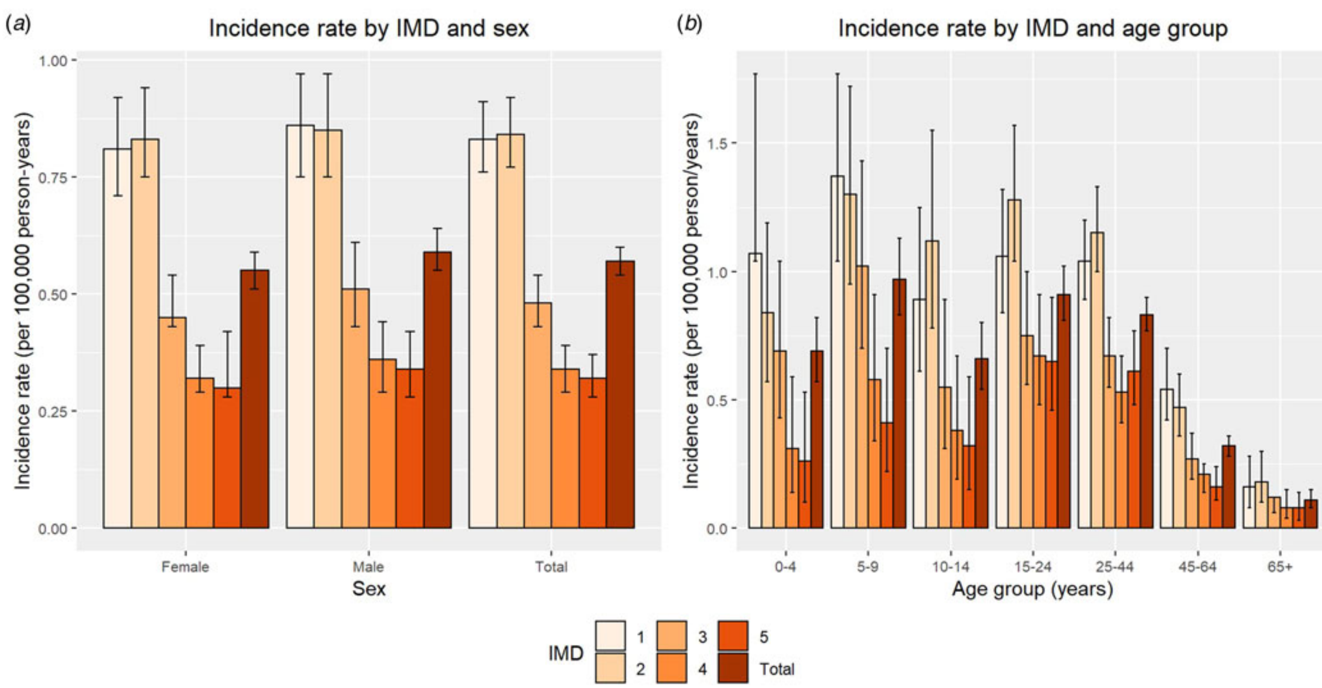

Fig. 2. Enteric fever incidence rates per 100 000 person-years described by IMD and sex (a) and IMD and age group (b) with 95% CIs calculated using Byar's method.

Association between ethnicity, IMD and admission to hospital, absence from school/work and symptom severity

The results of the fully adjusted (model 3) logistic regressions (Table 2) showed that individuals representing Pakistani (3.00, 95% CI 1.66–5.43), Indian (2.05, 95% CI 1.18–3.54) and Other/Other Asian (3.51, 95% CI 1.52–8.14) ethnicities had significantly higher odds of hospital admission than individuals representing White (British/Other) ethnicity, although all three groups had lower symptom severity scores (Table 3). There was no clear relationship between ethnicity and absence from school/work.

There was no clear pattern for hospital admissions nor symptom severity by IMD (Tables 2 and 3), although individuals from the second most deprived quintile had lower odds of hospital

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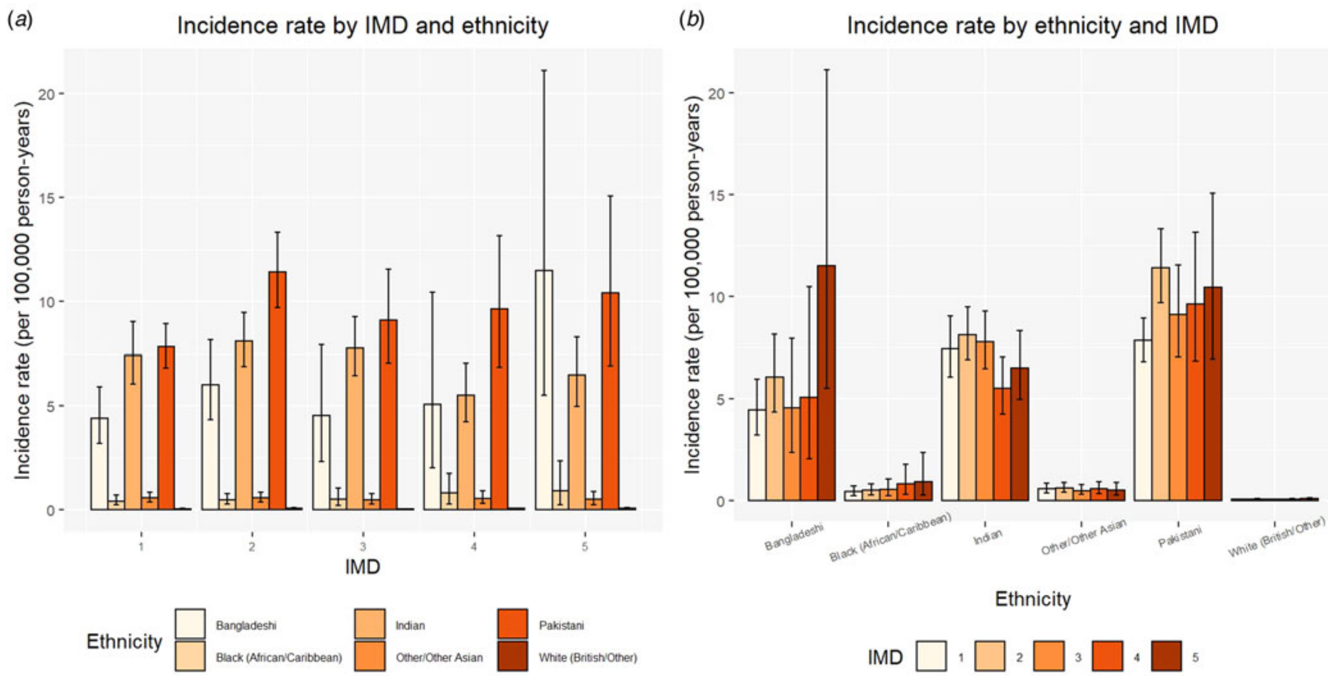

Fig. 3. Enteric fever incidence rates per 100 000 person-years described by ethnicity and IMD (a) and IMD and ethnicity (b) with 95% CIs calculated using Byar's method.

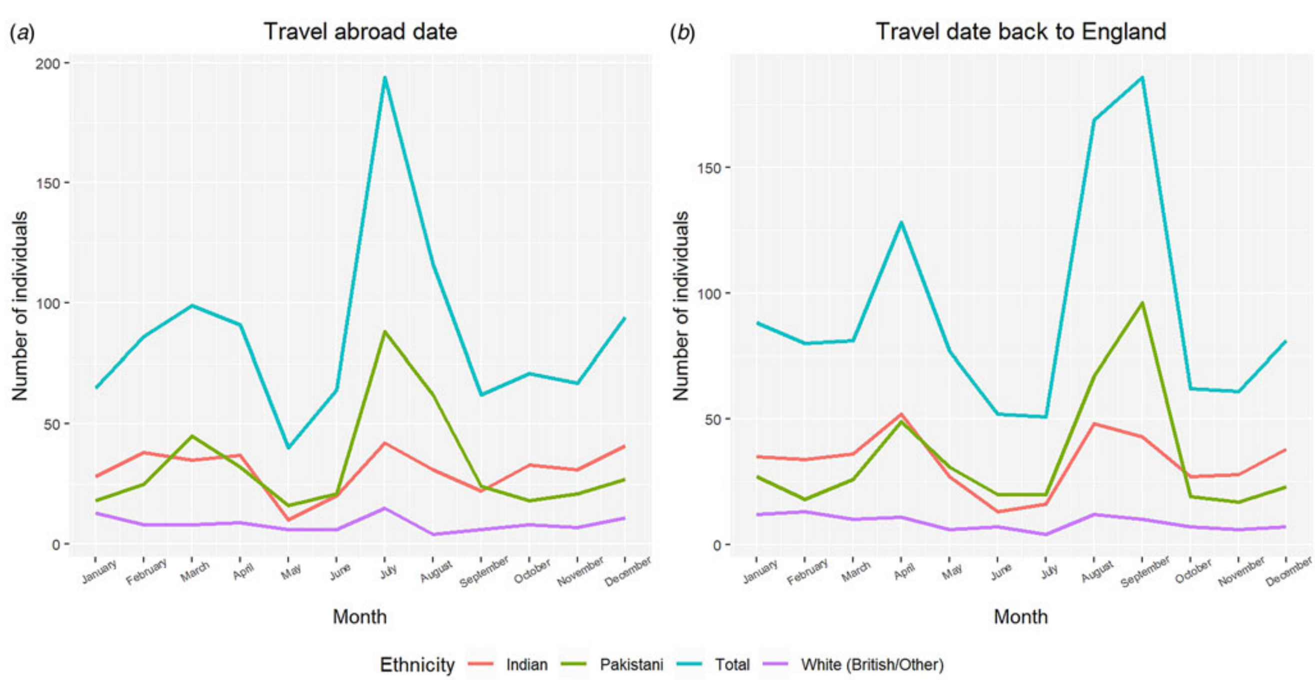

Fig. 4. Number of individuals travelling abroad (a) and coming back to England (b), grouped by month.

admission than individuals from the most deprived quintile (0.59, 95% CI 0.39–0.90). Individuals from the second least deprived quintile had lower odds of being absent from school/work than individuals from the most deprived quintile (0.56, 95% CI 0.33–0.96) (Table 4).

Females had lower odds of absence from school/work compared to males (0.68, 95% CI 0.49–0.93) (Table 4), although they had higher odds of higher symptom severity compared to males (1.29, 95% CI 1.06–1.57). Finally, *Salmonella* Paratyphi A cases had lower odds of hospital admission (0.60, 95% CI 0.42–0.83), as well as lower odds of high symptom severity (0.70, 95% CI 0.57–0.87), compared to *Salmonella* Typhi cases (Tables 2 and 3).

Ethnicity–travel abroad, IMD–residence and IMD–ethnicity interactions were not found to be statistically significant across

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Table 2. Binary and ordinal logistic regressions with ethnicity and IMD as explanatory variables and hospital admission as main outcome (n = 1412)

	Unadjusted model (explanatory variables only)		Model 1[a]		Model 2[b]		Model 3[c]	
Variable	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value
Outcome: hospital admission (n = 1412)								
Ethnicity								
White (British/Other)	Ref				Ref		Ref	
Bangladeshi	1.94 (1.04–3.64)	0.038*			1.97 (1.04–3.76)	0.039*	1.59 (0.78–3.26)	0.201
Pakistani	3.43 (2.10–5.62)	<0.001***			3.50 (2.09–5.88)	<0.001***	3.00 (1.66–5.43)	<0.001***
Indian	2.22 (1.41–3.51)	0.001**			2.43 (1.52–3.88)	<0.001***	2.05 (1.18–3.54)	0.011*
Black (African/Caribbean)	1.74 (0.76–3.97)	0.189			2.20 (0.94–5.16)	0.070	1.43 (0.57–3.62)	0.450
Other/Other Asian	3.92 (1.78–8.61)	0.001**			3.99 (1.79–8.89)	0.001**	3.51 (1.52–8.14)	0.003**
IMD quintile	Ref							
1 (most deprived)					Ref		Ref	
2	0.69 (0.46–1.02)	0.064			0.66 (0.44–0.98)	0.041*	0.59 (0.39–0.90)	0.015*
3	0.82 (0.51–1.32)	0.418			0.82 (0.51–1.32)	0.404	0.65 (0.40–1.08)	0.095
4	1.20 (0.68–2.14)	0.528			1.19 (0.67–2.14)	0.552	1.07 (0.58–1.99)	0.825
5 (least deprived)	0.79 (0.47–1.35)	0.394			0.76 (0.45–1.31)	0.327	0.69 (0.39–1.23)	0.206
Sex								
Male			Ref		Ref		Ref	
Female			0.92 (0.68–1.24)	0.575	0.90 (0.66–1.21)	0.483	0.95 (0.69–1.31)	0.757
Age								
25–44			Ref		Ref		Ref	
0–4			1.00 (0.55–1.81)	0.993	0.77 (0.42–1.42)	0.399	0.72 (0.37–1.39)	0.326
5–9			0.94 (0.57–1.56)	0.805	0.78 (0.47–1.32)	0.359	0.88 (0.50–1.53)	0.647
10–14			1.07 (0.57–2.02)	0.826	0.94 (0.49–1.79)	0.842	0.95 (0.48–1.88)	0.882
15–24			1.49 (0.94–2.38)	0.092	1.54 (0.96–2.49)	0.074	1.70 (1.03–2.83)	0.040*
45–64			0.50 (0.33–0.76)	0.001**	0.51 (0.33–0.77)	0.002**	0.50 (0.32–0.77)	0.002**
65+			0.52 (0.24–1.14)	0.100	0.63 (0.28–1.42)	0.268	0.61 (0.27–1.40)	0.242
Residence								
Urban							Ref	
Rural							1.52 (0.66–3.47)	0.322
Travel abroad							Ref	
No							0.68 (0.31–1.51)	0.347

Yes		
Antibiotic administration		
No	Ref	
Yes	16.15 (7.98–32.68)	<0.001***
Organism		
Salmonella Typhi	Ref	
Salmonella Paratyphi A	0.60 (0.42–0.83)	0.003**
Salmonella Paratyphi B	0.48 (0.22–1.07)	0.074

[a]Outcome, sex and age group included in the model.
[b]Outcome, explanatory variables, sex and age included in the model.
[c]Outcome, explanatory variables, sex, age, residence, travel abroad, antibiotic administration and organism included in the model.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

models with hospital admission, absence from school/work or symptom severity outcomes (Supplementary Table S6).

Sensitivity analysis

The sensitivity analysis using only cases who travelled abroad (Supplementary Table S7) provided very similar results to the main analysis. When inspecting the effect of additional confounders added to the model, we found that individuals travelling abroad for business (2.54, 95% CI 1.12–5.60) had higher odds of higher symptom severity compared to individuals travelling to VFR. Sensitivity analyses involving logistic regression with alternative severity score (Supplementary Table S8) did not find any additional associations and the results were very similar to the results of the main analysis.

Discussion

Analysis of the enteric fever surveillance data held by UK Health Security Agency (UKHSA) revealed that the highest incidence rate of infection was among the Pakistani community followed by other South Asian communities. Negative binomial regression analysis showed that there were relationships between both ethnicity and deprivation, but the stratified incidence rates calculations and multivariate analyses with disease severity outcomes suggest that the observed association with IMD can be explained by a differential distribution of ethnic groups by IMD quintile.

For all ethnic groups, the majority of cases were infected abroad, although travel details varied between the groups: those of Indian and Pakistani ethnicities were more likely to be VFR during the summer and were less likely to seek pre-travel advice. Although those of White (British/Other) ethnicity were more likely to report symptoms classed as severe, a higher proportion of individuals belonging to Indian and Pakistani ethnicities were more likely to be hospitalised.

Factors affecting incidence rate

There are no existing studies investigating the relationship between IMD, ethnicity and enteric fever incidence in the UK and Europe. However, a study from Kolkata, India, found that the individuals from the lowest socioeconomic class (highest deprivation) were at the highest risk of enteric fever infection [8]. However, the study was conducted in a lower-middle income country setting, which might not be comparable with data (mostly on travellers abroad) from England. A study conducted in Australia found that travelling to South Asia was associated with the highest crude incidence rate of typhoid among cases [21]. The results might be therefore caused by VFR group, which seemed to be the most vulnerable to typhoid fever in other studies too [22]. A systematic review investigating the safety of health care for ethnic minority patients across various high-income countries found that individuals representing ethnic minorities had an increased risk of safety events due to limited language proficiency, negative interactions with health professionals and specific beliefs about illness and treatment [23]. The same study found that ethnic minorities might also receive limited social support, have lower health literacy and have greater incidence of ill health. The study also reported that failure to provide qualified interpreting services to patients with poor English proficiency was a key contributor to poor health outcomes. Two studies conducted in England also suggested that South Asian ethnic groups had higher

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Table 3. Binary and ordinal logistic regressions with ethnicity and IMD as explanatory variables and symptom severity as main outcome ($n = 1412$)

	Unadjusted model (explanatory variables only)		Model 1[a]		Model 2[b]		Model 3[c]	
Variable	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value
Outcome: symptom severity ($n = 1412$)								
Ethnicity								
White (British/Other)	Ref				Ref		Ref	
Bangladeshi	0.65 (0.41–1.04)	0.075*			0.66 (0.41–1.06)	0.088	1.59 (0.78–3.26)	0.201
Pakistani	0.54 (0.37–0.78)	0.001**			0.54 (0.37–0.79)	0.002**	3.00 (1.66–5.43)	<0.001***
Indian	0.57 (0.40–0.81)	0.002**			0.57 (0.39– 0.82)	0.002**	2.05 (1.18–3.54)	0.011*
Black (African/Caribbean)	0.49 (0.26–0.92)	0.025*			0.52 (0.28–0.97)	0.041*	1.43 (0.57–3.62)	0.450
Other/Other Asian	0.59 (0.37–0.96)	0.035*			0.57 (0.35–0.93)	0.026*	3.51 (1.52–8.14)	0.003**
IMD quintile								
1	Ref				Ref		Ref	
2	0.90 (0.70–1.16)	0.406			0.86 (0.67–1.11)	0.251	0.59 (0.39–0.90)	0.015*
3	0.98 (0.73–1.33)	0.916			0.97 (0.72–1.32)	0.868	0.65 (0.40–1.08)	0.095
4	1.08 (0.76–1.53)	0.661			1.06 (0.75–1.50)	0.738	1.07 (0.58–1.99)	0.825
5	0.88 (0.62–1.25)	0.471			0.84 (0.59–1.20)	0.335	0.69 (0.39–1.23)	0.206
Sex								
Male			Ref		Ref		Ref	
Female			1.24 (1.02–1.51)	0.030*	1.26 (1.04–1.53)	0.021*	0.95 (0.69–1.31)	0.757
Age								
25–44			Ref		Ref		Ref	
0–4			0.40 (0.27–0.58)	<0.001***	0.42 (0.28–0.62)	<0.001***	0.72 (0.37–1.39)	0.326
5–9			0.91 (0.66–1.28)	0.601	0.97 (0.69–1.36)	0.867	0.88 (0.50–1.53)	0.647
10–14			0.73 (0.49–1.08)	0.118	0.76 (0.51–1.13)	0.177	0.95 (0.48–1.88)	0.882
15–24			1.11 (0.84–1.45)	0.467	1.09 (0.83–1.44)	0.522	1.70 (1.03–2.83)	0.040*
45–64			0.60 (0.44–0.81)	0.001**	0.59 (0.43–0.80)	0.001**	0.50 (0.32–0.77)	0.002**
65+			0.42 (0.23–0.78)	0.006**	0.38 (0.20–0.72)	0.003**	0.61 (0.27–1.40)	0.242
Residence								
Urban							Ref	
Rural							1.52 (0.66–3.47)	0.322
Travel abroad								
No							Ref	

Yes	1.14 (0.71–1.84)	0.597
Antibiotic administration		
No	Ref	
Yes	16.15 (7.98–32.68)	<0.001***
Organism		
Salmonella Typhi	Ref	
Salmonella Paratyphi A	0.60 (0.42–0.83)	0.003**
Salmonella Paratyphi B	0.48 (0.22–1.07)	0.074

[a]Outcome, sex and age group included in the model.
[b]Outcome, explanatory variables, sex and age included in the model.
[c]Outcome, explanatory variables, sex, age, residence, travel abroad, antibiotic administration and organism included in the model.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

rates of campylobacter compared to White individuals [24] and compared to non-Asian individuals [25].

Another factor affecting incidence rates was age: young individuals had higher incidence rate of enteric fever than the elderly. Similarly to our results, a study conducted in Australia found that higher risk of infection was also associated with younger age and being an immigrant returning to their country of birth [21]. Another retrospective study done in Copenhagen, Denmark, also found that patients presenting with typhoid fever in high-income countries were usually young adults of 40 years of age or younger [22] which would suggest that higher incidence rates in younger individuals reflect the epidemiology of enteric fever globally.

Severity of symptoms, hospitalisations and absence from school/work

Cases from the most deprived quintile were more likely to be admitted to the hospital than cases from the second most deprived quintile. A population-based study of Australian adults found that the prevalence rates of all GI symptoms tend to increase with decreasing social class [26]. Another study investigating total admissions from intestinal infectious disease in the UK (overwhelmingly not enteric fever) also found that individuals from lower socioeconomic status had higher rates of hospital admission. However, that might have been caused by increased symptom severity rather than increased infection risk [27]. A similar trend was seen in hospital admission among the most deprived groups in our study.

Indian, Pakistani and Other Asian/Other cases were more likely to be admitted to the hospital than White (British/Other) cases. However, Indian, Pakistani, Other Asian/Other and Black (African/Caribbean) cases had higher symptom severity scores than White (British/Other) cases. It is possible that the calculated symptom severity score underestimated true symptom severity: individuals representing ethnic minorities might have encountered language barrier while filling in the questionnaire in English and describing their symptoms as English might have not been their native language. It might also be because some individuals perceive symptom severity differently than the others, as previously shown with more deprived individuals [28]. Experience of pain activates stress-related physiological responses differently across various ethnic groups and different ethnic groups may show disparities in whether pain is seen as a clinical problem [29, 30]. We should also consider the fact that, in some cases, symptom onset was several weeks before completing the questionnaire. Recollection of symptoms might have therefore not been as vivid as it could have been if the time frame was shorter. Finally, we did not have information to assess whether the prevalence of other co-morbidities (that could affect the likelihood of hospital admission) varied by ethnicity.

A study investigating illness severity in Bangladesh, Nepal and Pakistan concluded that the high proportion of hospitalisations highlights illness severity [31]. However, this trend was not seen in our study. A study looking at symptom severity and sickness absence in people with infectious intestinal disease in the UK found that individuals of lower socioeconomic status were more likely to report severe symptoms and sickness absence [12] which was also not highlighted in our study. Interestingly, antibiotic administration was not correlated with symptom severity.

Although we did not find the association between ethnicity, deprivation and absence from school/work, previous research

Table 4. Binary and ordinal logistic regressions with ethnicity and IMD as explanatory variables and absence from school/work as main outcome ($n = 1020$)

	Unadjusted model (explanatory variables only)		Model 1[a]		Model 2[b]		Model 3[c]	
Variable	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value	Odds ratios (95% CI)	*P*-value
Outcome: absence from school/ work ($n = 1020$)								
Ethnicity								
White (British/Other)	Ref				Ref		Ref	
Bangladeshi	1.58 (0.75–3.34)	0.234			1.05 (0.48–2.30)	0.908	0.94 (0.41–2.14)	0.880
Pakistani	1.06 (0.63–1.78)	0.830			0.83 (0.48–1.45)	0.517	0.75 (0.41–1.37)	0.349
Indian	1.31 (0.79–2.20)	0.298			1.16 (0.67–1.99)	0.601	1.06 (0.58–1.93)	0.857
Black (African/Caribbean)	1.31 (0.48–3.57)	0.594			1.23 (0.44–3.48)	0.693	1.04 (0.35–3.04)	0.949
Other/Other Asian	1.71 (0.63–1.78)	0.830			1.45 (0.66–3.21)	0.358	1.47 (0.65–3.32)	0.353
IMD quintile								
1	Ref				Ref		Ref	
2	1.04 (0.70–1.56)	0.834			1.03 (0.68–1.57)	0.891	1.01 (0.66–1.54)	0.956
3	0.98 (0.60–1.58)	0.926			1.00 (0.60–1.66)	0.995	0.95 (0.57–1.58)	0.836
4	0.62 (0.37–1.02)	0.058			0.59 (0.35–1.00)	0.052	0.56 (0.33–0.96)	0.035*
5	0.83 (0.49–1.41)	0.492			0.77 (0.45–1.35)	0.365	0.73 (0.42–1.29)	0.277
Sex								
Male			Ref		Ref		Ref	
Female			0.68 (0.50–0.93)	0.016*	0.66 (0.48–0.91)	0.011*	0.68 (0.49–0.93)	0.018*
Age								
25–44			Ref		Ref		Ref	
0–4			0.29 (0.16–0.50)	<0.001***	0.29 (0.16–0.52)	<0.001***	0.29 (0.16–0.53)	<0.001***
5–9			2.78 (1.43–5.41)	0.003**	2.90 (1.47–5.69)	0.002**	3.09 (1.56–6.13)	0.001**
10–14			2.11 (0.98–4.58)	0.058	2.25 (1.03–4.91)	0.042*	2.33 (1.06–5.14)	0.035*
15–24			0.61 (0.41–0.91)	0.017*	0.65 (0.43–0.98)	0.039*	0.65 (0.43–0.98)	0.038*
45–64			0.63 (0.39–1.03)	0.063	0.64 (0.39–1.04)	0.070	0.62 (0.38–1.02)	0.057
65+			0.05 (0.01–0.19)	<0.001***	0.05 (0.01–0.18)	<0.001***	0.05 (0.01–0.18)	<0.001***
Residence								
Urban							Ref	
Rural							1.59 (0.65–3.87)	0.309

Travel abroad		
No	Ref	
Yes	1.08 (0.49–2.37)	0.854
Antibiotic administration		
No	Ref	
Yes	1.83 (0.80–4.21)	0.153
Organism		
Salmonella Typhi	Ref	
Salmonella Paratyphi A	0.82 (0.58–1.15)	0.257
Salmonella Paratyphi B	0.48 (0.21–1.12)	0.091

[a]Outcome, sex and age group included in the model.
[b]Outcome, explanatory variables, sex and age included in the model.
[c]Outcome, explanatory variables, sex, age, residence, travel abroad, antibiotic administration and organism included in the model.
$*P<0.05$, $**P<0.01$, $***P<0.001$.

suggests that high sickness absence correlates with lower socioeconomic status (higher deprivation) [32]. West Indians and Asians also had more work absence in a study done in South-east England [33]. Sickness absence can be due to differences in health, job satisfaction, social benefits, pain perception and working conditions [32–34] which we did not account for.

Seasonality and health advice

There were seasonal travel patterns in total travellers and individuals who were Pakistani or Indian with summertime being the key travelling season. Those results might be correlated with summer holidays and with weather changes. In a study done in Bangladesh, the highest number of enteric fever cases correlated with warmer weather, autumn and rainy season [35]. A study investigating global seasonal dynamics of typhoid and paratyphoid fevers found that among settings located 35°–11°N, the peak number of enteric fever cases occurs between May and October, which coincides with the monsoon season in many Asian countries [36]. The monsoon season is linked with excessive rainfall which often causes flooding, a risk factor of enteric fever due to mixing of drinking-water sources with open sewers that contain faecal matter [37].

Three-quarters of enteric fever cases occurred in individuals travelling to VFR. Less than a third of cases sought health advice before travelling. A study investigating the health advice-seeking behaviours among international travellers departing from Boston Logan International Airport found that 46% of travellers to low- and middle-income countries also did not seek health advice prior to their trip, mostly due to a lack of concern about health issues related to travel [36].

Strengths and limitations

One of the strengths of the study is the fact that a national surveillance questionnaire was used which is the most comprehensive database of enteric fever cases in England and one of the most comprehensive databases of enteric fever globally. Additionally, this is the first study to explore the social and demographic patterning of risk factors for enteric fever in England.

The conducted study was observational therefore causality could not be assessed. The total number of cases are likely to be under-estimated as not all cases are diagnosed (especially among asymptomatic individuals who might not be aware of their acquired infection), and this may vary by ethnicity and deprivation.

The validity of the results also depended upon the unbiased self-reporting of symptoms and sickness absence among cases. Moreover, several fields, such as ethnicity, admission to the hospital or absence from school/work, had data missing which could have affected the results. The questionnaire data did not contain information on total population by ethnicity and IMD; therefore, while fitting a negative binomial model, a different dataset was used, which in turn did not provide information on additional confounders, such as age or sex, which could have impacted the results.

It is also possible that IMD is on the causal pathway between ethnicity and enteric fever in England. Previous research done in the USA suggests that race/ethnicity influences socioeconomic status: in our study we also found that cases representing White (British/Other) ethnicity were present mostly in two least deprived quintiles while cases from all other ethnicities were present mostly in the most deprived quintiles. Adjusting for social class in racial/ethnic comparisons might therefore be an example of misspecification of the intermediates that biases estimates of total effect and leads to overadjustment bias [38].

Recommendations

The study highlights the need for better pre-travel counselling: the finding that only a third of cases received health pre-travel advice would appear to be a key area for improvement. Awareness of the need for travel advice needs to be improved through ethnicity-appropriate health promotion services. Travel health services should be made accessible to these groups. Our results suggest that the Pakistani group may be a particularly high priority group, that there should be advice specific to VFRs to the Indian subcontinent, and that pre-summer is likely to be the most effective time for re-enforcing prevention efforts. Travel advice should also reduce the risk of other diseases associated with travel to the Indian subcontinent, such as malaria and hepatitis. Pre-travel vaccination should also be promoted between July–September: there is evidence that non-vaccinated travellers returning from abroad were 10–11 times more likely to develop typhoid, compared to those who received their vaccine prior to travelling [22]. Previous studies have shown that foreign-born immigrants in the USA were willing to get vaccinated against typhoid fever. The trend was seen especially among younger respondents [39].

Enteric fever should also be considered in young febrile adults returning from a VFR-trip to the Indian subcontinent and more attention should be given to individuals living in deprived regions and of Pakistani, Indian and Bangladeshi ethnicities.

It would also be insightful to expand the fields covered by the enhanced surveillance of enteric fever questionnaire to identify more factors related to increased risk of enteric fever in England. Additional questions regarding travel itinerary (such as travel accommodation, activities done while travelling) would be particularly useful. Additionally, an improved system to measure symptom severity has to be established as it seems that individuals representing specific ethnicities/IMD quintiles might describe their symptoms differently.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0950268822001959.

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Author contributions. LB and MB conceptualised and designed the study. LB and CJ were responsible for supervision. MB was responsible for investigation, validation and formal analysis. HK and PK were responsible for data curation. MB was responsible for writing the original draft. JH was responsible for funding acquisition. MB, CJ, DH, JH, PK, HK and LB edited the manuscript. All authors read and approved the final manuscript.

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Ethical standards. No identifiable data were used in this study; therefore, ethical approval was not required. No new data were collected, and no data left the UKHSA NIS Gastrointestinal Infections team at Colindale.

Data availability. The data that support the findings of this study are available from UKHSA, but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Aggregated data are, however, available from the authors upon reasonable request and with the permission of UKHSA.

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