General practice

Study of infectious intestinal disease in England: rates in the community, presenting to general practice, and reported to national surveillance

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Abstract

Objective To establish the incidence and aetiology of infectious intestinal disease in the community and presenting to general practitioners. Comparison with incidence and aetiology of cases reaching national laboratory based surveillance.

Design Population based community cohort incidence study, general practice based incidence studies, and case linkage to national laboratory surveillance.

Setting 70 general practices throughout England.

Participants 459 975 patients served by the practices. Community surveillance of 9776 randomly selected patients.

Main outcome measures Incidence of infectious intestinal disease in community and reported to general practice.

Results 781 cases were identified in the community cohort, giving an incidence of 19.4/100 person years (95% confidence interval 18.1 to 20.8). 8770 cases presented to general practice (3.3/100 person years (2.94 to 3.75)). One case was reported to national surveillance for every 1.4 laboratory identifications, 6.2 stools sent for laboratory investigation, 23 cases presenting to general practice, and 136 community cases. The ratio of cases in the community to cases reaching national surveillance was lower for bacterial pathogens (salmonella 3.2:1, campylobacter 7.6:1) than for viruses (rotavirus 35:1, small round structured viruses 1562:1). There were many cases for which no organism was identified.

Conclusions Infectious intestinal disease occurs in 1 in 5 people each year, of whom 1 in 6 presents to a general practitioner. The proportion of cases not recorded by national laboratory surveillance is large and varies widely by microorganism. Ways of supplementing the national laboratory surveillance system for infectious intestinal diseases should be considered.

Introduction

Infectious intestinal disease causes substantial morbidity and economic loss in the United Kingdom and is responsible for over 300 deaths and 35 000 hospital admissions annually in England and Wales. [1] [2] Food poisoning notifications and laboratory reports of pathogens responsible for infectious intestinal disease have been rising since the early 1980s, and public awareness has risen following several large outbreaks, culminating in 1996 in the outbreak of *Escherichia coli* O157 infection in Scotland. [3] However, infectious intestinal disease can arise from various sources, of which food is only one.

The national surveillance system provides information about trends in incidence and outbreaks of infectious intestinal disease. [4] [5] Sources of data include voluntary reporting of organisms identified by public health and other diagnostic microbiology laboratories and reports of general outbreaks of infectious intestinal disease. The Public Health Laboratory Service Communicable Disease Surveillance Centre collates these data. National surveillance inevitably underestimates disease occurring in the community and seen in primary care. Many people do not seek medical attention, and of those that do only a proportion will have a stool specimen submitted for investigation. Not all of these stools will yield a pathogen, and not all pathogens identified are reported to the Communicable Disease Surveillance Centre. Because presentation rates and the sensitivity of laboratory identification vary according to the pathogen, the spectrum of pathogens reaching national surveillance may be different from that causing disease in the community. National surveillance data may also overestimate the proportion of cases in certain age groups or those who are part of outbreaks.

We studied the incidence and aetiology of cases of infectious intestinal disease presenting to general practitioners and in the community and how these related to national surveillance (laboratory reports). The study does not address under-reporting of food poisoning through statutory notifications.

Participants and methods

The methods have been described in full elsewhere. [6] The study was set in 70 general practices serving a total

population of 459 975. The practices were volunteers selected from the Medical Research Council's general practice research framework to meet specific criteria. Criteria were chosen to make the sample representative of all general practices nationally with respect to geographical location, urban and rural characteristics, and social deprivation index.[6] Practice recruitment was staggered over 18 months, and each practice participated for a complete year. Data were collected between 1993 and 1996. Approval was obtained from the Royal College of General Practitioners, participating research bodies, and all local research ethics committees.

The study estimated the incidence of infectious intestinal disease at five levels (community case, case presented to general practitioner, stool sent for test, positive test result, and reported to national surveillance).

Community cohort

We selected at random 200 people of all ages from each practice list by obtaining computer files of the age-sex registers and running a random selection program which stratified by age and sex. All those selected were invited to participate by letter and telephone. People who agreed to participate returned weekly postcards for six months declaring the absence of symptoms. Those with symptoms sent a stool specimen from home to Leeds Public Health Laboratory; the case definition is described elsewhere.[6] A second cohort was recruited for another six months.

Each cohort member was asked, on recruitment, to recall episodes of diarrhoea in the previous month to provide a retrospective estimate of the incidence of infectious intestinal disease.

General practice incidence study

All cases of infectious intestinal disease presenting to general practitioner were eligible. The practice research nurse recorded details on each case. Patients of all ages were included. Each practice was randomly allocated to one of two arms. In the first arm general practitioners asked all patients to provide a stool specimen for investigation at Leeds Public Health Laboratory (34 practices). In the enumeration arm the doctors' decision to request stool testing locally was observed without intervention (36 practices). Patients in the enumeration arm who had positive stool samples were sought in the national surveillance database by using names, dates of birth, and laboratory reference numbers.

Stool investigations

Stools were tested at Leeds Public Health Laboratory and public health laboratory service reference laboratories for a wide range of target organisms and bacterial toxins (table 1). Investigations were generally more extensive than those used in routine diagnostic laboratories. Selective and enrichment culture techniques were used for bacteria, except enterovirulent *E coli*, which were detected by DNA probes. Microscopy was used for protozoa and helminths and electron microscopy and commercial enzyme linked immunosorbent assays (ELISA) for detection of viruses. Microbiological methods are detailed elsewhere.[5] [7]

Statistical analysis

We calculated the incidence in the community using the number of person weeks of follow up of the two consecutive cohorts as the denominator and the incident cases as the numerator. Data were excluded from analysis if follow up infromation was incomplete. In the general practice component the denominator was the practice population adjusted for list inflation and combined with the exact period of practice participation (generally one year). Estimates of list inflation were derived from the community cohort study sampling frames, where the proportion of patients invited to participate who had died or moved away was recorded.[6] The numerator was the number of cases presenting to the general practitioner adjusted for suspected underascertainment—that is, failure to report a case. We conducted a detailed study of underascertainment to estimate the size of this adjustment. A researcher independently visited half the practices and compared computerised diagnostic records with case ascertainment details from the general practice incidence study.[8]

Organism specific incidences were based on cases for which a stool specimen was submitted to Leeds Public Health Laboratory. We assumed that the cases for which no stool sample was sent would have a similar distribution of organisms. Compliance data are presented elsewhere.[6] The organisms chosen for subanalysis were two bacteria (salmonella and campylobacter) and two viruses (rotavirus and small round structured virus) known to be important from surveillance and shown in our study to be common.

Statistical analysis was conducted with Stata software.[9] We calculated confidence intervals using the Poisson distribution with a random effects term for disease clustering within practices.[10] The ratios of the estimated incidence at each level were used to construct the reporting pyramid. Precise statistical confidence intervals for the ratios could not be calculated because of unquantifiable dependence between levels. Instead, sensitivity bounds were formed with similar calculations on the upper or lower 95% confidence limits of the rate ratios. The proportion of stools sent to the laboratory could not be estimated in organism specific reporting pyramids because the denominator of this proportion would require a knowledge of organisms in stools not tested.

Results

Community incidence

A total of 9776 people were recruited to the cohort (average of 140 in each practice) with a total follow up of 4026 person years. The response rate was 40% (9776 of the 24 399 invited; follow up information complete for 9296), and 82% (7623) of participants returned over 22 of the 26 weekly postcards. We ascertained 781 cases of infectious intestinal disease, an incidence of 19.4/100 person years (95% confidence interval 18.1 to 20.8) (table 1).

The retrospective estimate of reported diarrhoea in the month before recruitment to the cohort was 564/8674 (6.5%, 95% confidence interval 6.0% to 7.0%). Assuming independence of episodes from month to month extrapolation from this figure gives a rate of 55/100 person years, nearly three times the prospective estimate.

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Table 1 Incidence of infectious intestinal disease in community and reported to general practice by organism

	Community		General practice		
	No of cases*	Rate/1000 person years (95% CI)	No of cases	Rate/1000 person years (95% CI)	No of community cases/ GP case (95% CI)
Bacteria:					
Aeromonas spp	46	12.4 (9.4 to 16.7)	165	1.88 (1.48 to 2.37)	6.7 (4.9 to 9.1)
Bacillus spp (>10⁴/g)	0	0	4	0.05 (0.01 to 0.15)	—
Campylobacter spp	32	8.7 (6.1 to 12.3)	354	4.14 (3.34 to 5.13)	2.1 (1.5 to 3.0)
Clostridium difficile cytotoxin	6	1.6 (0.7 to 3.6)	17	0.20 (0.12 to 0.31)	8.0 (3.4 to 19.3)
Clostridium perfringens enterotoxin	9	2.4 (1.3 to 4.7)	114	1.30 (1.04 to 1.68)	1.9 (0.97 to 3.7)
E coli O157	0	0	3	0.03 (0.01 to 0.11)	—
E coli DNA probes:					
Attaching and effacing	20	5.4 (3.5 to 8.4)	119	1.32 (1.10 to 1.62)	4.1 (2.6 to 6.5)
Diffusely adherent	23	6.2 (4.2 to 9.4)	103	1.18 (0.92 to 1.52)	5.3 (3.4 to 8.2)
Enteroaggregative	18	4.9 (3.1 to 7.8)	141	1.62 (1.30 to 2.03)	3.0 (1.9 to 4.9)
Enteroinvasive	0	0	0	0	—
Enteropathogenic	1	0.27 (0.04 to 1.9)	4	0.05 (0.01 to 0.15)	5.4 (0.8 to 55.7)
Enterotoxigenic	10	2.7 (1.5 to 5.0)	52	0.59 (0.44 to 0.81)	4.6 (2.4 to 8.9)
Verocytotoxigenic (non-O157)	3	0.82 (0.26 to 2.5)	6	0.06 (0.02 to 0.17)	13.4 (3.6 to 49.6)
Salmonella spp	8	2.2 (1.1 to 4.3)	146	1.57 (1.19 to 2.06)	1.4 (0.7 to 2.8)
Shigella spp	1	0.27 (0.04 to 1.9)	23	0.27 (0.16 to 0.47)	1.0 (0.13 to 7.3)
Staphylococcus aureus (>10⁶/g)	1	0.27 (0.04 to 1.9)	10	0.11 (0.05 to 0.23)	2.5 (0.33 to 19.0)
Vibrio spp	0	0	1	0.01 (0.001 to 0.05)	—
Yersinia spp	25	6.8 (4.6 to 10.0)	51	0.58 (0.42 to 0.88)	11.7 (7.5 to 18.3)
Protozoa:					
Cryptosporidium parvum	3	0.81 (0.26 to 2.5)	39	0.43 (0.29 to 0.61)	1.9 (0.60 to 6.1)
Giardia intestinalis	2	0.54 (0.14 to 2.2)	28	0.28 (0.17 to 0.46)	1.9 (0.46 to 7.9)
Viruses:					
Adenovirus group F	11	3.0 (1.7 to 5.4)	81	0.88 (0.69 to 1.13)	3.4 (1.8 to 6.3)
Astrovirus	14	3.8 (2.3 to 6.4)	77	0.86 (0.67 to 1.13)	4.4 (2.5 to 7.6)
Calicivirus	8	2.2 (1.1 to 4.3)	40	0.43 (0.27 to 0.60)	5.1 (2.4 to 10.7)
Rotavirus group A	26	7.1 (4.8 to 10.4)	208	2.30 (1.80 to 2.94)	3.1 (2.1 to 4.6)
Rotavirus group C	2	0.54 (0.14 to 2.2)	6	0.06 (0.02 to 0.17)	8.9 (1.9 to 41.3)
Small round structured viruses	46	12.5 (9.4 to 16.7)	169	1.99 (1.45 to 2.73)	6.3 (4.6 to 8.6)
No organism identified	432	117.3 (107 to 129)	1305	14.82 (12.78 to 17.20)	7.9 (7.1 to 8.8)
Total	781	194 (181 to 208)	8770†	33.1 (29.4 to 37.5)	5.8 (5.4 to 6.3)

*Excluding cases where individual follow up was not known.

†Total cases are greater than the sum of individual organisms due to cases for which a stool sample was not sent for testing. The general practice total includes cases from the enumeration arm, for which full stool testing was not carried out.

General practice incidence

We ascertained 8770 cases presenting to general practitioners, a rate of 3.3/100 person years (2.94 to 3.75) after list inflation and underascertainment were corrected for. The uncorrected figure was 1.91 (1.70 to 2.14).

In the enumeration arm 4747 cases were ascertained. In 1262 (27%) cases stools were requested by the general practitioner (practice interquartile range 13%-36%). Pathogens were identified by the routine laboratory in 300/1262 (24%) of these cases (table 2), of which 208 (69%) were reported to national surveillance. Most were infections with campylobacter or salmonella.

The ratio of community incidence to general practice presentation rates was 5.8, suggesting that for every case presenting to general practice there are almost five more cases in the community. This ratio was high for cases associated with non-O157 verocytotoxin producing *E coli*, yersinia, rotavirus group C, *Clostridium difficile* cytotoxin, aeromonas, and small round structured viruses and for cases where no target organism was identified, although the confidence intervals were wide for *E coli* and rotavirus group C. In contrast, the ratio was lower for salmonella and shigella, suggesting that most people with these infections present to their general practitioner. Confidence intervals were wide for shigella.

Table 3 gives the reporting pyramids. For every isolate reported to the national surveillance scheme there were 1.4 positive laboratory results, 6.2 stools submitted to laboratories, 23 cases presenting to the

Table 2 Positive laboratory findings in stools sent for examination by general practitioners in enumeration arm and proportion reported to national surveillance*

Organism	No of laboratory positive cases	No (%)* reported to national surveillance	95% CI (%)
Bacteria:			
Aeromonas	3	0	
Campylobacter	148	94 (64)	56 to 71
E coli O157	1	1	
E coli (other)	3	3	
Salmonella	78	63 (81)	70 to 89
Shigella	13	10 (77)	46 to 95
Protozoa:			
Cryptosporidium	16	11 (69)	41 to 89
Giardia	4	3	
Viruses:			
Adenovirus	4	2	
Astrovirus	1	1	
Rotavirus	28	19 (68)	48 to 84
Small round structured virus	1	1	
Total	300	208 (69)	64 to 75

*Percentages given only where at least 10 cases.

Table 3 Reporting pyramids

	Community	Presenting to general practice	Stools sent for routine laboratory test*	Positive by routine laboratory test†	Reported to national surveillance
All infectious intestinal disease					
Rate per 1000 person years (95% CI)	194 (181 to 208)	33.1 (29.4 to 37.5)	8.8 (8.3 to 9.3)	2.1 (1.9 to 2.4)	1.5 (1.3 to 1.7)
Ratio to next column (95% CI)	5.8 (5.4 to 6.3)	3.8 (3.6 to 4.0)	4.3 (3.8 to 4.7)	1.4 (1.3 to 1.7)	
Ratio to final column (sensitivity bound)	136 (93 to 197)	23.2 (17.3 to 31.2)	6.2 (4.8 to 7.8)	1.4 (1.3 to 1.7)	1.0
% of community disease reported		17.1	4.5	1.1	0.7
Campylobacter					
Rate per 1000 person years (95% CI)	8.7 (6.1 to 12.3)	4.1 (3.3 to 5.1)		1.7 (1.4 to 2.0)	1.1 (0.9 to 1.3)
Ratio to next column (95% CI)	2.1 (1.5 to 3.0)	2.4 (2.0 to 2.9)		1.5 (1.2 to 2.0)	
Ratio to final column (sensitivity bound)	7.6 (3.6 to 17.4)	3.6 (2.4 to 5.8)		1.5 (1.2 to 2.0)	1.0
% of community disease reported		47.1		19.5	7.9
Salmonella					
Rate per 1000 person years (95% CI)	2.2 (1.1 to 4.3)	1.6 (1.2 to 2.1)		0.8 (0.7 to 1.0)	0.7 (0.5 to 0.9)
Ratio to next column (95% CI)	1.4 (1.0 to 2.8)	1.9 (1.4 to 2.5)		1.2 (1.0 to 1.7)	
Ratio to final column (sensitivity bound)	3.2 (1.4 to 12.0)	2.3 (1.4 to 4.3)		1.2 (1.0 to 1.7)	1.0
% of community disease reported		72.7		36.4	31.8
Rotavirus					
Rate per 1000 person years (95% CI)	7.1 (4.8 to 10.4)	2.3 (1.8 to 2.9)		0.3 (0.2 to 0.5)	0.21 (0.13 to 0.34)
Ratio to next column (95% CI)	3.1 (2.1 to 4.6)	7.5 (5.1 to 11.2)		1.5 (1.0 to 2.6)	
Ratio to final column (sensitivity bound)	35.0 (10.7 to 133.9)	11.3 (5.1 to 29.1)		1.5 (1.0 to 2.6)	1.0
% of community disease reported		32.4		4.2	3.0
Small round structured viruses					
Rate per 1000 person years (95% CI)	12.5 (9.4 to 16.7)	1.99 (1.5 to 2.7)		0.012 (0.003 to 0.09)	0.012 (0.003 to 0.09)
Ratio to next column (95% CI)	6.3 (4.6 to 8.6)	172.0 (24.1 to 1228)		1.4 (1.3 to 1.7)	
Ratio to final column (sensitivity bound)	1562 (140 to 17 424)	248 (30.4 to 2026)		1.4 (1.3 to 1.7)	1.0
% of community disease reported		15.9		0.9	0.06

*The proportion of stools sent for routine laboratory tests cannot be estimated for individual microbiological organisms.

†Ratio of number of positive for small round structured virus to number reported to national surveillance is assumed the same as for all infectious intestinal disease.

general practitioner, and 136 cases in the community. Among the organisms examined, this ratio was low for salmonella (3.2:1) and campylobacter (7.6:1) but much higher for the viruses (35:1 for rotavirus and 1562:1 for small round structured viruses). For small round structured viruses there was considerable statistical uncertainty in this ratio.

Discussion

Community rates
This study establishes the incidence of infectious intestinal disease in a large, representative population in England. We found that 1 in 5 people in the general population develop such disease each year, an estimated 9.4 million cases in England annually. Earlier studies in North America[11–13] found higher community rates but were family based and may reflect higher rates in children and parents compared with other groups. Although case definitions vary, our result is similar to that found in a recent Dutch study[14] but lower than those of other studies in England and Wales.[15 16]

The other British studies were based on recall rather than prospective follow up. We found much higher rates from retrospective assessment, probably because of recall bias—that is, the tendency to "telescope" illness events into the recent past. We believe the prospective, negative reporting method that we used did not underestimate incidence for two reasons: firstly, completeness of follow up was good,[6] and, secondly, participants were unlikely to send a postcard denying symptoms if they had them. Although the recruitment rate was not high (40%), partly due to difficulties in contacting people on practice lists, it was comparable with that in similar studies.[14] Moreover our cohort was large and broadly represented the national population in terms of age, sex, and social class.[6]

General practice rates
About 1 in 30 patients presented to their general practitioner with infectious intestinal disease in a year. The rate is similar to those reported in single practice studies in England,[17 18] a recent study in four practices in Wales,[16] and estimates derived from the Royal College of General Practitioners sentinel surveillance scheme.[19]

The study population was representative of the national population with respect to age, sex, geographical areas and urban and rural composition, but slightly underrepresented areas of low social deprivation.[11] We corrected for variable levels of list inflation using data from the cohort, and our overall estimate of 10% was similar to previous estimates.[20] We are confident that our correction for underascertainment of cases by general practitioners, although large, was accurate as it was derived from a detailed study of computerised records based in half the study practices.[8]

Reporting pyramid
We estimated that for every case detected by national laboratory surveillance, there are 136 in the community. One potential bias in this estimate is that we could not ensure that our sample contained a representative number of outbreaks. Outbreaks may have been underrepresented in the community sample because we excluded residential homes, prisons, universities, and long stay hospitals—sites where outbreaks are shown to occur.[21] We did, however, include schools. However, general outbreaks constitute less than 10% of laboratory reports of salmonella and less than 1% of reports of campylobacter.[22]

Key messages

- Infectious intestinal disease is common, with 9.4 million estimated cases each year in England

- In 1.5 million cases (1 in 6) patients present to their general practitioner

- Only a fraction of these cases are reported to national laboratory surveillance

- A greater proportion of cases due to common bacterial pathogens are reported than cases due to common viral pathogens

- Ways of supplementing the national laboratory surveillance system for infectious intestinal diseases should be considered

In conclusion, this study shows that the scale of infectious intestinal disease in England is large, with an estimated 9.4 million cases occurring in the community annually, and 1.5 million cases presenting to general practitioners. Greater understanding is needed of the risk factors to guide preventive strategies. The spectrum of microbiological agents in the population differs from that found in surveillance data. Surveillance figures for important bacterial pathogens that cause food poisoning, such as campylobacter and salmonella, are more representative of community rates than surveillance figures for common viruses. Methods of supplementing the national surveillance system for infectious intestinal diseases should be considered.

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A memorable patient
You can but try

He was old and very ill. He was one of those patients who becomes etched in the mind of a young and enthusiastic house officer working in a busy medical ward. He was admitted in the end stages of severe pulmonary hypertension having coped alone at home for many months. Now he had to accept the help of others in the final stages of his life. His ankles were grossly swollen and seeped fluid like sap from an ageing tree. He became as breathless as a marathon runner on walking the short distance to the nursing station. The rancorous smell in his room gave the impression of one who was already partly dead.

In the turmoil of admission to hospital his spectacles had been broken and he was rendered virtually sightless. My repeated attempts to get a new pair of glasses met with no success. Was it really worth while making them for someone who would be gone in a few weeks, inquired the optician. After all there was a six week waiting list.

Failing to restore his vision, I thought that I had to try to do something to improve his last few weeks of life. "Could we at least try and contact any remaining members of his family?" I asked.

"All dead," he stated matter of factly. "What all of them?" I inquired. "All," he replied.

Several weeks later as I was leaving his room after venesecting yet another quart of blood in an attempt to relieve his breathlessness, he mused, "There is a brother somewhere, America I think."

At last I thought I could do something for him in his twilight days. He stared a while and then reaffirmed, "Yes, definitely America."

It emerged that his brother had been working as a riveter in a ship. He had secured employment in the bowels of the vessel, stoking the furnaces, when it was launched a long time ago. Right, I would try to contact him or his family. There must be some way, someone would know. His name was quite unusual, after all.

Which ship, how long ago, which city did he go to in America?

An elderly neighbour provided the answers. This was Belfast, the year had been 1912 and the ship had been the *Titanic*.

You can but try.

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