A Report of the Study of Infectious Intestinal Disease in England

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London: The Stationery Office

Published with the permission of Food Standards Agency
on behalf of the Controller of Her Majesty's Stationery Office.

First published 2000

ISBN 0 11 322308 0

Printed in the United Kingdom for The Stationery Office.
TJ c10 11/00

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Abbreviations

This list is intended as an aid to reading the main text; definitions are given in the Glossary.

ACDP	Advisory Committee on Dangerous Pathogens
ACMSF	Advisory Committee on the Microbiological Safety of Food
AEEC	Attaching and effacing *E.coli*
CDSC	Communicable Disease Surveillance Centre of the Public Health Laboratory Service
CI	The Confidence Interval of a range of values
D	D-Value
DAEC	Diffusely adherent *E.coli*
DoH	Department of Health
DNA	Deoxyribonucleic acid
DoE	Department of the Environment
E.coli	*Escherichia coli*
EAggEC	Enteroaggregative *E.coli*
EHEC	Enterohaemorrhagic *E.coli*
EIEC	Enteroinvasive *E.coli*
ELISA	Enzyme-linked Immunosorbent Assay
EPEC	Enteropathogenic *E.coli*
ETEC	Enterotoxigenic *E.coli*
GPRF	General Practitioners' Research Framework
IID	Infectious intestinal disease
HACCP	Hazard analysis critical control point system
HUS	Haemolytic uraemic syndrome
Ig	Immunoglobulin, as in IgG, IgA, IgM
LPS	Lipopolysaccharide
MAFF	Ministry of Agriculture, Fisheries and Food
MID	Minimum infective dose
OPCS	Office of Population Censuses and Surveys
P	Probability value
pH	Index of acidity or alkalinity
PHLS	Public Health Laboratory Service
PCR	Polymerase chain reaction
R-TYPE	Antibiotic resistance type
RA	Risk assessment
SLTEC	Shiga-like toxin-producing *E.coli*
SRSV	Small Round Structured Virus
TTP	Thrombotic Thrombocytopaenia Purpura
VTEC	Verocytotoxin-producing *E.coli*
A_W	Water activity
WG	Working group

Chapter 1
Executive Summary

1.1 BACKGROUND

In 1989, in response to national epidemics of foodborne infection with *Salmonella enteritidis* phage type 4 and *Listeria monocytogenes*, the Secretary of State for Health and Minister of Agriculture, Fisheries and Food set up the Committee on the Microbiological Safety of Food, under the chairmanship of Professor Mark Richmond. This Committee recommended

> 'a study of the incidence of infectious intestinal disease based on GP consultations in which microbiological confirmation of the clinical diagnosis is carried out'

and that:

> 'the true incidence of infectious intestinal disease in the community needs to be ascertained. Thus we also recommend that a study including microbiological screening should be set up to provide information of the incidence of gastrointestinal illness in the community that can be linked to a microbiological cause. This should take place, if possible, in the same areas as the GP-based study'

In addition to these recommendations, the successors to the Richmond Committee decided that the value of the study would be enhanced by the collection of information on people without infectious intestinal disease, so that differences between the ill and the well could be identified. It was also decided that the clinical course of the disease, its long-term sequelae and socio-economic costs should be addressed.

1.2 AIMS AND OBJECTIVES

The principal aim of the study was to estimate the number of cases of gastroenteritis, or intestinal infectious diseases (IID), occurring in the population of England, and find out how many people with IID consulted their general practitioners (GPs).

We sought to identify as many as possible of the disease-causing organisms, or pathogens, responsible for IID. We then compared our estimate of the actual number of cases of IID in the population of England and presenting to their GPs, and the pathogens responsible for illness, with the routine national surveillance data from laboratory reports to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC). We also set out to identify the factors which might lead to IID, and the costs which might result.

Because it is impossible to separate out with any precision or reliability those cases of IID which result from food poisoning and those cases resulting from other causes, our study necessarily addressed all cases of IID and not merely the cases caused by eating contaminated food. We therefore included in our study cases infected with pathogens known to be spread predominantly from person to person, and cases with pathogens usually held responsible for food poisoning, as well as those cases who, although suffering from IID according to our definition, had no pathogen found in their stools. Our definition of IID was: any person with loose stools or significant vomiting

lasting less than two weeks, in the absence of a known non-infectious cause and preceded by a symptom-free period of three weeks. Vomiting was considered significant if it occurred more than once in a 24-hour period and if it incapacitated the case or was accompanied by other symptoms such as cramps or fever.

The study attempted to estimate the accuracy of laboratory reporting to the PHLS and CDSC; it did not attempt to determine the accuracy of national food poisoning statistics, which depend upon statutory notifications by doctors on the basis of clinical suspicion.

The specific objectives of the study were:

- To estimate the number and aetiology of cases of IID in the population, presenting to GPs, and having stool specimens sent routinely for laboratory examination.

- To compare these numbers and the aetiologies with those recorded by the national laboratory reporting surveillance system.

- To estimate the prevalence of asymptomatic infection with agents associated with IID.

- To document differences between cases of IID (in the population and presenting to GPs) and similar but well people (controls).

- To estimate the socio-economic burden of IID and its distribution.

1.3 METHODS

The study design was necessarily complex. It was based on an extensive review of previous studies, and on our own experience gained in carrying out a pilot study in 1992. Information from subjects was gathered between August 1993 and January 1996.

Seventy general practices in England were recruited from the Medical Research Council General Practice Research Framework. The practices were representative of all practices in England in terms of their geographical spread, urban or rural location, number of doctors and social deprivation. Groups of people representative of each practice population were invited to take part in a study. On average four out of ten did. For six months these people were asked to report every week whether or not they had suffered gastrointestinal disease. This was equivalent to following up 4,888 people for a full year. Cases who developed IID and matched controls (people similar but well) within these cohorts provided stool specimens for extensive laboratory investigation. In addition information was collected by questionnaire about their personal characteristics and things they may have done which could have had a bearing on whether or not they suffered illness, i.e., increased or decreased their risk of developing IID.

A further questionnaire was also sent out to cases some weeks after their illness. This included questions about how much their illness cost them, as well as questions about how much they would be prepared to pay for safer food and whom they saw as responsible for food safety. Some cases from the community presented themselves to their GPs and when this occurred, it was recorded. These parts of the study were the ‘population cohort component’ and ‘nested case-control’ components. The main results from these parts of the study were the rates of IID in the population.

As well as these cohorts from the 70 general practices, all cases who presented with IID to their GPs in 34 of the general practices over a 12-month period — and age and

sex matched controls — were asked to provide stool specimens for laboratory investigation. Information was obtained from them on personal characteristics, risk factors, and for cases, the same questions about costs and attitudes as in the population cohort component. This was the 'GP' component, and its main important results were the rates of cases of IID presenting to GPs and risk factors for acquiring IID.

In the remaining 36 similar practices, cases presenting with IID during the same 12-month period were identified. When cases presented themselves to these practices, the GPs' routine procedure for sending stool specimens was observed and recorded. Again, the personal characteristics of the cases were documented, and it was noted whether a stool specimen was obtained or not, and if so what the results were. Also, the same questions about costs and attitudes were asked as in the population cohort component and GP components. No controls were used for comparison in this part of the study. This was the 'enumeration' component and its most important result was an estimation of the rate of submission of stool specimens by GPs from cases of IID.

Two methods were then used to estimate the proportion of cases occurring in the population which are recorded in the national surveillance system. In the first — a direct method — the names of those cases for whom positive stools were obtained from the enumeration component were sought in the national database and the degree of under-reporting calculated.

In the second — an indirect method — we compared the rates of IID we estimated to occur in the whole population of England with the rates appearing in national surveillance, and the degree of under-reporting was calculated.

In total, we collected data and stools from over 6,000 cases of IID as well as from controls.

1.4 RESULTS

We estimated that 20% of the population of England suffered IID in a year, and 3% of the population presented themselves to their GP.

This means that nine and a half million cases of IID occur annually, of which one and a half million present to their GPs. Half a million have stools sent for microbiological examination. In our study, despite using extensive microbiological testing, no target organism was found in about two thirds of cases in the community, and nearly half those presenting to the GP. In normal practice, a much greater proportion of 'negative stools' is reported: over three-quarters of the stools submitted in the enumeration component of this study, which observed normal practice, were negative. This may be due to a number of factors: the diarrhoea may be non-infectious, or due to a pathogen which cannot be identified, or which is no longer present in sufficient numbers to be detectable, or whose identification is difficult, or not attempted.

Viruses, almost half of which are SRSV (Small Round Structured Viruses), account for about 16% of cases of IID in the community. *Yersinia* and *Aeromonas* are almost as common, or more common, in controls as cases, and their clinical significance is therefore unclear. If these are excluded from calculations, viruses are as common as bacteria in association with IID in the community in cases where a target organism was identified. In cases presenting to GPs, viruses were detected in over 20%, with rotavirus accounting for one third of these. Bacteria are, however, much commoner: excluding *Yersinia* and *Aeromonas*, nearly 40% of cases presenting to GPs have a bacterial pathogen identified.

We estimated by our direct method that for every 136 cases of IID in the community, 23 presented to a GP, 6.2 had a stool sent routinely for microbiological examination; 1.4 had a positive result; and one was reported to the PHLS' CDSC.

The ratio varies according to the organism. Approximately three cases of salmonellosis, a predominantly foodborne disease, occur in the community for every one reported to PHLS CDSC, whereas as many as 1,500 or more cases of SRSV infection, which is often spread from person to person, may occur for every one reported to the PHLS CDSC.

Put in another way: for every 1,000 cases of IID in the community, 160 presented to their GP, 45 had a stool sent routinely for microbiological examination, 10 had a positive result, and 7 were reported to PHLS, CDSC.

We estimated by our indirect method the ratio to be 88 cases in the community to every one reported to PHLS CDSC.

This ratio is lower than the ratio of 1:136 calculated by our direct method and this suggests that the indirect method may underestimate the community rate in relation to cases reported in the national data. This would occur if, as we suspect, national surveillance tends to over-represent the proportion of cases which are part of outbreaks. In other words, in estimating the ratio by this method, the national surveillance system's limitations in identifying apparently sporadic cases are partially offset by its greater efficiency in identifying cases which are part of outbreaks.

We found many differences between cases and controls.

When analysed by each of the enteropathogenic organisms, social factors and crowding, travel abroad, and bottle-feeding of infants were associated with an increased risk of IID. We also found that cases of infection with almost all organisms are consistently less likely than controls to have consumed certain foods (pulses, salads and rice prepared at home, fruit, pasteurised dairy products and fish) in the previous ten days. This may have arisen from the study design but we can find no evidence for this. It may therefore be a true association. We believe further research is warranted to confirm or refute this observation, as, if it is a true association, it may have implications for the prevention of IID.

We found the consumption of very few specific foods to be associated with an increased risk of suffering from IID.

There are a number of possible reasons for this, including the fact that most of our cases suffered from infection with organisms spread predominantly from person to person. A second explanation is that the time period we asked about — ten days prior to the onset of illness in cases — was too long to allow us to discriminate sufficiently between cases and controls, i.e., over that time period so many controls would also have eaten common foods that there was no difference between them and cases. If these explanations do not fully explain the lack of positive associations, a third explanation is that current understanding, based as it is almost completely on either the investigation of outbreaks or cases sufficiently ill to present to their GP, is not applicable to sporadic cases. The absence of an association between IID and, for example, the consumption of chicken in the home, in our study is indeed true of the mild, sporadic cases which constitute most of the burden of illness which occurs. This may be because such cases are linked to lightly contaminated foods, possibly as a result of cross-contamination from more heavily contaminated products.

We estimated the average cost of a case of IID, whatever its cause, in England to have been £79 at 1993–1995 prices.

About 36% of this cost falls to the NHS, 8% is a direct cost to the case and 55% is the cost to employers in lost production by the case or a carer. The average cost of a case presenting to a GP is £250; the average cost of a case presenting to a GP with *Salmonella*, a predominantly foodborne organism, is £606, and the average cost of a case presenting to a GP with SRSV, which is often spread from person to person, is £176. We estimated that IID in England cost at least three-quarters of a billion pounds a year. Cases presenting to their GP account for over half of this total. We found that cases presenting to the GP are ill for an average of 8.6 days. A quarter of these cases had symptoms persisting three weeks after illness.

1.5 CONCLUSIONS

The true burden of IID in England has been estimated: the number of cases, the associated microorganisms, and the costs. The identification of characteristics associated with the presence or absence of disease has raised questions to be answered by future studies, and which, if confirmed, have implications for reducing the burden of IID, whether foodborne or not.

Chapter 2
Background

2.1 MICROORGANISMS AND INFECTIOUS INTESTINAL DISEASE (IID)

2.1.1 Normal flora and pathogens

Over 400 different bacterial species have been described as part of the normal human bowel flora along with various yeasts and protozoa (Linton and Hinton 1990). The carriage of enteric viruses by healthy individuals has not been reported. The number of microorganisms in the normal stomach is low because of the presence of gastric acid but concentrations increase in the lower (distal) small intestine. In the large bowel the faecal contents contain more than 10^{11} bacteria per gram (Simon and Gorbach 1986, Guerrant 1995). Each individual has a relatively stable bacterial flora which helps to maintain the healthy state of the bowel and produces substances which may exclude pathogenic microorganisms. Major variations in diet may affect the bacterial flora and antibiotic use may cause significant changes (Simon and Gorbach 1986). There are differences between the flora of breast and bottle-fed infants before weaning and the complex adult-type flora is established by the age of about two years (Linton and Hinton 1990).

Certain bacteria, protozoa and viruses are recognised as pathogens causing intestinal disease (Guerrant 1995). These infectious intestinal diseases (IID) are typically associated with significant diarrhoea, vomiting, nausea and abdominal pain [Tables 2.1–2.3]. There may also be systemic upset with fever, but usually the illness is short-lived and resolves completely. Pathogens associated with IID may be food- or waterborne, for example *Salmonella enteritidis*, enterotoxigenic *Escherichia coli* and campylobacters. Others such as *Shigella sonnei*, *Clostridium difficile* and rotavirus are usually acquired by person-to-person contact. Several important food- or waterborne pathogens, such as *Clostridium botulinum*, *Listeria monocytogenes*, hepatitis A virus and poliovirus, cause systemic infection but little intestinal disease, and although these pathogens can be detected in faeces, they have not been sought in this study of IID. However, since this study of IID began there have been reports of foodborne *L.monocytogenes* infection characterised mainly by gastroenteritis and fever (Salamina *et al.* 1996, Dalton *et al.* 1997).

There are three major virulence characteristics that pathogens causing intestinal disease may possess (Guerrant 1995). These are the ability to:

i) Attach to intestinal epithelial cells
ii) Invade intestinal cells and epithelium
iii) Produce toxins that may be lethal to cells, produce inflammation, cause serious loss of fluid, or may be absorbed and affect the nervous system in some way, e.g., cause vomiting.

These virulence characteristics have been clearly identified for some microorganisms but not for all of the recognised pathogens (Poxton and Arbuthnot 1990, Sweet and Smith 1990, Guerrant 1995). Some microorganisms may possess more than one characteristic and the importance of each factor is difficult to determine. Studies of pathogenicity and virulence are usually carried out in animals, in tissue culture or in laboratory systems that are far removed from the complex ecosystem present within the human intestine.

In the diagnostic laboratory the identification of the virulence characteristics associated with disease is not routinely performed. More commonly the micro-organisms are identified and their pathogenic potential is inferred (Woods and Washington 1995, Collee 1996). In some cases, the differentiation of pathogenic from non-pathogenic strains of the same species or serotype is important but is only done in specialist laboratories. For example, the expression of enterotoxins and cytotoxins by *E.coli*, *Clostridium perfringens* type A, *Clostridium difficile* and *Staphylococcus aureus* is not a universal property of these species. In order to differentiate these strains, toxin production *in vitro* is determined by bioassay or immunoassay, or the gene encoding the toxin is identified by molecular techniques.

Generally, a microorganism causing disease will be present in patients with that disease and absent from normal control subjects. However, many microorganisms may be carried in the bowel for long periods following acute infection (Working Party of the PHLS *Salmonella* Committee 1995). In some cases subclinical (asymptomatic) infection occurs. Asymptomatic excreters can be a source of infection to others (Working Party 1995).

Multiple microorganisms presumed to be pathogens can, on occasion, be identified in an individual with IID at any one time. This may be because of a genuine mixed infection, some of the presumed pathogenic microorganisms may not be causing disease or they may have persisted in small numbers in the intestine as a result of previous infection.

Immunity may develop and protect against further infection (Guerrant 1995); however, this protection is often limited to the particular strain of microorganism which caused the original infection.

2.1.2 Major microorganisms with a recognised clinical significance

Brief descriptions of microorganisms are provided below to supplement the details given in Tables 2.1–2.3. The information given is that for typical presentation of the disease.

2.1.2.1 Bacteria

A range of bacteria are associated with IID and cause symptoms by a variety of methods, including attachment, tissue invasion and toxin production. Sensitive and selective culture methods are available for many but not all of these pathogenic bacteria, and some are identified only by DNA methods that detect virulence genes. Spread is mainly by ingestion of bacteria and/or their toxins in contaminated foods and waters, or by person-to-person (faecal-oral) spread. Some bacterial species causing IID may be part of the normal flora. Typing schemes such as serotyping and bacteriophage (‘phage’) typing are used to identify pathogenic strains within species. They may also be used to identify outbreaks.

Table 2.1 Major bacterial pathogens associated with IID

CAUSATIVE AGENT	USUAL INCUBATION PERIOD	USUAL DURATION OF SYMPTOMS	COMMON CLINICAL FEATURES	COMMON MODE OF TRANSMISSION	LABORATORY REPORTS 1995*
Aeromonas spp.	Unknown	varied	V, D	W, F	570
Bacillus cereus: Emetic syndrome	1–5 h	24 h	N, V, D, P	F	
Diarrhoeal syndrome	8–16 h	24 h	D, V, N, P	F	87 †
B.subtilis	1–4 h	24 h	N, V, D	F	
B.licheniformis	2–14 h	24 h	D, P	F	
Campylobacter spp.	2–5 d	2 d–1 wk	D, P, Fe,B	F, W, An	43,876
Clostridium difficile	<1 wk	varied	D, B	X	7,664
Clostridium perfringens	12–18 h	24 h	D, P	F	342
Enterovirulent *Escherichia coli*					
Attaching and effacing *E.coli* (AEEC)	unknown	unknown	D	F	
Diffusely adherent *E.coli* (DAEC)	unknown	unknown	D	unknown	
Enteroaggregative *E.coli* (EAggEC)	20–48 h	unknown	D, B	F	
Enteroinvasive *E.coli* (EIEC)	12–72 h	5–7 d	D, B	F, W	
Enteropathogenic *E.coli* (EPEC)	12–72 h	<2 wk	D	X, F, W	342
Enterotoxigenic *E.coli* (ETEC)	12–72 h	3–5 d	D	F, W	
Verocytotoxin-producing *E.coli* (VTEC)	1–6 d	4–6 d (not HUS)	D, B, HUS	F, X, W, An	792 #
Salmonellas (non-enteric fever)	12–72 h	<3 wk	V, D, Fe	F, X, An	29,314
Salmonella typhi/paratyphi	1–3 wk	10–14 d	N, Fe	F, X	435
Shigella spp.	1–7 d	<2 wk	D, B	X, F, W	4,113
Staphylococcus aureus	2–4 h	<12–48 h	V, P, Fe	F	59
Vibrio cholerae (O1, O139)	2–3 d	<7 d	D	W, F	10
Vibrio spp. (not *V.cholerae* O1, O139)	12–18 h	<7 d	D	F	66
Yersinia spp.	3–7 d	1–3 wk	D, P, Fe	F	280

Key – Clinical features

B	Blood in stool
D	Diarrhoea
Fe	Fever
HUS	Haemolytic Uraemic Syndrome
N	Nausea
P	Abdominal pain
V	Vomiting

Key – Mode of transmission

An	Animal Contact
F	Food
W	Water
X	Person-to-person (faecal-oral)

* CDSC data for England & Wales

† All *Bacillus* spp.

\# *E.coli* O157

h = hours

d = day(s)

wk = week(s)

Table 2.2 Major protozoal pathogens associated with IID

CAUSATIVE AGENT	USUAL INCUBATION PERIOD	USUAL DURATION OF SYMPTOMS	COMMON CLINICAL FEATURES	COMMON MODE OF TRANSMISSION	LABORATORY REPORTS 1995*
Cyclospora cayetanensis	5–7 d	variable	D, P	F, W	
Cryptosporidium parvum	2–5 d	<3 wk	D	W, An, X	5,691
Entamoeba histolytica	2–4 wk	variable	D, B	X	696
Giardia intestinalis	5–25 d	variable	D, P	W, X	6,171

Key – Clinical features
B Blood in stool
D Diarrhoea
P Abdominal pain

Key – Mode of transmission
An Animal Contact
F Food
W Water
X Person-to-person (faecal-oral)

* CDSC data for England & Wales
d = day(s)
wk = week(s)

Table 2.3 Major viral pathogens associated with IID

VIRUS	USUAL INCUBATION PERIOD	USUAL DURATION OF SYMPTOMS	COMMON CLINICAL FEATURES	COMMON MODE OF TRANSMISSION	LABORATORY REPORTS 1995*
Adenovirus types 40,41	7–8 d	9–12 d	D, V	X	1,157
Astrovirus	3–4 d	2–3 d	V, D, Fe	X, F, Aer	278
Calicivirus	1–3 d	1–2 d	V, D, Fe	X, F, Aer	139
Rotavirus	1–2 d	4–6 d	D, V	X	17,173
SRSV	1–3 d	1–3 d	V, D, Fe	X, F, Aer	2,366

Key – Clinical features
D Diarrhoea
Fe Fever
V Vomiting

Key – Mode of transmission
Aer Aerosol
F Food
X Person-to-person (faecal-oral)

* CDSC data for England & Wales
d = day(s)

Aeromonas and Plesiomonas
Aeromonas isolates from cases with IID can be divided into three species by phenotypic methods: *A.caviae, A.hydrophila* and *A.veronii* biotype *sobria*. *P.shigelloides* is similar phenotypically to *Aeromonas* and has also been reported to be associated with IID. These bacteria are commonly found in environmental waters such as rivers and lakes. Their pathogenicity has not been clearly established, although various virulence determinants have been proposed, including enterotoxin, cytotoxin and haemolysin production and invasiveness (Ljungh and Wadström 1989, Janda *et al.* 1995). Strains can be differentiated by serotyping.

Bacillus
B.cereus and members of the *'B.subtilis group'* (*B.licheniformis, B.pumilus, B.subtilis*) are associated with foodborne disease. These are ubiquitous spore-forming organisms, whose spores commonly contaminate a wide range of raw agricultural products, processed cereal products and pasteurised milks. They are not commonly found on raw or processed meat products. *B.cereus* is the species most frequently recognised as being associated with IID. Food poisoning results from the ingestion of large numbers (>10^5 cfu/g of food) of toxigenic bacteria or preformed emetic toxin. This may arise through inadequate temperature control of contaminated foods, classically fried rice. *B.cereus* strains can be differentiated by

serotyping (Kramer and Gilbert 1989). Enterotoxin is produced *in vivo* and in food and is associated with a wider range of foods.

Campylobacter
Campylobacters are the most commonly identified cause of acute diarrhoea in the UK, with *C.jejuni* being the most frequently isolated species. Meat, particularly poultry, is thought to be an important source of infection. A link between *Campylobacter* enteritis in man and infection in poultry has been established in many countries, and studies in the UK have supported this association (ACMSF 1993a). Almost all cases appear to be sporadic, but outbreaks have been described associated with inadequately cooked or cross-contaminated meat, with water, and with both pasteurised and raw milk.

The pathogenesis of *Campylobacter* infections is unclear, but probably involves invasion of the intestinal epithelium which may result in bacteraemia. Several toxins have been described; however, their role in disease is not established. Subtyping methods based on phenotypic properties such as serotype, biotype and phage type have been developed and these have recently been supplemented by molecular fingerprinting. Despite extensive research and numerous publications, there is, as yet, no consensus on the most appropriate method of typing for epidemiological purposes. Neither speciation nor typing of *Campylobacter* isolates (Skirrow 1990, Nachamkin 1992) was routine in England at the time of this study. A PHLS *Campylobacter* reference unit offering speciation and typing has been established since the study was completed.

The role of other *Campylobacter* species, *Arcobacter* species and intestinal *Helicobacter* (not *H.pylori*) in IID is unclear. Selective media and methods used for the isolation of *C.jejuni* may not be optimal for these organisms, and alternative techniques using selective and non-selective media have been proposed, including the use of membrane filters.

Clostridium difficile
C.difficile is an anaerobic spore-forming bacillus which can cause mild to severe colitis by means of two potent exotoxins, toxin A ('enterotoxin') and toxin B ('cytotoxin'). Not all strains produce toxins, but those that do so usually produce both toxins A and B. *C.difficile* is part of the normal intestinal flora of children under two years of age, who appear to be unaffected by the toxins. It is thought to be predominantly a hospital acquired pathogen of adults and children aged over two years, and requires the normal gut flora to be disturbed, usually by a broad spectrum antimicrobial agent, before it can establish itself in the bowel and symptoms occur. Infection is acquired from infected individuals or a contaminated environment (such as a hospital).

C.difficile-associated disease can be sporadic or occur as ward outbreaks, and the patients at highest risk are the elderly. *C.difficile* is the most common cause of nosocomial diarrhoea. Little is known about the role of *C.difficile* in community-acquired diarrhoea. In one study (Hirschhorn *et al.* 1994), the incidence of *C.difficile*-associated disease was low at 7.7 cases per 100,000 person-years. However, in another study the rate of *C.difficile* detection increased four-fold to 10.7% after GPs were encouraged to request *C.difficile* testing on specimens from patients with diarrhoea (Riley *et al.* 1995). Several typing methods have been applied in the investigation of outbreaks including serotyping and molecular fingerprinting (Joint DH/PHLS Working Group 1994).

Clostridium perfringens
C.perfringens is part of the normal faecal flora, generally present at $<10^5$ cfu/g of faeces in healthy adults. However, concentrations of $>10^5$ cfu/g occur in people

aged 60 years or more, in the absence of disease. Food poisoning is caused by ingestion of large numbers of *C.perfringens* organisms which form spores in the lower small intestine and release enterotoxin. *C.perfringens* also causes antibiotic-associated diarrhoea and may be spread directly from person to person, or via the environment. Isolates can be differentiated by serotyping and molecular methods are being developed (Labbe 1989).

Escherichia coli

Most *E.coli* are not pathogenic and are part of the normal human bowel flora. *E.coli* associated with diarrhoeal disease are referred to collectively as enterovirulent *E.coli.* Seven such groups can be defined based on the presence of known or putative virulence factors which include toxin production, adhesion and invasiveness (Nataro and Kaper 1998, Sussman 1997):

- Attaching and effacing *E.coli* (AEEC)
- Diffusely adherent *E.coli* (DAEC)
- Enteroaggregative *E.coli* (EAggEC)
- Enteroinvasive *E.coli* (EIEC)
- Enteropathogenic *E.coli* (EPEC)
- Enterotoxigenic *E.coli* (ETEC)
- Verocytotoxin-producing *E.coli* (VTEC)

The genes of these factors can be detected by DNA methods.

EPEC have been associated with outbreaks of IID in children aged one year or less in nurseries and hospital wards. ETEC is a common cause of infection in children in tropical countries and in travellers. EIEC are rare causes of diarrhoea and dysentery in travellers. EAggEC has been associated with diarrhoeal illness in infants and travellers. Less is known about AEEC and DAEC. VTEC infections are uncommon but can be serious, causing bloody diarrhoea, haemolytic-uraemic syndrome (HUS) and death. The most frequent serogroup isolated is O157, and this is easily identifiable in routine diagnostic laboratories. This microorganism is found in cattle, sheep and other farm animals and outbreaks have been associated with inadequately cooked meat and with contaminated milk (ACMSF 1995). VTEC infections may also be acquired by person-to-person spread. The infectious dose of VTEC is low. VTEC are also sometimes referred to as Shiga-like toxin-producing *E.coli* (SLTEC) or shiga toxin producing (STEC)because the verotoxin is related to Shiga toxin produced by *Shigella dysenteriae* type 1. They are also referred to as enterohaemorrhagic *E.coli* (EHEC). Strains of *E.coli* can be differentiated by serotyping and a phage typing scheme has been developed for VTEC O157 (Gyles 1994).

Outbreaks of VTEC O157 have been associated with inadequately cooked minced beef, such as beef-burgers, and milk, unpasteurised and contaminated post pasteurisation. In addition, food vehicles include yoghurt, cooked meats, cream cheese, salami, raw vegetables, unpasteurised apple juice and water. As well as contaminated foods, important transmission routes of infection with VTEC are direct or indirect contact with animals and person-to-person spread (Kaper and O'Brien 1998).

Salmonella

Salmonella are the second most commonly identified bacterial cause of IID in the UK. The illness most commonly manifests as acute diarrhoea with headache, abdominal cramps, nausea and sometimes vomiting. Salmonellae are thought to invade the intestinal epithelium. The role of enterotoxin in pathogenicity has not been established. A wide range of foodstuffs have acted as vehicles for the transmission of salmonellae and many animals, including farm animals, act as reservoirs for salmonellas. Person-to-person transmission has been identified as an important route of infection during outbreaks.

Over 2,000 types of *Salmonella* can be identified by serotyping. Currently in this country, human salmonellosis is most commonly associated with *S.enteritidis* and *S.typhimurium*. Phage typing provides a very useful epidemiological method for subdivision within the commonly isolated serotypes and is supplemented where appropriate with the application of DNA based techniques. *S.enteritidis* phage-type 4 is almost entirely associated with poultry and can be incorporated into eggs within the oviduct (ACMSF 1993b).

S.typhi and *S.paratyphi* cause serious systemic disease – typhoid and paratyphoid, respectively (the enteric fevers). They are usually acquired outside the UK, either directly or indirectly from other infected people or carriers (Old and Threlfall 1998).

Shigella

Four species comprise the genus *Shigella: S.boydii*, *S.dysenteriae*, *S.flexneri* and *S.sonnei*. *S.sonnei* is the major cause of shigellosis in the UK. Most infections associated with other species are acquired overseas and cause bacillary dysentery. The organism invades the superficial layers of the colonic epithelium causing loss of blood and inflammatory exudate. Some also produce potent toxins, in particular *Shigella dysenteriae* type 1 which produces the Shiga toxin. Infection may be caused by the ingestion of very few bacterial cells; therefore, person-to-person spread is common. It is often associated with poor hygiene and large outbreaks can occur. *Shigella* may also be transmitted in contaminated food or water. Shigellas are differentiated by serotyping and a phage typing system is used to subtype *S.sonnei* (Altwegg and Bockemüll 1998).

Staphylococcus aureus

Staph.aureus food poisoning is an intoxication caused by ingestion of one or more enterotoxins which have been produced as the organism multiplies within the contaminated food. Eight serologically distinct enterotoxins are recognised, all of which are heat stable. *Staph.aureus* is carried on the skin and in the anterior nares of up to 40% of healthy people and causes septic lesions, e.g., boils. It is also a common component of the normal faecal flora. Strains are differentiated by phage typing (Wieneke *et al.* 1993).

Vibrio

The *Vibrio* genus comprises over 30 species of which the most important is *V.cholerae* and this species can be subdivided into at least 140 serogroups. *V.cholerae* O1 and, recently, O139 are the causes of epidemic cholera which is predominantly a waterborne infection. The characteristic profuse watery diarrhoea of cholera is due mainly to the effects of a heat labile enterotoxin elaborated by the vibrio in the intestine; this toxin binds to enterocytes and alters water transport through inhibition of sodium absorption and stimulation of chloride secretion. Further differentiation of *V.cholerae* O1 is performed by biotyping and phage-typing. *V.parahaemolyticus* causes a milder illness and is acquired from raw or undercooked fish or shellfish (Lee 1990, Wachsmuth *et al.* 1994).

Yersinia

There are at least eleven species within the genus *Yersinia*; *Y.enterocolitica* is the major species associated with human diarrhoeal disease. Virulence has been correlated with the presence of a 70kDa plasmid, which carries genes which encode for epithelial invasion. Children are affected more frequently than adults and severe abdominal pain is a characteristic feature. Raw pork is thought to be an important source of infection. Immune-mediated complications may occur after the acute infection, particularly in adults, and may affect joints (arthritis), skin (rashes) and the eye (uveitis). Serotyping is used to differentiate strains and, in addition, biotyping is used for *Y.enterocolitica*.

2.1.2.2 Protozoa

The protozoal parasites are unicellular organisms which colonise the intestinal epithelium and form cysts. These are excreted and may survive for long periods in the environment. They are also resistant to the levels of chlorine found in tap water (Benenson 1995, Casemore 1991a).

Cryptosporidium
C.parvum causes an acute self-limiting diarrhoeal illness in immunocompetent individuals and chronic, debilitating disease in the immunosuppressed (Group of Experts on *Cryptosporidium* in Water Supplies 1990; Casemore 1991a). It may be acquired directly from infected persons, from pets, farm animals or contaminated water. Routine water treatment processes do not remove all oocysts from water supplies. Livestock grazing close to these supplies may be a source of contamination. Recent phenotyping and genotyping studies (by PCR) have shown that there are at least two lineages of *C.parvum*: human isolates belong to genotypes 1 or 2, whereas animal isolates are genotype 2 only; moreover, attempts to infect animals experimentally with genotype 1 strains have failed (Casemore 1998). This suggests that human infections may also arise from waters contaminated with human sewage, and recent outbreak investigations support this view (Patel *et al.* 1998). Epidemiological evidence suggests that previous exposure may lead to protective immunity (Casemore 1990, Heyworth 1992).

Cyclospora
Cyclospora has only recently been described as a cause of IID and the oocysts shed in faeces were previously described as *Cyanobacterium*-like bodies (CLB). *Cyclospora cayetanensis* infection causes an acute watery diarrhoea with abdominal cramps, vomiting and weight loss (Soave 1996). The illness may persist for weeks or months and follow a relapsing course. The illness is common in travellers. Infection can be asymptomatic. *Cyclospora* is acquired directly from food or water contaminated with oocysts. Patients excrete large numbers of oocysts in their faeces but these are infectious only after they have sporulated, which may take several days or weeks. Animal reservoirs of infection have not been described.

Giardia
G.intestinalis is a flagellate protozoan (Casemore 1991a, Healy and Garcia 1995). Giardiasis may cause chronic diarrhoea, malabsorption and weight loss, and is common in travellers. *Giardia* is acquired principally from contaminated water or by person-to-person transmission. Chlorination alone is not sufficient to kill cysts in water supplies. *Giardia* infection, particularly in children, is often asymptomatic.

Entamoeba
E.histolytica is one of seven species of amoebae that may live in the human bowel and is the only pathogenic species (Casemore 1991a, Healy and Garcia 1995). Certain strains are thought to be more pathogenic and are identified by isoenzyme typing (zymodeme analysis) and genetic methods (PCR). Pathogenic amoebae are an uncommon cause of IID in the UK.

2.1.2.3 Viruses

Many enteric viral infections are mild and of relatively short duration (Appleton 1991, ACMSF 1998). Most cases are probably not identified because specimens are not commonly examined for viruses and the detection methods (see 2.1.3.3) used routinely identify only two of the five groups of viruses known to cause IID. Transmission is mainly by person-to-person contact or inhalation of airborne droplets, but outbreaks of viral gastroenteritis associated with contaminated food

and water have been described (Appleton 1991, Hedberg and Osterholm 1993, ACMSF 1995, ACMSF 1998).

Adenovirus types 40,41
There are at least 41 types of adenovirus and most of these cause infections of the respiratory tract with two, types 40 and 41, in the enteric subgenus (Group F). Children under six years old are affected and infections occur throughout the year. Adenoviruses are responsible for up to 17% of hospital admissions of children with severe diarrhoea (Van *et al.* 1992).

Astrovirus
There are at least seven serotypes of astrovirus with type 1 responsible for over 70% of all human infections. The peak incidence of infection is in winter and spring. Astroviruses mainly infect children under 4 years and are responsible for 3% of hospital admissions of children with severe diarrhoea. Outbreaks have also occurred in elderly residents of nursing homes (Greenberg and Matsui 1992).

Calicivirus (classical)
There are at least three serotypes and children under five years old are the most susceptible group. World-wide, caliciviruses are responsible for 5% of hospital admissions for diarrhoea and outbreaks in day care centres have been described (Cubitt 1994). The classical caliciviruses are serologically and genotypically distinct from the related small round structured viruses.

Rotavirus
Rotavirus infection occurs predominantly in the winter months with children under three years of age and the elderly being most commonly affected. Rotaviruses are responsible for up to 50% of hospital admissions for diarrhoea in children under two years of age. Asymptomatic infections occur. Although most people have acquired specific antibodies by three years of age, reinfections can occur throughout life. Group A rotavirus infections are most common but group C strains which infect cattle and pigs also cause disease in humans (Kapikian 1993).

Small round structured virus (SRSV, Norwalk-like).
There are at least seven serotypes of SRSV and these viruses can also be divided into two main genotypes or genogroups. Strains are named after the outbreak locations (e.g., Norwalk, Desert Shield, Queen's Arms, Lordsdale, Snow Mountain). While this study was in progress, SRSV was reclassified with the calicivirus group (Cubitt *et al.* 1995) but the serotypes and genogroups are distinct from the 'classical' caliciviruses.

Outbreaks of SRSV are common in children and adults of all ages in hospitals, nursing homes, hotels and institutions. Foodborne outbreaks have been associated with infected food handlers and with shellfish or vegetables contaminated by human sewage (ACMSF 1998). Virus is present in vomitus and may be spread by aerosol; the infectious dose is considered to be very low (10–100 virus particles). Antibodies may protect from reinfection with SRSV of the same serotype but protective immunity is lost after 14 weeks. Some individuals appear to be more resistant to infection than others (ACMSF 1998).

2.1.3 Routine detection

The clinical diagnostic microbiology laboratory services in England comprise NHS, PHLS and university laboratories based in hospitals and a small number of private laboratories. Facilities vary, but most take part in voluntary National External Quality Assurance Schemes (NEQAS) and procedures and services are subject to peer review for the achievement of accreditation. The service is usually directed by a Consultant Medical Microbiologist or scientist of equivalent standing.

2.1.3.1 Bacteria

The routine isolation and identification of bacterial pathogens in faecal specimens relies on the use of direct culture on one or more agar based selective and differential isolation media. These media support the growth and aid the identification of colonies of the pathogen against the background of normal flora, the growth of which has been suppressed to a greater or lesser extent by antibiotics, dyes or other substances such as bile (Pedler and Orr 1990, Woods and Washington 1995). The sensitivity of detection of low numbers of pathogens is improved by enrichment culture in liquid media designed to maximise growth of small numbers of pathogens but selectively suppress the normal flora. This amplification step is followed by direct culture on selective and differential solid media. Some organisms require specific isolation methods, e.g., membrane filter culture for some campylobacters.

Spores of clostridia and bacilli are determined by differential culture following heat or ethanol treatment of the specimen; this kills vegetative cells but not the relatively resistant spores.

The significance of the detection of low numbers of a pathogen in faeces is usually interpreted with reference to recent symptoms, the known pathogenic potential of the organism isolated, and the delay in obtaining or processing the specimen following the onset of symptoms of disease (Guerrant 1995). The detection of low numbers of a putative pathogen may reflect either convalescent carriage following infection or true asymptomatic carriage.

Some potential pathogens, such as *Staph.aureus* and *C.perfringens,* are components of the normal flora (Collee 1996). An increase in numbers above normal values may indicate infection or overgrowth by pathogenic strains. This estimate of numbers is performed by standard quantitative culture methods using selective techniques and media.

Once isolated, the organisms are identified to genus or species level. In the case of some pathogens, e.g., salmonellas and vibrios, the majority of diagnostic laboratories send all isolates to a reference laboratory for confirmation of identification and for typing. With others, e.g., campylobacters and *C.difficile*, isolates are referred for typing only if they are part of a suspected outbreak. Most laboratories do not identify campylobacters to species level. Most enterovirulent *E.coli* are not further differentiated because simple diagnostic tests are not available.

2.1.3.2 Protozoa and helminths

Examination of a suspension of faeces by light microscopy can reveal protozoal pathogens and their cysts as well as small helminths and the ova of larger helminths (Lumsden and McMillan 1989, Jeffrey and Leach 1991, Healy and Garcia 1995). They are identified by their characteristic microscopic appearances (Jeffrey and Leach 1991). A concentration technique (differential centrifugation) is used to increase the sensitivity of detection of ova and cysts. Three separate specimens of faeces are usually requested for microscopy as it is recognised that the excretion of some parasites is intermittent and the sensitivity of the detection methods is low (Lumsden and McMillan 1989).

2.1.3.3 Viruses

Viruses may be detected by electron microscopy (EM) whereby characteristic particles are observed. This method is relatively insensitive and time consuming and

is usually only employed in the investigation of outbreaks, not of sporadic community cases of IID (ACMSF 1998). Other methods such as latex agglutination and enzyme-linked immunosorbent assay (ELISA) tests for viral antigen in faeces are available for rotavirus and enteric adenovirus (types 40/41) and many diagnostic laboratories use these, particularly for the investigation of diarrhoea in children (ACMSF 1995, ACMSF 1998). Immunological methods are not currently available for the routine detection of the less common serotypes of rotavirus affecting man, such as those of group C.

2.1.3.4 Toxins

The direct detection of toxin in faeces is usually limited to investigations for *C.difficile* toxins as this organism may be responsible for severe illness and death and causes large outbreaks in hospital populations (Joint DH/PHLS Working Group 1994). *C.difficile* toxins may be detected using cell culture cytotoxicity assays or immunological methods (usually ELISA). *C.perfringens* toxin, a cause of sporadic IID and outbreaks of food poisoning, is sought only if clinical factors suggest that the organism is a likely cause of the disease (Willis and Phillips 1988). Commercial test kits are available for the detection of *B.cereus*, *V.cholerae* and some *E.coli* toxins in faeces, but they are not used routinely in diagnostic laboratories.

2.2 REVIEW OF THE NATIONAL SURVEILLANCE SYSTEMS

2.2.1 Introduction

Nationally, there are three principal routine sources of data on foodborne disease and infectious intestinal disease in use in England and Wales (Wall *et al.* 1996):

i. Statutory notifications from clinicians of cases of food poisoning
ii. Voluntary reports from diagnostic laboratories of laboratory confirmed infections
iii. Standard report forms on general outbreaks of IID submitted by Consultants in Communicable Disease Control (CsCDC) on general outbreaks of infectious intestinal disease.

Data from the first are produced by the Office of National Statistics (ONS), formerly the Office of Public Censuses and Surveys (OPCS), and the other two by the PHLS Communicable Disease Surveillance Centre (CDSC).

In addition to these sources, the Royal College of General Practitioners (RCGP) runs a national primary care sentinel surveillance system for the voluntary reporting by participating GPs of cases of IID.

2.2.2 Statutory notifications from clinicians of cases of food poisoning

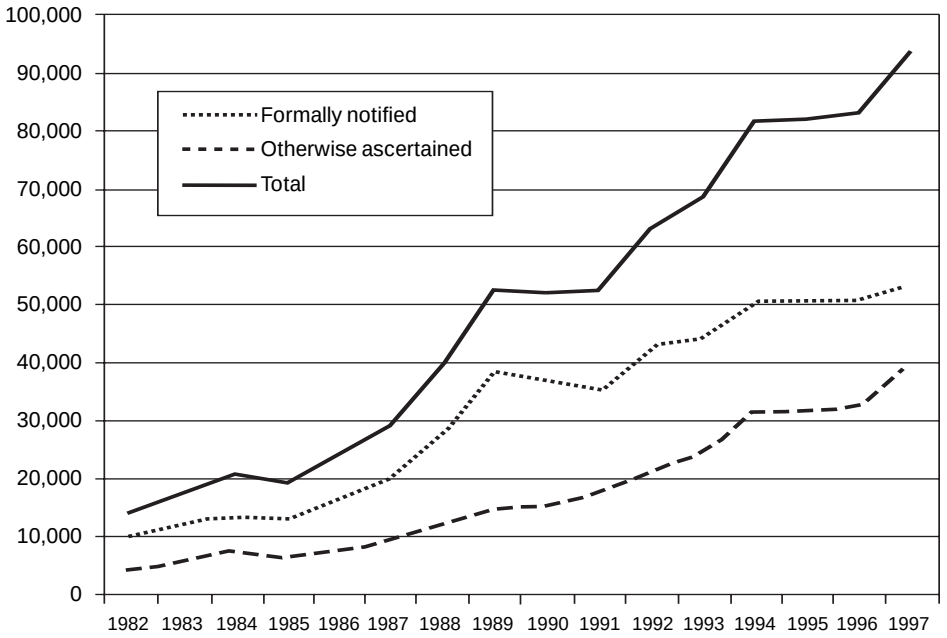
All doctors in clinical practice have a statutory duty to notify the proper officer of the local authority of cases, or suspected cases, of certain infectious diseases and of food poisoning. The meaning of the term ‘food poisoning’ is not defined in the relevant legislation, the Public Health (Control of Diseases) Act 1984, and this has previously led to confusion as to which cases should be reported. The ACMSF recommended a definition which was accepted by DH and circulated to all doctors in 1992. It defines food poisoning as: *‘any disease of an infectious or toxic nature caused by or thought to be caused by the consumption of food or water’*. The definition had been previously adopted by the World Health Organisation (Joint FAO/WHO Expert Committee on Food Safety 1984).

Notification is made by the attending clinician to the proper officer of the local authority (usually the CCDC) where the incident occurred. Notification is not contingent on laboratory confirmation of infection and delaying notification until laboratory confirmation is available defeats the purpose of a rapid notification system designed to enable effective and timely intervention at local level (Clarkson and Fine 1987).

In addition to those cases of food poisoning formally notified by clinicians, the local authority ascertains cases by other means, for example, cases detected in the course of investigations of outbreaks or as a result of complaints made by the general public (Figure 2.1). These notifications are collated locally and anonymized data on both formally notified and otherwise ascertained cases are forwarded as a legal requirement to the Registrar General at the ONS to produce the national food poisoning statistics (Public Health Regulations 1988).

Food poisoning notifications are a poor indication of the true incidence of food poisoning. The definition is deliberately wide to enhance its sensitivity in the detection of cases and outbreaks, but this vagueness reduces the system's value in the measurement of longer term trends. The system's sensitivity is also questionable as many do not consult their doctor, and only a proportion of those who do are notified. Since 1993 40% of the total number of notifications have been 'otherwise ascertained' which highlights the deficiencies of the formal system. Gross under-notification of food poisoning is recognised (Parliamentary Office of Science and Technology Report 1997) and is not surprising as it is well documented for more serious infections (Haward 1973, Crombie 1983, Clarkson and Fine 1985, McCormick 1987, Harvey *et al.* 1989, Zuckerman 1991).

Figure 2.1 Food Poisoning Notification in England and Wales (OPCS 1994, Anon 1996b, Anon. 1998)



2.2.3 Voluntary reports from diagnostic laboratories of laboratory confirmed infections

The CDSC is the epidemiology unit of the PHLS. It routinely receives reports of laboratory confirmed human infections from the laboratories and the reference laboratories of the PHLS network and from over 200 NHS laboratories and a small number of private laboratories throughout England and Wales. In 1995 the Strategic

Review of Pathology Services recommended that *'all pathology contracts should refer to the necessity for prompt reporting of data relevant to the epidemiology of communicable disease, both to the CCDC and to the PHLS CDSC'* (Anon 1995b). Most of the PHLS and some of the NHS laboratories report weekly via electronic links (Henry 1996). The remaining laboratories send paper reports to CDSC where they are entered into the central database (Grant and Eke 1993).

Most human isolates of *Salmonella* from England and Wales are forwarded to the PHLS Laboratory of Enteric Pathogens (LEP), which is the national *Salmonella* reference laboratory, for confirmation and further identification. LEP has an electronic link with CDSC and updates the salmonella figures daily. In addition all laboratories in England and Wales are encouraged to send isolates of *E.coli* O157 to LEP for further identification and definitive typing and the national returns on the incidence of O157 VTEC are based on LEP data. Isolates of *B.cereus, C.perfringens* and *Staph.aureus* are submitted to the PHLS Food Hygiene Laboratory (FHL) for typing and/or toxin testing and the national returns for these microorganisms are based on the FHL data.

The reports of laboratory confirmed gastrointestinal pathogens represents only a fraction of the true incidence of these pathogens as only a proportion of cases seek medical attention and only a subset of these have a specimen submitted for analysis (Figure 2.2) (Feldman and Banatvala 1994). Not all of these will have a pathogen identified and not all pathogens identified are reported to CDSC. The exact proportion in each category is unclear and may vary for different organisms. Laboratory reports are most likely to represent patients with the severe end of the spectrum of IID and are therefore not an unbiased sample.

The quality and quantity of information in laboratory reports to CDSC is dependent on the information included in the initial laboratory request form accompanying the specimen to the laboratory. Reports are not updated and therefore data on outcomes, including case fatality, are incomplete. In addition the system does not distinguish between specimens originating from patients in hospital, or specimens referred by GPs or Environmental Health Officers (EHOs) from patients in the community. The data do not include the patient's postcode or area of residence and the maps produced by CDSC are based on the geographic location of the reporting laboratory.

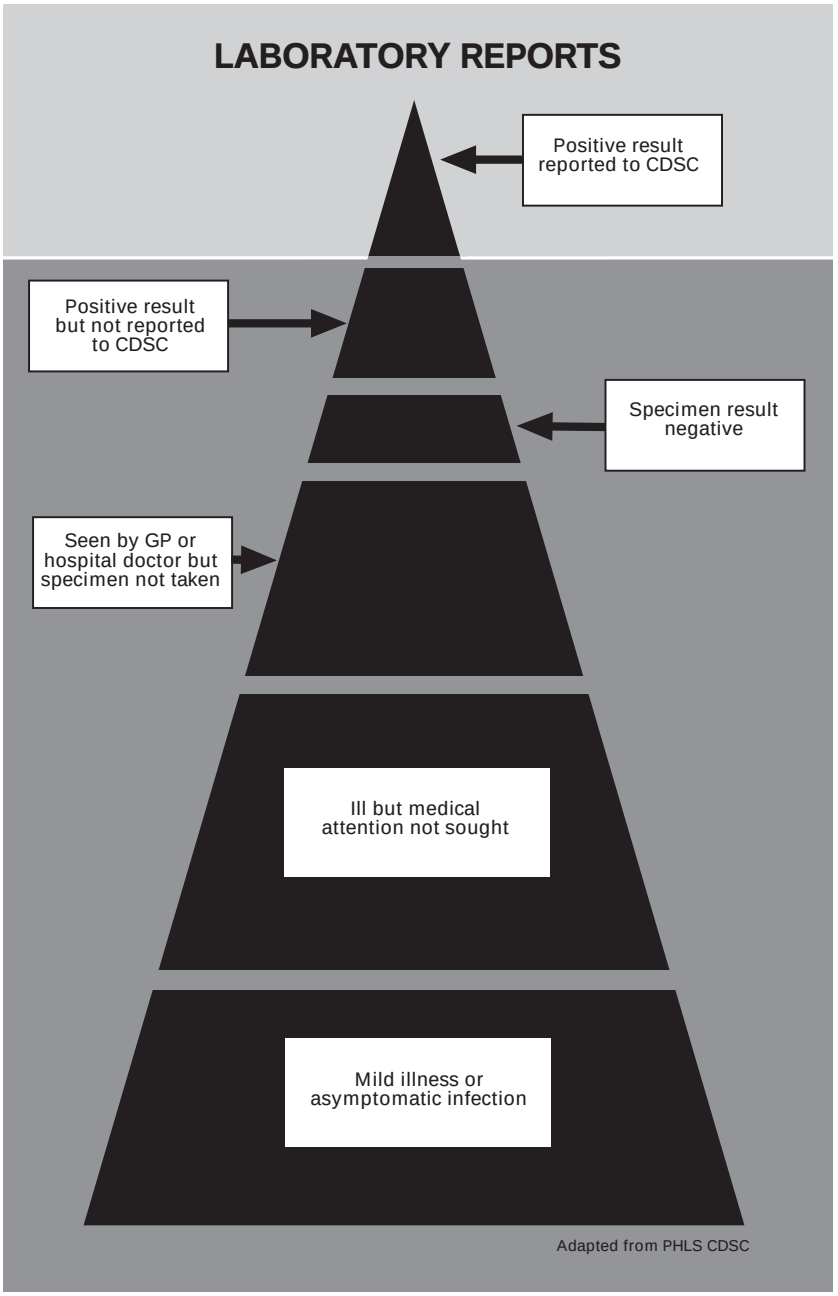
Regional incidence rates produced by CDSC are based on the populations of the Regional Health Authorities in which the reporting laboratories are located; however, laboratories vary greatly in their reporting practices. In addition, rates produced by CDSC assume that the patients reside in the same region as the laboratory which may not be the case. No data on negative specimens processed by each laboratory or the proportion of affected patients sampled are available at CDSC. As these factors may vary by region they can further distort the regional rates produced by CDSC (Wall *et al.* 1996).

Nationally there is no linkage between notified cases of food poisoning and laboratory reports of the identification of gastrointestinal pathogens. The degree of overlap between the two systems is therefore not quantifiable.

2.2.4 Standard report forms submitted by CsCDC on general outbreaks of infectious intestinal disease

A general outbreak is defined as one 'affecting members of more than one private residence or residents of an institution'. General outbreaks are distinct from family outbreaks affecting members of the same private residence only (Department of Health Working Group 1994). A surveillance system to investigate outbreaks was developed by the PHLS CDSC for England and Wales, in response to a recommendation by the Richmond Committee, and was introduced in 1992.

Figure 2.2 Reporting Pyramid: laboratory reports to PHLS CDSC represent only a proportion of the true prevalence of gastrointestinal pathogens and toxins



CDSC is made aware of possible general outbreaks of IID from a variety of sources, including the national laboratory reporting scheme, CsCDC, EHOs, microbiologists and others. A structured questionnaire is then dispatched to the appropriate CCDC with the request that the form is filled in by the lead investigator on completion of the outbreak investigation. Participation in the surveillance scheme is entirely voluntary. Analyses of data from this surveillance system appear regularly in CDSC's weekly Communicable Disease Reports (CDR) and review articles have been published in *Communicable Disease and Public Health*, formerly the *Communicable Disease Review* (Cowden *et al.* 1995, Djuretic *et al.* 1996b, Wall *et al.* 1996).

There are several areas of potential bias in the reporting of general outbreaks. Outbreaks at social functions affecting a defined cohort of people are more likely to be identified and investigated that those where cases are widely dispersed within the community such as those associated with contaminated products from retail or wholesale outlets (Palmer 1990). The reporting individual decides the probable

mode of transmission, and the faults likely to have contributed to the outbreak, and different individuals can classify similar outbreaks differently (Wall *et al.* 1996). Regional variations in the incidence of outbreaks may reflect a genuine difference but are more likely to reflect differences in laboratory interest, investigation policies, resources for communicable disease control and reporting to CDSC.

2.2.5 Primary care surveillance

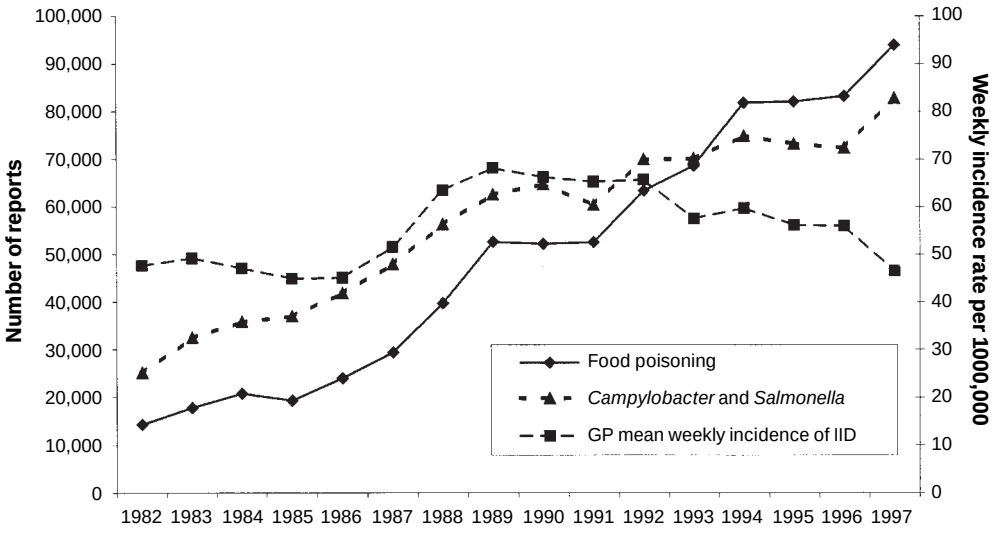
An additional source of data on infectious intestinal disease in the community is the RCGP Weekly Returns Service from its sentinel practice scheme. This provides information on weekly returns submitted by 99 general practices with a total population at risk of approximately 612,000. The data are on episodes of newly acquired IID. Microbiological confirmation of the clinical diagnosis is not required and not all cases will have resulted from food poisoning. However, this may give an approximation of the rate of case presentation of IID in general practice.

2.3 EPIDEMIOLOGICAL REVIEW

The mean weekly incidence rate for episodes of IID increased during the late 1980s (Figure 2.3) in parallel with the number of food poisoning notifications and laboratory reports of both *Campylobacter* and *Salmonella*. The increase in the notifications and laboratory reports after 1992 was not matched by a corresponding increase in GP consultations for IID, which raises the possibility that the release of the definition of food poisoning by ACMSF may have contributed to more complete formal and 'otherwise ascertained' notification.

Figure 2.3 Food poisoning notifications (notified and otherwise ascertained), laboratory reports of *Salmonella* and *Campylobacter*, and mean weekly incidence of IID in general practice

(Data courtesy of ONS, PHLS CDSC and RCGP)



2.3.1 National trends in IID

Campylobacter and *Salmonella* account for most of the laboratory reports and probably also of food poisoning notifications (Figure 2.3). Table 2.1 lists the most commonly reported bacterial pathogens causing IID in England and Wales.

The importance of *Campylobacter* as a human pathogen was recognised in the late 1970s and it is now the commonest gastrointestinal pathogen isolated from humans in the UK. There is a characteristic seasonal distribution of reports, with a peak in the early summer, in contrast to reports of *Salmonella* which reach their maximum in the late summer and autumn. There are also regional variations in the reporting of *Campylobacter* infections, which may reflect a higher incidence in rural than urban populations.

A rising incidence of antibiotic resistance, particularly to the fluoroquinolones, has been documented in campylobacters (Gaunt and Piddock 1996) and has also been attributed to antibiotic use in animal and poultry husbandry, but also to inappropriate treatment in man (ACMSF 1999). Until very recently, there was no national reference laboratory for *Campylobacter*, and this has hampered the detailed study of phenomena such as emerging antibiotic resistance.

There were four notable increases in *Salmonella* reports, the first in the mid-1950s, the second in the late 1960s and early 1970s, the third during the late 1970s and early 1980s and the fourth since 1985. This most recent increase in salmonellosis was due to an unprecedented increase in *S.enteritidis* phage type(PT)4, which began in 1983 and was associated with poultry and poultry products. Data from other European countries and the USA suggest that the increase in *S.enteritidis* PT4 seen in the UK was a global problem (Rodrigue *et al.* 1990).

S.typhimurium Definitive Type(DT)104 is now the second commonest *Salmonella* in human beings in England and Wales, increasing from less than 250 isolates in 1990 to 2873 in 1994 and 3837 in 1995. In 1995 87% of isolates were multiply antibiotic resistant to ampicillin (A), chloramphenicol (C), streptomycin (S), sulphonamides (Su) and tetracyclines (T) (R-type ACSSuT), with 27% and 6% of the strains being in addition resistant to trimethoprim and ciprofloxacin respectively (Threlfall *et al.* 1996).

Another important development has been the emergence of resistance to fluoroquinolone drugs in the poultry associated serotypes *S.hadar* and *S.virchow* (Frost *et al.* 1995). It has been suggested that the development of resistance in these serotypes is a consequence of the prophylactic and therapeutic use of the antibiotics in animals and poultry (Piddock *et al.* 1990, Piddock 1998). Regardless of the mechanism, the development of resistance has resulted in a reduction in options for the management of invasive salmonellosis in humans.

The enterovirulent *E.coli* include all those *E.coli* believed to be associated with diarrhoea. Several different serogroups of *E.coli* produce verocytotoxin but the most commonly recognised is O157. This organism was first identified as a human pathogen in 1982 (Riley *et al.* 1983) and has since emerged as a serious public health problem. Although the actual numbers of cases is small, with fewer than 1000 per year in England and Wales, *E.coli* O157 is of concern because of serious complications such as haemorrhagic colitis and HUS (Tarr 1995). Rates of infection vary across the UK. In 1994 the highest rate of infection was seen in Scotland with a rate of 4.73 per 100,000 population compared with 0.8 in England and Wales and 0.18 in Northern Ireland (ACMSF 1995). In November 1996 an outbreak in Central Scotland, caused by poor practices in a single butcher's shop, resulted in over 500 cases and 21 deaths (Cowden, JM, personal communication).

Between 1992 and 1995, *Shigella sonnei* was the third most commonly reported bacterial cause of IID after *Campylobacter* and *Salmonella* (Table 2.4). Although food-borne outbreaks have occurred (Frost *et al.* 1995) infection is more commonly spread directly from person to person, and most cases are sporadic. A national epidemic occurred in 1992/1993 (Newman 1993) in which most cases occurred in children.

There has been a steady increase in the number of reports of *C.difficile* infections from 1235 in 1992 to 2199 in 1995 and reports of toxin identification increasing from 1660 in 1992 to 7662 in 1995 (Djuretic *et al.* 1996b). A proportion of this increase in reports may be due to recent diagnostic improvements.

C.perfringens causes a mild disease of short duration and cases that are identified are usually part of general or family outbreaks. The number of cases identified by the PHLS has fallen from 1442 in 1991 to 342 in 1995. Reports of the other two toxin producing organisms traditionally regarded as important causes of food poisoning are rare: cases of *Staph.aureus* intoxication identified declined slightly from 61 in 1991 to 59 in 1995, and of *B.cereus* from 95 to 87 over the same period.

Cryptosporidium parvum is a coccidian protozoan parasite which was identified as an important human pathogen in 1976 (Nime *et al.* 1976). Infection rates in the UK show variation in both age and seasonal distribution (Casemore 1990, 1992). The age distribution suggests endemicity; few infections occur under the age of one year, probably due to a combination of passive maternal immunity and protection from exposure to the environment. An almost logarithmic increase is observed in toddlers and young children, moderately high rates in young adults, and few cases after the age of 40 years. Seasonal peaks occur in the spring and late autumn.

During the 1970s a number of viruses associated with acute IID were discovered and transmission by the food- or waterborne route has been documented for astroviruses and caliciviruses (human caliciviruses and Norwalk-like viruses) (Kapikian *et al.* 1972, Hedberg and Osterholm1993). Norwalk-like viruses, also known as small round structured viruses (SRSV), have become an important cause of both sporadic and epidemic gastro-enteritis (Blacklow and Greenberg 1991, Hedberg and Osterholm 1993).

Rotaviruses are a common cause of IID in young children in England and Wales and are associated with significant morbidity (Ryan *et al.* 1996). Infections are highly seasonal, peaking in January and February each year and 94% of reports are in children under five years of age (Ryan *et al.* 1996).

2.3.2 Sporadic/outbreak cases

Specimens tested as part of investigations into general outbreak investigations of IID account for only a small proportion of total laboratory reports. Table 2.4 compares the number of reports originating from identified general outbreaks of IID, irrespective of the mode of transmission, with the total number of laboratory reports between 1992 and 1994. The reports unaccounted for by general outbreaks may be genuine sporadic cases, arise from family outbreaks or from unrecognised or unreported general outbreaks.

2.3.3 Results of previous studies

Previous studies have reported incidence rates of IID in the population between 0.66 and 1.20 episodes per person-year (Table 2.5). In a Welsh study, less than 4% of people with gastroenteritis consulted a GP whereas two other studies (one in the USA and one in The Netherlands) reported that around 20% of cases presented themselves to a doctor. The RCGP reported a consultation rate of 0.029 episodes of IID per person in 1995, based on weekly returns from sentinel practices in England and Wales.

Campylobacter has been reported to be the most commonly detected pathogen in patients with diarrhoea in a number of studies, as shown in Table 2.6. The frequency

Table 2.4 Total number of laboratory reports compared to reports originating in all general outbreaks in England and Wales 1992–1995, ranked by number of laboratory reports. Reports include foodborne outbreaks, waterborne outbreaks, person-to-person spread, animal contact, and unknown mode of transmission

	NO. OF LABORATORY REPORTS*	LABORATORY REPORTS FROM GENERAL OUTBREAKS (% OF ALL REPORTS)		NO. OF OUTBREAKS**
Campylobacter spp.	166,290	272	(0.2)	24
All salmonellas	122,133	7,329	(6)	527
S.enteritidis PT4	60,377	4,316	(7)	331
S.enteritidis other PTs	13,428	960	(7)	59
S.typhimurium	22,393	1,002	(4)	80
S.virchow	7,609	334	(4)	19
other serotypes	18,326	717	(4)	38
Rotavirus	64,630	186	(0.3)	53
Shigella sonnei	32,622	895	(3)	46
Shigella flexneri	2,334	28	(1)	3
Giardia intestinalis	25,333	12	(0.05)	2
Cryptosporidium parvum	20,180	1,678	(8)	28
SRSV	6,375	2,054	(32)	709
Clostridium perfringens †	2,158	570	(26)	112
Escherichia coli 0157 #	2,058	164	(8)	27
Bacillus spp. †	387	22	(6)	29
Staphylococcus aureus †	273	15	(5)	11

* **Source:** laboratory reports from PHLS and NHS laboratories to CDSC under national laboratory reporting scheme
** **Source:** Surveillance system for general outbreaks of infectious intestinal disease
\# **Source:** PHLS Laboratory of Enteric Pathogens
† **Source:** PHLS Food Hygiene Laboratory

of detection of campylobacters ranged from 5.5% to 20.2% (mean 10.6%). The frequency of detection of *Salmonella* ranged from 2.7% to 4.3% (mean 3.5%).

In the two studies that examined all specimens for rotavirus, a higher frequency of detection than for campylobacters was reported (17.8% and 9.8% compared with 15.0% and 9.4%, respectively).

Table 2.5 Community rates and presentation rates of infectious intestinal illness reported by previous studies

COUNTRY (REFERENCE)	PERIOD OF STUDY	STUDY POPULATION	CASE DEFINITION	COMMUNITY RATE OF IID (RATE PER PERSON-YEAR)	PRESENTATION RATE OF IID (RATE PER PERSON-YEAR)
USA (Dingle *et al.* 1953)	Jan 1948–Dec 1950	292 (61 families)	Acute gastrointestinal illness	1.60	-
England (Tuckman *et al.* 1962)	Jan 1957–Dec 1958	8,041	Acute gastrointestinal illness <7 days	-	0.052
USA (Monto and Koopman 1980)	1965–1971	4,905	Diarrhoea, vomiting, upset stomach or nausea	1.20	0.22
England (Kendall 1982)	Jan 1978–Dec 1980	2,796	3 or more liquid stools within 48 h	-	0.056
Canada (Payment *et al.* 1991)	Mar–Jun 1988 Sep 88–Jun 89	2,408	Vomiting or diarrhoea, nausea with abdominal pain	controls: 0.76* water filter: 0.50	-
The Netherlands (Hoogenboom 1994)	Mar–Jul 1991	2,257	Mild: diarrhoea or vomiting plus 2 other symptoms within 1 week Severe: diarrhoea or vomiting plus 2 other symptoms for at least 2 days	Mild: 0.63 Severe: 0.18	Mild: 0.11 Severe: 0.04
Wales (Palmer *et al.* 1996)	Jan–Mar 1992 Aug–Oct 1992	1,557	Acute onset of diarrhoea and/or vomiting	0.89	0.033
Great Britain (Feldman and Banatvala 1994)	Oct 1992–Jan 1993	8,143 (adults)	3 or more loose stools	0.93	-

* randomised trial of water filters

Table 2.6 Studies reporting frequency (%) of detection of enteric pathogens in patients with symptoms of IID presenting to general practitioners in England and Wales

	STOOLS EXAMINED	*CAMPYLOBACTER*	*SALMONELLA*	*SHIGELLA*	*CRYPTOSPORIDIUM*	ROTAVIRUS	SRSV	*GIARDIA*
England 1977–8 (Rousseau 1983)	73	15.0	2.7	1.3	0	17.8	0	0
England 1978–80 (Kendall and Tanner 1982)	168	20.2	3.6	0.6	NT	NT	NT	NT
England 1983–4 (Hunt 1984)	867	5.7	4.3	0.8	5.0	2.2*	0*	2.0
England 1983–4 (Skirrow 1987)	33,857	5.5	3.4	0.8	NT	NT	NT	NT
England & Wales 1985–7 (Anon. 1990)	62,421	7.6	3.3	0.7	2.1	NT	NT	NT
Wales 1992 (Palmer *et al.* 1996)	255	9.4	3.5	1.2	0	9.8*	2.0*	0.4

NT: not tested
* not all specimens tested

2.3.4 Transmission of pathogens associated with IID

2.3.4.1 Zoonoses

Many of the food- and waterborne pathogens that cause IID have their reservoir in animals. These include *Salmonella* spp., *Campylobacter* spp., VTEC, *Yersinia* spp., and *Cryptosporidium parvum*.

Campylobacter spp. are found in poultry and a range of food animals and pets. Poultry can be colonised with *C.jejuni* at rates from 0 to 100% (ACMSF 1993a).

All salmonellae, excluding *S.typhi* and some *S.paratyphi*, are zoonotic (MAFF 1993). They are ubiquitous among domestic and wild animals, reptiles and avian species and one feature of salmonellas is their ability to adapt to different host species and to changing environmental factors. Although more than 2200 serotypes of salmonella are recognised, *S.enteritidis* and *S.typhimurium* account for three quarters of the reported human infections in the UK. The dramatic increase in salmonellosis in the UK since 1984 has been almost entirely due to *S.enteritidis*, particularly PT4, which is well documented to be largely associated with poultry and poultry products (Department of Health, 1988, Hopper and Mawer 1988, Lister 1988, Cowden *et al.* 1989). The intensive rearing of poultry using strains of poultry selected for food conversion efficiency and egg production, rather than disease resistance, combined with the pyramidal structure of poultry rearing, provided fertile ground for *S.enteritidis*. *S.enteritidis* PT4 causes an invasive infection in some poultry that leads to septicaemia and subsequent chronic infection of various organs; when the ovary is infected transmission of the organisms to the contents of the egg can occur (Humphrey *et al*. 1989). *S.virchow* and *S.hadar* are serotypes that also have their reservoir in poultry.

The epidemiological evidence indicates that multi-resistant *S.typhimurium* DT 104, although most commonly associated with cattle, is widely distributed in a variety of different food animals and poultry in which it can cause illness (Threlfall *et al.* 1996, Anon 1997). Therefore the potential exists for a diverse range of foodstuffs to become contaminated.

The reservoir of VTEC O157 is cattle and sheep; however, it does not usually cause illness in these animals (Chapman 1997). Other animals have also been documented to carry VTEC O157, including dogs, goats and horses. Non-O157 VTEC producing a variant verocytotoxin are also commonly found in pigs but are rarely associated with human disease.

The main reservoir for *Y.enterocolitica* is pigs; however, it is also found in poultry, rodents, rabbits, sheep, cattle, horses, cats and dogs.

Cryptosporidium parvum has been identified in a variety of animal species and may have important bovine and ovine reservoirs (Meinhardt *et al.* 1996, Fayer *et al.* 1997). However, recent genetic analysis indicates that approximately 30% of cases in the UK originate from human sources (McLauchlin *et al.* 1999).

Rotavirus infections occur in animals. However, the serogroups that affect humans are believed to be largely species specific, although serogroup C are also found in pigs. The explanation for the seasonality and the site of the inter-epidemic reservoir remains unresolved.

Humans are the only known reservoir for SRSVs.

2.3.4.2 Foodborne transmission

A wide range of enteric pathogens and their toxins can be transmitted via food, including *Campylobacter* spp., *Salmonella* spp., *Shigella* spp., enterovirulent *E.coli*, *Clostridium perfringens*, *Bacillus* species, *Staph.aureus* and SRSVs.

Campylobacter infections can be acquired from contaminated food particularly poultry (Harris *et al.* 1986, Butzler and Oosterom 1991, Neal and Slack 1995) and unpasteurised milk (Robinson and Jones1981, Woods *et al.* 1992, Fahey *et al.* 1995). Almost all cases are apparently sporadic and a proportion are associated with the consumption of poultry (Oosterom 1994). Outbreaks are rare and between 1992 and 1995 cases reported in outbreaks represented only 0.2% of all reports (Djuretic *et al.* 1996b). *Campylobacter* spp. do not multiply in food under normal circumstances and most of the larger outbreaks are due to the consumption of unpasteurised milk or to water contaminated with animal faeces.

A combination of the contamination of eggs and poultry meat, and an increasing consumption of poultry meat has led to the predominance of *Salmonella enteritidis* PT4 as a cause of human salmonellosis. Many European countries have also experienced a higher incidence of *S.enteritidis* PT4 infections and the organism has been isolated from human cases and food items in over ten European countries as well as from countries as far apart as Argentina and Japan (Baird-Parker 1990). In parts of the USA there have also been large increases in *S.enteritidis* infections associated with shell eggs (Morse *et al.* 1994). *S.virchow* and *S.hadar* are primarily associated with the consumption of poultry.

Although white and red meat, eggs, unpasteurised milk and products derived from these foods are the suspected vehicles of infection in many outbreaks of salmonellosis, salmonellas can contaminate an even wider range of foodstuffs; for example, outbreaks have been associated with contaminated yeast, chocolate, snack foods, and orange juice.

VTEC infection has been associated with the consumption of undercooked minced beef (Thomas *et al.* 1996, Anon 1993, Bell *et al.* 1994); however, a range of other foodstuffs including cooked meats, meat pies, dry cured salami, vegetables, fruit, fruit juice, cheese, milk and yoghurt have been implicated. Less than 10% of cases of VTEC O157 in England and Wales between 1992 and 1995 arose in general outbreaks where some of the above risk factors were identified. To establish the proportions of the remaining 90% of cases arising from the above or from other risk factors the DH has funded a national case control study which commenced in September 1996 (Adak *et al.* 1996).

Shigella sonnei is primarily spread by the person-to-person route; however, foodborne outbreaks can occur. In 1995 an outbreak of shigellosis occurred in several European countries, associated with the consumption of contaminated ‘iceberg’ lettuce (Frost *et al.* 1995).

Staphylococcus aureus food poisoning results from the ingestion of an enterotoxin produced by toxigenic strains of *Staph.aureus* in food.

Almost all outbreaks of *C. perfringens* food poisoning are associated with inadequately heated or reheated meat or meat products. Some spores can survive normal cooking temperatures and will then germinate and multiply rapidly during slow cooling or storage at ambient temperature. Heavy bacterial contamination ($>10^5$ organisms per gram of food) is usually required for clinical disease.

The spores of *Bacillus cereus* can survive boiling for short periods and will subsequently germinate and multiply in food that is stored unrefrigerated. The emetic toxin and the enterotoxin are formed in food and the enterotoxin is also formed in the intestine after ingestion of large numbers of organisms. The emetic toxin is heat stable and is not destroyed by brief rewarming of food.

In Northern Europe the ingestion of undercooked pork and cross-contamination of other foods by uncooked pork are important factors in the transmission of *Yersinia enterocolitica* infections (Tauxe *et al.* 1987).

The link between infection with SRSVs and the consumption of shellfish is well documented (Sockett *et al.* 1985, Scoging 1991, Rippey 1994, Dowell *et al.* 1995). Shellfish become contaminated if they are grown in areas contaminated with human sewage. Depuration does not remove all viruses from oysters (Scoging 1991). Humans are the only known reservoir for SRSVs emphasising the risk of growing shellfish in water contaminated by human sewage (Rippey 1994).

2.3.4.3 Waterborne transmission

A wide range of enteric pathogens can be transmitted in water including *C. parvum*, *G. intestinalis, Campylobacter* spp., *Salmonella* spp., *Shigella* spp., enterovirulent *E.coli*, *V. cholerae*, rotaviruses and SRSVs.

Human infection with *Cryptosporidium* occurs particularly after the consumption of treated water as the oocysts can withstand chlorination. Ingestion of as few as 10 oocysts may result in infection.

Other pathogens associated with the consumption of water in the UK include *Campylobacter* spp., *Giardia* and VTEC. These are usually associated with untreated water, borehole supplies and private wells, rather than treated public supplies. *Aeromonas* spp. are commonly found in environmental waters and it has been suggested that consumption of contaminated water is a major route of transmission.

2.3.4.4 Person-to-person spread

Most of the enteric pathogens can be transmitted by person-to-person spread, particularly in the very young and the elderly, those suffering from learning difficulties, and in circumstances where normal hygiene measures are difficult to maintain or ignored.

Nosocomial transmission, the transmission of infections within hospitals and residential healthcare facilities, is well described for a number of agents of IID, most notably *C. difficile*, *Salmonella*, SRSV and rotavirus. Several factors contribute to this mode of infection, including underlying disease, drug treatment, crowding, and breakdowns in hygiene.

Shigellosis is highly communicable, the causative organism being 100 times more infective than *Salmonella* (DuPont *et al.* 1989, Jawetz *et al.* 1989). *S.sonnei* is the most common species of *Shigella* in the UK and in recent years has accounted for over 90% of isolates reported to CDSC (Newman 1993). The principal route of transmission is faecal-oral which may be facilitated by a contaminated environment, particularly toilets, and is influenced by behavioural factors resulting in poor personal hygiene (Newman 1993). Similarly VTEC O157 also has a very low infectious dose (10–100 organisms) and is frequently spread from index cases by person-to-person transmission to family members and carers.

Almost all rotavirus infections are acquired by the person-to-person route and most children become infected within the first three years of life. Unlike many other enteric pathogens there is little evidence that the risk of exposure is different between developing and developed countries.

A large proportion of infections with SRSV are spread by person- to-person transmission. The predominant symptom of projectile vomiting creates a droplet aerosol and contaminates the environment. Individuals can then acquire infection by aerosol transmission or by direct transfer from contaminated surfaces and objects to their mouths with their hands. The low infectious dose facilitates transmission.

2.3.4.5 Direct contact with animals

All the zoonotic pathogens which have reservoirs in food and companion animals, exotic species of animals, birds and reptiles may be transmitted to humans by direct contact between humans and the natural host or its faeces. Visiting or working on farms has been associated with the acquisition of infections with *Salmonella* spp., *Campylobacter* spp., VTEC and *Cryptosporidium parvum*. In particular, *Cryptosporidium* and VTEC infection in children in close contact with young animals at farms which are open to the public has recently been recognised as a problem (Anon 1999). In addition companion animals like dogs and cats can act as a source for several pathogens including *Campylobacter* spp., *Salmonella* spp. and *Giardia*. The more exotic species such as reptiles have been associated with human cases of salmonellosis.

2.3.4.6 Factors influencing transmission

Food hygiene practices
Poor food hygiene practices such as inadequate heating, storing certain foods unrefrigerated, preparation of food too far in advance of consumption, cross-contamination from raw to cooked foods can all contribute to outbreaks and sporadic cases of food poisoning (Roberts 1982, Cowden *et al.* 1995).

Infected food handlers
Infected food handlers are the primary reservoirs for *Salmonella typhi* and SRSV and can potentially spread any enteric infection. During the acute phase of illness they are excreting large numbers of microorganisms and they should be excluded from work until they have been symptom-free for 48 hours (CDR 1995). Special recommendations exist for typhoid, paratyphoid, Hepatitis A and VTEC (CDR 1995). Infected food handlers can harbour *Staph.aureus* on infected skin lesions or in their nostrils and transfer it to food during preparation. Food handlers with septic lesions should be excluded from work until successfully treated. Nasal carriers do not need to be excluded but all food handlers should be aware of the possibility of transferring infection from their nostrils to food via their hands (Anon 1996a).

Travel abroad
Travel abroad may result in changes in people's eating behaviour and also in exposure to a wider range of pathogens. Infections acquired abroad include those caused by *Campylobacter*, *Salmonella*, *Shigella*, enterovirulent *E.coli*, *V.cholerae*, protozoa and helminths.

Up to 20% of cases of infection with non-typhoid *Salmonella* and with *Campylobacter* acquire their infection abroad. Most cases of infection with *Salmonella typhi*, *S.paratyphi*, *S. dysenteriae* and *S.boydii* are acquired abroad. Although apparently indigenous cases of *S. flexneri* occur in the UK, more than half of the cases report a history of recent foreign travel.

Antibiotic treatment
Disruption of the normal bowel flora as a result of antibiotic treatment allows *Clostridium difficile* to proliferate. *C.difficile* infection is nearly always associated with, and triggered by, the use of antibiotics, in particular cephalosporins, penicillins and clindamycin either used alone or in combination (Borriello and Larson 1981). Infection is more common in the elderly (>65 years) from whom over two thirds of the annual reports to CDSC arise. Recurrence of diarrhoea following apparently successful treatment is common, occurring in up to 20% of cases (Bartlett *et al.* 1985). In the majority of cases this has been shown to be due to reinfection rather than relapse due to germination of spores persisting in the bowel (Wilcox *et al.* 1998). Nosocomial outbreaks are common in settings with vulnerable patients.

Antibiotic-associated diarrhoea has also been associated with enterotoxigenic *C.perfringens* in hospital settings and can be as common a cause of nosocomial diarrhoea as *C.difficile* (Hancock 1997).

Gastric acid suppression
Gastric acid provides an effective barrier to the passage of gastrointestinal pathogens into the intestine from the stomach and factors that reduce gastric acid output, such as underlying disease or gastric surgery, increase the risk of IID. Pharmaceutical agents such as cimetidine, ranitidine and omeprazole suppress acid production and may also increase the risk of *Campylobacter* and *Salmonella* infection and intestinal carriage of *Listeria monocytogenes*. Volunteer challenge studies with ETEC and *Vibrio cholerae* have shown that use of recreational drugs such as cannabis may increase the risk and severity of IID by reducing gastric acid production.

Immune suppression
Immune suppression as a result of infection with HIV, cancer chemotherapy, or as a result of immunosuppressive therapy can leave individuals more susceptible to enteric pathogens. Both cryptosporidiosis and *Salmonella* septicaemia are AIDS-defining illnesses.

2.4 SOCIO-ECONOMIC REVIEW

2.4.1 Background

Estimates of national costs of salmonellosis requested by the Richmond Committee were submitted to the Committee, based on studies of *salmonellosis* (Sockett and Roberts 1991, Sockett 1993). It was estimated that the costs per case were between £789 and £861 which implied that the costs of salmonella in England and Wales in 1992 were between £350m and 502m. These estimates provided only a partial view of the national burden of IID. There are few reliable estimates of the size and distribution of the socio-economic burden of a comprehensive range of intestinal infectious diseases. Studies and methods used to assess this burden are reviewed below.

2.4.2 Economic evaluation

Economic evaluation is a technique that enables efficient choices to be made about the use of resources. Although there is a long history of economic evaluations in the field of public health (Cullens 1891)evaluations of intestinal infection are comparatively recent, stimulated by the increase in reported infections, particularly of *Salmonella* in the late eighties (Agriculture Committee 1989). The major types of economic evaluation are cost benefit analysis, cost effectiveness analysis, cost

utility analysis and cost of illness studies, sometimes referred to as studies of the socio-economic burden of disease.

Costs of illness studies are the earliest forms of economic evaluation and these are widely used in studies of intestinal infection (Sockett and Stanwell-Smith 1986, Sockett and Pearson 1987, Roberts *et al.* 1989, Sockett and Roberts 1991, Roberts 1988, 1989, Roberts and Marks 1995). All costs or burdens of illness are estimated and benefits are expressed as avoided costs that would arise from an intervention to prevent or contain the disease. The pool of resources used as a result of the infection are potentially available for other purposes. The method has been criticised because of its concentration on potential rather than realized benefits and because costs avoided may not reflect the value society places on avoiding illness. Benefits can also be assessed as the amount persons are willing to pay to avoid an illness. Estimates of willingness to pay have been undertaken but are difficult particularly when public health issues are involved.

2.4.3 Basis for assessment

Socio-economic burden of disease studies have been estimated using:

- population surveys
- studies of outbreaks
- projections using incidence rates
- assumptions about clinical severity and
- use of resource.

One of the very few surveys was undertaken by Sockett (1993) into the costs of laboratory confirmed cases of salmonellosis in England and Wales. This study estimated that the cost per case was £789. These costs included £106 for public health investigation and testing; £191 for health sector costs and £412 for lost productivity. Studies of outbreaks include a study of milk-borne *Salmonella* in Scotland in 1981, estimated to have cost £1l.3m (Cohen *et al.* 1983). Costs of an outbreak in 1982 of *S. napoli* were estimated as £504,808, the intervention having saved some £1,673,826 (Roberts, *et al.* 1989). As surveys are rare, estimates of national costs are usually based on projections of numbers from epidemiological sources and costs from outbreaks or from informed opinions about clinical severity. Such estimates of national costs of organisms include studies by Roberts (1988) for salmonellosis, who estimated costs in the USA to be $983m to 11.4m; Todd (1989), including different components of costs, estimated costs of salmonellosis in the USA in 1989 to be $3991m based on an average cost per case of $1350; Roberts and Marks (1995) estimated costs of *E. coli* O157 as being between $216.3m and $580.4m in the USA in 1992; and Roberts and Pinner (1990) estimated costs in the USA in 1986 of $1.8m for maternal cases and $231m for foetal cases for *Listeria monocytogenes*.

As a basis of estimating the socio-economic cost of disease, each estimation procedure has advantages and limitations and needs to be interpreted with caution. It is estimated that sporadic cases represent two-thirds of all reported infections of salmonellosis in England and Wales; projections from outbreaks might not represent sporadic cases adequately, but it is easier to estimate opportunity costs, the forgone benefits that arise because of the infection, the impact on industry and local health and community services from outbreak studies.

2.4.4 Underestimations of costs of intestinal infections

Underestimations occur because not all the clinical consequences of disease are taken into account. Most intestinal infections are self-limiting and of short duration.

Many infections do not come to the notice of clinicians, and even if they do, some go unreported. These submerged cases, though less severe, are numerous but research tends to concentrate upon cases that seek clinical care. Costs of submerged cases in an outbreak of salmonellosis were estimated to be £166,000 by Roberts *et al.* (1989). Costs of submerged cases of *E. coli* O157 were estimated to be between $29m and $58m by Marks and Roberts (1993). Submerged costs were also included by others including Krug and Rehm (1983) for Germany, and Curtin (1984) for Canada. Ratios of known to unknown cases and their relative costliness are needed for these estimates and these ratios vary with the organism, dose and vulnerability of those infected. Evidence on which to base such estimates is scant. Concentration on the acute phase of the illness underestimates the burden of disease if there are long-term sequelae. The socio-economic burden should be estimated over the course of the illness and appropriately discounted. Busby *et al.* (1997) estimated that the impact of Guillain-Barre Syndrome following campylobacteriosis was likely to be $197–902m for cases resulting from foodborne infections.

2.4.5 Cost categories included

Most studies concentrate upon the costs that occur as a result of infection, the *ex-post* costs that include costs to the public health sector such as costs of investigation and laboratory tests of food and human samples, costs to the health care sector distinguishing between costs to hospitals, general practice and community care, costs to those infected and their families and costs to industry and the wider economy. Few studies include a comprehensive range of these costs. Roberts *et al.* (1989) and Sockett (1993) included the public health costs incurred as a direct result of an outbreak. Both direct and indirect costs to patients and their families are included by Cohen *et al.* (1983) and Sockett and Roberts (1991). Most studies include only direct costs of medical care and indirect costs to families as reflected in time off work. The hospital costs are usually borne by health insurance schemes or national health services but may well be borne by individuals.

Costs to industry are often included in estimates of the national burden (Todd 1989). Some of these costs may represent the distribution of costs amongst firms in an industry and not net costs to society as a whole.

The infections investigated, the costs included in studies and the ways in which the costs are presented vary, making generalisations of the socio-economic burden of IID difficult. A summary of the findings of some of the major studies is provided in Table 2.7.

Table 2.7 Summary of the findings of major studies of the socio-economic burden of IID

PATHOGEN	AUTHORS AND DATE OF PUBLICATION	COUNTRY	TYPE OF STUDY	COSTS ESTIMATED
Salmonella	Cohen *et al.* (1983)	Scotland	CBA National Pasteurisation	£83 k
Salmonella	Krug and Rehm (1983)	Germany	COI National Modelled Estimates	DM108.25 m
Salmonella	Curtin (1984)	Canada	COI National Estimates	Can$83.7 m
Salmonella	Yule *et al.* (1986)	Scotland	CBA National Milk Irradiation	$25.3 k
Salmonella napoli	Roberts *et al.* (1989)	England & Wales	CBA Outbreak Control	£379 k
Salmonella	Sockett and Roberts (1989)	England & Wales	COI National Estimates	£330 –430 m
Multiple foodborne	Todd (1989)	Canada	COI/WTP National Estimates	Can$1.36 bn
Selected foodborne	Weiss *et al.* (1993)	USA	COI National Estimates	$5.6 bn
Campylobacter	Busby *et al.* (1997)	USA	COI National Estimates	$247.3–1,799.2 m
E.coli O157:H7	Roberts and Marks (1995)	USA	COI National Estimates	$29.4–59.9
E.coli O157:H7	Roberts and Upton (1997)	Scotland Great Britain	COI Outbreak COI National Estimates	£707 k £10.3 m

Key: CBA: Cost benefit analysis
COI: Cost of illness study
WTP: Willingness to pay study

Chapter 3
Methods

The study was designed to answer the main research questions identified by the Richmond Committee (Chapter 1).

3.1 STUDY DESIGN

3.1.1 The aim of the national study was:

To estimate the incidence and aetiology of cases of infectious intestinal diseases (IID) occurring in the population and presenting to GPs in England; and to compare these with national surveillance data. To identify the risk factors and socio-economic burden associated with illness.

The objectives of the study were:

i) To estimate the number and aetiology of cases of IID in the population, presenting to GPs and having stool specimens sent routinely for laboratory examination.

ii) To compare these numbers and the aetiologies with those recorded by the national laboratory reporting surveillance system.

iii) To estimate the prevalence of asymptomatic infection with agents associated with IID.

iv) To document differences between cases of IID (in the population and presenting to GPs) and similar but well people (controls).

v) To estimate the socio-economic burden of IID and its distribution.

3.1.2 Organisations involved in the study

The organisations involved in the study are shown in Figures 3.1 and 3.2. Those funded to carry out the work were:

- The Public Health Laboratory Service (PHLS) including the Communicable Disease Surveillance Centre (CDSC), London, Leeds Public Health Laboratory (PHL) and reference laboratories for specific organisms. These were the: Laboratory of Enteric Pathogens (LEP) and Food Hygiene Laboratory (FHL), Central Public Health Laboratory (CPHL), London and the PHLS Anaerobe Reference Unit (Cardiff).

- The Centre for Applied Microbiology and Research (CAMR), Salisbury.

- The Medical Research Council (MRC) Epidemiology and Medical Care Unit (EMCU) and the MRC's General Practice Research Framework (GPRF).

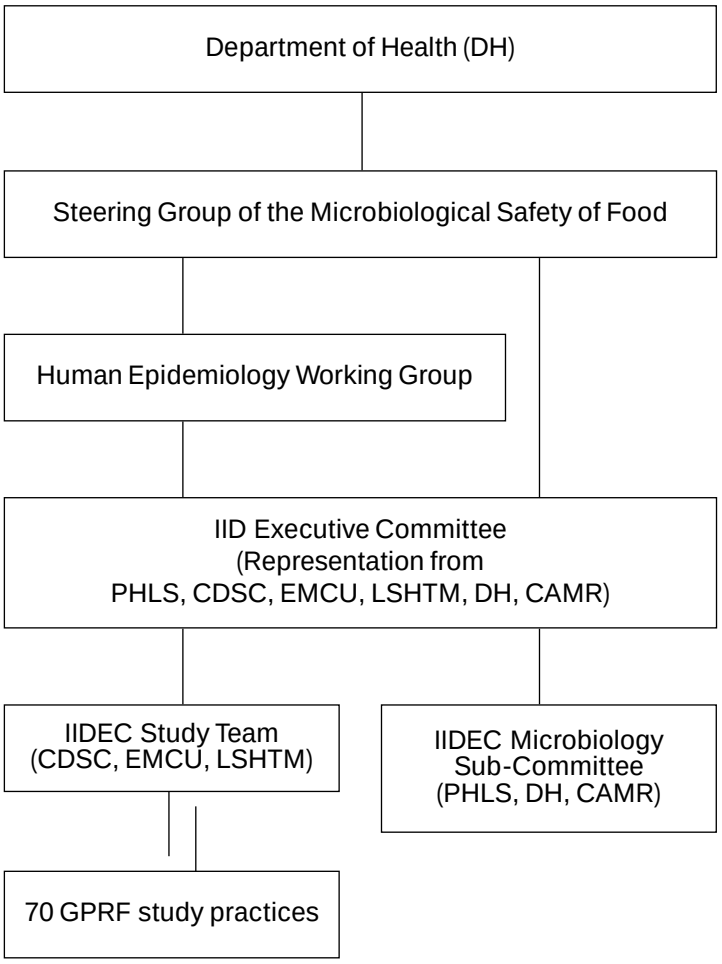
- The Communicable Disease Epidemiology Unit and Health Services Research Unit of the London School of Hygiene and Tropical Medicine (LSHTM).

These organisations shared responsibility for the study: CDSC, EMCU and LSHTM were responsible for the design of the study; EMCU for the local organisation of the study in the general practices and the collection and entry of the data; LSHTM for the entry and analysis of data; Leeds PHL and LEP for the first line microbiological testing. Isolates were sent to the relevant reference laboratories for confirmation and typing. CAMR was responsible for archiving the isolates and stool specimens.

A study team consisting of representatives from EMCU, LSHTM and CDSC co-ordinated practice recruitment, nurse training, data collection within the practices, quality assurance, data processing and coding. Representatives from each of the laboratories met with microbiologists from the Department of Health (DH) on a regular basis to review microbiological aspects of the study. Both groups reported to the Executive Committee, which met every three months to monitor progress and to advise on strategic and scientific issues.

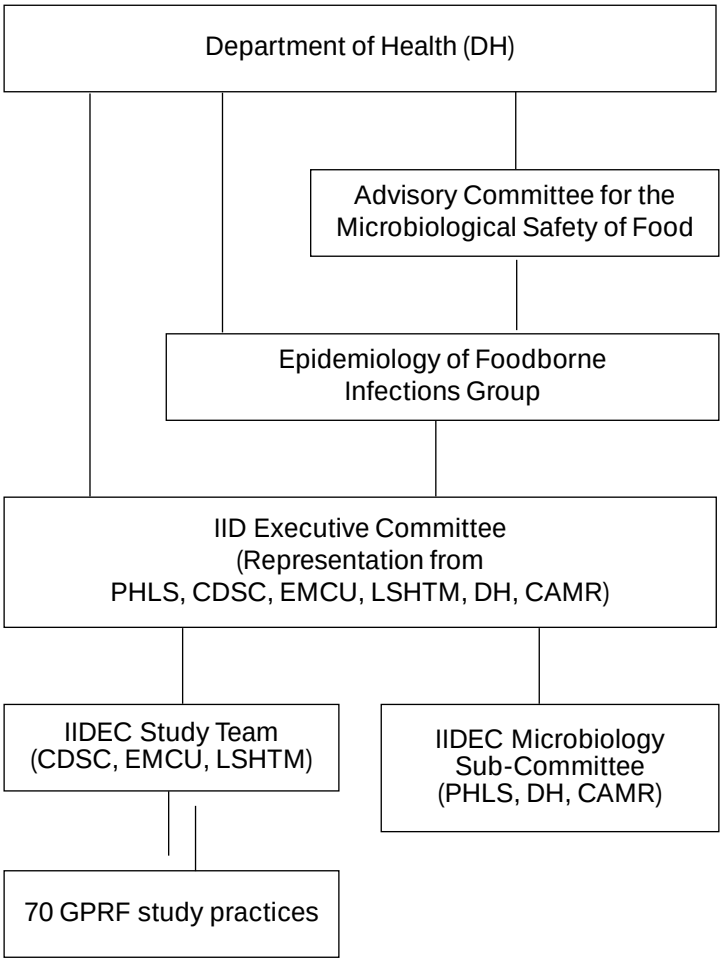
The Executive Committee reported to the Steering Group on the Microbiological Safety of Food (SGMSF), both directly and via its Human Epidemiology Working Group (HEWG). On 3 May 1995 the Government announced that the functions of the SGMSF would be merged with those of the Advisory Committee on the

Figure 3.1 Organisation responsibilities for reporting and running of the study of IID in England: Original Structure (to May 1996)



Microbiological Safety of Food (ACMSF) with the aim of ensuring a more efficient and streamlined consideration of food safety issues. Co-ordination of the Government's microbiological food safety surveillance programme was passed to two new groups, one the Microbiological Surveillance of Food Group (MSF)dealing with food and the other, the Epidemiology of Foodborne Infections Group (EFIG), dealing with human and animal epidemiology. The revised organisational responsibilities are shown diagramatically in Figure 3.2.

Figure 3.2 Organisation responsibilities for reporting and running of the study of IID in England: Final Structure (to May 1996)



3.1.3 Setting

The country was divided into three areas with approximately the same population in order that a geographical comparison might be made. The precise number of practices drawn in each area was in proportion to the area's total population from the 1981 census. The areas were: North (including the former health authority regions Northern, Yorkshire, North Western, Mersey), Midlands & Southwest (including East Anglia, West Midlands, Trent, South Western, Wessex) and the Southeast (the Thames Regions).

Seventy practices were selected to be representative of socio-economic characteristics of the area, and for urban or rural location. Tertiles of the population distribution of ward-based Jarman deprivation scores were used to stratify by socio-economic characteristics; scores were originally based on 1981 census information, later updated to 1991 information (Jarman 1984). For each area the

number of GPs chosen within a stratum reflected the Jarman score distribution of the area, and together the sample represented the Jarman score distribution of England and Wales. The urban/rural mix was chosen to represent each area as a whole. The sample attempted to include a mix of GPs with different OPCS Area Aggregate classifications (Inner London, Outer London, Other Metropolitan Districts, Principal Cities, Cities, Industrial, New Towns, Resort/Sea/Retired, Mixed Urban/Rural, Remote Rural) and a wide geographical spread within the area.

With these requirements it was not possible to obtain a stratified sample of GPs at random, given that a complete sampling frame which included these characteristics was not available, and GPs needed to be enthusiastic and resourced for research. Therefore GPs were volunteers selected from the MRC's GPRF to meet the criteria specified.

Figures 3.3–3.5 show the geographical distribution and classification of study practices by study component, Jarman index and Office of Population Census and Surveys (OPCS) area aggregate category respectively.

Figure 3.3 The Study of Infectious Intestinal Disease in England

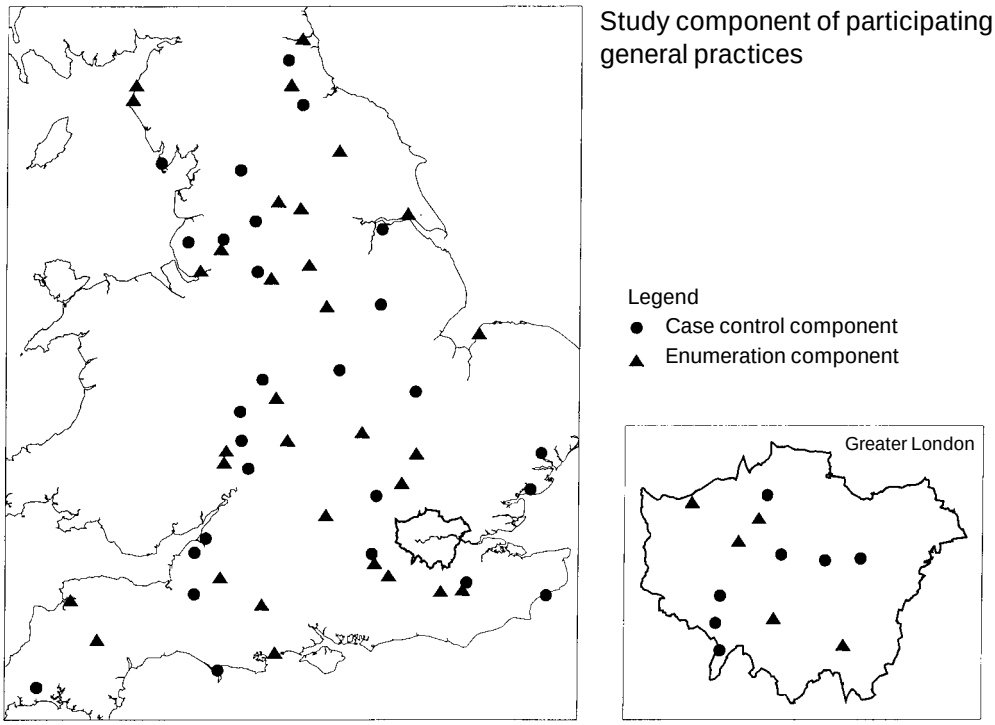


Figure 3.4 The Study of Infectious Intestinal Disease in England

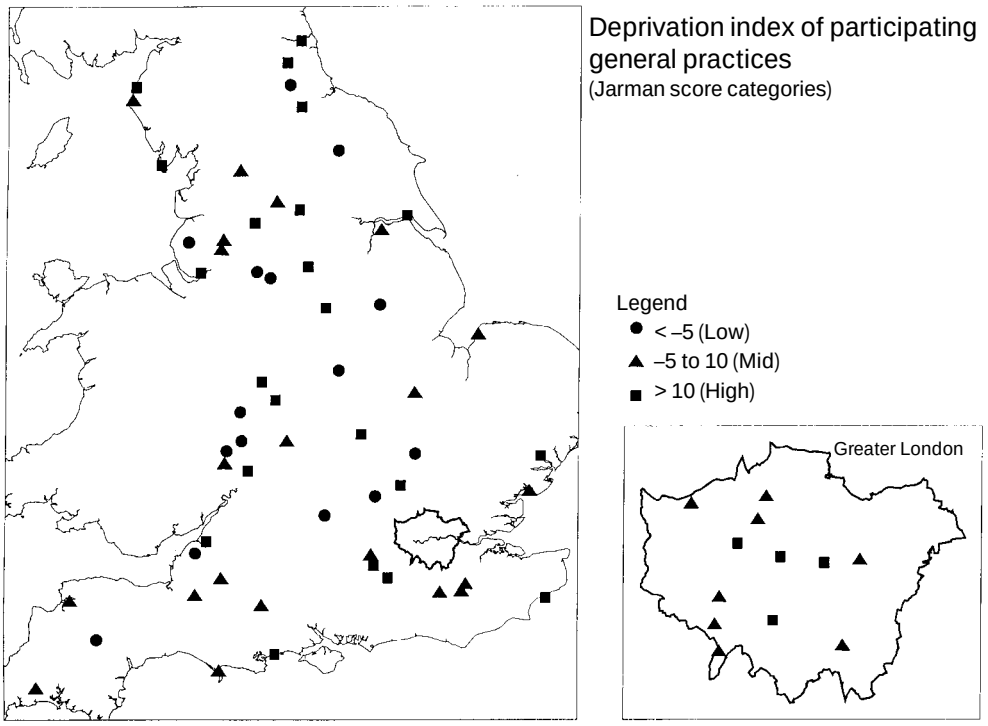
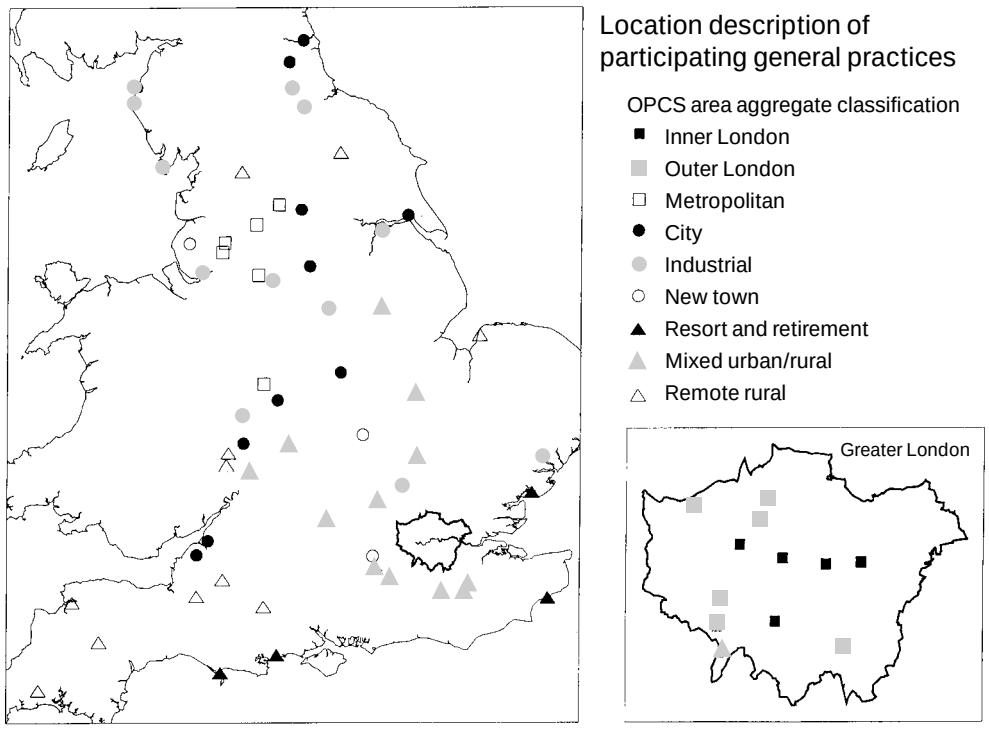


Figure 3.5 The Study of Infectious Intestinal Disease in England



3.1.4 Case definition

All components of the study used the same definitions for cases and controls:

Case of infectious intestinal disease (IID): Cases are persons with loose stools or significant vomiting lasting less than two weeks, in the absence of a known non-infectious cause and preceded by a symptom-free period of three weeks. Vomiting was considered significant if it occurred more than once in a 24-hour period and if it incapacitated the case or was accompanied by other symptoms such as cramps or fever.

Control: Cases are persons who have been free of loose stools or significant vomiting for three weeks prior to the onset of illness in the case, matched to case by age and sex according to the criteria in Appendix 1.

Non-infectious causes of diarrhoea such as Crohn's disease, ulcerative colitis, cystic fibrosis and coeliac disease, were excluded; non-infectious causes of vomiting such as surgical obstruction, excess alcohol, morning sickness, and regurgitation in infants were also excluded.

The decision tree used by GPs to ascertain cases is shown in Figure 3.6.

3.1.5 Study components

The study consisted of nine components (see Figure 3.7):

i) **A population cohort component** ('the community component') to estimate the incidence and aetiology of IID in the community.

ii) **A nested case-control component** based on cases ascertained in the cohort to identify risk factors for IID in the community.

iii) **A GP case-control component** ('the GP component') to identify risk factors and to estimate the incidence and aetiology of IID presenting to GPs.

iv) **An enumeration component** to estimate the incidence of IID presenting to GPs and the proportion of samples routinely sent for microbiological examination.

v) **An under-ascertainment component** to determine the degree of under-ascertainment of cases in components (iii) and (iv), to identify the practice and patient characteristics associated with ascertainment and to provide adjustment factors for the analysis of presentation rates.

vi) **The first under-reporting component** consisting of a search of the national database to identify cases corresponding to those reported to GPs in the enumeration study and from this to estimate the proportion of infections reported to national surveillance.

vii) **The second under-reporting component** consisting of a **questionnaire** survey of microbiological laboratories in England to determine the proportion of identifications reported to national surveillance. This also confirmed the representativeness of microbiological laboratories in the enumeration component in terms of the number of stool specimens analysed.

viii) **An Accident and Emergency (A&E) department component** to estimate the rate of presentation of IID to A&E.

ix) **A socio-economic costs component** to estimate the burden of illness of IID occurring in the community and presenting to GPs.

Figure 3.6 Decision tree used by GPs to ascertain cases

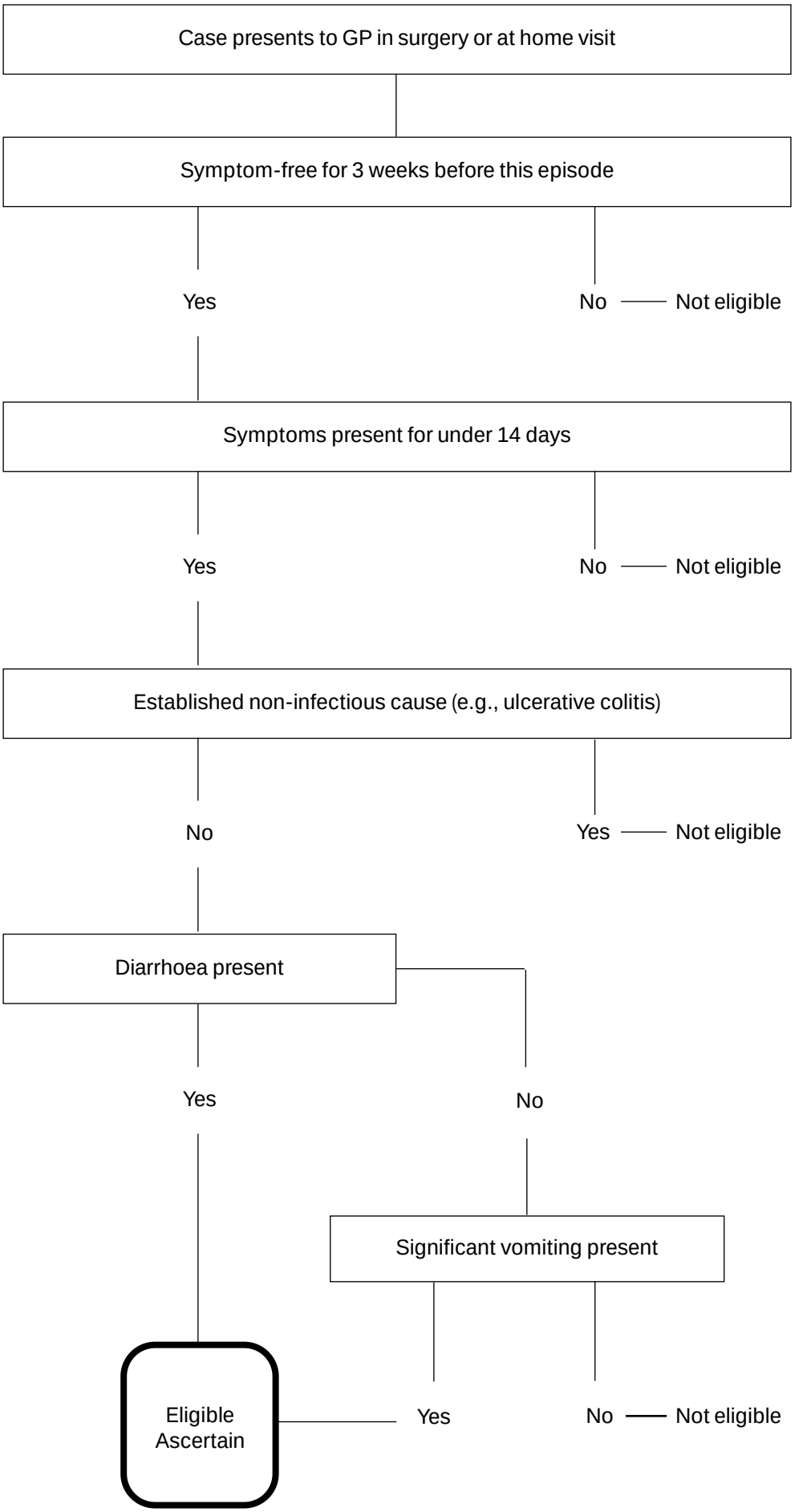
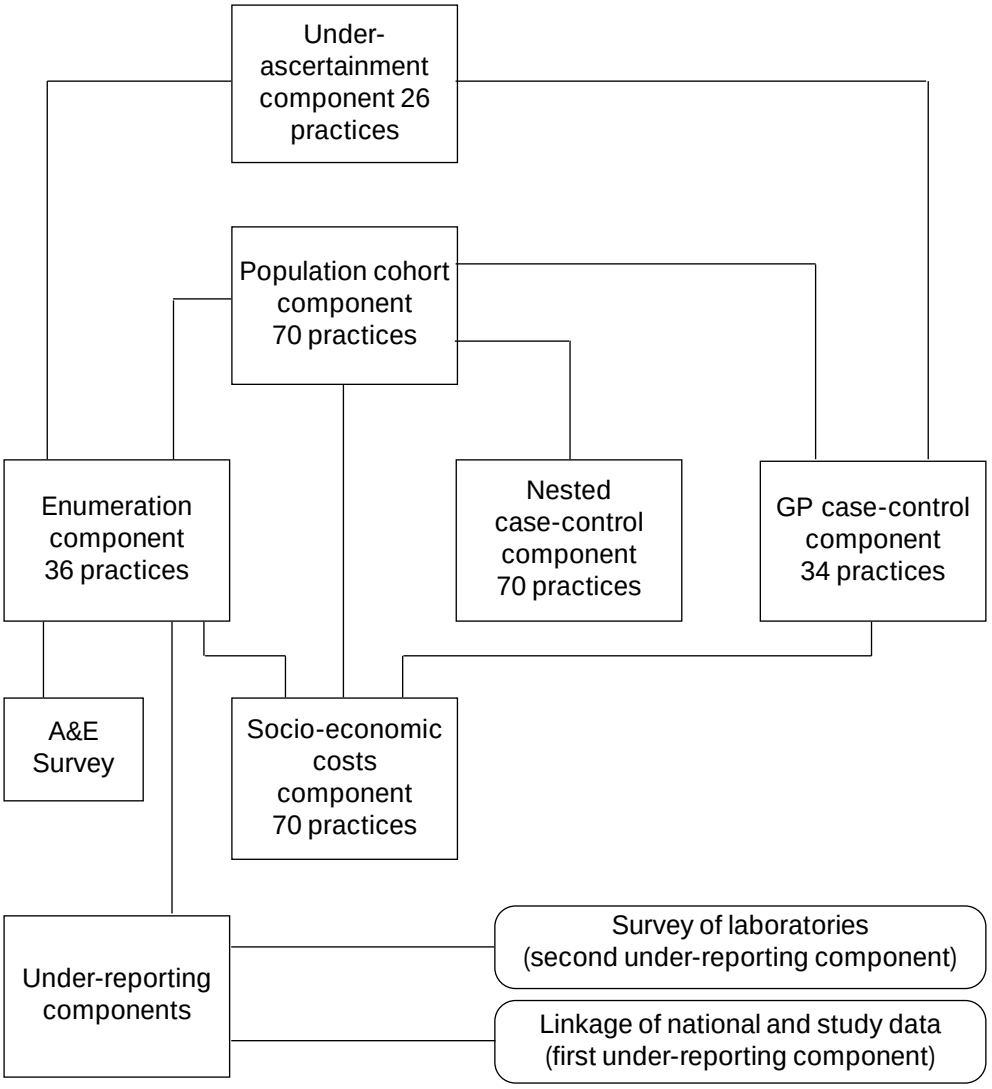


Figure 3.7 Design of Study of Infectious Intestinal Disease in England



3.1.5.1 **The population cohort component**

Study population. Persons were drawn at random from the age-sex register of the 70 GP practices and followed up for a period of six months. Two cohorts were recruited consecutively, so that a total period of 12 months' follow-up was conducted in each practice. The sampling of registers took place at the LSHTM using computerised copies of the register. Two hundred subjects were selected for each cohort. The second cohort was weighted according to the age-sex recruitment rates in the first cohort so that sufficient subjects were obtained in groups with a low recruitment rate. The cohort sample was then returned to the practice nurse who checked to ensure that the selected members were still registered with the practice. In most practices there was a short time gap between the end of the first cohort and beginning of the second. The effect on seasonal coverage is discussed below.

Study size. An average of 90 person-years of follow up in each of the 70 practices was calculated to enable a comparison of the incidence of IID. The total sample invited was 200 to allow for non-participation at the expected recruitment rate of 45% based on experience in the pilot study (Roderick *et al.*1995). This number would enable an estimate of the incidence of IID in the community with a precision of

± 10%, using a 95% confidence interval. This would permit estimates to be made separately in adults and children, with a precision of ± 20%. Area specific estimates could be made with ± 20% precision.

Recruitment. Persons, drawn at random from the practice registers, were invited to participate in the study using a letter signed by the study GP in their practice. The practice nurse followed this up with a phone-call, and by a letter (if there was no response or if there was no phone number available). Persons who refused were asked to complete a short 'non-participant's questionnaire about their socio-demographic factors and the reasons for refusal. The same questionnaire was sent to all other non-responders.

Briefing. Subjects agreeing to participate in the study were asked to attend a briefing session with the study nurse before the start of the study. Included with the invitation was a self-administered questionnaire to collect personal and household details similar to those collected in the GP case-control component. This was checked for completeness by the practice nurse at the briefing session.

In the briefing session the nurse explained the study, asked cohort members for written informed consent, and gave detailed instructions. Each cohort member was given written instructions and standard diary cards on which to report the presence or absence of any gastrointestinal illness, and a stool collection kit. They were instructed how to collect adequate stool specimens, pack the container, and post it to Leeds PHL using the pre-paid envelope.

Follow-up and collection of data. Diary cards were filled in by the cohort members every week and returned by post to the practice nurse irrespective of whether or not the member had IID. The practice nurse contacted everyone who failed to return their weekly diary card. Cohort members were asked to report by telephone, and to collect a stool specimen, if they passed a single loose stool or had significant vomiting. All cases fulfilling the case definition of IID were recruited into the nested case-control study.

GP records were reviewed at three months in those persons for whom no contact was made at the recruitment phase. The notesearch was performed to see if the person had made any contact with the practice in the three month period since the recruitment invitation. If there had been it was assumed that they were a true non-responder. If the practice records were not present (indicating that they had moved practice) it was possible that they might have been ineligible — if they had moved before the invitation. Persons who had no contact but whose notes were in the practice could not be classified.

3.1.5.2 The nested case-control component

Design and setting. A nested case-control study of cases arising in the population cohort component, and appropriate controls.

Study size. About 870 cases were expected to occur in cohort members, for which the same number of matched controls were to be selected.

Collection of data and stool samples. When an episode of illness was reported (or if it became apparent when either a diary card was sent, or the nurse contacted a defaulting participant) an age-sex matched control was selected from the population cohort in that practice according to the criteria as listed in Appendix 1. A stool specimen was provided by cases at the beginning of their illness, or when the illness was discovered, if they were still symptomatic. The control was also asked to provide a stool specimen. A standard set of questions on short-term risk factors was

asked of both cases and controls using a self-administered questionnaire. This was checked by the practice nurse for completeness and data quality and any problems were clarified with the subject. Cohort members who had already been a case were subsequently eligible to be controls as long as they fulfilled the criteria of no loose stools or significant vomiting in the previous three weeks. If an appropriate control could not be obtained from the cohort, they were selected from the practice age-sex register.

3.1.5.3 The GP case-control component ('the GP component')

Design and setting. A 12-month prospective case-control study of persons consulting their GP with IID and appropriate controls. As practice recruitment was staggered, the study was undertaken in each practice during different 12 month periods.

Case definition. A person presenting to their GP with a new episode of IID during a 12-month period.

Controls. Age and sex matched persons from the same practice register were chosen at random from the practice list. Criteria for age matching are listed in Appendix 1.

Study size. The study was run in 34 practices. It was estimated that between 2,000 and 4,000 adult cases and 1,000 and 2,000 child cases would present over the 12-month period. A size of 1,000 cases would be sufficient to enable detection of risk factors for IID which occur at least twice as often in cases than controls (i.e., a relative risk of at least two), and are observed in more than 10% and less than 85% of controls, with 80% power and at the 1% level of significance. The greater number of adult cases predicted allowed for greater statistical power, or alternatively enabled the detection of risk factors beyond the 10–85% range of prevalence amongst controls. The study was not designed to identify risk factors for specific organisms, but its size would allow a limited analysis of specific organisms, and possible identification of risk factors with relative risks in excess of two. A level of significance greater than the traditional 5% level was sought in anticipation of the problem of multiple testing in assessing a large number of potential risk factors.

Recruitment of controls. GPs completed a standard form for each patient presenting with IID (in the surgery or at home visits) and gave them a standard letter informing them about the study and inviting them to participate. Persons phoning for advice were not included. Cases consenting to enter the study were given a stool specimen pack and asked to provide a specimen before taking any medication. Practices which used a deputizing service for out of hours calls contacted that service to ascertain any potential cases of IID seen out of hours for the nurse to follow-up.

Controls. For each case the practice nurse selected up to five age and sex matched potential controls sequentially from the age-sex register. The nurse invited them in turn, by phoning twice a day for three days, until one accepted.

Collection of data. Cases and controls were contacted by phone or letter by the practice nurse and asked to complete a self-administered questionnaire on short-term risk factors, identical to that collected in the nested case-control component. Subjects were offered the alternative of an interview at which the practice nurse completed the questionnaire with them. The nurse asked the cases if they were aware of whether their infection was acquired in an outbreak of IID. If cases were hospitalized Leeds PHL were informed. Leeds PHL then liaised with the hospital to obtain a stool specimen. The questionnaire was completed after discharge.

Collection of stool samples and culture. Cases and controls were asked to provide a stool specimen for microbiological investigation.

3.1.5.4 **The enumeration component**

Design and setting. A 12-month prospective study of cases presenting to GPs with IID, determining whether a stool specimen was sent for microbiological investigation and, if so, the laboratory findings. No controls were used.

Case definition. The same definition was used as in the population cohort and case-control components.

Study size. The study was conducted in 36 practices which permitted an estimate of the difference between the incidence of IID presenting to GPs with a precision of ± 20%, using a 95% confidence interval.

Collection of data. GPs completed a standard form for each case presenting with IID. The nurse recorded each case's age, sex, name, address, and place of consultation, whether a stool specimen was sent, the laboratory results and whether the case was hospitalized.

Practices which used a deputizing service for out of hours calls contacted the service to ascertain any potential cases of IID seen out of hours for the nurse to follow up.

3.1.5.5 **The under-ascertainment component**

Design and setting. Twenty-six general practices in the GP case-control and enumeration components in which diagnoses were routinely entered on practice computers.

Definition of under-ascertainment. Cases of IID who presented to the practice but were not ascertained.

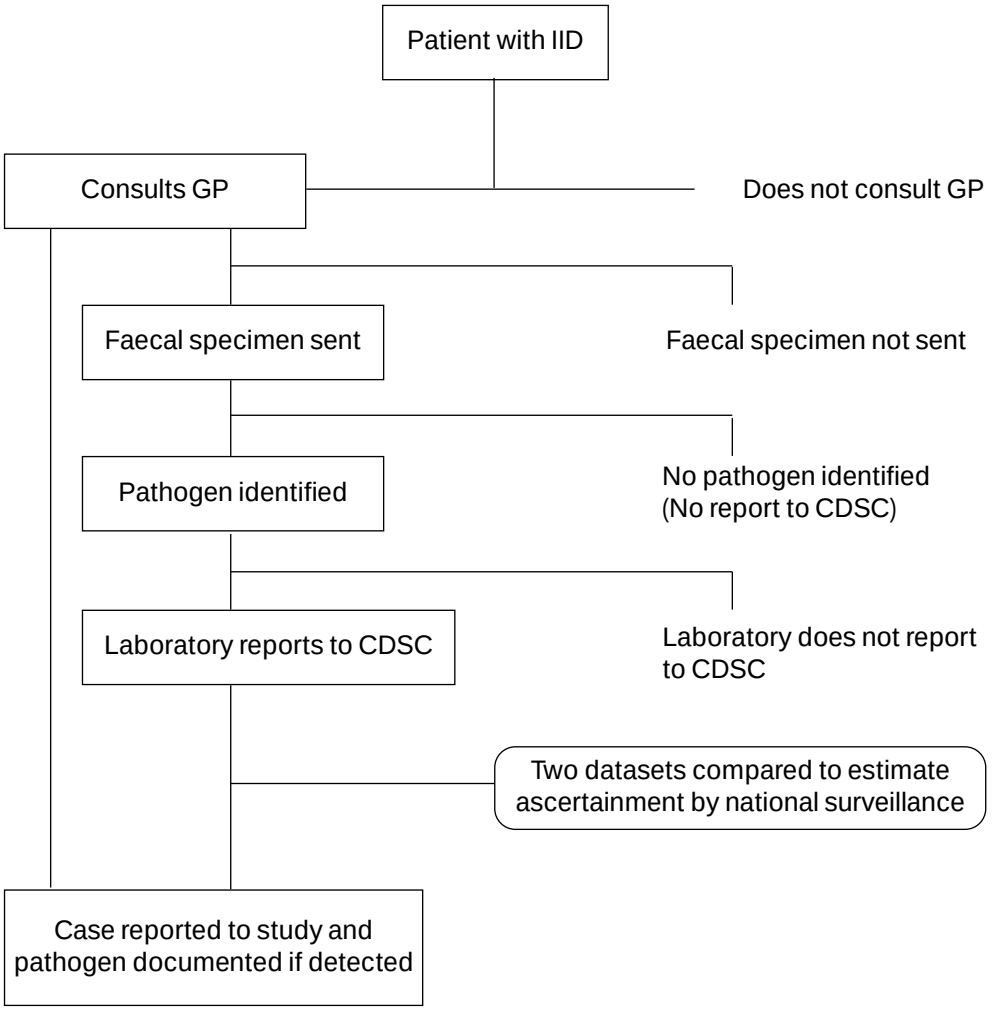
Collection of data. Persons potentially fulfilling the case definition were identified from the practice computer using Read code diagnoses of: IID, diarrhoea, vomiting, food poisoning and gastroenteritis. Practice computer records and case notes were studied to record information on personal and clinical details, presence of a non-infectious cause, treatment, place of consultation, and admission to hospital. Information on practice characteristics was also collected. Personal and clinical details of cases of IID were compared at the EMCU to determine if they had been ascertained.

3.1.5.6 **The first under-reporting component (by linkage of national and study data)**

Setting. Cases with isolates identified by laboratories serving in the enumeration component in whom organisms or toxins were identified and reports of identifications to the national surveillance centre.

Design. The national database at CDSC was examined to find records which matched laboratory reports sent to GPs in the enumeration component from the laboratories which served them. Search parameters were organism, laboratory number, name, sex, date of birth and date of specimen. Comparison of the numbers found in the national database with those reported to the study gave an estimate of under-reporting to CDSC (Figure 3.8).

Figure 3.8 Schematic representation of national laboratory surveillance and the first under-reporting component



3.1.5.7 **The second under-reporting component (by laboratory survey)**

Design. All PHLS and non-PHLS laboratories (both NHS and private) in England were surveyed by questionnaire. This asked about their total workload of faecal specimens and the number of selected gastrointestinal pathogens identified in 1994.

CDSC determined the number of reports of identifications of these pathogens received from these laboratories. Comparison with those reported by laboratories on their questionnaire gave an estimate of under-reporting to CDSC. This estimate was also used to confirm the representativeness of laboratories serving practices in the enumeration component

3.1.5.8 **Accident and Emergency component**

Design. Hospital A & E Departments whose catchment area included the practices in the enumeration component were identified. Those with computerised records were sent a questionnaire asking for details of any cases of IID from the practices who had presented. The survey requested details for the period during which each practice was participating in the enumeration component.

3.1.5.9 Socio-economic costs component

Design. Three weeks after inclusion in the poulation cohort, GP case-control or enumeration components cases received a questionnaire inquiring into the socio-economic burden of their infection. The practice nurses followed up any case not returning the questionnaire with a repeat questionnaire.

Study size. All cases were eligible to enter the socio-economic component.

Collection of data. Details on the characteristics of the case, the households, symptoms of the illness that persisted three weeks after the acute episode and the impact of these on the activities of daily living; the use of health sector resources and direct costs to the affected individuals and those who took care of them, and sickness related absence from work or school were collected. Information was also collected about willingness to pay for safe food and views about who was held responsible for food safety were sought.

3.1.6 Questionnaires

All subjects in the GP and community components received a self-administered questionnaire about risk-factors (see Table 3.4 and Appendix 6). The questionnaire was developed after a literature review for risk factors of IID, piloted and adapted for use.

Socio-demographic characteristics, clinical details and known and suspected risk factors for IID, both short- and long-term, were included. Short-term risk factors were those within ten days prior to the onset of symptoms whereas long-term risk factors were more persistent lifestyle factors. The text was adapted to produce separate questionnaires suitable for adult and child cases and controls. In the population cohort component a short questionnaire was sent to non-participants with questions on family size, social class and reasons for refusal.

The self-administered questionnaires used in the socio-economic component were developed from previous studies of the costs of salmonellosis and from the literature on economic effects of IID (see Chapter 2). The texts were adapted to allow details to be reported by cases, or carers, if cases were young children or adults not able to fill in the questionnaires themselves.

3.1.7 Training

Nurses. The GPRF had six regional nurse trainers who were responsible for nurse training in their area. Two training days at EMCU were held for the trainers whom were subsequently given regular updates about the study's progress. These trainers visited each participating practice in their area prior to the study starting to train the nurse, and continued to liaise with them throughout the study.

EMCU and LSHTM staff. Data processors and coders were trained by the LSHTM statistician and the study manager. This is discussed in the data management section of this chapter (see 3.4.1).

3.1.8 Ethics

Ethical approval was obtained from the Royal College of General Practitioners, LSHTM and PHLS ethics committees and from all 61 local research ethics committees within whose areas the 70 participating practices were located.

Written informed consent was obtained from all adults in the studies; consent for children was obtained from a parent or guardian.

3.2 STOOL COLLECTION AND MICROBIOLOGY

3.2.1 Stool collection

Stool collection kits comprised: a plastic 'universal' specimen pot (*c*.25ml) with screw cap and a label for identification of the subject, absorbent wadding, a sealable plastic bag, a small plastic spoon, a strong cardboard box of the design approved for the postage of pathological specimens and an adhesive postage-paid label with the laboratory address for Leeds PHL. The kit also included an instruction sheet with suggestions on how to collect a suitable specimen of stool and a sheet of greaseproof paper to aid the collection of liquid specimens (see Appendix 7 for details). A sufficient quantity of faeces (at least 10g) was requested to enable a full range of tests to be undertaken. A form was issued with each kit for return with the specimen to the laboratory. This included the name and address of the GP, the name, address, date of birth and study number of the participant, any special clinical details, the time of onset of illness (to be completed for cases but not controls) and the date that the specimen was taken.

3.2.2 Inter-relationship of laboratories

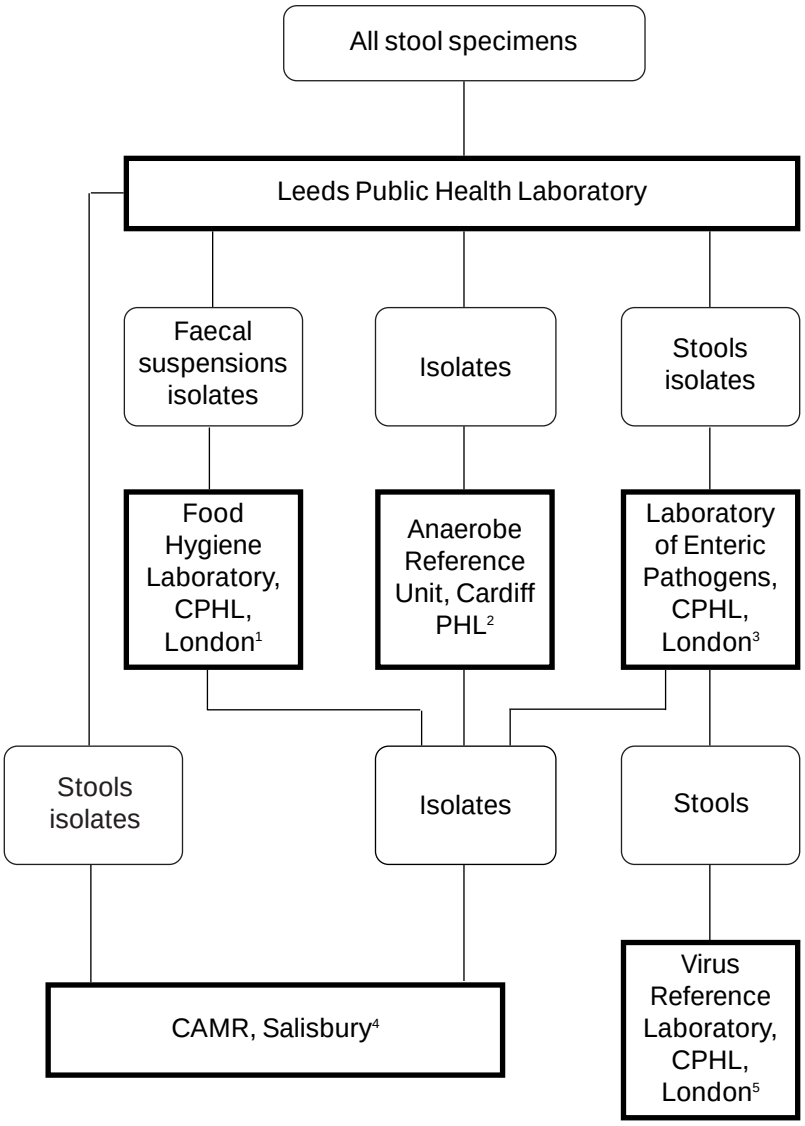
For the pilot study, participating practices submitted stool specimens to their local Public Health Laboratory. For the main study it was decided to use one primary laboratory: Leeds PHL. All stool specimens were submitted to this one centre which had sufficient space and equipment and where staff were trained to use a more extensive range of tests than that used normally in routine diagnosis. This enabled tests for the detection of spores of *Bacillus* spp. and *C. perfringens* to be carried out at Leeds PHL rather than at the Food Hygiene Laboratory, CPHL as had occurred in the pilot study. An aliquot of each faecal specimen was submitted to the Laboratory of Enteric Pathogens, CPHL for specialist *E.coli* investigations on the day of receipt or the next working day for specimens received on Saturdays. Cultures for *E.coli* O157 were carried out in Leeds PHL to minimize delay in the diagnosis of this serious infection. Clinically significant bacterial isolates were sent to reference laboratories for confirmation of identity, typing and archiving as indicated in Figure 3.9.

3.2.3 Processing of specimens at Leeds PHL

All stool specimens were weighed on receipt at Leeds PHL, using an electronic top-pan balance, tared with an empty specimen pot. Some specimens were received in containers other than those issued, and these faecal specimens were transferred to standard pots for weighing. Participant and GP details recorded on the request form were entered into the laboratory computer (Telepath). On completion of testing, computer-generated clinical reports (one for bacteriology/parasitology and another for virology) were posted to the GP. All positive findings deemed clinically significant by experienced clinical microbiologists were reported by telephone to the practice nurse or GP and, when appropriate, to the local consultant in Communicable Disease Control (CCDC). This ensured that subjects in the study received a high quality clinical service and that public health requirements and the collection of local epidemiological information were not compromised.

At the time of receipt all details except the participant's name and address (using study number and date of birth only as participant identifiers) were entered into a study data base (DataEase v4.2). The times of onset of symptoms, production of a stool specimen, posting (derived from postmark) and receipt of specimen were all recorded. Weekly summaries of this information along with the weights of the specimens were sent to the study manager at EMCU.

Figure 3.9 Movement of materials between laboratories



[1] *C.perfringens* enterotoxin tests by ELISA and sub-typing of *C.perfringens* and *Bacillus* spp.
[2] *C.difficile* toxin A testing by ELISA and typing
[3] Enterovirulent *E.coli* studies by DNA detection and typing of all enterobacterial isolates
[4] Archival storage of specimens and isolates
[5] Quality control for detection of viruses by EM

3.2.4 Rationale for selection of tests

Tests used were those in general use in clinical diagnostic laboratories and recommended by professional bodies in the UK. It was recognised that the volume of specimens, particularly from children, could be small and that the maximum information had to be derived from these. The national laboratory surveillance data were considered when the list of investigations was drawn up. All methods used were referenced.

A priority list was drawn up by the Executive Committee for the structured examination of specimens that were of inadequate volume for the full range of investigations; these are summarised in Table 3.1. When stool specimens of inadequate volume were received at the Leeds PHL staff attempted to contact the practice concerned to arrange for a larger specimen to be submitted if possible.

Table 3.1 Priority list for laboratory investigations

PRIORITY OF TESTING	PROCEDURE	TARGET ORGANISMS SOUGHT
Stage 1	Bacteriological culture	*Campylobacter* spp.
Stage 2	Bacteriological culture	*Aeromonas* spp., *Bacillus* spp., *Clostridium difficile*, *Salmonella* spp., *Shigella* spp., *Staphylococcus aureus*, *Vibrio* spp., *Yersinia* spp.
Stage 3	Bacteriological culture	*Escherichia coli* O157
	Direct microscopy	*Giardia intestinalis*
Stage 4	1–2g faeces to Laboratory of Enteric Pathogens (DNA probes)	Enterovirulent *Escherichia coli*
	Direct microscopy	*Cryptosporidium parvum*
Stage 5	Virology (Electron Microscopy and Enzyme Immunoassay)	adenovirus, astrovirus, calicivirus, rotavirus, SRSV (Norwalk-like)
Stage 6	Toxin tests; culture counts for vegetative cells and spores	*Clostridium difficile, Clostridium perfringens, Bacillus cereus, Staphylococcus aureus*
Stage 7	Concentration and Microscopy for ova, cysts and parasites	Protozoa and helminths
Stage 8	20% frozen suspension	Archiving at CAMR

3.2.5 Synopsis of laboratory methods

A full description of the laboratory methods used for detection of significant organisms is given in Appendix 7. Some of the methods for detection of bacterial pathogens have been published (SGMSF 1994). A synopsis of methods is given in Figure 3.10 for convenience.

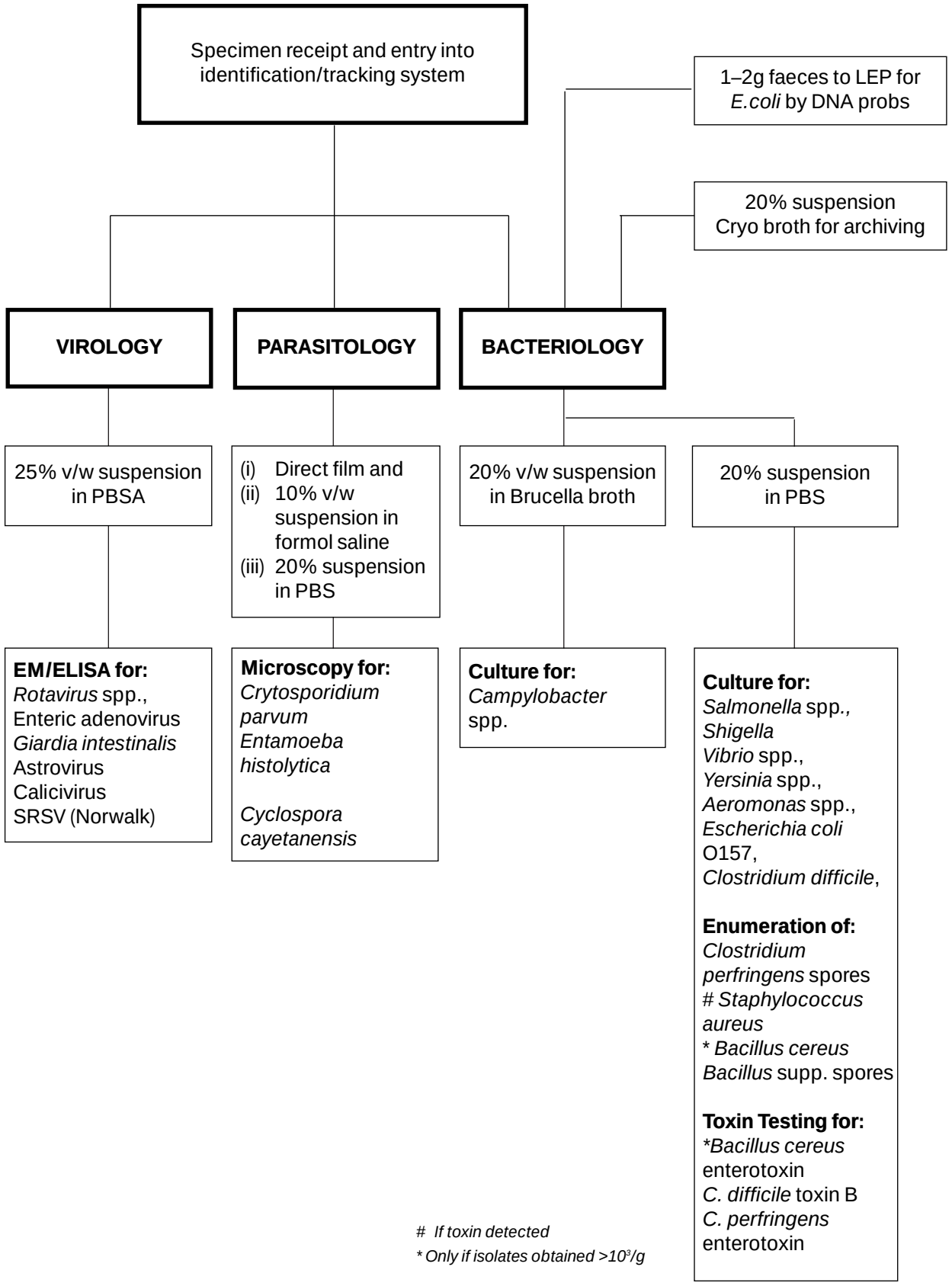
3.2.6 Archiving of stools and organisms

When there was sufficient residual specimen after all material had been taken for the full range of investigations, a 20% suspension of faeces was made in a cryoprotective broth and the suspension was stored at -70°C. All isolates of target organisms were similarly stored at -70°C at respective reference laboratories and *Staph. aureus* isolates at Leeds PHL. Stored faecal specimens and isolates were transported frozen in dry ice to the Centre for Applied Microbiology & Research (CAMR), Salisbury for storage at -70°C.

3.2.7 Quality assurance

There is a comprehensive quality control programme for media used at Leeds PHL. The laboratory participates in all relevant National External Quality Assurance Schemes (NEQAS) and is accredited for clinical microbiology by Clinical Pathology Accreditation UK Ltd (CPA) and for food and environmental microbiology by the UK

Figure 3.10 Summary Flowsheet of Microbiological Testing Procedures



Accreditation Service (UKAS). The CPHL reference laboratories (LEP, FHL) and the PHLS Anaerobe Reference Laboratory, Cardiff applied internal quality assurance schemes and achieved accreditation for clinical microbiology by Clinical Pathology Accreditation UK Ltd (CPA) during the study. CAMR is accredited in accordance with BS (EN) ISO 9001 for all services.

3.3 SOCIO-ECONOMIC COMPONENT

3.3.1 Social class and employment status

The highest social class status for the household (case or partner) was used for adult cases, the social class status of the main wage-earner was used for child cases. Data on social class for cases in the enumeration component were not collected.

3.3.2 Cost vectors used

Costs for hospital in-patient stay, A & E visits, and Out Patient Department (OPD) visits, were estimated using the generic Chartered Institute of Public Finance and Accounting Health Data (CIPFA 1995) for hospitals having similar characteristics to those admitting cases of acute infections. Costs of using GP and community services were estimated using estimates provided by the Personal Social Service Research Unit (PSSRU) data base. As the cases were admitted over two years the costs were aggregated and centred at the mid-point of the study. Costs of prescriptions were estimated using prescriptions charges as a guide. It was not possible to estimate an ingredient and administration cost for each drug as insufficient details were available. It was likely that the drugs used to treat the illness would have been inexpensive and except in extreme cases, the full cost of prescribing, dispensing and administering the drug would not have exceeded the cost of the prescription charge. Costs were attributed to the NHS or patient dependent on exemption status of the case. Costs of laboratory tests were estimated from a survey of participating laboratories interpreted in the light of the Audit Commission Report (Audit Commission 1995). The costs of stool testing under normal practice conditions were used as a basis to estimate the investigation costs. The rates of specimen tests in the enumeration component were applied to the GP and community. More precise estimates were not possible as only 13% of cases provided estimates of distance to the laboratory. The higher cost for blood tests (including culture and microscopy) was attributed to tests carried out while the cases were in hospital. The lower cost for a simple blood test (full blood count, urea and electrolytes) was used for all other blood tests. An average cost estimate was used for specimen collection by an EHO as only 13% of cases who had specimens collected gave information on the distance to the laboratory. An estimate of cost per case for postage of stool specimens from the enumeration study was applied to the GP and enumeration components.

Direct out-of-pocket expenses to cases were estimated and itemised by cases. Some adjustment for transport costs were made when private vehicles had been used and no cost mentioned. Costs of lost employment were estimated from the 1995 Earnings Survey and occupational groupings given by respondents broadly categorised into social class groupings. It was not possible to calculated costs adjusted for sex and social class in all categories. Social class was not known for cases in the enumeration component. The sex of carers was not always known and there was no detailed information on those taking time off work to accompany cases to the GP or hospital (see Table 8.5). For calculation of total costs the estimates of loss of employment costs unadjusted for sex and social class were used. The time spent caring at home was not included in the overall costs because of the difficulty of attributing the days of caring uniquely to care for cases. A value equivalent to the social class grade V employment cost per day (£55.70) was used to attribute value to this time.

3.4 DATA MANAGEMENT AND ANALYSIS

3.4.1 Data management

Data management was co-ordinated jointly by staff at the EMCU and the LSHTM. The EMCU was responsible for the day to day management of the data processing system and disseminated and received information from the general practices participating in the study. The LSHTM was responsible for the design of computer systems, quality control measures and questionnaire coding.

Table 3.2 Cost vectors in the socio-economic analysis

ITEM	£
GP home visit	47.00
GP surgery visit	17.00
Nurse visit	12.00
GP phone call — NHS	2.55
GP phone call — patient	1.00
Stool test	13.00
Blood test — culture and microscopy	14.00
Blood test — full blood count and urea and electrolytes	1.90
Urine test — including culture	9.00
Specimen collection by EHO — average cost	1.00
Postage cost for sample	0.50
Prescription charges — 1/4/93 to 31/3/94	4.75
Prescription charges — 1/4/94 to 31/3/95	5.25
Prescription charges — 1/4/95 to 31/3/96	5.50
Average cost of OPD visit	45.00
Average cost of A & E visit	27.00
Average cost of an in-patient day — infectious disease	225.00
Adult accompanying a child overnight in hospital	13.00
Average cost of ambulance journey if admitted to hospital	95.00
Average cost of arranged transport to OPD	27.00
Average cost of ambulance journey to GP	75.00
Average costs per mile for private transport	0.35
Average cost per mile for public transport	0.50
Average cost per mile for a taxi	1.50

Table 3.3 Employment cost vector — 1995 earnings survey

	ALL		MEN		WOMEN	
	PER WEEK (£)	PER DAY (£)	PER WEEK (£)	PER DAY (£)	PER WEEK (£)	PER DAY (£)
Overall	340.00	79.90	379.80	89.25	273.00	64.16
Social class						
I	497.30	116.87	544.40	127.93	372.70	87.58
II	470.80	110.64	506.00	118.91	413.40	97.15
III (non-manual)	310.00	72.85	327.70	77.01	193.80	45.54
III (manual)	246.00	57.81	273.00	64.16	233.00	54.76
IV	254.00	59.69	300.00	70.50	201.00	47.24
V	237.00	55.70	254.00	59.69	173.00	40.66

Figure 3.11 Flow of data between study participants and co-ordinating institutions

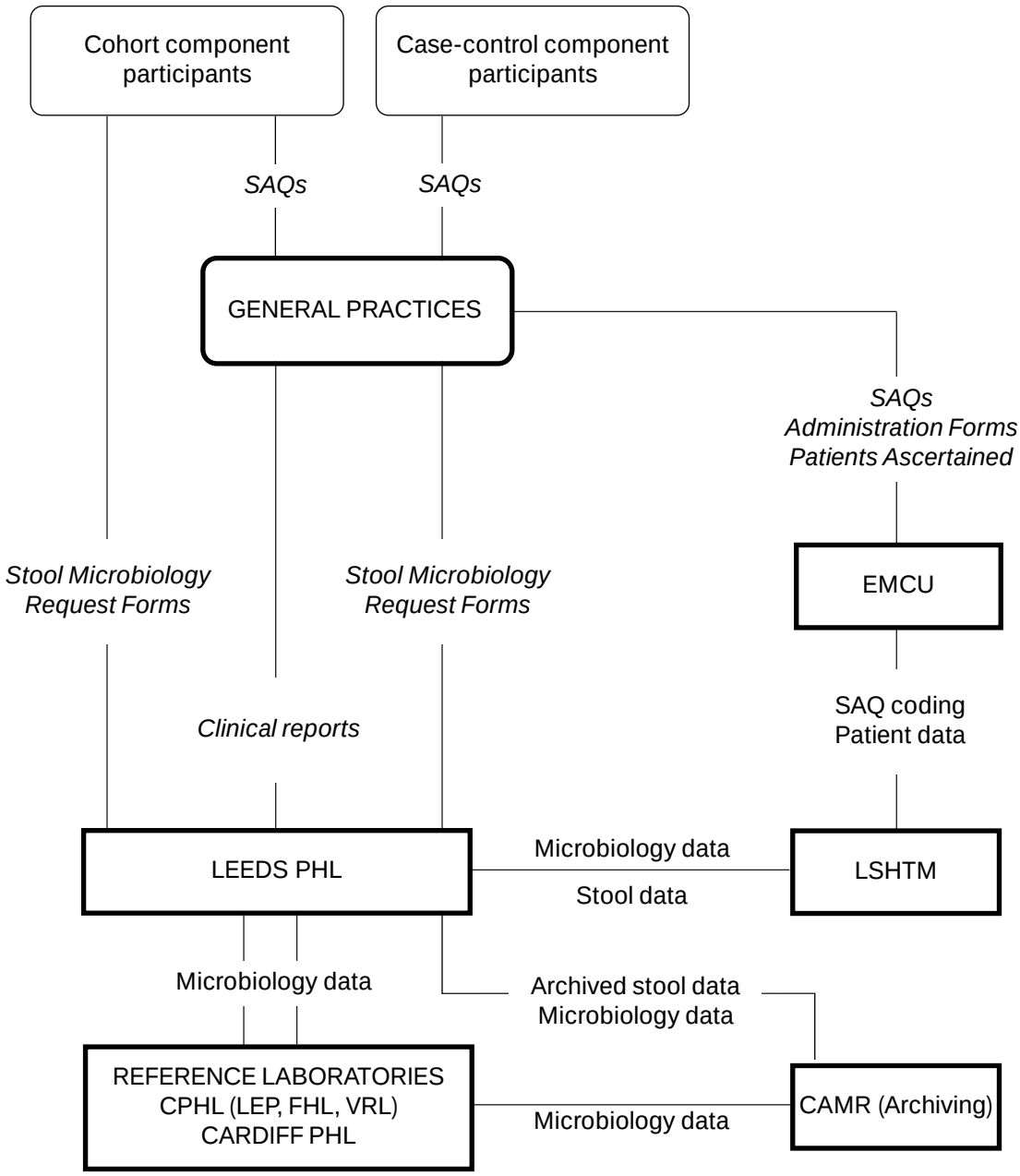


Figure 3.11 illustrates the various routes of information transfer via paper records or computerised data. Research nurses in each general practice sent weekly records of all participants entering the study to the EMCU. Study participants filled out self-administered questionnaires (SAQs) which were sent to the general practices and then to the EMCU. The research nurses also used various forms to administer the study which were sent periodically to the EMCU. Paper records were either processed at the EMCU or sent to the LSHTM for numerical coding. Final computerised data were sent to the LSHTM for analysis.

Stool samples were sent with a request form giving basic identifier information to Leeds PHL either from the general practices or direct from the study participants in the community component. The results of microbiological investigations were recorded on a database at Leeds PHL. The database was periodically transferred to the LSHTM. Results of further investigations at reference laboratories were recorded on in-house databases and transferred to the LSHTM.

3.4.1.1 Questionnaires and forms

These are summarised in Tables 3.4 and 3.5. Copies of the full questionnaires are located in Appendix 6.

Table 3.4 IID Study Questionnaires

SAQ NUMBER	STUDY COMPONENT	PURPOSE	QUESTIONS INCLUDED
1.1	Case control	Exposures in adult cases presenting to GP	Demographic, symptoms, foods, pets, travel, contacts, medicines, accommodation/kitchen, social, food handling
1.2	Case control	Exposures in child cases presenting to GP	Demographic, symptoms, foods, pets, travel, contacts, medicines, accommodation/kitchen, social, food handling
1.3	Case control	Exposures in adult controls presenting to GP	Demographic, foods, pets, travel, contacts, medicines, accommodation/kitchen, social, food handling
1.4	Case control	Exposures in child controls presenting to GP	Demographic, foods, pets, travel, contacts, medicines, accommodation/kitchen, social, food handling
2.1	Cohort	Adult baseline data	Demographic, accommodation/kitchen, social, food handling
2.2	Cohort	Child baseline data	Demographic, accommodation/kitchen, social, food handling
2.3	Cohort	Exposures in adult cases in the community	Symptoms, foods, pets, travel, contacts, medicines
2.4	Cohort	Exposures in child cases in the community	Symptoms, foods, pets, travel, contacts, medicines
2.5	Cohort	Exposures in adult controls in the community	Foods, pets, travel, contacts, medicines
2.6	Cohort	Exposures in child controls in the community	Foods, pets, travel, contacts, medicines
4B	Cost	Burden of disease in cases	Household composition, prolonged symptoms, income, days lost, use of health/transport services, carers, personal costs, willingness-to-pay
	A & E	Survey of A & E units	Use of computer diagnosis
	A & E	Details of IID cases seen	Demographic, diagnosis, admissions, stool investigations
	Under-ascertainment	Details of patient computerised notes	Demographic, how ascertained, symptoms, chronic illness, diagnosis, treatment, stool investigation, referrals

Table 3.5 IID Study Administrative Forms

FORM NUMBER	STUDY COMPONENT	PURPOSE	QUESTIONS INCLUDED
1.1	Case control	Case ascertainment by GPs	Symptoms, symptom history, non-infectious cause, where presented
1.2	Case control	Administer questionnaire and stool collection	Demographic, dates sent/received/reminded
1.3	Case control	Administer control recruitment	Contact details, matching information, availability, reason refuse
1.4	Case control	Notification of cases and controls to EMCU	ID, demographic
1.5	Case control	Evaluate ascertainment	Number ascertained vs computer notes
2.1	Cohort	Administer cohort recruitment	Contact details, reminders sent, acceptance/ refusal, baseline questionnaire receipt
2.2	Cohort	Record cohort withdrawals	Date and reason refused
2.3	Cohort	Record cohort follow-up in individuals	Weekly diary card returns, no contact, weeks become case/control
2.4	Cohort	Weekly diary card	ID, week number, presence of diarrhoea
2.5	Cohort	Administer case/control questionnaire and stool collection	Demographic, dates sent/received/reminded
2.6	Cohort	Notification of cases to EMCU	ID, demographic
2.7	Cohort	Administer control recruitment	Contact details, matching information, availability, reason refuse
2.8	Cohort	Non-participant details	Occupation, reason for refusal
3.1	Enumeration	Case ascertainment by GPs	Symptoms, symptom history, non-infectious cause, where presented
3.2	Enumeration	Patient details	Demographic, stool investigation, antibiotics prescribed, hospitalisation, chronic illness, diagnosis
3.3	Enumeration and stool results	Administer questionnaire	Stool sent/received, dates questionnaire sent/received
3.4	Enumeration	Evaluate ascertainment	Number ascertained vs computer notes
	Case control and cohort	Stool request form	GP details, clinical comments, ID, demographic, dates of onset, specimen and posting

ID — Identity

3.4.1.2 Computer software

At the EMCU data centre databases were developed using EPI INFO version 5.0. Separate questionnaire databases shared a common structure to provide consistency for data entry and to facilitate merging at the analysis stage. Separate databases were used for each administrative form. Further databases were used to manage the receipt of data at the EMCU (data logging). All procedures were made as user-friendly and versatile as possible by installing study specific menus and programs using MS-DOS.

Microbiology databases were developed using version 4.2 in-house software at the respective laboratories: EPI INFO version 5.0, DataEase, Excel or WordPerfect. Compatibility of data was ensured at the set-up phase by standardisation of patient identifier information on each database.

3.4.1.3 Data cycle at the EMCU data centre

All questionnaires and administrative forms received at the EMCU were processed according to the following sequence:

Logging
Data were logged on the computer on the day of receipt, recording the source general practice, basic patient identifier information, and subsequent file storage location. All paperwork received from the general practices was logged, and in addition weekly reports of stools received at Leeds PHL were logged.

Batching
Paperwork was sorted by questionnaire or form type and distributed into 'batches'. A batch formed a standard data processing unit which enabled pacing and monitoring of workloads, and also provided a storage reference. A batch consisted of 20 questionnaires or 50 forms. The progress of each batch through the system was charted on individual batch control sheets which were signed and dated by the appropriate data processor at each stage. Once batched, paper data were stored for later processing according to priorities.

Coding
Most data collected from study subjects were converted to numerical codes before being entered on the computer. The coding stage provided a visual check of the validity and consistency of responses as well as the standardisation of responses. Coding varied according to the type of question: tick box questions allowed limited response and had fixed coding frames, open-ended questions required coding frames to be developed progressively using standardised coding sheets. Data concerning patients' symptoms and medication were coded using the Read code (Read Clinical Classification, Computer Aided Medical Systems, 1987. Version 3. NHF Centre for Coding and Classification). Questions about respondents' occupation were coded using the OPCS Standard Occupational Classification (OPCS 1993).

Data entry
Coded data were independently double-entered by separate data clerks.

Validation
A report was produced to validate the double entry and was assessed by an independent data validator. Further consistency checks were performed before the data were finalised and added to a master database. All basic identifier information on the questionnaires and forms was rechecked against the information entered at the

logging stage for consistency and accuracy and to detect any paperwork that might be 'lost in the system'.

3.4.1.4 Quality control

Computerised checks or manual monitoring procedures were implemented at every stage to ensure accuracy. Data entered at the logging stage were checked by weekly computerised reports. The key information which was liable to transcription or typing error was the patient's ID code, which was checked for inaccuracies or duplications. Monthly reports summarising information received at EMCU were sent to each general practice for the nurses to cross-check with their records.

The coding stage was open to further undetected errors, and consistency between coders was encouraged by weekly coding meetings. Random spot checks were also conducted where several batches were fully double-coded. The average accuracy level achieved was 99.7%, i.e., 99.7% of numerical digits were correct. Of the remaining 0.3% errors, over half were detectable by later checks at the data entry or analysis stage.

At the data entry stage, automatic range and consistency checks were built into every field on the database so that inconsistencies were flagged up on entry. Double entry validation levels were monitored continuously and produced an average accuracy level of 99.6%. Almost all of these errors would have been detected and corrected by the double entry process.

After the data processing was complete, confirmation of every case and control recorded in the study was sought by collation of all sources of information referring to that person. Since case information at the general practices was not always sent to the EMCU immediately, and questionnaire and stool sample compliance was less than 100%, partial information existed on many cases. For all cases and controls where details could not be confirmed from at least two data sources, the practice nurse was contacted and the records checked, or the patient approached. For all cases and controls, basic identifier information and date information were cross-checked between all computerised and paper records for each general practice in turn.

The consistency of microbiological information from all the various data sources was monitored at the LSHTM by merging laboratory databases.

3.4.2 Statistical methods

3.4.2.1 Methods for data collected: completeness, representativeness and adjustment factors (see Chapter 4).

Representativeness was assessed by comparison of study characteristics with routine data from the census (ONS 1996), Jarman score data (Jarman 1983), and general practice statistics (Fleming *et al*. 1994).

Compliance was calculated as the proportion of subjects submitting a questionnaire or stool relative the total subjects in the study. Differences in compliance across age, sex or practice groups was assessed with the Pearson Chi-square test and multiple logistic regression.

Factors influencing under-ascertainment were investigated using multiple logistic regression. The inverse of the predicted under-ascertainment from this model was used as a multiplier for the number of cases reported in each practice, which took into account practice characteristics.

List inflation factors were calculated on the basis of ineligible people (died, moved away or living away) in the practice population identified during cohort recruitment. Information from cohort recruitment was incomplete, and reasons for non-recruitment included 'no contact' or no information. Nurses in the practices later performed a notesearch on these people, which was able to classify some of these as ineligible. In order to complete the estimate of ineligibles among those with incomplete records, the proportion ineligible was modelled using multiple logistic regression to identify practice characteristics that predicted ineligibility. The total number ineligible in a practice was therefore estimated as the proportion of known ineligibles plus the proportion of estimated ineligibles in the cohort list, multiplied by the total practice population.

3.4.2.2 Methods for microbiology results: frequency and seasonality (see Chapter 5)

Results of microbiological examinations were reported for all stool samples of sufficient volume for the first stage of testing (see section 3.2.4, Table 3.1). For target organisms investigated, the percentage identified was calculated only from the stools that reached the required stage of testing for that organism. The percentage identified among controls was standardised using the method of direct standardisation on the age distribution of England for 1994.

Age and seasonality incidence graphs for each target organism used denominators derived from the age/sex registers of the study practices. For each practice the age/sex register was received on two occasions (for selecting each of the study cohorts), and the one generated nearest in time to the middle of the study period was used to calculate denominators. Time plots of cases reported in each practice were scrutinised to decide the exact length of follow-up of the practice population, and allow for early finishing or gaps in reports due to nurse absence or other reasons. Practice populations were counted for fractions of the months when they started and finished. Seasonality plots were inspected for the full timespan of the study before combining the same month of all years together in the plots presented.

Pathogenicity was calculated as the ratio of the percentage of cases positive for a target organism to the percentage of controls positive for that organism. Confidence intervals were calculated using standard methods (Rothman 1986).

3.4.2.3 Methods for frequency and reporting of IID (see Chapter 6)

The incidence rate of IID in the community was calculated from the total number of cases reported in the population cohort component and the follow-up time of members of the cohort. Cohort members from whom a full record of person-weeks of follow-up was not received were excluded from the rate calculations regardless of whether they became cases or not. Practices with recruitment rates of less than 25% were also excluded from the rates on the basis that the recruited cohort was less likely to be representative of the practice population. Eight practices were excluded on this basis. The incidence rate of IID presenting to the GP was calculated from the total number of cases reported in the case-control and enumeration components and the follow-up time of all persons registered in the practice populations (see section 3.4.2.2). Practices that showed evidence of poor return of forms were excluded from the calculation; four practices were excluded on this basis. Adjustments were made to the numerator and denominator of the GP presentation. The contribution to the numerator from each practice was multiplied by a factor for under-ascertainment, derived from the under-ascertainment component and dependent on the characteristics of the practice and which study component it was. The contribution to the denominator from each practice was reduced by a factor for list inflation (see section 3.4.2.1).

Organism-specific incidence rates were calculated from the number of cases with each target organism identified, regardless of whether other organisms were present in the same case, and denominators as above. Under-ascertainment was assumed uniform for all organisms. Rates were also adjusted for non-compliance in submitting a stool sample, using an overall figure for compliance and therefore making the simplifying assumption that non-compliant cases would have the same identification rate for each organism as compliant cases. Confidence intervals were calculated by a method that did not increase the apparent precision due to this adjustment.

The expected number of repeat infections was calculated from the Poisson distribution.

Variation in rates was analysed using Poisson regression. Over-dispersion in GP presentation rates was modelled with a random effects term at the practice level. This effect was incorporated into all confidence intervals applied to GP presentation rates. No evidence of overdispersion at the practice level was seen with community rates and a fixed effects model was used. Analysis was based on episodes rather than subjects, assuming each episode to be independent. Interaction terms were examined but only presented if conclusions were affected.

Reporting pyramids were calculated from the overall incidence rates at each stage of reporting, by considering the ratios between these rates. The upper and lower sensitivity bands were derived by performing the same calculation on the upper and lower confidence intervals for the rate at each stage.

Additionally, the ratio of community rates to nationally reported cases was calculated by projecting the overall cohort incidence rates to the population of England (1994) and comparing with reports to CDSC from England during the years of the study fieldwork (1994 and 1995).

3.4.2.4 Methods for symptoms and duration of IID (see Chapter 7)

Symptom profiles for the acute phase were based on the subset of cases who returned a risk factor questionnaire and completed the symptom section. Specific target organisms were analysed in cases with only that organism identified, i.e., excluding cases with multiple organisms. Those target organism with at least ten cases reporting the presence of symptoms were presented. Calculation of the duration of symptoms during the acute phase, excluded cases who did not specify the duration on an individual symptom basis, and censored those with symptoms still present at the time of return of the questionnaire, using the method of Kaplan-Meier (Kaplan and Meier 1958). The Kaplan-Meier estimates of 25%, 50% and 75% symptom 'survival' were presented for all organisms having at least ten cases reporting duration of diarrhoea. The symptoms recorded in the socio-economic questionnaire, as persisting at three weeks, were analysed. The frequency and combination of symptoms were analysed by age, sex and target organism for the population cohort and GP case-control components. The frequency of reported symptoms at baseline, during the acute stage and three weeks after the acute illness were described where possible.

3.4.2.5 Methods of socio-economic analysis results (see Chapter 8)

The characteristics of households in each study component were analysed by age and relationship to other household members. The characteristics of the illness that had an impact on the activities of daily living were estimated. A scale of the impact of illness identified stages of illness for cases according to whether they were confined to bed or not, in hospital or at home, through to whether they were able to carry out normal activities in the home and outside. Numbers and percentages of those reporting spending time in each stage were calculated and the average time in

each stage was reported by study, age and organism. The health sector resources used were estimated and costed for general practice and community services and for hospital in-patient, A & E and out-patient services for each study, by age and organism, including the specific sub-types of target organisms where appropriate. The direct out-of-pocket expenses and the value of time lost from employment were calculated. Total and average costs were estimated. The overall means for duration of illness, use of resources and costs are estimates based on the whole sample, i.e., the denominator included those with no positive contribution to the particular estimate.

Geometric means with 95% confidence intervals for the component costs were calculated. A sensitivity analysis was conducted on all costs for each component. 10% interval bands (10%–50%) either side of the estimated cost were considered separately for each component cost to take into account the likely variation due to either the estimation of the number using services or the cost vector.

Costs for all IID in England were estimated using two different methods. The first was based solely on the estimate of average cost per case from the community component. The second divided cases into those presenting to the GP and those not presenting to the GP. For those presenting to the GP the estimate of average cost per case presenting to the GP was used. For those who did not present to the GP the average cost per case not presenting to the GP was used. In estimating total cost for all IID, the estimate of the average cost per case who presented to the GP in the GP component was used rather than the estimate from the enumeration component. This was consistent with the organism specific total cost estimates which could only be calculated using the estimate from the GP component. For number of cases, rates and ratios, refer to Chapter 6.

An estimate was made of the contribution of disease severity and duration of illness on the cost of illness, using multiple linear regression on log transformed data.

The costs and percentages expressed in the report have been rounded up, and therefore rounding errors may occur when the components are added together.

3.4.2.6 Methods for risk factors for disease (see Chapter 9)

Risk-factor analysis was conducted on matched pairs of cases and controls only. Since questionnaire compliance was imperfect, the number of pairs available for analysis was considerably reduced. Various options for relaxing the matching were explored but did not give substantial gain in numbers and presented difficulties in interpretation. All analyses used conditional logistic regression and produced odds ratios with 95% confidence intervals.

The analyses for ‘all IID’ and ‘no target organism identified’ used a structured modelling strategy based on the conceptual framework shown in Figure 9.1 (based on methods described by Victora *et al*. 1997). This framework led to the interpretation of the model at three stages.

Firstly, a model containing social variables only, which were considered to have a global influence on disease risk, and could be interpreted initially without modification by factors more directly related to disease risk.

Secondly, a model including factors thought to influence transmission via, or exposure to, more direct factors. For example: travel was thought to increase exposure to contaminated food and water; drugs, infant feeding and comorbidity were thought to influence transmission/infection through various routes. This model

included the factors found to be important at the first stage, and therefore demonstrated the degree to which factors which influence transmission explained the social factors.

The third model included factors that are the direct source of organisms that cause IID, including food and water. It also included the use of antibiotics which have a direct role in changing the gut flora and altering susceptibility to gut pathogens. This model included factors found to be important in the first two stages and could be used to demonstrate the degree to which these direct factors, as far as they can be measured accurately, explained the social and transmission factors.

Due to the large number of risk factors investigated, it was impossible to explore the influence of every combination of risk factors. Therefore, within the strategy outlined above, initial model reduction within each of the risk factor blocks shown in Figure 9.1 was used to select the strongest candidate variables (p value<0.1) to enter the combined model. In the final stages of reduction of the third stage model, a probablity (p-value) of <0.05 was used as a guide to statistical significance. After the final stage, selected interactions between risk factors were examined.

The 'all IID' and 'no target organism identified' models were intended to be exploratory, in order to generate hypotheses rather than to test them. No formal adjustment for multiple testing was made, but in the interpretation of the final results only factors that had p-values well beyond traditional significance levels, or showed consistent results over pre-selected subgroup models were taken to indicate importance.

Organism-specific models were developed on a different basis. These models were used to test a limited number of specific hypotheses. As the number of cases (including multiple organism cases) available for each specific organism analysis was small, additional controls were sought from the wider dataset which met the original matching criteria, and therefore maximised the cases included. Due to small numbers, extensive multiple variable models could not be run, and so the analyses were initially univariate, and finally adjusted for social and travel factors, where important.

3.5 MONITORING PERFORMANCE

3.5.1 GP performance

The 70 general practices were monitored by quality check visits from a regional research nurse, and by analysis of data received at the EMCU. Regional research nurse visits were made when the general practices started the study and four months later. Computer generated reports were produced at six weeks and three, six and nine months. Information in the three-month report was used to inform the regional nurse at the four months' visit. The reports were used firstly to monitor levels of case ascertainment to give early warning of levels that were outside expected limits as compared with estimates from the pilot study. Secondly, they gave details of control recruitment rates, and compliance with questionnaires and stool samples. Feedback was given to the general practices and any aspects that suggested under-performance were queried with the practice nurse or pursued by the regional nurse. In the population cohort study there was additional monitoring during the recruitment phase where nurses were asked for a summary of progress at two months.

3.5.2 Cohort follow-up

A quality check on cohort follow-up data was made in a selected number of practices by counting all diary cards returned to the practice nurse by every member of the cohort. Figures were checked against the administrative form used to record the follow-up.

3.5.3 Overall study performance

Overall study performance were monitored by the IID Executive Committee which met approximately every three months. Formal progress reports were produced every six months. The key aspects of data collection which were monitored were: general practice recruitment, case ascertainment, control recruitment, cohort recruitment and compliance with questionnaires and stool samples. The receipt and processing of microbiological data was also monitored using average monthly stool weights and delivery times and the proportion of stools reaching each stage of microbiological testing.

3.6 SAMPLE SIZE

3.6.1 Cohort component

The Committee on the Microbiological Safety of Food stated the following requirements for sample size:

i. 95% Confidence Interval (CI) for the incidence of IID nationally with a precision of 10% each side.

ii. 95% CIs for the incidence of IID in three specific geographical areas with a precision of 20% each side.

iii. 95% CIs for the incidence of IID by specific organisms, for organisms present in more than 15% of the population nationally, with a precision of 20% each side.

iv. Separate CIs for children and adults for the incidence of IID nationally with a precision of 20% each side.

In addition the study aimed to be representative of urban and rural, large and small, high and low social class practices, and to be large enough to study differences in incidence between these groups.

On this basis the component of the study aimed to recruit 72 practices nationally, 24 in each of three geographical areas, and to obtain at least 2,070 person-years follow-up per area.

3.6.2 Case-control component

The GP case-control component was designed to be able to detect a relative risk of two or more, for any risk factor present in at least 10% of controls, and with a 1% level of significance. On this basis the study aimed to recruit at least 987 adult and 987 child cases to allow a matched analysis to be performed. Figures allowed for data losses in recruitment of cases and controls. The study was not designed with the power to detect risk factors for all specific organisms, although it was recognised that significant risk factors could be detected in the more prevalent organisms if the relative risks were high.

Chapter 4
Completeness, Representativeness of the Data and Adjustment Factors

The following chapter summarises the main results on completeness, representativeness and adjustment factors for the data collected. Further details, figures and tables can be found in Appendix 1.

4.1 PRACTICE CHARACTERISTICS

Seventy practices took part in the community (population cohort)component; 36 of these also took part in the enumeration component and 34 in the GP case-control component. Practice participation over time is shown in Appendix 1.

4.1.1 GP practice characteristics compared to the rest of country

Table 4.1 shows that the distribution of the population in the IID study practices in the three geographical areas (the North, the Midlands & South West and the South East) is similar to the population of England.

The distribution of the population in the IID study practices and in England is shown as practice ward-based Jarman scores (Jarman 1983) in Table 4.2. The study population slightly under-represented the lower tertile (i.e., least deprived) (22% versus 30%) when compared to the population of England.

Table 4.1 Population distribution by three Areas (North, Midlands & South West and the South East) for the IID study population and population of England (mid-1994)

AREA	POPULATION			
	STUDY		COUNTRY	
	NO.	%	NO.	%
North	128,120	28.85	13,254,200	27.31
Midlands/South West	218,788	44.14	21,228,700	43.74
South East	148,758	30.01	14,049,800	28.95
Total	**495,666**		**48,532,700**	

Table 4.2 Population distribution by Jarman score tertiles for the IID study population and the population of England (1991)

JARMAN		POPULATION			
		STUDY		COUNTRY	
		NO.	%	NO.	%
<–5	Low	110,172	22.23	14,223,630	30.23
–5 to 10	Mid	201,813	40.72	14,870,582	31.61
>10	High	183,681	37.96	17,960,992	38.17
Total		**495,666**		**47,055,204**	

The IID study population under-represented GP practices with fewer than four partners and over-represented practices with five or more partners when compared to all practices in England (Appendix 1, Table A1.1).

The proportions of the study population whose general practice was based in an urban or rural location is almost identical to that of England and Wales (61% versus 62% for urban) (Appendix 1, Table A1.2). There is a lower proportion of the study practice population in metropolitan districts when compared to England and Wales but a higher proportion in areas classified as city and industrial. These differences reflect the distribution of practices in the MRC GPRF.

4.2 POPULATION COHORT COMPONENT CHARACTERISTICS

Representativeness and completeness of the population cohort component is shown schematically in Figure 4.1.

4.2.1 Numbers who enrolled, refused or were estimated to be ineligible for the population cohort component

Figure 4.2 shows that a total of 27,651 persons were invited to participate in the cohort study; of these 9,776 (35%) were enrolled and 6,686 (24%) refused to participate. Together these constituted the 16,462 persons who were eligible for enrolment as they were known to be alive and registered with the GP. Of the remaining 11,189 persons, 2,177 (8%) were known to be ineligible because they were no longer registered with the general practice, having died or moved away. In the case of the remaining 9,012 persons, the practice nurse could make no contact in 3,844, failed to record the reason for non-enrolment in 4,591, and lost the enrolment forms for 577 persons.

4.2.2 Persons enrolled amongst cohort invitees

The proportion of persons enrolled among all those invited to participate in the cohort study was 35%. There was practice variation, with a median enrolment of 36.8% (5th and 95th percentiles 13.3 and 55.5, respectively). Proportionally more females enrolled (40% versus 34%) and the age group with the lowest enrolment for both sexes was 15–24 years (Appendix 1, Table A1.6 and Fig. A1.2). There was lower enrolment in practices in an urban location, in the South East and with a high (most deprived) Jarman score (Appendix 1, Table A1.7).

4.2.3 Refusers

There were 6,686 persons (24%) who refused to participate in the cohort component and 4,133 of these (61.8%) returned a questionnaire with reasons for refusal and socio-demographic details. The reasons for refusal are summarised in Appendix 1, Table A1.8. The social class of persons who returned the refusers' questionnaire when compared with those who enrolled in the study is shown in Appendix 1, Table A1.9. There was a significant difference in social class distribution (chi squared=667, on 7 df $p<0.001$) with a higher proportion of refusers who were Class IV and V, whereas a higher proportion of those enrolled were Class I–III.

4.2.4 Known ineligibles

There were 2,177 persons (12%) ineligible (i.e., they had moved away or died) among the 18,639 in whom the eligibility was known (Appendix, Table A1.10). The median proportion by practice who were ineligible was 9.5% (5th and 95th percentiles 2.6 and 33.6, respectively). Ineligibility was significantly different by

Figure 4.1 Completeness and representativeness in the cohort component

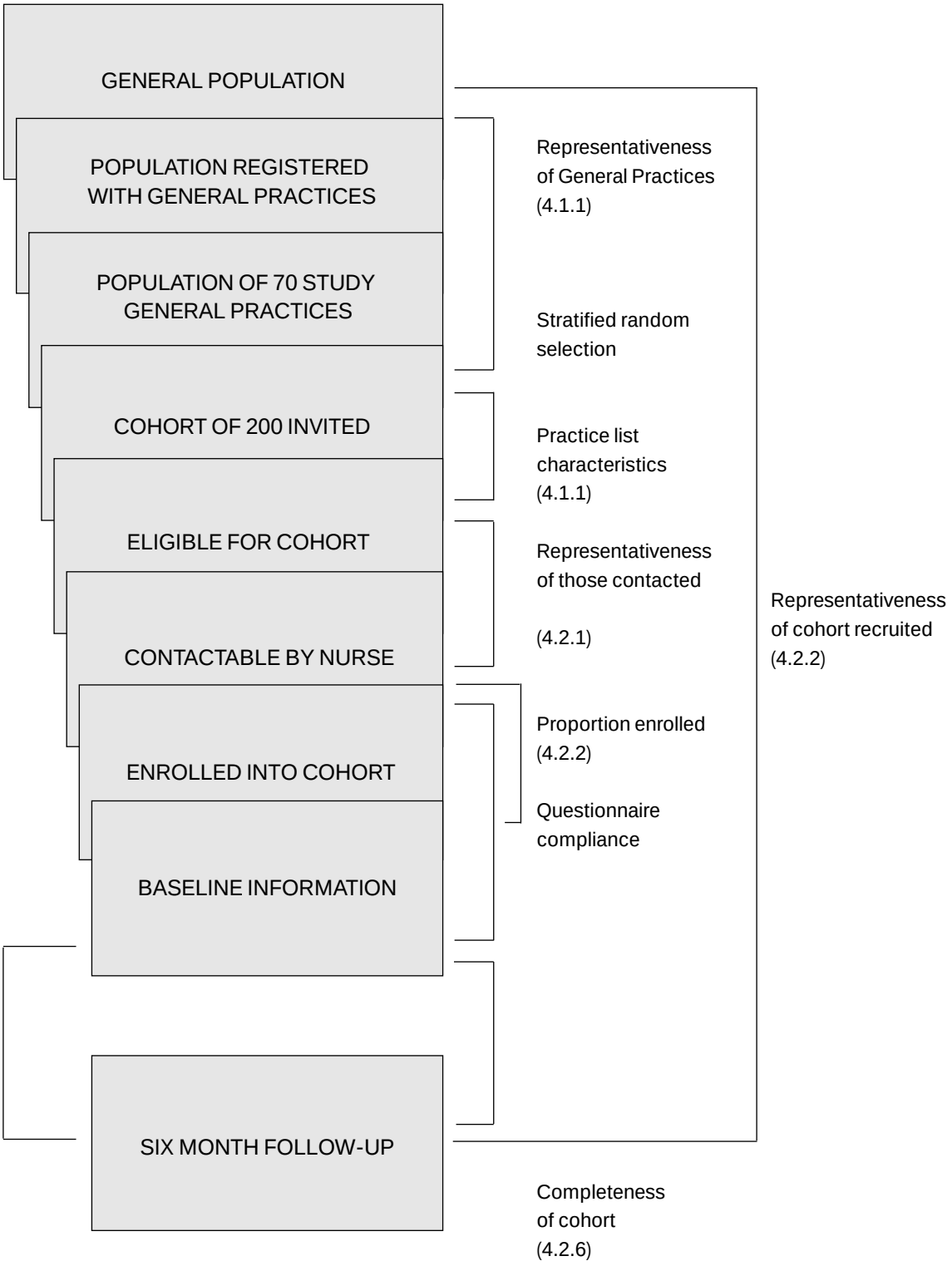
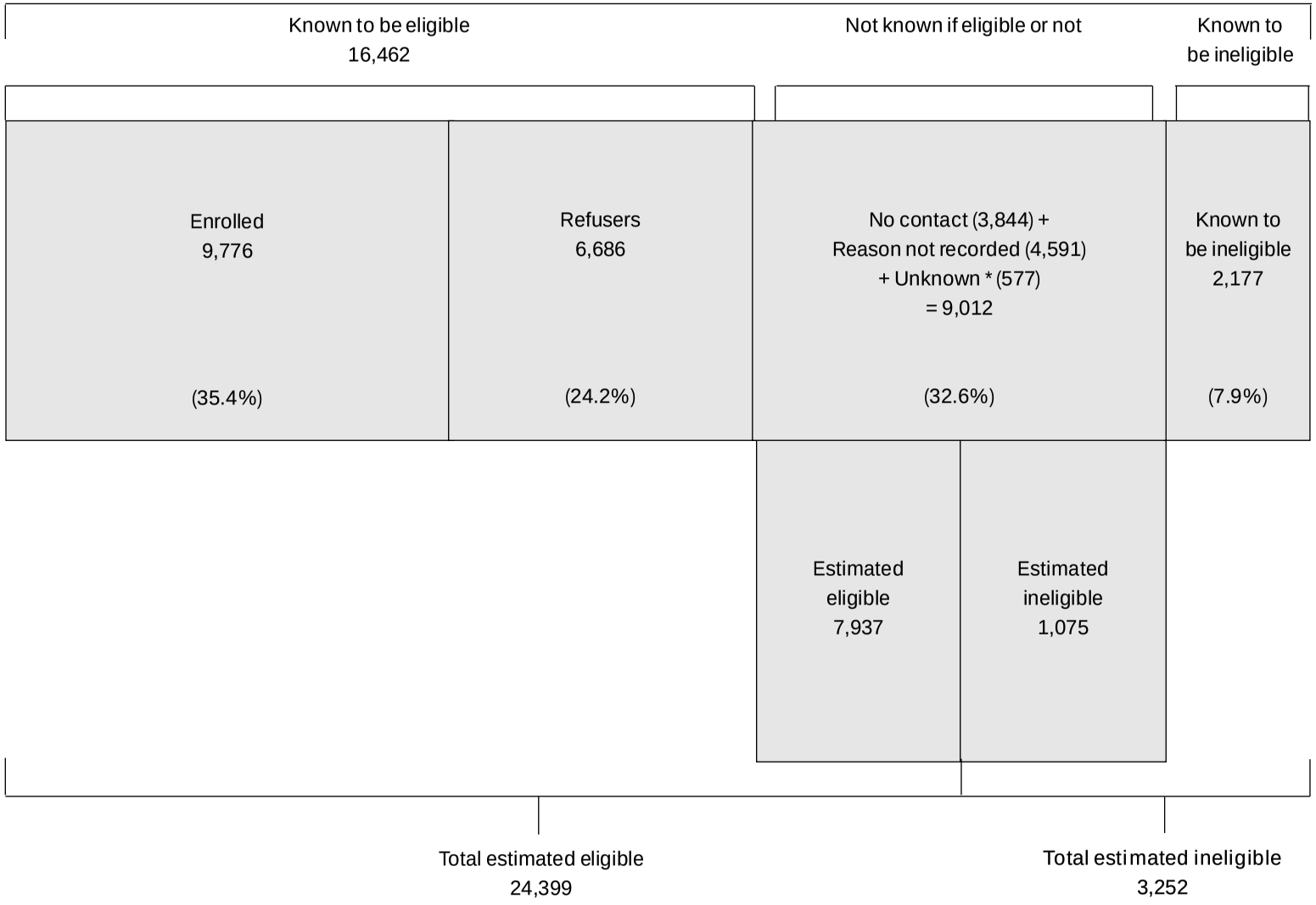


Figure 4.2 Numbers who enrolled, refused and were estimated to be eligible in cohort component practices; cohort selected for invitation 27, 651.



** Unknown: forms lost at two practices*

gender (chi ^{2}=23.2, p<0.001) being higher in males. There was a significant difference between age groups (chi ^{2}=988, p<0.001) and the highest proportion who were ineligible were aged between 15 and 34 years (Appendix 1, Table A1.11 and Figure A1.3). Ineligibility was highest in practices in the South East, in an urban location and with a high Jarman score (Appendix 1, Table A1.12).

4.2.5 Estimate of people who were ineligible

An estimate of the people who were ineligible was based on a notesearch of practice records among those with whom the practice nurse made no contact and persons where the practice nurse failed to record a reason for non-enrolment (Appendix 1, Table A1.13). A notesearch was performed on 3,007 of the 3,844 persons in whom no contact was made and 430 (14%) were found to be ineligible. Of these 14 had died and 416 had moved. 2,577 were presumed eligible because they had presented within the last three months (784), because they were still registered but had not presented (1,677) or for other reasons (116).

In the group in whom the reason for non-enrolment was not recorded (4,591) a notesearch was carried out in 1,238 and 10% were found to be ineligible. In the 577 persons whose forms were lost, it was assumed that 10% would also be ineligible. Thus the number of persons on practice registers who were estimated to be ineligible for enrolment was 1,075 and the total estimated to be ineligible was 3,252 (Figure 4.2). Therefore, the proportion enrolled of those who were eligible was 40%.

In order to correct for practice list size inflation in the calculation of rates of presentation of IID, due to those who had moved away or died, a multiple regression model was developed to predict proportions of ineligibility according to practice characteristics using the notesearch results from those with whom the nurse made no contact (Appendix 1, Table A1.14).

Ineligibility was highest in areas with a mid-tertile Jarman score, in rural areas, and in urban areas in the South East. The median number of ineligible persons per practice (of 400 invitees) was 41 or, in other words, 10.2% of those invited were ineligible (5th and 95th percentiles were 5.1 and 24.7 respectively). The median correction to list size was 89.8% (5th and 95th percentiles were 75.3 and 94.9).

4.2.6 Completeness of follow-up of the population cohort component

82% of the population cohort completed more than 23 out of a maximum possible 26 weeks of follow-up (Appendix 1, Table A1.15 and Fig. A1.4). 61% of persons completed all 26 weeks. Incomplete follow-up was higher among males and in the 15 to 24 year age group (Appendix 1, Table A1.16).

Of the 1,770 persons who completed less than 23 weeks, 200 completed a questionnaire giving a reason for early withdrawal from the study. Of these the three commonest reasons were: they were moving away, had no time or because they had developed another illness.

4.2.7 Completeness of return of baseline cohort questionnaire by those enrolled in the population cohort component

The baseline questionnaire was returned by 95% of the 9,776 persons enrolled. The median compliance per practice was 95.1% (5th and 95th percentiles 82.1 and 99.2, respectively). The age and sex distribution of the persons returning the baseline cohort questionnaire is shown in Appendix 1, Table A1.17. There was no significant difference between the sexes, but compliance varied significantly with

age (chi ^{2}=83.4, p<0.001). The 15–24 year age group had the lowest compliance. Compliance was lowest in persons registered with general practices with a high (most deprived) Jarman score and in the South East (Appendix 1, Table A1.18).

4.2.8 Representativeness of the population cohort recruited

Table 4.3 shows the age and sex distribution of persons who were enrolled in the population cohort component as compared to the population of England (ONS mid-1994 estimate). 45% of subjects were male compared to 49% of the national population. Enrolment was proportionately lowest in the 15–24 year age group when compared to the national population. Table 4.4 shows the social class distribution of the cohort and national populations. Enrolment was proportionately higher in social classes II and III (NM) when compared to the national population and lower in social class III(M) and persons classified as 'other inactive/missing'.

The study population was similar in ethnic composition to the national population; 95% of the study population and 94% of the national population were white (Appendix 1, Table A1.19). The cohort population differed from the national population in marital status: proportionally more were married (72% versus 58%) and fewer were single (15% verus 26%) (Appendix 1, Table A1.20). A smaller proportion were economically active when compared to the national population, 58% versus 61% and a larger proportion had retired (23% versus 19%), (Appendix 1, Table A1.21). A larger proportion owned the property where they lived (80%) when compared to the national population (71%) (Appendix 1, Table A1.22).

Table 4.3 Age and sex distribution of community population enrolled in the cohort study compared to population of England (mid-1994 estimate)

AGE	COHORT POPULATION				POPULATION OF ENGLAND IN THOUSANDS			
	MALE		FEMALE		MALE		FEMALE	
	NUMBER	%	NUMBER	%	NUMBER	%	NUMBER	%
<1	48	1.15	47	0.94	325.6	1.36	308.8	1.24
1–4	254	6.11	277	5.55	1,332.4	5.58	1,268.4	5.11
5–9	360	8.66	382	7.66	1,628.9	6.82	1,545.7	6.23
10–14	315	7.58	298	5.97	1,546.3	6.47	1,464.7	5.90
15–24	289	6.95	396	7.94	3,206.7	13.43	3,039.0	12.24
25–34	469	11.28	719	14.41	4,011.8	16.80	3,861.7	15.56
35–44	519	12.48	718	14.39	3,286.1	13.76	3,259.3	13.13
45–54	652	15.68	741	14.85	3,052.0	12.78	3,052.3	12.3
55–64	544	13.09	618	12.38	2,373.4	9.94	2,444.3	9.85
65–74	479	11.52	503	10.08	1,977.2	8.28	2,377.6	9.58
75+	228	5.48	291	5.83	1,142.6	4.78	2,203.5	8.88
Totals	**4,157**		**4,990**		**23,882.1**		**24,825.4**	

Table 4.4 Social class distribution of cohort study population and population of England (1991 census)

	COHORT POPULATION		ENGLAND 10% SAMPLE	
SOCIAL CLASS	**NUMBER**	**%**	**NUMBER**	**%**
I	458	4.85	222,583	4.89
II	2,322	24.57	999,138	21.93
III (NM)	1,425	15.08	393,815	8.64
III (M)	1,443	15.27	921,050	20.22
IV	910	9.63	437,888	9.61
V	249	2.63	142,854	3.14
Armed forces	27	0.29	32,304	0.70
Government scheme	0	0	20,553	0.50
Other inactive / missing	931	9.85	545,284	11.97
Retired	1,686	17.84	784,199	17.21
Total	**9,451**		**4,556,234**	

4.2.9 Nested case-control component

Population cohort members who developed IID were recruited to the nested case-control component and a matched control selected from the healthy cohort members (Appendix 1, Fig. A1.5).

Case-control matching
Matching of cases and controls by age and sex is shown in Appendix 1, Table A1.23 and Figure A1.6. It was lowest in the 10–14 year age group. Matching was highest in practices in the Midlands and South West and in practices with a low Jarman score (Appendix 1, Table A1.24). A matched control was found for 79% of the cases. There was variation at practice level (median, 5th–95th percentiles: 84.4, 0–100), no difference by sex, but a significant variation by age group (chi^2 = 26.2 11df , p = 0.006).

Compliance by cases
A total of 648 risk factor questionnaires were returned by the 817 cases, an overall mean compliance of 79% (Table 4.5). There was no difference by sex, but compliance varied by age group, being lowest in the 15–24 year age group (chi^2 = 30.8 11df, p = 0.001) (Appendix 1, Table A1.25 and Fig. A1.7). There was variation at practice level (median: 81%; 5th and 95th percentiles 0 and 100) (Table 4.5), with compliance being lowest in urban areas, in the South East and in practices with a high Jarman score (Appendix, Table A1.26). Compliance by cases in sending stools was higher at 90% in males and 88% in females (Appendix 1, Table A1.27). There was variation by practice (median 93.8, 5th and 95th percentiles 57 and 100) (Table 4.5), with compliance lowest in practices in urban areas in the South East (Appendix 1, Table A1.28). Sex did not influence stool specimen submission, although there was variation in compliance by age group, being lowest in the 10–24 year age group (chi^2 = 54.7 11df, p <.001) (Appendix 1, Table A1.29 and Figure A1.8).

Compliance by controls
Risk factor questionnaires were returned by 91% of the controls, and the median proportion returned by practices was 100% (5th and 95th percentiles 67 and 100,

Table 4.5 Risk-factor questionnaire, stool submission and socio-economic questionnaire compliance in GP case-control component and nested case-control component

		PROPORTION (%) RETURNED PER PRACTICE		
NESTED CASE-CONTROL COMPONENT	**NUMBER RETURNED**	**MEDIAN**	**5TH PERCENTILE**	**95TH PERCENTILE**
CASES (of 817)				
Risk-factor questionnaires	648	81.0	0	100
Stools submitted	761	93.8	57.1	100
Socio-economic questionnaire	555	66.7	0	91.7
CONTROLS (of 675)				
Risk-factor questionnaires	613	100	66.7	100
Stools submitted	555	87.5	50	100
GP CASE-CONTROL COMPONENT	**NUMBER RETURNED**	**MEDIAN**	**5TH PERCENTILE**	**95TH PERCENTILE**
CASES (of 4,026)				
Risk-factor questionnaires	2,642	69.8	40.0	81.3
Stools submitted	2,962	74.5	54.3	84.9
Socio-economic questionnaire	1,652	42.7	16.7	60.7
CONTROLS (of 2,871)				
Risk-factor questionnaires	2,429	87.8	67.9	100
Stools submitted	2,292	84.6	56.1	95.8
GP CASE-CONTROL COMPONENT (OF 4,744 CASES)	**NUMBER RETURNED**	**MEDIAN**	**5TH PERCENTILE**	**95TH PERCENTILE**
Socio-economic questionnaire	2,182	48.1	23	71.8

respectively) (Table 4.5). There was practice variation, being lower in practices from urban locations in the South East. There was no statistically significant difference by sex or age (Appendix 1, Tables A1.29 and A1.30 and Figure A1.9). Eighty-two percent sent stool specimens and there was practice variation, compliance being lowest in practices in an urban location (median, 5th–95th percentiles: 87.5, 50–100). There was no statistically significant difference by age and sex (Appendix 1, Tables A1.31 and A1.32 and Figure A1.10).

4.3 GP CASE-CONTROL AND ENUMERATION COMPONENTS

4.3.1 Under-ascertainment component

To estimate the extent of under-ascertainment of cases of IID to the study, data were collected from 26 GP practices who routinely entered diagnoses on their practice computer. By all measurable indices these practices were representative of those without this facility. The records of 2,021 persons with possible IID were examined. 1,514 fulfilled the case definition and should have been ascertained, but only 974 (64%) were ascertained into the GP component.

Logistic regression modelling was used to identify factors which were independently associated with ascertainment after taking other factors into account. This is described more fully in Appendix 1, A1.3.1.

The predicted percentage ascertainment according to practice characteristics was calculated from the final logistic regression model. Predicted under-ascertainment was higher in urban practices, with a large number of partners and without previous research experience (Table 4.6). These characteristics were then used to correct for the under-ascertainment at practice level.

Table 4.6 Regression model parameters for adjusting practice level incidence rates

VARIABLE	CATEGORY	ODDS RATIO	P-VALUE	95% CONFIDENCE INTERVAL
Study component	case control	1.0		
	enumeration	1.78	<0.001	1.39 to 2.29
Number of partners	1–2	1.0		
	3–4	0.63		0.55 to 0.73 per
	5–6	0.41		increase of
	7–8	0.26	<0.001	category
Location	urban	1.0		
	rural	2.27	<0.001	1.81 to 2.86
Previous research	no	1.0		
	yes	1.92	<0.001	1.49 to 2.48

4.3.2 Number of cases and controls in the GP case-control component

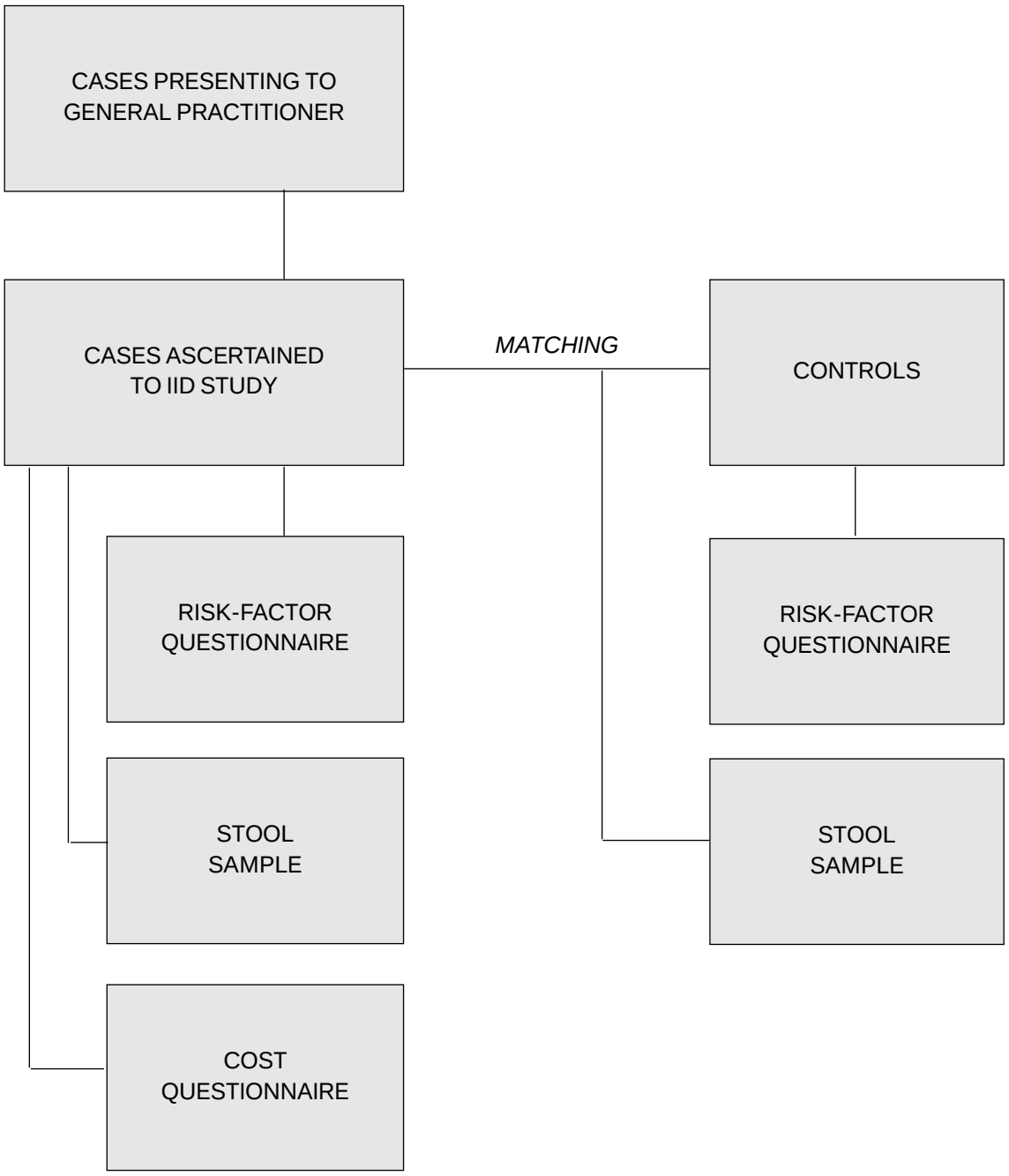
Compliance and representativeness of cases and controls are shown schematically in Figure 4.3. A total of 4,026 cases were ascertained in the 34 practices. There were 2,871 age and sex matched controls recruited for the 4,026 cases (overall matching 71%). There was variation at practice level matching and a median of 75.3% was achieved (5th and 95th percentiles 23.8 and 96.9, respectively). The median number of cases per practice was 119 and the median number of controls recruited was 77.

Matching was slightly higher in females than males (74% versus 71%) and lowest in the 15–24 year age group (Appendix 1, Table A1.36 and Figure A1.13). Higher matching was associated with practices in a rural location, in the Midlands & South West, and with a Jarman score in the mid-range (Appendix 1, Table A1.37).

Age and sex-matched controls were selected on the basis of the criteria and procedure described in A1.3.2.1 and Table A1.38 (Appendix 1) shows the number and proportion accepting in the order of invitiation. Half of the controls invited accepted, but this decreased to 13% when the fifth control was invited.

The time delay between case ascertainment and control recruitment was assessed by the time interval between the date of the case risk factor questionnaire and the date of the control risk factor questionnaire. In 57% of cases the control questionnaire was received within one month. In 83% of cases it was completed within two months (Appendix 1, Table A1.39 and Figure A1.14).

Figure 4.3 Representativeness and compliance in the case-control component



4.3.3 Compliance in completing risk-factor questionnaires and supplying stool specimens from cases

A total of 2,642 questionnaires were returned by the 4,026 cases, an overall mean compliance of 66% (median 70%, 5th and 95th percentiles 40 and 81, respectively) (Table 4.5). Females returned a higher proportion of questionnaires than males (Appendix 1, Table A1.40 and Figure A1.15). Overall 2,962 stool specimens were submitted by the 4,026 cases (mean compliance 74% median 75%). Fewer questionnaires and stool specimens were returned in the 15–24 year age group and from urban practices and from practices with the highest (most deprived) Jarman score (Appendix 1, Tables A1.41 and A1.43 and Figure A1.16). There was no difference in stool sample compliance between the sexes (Appendix 1, Table A1.42).

Amongst cases in the GP component, there was no difference in the severity of symptoms between those who complied by submitting stool specimens and those who did not.

4.3.4 Compliance in completing risk-factor questionnaires and supplying stool specimens among controls

There was a high overall mean compliance of 85% (median 88%, 5th and 95th percentiles 68 and 100, respectively), with 2,429 questionnaires being returned by the 2,871 controls (Table 4.5). Overall 2,281 stool specimens were submitted by the 2,871 controls, a mean compliance of 80% (median 85%, 5th and 95th percentiles 56 and 96). Low compliance in the submission of stool specimens was associated with practices with a high (most deprived) Jarman score (Appendix 1, Table A1.47). There was no difference in risk-factor questionnaire or stool specimen compliance between the sexes and compliance was lowest in the 15–24 year age band (Appendix 1, Tables A1.44 and A1.46 and Figures A1.17 and A1.18).

4.4 STOOL SPECIMENS

Stool weight was recorded for each specimen submitted for analysis. The dates of stool collection, postage and receipt by Leeds PHL were recorded, and the date of onset of symptoms was obtained from questionnaires.

4.4.1 Stool collection in each component

The numbers of stools collected from cases and controls for each study component by age and sex are given in Appendix 1, Tables A1.27, A1.31, A1.42, A1.46 and A1.48 . 5,243 stools were submitted for analysis from 6,897 subjects from the GP case-control component, an overall compliance rate of 76%. Compliance for controls was slightly better than for cases, and controls submitted fewer stools that were of insufficient weight for analysis (Appendix 1, Table A1.48).

4.4.2. Stool weights by age, study component and period of study

Stool weights for different age groups
The data are summarised in Appendix 1, Tables A1.49–52. For each age group, stool weights were comparable, but with a trend for more stool submitted by males than females. Stool weights were smaller for infants and children in most study components. The range of weights of specimens submitted was large in all study components, and some specimens in all age groups and study components were insufficient for all microbiological analyses.

Stool weights by study period
The median weights of stool specimens submitted for different quarters of the study period are given in Appendix 1, Tables A1.53–54, and exceeded 10g for more cases than controls in all age groups. The proportion of stool specimens less than 10g in weight was 34.3% and 23.1% for cases and controls respectively. Approximately 9g of stool was required for all microbiological analyses (to Stage 7) (Table 3.1). Only 12.1% of cases and 3.6% of controls failed to provide at least 5g of stool. There was a trend for an increase in the weight of stool specimen submitted during the study period, and it is likely that this reflected improved collection methods, which included the introduction of greaseproof paper for specimen retention, and the change-over to larger collection spoons, as well as clearer instruction sheets.

4.4.3 Time to testing

Data for times from onset of symptoms and voiding to receipt at Leeds PHL are given in Appendix 1, Tables A1.55–57 and Figures. A1.19 and A1.21. One third of specimens were received for analysis within four days of onset and 63%, 77.1% and 85% within 7, 10 and 14 days respectively. The time between voiding and receipt was comparable for cases and controls with 95% of specimens received within four days.

4.4.4 Priority of microbiological investigations

The numbers and proportions of specimens submitted to each of the stages of microbiological investigation are given in Appendix 1, Table A1.58. All specimens were examined to Stage 3 and more than 70% of all specimens were investigated to Stage 5 (Table 3.1).

4.4.5 Quality control

Bacteria
Most target bacteria isolated had identities confirmed and were typed at reference laboratories. A few isolates died in transit and could not be resuscitated at Leeds PHL.

Viruses
Part of every tenth specimen processed for virus detection at the Leeds PHL was sent to the Virus Reference Division (VRD), CPHL and examined by electron microscopy (EM) using their standard protocol. The two sets of results were compared at the end of the study period.

Table 4.7 Comparison of electron microscopy results for viruses obtained at VRD (CPHL) and at Leeds PHL

	VRD + LEEDS POSITIVE	LEEDS POSITIVE ONLY	VRD POSITIVE ONLY	TOTAL
Rotavirus	28	1	1	30
Adenovirus	10	0	0	10
SRSV	17	6	21	44
Astrovirus	17	0	2	19
Calicivirus	7	0	4	11

The results (Table 4.7) indicate:

Adenovirus — There was complete agreement between the two laboratories by EM. Only adenovirus types 40/41 were reported to the study and these comprised 77% of all the adenoviruses identified by EM.

Astrovirus— Good agreement was found between the two laboratories. Leeds PHL results were all confirmed by a second test, as approximately 5% of astroviruses EM positive findings cannot be confirmed by SPIEM, antigen capture EIA or culture. Only astroviruses confirmed by two tests were reported.

Rotavirus— There was good agreement between the two laboratories, as rotavirus is relatively easy to identify by EM. The two discrepant

results were specimens containing very low virus concentrations (i.e., around 10^5 particles/ml), where the one or two particles present may be seen or missed by chance.

SRSV/Calicivirus — There were 31 discrepancies between the two laboratories with these two groups of viruses.

The following points should be borne in mind with regard to detection of SRSV/caliciviruses:

i) It can be very difficult to distinguish between these two viruses if the morphology is obscured by antibody. Therefore the reporting of an SRSV by one laboratory as calicivirus in the other was counted as concordant. This applied to three results.

ii) SRSVs and caliciviruses frequently have an indistinct morphology and an identification may be difficult when virus is present in low numbers or in a degraded form. The approach taken at Leeds PHL was only to report results of which the microscopist was certain and to record uncertain results on the worksheets only. Examination of the worksheet notes often showed that microscopists at both laboratories had seen suspected virus particles but they were not reported at Leeds PHL. This accounts for some of the discrepant findings between the two laboratories and is demonstrated by the differences in sensitivity and specificity figures, with Leeds PHL having greater specificity and VRD having greater sensitivity (Table 4.8).

iii) A Polymerase Chain Reaction (PCR) confirmation technique developed at VRD was found to increase the detection capability 600-fold compared to the EM preparation method used at Leeds PHL (unpublished findings, data not shown). This PCR method detects only 90–95% of SRSV strains, because of the genetic diversity of these viruses. As a result, some PCR negative/ EM positive specimens will be genuine positives. PCR and EM were performed on the same virus suspensions. Results are shown in Table 4.8 and a summary of specificity and sensititivity in Table 4.9.

Table 4.8 SRSV validation – comparison of electron microscopy results with PCR results

	CORDANT	DISCORDANT		TOTAL
	VRD + LEEDS EM POSITIVE	LEEDS EM POSITIVE ONLY	VRD EM POSITIVE ONLY	
PCR positive	16	5	9	30
PCR negative	1	1	12	14
Totals	**17**	**6**	**21**	**44**

Table 4.9 Specificity and sensitivity of EM and PCR testing for SRSV

SPECIFICITY		
Leeds PHL EM positive and PCR confirmed	21/23	(91.3%)
VRD EM positive and PCR confirmed	25/38	(65.8%)
SENSITIVITY		
Leeds PHL EM positive / total PCR positive	21/30	(70%)
VRD EM positive/total PCR positive	25/30	(83%)

4.5 SOCIO-ECONOMIC COSTS QUESTIONNAIRE

4.5.1 Completeness and representativeness of those returning the socio-economic costs questionnaire in the GP, enumeration, and population cohort components

The questionnaire assessing the socio-economic costs of IID was sent to all cases. A total of 4,389 costs questionnaires were returned by cases in all three components (Table 4.5). Compliance by cases was 46% (2,261/4,876 questionnaires returned) in the enumeration component, 41% (1,652/4,026) in the GP component, and 68% (555/817) in the community component. Returns were higher in persons aged over 55 years and lowest in practices with a rural location, in the North and in those with a high (most deprived) Jarman score.

When considered as a proportion of cases who returned a risk-factor questionnaire, the proportions are 63% for the GP component, and 86% for the community component.

4.5.2 Characteristics and representativeness of cases returning socio-economic costs questionnaire when compared to cases who returned a risk-factor questionnaire

Age and sex characteristics
38.6% of cases responding to the socio-economic questionnaire were under 16 years of age. The age distribution of cases responding to the socio-economic costs questionnaire was similar to that of the GP, enumeration components and the community components (Table 4. 10 and Appendix 1, Figure A1.22).

Social class
Social class for the head of household was available for the cases arising from the GP and population cohort components. In the GP component, 33% of cases were social class I or II. In the population cohort component this proportion was 28% (Table 4.11 and Appendix 1, Figures A1.23 and A1.24). Social classes III (M) and III (NM) were commoner in cases presenting in the GP component than in the community. However, it should be noted that social class was missing for 38% of the sample. There were more males than females in social class I, II, III(NM) and more females than males in social class III (M) and IV, and in those whose social class was unknown. Most of the cases in children were in households in which the head of household was in social class II or III(NM). The over 60 year olds were primarily in social class II.

Employment status
The employment status of the main earner was determined for responders to the employment status question. The responders to the socio-economic questionnaire had a similar pattern of employment to those in other study components. In the GP component more than 65% of males and 36% of females were employed full-time. More females than males were employed part-time (17% and 2%, respectively) (see Table 4.12).

Income
Information on household income was provided by 1,134 cases in the GP component, 391 cases in the community component and 1,440 cases in the enumeration component. The distribution of reported income for each study component was similar (Appendix 1 Table A1.61).

Table 4.10 Age and sex distribution of cases in the GP case-control component and population cohort component who returned a socio-economic questionnaire, compared to all who returned a risk-factor questionnaire cases in each study component

SOCIO-ECONOMIC COSTS QUESTIONNAIRE RETURNERS					ALL CASES			
	GP CASE-CONTROL COMPONENT							
AGE GROUP	MALE		FEMALE		MALE		FEMALE	
	N	%	N	%	N	%	N	%
< 1 year	76	11.1	66	7.5	138	11.5	109	7.7
1–4 years	174	25.5	145	16.6	305	25.5	237	16.8
5–15 years	70	10.3	67	7.7	110	9.2	101	7.2
16–60 years	272	39.9	451	51.7	518	43.3	761	54.0
60+ years	88	12.9	142	16.3	122	10.2	195	13.8
Missing	2	0.3	2	0.2	4	0.3	7	0.5
Total *	**682**		**873**		**1,197**		**1,410**	

** 97 cases age/sex data missing*

AGE GROUP	POPULATION COHORT COMPONENT							
	N	%	N	%	N	%	N	%
< 1 year	5	2.1	12	4.4	7	2.3	15	4.1
1–4 years	55	22.6	56	20.6	70	23.0	75	20.6
5–15 years	54	22.2	36	13.2	68	22.3	50	13.7
16–60 years	88	36.2	139	51.3	112	36.7	184	50.6
60+ years	41	16.9	28	10.3	48	15.7	40	11.0
Total *	**243**		**271**		**305**		**364**	

41 cases age/sex data missing

Table 4.11 Social class distribution of cases in the GP case-control component and population cohort component who returned a socio-economic questionnaire compared to all cases in each study

	SOCIO-ECONOMIC QUESTIONNAIRE RETURNERS		ALL CASES	
	POPULATION COHORT COMPONENT			
SOCIAL CLASS	**N**	**%**	**N**	**%**
I	18	3.2	31	4.6
II	135	24.3	199	29.5
III (N)	69	12.4	140	20.7
III (NM)	49	8.8	87	12.9
IV	45	8.1	80	11.9
V	3	0.5	11	1.6
Other	23	4.1	45	6.7
Missing	213	38.4	82	12.1
Total	**555**		**675**	
	GP CASE-CONTROL COMPONENT			
SOCIAL CLASS	**N**	**%**	**N**	**%**
I	102	6.2	71	2.7
II	445	26.9	417	15.9
III (N)	295	17.9	352	13.4
III (NM)	270	16.3	225	8.6
IV	183	11.1	220	8.4
V	40	2.4	48	1.8
Other	139	8.4	188	7.2
Missing	178	10.8	1,104	42.0
Total	**1,652**		**2,625**	

Table 4.12 Employment status of adult cases who responded to the relevant questions, by study component and sex

	SOCIO-ECONOMIC COSTS QUESTIONNAIRE RETURNERS				ALL CASES			
	GP CASE-CONTROL COMPONENT							
EMPLOYMENT STATUS	MALE	%	FEMALE	%	MALE	%	FEMALE	%
Full-time	235	65.3	213	35.9	431	67.2	367	38.3
Part-time	8	2.2	104	17.5	19	3.0	167	17.4
Unemployed	9	2.5	11	1.9	28	4.4	27	2.8
Temporarily sick	3	0.8	9	1.5	4	0.6	13	1.4
Disabled	20	5.6	24	4.0	28	4.4	40	4.2
Retired	59	16.4	89	15.0	82	12.8	125	13.1
Student	15	4.2	18	3.0	26	4.1	30	3.1
Not seeking employment	4	1.1	95	16.0	5	0.8	142	14.8
Missing	7	1.9	31	5.2	18	2.8	47	4.9
Total	**360**		**594**		**641**		**958**	
	POPULATION COHORT COMPONENT							
EMPLOYMENT STATUS	MALE	%	FEMALE	%	MALE	%	FEMALE	%
Full-time	119	56.1	92	37.3	146	54.9	127	37.8
Part-time	17	8.0	53	21.5	24	9.0	74	22.0
Unemployed	7	3.3	7	2.8	9	3.4	8	2.4
Waiting to start job	1	0.5	0	0	1	0.4	0	0
Disabled	8	3.8	10	4.1	11	4.1	13	3.9
Retired	47	22.2	39	15.8	55	20.7	54	16.1
Student	4	1.9	2	0.8	6	2.3	3	0.9
Not seeking employment	5	2.4	35	14.2	8	3.0	44	13.1
Missing	4	1.9	9	3.6	6	2.3	12	3.9
Total	**212**		**247**		**266**		**336**	

4.5.3 Proportion of cases returning socio-economic costs questionnaire according to organism identified

The organisms identified in cases who returned a socio-economic costs questionnaire were distributed in a broadly similar way to those in the other components. Approximately 50% of cases with target organisms in the GP component returned a socio-economic questionnaire, with the exception of the lower response from cases with *E.coli* O157, enteropathogenic *E.coli* (EPEC) and *Shigella*.

4.6 THE REPRESENTATIVENESS OF MICROBIOLOGY LABORATORIES IN THE ENUMERATION STUDY

The representativeness of the laboratories serving GP practices in the enumeration component was examined on the basis of the proportion belonging to PHLS, the proportions of organisms isolated and the number of stools tested. There were 11 PHL laboratories who served the enumeration component (33% of total) compared to 52 in England (21%). There were 33 laboratories who routinely received stool samples from the 36 enumeration practices. Of these, 11 belonged to the PHLS and 22 did not. Information was also obtained on faecal workload and positive isolates for 1994 by sending questionnaires to all microbiology labs in England. There was a reply from 46/52 PHLS laboratories (88%) and from 132/190 non-PHLS laboratories (69%). Of laboratories receiving samples from the enumeration component, only 10 (of 11) and 11 (of 22) laboratories replied, respectively. Together the enumeration labs tested 16.7% of the stools and identified 16.5% of the isolates (Table 4.13). The proportion that were positive was similar to the national laboratories (12%). On this basis it is likely that they were reasonably representative of all microbiology labs in England.

The number of laboratories that had a computerised microbiological data recording system was also compared as it was thought that this might influence reporting to CDSC. Of those who replied to the questionnaire, 9 of the 10 PHLS laboratories (90%) in the enumeration component had a computerised system, compared to 44 of 46 nationally (96%). Of the non-PHLS laboratories 82% in the enumeration component (9 of 11) had a computer versus 75% nationally (99 of 132).

Table 4.13 Total number of stools tested and target isolates identified by the enumeration laboratories compared to all laboratories in England amongst laboratories responding to the questionnaire

LABORATORY	TOTAL STOOLS EXAMINED IN 1994	TOTAL STOOLS POSITIVE	PERCENT POSITIVE
Enumeration labs (n=21)	146,902 (16.7%)	17,868 (16.5%)	12.2
All labs in England (n=178)	878,247	108,180	12.3

4.7 CONCLUSIONS

4.7.1 Practice characteristics

The study population was representative of that of England as judged by age, sex, geographical areas (North, Midlands & South West and South East), and by urban or rural location. It slightly under-represented the lower (least deprived) Jarman tertile and GP practices with fewer than four partners when compared to the population of England. These differences were only slight and reflected the distribution of practices in the GPRF.

4.7.2 List inflation

On the basis of notesearches carried out during cohort recruitment, it was estimated that 10.2% of the population who were still registered with their GP should not have been because they had moved away or died. This figure is in keeping with other estimates of list inflation which range from 1 to 30% (Fraser 1978, Sheldon 1984, Roe *et al*. 1989, O'Mahoney *et al*. 1997). Thus adjustments were made for each practice ensuring that any inflation in the denominator for the calculation of presentation rates was corrected for.

4.7.3 Under-ascertainment to the study

Under-ascertainment by GPs to the study was estimated by using practices with computerised diagnosis to identify patients who should have been ascertained but were not. Overall ascertainment was 64% and varied according to the number of partners in the practice, urban or rural location, study component and experience of previous research. These characteristics were then used to adjust for individual practices to obtain a more accurate correction than would have resulted from a crude adjustment for under-ascertainment. Under-ascertainment is a common problem in epidemiological studies, disease registers and surveillance, and adjustment is needed (Doll 1991).

The representativeness of the population, and the adjustments for list inflation and under-ascertainment ensured that the corrected presentation rate was as accurate as possible.

4.7.4 Cohort population

The characteristics of the cohort population were very similar to the population of England; there were only slight differences in terms of age, sex, ethnicity and social class. Enrolment was lower in the 15–24 year age group and in social classes I, III(M) and V when compared to the national population. A larger proportion were married, retired and were owner-occupiers. As data were collected on these characteristics, correction factors could theoretically be used to adjust for community rates. Accurate follow-up data were obtained because of the weekly report cards, and 82% completed more than 23 weeks of follow-up. Compliance in the baseline questionnaire return was lowest in the 15–24 year age group, practices with a high (most deprived) Jarman score and in the South East.

4.7.5 Compliance

Compliance of cases in returning risk-factor questionnaires (69%) and in submitting stool specimens (74%) was high. It was lowest in the 15–24 year age group and in males. Practice characteristics associated with lower compliance were high (most deprived) Jarman score and urban location. Matching of controls to cases was also

high (median 75%). Compliance in controls was generally higher, as they had already self-selected to participate in the study.

4.7.6 Stool specimens

The overall compliance with stool collection was high (76%). Over 70% of all specimens were tested to Stage 5 and the proportion of stools that were less than 10g was 34% for cases and 23% for controls; these may not therefore have had comprehensive microbiological testing and archiving. Specimen weights were smaller for children. There was an inevitable time interval between onset of symptoms and testing; however, 63% of specimens were received within one week of the onset of symptoms and 85% within a fortnight. The time between voiding and receipt of specimen was small and 95% were received within four days.

4.7.7 Microbiology laboratories in the enumeration study

Microbiology laboratories serving practices in the enumeration study were representative of those of England in that they undertook 17% of the national workload and they identified a similar proportion of positive stools.

4.7.8 Socio-economic costs questionnaire

Compliance overall was not high but 63% of those who returned their risk-factor questionnaire also returned a socio-economic costs questionnaire. The social class distribution and age and sex distribution was very similar to that in the GP and community components.

Chapter 5
Microbiological Findings

5.1 LABORATORY RESULTS OF STOOL EXAMINATIONS

5.1.1 Target organisms and toxins

Target organisms and toxins identified in faecal specimens from cases and controls in the GP case-control and population cohort components are listed in Tables 5.1 and 5.2. These tables are intended to provide a synopsis of the microbiological findings of the study, to give an indication of the relative numerical importance of each of the organisms and to enable comparisons to be made with other published information.

The volumes of faeces received were insufficient to test for every target organism in every specimen and the number tested reflect the priority list given in Table 3.1. For some organisms, data for different species have been aggregated although it is recognised that there may be both intra- and inter-species variation in terms of pathogenicity. Some of the organisms listed, although recognised as putative gastro-intestinal pathogens, are also frequently identified in the normal intestinal flora of healthy individuals; these include *Aeromonas* spp., *Clostridium difficile* in children aged less than 2 years, *Clostridium perfringens* and *Staphylococcus aureus*.

Many enteropathogens produce toxins, but in two instances, *C.perfringens* and *C.difficile* (in adults and children aged 2 years and above), specific toxin detection in the faeces is considered diagnostic of a pathogenic role for these particular bacteria, as non-toxin-producing strains are also found in the normal flora. Numbers quoted for *C.perfringens* enterotoxin are for specimens giving positive reactions in the Perfringens enterotoxin reverse passive latex agglutination (PET-RPLA) test conducted at Leeds Public Health Laboratory (PHL) that were also confirmed as enterotoxin positive by ELISA at the PHLS Food Hygiene Laboratory. Ingestion of pre-formed *Staph.aureus* enterotoxin in food causes IID but it is not possible to detect the enterotoxin in faecal specimens. As a correlate of intoxication by this pathogen, high counts of *Staph.aureus* were identified in this study and the isolates subsequently tested for enterotoxin production.

There was a high percentage of cases in both study components (45% for cases presenting to GPs and 63% in the population cohort) in which no target organism was identified. This finding is discussed in section 5.5.

5.1.2 Overview of relative frequencies and comparisons with previous studies

Target organisms were identified more frequently in cases in the GP component (55%) than in the population cohort component (37%). SRSV was the most commonly identified target organism in cases in the population cohort component and may, therefore, be considered the most frequent cause of IID in the community. *Campylobacter* spp. and rotavirus group A were more common than SRSV in cases in the GP component. The severity of disease associated with each target organism is described in Chapter 7.

Although most target organisms were found in at least some controls, the numbers of positives in controls were generally small in comparison to cases. The total

numbers of target organisms identified in the controls were small, particularly in the population cohort component. However, the percentages positive for each target organism in controls for both studies were similar as would be expected from independent random samples of healthy individuals. Comparing the percentages positive for cases from the GP and population cohort components, higher percentages were found for each of the target organisms in the GP component (excluding *Aeromonas* spp., *Yersinia* spp. and SRSV).

It is not possible to make a direct comparison with national reports of gastrointestinal pathogens because of the way in which these data are collected; however, the relative frequencies are presented in Table 5.3 and discussed further in Chapter 6.

Although no target organisms were identified in 45% of cases in the GP component and 63% of cases in the population cohort component, there was a higher frequency of detection for the common bacterial enteropathogens in this study compared with other UK studies (Table 5.4). This may reflect the methods used in this study to maximise recovery of pathogens. In a recent study in Wales (Palmer *et al.* 1996), specimens were examined from 255 cases of presumed IID presenting to four general practices. Two studies were also carried out in the mid-1980s to establish the significance of *Cryptosporidium parvum* as a human pathogen. In the first, specimens were examined from 867 patients at Bristol PHL (Hunt *et al.* 1984) and in the second, specimens were examined from 62,421 patients at 16 PHLS laboratories (Anon. 1990). The different methods used in each study may have influenced the detection rates.

5.1.3 Relative frequencies of organisms in different age groups

The aggregated information from Tables 5.1 and 5.2 was broken down according to age group, for infants (aged under 1 year), young children (aged between 1 and 4 years), older children (aged between 5 and 14 years), adults (aged between 15 and 74 years) and the elderly (aged 75 years and older). Tables A2.1–A2.5 (see Appendix 2) show that *C.difficile* cytotoxin was detected most frequently in both cases and controls aged under 1 year, confirming previous reports, with a second increase in frequency in cases in the elderly. *Campylobacter* and *Salmonella* infections were more common in older children and adults than in young children. Among the enterovirulent *E.coli*, EPEC infections were uncommon and did not occur in infants, which was the age group noted for outbreaks of infection with certain serotypes of EPEC in the 1950s and 1960s. ETEC infections were found most frequently in adult cases. *C. parvum* infections were most common in children. All viral infections were most frequent in cases in young children and infants.

5.1.4 Multiple organisms and pathogenicity

Two or more target organisms were identified in 11% of cases presenting in the GP component, in 7% of the population cohort component and less than 2% of controls (Table 5.5). Many different combinations were observed with no common association predominating. Some target organisms were seen more commonly as sole isolates whereas others were observed more frequently in association with other target organisms (Table 5.6). No comparable figures are given for target organisms detected in cases and controls in the population cohort component, because numbers were insufficient for analysis; however, for cases in the population cohort component with *Campylobacter* spp., *Salmonella* spp., rotavirus A and SRSV infection, the percentage for each organism identified as the sole was virtually identical to that of the GP component. A complete list of the combinations of enteropathogens detected is given in Appendix 2.

For a selected number of target organisms identified as multiple isolates in the same stool sample, statistical tests were used to test whether both organisms were

identified in the same stool more often than would be expected to occur by chance. The presence of *Salmonella* spp. and *Campylobacter* spp. in the same stool sample occurred significantly less frequently than expected by chance (two instances instead of 12.5 expected, P=0.0013) and this finding requires further study.

Some organisms (*Aeromonas* spp. (DAEC)) whose pathogenicity is not fully established were detected more frequently in the presence of other pathogens than as sole isolates. This feature also applied to *Shigella*, an accepted pathogen. Ratios of proportions of the isolation of target organisms in cases compared with controls are given in Table 5.6, in an attempt to identify those target organisms statistically significantly associated with disease. For example, a high case to control ratio is seen with *C. jejuni*, and *S. enteritidis*, whereas an inverse ratio is seen with DAEC and *Yersinia* spp. However, as indicated above, in some instances individual species or genotypes of enterovirulent *E.coli* have been identified, whereas for other target organisms data for a genus are aggregated.

5.1.5 Effects of time and other factors on microbiology results

The time delay between the onset of symptoms, taking a stool specimen and the specimen being received at Leeds PHL varied considerably (Appendix 1, Figures A1.20 and A1.21 and Tables A1.56 and A1.57). The time delay between the onset of symptoms and receipt of the specimen ranged from 1 to 77 days (median=6, mode=5) in the GP component and 0 to 58 days (median=3, mode=2) in the population component (Figures 5.1 and 5.2). The length of time did not appear to influence the positivity rate up to one week after onset, with a slow decline in positivity rates thereafter; the median time delay in the GP component was six days for positive stools and seven days for negative stools and was three days for both positive and negative stools in the population cohort component (Figure 5.2).

The proportion of stools with one or more target organism identified does not simply decrease with increasing time from the onset of symptoms to the receipt of the specimen. In the GP component there was a slightly increasing proportion 'positive' up to seven days followed by a gradually decreasing proportion 'positive' beyond seven days in the GP component (Figure 5.1). A similar effect was seen in the population cohort component (Figure 5.2). The reasons for this are not clear. The proportion of stools with more than one pathogen detected appears to reflect the same pattern (Tables A2.6–2.14).

The effect of length of time from onset of symptoms to the specimen being taken or received in the laboratory is shown for selected target organisms (Figures A2.1–2.8). *Salmonella* detection was unaffected by the length of time, which is consistent with our knowledge of *Salmonella* excretion. In contrast, *Campylobacter* detection was very sensitive to time; proportions detected were high between 3–8 days and fell sharply outside of this range. The effect of time on detection of the two most common viruses, SRSV and rotavirus, also differed. The peak for detection of SRSV was two days with a sharp decline after five to seven days, whereas high rates of rotavirus detection started to fall after eight days.

Others have shown that *C.perfringens* enterotoxin can be detected in 75% of faecal specimens from cases of food poisoning collected within two days of onset of symptoms, but in only 33% of specimens collected after that time (Bartholomew *et al*. 1985). Similarly, *C.difficile* toxins deteriorate in stool specimens stored at ambient temperature (Bowman and Riley 1986), but these effects were not analysed in this study.

Not all stool specimens were of sufficent weight to allow the complete range of microbiological tests to be performed; this might be expected to affect the frequency of isolation of multiple organisms. Table 5.7 shows the frequency of isolation of one or more target organisms from only those stool specimens from IID that were subjected to all tests (to stage 7), and that were received within eight days of onset of symptoms. The frequency distributions in the GP and population cohort components are comparable with those presented for all specimens, regardless of the extent of testing or time lapse (Table 5.5).

These results indicate that delays in sampling and transport had little effect on the detection of organisms in this study, as most stools were received before deterioration in detection rates caused by delays would have taken effect.

5.1.6 Enrichment methods

Table 5.8 shows the proportion of selected target organisms isolated only after enrichment methods were used. Tables 5.9 and 5.10 show how this varied with time delay between onset of symptoms and receipt at the laboratory for *Campylobacter* spp. and *Salmonella* spp. isolations, respectively.

A high proportion of *Yersinia* spp. and *Aeromonas* spp. isolates in cases of IID were detected only after enrichment (60–80%). Therefore, although these two were among the more frequently identified target organisms in both cases and controls, they were usually present in low numbers. For cases with *Salmonella* spp. the proportion of specimens requiring enrichment was around 30%, but for *Campylobacter* spp. this was much lower at around 5%.

Specimens from controls required enrichment more frequently than specimens from cases for the detection of *Salmonella* and *Yersinia*, suggesting that these bacteria were present in lower numbers in controls than in cases. No *Campylobacter* were detected by enrichment alone in controls; however, the number of controls in which *Campylobacter* was found was small. There was little difference in the effect of enrichment on the isolation of *Aeromonas* in cases and controls. The effect of enrichment on isolation rates was more pronounced with increasing time between onset of symptoms and receipt of the specimen in the laboratory for both *Salmonella* and *Campylobacter* (Tables 5.9 and 5.10).

G. intestinalis was detected by direct microscopic examination of the stool specimen and following a concentration procedure. Concentration was required for the detection of almost 25% of cases but did not identify more asymptomatic excreters than direct microscopy alone (Table 5.8); this apparent anomaly is likely to be due to small numbers in the latter group.

5.2 AGE AND SEX DISTRIBUTION OF CASES OF IID

The distribution of cases by age and sex was expressed using incidence rates. It is described in detail in Chapter 6. GP presentation rates for IID varied substantially by age with the highest rate in those under 5 years, particularly in the under 2 years age group (Figure 5.3). In adults aged over 20 years, rates decreased with increasing age. Community IID rates were higher than rates of presentation to the GP in all ages, but showed a similar pattern with high rates in children and a decline, albeit less marked, with increasing age (Figure 5.4). Sex differences were small and inconsistent in both studies. The significance of these observations is discussed in Chapter 6.

Age-specific rates of IID in cases presenting in the GP component with specific target organisms isolated, and, where justified by numbers, age distributions of the proportion of controls asymptomatically excreting those organisms, are shown in Figures A2.11–A2.34. Figures A2.25 and A2.26 shows the same paired data for IID with no target organism isolated. There were insufficient community cases with specific organisms for graphical presentation.

Cases
For most target organisms, presentation rates were highest in the under 2 years age group, however, for *Cryptosporidium parvum* the peak occurred in the 2– 4 year group (Figure A2.28), and for *Shigella* and ETEC most cases presenting were adults (Figures A2.25 and A2.23 respectively). Few adult cases of Calicivirus and Adenovirus infection were identified and Rotavirus, Astrovirus and SRSV infections were also predominantly found in children (Figures A2.30–2.34). Rotavirus Group A was the most common target organism identified in children under 5 years of age presenting to GPs, whereas in the population cohort component SRSV was slightly more frequent in cases in this age group.

Controls
The numbers of positive controls were insufficient to give a clear pattern of age distribution except with five target organisms, of which three were different types of enterovirulent *E.coli*. DAEC was excreted by 30–50% of all age groups, AEEC by 60–70% aged 0– 9 years and 10–25% of the older population and EAggEC by 15–35% aged 0–19 years and 10–25% of the adult population. Greater proportions of asymptomatic children excreted *Aeromonas* and *Yersinia* than adults. *Aeromonas* was isolated from 60–75% of children aged 0–9 years and 20–50% of older age groups, whilst *Yersinia* were isolated from 40–50% of children aged under 2 years, 40–50% of children aged 2–9 years and 15–30% of older age groups.

5.3 SEASONAL DISTRIBUTION OF CASES OF IID

The distribution of cases by season was expressed using incidence rates. It is described in Chapter 6. There was no discernible seasonality in the number of cases of IID in the GP or population cohort components (Figures 5.5 and 5.6).

The seasonal distribution of specific target organisms in cases in the GP component and for controls, are shown in Figures A2.37–2.61. Figures A2.62 and A2.63 show the same paired data for IID with no target organism isolated. There were insufficient cases in the population cohort component with specific organisms for meaningful seasonality analysis.

In general, the results confirm what is widely accepted for those organisms for which good national surveillance data are available, for example, the increased incidence in the summer months of *Salmonella* infection, and the marked increase in rotavirus infections in the first few months of the year (Figures A2.51 and A2.60, respectively).

These results are nevertheless valuable as it has always been possible to argue from existing evidence that at least some of these seasonal trends could have been due to ascertainment bias; clinicians or microbiologists could have sought more assiduously those organisms believed to be commoner at the appropriate time of year. These results are subject to no such bias.

AEEC was the only organism for which there was a convincing seasonal variation in both the rates of isolation of the organism from cases of IID and the proportion of controls carrying the organism (Figures A2.44 and A2.45, respectively). This is

interesting in that this is one of the few target organisms studied whose pathogenicity is not clearly established, and for which the incidence in cases was not statistically significantly different from the incidence in controls. The rates of carriage of this organism may vary independently of any disease although a subset may be pathogenic.

Further details relating to the seasonality observed with individual enteropathogens are discussed below.

5.4 ANALYSIS OF RESULTS FOR EACH TARGET ORGANISM

Notable results for each of the target organisms are presented below. Full details of sub-species identified and typing results are presented in Appendix 3.

5.4.1 Bacteria

Aeromona

Aeromonas spp. were isolated frequently with 4% to 6% of specimens positive for these organisms in cases and controls in both the GP and population cohort components. Thus, it was the second most commonly isolated target bacterium in the study but was as common in controls as cases. The proportion of controls positive for *Aeromonas* was higher than for any other organisms in both the GP and population cohort components. This suggests that many of the isolates from cases were not responsible for the IID but an incidental finding. About 80% of the *Aeromonas* were isolated only after enrichment (section 5.1.6). There was no clear seasonal variation in the isolation of *Aeromonas* spp. from cases or controls (Figure A2.37 and A2.38).

The highest age-specific rate in cases presenting to the GP was in the under 2 years age group (Figure A2.11). In cases in the GP component about 30% were children of less than one year of age. Over 75% of the strains from cases in the GP component were *A.caviae* followed by *A.hydrophila* (less than 20%) and *A.veronii* subspecies *sobria* (less than 5%). Few of the *Aeromonas* strains belonged to currently recognised O serogroups. In the period 1991–1994 isolates of *Aeromonas* spp. referred to LEP were as follows: *A.caviae* (45%), *A.hydrophila* (37%) and *A.veronii* subspecies *sobria* (18%). The results from this study suggest that only a subset of *Aeromonas* spp. is likely to be pathogenic. Identification of this subset requires further study of virulence properties.

Bacillus

A cut-off level of 10^4 cfu/g faeces was chosen, as *Bacillus* spp. can be present in low numbers in normal faecal specimens. High counts were very infrequent and occurred more often in controls than cases. The species isolated were: *B.cereus* (3 isolates), *B.subtilis* (1), *B.licheniformis* (1), *B.pumilus* (1) and *B.firmus* (6). None was the sole pathogen identified. There were insufficient isolates for useful interpretation of seasonality or age distribution.

Campylobacter

There were 44,414 and 43,876 laboratory reports of *Campylobacter* isolations in England and Wales in 1994 and 1995, respectively; and the number of *Campylobacter* reports exceeded 50,000 in 1997.

Campylobacter spp. were the most frequently isolated of all the bacteria sought in the study. Twelve per cent of cases in the GP component and 4% in the population

cohort component had *Campylobacter* spp. in their stools. The frequency of isolation in controls for both studies was only 0.7% (Tables 5.1 and 5.2).

A small number of *Campylobacter* spp. (4%) were isolated by enrichment but no controls were positive by enrichment alone (Table 5.8). Enrichment improved isolation rates slightly when specimen receipt in the laboratory was delayed (Table 5.9).

Campylobacteriosis was common throughout the year; in no month did the incidence amongst cases in the GP component fall below 100 cases/100,000 person-years (Figure A2.39). For eight months of the year, from March to August and October and November, the monthly number of cases was over 150 cases/100,000 person-years; the cases in these periods represented 54% and 25% respectively of all cases, suggesting a bimodal seasonality.

The highest age-specific rate was observed in the under 2 years age group, but over 70% of the cases were adults aged between 20 and 69 years. For adults the highest age-specific rate was in the 20–29 year olds (Figure A2.13).

C.jejuni was the predominant species identified (89% of GP cases) and a large number of different Penner O serotypes were identified, with the most frequent serotypes being Penner 1, 2 and the '4 complex' comprising serotypes 4, 13, 16, 50 and 64. *C.coli* was the only other species identified in significant numbers (8% of GP cases) but nevertheless at a much lower frequency.

We used a combination of isolation methods, including a membrane filter method, to enhance the recovery of Campylobacters. Nevertheless, only occasional strains of other non-'thermophilic' species (*C.upsaliensis, C.fetus* and *C.hyointestinalis*) were encountered and in remarkably few cases; there was one isolate of *Arcobacter cryaerophilus* from a case presenting to a GP.

Clostridium difficile

The positive *C.difficile* cytotoxin results presented in Table 5.1 are for all age groups. It is recognised that *C.difficile* is part of the normal flora in children up to the age of 2 years and *C.difficile* toxin may be detected in asymptomatic children at this age (Joint Department of Health and Public Health Laboratory Services Working Group 1994, Riley 1994). Re-analysis of the two age groups reveals equivalent colonisation and toxin detection rates in cases and controls aged under 2 years in the population cohort and a lower frequency of toxin positive specimens in cases compared with controls in this age group presenting to GPs (Tables A2.1–A2.5 and A2.9, A2.10; Figures A2.14, A2.15).

In older children and adults presenting to GPs there was a 2.5-fold increase in frequency of colonisation in cases compared with controls and a 5-fold increase in toxin detection. Cytotoxin was not detected in control subjects in this older age group in the population cohort component. This indicates that *C.difficile* may be responsible for a small but significant number of cases of IID in patients aged over 2 years outside hospitals. There are no published studies giving community rates of *C.difficile* in the UK; however, in the USA 3–5% of healthy adults are asymptomatic carriers (Joint Working Group 1994). In Australia, *C.difficile* or its cytotoxin was found in 4.7–5.5% of patients in the community with IID and was associated with antibiotic use (Riley 1994).

Seasonal variations, based on cytotoxin results, showed increased rates in winter and spring for cases aged under 2 years old, but an autumn increase for cases aged over 2 years. In controls aged under 2 years old rates increased in spring and autumn (Figures A2.40–A2.42).

The PHLS Anaerobe Reference Unit (Cardiff PHL) confirmed the identity of 375 isolates of *C.difficile*. All isolates were typed by the PCR ribotyping method of O'Neill *et al*. (1996) and tested for enterotoxin (Toxin A) production by an enzyme immunoassay method (Tox A Test, TechLab). 57% of isolates were toxigenic and 43% were non-toxigenic by this method. The numbers of each ribotype and toxigenicity are given in Appendix 3. Overall, 58 different ribotypes were identified in the study populations. Toxigenic strains were generally capable of producing both the enterotoxin (Toxin A) as well as the cytotoxin (Toxin B) which was detected in the diagnostic tests performed on the faecal specimens; the exception was Type 17 which produced Toxin B only. The most prevalent PCR ribotypes were Type 10 (non-toxigenic) which accounted for 16% of isolates and Type 20 (toxigenic) which accounted for 12%. The fourth most common ribotype at 4.8% was Type 1 (toxigenic) which accounts for over 54% of hospital strains analysed by the PHLS Anaerobe Reference Unit.

Clostridium perfringens

A positive result for this organism was defined as a specimen with a positive PET-RPLA result which was confirmed by ELISA. Using these criteria, *C.perfringens* enterotoxin was detected in 4% of cases and in 0.7% of controls in the GP component. The incidence was lower in the population cohort component (Tables 5.1 and 5.2).

The presence of enterotoxin was confirmed by ELISA in RPLA-positive specimens from both components in 123 out of 376 cases (33%) and 18 out of 328 controls (5%), and, in specimens with an equivocal RPLA result, in 1 of 10 cases and 1 of 9 controls (Table 5.14). Enterotoxin was detected by ELISA in 17% of 222 RPLA-negative cases and 1% of 218 RPLA-negative controls. Because it was not practical to test all specimens by ELISA, it is likely that the number of enterotoxin positive results was underestimated.

No other target organism was found in 47% of cases with *C.perfringens* (Table 5.6). In 15 of the 60 cases with more than one organism detected *Campylobacter* was the second most common organism isolated. Adenovirus and Rotavirus were detected in six and five of these cases, respectively. 179 different serotypes of *C.perfringens* were isolated; 10 serotypes were isolated only from cases, 138 only from controls and 31 from both cases and controls. The most frequently isolated serotypes from enterotoxin positive cases were 33,61 (10 isolates); 55 (6 isolates) and TW40,PS67 (4 isolates); serotype 71; serotypes 27 and TW24 were most common in enterotoxin negative specimens (16, 11, 11 isolates respectively). None of the serotypes isolated in the IID study corresponded to serotypes isolated from food poisoning outbreaks during the study period.

The total viable count and the number of spores were $\geq 10^5$ cfu/g faeces in 19 (15%) and 17 (14%) of enterotoxin-positive cases respectively and in 5 (2%) and 6 (3%) of enterotoxin-negative controls.

The highest rate of cases presenting to a GP occurred in the under 2 years age group. This rate decreased in the 2–4 years age group and thereafter remained relatively constant. Enterotoxin was detected in very low numbers of controls of most ages (Figure A2.16).

Cases occurred most frequently in April, June and October to December (Figure A2.43). Numbers were lowest between July and September. The small number of positive controls were most frequent in April, June, October and November.

Enterovirulent *E.coli*

Verocytotoxin-producing *E.coli* (VTEC) serogroup O157 was isolated from only three cases (0.1%), all in the GP component and not from controls or cases in the population cohort (Tables 5.1 and 5.2). VTEC belonging to at least ten serogroups other than O157 were also detected at low frequencies in both study components and there were higher levels in the controls (0.4% and 1%) than the cases (0.2% and 0.4%) in the GP and population cohort components.

Enteroaggregative *E.coli* (EAggEC) were the most commonly isolated enterovirulent *E.coli* in cases in the GP component (5.1%) and this frequency in cases was 2.7 times that in the controls (Tables 5.1 and 5.2). EAggEC were identified in over half of the cases in which EAggEC were present (Table 5.6). Of the other *E.coli* groups AEEC and DAEC were detected relatively frequently in cases and controls in both components.

ETEC were identified in between 1 and 2% of cases in both study components and none was detected in the controls, highlighting the pathogenic role of this *E.coli* group.

Numbers were sufficient for seasonality analyses for some but not all enterovirulent *E. coli* (Figures A2.44–A2.50). There were not very clear seasonal patterns for EAggEC and DAEC; the presentation of cases with EAggEC was highest in May, June and October and for DAEC in January, June and October. However, for AEEC there was a peak of cases in the GP component in the summer months and this was also observed in controls. A summer peak was also seen in cases with ETEC with the highest rates in June and very few cases between November and March.

The age distributions for enterovirulent *E.coli* are shown in Figures A2.17–A2.23. Cases with AEEC in the GP component showed that over 40% were from children less than two years whereas only about 20% of cases with EAggEC and DAEC were under one year; for ETEC the figure was less than 4%. Approximately half the cases with EAggEC and DAEC were from adults aged 20 to 59 years whereas only 28% of cases with AEEC were in this group. For ETEC over 80% of cases in the GP component were adults in this age range.

Results of serotyping the enterovirulent *E.coli* showed that for each group a large number of different O serogroups was identified (Appendix 3). However, for AEEC, EAggEC and DAEC 30% or more of the isolates did not belong to serogroups O1 to O173. There has been no laboratory based information available for the incidence of enterovirulent *E.coli* in England before this study other than for VTEC O157 and studies of EPEC as a cause of infantile gastroenteritis. Both EAggEC and AEEC have recently been associated with outbreaks of gastroenteritis in the UK (Smith *et al*. 1997; Wight *et al*. 1997)

Plesiomonas shigelloides

There was one isolate of *P.shigelloides*, from a case in the GP component.

Salmonella

Salmonella spp. were the fourth most frequently isolated target bacteria after *Campylobacter, Aeromonas* and EAggEC in cases in the GP component. In cases in the GP component 5% were positive but *Salmonella* spp. were isolated from only 1% of cases in the population cohort component. In both studies *Salmonella* spp. were found in only 0.4% of controls (Tables 5.1 and 5.2). Approximately 30% of *Salmonella* spp. from cases and 60% from controls were isolated by enrichment only (Table 5.8) with the proportion increasing when specimen receipt in the laboratory was delayed (Table 5.10). There was a marked seasonality, with about

70% of cases in the GP component presenting between June and October (Figure A2.51); this was not seen in the small number of *Salmonella* spp. isolated from controls. Only 10% of cases were children aged less than two years and over 60% of cases were adults aged between 20 and 59 years (Figure A2.24). In this study the most common type was *S.enteritidis* PT4 (45%) followed by *S.typhimurium* DT104 (10%). These results agree well with national surveillance data for the period of the study.

Shigella

Shigella spp. were isolated at low frequency, less than 1%, in cases in the GP component and none was present in controls in both studies. There was only one *Shigella* spp. identified in a case in the population cohort component (Tables 5.1 and 5.2). In contrast to other well recognised bacterial enteric pathogens *Shigella* spp. were detected as the sole pathogen in only 35% of cases where they were present (Table 5.6).

There was no clear seasonality in the isolation of *Shigella* spp. although the highest rates were seen in June and August (Figure A2.52). Nearly 80% of the isolates were from adults between 20 and 59 years (Figure A2.25). *S.sonnei* was the predominant species (21 of the total of 24), with two isolates of *S.flexneri* and one of *S.boydii*. This agrees with national surveillance data for *Shigella* spp. during the study period. Six different types of *S.sonnei* were identified in this study, including phage types 2 and L; these were the phage types identified in the outbreak of shigellosis in June/July 1995 associated with imported iceberg lettuce (Frost *et al*. 1995).

Staphylococcus aureus

A cut-off value of 10^6 cfu/g faeces was chosen, as *Staph.aureus* can occur in low numbers in normal faecal specimens. High counts of *Staph.aureus* were detected in 0.4% of cases presenting to GPs and 0.1% in the population cohort (Tables 5.1 and 5.2). Strains that produced staphylococcal enterotoxins occurred at a similar frequency in cases and controls (Table A5.15). There were insufficient isolates for useful analysis of age distribution and seasonality. Over half of the food poisoning outbreaks caused by staphylococcal enterotoxin occur between June and August (Wieneke *et al.* 1993).

Vibrio

There was only one *Vibrio cholerae* non-O1 isolate from a case presenting to a GP; the patient had recently returned from North Africa.

Yersinia

Yersinia spp. were isolated more frequently in controls than in cases in the GP component; less than 2% of the cases were positive. Similarly, in the population cohort component *Yersinia* spp. were isolated from 3.4% of cases and 2.9% of controls (Tables 5.1 and 5.2, respecitively). Over 60% of *Yersinia* spp. were isolated only after enrichment (Table 5.8).

The isolation of *Yersinia* spp. from cases was highest in the autumn with 51% of cases between September and November. This seasonality was not seen in the controls. (Figures A2.53 and A2.54). Over half of the isolates from cases were from adults aged 20 to 60 years and only 14% were from infants under two years (Figure A2.26). There are few national data on the incidence of *Yersinia* spp. 66% of the isolates in this study were *Y.enterocolitica* and the other species were *Y.frederiksenii, Y.intermedia, Y.mollaretii, Y.bercovieri* and *Y.rohdei*.

Most *Y.enterocolitica* isolates did not belong to the recognised 'pathogenic' serogroups such as O:3, O:5, 27, O:8 and O:9. Eighteen different serogroups of *Y.enterocolitica* were isolated but about 30% of strains did not belong to currently

recognised serogroups. Only a subset of the *Yersinia* spp. may be pathogenic and carry the recognised *Yersinia* virulence factors.

5.4.2 Protozoa

Cryptosporidium
C. parvum was identified in 1% of cases and 0.1% of controls in the GP component (Table 5.1). Few positive cases (0.4%) were found in the population cohort component (Table 5.2). These data indicate that *C.parvum* is one of the less common pathogens causing sporadic IID in England. In the mid-1980s the positivity rate for *C.parvum* in faecal specimens submitted from general practice was 2%, with a higher rate in children (PHLS 1990). The annual incidence of laboratory reports peaked in 1989 but can be affected by large outbreaks associated with drinking water supplies (Anon. 1995a). The peak seasons for infection in the British Isles are spring and late autumn (Badenoch 1990) but no clear pattern was seen with the small numbers in this study (Figure A2.56).

Cryptosporidiosis is reported most commonly in children aged 1 to 5 years (Badenoch 1990) and this age profile was observed in the present study (Figure A2.28).

Giardia
Giardia intestinalis was one of the least common of the target organisms, being detected in 1% of cases in the GP component and 0.4% of controls were asymptomatic cyst excreters (Table 5.1). In the population cohort component the rate of 0.4% of positive cases was exceeded by 0.5% of controls, although the numbers were small (Table 5.2). Many people infected by *G.intestinalis* are asymptomatic and may excrete cysts for several months (Flanagan 1992, Hill 1995). In developed countries the prevalence of infection may be 2 to 5% (Smith *et al.* 1995). Cases are said to be more common in cooler, wetter seasons worldwide (Smith *et al.* 1995). Our study identified few cases, and no seasonal pattern was observed (Figure A2.56). Infections with *Giardia* were most frequent in young children, with a second peak in the 30–39 year age group (Figure A2.29). Previous studies have described this second peak in young adults (Flanagan 1992, Hill 1995).

Other protozoa and helminths
No other pathogenic protozoa, such as *Entamoeba histolytica* and *Cyclospora cayetanensis*, or helminth ova were detected in stool specimens in this study.

5.4.3 Viruses

There have been no previous comprehensive UK studies estimating the incidence of enteric viral pathogens in the community. Previously, information has been derived largely from the surveillance of outbreaks of IID (ACMSF 1998) and it is widely recognised that IID due to viruses is under-reported. Historically, the examination of faecal specimens for virus particles has been by EM, which is not widely available and is accepted to be relatively insensitive. Both EM and enzyme immunoassays were used for the detection of virus in faecal specimens in this present study.

The relative frequencies of detection of the different viruses determined in this study are given in Table 5.16. For comparison, Table 5.17 presents data for a study of children admitted to hospital in Liverpool with IID (Hart and Cunliffe 1996).

Adenovirus
Only Adenovirus types 40, 41 ('enteric' group F) have been consistently associated with diarrhoea and were sought in this study. Other types are predominantly

associated with respiratory symptoms. In this study all Adenoviruses present in faecal specimens were detected by EM and an enzyme immunoassay technique was used to detect Adenovirus types 40, 41. A total of 127 specimens were found to have adenoviruses by EM examination and 77% of these were types 40, 41. The ratio of types 40, 41 to other (respiratory) Adenoviruses was 4.2:1 in the GP component and 3.3:1 in the population cohort component. In 19 of the 20 cases presenting to GPs in which non-types 40, 41 Adenovirus were detected, no other target organism was detected (*Aeromonas* was the single exception). Only one of these 20 cases was over 5 years old (aged 34 years), suggesting that infection with 'respiratory' Adenoviruses (non-types 40, 41) may give rise to IID in children under 5 years of age.

Adenovirus types 40, 41 were the third most common target organism identified in cases aged 1– 4 years in the GP component (Table A2.2). Expressed as a proportion of the total number of viruses identified in cases, Adenoviruses constituted 14% and 11% in the GP component and in the population cohort component, respectively. This is similar to the value of 12.8% for hospital admissions of children in Liverpool (Table 5.17).

Adenoviruses were identified most frequently in July to November with rates of over 40 per 100,000 person-years (Figure A2.57). The age-specific rates for Adenovirus types 40, 41 in cases in the GP component (the only group with sufficient numbers to analyse) indicated low rates in cases 5 years and over, but with very high incidences (400 and 800 cases per 100,000 person-years) in children aged 2–4 years and 0–1 year respectively (Figure A2.30). Adenovirus types 40, 41 were identified as the only target organism present in 77% of the cases in which they were found (Table 5.6).

Astrovirus

Astrovirus was most frequently detected in cases aged 1–4 years in the GP component (6.7% of cases) (Table A2.2). Expressed as a proportion of the total number of viruses identified in cases, Astroviruses constituted 13% and 12% of cases in the GP and population cohort components; this was slightly higher than the value of 10.9% for hospital admissions of children in Liverpool (Table 5.17).

Astroviruses were identified most frequently in November and December with rates over 50 per 100,000 person-years (Figure A2.58). The age-specific rates for Astrovirus in cases in the GP component (the only group with sufficient numbers for analysis) indicated high rates in children under 5 years old, with incidences of 175 and 550 cases per 100,000 person-years in 2–4 years and 0–1 year age groups, respectively (Figure A2.31). Astrovirus was identified as the only target organism present in 71% of the cases in which it was found (Table 5.6).

Calicivirus

Calicivirus was identified most frequently in children aged 1 to 4 years. As a proportion of the total number of viruses identified in the GP component, Caliciviruses constituted 7.% of cases. This was slightly greater than the value of 5.2% for hospital admissions of children in Liverpool (Table 5.17).

With so few cases, it was difficult to discern a seasonality to Calicivirus identifications (Figure A2.59). Like Astroviruses, caliciviruses were most common in those under five years old in cases in the GP component (the only group with sufficient numbers for analysis) with an even higher incidences of 150 and 460 cases per 100,000 person-years in those aged 2–4 years and the under 2 years age groups, respectively (Figure A2.32). Caliciviruses were identified as the only target organism present in 70% of the cases in which they were found (Table 5.6).

Rotavirus group A

Rotavirus group A was the second most common target organism in cases in the GP component, comprising 8% of the total cases and was by far the most common enteric pathogen detected in children aged up to 4 years (Tables A2.1 and A2.2). It ranked fourth in cases in the population cohort component and was twice as common in cases in the GP component as in the population cohort component (Tables 5.1 and 5.2). Rotavirus group A was detected in 36% and 25% of cases with viral infection in the GP and population cohort component, respectively. This compared with 42% for hospital admissions of children in Liverpool (Table 5.17).

Rotavirus group A were identified most frequently in January to April with rates of more than 100 per 100,000 person-years, peaking in March at rates of more than 250 per 100,000 person-years (Figure A2.60). The age specific rates for rotavirus group A in cases in the GP component (the only group with sufficient numbers for analysis) indicated particularly high rates in children aged less than 5 years, with high incidence of 500 and 2,250 per 100,000 person-years in the 2–4 year and under 2 years age groups, respectively. This suggests that over 2% of children will suffer from rotavirus group A infection before their first birthday. Rotavirus group A was identified as the only target organism present in 82% of the cases in which it was found.

Table 5.13 indicates the importance of rotavirus group A as a cause of IID in children under 5 years old in the winter months, with over 10% of cases in the population cohort and almost 30% of cases in the GP component having Rotavirus group A detected. These results confirm national surveillance data which have shown Rotavirus group A to be the commonest cause of childhood diarrhoea.

Rotavirus group C

The identification of rotavirus group C virus in cases, but not controls, in both study components indicated that virus is present in the population and causes IID. The virus has very rarely been reported in sporadic cases of diarrhoea admitted to hospital but was clearly responsible for 0.3% of IID in the community (this study). This finding is in keeping with a population study that found increasing sero-prevalence of Rotavirus group C antibody with age (Bridger 1994). Seven of the eight cases in this study occurred in children under 10 years old.

Small Round Structured Virus (SRSV or Norwalk-like virus)

SRSVs were the third most commonly identified target organism in cases in the GP component and the most common in cases in the population cohort component, where they comprised 7% of the total cases (Tables 5.1 and 5.2). SRSV constituted 29% and 43% of all viruses identified in cases in the GP and population cohort components, respectively. These proportions are considerably greater than the detection rate of 1.6% found for SRSV in children admitted to hospital in Liverpool (Table 5.17).

SRSV appears to be endemic in the population with rates of over 40/10,000 person-years every month except February (Figure A2.61); the data suggest a bimodal seasonality with peaks of incidence in May and October. The age-specific rates for SRSV in cases in the GP component (the only group with sufficient numbers for analysis) show that 50% of cases were found in the over 5 years of age group. High incidence rates were observed in those aged 2–4 and under 2 years old: 300 and 1,200 per 100,000 person-years, respectively (Figure A2.34). This suggests that over 1% of children will suffer from SRSV infection before their first birthday. SRSV was identified as the only target organism present in 72% of the cases where they were found.

Although laboratory reports of SRSV increased sharply during the 1990s, only 2366 reports were recorded for England and Wales in 1995. It was recognised that these figures probably significantly underestimated the true incidence of SRSV infection (ACMSF 1998).

Other viruses
EM examination of faecal specimens occasionally revealed virus and virus-like particles which could not be ascribed to recognised agents of gastrointestinal illness; although this information was recorded on worksheets in the laboratory, data have not been analysed here.

5.5 ANALYSIS OF RESULTS IN EPISODES IN WHICH NO TARGET ORGANISM WAS DETECTED

In this study there were higher overall rates of detection for many of the common pathogens than has been described for previous studies (Table 5.3). Also, a wider range of pathogens was sought in this study than in other studies that have been carried out in the UK. Nevertheless, there was a high percentage of cases both in the GP and population cohort components where no target organism was identified.

There are several possible causes for the episodes of presumed IID where no potentially pathogenic organisms or toxins were identified in the stool specimens. These include:

- microbiological methods are not 100% sensitive; for example, EM for detection of viruses in stool is recognised as being relatively insensitive;
- only a single stool specimen was examined;
- some stool specimens were of insufficient volume to complete all analyses;
- for some specimens, the time lapse (a) between onset of illness and collection of a specimen, or (b) between collection of the specimen and receipt in the laboratory, could have resulted in some of the target organisms or toxins becoming undetectable;
- there may be unrecognised causes of IID;
- some organisms were not sought because they do not cause gastroenteritis as their main symptom. Nevertheless they have been reported as sometimes causing IID (e.g., *Listeria monocytogenes*, enterococci, microsporidia);
- no clinical case definition can be 100% specific, and non-infective causes of intestinal disease may have been included in the study.

Delay in obtaining faecal specimens after the onset of illness and in sending these specimens to the laboratory does not appear to have been a major contributing factor for the failure to identify target micro-organisms (section 5.1.5). The symptom profile for individuals with no target organisms was similar to that observed for all cases. This would suggest that no single category of target organism, e.g., viruses, was being missed.

The pattern of age-specific rates among cases in the GP component with no target organism closely resembled the pattern for all cases of IID (Figures A2.35 and A2.3). Asymptomatic controls would be expected to have a low incidence of target organisms, however, over 20% of children aged 5 years or less had target organisms detected in this study, with fewer detected in older children and adults (Figure A2.36). *C.difficile*, which is part of the normal flora of infants and young children, would account for some of this over-representation, but the remainder is unexplained. Although there were monthly variations in the detection of target organism in cases in the GP component it is difficult to distinguish clear seasonal patterns (Figure A2.62). There was little variation in the monthly proportion of

controls with no target organisms detected, but an increased detection of target organisms in controls in the latter half of the year (Figure A2.63). The reasons for this are unclear.

5.6 SUMMARY

- This is the first British investigation to use such a wide variety of methods in large populations. 37% of cases in the population cohort component and 55% of cases in the GP component had target organisms or toxins identified in faecal specimens. More than one organism or toxin was identified in 7% of cases in the population cohort component and 11% of cases in the GP component.

- Viruses were confirmed as the most common causes of IID in the community, particularly in children, and rotavirus group A was by far the commonest cause of IID in the under 5 year olds presenting to GPs. SRSVs were the most frequently identified pathogens in the population cohort component. The relative proportions of target organisms identified in cases in the GP component differed from those in the population cohort component: *Campylobacter* and rotavirus group A were more frequently identified than SRSV in cases in the GP component and *Salmonella* spp. were present in 5% of cases in the GP component compared with 1% of cases in the population cohort component.

- Target organisms and toxins were identified more frequently in cases in the GP component than in the population cohort component except for *Aeromonas*, *Yersinia* spp, SRSV, VTEC (non-O157) and rotavirus group C, although the numbers of cases in the last two categories were small.

- In controls, the highest frequencies of target organisms detected were *Aeromonas* (5%), *Yersinia* spp. (3%), DAEC (2%) and AEEC (2%) in the population cohort component, and *Aeromonas* spp. (4%), DAEC (4%), AEEC (3%) and *Yersinia* spp. (3%) in the GP component.

- National surveillance data showing *Campylobacter* spp. and rotavirus group A as the major bacterial and viral causes of IID presenting to GPs were confirmed.

- *Clostridium perfringens* enterotoxin was confirmed as an important cause of IID in the community and more commonly in cases presenting to GPs. *C. difficile* toxin was most frequently identified in both cases and controls aged less than 2 years, confirming previous reports, but was also found in a small number of older cases in the GP component.

- Highest rates of IID were found in children, particularly in infants. Overall, there was little seasonal variation in presentation of IID. Expected seasonal variations were observed in some of the target organisms, e.g., Rotavirus, *Salmonella* and ETEC, but not in others, e.g., *Campylobacter* and SRSV.

- The evidence from studies world-wide that enterovirulent *E.coli* are an important and frequent cause of IID was substantiated. VTEC serotype O157 was identified in only three cases (0.1%) in the GP component. Other VTEC serogroups were found more frequently in controls than in cases. In contrast to AEEC, DAEC and EPEC, EAggEC were found markedly more frequently in cases than in controls, and ETEC were found only in cases.

- Target organisms were not identified in 63% of cases in the population cohort component and 45% of cases in the GP component. This is a lower negativity

rate than other studies but still represents a substantial number of cases with no microbiological cause identified for their illness. Information from this study suggests that delay in receipt of specimens in the laboratory was not a major contributory factor to the cases with negative microbiological findings. Lack of sensitivity of some tests, e.g., EM for virus particles, is a likely cause of some cases with no target organism detected.

Table 5.1 Organisms identified in the GP case-control component

	CASES			CONTROLS			
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	STANDARDISED PERCENT *
Bacteria							
Aeromonas spp.	165	2,893	5.7	96	2,264	4.2	3.2
Bacillus spp. (>10^4/g)	4	2,571	0.2	8	2,176	0.4	0.3
Campylobacter spp.	354	2,893	12.2	16	2,264	0.7	0.5
Clostridium difficile cytotoxin	38	2,259	1.7	41	2,039	2.0	0.4
Clostridium perfringens enterotoxin	114	2,871	4.0	15	2,256	0.7	0.5
E. coli O157	3	2,893	0.1	0	2,264	0	0
E. coli DNA probes:							
Attaching and effacing	119	2,774	4.2	67	2,230	3.0	1.5
Diffusely adherent	103	2,774	3.7	93	2,230	4.2	3.8
Enteroaggregative	141	2,774	5.1	43	2,230	1.9	1.8
Enteroinvasive	0	2,774	0	0	2,230	0	0
Enteropathogenic	4	2,774	0.1	6	2,230	0.3	0.2
Enterotoxigenic	52	2,774	1.9	0	2,230	0	0
Verocytotoxigenic (non O157)	6	2,774	0.2	9	2,230	0.4	0.5
Salmonella spp.	146	2,893	5.0	10	2,264	0.4	0.4
Shigella spp.	23	2,893	0.8	0	2,264	0	0
Staphylococcus aureus (>10^6/g)	10	2,568	0.4	5	2,172	0.3	0.1
Vibrio spp.	1	2,893	0.03	0	2,264	0	0
Yersinia spp.	51	2,893	1.8	56	2,264	2.5	2.4
Protozoa							
Cryptosporidium parvum	39	2,892	1.3	2	2,264	0.1	0.0
Giardia intestinalis	28	2,893	1.0	10	2,264	0.4	0.3
Viruses							
Adenovirus types 40, 41	81	2,612	3.1	3	2,210	0.1	0.0
Astrovirus	77	2,612	3.0	5	2,210	0.2	0.0
Calicivirus	40	2,612	1.5	4	2,210	0.2	0.0
Rotavirus Group A	208	2,709	7.7	9	2,211	0.4	0.1
Rotavirus Group C	6	2,709	0.2	0	2,211	0	0
SRSV	169	2,612	6.5	6	2,210	0.3	0.1
No organism identified	1,305	2,893	45.1	1,834	2,264	81.0	85.2

* Percent standardised by the population age distribution (Office for National Statistics, 1997)

Table 5.2 Organisms identified in the population cohort component

	CASES			CONTROLS			
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	STANDARDISED PERCENT *
Bacteria							
Aeromonas spp.	46	761	6.0	28	555	5.0	5.2
Bacillus spp. (>10^4/g)	0	684	0	2	526	0.4	0.4
Campylobacter spp.	32	761	4.2	4	555	0.7	0.9
Clostridium difficile cytotoxin	9	614	1.5	5	487	1.0	0.3
Clostridium perfringens enterotoxin	9	756	1.2	3	551	0.5	1.1
E. coli O157	0	761	0	0	555	0	0
E. coli DNA probes:							
Attaching and effacing	23	732	3.1	10	542	1.9	1.0
Diffusely adherent	23	732	3.1	13	542	2.4	2.0
Enteroaggregative	21	732	2.9	4	542	0.7	0.5
Enteroinvasive	0	732	0	0	542	0	0
Enteropathogenic	1	732	0.1	2	542	0.4	0.2
Enterotoxigenic	12	732	1.6	0	542	0	0
Verocytotoxigenic (non O157)	3	732	0.4	6	542	1.1	1.0
Salmonella spp.	8	761	1.1	2	555	0.4	0.2
Shigella spp.	1	761	0.1	0	555	0	0
Staphylococcus aureus (>10^6/g)	1	683	0.1	1	524	0.2	0.0
Vibrio spp.	0	761	0	0	555	0	0
Yersinia spp.	26	761	3.4	16	555	2.9	3.1
Protozoa							
Cryptosporidium parvum	3	761	0.4	0	555	0	0
Giardia intestinalis	3	761	0.4	3	555	0.5	0.5
Viruses							
Adenovirus types 40, 41	13	715	1.8	1	535	0.2	0.0
Astrovirus	14	715	2.0	1	535	0.2	0.0
Calicivirus	8	715	1.1	1	535	0.2	0.0
Rotavirus Group A	29	718	4.0	0	535	0	0
Rotavirus Group C	2	718	0.3	0	535	0	0
SRSV	50	715	7.0	3	535	0.6	0.5
No organism identified	480	761	63.1	462	555	83.2	83.9

* Percent standardised by the population age distribution (Office for National Statistics, 1997)

Table 5.3 Proportion of each organism as percentage of total positive identifications in the population cohort and GPCC studies compared with percentage of total positive reports to CDSC in 1995.

	POPULATION COHORT STUDY	GPCC STUDY	CDSC REPORTS 1995
BACTERIA			
Aeromonas spp.	13.6	8.3	0.5
Bacillus spp. (>10^4/g)	0	0.2	>0.1
Campylobacter spp.	9.5	17.9	36.0
Clostridium difficile cytotoxin	2.7	1.9	6.3
Clostridium perfringens enterotoxin	2.7	5.8	0.3
E.coli O157	0	0.2	0.6
E.coli DNA probes:			
Attaching and effacing	6.8	6.0	NI
Diffusely adherent	6.8	5.2	NI
Enteroaggregative	6.2	7.1	NI
Enteroinvasive	0	0.0	NI
Enteropathogenic	0.3	0.2	0.3
Enterotoxigenic	3.6	2.6	NI
Verocytotoxigenic (non O157)	0.9	0.3	NI
Salmonella spp.	2.4	7.4	24.7
Shigella spp.	0.3	1.2	3.4
Staphylococcus aureus (>10^6/g)	0.3	0.5	<0.1
Vibrio spp.	0	<0.1	<0.1
Yersinia spp.	7.7	2.6	0.2
PROTOZOA			
Cryptosporidium parvum	0.9	2.0	4.7
Giardia intestinalis	0.9	1.4	5.1
VIRUSES			
Adenovirus types 40/41	3.9	4.1	0.9
Astrovirus	4.2	3.9	0.2
Calcivirus	2.4	2.0	0.1
Rotavirus group A	8.6	10.5	14.1
Rotavirus group C	0.6	0.3	NI
SRSV	14.8	8.5	1.9

NI = no information

Table 5.4 Frequency of detection of enteric pathogens in patients with symptoms of IID presenting to General Practitioners (%)

PERIOD OF INVESTIGATION	BRISTOL STUDY (1983–84)	CRYPTOSPORIDIOSIS STUDY (1985–87)	WELSH STUDY (1992)	IID IN ENGLAND STUDY (1994–96)
Number examined	867	62,421	255	2,893
Campylobacter	5.7	7.6	9.4	12.2
Salmonella	4.3	3.3	3.5	5.0
Shigella	0.8	0.7	1.2	0.8
Cryptosporidium	5.0	2.1	0	1.3
Rotavirus	2.2*	NT	9.8*	7.7
SRSV	0*	NT	2.0*	6.5
Giardia	2.0	NT	0.4	1.3

NT not tested

** not all specimens tested*

Table 5.5 Frequency of specimens with multiple target organisms

NUMBER OF ORGANISMS IDENTIFIED	GP CASES	%	COMMUNITY CASES	%	CONTROLS	%	TOTAL	%
0	1,305	45.1	480	63.1	2,296	81.5	4,081	63.1
1	1,261	43.6	232	30.5	478	17.0	1,971	30.5
2	276	9.5	48	6.3	41	1.5	365	5.6
3	48	1.7	1	0.1	4	0.1	53	0.8
4	3	0.1	0	0.0	0	0.0	3	0.1
Total	2,893	100.0	761	100.0	2,819	100.0	6,473	100.0

Table 5.6 Proportion of cases in the GP component in which individual target organisms were identified as the single organism, and comparison with the control group

	GP CASES			GP CASE/CONTROL COMPARISON	
	NUMBER IDENTIFIED	NUMBER SINGLE ORGANISM	PERCENT SINGLE ORGANISM	RELATIVE PROPORTION IDENTIFIED (CASE/ CONTROL)	95% CONFIDENCE INTERVAL
Bacteria					
Aeromonas spp.	165	81	49	1.35	1.05, 1.72
A. caviae	126	70	56	1.28	0.97, 1.69
A. hydrophila	31	10	32	1.73	0.92, 3.25
other spp.	8	1	13	1.25	0.41, 3.82
Bacillus spp. (>10^4/g)	4	0	0	0.42	0.13, 1.40
Campylobacter spp.	354	257	73	17.31	10.52, 28.49
C. jejuni	315	229	73	20.54	11.57, 36.46
C. coli	30	21	70	11.74	2.81, 49.07
other spp.	9	7	78	3.52	0.76, 16.28
Clostridium difficile (> 1 year old)	25	13	52	6.05	1.81, 20.26
Clostridium perfringens enterotoxin	114	54	47	5.96	3.49, 10.17
E. coli O157	3	3	100	no positive control	
E. coli DNA probes:					
Attaching and effacing	119	58	49	1.43	1.06, 1.92
Diffusely adherent	103	44	43	0.89	0.68, 1.17
Enteroaggregative	141	77	55	2.64	1.88, 3.69
Enteroinvasive	0	0	0	-	-
Enteropathogenic	4	2	50	0.54	0.15, 1.90
Enterotoxigenic	52	34	65	no positive control	
Verocytotoxigenic (non O157)	6	1	17	0.54	0.19, 1.50
Salmonella spp.	146	109	75	11.43	6.03, 21.63
S. enteritidis	85	67	79	33.26	8.19, 135.01
S. typhimurium	29	24	83	11.35	2.17, 47.50
other serotypes	32	18	56	4.17	1.75, 9.96
Shigella spp.	23	8	35	no positive control	
Staphylococcus aureus (>10^6/g)	10	5	50	1.69	0.58, 4.94
Vibrio spp.	1	1	100	no positive control	
Yersinia spp.	51	26	51	0.17	0.49, 1.04
Y. enterocolitica	40	21	53	0.95	0.60, 1.50
Y. frederiksenii	10	4	40	0.41	0.19, 0.88
other spp.	1	1	100	0.20	0.02, 1.75
Protozoa					
Cryptosporidium parvum	39	27	69	15.27	3.69, 63.15
Giardia intestinalis	28	17	61	2.54	1.24, 5.21
Viruses					
Adenovirus types 40, 41	81	62	77	22.84	7.23, 72.23
Astrovirus	77	55	71	13.03	5.28, 32.14
Calicivirus	40	28	70	8.46	3.03, 23.16
Rotavirus Group A	208	171	82	18.86	9.70, 36.68
Rotavirus Group C	6	6	100	no positive control	
SRSV	169	122	72	23.83	10.58, 53.69

Table 5.7 Frequency of multiple organism isolations in IID for specimens received within 8 days of onset which were subjected to the complete range of tests (to stage 7)

NUMBER OF ORGANISMS IDENTIFIED	GP CASES	%	COMMUNITY CASES	%
0	547	38.8	270	60.5
1	672	47.6	143	32.6
2	160	11.3	32	7.2
3	29	2.1	1	0.2
4	3	0.2	0	0.0
Total	**1,411**	**100.0**	**446**	**100.0**

Table 5.8 Proportion of targets organisms identified in cases and controls only after enrichment

	CASES		CONTROLS	
	TOTAL NUMBER OF IDENTIFICATIONS	IDENTIFIED ONLY AFTER ENRICHMENT (%)	TOTAL NUMBER OF IDENTIFICATIONS	IDENTIFIED ONLY AFTER ENRICHMENT (%)
All *Salmonella*	149	47 (31.5)	12	7 (58.3)
S.enteritidis PT4	69	18 (26.1)	3	2 (66.7)
other *Salmonella*	80	29 (36.2)	9	5 (55.6)
Aeromonas caviae	149	116 (77.8)	99	87 (87.9)
other *Aeromonas*	51	41 (80.4)	25	18 (72.0)
All *Campylobacter*	380	17 (4.5)	20	0 (0.0)
C.jejuni	334	17 (5.1)	15	0 (0.0)
C.coli	31	0 (0.0)	2	0 (0.0)
Yersinia enterocolitica	54	36 (66.7)	43	36 (83.7)
other *Yersinia*	20	12 (60.0)	28	23 (82.1)
Giardia intestinalis†	29	7 (24.1)	11	0 (0.0)

Note: A small number of specimens (30) had missing data on enrichment

† In the case of *G. intestinalis* only, enhanced detection was based upon concentration of the specimen rather than enrichment

Table 5.9 Effect of time on the identification of *Campylobacter* spp. by enrichment

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN	TOTAL IDENTIFICATIONS	IDENTIFIED ONLY AFTER ENRICHMENT (%)
0–2 days	19	0 (0.0)
3–5 days	176	5 (2.8)
6–10 days	149	8 (5.4)
11–15 days	16	2 (12.5)
16+ days	5	1 (20.0)
Unknown	35	1 (2.9)
Total	**400**	**17 (4.2)**

(enrichment data unavailable for six specimens)

Table 5.10 Effect of time on the identification of *Salmonella* spp. by enrichment

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN	TOTAL IDENTIFICATIONS	IDENTIFIED ONLY AFTER ENRICHMENT (%)
0–2 days	9	2 (22.2)
3–5 days	59	16 (27.1)
6–10 days	47	15 (31.9)
11–15 days	15	7 (46.7)
16+ days	6	3 (50.0)
Unknown	25	11 (44.0)
Total	**161**	**54 (33.5)**

(enrichment data unavailable for five specimens)

Table 5.11 *Clostridium difficile*: colonisation and toxin detection in young children (< 2 years) and others: GP case-control component

	CASES			CONTROLS		
	NUMBER POSITIVE	NUMBER TESTED	% OF TESTED	NUMBER POSITIVE	NUMBER TESTED	% OF TESTED
Under 2 years :						
Toxin B positive	17	391	4.3	38	423	9.0
Culture positive, toxin negative	90	374	24.1	75	385	19.5
Culture positive, toxin NT	52	204	25.5	13	61	21.3
2 years and over:						
Toxin B positive	21	1,866	1.1	3	1,616	0.2
Culture positive, toxin negative	18	1,845	1.0	6	1,613	0.4
Culture positive, toxin NT	4	430	0.9	1	164	0.6

Table 5.12 *Clostridium difficile*: colonisation and toxin detection in young children (< 2 years) and others: community component

	CASES			CONTROLS		
	NUMBER POSITIVE	NUMBER TESTED	% OF TESTED	NUMBER POSITIVE	NUMBER TESTED	% OF TESTED
Under 2 years :						
Toxin B positive	7	61	11.5	5	48	10.4
Culture positive, toxin negative	9	54	16.7	7	43	16.3
Culture positive, toxin NT	4	22	18.2	2	8	25.0
2 years and over:						
Toxin B positive	2	553	0.4	0	439	0
Culture positive, toxin negative	2	551	0.4	1	439	0.2
Culture positive, toxin NT	0	125	0	0	60	0

Table 5.13 Target organisms identified in children aged less than 5 years who were cases during the winter months (December to February)

	GP CASES CONTROL COMPONENT			CONTROL COMPONENT		
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED
Bacteria						
Aeromonas spp.	9	195	4.6	1	39	2.6
Bacillus spp. (>10^4/g)	0	165	0	0	37	0
Campylobacter spp.	10	195	5.1	2	39	5.1
Clostridium difficile cytotoxin	6	143	4.2	1	30	3.3
Clostridium perfringens enterotoxin	10	195	5.1	0	39	0
E. coli O157	0	195	0	0	39	0
Enterovirulent *E. coli* (DNA probes)						
Attaching and effacing (AEEC)	5	186	2.7	0	38	0
Diffusely adherent (DAEC)	9	186	4.8	1	38	2.6
Enteroaggregative (EAggEC)	4	186	2.1	1	38	2.6
Enteroinvasive (EIEC)	0	186	0	0	38	0
Enteropathogenic (EPEC)	0	186	0	0	38	0
Enterotoxigenic (ETEC)	1	186	0.5	0	38	0
Verocytotoxigenic (VTEC, non O157)	1	186	0.5	0	38	0
Salmonella spp.	2	195	1.0	0	39	0
Shigella spp.	0	195	0	0	39	0
Staphylococcus aureus (>10^6/g)	0	165	0	0	37	0
Vibrio spp.	0	195	0	0	39	0
Yersinia spp.	2	195	1.0	2	39	5.1
Protozoa						
Cryptosporidium parvum	5	195	2,6	1	39	2.6
Giardia intestinalis	2	195	1.0	0	39	0
Viruses						
Adenovirus types 40,41	9	179	5.0	2	38	5.3
Astrovirus	14	179	7.8	4	38	10.5
Calicivirus	5	179	2.8	1	38	2.6
Rotavirus Group A	53	179	29.6	4	38	10.5
Rotavirus Group C	2	179	1.1	1	38	2.6
SRSV	14	179	7.8	2	38	5.3
No organism identified	61	195	31.3	18	39	46.1

Table 5.14 Comparison of *C.perfringens* enterotoxin assay results on specimens tested at Leeds PHL and FHL

CASES *FHL RESULTS* ELISA	RPLA RESULTS - LEEDS NEGATIVE	(%)	EQUIVOCAL	(%)	POSITIVE	(%)	TOTAL	(%)
Negative	185	(83)	9	(90)	253	(67)	448	(88)
Positive	37	(17)	1	(10)	123	(33)	161	(12)
Total	222	(100)	10	(100)	376	(100)	509	(100)
RPLA								
Negative	61	(66)	6	(55)	34	(39)	101	(54)
Equivocal	14	(16)	3	(27)	12	(14)	29	(15)
Positive	15	(17)	2	(18)	41	(47)	58	(31)
Total	90	(100)	11	(100)	87	(100)	188	(100)
ALL CONTROLS *FHL RESULTS* ELISA	RPLA RESULTS - LEEDS NEGATIVE	(%)	EQUIVOCAL	(%)	POSITIVE	(%)	TOTAL	(%)
Negative	215	(99)	8	(89)	310	(95)	533	(96)
Positive	3	(1)	1	(11)	18	(5)	22	(4)
Total	218	(100)	9	(100)	328	(100)	555	(100)
RPLA								
Negative	71	(83)	3	(38)	29	(58)	103	(72)
Equivocal	13	(15)	5	(62)	14	(28)	32	(22)
Positive	2	(2)	0	(0)	7	(14)	9	(6)
Total	86	(100)	8	(100)	50	(100)	144	(100)

** Results on all RPLA tests carried out at FHL, regardless of ELISA result*

Table 5.15 *S. aureus* typing and toxin production

	TOXIN PRODUCED	PHAGE GROUP	PHAGE TYPE
Cases presenting to GPs	A	I	29,79, 42E+
	B	III	54+
	B	V	94++
	B	NT	NT
	NEG	I	29, 52, 79, 80++
	NEG	I	52, 52A, 79, 80, 95++
	NEG	I	29, 52, 80, 81++; 79, 95, 24E+
	NEG	II	3A, 55, 71++; 3C±
	NEG	NT	NT
	NEG	NT	NT
Controls presenting to GPs	A	I	29++
	B	NT	NT
	C	I	29, 52, 79, 80++; 55±
	D	95	95++; 29, 42E+; 80±
	NEG	II	6, 42E, 47, 54, 75, 84, 81++; 53, 85+
Community cohort case	NEG	80/81	80+; 52±
Community cohort control	NEG	NT	NT

Table 5.16 Comparison of frequencies of viruses in cases and controls

VIRUS	GPCC STUDY		FREQUENCY	COHORT STUDY		FREQUENCY
	CASE	CONTROL	CASE: CONTROL	CASE	CONTROL	CASE: CONTROL
Adenovirus*	3.1	0.1	x31	1.8	0.2	x 9
Astrovirus	3.0	0.2	x15	2.0	0.2	x10
Calicivirus	1.5	0.2	x7.5	1.1	0.2	x5.5
Rotavirus group A	7.7	0.4	x19	4.0	0.0	-
Rotavirus group C	0.2	0.0	-	0.3	0.0	-
SRSV	6.5	0.3	x22	7.0	0.6	x12

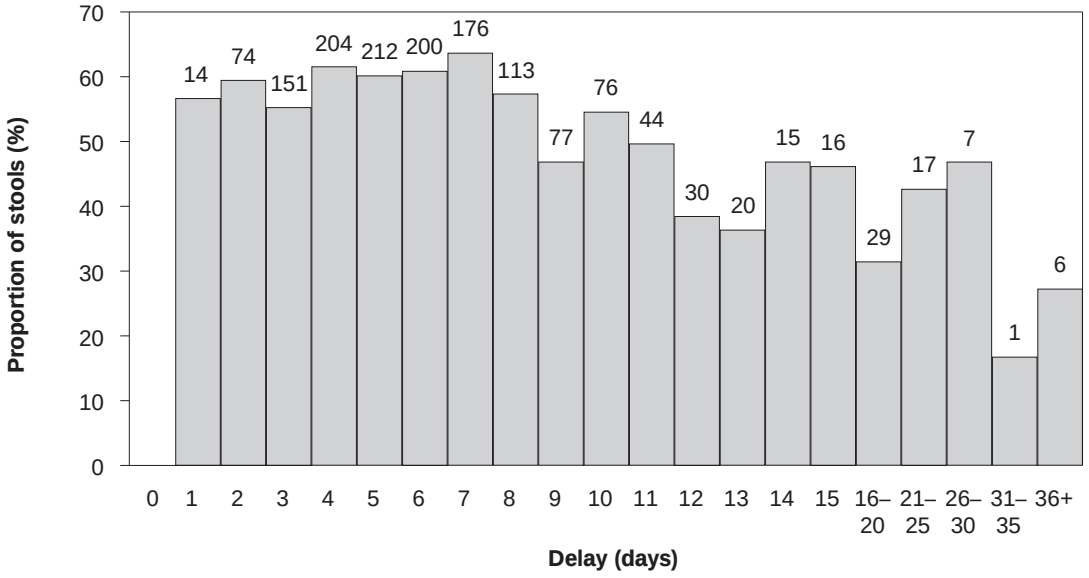
** Enteric adenoviruses (types 40, 41) only*

Table 5.17 Frequencies of enteric viruses detected in cases (aged <16 years) in two components of the IID study compared with a published study of children admitted to a hospital.

VIRUS	IID STUDY: GP CASE CONTROL COMPONENT (581 CASES)		IID STUDY COMMUNITY COMPONENT (116 CASES)		HOSPITAL† (1034 CASES)	
	% OF CASES	RANK	% OF CASES	RANK	% OF CASES	RANK
Adenovirus*	14.1	3	11.1	4	12.8	2
Astrovirus	13.3	4	12.1	3	10.9	3
Calicivirus	6.8	5	6.8	5	5.2	4
Rotavirus group A	35.6	1	25.0	2	42.3	1
Rotavirus group C	1.0	6	1.7	6	0.0	-
SRSV	29.1	2	43.1	1	1.6	5

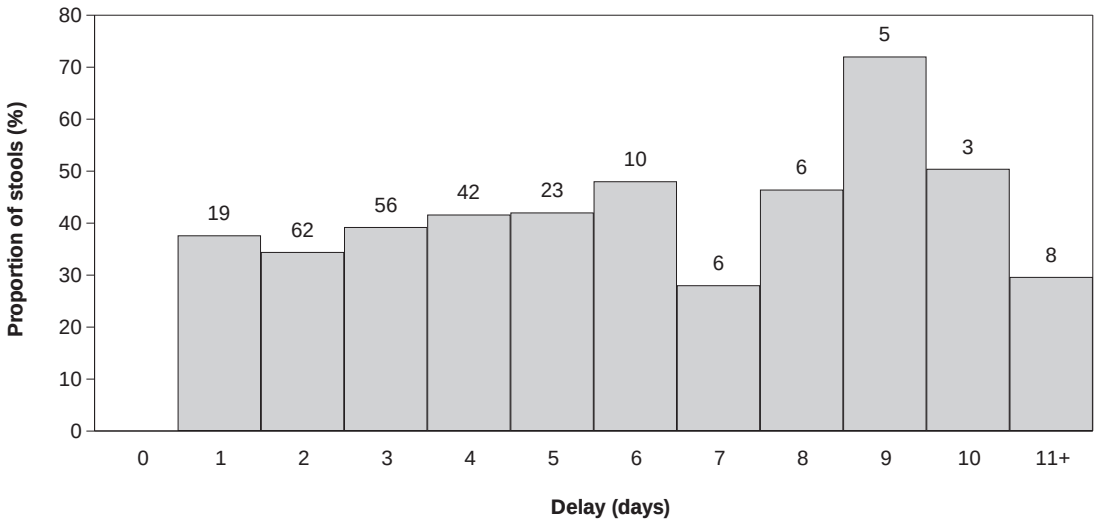
** Enteric adenoviruses (types 40, 41) only*
† Data from Hart and Cunliffe 1996

Figure 5.1 Proportion of stools with one or more target organisms by delay between onset of symptoms and receipt of specimen: GP case control study – cases



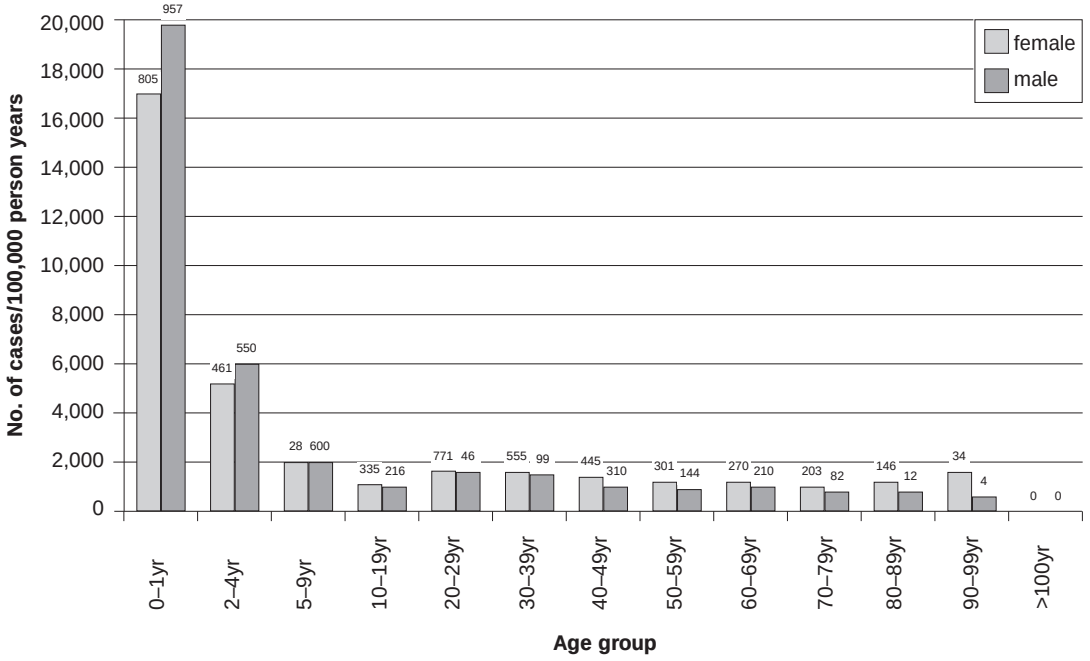
Note. Figures above the bars represent the number of stools positive for the organism

Figure 5.2 Proportion of stools with one or more target organisms by delay between onset of symptoms and receipt of specimen: Population cohort study – cases only



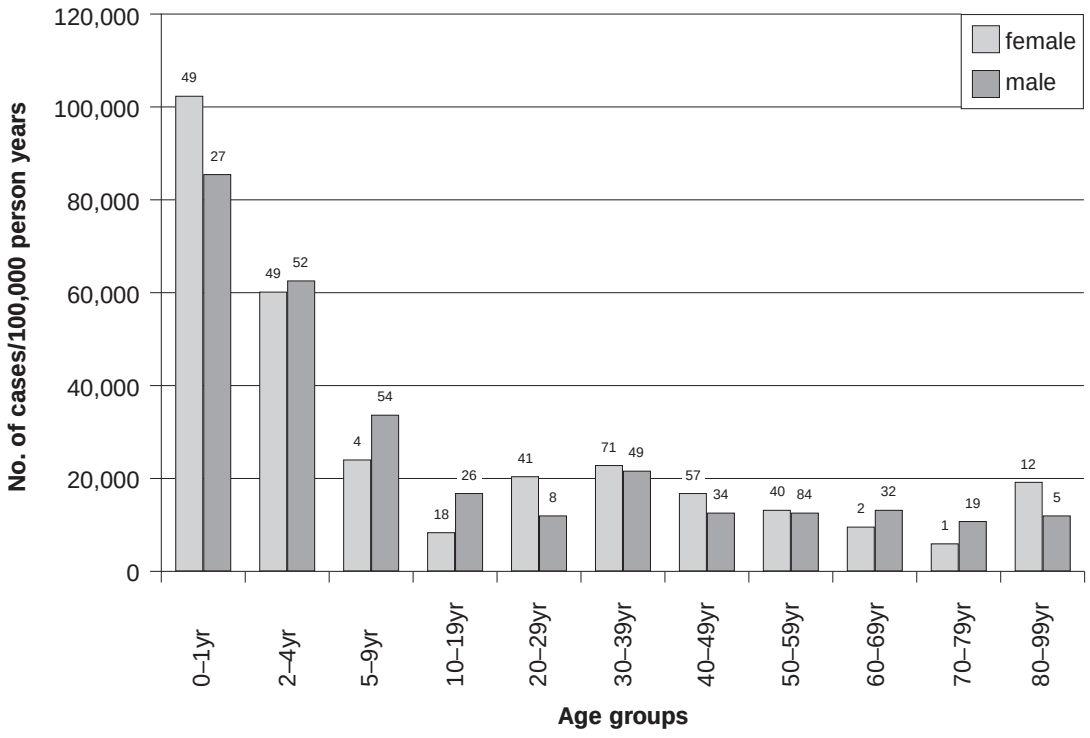
Note. Figures above the bars represent the number of stools positive for the organism

Figure 5.3 Age-specific rate of all IID cases presenting to the GP, by sex



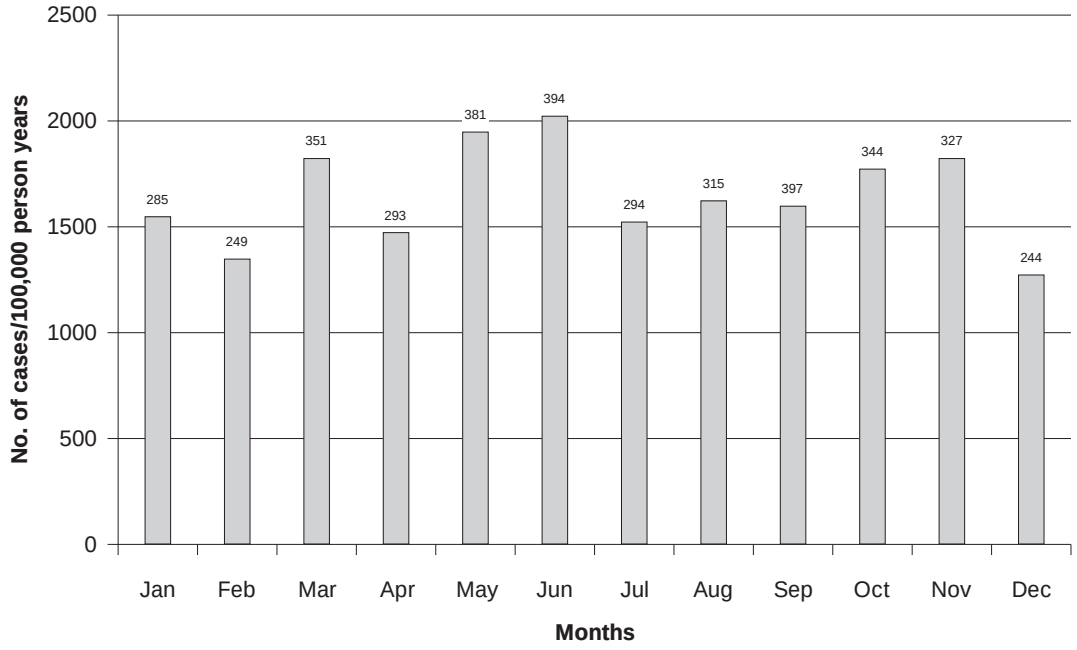
Note. Figures above the bars represent the number of cases/controls per age group

Figure 5.4 Age-specific rate of all IID cases in the community, by sex



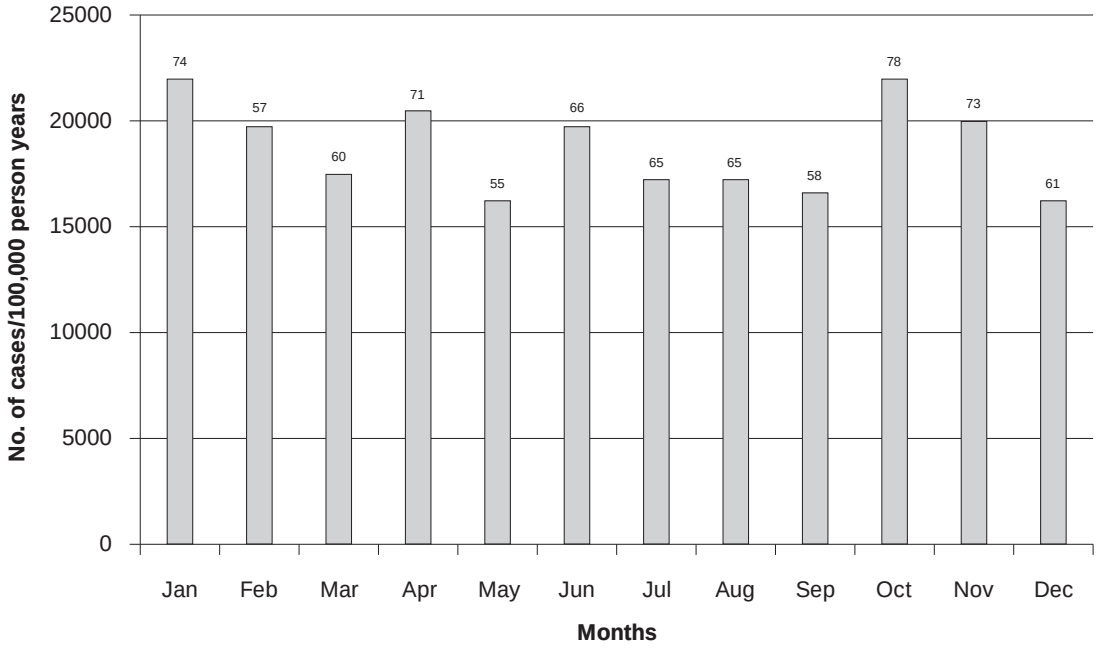
Note. Figures above the bars represent the number of cases/controls per age group

Figure 5.5 Seasonal distribution of cases presenting to the GP



Note. Figures above the bars represent the number of cases/controls per month

Figure 5.6 Seasonal distribution of cases in the community



Note. Figures above the bars represent the number of cases/controls per month

Chapter 6
Frequency and Reporting of Infectious Intestinal Disease (IID)

6.1 OVERALL RATES OF IID

6.1.1 Rates of IID in the community

The incidence rate of IID in the community was calculated from the total number of cases reported in the community component and the follow-up time of all the cohort members. The rate of IID in the community was 19.4 per 100 person-years (Table 6.1). Therefore, about a fifth of the overall population was estimated to suffer from IID in a year. This figure includes all IID, not merely that fraction caused by the consumption of contaminated food.

Table 6.1 Overall incidence rates of IID

	NUMBER OF CASES OF IID	PERSON-YEARS	RATE PER 100 PERSON-YEARS	95% CONFIDENCE INTERVAL
Community	781	4,026	19.4	18.1, 20.8
Presenting to the GP (unadjusted)	8,770	459,975	1.91	1.70 , 2.14
Presenting to the GP (adjusted for list inflation and underascertainment)	13,619	409,878	3.31	2.94 , 3.75

Few studies have calculated community incidence rates for predominantly sporadic cases of IID. The community rate in this study is much lower than rates found in the USA and Canada (Table 6.2). Possible reasons for the higher rates in these studies may be the greater proportion of children in the family-based study populations, and the use of broader case definitions (Dingle *et al.* 1953, Monto and Koopman 1980, Payment *et al*. 1991). However, our rate is comparable to the rate found in the more recent Dutch study, using their definition of severe illness which is closer to our own case definition (Hoogenboom-Verdegaal *et al*. 1994).

Age- and sex-specific rates are shown in Table 6.3. As noted in Chapter 5 the rates are particularly high in children under 5 years of age. Among adult males the rate is fairly constant across age groups, but in females higher rates at reproductive age can be seen, although the confidence intervals overlap with those for males.

6.1.2 Rates of IID presenting to GPs

The rate of IID presenting to GPs was calculated from the total number of cases reported in the GP case-control and enumeration components and the follow-up time of all the persons registered with the GPs in the study practices. The corrected rate of IID presenting to the GPs was 3.3 per 100 person-years (Table 6.1). Thus one in 30 of the population presented to their GP with IID in a year.

The corrected rates are a more accurate estimate than the uncorrected rates because they take into account: (i) the persons on GP lists who may have moved away or died, and (ii) the levels of under-reporting identified and corrected for in the

Table 6.2 Incidence rates of IID compared to other studies

STUDY	DEFINITION	PRESENTATION RATE OF IID PER 100 PERSON YEARS	COMMUNITY RATE OF IID PER 100 PERSONS YEARS
USA (Dingle *et al*. 1953)	Acute gastrointestinal illness	-	160
USA (Monto and Koopman 1980)	Diarrhoea, vomiting, upset stomach or nausea	22	120
Canada (Payment *et al.* 1991)	Vomiting or diarrhoea, nausea with abdominal pain	-	76
England (Tuckman *et al.* 1962)	Acute gastrointestinal illness < 7 days	5.2	-
England (Kendall and Tanner 1982)	3 or more liquid stools within 48 hrs	5.6	-
Scotland (Nathwani *et al.* 1994)	Presumed infective diarrhoea	1	-
The Netherlands (Hoogenboom-Verdegaal *et al.* 1994)	Mild: Diarrhoea or vomiting plus 2 other symptoms within 1 week Severe: Diarrhoea or vomiting plus 2 other symptoms for at least 2 days	Mild: 11 Severe: 4	Mild: 63 Severe 18
Wales (Palmer *et al.* 1996)	Acute onset of diarrhoea and/ or vomiting	3.3	-
IID Study in England	Diarrhoea or vomiting for <2 weeks with preceding 3 weeks symptom-free	3.3	19

Table 6.3 Incidence rates of IID by age and sex in the community component

	FEMALES				MALES			
AGE GROUP	NO. OF CASES OF IID	PERSON-YEARS	RATE PER 100 PERSON-YEARS	95% CONFIDENCE INTERVAL	NO. OF CASES OF IID	PERSON-YEARS	RATE PER 100 PERSON-YEARS	95% CONFIDENCE INTERVAL
0–1	19	17	114	73–178	10	16	64	35–120
2–4	79	113	70	56–87	79	110	72	58–90
5–9	41	174	24	17–32	54	161	33	26–44
10–14	14	137	10	6–17	26	141	19	13–27
15–24	17	169	10	6–16	17	123	14	9–22
25–34	67	292	23	18–29	37	195	19	14–26
35–44	62	303	20	16–26	38	233	16	12–22
45–54	50	338	15	11–20	34	293	12	8–16
55–64	29	280	10	7–15	37	247	15	11–21
65–74	18	225	8	5–13	21	220	10	6–15
75+	17	137	12	8–20	15	101	15	9–25
Total	**413**	**2,185**	**19**	**20–21**	**368**	**1,840**	**20**	**18–22**

under-ascertainment component. The disappearance of the apparently higher rate of presentation to GPs in the enumeration component compared to the GP component after correction supports this view.

Comparison of these results with previous studies (Table 6.2) shows that the presentation rate to GPs is similar to that found in the most recent studies in Wales, Scotland and in the Netherlands (in relation to illness defined as severe), (Hoogenboom-Verdegaal *et al.* 1994, Nathwani *et al.* 1994, Palmer *et al.* 1996), and is very close to estimates derived from the Royal College of General Practitioners sentinel surveillance scheme (Fleming *et al.* 1994). It is somewhat lower than previous studies in England (Tuckman *et al.* 1962, Kendall and Tanner 1982). The latter studies were single practice studies and took place more than 15 years ago. The presentation rate to GPs is much lower than rates found in the USA, probably due to the greater proportion of children, who suffer higher rates of IID, in these family-based study populations. There were also differences in case definition.

Adjusted age- and sex-specific rates are shown in Table 6.4. In this component the rates in children under five years old show a greater differential with respect to other age groups than in the community component, suggesting a greater tendency for parents to take young children to the GP than for other age groups to present. Boys under 1 year old present at a higher rate than girls. Over the age of 15 years, females present to the GP at consistently higher rates than males; this observation is statistically significant.

6.1.3 Patients presenting to hospital Accident and Emergency Departments (A&E)

Patients from the enumeration component practices who may have presented to A&E instead of their GP were identified to determine whether this was an important route of

Table 6.4 Incidence rates of IID by age and sex presenting to the GP (adjusted for list inflation and underascertainment)

	FEMALES				MALES			
AGE GROUP	NO. OF CASES OF IID	PERSON-YEARS	RATE PER 100 PERSON-YEARS*	95% CONFIDENCE INTERVAL*	NO. OF CASES OF IID	PERSON-YEARS	RATE PER 100 PERSON-YEARS*	95% CONFIDENCE INTERVAL*
0–1	1,260	4,204	29.4	25.0–34.6	1,511	4,366	35.0	29.8–41.4
2–4	701	7,779	9.5	8.0–11.3	850	8,228	11.1	9.6–12.9
5–9	442	12,703	3.9	3.1–4.9	450	13,154	3.6	2.9–4.3
10–14	212	12,057	1.8	1.5–2.2	277	12,941	2.3	1.8–2.8
15–24	877	25,191	3.5	3.0–4.1	586	25,619	2.3	1.9–2.8
25–34	1,148	31,975	3.7	3.3–4.3	930	32,732	2.9	2.6–3.3
35–44	745	27,714	2.8	2.4–3.3	587	28,696	2.1	1.8–2.4
45–54	556	26,432	2.4	1.9–2.8	482	27,688	1.8	1.5–2.1
55–64	449	20,356	2.4	2.1–2.9	366	20,278	1.9	1.6–2.3
65–74	389	20,250	2.0	1.7–2.5	241	17,123	1.5	1.3–1.8
75+	414	19,870	2.2	1.7–2.8	142	10,524	1.6	1.2–2.1
Total	**7,193**	**208,530**	**3.5**	**3.3–3.6**	**6,421**	**201,348**	**3.2**	**3.2–3.4**

** Rate estimates and 95% confidence intervals derived from random effects models*

presentation. 54 patients from 14 practices presented with IID to 15 A&E departments during the year of ascertainment. These 15 A&E departments were selected because they routinely entered diagnoses on the A&E computer. They form a subset of the 44 A&E departments serving all enumeration study practice areas. Using the practice denominators the overall A&E attendance rate was 0.065 per 100 person-years in the 15 selected departments, leading to an estimated rate of 0.19 per 100 person-years overall. The presentation rate to GPs in the GP component was 3.3 per 100 person-years, suggesting that there was a negligible 6% loss to the study because cases presented to A&E instead of their GP. Of the 54 cases, three were also ascertained in the study as they also consulted their GP.

6.1.4 Organism specific rates in the community and presenting to GPs

Table 6.5 shows rates of IID in the community versus those presenting to GPs for each target organism. Rate ratios of incidence in the community and incidence of cases presenting to GPs in the GP component have been calculated. For all IID this ratio was 5.8, suggesting that for every case presenting to the GP there are almost five more cases in the community who do not present. The ratio of cases in the community to cases presenting to GPs is high (greater than six to one) in SRSV, VTEC (non O157), *Yersinia* spp., rotavirus group C, *C.difficile, Aeromonas* spp. and EPEC, suggesting that many people with IID associated with these organisms do not consult their GP. The confidence intervals for VTEC, *C.difficile* and EPEC were notably wide. The ratio is also high for cases where no organism was identified. Carriage of an organism with a low rate of pathogenicity would be expected to occur much more frequently in the community than in cases presenting to GPs in the GP component. This is true of *Yersinia* spp. and *Aeromonas* spp. This does not, however, exclude the possibility that some sub-types of *Yersinia* or *Aeromonas* are pathogenic, and this cannot be determined from this study.

In contrast, the ratio of community to GP cases is particularly low (less than two to one) for *Salmonella* spp. and *Shigella* spp. suggesting most cases present to their GP. Confidence intervals are wide for *Shigella* spp. because of the small number of cases.

Comparison of organism specific rates from this study with estimates based on laboratory reports to CDSC are shown in Table 6.6. In the community the four most frequent target organisms identified were (in rank order): SRSV, *Aeromonas* spp., *Campylobacter ssp.*, rotavirus group A. In contrast, the commonest target organism in cases presenting to GPs were, in rank order: *Campylobacter* spp., rotavirus group A, SRSV and *Aeromonas* spp. At the national level, the four most frequently reported target organisms, in rank order, are: *Campylobacter* spp., *Salmonella* spp., rotavirus group A and *C. difficile* cytotoxin, respectively. The surveillance of gastrointestinal pathogens in national surveillance therefore presents a different ranking, as we might expect, to that provided by comprehensive stool testing in the community and in cases presenting to GPs.

6.1.5 Repeat infections

The study identified cases who had IID more than once during the study. Repeat infections were more common in the community component where 9% of cases had two or more episodes of infection (Table 6.7). One case experienced up to five episodes in the six months of follow-up. If all infections occurred independently, i.e., if every individual was equally prone to disease, we would expect repeat infections in 38 people. The observed number of people with two or more infections was in fact 69, suggesting clustering of disease in those cases of people who were particularly prone to infection.

Table 6.5 Incidence rates of IID by organism and in total in both study components, and the rate ratios between those components

	POPULATION COHORT COMPONENT			GP COMPONENT			RATIO COHORT:GP	
	NUMBER OF CASES	RATE PER 1,000 PERSON-YEARS	95% CI	NUMBER OF CASES	RATE PER 1,000 PERSON-YEARS	95% CI	RATE RATIO	95% CI
Bacteria								
Aeromonas spp.	46	12.4	9.4 , 16.7	165	1.88	1.48 , 2.37	6.7	4.9 , 9.1
Bacillus spp. (>10^4/g)	0	0	-	4	0.05	0.01 , 0.15	-	-
Campylobacter spp.	32	8.7	6.1 , 12.3	354	4.14	3.34 , 5.13	2.1	1.5 , 3.0
Clostridium difficile cytotoxin*	9	1.6	0.7 , 3.6	17	0.20	0.12 , 0.31	8.0	3.4 , 19.3
Clostridium perfringens enterotoxin	9	2.4	1.3 , 4.7	114	1.30	1.04 , 1.68	1.9	0.97 , 3.7
E. coli O157	0	0	-	3	0.03	0.01, 0.11	-	-
E. coli DNA probes:								
Attaching and effacing	23	5.4	3.5 , 8.4	119	1.32	1.10 , 1.62	4.1	2.6 , 6.5
Diffusely adherent	23	6.2	4.2 , 9.4	103	1.18	0.92 , 1.52	5.3	3.4 , 8.2
Enteroaggerative	21	4.9	3.1 , 7.8	141	1.62	1.30 , 2.03	3.0	1.9 , 4.9
Enteroinvasive	0	0	-	0	0	-	-	-
Enteropathogenic	1	0.27	0.04 , 1.9	4	0.05	0.01 , 0.15	5.4	0.8 , 55.7
Enterotoxigenic	12	2.7	1.5 , 5.0	52	0.59	0.44 , 0.81	4.6	2.4 , 8.9
Verocytotoxigenic (non O157)	3	0.82	0.26 , 2.5	6	0.06	0.02 , 0.17	13.4	3.6 , 49.6
Salmonella spp.	8	2.2	1.1 , 4.3	146	1.57	1.19 , 2.06	1.4	0.7 , 2.8
Shigella spp.	1	0.27	0.04 , 1.9	23	0.27	0.16 , 0.47	1.0	0.13 , 7.3
Staphylococcus aureus (>10^6/g)	1	0.27	0.04 , 1.9	10	0.11	0.05 , 0.23	2.5	0.33 , 19.0
Vibrio spp.	0	0	-	1	0.01	0.001 , 0.05	-	-
Yersinia spp.	26	6.8	4.6 , 10.0	51	0.58	0.42 , 0.88	11.7	7.5 , 18.3
Protozoa								
Cryptosporidium parvum	3	0.81	0.26 , 2.5	39	0.43	0.29 , 0.61	1.9	0.60 , 6.1
Giardia intestinalis	3	0.54	0.14 , 2.2	28	0.28	0.17 , 0.46	1.9	0.46 , 7.9
Viruses								
Adenovirus Group F	13	3.0	1.7 , 5.4	81	0.88	0.69 , 1.13	3.4	1.8 , 6.3
Astrovirus	14	3.8	2.3 , 6.4	77	0.86	0.67 , 1.13	4.4	2.5 , 7.6
Calicivirus	8	2.2	1.1 , 4.3	40	0.43	0.27 , 0.60	5.1	2.4 , 10.7
Rotavirus Group A	29	7.1	4.8 , 10.4	208	2.30	1.80 , 2.94	3.1	2.1 , 4.6
Rotavirus Group C	2	0.54	0.14 , 2.2	6	0.06	0.02 , 0.17	8.9	1.9 , 41.3
SRSV	50	12.5	9.4 , 16.7	169	1.99	1.45 , 2.73	6.3	4.6 , 8.6
No target organism identified	480	117.3	107, 129	1,305	14.82	12.78 , 17.20	7.9	7.1 , 8.8
ALL IID	781	194	181, 208	8,770	33.1	29.4 , 37.5	5.8	5.4 , 6.3

* cases > 2 years old

Table 6.6 Incidence rates per 1000 person-years of organisms in the community and GP components compared with those from positive laboratory reports to CDSC 1995

	POPULATION COHORT COMPONENT	GP COMPONENT	CDSC REPORTS 1995
BACTERIA			
Aeromonas spp.	12.4	1.9	0.01
Bacillus spp. (>10^4/g)	0	0.05	0.002
Campylobacter spp.	8.7	4.1	0.84
Clostridium difficile cytotoxin	1.6	0.2	0.14
Clostridium perfringens enterotoxin	2.4	1.3	0.007
E.coli O157	0	0.03	0.01
Salmonella spp.	2.2	0.6	0.6
Shigella spp.	0.3	0.3	0.08
Staphylococcus aureus (>10^6/g)	0.3	0.1	0.001
Vibrio spp.	0	0.008	0.001
Yersinia spp.	6.8	0.6	0.004*
PROTOZOA			
Cryptosporidium parvum	0.8	0.4	0.41
Giardia intestinalis	0.5	0.3	0.1
VIRUSES			
Adenovirus types 40,41	3.0	0.9	0.02
Astrovirus	3.8	0.9	0.005
Calcivirus	2.2	0.4	0.003
Rotavirus group A	7.1	2.3	0.3
SRSV	12.5	2.0	0.05

** CDSC data for Y.enterocolitica only*

Two percent of cases presenting to the GP had two or more episodes of infection, although the proportion may have been 2.5% if repeat episodes which could not be verified by available data are included. A single person experienced up to three episodes in the 12 months of follow-up of the practice population. If all infections occurred independently, i.e., every individual was equally prone to IID, we would expect repeat infections in 82 people. The observed number of people with two or more infections was between 82 and 98, giving little evidence of clustering of disease presentation within cases.

The case definition excluded any cases which had not been asymptomatic for the three week period prior to the episode. Thus each episode could be regarded as a separate infection rather than a recurrence of infection in the same person. This was supported by the microbiology results on repeat episode cases, which showed no repeat episodes with the same organism in the community component and only one with the same organism (*C. perfringens*) in the GP component. However, in most cases two positive stools from both episodes were not available.

6.2 VARIATION IN RATES OF IID

6.2.1 Comparison of prospective and retrospective ascertainment in the community component

In other studies rates of IID, when estimated by a person's recall of past diarrhoea rather than prospective follow-up, have tended to be high. To compare recall rates with prospective rates in this study we obtained an estimate of recall rates equivalent

Table 6.7 Repeat episodes of IID

NUMBER OF EPISODES PER PERSON	CASES IN THE GP CASE-CONTROL COMPONENT			CASES IN THE COMMUNITY COMPONENT		
	NUMBER OF CASES	NUMBER OF PEOPLE	PERCENT OF CASES	NUMBER OF CASES	NUMBER OF PEOPLE	PERCENT
1	3856 (3824*)	3856 (3824)	97.9	671	671	90.7
2	158 (190*)	79 (95)	2.0	126	63	8.5
3	9	3	0.1	15	5	0.7
4	0	0	0	0	0	0
5	0	0	0	5	1	0.1
Total	4026	3938	100	817	740	100

** Including probable repeat cases that could not be confirmed by available information*

to that in the 1994 Omnibus Survey in Great Britain (Feldman and Banatvala 1994) by asking participants in the population cohort the following question at the recruitment stage: *'During the last month have you suffered from diarrhoea (3 or more loose bowel movements in any 24-hour period)?'*

The overall percentage who reported diarrhoea in the last month was 6.5% (564/8,674). This is close to estimates from studies using similar retrospective methods: the Omnibus Survey reported a monthly rate of 7.9% and Palmer reported average monthly rates between 6.3% and 8.9% (Palmer 1996, Feldman 1994). Extrapolation of this result, assuming independence from month to month, estimates a rate of 55 per 100-person years. This rate is three times higher than that calculated in the population cohort component by prospective follow-up, which suggested that around 19% of the population would experience IID in a year. This highlights the danger of recall bias when attempting to enumerate events over time. We suggest that the rate from the population cohort component, being prospective, is the more accurate estimate: i.e., 19.4 per 100 person-years. Studies which have used the recall method are likely to over-estimate the true rate of IID in the community.

6.2.2 Variation in rates of IID in the community

The estimated rate of IID in the community varied between different practice cohorts from 7.1 to 31.3 per 100 person-years (5th, 95th percentile), with a median value of 18.8. The geographical distribution of these rates is shown in Figure 6.1. The only discernible patterns are consistently high rates in the South West of England and occurrence of the highest rates in central London.

Regression analysis identified type of location as the only significant practice characteristic associated with rate of IID in the community (Table 6.8). Rates were highest in London but otherwise generally higher in rural than in urban practices (p=0.001). There was no statistically significant difference between regions after allowing for urban/rural differences. Apart from age and sex, personal characteristics which significantly influenced community rates were social class, which showed lower rates in the middle classes, social classes III(NM), III(M) and IV, than in the highest and lowest classes. The rate in the economically inactive (students, housewives and carers without other earners in the household) is significantly lower than social class I but not

Figure 6.1 The Study of Infectious Intestinal Disease in England

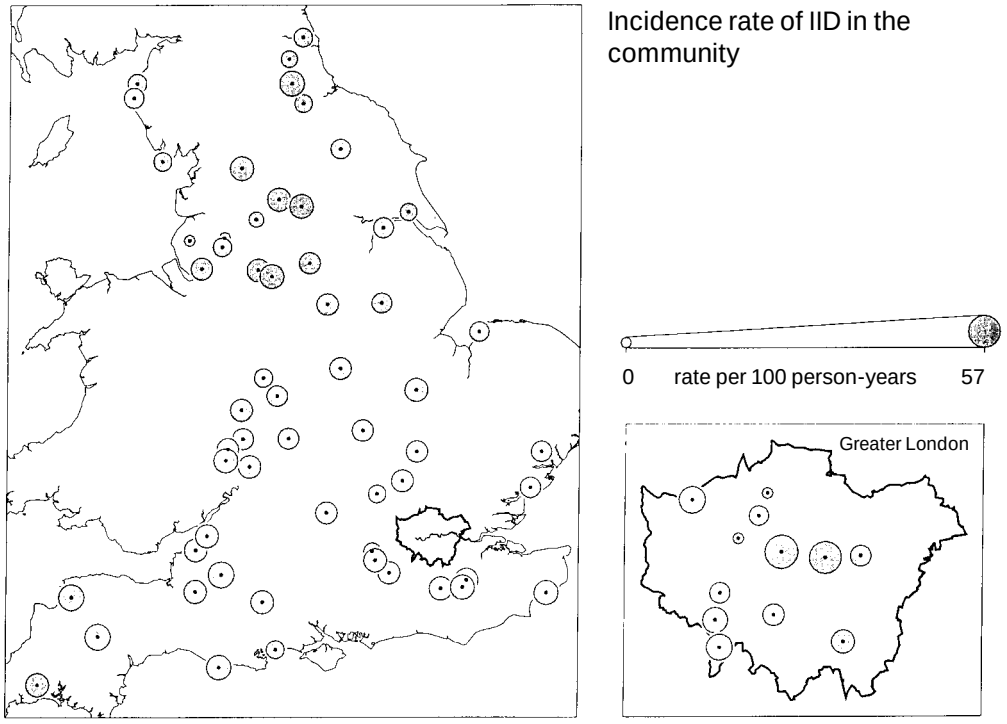


Figure 6.2 The Study of Infectious Intestinal Disease in England

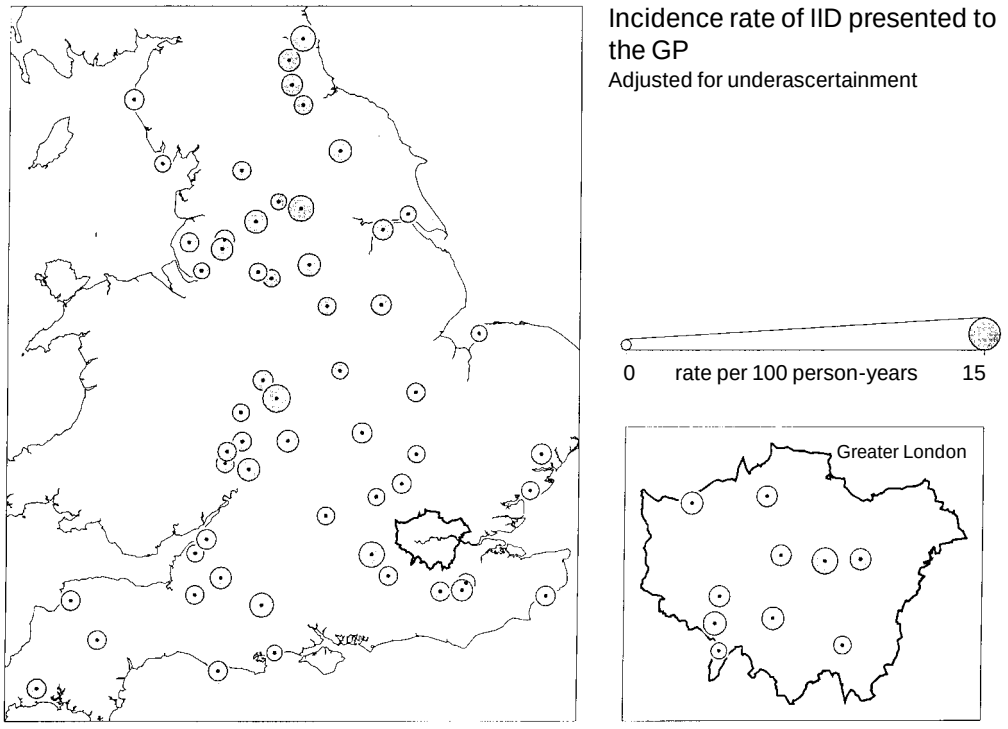


Table 6.8 Variation in rates of IID in the community component (after controlling for age and sex)

FACTOR		RATE RATIO	P-VALUE	95% CI
Location				
	Urban	1.00		
	Rural	1.33	0.001	1.13–1.58
	London	1.51	0.008	1.11–2.05
Social Class				
	I	1.00		
	II	0.99	0.93	0.77–1.26
	III (NM)	0.70	0.02	0.52–0.94
	III (M)	0.73	0.03	0.55–0.97
	IV	0.86	0.39	0.61–1.21
	V	0.93	0.80	0.53 –1.63
	Forces	1.19	0.71	0.48–2.96
	Economically inactive	0.56	0.011	0.36–0.86
	Missing	0.87	0.64	0.49–.54

Table 6.9 Variation in rates of IID presenting to the GP (after controlling for age and sex)

FACTOR		RATE RATIO	P-VALUE	95% CI
Region	North	1.00		
	Southwest/Midland	0.88	0.35	0.67–1.15
	Southeast	0.63	0.016	0.43–0.92
Location	Urban	1.00		
	Rural	1.09	0.52	0.84–1.42
	London	1.80	0.009	1.16–2.78
Jarman Score				
	1st quintile (least deprived)	1.00		
	2nd–4th quintile	1.23	0.12	0.95–1.60
	5th quintile	1.65	0.003	1.19–2.28

social classes III(M) and III(NM). Other social factors investigated that were not significant were Jarman score of the practice and regional unemployment levels.

6.2.3 Variation in rates of IID presenting to GPs

The estimated rate of IID presenting to GPs in the GP component varied between practices from 1.3 to 7.6 per 100-person years (5th, 95th percentile) with a median value of 3.1. The geographical distribution of these rates is shown in Figure 6.2, from which no clear patterns are discernible.

Regression analysis revealed that the region, type of location and Jarman score of the general practice were all statistically significantly associated with the rate of IID, after adjusting for age and sex, under-ascertainment and list inflation (Table 6.9). Presentation rates to GPs were highest in the North, and the difference compared to the South East was statistically significant ($p=0.016$) after allowing for the different rates in London. Presentation rates were higher in London, but with no other clear urban/rural differential. They were also higher in the most deprived regions as measured by the fifth quintile of the Jarman score distribution ($p<0.01$). There was no significant difference in presentation rates between practices with four or more partners and practices with three or fewer. There was evidence of disease clustering within certain practices: some had much higher rates than others. This was modelled in the statistical analysis but was not fully explained by all the above factors.

6.2.4 Variation in rates of IID presenting to GPs by organism

Regression analysis was used to investigate jointly variations by region, Jarman score and location of the practice, after controlling for age and sex. This was carried out for each organism which was identified in at least 25 cases in order to have a sufficient sample for analysis. The results in Table 6.10 show that for many bacteria and viruses the rates in the least deprived (low Jarman score) practices were lower than in more deprived practices. Both *Giardia* and *Cryptosporidium* had significantly higher rates in rural than in urban settings, whilst many of the bacteria appeared to have a higher incidence in urban settings, although this was only statistically significant for DAEC. There was little evidence of regional variation, apart from lower rates of *Aeromonas* spp. and higher rates of *Cryptosporidium* spp. in the North. The statistical power to detect significant differences was low for the individual target organisms, especially after allowing for disease clustering within practices.

Only a few organisms were isolated sufficiently frequently to analyse variation in rates of IID in the community, and no significant associations were found.

Table 6.10 Variation in organism specific rates in cases presenting to the GP

TARGET ORGANISM	SIGNIFICANT VARIABILITY AFTER ADJUSTING FOR AGE AND SEX		
	REGION	LOCATION	JARMAN SCORE
Bacteria			
Aeromonas spp.	Mid/SW > North *		Mid > Low *** High > Low *
Campylobacter spp.			High > Low *
Clostridium perfringens enterotoxin			
Enterovirulent *E. coli* (DNA probes):			
Attaching and effacing			Mid > Low *
Diffusely adherent	-	Rural < Urban *	-
Enteroaggregative	-	-	-
Enterotoxigenic	-	-	-
Salmonella spp.			Mid > Low * High > Low *
Shigella spp.	-	-	-
Yersinia spp.			High > Low *
Protozoa			
Cryptosporidium parvum	Mid/SW < North * SE < North *	Rural > Urban ***	
Giardia intestinalis		London > Urban * Rural > Urban *	
Viruses			
Adenovirus types 40,41			Mid > Low * High > Low *
Astrovirus			
Calicivirus			High > Low **
Rotavirus Group A	-	-	-
SRSV			Mid > Low ***
No target organisms identified			Mid > Low *** High > Low ***

* 0.01 < p 0.05
** 0.001 < p 0.01
*** p ≥ 0.001

6.3 REPORTING TO THE NATIONAL LABORATORY SURVEILLANCE SYSTEM

6.3.1 Proportion of stools requested routinely from cases presenting to GPs, those with isolates, and those reported nationally

During a one year prospective follow-up in the 36 practices in the enumeration component, 4,884 cases were ascertained. The median number of cases presenting per practice was 119 and the 5th and 95th percentiles were 24 and 316, respectively. Complete information was obtained for 4,747. Of these 1,262 (27%) had stool examination requested by the GP on clinical grounds. The specimens were sent to the usual laboratory serving the GP practice, and were tested for organisms or toxins as required by the clinical information provided, and according to local laboratory protocols. Pathogens were identified in 300/1,262 (24%) of these cases.

6.3.2 The overall proportion of isolates reported nationally

Thirty-two microbiology laboratories were identified which received routine stool specimens from the 36 practices in the enumeration component (Table 6.11). These laboratories were representative of others in England (see Chapter 4). Twelve belonged to the PHLS, 19 were NHS laboratories and one was independent. The personal details and laboratory numbers of cases on whom isolates were reported to the GP practice were checked at CDSC to identify those laboratory isolates which had been reported. A total of 207/300 (69%) isolates had been reported. There was no difference between PHLS and non-PHLS laboratories.

6.3.3 The proportion of isolates reported nationally, by organism

Table 6.12 shows the proportion of isolates identified by the laboratories serving practices in the enumeration component which were reported to CDSC. Considering only those organisms where there were at least 10 isolates, the proportion reported was highest for *Salmonella* spp.(81%) and lowest for *Campylobacter* spp.(64%).

6.4 THE RATIO OF LABORATORY ISOLATES REPORTED NATIONALLY TO CASES PRESENTING TO GPS AND TO CASES IN THE COMMUNITY: ALL IID AND BY ORGANISM

A reporting pyramid can be constructed from the various estimates of disease frequency at different levels of reporting. The proportion of cases in the community component that present to the GP can be seen from the ratio of the incidence rates described in Table 6.5. The number of GP cases that have stools sent for routine laboratory analysis was estimated in the enumeration component, as well as the proportion that were positive for target organisms (see section 6.3.1). The proportion of these reports teaching the CDSC was established in the first under-reporting component (see sections 3.1.6.6 and 6.33), based on identifying the number of cases identified by the study who were on the national database of laboratory isolates at CDSC (Table 6.12).

Table 6.11 Positive laboratory findings in stools sent for examination by general practitioners in the enumeration arm and the proportion reported to national surveillance (CDSC) by PHL and non-PHL laboratories

TYPE OF LAB	NUMBER OF LABS	NUMBER OF ISOLATES REPORTED TO CDSC	TOTAL NUMBER OF ISOLATES IDENTIFIED	PERCENTAGE REPORTED TO CDSC (95% CI)
PHL	12	78	113	69.0 (60.5–77.6)
non-PHL	20	129	187	69.0 (62.4–75.6)
ALL	**32**	**207**	**300**	**69.0**

Table 6.12 Positive laboratory findings in stools sent for examination by general practioners in the enumeration arm and proportion reported to national surveillance*

ORGANISM	LABORATORY POSITIVE CASES	REPORTED TO NATIONAL SURVEILLANCE	PERCENTAGE REPORTED (95% CI) WHERE AT LEAST 10 POSITIVE CASES
Bacteria			
Aeromonas	3	0	
Campylobacter	148	94	63.5 (55.8–71.3)
E.coli O157	1	1	
E.coli (other)	3	3	
Salmonella	78	63	80.8 (70.3–88.8)
Shigella	13	10	77.0 (46.2–95.0)
Protozoa			
Cryptosporidium	16	11	68.8 (41.3–89.0)
Giardia	4	3	
Viruses			
Adenovirus	4	2	
Astrovirus	1	1	
Rotavirus	28	19	67.9 (47.7–84.1)
SRSV	1	1	
Total	**300**	**208**	**69.3 (64.1–74.6)**

** Percentages only given where at least 10 cases*

Table 6.13 summarises these various estimates for all IID and, by considering the ratios between them, shows the number of cases at each stage that contribute to a single case being reported to CDSC. The upper and lower sensitivity bands are derived by performing the same calculation on the upper and lower confidence limits at each stage.

For every report of an identification of any target organism made to CDSC there are 1.4 laboratory identifications, 6.2 stools submitted to laboratories, 23 cases presenting to the GP and 136 cases in the community, as illustrated in Figure 6.3. This final figure for community cases may be as high as 197 or as low as 93.

Reporting pyramids have been calculated for certain individual organisms, using the organism specific rates in Table 6.5 and the results from the laboratory linkage study in Table 6.12 (Table 6.14 and Figures 6.3–6.8). The organisms selected for this

Table 6.13 Reporting pyramid for all IID

	COMMUNITY	PRESENTING TO GP	STOOLS SENT FOR ROUTINE LABORATORY TEST	POSITIVE BY ROUTINE LABORATORY TEST	REPORTED TO NATIONAL SURVEILLANCE ALL IID
Rate per 1000 py (95% CI)	194 (181, 208)	33.1 (29.4, 37.5)	8.8 (8.3, 9.3)	2.1 (1.9, 2.4)	1.5 (1.3, 1.7)
Ratio to next column (95% CI)	5.8 (5.4, 6.3)	3.8 (3.6, 4.0)	4.3 (3.8, 4.7)	1.44 (1.26, 1.65)	
Ratio to final column (sensitivity bound)	136 (93, 197)	23.2 (17.3, 31.2)	6.2 (4.8, 7.8)	1.44 (1.26, 1.65)	1.0

Table 6.14 Reporting Pyramid for Specific Organisms

	COMMUNITY	PRESENTING TO GP	STOOLS SENT FOR ROUTINE LABORATORY TEST[1]	POSITIVE BY ROUTINE LABORATORY TEST[2]	REPORTED TO NATIONAL SURVEILLANCE
Campylobacter					
Rate per 1000 py (95% CI)	8.7 (6.1 , 12.3)	4.1 (3.3 , 5.1)		1.7 (1.4 , 2.0)	1.1 (0.9 , 1.3)
Ratio to next column (95% CI)	2.1 (1.5 , 3.0)	2.4 (2.0 , 2.9)		1.5 (1.2 , 2.0)	
Ratio to final column (sensitivity bound)	7.6 (3.6 , 17.4)	3.6 (2.4 , 5.8)		1.5 (1.2 , 2.0)	1.0
Salmonella					
Rate per 1000 py (95% CI)	2.2 (1.1 , (4.3)	1.6 (1.2 , 2.1)		0.8 (0.7 , 1.0)	0.7 (0.5 , 0.9)
Ratio to next column (95% CI)	1.4 (1.0 , 2.8)	1.9 (1.4 , 2.5)		1.2 (1.0 , 1.7)	
Ratio to final column (sensitivity bound)	3.2 (1.4 , 12.0)	2.3 (1.4 , 4.3)		1.2 (1.0 , 1.7)	1.0
Rotavirus					
Rate per 1000 py (95% CI)	7.1 (4.8 , 10.4)	2.3 (1.8 , 2.9)		0.3 (0.2 , 0.5)	0.21 (0.13 , 0.34)
Ratio to next column (95% CI)	3.1 (2.1 , 4.6)	7.5 (5.1 , 11.2)		1.5 (1.0 , 2.6)	
Ratio to final column (sensitivity bound)	35.0 (10.7 , 133.9)	11.3 (5.1 , 29.1)		1.5 (1.0 , 2.6)	1.0
SRSV					
Rate per 1000 py (95% CI)	12.5 (9.4 , 16.7)	1.99 (1.5 , 2.7)		0.12 (0.003 , 0.09)	0.12 (0.003 , 0.09)
Ratio to next column (95% CI)	6.3 (4.6 , 8.6)	172.0 (24.1 ,1228)		1.44 (1.26 , 1.65)	
Ratio to final column (sensitivity bound)	1,562 (140 , 17,424)	248 (30.4 , 2026)		1.44 (1.26 , 1.65)	1.0
No target organism					
Rate per 1000 py (95% CI)	1,173 (107 , 129)	14.8 (14.2 , 15.5)		10.8 (10.1 , 11.5)	
Ratio to next column (95% CI)	7.9 (7.1 , 8.8)	1.4 (1.3 , 1.5)			
Ratio to final column (sensitivity bound)	11.1 (9.2 , 12.2)	1.4 (1.3 , 1.5)		1.0	

1 The proportion of stools sent for routine laboratory tests cannot be estimated for individual microbiological organisms
2 Ratio of number of positive SRSV to number reported to national surveillance is assumed the same as for all IID

analysis were two bacteria and two viruses known to be important from surveillance and shown in our study to be common. For SRSV the estimated proportion reported to CDSC was assumed to be the same as for all IID, since this proportion could not be estimated precisely from the single laboratory positive case of SRSV. It is not possible in organism-specific pyramids to estimate what proportion of stools with the organism was 'sent to the laboratory', because the number of stools with the organism which were not sent (the other part of the denominator) cannot be known.

Table 6.14 and Figure 6.4 suggest that the ratio of isolates nationally reported to cases occuring in the community is lowest for *Salmonella* spp.(1 to 3.2), because many community cases present to the GP and because the laboratory reporting of *Salmonella* spp. is high. The ratio is also low for *Campylobacter* spp.(1 to 7.6) (Figure 6.5).

For rotavirus the estimated ratio of nationally reported isolates to community cases is much higher (1 to 35) (Figure 6.6), although not as high as the ratio for all IID.

Table 6.15 Ratio of community rates of all IID and specified target organisms calculated from this study to total number of laboratory isolates in England reported to CDSC in 1995

ORGANISM	COMMUNITY RATE PER 1,000 PERSON YEARS	PROJECTED NUMBER OF CASES AMONG POPULATION OF ENGLAND PER YEAR[1]	REPORTED IN ENGLAND TO CDSC PER YEAR[2]	RATIO OF COMMUNITY TO REPORTED IN ENGLAND	RATIO OF COMMUNITY TO REPORTED IN IID STUDY (CI)	RATIO COMPARISON COL5/COL6
All IID	194	9,415,208	110,807	85	136 (93 , 197)	1.5
Campylobacter	8.7	422,200	40,940	10.3	7.6 (3.6 , 17.4)	0.7
Salmonella	2.2	106,800	28,015	3.8	3.2 (1.4 , 12.0)	0.8
Rotavirus	7.1	344,600	15,316	22.5	35.0 (10.7 , 133.9)	1.6
SRSV	12.5	606,700	1,926	315	1562 (140 , 17424)	5.0

1 Population of England taken as 48,532,000 (1994 estimate)
2 Total annual laboratory reports to CDSC from England, averaged over 1994/95

For SRSV the ratio of nationally reported to community cases is very high (1 to 1,562) (Figure 6.7). This is because firstly, only a small proportion present to the GP and secondly, because only one SRSV positive report arose from routine investigation in the enumeration study. The sensitivity bounds for this estimate are wide. Figure 6.8 illustrates the pyramid for specimens with no target organism shows 1:11 infections where no target organism was identified in the laboratory. Negative results do not reach the national surveillance system. The ratio reflects the fact that laboratory examinations carried out as part of this study were more extensive than those normally performed in routine diagnosis.

The second under-reporting component was a simpler calculation, made to link the community rate from this study to the total annual reports to CDSC (see section 3.1.6.2). These include routine laboratory reports from both sporadic and general outbreak sources. The ratio of community to reported cases of all IID estimated by using this method of calculation was lower than the direct method described above by a factor of 1.5 (Table 6.15). The ratio is closer to 1 for *Salmonella* spp. and *Campylobacter* spp., but further from 1 for the viruses. This demonstrates that the degree of under-reporting estimated from the study in respect of viruses is higher than that estimated from the projection to all reported cases.

6.5 DISCUSSION

It is important to note that this study addresses all IID, not merely that fraction caused by the consumption of contaminated food. The study makes no attempt to quantify the accuracy of statutory notifications of food poisoning, but addresses the relationship of the national surveillance of the reporting of laboratory identifications by PHLS CDSC to IID, whatever its aetiology, presenting to GPs and in the community.

One in five population cohort members suffered from IID in one year. This result is comparable to that found in a recent European study (Hoogenboom-Verdegaal *et al*. 1994). The rate determined by this prospective method of follow-up is likely to be

more accurate than that determined by recall, which gave a rate of five out of ten persons developing IID in any one year. This may be explained by the tendency for study responders to telescope events into a given period of time. In this present study, one person in 30 presented to their GP with IID in one year, again similar to the recent European study (Hoogenboom-Verdegaal *et al.* 1994). The presentation rate to A&E departments was low, suggesting that primary care of IID was almost always in general practice. Only the A&E departments with computerised records were included in this study, but these represented approximately 30% of all such departments in the study areas. In view of the study design and large sample size it was possible to make reasonably accurate adjustments for GP practice list inflation and under-ascertainment. Many community cases do not present to a GP. This may be due to personal inclination or the mildness of symptoms, but accessibility to services is also likely to be important. This study demonstrated higher rates of illness in the population of rural rather than urban areas but not in rates of presentation to the GP.

Rates of IID both in the community and amongst those presenting to GPs varied by age and sex. In the community, rates were highest in children under five years old and in females in their reproductive years; this may be due to the greater exposure to infectious agents in children whilst acting as carers. The rates in the elderly may be underestimated as the study did not recruit from residential homes, which are a common site of outbreaks of IID. Rates of presentation to GPs reflected the pattern in the community, with higher rates in children under the age of five years, but rates were also higher in all females in all age groups over the age of 15 years when compared to men. This pattern was not seen in the community, possibly because of the smaller sample. Alternatively it could be explained by different health-seeking behaviours of men and women.

There was also variation in rates of IID according to the population's characteristics. Higher rates in rural rather than urban communities might be explained by their closer proximity to animal sources of infection, although within the locations defined as rural there was no clear difference between more remote locations and suburban ones. The higher rates in London are difficult to explain, and need to be explored further. One possible reason might be the greater opportunities for eating out, although it is difficult to demonstrate that eating out carries a higher risk of foodborne disease than eating at home. Community rates were higher in social classes I, II and V. Higher rates among the lowest social class might be due to poorer housing conditions, hygiene behaviour (reflecting education) and nutrition. Among the highest social class, more frequent travel and eating out may contribute. This U-shaped pattern may have been the reason for finding no association with the practices' Jarman score. Rates of presentation to GPs were higher in London and in the North. Further work needs to be done to compare these data with regional patterns in health seeking behaviour for other diseases. Presentation rates were higher in areas with the highest Jarman score, and this may reflect different patterns of health service use, or more severe disease in areas with higher Jarman scores. In the GP component, Jarman score was the only deprivation marker available and social class could not be examined.

The study estimated that for, every case of IID detected by national laboratory reporting surveillance, there are another 135 undetected in the community. The reporting pyramid was found to vary by organism. Under-ascertainment by national surveillance of community cases was estimated to be greatest for SRSV where for every case reported there were 1,562 in the community. As the diagnostic test for SRSV is available at only a small number of laboratories in England, routine investigations are carried out only when a number of individuals are suspected of being part of an outbreak of viral gastroenteritis. In addition, persons experiencing mild symptoms in the community may not seek help from the GP, and stool specimens

are less likely to be requested by the GP on clinical grounds. Under-ascertainment was least for *Salmonella* spp. with three cases in the community for each case identified nationally. This may be because a greater proportion of cases sought help from their GP because their illness was more severe, but also because laboratory reporting nationally is more complete. Thus it would appear that severe disease, mainly due to pathogenic bacteria, is less under-ascertained nationally than milder forms of IID, which are mainly due to viruses.

Comparison of the reporting pyramids estimated by the study (Table 6.14) and results achieved by extrapolation of the study results to national figures (Table 6.15) demonstrated different estimates of the ratio of reports to community incidence. This suggests that a greater proportion of IID is reported nationally than predicted by the study. Reasons for this discrepancy have been considered. The study was large enough to produce robust estimates, as the GP population represented about 1% of the population of England. The routine laboratories within the GP areas were also shown to be representative of all laboratories nationally in terms of number and type of reports. It is possible that repeat specimens taken for diagnostic or public health reasons could have spuriously inflated the CDSC reports, although this is unlikely to have had an important effect. Efforts are made to eliminate duplicate reports at CDSC but they depend on the quality of the identifier information sent. In the enumeration component nurses may have failed to record positive laboratory results received late, although this possibility was minimised by a follow-up mailing to all practices to check on delayed reports.

The most likely explanation for this discrepancy between the two methods of calculation is cases originating from outbreaks, which may often reach CDSC having bypassed the GP. During outbreaks, identified cases may be asked to send stool specimens directly to the laboratory, and it is likely that the GP would not be aware of such cases. Many outbreaks are recorded in hospitals, where stool specimens are easily obtained, and these would also go directly to a laboratory without any GP involvement. If an outbreak occurs at a social function, cases may disperse and visit their own GPs in many different areas, so a study based in scattered GP practices will tend to pick up just a few cases from the outbreak. Outbreak cases may have appeared in our community study, even if the link through the GP was not made, but with a cohort of just 6,000 it is possible that outbreak cases were missed by chance alone. However, the community component did not, for logistical reasons, include residential institutions. We excluded residential homes, prisons, universities, and long-stay hospitals, but included schools. Within our study data for both community and GP cases it was only possible to identify one outbreak where there was sufficient evidence of spatial and temporal clustering with consistent laboratory findings.

Organism-specific pyramids were also compared with the extrapolated figures (Table 6.15) and, although the viruses remain poorly reported compared to the bacteria, the discrepancy between figures varied by organism. Two simplifying assumptions used for the calculation of the pyramids may explain some of the discrepancy. Firstly, we assumed that under-ascertainment in our study was constant for all organisms. We believe this assumption to be substantially true despite some evidence that ascertainment was poorer among cases presenting with vomiting only. This might suggest that greater under-ascertainment of viral IID occurs. However, such cases were few, and our belief is further justified by the fact that the strongest predictors of under-ascertainment reflected the GPs ability to participate in research, which is unlikely to result in different levels of reporting for different target organisms. Secondly, we assumed that compliance in submitting a stool specimen was the same for all organisms. It could be argued that compliance might be better in either the milder cases, who may feel more able to participate in the study or the more severe cases who have a greater motivation to comply, but neither hypothesis could be confirmed

from the study. We believe the assumption to be true because a comparison of severity of symptoms between cases sending a stool specimen and cases not sending a stool specimen showed them to be the same suggesting that severity, and hence underlying organism, did not influence compliance.

If it were true that outbreaks were the reason for the discrepancy between the two estimates of completeness of ascertainment at the national level we would have expected to see good agreement for organisms rarely associated with outbreaks, and poorer agreement for those organisms which more commonly cause outbreaks. The proportion of reports of *Salmonella* spp., *Campylobacter* spp., rotavirus group A and SRSV from outbreaks are 5%, 0.04%, 0.4% and for 47% respectively (Cowden *et al*. 1995). In fact, *Salmonella* showed good agreement with external estimates. Figures for *Campylobacter* spp. and rotavirus showed reasonable agreement and SRSV showed poorest, most likely due to its more frequently being reported as part of an outbreak.

The national statistics on the percentage of cases due to outbreaks are not precise. During an outbreak not all cases have stool specimens investigated either due to patient compliance or because it is not deemed necessary on clinical, epidemiological or public health grounds. The proportion of cases of viral gastroenteritis occurring as part of an outbreak has increased four-fold between 1992 and 1996. This may be due to increased reporting of outbreaks or, less likely, to a deterioration in the ascertainment of sporadic cases.

The outstanding discrepancy between the two rotavirus estimates, and the two *Campylobacter* estimates remains unexplained, as the number of outbreaks reported is very low. However, the external estimates lie within the sensitivity bounds of the study estimate, and the difference could be attributableto sampling error and to imprecision of one or more stages of estimation in the reporting pyramid.

Figure 6.3

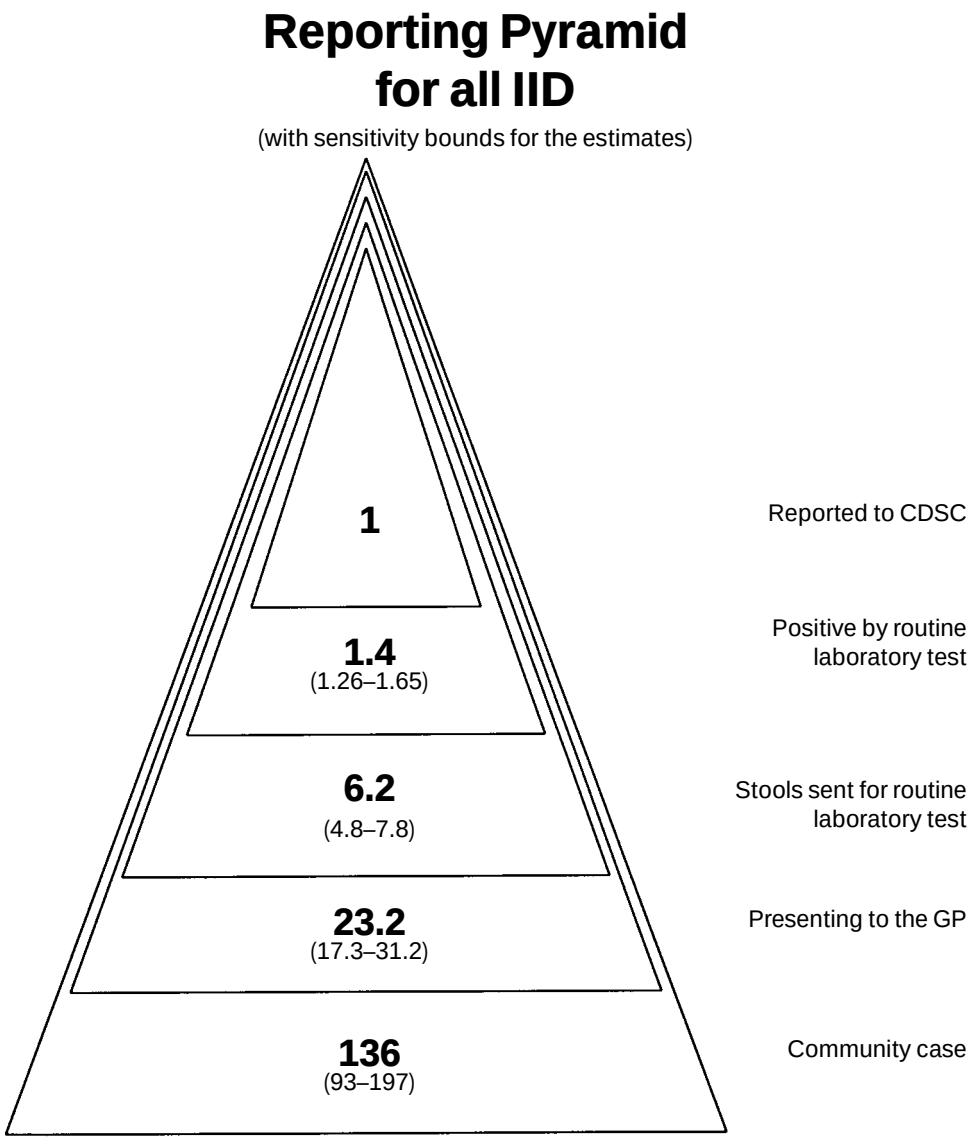

Reporting Pyramid for all IID
(with sensitivity bounds for the estimates)
1
Reported to CDSC
1.4
(1.26–1.65)
Positive by routine laboratory test
6.2
(4.8–7.8)
Stools sent for routine laboratory test
23.2
(17.3–31.2)
Presenting to the GP
136
(93–197)
Community case

Figure 6.4

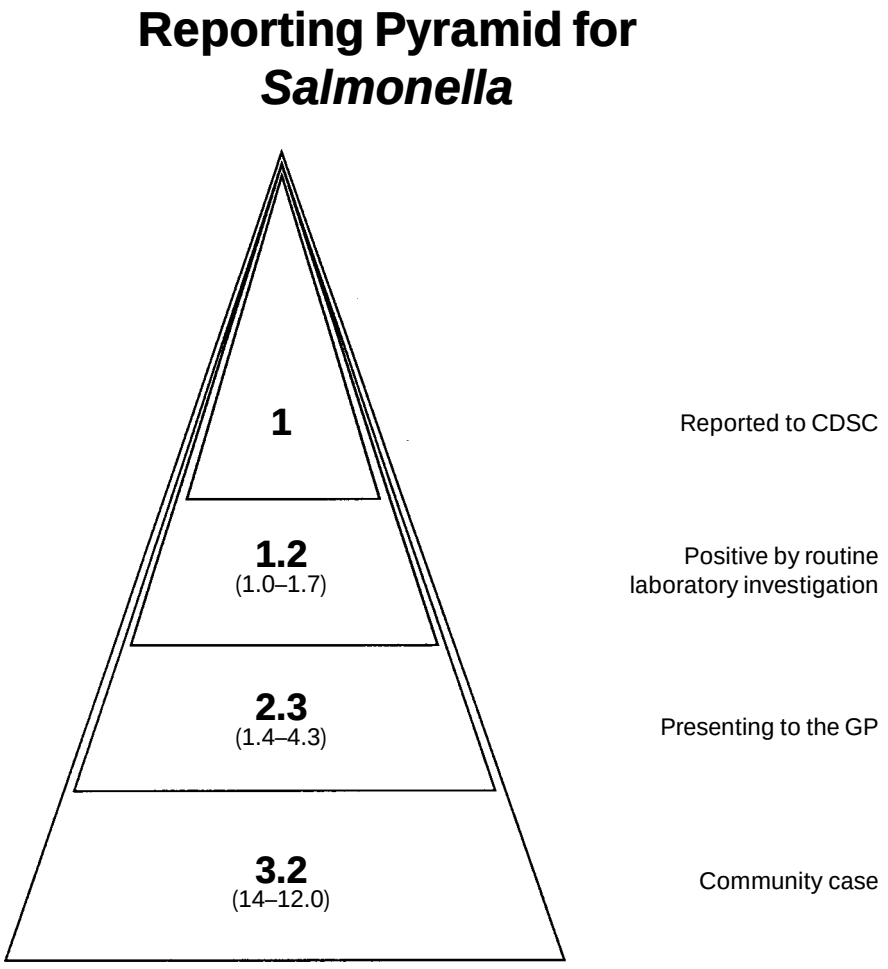

Reporting Pyramid for
Salmonella
1
Reported to CDSC
1.2
(1.0–1.7)
Positive by routine
laboratory investigation
2.3
(1.4–4.3)
Presenting to the GP
3.2
(14–12.0)
Community case

Figure 6.5

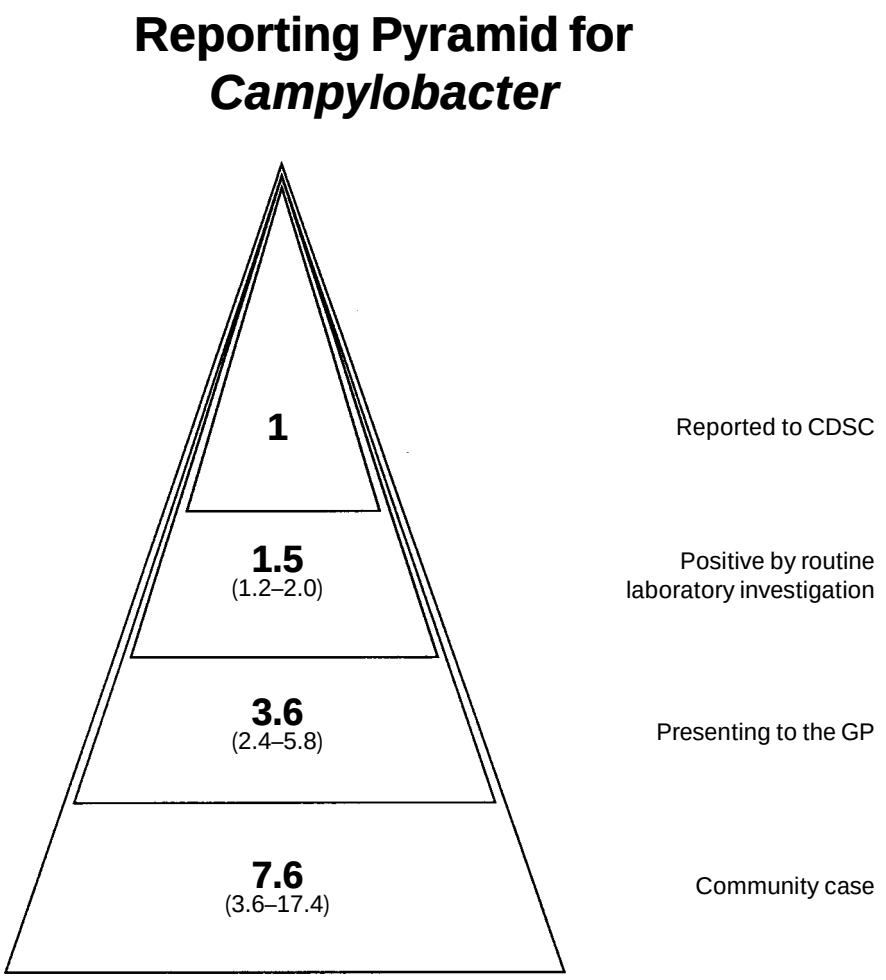

Reporting Pyramid for
Campylobacter
1
Reported to CDSC
1.5
(1.2–2.0)
Positive by routine
laboratory investigation
3.6
(2.4–5.8)
Presenting to the GP
7.6
(3.6–17.4)
Community case

Figure 6.6

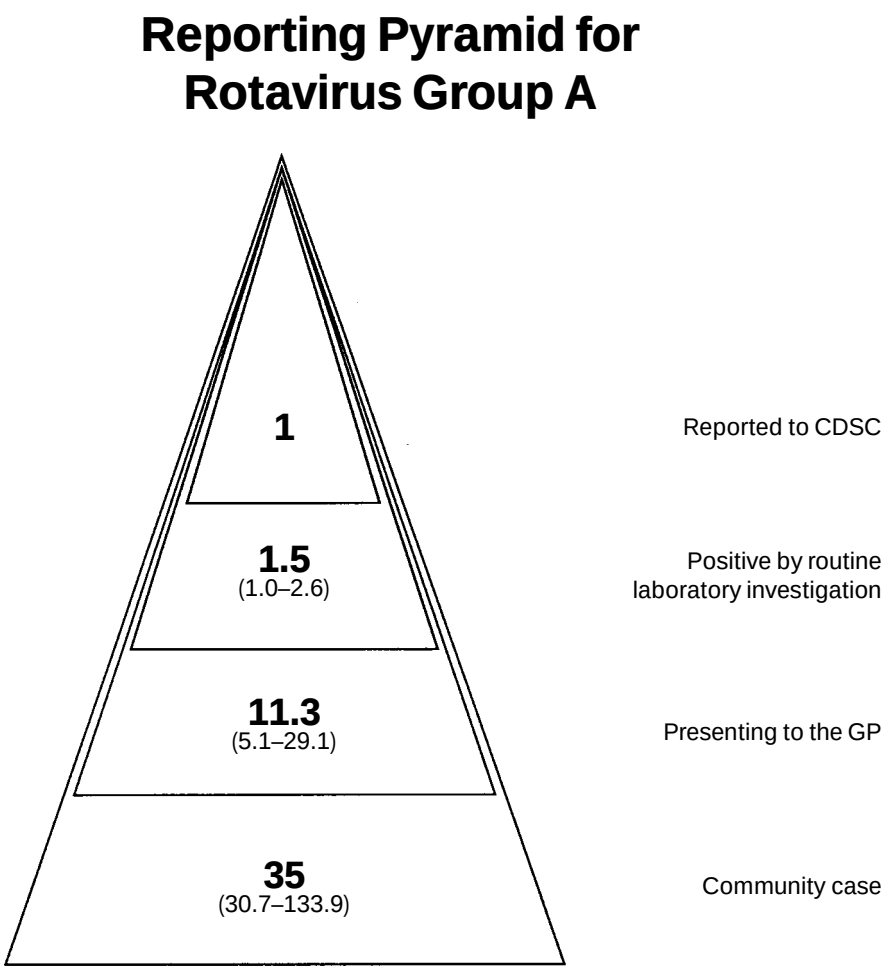

Reporting Pyramid for Rotavirus Group A
1
Reported to CDSC
1.5
(1.0–2.6)
Positive by routine laboratory investigation
11.3
(5.1–29.1)
Presenting to the GP
35
(30.7–133.9)
Community case

Figure 6.7

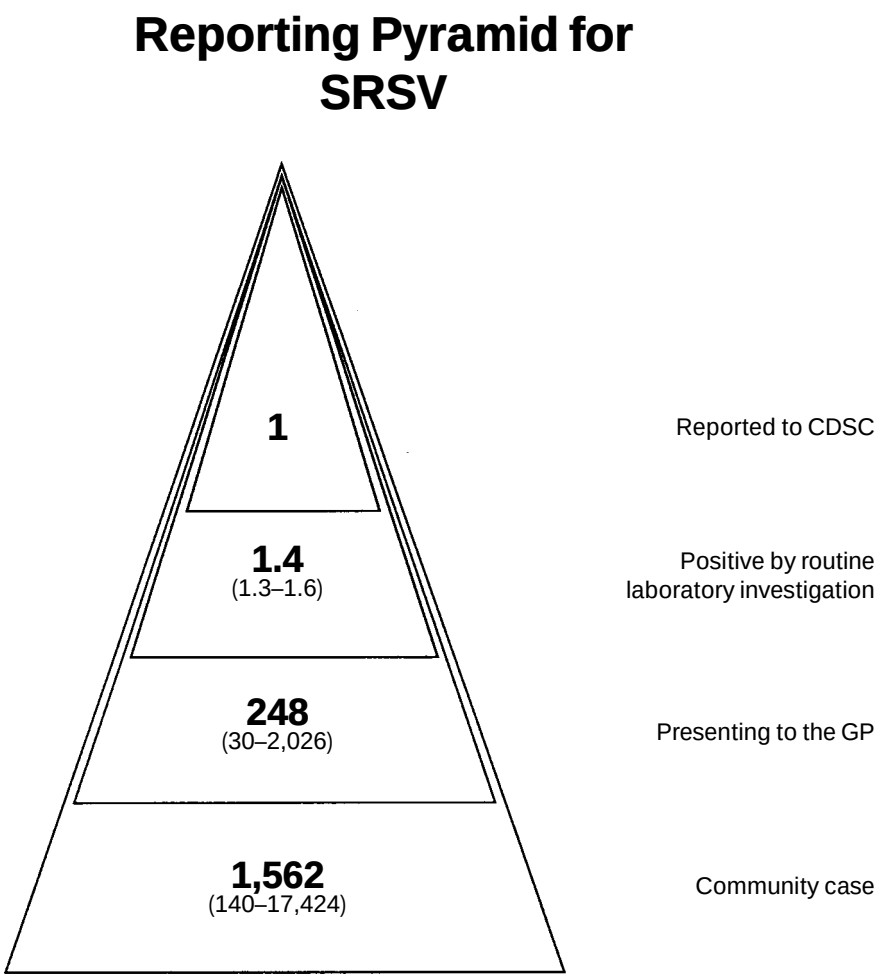
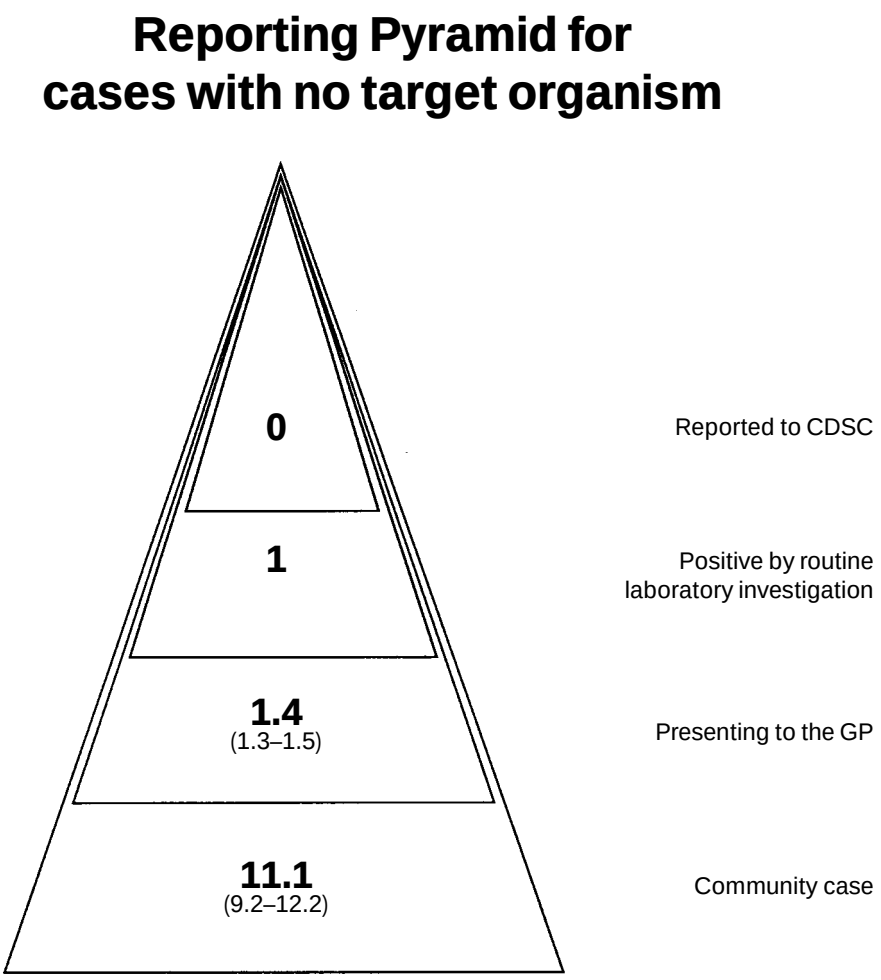

Reporting Pyramid for SRSV
1
Reported to CDSC
1.4
(1.3–1.6)
Positive by routine laboratory investigation
248
(30–2,026)
Presenting to the GP
1,562
(140–17,424)
Community case

Figure 6.8


Reporting Pyramid for cases with no target organism
0
1
1.4
(1.3–1.5)
11.1
(9.2–12.2)
Reported to CDSC
Positive by routine laboratory investigation
Presenting to the GP
Community case

Chapter 7
Symptoms and Duration of Infectious Intestinal Disease (IID)

7.1 SYMPTOMS

7.1.1 Introduction

Frequency, severity and duration of symptoms were reported by cases in the GP and community components on completion of the initial risk-factor questionnaire. Results for children (cases aged up to 15 years) were analysed separately from results for adults (cases aged 15 years and above). Results by organism are presented only for cases where that organism was identified as a single pathogen to avoid confounding symptom profiles produced by mixed infections. Details of symptoms were also requested in the socio-economic questionnaire administered three weeks after the onset of illness and responses are presented separately in section 7.2. A list of symptoms included on the case questionnaires can be found in Appendix 4.

7.1.2 Symptoms in cases

The questionnaire requested details of the presence and severity of 15 separate symptoms, six related specifically to gastrointestinal upset and nine to general symptoms. Separate symptom profiles are shown graphically for both children and adults either presenting to the GP or in the community components. For each of these four groups, analyses are presented for all responses in the group (Figures 7.1 to 7.4), for cases who had no target organism identified (Figure 7.5 and 7.8), and for cases where specific target organisms were identified (Appendix 4, Figures A4.5 –A4.30). Results are presented for target organisms only when there were at least ten cases in the category with the organism identified. Figures are presented without confidence intervals for reasons of clarity. However, Table 7.1 gives examples of confidence intervals depending on the sample size and symptom prevalence. It should be noted that either diarrhoea or vomiting were the symptoms used in the case definition to identify cases for inclusion in the study.

In each of the four groups there were more cases with no target organism identified than there were with any specific target organism (Tables 7.2–7.5). The symptom profile for both adults and children with no target organism was virtually identical to the symptom profile for the whole group. This was true for cases in both the community and GP components.

Diarrhoea, abdominal pain, loss of appetite and nausea were the four most common symptoms in adult cases in both the GP and community components (Figures 7.1 and 7.2). In general, symptoms were more prevalent and severe in adults in the GP component than in the community component. The most common general symptoms reported by adults with IID were high temperature and headache. However, the symptoms of cases must be considered in the light of symptoms experienced by the controls (see paragraph 7.1.3). The four most common symptoms in children in the GP and community components were diarrhoea, loss of appetite, vomiting and abdominal pain (Figures 7.3 and 7.4). Many children in the study were aged under one year and this influences the symptoms reported. As with adult cases, symptoms in children were more severe in the GP component. The

most frequent general symptoms were high temperature and respiratory symptoms. Comparisons of the frequencies of symptoms associated with different organisms are shown in Tables 7.2 –7.5.

The symptom profiles for adults and children were quite different. Overall, fewer symptoms were reported by children with much less frequent reporting of general symptoms except for high temperature. Respiratory symptoms were more common in children. Whereas nausea was more common than vomiting in adults, this was reversed in children. The more obvious signs of illness apparent to parents were more likely to be reported for cases in children.

Considering all cases in each group, the frequency of reports of diarrhoea was similar in both GP and community components for adults, although the diarrhoea was less severe in the community component. Few cases met the case definition of vomiting alone. Whereas 96% of children presenting in the GP component had diarrhoea, identical to the percentage of adults with this symptom, only 80% of children in the community component had diarrhoea. This may reflect the tendency for cases who had only vomited not to present, or may reflect their under-ascertainment in the GP component (see Chapter 4). In general, the overall symptom profiles in cases in the community and in those presenting to the GP were similar, but frequency and severity, were reduced in cases in the community component.

7.1.3 Symptoms in controls compared to cases

The symptoms in cases must be considered in the light of symptoms experienced by the controls. Information was collected from controls about symptoms that were experienced in the three weeks prior to the receipt of the questionnaire (Figures 7.9 and 7.10). It should be noted that the recall period of three weeks for controls was greater than the ten days for cases, making direct comparisons invalid.

In children, only one symptom, loss of appetite, was reported by over 10% of controls in the three weeks prior to completing the questionnaire. In adults, on the other hand, over 10% of controls experienced abdominal pain, over 15% loss of appetite and muscle ache, over 20% joint pains and/or stiffness and/or neck pain and over 30% headache in the three weeks prior to completing the questionnaire. Despite the high incidence in controls, the data do suggest that some of the headaches, and muscle ache and most of the dizziness/faintness reported by cases was attributable to IID. However, the joint and back/neck pain reported was less likely to be due to IID. Respiratory symptoms were common in cases irrespective of the organism identified, particularly in children. Controls were not questioned about respiratory symptoms, nausea and high temperature. As there is no information on respiratory symptoms in controls, it is impossible to estimate any association between IID and the respiratory symptoms described (Figures 7.1 to 7. 4).

7.1.4 Duration of symptoms evaluated at time of acute illness

The duration of five gastrointestinal symptoms in adults presenting to the GP with IID is shown in Figure 7.11. Half of all cases had diarrhoea and abdominal pain lasting at least five days with a quarter of cases still having these symptoms ten days after onset of illness. Nausea, vomiting and bloody diarrhoea, if present, lasted for shorter periods of time. Diarrhoea was present for a slightly shorter time (four days in half of the cases) when no IID target organism was identified (Figure 7.12).

Cases with bacterial target organisms identified had symptoms for longer than cases with viral target organisms. Cases with EAggEC and ETEC infections had the most prolonged symptoms in adults presenting to the GP with a median duration for

diarrhoea of ten and nine days, respectively (Appendix 4, Figures A4.32 and A4.33). In the GP component, children were ill for a longer period than adults, with the median duration of diarrhoea being seven days (compared with five days in adults) and the median duration of vomiting being two days (compared to one in adults) (Figures 7.11 and 7.13). Overall, there was no difference in gastrointestinal symptom duration for all IID cases in children from whom a target organism was identified compared with children in whom no target organism was identified (Figures 7.13 and 7.14).

For adults and childhood cases in the community component (Figures 7.15 and 7.16) the duration of gastrointestinal symptoms was less than for cases in the GP component (Figures 7.11 and 7.13). For all cases in the community component, the median duration of diarrhoea, nausea and abdominal pain was two days and for vomiting it was one day in adults and two days in children. The duration of general symptoms is shown in Figures 7.19 and 7.22.

7.1.5 Incapacity

Cases in the GP component were asked whether they considered themselves to have been incapacitated by their IID (Tables 7.6 and 7.7). Incapacity was defined as being prevented from going about their normal duties. Of adult cases with a target organism identified, 82% reported incapacity, although incapacity was reported by slighty fewer cases in which no target organism was detected (75%). Only 59% of children with a target organism identified were reported to be incapacitated by their illness and again this was reported in slightly fewer (53%) children with no target organism.

7.1.6 Particular symptoms associated with specific organisms

In this section, attention is drawn to symptoms that were remarkable in their frequency, or rarity, in association with specific target organisms relative to all cases of IID (Tables 7.2–7.5). Duration of symptoms, particularly diarrhoea, the most common symptom overall, is also highlighted in Appendix 4, Figures A4.27–A4.42.

7.1.6.1 *Aeromonas*

Of adult cases in the GP component, 6% had bloody diarrhoea and 37% respiratory symptoms. Of cases in children in the GP component, 78% had diarrhoea, 61% respiratory symptoms, 30% headache and 91% vomiting. In the community component, 17% of adult cases had bloody diarrhoea and general symptoms were common with 58% having dizziness and 42% respiratory symptoms. 91% of children had diarrhoea and 36% had headache, vomiting and respiratory symptoms. The median duration of diarrhoea in adult cases was four days in the GP component and two days in the community component (Appendix 4, Figure A4.27).

7.1.6.2 *Campylobacter*

Campylobacter infection was associated with severe symptoms. Of adult cases in the GP component, 17% had bloody diarrhoea, 92% abdominal pain and 76% had a high temperature. Of cases in children in the GP component, 31% had bloody diarrhoea, 81% abdominal pain, 77% a high temperature and 38% headache. The median duration of diarrhoea for adult cases in the GP component was six days, and for children it was seven days. Diarrhoea was severe in 60% of adults and over 50% of children. 45% of the adults with abdominal pain described it as severe. In the community component, 91% of adults had abdominal pain, 91% loss of appetite, 64% a high temperature and 36% bloody diarrhoea. Only 20% of children with *Campylobacter* infection in the community component had vomiting; however, 50% had a high temperature and 80% had abdominal pain (Appendix 4, Figure A4.4).

7.1.6.3 *Clostridium difficile*

There were insufficient cases aged over two years of age in whom *C.difficile* toxin alone was detected for meaningful analysis.

7.1.6.4 *Clostridium perfringens*

Of adult cases in the GP component in whom *C.perfringens* enterotoxin was detected, a greater than average number reported headache (70%), 30% of which was described as severe. There was also an increase in reports of vomiting (60%) but a decrease in the number (45%) reporting high temperature (Appendix 4, Figure A4.5). Childhood cases in the GP component with *C.perfringens* enterotoxin detected also had fewer reports of high temperature than children with other IID and there was decreased reporting of nausea and vomiting. There was an increased reporting of respiratory symptoms and increased severity of these compared with children with IID associated with other target organisms.

In adult cases in the GP component diarrhoea lasted for at least four days in half the cases and there was a median duration of abdominal pain of six days. In the community component, adults with *C.perfringens* enterotoxin had symptoms for half this time with a median duration of two days for diarrhoea and three days for abdominal pain (Appendix 4, Figure A4.30). There were insufficient children with *C.perfringens* enterotoxin and no other target organism for analysis.

7.1.6.5 Enterovirulent *Escherichia coli*

AEEC 69% of adult cases in the GP component had muscle ache and 46% had vomiting, with over 30% having severe vomiting (Appendix 4, Figure A4.7). Vomiting was less frequent in children with only 29% reporting this symptom (Appendix 4, Figure A4.8).

DAEC 68% of adult cases in the GP component had muscle ache, 59% back/neck pain and 9% bloody diarrhoea. The median duration of diarrhoea and abdominal pain was six days. Of children seeing the GP, 9% had bloody diarrhoea and 55% respiratory symptoms (Appendix 4, Figures A4.9, A4.10, and A4.31).

EAggEC 10% of adult cases in the GP component had bloody diarrhoea and were ill for longer then the average for the study, with half the cases still having diarrhoea ten days after onset. 5% of children had bloody diarrhoea and vomiting was relatively uncommon with 30% reporting this symptom (Appendix 4, Figures A4.11 and A4.12).

ETEC As this organism was infrequently identified in children, data for childhood cases is not presented. In adult cases in the GP component, diarrhoea was common with over 60% reporting severe diarrhoea and only 11% vomiting. Duration of illness was prolonged with a median duration of diarrhoea of nine days. Abdominal pain was present in 93%. General symptoms were uncommon (Appendix 4, Figures A4.13 and A4.33).

7.1.6.6 *Salmonella*

This organism was associated with severe symptoms. Of adult cases in the GP component, 92% had abdominal pain, 94% loss of appetite, 20% bloody diarrhoea, 86% high temperature, 73% headache, 72% muscle ache and 59% faintness/ dizziness. The median duration of diarrhoea was six days but 25% still had diarrhoea at fourteen days. Over 70% of adults had severe diarrhoea and over 60% had severe abdominal pain. Children presenting in the GP component also had severe symptoms with 25% having bloody diarrhoea, 59% nausea (not a symptom commonly reported by children), 75% abdominal pain, 100% loss of appetite, 88% a high temperature, 50% a headache, 29% muscle ache and 19% joint and neck pain (the last three symptoms were uncommon in children with other, or no, target organisms). Diarrhoea was said to be severe in over 50% of the children (Appendix 4, Figure A4.15). There were insufficient cases in the community component for analysis.

7.1.6.7 *Shigella*

There were insufficient cases with *Shigella* as the sole organism identified for meaningful analysis.

7.1.6.8 *Yersinia*

There were 86% of adult cases in the GP component with diarrhoea (a relatively low figure when compared to IID associated with other organisms). However, of these, 14% reported having blood in the stool. Respiratory symptoms were common (50%) whereas abdominal pain (64%) and high temperature (29%) were relatively uncommon. Diarrhoea in adults had a median duration of five days with abdominal pain having a longer median duration of nine days in the small number of cases reporting this symptom (Appendix 4, Figures A4.16 and A4.35) Abdominal pain has been documented as occurring in infection with known pathogenic types of *Yersinia*.

7.1.6.9 *Cryptosporidium*

There were insufficient cases in adults for analysis. 95% of cases in children in the GP component had diarrhoea, with a median duration of seven days. General symptoms such as high temperature and headaches were relatively uncommon, 32% and 5%, respectively (Appendix 4, Figure A4.17).

7.1.6.10 *Giardia*

There were insufficient cases in children for analysis. Diarrhoea in adults in the GP component had a lengthy duration of eight days with 25% still reporting diarrhoea at 13 days. General symptoms were relatively uncommon with the lowest reported frequencies of loss of appetite (58%), headaches (33%) and muscle ache (25%) associated with any of the target organisms (Appendix 4, Figure A4.18).

7.1.6.11 *Adenoviruses*

Diarrhoea due to adenovirus infection had a median duration of six days in cases in children in the GP component (Appendix 4, Figure A4.36). In cases in children in the community component, 82% had vomiting but headache was infrequently reported (10%) (Appendix 4, Figure A4.19).

7.1.6.12 *Astroviruses*

Diarrhoea was reported by all adult cases in the GP component and over 60% described the diarrhoea as severe. 95% had loss of appetite but respiratory symptoms were uncommon (10%) (Appendix 4, Figure A4.20). In cases in children in the GP component, abdominal pain was a notable feature, being described in 82%, and again diarrhoea was present in every individual with this organism (Appendix 4, Figure A4.21). The median duration of diarrhoea was four days in adults and seven days in children presenting in the GP component (Appendix 4, Figures A4.37 and A4.38).

7.1.6.13 *Caliciviruses*

This organism was found in sufficient numbers for analysis only in cases in children in the GP component. All had diarrhoea, with a median duration of eight days, and 84% had vomiting. General symptoms were uncommon, for example high temperature occurred in only 26% of children (Appendix 4, Figure A4.22).

7.1.6.14 *Rotaviruses*

Of the five virus types included in the target organisms identified, rotaviruses produced the most severe symptoms. In the GP component, 81% of adult cases experienced nausea. However, vomiting was no more common (42%), than with other, or no target organisms. 92% had loss of appetite and 50% back pain (Appendix 4, Figure A4.23). Vomiting was a prominent feature of rotavirus infection in childhood cases in the GP component with 97% experiencing this symptom, 86% reported loss of appetite and 60% a high temperature. It was the highest

frequency for high temperature in childhood cases in the GP component with any of the viral causes of IID. Diarrhoea was described as severe in over 60% of the adults and over 50% of the children with rotavirus in the GP component, and had a median duration of four days in adults and six days in children. 25% of children still had diarrhoea at ten days and 25% of adults still had nausea at seven days after onset. In the community, 94% of children had vomiting and 82% had diarrhoea and loss of appetite. There were insufficient adult cases with rotavirus in the community component for analysis (Appendix 4, Figures A4.23, A4.24, A4.39 and A4.40).

7.1.6.15 *SRSVs*

Vomiting was a notable symptom of infection with SRSVs. In the GP component, 82% of adult cases experienced nausea and 77% vomiting, with 91% having loss of appetite and 64% muscle aches. 95% of cases in children in the GP component had vomiting whilst 83% had loss of appetite and 61% high temperature. In the community component, 75% of adult cases had nausea and 69% vomiting. 69% of cases in children in the community component had nausea, 92% had vomiting and 92% loss of appetite, with 69% having a high temperature and 54% respiratory symptoms. The vomiting was described as severe in over 50% of adults in both the GP and community components. The median duration of symptoms in adults, including diarrhoea, was relatively short, being two days in both the GP and community components. SRSV infection in children caused a more prolonged illness than in adults, with diarrhoea continuing for a median duration of five days in cases in children in the GP component. There were insufficient cases in children in the community component for analysis (Appendix 4, Figures A4.25, A4.26, A4.41 and A4.42).

7.1.6.16 *No target organism detected*

Symptom profiles, in terms of both frequency and severity, of cases with no target organism detected were virtually identical to those of all cases of IID (Figure 7.5). The duration of gastrointestinal symptoms was also identical for those with no target organism for all adult cases in the community component (Figure 7.15). However, for adult cases in the GP component the median duration of diarrhoea was five days for all cases and four days for those with no target organism detected (Figure 7.11).

7.2 DURATION OF THE ILLNESS, AND SYMPTOMS AFTER THE ACUTE PHASE

The characteristics of the illness in the post-acute phase (reported three weeks after the onset of the illness) were also collected. This information has been analysed for those responding to the economic questionnaire, a sub-group of 4,389 respondents. The analysis of data by organism was restricted to target organisms that were represented in sufficient numbers for statistical analysis. The questions were also less specific. As a result, this information complements, but is not directly comparable with, information from the analysis of the risk-factor questionnaire reported in section 7.1 above.

7.2.1 Duration of the illness by study component, sex and age

The duration of illness has important implications for the socio-economic burden of disease. It is difficult to obtain accurate estimates for duration of illness from studies that rely upon the return of questionnaires because the administration of the research instrument (date questionnaire was delivered, reminders sent and return of questionnaire) affects the estimate. In the socio-economic component, estimates relate to the interval between consultation and the completion of the questionnaire that was sent at three weeks. 73% of questionnaires were returned within seven weeks, but 10% were returned after 35 weeks. The conventions adopted to assess the duration of the illness are described in Chapter 3.

7.2.1.1 *Duration of illness by study component, sex, and age*

The patterns of illness reported in the GP component and enumeration component were very similar. The mean duration of illness was 8.6 days and 7.9 days, respectively, and the maximum length of illness was 80 days. Cases in the community component reported illness of shorter duration, 3.9 days on average, with a maximum length of 40 days and fewer reporting illness lasting beyond seven days. The 149 cases in the community component who had also seen their GP reported an average of 6.9 days illness (range 0.5–40), compared to 2.8 days (range 0–21) in those who had not seen their GP.

55% and 58% of cases in the GP and enumeration components respectively reported that they were ill for seven days or less, whilst 75% and 83% respectively, were ill for 14 days or less. This was consistent with estimates from the questionnaire administered in the acute phase. 88% and 90% of cases, respectively, were ill for 21 days or less and 90% of cases in both components were ill for 28 days or less. Two cases in the GP component were ill for longer than ten weeks and four cases in the enumeration component were ill for eight weeks or more.

The duration of illness amongst cases in the community component who did not consult a GP was much shorter: 86% of the cases were ill for five days or less, 91% ill for seven days or less and 93% were ill for 14 days or shorter. The longest duration of illness was 21 days. The duration of illness in cases in the community component who consulted a GP was similar to that in the GP and enumeration component, 64% of cases reported that they were ill for seven days or less, 82% were ill for 14 days or less, 86% were ill for 21 days or less and 88% of cases in this component were ill for 28 days or less (Appendix 4, Figure A4.45).

The duration of illness in men and women in the GP component was similar, 8.6 days. The range was wider for women (0–80 days), than for men (0–56 days). The mean duration of illness was longest for adults of working age (9.5 days), followed by the elderly (8.2 days). It was shortest for children of school age (7 days). Children under one and of school age had the narrowest range of duration of illness, 0–27 and 0–28 days, respectively.

In the enumeration component, males were ill for an average of 8.0 days. However, the range was 0–80 days for women and 0– 58 days for men. There was no discernible age pattern in the cases in the enumeration component.

In the community component, women had the longest mean length of illness, 4.4 days compared to 3.3 days for men, with ranges of 0–35 days and 0–40 days, respectively. In the community component, children under one year old were ill for longer than adults.

7.2.2 **Duration of the illness by organism**

For cases in the GP and community components it was possible to analyse the duration of illness by target organism for the main target organisms.

For those cases in the GP component with no target organism identified, 663 cases were ill for a total of 5,522 days. This represents a mean of 8.3 days (range 0–80 days). The longest mean length of illness for any organism was 11.1 days (range 5–74 days), for cases with EAggEC. A total of 2,193 days illness was recorded for 198 cases. In 80% of cases with EAggEC, illness lasted up to 14 days, but in 20% of cases it extended beyond this point, lasting up to six weeks, with one case being ill for ten weeks.

The mean duration of illness was similar for cases of infection with *Salmonella* and *Campylobacter*, 10.9 and 9.3 days, respectively, although the range of illness differed. Ninety cases of *Salmonella* infection were ill for between 2.5 and 42 days,

and 192 cases of *Campylobacter* infection were ill for between 1 and 56 days. No cases of *Salmonella* infection persisted beyond six weeks. The median reported duration for *Campylobacter* illness was seven days although three cases persisted for five weeks or more. Cases due to *C.difficile* and rotavirus group A infection reported very similar mean durations of illness and the range was also very similar. The duration of illness for cases with *C.difficile* peaked twice, at four and nine days. Most had recovered by eight days but two cases persisted for 20 days and five weeks respectively. The median duration of illness for rotavirus group A was six days. Most cases had recovered within 15 days, but two cases persisted for 21 days and 28 days, respectively. SRSV produced the shortest duration of illness with a median of 5.8 days and the narrowest range of duration (1 to 21 days). Only two cases were ill beyond 14 days (Appendix 4, Figure A4.59).

Most cases in the community component had recovered by ten days and the median length of illness was four days. In one case the illness persisted for 21 days. There were only four cases of *Salmonella* infection in the community component and these cases were ill for between 3.5 and 14 days. Cases of rotavirus group A infection were largely resolved by seven days with one case persisting for 11 days. For cases of SRSV infection the median duration was two days. All cases had recovered by the eighth day (Appendix 4, Figure A4.59).

7.2.3 Symptoms after the acute phase

The socio-economic questionnaire was administered three weeks after the onset of the illness to all cases and provided an opportunity to assess the symptoms that had persisted. The symptoms included some that were asked about initially and some that were added in order to explore aspects that might indicate longer term sequelae. The symptom profiles were collected for each component of the study, for adults and children and for the most important target organisms. The persistence of and combination of symptoms is explored by study component, and by target organism, for adults and children.

7.2.3.1 *Symptoms after the acute phase by study component*

After the acute phase 42% of cases in the GP component, 58% in the community component and 32% of the enumeration component recorded persistent symptoms. Only 17 cases recorded more than ten symptoms, 3% of the cases in the community component, 6% in the GP component and 9% in the enumeration component.

The symptoms most commonly reported at three weeks were diarrhoea, tiredness and abdominal pain. 28% of all cases in the GP component (29% of the adults and 25% of the children) had diarrhoea at three weeks. In the enumeration component, 39% of adults and 36% of children reported diarrhoea, and in the community component 17% of adults and 16% of children did so. Tiredness was reported by 29% of cases in the GP component, 35% in the enumeration component and 18% of cases in the community component. Abdominal pain was the next most common symptom, reported by 25% of cases in the GP component, 34% of cases in the enumeration component and 18% of cases in the community component. More adults than children reported abdominal pain. In cases in the GP component, 30% of adults and 16% of children reported abdominal pain, as did 38% of cases in adults and 28% of cases in children in the enumeration component and 19% of the cases in adults and 15% of cases in children in the community component.

Bloody diarrhoea was reported by 3% of all cases in the GP component (4% of the adults and 0.5% of the children), 4% of cases in the enumeration component (5% of adults and 2% of children) and 2% of the cases in the community component (3% adults and 1% children) (Appendix 4, Table A4.8).

Loss of appetite was a common symptom in cases in the GP component, reported by 23% of adults and 18% of children. It was reported more frequently in the enumeration component, 33% in adults and children, but less frequently in cases in the community component, 11% and 16% for adults and children, respectively. Cases reported loss of appetite more frequently than controls. Flatulence was reported most frequently by cases in the enumeration component, 25% of adults and 18% of children (Appendix 4, Table A4.8).

Pain, whether general aches, headaches or pains in joints or limbs, was reported more frequently by adults than children. Headache was reported by 20% of adult cases and 10% of cases in children in the GP component. Dizziness, double vision, unsteadiness, pins and needles and hand and leg weakness were commoner in adults than children in all components. Clumsiness, however, was commoner in adults in the community component. These symptoms were all less common in cases in the community than in the enumeration component or GP components. Controls were not asked about these symptoms. Rashes were most common in children in all study components (Appendix 4, Table A4.8)

Red eyes were most commonly reported by cases in the enumeration component followed by the GP component. It was reported by 6% and 5% of adult cases, respectively, and 4% and 3% of cases in children (Appendix 4, Table A4.8).

7.2.3.2 *Symptoms after the acute phase for five selected target organisms*

Symptoms by organism at three weeks are reported for the GP component only as numbers in the community component were too small for analysis at this level.

Campylobacter

In the post-acute period, 32 children in the GP component who had *Campylobacter* infection reported symptoms. Six cases (19%) reported tiredness, five (16%) reported abdominal pain, three (10%) diarrhoea and two(6%) weight loss. Adult cases of *Campylobacter* infection also reported symptoms: 64 adults (41%) reported tiredness, 57 (36%) abdominal pain (three times that reported by the controls), 51 (32%) diarrhoea, 40 (25%) sleepiness and weight loss, flatulence and aches were reported by 22% of adults. 18% reported headaches, slightly higher than for rotavirus infection. Backache was reported by fewer cases than controls (Appendix 4, Table A4.9).

Salmonella

15 (22%) adults and 7 (32%) children in the GP component who had *Salmonella* infection reported diarrhoea in the post-acute period of their illness. Six of the children (27%) reported abdominal pain, a higher proportion than in controls. 33 (50%) adult cases reported tiredness and 19 (29%) reported abdominal pain, 2.9 times the proportion of controls (Appendix 4, Table A4.9).

EAggEC

12 (28%) adults and 3 (10 %) children reported diarrhoea. Two cases of bloody diarrhoea were reported by adults (Appendix 4, Table A4.9).

Rotaviruses

Two adults and four children reported diarrhoea in the post-acute period (but there were no reports of bloody diarrhoea). Abdominal pain and loss of appetite were the next most common symptoms.

SRSVs

13 children (31%) with SRSV reported diarrhoea, 11 (26%) tiredness, 10 (24%) loss of appetite. This was higher than the proportion reported in controls.

7.2.3.3 *Comparison of symptoms in the acute and post-acute phase*

21% of the cases that reported diarrhoea in the acute phase also reported diarrhoea in the post-acute phase. 46% of cases reporting bloody diarrhoea also reported continuation of the symptom, as did 20% of those who reported vomiting and 29% of those with abdominal pain. Continuation of symptoms was also reported by 64% of those reporting back pain by 39% of those with general aches and pains, and by 35% of those with headache. 31% of cases reporting dizziness and 73% of those reporting red eyes during the acute phase also reported them during the post-acute period.

In the GP component, diarrhoea persisted at three weeks in 31% of those who suffered it in the acute phase: bloody diarrhoea persisted in 39% of cases acutely affected, and vomiting in 20% of cases, abdominal pain in 37%, and loss of appetite in 31%. 77% of those reporting joint pain initially and 93% of those reporting joint swelling reported symptoms persisting, as did 35% of those with back pain, 40% with headache, 29% with dizziness and 69% with red eyes.

7.3 SUMMARY

7.3.1 The duration of the symptoms and severity of the illness in the acute phase

Not surprisingly, symptoms were more severe, more frequent and of longer duration in cases in the GP component than in cases in the community component.

Children were less likely to report non-gastrointestinal symptoms than adults. In the GP component, the duration of illness was longer in children than in adults but the duration was similar in children and adults in the community component.

Campylobacter and *Salmonella* infection caused the most severe illness with raised temperature and bloody motions being most frequently reported in association with these pathogens in both adults and children in the GP component.

Vomiting was most frequently reported in association with SRSV infection in adult cases and with SRSV and rotavirus group A infection in children.

Although the most target organism in the community component was SRSV, illness was generally short-lived with a median duration of only two days in adults.

The frequency and severity of symptoms, and the duration of gastrointestinal symptoms, in cases in whom there was no target organism or toxin identified, were very similar to the symptoms for all cases of IID combined. This group's symptomatology does not resemble the characteristic symptom pattern of SRSV infection, strongly suggesting that undetected SRSV infections are not responsible for the majority of these microbiologically negative cases.

7.3.2 Duration and characteristics of symptoms in the post-acute phase

There are considerable difficulties in measuring the duration of symptoms using questionnaires, as distortions may arise because of the timing of them. There is possibly some under-reporting as a result. One of the reasons for not returning a questionnaire may have been severity of illness or hospitalisation. The numbers of rare but serious illnesses such as *E.coli* O157 and *Shigella* infection were, in our study, small and response rates were disproportionately low (see Chapter 4). This may have introduced bias, which may have underestimated the duration of illness and the symptoms experienced. The numbers were very small in many categories and interpretation at organism level should be viewed with caution.

There was considerable morbidity in the days following the acute attack. The duration of the illness was longer for bacterial infections than for the viruses and appears to be longer than is often reported in the literature.

The proportion of cases reporting persistent symptoms was large. In general, adults reported more symptoms than children. This may reflect biases in reporting symptoms that may be less obvious in young children. Children were, however, more likely to have rashes.

Persistent symptoms included tiredness and abdominal pain, and these were much commoner in cases than in controls.

Following *Campylobacter* infection, general weakness, pins and needles and clumsiness were more commonly reported than in controls or other cases of IID. Headaches and backaches, and joint aches and pains were reported less commonly than in controls.

7.3.3. Comparison with published literature

The symptoms and duration of illness reported by cases in this study are generally consistent with descriptions in standard texts (Mandell *et al*. 1995, Collier *et al.* 1998), particularly for disease associated with *Campylobacter*, *Salmonella*, *Cryptosporidium*, *Giardia*, adenoviruses, astroviruses, caliciviruses, rotaviruses and SRSVs. There is less information about symptoms associated with the enterovirulent *E.coli,* but watery diarrhoea is usually the predominant presentation (Nataro and Kaper 1998, Smith and Cheasty 1998). Pathogenic *Yersinia* spp. cause an enterocolitis with diarrhoea, fever and abdominal pain lasting from one to three weeks (Butler 1995). Our results probably include a mixture of cases either with pathogenic or with non-pathogenic strains thus complicating the picture. The clinical presentation of disease associated with *Aeromonas* spp. is varied, with watery diarrhoea being the most common symptom. Occasionally, the disease presents with fever, abdominal pain, bloody stools and a protracted course (Smith and Cheasty 1998). The cases in this study probably included a mixture of individuals with pathogenic and non-pathogenic strains. Symptoms reported in this study associated with *C.perfringens* enterotoxin are not consistent with previous reports, where the information has largely been derived from outbreaks. In cases such as these, symptoms are predominantly watery diarrhoea and abdominal pain with a small minority describing nausea, fever and vomiting, and a short duration of six to twenty-four hours (Lorber 1995, Gilbert and Humphrey 1998). In this study, symptoms were more varied and of longer duration. *C.perfringens* has been described as a cause of antibiotic associated diarrhoea and of infectious diarrhoea which may occur as an outbreak. It is possible that sporadic cases have a different clinical presentation to cases associated with outbreaks (Larson and Borriello 1988).

Table 7.1 Confidence intervals for symptom profiles

PERCENT WITH SYMPTOM	SAMPLE SIZE (N)						
	10	20	30	50	100	500	1000
10	0.3 , 44	1 , 32	2 , 27	3 , 22	5 , 18	7 , 13	8 , 12
30	7 , 65	12 , 54	15 , 49	18 , 45	21 , 40	26 , 34	27 , 33
50	19 , 81	27 , 73	31 , 69	36 , 64	40 , 60	45 , 54	47 , 53
70	35 , 93	46 , 88	51 , 85	55 , 82	60 , 79	66 , 74	67 , 73
90	55 , 99	68 , 98	73 , 98	78 , 97	82 , 95	87 , 93	88 , 92

Confidence intervals for the bars depend on the sample size and the height of the bar (percent of cases with the symptom).

Table 7.2 Symptoms in adults presenting to the GP. For all cases and target organism (percent with symptom regardless of severity)

	ALL	AEEC	AERO	ASTRO	CAMP	CPERF	DAEC	EAGGEC	ETEC	GIARD	ROTA	SALM	SRSV	YERS	NO ORG
Size of sample	1,615	13	35	21	186		22	39	28	12	21	71	56	14	698
Diarrhoea	96	100	91	100	99	100	95	97	100	100	100	100	93	86	94
Blood in stool	11	0	6	0	17	11	9	10	7	0	0	20	2	14	10
Nausea	69	69	74	71	59	78	73	67	50	75	81	70	82	71	70
Vomiting	44	46	49	29	30	59	50	41	11	42	42	35	77	50	45
Abdominal pain	85	85	77	67	92	96	77	87	93	75	77	92	86	64	84
Loss of appetite	80	69	77	95	81	85	91	69	68	58	92	94	91	64	77
High temperature	58	54	49	43	76	44	55	49	39	42	65	86	61	29	54
Headace	57	69	51	57	62	70	55	54	36	33	58	73	59	50	55
Muscle ache	50	69	60	62	59	56	68	49	32	25	58	72	64	50	46
Dizzy/Faint	43	38	40	48	38	44	36	36	18	42	54	59	48	29	43
Cough/Nose/Throat	24	23	37	10	23	22	27	36	14	50	12	8	27	50	25
Red eyes	8	8	6	10	5	7	0	13	4	8	12	6	7	70	9
Joint pain/Stiffness	28	31	34	43	33	30	23	26	4	8	38	41	36	21	25
Back/Neck pain	37	46	29	33	44	22	59	26	29	25	50	46	36	29	36
Joint swelling	5	15	9	5	5	7	0	3	4	0	4	6	2	7	7
Other symptoms	9	23	9	24	12	4	5	5	7	17	15	7	2	7	10

ALL = All cases
AEEC = Attaching and effacing *E.coli*
AERO = *Aeromonas*
ASTRO = *Astroviruses*
CAMP = *Campylobacter*
CPERF = *Clostridium perfringens*
DAEC = Diffusely adherent *E.coli*
EAGGEC = Enteroaggregative *E.coli*
ETEC = Enterotoxigenic *E. coli*
GIARD = *Giardia*
ROTA = Rotaviruses
RSSV = Small round structured viruses
YERS = *Yersinia*
NO ORG = No target organism or toxin detected

Table 7.3 Symptoms in children presenting to the GP. For all cases and by target organism (percent with symptom regardless of severity)

	ALL	ADENO	AEEC	AERO	ASTRO	CALIC	CAMP	CPERF	CRYPT	DAEC	EAGGEC	ROTA	SALM	SRSV	NO ORG
Size of sample	1,009	48	31	23	24	23	29	15	19	11	20	112	17	44	316
Diarrhoea	96	100	97	78	100	100	100	100	95	100	95	98	100	93	95
Blood in stool	4	2	0	0	4	0	28	0	0	9	5	0	24	0	3
Nausea	34	23	26	39	42	26	48	20	42	36	35	42	59	39	28
Vomiting	68	73	29	91	75	83	66	47	47	55	30	97	59	95	61
Abdominal pain	54	50	42	43	79	43	83	60	63	55	60	53	76	48	53
Loss of appetite	77	88	58	87	92	78	79	80	74	73	65	87	100	82	69
High temperature	47	38	42	61	42	30	72	20	32	45	30	60	88	59	42
Headache	17	10	6	30	17	4	45	7	5	9	25	9	47	14	18
Muscle ache	10	4	10	9	8	0	24	0	11	9	5	8	29	7	10
Dizzy/Faint	9	4	10	13	8	4	21	7	0	9	10	9	12	11	8
Cough/Nose/Throat	43	46	26	61	42	35	41	67	37	55	40	44	35	41	45
Red eyes	9	4	3	17	4	0	7	0	16	18	5	10	0	5	9
Joint pain/Stiffness	4	0	0	0	0	0	0	0	0	9	5	4	24	2	4
Back/Neck pain	5	2	0	9	8	4	10	0	0	9	5	3	18	2	6
Joint swelling	1	0	0	0	0	0	3	0	0	9	0	1	0	0	0
Other symptoms	9	6	3	9	13	13	10	20	5	9	0	10	12	5	10

ALL = All cases
AEEC = Attaching and effacing *E.coli*
AERO = *Aeromonas*
ASTRO = *Astroviruses*
CAMP = *Campylobacter*
CPERF = *Clostridium perfringens*
DAEC = Diffusely adherent *E.coli*
EAGGEC = Enteroaggregative *E.coli*
ETEC = Enterotoxigenic *E. coli*
GIARD = *Giardia*
ROTA = Rotaviruses
RSSV = Small round structured viruses
YERS = *Yersinia*
NO ORG = No target organism or toxin detected

Table 7.4 Symptoms in adults in the population cohort component and most common target organism (percent with symptom regardless of severity)

	ALL	AERO	CAMPYL	SRSV	NO ORG
Size of sample	389	12	11	169	250
Diarrhoea	94	100	100	94	92
Blood in stool	5	17	36	6	5
Nausea	49	50	64	75	45
Vomiting	31	25	18	69	30
Abdominal pain	72	58	91	69	72
Loss of appetite	60	75	91	63	56
High temperature	30	50	64	25	27
Headache	39	58	45	44	39
Muscle ache	25	33	36	25	25
Dizzy/Faint	22	58	18	6	20
Cough/Nose/Throat	16	42	0	19	14
Red eyes	4	0	9	0	5
Joint pain/Stiffness	15	33	9	13	16
Back/Neck pain	20	33	36	19	20
Joint swelling	6	8	0	6	7
Other symptoms	10	17	9	13	12

ALL = All cases
AERO = *Aeromonas*
CAMPL = *Campylobacter*
SRSV= Small round structured viruses
NO ORG = No target organism or toxin detected

Table 7.5 Symptoms in children in the population cohort component and by most common target organism (percent with symptom regardless of severity)

	ALL	ADENO	AERO	CAMPYL	ROTA	SRSV	NO ORG
Size of sample	290	11	11	10	17	14	130
Diarrhoea	80	91	91	100	82	79	75
Blood in stool	1	0	0	0	0	0	1
Nausea	35	36	55	10	29	64	31
Vomiting	57	82	36	20	94	93	48
Abdominal pain	60	55	55	80	47	57	58
Loss of appetite	67	82	73	60	82	93	58
High temperature	34	27	27	50	47	64	30
Headache	22	9	36	20	24	14	22
Muscle ache	9	9	18	20	18	14	6
Dizzy/Faint	8	9	36	0	6	7	8
Cough/Nose/Throat	33	27	36	40	41	50	30
Red eyes	4	0	18	20	6	0	2
Joint pain/Stiffness	3	0	9	10	0	7	2
Back/Neck pain	4	9	9	0	0	7	6
Joint swelling	0	0	0	0	0	0	0
Other symptoms	9	9	27	10	12	7	8

ALL = All cases
ADENO = *Adenoviruses*
AERO = *Aeromonas*
CAMPYL = *Campylobacter*
ROTA = Rotaviruses
RSSV= Small round structured viruses
NO ORG = No target organism or toxin detected

Table 7.6 Proportion of cases incapacitated by illness in the GP component: children

ORGANISM	INCAPACITATED	
All IID	568/995	(59%)
Bacteria		
Aeromonas spp.	17/23	(74%)
Bacillus spp. (>10^4/g)		
Campylobacter spp.	21/28	(75%)
Clostridium difficile cytotoxin	4/6	(67%)
Clostridium perfringens enterotoxin	3/15	(20%)
AEEC	10/31	(32%)
DAEC	5/11	(45%)
EAggEC	12/20	(60%)
EIEC		
EPEC		
ETEC	2/2	(100%)
VTEC		
Salmonella spp.	16/17	(94%)
Shigella spp.	1/1	(100%)
Staphylococcus aureus (>10^6/g)		
Vibrio spp.		
Yersinia spp.	3/8	(37%)
Protozoa		
Cryptosporidium parvum	7/18	(39%)
Giardia intestinalis	2/2	(100%)
Viruses		
Adenovirus types 40,41	24/47	(51%)
Astrovirus	14/23	(61%)
Calicivirus	10/23	(43%)
Rotavirus group A	84/111	(76%)
Rotavirus group C	3/4	(75%)
SRSV		
No target organism	165/313	(53%)

Table 7.7 Proportion of cases incapacitated by illness in the GP component: adults

ORGANISM	INCAPACITATED	
All IID	1,268/1,605	(82%)
Bacteria		
Aeromonas spp.	28/37	(76%)
Bacillus spp. (>10^4/g)		
Campylobacter spp.	166/195	(85%)
Clostridium difficile cytotoxin	9/9	(100%)
Clostridium perfringens enterotoxin	24/27	(89%)
E. coli O157	2/2	(100%)
AEEC	12/15	(80%)
DAEC	17/23	(74%)
EAggEC	27/42	(64%)
EIEC		
EPEC	2/2	(100%)
ETEC	20/29	(69%)
VTEC	1/1	(100%)
Salmonella spp.	70/75	(93%)
Shigella spp.	4/5	(80%)
Staphylococcus aureus (>10^6/g)	3/4	(75%)
Vibrio spp.	1/1	(100%)
Yersinia spp.	11/15	(73%)
Protozoa		
Cryptosporidium parvum	4/5	(80%)
Giardia intestinalis	8/11	(73%)
Viruses		
Adenovirus types 40,41	3/3	(100%)
Astrovirus	19/22	(86%)
Calicivirus	1/3	(33%)
Rotavirus group A	23/28	(82%)
Rotavirus group C	1/1	(100%)
SRSV		
No target organism	544/726	(75%)

Symptom profile of all IID cases (adults): presenting to GPs

Figure 7.1 Presenting to the GP

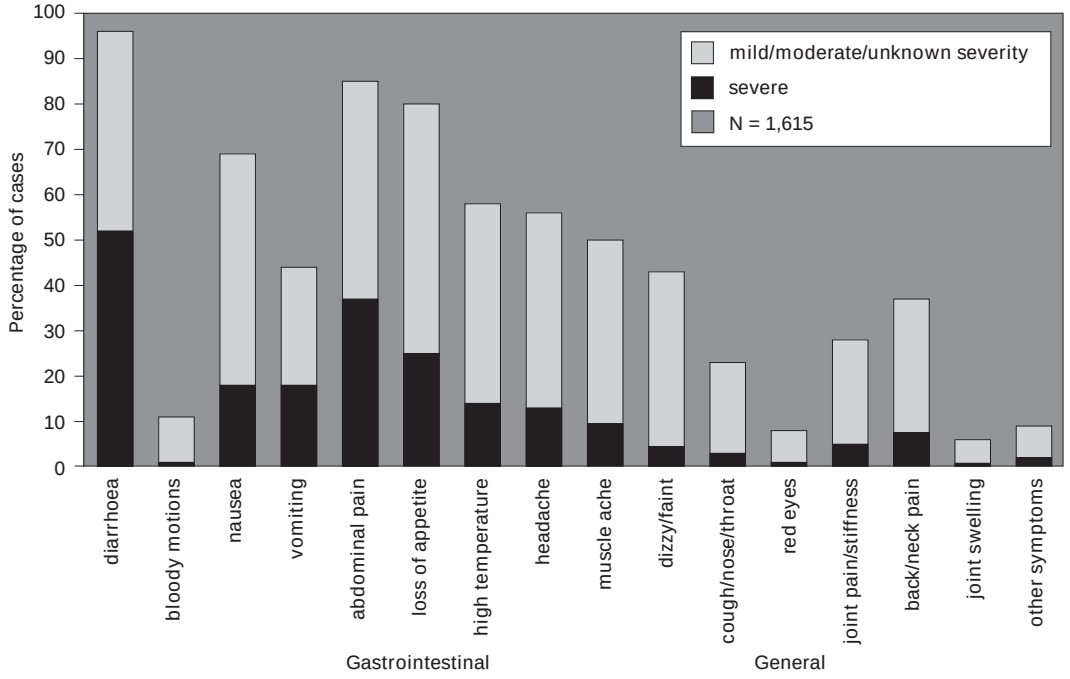
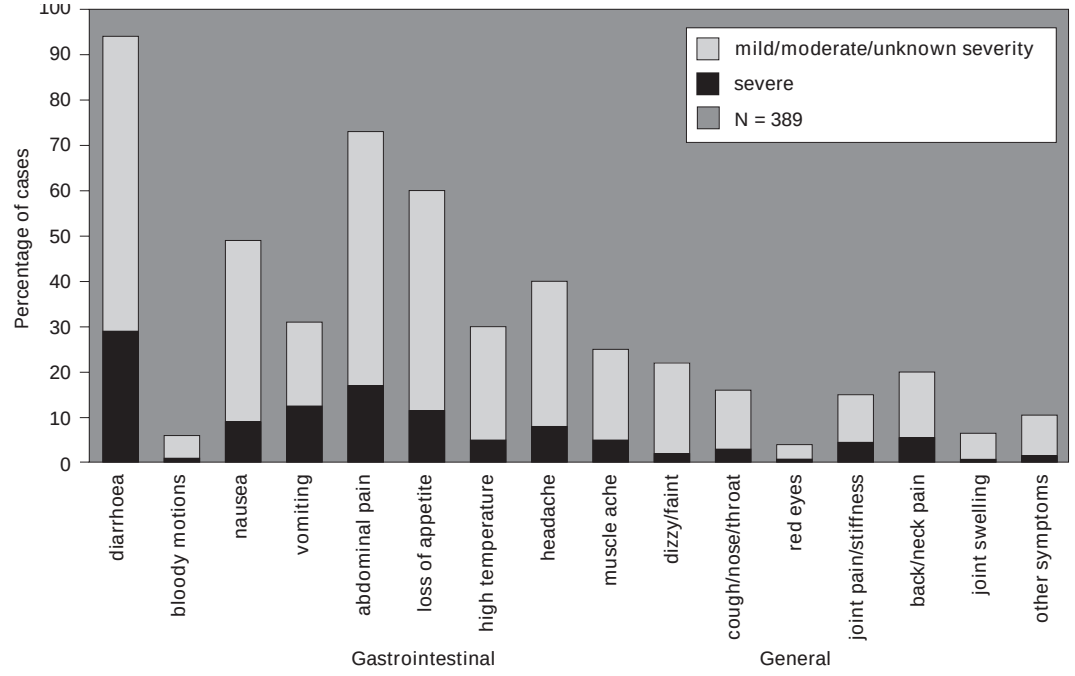


Figure 7.2 In the population cohort component



Symptom profile of all IID cases (children)

Figure 7.3 Presenting to the GP

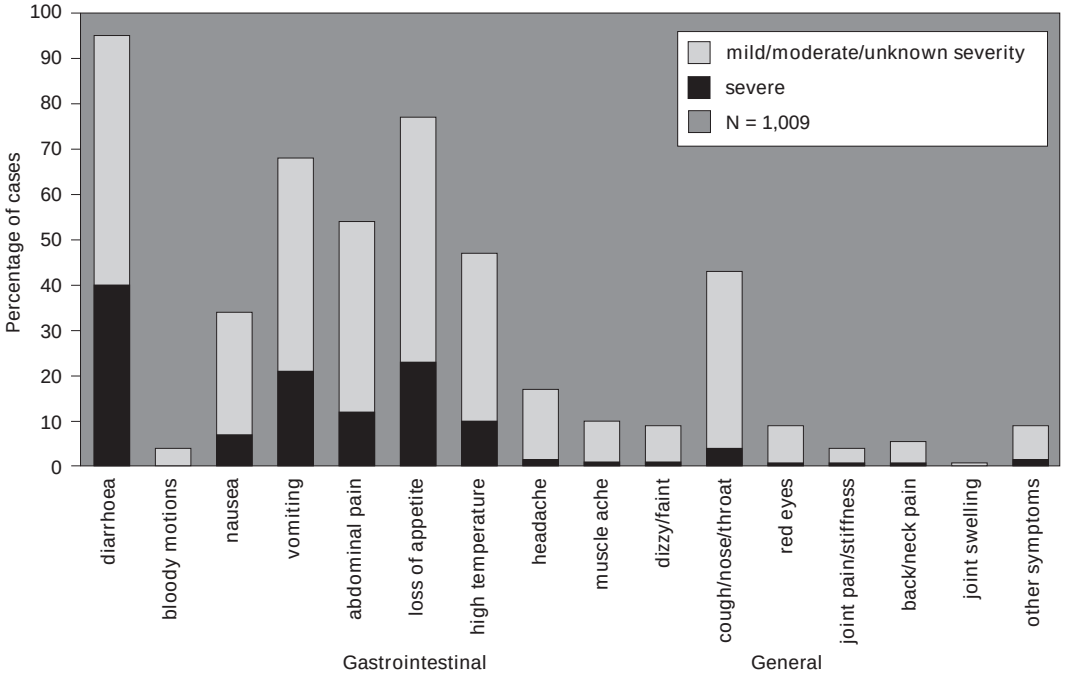
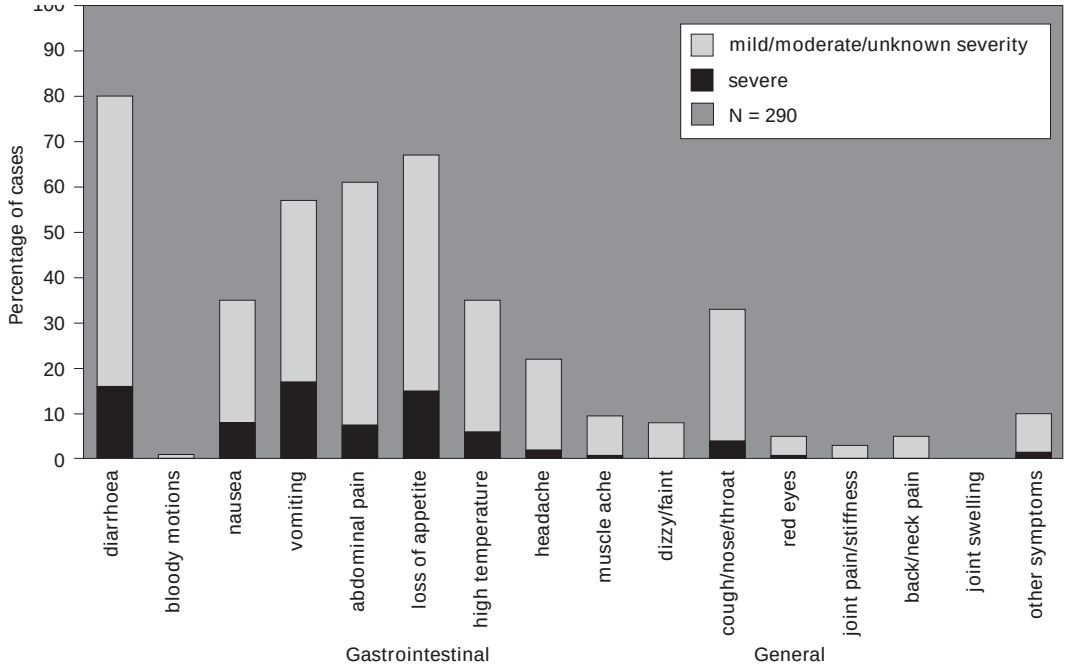


Figure 7.4 In the population cohort component



Symptom profile of all cases with no target organism (adults)

Figure 7.5 Presenting to the GP

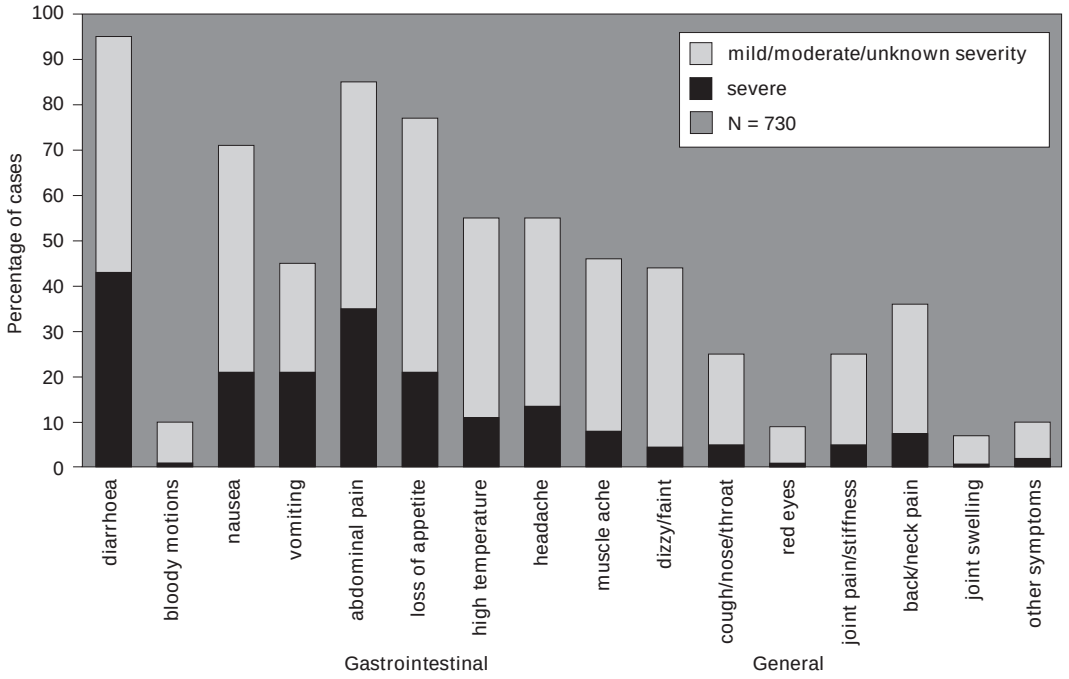
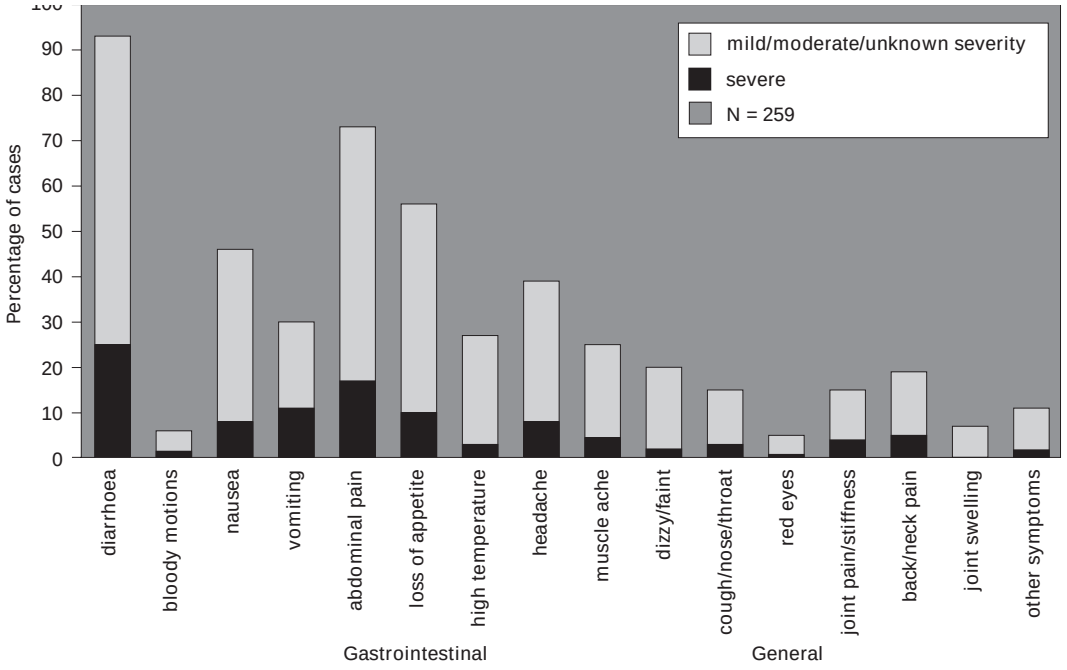


Figure 7.6 In the population cohort component



Symptom profile of all cases with no target organism (children)

Figure 7.7 Presenting to the GP

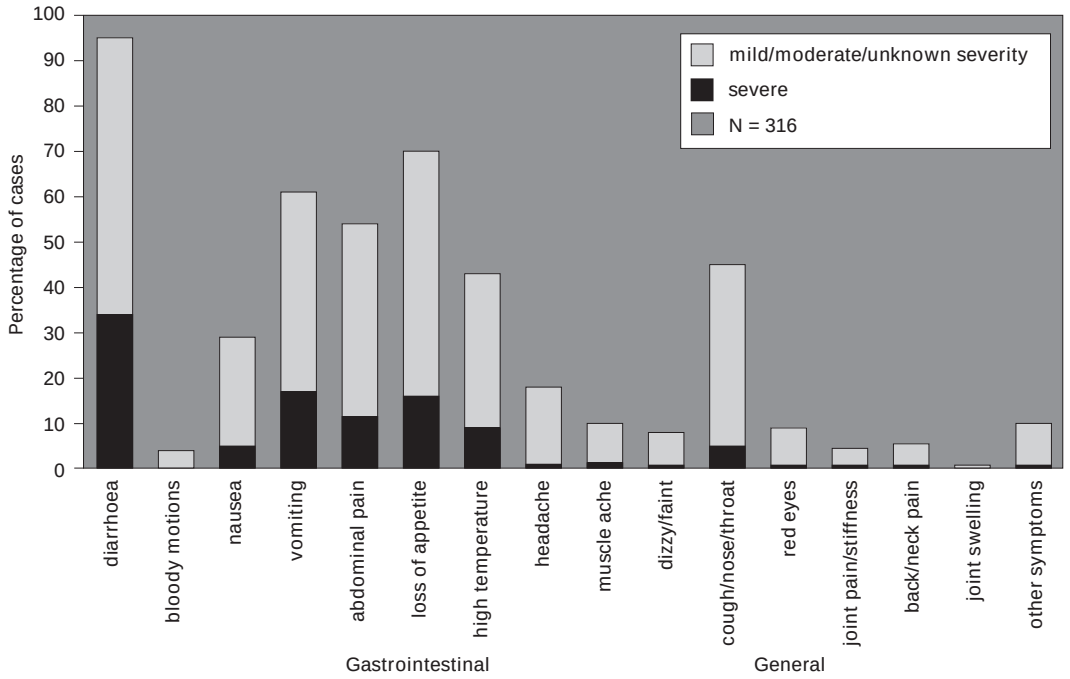
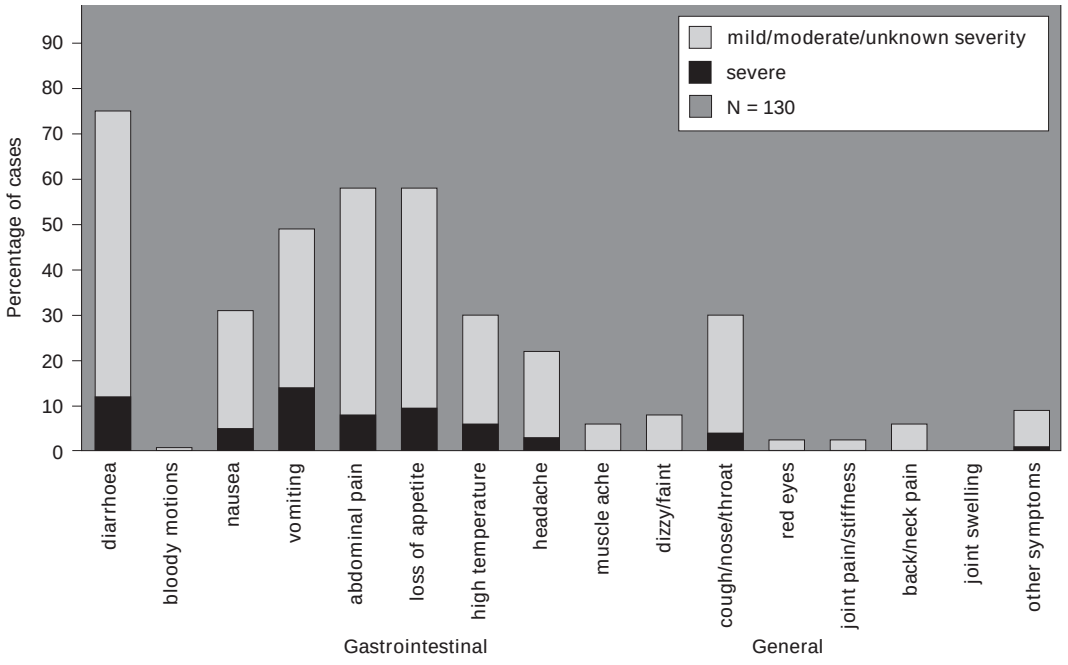


Figure 7.8 In the population cohort component



Symptom profiles of controls

Figure 7.9 Adults from GP population – symptoms experienced in the last 3 weeks

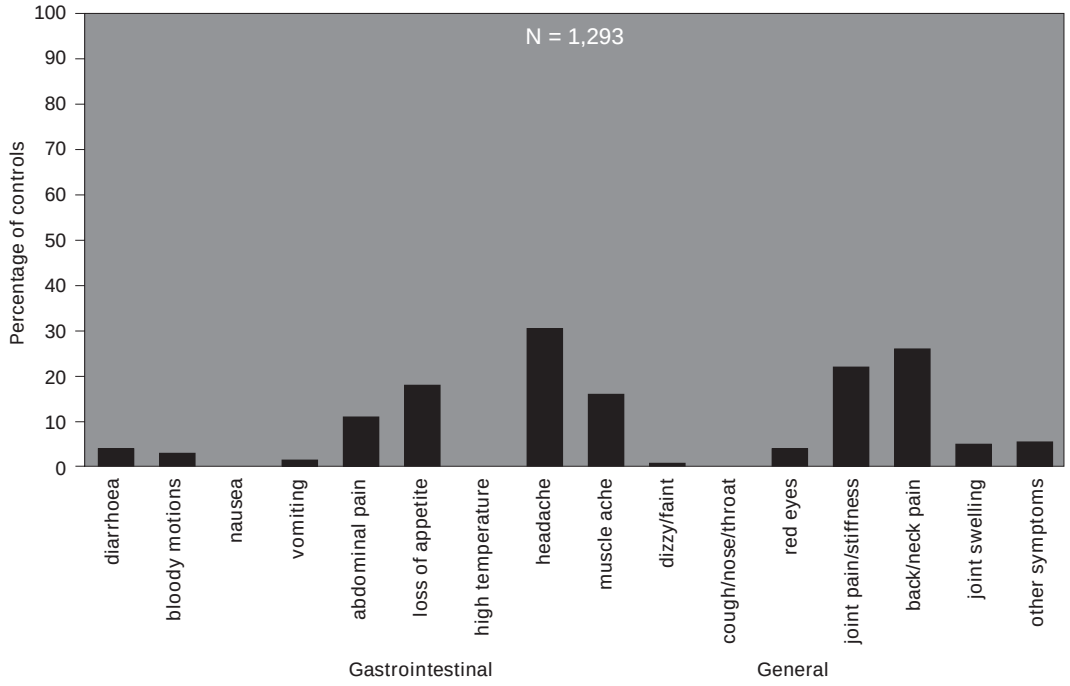
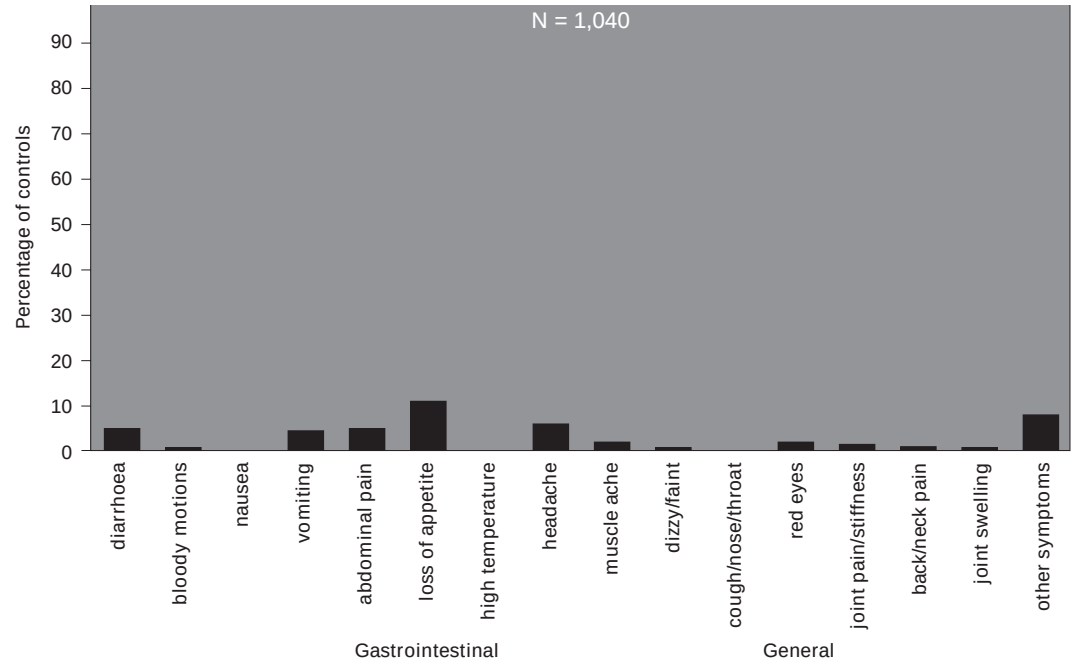
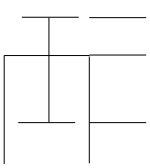


Figure 7.10 Children from GP population – symptoms experienced in the last 3 weeks



Key

Number of days after onset at which:



25% of cases continue to have the symptom

50% of cases continue to have the symptom

75% of cases continue to have the symptom

Duration of general symptoms in all cases

Figure 7.19 Adults presenting to the GP

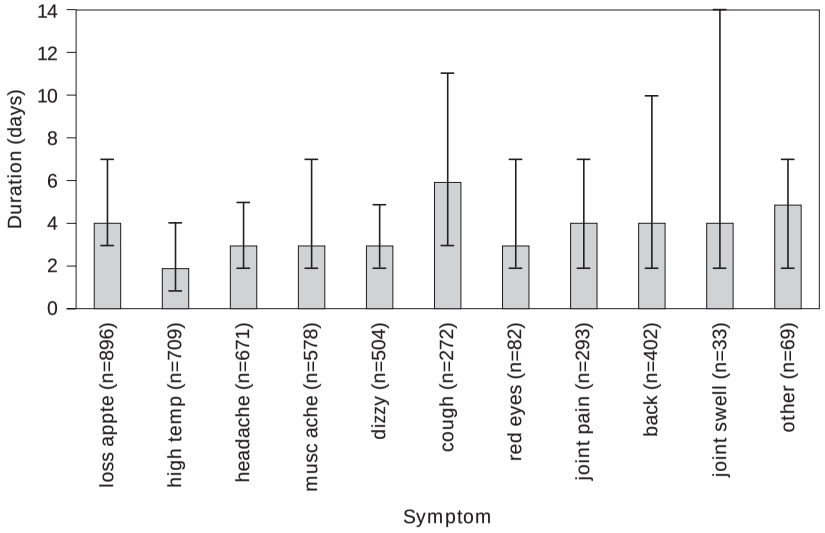


Figure 7.20 Children presenting to the GP

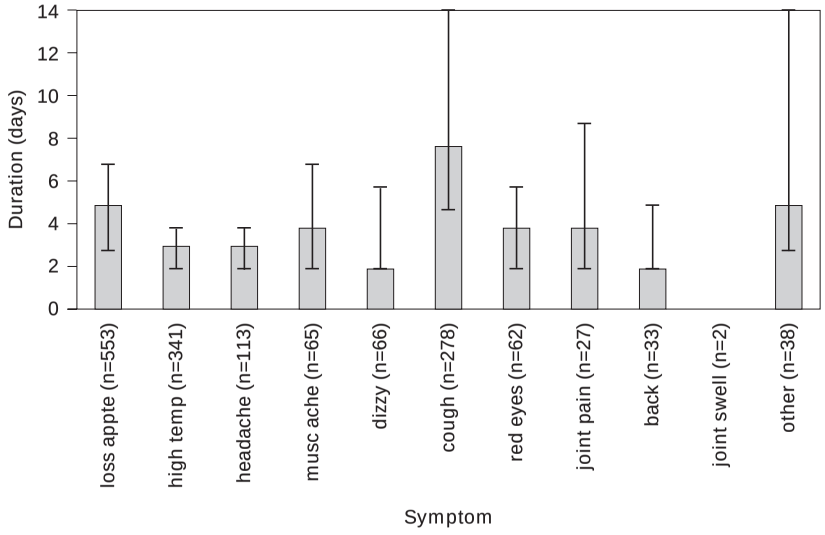


Figure 7.21 Adults in the population cohort component

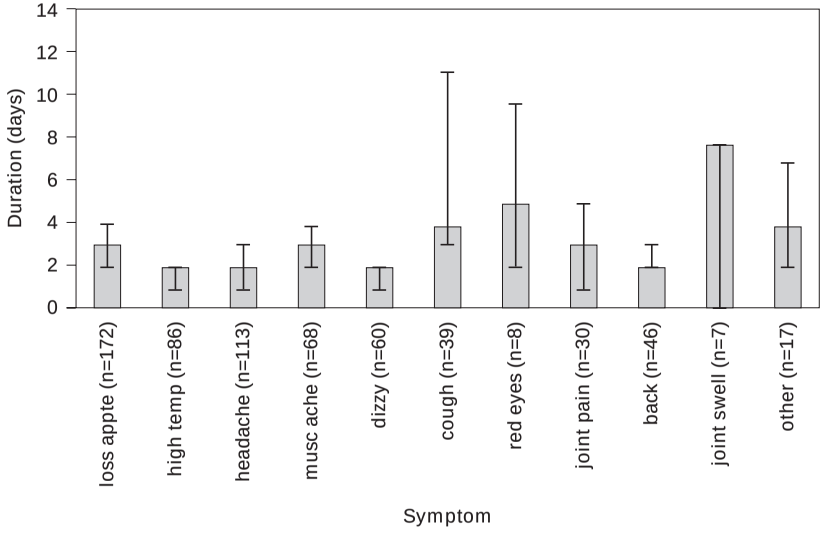
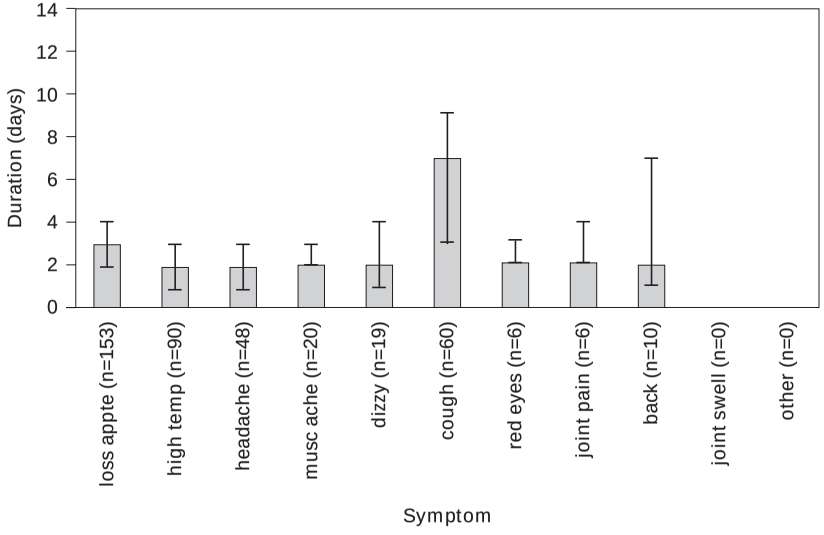


Figure 7.22 Children in the population cohort component



Duration of gastrointestinal symptoms of all IID cases

Figure 7.11 Adults presenting to the GP

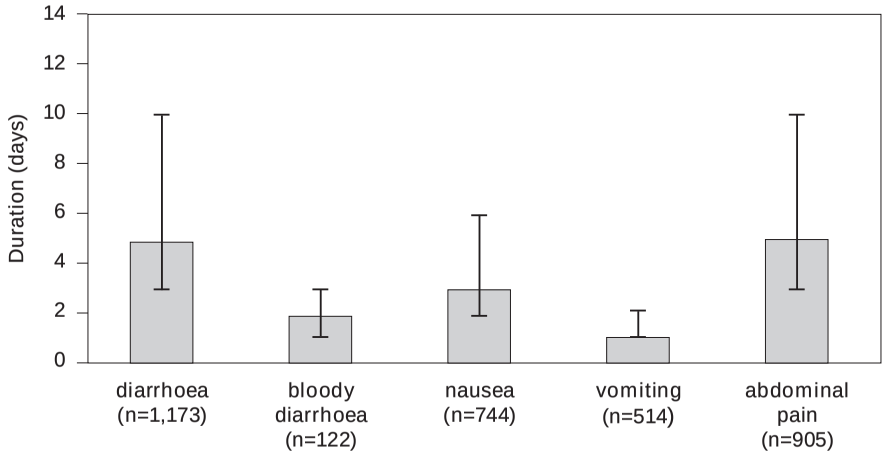


Figure 7.15 Adults in population community cohort

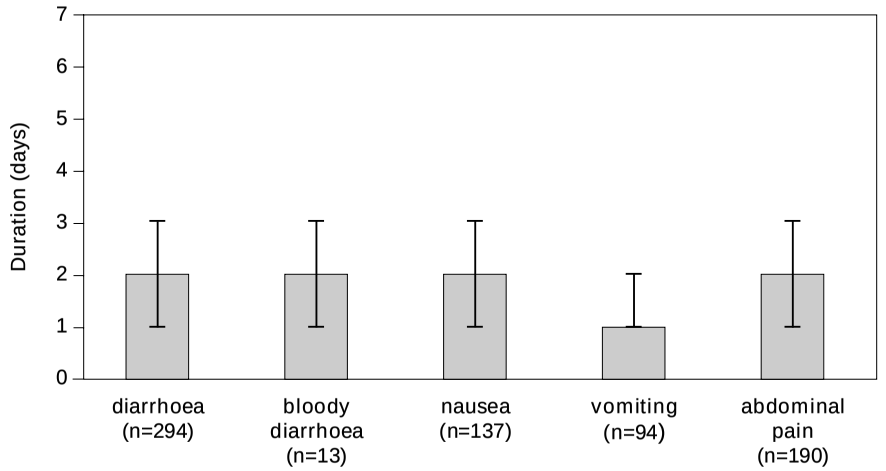


Figure 7.13 Children presenting to the GP

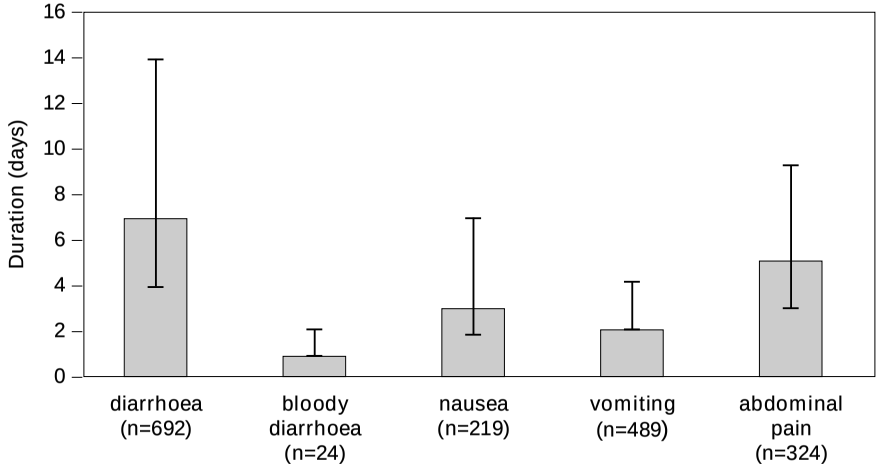
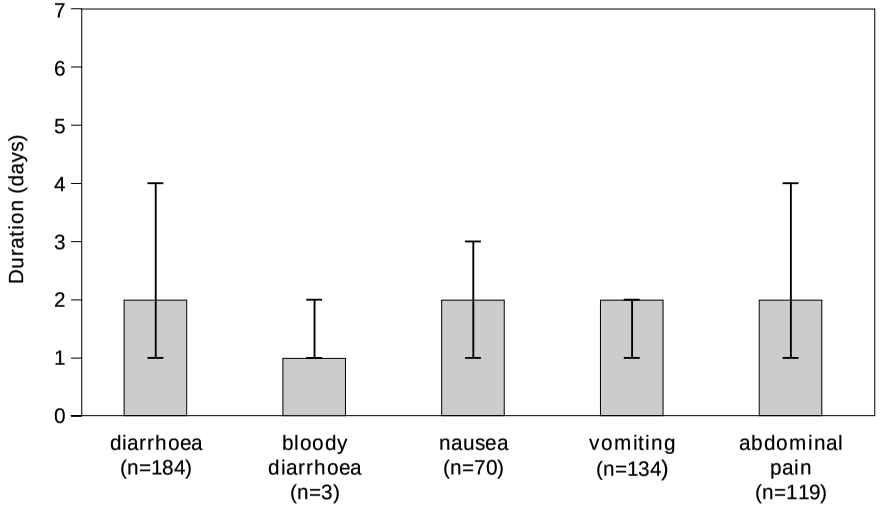


Figure 7.16 Children in the population cohort component



Duration of gastrointestinal symptoms in cases with no target organism

Figure 7.12 Adults presenting to the GP

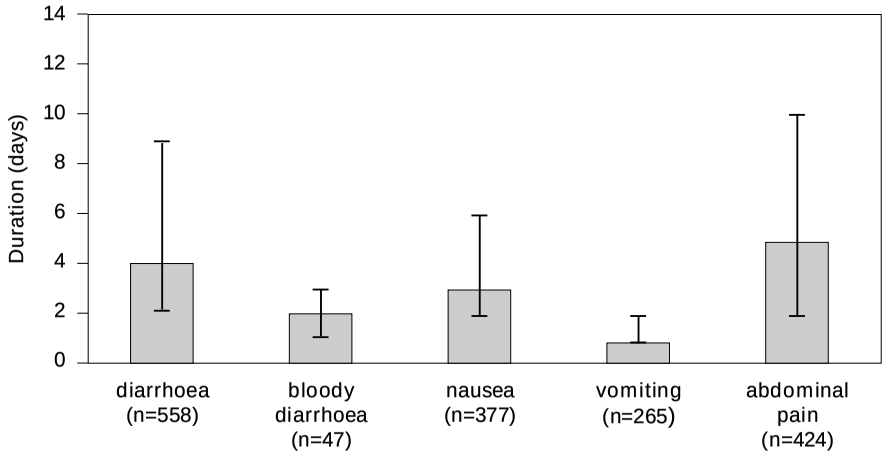


Figure 7.17 Adults in population community cohort

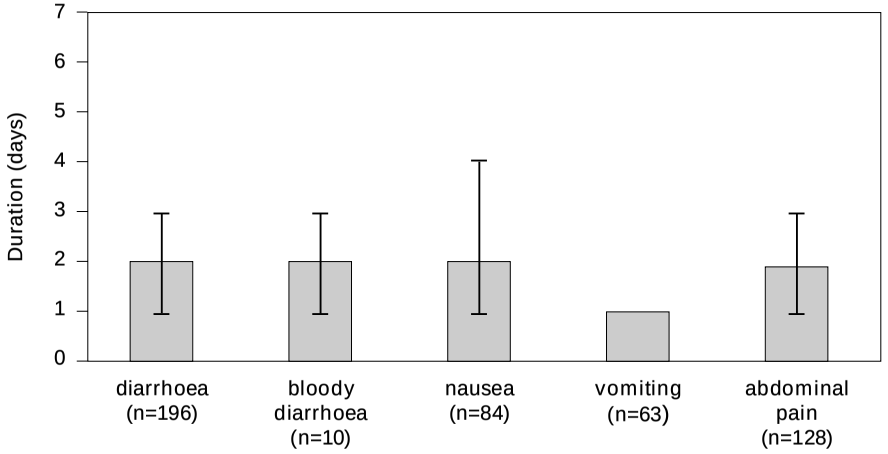
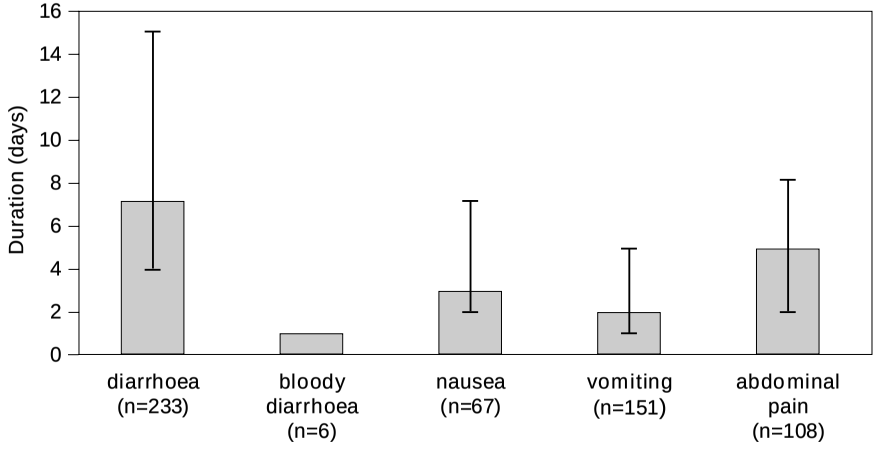
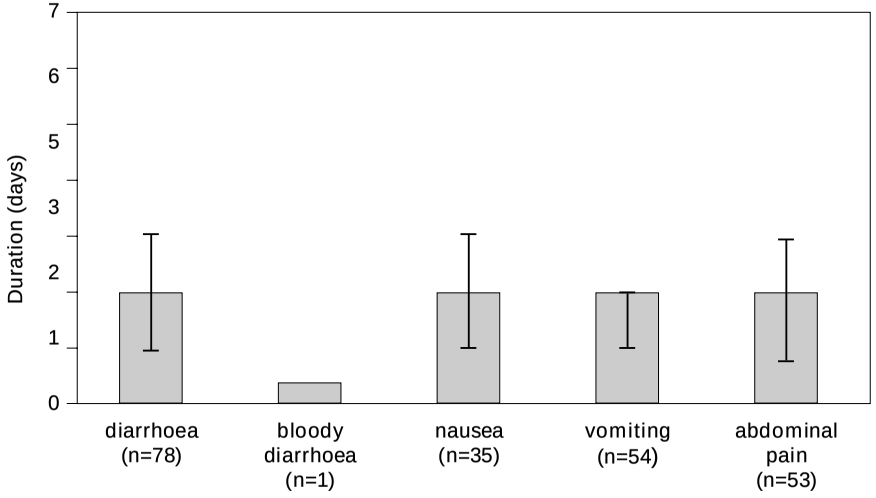


Figure 7.14 Children presenting to the GP



75 percentile figure for bloody diarrhoea not available

Figure 7.18 Children in the population cohort component



Chapter 8
Socio-economic Analysis Results

8.0 INTRODUCTION

The total number of socio-economic questionnaires returned by cases was 4389. The response rate was 46% (2,216/4,876) for the enumeration component, 41% (1,652/4,026) in the GP cohort component and 80% (555/675) in the community component. 63% of those in the GP component and 82% in the community component who returned a risk questionnaire also returned the socio-economic questionnaire. The socio-demographic characteristics of those returning the socio-economic questionnaires were similar to those who returned the risk questionnaire. See Chapter Four, paragraph 4.5.2.

The results of the socio-economic analysis are presented for each component of the study and for all cases who completed the questionnaire. The analysis includes those target organisms that were associated with a large number of cases. Where there are sufficient numbers, organism sub-groups are analysed. The categories include all salmonellas and *S.enteritidis*; all campylobacters and *C.jejuni*; all enterovirulent *E.coli* and enteroaggregative *E.coli* (EAggEC); all rotavirus and rotavirus group A, *C.difficile* and SRSV. These are also the target organisms analysed in the risk factor analysis (Chapter 9). The methods are described in Chapter 3.

This analysis begins with a description of households and the impact of illness on the activities of daily living. The resources used and the financial burden of the illness to the cases and the health sector are then estimated. In addition to organisms, the costs are linked to the reported severity of illness.

The questionnaire invited responses to several questions related to food safety, although it was recognised that not all cases of IID would be food-related. We analyse how much cases would be prepared to pay for safer food and their response is linked to expenditure on food and to personal income. We conclude with a discussion as to who the respondents considered to have responsibility for food safety, whether government or local authority agencies, food manufacturers, retailers or consumers. It should be stressed that these responses represent the personal views of respondents who had suffered an illness whether or not this was related to food.

8.1 STRUCTURE OF HOUSEHOLDS

Household structure indicates both the support available for those who are ill and the potential for secondary spread amongst close contacts.

8.1.1 Number in household

Most cases responding to the socio-economic questionnaire were in households of up to three individuals. The proportion of responders in households of this type was 58% in the GP component, 46% in the community component and 56% in the enumeration component. In the GP component, 96% of cases were in households of up to six persons. It was difficult to establish precisely the number of cases living

in institutions, but it was estimated that the percentage was less than 2 (Appendix 5, Table A5.1).

8.1.2 Composition of households

Information on household composition was available from the socio-economic analysis for 3,177 households. About 54% of households consisted of two parents and their children; 3% of households consisted of only one adult and one child under 16 years of age; while 3% of households consisted of one adult and more than one child under 16 years of age. Many households included grandparents and other relatives and friends (Appendix 5, Table A5.2)

8.1.3 Household illness

In all study components it was likely that the case was the only person affected in the household. This was so for 82% of adults and 61% of the children in the GP component and 84% of adults and 59% of children in the community component. There were more households with multiple cases in the enumeration component than in other components: 75% of the adult cases and 52% of the cases in children being the only ones affected in the household. The second person in the household most likely to be ill if the case was a child, was the mother. If the case was an adult, the other person most likely to be ill was the spouse. This probably reflects the level of exposure, i.e. mothers caring for ill children and adults caring for their spouses or partners (Appendix 5, Tables A5.3–A5.5).

The percentage of the household ill varied with the size of the household. A smaller percentage of members of larger households were ill. In no households of more than six persons were all members ill (Appendix 5, Tables A5.3–A5.5).

8.2 CHARACTERISTICS OF THE ILLNESS – ACTIVITIES OF DAILY LIVING

The impact of the illness on the activities of daily living were measured in addition to the duration and symptoms (discussed in Chapter 7). These measures were linked to the major target organisms. The impact was categorised on a scale that began with a hospital admission where the case was confined to bed, and broadly followed a Guttman Scale ordering until cases were able to participate in all normal activities in the home and outside. The proportion of cases in each stage are reported for each study component, by sex, age and organism (Figures 8.1–8.8, and Appendix 5, Tables A5.6– A5.18).

8.2.1 Impact of the illness

In each study component the most frequently reported stages were ‘at home but not able to do normal activities’ and ‘at home able to undertake normal activities’. Cases who saw their GP in the community component represented a similar pattern of illness to those presenting to their GP in the other study components (Figures 8.1 and 8.2).

Over 40% of cases in the enumeration component and 38% in the GP component were ‘confined to bed’ for an average of three days and 25% of cases in the community component reported being ‘confined to bed’ for nearly two days. On average, cases in the GP component and the enumeration component spent more than five days ‘feeling ill but able to go out to shop, etc.’ (Figures 8.1 and 8.3).

In the GP component for all age groups, except children under one year old, the most frequently reported category of illness was ‘at home unable to do normal activities’

followed by ‘at home able to do normal activities’. Over 45% of adults aged 16–60, 30% of children aged 5–15 years and 24% of adults over 60 years old reported going about normal activities outside the home whilst feeling ill. Most adults 16–60 years of age reported spending some time in bed at home because of illness. A small percentage of cases (2%), mostly children under one year old (4%), were hospitalised (Figure 8.4). Proportionately fewer cases were admitted to hospital from the GP component than for cases from other study components that consulted a GP (Appendix 5, Table A5.19).

Compared to the profile for all IID, a higher percentage of cases with *Salmonella* and *Campylobacter* in the GP component reported being at home ‘confined to bed’ and ‘not able to do normal activities’. Cases with rotavirus infection also reported a high percentage of cases ‘at home not able to do normal activities’ (Figure 8.7 and Appendix 5, Table A5.9).

In the community component ‘at home but able to do normal activities’ was most frequently reported for children aged 1–4 years and adults aged over 60 years old. Adults 16–60 years old reported ‘feeling ill but able to go to the shops’ most frequently followed by ‘at home but not able to do normal activities’ and ‘at home but able to do normal activities’. The percentage reported being ‘confined to bed at home’ was over 20% for all age groups other than children under five years of age (Figure 8.5).

In the community component more cases with SRSV infection reported being ‘at home unable to do normal activities’ and ‘at home confined to bed’, compared to the profile for all IID. A higher proportion of cases with *Salmonella* and *Campylobacter* infection reported going about normal activities within and outside the home whilst feeling ill than for cases with other organisms (Figure 8.8 and Appendix 5, Table A5.11).

Cases in the enumeration component reported more severe illness (Figure 8.1). The hospitalisation rate for children under one year old was 8% and for older children and adults over 60 years of age it was 4%. The percentage reporting being ‘at home not able to do normal activities’ was very high: over 50% for all age groups, 70% for children aged 5–15 years and adults 16–60 years of age. The percentage reporting being ‘at home but able to do normal activities’ and ‘feeling ill but able to go out’ was also high (Figure 8.6 and Appendix 5, Table A5.15).

8.2.2 Days off work

In the GP component, 42% of adult cases of working age lost an average of six days away from paid employment (Appendix 5, Tables A5.6 and A5.13). Females were off work on average for slightly less time than males; however, the maximum time off was longer, 80 days compared to 56 days for men (Appendix 5, Table A5.13). Cases with *Salmonella* infection reported an average of nine days off work, those with *S.enteritidis* an average of 7.5 days, *Campylobacter* cases 6.5 days, enterovirulent *E.coli* five days, rotavirus four days and SRSV three days (Appendix 5, Table A5.10).

In the community component only 20% of adults of working age reported time off work because of the illness (Appendix 5, Table A5.7). The cases who had consulted a GP reported an average of three days off work, whilst those who had not presented to their GP reported two days off work. Numbers of cases for each target organism were insufficient for meaningful analysis (Appendix 5, Table A5.12).

In the enumeration component, 40% of cases lost an average of five days work – 34% of female and 49% of male cases (Appendix 5, Table A5.8). On average, females were off work for slightly longer than males. The maximum time lost was 85 days and 22 days for females and males, respectively (Appendix 5, Table A5.8 and A5.15).

Figure 8.1 The impact of illness: percentage of cases reporting spending time in the different stages, by study

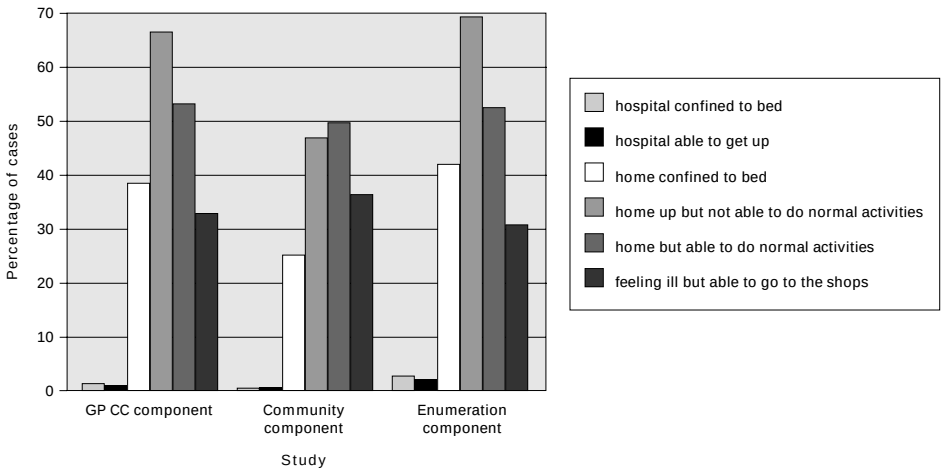


Figure 8.2 The impact of illness: percentage of cases reporting spending time in the different stages in the Community component, by GP consultation

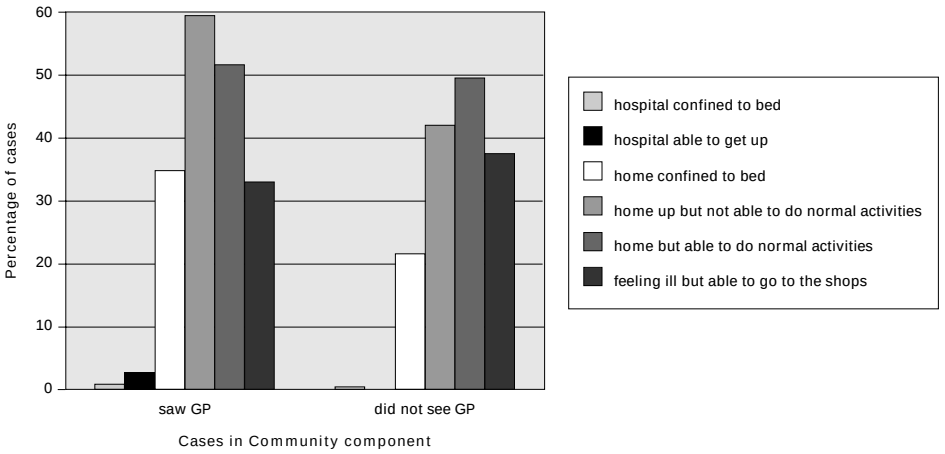


Figure 8.3 Mean number of days in different stages of illness for those reporting, by study

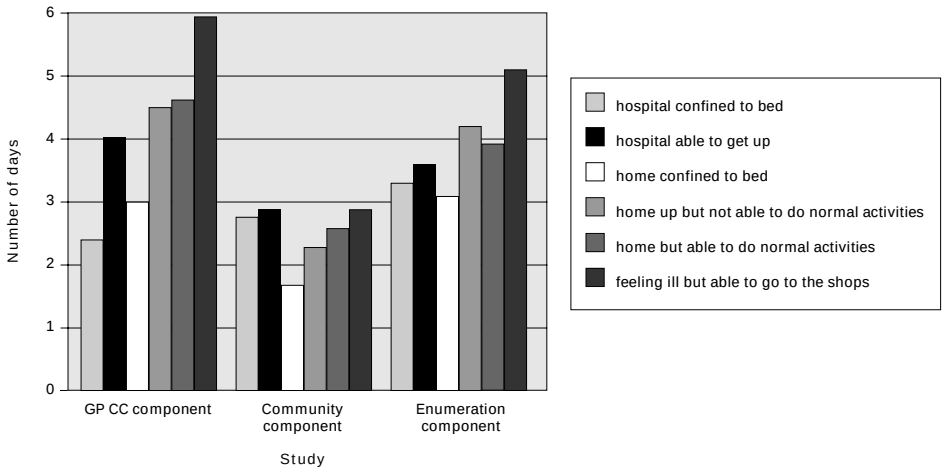


Figure 8.4 Impact of illness: Percentage of cases in the GP case control component reporting spending time in the different stages of illness, by age

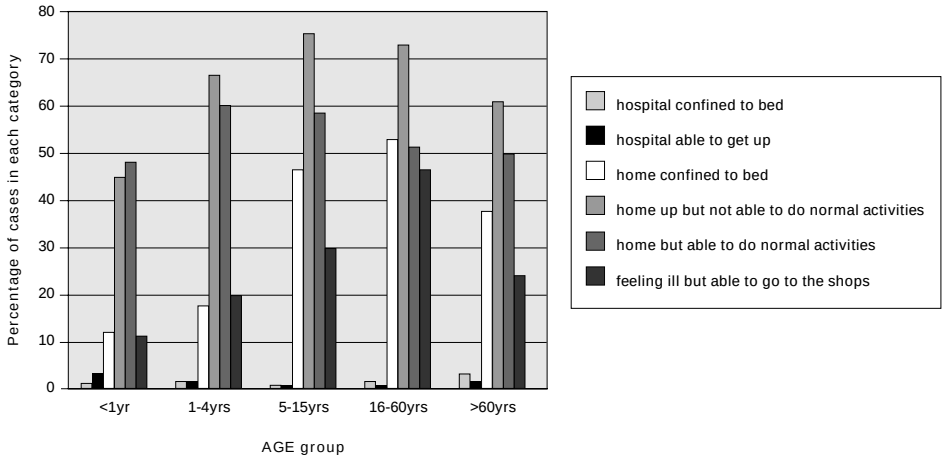


Figure 8.5 Impact of illness: Percentage of cases in the Community component reporting spending time in the different stages of illness, by age

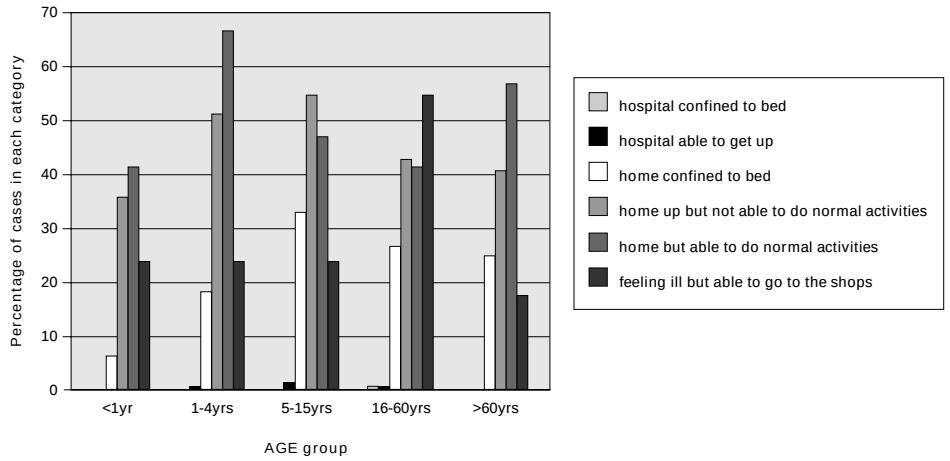


Figure 8.6 Impact of illness: Percentage of cases in the Enumeration component reporting spending time in the different stages of illness, by age

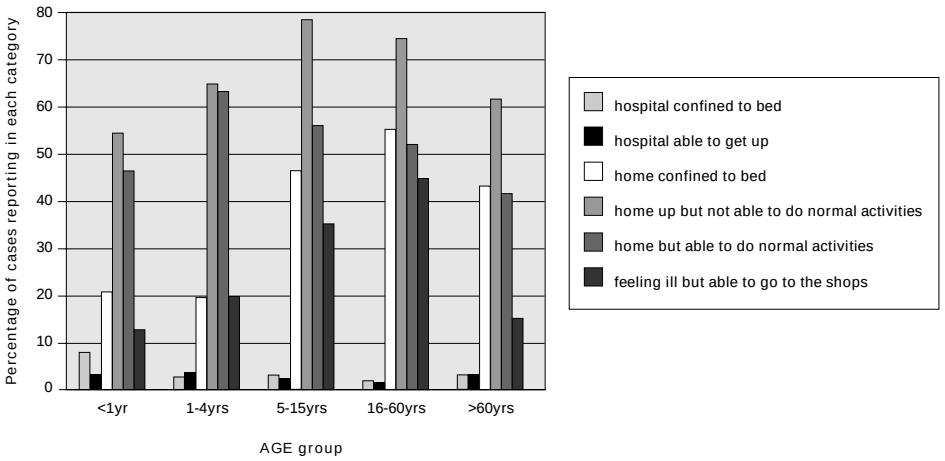


Figure 8.7 Percentage of cases in the GP case-control component reporting spending time in the different stages of the illness, by organism

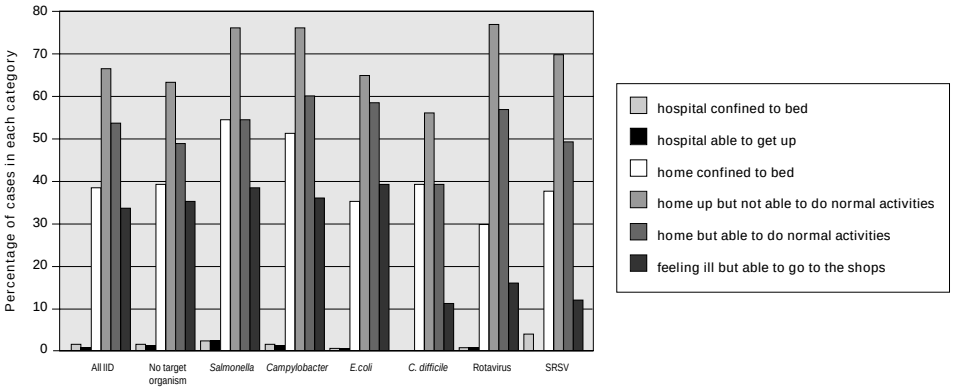
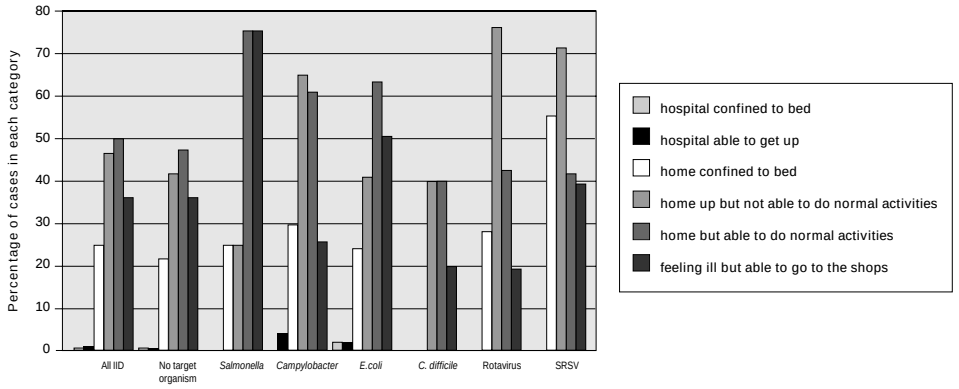


Figure 8.8 Percentage of cases in the Community component reporting spending time in the different stages of the illness, by organism



8.2.3 Days of education lost

In the GP component 30% of cases reported an average of five days lost from education because of their illness (Appendix 5, Table A5.6). In cases with no target organism identified 33% lost time from education compared to 54% with *Salmonella* and 27% with enterovirulent *E.coli*. Eight cases with EAggEC reported the longest time off with an average of eight days (Appendix 5, Table A5.10).

In the community component 31% lost an average of three days education (Appendix 5, Table A5.7). Those who consulted a GP lost four days and those who did not lost two days (Appendix 5, Table A5.7a and A5.7b). Numbers reporting in this category by organism were small (Appendix 5, Table A5.12).

In the enumeration component 30% of cases lost an average of 4.5 days education, with a range of 0–90 days (Appendix 5, Table A5.8).

8.2.4 Exclusions from work or school due to illness

In the GP and enumeration components about 5% of cases reported exclusion for an average of six days from work or school because of their illness (Appendix 5, Tables A5.6 and A5.8). The numbers reporting exclusion, by organism, were small, but five cases of *Salmonella* reported an average of 16 days exclusion in the GP component (Appendix 5, Table A5.10).

In the community component 3% of cases were excluded from work or school for an average of two days. None of these cases had seen a GP (Appendix 5, Table A5.7).

8.2.5 Ability to conduct normal household duties

In each study component the proportion of cases in this category reflected those who were in a position potentially to perform 'normal household activities', i.e. the adult group.

In the GP component 39% of cases, (26% of men and 49% of women), reported not being able to undertake normal household duties for an average of five days with a range of 0.5 – 55 days (Appendix 5, Table A5.6 and A5.13). In 50% of *Salmonella* cases and 39% of *C.difficile* and SRSV cases an average abstinence of seven days, and three days was reported respectively (Appendix 5, Table A5.10).

In the community component 25% of cases reported an average of two days (range 1–18 days) being unable to perform normal households duties (Appendix 5, Table A5.7). The number of cases, by organism, reporting in this category was small; eight cases of enterovirulent *E.coli* reported an average of four days and three cases of rotavirus Group A reported an average of four days. Of those with no target organism identified 3% reported an average of two days (range 0.5–11 days). (Appendix 5, Table A5.12).

In the enumeration component an average of five days was recorded for those not being able to undertake normal household duties – an overall average of one day for males and three days for females (Appendix 5, Table A5.8 and A5.15).

8.2.6 Lost leisure time

In the GP component 724 cases (44%) reported an average of eight days lost leisure time (range 0.5–60 days) (Appendix 5, Table A5.6). The mean time lost by children was lower (six days) than adults, six and eight days, respectively. Cases of EAggEC

and *Salmonella* infection reported an average of 10 and 11 days lost leisure time, respectively and rotavirus and SRSV cases an average of seven and five days, respectively (Appendix 5, Table A5.10).

In the community component 192 (34%) cases reported lost leisure time with an average of four days, and range of 0.5–22 days (Appendix 5, Table A5.7). Of those who had consulted a GP, 36% reported six days (range 1–22 days) lost leisure time compared to 34% of those who did not consult a GP who reported three days (range 0.5–14 days) (Appendix 5, Tables A5.7a and A5.7b). Cases with *Salmonella* and *Campylobacter* reported the longest time unable to take part in normal leisure activities, seven and six days respectively. Of the cases that had no target organism identified 36% reported an average of four days (range 0.5–14 days) in this category (Appendix 5, Table A5.12).

In the enumeration component 989 cases (45%) lost an average of eight days (range 0.5–63 days) leisure time. Females lost slightly more than males, eight days and seven days, respectively (Appendix 5, Tables A5.8 and A5.15).

8.3 USE OF RESOURCES

The pattern of illness described above is reflected in the use of health sector resources and the direct and indirect expenses associated with the illness to cases and those who cared for them.

8.3.1 Days spent in hospital

In the GP component 29 cases (2%) were hospitalised for four days on average; a total of 115 days. Of these 55% were in hospital for up to two days and 83% were discharged before seven days. In children under one year of age 4% were hospitalised (Appendix5, Tables A5.19 and A5.20).

Only six cases from the community component were admitted to hospital. These cases comprised two older children, three adults (two under 60 years of age and one over 60 years of age) and one case with no data available on age. Three of the cases were in hospital for one to two days and five were discharged within a week. One case remained in hospital for 18 days. Of those who consulted a GP, 4% were hospitalised, but none of those who did not consult a GP were. (Appendix 5, Tables A5.19 and A5.20).

79 cases (4%) in the enumeration component were hospitalised, a higher proportion than in the GP component for each age group, but the average duration of the stay was similar (four days) (Appendix 5, Tables A5.19 and A5.20). This suggests an under ascertainment of severe cases in the GP component.

8.3.2 Hospital out-patient visits

Children under one year old and adults were most likely to be seen in out-patient departments (Appendix 5, Table A5.21).

In the GP component 20 cases (1%) attended out-patient departments, 1% of the adults aged under 60 years of age and 2% of children under one year of age. (Appendix 5, Table A5.21).

In the community component seven cases (1%) visited out-patient departments, all but one case being adults. Of those over 60 years of age, 3% visited an out-patient department. All cases visiting out-patient departments had either seen a GP or had

been admitted to hospital. In cases seeing a GP, 5% had had an out-patient appointment (Appendix 5, Table A5.21).

In the enumeration component 57 cases (2.6%) visited out-patient departments. The lowest attendances were from children aged 1–4 years (1%). The attendances for all age groups in the enumeration component were higher than those in the GP component, perhaps reflecting the higher hospitalisation rate of this group (Appendix 5, Table A5.21).

8.3.3 Hospital Accident & Emergency (A&E) department visits

The number of attendances at A&E departments was provided and analysed for each component of the study for age and organism. There were 23 cases (1%) in the GP case-control component where a visit was made to an A&E department. All those under one year of age and over 60 years old were then admitted to hospital. Six cases (1%) in the community component visited A&E departments, four of whom were admitted. All those visiting A&E departments had previously seen a GP. In the enumeration study 72 cases (3%) visited A&E departments and 49% of these were admitted to hospital. This included 86% of the elderly cases, 40% of cases under one year old and 55% of cases aged 1–4 years Appendix 5, Table A5.20).

There were no visits to A&E departments by patients with *S.enteritidis* and *C.difficile*. Two cases in the GP component, both adults aged less than 60 years old with *C.jejuni* infection, visited an A&E department and one was admitted. Three children, one each with EAggEC, rotavirus group A and SRSV, visited A&E departments but none were admitted. Nine cases with no IID target organism identified visited A&E departments and five of these cases were admitted.

8.3.4 Use of GP services

Consultations with GPs took place in the surgery, in the patients' homes and by telephone. Practice nurses also visited cases.

8.3.4.1 GP consultations

All cases in the GP and enumeration components should, according to the study design, have had a consultation with a GP. In the community component 149 (27%) cases reported consulting a GP.

8.3.4.2 GP consultations at home

In the GP component, 352 cases (23%) were visited at home, 18% of cases were visited once and 5% were visited twice or more. The largest number of home visits were to those aged over 60 years, 33% of whom were visited once and 8% were visited on two or more occasions (Appendix 5, Table A5.23).

In the community component 7% of cases had a GP consultation at home. Higher proportions of infants and the elderly received home visits (Appendix 5, Table A5.24).

In the enumeration component 27% received a home visit, comparable to that in the GP component. Of those over 60 years of age, 52% received a visit, as did 29% of children under one year old (Appendix 5, Table A5.25).

8.3.4.3 GP consultations in the surgery

In the GP component 87% of cases visited the GP surgery, 63% made one visit and 24% more than one visit. The highest proportion of multiple visits were made by children under one year of age, 35% of whom made two or more visits (Appendix 5, Table A5.23).

In the community component 80% of cases who consulted a GP visited the GP in the surgery; 59% visited once and 22% visited twice or more. A higher proportion of adults under 60 years old and children under one year old made surgery visits. Of those over 60 years old who consulted a GP, 35% did not visit the surgery reflecting the higher number of home visits in this group (Appendix 5, Table A5.24).

In the enumeration component 81% of cases made a surgery visit. The pattern of visits, by age, was similar to that in the GP component, with the highest proportions of visits made by children under one year old (Appendix 5, Table A5.25).

8.3.4.4 Telephone calls to GPs

In addition to face-to-face consultations, telephone calls relating to the illness were made to GPs. The pattern was similar in each component with between 20% and 29% of cases phoning their GP. The proportion calling was higher for cases under five years old and highest for infant cases (Appendix 5, Tables A5.26–A5.28).

8.3.4.5 Visits by practice nurses

In each component about 2–2.5% of cases were visited by a nurse. The proportion of nurse visits was higher for infant and elderly cases. All nurse visits in the community component were to cases who had seen a GP (Appendix 5, Tables A5.26–A5.28).

8.3.5 Investigations

Investigations of those in the GP and the comunity components were undertaken as a salient part of the study. These were study costs, not costs of illness, and were thus not included in the cost analysis. The assumption was made that in routine clinical management cases would have had the same chance of having a faecal specimen taken for laboratory investigations and the same testing procedures applied as for cases included in the enumeration component and costed accordingly (see Chapter 3).

8.3.5.1 Numbers of stool tests requested

If the same proportion had one stool test in the GP and community components as in the enumeration component, then 427 cases in the GP component and 41 cases in the community component would have had one stool test. In addition, 282 stool tests in the GP component and 60 in the community component were carried out on cases who had two or more stool tests. This gives an estimated 709 tests in the GP component cases and 101 tests in the community component cases having had a stool test under normal practice conditions.

Stool tests were recorded for 91% of cases in the GP component (9% had missing information). Of these 84% recorded one test and 7% recorded two or more tests (range 0 – 10) (Appendix 5, Table A5.29).

In the community component, 25 cases (17%) had missing information. 65% recorded having one test and 18% as having multiple tests (range 0 – 4 tests) (Appendix 5, Table A5.29).

In the enumeration component 33% of cases had a stool test. 27% reported one test and 5% reported multiple tests (range 0–6) (Appendix 5, Table A5.29).

8.3.5.2 **Blood tests**

In each study component approximately 4% of cases reported having had a blood test of some kind (Appendix 5, Table A5.29).

8.3.5.3 **Urine tests**

In each study component approximately 6% of cases reported having had a urine test (Appendix 5, Table A5.29).

8.3.5.4 **Miscellaneous tests**

1% of cases reported having further unspecified tests (Appendix 5, Table A5.29).

8.3.6 **Treatments**

For cases who had consulted a GP the proportion receiving a prescription was similar in each study component (range 41–44%). Although information was requested only for items prescribed for the IID illness, it is possible that some drugs were prescribed for other illnesses. In each study component, an average of 1.4 prescriptions were given. Multiple prescriptions as a proportion of prescriptions increased with age, suggesting that co-morbidity prescriptions may have been included in the number of prescriptions reported by the elderly (Appendix 5, Table A5.30–A5.32).

8.3.7 **Resource use by cases and carers**

8.3.7.1 **Direct out-of pocket expenses**

Information was collected about the resources used to purchase different items of food for those who were sick, cleaning materials, replacements for items spoilt as a result of the illness and the impact on leisure activities. Similarly, information on resources used by those persons who accompanied cases visiting GP surgeries and hospitals and staying with children in hospitals was also collected. The value of these items was collected from individuals who were asked to estimate the costs (Appendix 5, Table A5.34–A5.36).

8.3.7.2 **Caring activities and relationship of carer**

In most instances, the person who accompanied the case to the GP was likely to be the mother or female paid carer (65%, 74% and 64% of cases for the GP, community and enumeration components, respectively). Fathers accompanied children to visit the GP for 9–13% of cases. Where two persons accompanied the case to the GP the second person was the father in 44–60% of cases. In 82% of cases the mother stayed in hospital with an ill child. In contrast, persons other than the mother were more likely to be involved in visits to hosptal A & E and out-patient departments (Appendix 5, Table A5.33).

In the GP component 58% of cases did not receive care at home. In the 706 cases that did this was for an average of 7.5 days (range 0.5–84 days). In 90% of cases they were cared for for less than 10 days, however, 2% received care for more than 20 days. Cases that needed to be cared for at home and who were cared for by one parent, were predominately cared for by mothers. More male (114) than female (99) partners were carers. Female grandparents were the most likely other person to be caring for cases at home and they were the only carer in 3% of cases (Appendix 5, Table A5.33).

In the community component 211 cases (42%) were cared for at home for an average of four days (0.5–34 days). Of these, 20% had care for up to two days, and 92% for

less than five days; the longest time a case needed to be cared for at home was 34 days. Where there was only one parent at home caring 77% of these were mothers. More male (34) than female (27) partners looked after cases at home (Appendix 5, Table A5.33).

In the enumeration component 984 cases (45%) were cared for at home for an average of eight days (range 0.5–56 days). Of these 10% received care for two days and 2.5% received care for more than 20 days. For 94% of those cared for by only one parent at home that carer was the mother. More males (169) than females (149) cared for partners (Appendix 5, Table A5.33).

8.4 COSTS OF RESOURCES USED

The methods used to derive cost vectors are described in Chapter 3. The estimates of costs are provided in the following sections by category of cost, and include: NHS costs including estimates of hospital bed days by study component and age group, GP consultation costs, and costs of telephone calls and nurse visits. Investigations and treatment costs were derived and prescription costs estimated. The NHS costs were reduced by the amount of prescription payments made by patients. The direct out of pocket expenses to cases and their families and the indirect costs of lost work or time lost from normal activities by cases and their carers were estimated.

The total costs were derived from the resources used by each case in the study. The average costs are the totals divided by the number of cases in the study – they do not refer to the average for those reporting the use of a resource.

8.4.1 NHS costs

The cost per case was £62.62 (£100,229 total), for cases in the GP component, £24.80 per case (£15,975 total) for cases in the community component, with £107.22 per case for those cases in the community component who consulted a GP. The cost per case was £85.96 (£182,333 total) for cases in the enumeration component (Tables 8.1 and 8.2).

8 4. 1.1 Hospital admission costs

In the GP component the hospital admission costs were £25,875, with a cost of £892 for each case admitted and an average cost of £15.66 per case for all cases in the study component. In the community component the hospital admission costs were £7,313, with an average cost of £1,220 per hospitalised case and an average cost of £13.18 per case for all cases in this study component. All costs relate to cases who had consulted a GP. In the enumeration component the total hospital admission costs was £70,875 with an average cost per case of £32.48 and £897 per hospitalised case (Tables 8.1 and 8.2).

8.4.1.1.1 Hospital out-patient costs

The total cost for hospital out-patient department (OPD) visits by cases in the GP component was £1,665, an average of £1.01 per case. In the community component the estimated cost for the 149 cases who had seen a GP was £945, an average cost per case of £6.34. In the enumeration component the total costs for out-patient visits was estimated to be £3,150, at an average cost per case of £1.44 (Tables 8.1 and 8.2).

Costs of out-patient appointments for cases with no target organism identified were £1.63 per case for the GP component and £1.26 per case for all cases in the community component (Tables 8.3–8.6).

8.4.1.1.2 Visits to hospital A & E departments

The costs of A&E visits in the enumeration and the community components for cases that consulted a GP were very similar, £1.11 and £1.09 per case respectively, compared to £0.49 in the GP component (Table 8.2).

8.4.1.2 Cost to General Practice

8.4.1.2.1 Costs of home visits

In the GP component the mean cost for those visited at home was £61 and the average for all cases in the component was £13.59. Of this cost 61% was for cases visited once and the remainder for those who were visited on two or more occasions (Table 8.33). Cases of *Salmonella* infection had the highest cost of home visits per case followed by those with rotavirus infection (Table 8.4).

In the community component the mean costs of home visits were £4.49 per case for all cases in the study component, £16.72 per case consulting a GP and £60.76 per case receiving a home visit (Table 8.2). SRSV cases had the highest costs per case, £6.18 (Table 8.6).

In the enumeration component there were fewer cases consulting a GP at home. The mean cost for GP home visits was £18.45 per case, (£65.25 per case for those who were visited). Those over 60 years of age (16% of the study population) engendered 30% of the costs (Table 8.2).

8.4.1.2.2 Costs of surgery visits

The mean cost of visits to the GP surgery in the GP component was £20.45 per case for each case in this component (Table 8.2). Nearly half (45%) was spent on cases of working age. Surgery visit costs were highest for cases with *C.difficile* infection at £23.61 per case (Table 8.4). In the community component the average cost of visiting the GP at the surgery was £18.48 per case, an average of £4.96 for each case in the study component. Surgery visit costs were highest for cases with *Campylobacter* infection. In the enumeration component the cost was £24.27 per case visiting the surgery and £18.64 for each case in the study (Table 8.2).

8.4.1.2.3 Prescription costs to the NHS

Many of those receiving prescriptions were exempt from payment. This affects the distribution of costs between the patient and the NHS. Total costs to those who paid a prescription fee were included in the patient costs and subtracted from the costs of prescribed medicines to the NHS. The cost of prescriptions were difficult to estimate as the full details and dosage of the drugs prescribed were not available. In the GP component the highest costs for prescriptions were for cases with enterovirulent *E.coli* and rotavirus infections (Table 8.4). In the community component the highest costs was for *Salmonella* infection (Table 8.6). Prescription costs were higher in the enumeration component, £2.62, than in the GP component, £2.19; they were lowest in the community component, at 72p per case overall and £2.69 for those consulting a GP (Table 8.2).

8.4.1.3 Costs of specimen testing, transport, etc

Stool testing was estimated at £5.30 per case for all study cases consulting a GP and an average of £1.42 for each case in the community component. Costs for blood and urine tests, were lowest in the community component (Table 8.2).

8.4.1.4 Total costs of IID to the NHS by study component

The cost per case was £253.78 in the GP component and £262.47 in the enumeration component. Both the total cost per case and the percentage distribution of costs borne by the NHS differed for cases presenting to a GP. In the community component the cost was estimated to be £201.77 for those who had consulted a GP and £34.31 for those who had not (Table 8.7).

Total NHS costs and costs per case in each study component are presented in Tables 8.8–8.13. The NHS costs represented 25% of total costs in the GP component, 33% in the enumeration component and 53% in the community component for those who consulted a GP (Table 8.7). Hospital costs were the largest category of cost in the community component (31%) and 21% for those who saw a GP. Primary care costs, costs of consultations and treatments represent 15% of costs in the GP component, 16% in the enumeration component and 31% for those who saw a GP in the community component.

8.4.1.5 Total cost to the NHS by organism

The highest cost per case to the NHS by organism was £134.10 for *Salmonella* cases in the GP component. The percentage of the cost borne by the NHS in the GP component was 22%, more than the costs for *Campylobacter* (16%), but lower than that for cases with rotavirus (28%). Costs to the NHS by other organisms in the GP component were very similar ranging from £54 for enterovirulent *E.coli* to £37 for SRSV (Table 8.14). Direct out-of-pocket expenses was a similar proportion of costs in each study component; the absolute costs in the GP component were highest for *Salmonella* (£32) and lowest for SRSV (£12) (Appendix 5, Table A5.41–A5.44)

8.4.2 Costs to patients and families

8.4.2.1 Direct cost to cases

Out-of-pocket expenses per case were £15 in the GP component, £14 in the enumeration component and £6 for all cases in the community component, but £13 for those who saw a GP (Appendix 5, Tables A5.37–A5.40). Direct costs of caring for cases at home was the largest component of direct costs. Nappies, bleach and washing powder represented a large element of costs in all study components, and the next most common major costs was loss of prepaid fees (Appendix 5, Tables A5.34–A5.36).

Cases with *S.enteritidis* had the highest cost per case in both the GP component (£31.89) and in the community component (£12.25). SRSV cases in the GP component cost £12.11 and £6.67 in the community component, similar to cases who had no target IID organism identified (£12.21 and £5.54, respectively (Appendix 5, Tables A5.41–A5.44).

8.4.2.2 Indirect costs — time costs

The average costs of days lost employment per case was £139.97 in the GP component, £121.68 in the enumeration component and £26.63 in the community

component. When employment costs were adjusted for sex, the impact of the lower earnings of females reduced costs, whereas adjustment for social class increased the costs for cases in the GP component. However, the combined adjustment by social class and sex reduced the costs still further in the GP component (Appendix 5, Tables A5.45–A5.46).

In the GP component carers lost work worth £35,715, a cost per case of £21.62. In the community component carers lost work worth £15.48 per case. In the enumeration component the costs per case were £27.68. Adjustment for social class did not significantly affect the costs (Appendix 5, Tables A5.47–A5.49). An adjustment for sex could not be made as for cases, as the gender for many carers was not known.

Persons accompanying cases lost work worth £14.36 per case, in the GP component, £1.87 per case in the community component, and £12.77 per case in the enumeration component (Appendix 5, Table A5.50).

8.4.2.3 Value of lost education

Time lost from education was estimated and reported earlier in the chapter. This time was undoubtedly valuable to those affected and may have had considerable impact if it occurred at crucial times in the educational year. However, no value has been placed upon it.

8.4.3 Sensitivity test

Confidence intervals have been produced for numbers of visits and contacts with GPs, home visits by nurses, tests, prescriptions, and visits to hospital A&E departments (Table 8.15). The 95% confidence intervals for the use of these services in the GP component indicated that the numbers varied between 0.5 and 3.5 visits about a geometric mean of 1.2–3. The confidence limits for hospital admissions, out-patient visits and accommodation in hospital were larger, between 4 and 16 around a geometric mean of 1.6–2.6. The largest variation was for days ill at home (number of cases 1,194, geometric mean of 6.2 days, confidence interval 0.3–113) and for cases who were ill on holiday (41 cases, geometric mean 14.6 days, confidence interval 0.9–242). This pattern was similar to the pattern found in the community and the enumeration components (Table 8.15). It confirms the pattern expected from the diversity of conditions, the range of severity and the small number of cases in some categories, i.e. the small number of hospitals admissions (Appendix 5, Tables A5.19–A5.20).

Costs estimates are based for the most part (excluding direct out of pocket expenses) on vectors of costs for items of service, e.g. a GP visit or a day spent in hospital or a test. These cost vectors are applied to the estimates of items used. Had the cost vectors been under or over estimated, the estimated costs would have varied accordingly. A sensitivity analysis was used to indicate the impact of possible variability of cost of any item on total costs. The analysis estimated the costs if the vectors had been increased or decreased by 10%, 20%, or 50%. Estimated direct costs to cases and those who looked after them are also not likely to exceed the 20% levels. Hospital admissions varied widely by study and costs estimates for the enumeration component may well have been a more accurate representation of these costs. If hospitalised case were under reported then this would make a substantial difference to costs. Time costs were not estimated for the full period of the illness because adjustments would have been needed for time taken on combined activities, and these could not be made without further studies using different methods.

8.5 ANNUAL ESTIMATION OF COST OF IID IN ENGLAND AT 1993–1995 PRICES

Using the estimates of ratios of reports to actual cases and applying these to the cases in the community component some broad calculations of the total costs of IID were made. These are based on the reporting adjustments described in Chapter 6, and assuming that the illness experienced by cases who completed the cost questionnaire reflected the illness in the community component. It was estimated that the total costs of cases of IID in England during the study period was £742.8 million or £78.89 per case (Table 8.16). The NHS costs were 37% of these costs. Using an alternative assumption for the costs based on the estimated cost for those who did not see a GP in the community component and those who saw a GP in the GP component study, the cost was £676.9 million (Table 8.16). The cost estimated on this basis was £46.4m for *Salmonella*, £69.5m for *Campylobacter*, £69.3m for enterovirulent *E.coli*, £5.6m for *C.difficile*, £16.5m for Rotavirus and £24.4m for SRSV (Table 8.17). NHS costs comprised GP costs (14%), hospital costs (21%) and laboratory costs (2%). Direct costs to cases and families were 8% and the value of lost employment was 34% for cases and 22% for carers (Tables 8.7–8.8 and Appendix 5, Tables A5.45–A5.50).

8.6 FOOD SAFETY: ATTITUDES TO FOOD SAFETY REFLECTED IN WILLINGNESS TO PAY FOR SAFER FOOD AND ORGANISATIONS HELD RESPONSIBLE FOR FOOD SAFETY

This investigation is a cost of illness study not a cost-effectiveness study nor a cost benefit study. It was thus not possible to assess the value of any interventions to reduce infection nor cost such interventions. We were however asked to assess the values people attached to reduction in risk of foodborne infection by conducting a willingness to pay study. It should be remembered that our subjects had suffered from IID, not necessarily food poisoning.

8.6.1 Willingness to pay estimates

A section of the socio-economic study was designed to assess cases attitudes to food safety expressed as an amount that they were willing to pay for food if improvements were made that led to safer food. The information on willingness to pay reflects the values of cases and those who expressed values on their behalf by filling in the questionnaires for them. Adults were most likely to complete a questionnaire on behalf of a child in the community component (41.4%) and most likely to fill it in for another adult in the enumeration study (1.8%) (Appendix 5, Table A5.51)

The first set of questions asked whether cases, or those reporting on their behalf, would be willing to pay for safer food. Over 60% in all study components said they were willing to pay extra for food with a lower risk of spreading infection (Table 8.18).

Of those households willing to pay more, 65% spent between £100 and £300 on food each month and were more likely to be willing to pay more than those spending more or less (Appendix 5, Table A5.53)

About 50% in each study component reported themselves willing to pay up to 10% extra to ensure the lowest possible risk. A small proportion said they were willing to pay between 50–100% more. Some persons did not answer the question, 28% in the GP component, 26% in the community component and 28.4% in the enumeration component (Table 8.19)

In each study component, those willing to pay between 50–100 pence more per bird to achieve a negligible level of risk of *Salmonella* in chicken was about 3% whilst

those willing to pay this amount to achieve a halving of the risk was only 0.7%. Although the question was not expressed in a way that tested for numerical symmetry, it did appear that a reduction to a 'negligible risk' was valued 2–5 times more highly than a reduction to 'half the risk' (Table 8.20).

Irradiated meat, expressed as being 99% free of *Salmonella* was regarded rather differently. Irradiation offers a perceived trade-off of risks. In all study components, the number who did not answer the question was small at about 8.5%. In all study components 17.5–24.5% of responders said they would not buy the irradiated meat at any price (Table 8.21). This decreased to 6.3–8.5% if consumers were assured that the meat was absolutely safe and the taste would not be affected, however, a large proportion did not answer this second question (Tables 8.22 and Appendix 5, Tables A5.54–A5.59).

8.6.2 Responsibility for food safety

When asked to rank those responsible for food safety, about 35% ranked national government first, 27% food manufacturers, 22% food producers, 5% food retailers and 1.5% local authorities. Customers were only placed in first position by 10% of cases and over 50% placed them last in order of responsibility (Appendix 5, Tables A5.60–A5.61).

8.7 SUMMARY

Responders to the socio-economic questionnaire were predominately cases from households and few institutionalised cases were included. The modal size of household consisted of four persons and most were parents with two children.

If the index case was a child there were more likely to be other cases in the household: 61% of childhood index cases in the GP component, 59% in the community component, and 52% in the enumeration component were the only ones ill. If the index case was an adult then fewer other cases were likely: in the GP component 82% of adults were the index case, 84% in community component and 75% in the enumeration component.

If children were ill the other most likely member of the household to be affected was the mother; if an adult was affected the other adult most likely to be affected was the spouse or partner.

In the GP component cases were ill for an average of nine days, in the community component cases were ill for 4 days, and in the enumeration component cases were ill for 8 days. The range of values was wide (up to 80 days). Illness caused prolonged morbidity that led to time off work or school and disrupted normal household duties and leisure activities. In 2.7% of cases they were barred from work or school for an average of two days because they were seen to pose a risk of infecting others.

There were 112 cases admitted to hospital for 1–21 days. These cases absorbed 7% of total costs in the GP component, 14% in the enumeration study and 30 % of the community component cases that consulted a doctor. Most of the cases were treated at home, either 'at home in bed' or 'at home not able to undertake normal activities'.

The illness was treated mainly by GPs. Use of GP services was estimated from the community component in which 27% of cases visited a GP. Those who visited the GP were more severely affected by the illness than those who did not. The number

of home visits was highest for cases over 60 years and children under one year of age. Adults under 60 years of age and young children made the most GP surgery visits.

Bacterial infections were more prolonged and severe than viral infections. SRSV was less prolonged than rotavirus infection but both were less severe than *Salmonella*, *Campylobacter* and enterovirulent *E.coli*. Within these groups *Salmonella* serotypes in general were more severe than *S.enteritidis*.

Stool samples were requested as part of the study in the GP and community components. The pattern of testing cases was obtained from the enumeration component in which 33% of cases received a stool test. There were 7% of cases in the GP component, 18% in the community component and 5% in the enumeration component who received more than one test.

A higher proportion of young children and the elderly received more than one prescription. In each study component an average of about 1.4 prescriptions were issued per case.

Most cases were taken care of by females, usually mothers of young children; fathers and other relatives were likely to be involved when cases visited health service premises. Adult cases were most likely to be cared for by partners.

Average miscellaneous out-of-pocket expenses per patient were £15.21in the GP component, £6.11 in the community component and £14.38 in the enumeration component. For the cases in the community component that saw a GP the average cost was £12.77 and for those who did not £3.72.

The average cost per case associated with lost employment was £176 in the GP component, £44 in the community component (and cases that saw a GP were more costly than those who did not — £82 compared to £31) and £162 in the enumeration component.

The average cost per case for cases in the GP component was highest for cases with *Salmonella* at £606 per case. The largest component of this cost (73%) was for lost employment, followed by cost to the NHS (22%). *Campylobacter* infection was the next highest cost at £315 per case. The NHS cost for *Campylobacter* cases was less than for *Salmonella*, at only 16% of the total, but the percentage of costs for lost employment for *Campylobacter* was the highest for any organism at 78%. Cases with SRSV were the least costly followed by enterovirulent *E.coli* and *Campylobacter*. The costs of viral infections were lower than for bacterial infections.

Costs to the NHS were estimated as £62.62 per case in the GP component, £28.80 in the community component and £85.96 in the enumeration component. NHS costs to cases in the community component were incurred only by cases who visited a GP, and the estimated cost for these cases was £107.22.

Total costs of cases of IID presenting in the population in England in 1994 were estimated as £742.8 million or £78.89 per case based on the community component.

Approximately 50% of people with IID, which was not necessarily a result of food poisoning, reported themselves to be willing to pay 10% more for safe food and some would pay more if the food was guaranteed to be 99% safe, rather than if the risk was halved.

51% would be willing to pay up to 50 pence more for irradiated poultry. Some would only buy if the price was less and some would not buy at any price — although this proportion could be reduced if safety and taste could be assured.

National government and the food industry were ranked highest as those most responsible for food safety. Consumers were placed lowest by 51% of those responding in the GP component.

8.8 DISCUSSION

The burden of illness is predominantly felt in the community but the few cases admitted to hospital represented 58% of the NHS costs in the community component amongst those who had seen a GP, 43% in the enumeration component and 28% in the GP component. The proportion of costs in all study components were less than those found in a survey of 1,481 laboratory confirmed cases of *Salmonella* in 1988/89 (Sockett *et al*. 1993). More cases were hospitalised (18.3%) in that study and those hospitalised were in hospital for longer, (6.4 days). Whilst rates of hospitalisation and length of stay have changed since then, the size of the deviation suggests that, although the case definition used in the survey of salmonella cases represents possibly more severe cases, the hospitalised cases may have been under represented in this survey.

Cases with IID use up resources that could be used for other patients. The costs are thus likely to reflect the opportunity costs of use of scarce hospital resources and GP time. The avoidance of these costs may not result in financial savings in the short term but investment to reduce the incidence of the illness may show long term savings.

Cases who consult GPs report more severe symptoms (Chapter 7) than those who do not, their illness lasts longer and they incur more NHS and personal costs. The low costs of those who do not see a GP are striking and do not reflect the normal understanding of these cases. This difference may be because the IID cases in this study are mainly infected with viruses whilst those usually reported in estimations of the costs of foodborne infection are infected with bacteria such as *Salmonella*.

Illness due to all *Salmonella* serotypes appeared to last longer and be more severe than illness due to *S.enteritidis*. This has been noted in other studies (Sockett *et al*. 1993). SRSV illness was of short duration with fewer symptoms persisting at three weeks and lower costs.

The different pattern of illness and costs for cases in the community component from those in the other study components are largely resolved when the cases visiting their GP are considered separately. The higher costs per case in the enumeration component can be attributed to the number of cases hospitalised, that may have been under represented in the GP component.

The costs of IID captured in this study are likely to be an underestimate of the costs to society. The public health costs of monitoring and investigation, apart from the costs of some laboratory tests, have not been included; these are often substantial in outbreak investigations. These costs were estimated as 19% of Public Sector costs in the survey of *Salmonella* by Sockett and Roberts (1991). The costs do not include any estimates for the value of the impact of morbidity on normal activities within the home or on education. No estimate has been made of the impact of IID in institutions, apart from the small proportion included in this study. No value is placed on loss of life attributable directly or indirectly to IID, nor are the costs of sequelae

included. If this were included, either at the value used by road transport estimates (£784,000), or by Railtrack for estimating safety standards when major accidents including many people are concerned (£2.3m), then the costs would rise sharply. No costs to industry apart from lost productivity have been estimated.

Some rare organisms, that are likely to be more expensive to treat, were not detected in sufficient numbers in this study to estimate costs reliably. For example only four cases of *E.coli* O157 were included. Some of the more severe cases of IID may not have been captured because cases were either in hospital or too sick to participate.

Comparable costs from other studies are only available for the *Salmonella* cases. The costs appear to be slightly lower than those estimated elsewhere (Roberts and Sockett 1994).This difference is probably explained by the case mix and the items of costs included. Many of the previous studies have estimated costs in outbreaks that may have had more tests and more expensive tests and which will absorb more public health investigative resources. Some of the difference in costs is explained by previous assumptions about the severity of submerged cases. Costs estimated in studies in the USA are available from models based on the incidence of infections and estimated use of medical services and time off work. These, particularly the costs of *Campylobacter*, are not directly comparable as they include the costs of sequelae and values for lives lost (Busby 1997).

Statistical analysis of a study where two vectors are combined, in this case numbers and costs, presents a problem for estimations of the relevant confidence intervals. For this reason confidence intervals have been provided for the estimated number of events and a sensitivity analysis has been used to estimate the likely boundaries of costs. This analysis indicates how changes in the underlying assumptions might affect the estimates and enables others to use estimates making different assumptions either about service use or the cost vectors applicable. Apart from hospitalisation and use of out-patient services, the estimates appear to be robust.

The study provides one of the few estimates of morbidity of IID, as assessed by those who have experienced the illness. It has demonstrated the severity of the illness especially that attributed to bacterial infection. The short illness associated with SRSV explains the low rate of reporting of this illness and the low costs associated with these cases. The study does not include a measure of health status of case's experience of the illness. There are methodological problems in applying these measures during the acute phase of an illness. Health Status measures have been used in a long term follow up study currently underway.

Some estimates have been made to explain costs by the duration and severity of the illness. These indicated that duration and severity were significant factors in explaining costs although the proportion of costs explained was low.

People do appear to be willing to pay for safer food but this is an attitude study and it is not clear that this willingness would be translated into demand for safe goods at higher prices. Irradiated produce is viewed with suspicion by many although some might be convinced by adequate assurance of its safety.

The responsibility for food safety is placed with National Government and few seem to see any responsibility for food safety residing with local authorities or consumers.

Table 8.1 Breakdown of total NHS costs (£), by study component

	GP COMPONENT N = 1652	COMMUNITY COMPONENT N = 149 *	ENUMERATION COMPONENT N = 2182
GP home visit	21479	2491	37976
GP surgery visit	32317	2754	38352
Transport to GP	1500	0	2625
Phone GP	1550.40	114.75	2050.20
Nurse home visit	960	36	1272
Stool test	8373.69	789.67	10907
Blood test	277.30	33	734.30
Urine test	918	81	1332
Specimen collection	33.78	3.2	44
Specimen postage	14.59	1.38	19
Prescriptions	3467.50	401.25	5396.25
A & E visit	810	162	2430
Hospital admission	25875	7312.50	70875
OPD visit	1665	945	3150
Transport to hospital	637	760	3974
Accommodation of parent in hospital	351	91	1196
TOTAL	**100229.26**	**15975.75**	**182332.75**

*cases who saw a GP

Table 8.2 Breakdown of NHS costs per case (£), by study component

	GP COMPONENT N = 1652	COMMUNITY COMPONENT N = 149 *	ENUMERATION COMPONENT N = 2182
GP home visit	13.59	16.72	18.45
GP surgery visit	20.45	18.48	18.64
Transport to GP	0.95	0	1.28
Phone GP	0.98	0.77	1.00
Nurse home visit	0.61	0.24	0.58
Stool test	5.30	5.30	5.30
Blood test	0.18	0.22	0.36
Urine test	0.58	0.54	0.65
Specimen collection	0.02	0.02	0.02
Specimen postage	0.01	0.01	0.01
Prescriptions	2.19	2.69	2.62
A & E visit	0.49	1.09	1.11
Hospital admission	15.66	49.08	32.48
OPD visit	1.01	6.34	1.44
Transport to hospital	0.39	5.10	1.82
Accommodation of parent in hospital	0.21	0.61	0.55
TOTAL	**62.62**	**107.22**	**85.96**

Table 8.3 Total NHS costs, by organism and study component

GP CASE CONTROL COMPONENT

GENERAL PRACTICE COMPONENT	NO IID ORGANISM N=663	*SALMONELLA* SP. N=90	*S.ENTERITIDIS* N=59	*CAMPYLOBACTER* SP. N=192	*C.JEJUNI* N=172	ENTEROVIR *E.COLI.* N=197	EAGGEC N=65	*C.DIFFICILE* N=18	ROTAVIRUS SP. N=122	ROTAVIRUS GP 3 N=119	SRSV N=83
GP home visit	7661	1927	1457	3102	2773	1692	658	188	2444	2397	1081
GP surgery visit	12410	1938	1139	3723	3315	4301	1428	425	2482	2448	1394
Transport to GP	525	0	0	150	150	75	0	75	75	75	0
Phone GP	492.15	142.80	99.45	247.35	211.65	140.25	45.90	20.4	204	201.45	66.30
Nurse home visit	336	84	60	132	132	132	12	0	108	108	24
Blood test	112.30	17.80	0	13.30	13.3	26.6	15.2	1.9	0	0	3.8
Urine test	513	36	27	18	9	63	18	0	45	45	27
Specimen collection	11	6	0	5	5	3	0	2	0	0	1
Prescriptions	1278.25	153	60.50	403.75	343.25	619.75	181.00	33.00	341	341.00	192.50
A & E visit	270	54	0	54	54	108	54	0	0	0	27
Hospital admission	10575	7312.50	0	1687.50	1012.50	3150	0	0	0	0	225
OPD visit	1080	0	0	45	0	135	0	0	0	0	45
Transport to hospital	162	190	0	0	0	95	0	0	0	0	0
Accommodation of parent in hospital	52	208	0	91	0	182	0	0	0	0	13
TOTAL	**35477.70**	**12069.10**	**2842.95**	**9671.90**	**7928.70**	**10722.60**	**2412.10**	**745.30**	**5699.00**	**5615.45**	**3099.60**

Table 8.4 NHS costs per case, by organism and study component

GP CASE CONTROL COMPONENT

GENERAL PRACTICE COMPONENT	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI.*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
GP home visit	11.56	21.41	24.69	16.16	16.12	8.59	10.12	10.44	20.03	20.14	13.02
GP surgery visit	18.72	21.53	19.31	19.39	19.27	21.83	21.97	23.61	20.34	20.57	16.80
Transport to GP	0.79	0	0	0.78	0.87	0.38	0	4.17	0.61	0.63	0
Phone GP	0.74	1.59	1.69	1.29	1.23	0.71	0.71	1.13	1.67	1.69	0.80
Nurse home visit	0.51	0.93	1.02	0.69	0.77	0.67	0.18	0	0.89	0.91	0.29
Blood test	0.17	0.20	0	0.07	0.08	0.14	0.23	0.11	0	0	0.05
Urine test	0.77	0.40	0.46	0.09	0.05	0.32	0.28	0	0.37	0.38	0.33
Specimen collection	0.02	0.07	0	0.03	0.03	0.02	0	0.11	0	0	0.01
Prescriptions	1.78	1.70	0.94	2.10	1.85	3.15	2.56	1.68	2.80	2.63	2.13
A & E visit	0.41	0.60	0	0.28	0.31	0.55	0.83	0	0	0	0.33
Hospital admission	15.95	81.25	0	8.79	5.89	15.99	0	0	0	0	2.71
OPD visit	1.63	0	0	0.23	0	0.69	0	0	0	0	0.54
Transport to hospital	0.24	2.11	0	0	0	0.48	0	0	0	0	0
Accommodation of parent in hospital	0.08	2.31	0	0.47	0	0.92	0	0	0	0	0.16
TOTAL	**53.37**	**134.10**	**48.10**	**50.37**	**46.47**	**54.44**	**36.89**	**41.14**	**46.71**	**46.95**	**37.15**

Table 8.5 Total NHS costs, by organism and study component

COMMUNITY COMPONENT	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI.*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
	N=663	N=90	N=59	N=192	N=172	N=197	N=65	N=18	N=122	N=119	N=83
GP home visit	1222	0	0	94	94	188	47	0	94	94	235
GP surgery visit	1241	34	34	238	170	204	68	85	153	153	289
Transport to GP	0	0	0	0	0	0	0	0	0	0	0
Phone GP	53.55	2.55	2.55	15.3	10.20	2.55	2.55	0	5.1	5.1	5.1
Nurse home visit	12	0	0	12	12	0	0	0	0	0	0
Blood test	11.40	0	0	0	0	0	0	0	0	0	1.9
Urine test	27	0	0	0	0	9	0	0	0	0	0
Specimen collection	0	0	0	2	2	0	0	0	0	0	0
Prescriptions	137.50	11	11.00	33	33.00	33	11.00	5.25	11	11.00	49.50
A & E visit	27	0	0	27	0	27	0	0	0	0	0
Hospital admission	225	0	0	1575	0	1125	0	0	0	0	0
OPD visit	405	0	0	0	0	0	0	0	0	0	0
Transport to hospital	0	0	0	0	0	0	0	0	0	0	0
Accommodation of parent in hospital	0	0	0	0	0	0	0	0	0	0	0
TOTAL	**3361.45**	**47.55**	**47.55**	**1996.30**	**321.20**	**1588.55**	**128.55**	**90.25**	**263.10**	**263.10**	**580.50**

Table 8.6 NHS costs per case, by organism and study component

COMMUNITY COMPONENT	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
GP home visit	3.81	0	0	4.09	5.22	3.92	3.92	0	4.48	4.95	6.18
GP surgery visit	3.87	8.5	17	10.35	9.44	4.25	5.67	17	7.29	8.05	7.61
Transport to GP	0	0	0	0	0	0	0	0	0	0	0
Phone GP	0.17	0.64	1.28	0.67	0.57	0.05	0.21	0	0.24	0.27	0.13
Nurse home visit	0.04	0	0	0.52	0.67	0	0	0	0	0	0
Blood test	0.04	0	0	0	0	0	0	0	0	0	0.05
Urine test	0.08	0	0	0	0	0.19	0	0	0	0	0
Specimen collection	0	0	0	0.09	0.11	0	0	0	0	0	0
Prescriptions	0.39	2.75	5.05	1.43	1.68	0.69	0.4	1.01	0.52	0.53	1.20
A & E visit	0.08	0	0	1.17	0	0.56	0	0	0	0	0
Hospital admission	0.70	0	0	68.48	0	23.44	0	0	0	0	0
OPD visit	1.26	0	0	0	0	0	0	0	0	0	0
Transport to hospital	0	0	0	0	0	0	0	0	0	0	0
Accommodation of parent in hospital	0	0	0	0	0	0	0	0	0	0	0
TOTAL	**10.44**	**11.89**	**23.33**	**86.80**	**17.69**	**33.09**	**10.64**	**18.01**	**12.53**	**13.80**	**15.17**

Table 8.7 Summary costs per case for all IID

Community component (All cases)

COSTS (£)		(%)
GP COSTS	12.08	(15.3)
HOSPITAL COSTS	16.72	(21.2)
DIRECT PERSONAL	6.11	(7.7)
LOSS OF EMPLOYMENT:		
CASE	26.63	(33.8)
CARER	17.35	(22.0)
TOTAL	**78.89**	**(100)**

Community component cases who did see the GP (n=149)

COSTS (£)		(%)
GP COSTS	44.99	(22.3)
HOSPITAL COSTS	62.23	(30.8)
DIRECT PERSONAL	12.77	(6.3)
LOSS OF EMPLOYMENT:		
CASE	52.82	(26.2)
CARER	28.96	(14.4)
TOTAL	**201.77**	**(100)**

Community component cases who did not see the GP (n=397)

COSTS (£)		(%)
GP COSTS		0
HOSPITAL COSTS		0
DIRECT PERSONAL	3.72	(10.8)
LOSS OF EMPLOYMENT:		
CASE	17.21	(50.2)
CARER	13.38	(39.0)
TOTAL	**34.31**	**(100)**

GP case control component

COSTS (£)		(%)
GP COSTS	44.80	(17.6)
HOSPITAL COSTS	17.82	(7.0)
DIRECT PERSONAL	15.21	(6.0)
LOSS OF EMPLOYMENT:		
CASE	139.97	(55.2)
CARER	35.98	(14.2)
TOTAL	**253.78**	**(100)**

Enumeration component

COSTS (£)		(%)
GP COSTS	48.83	(18.6)
HOSPITAL COSTS	37.13	(14.1)
DIRECT PERSONAL	14.38	(5.5)
LOSS OF EMPLOYMENT:		
CASE	121.68	(46.4)
CARER	40.45	(15.4)
TOTAL	**262.47**	**(100)**

Table 8.8 Total NHS costs, by study component

GP CASE CONTROL COMPONENT

	-50%	-40%	-30%	-20%	-10%	BEST ESTIMATE	+10%	+20%	+30%	+40%	+50%
GP home visit	10739.5	12887.4	15035.3	17183.2	19331.1	21479	23626.9	25774.8	27922.7	303373.6	32218.5
GP surgery visit	16158.5	19390.2	22621.9	25853.6	29085.3	32317	35548.7	38780.4	42012.1	45243.8	48475.5
Transport to GP	750	900	1050	1200	1350	1500	1650	1800	1950	2100	2250
Phone GP	775.2	930.24	1085.28	1240.32	1395.36	1550.4	1705.44	1860.48	2015.52	2170.56	2325.6
Nurse home visit	480	576	672	768	864	960	1056	1152	1248	1344	1440
Stool test	4186.845	5024.21	5861.58	6698.95	7536.32	8373.69	9211.06	10048.4	10885.8	11723.2	12560.5
Blood test	138.65	166.38	194.11	221.84	249.57	277.3	305.03	332.76	360.49	388.22	415.95
Urine test	459	550.8	642.6	734.4	826.2	918	1009.8	1101.6	1193.4	1285.2	1377
Specimen collection	16.89	20.268	23.646	27.024	30.402	33.78	37.158	40.536	43.914	47.292	50.67
Specimen postage	7.295	8.754	10.213	11.672	13.131	14.59	16.049	17.508	18.967	20.426	21.885
Prescriptions	1733.75	2080.5	2427.25	2774	3120.75	3467.5	3814.25	4164	4507.75	4854.5	5201.25
A & E visit	405	486	567	648	729	810	891	972	1053	1134	1215
Hospital admission	12937.5	15525	18112.5	20700	23287.5	25875	28462.5	31050	33637.5	36225	38812.5
OPD visit	832.5	999	1165.5	1332	1498.5	1665	1831.5	1998	2164.5	2331	2497.5
Transport to hospital	318.5	382.2	445.9	509.6	573.3	637	700.7	764.4	828.1	891.8	955.5
Accommodation of parent in hospital	175.5	210.6	245.7	280.8	315.9	351	386.1	421.2	456.3	491.4	526.5
TOTAL	**50114.63**	**60137.6**	**70160.5**	**80183.4**	**90206.3**	**100229**	**110252**	**120275**	**130298**	**140321**	**150344**

Table 8.9 NHS costs per case, by study component

GP CASE CONTROL COMPONENT

	-50%	-40%	-30%	-20%	-10%	BEST ESTIMATE	+10%	+20%	+30%	+40%	+50%
GP home visit	6.795	8.154	9.513	10.872	12.231	13.59	14.949	16.308	17.667	19.026	20.385
GP surgery visit	10.225	12.27	14.315	16.36	18.405	20.45	22.495	24.54	26.585	28.63	30.675
Transport to GP	0.475	0.57	0.665	0.76	0.855	0.95	1.045	1.14	1.235	1.33	1.425
Phone GP	0.49	0.588	0.686	0.784	0.882	0.98	1.078	1.176	1.274	1.372	1.47
Nurse home visit	0.305	0.366	0.427	0.488	0.549	0.61	0.671	0.732	0.793	0.854	0.915
Stool test	2.65	3.18	3.71	4.24	4.77	5.3	5.83	6.36	6.89	7.42	7.95
Blood test	0.09	0.108	0.126	0.144	0.162	0.18	0.198	0.216	0.234	0.252	0.27
Urine test	0.29	0.348	0.406	0.464	0.522	0.58	0.638	0.696	0.754	0.812	0.87
Specimen collection	0.01	0.012	0.014	0.016	0.018	0.02	0.022	0.024	0.026	0.028	0.03
Specimen postage	0.005	0.006	0.007	0.008	0.009	0.01	0.011	0.012	0.013	0.014	0.015
Prescriptions	1.095	1.314	1.533	1.752	1.971	2.19	2.409	2.628	2.847	3.066	3.285
A & E visit	0.245	0.294	0.343	0.392	0.441	0.49	0.539	0.588	0.637	0.686	0.735
Hospital admission	7.83	9.396	10.962	12.528	14.094	15.66	17.226	18.792	20.358	21.924	23.49
OPD visit	0.505	0.606	0.707	0.808	0.909	1.01	1.111	1.212	1.313	1.414	1.515
Transport to hospital	0.195	0.234	0.273	0.312	0.351	0.39	0.429	0.468	0.507	0.546	0.585
Accommodation of parent in hospital	0.105	0.126	0.147	0.168	0.189	0.21	0.231	0.252	0.273	0.294	0.315
TOTAL	**31.31**	**37.572**	**43.834**	**50.096**	**56.358**	**62.62**	**68.882**	**75.144**	**81.406**	**87.668**	**93.93**

Table 8.10 Total NHS costs, by study component

COMMUNITY COMPONENT

	-50%	-40%	-30%	-20%	-10%	BEST ESTIMATE	+10%	+20%	+30%	+40%	+50%
GP home visit	1245.5	1494.6	1743.7	1992.8	2241.9	2491	2740.1	2989.2	3238.3	3487.4	3736.5
GP surgery visit	1377	1652.4	1927.8	2203.2	2478.6	2754	3029.4	3304.8	3580.2	3855.6	4131
Transport to GP	0	0	0	0	0	0	0	0	0	0	0
Phone GP	57.375	68.85	80.325	91.8	103.275	114.75	126.225	137.7	149.175	160.65	172.125
Nurse home visit	18	21.6	25.2	28.8	32.4	36	39.6	43.2	46.8	50.4	54
Stool test	394.835	743.802	552.769	631.736	710.703	789.67	868.637	947.604	1026.571	1105.538	1184.505
Blood test	16.5	19.8	23.1	26.4	29.7	33	36.6	39.6	42.9	46.2	49.5
Urine test	40.5	48.6	56.7	64.8	72.9	81	89.1	97.2	105.3	113.4	121.5
Specimen collection	1.6	1.92	2.24	2.56	2.88	3.2	3.52	3.84	4.16	4.48	4.8
Specimen postage	0.69	0.828	0.966	1.104	1.242	1.38	1.518	1.656	1.794	1.932	2.07
Prescriptions	200.625	240.75	280.875	321	361.125	401.25	441.375	481.5	521.625	561.75	601.875
A & E visit	81	97.2	113.4	129.6	145.8	162	178.2	194.4	210.6	226.8	243
Hospital admission	3656.25	4387.5	5118.75	5850	6581.25	7312.5	8043.75	8775	9506.25	10237.5	10968.75
OPD visit	472.5	567	661.5	756	850.5	954	103.5	1134	1228.5	1323	1417.5
Transport to hospital	380	456	532	608	684	760	836	912	988	1064	1140
Accommodation of parent in hospital	45.5	54.6	63.7	72.8	81.9	91	100.1	109.2	118.3	127.4	136.5
TOTAL	**7987.88**	**9585.45**	**11183.03**	**12780.6**	**14378.18**	**15975.75**	**17573.33**	**1917.9**	**20768.48**	**22366.05**	**23963.63**

Table 8.11 NHS costs per case, by study component

COMMUNITY COMPONENT

	-50%	-40%	-30%	-20%	-10%	BEST ESTIMATE	+10%	+20%	+30%	+40%	+50%
GP home visit	2.245	2.694	3.143	3.592	0.041	4.49	4.939	5.388	5.837	6.286	6.735
GP surgery visit	2.48	2.976	3.472	3.968	4.464	4.96	5.456	5.952	6.448	6.944	7.44
Transport to GP	0	0	0	0	0	0	0	0	0	0	0
Phone GP	0.105	0.126	0.147	0.168	0.189	0.21	0.231	0.252	0.273	0.294	0.315
Nurse home visit	0.03	0.036	0.042	0.048	0.054	0.06	0.066	0.072	0.078	0.084	0.09
Stool test	0.71	0.852	0.994	1.136	1.278	1.42	1.562	1.704	1.846	1.988	2.13
Blood test	0.03	0.036	0.042	0.048	0.054	0.06	0.066	0.072	0.078	0.084	0.09
Urine test	0.075	0.09	0.105	0.12	0.135	0.15	0.165	0.18	0.195	0.21	0.225
Specimen collection	0.01	0.012	0.014	0.016	0.018	0.02	0.022	0.024	0.026	0.028	0.03
Specimen postage	0.005	0.006	0.007	0.008	0.009	0.01	0.011	0.012	0.013	0.014	0.015
Prescriptions	0.36	0.432	0.504	0.576	0.648	0.72	0.792	0.864	0.936	1.008	1.08
A & E visit	0.145	0.174	0.203	0.232	0.261	0.29	0.319	0.348	0.377	0.406	0.435
Hospital admission	6.56	7.908	9.226	10.544	11.862	13.18	14.498	15.816	17.134	18.452	19.77
OPD visit	0.85	1.02	1.19	1.36	1.53	1.7	1.87	2.04	2.21	2.38	2.55
Transport to hospital	0.685	0.822	0.959	1.096	1.233	1.37	1.507	1.644	1.781	1.918	2.055
Accommodation of parent in hospital	0.08	0.096	0.112	0.128	0.144	0.16	0.176	0.192	0.208	0.224	0.24
TOTAL	**14.4**	**17.28**	**20.16**	**23.04**	**25.92**	**28.8**	**31.68**	**34.56**	**37.44**	**40.32**	**43.2**

Table 8.12 Total NHS costs, by study component

ENUMERATION COMPONENT

	-50%	-40%	-30%	-20%	-10%	BEST ESTIMATE	+10%	+20%	+30%	+40%	+50%
GP home visit	18988	22785.6	26583.2	30380.8	34178.4	37976	41773.6	45571.2	49368.8	53166.4	56964
GP surgery visit	19176	23011.2	26846.4	30681.6	34516.8	38352	42187.2	46022.4	49857.6	53692.8	57528
Transport to GP	1312.5	1575	1837.5	2100	2362.5	2625	2887.5	3150	3412.5	3675	3937.5
Phone GP	1025.1	1230.12	1435.14	1640.16	1845.18	2050.2	2255.22	2460.24	2665.26	2870.28	3075.3
Nurse home visit	636	763.2	890.4	1017.6	1144.8	1272	1399.2	1526.4	1653.6	1780.8	1908
Stool test	5453.5	6544.2	7634.9	8725.6	9816.3	10907	11997.7	13088.4	14179.1	15269.8	16360.5
Blood test	367.15	440.58	514.01	587.44	660.87	734.3	807.73	881.16	954.59	1028.02	1101.45
Urine test	666	799.2	932.4	1065.6	1198.8	1332	1465.2	1598.4	1731.6	1864.8	1998
Specimen collection	22	26.4	30.8	35.2	39.6	44	48.4	52.8	57.2	61.6	66
Specimen postage	9.5	11.4	13.3	15.2	17.1	19	20.9	22.8	24.7	26.6	28.5
Prescriptions	2698.125	3237.75	3777.375	4317	4856.625	5396.25	5935.875	6475.5	7015.125	7554.75	8094.375
A & E visit	1215	1458	17.01	1944	2187	2430	2673	2916	3159	3402	3645
Hospital admission	35437.5	42525	49612.5	56700	63787.5	70875	77962.5	85050	92137.5	99225	106312.5
OPD visit	1575	1890	2205	2520	2835	3150	3465	3780	4095	4410	4725
Transport to hospital	1987	2384.4	2781.8	3179.2	3576.6	3974	431.4	4768.0	5166.2	5563.6	5961
Accommodation of parent in hospital	598	717.6	837.2	956.8	1076.4	1196	1315.6	1435.2	1554.8	1674.4	1794
TOTAL	**91166.375**	**109399.65**	**127632.925**	**145866.2**	**164099.475**	**182332.75**	**200566.025**	**218799.3**	**237032.575**	**255265.85**	**273499.125**

Table 8.13 NHS costs per case, by study component

ENUMERATION COMPONENT

	-50%	-40%	-30%	-20%	-10%	BEST ESTIMATE	+10%	+20%	+30%	+40%	+50%
GP home visit	9.225	11.07	12.915	14.76	16.605	18.45	20.295	22.14	23.985	25.83	27.675
GP surgery visit	9.32	11.184	13.048	14.912	16.776	18.64	20.504	22.368	24.232	26.096	27.96
Transport to GP	0.64	0.768	0.896	1.024	1.152	1.28	1.408	1.536	1.664	1.792	1.92
Phone GP	0.5	0.6	0.7	0.8	0.9	1	1.1	1.2	1.3	1.4	1.5
Nurse home visit	0.29	0.348	0.406	0.464	0.522	0.58	0.638	0.696	0.754	0.812	0.87
Stool test	2.65	3.18	3.71	4.24	4.77	5.3	5.83	6.36	6.89	7.42	7.95
Blood test	0.18	0.216	0.252	0.288	0.324	0.36	0.396	0.432	0.468	0.504	0.54
Urine test	0.325	0.39	0.455	0.52	0.585	0.65	0.715	0.78	0.845	0.91	0.975
Specimen collection	0.01	0.012	0.014	0.016	0.18	0.02	0.022	0.024	0.026	0.028	0.03
Specimen postage	0.005	0.006	0.007	0.008	0.009	0.01	0.011	0.012	0.013	0.014	0.015
Prescriptions	1.31	1.572	1.834	2.096	2.358	2.62	2.882	3.144	3.406	3.668	3.93
A & E visit	0.555	0.666	0.777	0.888	0.999	1.11	1.221	1.332	1.443	1.554	1.665
Hospital admission	16.24	19.488	22.736	25.984	29.232	32.48	35.728	38.976	42.224	45.472	48.72
OPD visit	0.72	0.864	1.008	1.152	1.296	1.44	1.584	1.728	1.872	2.016	2.16
Transport to hospital	0.91	1.092	1.274	1.456	1.638	1.82	2.002	2.184	2.366	2.548	2.73
Accommodation of parent in hospital	0.275	0.33	0.385	0.44	0.495	0.55	0.605	0.66	0.715	0.77	0.825
TOTAL	**42.98**	**51.576**	**60.172**	**68.768**	**77.364**	**85.96**	**94.556**	**103.152**	**111.748**	**120.344**	**128.94**

Table 8.14 Summary costs per case, by organism

	PRESENTING TO GP (GP CASE CONTROL COMPONENNT)				
			LOSS OF EMPLOYMENT		
	NHS	**DIRECT**	**CASE**	**CARER**	**TOTAL**
organism					
All IID	62.62	15.21	139.97	35.98	253.78
No IID organism	53.51	12.21	130.27	24.83	220.82
Salmonella	134.10	31.88	369.76	70.58	606.33
Campylobacter	50.37	17.80	214.32	32.46	314.95
Enterovir *E.coli*	54.43	19.25	108.49	32.04	214.21
C. difficile	41.41	19.69	150.92	75.46	287.48
Rotavirus	46.71	17.07	23.58	76.63	163.99
SRSV	37.34	12.10	78.94	48.13	176.51
	IN THE COMMUNITY — CASES WHO DID SEE THE GP				
			LOSS OF EMPLOYMENT		
	NHS	**DIRECT**	**CASE**	**CARER**	**TOTAL**
organism					
All IID	107.22	12.77	52.82	28.96	201.77
No IID organism	46.69	12.37	63.81	36.62	159.49
Salmonella	23.78	12.78	39.95	0	76.50
Campylobacter	160.56	15.87	79.90	18.44	274.77
Enterovir *E.coli*	126.89	9.61	33.80	18.44	188.74
C. difficile	30.09	14.32	0	0	44.40
Rotavirus	37.59	8.46	0	28.54	74.59
SRSV	54.53	16.59	29.96	49.94	151.02
	IN THE COMMUNITY — CASES WHO DID NOT SEE THE GP				
			LOSS OF EMPLOYMENT		
	NHS	**DIRECT**	**CASE**	**CARER**	**TOTAL**
organism					
All IID	0	3.72	17.21	13.38	34.31
No IID organism	0	3.70	16.25	12.10	32.05
Salmonella	0	3.75	0	0	3.75
Campylobacter	0	4.20	23.97	0	28.17
Enterovir *E.coli*	0	4.17	4.44	22.19	30.80
C. difficile	0	1.10	0	39.95	41.05
Rotavirus	0	0	0	0	0
SRSV	0	2.18	0	12.20	14.48

Table 8.15 Table of geometric means and 95% confidence intervals of data used for calculating total costs

	GP CASE CONTROL COMPONENT			COMMUNITY COMPONENT			ENUMERATION COMPONENT		
	N=1652	GEOMETRIC MEAN	95% CONFIDENCE INTERVAL	N=555	GEOMETRIC MEAN	95% CONFIDENCE INTERVAL	N=2182	GEOMETRIC MEAN	95% CONFIDENCE INTERVAL
Items which contribute to NHS costs	n			n			n		
GP home visits	352	1.19	0.58–2.43	41	1.19	0.59–2.41	582	1.25	0.55–2.80
GP surgery visits	1329	1.27	0.55–2.91	115	1.26	0.56–2.87	1580	1.28	0.56–2.88
Phone calls to GP	420	1.30	0.57–2.99	34	1.22	0.58–2.55	586	1.24	0.56–2.73
Nurse home visits	53	1.28	0.49–3.37	3	1		64	1.28	0.45–3.63
Stool tests								1.15	0.59–2.24
Blood tests	60	1.36	0.54–3.45	6	1.59	0.52–4.81	88	1.17	0.52–2.64
Urine tests	82	1.16	0.60–2.23	9	1		133	1.08	0.67–1.73
Specimen collection	26	1.20	0.56–2.55	3	1		33	1.20	0.53–2.67
Specimen postage							30	1.18	0.60–2.33
Prescriptions	403	1.29	0.53–3.15	46	1.35	0.53–3.43	660	1.29	0.56–3.00
Items which contribute to personal costs									
Prescriptions	267	1.30	0.54–3.11	20	1.28	0.58–2.83	304	1.24	0.60–2.58
A & E visit	20	1.37	0.60–3.11	5	1.15	0.63–2.11	65	1.23	0.53–2.84
Hospital admission	29	2.49	0.38–16.40	6	2.61	0.17–39.97	77	2.78	0.50–15.46
OPD visit	18	1.59	0.45–5.58	7	2.48	0.72–8.58	51	1.25	0.57–2.75
Transport to hospital									
Accommodation of parent in hospital	27	2.63	0.43–16.11	5	3.62	0.59–22.20	73	2.85	0.53–15.41
Ill on holiday	41	14.62	0.88–242.25	7	6.36	0.87–46.47	41	9.53	0.70–130.47
Ill at home	1194	6.24	0.34–113.23	287	3.83	0.18–82.27	1507	6.13	0.33–113.62

Table 8.16 Total cost of IID in the community, in England, per year

ESTIMATED TOTAL COST FOR ALL IID USING COMMUNITY COMPONENT ESTIMATE											
	-50%	-40%	-30%	-20%	-10%	BEST EST. MILLION £	+10%	+20%	+30%	+40%	+50%
All IID	371	446	520	594	669	742.8	817	891	966	104	1114
ESTIMATED TOTAL COST FOR ALL IID USING ESTIMATES FROM COMMUNITY COMPONENT FOR THOSE WHO DID NOT SEE A GP AND ESTMATES FROM THE GP CASE CONTROL COMPONENT FOR THOSE PRESENTING TO A GP											
All IID	338	406	474	542	609	676.9	745	812	880	948	1015

Table 8.17 Total cost of IID in the community, in England, per year, by organism

ORGANISM	-50%	-40%	-30%	-20%	-10%	BEST EST. MILLION £	+10%	+20%	+30%	+40%	+50%
All IID	338	406	474	542	609	676.9	745	812	880	948	1015
No target organism	159	191	223	255	287	318.5	350	382	414	446	478
Salmonella	23.2	27.8	32.5	37.1	41.8	46.4	51	55.7	60.3	65	69.6
Campylobacter	34.8	41.7	48.7	55.6	62.6	69.5	76.5	83.4	90.4	97.3	104
E.coli	34.7	41.6	48.5	55.4	62.4	69.3	76.2	83.2	90.1	97.0	104
C.difficile	2.8	3.36	3.92	4.48	5.04	5.6	6.16	6.72	7.28	7.84	8.4
Rotavirus	8.25	9.9	11.6	13.2	14.9	16.5	18.2	19.8	21.5	23.1	24.8
SRSV	12.2	14.6	17.1	19.5	22	24.4	26.8	29.3	31.7	34.2	36.6

Table 8.18 Would you be willing to pay more on your food bill for measures to reduce the risk to yourself and other people?

	GP CASE CONTROL COMPONENT		COMMUNITY COMPONENT		ENUMERATION COMPONENT	
	N	%	N	%	N	%
Yes	1053	63.7	367	66.1	1331	61.0
No	326	19.7	114	20.5	458	21.0
Missing	273	16.6	74	13.4	393	18.0
Total	1652	100	555	100	2182	100

Table 8.19 Willing to pay how much extra, for every £1 spent on regular monthly food bill, to ensure the lowest possible risk of causing food poisoning

AMOUNT (P)	GP CASE CONTROL COMPONENT		COMMUNITY COMPONENT		ENUMERATION COMPONENT	
	N	%	N	%	N	%
1	88	6.4	45	9.4	152	8.5
2–5	296	21.5	113	23.5	364	20.3
6–10	325	23.6	126	26.2	396	22.1
11–25	128	9.3	38	7.9	157	8.8
26–50	145	10.5	32	6.7	198	11.1
51–100	4	0.3	1	0.2	11	0.6
more than 100 [150–1000]	2	0.1	1	0.2	3	0.2
missing	391	28.4	125	26.0	508	28.4
Total	1379	100	481	100	1789	100

Table 8.20 If a fresh chicken (weight about 3lb) normally costs about £2.50, how much more would you be willing to pay for a chicken which had been treated to reduce the chance of it having *Salmonella* food poisoning bacteria on it

	GP CASE CONTROL COMPONENT				COMMUNITY COMPONENT				ENUMERATION COMPONENT			
	NEGLIGIBLE RISK OF INFECTION		HALF THE RISK OF INFECTION		NEGLIGIBLE RISK OF INFECTION		HALF THE RISK OF INFECTION		NEGLIGIBLE RISK OF INFECTION		HALF THE RISK OF INFECTION	
AMOUNT (P)	N	%	N	%	N	%	N	%	N	%	N	%
1	18	1.3	44	3.2	4	0.8	19	4.0	36	2.0	80	4.5
2–5	54	3.9	128	9.3	23	4.8	42	8.7	81	4.5	149	8.3
6–10	134	9.7	157	11.4	41	8.5	60	12.5	170	9.5	199	11.1
11–25	210	15.2	169	12.3	77	16.0	62	12.9	282	15.8	198	11.1
26–50	525	38.1	209	15.2	179	37.2	67	13.9	623	34.8	255	14.3
51–100	39	2.8	7	0.5	11	2.3	3	0.6	47	2.6	17	1.0
more than 100 [125–275]	11	0.8	2	0.1	1	0.2	0	0.0	14	0.8	4	0.2
missing												
Total	1379	100	1379	100	481	100	481	100	1789	100	1789	100

Table 8.21 If you were offered poultry meat which had been irradiated and could be guaranteed 99% free of *Salmonella*, would you be prepared to buy it in preference to non-irradiated poultry if any of the following applied?

WILLINGNESS TO PAY	GP CASE CONTROL COMPONENT		COMMUNITY % COMPONENT		ENUMERATION COMPONENT	
	N	%	N	%	N	%
MORE	848	51.3	267	48.1	1137	52.1
SAME PRICE	223	13.5	72	13.0	305	14.0
LESS	109	6.6	32	5.8	155	7.1
NOT AT ANY PRICE	338	20.5	136	24.5	379	17.4
MISSING	134	8.1	48	8.6	206	9.4
TOTAL	1652	100	555	100	2182	100

Table 8.22 Which category in the above table would have been ticked if you could be assured that irradiated meat is absolutely safe and tastes the same as non-irradiated meat?

WILLINGNESS TO PAY	GP CASE CONTROL COMPONENT		COMMUNITY % COMPONENT		ENUMERATION COMPONENT	
	N	%	N	%	N	%
MORE	812	49.2	247	49.4	986	45.2
SAME	216	13.1	100	18.0	346	15.9
LESS	43	2.6	14	2.5	83	3.8
NOT AT ANY PRICE	129	7.8	47	8.5	137	6.3
MISSING	452	27.4	120	43.8	630	28.8
TOTAL	1652	100	555	100	2182	100

Chapter 9
Risk Factors for Intestinal Infectious Disease

This chapter presents the results of the analysis of statistical associations between various characteristics and exposures reported by subjects and the presence or absence of IID. Results for all cases of IID are presented in section 9.1 and results according to which organism, if any, was identified in the stools in section 9.2, where a smaller selection of risk factors was studied. The selection of factors for each organism was based on previous knowledge of established or suspected risk factors. Each section includes a brief discussion. Summary tables are presented in the text. Findings are summarised in section 9.3, and an overall discussion is presented in section 9.4.

The statistical associations which the study has identified are real, but as in any epidemiological study, it is not possible to establish with certainty whether these associations are causal, i.e., whether the risk factors are causally associated with illness or infection. The issue of possible causality is addressed in the discussion.

9.1 RISK FACTORS FOR ALL CASES OF IID

This section presents statistical associations between risk factors and cases of IID, irrespective of whether or not a target organism was found in the stool. The risk factors are listed in Table 9.1 and the full risk-factor questionnaire is in Appendix 6.

Subjects were analysed in three groups from the GP case-control component: 753 adults (those aged over 15 years), 463 children (those aged 1 to 15 years) and 133 infants (those aged less than one year). Analyses were confined to matched case-control pairs who had completed the appropriate questionnaires. Data from the cohort study is still being analysed.

9.1.1 Conceptual framework

The conceptual framework described below was used in its entirety only for the study of all cases of IID and for cases of IID without a target organism in the stool. When the conceptual framework was used in its entirety, a large number of variables was included, not only those based on specific hypotheses. This is extremely useful for generating new hypotheses, but some of the associations are likely to be spurious because when a large number of tests are carried out, the likelihood that some statistically significant results are found as a result of chance increases.

The conceptual framework assumed three levels of association with IID (see Figure 9.1):

- **Social factors:** social class, employment status, educational levels, aspects of housing (house ownership, crowding).These affect the next level:
- **Intermediate factors:** factors indirectly affecting the likelihood of being exposed to relevant organisms: hygiene behaviour, housing conditions (e.g., size of kitchen), travel, chronic diseases and medication. These affect the next level:
- **Direct factors:** factors immediately related to the likelihood of infection with relevant organisms: food consumption, swimming, pets and contact with people with diarrhoea and/or vomiting.

Figure 9.1 Conceptual framework for analysis of risk factors

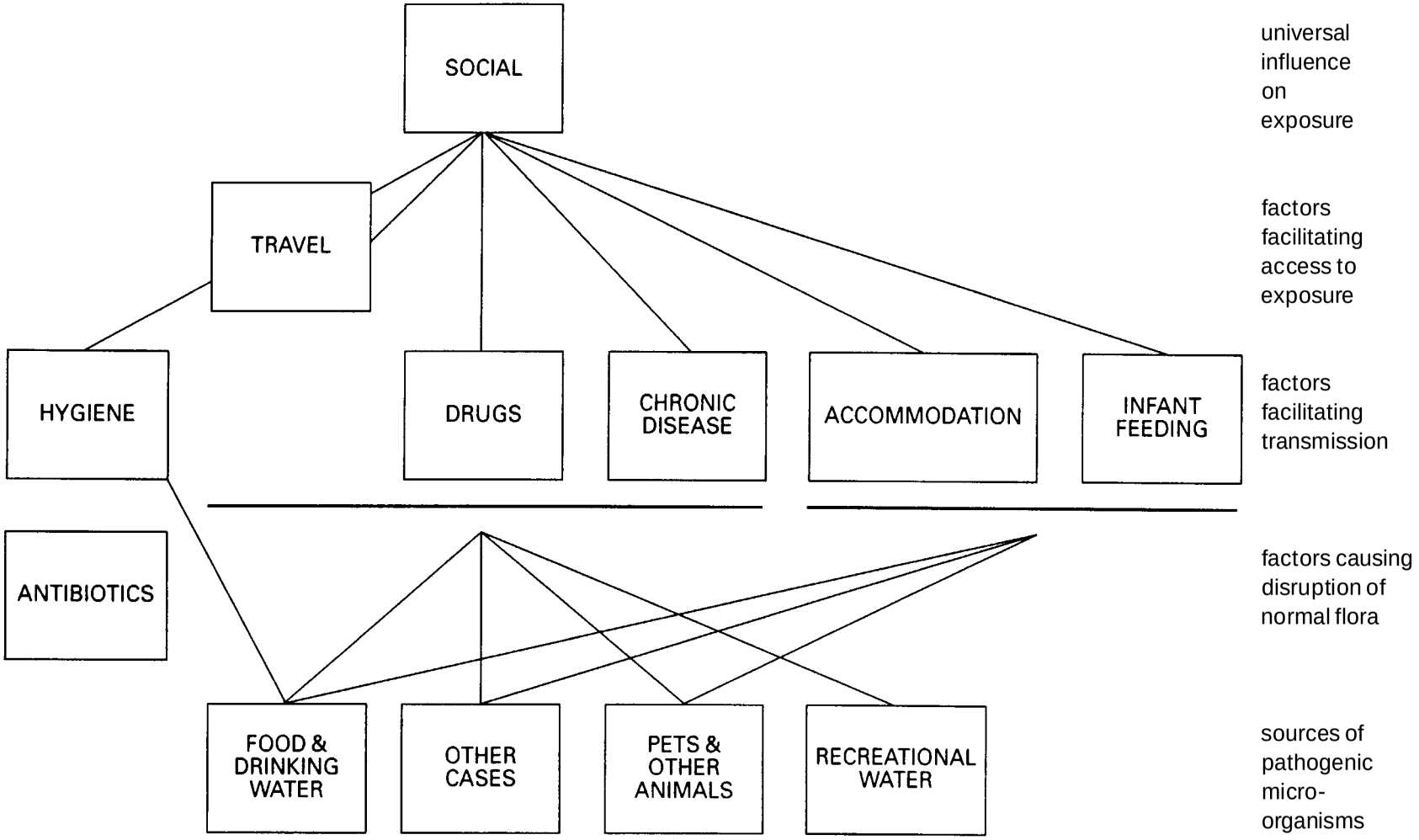


Table 9.1 Summary of risk factors investigated

SOCIAL FACTORS	
Marital status	
Ethnic group	
Employment status	
Occupation(of patient and/or spouse/partner)	
Education level	
Accommodation	house type/size
	shared accommodation
OTHER FACTORS	
Travel	UK
	abroad
Swimming/water sports	
Pets	type
	exposure to pet faeces
Exposure to other animals (e.g. zoo, farm)	
Drinking water (source and use of jug water filters)	
Foods	meat (by type)*
	fish and shellfish (by type)
	salads, raw fruit and vegetables (by type)
	rice (boiled or fried)
	milk*
	cakes and tarts
	eggs and egg dishes
	*plus more detailed questions about chicken, cold sliced meats and dairy products
Meals outside the home (by venue)	
Shopping habits frequency	
	checking of labels/packaging
Domestic hygiene	kitchen/work surface size
	kitchen facilities/equipment
	food storage practice
	refrigerator temperature control
	defrosting of frozen chicken
	use of chopping boards
	dealing with leftovers
Beliefs about food hygiene/food poisoning	
Medicines	antibiotics
	antacids
	other

The analysis, which was repeated for each of the three age groups, selected a first model by including only social factors, then selected a second model adding the intermediate factors to the first model, and a final model, adding direct factors to the second model.

9.1.2 Presentation

For each of the three age groups, the tables present factors which were statistically significant in each of the three models, at the traditional probability value of p=0.05 for statistical significance; with odds ratios (OR) and probability (p)-values. An OR of 4 means that the frequency of disease was four times higher in people who reported the factor than in those who did not report it; and an OR of 0.5 means that those reporting the factor had IID half as frequently as those who did not report it. Factors of interest, because of the existing hypothesis or because they were statistically significant in other analyses, and those with borderline significance are also reported.

We present below the results of the risk-factor analysis for three groups of all IID: adults, children and infants presenting to the GP in the GP case-control component (the GP component).

9.1.3 Adults (aged 16 years and over)

This was the largest of the groups with 753 cases in the analysis. The frequency of organisms identified is presented in Table 9.2. *Campylobacter* was identified in 15% of cases, *Salmonella* in 7% and viruses in 8.7% of cases. 51% of cases had no target organism identified in the stool. The analysis of risk factors is summarised in Table 9.3.

Table 9.2 Organisms identified in adult cases (>15 years of age) presenting to the GP, matched to controls and included in the risk-factor analysis (n = 753). Cases in which more than one organism was identified appear more than once in this table.

	ADULTS	
	NUMBER IDENTIFIED	**PERCENT OF THOSE TESTED**
Bacteria		
Aeromonas spp.	38	5.1
Bacillus spp. (>10^4/g)	2	0.3
Campylobacter spp.	117	15.5
Clostridium difficile cytotoxin	7	1.1
Clostridium perfringens enterotoxin	24	3.2
E. coli O157	0	0
Enterovirulent *E. coli*		
AEEC	24	3.3
DAEC	29	4.0
EAggEC	43	5.9
EIEC	0	0
EPEC	0	0
ETEC	21	2.9
VTEC (non O157)	0	0
Salmonella spp.	54	7.2
Shigella spp.	9	1.2
Staphylococcus aureus (>10^6/g)	3	0.4
Vibrio spp.	0	0
Yersinia spp.	12	1.6
Protozoa		
Cryptosporidium parvum	2	0.3
Giardia intestinalis	9	1.5
Viruses		
Adenovirus group F	1	0.2
Astrovirus	12	1.8
Calicivirus	2	0.3
Rotavirus group A	13	1.8
Rotavirus group C	0	0
SRSV	31	4.6
No target organism identified	384	51.0
Total number of cases	**753**	

Results

Social factors: when compared to social classes I and II, the risk of IID was 50% higher in social classes III and IV, although this was not statistically significant, and four times higher in social class V. There was a statistically significant effect of working part time (30% lower risk) when compared to working full time. There was no statistically significant effect of unemployment, but there was a statistically significant three-fold increase of risk in those not working because of a disability.

Table 9.3 Risk factors for IID in adults presenting to the GP. Odds ratios (OR) and probability (p) values for three models: social factors alone, social plus intermediate factors, and social plus intermediate plus direct factors. Factors presented were significant in one of the models (n = 753 pairs).

		MODEL 1: SOCIAL		MODEL 2: INTERMEDIATE		MODEL3: DIRECT	
SOCIAL FACTORS		**OR**	**P**	**OR**	**P**	**OR**	**P**
Social class							
	III	1.6	ns	1.8	0.01	1	ns
	IV	1.5	ns	1.7	0.05	1.2	ns
	V	4.0	0.002	4.9	0.002	2.8	ns
Employment							
	part-time	0.7	0.01	0.7	ns	0.9	ns
	disabled	3.4	0.002	3.7	0.03	2.2	ns
INTERMEDIATE FACTORS							
Travel (no travel = 1)							
	UK/N Europe			1	ns	1.1	ns
	SE Europe/Med/M East			9	0.001	10.2	<0.00
	Africa/Caribbean			30.9	0.001	40.1	0.01
Domestic practices							
Shops once a week				0.7	0.002	0.6	0.02
Obeys storage instructions sometimes				0.6	<0.001	0.6	0.02
Chronic Illness							
	Asthma			2.4	0.02	2.5	0.05
	Diabetes			4.8	0.03	6.7	0.02
Medication	Antacids			1.8	0.01	1.9	0.02
	CNS			0.7	0.004		
Water Jug Filter				0.6	0.004	0.4	<0.001
DIRECT FACTORS							
Contacts							
	Household – child					10.1	<0.001
	Outside – yes/not sure					2.7/3.3	<0.001
Pets							
	Unusual pets					3.7	0.03
	Dog (except when mess cleared up)					0.5	0.04
	Cat					0.6	0.03
	Rabbit					0.5	0.01
	Cooks pet food at home					0.7	0.05
Any recreational swimming (controlling for travel abroad)						**0.6**	**0.05**
Food							
	Oysters					7.0	0.02
	Pulses					0.5	<0.001
	Fruit (edible skin)					0.5	<0.001
	Dried fruit					0.5	<0.001
	Freshly boiled rice					0.7	0.02
	Take-away sandwich					0.6	0.02
	Pasteurised dairy products					0.5	<0.001

ns = non-significant

Intermediate factors: travel to countries outside northern Europe was associated with a marked increase in risk: nine- fold for travel to countries around the Mediterranean and Middle East, and 31-fold for travel elsewhere. Of over 30 domestic practices investigated, only three were statistically significantly

associated with an altered risk of IID: (i) shopping for food once a week (as opposed to more or less frequently) reduced risk of disease by 30%; (ii) obeying storage instructions sometimes (as opposed to always or never) reduced the risk by 40%; and (iii) using jug filters for water also reduced the risk by 40%. No other domestic practice had a statistically significant effect on risk of disease. Chronic illness increased the risk of IID: asthma by 2.5-fold and diabetes by five-fold. Use of antacids almost doubled the risk of disease, and reported use of central nervous system drugs (mostly against epilepsy) reduced it by 30%.

When these intermediate variables were introduced, the effect of both disability leave and social class increased, with the risk of IID in those in social class III and IV becoming statistically significant. Most of this effect was due to the introduction of travel abroad into the model.

Direct factors: risks were increased ten-fold for those who reported contact with children with diarrhoea and/or vomiting in the household and three-fold for contact with adults with diarrhoea and/or vomiting outside the household. Both associations were statistically significant. Eating oysters and having unusual pets increased the risk by seven- and four-fold, respectively. No other food was found to be statistically significantly associated with increase risk of disease.

All the remaining direct factors which were statistically significantly associated with IID reduced the risk. Pet ownership reduced the risk by 40% in the case of cats and 50% for rabbits or dogs, except for those responsible for cleaning up the dog's mess. Recreational swimming reduced the risk by 40% but only if travel abroad was included in the model, and the level of significance was low ($p=0.05$). Eating any of the following foods in the previous ten days was statistically significantly associated with a 50% lower risk of IID: pulses, fruit (either fresh fruit with edible skin or dried fruit), boiled rice cooked and eaten immediately, pasteurised products and take-away sandwiches.

Introducing the direct variables into the model removed most of the effect of social factors and had practically no impact on the effect of intermediate variables. This suggests that most of the effect of the social factors, but not the effect of the intermediate factors, is mediated by the direct factors.

For many of the questions, people who ticked the 'do not know' box, or failed to complete the question, had a higher risk of IID that those who gave a definite reply, irrespective of what that reply was. For example those who ticked the 'do not know' box or failed to answer the question about years of schooling had an increased risk of disease, when compared with those who replied to the question, irrespective of what that reply was.

Summary

The analysis of risk factors in adults presenting to GPs with IID showed, for social factors, a marked association with social class, those unable to work because of disability, and part-time employment, mediated in some degree by the direct factors. Of the intermediate factors, travel outside northern Europe, presence of diabetes and asthma and use of antacids were associated with increased risk. Intermediate factors associated with lower risk included shopping once a week, using a jug filter for water, and the use of CNS drugs. Of the direct factors, contact with children and adults with diarrhoea and/or vomiting, eating oysters and having an unusual pet increased the risk of disease. No other reported food consumption carried a risk. Having a cat, dog or rabbit; recreational swimming; and eating pulses,

fruit, freshly cooked rice, pasteurised products and take-away sandwiches were all statistically associated with a reduced risk of suffering IID.

Discussion

There is one caveat which should be observed when interpreting these data. The cases were a selected sub-group of all IID. They were those cases who presented to their GP. It is therefore possible that some of the risk factors identified here are determinants not of disease, but of presentation. We have shown that the strongest determinants of presentation to the GP are the severity and duration of disease. This may be of particular relevance to the association with co-existing chronic illnesses, like diabetes and asthma, which may influence presentation. Similarly it is plausible that cases who report contact with another person with diarrhoea and/or vomiting may be more likely to present to their GP.

The most striking result from this analysis is the absence of a statistically significant association between IID and the consumption of foods known to be associated with food poisoning. With the exception of oysters, why were foods such as chicken and eggs, which have been clearly shown to cause outbreaks and, which have also been associated, albeit less frequently, with sporadic cases, not associated with increased risk in this study? There are a number of possible reasons for this.

The first possible reason is that our case definition included all IID, whether or not a target organism was identified and irrespective of the nature of the organism if one was identified. Some of the cases will have resulted from non foodborne modes of spread, particularly person-to-person contact. The risks of some foods may have been masked by including among our cases people who contracted their illness through different routes. This will be re-examined when discussing risk factors for *C.jejuni*.

The second possible reason is that our study may have lacked precision because it sought information on food consumption in the ten days prior to the onset of illness. The incubation period for a number of the organisms we addressed could have been much shorter than this. So, for example, while cases may indeed have eaten more chicken than controls in the three days before they were ill, the difference between cases and controls over a ten-day period is likely to have been less for commonly eaten foods, and therefore it is less easy to demonstrate an association without much larger numbers of cases.

The third possible reason is simply that of recall. Cases and controls may not have been able to remember food intake correctly, or may actually have a biased perception of their food intake. We think this unlikely, as recall of food consumption is usually good enough in most outbreaks to lead to identification of the cause.

The fourth possible reason is that our findings are a closer approximation to what happens on a day-to-day basis than the existing data on which our understanding of risk factors is based. Our study mainly addressed apparently sporadic cases, many of which were only mildly ill, whereas current understanding is based on data originating from outbreak investigations or studies of sporadic cases who were sufficiently ill to be identified by routine surveillance. However, cases included in this analysis were ill enough to present to their GP. If outbreaks were caused by the relatively rare occurrence of heavily contaminated food vehicles, and sporadic cases by the much more frequent occurrence of light contamination, the result would be that hardly anyone exposed in an outbreak would escape infection (and the vehicle would be easier to identify) but that few of those people exposed sporadically would be affected. Whether a sporadically exposed person became ill

or not would depend mainly on their individual susceptibility. The hypothesis is that many cases and controls are exposed to contaminated vehicles, but that exposure, although necessary, is not a sufficient cause of infection. The difference in exposure between cases and non-cases was too small to be detected in our study.

It should be remembered that statistical significance is not a measure of the importance of a risk factor: an increased risk may be so small as to be statistically insignificant even in studies with large sample sizes and still, if caused by an extremely common exposure, be responsible for more cases than an exposure associated with a large statistically significant risk which is only rarely encountered.

A fifth possible reason, related to the fourth, may be that many different food vehicles are contaminated, but each type only occasionally. The absence of a demonstrable risk in our study would then be an accurate estimate of the average risk of infection with each organism associated with each food. In other words, again, the risk per exposure may be small, though important because the number of people exposed is immense.

A sixth possible reason is that target organisms may contaiminate a range of different foods and this confounds interpretation of direct risk factors. So, while exposure to undercooked poultry in the ten days prior to illness, for example, may be a risk factor for the acquisition of infection with a poultry associated *Salmonella*, the risk would be masked or obscured by the inclusion of cases with a bovine associated *Salmonella*. The masking would occur because a proportion of cases would not have been exposed to poultry but to beef. This phenomenon would be multiplied many-fold in this analysis where we have aggregated not merely all cases of *Salmonella* infection, but all other organisms, whether foodborne or not, and whatever their incubation period. In the analysis of this group we can only hope to identify those factors whose influence is either very strong for a particular aetiological sub-group, or which operates across them all. The analysis for specific organisms is presented in section 9.2.

What is the interpretation of the effect of possession of a food processor or water filter jug? Again, this could be an artefact: people who are health conscious may be at a lower risk of IID and may also own a food processor or a water filter; the possession of these items may not in itself confer protection against IID. In other words the association may not be causal. This phenomenon is known as confounding. Although the association between possession of these items and IID may be confounded by other characteristics — obviously mere possession could not prevent IID — the relationship may be a close one if, for example, possession of a food processor was associated with preparing fresh food at home, particularly vegetables and fruit. It might even be direct if, for example, use of a water filter jug had a significant effect on the microbiological flora in drinking water and did reduce contamination of the water consumed.

Why did we find no effect of food hygiene and kitchen practices? There are a number of possible explanations. Kitchen practices are difficult to measure. Firstly, people may not have told the truth. Secondly, even if subjects were honest, they may have had difficulty answering the questions accurately. Thirdly, we asked about usual practices rather than specific practices during the period in which infection presumably occurred. Infection may have been due to a lapse we did not identify rather than the habits which we did. Fourthly, it is possible that our measurement of kitchen practice was not sufficiently sensitive to identify the minor types of bad practice which may occur habitually, but do not commonly lead to infection. In other words, kitchen practice which falls within the norm, and may be accepted as ‘good’, may still, on occasion, be an inadequate safeguard against infection. This is the

same argument rehearsed above: a very small increase in risk — insufficient for a study such as ours to identify — when multiplied by every household in the country, may lead to a large number of cases. This would have important consequences for food safety policy as it would imply that even educating people to the highest achievable standard in domestic hygiene might have little effect on the incidence of sporadic cases of IID.

The final explanation is, of course, that the failure to demonstrate an association reflects a true lack of effect of the domestic hygiene practices investigated. Why would kitchen practices not have an effect? This would occur if most contamination of vehicles of infection occurred outside home, or, again, if individual susceptibility was more important than exposure resulting from lapses in practice. Again, this analysis cannot exclude poor kitchen practice as a risk factor for a particular aetiologic sub-group of IID, which will be addressed in section 9.2. If the sub-group were small, its effect could be swamped by the other aetiologies and modes of spread.

Why did we find an increased risk in subjects who replied 'don't know"'to various questions? This could be due to the phenomenon of reverse causation (i.e., cases were not feeling well enough to bother to reply to all questions); or 'not knowing' may be an indirect (but powerful) measure of a subject's inability to be effective in avoiding IID in general.

Why were the reported consumption of some foods (salads, fruit, freshly cooked rice), the ownership of some pets (cats, dogs and rabbits) and swimming (as long as it was not abroad) associated with lower risk? This may be an artefact of the study, or may reflect a real effect of those factors in lowering the risk of disease. Artefacts could include, firstly, confounding factors. This could have occurred if, for example, these factors were markers for a health conscious lifestyle, analogous to responses on ownership of food-processors and water filter jugs, and that some other aspect of such a life-style which we did not measure was the real cause of the low risk of IID. Secondly, our controls could have been subject to selection bias. This could have occurred if people whom we invited to be controls were more likely to accept if they ate vegetables and fruit, had pets and went swimming, and less likely to accept if they did not. Thirdly, there could have been information bias. For this to have occurred, the answers of cases and controls would have to have been influenced by the belief that these characteristics were protective, and controls erroneously reported them more frequently, or cases less frequently, than was actually the case. We believe this to be unlikely, as the foods and pets we found to be associated with a lower risk of disease are not generally regarded as 'protective'.

Alternatively, this may be a true effect. There are a number of ways in which such an effect could be mediated. One is by enhancing individual immunity to gastro-intestinal pathogens. There are a number of biologically plausible ways in which this could occur. Firstly, frequent exposure to low doses of a range of pathogenic and antigenically-related non-pathogenic organisms could enhance both general and organism-specific immunity. Contact with pets (and possibly some foods eaten raw) could lead to such repeated exposure. Secondly, ingestion of micronutrients, particularly anti-oxidants, in food, is known to enhance general immunity. Fruit and fresh vegetables are relatively rich in antioxidants and this has been put forward as the reason they have a protective effect against cancer of the gastrointestinal tract (in particular of the stomach and colon) (AICRWCRF 1997; Kimura *et al*. 1997; Coconnier *et al.* 1997; Erskine *et al.* 1989) and decrease severity of diarrhoea in developing countries (Barreto *et al.* 1994) . This is a particularly attractive hypothesis as consumption of antioxidants is known to be related to social inequality, and so could explain the disappearance of a social class effect when the reported

consumption of fruit and vegetables was controlled for. We resume this discussion in section 9.4.

9.1.4 Children (aged between 1 and 15 years)

There were 463 cases in this group. The frequency of organisms identified is presented in Table 9.4. 42% had viruses, 34% bacteria, and only 32% no target organisms in stools (some had more than one organism type which is why the total exceeds 100%). The results are summarised in Table 9.5.

Table 9.4 Organisms identified in children (>1 year old) presenting to the GP, matched to controls and included in the analysis of risk factors (n = 463). Cases in which more than one organism was identified appear more than once in this table.

	CHILDREN (OVER 1 YEAR OLD)	
	NUMBER IDENTIFIED	PERCENT OF THOSE TESTED
Bacteria		
Aeromonas spp.	26	5.6
Bacillus spp. (>10^4/g)	0	0
Campylobacter spp	32	6.9
Clostridium difficile cytotoxin	5	1.4
Clostridium perfringens enterotoxin	22	4.8
E. coli O157	0	0
Enterovirulent *E. coli*		
AEEC	35	7.9
DAEC	14	3.1
EAggEC	21	4.7
EIEC	0	0
EPEC	1	0.2
ETEC	3	0.7
VTEC (non O157)	1	0.2
Salmonella spp.	15	3.2
Shigella spp.	0	0
Staphylococcus aureus (>10^6/g)	0	0
Vibrio spp.	0	0
Yersinia spp.	10	2.2
Protozoa		
Cryptosporidium parvum	19	4.1
Giardia intestinalis	6	1.8
Viruses		
Adenovirus group F	37	8.7
Astrovirus	27	6.4
Calicivirus	15	3.5
Rotavirus group A	64	14.7
Rotavirus group C	3	0.7
SRSV	39	9.2
No target organism identified	151	32.6
Total number of cases	**463**	

Results

Social factors: only marital status of the head of the household was significantly associated with risk of IID in children. We think it is safe to assume that in most households with children, the head of the household is a parent of the child. Compared to children living with married heads of household, those living with single (never married) heads of household had a two-fold increase in risk. Children living with divorced and widowed heads of household seemed to have a reduced

Table 9.5 Risk factors for IID in children (>1 year old) presenting to the GP. Odds ratios (OR) and probability (p) values for three models: social factors alone, social plus intermediate factors, and social plus intermediate plus direct factors. Only statistically significant factors are shown (n = 463 pairs).

	MODEL 1: SOCIAL		MODEL 2: INTERMEDIATE		MODEL3: DIRECT	
SOCIAL FACTORS	**OR**	**P**	**OR**	**P**	**OR**	**P**
Marital status of main wage-earner						
married	1		1		1	
single	2.1	0.03	1.57	0.26	1.80	0.26
divorced/widowed	0.8	0.47	0.62	0.11	0.48	0.07
INTERMEDIATE FACTORS						
Accommodation ownership						
owned/mortgaged			1		1	
rented – council			2.8	<0.001	3.5	<0.001
rented – private			1.2	0.50	0.95	0.89
tied			1.5	0.49	1.88	0.34
Own food mixer			0.64	0.002	0.67	0.04
Crowding index *						
0 – 0.49			1		1	
0.5 – 0.99			0.60	0.02	0.47	0.009
≥1			0.83	0.52	0.66	0.26
Travel						
UK			0.85	0.41	0.83	0.47
Abroad			5.73	0.003	4.91	0.01
Drugs						
Respiratory system			0.46	0.007	0.32	0.001
Hygiene practices						
Check use-by-date on food products						
always			1			
sometimes			0.63	0.03		
never			1.99	0.35		
DIRECT FACTORS						
Contacts with diarrhoea and/or vomiting						
Other person ill within household				2.24	0.002	
Other person ill outside household						
1 –2 people					3.69	<0.001
3 –30 people					11.12	0.001
Food						
Dairy products made abroad					1.48	0.03
Non-oily fish					0.54	0.002
Salad at home					0.60	0.008
Pulses					0.47	0.001

** Number of people per room (excluding WC, hall and landing)*

risk of disease. None of the other social factors (education, employment status, social class) was statistically significantly associated with IID.

Intermediate factors: living in rented council accommodation was associated with a three-fold increase in risk. When this was added to the model, the effect of marital status of the head of household decreased and was no longer statistically significant, suggesting that the risk associated with living in a single parent household is mediated by living in rented council accommodation. Children living in households with few members tended to also be living in reduced living space. This was associated with a larger risk.

Owning a food mixer was again associated with a lower risk of illness, reducing it by 30%. The only other hygiene practice to be statistically significantly associated with IID was whether the subject's parent or guardian respected "use by date" advice. Respecting the 'use by date' instruction 'sometimes' in relation to respecting it 'always' was associated with lower risk (40% reduction); in contrast, 'never' respecting it was associated with increased risk, but this was not statistically significant. Travel abroad carried a five-fold increase in risk. Children receiving drugs for respiratory illnesses (mainly against asthma) had a reduced risk of IID.

Direct factors: contact with another child with diarrhoea and/or vomiting in the household, or anyone with diarrhoea and/or vomiting outside of the household, increased the risk of becoming a case.

Consumption of dairy products made abroad carried an increased risk (OR 1.5). All other foods found to be statistically significantly associated with IID (pulses, salad at home and non-oily fish) led to lower risks.

Summary

In summary, for children in the GP component, the only social factor associated with an increased risk was having, as head of household, a single person (this risk was mediated by living in rented council accommodation), and there was a lower risk for children with widowed or divorced parents. Other intermediate factors associated with an increased risk of disease were crowding in the household and travel. Contact with other cases of diarrhoea and/or vomiting, and eating dairy products made abroad carried an increased risk. Respiratory drugs, owning a food processor, and eating pulses, salad at home and non-oily fish were associated with lower risk.

Discussion

What is the interpretation of the increase in risk associated with single parents, rented council accommodation and crowding? These are likely to reflect an effect of increased number of potentially infectious contacts. Of the direct factors, an association with lower risk of disease was found for some of the same foods as for adults, and for pets. The possible reasons – artefactual and real – for this finding have been discussed above, but the repetition of the finding in children as well as adults, groups whose aetiologies and risk factors are likely to be different, suggests that it is either a consistent bias, or a true finding.

9.1.5 Infants (aged under 1 year)

There were 133 cases in this group. The frequency of organisms identified is presented in Table 9.6 and the results are summarised in Table 9.7.

Social factors: the risk of IID showed a gradient with levels of deprivation as measured by social class. This was statistically significant only for social class IV (where the risk of IID was doubled) and social class V and 'others' (where there was a four-fold increase in risk).
Intermediate factors: breast-feeding showed a marked protective effect, with a three-fold increase in risk for bottle-fed infants. Table 9.8 shows the effect of different methods used for cleaning the bottle used to feed the infant. Risks in this table are relative to breast-feeding and are controlled for social class only (because of the small number of cases). All methods of sterilising the bottle showed a statistically significant increase in risk of IID in infants, when compared to breastfeeding. There was a high increase in risk of IID associated with using boiling water to clean bottles.

Table 9.7 shows that using a saucepan to re-heat leftovers (rather than a microwave oven or traditional oven) halved the risk of IID. Sharing a bathroom with another family increased the risk in infants 30-fold, but this was a rare event, even among cases. Travelling carried a risk (five-fold increase) but only if the travel was for reasons other than holidays. This was independent of the country to which the infants travelled, but almost all travel was in England. Adding intermediate factors to the model increased the effect of social class, raising the effect in social class IV from two- to five-fold.

Direct factors: ownership of pets, swimming and contact with other cases of gastroenteritis were not statistically significantly associated with risk of IID.

Table 9.6 Organisms identified in the stools of infants (<1 year old) presenting to the GP, matched to controls and included in the analysis of risk factors (n = 113). Cases in which more than one organism was identified appear more than once in this table.

	INFANTS	
	NUMBER IDENTIFIED	**PERCENT OF THOSE TESTED**
Bacteria		
Aeromonas spp.	11	8.3
Bacillus spp. (>10^4/g)	0	0
Campylobacter spp.	1	0.8
Clostridium difficile cytotoxin	7	8.3
Clostridium perfringens enterotoxin	6	4.5
E. coli O157	0	0
Enterovirulent *E. coli*		
AEEC	10	7.8
DAEC	4	3.1
EAggEC	4	3.1
EIEC	0	0
EPEC	0	0
ETEC	0	0
VTEC (non O157)	0	0
Salmonella spp.	4	3.0
Shigella spp.	0	0
Staphylococcus aureus (>10^6/g)	1	0.9
Vibrio spp.	0	0
Yersinia spp.	1	0.8
Protozoa		
Cryptosporidium parvum	1	0.8
Giardia intestinalis	2	2.8
Viruses		
Adenovirus group F	10	8.4
Astrovirus	1	0.8
Calicivirus	6	5.0
Rotavirus group A	30	24.8
Rotavirus group C	0	0
SRSV	9	7.6
No target organism identified	55	41.4
Total number of cases	**133**	

Summary

There was a marked increase in risk the lower the social class, with sharing a bathroom and with non-holiday travel even if in England. Breast-feeding was protective, and bottle-feeding carried a risk whatever method was used to clean the bottle; however, using steam or cold water with chemicals was better than using boiling water to clean the bottle.

Table 9.7 Risk factors for IID in infants presenting to the GP. Odds ratios (OR) and probability (p) values for three models: social factors, social plus intermediate factors, and social plus intermediate plus direct factors. Only statistically significant factors are shown (n =133 pairs).

	MODEL 1: SOCIAL		MODEL 2: INTERMEDIATE		MODEL3: DIRECT	
SOCIAL FACTORS	**OR**	**P**	**OR**	**P**	**OR**	**P**
Social class						
I	1	ns	1.2	ns	1.0	ns
II	1.3	ns	2.5	ns	1.0	ns
III	1.5	ns	2.5	ns	1.0	ns
IV	1.8	0.04	5.1	0.02	1.1	ns
V/other	4.3	0.02	5.8	0.02	1.1	ns
INTERMEDIATE FACTORS						
Feeding						
Breast feeding			1		1	
Bottle			2.9	0.04	3.14	ns
Accommodation						
Family owns food mixer			0.3	0.003	0.3	0.02
Family shares a bathroom					31.3	0.01
Hygiene						
Food for household reheated in saucepan			0.47	0.04	0.3	ns
Travel in the UK						
on holidays					0.5	ns
for other reasons					5.4	0.01

Table 9.8 Effect of method used to sterilize bottle, compared with breast-feeding, on risk of IID in infants presenting to a GP. Odds ratios (OR) and probability (p) values, adjusted for social class only.

FEEDING MODE AND METHOD OF CLEANING BOTTLE	OR	P VALUE
Breast feeding	1	
Cold water and chemicals	3.4	0.007
Boiling water	12.8	0.004
Steam	3.1	0.01
Other	5.7	0.008

Discussion

Breast-feeding was protective, and lower social class a risk, as expected. What can be behind the effect of travelling 'but only if travel was for reasons other than holidays'? This is possibly the result of disrupting routine leading to the potential for a varity of exposures, including food and contacts with cases of diarrhoea and/or vomiting.

9.2 RISK FACTORS FOR IID BY INDIVIDUAL TARGET ORGANISM AND IN THOSE WITH NO TARGET ORGANISM IN THE STOOL

Separate analyses were carried out for cases where no target organism was identified in the stool, and for cases with each of the following six organisms in the stool: *Salmonella enteritidis* phage type (PT) 4, enteroaggregative *Escherichia coli* (EAggEC), *Clostridium difficile*, *Campylobacter jejuni*, SRSV and rotavirus group A. If a case had more than one target organism identified in the stool, it was included in the analysis for each of the target organisms identified.

The age groups used in the analyses of cases with organisms identified in stools were selected on the basis of what was known about the epidemiology and risk factors for each organism, in an effort to select a uniform group. For example, for rotavirus, we analysed only cases under 15 years of age, with some sub-group analysis for cases under 5 years of age. Cases identified in the population cohort component and presenting to GPs were included.

Cases were compared to their age-matched controls and we did not exclude controls who had organisms identified in their stools. The number of cases in each group is the number of cases with the organism, who fulfilled the criteria for analysis, had a matched control, and where case and control completed the questionnaire.

9.2.1 Conceptual framework

The conceptual framework and strategy for the analysis of cases without a target organism in the stool was the same as that for all cases of IID, described in section 9.1.1.

For cases with a target organism in the stool, only the specific hypotheses raised for that organism were investigated, because of the smaller sample size. A second reason for doing this was to avoid spurious associations as the result of multiple testing. As only a selection of factors were analysed for each organism, the number of models selected varied. The groups of variables investigated for each organism were:

S.enteritidis PT4:	social factors, hygiene behaviour, travel, eating out, antacids; contact with other people with diarrhoea and/or vomiting, pets and food
EAggEC:	social factors, travel, recreational water contact, and food
C.difficile:	social factors and use of antibiotics
C.jejuni:	social factors, travel, recreational water contact, food, drinking water, antacids and contact with animals
SRSV:	social factors, travel, recreational water contact, food, accommodation and contact with subjects with diarrhoea and/or vomiting
Rotavirus group A:	social factors, travel, recreational water contact, food, accommodation and contact with subjects with diarrhoea and/or vomiting.

9.2.2 Presentation of the results

For each of the groups, tables present factors which were statistically significant in the relevant models, at the traditional probability level of p = 0.05; with OR and p values, from a univariate analysis. Multivariate analysis to investigate the independent effect of more than one variable was undertaken only when findings suggested that this was necessary for the understanding of the results (i.e., more than one factor was statistically significant or a previous hypothesis was found not to be confirmed).

9.2.3 *Salmonella enteritidis* PT4

All age groups were analysed. There were 70 cases of *S.enteritidis* PT4 infection of which 51 had a matched control where both case and control had completed the questionnaire. For this organism the hypotheses investigated included social factors; intermediate factors included hygiene behaviour, travel, eating out, use of antacids; direct factors investigated included contact with other people with

diarrhoea and/or vomiting, contact with pets and the consumption of certain foods. The results are presented in Table 9.9, and include only those factors which were statistically significant. Table 9.10 summarises the results for consumption of chicken or egg. Although these were not statistically significant, the association between consumption of chicken and IID with *Salmonella* in the stool was one of the initial hypotheses and therefore these results remain of interest.

Results

Social and intermediate factors: these included hygiene behaviour, travel, eating out and use of antacids. None showed an association.

Table 9.9 Risk factors for IID with *Salmonella enteriditis* PT4 in the stool with odds ratios (OR) and probability (p) values; univariate analysis. Only statistically significant factors are shown.

		CONTROLS	CASES	UNADJUSTED	
		NO.	NO.	ODDS RATIO	P-VALUE
Boiled rice, eaten immediately					
	No	18	32		
	Yes	33	19	0.33	0.012
Pulses					
	No	29	40		
	Yes	22	11	0.31	0.023
Raw salad, prepared and eaten at home					
	No	15	26		
	Yes	36	25	0.42	0.040
Prawns					
	No	33	42		
	Yes	18	9	0.36	0.048
Lamb/mutton					
	No	29	39		
	Yes	22	12	0.42	0.048

Direct factors: very few factors showed a statistically significant association with *S.enteritidis* PT4 infection. No food was statistically significantly associated with an increased risk of infection with *S.enteritidis* PT4. Consumption of the following foods in the previous ten days was statistically significantly associated with lower risk: rice freshly cooked and eaten at home, salad eaten at home, prawns and lamb (the latter two foods each had p-values of 0.048).

None of the many ways of eating chicken that were investigated showed a statistically significant association with *S.enteritidis* PT4 infection (Table 9.10), and the trends in association do not show a consistent direction.

Summary

No factor, and specifically no food vehicle, was statistically significantly associated with an increased risk of *S.enteritidis* PT4 infection. Four foods were associated with lower risk; and two of these were also found in the analysis of all cases of IID in adults: fresh rice, and salad eaten at home. The other two, lamb and prawns, were only marginally significant. No effect of consumption of chicken or egg in the previous ten days was detected.

Discussion

Why did the study fail to show an association between *S.enteritidis* PT4 infection and consumption of foods well demonstrated elsewhere as risks? The explanations are similar to those for all cases of IID in section 9.1.3. There is a possibility that

Table 9.10 Consumption or preparation of chicken and risk of *Salmonella enteriditis* PT4

CHICKEN FACTOR		CONTROLS NO.	CASES NO.	UNADJUSTED ODDS RATIO	UNADJUSTED PROBABILITY VALUE
Any Chicken					
	No	7	7		
	Yes	44	44	1.0	1.0
Fresh ready gutted chicken with giblets					
	No	49	44		
	Yes	2	7	3.5	0.118
Ready gutted with giblets, frozen					
	No	44	48		
	Yes	7	3	0.33	0.178
Ready gutted without giblets, fresh					
	No	29	32		
	Yes	22	19	0.75	0.514
Ready gutted without giblets, frozen					
	No	43	46		
	Yes	8	5	0.57	0.372
Bought raw fresh, eaten at home					
	No	27	30		
	Yes	24	21	0.80	0.565
Bought raw frozen, eaten at home					
	No	36	40		
	Yes	15	11	0.64	0.350
Bought precooked, eaten hot					
	No	43	47		
	Yes	8	4	0.43	0.220
Bought precooked, eaten cold					
	No	48	49		
	Yes	3	2	0.67	0.657
Take-away					
	No	43	46		
	Yes	8	5	0.5	0.327
Fast food chicken					
	No	42	47		
	Yes	9	4	0.44	0.177
Restaurant/canteen					
	No	45	40		
	Yes	6	11	1.83	0.232
Barbecued					
	No	48	48		
	Yes	3	3	1.0	1.0
Number of times chicken was eaten					
	0	6	5		
	1–2	28	34	1.25	0.739
	3–5	14	7	0.57	0.572
	6+	2	2	0.85	0.894
	Not stated	1	3	3.18	0.391
Prepared fresh chicken for eating					
	No	35	33		
	Yes	16	18	1.14	0.796

sporadic cases are different from outbreak cases in terms of the vehicles of infection. A more likely explanation is that an individual piece of chicken or an individual egg presents too small a risk to achieve significance in this study, and that, to become infected, a case must have other characteristics, such as individual susceptibility or a lapse in hygiene behaviour. Indeed, unless one consumes the chicken or the egg raw or partly cooked, to acquire infection from them inevitably requires a lapse in hygiene practice. We found no increased risk associated with poor hygiene practices among those who consumed chicken. However, the study was unlikely to be able to detect trivial deficiencies which may lead to infection. This analysis includes few cases: which may have contributed to the lack of statistical association with chicken consumption, or an interaction between chicken consumption and lack of hygiene. This is also consistent with the lack of a statistically significant association with social factors, travel, and other intermediate

Table 9.11 Risk factors for IID with *C.jejuni* in the stool, with odds ratios and probability (p) values; univariate and adjusted for employment, ethinicity and travel.

	CONTROLS	CASES	UNADJUSTED		ADJUSTED FOR EMPLOYMENT/ ETHNICITY		ADJUSTED FOR TRAVEL	
INTERMEDIATE	**NO.**	**NO.**	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**
Travel abroad								
No	220	199	1.00		1.00			
Yes	9	30	3.62	0.001	3.55	0.002		
Recreational water sport								
No	188	193	1.00		1.00		1.00	
Yes (did not swallow water)	19	10	0.53	0.108	0.46	0.058	0.32	0.017
Yes (swallowed water)	22	26	1.20	0.582	1.30	0.449	0.76	0.488
FOOD								
Boiled rice, eaten immediately								
No	104	145	1.00		1.00		1.00	
Yes	125	84	0.45	<0.001	0.42	<0.001	0.42	<0.001
Pulses								
No	143	187	1.00		1.00		1.00	
Yes	86	42	0.39	.<0.001	0.36	<0.001	0.36	<0.001
Fruit with edible skins								
No	46	77	1.00		1.00		1.00	
Yes	183	152	0.48	0.001	0.44	0.001	0.44	<0.001
Peeled fruit								
No	45	93	1.00		1.00		1.00	
Yes	184	136	0.34	<0.001	0.30	<0.001	0.34	<0.001
Dried fruit								
No	135	191	1.00		1.00		1.00	
Yes	94	38	0.25	<0.001	0.26	<0.001	0.27	<0.001
Salad at home								
No	64	117	1.00		1.00		1.00	
Yes	165	112	0.34	<0.001	0.34	<0.001	0.36	<0.001
Oily fish								
No	132	154	1.00		1.00		1.00	
Yes	97	75	0.65	0.033	0.69	0.068	0.63	0.023
Non-oily fish								
No	112	134	1.00		1.00		1.00	
Yes	117	95	0.69	0.045	0.69	0.060	0.65	0.026
Pasteurised dairy products								
No	97	137	1.00		1.00		1.00	
Yes	132	92	0.48	<0.001	0.48	0.001	0.48	<0.001
Cold sliced meats from shops other than supermarkets or delicatessens								
No	217	205	1.00		1.00		1.00	
Yes	12	24	2.09	0.044	2.03	0.066	2.06	0.051
Hot/cold chicken at a restaurant								
No	208	186	1.00		1.00		1.00	
Yes	21	43	2.38	0.004	2.41	0.005	1.86	0.049
Poultry other than chicken								
No	167	187	1.00		1.00		1.00	
Yes	62	42	0.57	0.020	0.60	0.039	0.53	0.014
Burgers								
No	151	168	1.00		1.00		1.00	
Yes	78	61	0.67	0.067	0.70	0.126	0.61	0.034
Home-made sauce with raw eggs								
No	209	218	1.00		1.00		1.00	
Yes	20	11	0.53	0.100	0.52	0.098	0.43	0.036
Home-made desserts with raw eggs								
No	194	213	1.00		1.00		1.00	
Yes	35	16	0.41	0.006	0.37	0.004	0.37	0.004
Cakes with artificial cream								
No	184	204	1.00		1.00		1.00	
Yes	45	25	0.53	0.015	0.51	0.015	0.50	0.010

factors. The finding of some foods associated with a lower risk, as in the analysis of all cases of IID, suggests that the study had power to find some associations, but not necessarily weak ones.

9.2.4 *Campylobacter jejuni*

All age groups were analysed. There were 342 cases of *C.jejuni* infection; the analysis included all 229 that had a matched control, where case and control had completed a questionnaire. The hypotheses investigated included social factors, intermediate factors (including travel, antacids, hygiene), and direct factors (including foods, pets, and recreational water sports). Table 9.11 presents risk factors for *C.jejuni*, adjusted for employment status, ethnicity, and for travel.

Results

Social factors: although part-time workers had half the risk, and non-white subjects twice the risk of *C.jejuni* infection, neither these nor any other social factor were statistically significantly associated with *C.jejuni* infection.

Intermediate factors: the factors with a statistically significant effect were travelling abroad (associated with a 3.6-fold increase in risk) and recreational water sports (associated with half the risk), as long as this was not done abroad and no water was swallowed. Subjects were asked if they had taken antibiotics recently and also to name any medication they were taking at the time of the onset of illnes. This was then Reed-coded. In both instances there was an increase in risk (up to 1.8-fold increase when coded for new potent antacids only), but the effect did not reach statistical significance.

Direct factors: consumption of two foods showed a statistically significant increase in risk: eating chicken (whether cold or hot) at a restaurant; and eating cold sliced meats bought in shops other than supermarkets, butchers' or delicatessens. After controlling for travel, the significance of the association was borderline. Drinking milk from a bottle pecked by a bird carried a six-fold increase in risk, and eating barbecued chicken doubled the risk of infection, but these were not statistically significant. Many foods were statistically significantly associated with a lower risk of *C.jejuni* infection: rice freshly cooked and eaten at home, salad eaten at home, pulses, fruits (with edible skins, without edible skins, dried), fish (oily and non-oily), pasteurised products, other poultry (mainly turkey), home-made desserts and sauces made with raw eggs, cake made at home, and burgers.

Drinking untreated water from rivers and lakes doubled the risk, and drinking water from a jug filter decreased it by 40%, but these were not statistically significant. Contact with pets had no statistically significant effect, although contact with puppies more than doubled the risk, and contact with any pet with diarrhoea nearly doubled it.

Summary

Statistically significant associations with higher risk of *C.jejuni* disease were found only with travel abroad, eating chicken at a restaurant, and eating sliced cold meats from shops other than supermarkets, butchers' or delicatessens. Statistically significant associations with lower risk of disease included: recreational water sports and some of the foods associated with lower risk for other organisms: salad and rice eaten at home, fruit, pulses, pasteurised products and fish. Other foods associated with a lower risk were: other poultry, desserts and sauces made at home using raw eggs, and burgers. Associations which were not statistically significant, but of interest, included a higher risk in those who drank milk from bottles pecked by

a bird, ate barbecued chicken, or took antacids, and a lower risk in those who used a domestic water jug filter.

Discussion

The association between eating chicken at restaurants and infection with *C.jejuni* was not unexpected as many chickens are colonised with *C jejuni*, and poultry meat on retail sale in the UK is often contaminated. We have postulated earlier that the study's inability to link recent consumption of foods known to be common vehicles of infection to an increased risk of IID may be because sporadic cases result from widespread low level contamination which does not often cause illness. If this is true, our finding of an increased risk of *C.jejuni* infection associated with the consumption of chicken in restaurants and cold cooked meat from small shops would imply frequent and heavy contamination of these food vehicles. The fact that it was a risk only when eaten at restaurants may suggest poorer hygiene at restaurants than in the average home. The problems of cold cooked meats are now well documented (Pennington Group 1997).

Was it surprising to find that domestic consumption of chicken was not associated with an increased risk of IID with *C.jejuni*? Some outbreaks of *C.jejuni* are associated with the consumption of chicken. However, the data on sporadic infections are less clear. In England, a previous study of sporadic *Campylobacter* infection has shown consumption of poultry in the previous three days to be associated with a reduced risk (Adak *et al*. 1995). The lack of association in our study could be an artefact. We asked about consumption of chicken in the 10 days

Table 9.12 Risk factors for IID with Enteroaggregative *E.Coli* (EAggEC) in the stool. Odds ratios and probability (p) values; univariate, adjusted for education, and for travel abroad (n = 108).

	UNADJUSTED		ADJUSTED FOR EDUCATION		ADJUSTED FOR TRAVEL ABROAD	
SOCIAL FACTORS	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**
Stayed in education after the age of 16						
No	1.00				1.00	
Yes	1.94	0.026			1.88	0.081
INTERMEDIATE FACTORS						
Travel abroad						
No	1.00		1.00			
Yes	45.0	<0.001	42.51	<0.001		
DIRECT FACTORS						
Hot/cold chicken at canteen/restaurant						
No	1.00		1.00		1.00	
Yes	3.60	<0.001	3.39	0.001	1.13	0.786
Salad at restaurant						
No	1.00		1.00		1.00	
Yes	5.14	<0.001	3.43	<0.001	4.22	0.012
Tropical fruit						
No	1.00		1.00		1.00	
Yes	3.75	0.019	3.43	0.030	3.64	0.364
Cold meat bought from the supermarket						
No	1.00		1.00		1.00	
Yes	0.23	<0.001	0.26	0.001	0.35	0.29
Sausages						
No	1.00		1.00		1.00	
Yes	0.45	0.014	0.51	0.046	0.69	0.45

prior to the onset of symptoms and numbers were relatively small although, as for *S .enteritidis* PT4 infection, other factors were found to be significantly associated with this infection.

It has been suggested that sporadic cases of *Campylobacter* infection are more likely to occur because of cross-contamination from raw chicken than because of direct consumption (Cowden 1992; ACMSF 1993a). The scenario described in section 9.1.3 is more relevant to *C.jejuni* than to many other organisms. Specifically for *Campylobacter*, the suggestion is that although chicken may often be the source, it is most likely not the vehicle of infection for sporadic cases. This would explain the difference between vehicles identified with outbreaks and with sporadic cases. Chicken would not be identified as a risk for sporadic cases if studies collect information only about food consumed by cases and not about food prepared in the household. If a vehicle is heavily contaminated, the important determinant of illness is whether a subject ate the contaminated food; whereas if, in sporadic cases, the vehicle is only lightly contaminated, individual susceptibility would play a larger role.

The findings here are consistent with some foods being associated with lower risk because they confer protection against some diseases. Salad eaten at home and rice prepared and eaten at home, fruit, pulses, pasteurised products and fish were all associated with a lower risk of *C.jejuni* . Mechanisms were suggested in section 9.1.3 for the protective effect associated with consumption of these foods.

9.2.5 Enteroaggregative *E.coli* (EAggEC)

All age groups were analysed. 108 case-control pairs were included in the analysis. Hypotheses investigated included social factors, travel, swimming and food consumption. Only education and travel had a statistically significant effect on the univariate analysis.

Results

Social factors: continuing formal education after age 16 was associated in the univariate analysis with a statistically significant doubling of risk but this was no longer significant when travel was taken into account, indicating that those receiving better education had a greater risk of IID due to EAggEC because they travel abroad more frequently. No other social factor was statistically significant.

Intermediate factors: travel abroad had a large effect, with a statistically significant 40-fold increase in risk of EAggEC. However, only 40% of cases reported travelling abroad.

Direct factors: many direct factors were associated with an increase in risk in the univariate analysis; but this association disappeared when travel was controlled for. It is likely that these factors were only markers for whether the person had travelled abroad. For those who did not travel abroad, eating salad at a restaurant was associated with a four-fold increase in risk of EAggEC infection. Eating cold meat bought from a supermarket and eating sausages were associated with lower risk, and this was statistically significant. When travel was controlled for, this association was no longer significant.

Summary

Only two risk factors were clearly identified with increased risk of EAggEC infection: travel abroad and, for those not travelling abroad, eating salads at a restaurant. Other foods were associated with increased or decreased risk, but this disappeared when travel was taken into account.

Discussion

Travel is known to be a risk factor for EAggEC infection (Gascon *et al*. 1998). The effect of eating salad at a restaurant is a new finding, and suggests that risks are associated with eating raw foods, such as salads, particularly when they may have been imported. An international outbreak of *Shigella sonnei* infection associated with imported lettuce which had been flood irrigated with untreated human sewage has been reported (Frost *et al.* 1995). Although our study did not identify whether the salad ingredients were imported, and home gown produce may also present a risk, the increasing world trade in food does mean that people no longer need to travel abroad to acquire infections which are normally considered to be travel related.

9.2.6 *Clostridium difficile*

There were only 18 cases of *C.difficile* infection that were over 2 years of age, had a matched control, and in which both case and control had answered the questionnaire. The main hypothesis of interest was that the use of antibiotics prior to the IID was a risk. This was investigated by asking whether the subject had taken antibiotics recently, and to name any medication they were taking at the time of the start of the illness. The responses were Reed-coded. Social factors were also investigated, and the association with antibiotics was investigated after controlling for social factors. This data is presented in Table 9.13.

Table 9.13 Risk factors for IID with *Clostridium difficile*, in those aged 2 years and older, with number of cases and controls, odds ratios and probability (p) values; univariate, and adjusted for social class

	CASE	CONTROL	UNADJUSTED		ADJUSTED FOR SOCIAL CLASS	
FACTORS	**NO.**	**NO.**	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**
Social Class						
Non Manual	12	13	1.00			
Manual	5	5	0.67	0.657		
Subject reports taking an antibiotic						
No	16	6	1.00		1.00	
Yes	1	10	9.00	0.037	10.44	0.044
Subject reports the name of a drug taken and this is subsequently coded as an antibiotic						
No	17	12	1.00		1.00	
Yes	12	6	6.00	0.097	9.13	0.092

Results

Social factors: there was no statistically significant association with social factors.

Intermediate factors: reported use of antibiotics was associated with a ten-fold increase in risk. When use of antibiotic was ascertained by coding the name of the drugs reported to have been used, there was a 6-fold increase in risk when social class was not controlled for, and a 9 -fold increase when it was, although these associations were not statistically significant (Table 9.13). This resulted from more controls and fewer cases being classified as using antibiotics when this method was used. The population attributable fraction, i.e., the proportion of IID with *C.difficile* in stools in subjects aged 2 or older attributed to use of antibiotics, was only 33%.

Direct factors: none were investigated.

Summary

Use of antibiotics was associated with an increased risk of *C.difficile* infection. This association was more marked when the case reported taking 'an antibiotic' than when the name of the drug was reported and classification undertaken by the study team.

Discussion

Although the number of cases was small, the hypothesis that the prior use of antibiotics increases the risk of *C.difficile* illness in the over 2 year olds, even outside the hospital environment, is confirmed. The explanation for the difference in risk with reported use of antibiotics versus use derived from coding the names of medicines is unclear.

Table 9.14 Risk factor for IID with rotavirus in the stool in children under 15 years of age. Number of cases and controls, with odds ratios and probability (p) values; univariate, adjusted for social class and adjusted for contact with another person with diarrhoea and/or vomiting. Only factors which remain statistically significant are shown.

	CONTROLS	CASES	UNADJUSTED		ADJUSTED FOR SOCIAL CLASS		ADJUSTED FOR CONTACT WITH ANY PERSON WITH DIARRHOEA AND/ OR VOMITING	
SOCIAL FACTORS	**NO.**	**NO.**	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**	**ODDS RATIO**	**P-VALUE**
Social class								
Non Manual	84	71	1.00					
Manual	52	51	1.20	0.501				
INTERMEDIATE FACTORS								
Accommodation								
Detached/Semi/Terraced	133	121	1.00		1.00		1.00	
Rooms or flat	6	18	7.00	0.010	6.49	0.015	5.46	0.033
Ownership of property								
Owned	125	100	1.00		1.00		1.00	
Rented from Council	6	23	5.10	0.001	3.60	0.032	5.73	0.001
Number of rooms in household								
4	13	24	1.00		1.00		1.00	
5	14	31	1.30	0.632				
6	36	36	0.60	0.287				
7	28	18	0.38	0.092				
8	19	6	0.17	0.01				
9	6	4	0.16	0.05				
10+	8	4	0.42	0.262				
Trend			0.70	0.001	0.76	0.009	0.69	0.002
DIRECT FACTORS								
CONTACT WITH PERSON WITH DIARRHOEA AND/OR VOMITING								
Contact in household								
No	127	100	1.00					
Yes	12	39	3.70	<0.001	5.10	<0.001		
Contact outside								
No	101	63	1.00		1.00			
Pre-school	5	16	3.94	0.015	4.78	0.008		
School	7	18	3.62	0.009	5.24	0.007		
Social/Other	2	6	5.03	0.059	7.46	0.025		
Not sure	24	13	2.22	0.015	2.49	0.009		
Any contact								
No	96	47	1.00	<0.001	1.00			
Yes	43	92	3.45		4.57	<0.001		

Table 9.14 ***continued***

DIRECT FACTORS FOOD		CONTROLS NO.	CASES NO.	UNADJUSTED ODDS RATIO	UNADJUSTED P-VALUE	ADJUSTED FOR SOCIAL CLASS ODDS RATIO	ADJUSTED FOR SOCIAL CLASS P-VALUE	ADJUSTED FOR CONTACT WITH ANY PERSON WITH DIARRHOEA AND/ OR VOMITING ODDS RATIO	ADJUSTED FOR CONTACT WITH ANY PERSON WITH DIARRHOEA AND/ OR VOMITING P-VALUE
Fruit with edible skin									
	No	25	47	1.00		1.00		1.00	
	Yes	114	92	0.35	0.002	0.45	0.023	0.35	0.004
Peeled fruit									
	No	27	58	1.00		1.00		1.00	
	Yes	112	81	0.26	<0.001	0.31	0.002	0.26	<0.001
Dried fruit									
	No	87	109	1.00		1.00		1.00	
	Yes	52	30	0.37	0.002	0.40	0.005	0.31	0.001
Salad at home									
	No	79	112	1.00		1.00		1.00	
	Yes	60	27	0.30	<0.001	0.32	<0.001	0.29	<0.001
Non-oily fish									
	No	66	95	1.00		1.00		1.00	
	Yes	73	44	0.31	<0.001	0.33	<0.001	0.36	0.003
Pasteurised dairy products									
	No	24	41	1.00		1.00		1.00	
	Yes	115	98	0.29	0.004	0.38	0.032	0.31	0.012
Fresh chicken eaten at home									
	No	26	48	1.00		1.00		1.00	
	Yes	113	91	0.35	0.002	0.39	0.011	0.32	0.003

The population attributable fraction was relatively small: only 33% of cases were attributable to antibiotics. What caused the other 67%? There are three possible causes: firstly, these cases may have IID where *C.difficile*, albeit present, was not the cause of the IID, as many controls also had this organism; secondly, use of antibiotics may not have been perfectly recorded; and finally, some IID caused by *C.difficile* may have had other causes, which were not identified since only a limited range of factors were analysed.

9.2.7 Rotavirus

139 cases were under 15 years of age, had a matched control, and both case and control answered a questionnaire. The hypotheses investigated for rotavirus in this age group include associations with social factors, intermediate factors (including crowding and travel) and direct factors (including contacts with other people with diarrhoea and/or vomiting and food).

Table 9.14 presents the results, adjusted for social class and contact with a person with diarrhoea and/or vomiting. A separate analysis was done for 39 infants (cases under 1 year of age) and 123 cases in young children and in infants (under 5 years of age), to study the effect of breast feeding and of frequenting a crèche or nursery, and these data are presented in Tables 9.15 and 9.16.

Results

Social factors: membership of a manual social class increased the risk by 20%, but this was not statistically significant. There was a clear risk associated with living conditions and overcrowding: living in rented council accommodation increased the risk five- fold (3.6-fold when controlled for social class), living in purpose-built flats or rooms in a converted house increase the risk seven-fold, and living in houses with

Table 9.15 Effect of breast-feeding and of frequenting a nursery or crèche on the risk of developing IID with rotavirus in the stool in infants (under 1 year of age). Number of cases and controls with odds ratios and probability values and 95% confidence intervals; univariate, adjusted for social class and adjusted for contact with another person with diarrhoea and/or vomiting.

	CONTROLS		CASES		UNADJUSTED				ADJUSTED FOR SOCIAL CLASS				ADJUSTED FOR CONTACT WITH ANY PERSON WITH DIARRHOEA AND/OR VOMITING			
	NO.	%	NO.	%	ODDS RATIO	95% CI		P-VALUE	ODDS RATIO	95% CI		P-VALUE	ODDS RATIO	95% CI		P-VALUE
Currently fed																
Breast-fed only	8	24.24	1	2.56	1.00				1.00				1.00			
Bottle and breast-fed	16	48.48	35	89.74	8.00	1.00	63.96	0.050	4.82	0.56	41.63	0.153	8.16	1.00	66.56	0.050
Other	9	27.27	3	7.69	-				-			1.000	-			1.000
Not known	6		0													
Attends nursery/creche																
No	17	45.95	16	51.61	1.00				1.00				1.00			
Yes	21	54.05	15	48.39	0.83	0.25	2.73	0.763	1.67	0.40	7.07	0.482	0.76	0.22	2.59	0.659
Not known	2		8													

Table 9.16 Effect of frequenting a nursery or crèche on the risk of developing IID with rotavirus in the stools in infants and children (under 5 years of age). Numbers of cases and controls, with odds ratios, probability values and 95% confidence intervals; univariate, adjusted for social class and adjusted for contact with another person with diarrhoea and/or vomiting.

	CONTROLS		CASES		UNADJUSTED				ADJUSTED FOR SOCIAL CLASS				ADJUSTED FOR CONTACT WITH ANY PERSON WITH DIARRHOEA AND/OR VOMITING			
	NO.	%	NO.	%	ODDS RATIO	95% CI		P-VALUE	ODDS RATIO	95% CI		P-VALUE	ODDS RATIO	95% CI		P-VALUE
Attends nursery/creche																
No	31	27.68	36	34.95	1.00				1.00				1.00			
Yes	81	72.32	67	65.05	0.56	0.29	1.12	0.100	1.06	0.47	2.35	0.890	0.52	0.26	1.07	0.076
Not known	12															

fewer than six rooms also increased the risk. These were all statistically significant associations.

Intermediate factors: travel abroad increased the risk five-fold, but only five of the 139 cases were exposed to this risk factor and the association was not statistically significant.

Direct factors: there was a marked increase in risk associated with contact with another person with diarrhoea and/or vomiting. However, this did not explain the risk associated with housing. The foods associated with lower risk for IID with other organisms were also statistically significantly associated with lowering the risk of rotavirus infection in infants and children under 15 years of age. Reported consumption of the following foods reduced the risk of rotavirus infection by between 50% and 70%: salad eaten at home, fresh fruit (with and without edible skin), dried fruit, pasteurised milk, fresh chicken eaten at home, and non-oily fish.

Table 9.15 presents the results for infants. Breast-feeding was protective, as evidenced by an eight-fold increase in those who had been bottle fed as well. When social class is controlled for the increase was only five-fold and was no longer statistically significant.

Table 9.16 presents results for children under 5 years old. Frequenting a nursery or crèche reduced the risk of IID. However, this effect disappeared when social class was controlled for.

Summary

For rotavirus infection in infants and children under 15 years of age, living conditions, in particular rented council accommodation and overcrowding, and of contact with other people with diarrhoea and/or vomiting had a marked effect on risk. Frequenting a crèche or nursery was not a risk factor for infants and children under 5 years old. Breast-feeding was protective, but statistical significance was lost when social class was controlled for. Foods identified as associated with lower risk of all IID and of IID due to other selected target organisms were also associated with a lower risk of rotavirus in this group. These foods included salad at home, fruits, fish and pasteurised products.

Discussion

The increase in risk associated with living conditions suggests that this is mediated by an increased chance of being exposed to an infective contact. Why then does controlling for contact not decrease the risk associated with living conditions? A possible explanation is that living in council rented accommodation increases exposure to infective contacts with people not known to be infective by those completing the questionnaire. The fact that attendance at a crèche or nursery did not increase the risk suggests that most transmission in that age group does not occur in these settings. The interpretation of the lower risk conferred by the consumption of various foods is similar to that for other selected target organisms, but adds to the credibility of the hypothesis that these foods in some way increase resistance to infection, rather than that they replace more risky foods, because rotavirus infection is only very rarely foodborne.

9.2.8 SRSV

There were 219 cases of SRSV infection. Of these,155 had a control and questionnaires for both case and control. The analysis was restricted to the 81 pairs

Table 9.17 Risk factors for IID with SRSV in the stool, in subjects aged over 5 years. Number of cases and controls, with odds ratios and probability (p) values; univariate, adjusted for contact with a person with diarrhoea and/or vomiting.

	CONTROLS	CASES	UNADJUSTED		ADJUSTED FOR SOCIAL CLASS		ADJUSTED FOR CONTACT WITH ANY PERSON WITH DIARRHOEA AND/OR VOMITING	
SOCIAL FACTORS	NO.	NO.	ODDS RATIO	P-VALUE	ODDS RATIO	P-VALUE	ODDS RATIO	P-VALUE
Social class								
Non-manual	63	46	1.00				1.00	
Manual	12	31	3.72	0.002			3.15	0.012
DIRECT FACTORS CONTACTS WITH PERSONS WITH DIARRHOEA AND/OR VOMITING								
Contact with other ill person in household								
No	75	60	1.00		1.00			
Yes	6	21	4.00	0.006	3.74	0.013		
Contact with other ill person outside the home								
No	63	48	1.00		1.00			
Yes	4	19	8.85	0.004	7.89	0.008		
DIRECT FACTORS FOOD								
Desiccated coconut								
No	70	78	1.00		1.00		1.00	
Yes	11	3	0.20	0.038	0.18	0.049	0.25	0.101
Salad at a restaurant								
No	74	61	1.00		1.00		1.00	
Yes	7	20	4.25	0.009	4.28	0.013	4.63	0.012
Hot/cold chicken at a restaurant								
No	76	62	1.00		1.00		1.00	
Yes	5	19	3.80	0.008	3.29	0.024	3.20	0.030
Precooked chicken eaten at home hot								
No	69	78	1.00		1.00			
Yes	12	3	0.18	0.027				

over 5 years of age, as we assumed that risk factors in the under-fives would be different from those in the over-fives. Hypotheses investigated included association of infection with social factors, intermediate factors (including travel and accommodation) and direct factors (including water sports, food and contact with other people with diarrhoea and/or vomiting). Table 9.17 shows the results.

Results

Social factors: the risk was trebled in those who belonged to the manual social classes, and this was statistically significant. No other social factors were statistically significant, although living in a household where the head was single doubled the risk of infection.

Intermediate factors: foreign travel was statistically significantly associated with a seven-fold increase in risk. Accommodation showed no statistically significant

association with SRSV. Living in rented rooms and flats did not increase risk, and none of our 81 cases lived in an institution.

Direct factors: contact with another person with diarrhoea and/or vomiting increased the risk four-fold if the person was in the same household, and nine-fold if they were from outside the household. Reported consumption of two foods, chicken (either cold or hot) and salad at a restaurant, was statistically significantly associated with an increased risk for SRSV infection (three-fold and four-fold, respectively). The only food that remained statistically significantly associated with lower risk after controlling for contact was pre-cooked chicken eaten at home. This reduced the risk to 20%. Consumption of shellfish and oysters were not statistically significantly associated with increased risk of SRSV infection in this dataset, although exposure was very rare in cases and controls.

Summary

Statistically significant factors associated with an increased risk of SRSV infection were manual social class, contact with other cases of diarrhoea and/or vomiting and eating chicken and salad at a restaurant. Eating prepared chicken at home was associated with a lower risk. Living in an institution, over-crowding and eating oysters were not found to be statistically significant risks.

Discussion

Contact with a child with diarrhoea and/or vomiting within the household or with a person with diarrhoea and/or vomiting outside the household increased the risk of SRSV infection, as it did for rotavirus in infants and children under 15 years of age, emphasising the importance of person-to-person transmission for these organisms. Consumption of certain foods increased the risk, but only eating chicken and salad at restaurants. SRSV was the only organism analysed for which the foods identified with a lower risk of disease for all IID and other organisms did not confer protection. The under-representation of residential institutions in our sample may explain the absence of any association with living in one.

9.2.9 Adult cases of IID with no target organism in the stool

1282 cases, all adults, were included in the analysis. Children were not looked at because of the possibility that the risk factors were different for children and adults. The conceptual framework used was the same as for all IID. Results are summarised in Table 9.18.

Results

Social factors: only those not working because of a disability had a statistically significant five-fold increase in risk. Part-time workers had a lower risk, but this was not statistically significant.

Intermediate factors: travel abroad to countries other than Northern Europe increased the risk of IID without target organisms in the stool (8-fold for travel to Southern Europe and Mediterranean countries, and 10-fold for other countries). Asthma increased the risk of IID without target organisms in the stool by five-fold. There was a dose response relationship between risk of IID with no organism and length of work surface in the kitchen used to prepare food. Compared with a length of two metres or more, a length between one and two metres increased the risk by 50%, and less than 1 metre increased the risk 2.5-fold. All associations were statistically significant.

Table 9.18 Adult cases (>15 years of age) with target organism detected in the stool, presenting to the GP, matched to controls and included in the risk factor analysis

FINAL STAGE 3 MODEL

FACTOR		ODDS RATIO (MATCHED)	95% CONFIDENCE INTERVAL		P-VALUE
Employment status					
	Full-time	1.00			
	Part-time	0.66	0.40	1.09	0.104
	Unemployed	0.77	0.32	1.82	0.550
	Sick	1.32	0.23	7.66	0.756
	Disabled	5.61	1.85	17.00	0.002
	Retired	0.65	0.30	1.44	0.288
	Student	1.51	0.50	4.49	0.463
	Not seeking employment	0.82	0.46	1.46	0.502
Social Class					
	I	1.00			
	II	1.27	0.77	2.12	0.351
	III (NM)	1.43	0.81	2.52	0.224
	III (M)	1.05	0.56	1.97	0.876
	IV	1.16	0.54	2.50	0.698
	V	1.84	0.33	10.12	0.485
	Other	0.66	0.27	1.59	0.350
TRAVEL	Travel Abroad	1.00			
	UK Only	0.87	0.56	1.36	0.547
	S.Europe/Mediterranean	8.44	2.08	34.21	0.003
	N.Europe	1.37	0.37	5.01	0.639
	Other	10.64	2.59	43.72	0.001
CHRONIC DISEASE	**Neoplasm**	5.01	0.91	27.67	0.065
	Asthma	4.97	1.64	15.11	0.005
HYGIENE					
	'Food poisoning germs are killed by proper cooking'				
	Agree	1.00			
	Disagree	1.00	0.65	1.51	0.981
	Not Sure	2.41	1.42	4.12	0.001
	Missing	15.26	1.22	191.44	0.035
	Total length of work surface				
	>2 metres	1.00			
	1–2 metres	1.57	1.13	2.19	0.007
	<1 metre	2.40	1.10	5.21	0.027
	Missing	1.40	0.72	2.70	0.317
CONTACT WITH OTHER PERSON WITH DIARRHOEA AND/OR VOMITING	**Contact at home**				
	No	1.00			
	Child case	4.11	1.67	10.11	0.002
	Adult case	0.72	0.34	1.52	0.392
	Both	0.46	0.09	2.42	0.359
	Contact outside the home				
	No	1.00			
	Yes	2.85	1.74	4.66	<0.001
	Not sure	3.52	2.28	5.44	<0.001
FOOD & WATER	Whelks	31.23	3.08	316.28	0.004
	Offal	0.50	0.29	0.87	0.015
	Pulses	0.52	0.37	0.74	<0.001
	Fruit with edible skins	0.59	0.40	0.86	0.007
	Peeled fruit	0.66	0.45	0.97	0.032
	Dried fruit	0.54	0.38	0.76	<0.001
	Take-out from sandwich bar	0.42	0.27	0.65	<0.001

Table 9.18 ***continued***

FINAL STAGE 3 MODEL

FACTOR		ODDS RATIO (MATCHED)	95% CONFIDENCE INTERVAL		P-VALUE
ANIMAL CONTACT					
	Contact with pets with diarrhoea				
	No	1.00			
	Yes	2.52	1.05	6.01	0.038
	Not sure	41.99	4.47	394.46	0.001
	Feeds pets meat/fish cooked at home	0.66	0.42	1.03	0.066
	Cleans up pet's mess	0.57	0.39	0.83	0.003
	Contact with animals outside the home	0.49	0.34	0.71	<0.001

Direct factors: contact with children with diarrhoea and/or vomiting within the household increased the risk four-fold, and contact with people with diarrhoea and/or vomiting outside the household increased it three-fold. Contacts with pets with diarrhoea increased the risk 2.5-fold. Contact with animals outside the house or being the person who cleans up a pet's mess halved the risk of IID in this sub-group. Reported consumption of whelks increased the risk markedly (30-fold) but not many cases reported this exposure. Reported consumption of a number of foods was associated with a statistically significant lower risk: pulses, fruit (skinless, with edible skins and dried) or food from sandwich bars.

Summary

Being off work because of a disability increased the risk. Travel abroad also increased the risk, but the magnitude of the effect is much less marked than for all IID. Asthma, short kitchen work surfaces, contact at home with children with diarrhoea and/or vomiting or pets with diarrhoea, and consumption of whelks increased the risk. Decreased risk was associated with contact with animals outside the house, cleaning up pets' mess, and the consumption of pulses, fruit and food from sandwich bars.

Discussion

It is likely that this group consists of a 'heterogeneous' mixture of infections rather than a homogeneous group. The mix within the group, however, is unlikely to be the same as for all IID. The group may contain a higher proportion of infections with target organisms which were difficult to identify, and cases infected with recognised or novel pathogens which were not sought in our study. It is also the group most likely to include undiagnosed non-infectious intestinal disease. Attempts to interpret contradictory or counter-intuitive associations may prove futile. It is of note that the lower risk associated with eating certain foods is consistent across organisms, suggesting either a consistent bias or a true effect.

9.3 SUMMARY OF FINDINGS

9.3.1 Social factors, housing and contact with people with gastroenteritis

There was a small but pervasive effect of social factors on all IID, and on infection with the two viruses investigated, rotavirus infection (in infants and children under 15 years of age) and SRSV. Social class had an impact on infection in adults, whilst

disease in children was associated with single status of the head of the household. The effect of social class disappeared when controlled for foods associated with lower risk; the effect of single status decreased when controlled for housing.

Poor housing conditions were associated with an increased risk of viral IID. In infants, this was linked to sharing a bathroom (a very strong effect, but very few subjects exposed). In infants and children under 15 years of age, rotavirus infection was associated with living in rooms or flats. This effect tended to persist when contact with a person with diarrhoea and/or vomiting was taken into account.

People reporting contact with another person with diarrhoea and/or vomiting outside the household were at increased risk of infection in all age groups for which this factor was investigated: all IID in adults and children, rotavirus in infants and children under 15 years of age, and SRSV in subjects over 5 years of age. Contact with a child with diarrhoea and/or vomiting in the household carried a risk for all IID, IID with no target organism in the stool, and for the two viruses investigated. Attending crèches, play groups, school and child minders was not associated with increased risk for children. In fact, they tended to be associated with a lower risk, since use of such facilities was more common in families of higher social class.

9.3.2 Travel

Travel abroad had a marked effect on all IID for adults and children, and on *C.jejuni* and EAggEC infection. The effect was present (but not as strong as for all IID) for IID with no target organism detected. Numbers travelling abroad were too small to reach statistical significance for infection with SRSV, rotavirus in infants and children under 15 years of age, and all IID in infants. This suggests that, even if travel is a risk factor for infection with these organisms, its contribution to the total burden is small. Only for all IID and all IID with no target organisms in adult subjects were the numbers sufficient to investigate risk by country visited. The pattern was similar in both groups, but the effect was smaller for IID with no target organism identified. Travel to northern Europe carried no statistically significant increase in risk, whereas, for travel to southern Europe/ Mediterranean countries and the Middle East, the risk was intermediate and, for travel to other countries, it was large. Travel in the UK where the travel was not for holidays carried a risk of all IID in infants.

9.3.3 Other disease and medications

Other disease and medications were investigated only for some groups, because of limited numbers. Asthma in adults was associated with an increase in risk of all IID and of IID with no target organism identified. Diabetes was associated with an increased risk of all IID in adults.

Use of antacids increased the risk of all IID in adults, and also of *C.jejuni* infection but, in the latter case, this was not statistically significant. Antibiotics increased the risk of *Clostridium difficile in* subjects over 2 years of age, but this was responsible for less than half of all cases. Medication for respiratory illnesses (mostly asthma) was associated with lower risk of all IID in children.

9.3.4 Swimming and contact with pets

Swimming was associated with a lower risk of all IID in adults and in children, and of IID with *C.jejuni*, but only when travel and swallowing water were controlled for.

Having ‘unusual pets’ was associated with an increased risk for all IID in adults. However, pets such as rabbits, cats and dogs (as long as the subject was not

Table 9.19 Foods with a statistically significant association with all IID in adults, children and infants, or with selected target organisms in the stool. Where a reduced risk of IID is shown, foods are included only if the effect was shown in at least two analyses. Adjusted for travel, except in the case of rotavirus and *Salmonella enteritidis* PT 4, where either the effect or the numbers were too small.

	ADULTS		CHILDREN		INFANTS		*S.ENTERITIDIS* PT4		*C.JEJUNI*		EAggEC		ROTAVIRUS		SRSV		NO TARGET ORGANISM
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P	DETECTED
pulses	0.5	<0.001	0.5	0.000	0.05	0.07	0.3	0.023	0.4	<0.001							0.5 <0.001
fruit with edible skin	0.5	<0.001							0.4	<0.001			0.4	0.004			0.6 0.007
peeled fruit									0.3	<0.001			0.3	<0.001			0.7 0.032
dried fruit	0.5	<0.001							0.3	<0.001			0.3	0.001			0.5 <0.001
salad eaten at home			0.6	0.005			0.4	0.04	0.4	<0.001			0.3	<0.001			
rice eaten at home	0.7	0.020					0.3	0.012	0.4	<0.001							
non-oily fish			0.6	0.003							0.7	0.026			0.4	0.003	
pasteurised dairy products	0.5	<0.001							0.5	<0.001			0.3	0.012			
dairy products made abroad			1.5	0.031													
salad at restaurant											4.22	0.012			4.63	0.012	
chicken at restaurant									1.9	0.049					3.2	0.03	
oysters	7.0	0.02															
whelks																	31.2 0.004

responsible for cleaning up the dog's mess) were associated with lower risk. Contact with dogs and cats (outside the home), and feeding the pet outside the kitchen was also associated with lower risk of all IID. For IID in adults with no target organism detected, contact with animals outside the home and cleaning up the dog's mess were associated with lower risk. Having a pet with diarrhoea increased the risk.

9.3.5 Kitchen practices, hygiene practices and knowledge

Kitchen practices and hygiene, as measured in the study, had remarkably little effect on risk of IID of any aetiology. Having a jug filter for water and shopping once a week were associated with a lower risk of all IID. Having a kitchen counter of 2 metres or longer was associated with a lower risk of IID in adults without a target organism.

None of the other 50 hygiene practices and 10 hygiene beliefs investigated were statistically significant in an interpretable way. A number of practices were associated with risk when the respondent 'didn't know' what they did, and some were associated with lower risk when the respondent followed instructions 'sometimes, but not always' or 'never'.

9.3.6 Breast-feeding practices

Breast-feeding was highly protective against all IID in infants. How the bottle was cleaned also was associated with variations in risk for all IID. For rotavirus infection in infants, breast-feeding was protective, but lost statistical significance when social class was controlled for.

9.3.7 Food

Table 9.19 presents a summary of the statistically significant associations found between food consumption and IID for all sub-analysis undertaken.

9.3.7.1 Foods associated with a higher risk of disease

Consumption of very few foods was found to be statistically significantly associated with increased risk. There was a higher risk of disease associated with: oysters, for all IID in adults; dairy products made abroad, for all IID in children; chicken (eaten at a restaurant) and cold sliced meats (bought at a shop, that is, not a supermarket, butcher or delicatessen) for *C.jejuni* infection; salad at a restaurant, for EAggEC infection, particularly for those not travelling abroad; and whelks, for those without a target organism detected.

Consumption of chicken and eggs was not found to be associated with an increased risk of *Salmonella enteritidis* PT4. Consumption of shellfish and oysters was not associated with risk of SRSV infection, but numbers were small.

9.3.7.2 Foods associated with lower risk of disease

A group of five foods showed a very consistent, highly statistically significant association with a lower risk of disease. The effect typically reduced the risk of IID for a variety of aetiologies by between 30% and 70%.

The consumption of pulses reduced the risk of all IID in adults and in children, and of *Salmonella enteritidis* PT4, *C.jejuni*, and IID with no target organism. Consumption of pulses also reduced the risk of infection with rotavirus, SRSV and EAggEC in the age groups analysed.

Consumption of salad (at home) was associated with a reduced risk of all IID in children, and IID caused by *S.enteritidis* PT4, *C.jejuni*, and rotavirus.

Fruit (fresh with edible skin, fresh without edible skin, dried and desiccated coconut) was statistically significantly associated with a lower risk IID for selected target organisms. Fruit of these four types was associated with a reduced risk of all IID in adults, *C.jejuni*, rotavirus, SRSV and IID in adults with no target organism identified. Freshly cooked rice that was eaten immediately at home was associated with a reduced risk of all IID in adults, *S.enteritidis* PT4, and *C.jejuni*.

Fish associated with a reduced risk of all IID in children, *C.jejuni* and rotavirus.

Other foods were associated with a statistically significant reduced risk in one or two sub-analyses only and the effect tended to be less statistically significant. Take-away sandwich bars were associated with a reduced risk of all IID in adults, and IID with no target organism. Beef and prawns were associated with a lower risk of all IID in children aged 1 to 15 years; pork and frozen chicken prepared at home were associated with a lower risk of IID in infants aged under 1 year. Lamb and prawns were associated with a lower risk of *S.enteritidis* PT4 infection. Pasteurised dairy products, desserts, sauces and cakes made at home, other poultry (mainly turkey) and burgers were associated with a lower risk of *C.jejuni*, infection. Cold meat from a supermarket and sausages were associated with a lower risk of EAggEC infection. Pasteurised dairy products were associated with a lower risk of rotavirus infection.

9.4 DISCUSSION

We discuss the findings risk factor by risk factor, having discussed them by organism in the body of this chapter. The finding of an association between IID and social class, and IID and housing conditions was not unexpected. Illness is not evenly distributed in society and increased morbidity from many causes is associated with lower social class and poorer living conditions (Black 1991).

Contact with a person with diarrhoea and/or vomiting outside the household was associated with higher risk for rotavirus in infants and children under 15 years of age, and for SRSV, *S.enteritidis* PT4 and *C.jejuni*. Rotavirus and SRSV are primarily spread by the person-to-person route. Contact with a child with diarrhoea and/or vomiting the household was a risk for infection with both rotavirus (in infants and children under 15 years of age) and SRSV. This finding was not unexpected and emphasises the need to determine the mechanism of transmission between children and adults.

The protective effect of breast-feeding was an expected finding, as was the influence of the method of cleaning the baby's bottle on illness.

Travel associated illness is widespread and is becoming an increasing problem (Farthing 1993). Gastrointestinal upset is the commonest illness reported by travellers returning to the UK , affecting at least 25% of the 28 million UK residents who travel abroad each year (Packham 1995). Much of this illness is infectious in origin (Farthing 1993) and is potentially preventable by specific risk avoiding behaviour. However, the practical difficulties of adhering to preventive advice have been recognised (Kozicki *et al.* 1985; Farthing 1993). Those at greatest risk in the population are those travelling to high risk areas (Cossar *et al.* 1990, Behrens and McAdam 1993). Notified cases of food poisoning in those returning from abroad represent substantial work for those responsible for infection control in the community. A survey undertaken in 1993/1994 included 123 cases of infection

acquired abroad of whom 104 were food poisoning and 19 were malaria (Packam 1995). In this study, 11% of notified cases of food poisoning were directly attributed to travel abroad. It is often difficult for travellers consistently to adhere to advice (Kozicki *et al.* 1985). Even when travellers are careful, they can often become ill. Bacterial pathogens are able to survive on food that is too hot to touch (Bandres *et al*. 1988) and bacteria in ice cubes can be recovered from cocktails containing tequilla, whisky and other spirits (Dickens *et al.* 1985).

In England and Wales, data from the PHLS Laboratory of Enteric Pathogens suggests that 10 to 20% of non-typhoid salmonellas and *Campylobacter* infections have been acquired abroad. For typhoid, the figure approaches 90%. However, these data are based on a passive surveillance system. The fact that the request accompanying a stool specimen to a laboratory does not specify that the case has travelled abroad does not exclude the possibility. The proportion of cases who have acquired their infection abroad may therefore be much higher than surveillance data suggests. The response of the travel industry to diarrhoeal outbreaks has often been low key despite the fact that the symptoms are so common. According to some surveys, they affect 30–40% of travellers (Cossar *et al.* 1990). The low key response is probably because symptoms are often mild and short-lived. However, what may be a mild illness for a robust young adult can be life threatening for an infant, a frail elderly person or an immunocompromised person, and may occasionally lead to hospitalisation and even death. Furthermore, the economic consequences can be considerable. The average cost to the individual and health service of a case of *S. enteritidis* infection has been estimated at £800 (Roberts and Sockett 1994) but the loss incurred by someone on an expensive holiday could be much greater. However, with the recent enactment in English law of the European Directive on Package Holidays (90/314/EEC), tour operators are responsible for anything that goes wrong, irrespective of whether the service at fault is provided by the operator itself or by somebody else (Council Directive 90/314/EEC; Department of Trade and Industry 1992). With the possibility of financial compensation that this legislation provides, increasing numbers of travel associated infections, particularly those occurring as part of outbreaks, are being reported to the PHLS CDSC.

It was not unexpected to find unusual pets associated with an increased risk of IID as infections with salmonella are well documented in individuals who keep exotic pets, particularly reptiles (D'Aoust *et al.* 1990; Shane *et al.* 1990; Mermin *et al.* 1997). What is disturbing is that a high percentage of parents appear oblivious to the risks posed by pet iguanas and other reptiles in the household (Mermin *et al.* 1997). Even though young children and infants were often not permitted to touch or come into contact with these animals, Mermin *et al.* (1997) showed clear evidence that when the animals were present in household bacteria were carried on the hands of other household members or were present on surfaces in the household. Forbidding a child to touch such a pet may therefore not be enough to prevent infection, particularly in susceptible individuals. Mermin *et al.* (1997) recommend that any household with highly susceptible individuals should not keep reptiles. Handwashing, surface disinfection and other hygienic measures must be followed whenever dealing with reptiles as well as pet birds and other animals potentially capable of transmitting *Salmonella* and other pathogens.

The patterns of risk associated with keeping dogs and cats are difficult to explain. Both dogs and cats have been associated with the spread of *Campylobacter*, *Salmonella* and other pathogens (Hastings 1978) although a reduced risk of diarrhoea in children associated with ownership of pets has also been described (Franti *et al*. 1980). Contact with pets with diarrhoea was associated with a higher risk of IID in adults with no identified target organism. When animals are ill they shed more pathogens and even house-trained pets are liable to mess in the house. The

finding of an association with IID is not unexpected but the fact that in most cases no pathogen was identified is surprising. The finding that healthy dogs and cats did not pose a risk is surprising given that asymptomatic animals can carry pathogens and that these animals, especially cats, live in very close proximity to their owners and often have access to work surfaces in the kitchen (Wall *et al.*1996c). The study did not ask whether the pets were newly arrived in the household or the age of the pets. It has been suggested that continuous exposure to low doses of infectious agents from pets may cause some degree of organism specific immunity although this has not been documented (Salfield and Pugh 1987, Evans 1993).

Asthma and diabetes were associated in adults with an increased risk of presenting to the GP with IID. Asthma can be triggered by infections, so these patients may be more likely to present to their GPs. Whilst persons with chronic diseases may have been less willing to participate in the study as controls, thereby exaggerating the association between IID and asthma and diabetes, increased susceptibility to infection is a well-documented side-effect of diabetes.

The finding of an association between antibiotic use and *C.difficile* infection was expected, as *C.difficile* is the principal agent of antibiotic-associated diarrhoea. However, it is noteworthy that this occurred in a non-hospital setting. Community-acquired antibiotic-associated diarrhoea due to *C.difficile* has been documented in several countries but this is the first study of prevalence in the UK.

The finding of such a small effect of hygiene and kitchen practices was surprising. Possible explanations are discused above in section 9.3.5. Hygiene practices and knowledge are, however, notoriously difficulty to measure. It may be that subjects knew how they should behave in their kitchen and answered the questions accordingly, irrespective of their actual behaviour. In addition, even if the respondents were honest, the study collected information on usual practice not practice in the days before illness, and so it may have missed the lapse which caused the infection. Surveillance data on general outbreaks of IID in England and Wales show that the most usually reported faults contributing to outbreaks are inadequate refrigeration, cross-contamination and inadequate heat treatment (Cowden *et al.* 1995). The lower risk of disease in those with a kitchen working surface of two metres or longer may be due to its facilitating the separation of raw and cooked food and reducing the risk of cross-contamination.

Very few foods were associated with an increased risk of IID. They fell into two groups: certain shellfish (whelks and oysters) and chicken and salad from restaurants. Oysters are well-documented vehicles of food poisoning (Le Guyader *et al.* 1996). Many shellfish are bivalve mollusca filter feeders and accumulate both bacteria and viruses if exposed to sewage contamination from the water in which they grow. They can be cleared of bacterial pathogens by depuration. However, depuration may not eliminate viruses, and outbreaks of SRSV infection related to oyster consumption are well described (Luthi *et al.* 1996). Is is not clear why oysters had a statistically significant association with all IID and IID with no target organism given the small numbers exposed.

The association between eating chicken at restaurants and infection with *C.jejuni* is not an unexpected finding as many chickens are colonised with *C.jejuni,* and surveys have shown poultry meat on retail sale in the UK is often contaminated (Atabay and Corry 1997). We failed to show a similar association with *S.enteritidis* PT4 infection, even though this is an organism overwhelmingly associated with poultry and egg sources. Sources and vehicles of infection, however, are not necessarily the same. The fact that, unlike *Campylobacter*, *Salmonella* spp. can grow on food, could lead to a much wider range of food vehicles being responsible

for *S.enteritidis* PT4 infection, and explain the lack of a statistically significant association with poultry consumption. The association between salads in restaurants and EAggEC is an interesting finding as this is a pathogen that is not routinely looked for by diagnostic microbiology laboratories in England. This study suggests that it is an important cause of IID and should be considered in the investigation of cases.

Except for the association discussed above, consumption of chicken and eggs was not associated with an increased risk of IID in this study. This could be an artefact as discussed in section 9.1.3. We asked subjects about their food consumption in the ten days prior to the onset of the illness, and this is longer than the typical incubation period for *Campylobacter* and *Salmonella*. The study's power to identify poultry and eggs as risk factors would therefore have been reduced. In other words, cases may have eaten more chicken than controls in the three days prior to illness (for which we have no data) but not in the ten days prior to illness (for which we do). This limitation would have reduced our chances of showing direct associations with any of the shorter incubation period target organisms. However, choosing a shorter period would have reduced our chances of identifying associations with target organisms of longer incubation period. Another less likely possibility is that subjects' responses were systematically biased: those cases who had eaten chicken denying it, or controls who had not eaten chicken claiming to having done so. However, the absence of an increased risk of *S.enteritidis* PT4 or *C.jejuni* infection associated with poultry consumption in sporadic cases is not unprecedented. Studies by Cowden *et al.* (1989) and Adak *et al.* (1995) have shown consumption of poultry in the previous three days to be associated with a reduced risk of *S.enteritidis* PT4 and *Campylobacter* infection respectively. Possible explanations are that continuous exposure to low doses of the infectious agents confers a degree of immunity; or that other vehicles are responsible for most sporadic disease.

Most outbreaks of *S.enteritidis* PT4 infection in England and Wales are associated with the consumption of chicken, egg or egg based dishes (Cowden *et al.* 1995, Djuretic *et al.* 1996b). Outbreaks of *Campylobacter* infection, although much rarer, have also been linked to the consumption of chicken. The apparent discrepancy between food vehicles causing outbreaks and those causing sporadic cases could be explained by the fact that, in an outbreak, the vehicle is heavily contaminated, and the determinant of illness is whether a subject ate it. In sporadic cases, on the other hand, the vehicle might be only lightly contaminated, and the determinant of illness might be the individual's susceptibility. The individual's resistance may indeed be increased if they regularly eat food contaminated with small numbers of pathogens.

Another explanation for so few foods being associated with an increased risk of IID is that cross-contamination in the domestic or catering kitchen, or during manufacture, results in a wider range of intermittently and lightly contaminated foods than is usually supposed.

Why did we find a lower risk of disease in people consuming pulses, salad and rice at home, fruit and fish? The questionnaire asked 60 specific questions on food consumption but only these five foods were consistently associated with lower risk. This could be an artefact as discussed in section 9.1.3. People that reported eating these foods may have a health conscious lifestyle which lowers their risk of IID by some practice not measured in the study. We think this improbable. It is difficult to imagine what this practice could be, as information was collected about a large range of social, educational, and hygienic practices, and none is as strongly associated with lower risk as these foods. The finding could be due to selection bias, if people who agreed to be a control in the study were more likely to eat these foods. A preliminary analysis of the

data from the nested population case-control study indicates that these five foods are associated with lower risk in the community component. As acceptance rates for controls were higher in the community component we believe selection bias is unlikely to explain the effect. Reverse causation is another possible artefact. This could occur if people changed their eating habits after developing the disease and this biased their recall of what food they consumed before the disease. We think this an unlikely explanation.

We believe the lower risk of IID associated with pulses, salad and rice eaten at home, fruit and fish may be a true finding which merits further investigation. Proposed causal mechanisms which could be studied include:

(i) The effect of diet on the intestinal flora. It is possible that the food one consumes changes the composition of the intestinal flora. For example, increasing the endogenous intestinal populations of bifidobacteria has been cited as protecting against some forms of food poisoning (Kimura *et al*. 1997).

(ii) Boosting of specific immunity to various foodborne pathogens by repeated exposure to low doses of them in food. Although this may explain why some studies have, for example, found consumption of poultry to be protective, we believe it is less likely to be true for the foods found to be protective in this study as there is no evidence of widespread contamination of these products with the main foodborne pathogens.

(iii) Boosting of general immunity to infection. This could be mediated by micronutrients, for example selenium and other antioxidants, in the protective foods. Selenium deficiency has been cited as a risk factor in the acquisition of *E.coli* O157 infection (Erskine *et al.* 1989). Vitamin A has been shown to reduce severity of diarrhoea in developing countries (Barreto *et al*. 1994). Fruit, salad and pulses are rich in antioxidants.

In summary, social factors were associated with a higher risk of IID, and this was mediated mostly by living conditions. Contact with another person with IID was identified as a risk factor, highlighting the importance of person-to-person spread of viral IID in the community. Travel abroad was associated with higher risk of all IID and of IID caused by some target organisms. Breastfeeding was highly protective.

The study showed no association between domestic practices or hygiene and an increased risk of IID, not even for those organisms known to be foodborne. This could be an artefact since hygiene practices and knowledge are difficult to measure; it could be because we asked about normal practice; or it could be real, either because major lapses of hygiene are not necessary for sporadic disease, or if most contamination occurs outside the home.

Very few foods were found to be associated with increased risk. This could be an artefact, as we asked about the ten days before the onset of symptoms; or it might be true for sporadic cases. Contaminated chicken may, for example, cause many outbreaks of *Salmonella* and *Campylobacter*, but few of the sporadic cases which account for 95% or more of the total. In that sense, it may present a small risk overall. Alternatively, it may be because contamination of many food types is rare and insufficient to endanger most people's health, and infection is caused from eating one of a wide variety of lightly contaminated foods.

In contrast, we found that a group of five foods was associated with a very consistent and statistically significant lower risk of disease. The effect typically reduced the risk of IID by between 30% and 70%. These foods were pulses, salad, fruit, rice and fish . It is possible that the lower risk of being a case associated with consumption of these foods is an artefact, or reflects some characteristic which is

itself associated with lower risk: perhaps eating freshly prepared food. It is possible, however, that the effect is causal. Consumption of fruit and vegetables has been shown to be associated with a lower risk of cancer of the intestinal tract, and possible causal mechanisms for protection against IID include: the effect of diet on the intestinal flora, or a boost to general immunity against infection mediated by micronutrients including antioxidants.

Chapter 10
Summary

This was the largest microbiological epidemiological and economic study of IID yet undertaken. Seventy general practices were involved, covering a population of nearly a half a million (1% of the national population). The sample was broadly representative of the population of England in terms of age and sex distribution, residence in a particular geographical area (the North, Midlands and South West and the South East) and an urban or rural location. The general practices were also geographically representative but tended to be larger than average, reflecting the characteristics of practices in the MRC's General Practice Research Framework. In contrast, previous studies of IID in general practice have been small, involving one or a few general practices.

The study was necessarily complex to address the study objectives:

- To estimate the number and aetiology of cases of IID in the population, presenting to GPs, and having stool specimens sent routinely for laboratory examination.
- To compare these numbers and the aetiologies with those recorded by the national laboratory reporting surveillance system.
- To estimate the prevalence of asymtomatic infection with agents associated with IID.
- To document differences between cases of IID (in the population and presenting to GPs) and similar but well people (controls).
- To estimate the socio-economic burden of IID and its distribution.

10.1 THE INCIDENCE AND MICROBIOLOGICAL CAUSE OF IID IN THE COMMUNITY AND PRESENTING TO GPS

10.1.1 Community rates

Two large population based cohorts were recruited and followed prospectively for six months to obtain a complete year of follow-up. Although uptake was only 40%, this was consistent with other studies and was perhaps expected, given the nature of the study. The final cohort was reasonably representative of the national population in terms of age and sex except amongst males aged 15–24 years, and where there were slight differences in social status and social class.

There was a very high level of compliance with follow-up which used a weekly negative reporting system. This gives more valid results than a prospective positive reporting system (i.e., only IID events are reported) or a retrospective recall.

Microbiological sampling was satisfactory with high compliance, minimal delays in postage and transport, and standardised and comprehensive testing of faecal specimens in one main laboratory, Leeds PHL. Specialist laboratories were used for more specific tests. The majority of specimens had all the planned tests performed on them, and in two thirds there was sufficient stool remaining to be archived for possible future testing. All isolates were also archived.

One in five of the study population had an episode of IID in the course of the year. The rate was highest in children under 5 years of age and was also high in women of reproductive age. The results are similar to a recent Dutch population based survey. Previous studies in the US found higher rates which may reflect the selective nature of the populations studied (e.g., with more families and young children).

If we discount Aeromonas which were found in almost as many controls as in cases, target microbial pathogens or their toxins were identified in only a third of cases, most frequently SRSV and *Campylobacter*.

10.1.2 General practice rates

Robust estimates of GP presentation rates were achieved, firstly by adjusting the denominators for practice list inflation, derived from the cohort study above. The average level was 10%. Previous studies report a range from 5–30%. Secondly, the numerator was adjusted for the estimated underascertainment of cases by GPs.

Compliance by the subjects with microbiological sampling was reasonable (74% from cases and 80% from controls) given the difficulties of collecting stool specimens from individuals suffering from presumed IID. For example, a primary care based study in Wales had a 67% compliance rate with stool sampling.

A higher proportion (55%) of cases had an organism identified than in the population cohort study (37%). Frequently identified target organisms included *Campylobacter* in 12%; rotavirus in 8%; SRSV in 7% and *Salmonella* in 5%. There were only three isolates of *E.coli* O157. This pattern is similar to that found in national surveillance.

Overall, one in 30 people presented to the GP (or one in six of those with IID identified in the community). The rate of presentation to A & E was low, suggesting patients largely used primary care for consultations. These rates are similar to other UK-based primary care studies and to a recent Dutch study. The rate was again higher in children under 5 years of age and greater in adult females than in males.

Severity of illness, use of primary health care services and accessibility to services may explain some of this difference. Symptoms were more severe, more frequent and of longer duration in both adults and children presenting to GPs compared with cases in the population cohort component. There were similar distinctions between bacterial and viral infections in general, although some rotavirus infections in children were more severe than many of the bacterial infections.

Symptoms were evaluated when there were sufficient cases associated with individual target organisms. Of those evaluated, *Campylobacter* and *Salmonella* were associated with severe illness. Raised temperature and bloody motions being most frequently reported with these pathogens both in adults and children presenting to a GP. Vomiting was most frequently reported in association with SRSV infection in adults and with SRSV and rotavirus group A in children. The most frequent infection in the population cohort component, SRSV, generally caused a

short-lived illness with a median duration of only two days, even in those adults presenting to a GP. Rates of target organism or toxin detection were higher than in previous studies. The relative proportions of *Salmonella* types identified were similar to those identified routinely through national reference laboratory surveillance, thus showing the value of the current surveillance system in monitoring trends in sub-types of this organism. The most commonly identified serotype was *S.enteritidis*, and in particular PT4. The second most common was *S.typhimurium*, in particular DT 104. We found relative proportions of the different types of enterovirulent *E.coli* that was markedly different from those identified routinely; the importance of EAggEC as a cause of IID was particularly noteworthy. The very small number of sporadic cases of *E.coli* O157, which may cause serious disease, reflected the national reported figures. This was also the case with *Vibrio, Giardia intestinalis* and *Cryptosporidium parvum*. *Clostridium perfringens* was shown to be a common cause of sporadic IID. The importance of SRSV as a common cause of sporadic, community-acquired IID which was relatively mild in duration and severity was demonstrated. Other viruses, notably rotavirus followed by adenoviruses, astroviruses and, to a lesser extent, caliciviruses, were important causes of IID presenting to GPs.

Results on age and seasonality of IID in England are consistent with previous studies. The study did not clarify the role of *Aeromonas, Yersinia* and some of the enterovirulent *E.coli* in sporadic IID in the community in England since these were found in similar proportions in cases and controls.

A high proportion of cases had no target organism or toxin identified. This was not explained by the time lapse between voiding and testing of stool specimens, or completeness of testing, although there were some delays, and 30% of samples were insufficient for complete analysis. The most likely explanations are the limited sensitivity of the tests used, compounded by the inevitable time-lag between the onset of symptoms and the production of a stool specimen, the occurrence of IID due to as yet unrecognised organisms and toxins, and the inclusion of patients with non-infectious causes (despite the application of a clear case definition).

It is likely that the routine use of modern molecular tests such as polymerase chain reaction (PCR) amplification for pathogens and toxins would have improved the study's sensitivity. The improvement might not have been great for bacterial pathogens such as VTEC, where the gene probe used detected no more cases of *E.coli* O157 than the culture method chosen. On the other hand, the PCR technique might have increased the identification rate for viral pathogens more significantly, as it is well recognised that electron microscopy is a subjective and relatively insensitive technique. The quality control exercise undertaken during the study confirmed this assessment and, although viruses were pre-eminent as a cause of IID, it is likely that the true number of cases of viral infection (excluding rotavirus group A which were identified by EIA) was even greater than that reported in this study.

Other important issues remain unanswered. For example, the data on infection with multiple organisms were complex and require further analysis. This study provides a very valuable source of information and materials for further studies, which should include the development of methods for detection and isolation of organisms, and typing and virulence properties.

10.2 COMPARISON OF COMMUNITY AND GP RATES OF IID WITH NATIONAL LABORATORY SURVEILLANCE DATA

Routine stool sampling practice was observed in 36 general practices. The laboratories used by these practices were representative in terms of whether they belonged to the PHLS or not, and their size. Overall, the normal practice of GPs was to request stool samples from about a quarter of the patients who presented to them with IID. This reflects a tendency to request stool specimens on clinical grounds, rather than for surveillance purposes. Our study will provide valuable evidence to assist in the formulation of advice to GPs on which patients should have specimens taken in order to achieve epidemiological and public health objectives.

Two methods were used to estimate the factor by which national surveillance data should be multiplied to describe the incidence of IID in the population and the number of cases presenting to GPs, the so-called reporting pyramid. In the first — a direct method — the names of those cases for whom positive stools were obtained in the enumeration component were searched for in the national database and the degree of under-reporting calculated.

In the second — an indirect method — we compared the rates of IID which we estimated to occur in the whole population of England with the rates appearing in national surveillance figures and the degree of under-reporting was calculated.

By our own direct method we estimated that for every 136 cases of IID in the community 22 presented to a GP, 6.2 had a stool sent routinely for microbiological examination, 1.4 had a positive result, and one was reported to PHLS CDSC.

By our indirect method we estimated the ratio to be 88 cases in the community for every one reported to CDSC.

Our first estimate of the proportion of actual cases in the community appearing in CDSC's surveillance statistics based on the direct method may be pessimistic. This is because this estimate included only those cases reported to CDSC after presenting to their GPs. Cases may also arise in outbreaks, and these may be reported to CDSC by routes other than the GP. For example, outbreak cases identified by EHOs may be asked to send stool samples directly to laboratories. The direct method would identify these cases in the community, but not in the enumeration component, leading to an under estimate of the system's sensitivity. Another reason could be that our study did not include certain institutions (e.g., prisons, hospitals or long-stay institutions) from which stool samples would go direct to laboratory without any GP involvement. Two effects may act in the opposite direction leading to a spurious overestimate of the sensitivity of the national surveillance system. Firstly, it is possible that repeat specimens, specimens of materials other than stools, and specimens taken for research purposes could artificially inflate the CDSC reports, despite the efforts made to remove them from CDSC's data. Secondly, study nurses may have failed to record positive laboratory results.

The proportion of different target organisms causing IID identified in the population and presenting to GPs varied, and these proportions were different again from those were routinely identified in laboratories and reported to the national surveillance scheme.

This reporting pyramid was estimated to be steepest for SRSV where for every case reported to CDSC there were about 1,500 in the community. This is entirely

understandable, for four reasons: firstly, people experiencing mild symptoms in the community are much less likely to consult their GP; secondly, the GP, being motivated by clinical considerations, is much less likely to request a stool specimen for cases with mild short-lived illness; thirdly, unless a case is part of a known outbreak, the laboratory is unlikely to perform EM for SRSV; and, fourthly, even when a stool specimen is sent to the laboratory, the routinely available tests for SRSVs (EM) are less sensitive than the culture test used for detection of the common bacterial pathogens. In contrast, there were three cases of *Salmonella* infection in the community for each case reported to CDSC. This may be because a higher proportion of cases of salmonellosis than viral gastroenteritis consulted their GP because their illness was more severe, or because laboratory tests are more sensitive for salmonellas than SRSV, or because laboratory reporting to CDSC is more complete, or a combination of all three. Thus it would appear that severe cases of IID, that are mainly due to bacterial infection, tend to be less under reported than milder forms of IID mainly due to viral infection. It is worth noting that a consequence of this is that national laboratory surveillance is at its most efficient in identifying what matters most: the more severe end of the spectrum of IID, and, as it is bacterial, IID more likely to have resulted from the consumption of contaminated food.

Organism specific results from the direct and indirect estimating methods of completeness of reporting to CDSC were compared. The viruses appear to be poorly reported by both estimates compared with the bacteria. If it were true that outbreaks were the reason for the discrepancy between the direct and indirect estimates we would have expected it to be less for *Salmonella*, *Campylobacter* and rotavirus infections where outbreaks are relatively uncommon (5%, 0.04%, 0.4% percent of reports from outbreaks, respectively 1995 data) and rather worse for SRSV (47% of reports from outbreaks in 1995). This was indeed the case. Both estimates showed a similar reporting ratio for *Campylobacter* and *Salmonella*. The estimate from the indirect method was well within the confidence intervals for the direct method. With SRSV the discrepancy was even greater than we had anticipated. This is probably because the actual proportion of cases recorded as part of an outbreak is unpredictable, as EHOs usually obtain stool specimens from only very few cases in an outbreak. This is understandable, given that it is seldom possible to contact all cases, and that once the organism responsible for an outbreak is identified, it is reasonable to assume that other cases are due to the same organism if they are clinically similar. There may also be an artefactual trend in the reporting of outbreaks, since the number reported is increasing, particularly those due to viruses, which have increased 4-fold from 1992–96. The two-fold discrepancy between our two estimates of the under-reporting of rotavirus remains unexplained, as the few outbreaks associated with this virus are almost always localised outbreaks in young children, which should have been identified by both our direct and indirect estimates. The indirect estimate does, however, lie within the confidence intervals of the direct estimate, and the difference could thus be due to chance.

In summary, IID is very common in the community and presenting to GPs but only a proportion is reported to national surveillance, this figure varying by organism. This suggests that a primary care based sentinel IID surveillance scheme with microbiological testing is required to assist in the monitoring of trends.

10.3 RISK FACTORS FOR IID

Most existing information on IID risk factors is derived from outbreaks or sporadic cases reported to routine surveillance. Such cases may not reflect the generality of IID in the community or in primary care.

The data on risk factors in this study were based on a case control design in the GP study and a nested case-control design within the population cohort component. Cases and controls completed risk-factor questionnaires and provided stools. Matching of controls was quite high though not complete despite up to five attempts to obtain an appropriate control. Most cases and controls completed questionnaires and provided stools. Controls had a higher compliance than cases, probably as they had self-selected to participate in the study. As expected, compliance was even higher in the nested case-control study of the cohort. This design is less prone to selection bias than the GP study but the numbers of cases was smaller, limiting the power to detect significant differences. Risk factors of all IID were estimated from subjects in the GP case-control study, and risks by target organism from subjects in both the GP case-control study and the population cohort component study.

Despite the size of this study, it was not designed to demonstrate risk factors for specific organisms, or sub-groups of organisms, and the number of cases was too small to allow it to do so for many of the target organisms studied. Studies targeted specifically at certain organisms or toxins are required to obtain meaningful information on risk factors for these. However, the present study is unique in defining the relative numerical importance of the different organisms and toxins sought.

Social factors were associated with a higher risk of all IID, SRSV and rotavirus. The influence of social factors on viral IID was mediated by living in purpose-built flats or rented accommodation. Contact with another ill person outside the home was associated with higher risk for all organisms for which it was investigated (rotavirus, SRSV, *Salmonella* and *Campylobacter*). Contact with an ill child in the household carried a risk for rotavirus and SRSV. These findings highlight the importance of person to person spread of viral IID in the community.

Travel abroad was associated with higher risk of all IID for adults and children, IID with no target organism in adults, and *C.jejuni* and enteroaggregative *E.coli*. The effect was restricted to trips outside northern Europe, except for babies. Swimming was associated with lower risk of all IID in adults and in children.

As anticipated, breastfeeding was highly protective against all IID in infants. How the bottle was disinfected was also associated with risk of all IID.

The study showed no association between domestic practices and hygiene and an increased risk of IID. This may be because our case definition included all infectious intestinal disease, not merely that acquired from food.

None of the 50 hygiene practices and 10 hygiene beliefs showed a consistent association with risk. This lack of association could be an artefact, since hygiene practices and knowledge are notoriously difficult to measure, and we asked about normal practice, not practice in the days before illness. If real, the lack of effect could mean that the current levels of contamination of foods entering the domestic kitchen are so low that individual susceptibility is a more important determinant of sporadic illness than kitchen hygiene. Another explanation could be that most transmission occurs outside home.

Another unexpected finding was that reported consumption of very few foods was found to be associated with increased risk. For example, reported consumption of chicken and eggs was not associated with IID due to *Salmonella enteritidis* PT4. This could be an artefact: the study was not designed to provide precise data on food eaten. The questionnaire sought information on foods eaten in the ten days before the onset of symptoms, which is longer than the usual incubation period for

most food poisoning pathogens. This reduces the power of the study to identify food vehicles. Responses may have been biased (although cases would be more likely to bias their answers so as to implicate foods they consider to be risks, such as chicken and eggs).

Alternatively, it might give a truer picture of the overall risk of those foods. Contaminated chicken may, for example, cause many outbreaks, but few of the sporadic cases which account for 95% of the total and in that sense present a small risk overall.

A plausible explanation of our not finding an association between IID and most food types could include intermittent low dose contamination of many food types exists to a degree that would be insufficient to endanger most people's health. If this were the case, we could postulate that most sporadic cases result from eating one of a wide variety of lightly contaminated foods, rather than one of a narrow range of heavily contaminated foods with individual variation in susceptibility, rather than the type of food consumed, determining who develops disease.

In contrast, we found that a group of six foods was associated with a very consistent and statistically significant lower risk of disease. The effect typically reduced the risk of IID by between 30% and 70%. These foods were pulses, salad, fruit, rice, fish and pasteurised dairy products.

This could be artefactual, due to confounding factors: people who report eating these foods may have a lower risk of IID for reasons we did not measure, or measured imprecisely. Although this is unlikely because we collected and analysed comprehensive information about a large range of social, educational, and behavioural practices .

Alternatively, it could be due to selection bias: people who agreed to be a control in the study may have been more likely than cases to eat those foods. This is also unlikely, as a preliminary analysis of the data from the nested case-control study suggests that the effect is also present in this study. The community controls had a much lower refusal rate, lessening the likelihood of selection bias. It is unlikely that reporting bias caused this effect, as there is no widespread belief that the foods protect against diarrhoea. Reverse causation is a possible source of artefact, if people change their eating habits after their illness and fail to remember or deliberately misreport their consumption before they fell ill. If none of these biases exist, then these foods may actually reduce the risk of IID. Causal mechanisms for such an effect could include food consumption changing the intestinal flora (by exposure to other micro-organisms, fibre) or boosting general or specific immunity. Specific immunity could be boosted by repeated exposure to low dose of microorganisms in food. General immunity could be boosted by ingestion of micronutrients, particularly antioxidants, in food. Fruit and fresh vegetables are rich in antioxidants.

Interpretation of risk factors from the GP case-control study should be cautious for a number of reasons. Cases were atypical in that they presented to GPs so risk factors for contracting IID may be different from the average case. The fact that they were atypical in one respect, their presentation to GPs, introduces the possibility of confounding, and selection bias. In other words, the risks identified may be risks associated with presentation to GPs rather than with IID itself, and risks of IID even if correctly identified may be different in cases who present to GPs when compared with all cases occuring in the community. In addition, as many associations were sought, some may be statistically associated with IID merely by chance.

In summary, we found many differences between cases and controls; however we

were generally unable to demonstrate an association between specific food vehicles, or domestic hygiene practices and IID, even for organisms which are predominantly transmitted in food. Factors favouring person-to-person transmission were important in the acquisition to IID due to viruses. We found the consumption of certain foods to be associated with a lower risk of IID.

10.4 COSTS OF IID

The cost questionnaire had a lower overall response rate, perhaps because it was a detailed questionnaire which coincided with the reminder for the main risk-factor questionnaire that had been sent three weeks before. However, the response rate from those who had responded to the risk factor questionnaire was high. Responders were representative, in terms of age and social class, of all cases in the study.

The overall national cost of predominantly community acquired IID was estimated at £745 million at 1994/95 prices. Of this total, 37% fell to the NHS, 8% to individuals and 56% were employment costs.

The costs of community cases who did not see a GP were low. This is because such cases generally had milder and shorter lived symptoms than those who saw a GP. The overall costs identified in our study appear to be lower than those estimated elsewhere. There are a number of possible reasons for this. Firstly, our study, unlike previous studies, was of a representative sample of all cases, including the mild cases not normally seen by the health services. Secondly, our study measured the costs of these milder cases to be less than many previous estimations. Thirdly, our study did not measure costs to the public health services from investigating IID apart from the costs of the laboratory tests. Fourthly, as our study did not include deaths, we have placed no value on the raised risk of mortality caused by illness. And fifthly, our study did not measure any of the costs due to outbreaks, which may involve more tests and more expensive tests and which will absorb more public health investigative resources.

NHS costs are mostly GP costs. They represent the opportunity costs of use of hard-pressed GP time but not directly representing financial outlay. Whilst average costs per case are useful for aggregating up to national figures, hospitals attempting to cost the impact of IID may be more interested in the cost of average cases presenting for treatment. The costs to in-patients are quite high and this study may have underestimated the hospitalisation rate for IID from general practice.

The largest item of cost is loss of time in paid employment. However, time off normal activities at home and leisure are not costed here.

The range of cost per case varied almost as much amongst cases with any particular organism as amongst cases infected by different organisms. The SRSV cases are the exception to this with short duration, fewer symptoms persisting at three weeks and lower costs.

People do appear to be willing to pay for safer food but this is an attitude study and it is not clear that this willingness would be translated into demand for safer goods at higher prices. The responsibility for food hygiene is placed firmly with National Government. Irradiated produce is viewed with suspicion by many although some might be convinced of its safety.

Suggestions for the future:

1. We suggest that consideration is given to raising public and professional

awareness of the importance of viral gastroenteritis.

2. We suggest that consideration should be given to formulating advice to GPs on which cases they should obtain stool specimens from for microbiological testing to aid surveillance.

3. We suggest consideration be given to setting up primary care sentinel surveillance schemes to monitor the aetiology of IID presenting to GPs and in the community in the longer term. The latter could entail repeated population based cohorts.

4. We suggest national laboratory reporting should continue to develop, with particular emphasis on obtaining more complete reporting by laboratories. The system would also benefit from the addition of denominator data, i.e., the reporting of negative as well as positive tests, and linkage to primary care sentinel surveillance of clinical IID, and to the statutory notification of food poisoning.

5. We suggest that consideration be given to a review of which organisms should be routinely sought in diagnostic microbiology laboratories for clinical and surveillance purposes, and that particular consideration be given to enteroaggregative and other enterovirulent *E.coli*, and viruses. Any review should address the issue of laboratory funding for tests whose main use lies in surveillance rather than in clinical management.

6. We suggest urgent consideration of a scheme to require the statutory notification of laboratory identification of certain organisms.

7 We suggest research to clarify the pathogenic role of some of the target organisms in the study, notably *Aeromonas* and *Yersinia*.

8. We suggest that resources earmarked for the prevention of IID be targeted particularly at areas with social disadvantage and crowding as this is where most IID occurs, and therefore effective prevention in these areas promises the greatest health gain.

9. We suggest that tour operators should ensure that travellers receive advice before travelling to high-risk areas. In addition, tour operators should be made aware of their obligation to monitor their providers closely to ensure that they maintain the best hygiene standards.

10. We suggest that the national and international surveillance of travel associated IID should be developed so that problem areas can promptly be identified and investigated.

11. We suggest that eating of pulses, salads, fruit and fish already recommended for the prevention of heart disease or cancers may also have a protective effect against IID.

12. We suggest that efforts continue to be made to educate foodhandlers in the commercial and domestic setting of the necessity of scrupulous food hygiene, especially in the preparation of poultry, and foods such as salads which do not require heat treatment.

13. We suggest that breast-feeding should continue to be promoted, and when it is not possible scrupulous care should be taken in the disinfection of bottles.

Appendix 1
Completeness, Representiveness of the Data, and Adjustment Factors

SUPPLEMENTARY DATA, TABLES AND FIGURES FOR CHAPTER 4

A1.1 PRACTICE CHARACTERISTICS

The participation of practices over time is shown in Figure A1.1. Seventy practices took part in the first cohort and 68 in the second; 36 of these took part in the enumeration component and 34 in the case-control component.

A1.1.1 GP practice characteristics compared to the rest of country

The country was divided into three geographical areas: North (including the former health regions Northern, Yorkshire, North Western, Mersey), Midlands and South West (comprising East Anglia, West Midlands, Trent, South Western, Wessex) and the South East (the Thames Regions). Practices were selected from these three areas to be representative of Jarman score, GP partnership size, and rural or urban area.

The number and proportions of the study population whose general practice was based in an urban (61.3%) or rural location is similar to that of England and Wales (62.4%) (Table A1.2). The population distribution according to ONS aggregate area is also shown in Table A1.2.

Table A1.3 shows the distribution of population by Jarman score tertiles for the three areas (North, Midlands/South West and South East) for the study practice population compared with that of England. There are some mismatches when the proportions between the study and national population are compared. In particular, the study practice population is under represented in the North and South East in practices with a low (least deprived) Jarman score. Population distributions by area and GP partnership size are shown for the country and for the study in Table A1.4.

A1.1.2 Practice list characteristics

The age and sex distribution of all persons registered with the 70 practices when compared to the population of England registered with general practices is shown in Table A1.5. The practice population of the study is very similar to the population of England by age and sex.

Table A1.5 also shows that there is little difference in the age and sex distribution of the registered population of England when compared to the ONS population estimate for 1994. The difference between the totals of the population of England as determined by ONS (48,707,500) and that registered with general practices (50,471,199) was 3.6% (1,763,699). There is a time delay for changes to be made in GP registration after persons have either moved to a new area or have died. In view of this it is necessary to make a correction for practice list inflation in the present study (Section 4.2.5).

Figure A1.1 GP practices involved in the study: participation over time

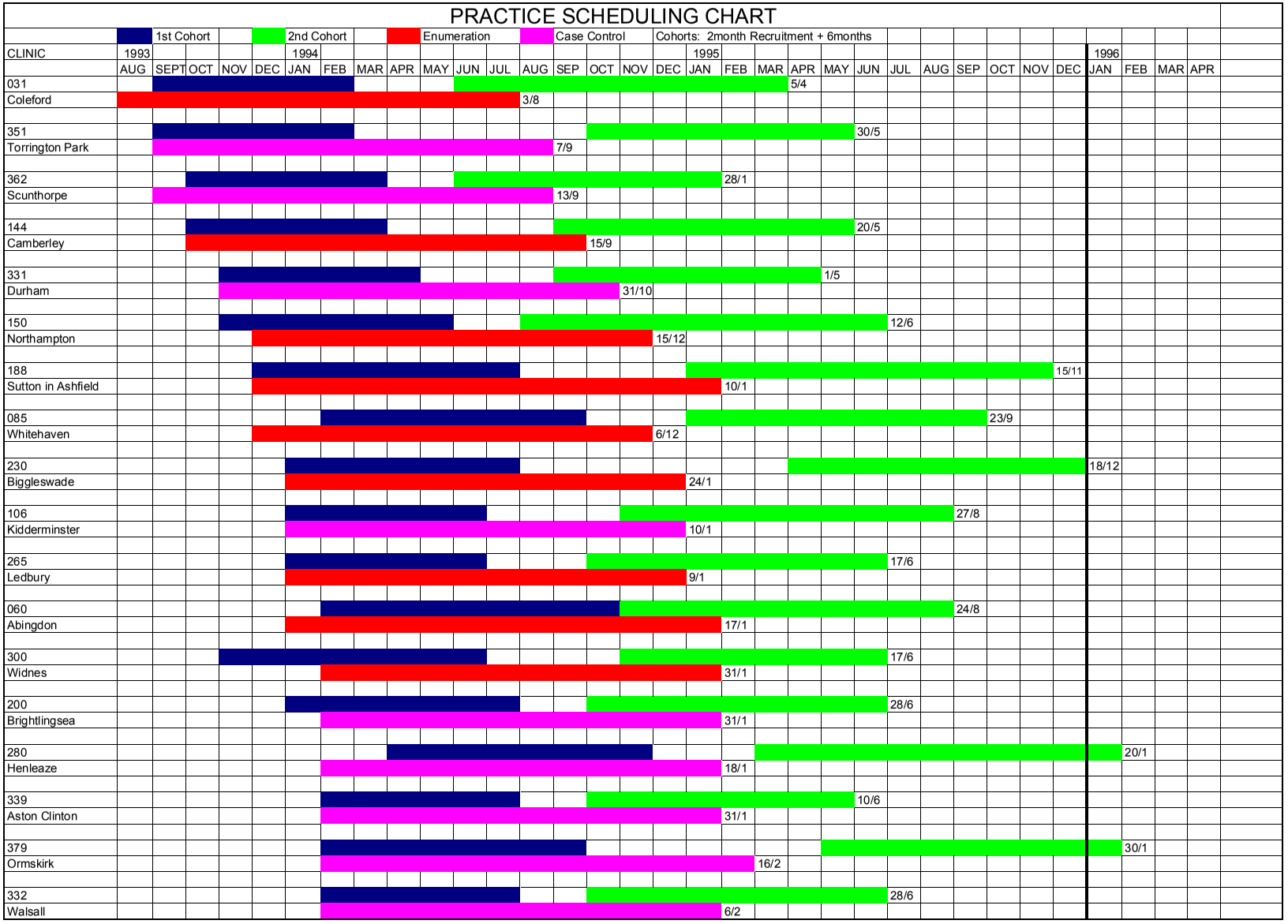


Figure A1.1 (cont.)

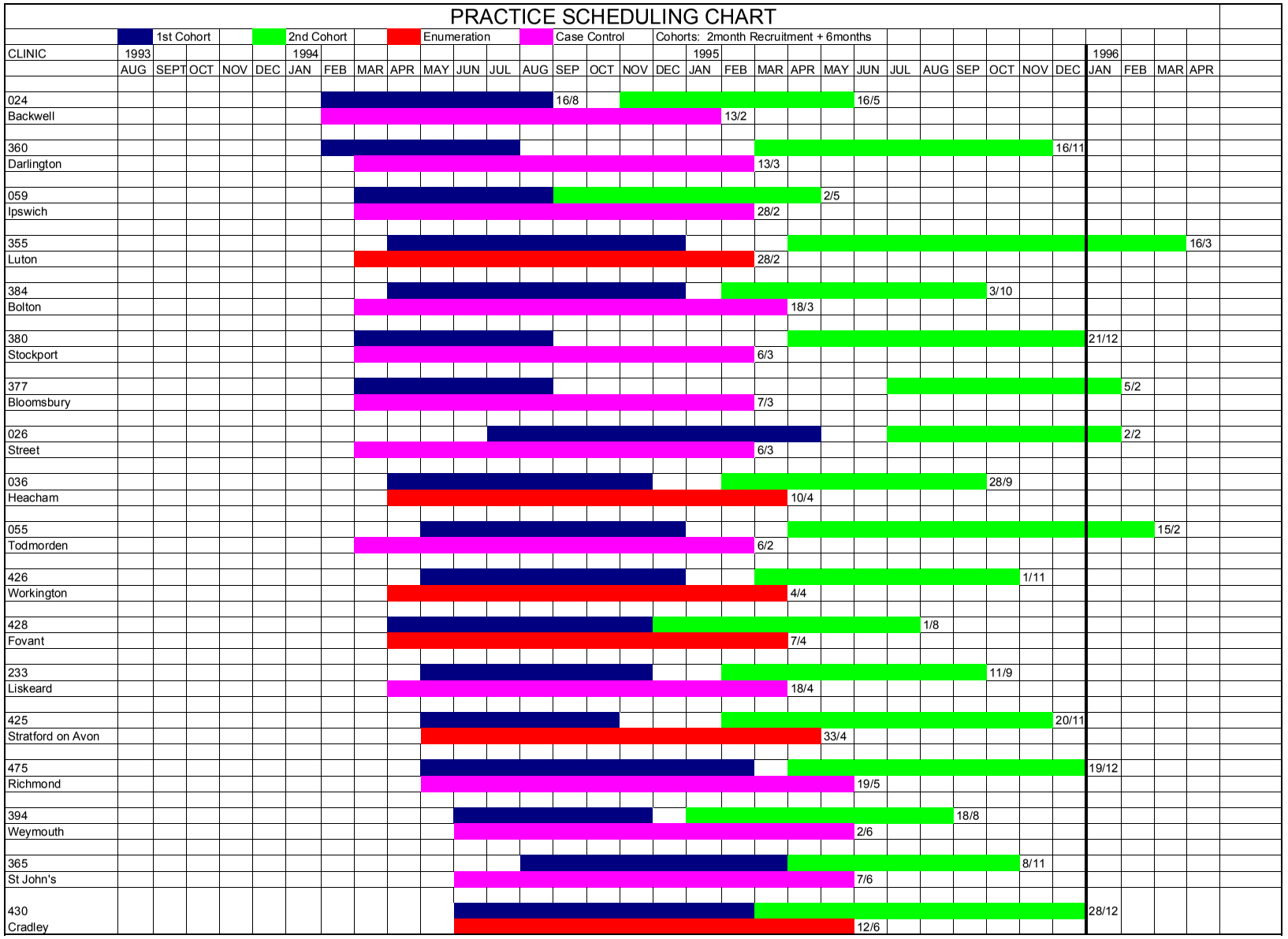


Figure A1.1 (cont.)

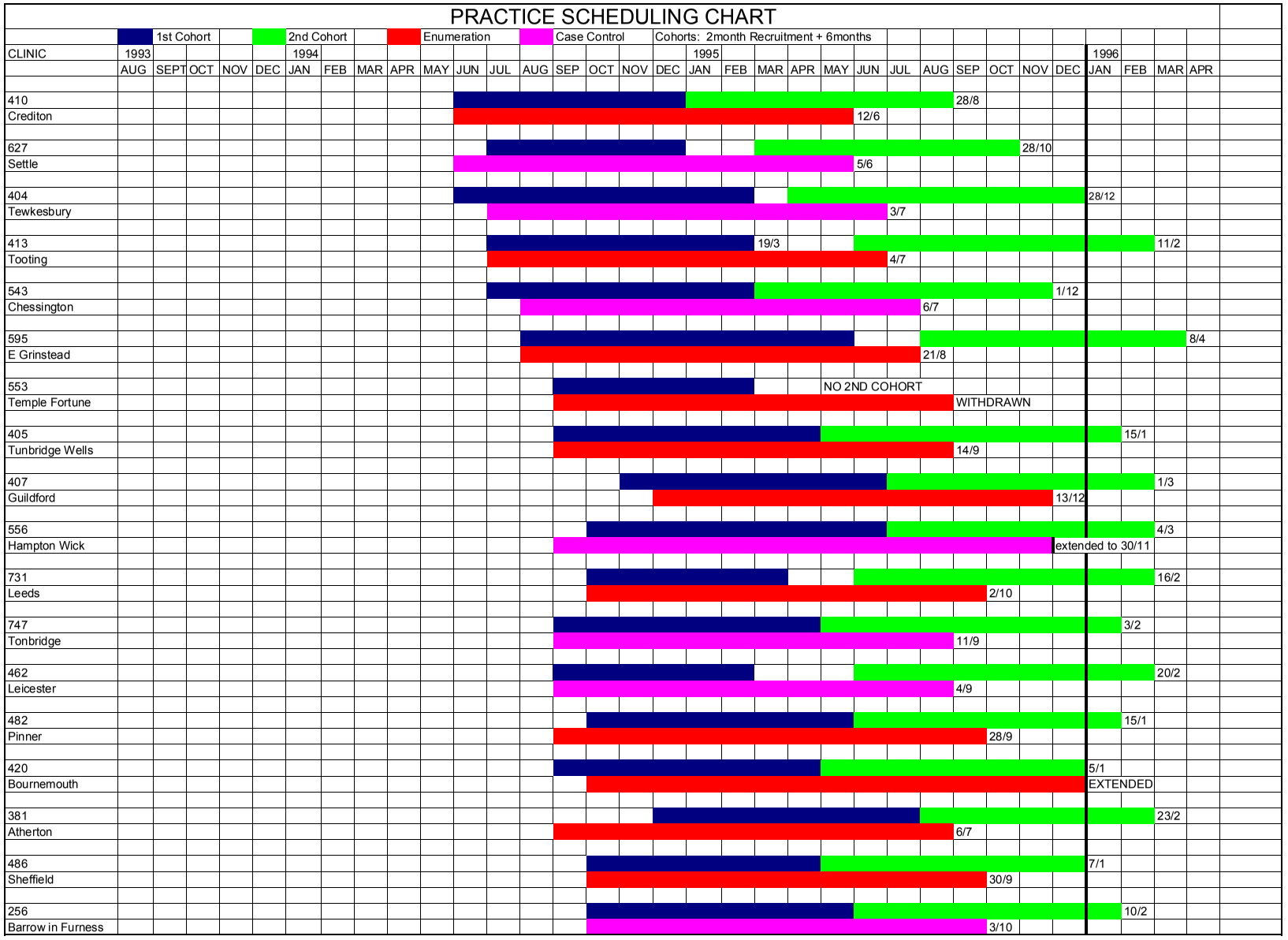


Figure A1.1 (cont.)

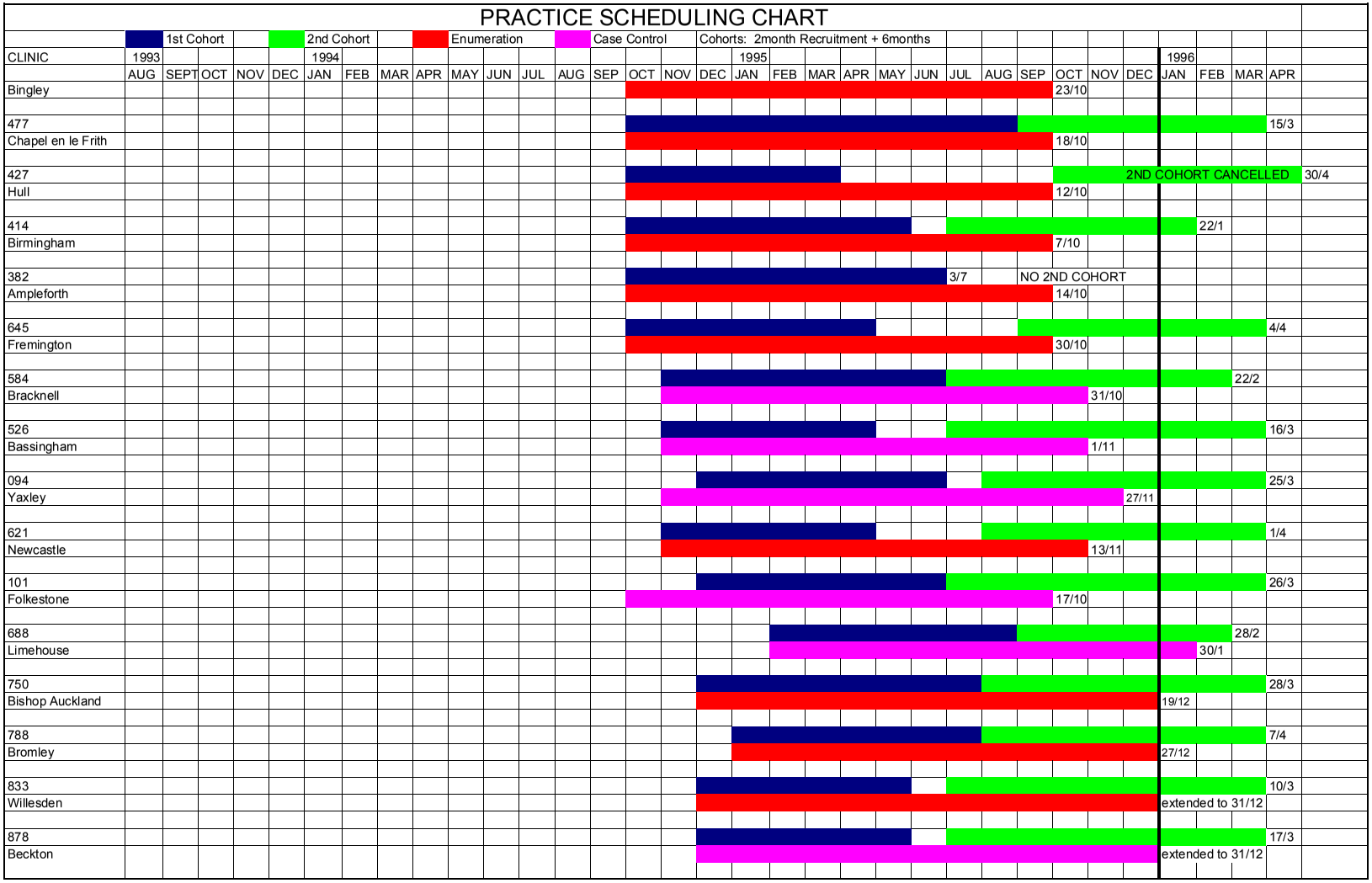


Table A1.1 Population distribution by partnership size for IID study population and population of England (Oct 94)

	POPULATION			
	STUDY		COUNTRY	
GP PARTNER SIZE	NO	%	NO	%
1–2	65,972	13.31	12,936,000	24.35
3–4	147,938	29.85	17,836,000	33.57
5–6	193,986	39.14	15,066,000	28.36
7–>9	87,770	17.71	7,284,000	13.71
Total	495,666		53,122,000*	

* calculated making the assumption that standard list size per GP is 2,000

Table A1.2 Population distribution by ONS area aggregates and urban or rural location for IID study population and population of England and Wales (1993)

	POPULATION			
	STUDY		COUNTRY	
AREA AGGREGATE	NO	%	NO	%
Urban				
Inner London	20,930	4.22	2,647,400	5.15
Outer London	33,682	6.79	4,285,600	8.33
Metropolitan	34,562	6.97	11,199,200	21.77
City	67,471	13.61	4,710,400	9.16
Industrial	115,234	23.25	6,882,400	13.38
New Town	31,918	6.44	2,391,200	4.65
Urban Total	303,797	61.29	32,116,200	62.44
Rural				
Resort/Retirement	24,242	4.89	3,662,000	7.12
Mixed Urban/Rural	104,808	21.14	10,068,800	19.57
Remote Rural	62,819	12.67	5,592,200	10.87
Rural Total	191,869	38.71	19,323,000	37.56
Overall Total	495,666		51,439,200	

Table A1.3 Distribution of population by Jarman score (low, mid or high) for three areas (N, M/SW, SE) for IID study population and population of England (1991)

	STUDY POPULATION						POPULATION OF ENGLAND					
	<-5 LOW		>-5 TO <10 MID		>10 HIGH		<-5 LOW		>-5 TO <10 MID		>10 HIGH	
AREA	POP.	%	POP.	%	POP.	%	POP.	%	POP.	%	POP.	%
North	16,785	13.10	43,284	33.78	68,051	53.12	3,496,475	27.16	3,785,499	29.4	5,592,990	43.44
Midlands/ South West	77,908	35.61	86,607	39.58	54,273	24.81	7,275,565	35.65	6,992,156	34.26	6,141,821	30.09
South East	15,479	10.41	71,922	48.35	61,357	41.25	3,464,176	25.16	4,087,922	29.69	6,218,600	45.16
Total	110,172		201,813		183,681		14,236,216		14,865,577		17,953,411	

Table A1.4 Distribution of IID study population and population of England by partnership size for each of 3 Areas (N, M/SW, SE)

	PARTNERSHIP SIZE IN STUDY									
AREA	1–2 PARTNERS		3–4 PARTNERS		5–6 PARTNERS		7–9 PARTNERS		TOTAL	
	POP.	%	POP.	%	POP.	%	POP.	%	POP.	%
North	16,894	13.19	12,321	9.62	85,087	66.41	13,818	10.79	128,120	25.89
Midlands/ South West	28,510	13.03	61,876	28.28	54,450	24.89	73.952	33.8	218,788	44.14
South East	20,568	13.83	73,741	49.57	54,449	36.60	-		148,758	30.01
Total	65,972		147,938		193,986		87,770		495,666	

	PARTNERSHIP SIZE IN ENGLAND									
AREA	1–2 PARTNERS		3–4 PARTNERS		5–6 PARTNERS		7–9 PARTNERS		TOTAL	
	POP. (thousands)	%	POP. (thousands)	%	POP. (thousands)	%	POP. (thousands)	%	POP. (thousands)	%
North	3,560	24.94	5,202	36.44	3,370	26.13	1,780	12.47	14,272	26.87
Midlands/ South West	4,584	19.08	7,892	32.85	7,678	31.96	3,870	16.11	24,024	45.22
South East	4,792	32.32	4,742	31.98	3,658	24.67	1,634	11.02	14,826	27.91
Total	12,936		17,836		14,706		7,284		53,122	

Table A1.5 Distribution by age and sex of study practice population, ONS census population of England (1994 estimate) and population of England registered with general practices (October 1994)

AGE	STUDY PRACTICE POPULATION				ONS POPULATION OF ENGLAND				GP REGISTERED POPULATION OF ENGLAND			
	MALE		FEMALE		MALE		FEMALE		MALE		FEMALE	
	NUMBER	%	NUMBER	%	NUMBER	%	NUMBER	%	NUMBER	%	NUMBER	%
0-4	14,805	6.30	14,072	5.79	1,658,000	6.94	1,577,200	6.35	1,616,466	6.47	1,538,075	6.03
5-15	33,509	14.26	31,880	13.12	3,479,200	14.57	3,820,900	15.39	3,514,102	14.08	3,347,341	13.12
16-44	99,124	42.17	96,824	39.84	10,200,600	42.71	9,873,200	39.77	10,767,291	43.13	10,368,876	40.65
45-64	55,910	23.78	54,270	22.33	5,425,400	22.72	5,496,600	22.14	5,799,853	23.23	5,593,330	21.93
65-74	19,677	8.37	23,179	9.54	1,977,200	8.28	2,377,600	9.58	2,058,935	8.25	2,418,895	9.48
75+	12,044	5.12	22,828	9.39	1,141,600	4.78	2,203,500	8.88	1,208,678	4.84	2,239,357	8.78
Totals:	235,069		243,056		23,882,100		24,825,400		24,965,325		25,505,874	

A1.2 COHORT CHARACTERISTICS

Table A1.6 Enrolment into the population cohort by age and sex

AGE	FEMALES			MALES		
	NUMBER ENROLLED	NUMBER INVITED	%	NUMBER ENROLLED	NUMBER INVITED	%
<1	60	118	50.9	59	143	41.3
1-4	279	590	47.3	268	606	44.2
5-9	390	779	50.1	388	822	47.2
10-14	310	694	44.7	319	729	43.8
15-24	416	1,592	26.1	319	1,742	18.3
25-34	742	2,092	35.5	492	2,130	23.1
35-44	715	1,563	45.8	528	1,764	29.9
45-54	748	1,542	48.5	639	1,631	39.2
55-64	600	1,212	49.5	538	1,204	44.7
65-74	503	1,182	42.6	479	1,013	47.3
75+	290	1,431	20.3	221	665	33.3
Totals	5,053	12,795	39.5	4,250	12,449	34.1

Note: 999 people had missing sex information

Figure A1.2 Enrolment in the population cohort by age and sex

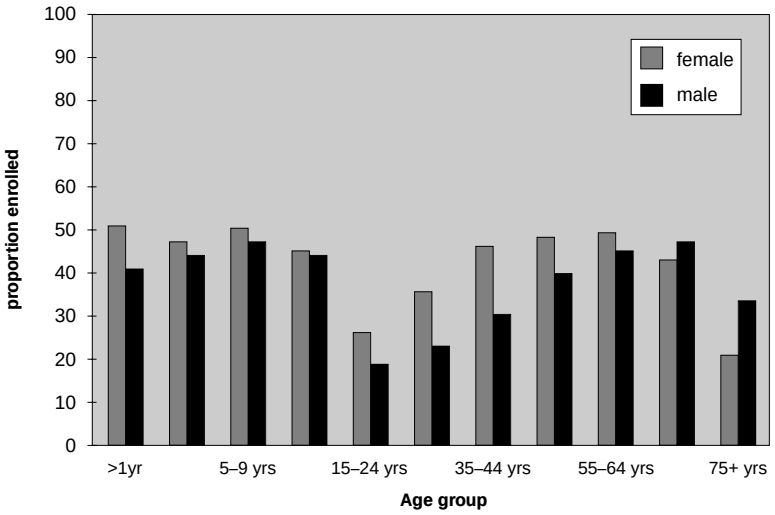


Table A1.7 Enrolment into the population cohort by practice characteristics

	CATEGORY	NUMBER ENROLLED	NUMBER INVITED	%	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	5,360	16,287	32.9	
	Rural	4,416	10,787	40.9	(χ^2 = 181.3, P<0.001)
Geographical Region	North	2,831	7,210	39.3	
	South West / Midlands	4,456	11,368	39.2	
	South East	2,489	8,496	29.3	(χ^2 = 249.1 P <0.001)
Jarman Score	Low	2,279	5,814	39.2	
	Mid	4,513	11,083	40.7	
	High	2,984	10,177	29.3	(χ^2 = 329.5, P <0.001)

A1.2.1 Characteristics of refusers

Table A1.8 Reasons for refusal for cohorts 1 and 2

REASON FOR REFUSAL	N	%
Refused, reason not specified	2,850	42.6
Too busy to participate	1,046	15.7
Initially agreed but changed mind and withdrew	130	2.0
Frequently absent for work or other reasons	749	11.2
Patient has current illness	239	3.6
Patient has gastro-intestinal illness	306	4.6
Waiting to go in, in hospital or just out of hospital	86	1.3
Patient is pregnant or has new baby	48	0.7
Patient experienced recent crisis or is suffering from anxiety	86	1.3
Child/student busy studying	36	0.5
Patient caring for relative or friend	50	0.7
Patient objects to study or being asked to take samples	73	1.1
Problems with travel to surgery, P.O. etc	21	0.3
Patient or other family member involved in a trial	72	1.1
Parental refusal on behalf of child	42	0.6
Considered unreliable or unable to cope	137	2.0
Illiterate or has language problems	47	0.7
Physical or mental disability	158	2.4
In residential home or too old	310	4.6
Patient suffering from chronic illness e.g. cancer, senile dementia, alcoholism	200	3.0
	6,686	100

Table A1.9 Social class comparison between cohort participants and refusers

	REFUSERS		PARTICIPANTS	
SOCIAL CLASS	NUMBER	PERCENTAGE (EXCL. MISSING)	NUMBER	PERCENTAGE (EXCL. MISSING)
I	105	3.3	540	5.9
II	613	19.0	2,826	30.7
III(NM)	473	14.7	1,806	19.6
III(M)	577	17.9	1,746	19.0
IV	475	14.7	1,088	11.8
V	156	4.9	308	3.3
forces	10	0.3	43	0.5
economically inactive	815	25.3	857	9.3
missing	909	-	237	-
total	4,133		9,451	

A1.2.2 Ineligibility

Table A1.10 Reasons for ineligibility for cohorts 1 and 2

REASON FOR INELIGIBILITY	N	%
Ulcerative colitis or Crohn's disease	53	2.4
Deceased	157	7.2
Not possible to contact (moved away/left practice/wrong address)	1,799	82.7
Currently away, so unable to contact (prison, Armed Forces, hospital, University)	168	7.7
	2,177	100

Table A1.11 Ineligibility in the population cohort by age and sex

	FEMALES			MALES		
AGE	NUMBER INELIGIBLE	NUMBER INVITED (ELIGIBILITY KNOWN)	%	NUMBER INELIGIBLE	NUMBER INVITED (ELIGIBILITY KNOWN)	%
<1	4	81	4.9	9	98	9.2
1–4	38	423	9.0	47	410	11.5
5–9	43	548	7.9	43	567	7.6
10–14	41	484	8.5	49	514	9.5
15–24	238	990	24.0	229	1,013	22.6
25–34	227	1,356	16.7	253	1,198	21.1
35–44	105	1,114	9.4	141	1,095	12.9
45–54	80	1,171	6.8	103	1,123	9.2
55–64	47	961	4.9	76	906	8.4
65–74	39	968	4.0	42	810	5.2
75+	103	1,137	9.1	58	532	10.9
Total	965	9,233	10.5	1,050	8,266	12.7

Note: 568 people had missing sex information

Figure A1.3 Ineligibility in the population cohort by age and sex

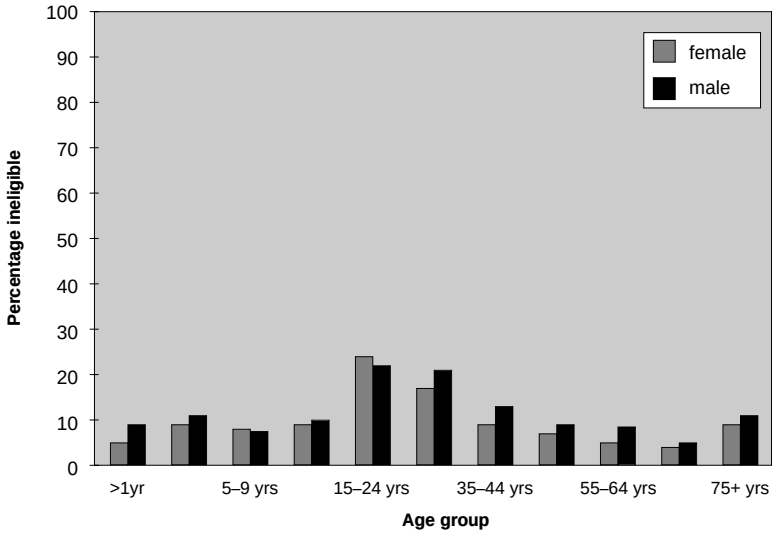


Table A1.12 Ineligibility in the population cohort by practice characteristics

	CATEGORY	NUMBER ENROLLED	NUMBER INVITED	%	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	1,368	10,726	12.85	
	Rural	809	7,913	10.2	(χ^2 = 28.3, P<0.001)
Geographical Region	North	450	5,246	8.6	
	South West / Midlands	873	8,207	10.6	
	South East	854	5,186	16.5	(χ^2 = 172.8, P <0.001)
Jarman Score	Low	435	4,208	10.3	
	Mid	963	8,107	11.9	
	High	779	6,324	12.3	(χ^2 = 10.2, P <0.006)

A1.2.3 Estimate of people who were ineligible

It was possible to calculate the proportion of the whole sample who were ineligible. The following equatiion was used:

Total predicted number ineligible in each practice = number ineligible (reason known) + Predicted proportion ineligible among 'no contact' notesearch (n%) x number of 'no contacts + overall proportion ineligible in 'not recorded' notesearch (10%) x number of 'not recordeds' where n is predicted proportion of ineligibles using the logistic model.

The overall number predicted as ineligible was 3,252 (11.8% of those invited), as derived from:

2177 + (430/3007 x 3877) + (122.1238 x 5168).

Table A1.13 Notesearch of people whose eligibility to join the cohort was unknown

	NURSE COULDN'T CONTACT NUMBER	%	NURSE RECORDS INCOMPLETE NUMBER	%
Proportion with notesearch	3,007/3,844	78	1,238/4,591	27
Notesearch results				
Ineligible:	430	14	122	10
Died	14	0.5	5	0.4
Notes to FHSA	149	5	51	4
Left practice	267	9	66	5
Presumed eligible:	2,577	86	1,116	90
Presented in last 3 months	784	26	314	25
Registered but had not presented in the last 3 months	1,677	56	745	60
Other	116	4	57	5
Total	3,007		1,238	

Table A1.14 Predicted proportion ineligible by practice characteristics among people who the nurse couldn't contact

	JARMAN SCORE		
LOCATION	LOW	MEDIUM	HIGH
Urban: North, Midlands /South West	6.6	12.7	9.0
Urban: South East	12.6	22.9	16.8
Rural	13.5	24.3	18.0

A1.2.4 Completeness of follow-up

Table A1.15 Completeness of follow-up in the population cohort component

WEEKS OF FOLLOW-UP	NUMBER	CUMULATIVE %
26	5,692	61.2
25	1,059	72.6
24	582	78.9
23	320	82.3
22	202	84.5
21	163	86.3
20	119	87.5
19	105	88.7
18	68	89.4
17	74	90.2
16	78	91.0
15	70	91.8
14	64	92.5
13	59	93.1
12	64	93.8
11	48	94.3
10	51	94.9
9	58	95.5
8	58	96.1
7	46	96.6
6	65	97.3
5	53	97.9
4	52	98.4
3	42	98.9
2	48	99.4
1	56	100.0
Total	**9,296**	

Figure A1.4 Completeness of follow-up in the population cohort component

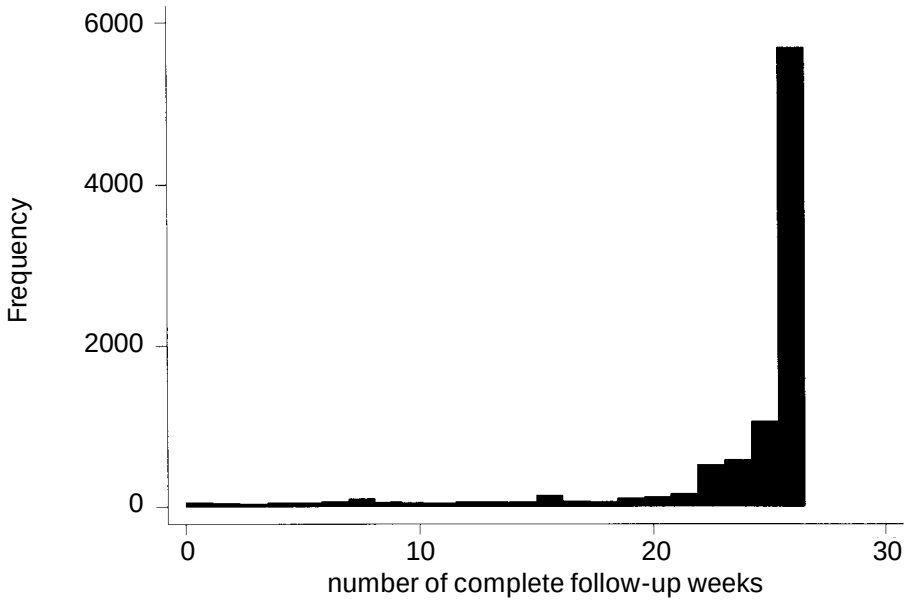


Table A1.16 Incomplete follow-up by age and sex in the cohort component

	FEMALES			MALES		
AGE	FOLLOW-UP <23 WEEKS	TOTAL	%	FOLLOW-UP <23 WEEKS	TOTAL	%
<1	9	56	16.10	10	51	19.61
1–4	57	260	21.92	58	255	22.75
5–9	82	371	22.10	72	371	19.41
10–14	62	297	20.90	52	298	17.45
15–24	118	397	29.72	89	295	30.20
25–34	165	688	24.00	99	464	21.34
35–44	103	665	15.50	74	499	14.83
45–54	95	707	13.44	77	614	12.54
55–64	69	582	11.90	66	521	12.70
65–74	49	479	10.23	54	461	11.71
75+	37	282	13.12	26	211	12.32
Total	**846**	**4,784**	**17.70**	**677**	**4,040**	**16.80**

Note: 247 people had missing sex information

Table A1.17 Baseline questionnaire: compliance in the population cohort component by age and sex

	FEMALES			MALES		
AGE	NUMBER POPULATION	TOTAL	%	NUMBER POPULATION	TOTAL	%
<1	60	60	100.0	56	59	94.9
1–4	257	279	92.1	247	268	92.2
5–9	362	390	92.8	365	388	94.1
10–14	285	310	91.9	293	319	91.8
15–24	379	416	91.1	282	319	88.4
25–34	707	742	95.3	458	492	93.1
35–44	687	715	96.1	497	528	94.1
45–54	717	748	95.9	614	639	96.1
55–64	576	600	96.0	521	538	96.8
65–74	493	503	98.0	459	479	95.8
75+	277	290	95.5	214	221	96.8
Total	**4,800**	**5,053**	**95.0**	**4,006**	**4,250**	**94.3**

Note: 248 people had missing sex information

Table A1.18 Baseline questionnaire: compliance in the population cohort component by practice characteristics

	CATEGORY	NUMBER POPULATION	TOTAL	%	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	5053	5360	94.3	
	Rural	4186	4416	94.8	(χ^2 = 1.26, P=0.262)
Geographical Region	North	2706	2831	95.6	
	South West / Midlands	4240	4456	95.1	
	South East	2293	2489	92.1	(χ^2 = 37.11 P <0.001)
Jarman Score	Low	2194	2279	96.3	
	Mid	4236	4513	93.9	
	High	2809	2984	94.1	(χ^2 = 18.06, P <0.001)

A1.2.5 Representativeness of the cohort

Table A1.19 Distribution of ethnic groups in the cohort study population and the population of England (1991 census)

POPULATION	COHORT STUDY		ENGLAND	
	NUMBER	%	NUMBER	%
White	8,980	94.99	44,911,778	93.8
Black Carribean	54	0.57	495,682	1.05
Black African	28	0.30	206,918	0.44
Black Other	47	0.5	172,282	0.37
Indian	65	0.69	823,821	1.8
Pakistani	94	0.99	449,646	0.96
Bangladeshi	14	0.15	157,881	0.34
Chinese	14	0.15	141,661	0.30
Other Asian	9	0.10	189,253	0.40
Other	23	0.24	273,721	0.58
Missing	126	1.33	0	0
Total	9,454		47,055,204	

Table A1.20 Distribution of population by marital status and gender for persons over 16 years of age in the cohort study compared to the population of England (mid 1994 estimate)

AGE	COHORT STUDY POPULATION				POPULATION OF ENGLAND OVER 16			
	MALE		FEMALE		MALE		FEMALE	
	PERSONS	%	PERSONS	%	PERSONS	%	PERSONS	%
Married	2,433	75.05	2,797	69.04	10,915,249	60.71	11,015,216	56.09
Single	512	15.79	592	14.61	5,397,788	30.02	4,548,709	23.16
Divorced	145	4.47	250	6.17	991,039	5.51	1,339,650	6.82
Widowed	127	3.92	385	9.50	675,797	3.76	2,735,449	13.93
Missing	25	0.77	27	0.67				
Totals	3,242		4,051		17,979,873	100	19,639,024	100

** There was information on sex missing in 40 persons*

Table A1.21 Employment status of persons over 16 years of age in the cohort study population and in the population of England (1991 census)

	COHORT POPULATION		ENGLAND 10% SAMPLE	
	NUMBER	%	NUMBER	%
Economically active	**4,272**	**58.25**	**2,265,781**	**61.30**
Working full time	3,012	41.07	1,747,814	47.29
Working part time	1,021	13.92	446,267	12.07
Unemployed	235	3.21	208,560	5.64
On government scheme	4	0.05	28,116	0.76
Economically inactive	**2,923**	**39.86**	**1,430,558**	**38.7**
Student	252	3.44	141,359	3.82
Permanently sick	219	2.99	137,906	3.73
Retired	1,688	23.02	707,110	19.13
Other inactive/ Not seeking work	764	10.42	444,183	12.02
Missing	139	1.90		
Total	**7,334**		**3,696,339**	

Table A1.22 Distribution of tenure of accommodation of cohort study population and population of England

	COHORT STUDY POPULATION		POPULATION OF ENGLAND	
TENURE CATEGORY	PERSONS	%	PERSONS	%
Owner/occupier	7,584	80.25	32,923,405	71.05
Rented council	1,174	12.42	9,707,276	20.95
Rented private	468	4.95	2,739,584	5.91
Tied to job	108	1.14	967,103	2.09
Other	29	0.03		
Missing	88	0.93		
	9,451		46,337,368	

A1.2.6 Nested case-control component

Figure A1.5 Schematic representations of nested case-control component

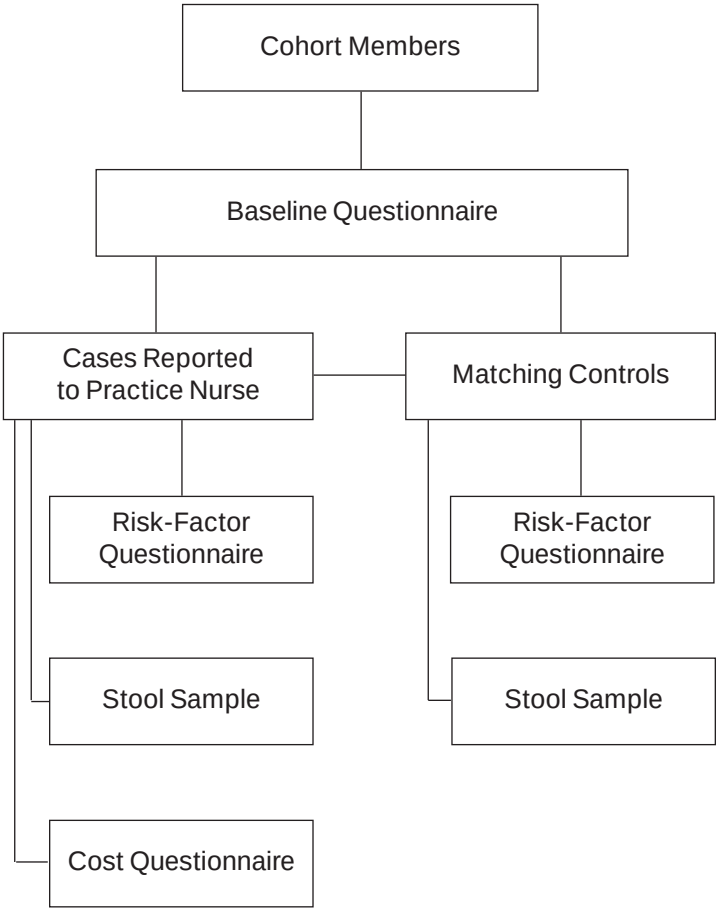


Table A1.23 Case control matching in the nested case-control component by age and sex

	FEMALES			MALES		
	NUMBER OF MATCHED CONTROLS	NUMBER OF CASES	% MATCHED	NUMBER OF MATCHED CONTROLS	NUMBER OF CASES	% MATCHED
<1	15	20	75.0	9	10	90.0
1–4	71	83	86.0	68	81	84.0
5–9	34	43	79.1	45	56	80.4
10–14	10	15	66.7	19	26	73.1
15–24	12	16	75.0	13	16	81.3
25–34	55	67	82.1	27	38	71.1
35–44	56	68	82.4	29	39	74.4
45–54	37	52	71.2	27	34	79.4
55–64	25	30	83.3	31	41	75.6
65–74	15	20	75.0	20	25	80.0
75+	10	17	59.0	12	15	80.0
Totals	340	431	78.9	300	381	78.7

Note: 5 cases had missing age/sex information

Figure A1.6 Case-control matching in the nested case-control component by age and sex

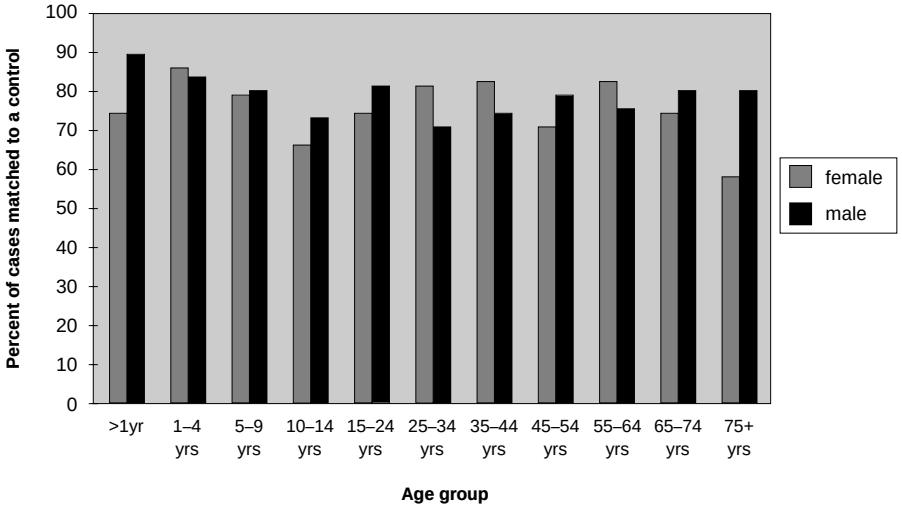


Table A1.24 Case-control matching in the nested case-control component by practice characteristics

	CATEGORY	NUMBER OF MATCHED CONTROLS	NUMBER OF CASES	% MATCHED	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	305	393	77.6	
	Rural	335	424	79.0	(χ^2 = 0.24, P = 0.63)
Geographical Region	North	135	182	74.2	
	South West/ Midlands	330	401	82.3	
	South East	175	234	74.8	(χ^2 = 7.3, P = 0.03)
Jarman Score	Low	166	197	84.3	
	Mid	307	408	75.3	
	High	167	212	78.8	(χ^2 = 6.4, P = 0.041)

A1.2.7 Compliance in the nested case-control study

Table A1.25 Risk factor questionnaire compliance among cases in the nested case-control component by age and sex

	FEMALES			MALES		
AGE	QUESTIONNAIRE RETURNED	NUMBER OF CASES	% COMPLIANCE	QUESTIONNAIRE RETURNED	NUMBER OF CASES	% COMPLIANCE
<1	15	20	75.0	7	10	70.0
1–4	72	83	86.8	67	81	82.7
5–9	36	43	83.7	47	56	83.9
10–14	11	15	73.3	20	26	76.9
15–24	11	16	68.8	10	16	62.5
25–34	50	67	74.6	28	38	73.7
35–44	58	68	85.3	28	39	71.8
45–54	45	52	86.5	26	34	75.6
55–64	26	30	86.7	31	41	76.0
65–74	12	20	60.0	22	25	88.0
75+	13	17	76.5	13	15	86.7
Total	349	431	81.0	299	381	78.5

Note: 5 cases had missing age/sex information

Figure A1.7 Risk factor questionnaire compliance among cases in the nested case-control component by age and sex

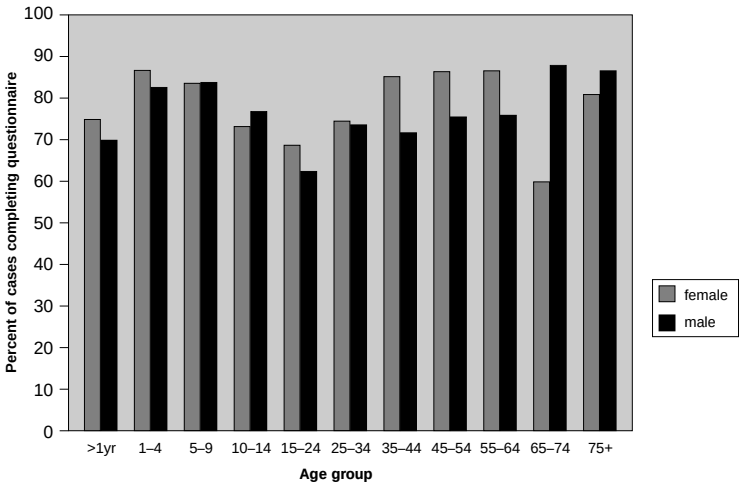


Table A1.26 Risk factor questionnaire compliance among cases in the nested case-control component by practice characteristics

	CATEGORY	QUESTIONNAIRE RETURNED	NUMBER OF CASES	% COMPLIANCE	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	300	393	76.3	
	Rural	348	424	82.1	(χ^2 = 4.10, P = 0.043)
Geographical Region	North	144	182	79.1	
	South West/ Midlands	331	401	82.5	
	South East	173	234	73.9	(χ^2 = 6.70, P = 0.04)
Jarman Score	Low	170	197	86.3	
	Mid	323	408	79.2	
	High	155	212	73.1	(χ^2 = 10.8, P = 0.004)

Table A1.27 Compliance in sending a stool sample among cases in the nested case-control component by age and sex

	FEMALES			MALES		
AGE	STOOL SENT	NUMBER OF CASES	% COMPLIANCE	STOOL SENT	NUMBER OF CASES	% COMPLIANCE
<1	20	20	100.0	10	10	100.0
1–4	73	83	88.0	73	81	90.1
5–9	37	43	86.1	50	56	89.3
10–14	9	15	60.0	22	26	84.6
15–24	12	16	75.0	14	16	87.5
25–34	60	67	89.6	34	38	89.5
35–44	59	68	86.8	36	39	92.3
45–54	49	52	94.2	33	34	97.1
55–64	27	30	90.0	37	41	90.2
65–74	18	20	90.0	21	25	84.0
75+	14	17	82.4	13	15	86.7
Totals	378	431	87.7	343	381	90.0

Note: 5 cases had missing age/sex information, 40 stools had missing linkage information

Figure A1.8 Stool sample compliance among cases in the nested case-control component by age and sex

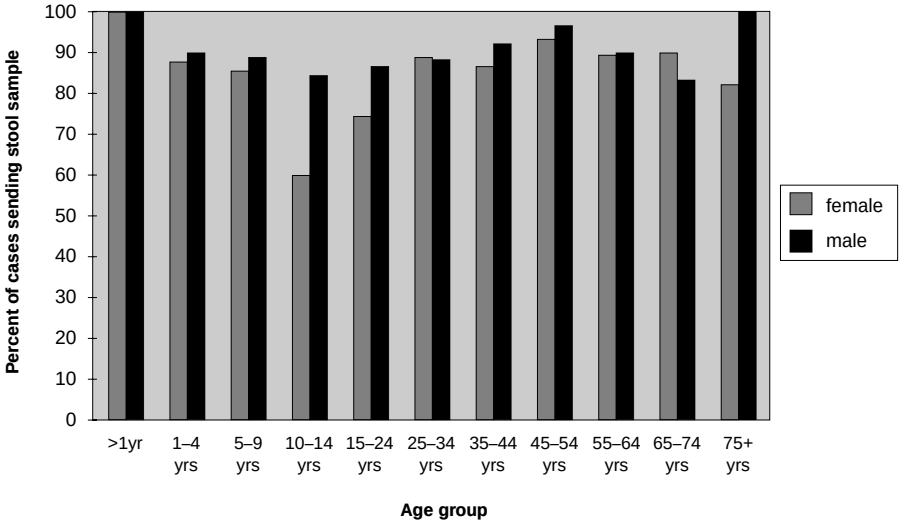


Table A1.28 Compliance in sending a stool sample among cases in the nested case-control component by practice characteristics

	CATEGORY	STOOL SENT	NUMBER OF CASES	% COMPLIANCE	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	338	393	86.0	
	Rural	383	424	90.3	(χ^2 = 3.7, P = 0.055)
Geographical Region	North	166	182	91.2	
	South West / Midlands	363	401	90.5	
	South East	192	234	82.1	(χ^2 = 12.2, P = 0.002)
Jarman Score	Low	181	197	91.9	
	Mid	353	408	86.5	
	High	187	212	88.2	(χ^2 = 3.7, P = 0.16)

Table A1.29 Risk factor questionnaire compliance among controls in the nested case-control component by age and sex

	FEMALES			MALES		
AGE	QUESTIONNAIRE RETURNED	NUMBER OF CONTROLS	% COMPLIANCE	QUESTIONNAIRE RETURNED	NUMBER OF CONTROLS	% COMPLIANCE
<1	9	10	90.0	9	9	100.0
1–4	71	84	84.5	54	60	90.0
5–9	32	34	94.1	35	41	85.4
10–14	9	10	90.0	19	22	86.4
15–24	14	17	82.4	9	10	90.0
25–34	51	53	96.2	28	31	90.3
35–44	55	58	94.8	27	31	87.1
45–54	38	39	97.4	28	32	87.5
55–64	21	21	100.0	32	32	100.0
65–74	20	20	100.0	28	28	100.0
75+	10	10	100.0	3	5	60.0
Total	330	356	92.7	272	301	90.4

Note: 18 controls had missing age/sex information, 14 stools had missing linkage information

Figure A1.9 Risk factor questionnaire compliance among controls in the nested case-control component by age and sex

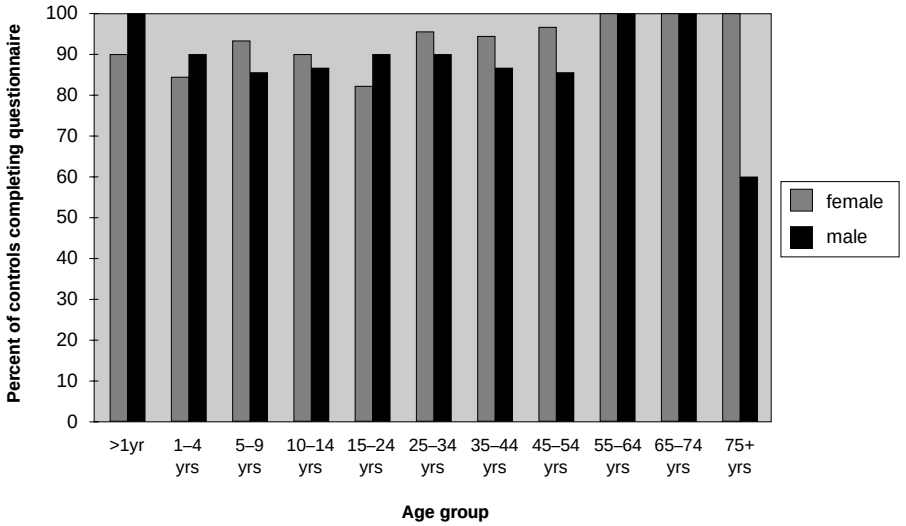


Table A1.30 Risk factor questionnaire compliance among controls in the nested case-control component by practice characteristics

	CATEGORY	NUMBER OF CONTROLS	NUMBER OF CASES	% MATCHED	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	283	322	87.9	
	Rural	330	353	93.5	(χ^2 = 6.32, P = 0.012)
Geographical Region	North	128	145	88.3	
	South West / Midlands	323	343	94.2	
	South East	162	187	86.6	(χ^2 = 9.7, P = 0.008)
Jarman Score	Low	162	171	94.7	
	Mid	297	334	88.9	
	High	154	170	90.6	(χ^2 = 4.6, P = 0.10)

Table A1.31 Compliance in sending a stool sample among controls in the nested case-control component by age and sex

	FEMALES			MALES		
AGE	STOOL SENT	NUMBER OF CONTROLS	% COMPLIANCE	STOOL SENT	NUMBER OF CONTROLS	% COMPLIANCE
<1	9	10	90.0	9	9	100.0
1–4	67	84	79.8	49	60	81.7
5–9	27	34	79.4	30	41	73.2
10–14	6	10	60.0	18	22	81.8
15–24	12	17	70.6	8	10	80.0
25–34	46	53	86.8	26	31	83.9
35–44	47	58	81.0	22	31	71.0
45–54	34	39	87.2	29	32	90.6
55–64	19	21	90.5	27	32	84.4
65–74	19	20	95.0	25	28	89.3
75+	9	10	90.0	3	5	60.0
Totals	295	356	82.9	246	301	81.7

Note: 18 controls had missing age/sex information

Figure A1.10 Stool sample compliance among controls in the nested case-control component by age and sex

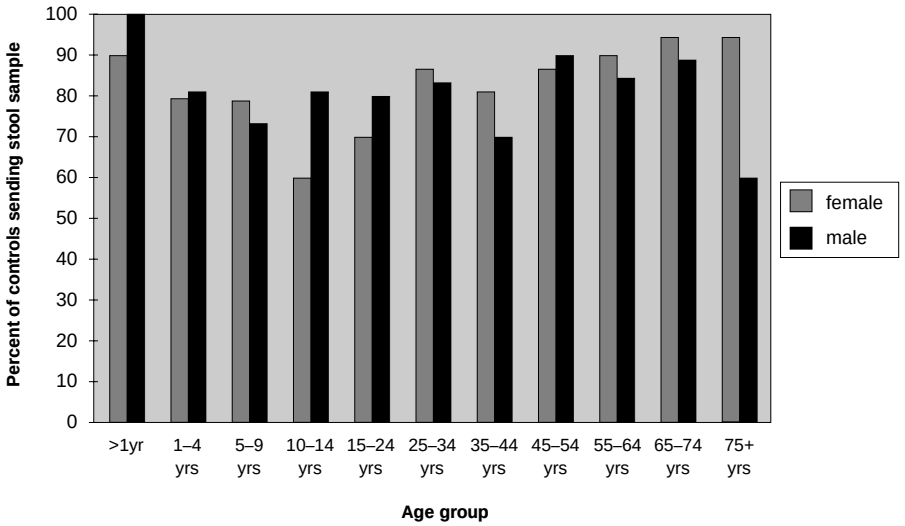


Table A1.32 Compliance in sending a stool sample among controls in the nested case-control component by practice characteristics

	CATEGORY	STOOL SENT	NUMBEROF CASES	% COMPLIANCE	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	247	322	76.7	
	Rural	300	353	85.0	(χ^2 = 7.51, P = 0.006)
Geographical Region	North	116	145	80.0	
	S. West / Midlands	283	343	82.5	
	S. East	148	187	79.1	(χ^2 = 1.02, P = 0.601)
Jarman Score	Low	142	171	83.0	
	Mid	263	334	78.7	
	High	142	170	83.5	(χ^2 = 2.3, P = 0.320)

A1.3 CASE CONTROL AND ENUMERATION COMPONENTS

Thirty-six practices took part in the enumeration component and 34 in the case-control component . Figure A1.11 is a schematic representation of ascertainment to the study, and compliance with risk factor and socio-economic questionnaire and stool samples. Cases were ascertained to the study if they fulfilled the definition of IID. Whereas efforts were made to make this as complete as possible (see Chapter 3), under-ascertainment could not be avoided on the whole and had to be estimated and corrected for. Figure A1.12 is a schematic representation of the enumeration component.

A1.3.1 Assessment of under-ascertainment

Cases of presumed IID which presented to general practice in the national study should have been ascertained by their GP in both the case-control and enumeration components. However ascertainment was not complete and a sub-study was carried out in order to estimate and correct the degree of under-ascertainment. In 26 computerised general practices in which diagnoses were routinely entered onto the practice computer, cases suggestive of IID were identified retrospectively. Cases which fulfilled the case definition of IID and should have been ascertained to the MRC EMCU, but were not, represented the level of under-ascertainment

A1.3.1.1 Data collected

The characteristics of the 26 GP practices with computerised diagnostic recording systems which took part in the under-ascertainment study were compared with those of all practices in the IID study and are shown in Table A1.33. There was no significant difference in terms of study component, urban or rural setting, geographical location, Jarman score and number of partners, suggesting that the practices with computerised diagnostic recording systems were representative of all study practices.

The total number of records examined was 2,021 in the 26 practices (median 78, range 37 to 83). Of these, 1,514 (75%) were eligible, based on the case definition of IID. Further analysis was restricted to these eligible cases, all of which should have been ascertained. Of the 1,514 eligible cases, only 974 (64.3%) were ascertained to the study. This could be used simplistically, to derive an overall adjustment factor (100/64.3 = 1.56) for the true presentation rate of IID to general practice. Variation in ascertainment between practices ranged from 30% to 93%.

A1.3.1.2 Univariate analysis

Univariate analysis showed that, of patient related factors, there was no strong evidence that age and sex were associated with ascertainment (Table A1.34). Males had a slightly higher ascertainment than females (p=0.06). Cases who complained of loose stools, with or without vomiting, were more likely to be ascertained rather than those with vomiting alone (70% versus 43%, p<0.001). Consultation in the surgery as opposed to home (67% versus 49%, p<0.001), and by the GP as opposed to deputising agency (65% versus 36%, p<0.001) were also associated with higher ascertainment.

Practice characteristics were examined to see if they were associated with ascertainment. Ascertainment was higher in enumeration practices versus GP case-control component practices(70% versus 58%, p<0.001), and in rural practices versus urban (75% versus 53%, p<0.001). It decreased as the number of partners per practice increased, from 70% with 1–2 partners, to 44% in practices with 7–8 partners (p<0.001 test for trend). Ascertainment varied with practice Jarman score but there was no trend. It was lowest in practices located in the North.

Figure A1.11 Schematic representation of the case-control component

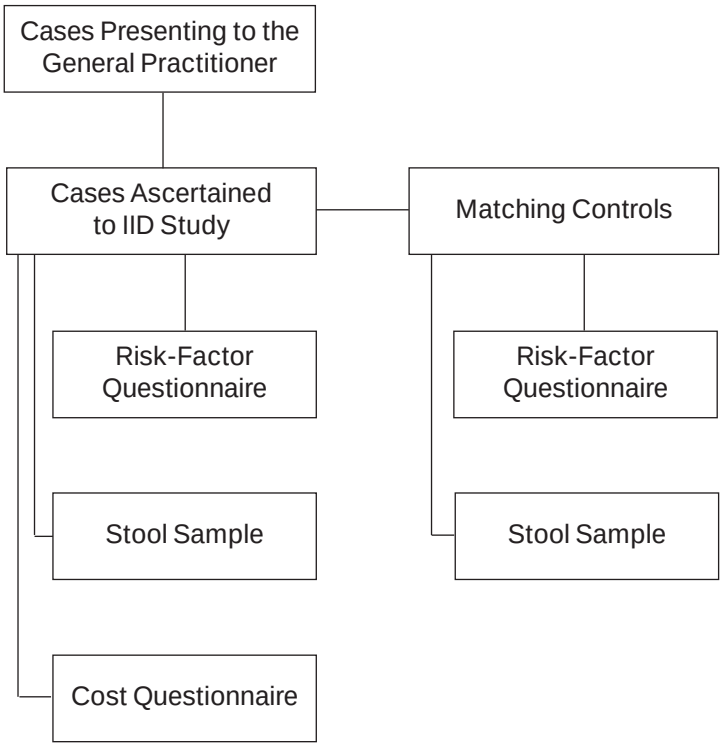


Figure A1.12 Schematic representation of the enumeration component

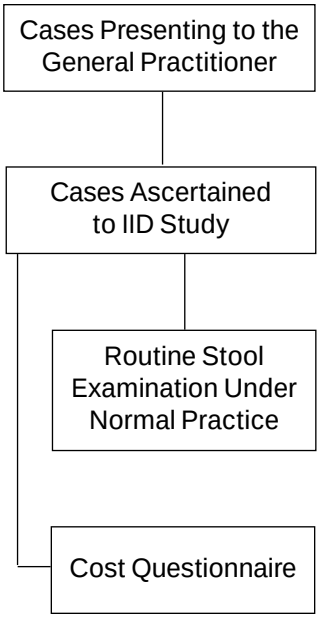


Table A1.33 Comparison of characteristics of practices in IID study with those who took part in the assessment of under-ascertainment.

CHARACTERISTIC	ALL IID STUDY PRACTICES	PERCENTAGE	UNDER-ASCERTAINMENT STUDY	PERCENTAGE
Study component				
Case control	34	49	14	54
Enumeration	36	51	12	46
Urban or rural location				
Urban	28	40	13	50
Rural	42	60	13	50
Geographical region				
North	19	27	6	23
Midlands/ South West	29	41	13	50
South East	22	31	7	27
Jarman score				
High	26	37	7	27
Mid	29	41	12	46
Low	15	21	7	27
Number of partners				
1–2	24	34	8	31
3–4	22	31	11	42
5–6	18	26	4	15
7–9	6	9	3	12
Totals	70		26	

Table A1.34 Factors associated with under-ascertainment (unadjusted)

FACTOR	CATEGORIES	n	PERCENTAGE ASCERTAINED	P-VALUE
All		1,516	64.3	
Sex	male	728	66.8	
	female	781	62.1	0.06
	missing	7		
Age	agebands within males			0.10
	agebands within females			0.23
Symptom	loose stool/stool+vomiting	1,185	70.0	
	vomiting only	162	42.6	
	missing	169	45.5	<0.001
Home visit	yes	269	48.9	
	no	1,231	67.4	
	missing	16		<0.001
Deputising service	yes	50	36.0	
	no	1,457	65.4	
	missing	9		<0.001
Study component	case control	753	58.3	
	enumeration	763	70.3	<0.001
Number of partners	1–2	451	70.3	
	3–4	718	65.2	
	5–6	226	60.4	<0.001
	7–8	121	44.2	(trend)
Jarman score	<-5	328	56.1	
	-5 to 10	784	68.6	
	>10	404	62.8	<0.001
Geographical region	north	344	50.3	
	mid/south west	777	69.5	
	south east	395	66.5	<0.001
Location	urban	717	52.8	
	rural	799	74.7	<0.001
GP spotter scheme	yes	275	49.5	
	no	1,241	67.6	<0.001
Questionnaire	scanned	1,242	63.6	
	coded	274	67.7	0.21
Time period	early in practice's year	760	63.6	
	late in practice's year	756	61.2	0.50
Previous research experience	yes	744	65.4	0.41
	no	772	63.3	

Ascertainment did not vary according to whether the period examined was early or late in the study period. There was lower ascertainment in spotter practices that belonged to the Royal College of General Practitioners Weekly Returns Service when compared with those that did not (50% versus 68%, p<0.001).

A1.3.1.3 Logistic regression model

Logistic regression modeling was used to identify variables which were independently associated with ascertainment after taking other variables into account. Of the factors related to patients (age, sex, symptoms, home visit and seen by a deputising agency) those that were independent were: i) vomiting only, as opposed to diarrhoea with orwithout vomiting (OR 0.37, 95% CI 0.28 to 0.49) and ii) consultation in the surgery as opposed to at home (OR 2.18, 95% CI 1.63 to 2.90).

Patient level characteristics were not used to predict ascertainment because: i) the severity of the symptoms may have influenced the GP's interpretation of whether the case definition of IID was met and ii) it would have been difficult to obtain denominator data for patients visited at home for adjustment of ascertainment rates.

Practice related factors independently associated with ascertainment were: i) study component (enumeration versus GP case-control, OR 1.78), ii) the number of partners (OR 0.3 for 7–8 partners, test for trend p<0.001), iii) urban or rural location (urban versus rural, OR 2.27) and iv) previous research experience (OR 1.92). Factors that were no longer significant included sex (p=0.14), Jarman score (p=0.46) and geographical region (p=0.21). There were no significant interaction terms.

The predicted percentage ascertainment according to practice characteristics was calculated from the final logistic regression model. Predicted under-ascertainment was higher in urban practices, in practices with a large number of partners and in those practices without previous research experience. These characteristics were then used to correct for the under ascertainment at practice level.

A1.3.2 Matching and compliance in case-control component

A1.3.2.1 Selection of controls

Age and sex matched controls selected on the basis of the criteria listed below were invited from the practice lists:

Controls were selected from the cohort lists (in the population cohort study) or from the practice age-sex register (in the GP case control study). The next patient alphabetically on the list who fulfilled the matching criteria was selected. If this control was unwilling to participate or was not obtainable, the next appropriate control was selected. The matching criteria were as follows:

Sex

Cases of 5 years old and over had controls matched for sex as well as age.

Age

0–5 months:	within age band
6–11 months:	within age band
1–4 years:	within one year on either side of case, but not below 11 months
5–19 years:	within two years on either side of case, but not below 4 years
20 and over:	within 5 years on either side of case, but not below 18 years

If the first potential control refused, then a second, third, fourth or fifth control were invited until one that accepted was found. Table A1.38 shows the number and proportion accepting in the order of invitation. Half of the first controls invited accepted but this decreased to 13% when the 5th control was invited.

Time delay between case recruitment and control recruitment
This was assessed by the time delay between the case risk factor questionnaire and the control risk factor questionnaire. (Table A1.39, Figure A1.14).

Table A1.35 Case-control matching in the case-control component by age and sex

	FEMALES			MALES		
AGE	NUMBER OF CONTROLS	NUMBER OF CASES	% MATCHED	NUMBER 0F CONTROLS	NUMBER OF CASES	% MATCHED
<1	117	158	74.1	173	218	79.4
1–4	300	386	77.7	358	452	79.2
5–9	84	106	79.3	82	112	73.2
10–14	39	53	73.6	44	65	67.7
15–24	136	245	55.5	75	164	45.7
25–34	261	360	72.5	166	292	56.9
35–44	178	222	80.2	114	171	66.7
45–54	133	164	81.1	108	141	76.6
55–64	102	129	79.1	87	109	79.8
65–74	83	99	83.8	50	62	80.7
75+	50	85	58.8	25	32	78.1
Missing	12	23	52.2	7	11	63.6
Totals	1,495	2,030	73.7	1,289	1,829	70.5

Note: 167 cases had missing sex information

Figure A1.13 Matching of cases and controls in the case-control component by age and sex

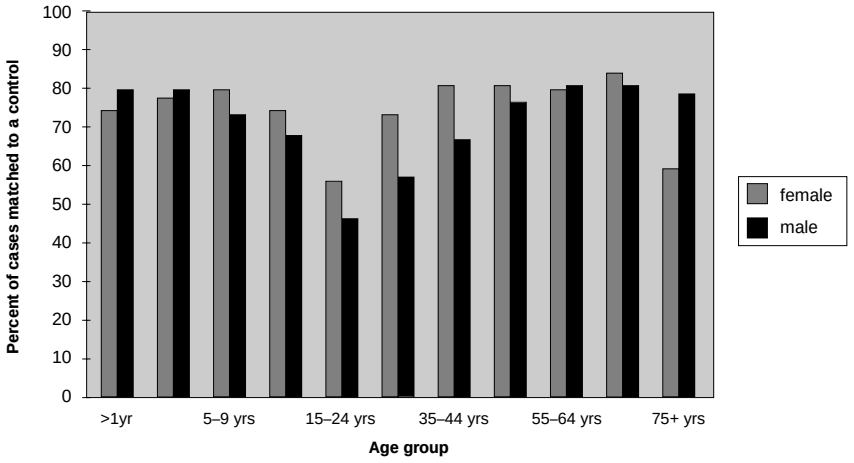


Table A1.36 Case-control matching in the case-control component by practice characteristics

	CATEGORY	NUMBER OF CONTROLS	NUMBER OF CASES	% MATCHED	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	1,671	2,596	64.4	
	Rural	1,193	1,430	83.4	(χ^2 = 163.12, P = <0.001)
Geographical Region	North	705	1,014	69.5	
	South West / Midlands	1,352	1,833	73.8	
	South East	807	1,179	68.5	(χ^2 = 11.57, P = 0.003)
Jarman Score	Low	420	597	70.4	
	Mid	1,619	2,098	77.2	
	High	825	1,331	62.0	(χ^2 = 91.67, P = <0.001)

Table A1.37 Number of people invited before matched control agreed to participate

Information available for 3,186 out of 4,026 cases (79.1%)

	NUMBER INVITED	NUMBER REFUSED TO PARTICIPATE	NUMBER AGREED TO PARTICIPATE	% AGREED OF THOSE INVITED	CUMULATIVE NUMBER AGREED	CUMULATIVE % AGREED	% AGREED AT EACH INVITE
1st control invited	3,186	1,595	1,591	49.9	1,591	49.9	62.4
2nd control invited	1,476	930	546	37.0	2,137	67.1	21.6
3rd control invited	851	621	230	27.0	2,367	74.3	9.1
4th control invited	575	470	105	18.3	2,472	77.6	4.2
5th control invited	408	355	53	13.0	2,525	79.3	2.1

Table A1.38 Time delay between case risk factor questionnaire and control risk factor questionnaire in the case-control component

DELAY (MONTHS)	NUMBER	CUMULATIVE PERCENTAGE
up to 2 months prior	2	0.2
up to 1 month prior	38	3.4
up to 1 month delay	645	57.3
up to 2 months delay	309	83.2
up to 3 months delay	119	93.1
up to 4 months delay	40	96.5
up to 5 months delay	20	98.2
up to 6 months delay	7	98.7
up to 7 months delay	9	99.5
up to 8 months delay	3	99.8
up to 9 months delay	3	100.0
total	1,195	

Notes: Data presented for 1,195 cases out of 1,714 with a matched control, where dates on each questionnaire were verified closely by dates of receipt of the questionnaire.

Figure A1.14 Time delay (in days) between case risk factor questionnaire and control risk factor questionnaire in the case-control component

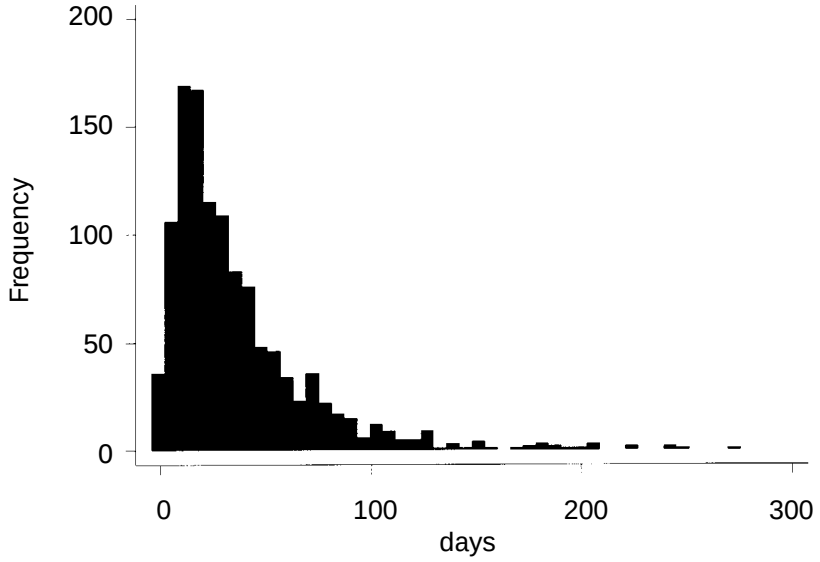


Table A1.39 Risk factor questionnaire compliance among cases in the case-control component by age and sex

	FEMALES			MALES		
AGE	QUESTIONNAIRE RETURNED	NUMBER OF CASES	% COMPLIANCE	QUESTIONNAIRE RETURNED	NUMBER OF CASES	% COMPLIANCE
<1	102	158	64.5	125	218	57.3
1–4	237	386	61.4	305	452	67.5
5–9	68	106	64.2	63	112	56.3
10–14	32	53	60.1	37	65	57.0
15–24	142	245	58.0	80	164	48.8
25–34	247	360	68.6	167	292	57.2
35–44	158	222	71.2	115	171	67.3
45–54	129	164	78.7	102	141	72.3
55–64	101	129	78.3	78	109	71.2
65–74	79	99	79.9	51	62	82.3
75+	58	85	68.4	23	32	71.2
Missing	14	23	60.1	7	11	63.6
Total	1,367	2,030	67.3	1,153	1,829	63.0

Note: 167 cases had missing sex information

Figure A1.15 Risk factor questionnaire compliance among cases in the case-control component by age and sex

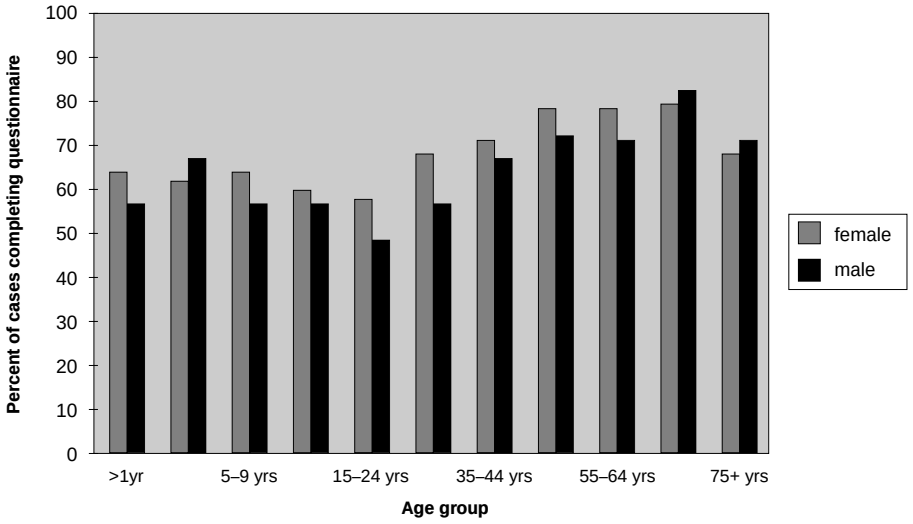


Table A1.40 Risk factor questionnaire compliance among cases in the case-control component by practice characteristics

	CATEGORY	QUESTIONNAIRE RETURNED	NUMBER OF CASES	% COMPLIANCE	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	1,631	2,596	62.8	
	Rural	1,011	1,430	70.7	(χ^2 = 25.33, P = < 0.001)
Geographical Region	North	650	1,014	64.1	
	South West / Midlands	1,214	1,833	66.2	
	South East	778	1,179	66.0	(χ^2 = 1.41, P = 0.50)
Jarman Score	Low	406	597	68.0	
	Mid	1,413	2,098	67.4	
	High	823	1,331	61.2	(χ^2 = 12.75, P = 0.002)

Table A1.41 Compliance in sending a stool sample among cases in the case-control component by age and sex

	FEMALES			MALES		
AGE	STOOL SENT	NUMBER OF CASES	% COMPLIANCE	STOOL SENT	NUMBER OF CASES	% COMPLIANCE
<1	116	158	73.4	157	218	72.0
1–4	276	386	71.5	343	452	75.6
5–9	68	106	64.2	74	112	66.1
10–14	34	53	64.2	39	65	60.0
15–24	150	245	61.2	87	164	53.1
25–34	249	360	69.2	201	292	68.8
35–44	181	222	81.5	131	171	76.6
45–54	137	164	83.6	116	141	82.3
55–64	117	129	90.7	88	109	80.7
65–74	90	99	90.9	54	62	87.1
75+	73	85	85.9	24	32	75.0
Missing	12	23	52.2	6	11	54.6
Totals	1,503	2,030	74.0	1,320	1,829	72.2

Note: 167 cases had missing sex information

Figure A1.16 Stool sample compliance among cases in the case-control component by age and sex

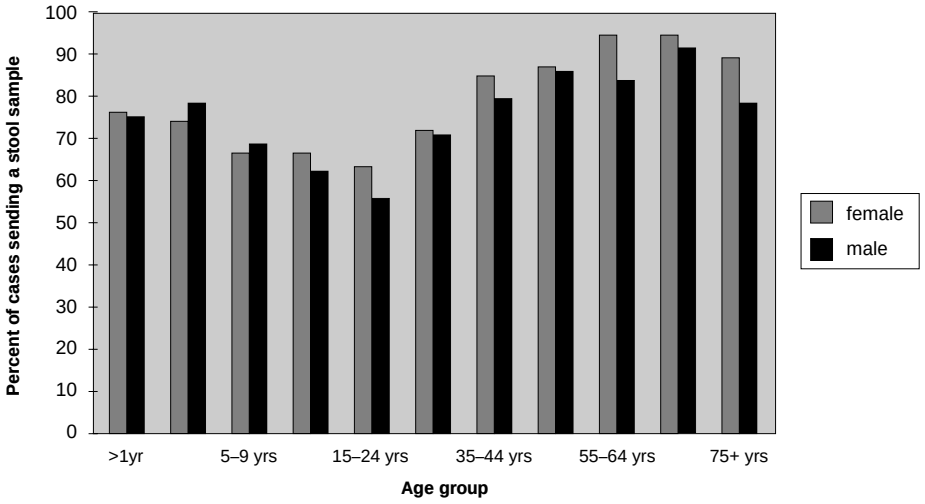


Table A1.42 Compliance in sending a stool sample among cases in the case-control component by practice characteristics

	CATEGORY	STOOL SENT	NUMBER OF CASES	% COMPLIANCE	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	1,631	2,596	71.2	
	Rural	1,099	1,430	76.7	(χ^2 = 12.28, P = <0.001)
Geographical Region	North	769	1,014	75.8	
	South West/ Midlands	1,327	1,833	72.4	
	South East	866	1,179	73.5	(χ^2 = 3.99, P = 0.14)
Jarman Score	Low	429	597	71.9	
	Mid	1,620	2,098	77.2	
	High	913	1,331	68.6	(χ^2 = 32.19, P = <0.001)

Table A1.43 Risk factor questionnaire compliance among controls in the case-control component by age and sex

	FEMALES			MALES		
AGE	QUESTIONNAIRE RETURNED	NUMBER OF CONTROLS	% COMPLIANCE	QUESTIONNAIRE RETURNED	NUMBER OF CONTROLS	% COMPLIANCE
<1	95	109	87.2	114	124	91.9
1–4	256	307	83.4	284	334	85.0
5–9	69	77	89.6	71	83	85.5
10–14	38	42	90.5	35	43	81.4
15–24	81	125	64.8	44	67	67.7
25–34	213	262	81.3	114	163	69.9
35–44	128	147	87.1	76	99	76.8
45–54	121	132	91.7	88	103	85.4
55–64	91	94	96.8	58	72	80.6
65–74	69	73	94.5	51	53	96.2
75+	44	52	84.6	22	24	91.7
Missing	3	4	75.0	2	2	100.0
Total	1,208	1,424	84.8	959	1,167	82.2

Note: 280 controls had missing sex information

Figure A1.17 Risk factor questionnaire compliance among controls in the case-control component by age and sex

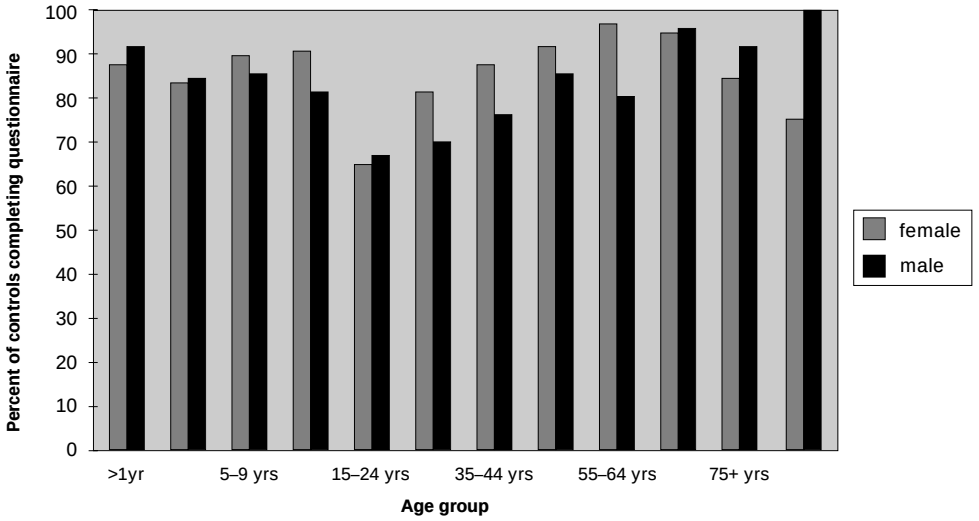


Table A1.44 Risk factor questionnaire compliance among controls in the case-control component by practice characteristics

	CATEGORY	STOOL SENT	NUMBER OF CASES	% MATCHED	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	1,410	1,660	84.9	
	Rural	1,019	1,193	85.4	(χ^2 = 0.13, P = 0.7)
Geographical Region	North	587	705	83.3	
	South West / Midlands	1,139	1,339	85.1	
	South East	703	809	86.9	(χ^2 = 3.95, P = 0.14)
Jarman Score	Low	363	415	87.5	
	Mid	1,378	1,616	85.3	
	High	688	822	83.7	(χ^2 = 3.15, P = 0.21)

Table A1.45 Compliance in sending a stool sample among controls in the case-control component by age and sex

	FEMALES			MALES		
AGE	STOOL SENT	NUMBER OF CONTROLS	% COMPLIANCE	STOOL SENT	NUMBER OF CONTROLS	% COMPLIANCE
<1	95	109	87.2	105	124	84.7
1–4	246	307	80.1	267	334	79.9
5–9	62	77	80.5	65	83	78.3
10–14	33	42	78.8	31	43	72.1
15–24	69	125	55.2	37	67	55.2
25–34	189	262	72.1	110	163	67.5
35–44	116	147	78.9	74	99	74.8
45–54	117	132	88.6	87	103	84.5
55–64	87	94	92.6	59	72	81.9
65–74	67	73	91.8	50	53	94.3
75+	41	52	78.6	19	24	79.2
Missing	3	4	75.0	2	2	100.0
Totals	1,125	1,424	79.0	906	1,167	77.6

Note: 280 controls had missing sex information

Figure A1.18 Stool sample compliance among controls in the case-control component

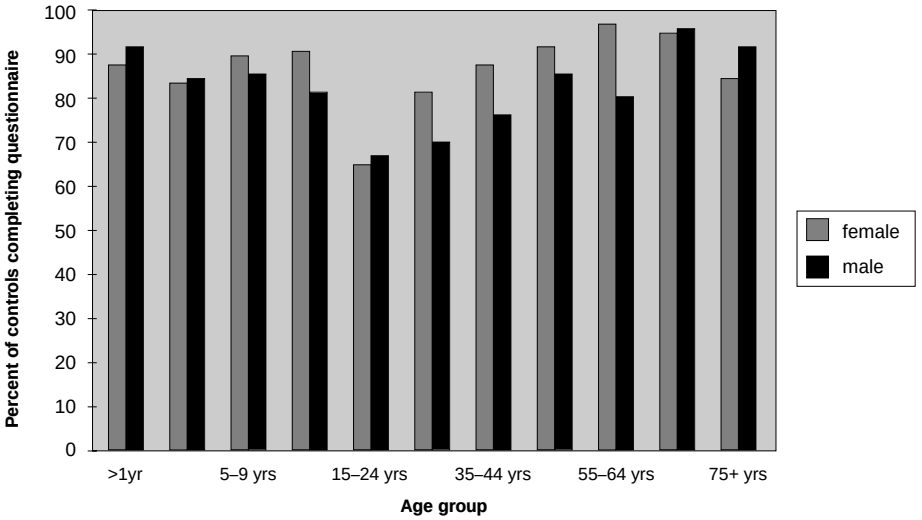


Table A1.46 Compliance in sending a stool sample among controls in the case-control component by practice characteristics

	CATEGORY	STOOL SENT	NUMBER OF CASES	% COMPLIANCE	TEST FOR DIFFERENCE BETWEEN CATEGORIES
Rural / Urban Location	Urban	1,299	1,660	78.3	
	Rural	964	1,193	80.1	(χ^2 = 2.76, P = <0.10)
Geographical Region	North	554	705	78.6	
	S. West/ Midlands	1,065	1339	79.5	
	S. East	644	809	79.6	(χ^2 = 0.31, P = 0.86)
Jarman Score	Low	345	415	83.1	
	Mid	1,296	1,616	80.2	
	High	622	822	75.7	(χ^2 = 11.12, P = 0.004)

A1.4 STOOL SPECIMENS

Table A1.47 Compliance with stool submission in each study component

	GP CASE CONTROL COMPONENT		NESTED CASE CONTROL COMPONENT	
	CASES	CONTROLS	CASES	CONTROLS
Number ascertained/ recruited	4,026	2,871	817	675
Number of stools analysed	2,893	2,264	761	555
Total number of stools received, including those of insufficient weight	2,962	2,281	767	555
% compliance	73.6	79.4	93.9	82.2

Table A1.48 Stool weights in grams by age/sex among cases in the case-control component

AGE GROUP	MALES			FEMALES		
	NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)		NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)	
<1	167	9.1	(2.0,18.4)	130	8.2	(2.1,17.7)
1–4	329	12.1	(2.8,21.5)	268	12.1	(3.7,19.6)
5–9	78	12.5	(3.7,18.6)	68	10.6	(3.3,19.8)
10–14	39	11.0	(4.5,23.0)	35	10.0	(2.7,21.2)
15–24	92	11.1	(2.6,20.0)	160	13.3	(2.8,21.7)
25–34	206	13.8	(3.4,21.9)	258	13.5	(3.3,22.9)
35–44	136	14.2	(3.9,23.0)	186	13.8	(2.4,21.7)
45–54	118	15.3	(4.0,23.1)	142	14.7	(3.6,22.8)
55–64	94	15.1	(4.1,24.5)	120	13.9	(3.3,23.5)
65–74	51	16.4	(3.4,24.6)	94	12.7	(3.5,23.3)
75+	21	13.7	(4.7,22.2)	73	14.9	(3.2,25.4)
Missing	1	18.9	(18.9,18.9)	5	11.9	(4.2,23.8)

Note: 49 samples had missing information for sex

Table A1.49 Stool weights by age/sex among controls in the case-control component

AGE GROUP	MALES			FEMALES		
	NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)		NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)	
<1	125	12	(4.2,20.3)	106	12.2	(3.3,19.9)
1–4	305	14.2	(3.8,22.2)	260	13.4	(5.5,22.9)
5–9	69	14	(5.5,23.2)	66	12.2	(4.1,21)
10–14	34	12.6	(6.5,21.8)	31	12.4	(3.8,19.3)
15–24	40	13	(7.45,20.5)	76	12.1	(5.6,21.4)
25–34	118	13.3	(6.6,23.8)	210	13.1	(6.2,24.1)
35–44	83	14.9	(5.7,22.8)	136	13.7	(5.6,25.1)
45–54	95	16.5	(6.3,26)	132	15.1	(4.9,23)
55–64	68	15.9	(5.9,23.8)	97	15.5	(5.6,24.1)
65–74	54	17.3	(8.3,23.1)	77	16.2	(6,25.3)
75+	22	15.4	(5.2,24.1)	44	15.1	(5.1,26.8)
Missing	2	15.7	(10.4,20.6)	0		

Table A1.50 Stool weights by age/sex among cases in the nested case-control component

AGE GROUP	MALES		FEMALES	
	NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)	NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)
<1	12	10.5 (2.9,17.9)	19	10.2 (4.7,23.9)
1–4	76	13.2 (3.6,20.1)	78	12.3 (2.4,23.7)
5–9	50	12.2 (2.3,22.4)	41	12.8 (3.25,23.15)
10–14	22	10.9 (1.8,20.7)	9	10.2 (3.5,23.2)
15–24	13	12.5 (1.9,22.9)	13	14.4 (3.1,19.6)
25–34	40	15.6 (5.3,24.8)	62	13.9 (3.4,21)
35–44	36	15.1 (1.9,25.9)	62	12.7 (4.4,20.7)
45–54	34	17.2 (3.3,28.5)	50	14.6 (4.8,24.2)
55–64	38	13.85 (2.2,23.2)	28	14.9 (4.8,23.5)
65–74	28	16.95 (4.7,22.7)	19	11.7 (2.2,21.9)
75+	8	7.25 (1.8,21.4)	16	15.2 (5.2,22.7)
Missing	0		0	

Table A1.51 Stool weights by age/sex among controls in the nested case-control component

AGE GROUP	MALES		FEMALES	
	NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)	NUMBER OF STOOLS	MEDIAN WEIGHT (5TH, 95TH PERCENTILE)
<1	9	13.6 (8.5,22.1)	12	11.5 (4.1,20.7)
1–4	61	11.4 (3.8,18.3)	56	11.3 (3.4,19.9)
5–9	29	15.1 (5.1,23.3)	27	10.5 (2.9,23)
10–14	18	15.9 (7,24.9)	9	10.4 (2,20.5)
15–24	8	12.5 (2.3,17.7)	10	10.9 (7.3,18.5)
25–34	26	15.5 (9.7,23.3)	49	13.6 (3.8,20.9)
35–44	22	17.3 (11.1,23.7)	47	12.7 (3.3,22.5)
45–54	27	12.1 (4.9,22.4)	37	14.1 (4.7,22.1)
55–64	26	13.6 (8.5,23.1)	20	11.9 (3.9,23.2)
65–74	25	18.7 (2.1,25.4)	19	16.1 (6.5,24)
75+	3	20.1 (12.4,20.9)	9	19.6 (10.3,26.3)
Missing	0		0	

Table A1.52 Stool weights (in grams) in cases for different study periods

QUARTER /YEAR	NUMBER OF STOOLS	NUMBER/PERCENT <10g	NUMBER/PERCENT <5g	MEDIAN WEIGHT (g)
3/93 + 4/93	103	44 (42.7)	19 (18.4)	13.5
1/94	293	112 (38.2)	35 (11.9)	13.2
2/94	560	199 (35.5)	60 (10.7)	13.5
3/94	629	203 (32.3)	77 (12.2)	13.7
4/94	723	226 (31.3)	76 (10.5)	14.1
1/95	521	194 (37.2)	67 (12.9)	14.1
2/95	411	136 (33.1)	49 (11.9)	13.9
3/95	269	83 (30.9)	38 (14.1)	13.9
4/95 +1/96	145	57 (39.3)	22 (15.2)	13.1

Table A1.53 Stool weights (in grams) in controls for different study periods

QUARTER /YEAR	NUMBER OF STOOLS	NUMBER/PERCENT <10g	NUMBER/PERCENT <5g	MEDIAN WEIGHT (g)
3/93 + 4/93	58	11 (19.6)	1 (0.02)	10.2
1/94	195	42 (21.5)	5 (2.6)	12.3
2/94	357	73 (20.5)	18 (5.0)	12.2
3/94	506	122 (24.1)	25 (4.9)	13.4
4/94	524	110 (20.9)	23 (4.4)	13.2
1/95	483	119 (24.6)	21 (4.4)	12.5
2/95	342	84 (24.6)	19 (5.6)	13.4
3/95	219	53 (24.2)	11 (5.0)	13.7
4/95 +1/96	135	36 (26.7)	10 (0.07)	12.5

Table A1.54 Time from onset of illness to receipt of stool in the laboratory (cases)

DAYS BETWEEN ONSET AND RECEIPT	NUMBER OF STOOLS	%
0	1	0.0
1	75	2.1
2	305	8.4
3	415	11.4
4	435	11.9
5	409	11.2
6	351	9.6
7	298	8.2
8	211	5.8
9	171	4.7
10	147	4.0
11	92	2.5
12	84	2.3
13	59	1.6
14	36	0.9
15	36	0.9
16	41	1.1
17	22	0.6
18	17	0.5
19	14	0.4
20	6	0.2
21	9	0.3
22	10	0.3
23	8	0.2
24	6	0.2
25	8	0.2
26	2	0.1
27	5	0.1
28	5	0.1
29	2	0.1
30+	31	0.9
Missing	343	9.4
Total	3,654	100.0

Figure A1.19 Number of days from onset of symptoms to receipt of stool sample at Leeds PHL

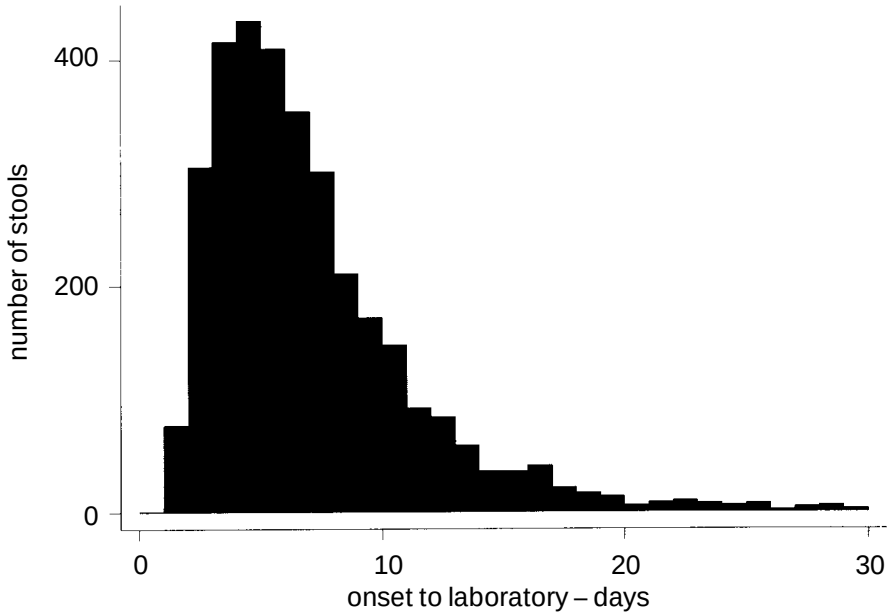


Table A1.55 Time from voiding to receipt of the stool in the laboratory

	CASES		CONTROLS	
DAYS BETWEEN VOIDING AND RECEIPT	NUMBER OF STOOLS	%	NUMBER OF STOOLS	%
0	13	0.4	4	0.2
1	1,256	36.3	1,103	42.4
2	1,237	35.7	931	35.8
3	546	15.8	307	11.8
4	218	6.3	117	4.5
5	80	2.3	52	0.2
6	44	1.3	36	1.4
7	26	0.8	15	0.6
8	11	0.3	10	0.4
9	7	0.2	7	0.3
10	26	0.8	18	0.7
Total	3,464	100	2,600	100

Figure A1.20 Number of days from voiding to receipt of stool samples at Leeds PHL – controls

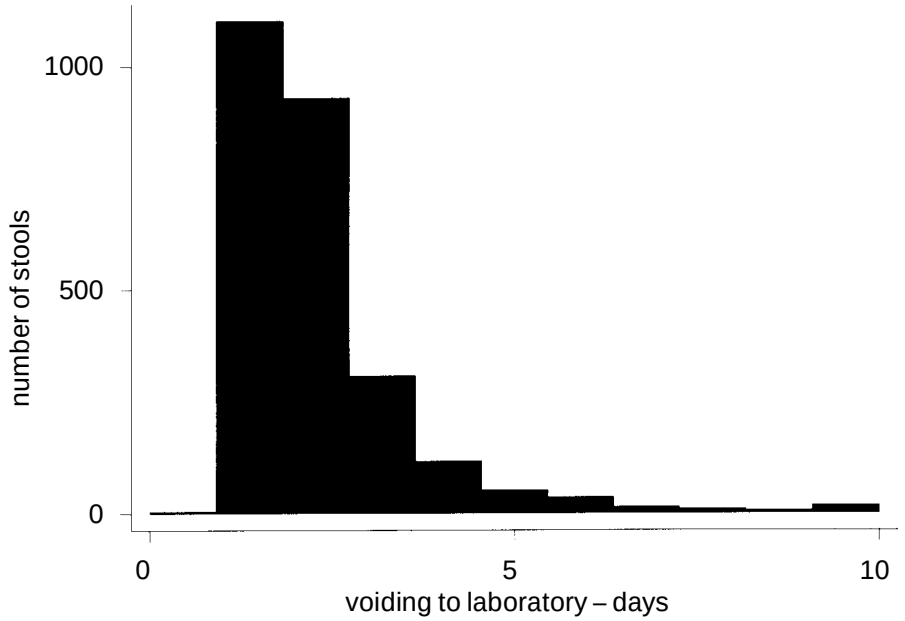


Figure A1.21 Number of days from voiding to receipt of stool sample at Leeds PHL – cases

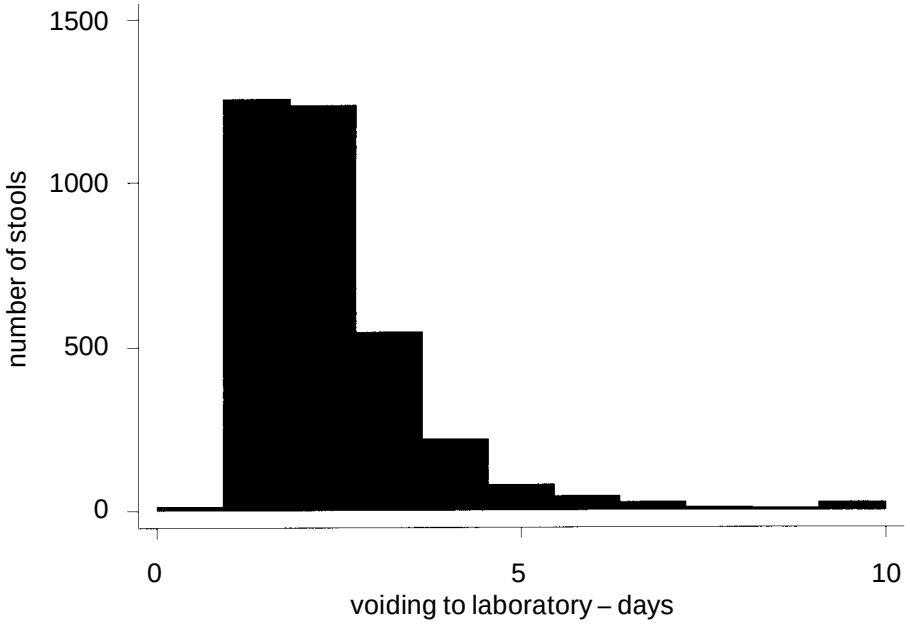


Table A1.56 Median delays between onset of symptoms or voiding of stool and receipt in the laboratory for different study periods in cases and controls

QUARTER YEAR	CASES		CONTROLS
	ONSET TO RECEIPT MEDIAN	VOIDING TO RECEIPT MEDIAN	VOIDING TO RECEIPT MEDIAN
3/93 + 4/93	5	2	2
1/94	5	2	2
2/94	6	2	2
3/94	6	2	2
4/94	6	2	2
1/95	6	2	2
2/95	5	2	2
3/95	5	2	2
4/95 + 1/96	4	2	2

Table A1.57 Number of stools sufficient for each analytical stage in cases and controls

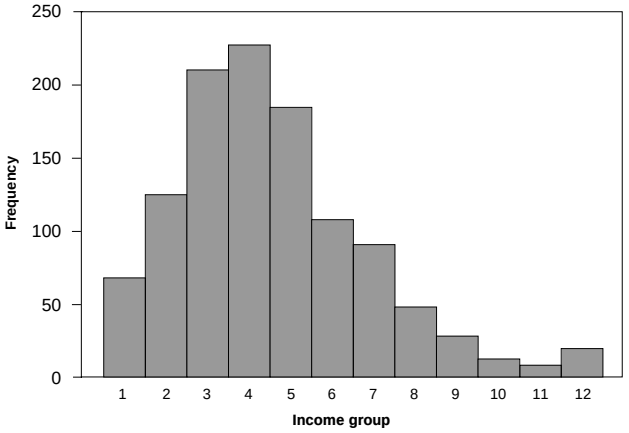
AMOUNT	CASES		CONTROLS	
	NUMBER OF STOOLS	PERCENT (CUMULATIVE)	NUMBER OF STOOLS	PERCENT (CUMULATIVE)
Sufficient for all tests + CAMR (Stage 8)	2,441	67	2,221	79
Up to Stage 7	2,701	75	2,538	79
Up to Stage 6	-	-	-	-
Up to Stage 5	3,327	91	2,745	97
Up to Stage 4	3,538	97	2,793	99
Up to Stage 3	3,654	100	2,820	100
All Received	3,654	100	2,820	100

Stages of Testing

Stage 8 Archived at CAMR
Stage 7 Protozoal parasites
Stage 6 Bacterial toxins
Stage 5 Virology
Stage 4 DNA probes for enterovirulent E.coli, and direct microscopy for *Cryptosporidium parvum*
Stage 3 *E coli* O157
Stage 2 *Salmonella, Shigella, Yersinia, Aeromonas, Vibrio, Clostridium*
Stage 1 Campylobacter

Figure A1.22 Distribution of income, by study, for those completing a socio-economic questionnaire

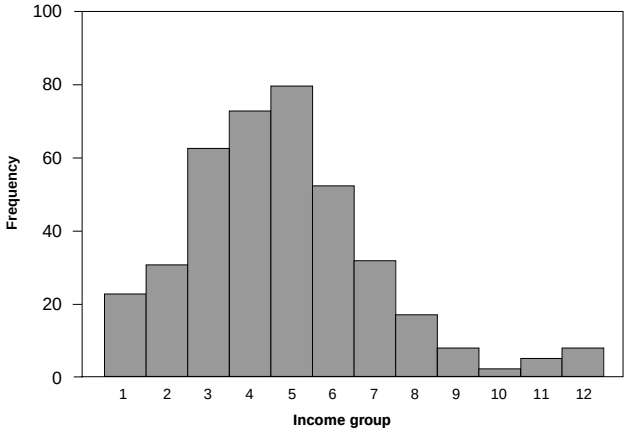
GP case control component



Income group
1 = <2,500 pa
2 = 2,501–5,000 pa
3 = 5,001–10,000 pa
4 = 10,001–15,000 pa
5 = 15,001–20,000 pa
6 = 20,001–25,000 pa
7 = 25,001–30,000 pa
8 = 30,001–35,000 pa
9 = 35,001–40,000 pa
10= 40,001–45,000 pa
11= 45,001–50,000 pa
12= >50,000 pa

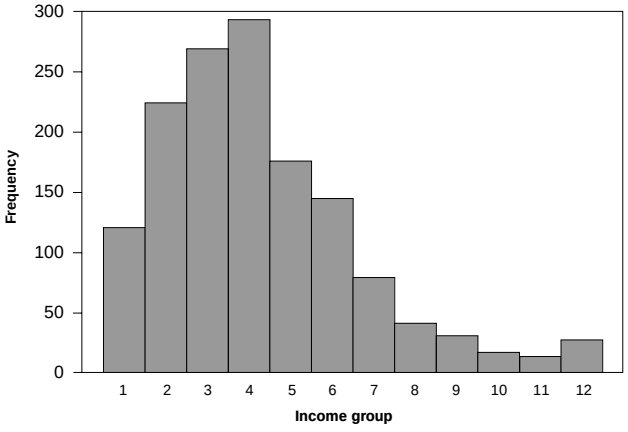
Missing data on 518 (31%) of cases

Community case-control component



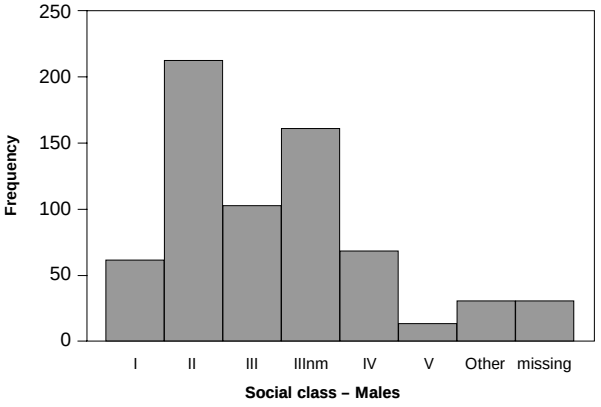
Missing data on 164 (30%) of cases

Enumeration component



Missing data on 742 (34%) of cases

Figure A1.23 Social class and sex distribution of cases in the GP case-control component who returned a socio-economic questionnaire



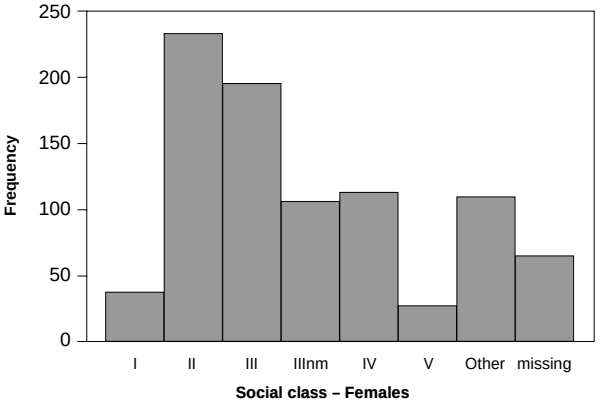


Figure A1.24 Social class and sex distribution of cases in the population cohort component who returned a socio-economic questionnaire

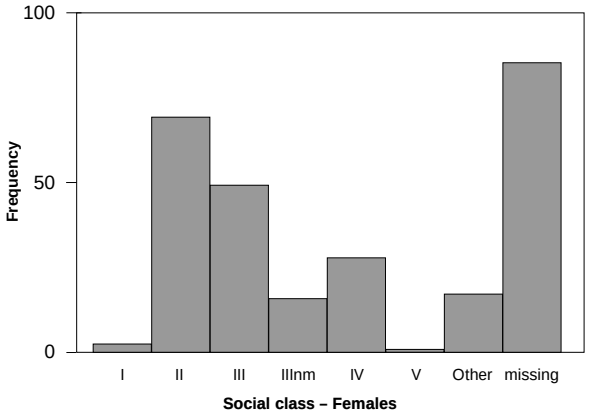
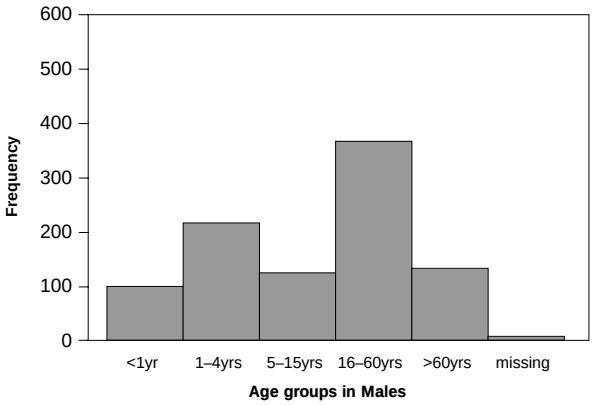


Figure A1.25 Age and sex distribution of cases in the enumeration component who returned a socio-economic costs questionnaire

Age distribution in males



Age distribution in females

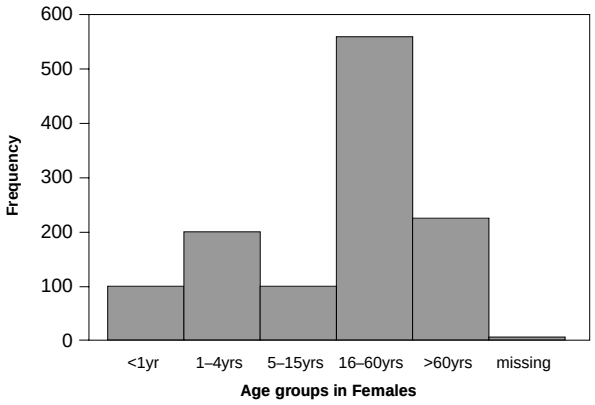


Table A1.58 Social class and age distribution of cases who returned a socio-economic questionnaire in the GP case control component

	AGE GROUP											
SOCIAL CLASS	<1 YR	(%)	1–4 YRS	(%)	5–15YRS	(%)	16–60 YRS	(%)	>60 YRS	(%)	TOTAL	(%)
I	11	(7.7)	33	(10.3)	12	(8.8)	37	(5.0)	9	(3.8)	102	(6.5)
II	42	(29.4)	101	(31.7)	46	(33.6)	207	(28.3)	49	(20.8)	445	(26.9)
III	18	(12.6)	37	(11.6)	22	(16.1)	181	(24.8)	37	(15.7)	295	(17.9)
IIInm	33	(23.1)	85	(26.7)	25	(18.3)	95	(12.9)	32	(13.6)	270	(17.2)
IV	15	(10.5)	32	(10.0)	14	(10.2)	97	(13.2)	25	(10.6)	183	(11.7)
V	4	(2.8)	2	(0.6)	5	(3.7)	21	(2.9)	8	(3.4)	40	(2.4)
Other	8	(5.6)	15	(4.7)	6	(4.4)	75	(10.2)	35	(14.8)	139	(8.9)
Missing	12	(8.4)	14	(4.4)	7	(5.1)	18	(2.5)	40	(17.0)	178	(10.8)
Total	143	(100)	319	(100)	137	(100)	731	(100)	235	(100)	1652	(100)

Table A1.59 Social class and age distribution of cases who returned a socio-economic questionnaire in the population cohort component

	AGE GROUP											
SOCIAL CLASS	<1 YR	(%)	1–4 YRS	(%)	5–15YRS	(%)	16–60 YRS	(%)	>60 YRS	(%)	TOTAL	(%)
I	0	(0.0)	3	(2.6)	0	(0.0)	10	(4.4)	5	(7.2)	18	(3.2)
II	4	(23.5)	9	(7.9)	11	(12.2)	88	(38.8)	23	(33.3)	135	(24.3)
III	0	(0.0)	3	(2.6)	2	(2.2)	55	(24.2)	9	(13.0)	69	(12.4)
IIInm	1	(5.9)	10	(8.8)	6	(6.7)	25	(11.0)	7	(10.1)	49	(8.8)
IV	0	(0.0)	1	(0.9)	1	(1.1)	34	(15.0)	9	(13.0)	45	(8.1)
V	0	(0.0)	1	(0.9)	0	(0.0)	2	(0.9)	0	(0.0)	3	(0.5)
Other	0	(0.0)	0	(0.0)	2	(2.2)	13	(5.7)	8	(11.6)	23	(4.1)
Missing	12	(70.6)	87	(76.3)	68	(75.6)	0	(0.0)	8	(11.6)	213	(38.4)
Total	17	(100)	114	(100)	90	(100)	227	(100)	69	(100)	555	(100)

Table A1.60 Income distribution of cases in the GP case control component, population cohort component and enumeration component who returned a socio-economic questionnaire

	GP CASE CONTROL COMPONENT		COMMUNITY CASE CONTROL COMPONENT		ENUMERATION COMPONENT	
INCOME (£) P.A.	n	(%)	n	(%)	n	(%)
Up to 2,500	67	(4.0)	22	(4.0)	121	(5.5)
2,501–5,000	124	(7.5)	30	(5.4)	224	(10.3)
5,001–10,000	211	(12.7)	63	(11.4)	267	(12.2)
10,001–15,000	229	(13.9)	73	(13.2)	291	(13.3)
15,001–20,000	183	(11.1)	79	(14.2)	176	(8.1)
20,001–25,000	109	(6.6)	52	(9.4)	145	(6.7)
25,001–30,000	90	(5.4)	31	(5.6)	80	(3.7)
30,001–35,000	48	(2.9)	17	(3.1)	44	(2.0)
35,001–40,000	30	(1.8)	8	(1.4)	33	(1.5)
40,001–45,000	13	(0.8)	3	(0.5)	17	(0.8)
45,001–50,000	11	(0.7)	5	(0.9)	15	(0.7)
50,001–60,000	14	(0.9)	5	(0.9)	18	(0.8)
more than 60,001 [60,001–105,000]	5	(0.3)	3	(0.4)	9	(0.4)
Missing	518	(31.4)	164	(29.6)	742	(34.0)
Total	1,652	(100)	555	(100)	2,182	(100)

Table A1.61 Structure of household and estimated number institutionalised for all cases who returned a socio-economic costs questionnaire by study component

	TYPE OF ACCOMMODATION					
	GP CASE CONTROL COMPONENT		POPULATION CASE CONTROL COMPONENT		ENUMERATION COMPONENT	
	NOT INST.	INST.	NOT INST.	INST.	NOT INST.	INST.
NO. IN HOUSEHOLD	n (% OF TOTAL)	n (% OF GROUP)	n (% OF TOTAL)	n (% OF GROUP)	n (% OF TOTAL)	n (% OF GROUP)
1–3	943 (57.9)	4	255 (46.3)	1	1,217 (56.1)	0
4–6	630 (38.7)	7	258 (46.8)	0	832 (38.4)	0
76	21 (1.3)	8	12 (2.2)	1	44 (2.0)	7
Missing	34 (2.1)	1	26 (4.7)	0	75 (3.5)	0
Total	1,628 (100)	20	551 (100)	2	2,168 (100)	7
Range	0–9	2–23	0–10	3–51	0–65	10–43

Appendix 2
Supplementary Results for Chapter 5

Key to organisms abbreviations

AD	Adenovirus
AE	Aeromonas
AS	Astrovirus
BA	Bacillus
CA	*Campylobacter*
CD	*Clostridium difficile*
CP	*Clostridium perfringens*
CR	*Cryptosporidium*
CV	Calicivirus
E1	Enterotoxigenic *E. coli*
E2	Verocytotoxin producing *E. coli*
E3	Enteroinvasive *E. coli*
E4	Attaching and effacing *E. coli*
E5	Enteropathogenic *E. coli*
E6	Enteroaggregative *E. coli*
E7	Diffusively adherent *E. coli*
EC	*E. coli* O157
GI	Giardia
RC	Rotavirus group C
RV	Rotavirus group A
SA	*Salmonella*
SH	*Shigella*
SR	SRSV
ST	*Staphylococcus aureus*
VB	Vibrio
YS	*Yersinia*

Table A2.1 Target organisms identified in all components: under 1 year

	GP CASE			GP CONTROL			COHORT CASE			COHORT CONTROL		
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED
Bacteria												
Aeromonas spp.	31	302	10.3	16	233	6.9	2	31	6.4	1	21	4.8
Bacillus spp. (>10^4/g)	0	235	0	1	217	0.5	0	27	0	0	21	0
Campylobacter spp.	6	302	2.0	1	233	0.4	2	31	6.4	0	21	0
Clostridium difficile cytotoxin	13	180	7.2	33	199	16.6	6	21	28.6	4	19	21.0
Clostridium perfringens enterotoxin	12	302	4.0	3	229	1.3	0	31	0	0	20	0
E. coli O157	0	302	0	0	233	0	0	31	0	0	21	0
E. coli DNA probes:												
Attaching and Effacing	17	278	6.1	10	229	4.4	2	31	6.4	1	21	4.8
Diffusely adherent	10	278	3.6	13	229	5.7	3	31	9.7	0	21	0
Enteroaggregative	11	278	4.0	3	229	1.3	2	31	6.4	0	21	0
Enteroinvasive	0	278	0	0	229	0	0	31	0	0	21	0
Enteropathogenic	0	278	0	0	229	0	0	31	0	1	21	4.8
Enterotoxigenic	0	278	0	0	229	0	0	31	0	0	21	0
Verocytotoxigenic (non O157)	0	278	0	0	229	0	0	31	0	0	21	0
Salmonella spp.	7	302	2.3	1	233	0.4	0	31	0	0	21	0
Shigella spp.	0	302	0	0	233	0	0	31	0	0	21	0
Staphylococcus aureus (>10^6/g)	3	234	1.3	2	217	0.9	0	27	0	0	21	0
Vibrio spp.	0	302	0	0	233	0	0	31	0	0	21	0
Yersinia spp.	1	302	0.3	1	233	0.4	0	31	0	0	21	0
Protozoa												
Cryptosporidium parvum	2	301	0.7	1	233	0.4	0	31	0	0	21	0
Giardia intestinalis	3	302	1.0	0	233	0	0	31	0	0	21	0
Viruses												
Adenovirus Group F	18	259	6.9	1	224	0.4	2	28	7.1	0	21	0
Astrovirus	5	259	1.9	4	224	1.8	2	28	7.1	0	21	0
Calicivirus	15	259	5.8	1	224	0.4	2	28	7.1	1	21	4.8
Rotavirus Group A	56	263	21.3	3	224	1.3	3	29	10.3	0	21	0
Rotavirus Group C	0	263	0	0	224	0	0	29	0	0	21	0
SRSV	23	259	8.9	1	224	0.4	3	28	10.7	1	21	4.8
No organism identified	127	302	42.0	176	233	75.5	9	31	29.0	16	21	76.2

Table A2.2 Target organisms identified in all components: 1–4 years

	GP CASE			GP CONTROL			COHORT CASE			COHORT CONTROL		
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED
Bacteria												
Aeromonas spp.	26	606	4.3	34	568	6.0	7	156	4.5	6	119	5.0
Bacillus spp. (>10^4/g)	0	537	0	1	540	0.2	0	134	0	0	109	0
Campylobacter spp.	33	606	5.4	9	568	1.6	10	156	6.4	2	119	1.7
Clostridium difficile cytotoxin	8	468	1.7	5	510	1.0	1	116	0.9	1	98	1.0
Clostridium perfringens enterotoxin	34	603	5.6	5	564	0.9	3	154	1.9	0	118	0
E. coli O157	1	606	0.2	0	568	0	0	156	0	0	119	0
E. coli DNA probes:												
Attaching and Effacing	57	580	9.8	37	557	6.6	8	149	5.4	5	118	4.2
Diffusely adherent	17	580	2.9	25	557	4.5	3	149	2.0	4	118	3.4
Enteroaggregative	32	580	5.5	15	557	2.7	5	149	3.4	2	118	1.7
Enteroinvasive	0	580	0	0	557	0	0	149	0	0	118	0
Enteropathogenic	1	580	0.2	3	557	0.5	0	149	0	0	118	0
Enterotoxigenic	3	580	0.5	0	557	0	0	149	0	0	118	0
Verocytotoxigenic (non O157)	2	580	0.3	1	557	0.2	1	149	0.8	1	118	0.8
Salmonella spp.	15	606	2.5	3	568	0.5	3	156	1.9	1	119	0.8
Shigella spp.	2	606	0.3	0	568	0	0	156	0	0	119	0
Staphylococcus aureus (>10^6/g)	0	536	0	1	538	0.2	1	135	0.7	1	109	0.9
Vibrio spp.	0	606	0	0	568	0	0	156	0	0	119	0
Yersinia spp.	12	606	2.0	23	568	4.0	8	156	5.1	4	119	3.4
Protozoa												
Cryptosporidium parvum	17	606	2.8	1	568	0.2	2	156	1.3	0	119	0
Giardia intestinalis	7	606	1.2	6	568	1.1	0	156	0	1	119	0.8
Viruses												
Adenovirus Group F	57	553	10.3	2	546	0.4	9	148	6.1	1	112	0.9
Astrovirus	37	553	6.7	1	546	0.2	6	148	4.0	1	112	0.9
Calicivirus	21	553	3.8	3	546	0.5	3	148	2.0	0	112	0
Rotavirus Group A	98	567	17.3	4	547	0.7	13	148	8.8	0	112	0
Rotavirus Group C	2	567	0.3	0	547	0	1	148	0.7	0	112	0
SRSV	61	553	11.0	4	546	0.7	17	148	11.5	0	112	0
No organism identified	187	606	30.9	404	568	71.1	70	156	44.9	95	119	79.8

Table A2.3 Target organisms identified in all components: 5–14 years

	GP CASE			GP CONTROL			COHORT CASE			COHORT CONTROL		
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED
Bacteria												
Aeromonas spp.	16	221	7.2	7	201	3.5	9	123	7.3	9	83	10.8
Bacillus spp. (>10^4/g)	1	193	0.5	0	189	0	0	107	0	0	80	0
Campylobacter spp.	25	221	11.3	1	201	0.5	4	123	3.2	0	83	0
Clostridium difficile cytotoxin	1	167	0.6	1	177	0.6	0	94	0	0	72	0
Clostridium perfringens enterotoxin	10	220	4.5	1	200	0.5	2	123	1.6	0	82	0
E. coli O157	0	221	0	0	201	0	0	123	0	0	83	0
E. coli DNA probes:												
Attaching and Effacing	7	214	3.3	10	194	5.1	5	116	4.3	3	81	3.7
Diffusely adherent	5	214	2.3	9	194	4.6	2	116	1.7	4	81	4.9
Enteroaggregative	10	214	4.7	4	194	2.0	4	116	3.4	0	81	0
Enteroinvasive	0	214	0	0	194	0	0	116	0	0	81	0
Enteropathogenic	1	214	0.5	0	194	0	0	116	0	0	81	0
Enterotoxigenic	1	214	0.5	0	194	0	1	116	0.9	0	81	0
Verocytotoxigenic (non O157)	1	214	0.5	0	194	0	2	116	1.7	0	81	0
Salmonella spp.	13	221	5.9	0	201	0	3	123	2.4	0	83	0
Shigella spp.	1	221	0.4	0	201	0	0	123	0	0	83	0
Staphylococcus aureus (>10^6/g)	0	193	0	1	188	0.5	0	106	0	0	80	0
Vibrio spp.	0	221	0	0	201	0	0	123	0	0	83	0
Yersinia spp.	4	221	1.8	6	201	3.0	6	123	4.9	2	83	2.4
Protozoa												
Cryptosporidium parvum	11	221	5.0	0	201	0	1	123	0.8	0	83	0
Giardia intestinalis	4	221	1.8	2	201	1.0	1	123	0.8	0	83	0
Viruses												
Adenovirus Group F	2	201	1.0	0	195	0	2	111	1.8	0	81	0
Astrovirus	6	201	3.0	0	195	0	1	111	0.9	0	81	0
Calicivirus	1	201	0.5	0	195	0	3	111	2.7	0	81	0
Rotavirus Group A	14	208	6.7	0	195	0	5	111	4.5	0	81	0
Rotavirus Group C	3	208	1.4	0	195	0	1	111	09	0	81	0
SRSV	11	201	5.5	0	195	0	8	111	7.2	0	81	0
No organism identified	101	221	45.7	163	201	81.1	76	123	61.8	65	83	78.3

Table A2.4 Target organisms identified in all components: 15–74 years

	GP CASE			GP CONTROL			COHORT CASE			COHORT CONTROL		
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED
Bacteria												
Aeromonas spp.	85	1,664	5.1	37	1,194	3.1	25	427	5.8	12	320	3.7
Bacillus spp. (>10^4/g)	3	1,515	0.2	6	1,165	0.5	0	395	0	2	303	0.7
Campylobacter spp.	281	1,664	16.9	4	1,194	0.3	15	427	3.5	1	320	0.3
Clostridium difficile cytotoxin	10	1,360	0.7	2	1,091	0.2	1	364	0.3	0	286	0
Clostridium perfringens enterotoxin	53	1,647	3.2	6	1,189	0.5	4	425	0.9	3	319	0.9
E. coli O157	2	1,664	0.1	0	1,194	0	0	427	0	0	320	0
E. coli DNA probes:												
Attaching and Effacing	36	1,606	2.2	10	1,185	0.8	8	414	1.9	1	309	0.3
Diffusely adherent	69	1,606	4.3	45	1,185	3.8	13	414	3.1	5	309	1.6
Enteroaggregative	86	1,606	5.3	21	1,185	1.8	10	414	2.4	2	309	0.6
Enteroinvasive	0	1,606	0	0	1,185	0	0	414	0	0	309	0
Enteropathogenic	2	1,606	0.1	3	1,185	0.2	1	414	0.2	1	309	0.3
Enterotoxigenic	48	1,606	3.0	0	1,185	0	11	414	2.7	0	309	0
Verocytotoxigenic (non O157)	3	1,606	0.2	8	1,185	0.7	0	414	0	5	309	1.6
Salmonella spp.	111	1,664	6.7	5	1,194	0.4	2	427	0.5	1	320	0.3
Shigella spp.	20	1,664	1.2	0	1,194	0	1	427	0.2	0	320	0
Staphylococcus aureus (>10^6/g)	7	1,514	0.5	1	1,164	0.1	0	394	0	0	302	0
Vibrio spp.	1	1,664	0.1	0	1,194	0	0	427	0	0	320	0
Yersinia spp.	34	1,664	2.0	24	1,194	2.0	12	427	2.8	10	320	3.1
Protozoa												
Cryptosporidium parvum	9	1,664	0.5	0	1,194	0	0	427	0	0	320	0
Giardia intestinalis	14	1,664	0.8	2	1,194	0.2	2	427	0.5	2	320	0.6
Viruses												
Adenovirus Group F	3	1,504	0.2	0	1,179	0	0	406	0	0	308	0
Astrovirus	27	1,504	1.8	0	1,179	0	5	406	1.2	0	308	0
Calicivirus	3	1,504	0.2	0	1,179	0	0	406	0	0	308	0
Rotavirus Group A	36	1,575	2.3	2	1,179	0.2	8	408	2.0	0	308	0
Rotavirus Group C	1	1,575	0.1	0	1,179	0	0	408	0	0	308	0
SRSV	63	1,504	4.2	1	1,179	0.1	21	406	5.2	2	308	0.6
No organism identified	835	1,664	50.2	1,030	1,194	86.3	309	427	72.4	275	320	85.9

Table A2.5 Target organisms identified in all components: > 74 years

	GP CASE			GP CONTROL			COHORT CASE			COHORT CONTROL		
	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED	NUMBER IDENTIFIED	NUMBER TESTED	PERCENT IDENTIFIED
Bacteria												
Aeromonas spp.	7	94	7.4	2	66	3.0	3	24	12.5	0	12	0
Bacillus spp. (>10^4/g)	0	86	0	0	63	0	0	21	0	0	12	0
Campylobacter spp.	9	94	9.6	1	66	1.5	1	24	4.2	1	12	8.3
Clostridium difficile cytotoxin	6	79	7.6	0	60	0	1	19	5.3	0	12	0
Clostridium perfringens enterotoxin	5	93	5.4	0	66	0	0	23	0	0	12	0
E. coli O157	0	94	0	0	66	0	0	24	0	0	12	0
E. coli DNA probes:												
Attaching and Effacing	2	90	2.2	0	63	0	0	22	0	0	12	0
Diffusely adherent	2	90	2.2	1	63	1.6	2	22	9.1	0	12	0
Enteroaggregative	2	90	2.2	0	63	0	0	22	0	0	12	0
Enteroinvasive	0	90	0	0	63	0	0	22	0	0	12	0
Enteropathogenic	0	90	0	0	63	0	0	22	0	0	12	0
Enterotoxigenic	0	90	0	0	63	0	0	22	0	0	12	0
Verocytotoxigenic (non O157)	0	90	0	0	63	0	0	22	0	0	12	0
Salmonella spp.	0	94	0	1	66	1.5	0	24	0	0	12	0
Shigella spp.	0	94	0	0	66	0	0	24	0	0	12	0
Staphylococcus aureus (>10^6/g)	0	86	0	0	63	0	0	21	0	0	12	0
Vibrio spp.	0	94	0	0	66	0	0	24	0	0	12	0
Yersinia spp.	0	94	0	2	66	3.0	0	24	0	0	12	0
Protozoa												
Cryptosporidium parvum	0	94	0	0	66	0	0	24	0	0	12	0
Giardia intestinalis	0	94	0	0	66	0	0	24	0	0	12	0
Viruses												
Adenovirus Group F	1	89	1.1	0	64	0	0	22	0	0	12	0
Astrovirus	1	89	1.1	0	64	0	0	22	0	0	12	0
Calicivirus	0	89	0	0	64	0	0	22	0	0	12	0
Rotavirus Group A	4	90	4.4	0	64	0	0	22	0	0	12	0
Rotavirus Group C	0	90	0	0	64	0	0	22	0	0	12	0
SRSV	9	89	10.1	0	64	0	1	22	4.5	0	12	0
No organism identified	52	94	55.3	59	66	89.4	16	24	66.7	11	12	91.7

Table A2.6 The effect of delay between onset of symptoms and receipt of specimen (days) on the recovery of target organisms: all samples

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0–2	169 (44.5)	380
3–5	688 (54.6)	1260
6–10	672 (57.0)	1178
11–15	130 (42.4)	307
16–20	31 (31.0)	100
21–25	17 (41.5)	41
26+	15 (34.1)	44
Unknown	147 (42.7)	344
Total	**1869 (51.2)**	**3654**

Pearson chi2(6) = 60.6734 Pr = 0.000 (excluding unknown group)

Table A2.7 The effect of delay between onset of symptoms and receipt of specimen (days) on the recovery of target organisms: GP case-control component

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0–2	88 (58.7)	150
3–5	567 (58.9)	962
6–10	642 (57.8)	1110
11–15	125 (43.1)	290
16–20	29 (31.5)	92
21–25	17 (42.5)	40
26+	14 (32.6)	43
Unknown	106 (51.5)	206
Total	**1588 (54.9)**	**2893**

Table A2.8 The effect of delay between onset of symptoms and receipt of specimen (days) on the recovery of target organisms: Community case-control component

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0–2	88 (58.7)	150
0–2	81 (35.2)	230
3–5	121 (40.6)	298
6–10	30 (44.1)	68
11–15	5 (29.4)	17
16–20	2 (25.0)	8
21–25	0 (0.0)	1
26+	1 (100.0)	1
Unknown	41 (29.7)	138
Total	**281 (36.9)**	**761**

Table A2.9 The effect of delay between onset of symptoms and taking of the specimen (days) on the recovery of target organisms: all samples

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0–2	592 (48.6)	1217
3–5	654 (60.1)	1088
6–10	316 (51.2)	617
11–15	68 (39.3)	173
16–20	16 (39.0)	41
21–25	14 (43.8)	32
26+	8 (29.6)	27
Unknown	201 (43.8)	459
Total	**1869 (51.2)**	**3654**

Pearson chi2(6) = 54.4988 Pr = 0.000 (excluding unknown group)

Table A2.10 The effect of delay between onset of symptoms and taking of the specimen (days) on the recovery of target organisms: GP case-control component

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL	
0–2	416 (56.7)	734	
3–5	613 (61.6)	996	
6–10	301 (51.0)	590	
11–15	63 (39.4)	160	
16–20	15 (38.5)	39	
21–25	14 (45.2)	31	
26+	8 (29.6)	27	
Unknown	158 (50.0)	316	
Total	**1588 (54.9)**	**2893**	

Table A2.11 The effect of delay between onset of symptoms and taking of the specimen (days) on the recovery of target organisms: Community case-control component

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0–2	176 (36.4)	483
3–5	41 (44.6)	92
6–10	15 (55.6)	27
11–15	5 (38.5)	13
16–20	1 (50.0)	2
21–25	0 (0.0)	1
26+	0 (0.0)	0
Unknown	43 (30.1)	143
Total	281 (36.9)	761

Table A.12 The effect of the delay between taking of the specimen and it's receipt in the laboratory on the recovery of target organisms: all samples

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0	5 (38.5)	13
1	672 (53.6)	1255
2	630 (50.7)	1242
3	286 (52.4)	546
4	106 (48.8)	217
5	32 (40.0)	80
6+	47 (42.3)	111
Unknown	91 (47.9)	190
Total	**1869 (51.2)**	**3654**

Pearson chi2(6) = 8.3443 Pr = 0.214

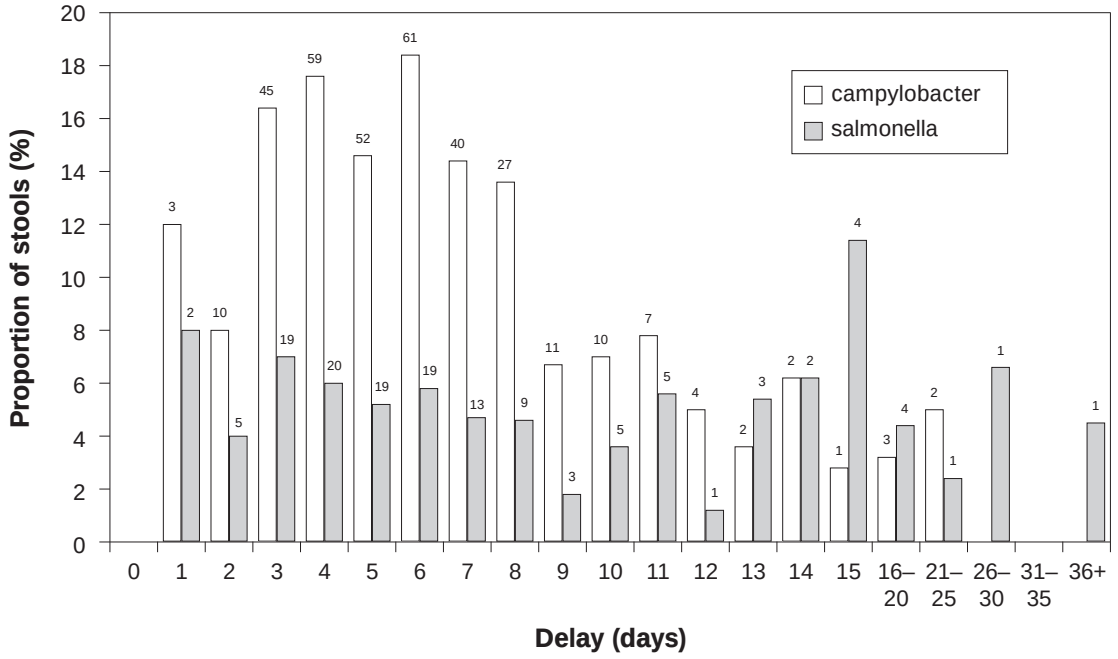
Table A.13 The effect of the delay between taking of the specimen and it's receipt in the laboratory on the recovery of target organisms: GP case-control study

DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0	5 (41.7)	12
1	568 (57.1)	994
2	523 (54.9)	952
3	239 (56.2)	425
4	91 (52.3)	174
5	31 (45.6)	68
6+	46 (46.0)	100
Unknown	85 (50.6)	168
Total	**1588 (54.9)**	**2893**

Table A.14 The effect of the delay between taking of the specimen and it's receipt in the laboratory on the recovery of target organisms: Community case-control study

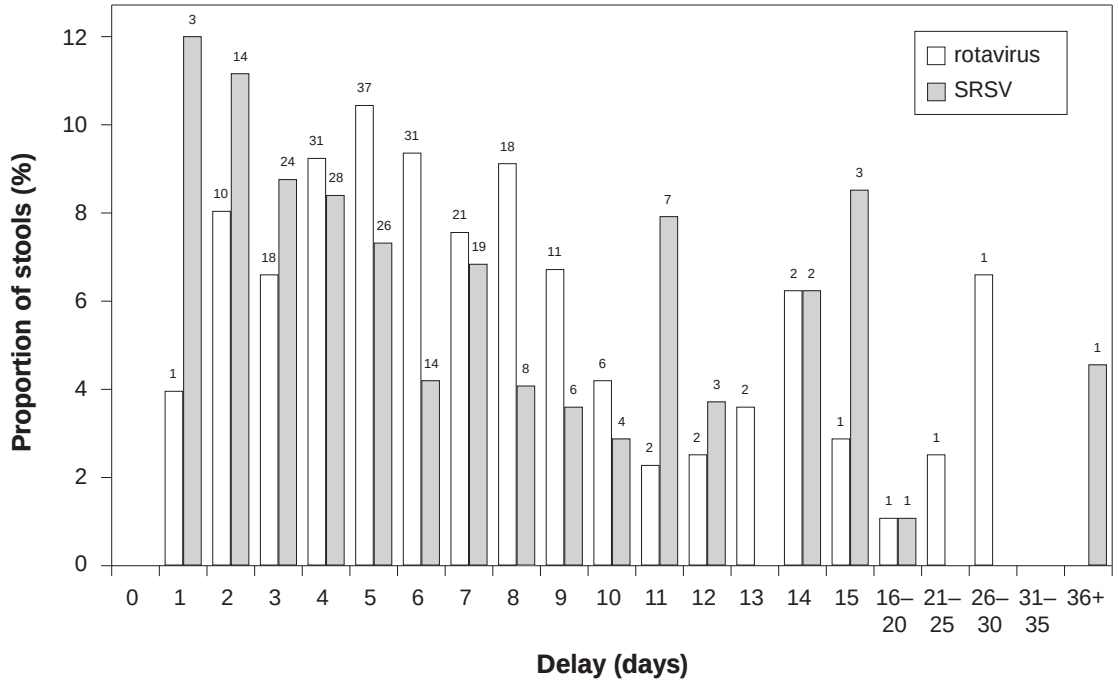
DELAY BETWEEN ONSET OF SYMPTOMS AND RECEIPT OF SPECIMEN (DAYS)	NUMBER OF SPECIMENS IN WHICH ONE OR MORE ORGANISMS WERE IDENTIFIED (%)	TOTAL
0	0 (0.0)	1
1	104 (39.8)	261
2	107 (36.9)	290
3	47 (38.8)	121
4	15 (34.9)	43
5	1 (8.3)	12
6+	1 (9.1)	11
Unknown	6 (27.3)	22
Total	**281 (36.9)**	**761**

Figure A2.1 Proportion of stools with *Campylobacter* or *Salmonella* identified by delay between onset of symptoms and receipt of specimen: GP case-control study cases



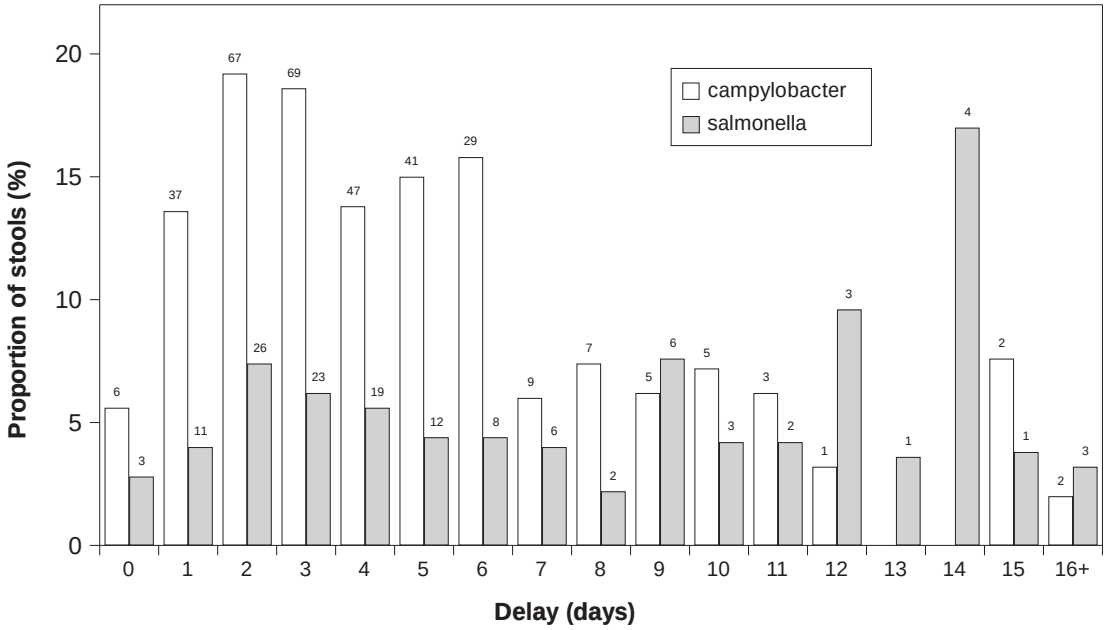
Note. Figures above the bars represent the number of stools positive for the organism

Figure A2.2 Proportion of stools with Rotavirus or SRSV identified by delay between onset of symptoms and receipt of specimen



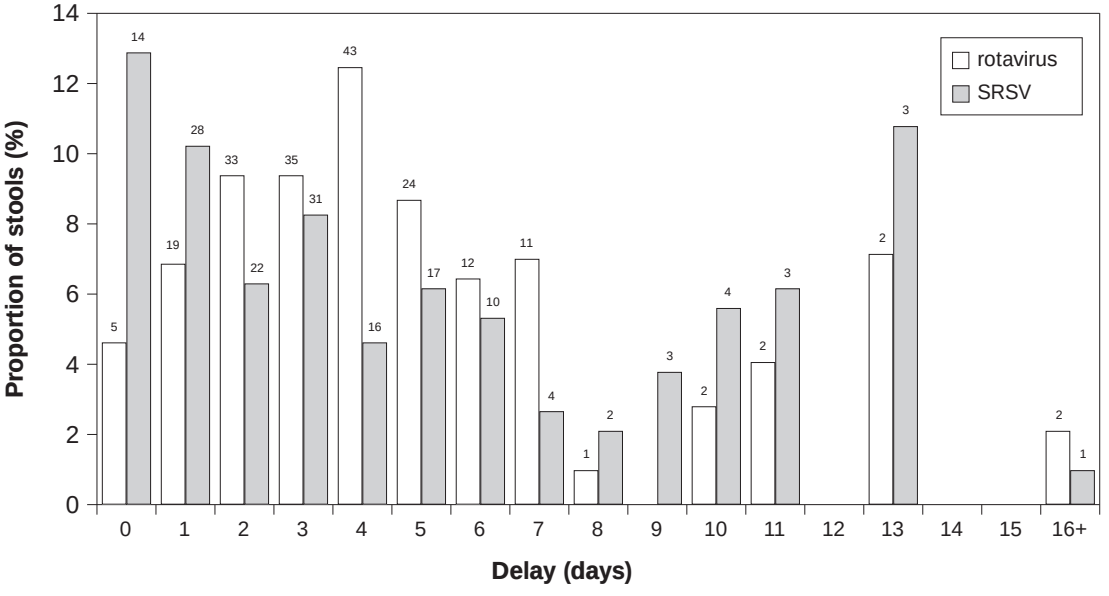
Note. Figures above the bars represent the number of stools positive for the organism

Figure A2.3 Proportion of stools with *Campylobacter* or *Salmonella* identified by delay between onset of symptoms and specimen being taken: GP case-control study



Note. Figures above the bars represent the number of stools positive for the organism

Figure A2.4 Proportion of stools with Rotavirus or SRSV identified by delay between onset of symptoms and specimen being taken: GP case-control study



Note. Figures above the bars represent the number of stools positive for the organism

Figure A2.5 Proportion of stools with *Campylobacter* or *Salmonella* identified by delay between onset of symptoms and receipt of specimen: population cohort study – cases only

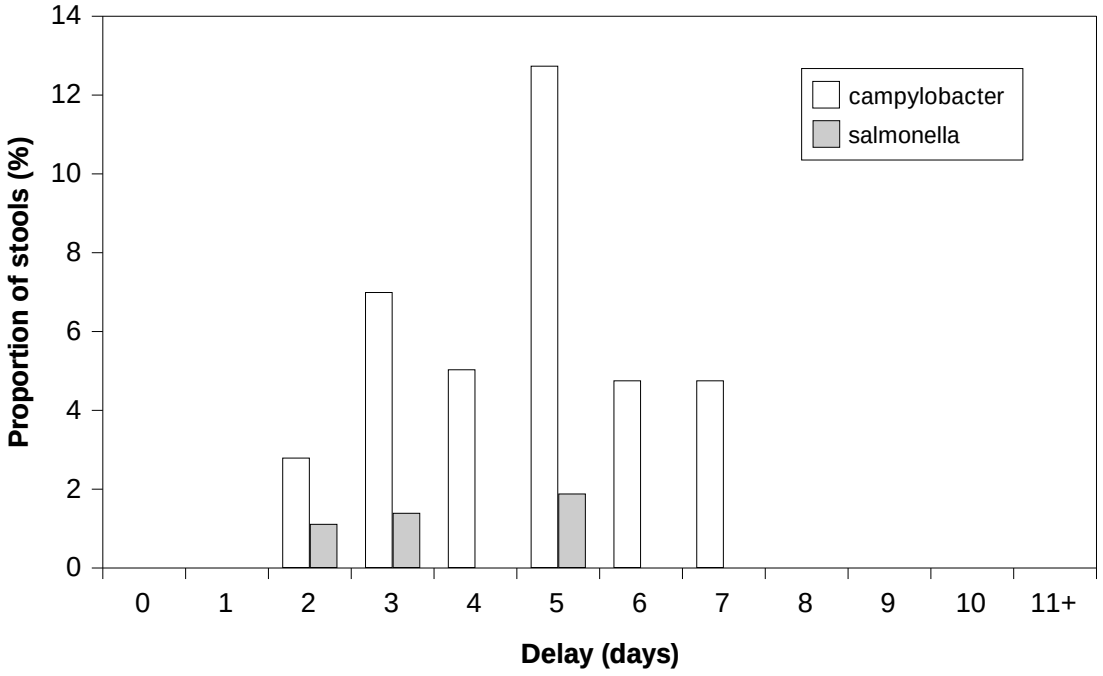


Figure A2.6 Proportion of stools with Rotavirus or SRSV identified by delay between onset of symptoms and receipt of specimen: population cohort study – cases only

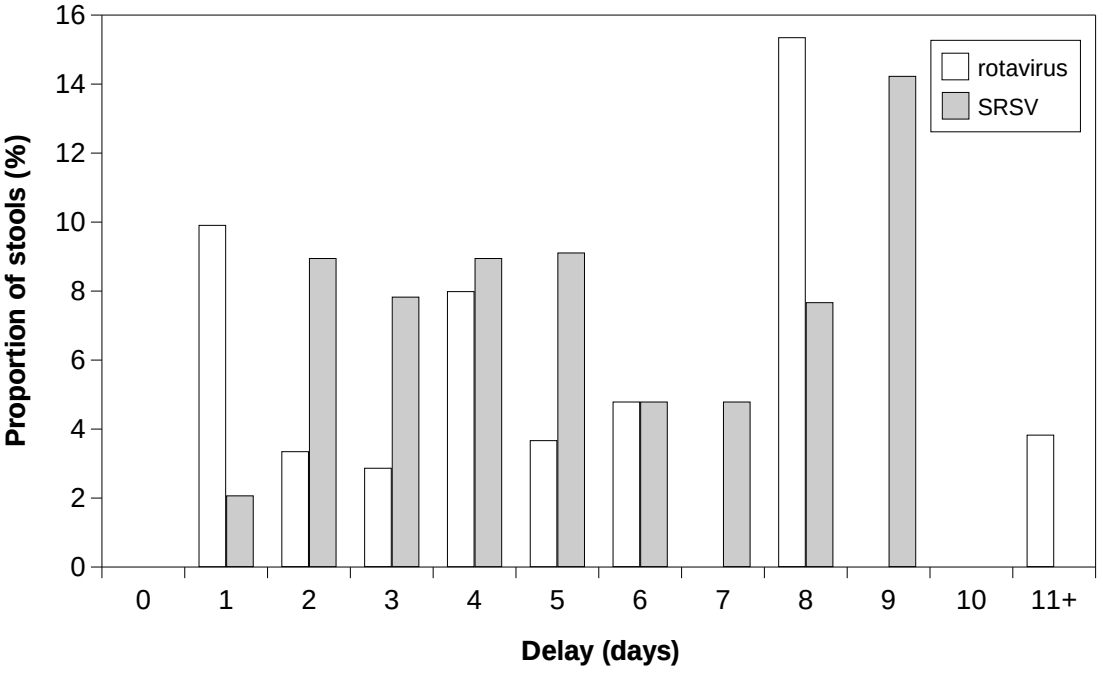


Figure A2.7 Proportion of stools with *Campylobacter* or *Salmonella* identified by delay between onset of symptoms and specimen being taken: population cohort study – cases only

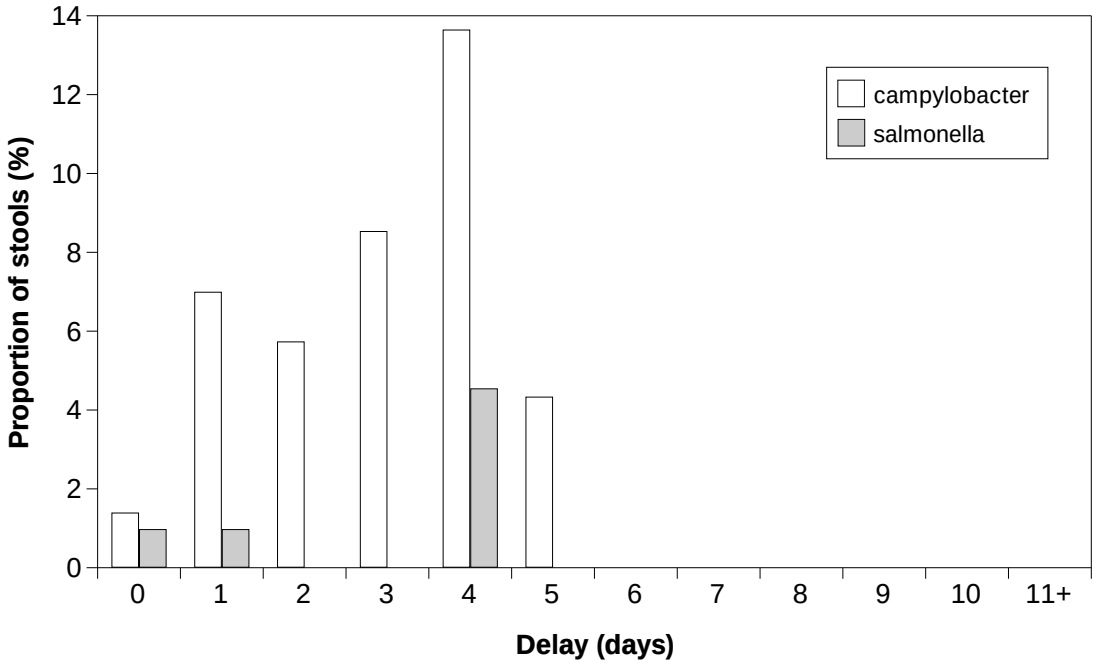


Figure A2.8 Proportion of stools with Rotavirus or SRSV identified by delay between onset of symptoms and receipt of specimen: population cohort study – cases only

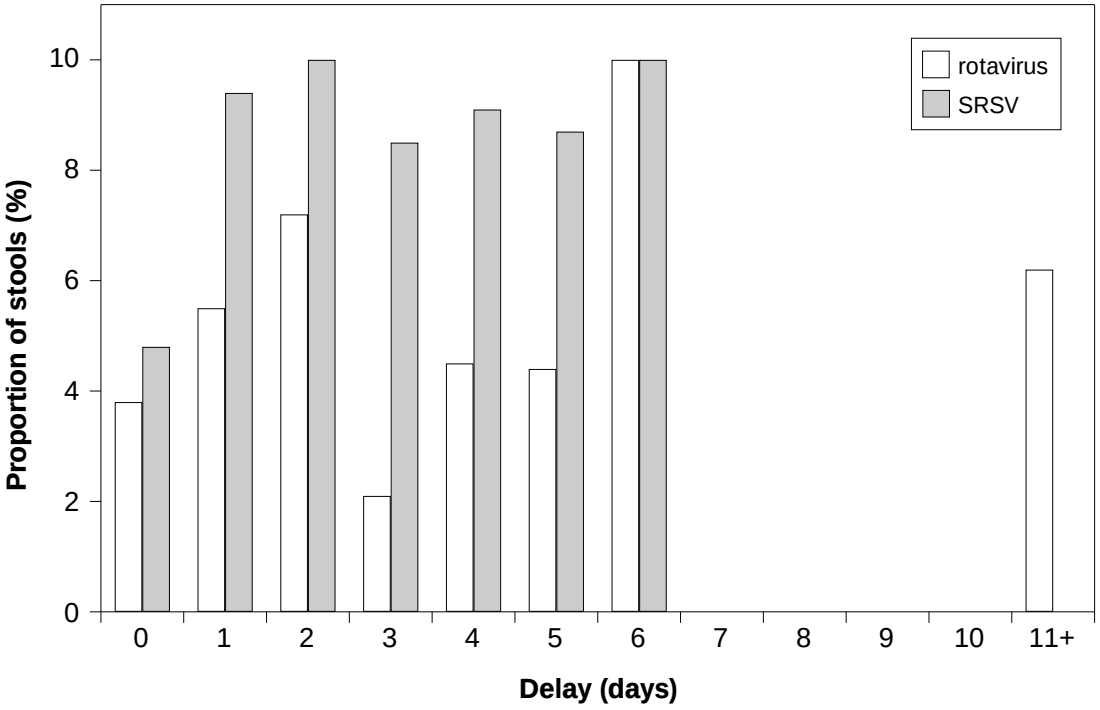
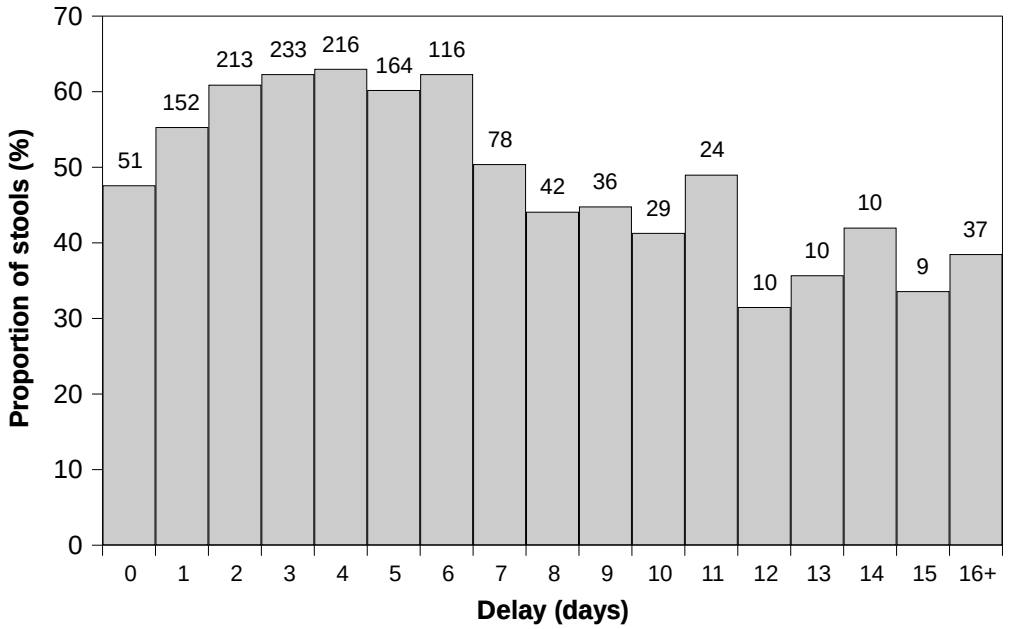


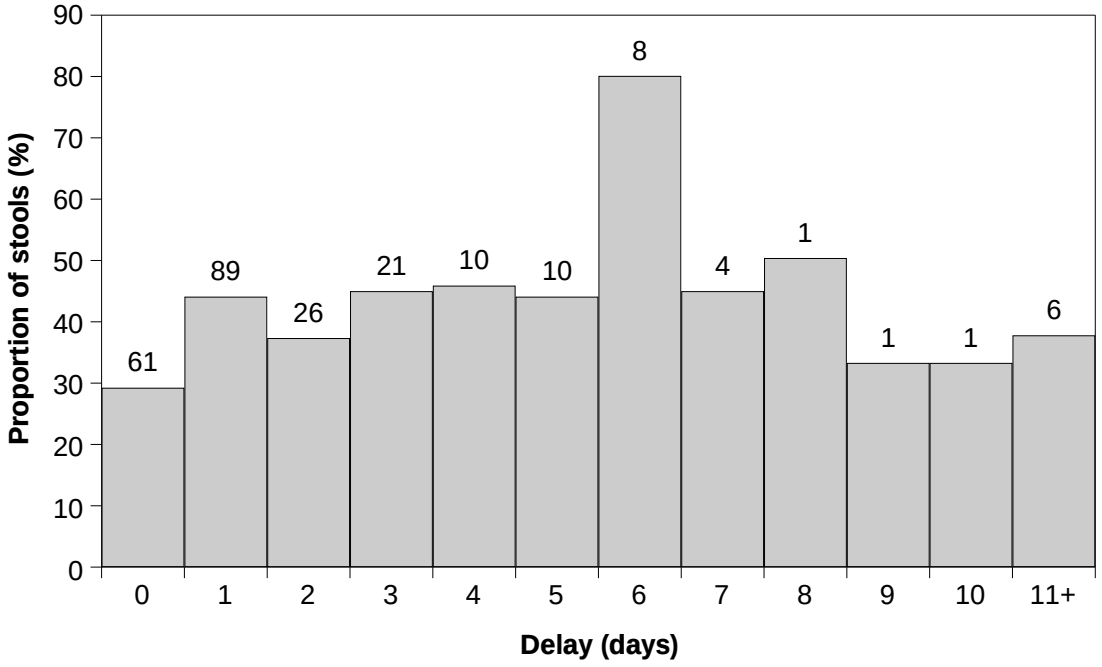
Figure A2.9 Proportion of stools with one or more target organisms by delay between onset of symptoms and specimen being taken: GP case-control component



Note: The delay between onset of symptoms and taking a specimen ranged from 0 to 73 days (median=4 days, mode=3 days). The median delay for both positive and negative stools was 4 days.

Note. Figures above the bars represent the number of stools positive for the organism

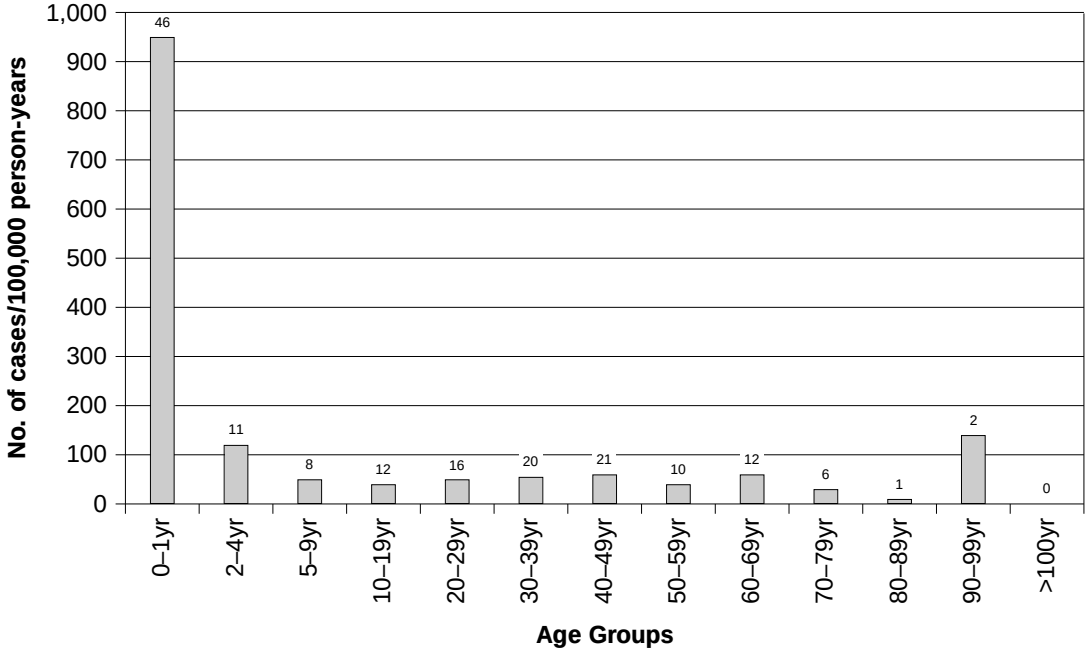
Figure A2.10 Proportion of stools with one or more target organisms by delay between onset of symptoms and specimen being taken: population cohort study – cases only



Note: The delay between onset of symnptoms and taking a specimen ranged from 0 to 22 days (median=1 day, mode=0 day). The median delay for both positive and negative stools was 1 day.

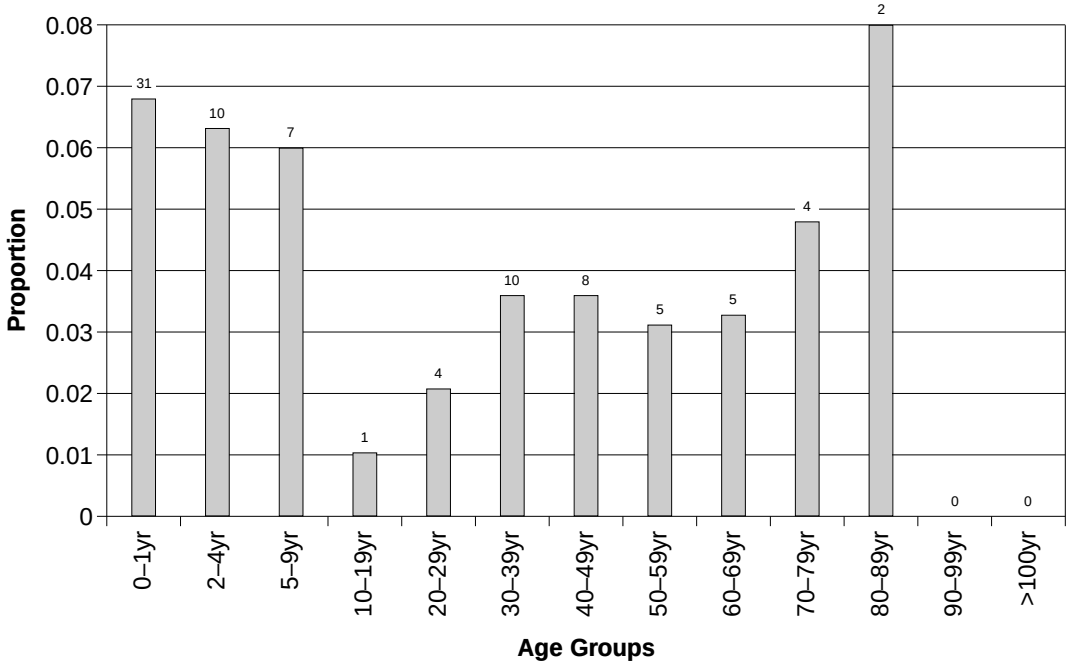
Note. Figures above the bars represent the number of stools positive for the organism

Figure A2.11 Age-specific rates of *Aeromonas* among cases presenting to the GP



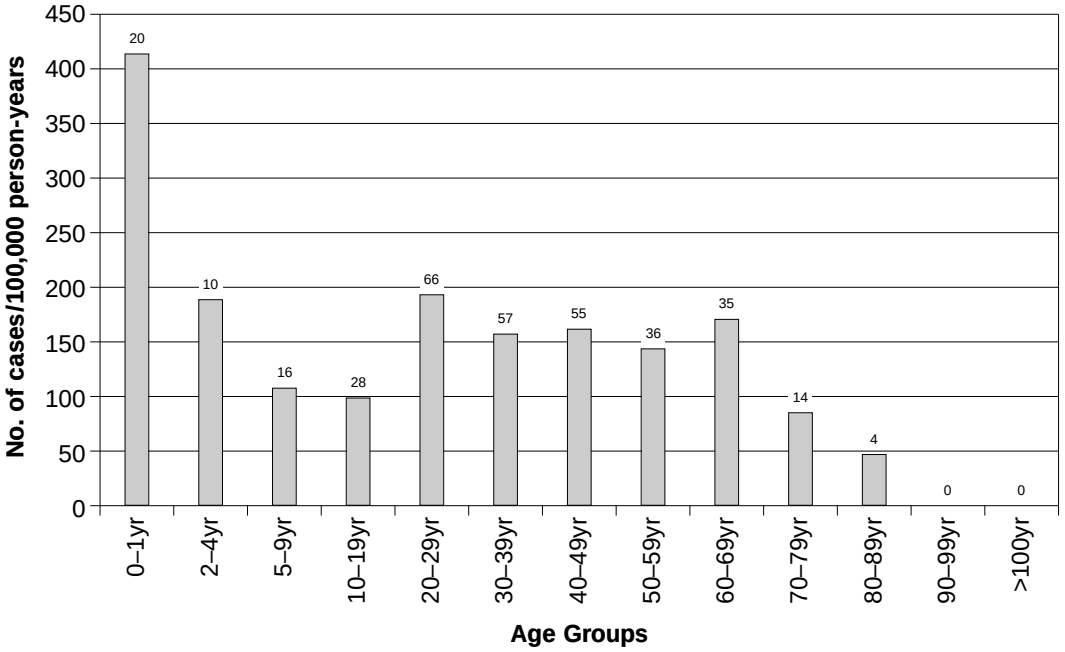
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.12 Age distribution of prevalence of *Aeromonas* among controls



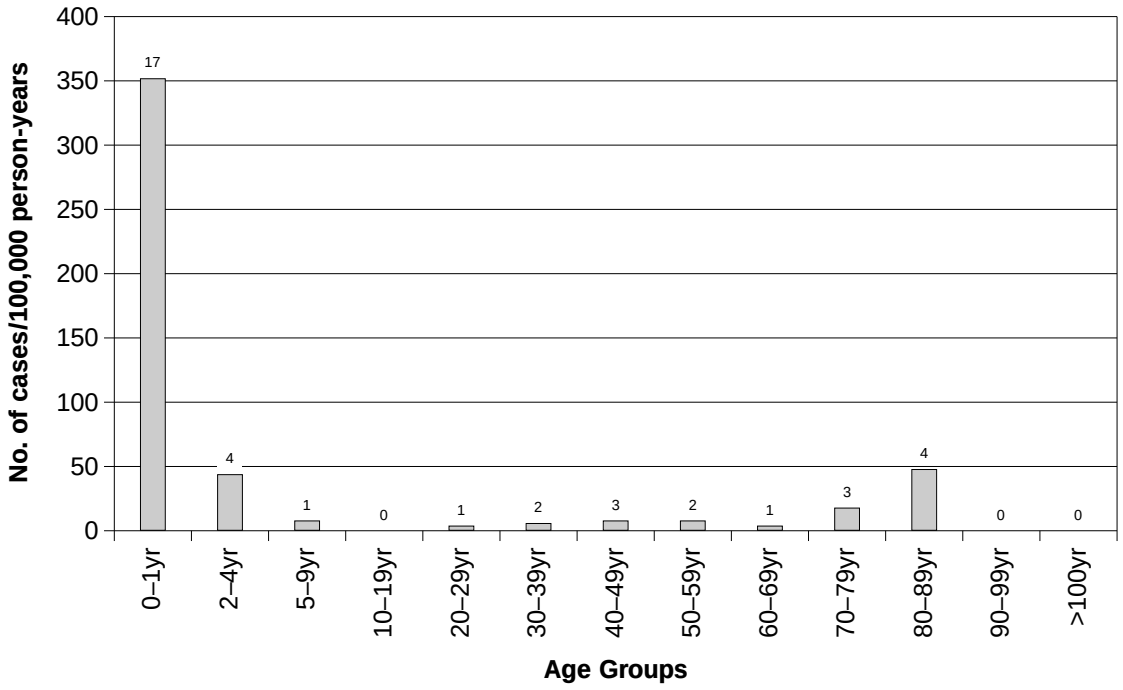
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.13 Age-specific rates of *Campylobacter* among cases presenting to the GP



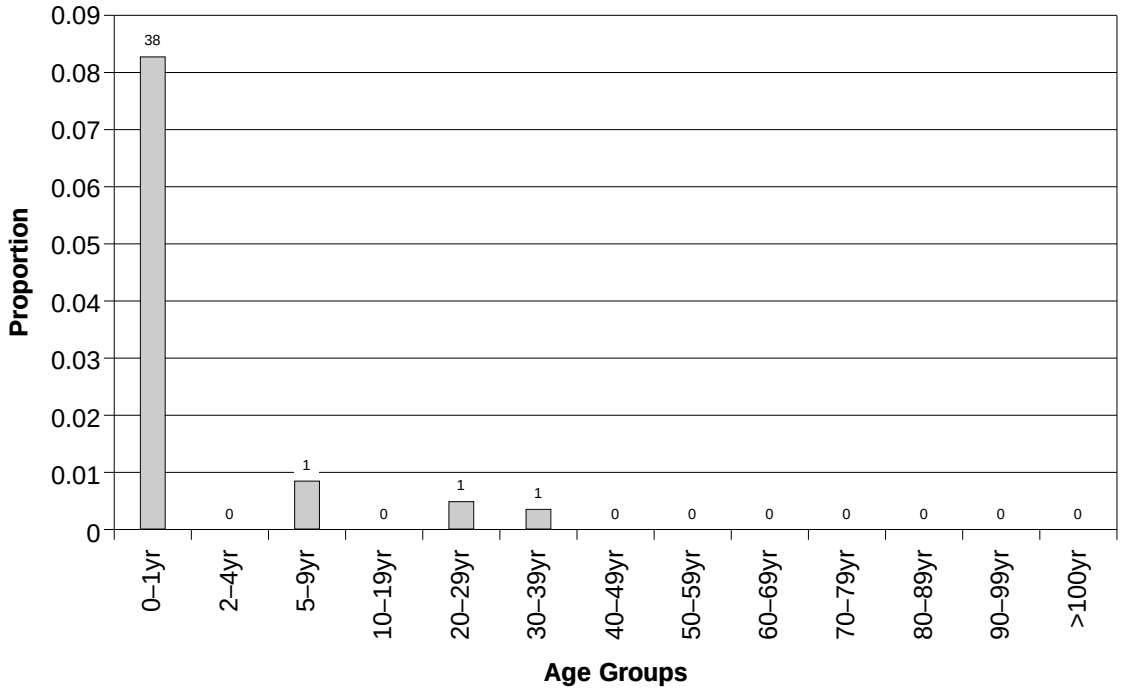
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.14 Age-specific rates of *C.difficile* among cases presenting to the GP



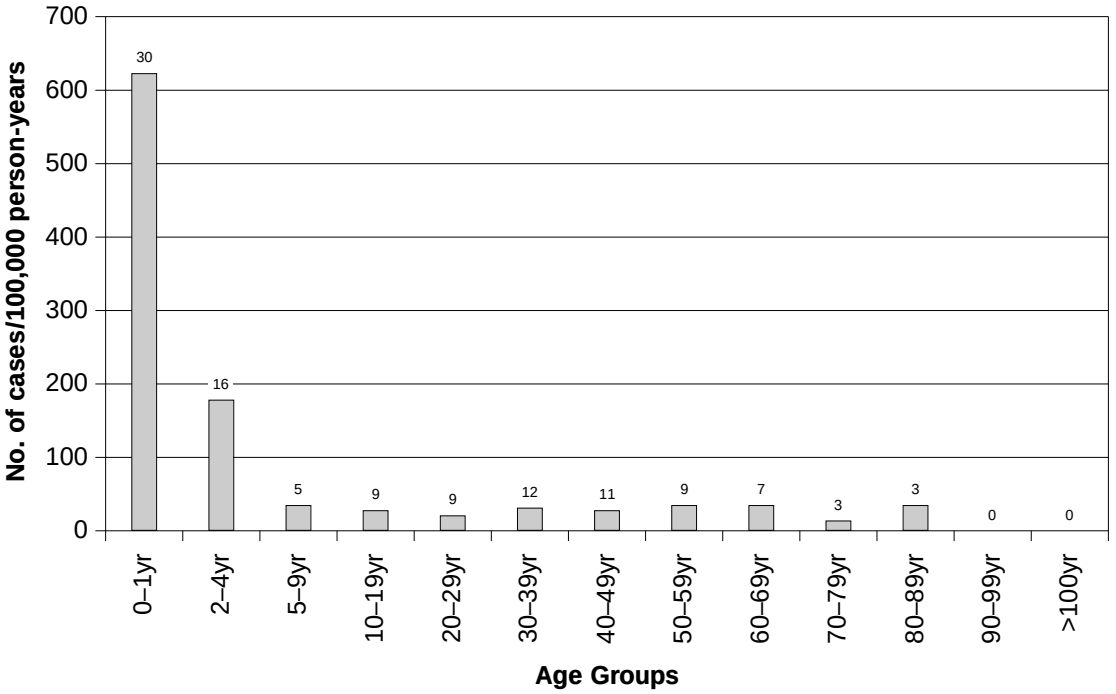
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.15 Age distribution of prevalence of *C.difficile* among controls



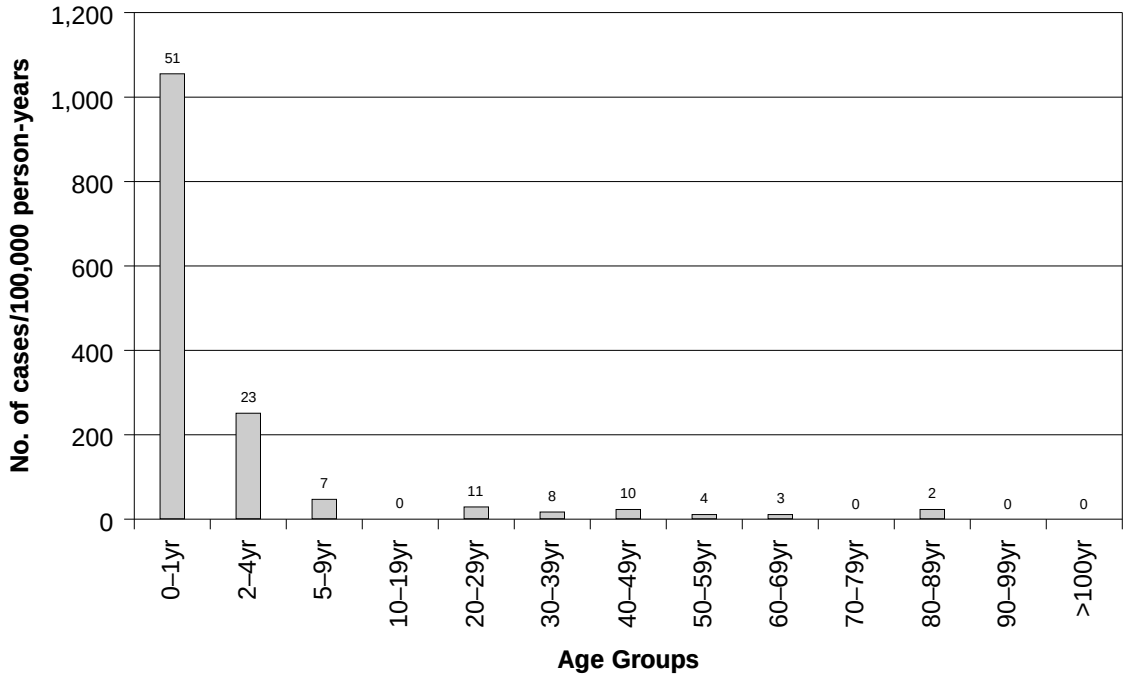
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.16 Age-specific rates of *C.perfringens* among cases presenting to the GP



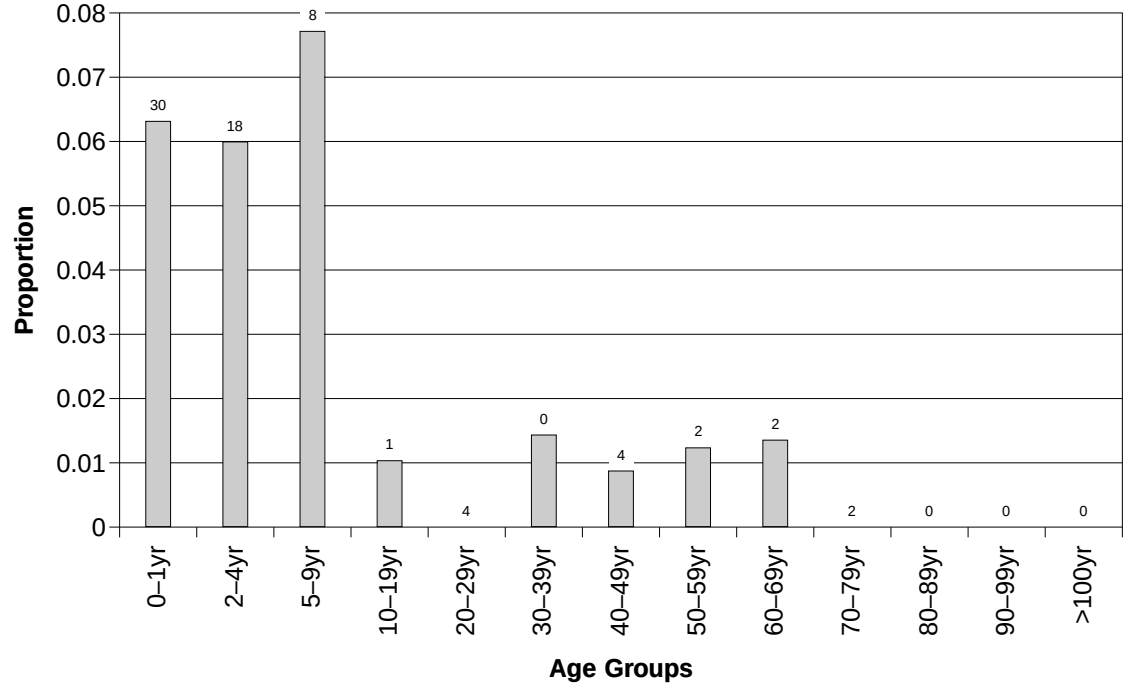
Note. Figures above the bars represent the number of cases/controls per age group. There were only 15 isolates of *C.perfringens* in controls

Figure A2.17 Age-specific rates of AEEC among cases presenting to the GP



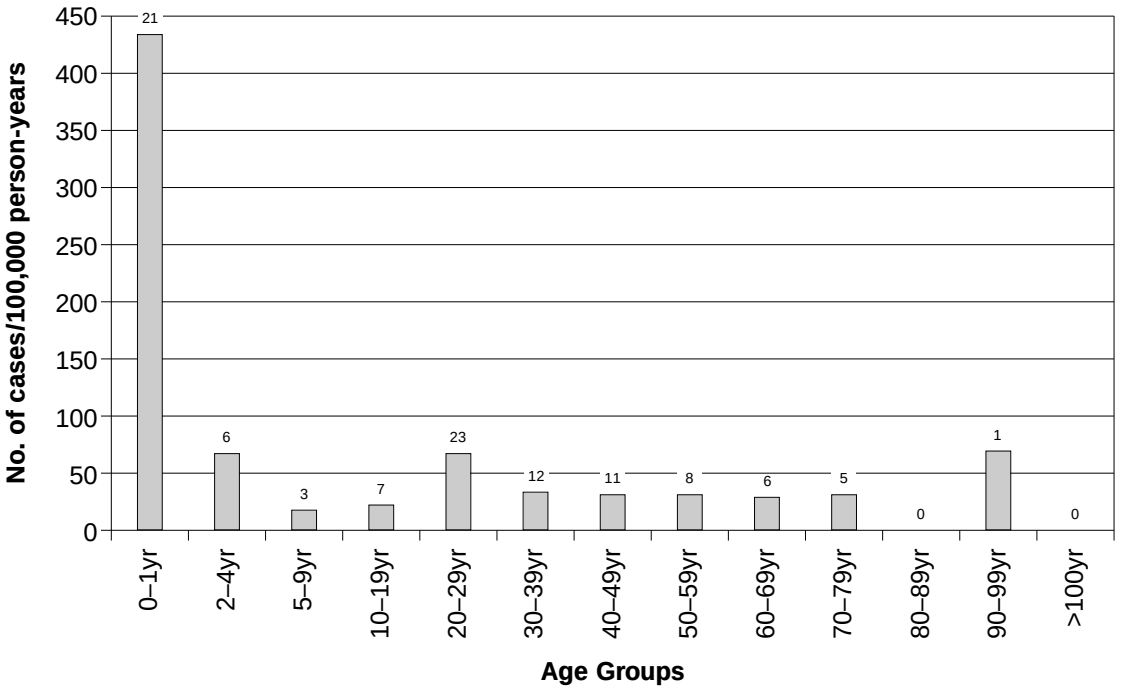
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.18 Age distribution of prevalence of AEEC among controls



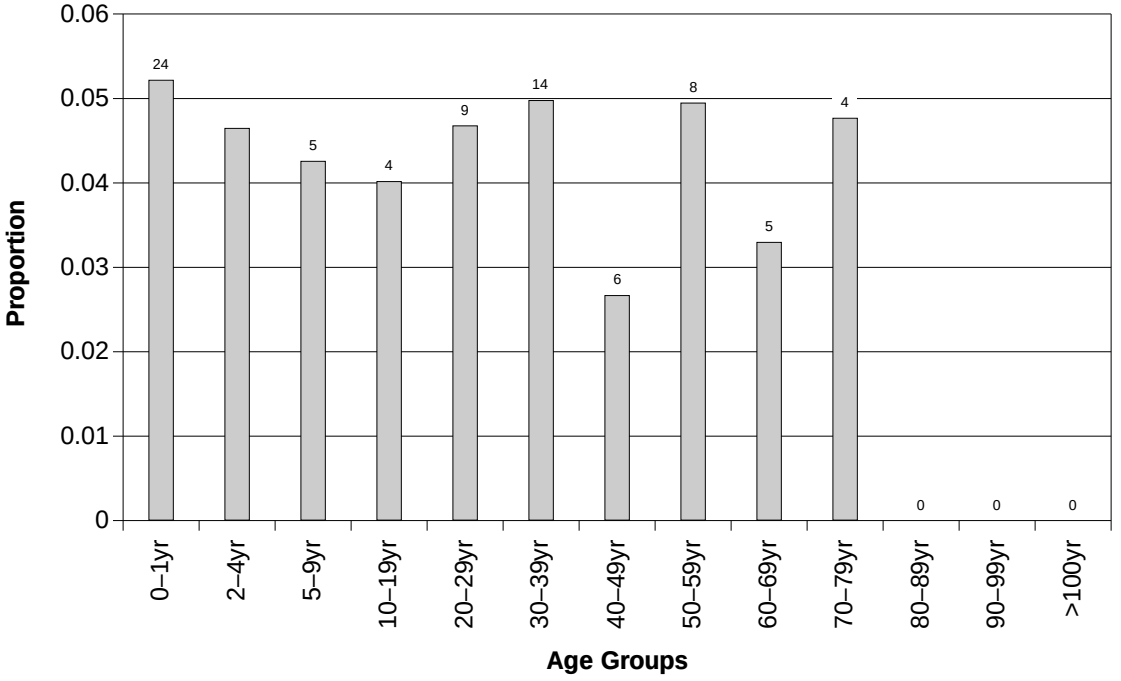
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.19 Age-specific rates of DAEC among cases presenting to the GP



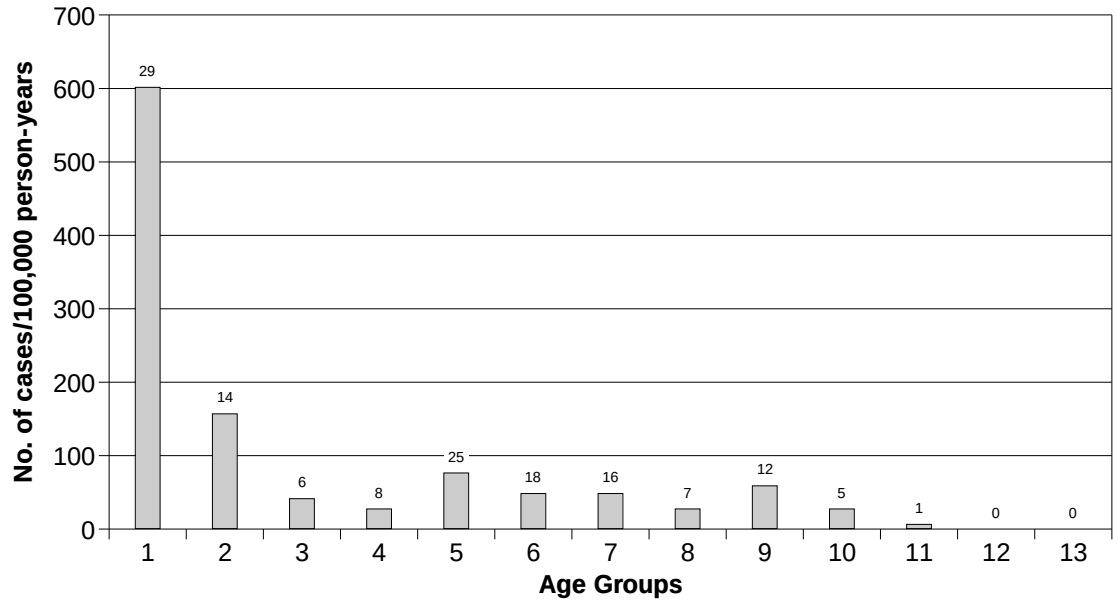
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.20 Age distribution of prevalence of DAEC among controls



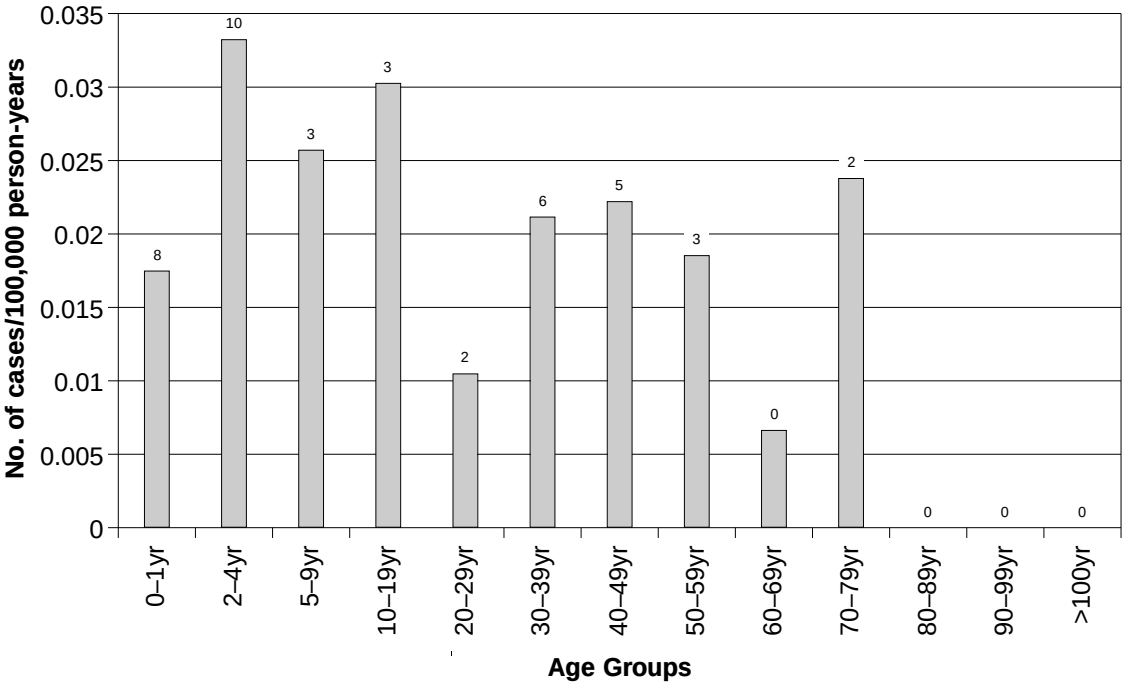
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.21 Age-specific rates of EAggEC among cases presenting to the GP



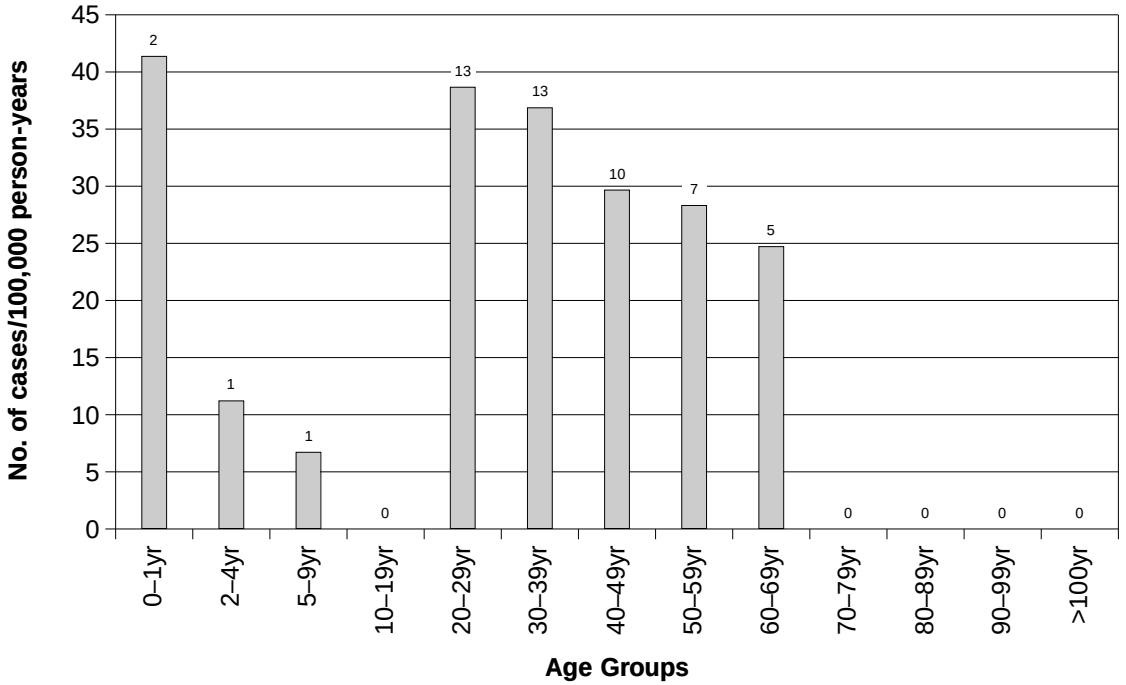
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.22 Age distribution of prevalence of EAggEC among controls



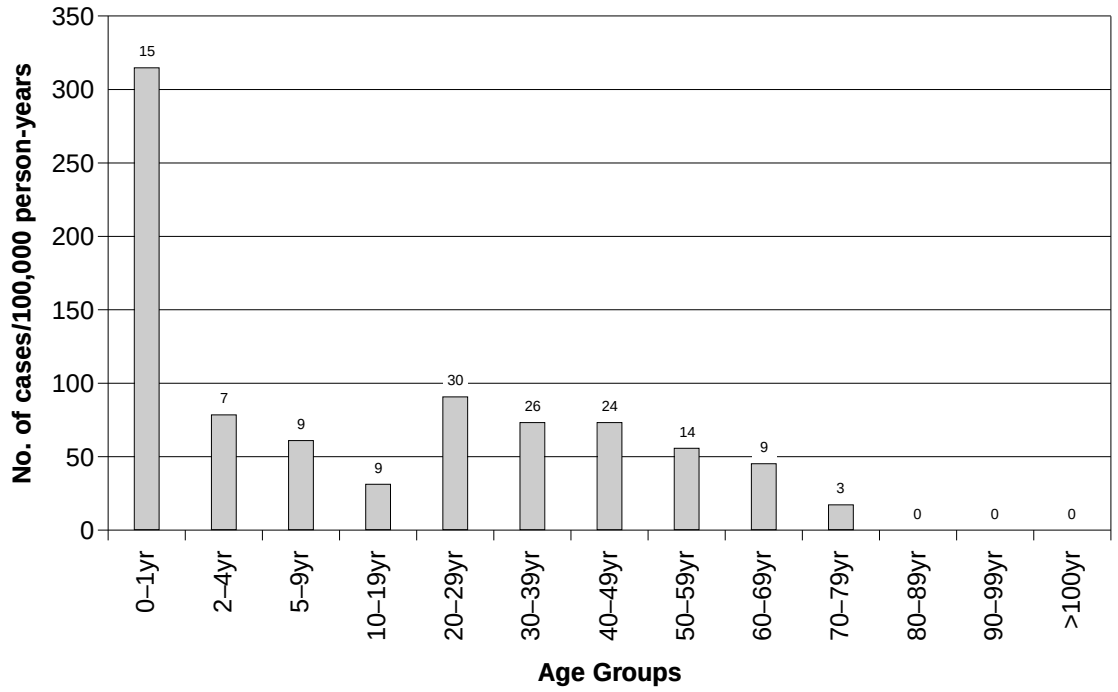
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.23 Age-specific rates of ETEC among cases presenting to the GP



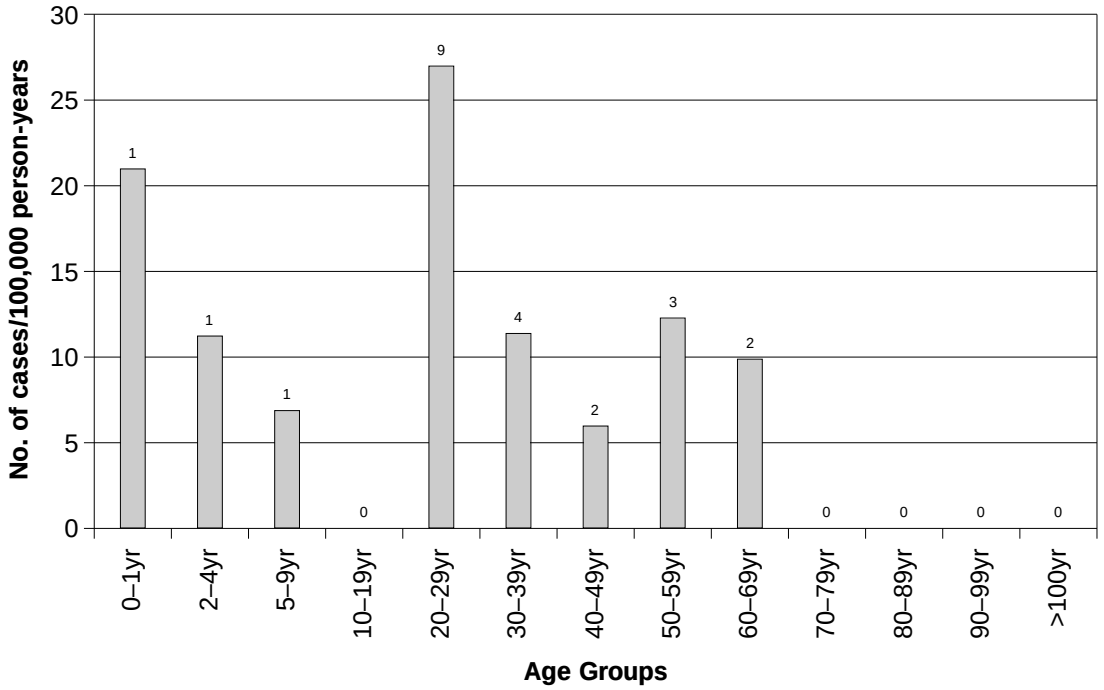
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.24 Age-specific rates of *Salmonella* among cases presenting to the GP



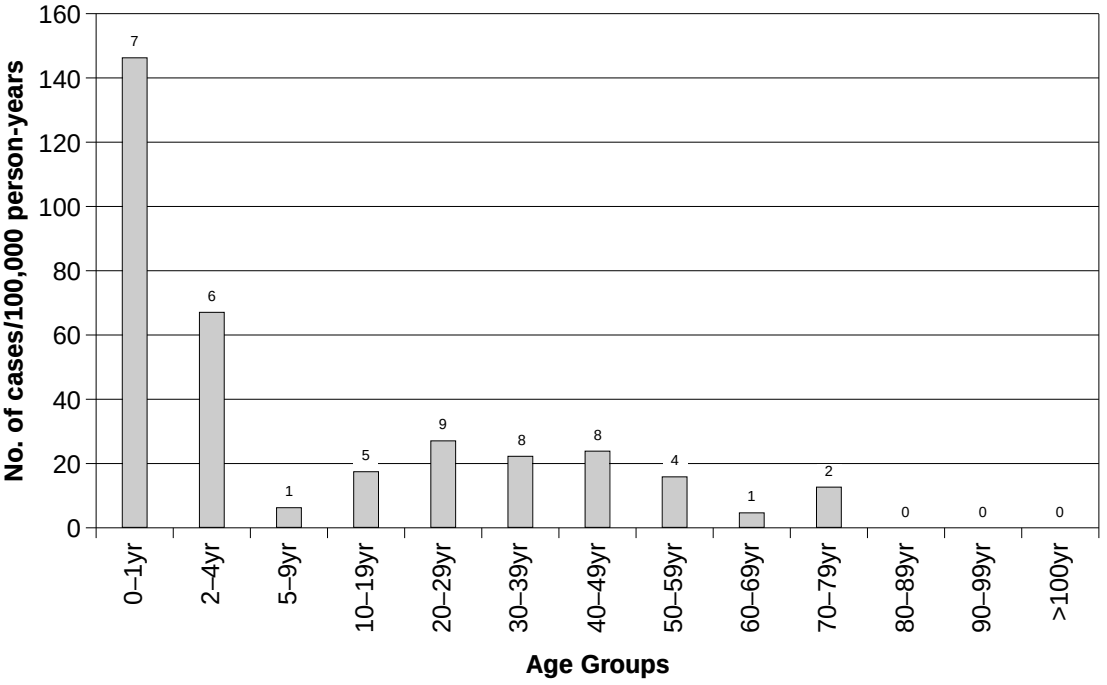
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.25 Age-specific rates of *Shigella* among cases presenting to the GP



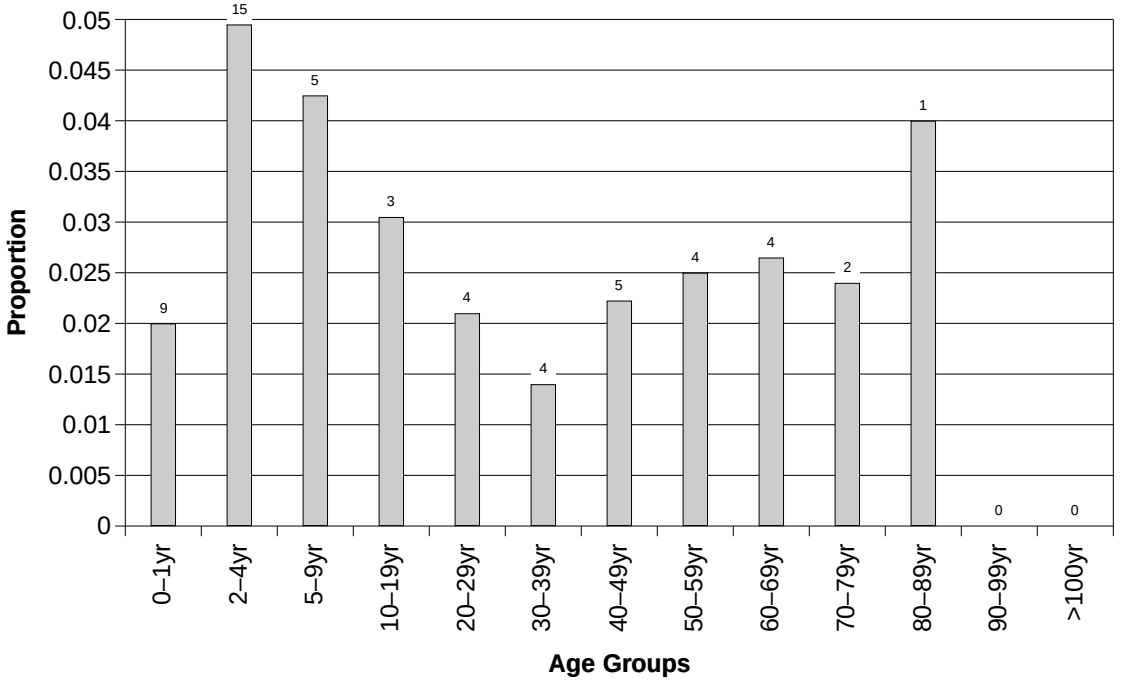
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.26 Age-specific rates of *Yersinia* among cases presenting to the GP



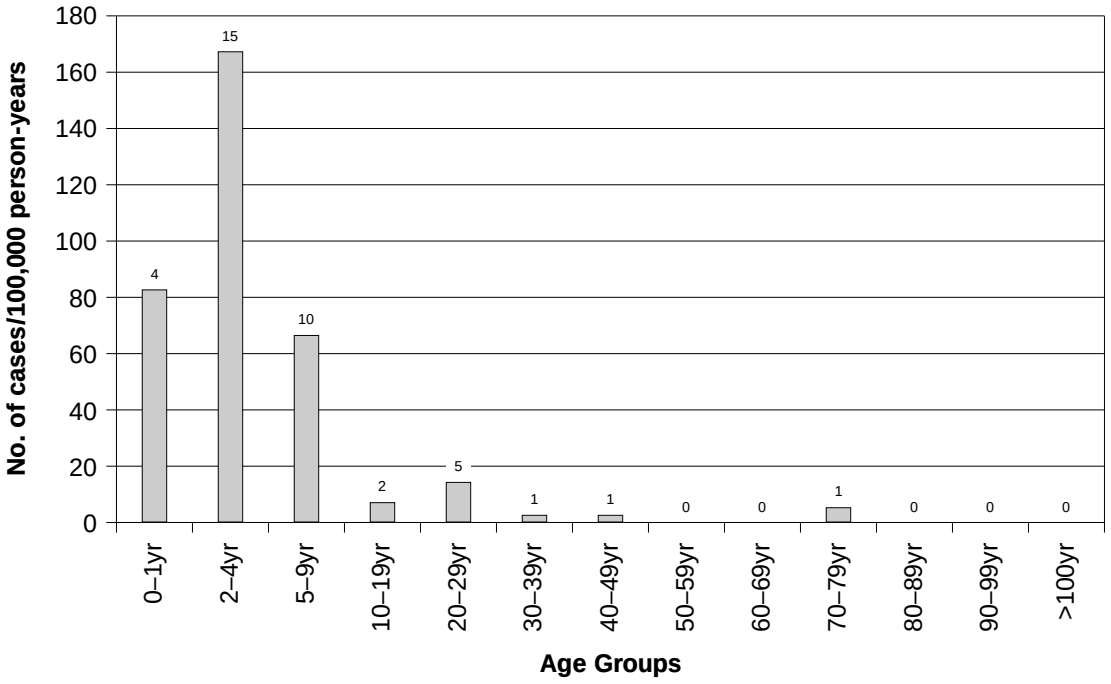
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.27 Age distribution of prevalence of *Yersinia* among controls



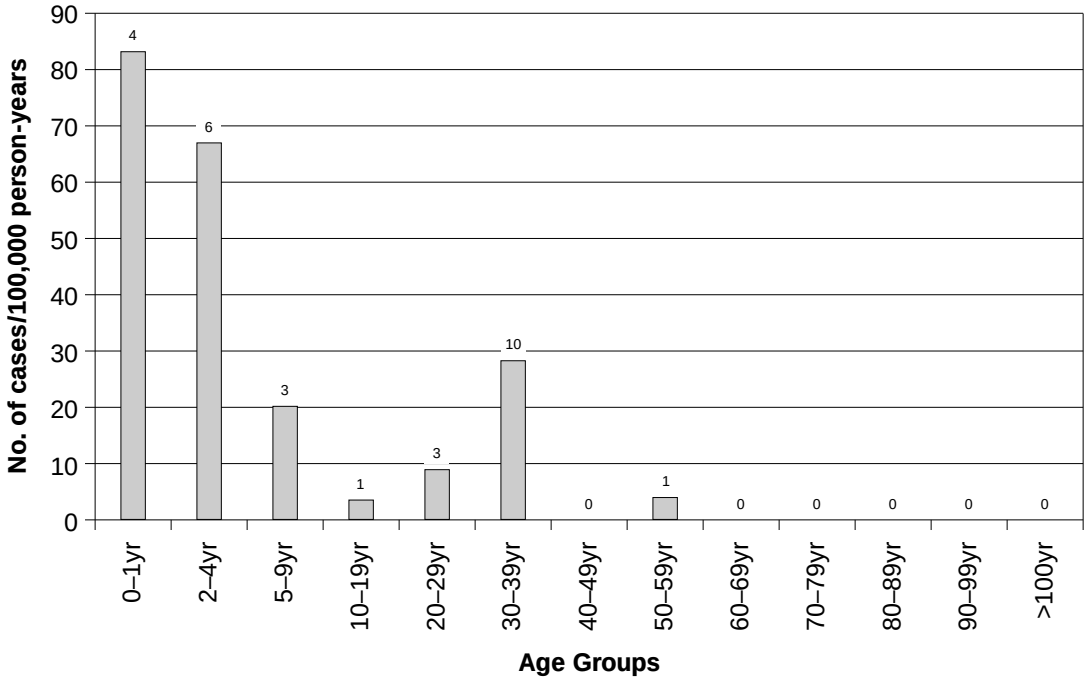
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.28 Age-specific rates of *Cryptosporidium* among cases presenting to the GP



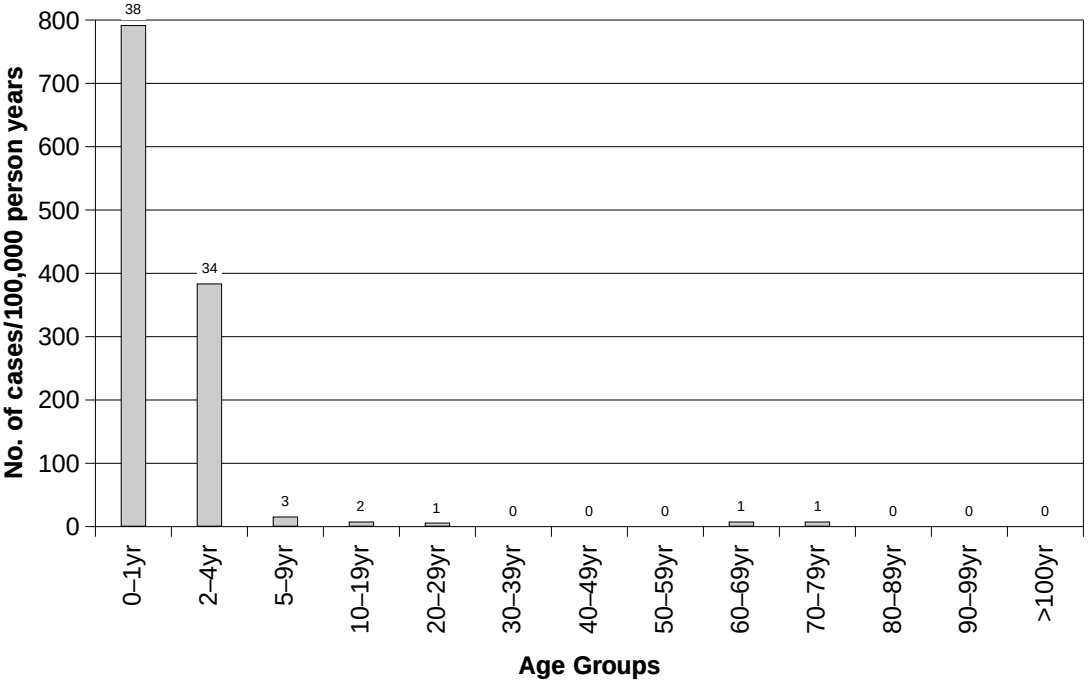
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.29 Age-specific rates of *Giardia* among cases presenting to the GP



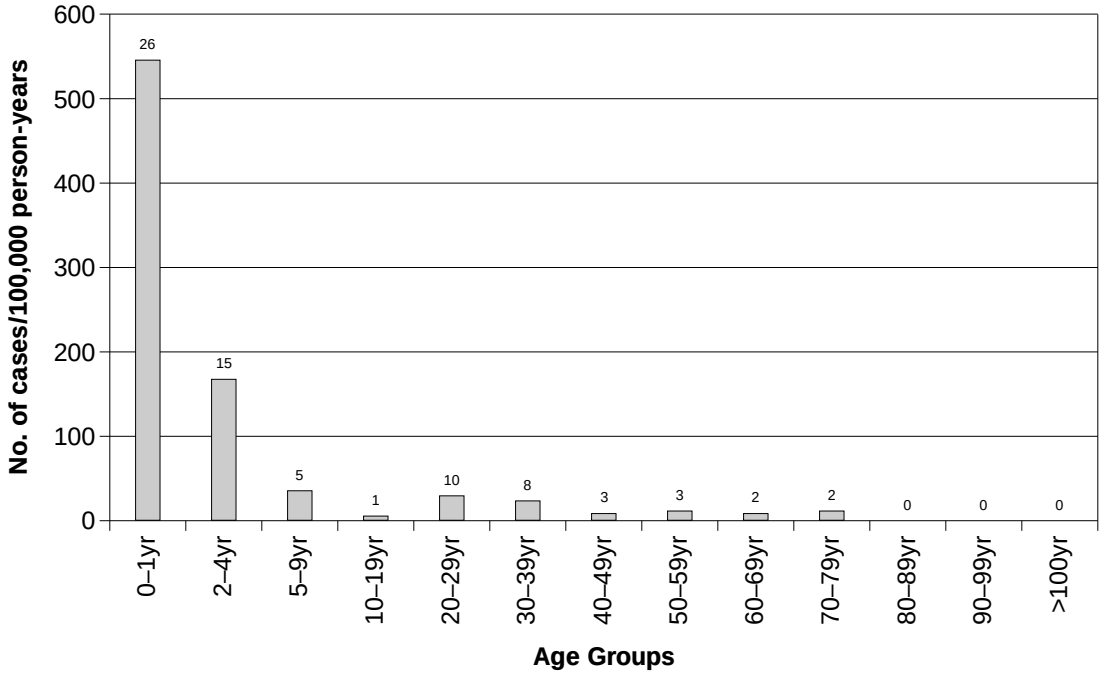
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.30 Age-specific rates of Adenovirus types 40, 41 among cases presenting to the GP



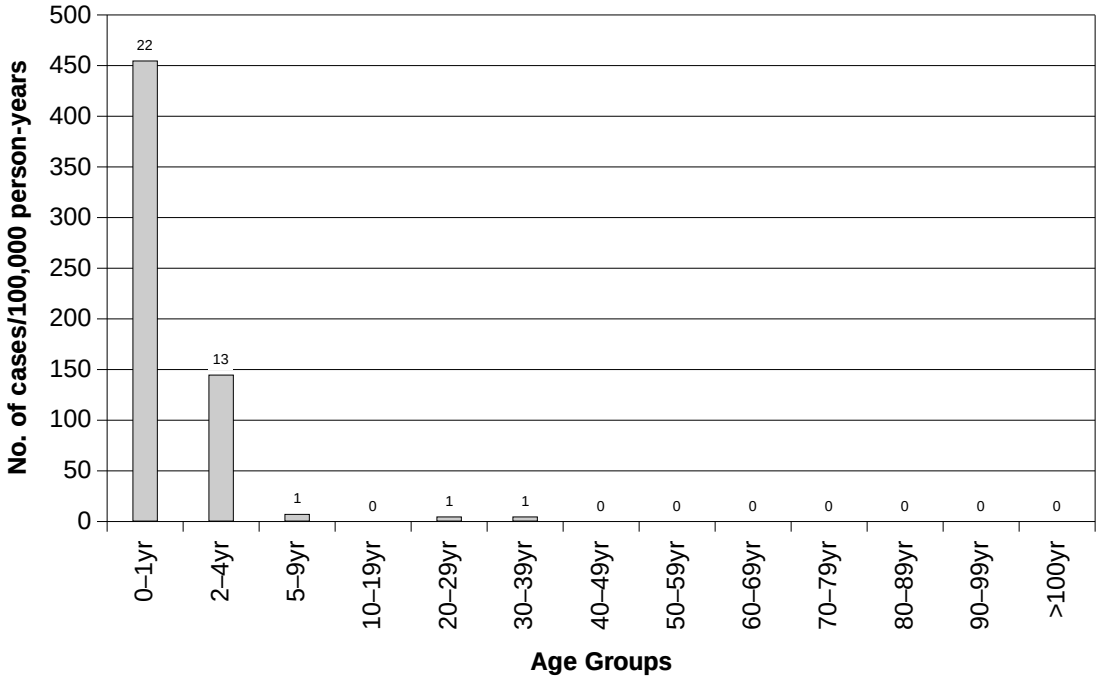
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.31 Age-specific rates of Astrovirus among cases presenting to the GP



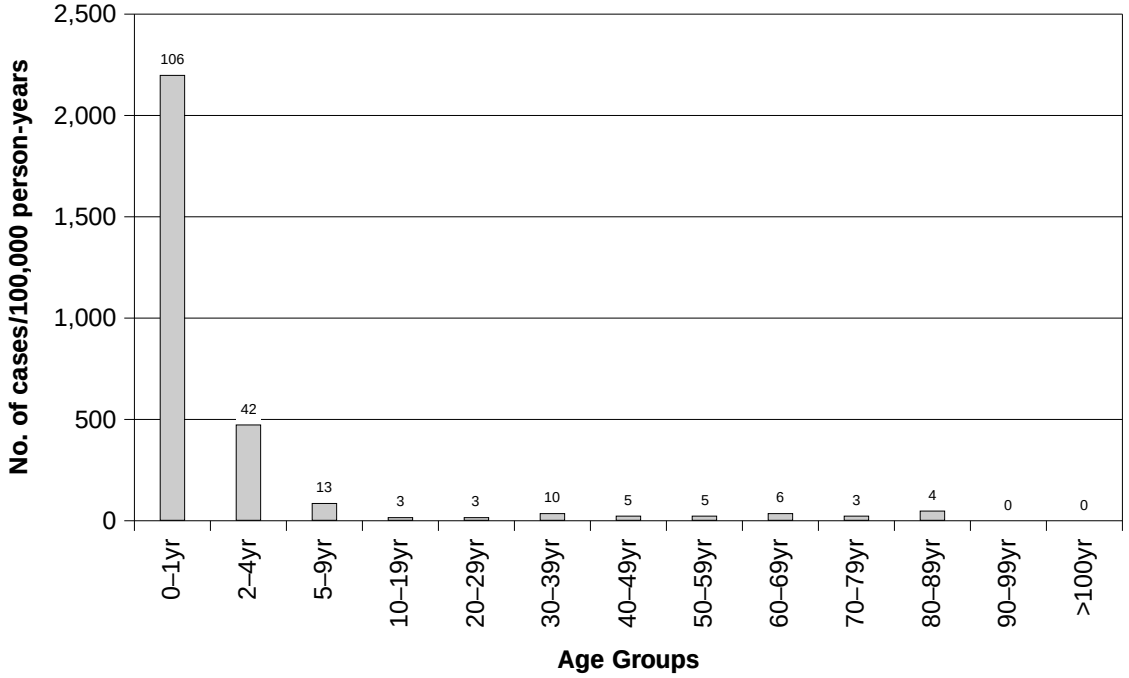
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.32 Age-specific rates of Calicivirus among cases presenting to the GP



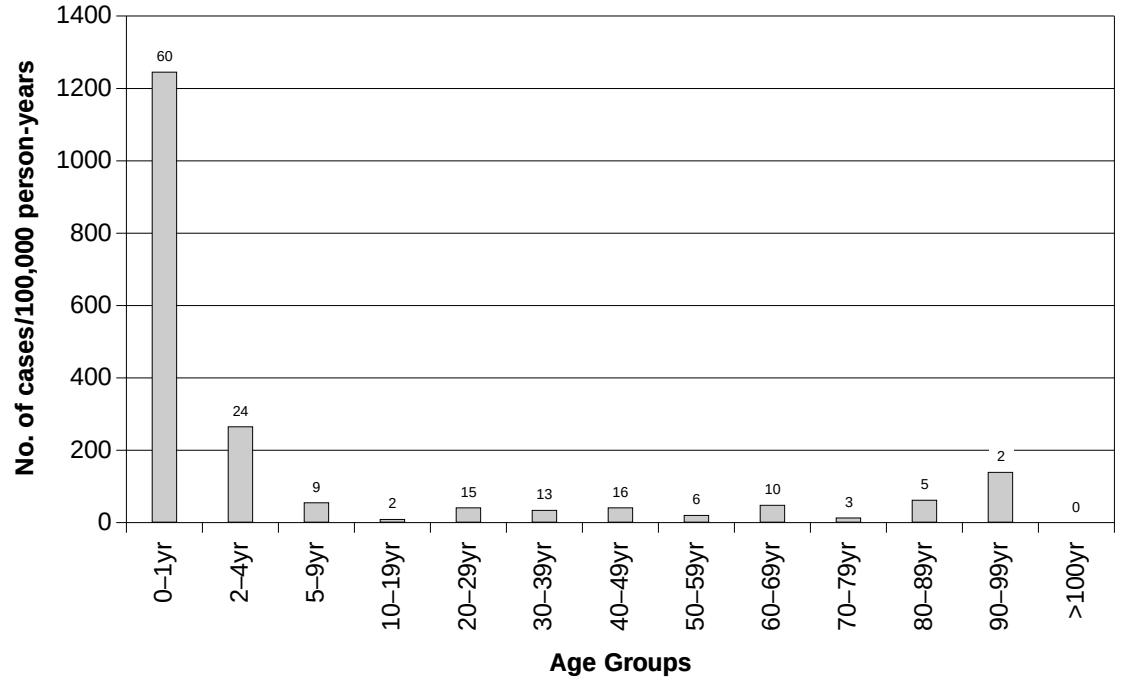
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.33 Age-specific rates of Rotavirus among cases presenting to the GP



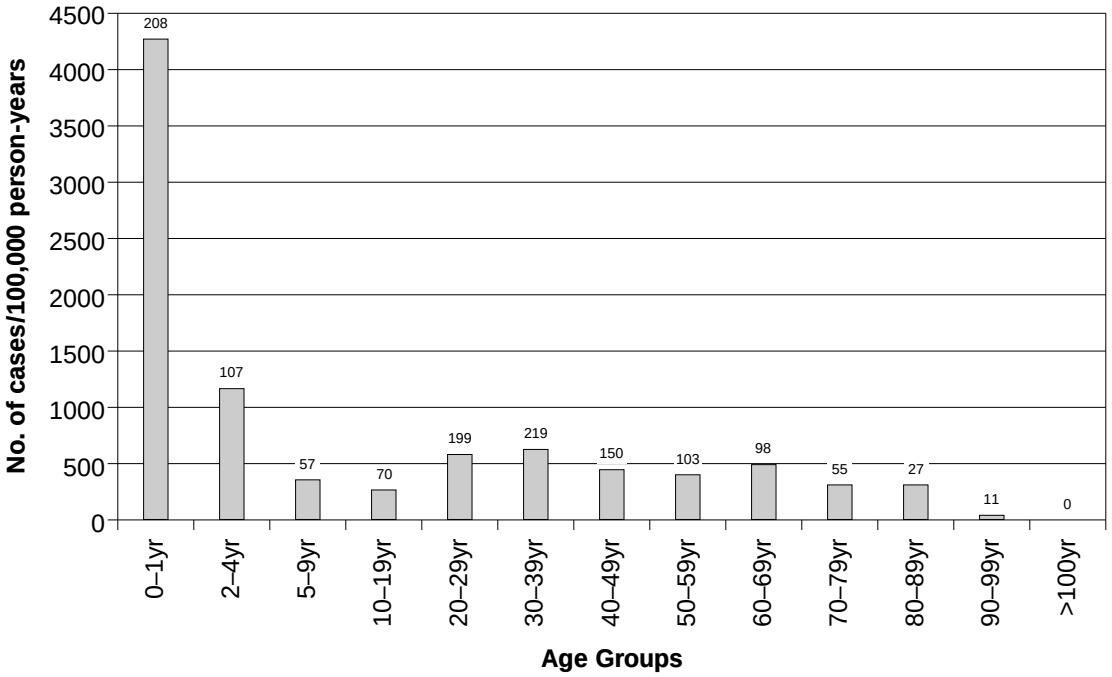
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.34 Age-specific rates of SRSV among cases presenting to the GP



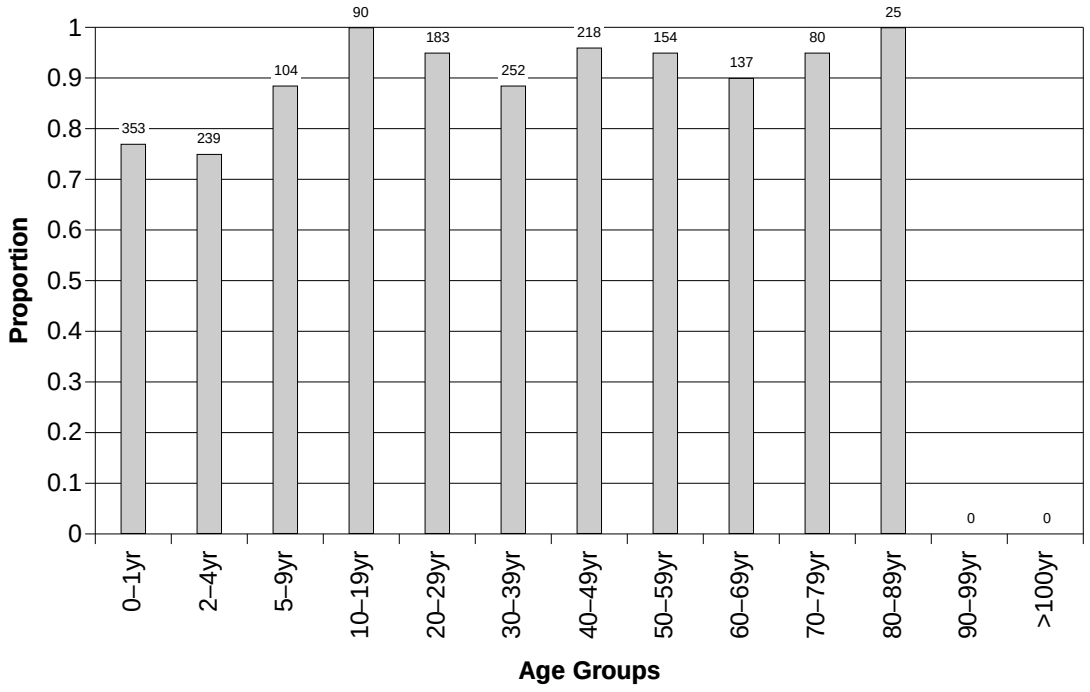
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.35 Age-specific rates among cases with no positive organism presenting to the GP



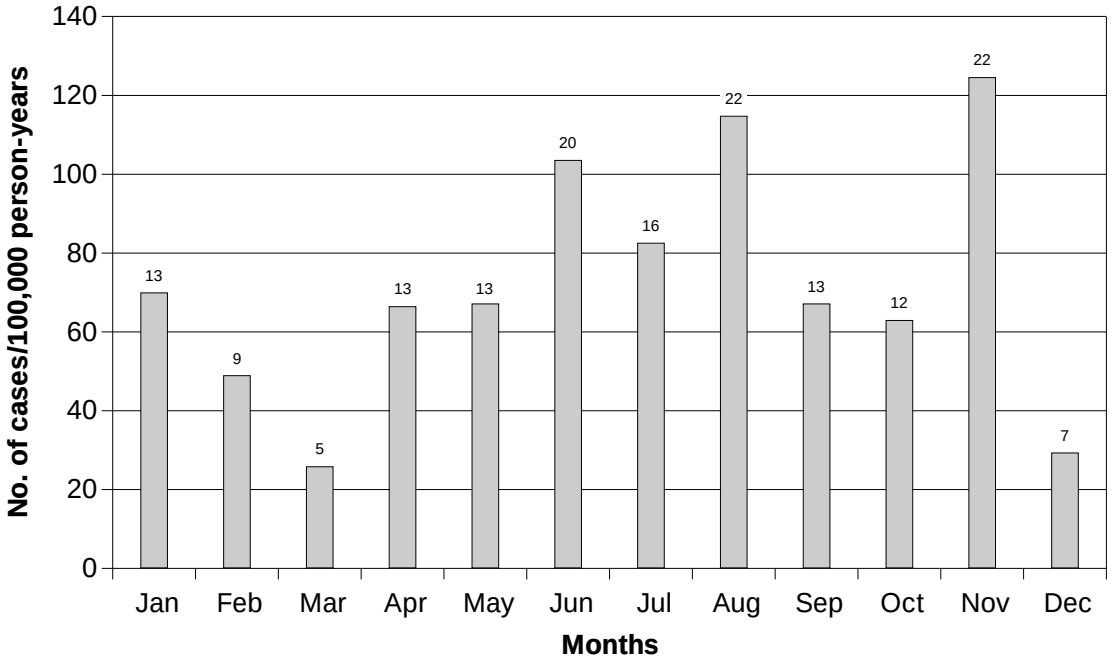
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.36 Age distribution of prevalence of controls with no positive organism



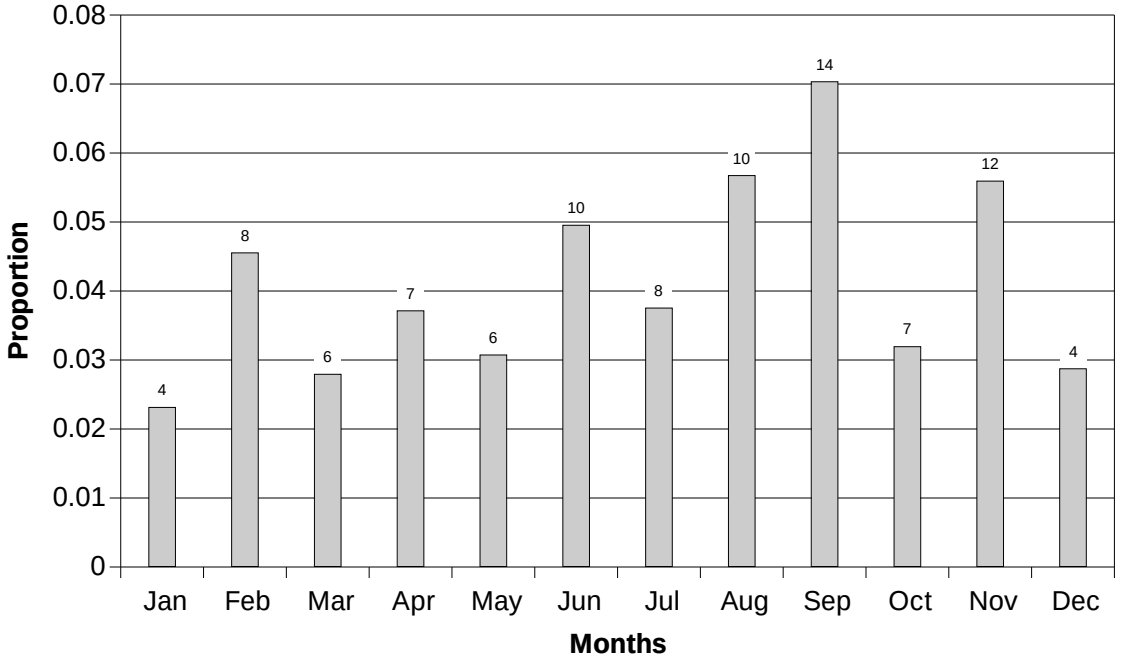
Note. Figures above the bars represent the number of cases/controls per age group.

Figure A2.37 Seasonal distribution of *Aeromonas* among cases presenting to the GP



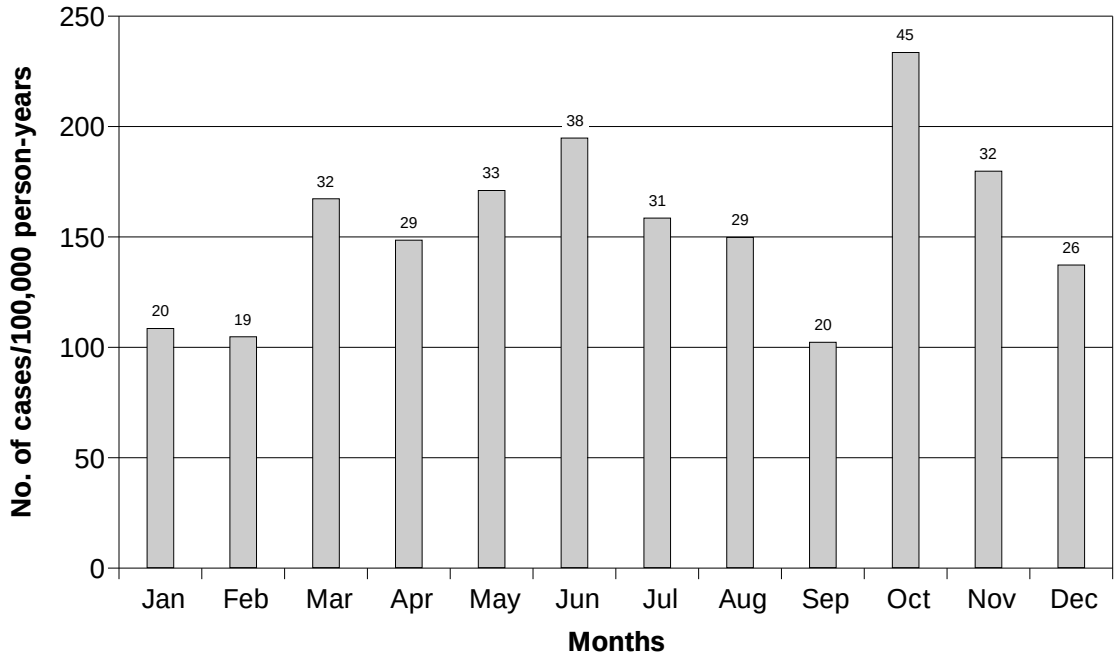
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.38 Seasonality of prevalence of *Aeromonas* among controls



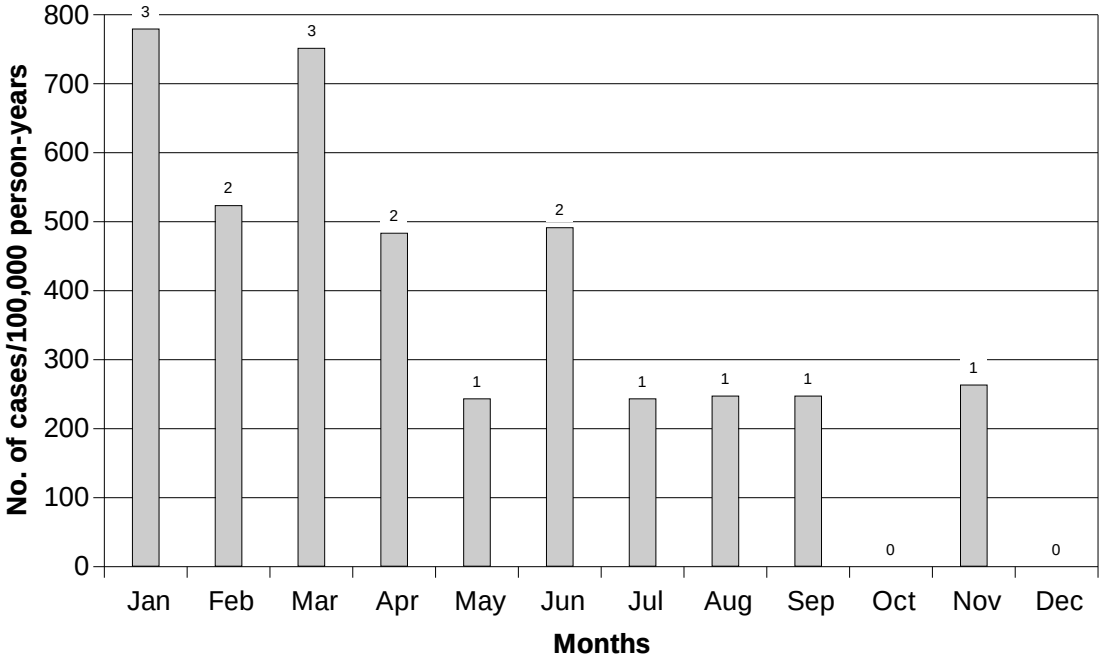
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.39 Seasonal distribution of *Campylobacter* among cases presenting to the GP



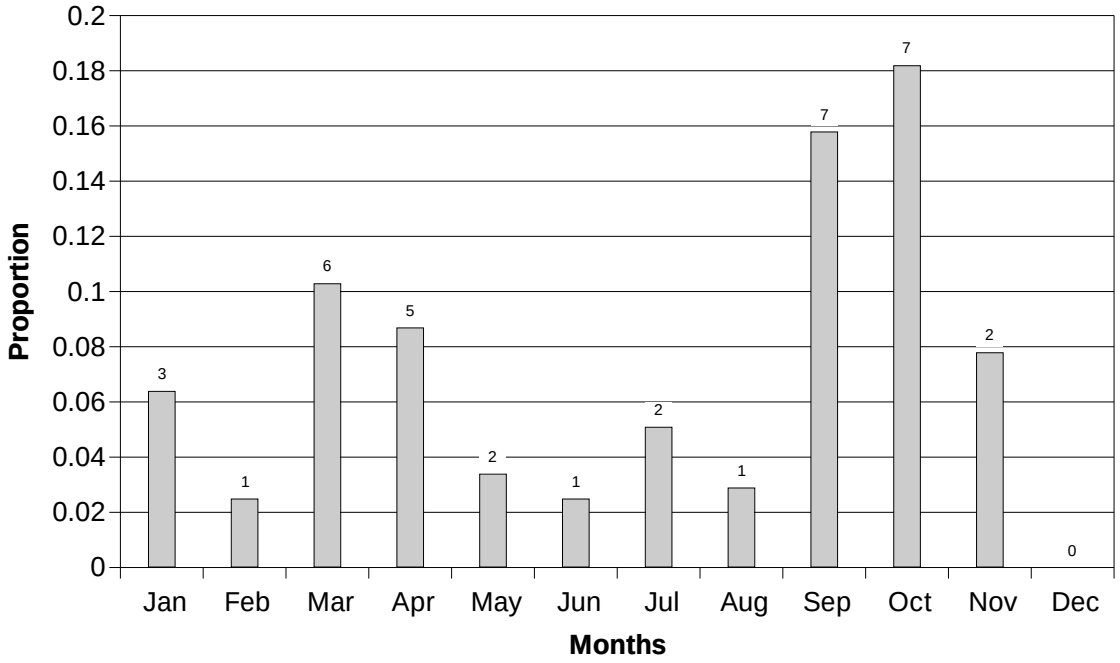
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.40 Seasonality distribution of *C.difficile* among cases age <2 years, presenting to the GP



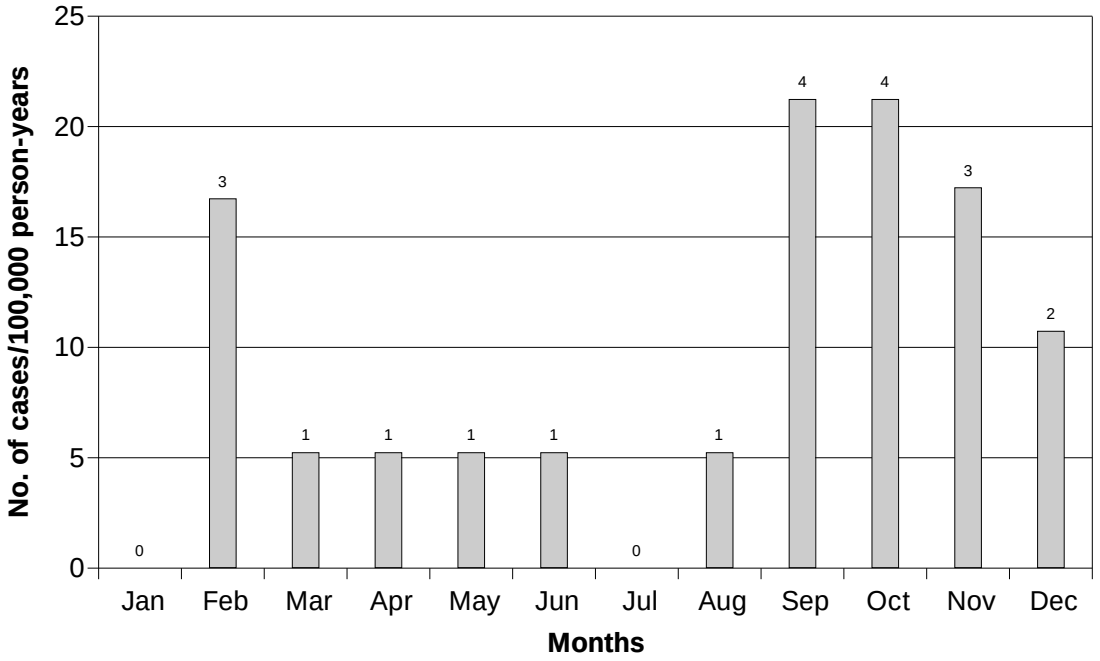
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.41 Seasonality of prevalence of *C.difficile* among controls age <2 years



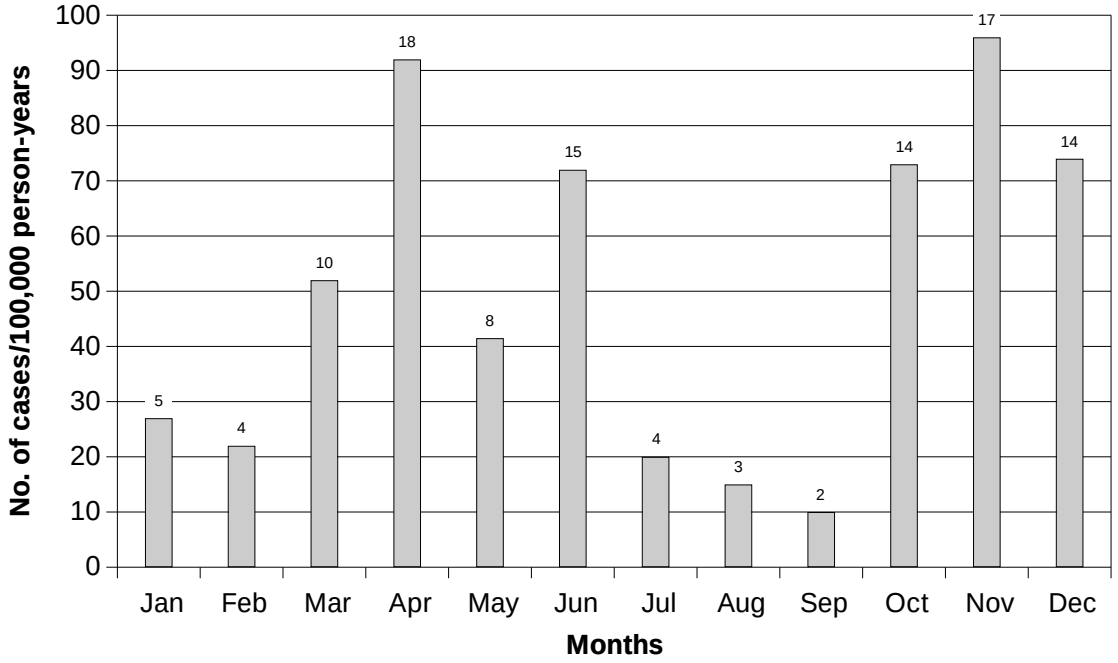
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.42 Seasonality distribution of *C.difficile* among cases age >2 years, presenting to the GP



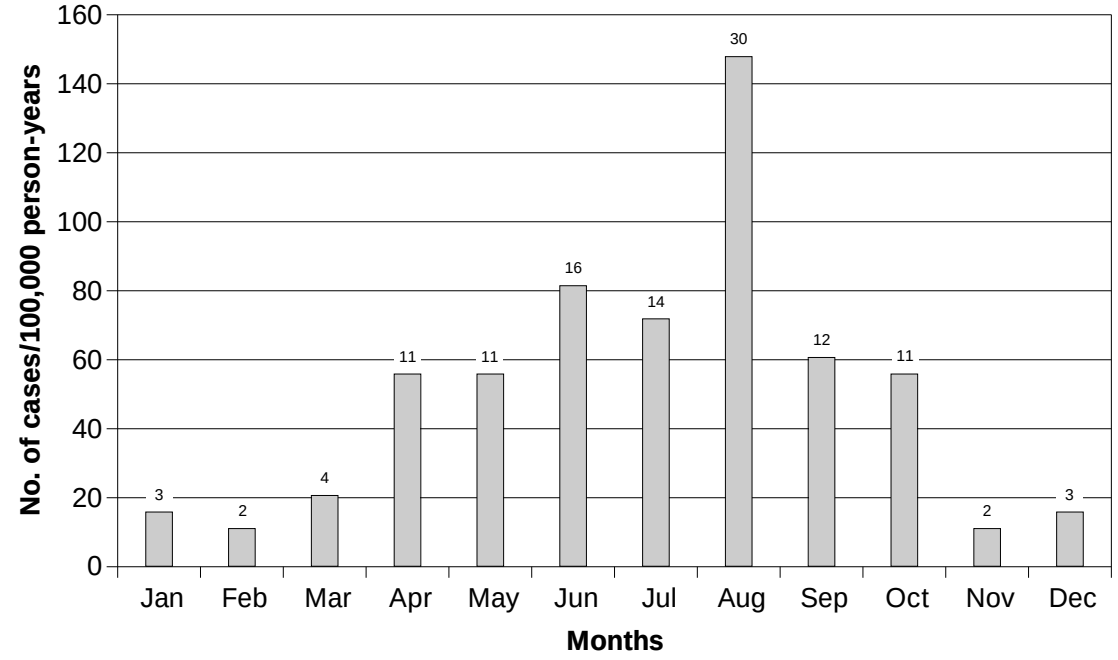
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.43 Seasonality distribution of *C.perfringens* among cases presenting to the GP



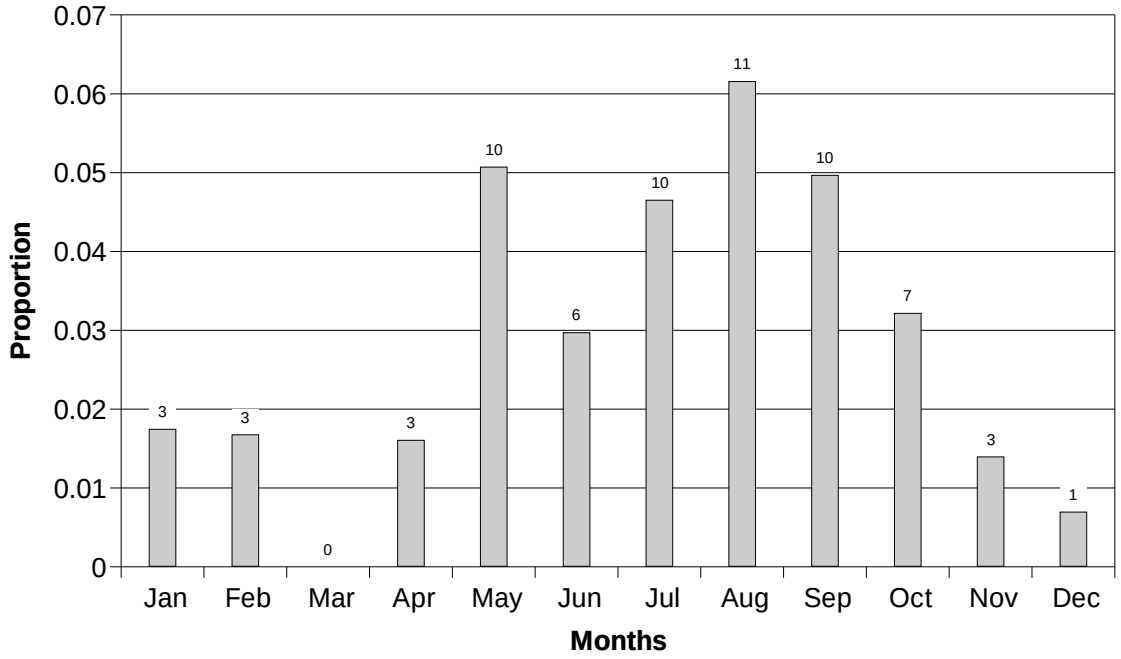
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.44 Seasonal distribution of AEEC among cases presenting to the GP



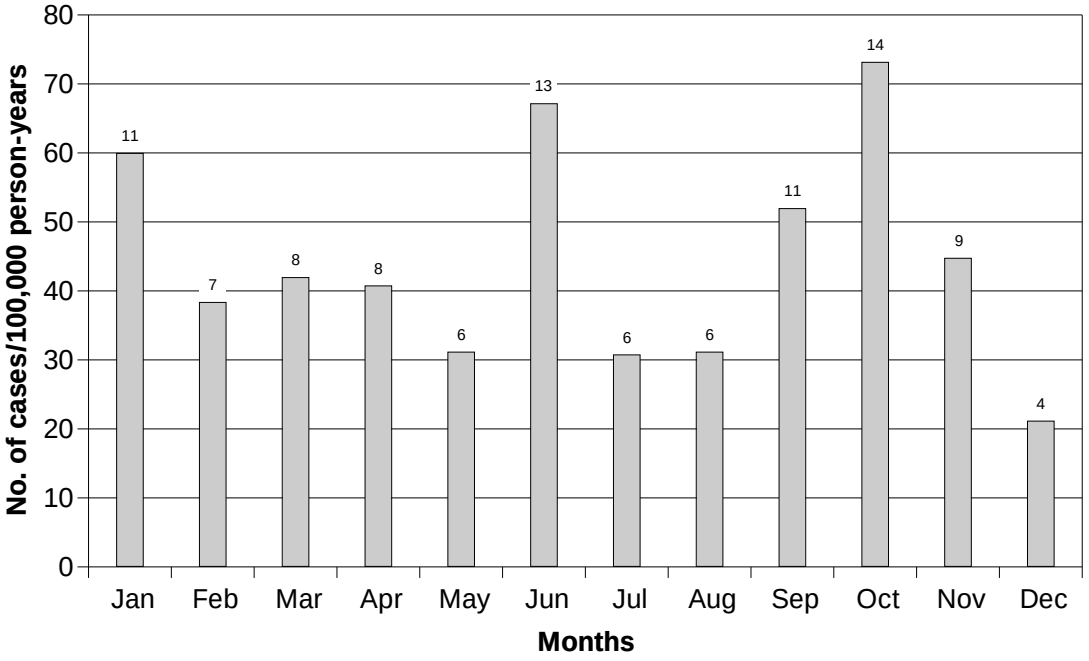
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.45 Seasonality of prevalence of AEEC among controls



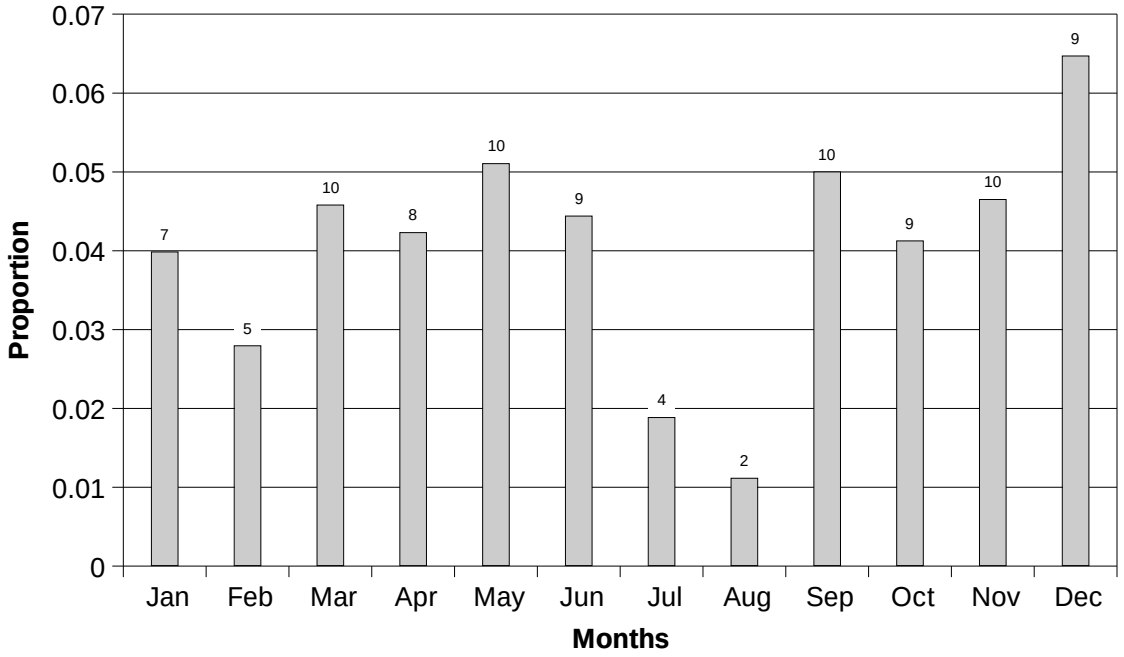
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.46 Seasonal distribution of DAEC among cases presenting to the GP



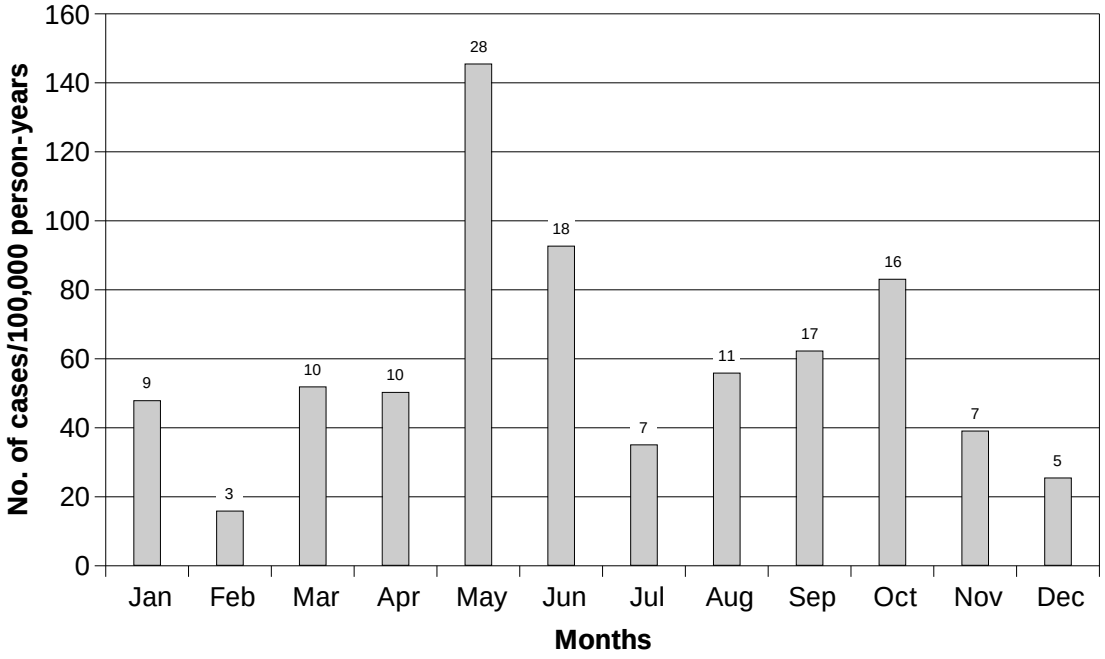
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.47 Seasonality of prevalence of DAEC among controls



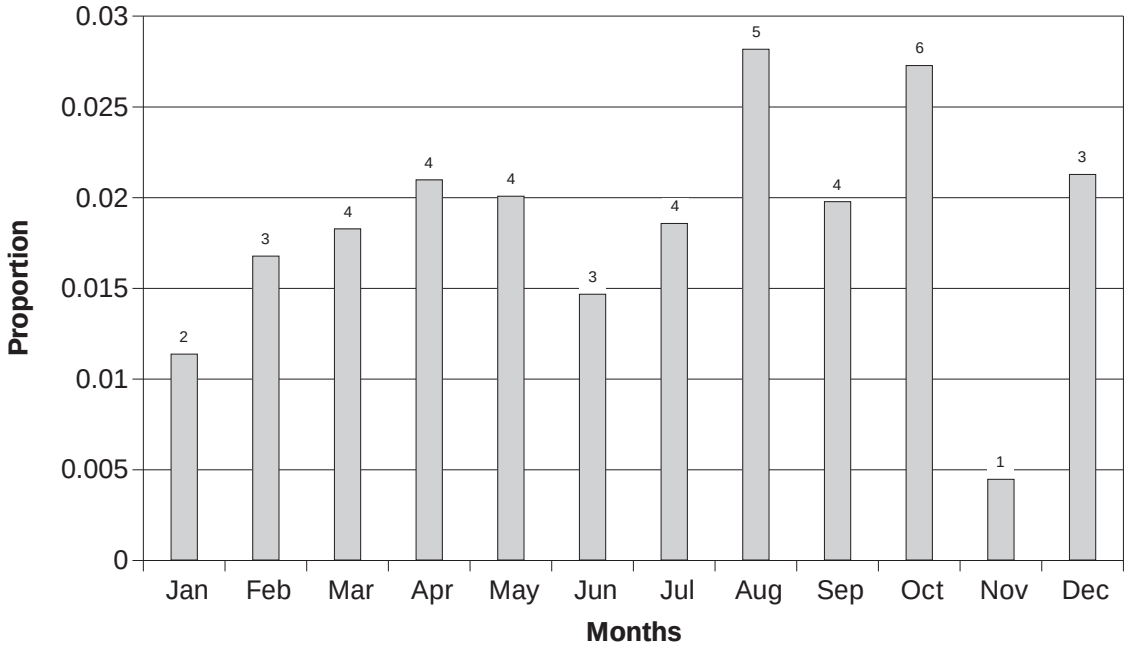
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.48 Seasonal distribution of EAggEC among cases presenting to the GP



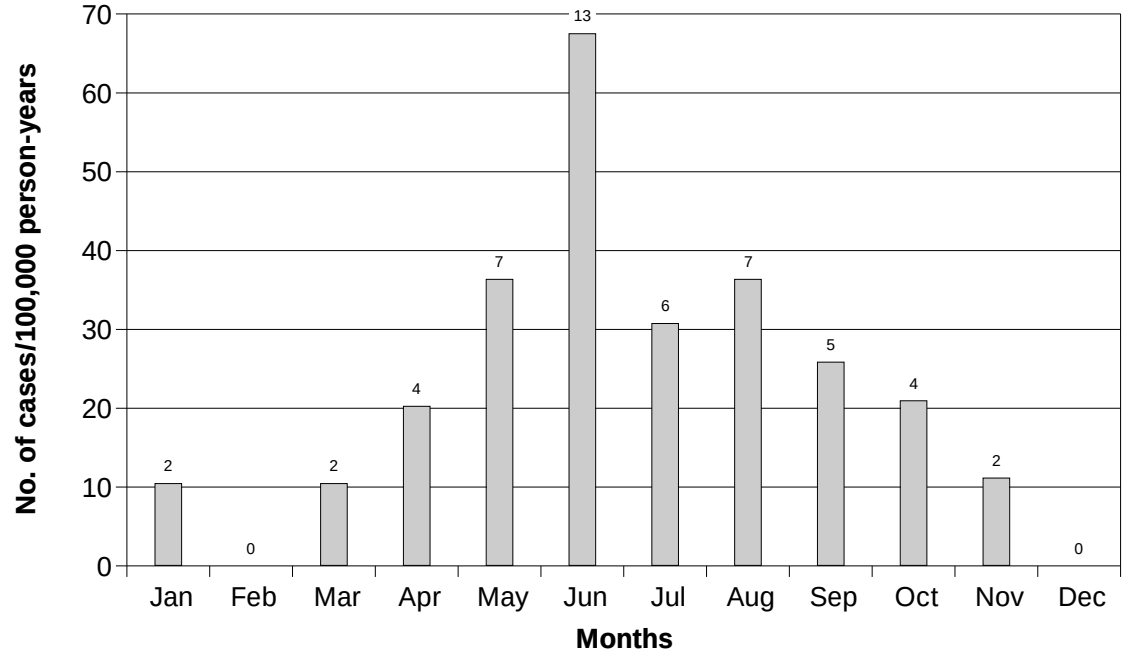
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.49 Seasonality of prevalence of EAggEC among controls



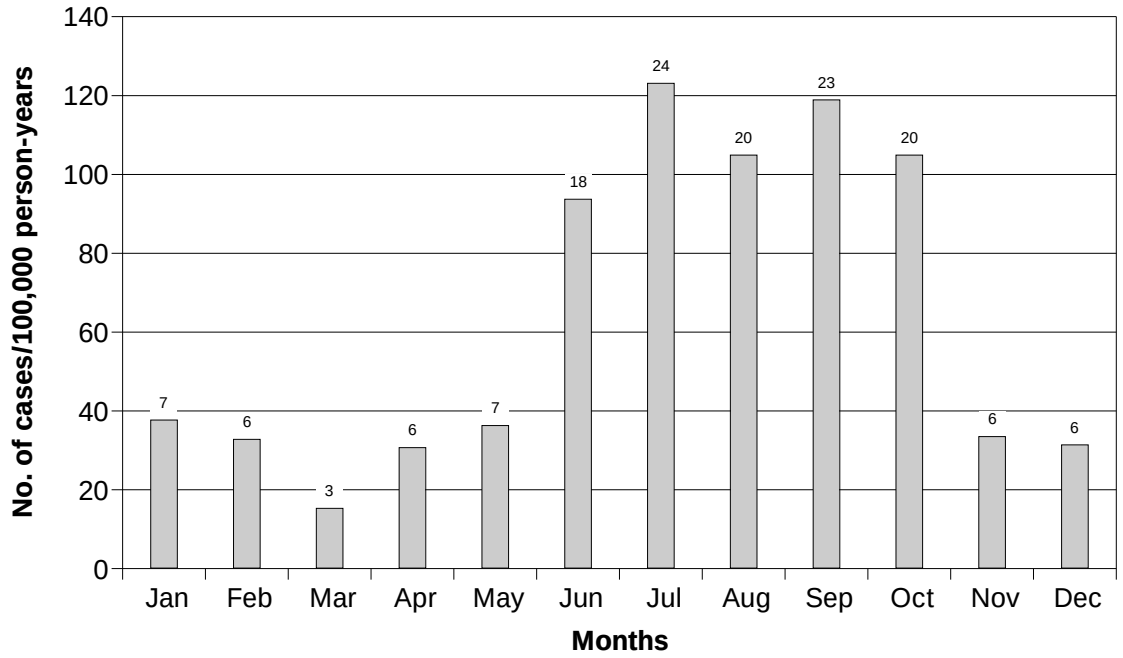
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.50 Seasonal distribution of ETEC among cases presenting to the GP



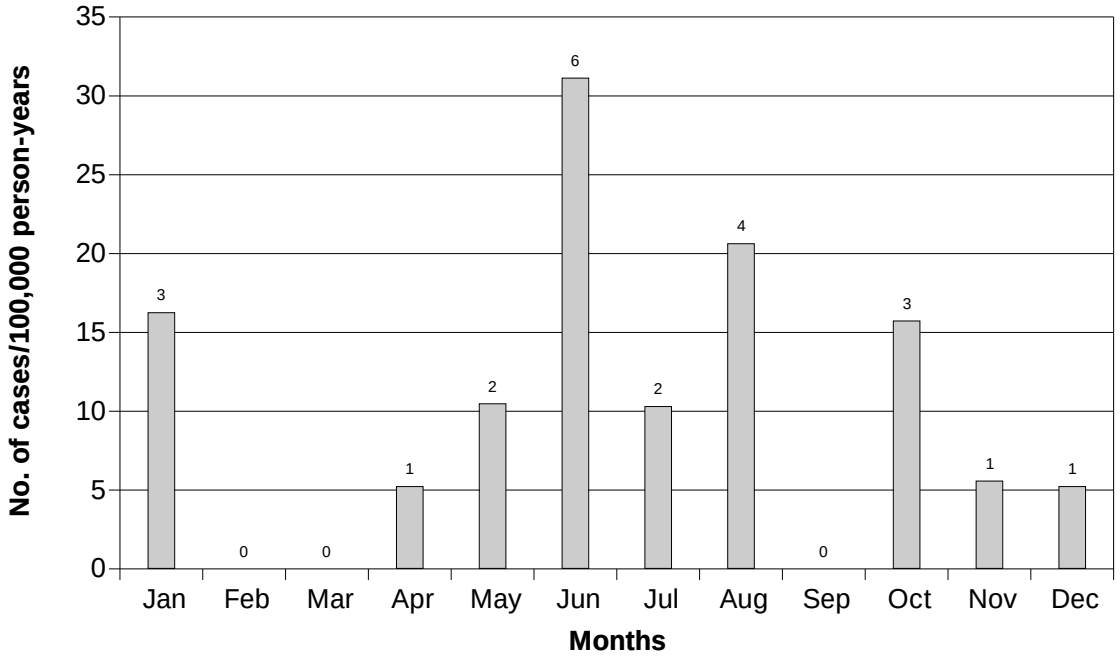
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.51 Seasonal distribution of *Salmonella* among cases presenting to the GP



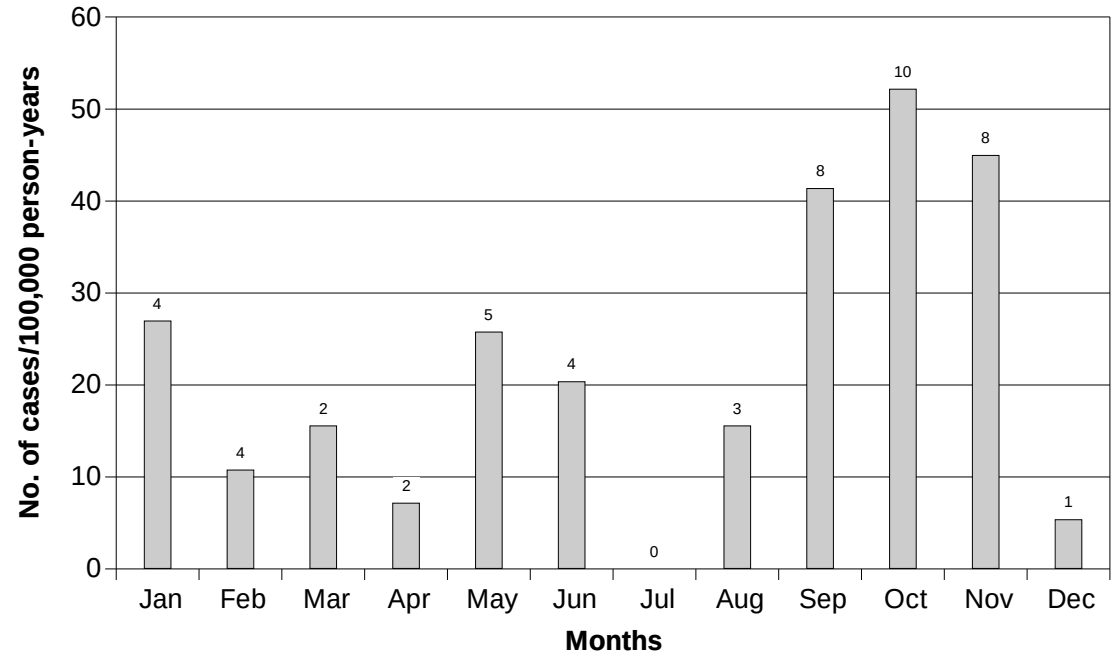
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.52 Seasonal distribution of *Shigella* among cases presenting to the GP



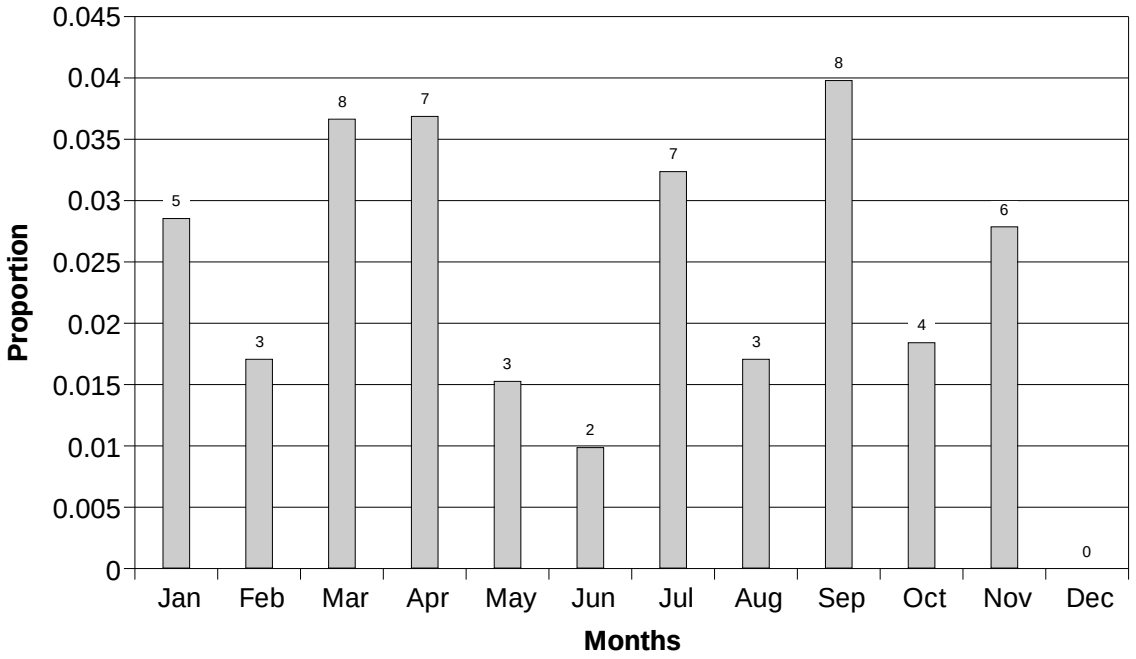
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.53 Seasonal distribution of *Yersinia* among cases presenting to the GP



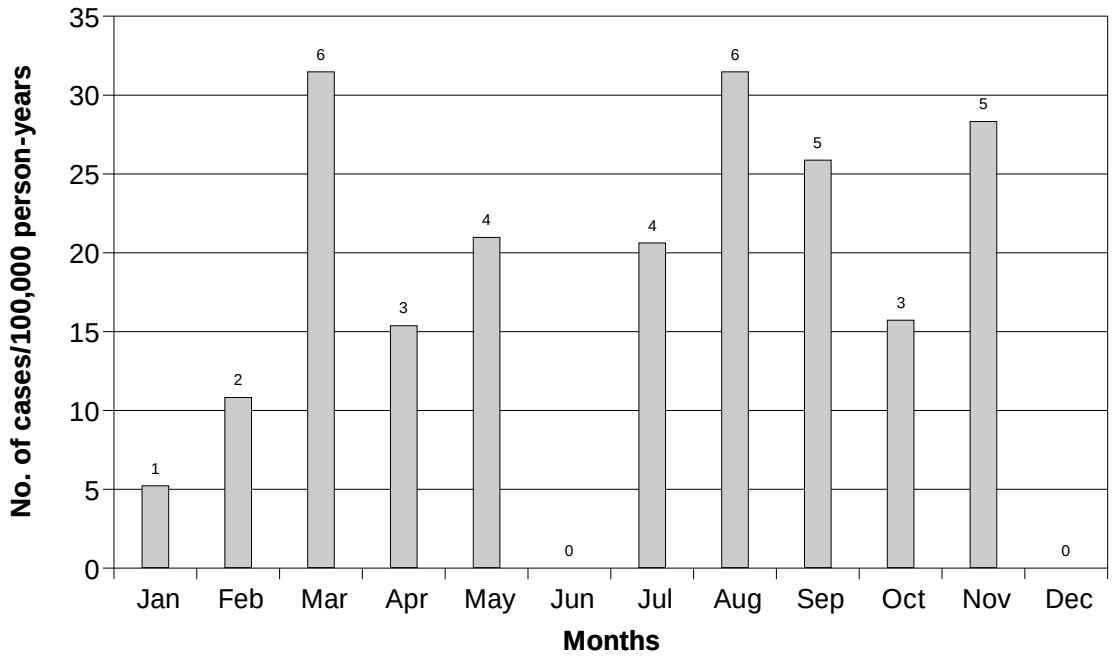
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.54 Seasonality of prevalence of *Yersinia* among controls



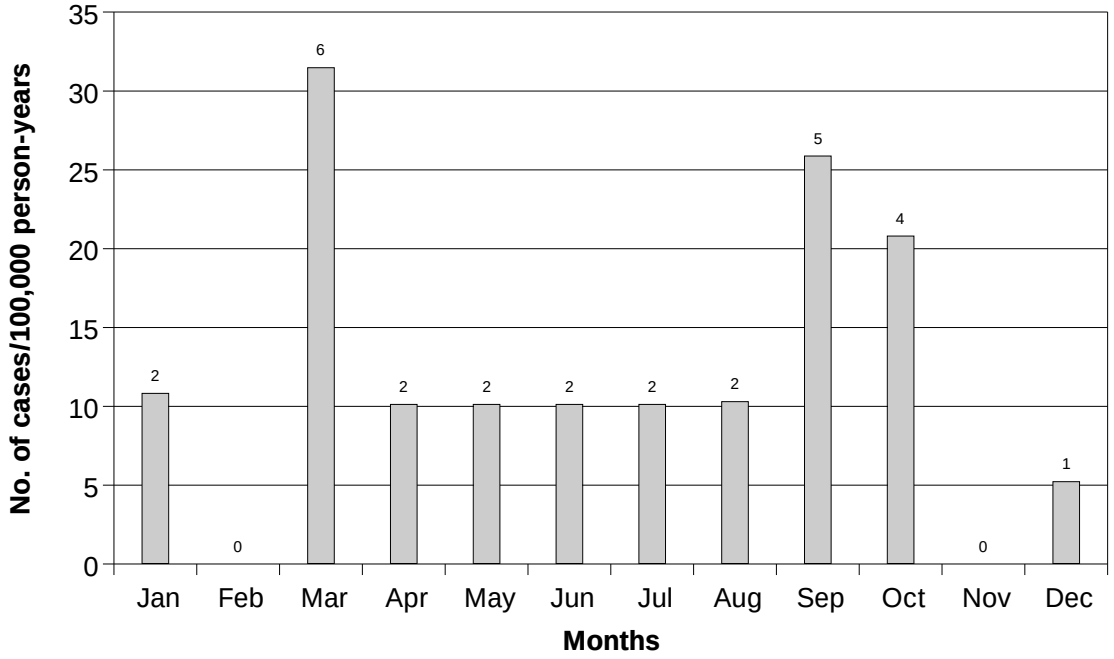
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.55 Seasonal distribution of *Cryptosporidium* among cases presenting to the GP



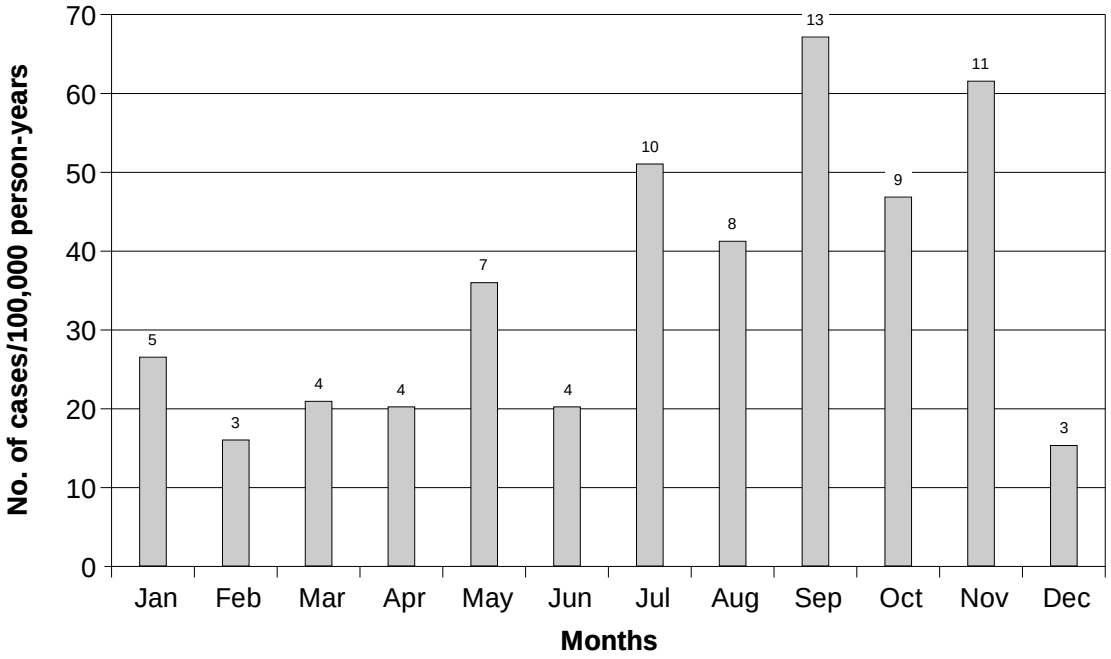
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.56 Seasonal distribution of *Giardia* among cases presenting to the GP



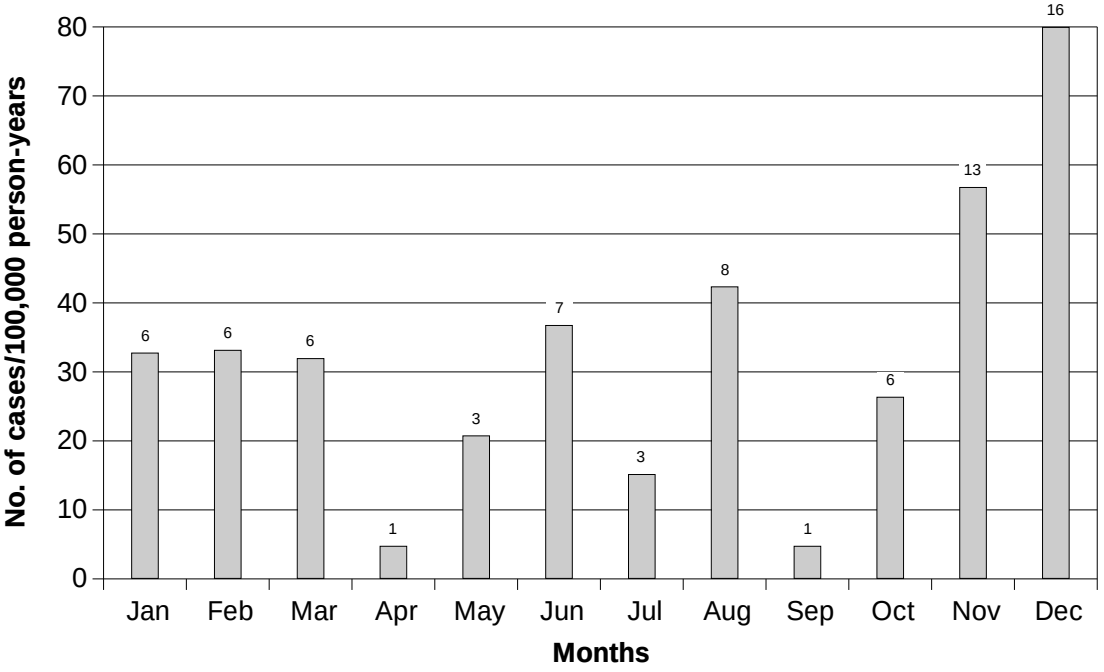
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.57 Seasonal distribution of Adenovirus among cases presenting to the GP



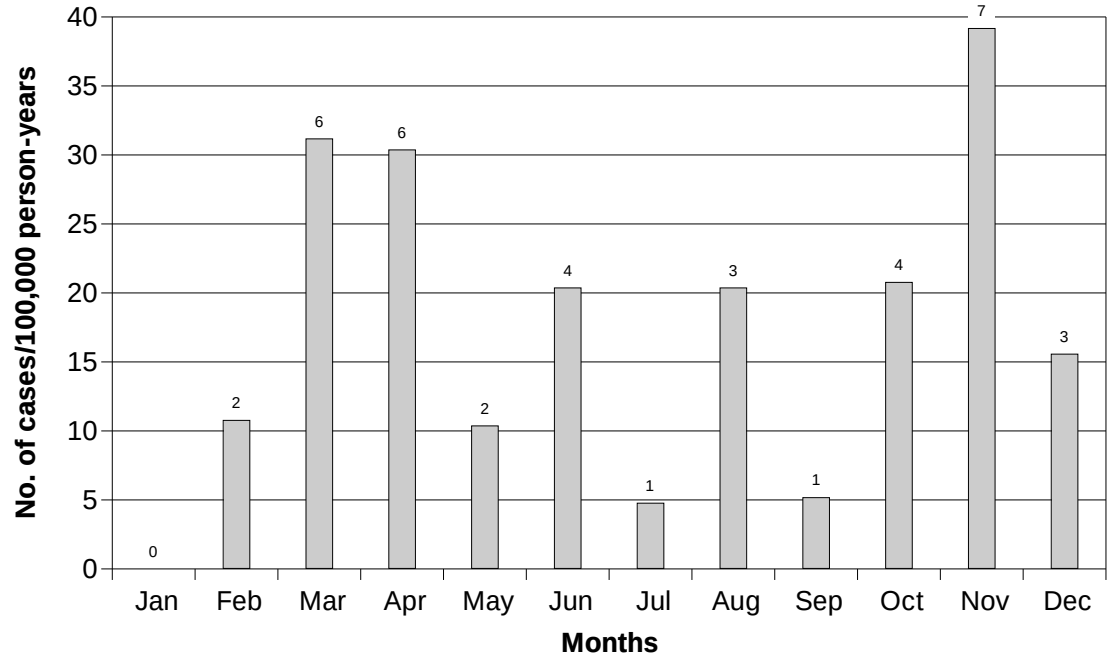
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.58 Seasonal distribution of Astrovirus among cases presenting to the GP



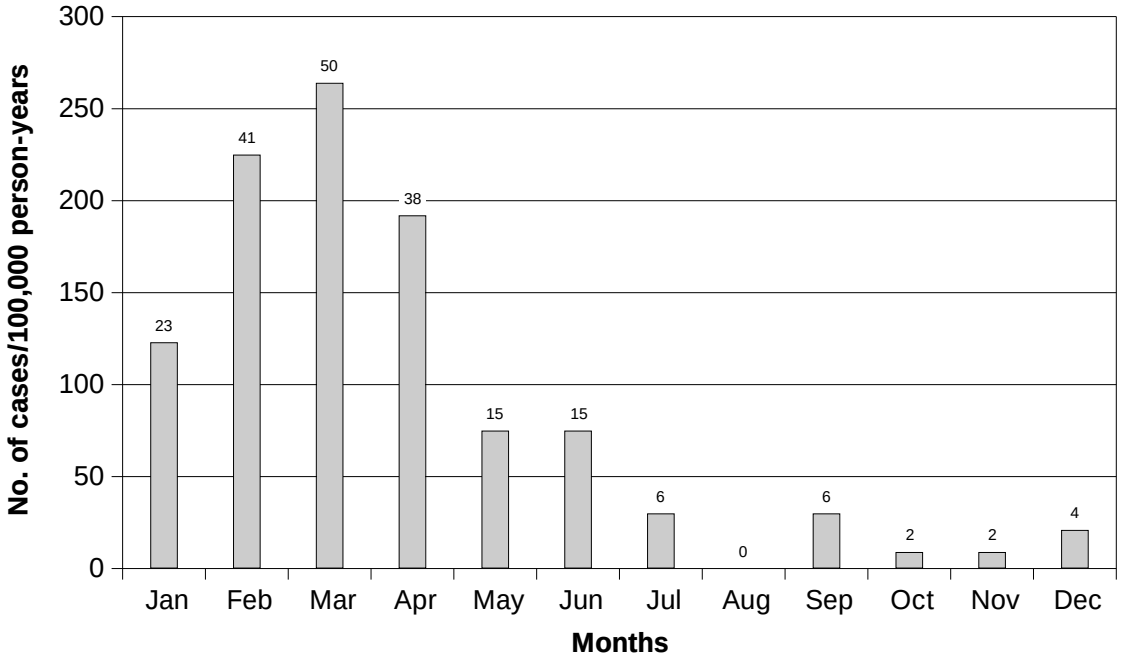
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.59 Seasonal distribution of Calicivirus among cases presenting to the GP



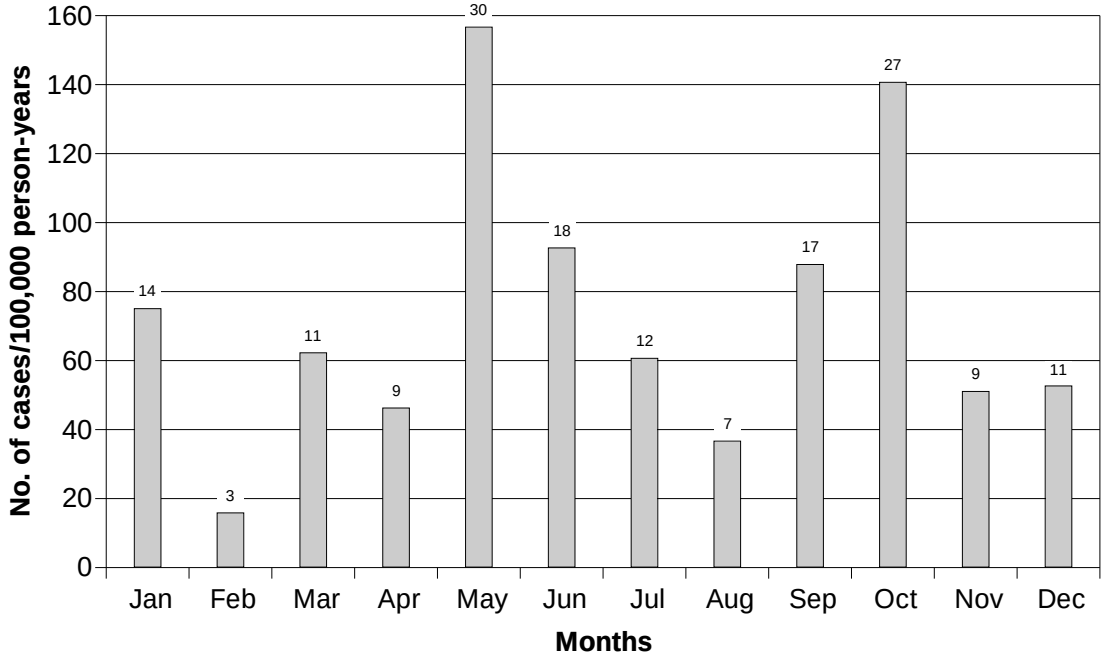
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.60 Seasonal distribution of Rotavirus among cases presenting to the GP



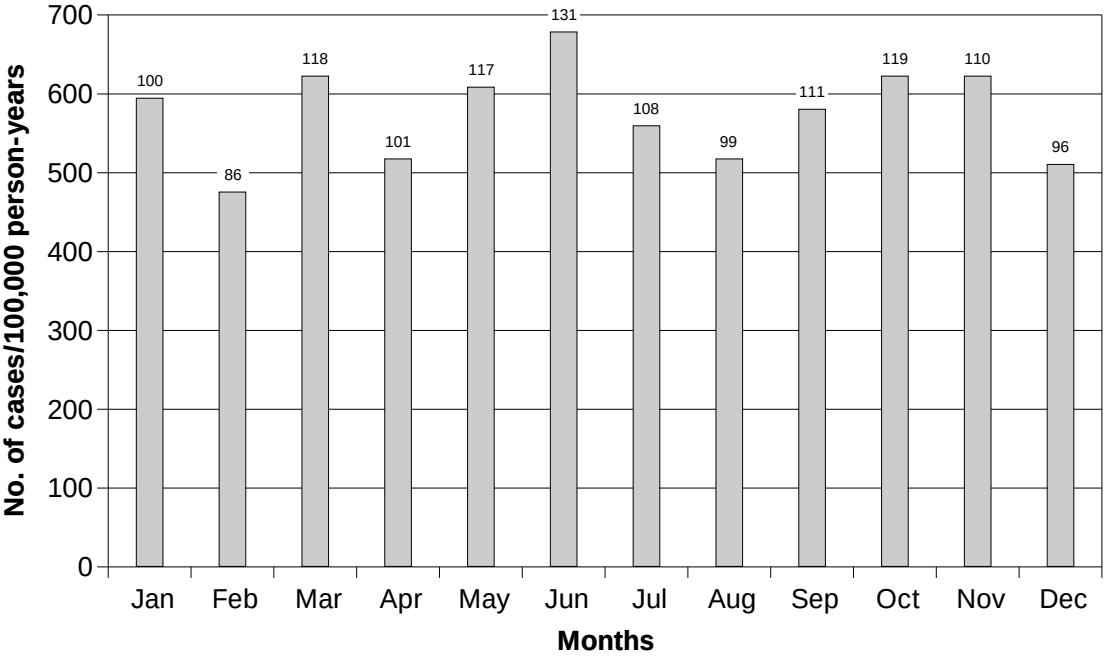
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.61 Seasonal distribution of SRSV among cases presenting to the GP



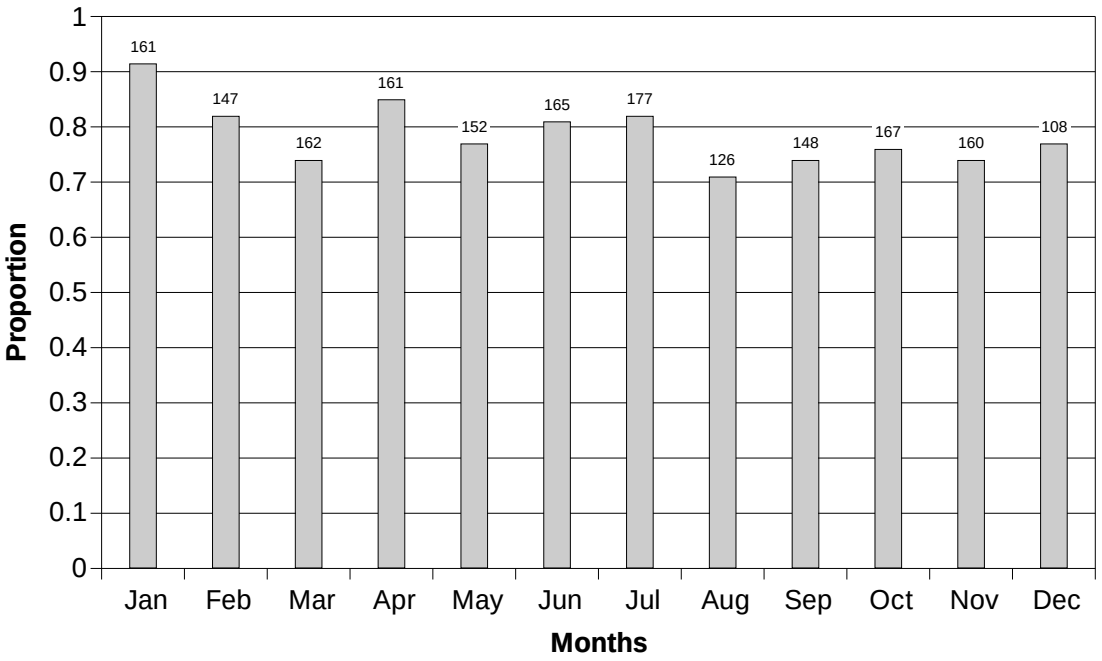
Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.62 Seasonal distribution of cases with no target organism, among cases presenting to the GP



Note. Figures above the bars represent the number of cases/controls per month.

Figure A2.63 Seasonality of prevalence of controls with no target organism



Note. Figures above the bars represent the number of cases/controls per month.

Table A2.15 Multiple organisms including Adenovirus

	GP CASE	COMM CASE	CONTROL	Total
AD	62	13	4	79
AD+AE	1	0	0	1
AD+AE+E7	1	0	0	1
AD+CP 6	6	0	0	6
AD+CV 1	1	0	0	1
AD+E2	1	0	0	1
AD+E4	4	0	0	4
AD+E6	1	0	0	1
AD+E6+SR	1	0	0	1
AD+E7	2	0	0	2
AD+YS	1	0	0	1
Total	**81**	**13**	**4**	**98**

Table A2.16 Multiple organisms including *Aeromonas*

	GP CASE	COMM CASE	CONTROL	Total
AD+AE	1	0	0	1
AD+AE+E7	1	0	0	1
AE	81	29	107	217
AE+AS	3	1	0	4
AE+AS+SA	1	0	0	1
AE+CA	20	4	1	25
AE+CA+CP	2	0	0	2
AE+CA+CP+E7	1	0	0	1
AE+CA+E4	1	0	0	1
AE+CA+E6	1	0	0	1
AE+CA+E7	3	0	0	3
AE+CA+YS	1	0	0	1
AE+CD	0	0	1	1
AE+CD+CP	1	0	0	1
AE+CD+YS	1	0	0	1
AE+CP	2	1	0	3
AE+CP+CV	1	0	0	1
AE+CP+E7	1	0	0	1
AE+CP+RV	1	0	0	1
AE+CP+SA	1	0	1	2
AE+CP+SR	1	0	0	1
AE+CR	2	0	0	2
AE+CV	0	1	0	1
AE+E1	0	2	0	2
AE+E1+E6	1	0	0	1
AE+E4	5	2	3	10
AE+E4+E7	1	0	0	1
AE+E4+SA	4	0	0	4
AE+E6	4	0	2	6
AE+E6+RV	1	0	0	1
AE+E6+SR	1	0	0	1
AE+E7	2	0	6	8
AE+E7+SA	1	0	0	1
AE+RV	3	0	0	3
AE+SA	7	0	0	7
AE+SA+ST	1	0	0	1
AE+SH	1	0	0	1
AE+SR	6	3	0	9
AE+ST	0	0	1	1
AE+YS	0	3	2	5
Total	**165**	**46**	**124**	**335**

Table A2.17 Multiple organisms including Astrovirus

	GP CASE	COMM CASE	CONTROL	Total
AE+AS	3	1	0	4
AE+AS+SA	1	0	0	1
AS	55	9	6	70
AS+CA	1	0	0	1
AS+CA+CP	1	0	0	1
AS+CD	0	1	0	1
AS+CP	3	0	0	3
AS+E4	2	0	0	2
AS+E6	3	1	0	4
AS+E7	4	1	0	5
AS+RV	1	0	0	1
AS+SA	0	1	0	1
AS+SR	1	0	0	1
AS+YS	2	0	0	2
Total	**77**	**14**	**6**	**97**

Table A2.18 Multiple organisms including Bacillus

	GP CASE	CONTROL	Total
BA	0	9	9
BA+CA	1	0	1
BA+E4	1	0	1
BA+E6+E7	0	1	1
BA+RV	1	0	1
BA+SR	1	0	1
Total	**4**	**10**	**14**

Table A2.19 Multiple organisms including *Campylobacter*

	GP CASE	COMM CASE	CONTROL	Total
AE+CA	20	4	1	25
AE+CA+CP	2	0	0	2
AE+CA+CP+E7	1	0	0	1
AE+CA+E4	1	0	0	1
AE+CA+E6	1	0	0	1
AE+CA+E7	3	0	0	3
AE+CA+YS	1	0	0	1
AS+CA	1	0	0	1
AS+CA+CP	1	0	0	1
BA+CA	1	0	0	1
CA	257	24	16	297
CA+CD+GI	1	0	0	1
CA+CP	15	0	0	15
CA+CR	1	0	0	1
CA+CV	2	0	0	2
CA+E1	2	0	0	2
CA+E1+E6	1	0	0	1
CA+E2	1	0	0	1
CA+E2+E4	1	0	0	1
CA+E4	4	0	1	5
CA+E4+GI	0	0	1	1
CA+E6	4	0	0	4
CA+E6+RV	1	0	0	1
CA+E6+YS	1	0	0	1
CA+E7	13	0	0	13
CA+E7+YS	1	0	0	1
CA+GI	1	0	0	1
CA+RV	1	0	0	1
CA+SA	3	0	0	3
CA+SR	1	1	0	2
CA+SR+YS	1	0	0	1
CA+ST	3	0	0	3
CA+YS	7	3	1	11
Total	**354**	**32**	**20**	**406**

Table A2.20 Multiple organisms including *Clostridium difficile*(>1 year olds)

	GP CASE	COMM CASE	CONTROL	Total
AE+CD	0	0	1	1
AE+CD+CP	1	0	0	1
AE+CD+YS	1	0	0	1
AS+CD	0	1	0	1
CA+CD+GI	1	0	0	1
CD	13	2	7	22
CD+CP	3	0	0	3
CD+CP+E6+SR	1	0	0	1
CD+E4	0	0	1	1
CD+E6	1	0	0	1
CD+E6+SR	1	0	0	1
CD+RV+YS	1	0	0	1
CD+SR	1	0	0	1
CD+YS	1	0	0	1
Total	**25**	**3**	**9**	**37**

Table A2.21 Multiple organisms including *Clostridium perfringens*

	GP CASE	COMM CASE	CONTROL	Total
AD+CP	6	0	0	6
AE+CA+CP	2	0	0	2
AE+CA+CP+E7	1	0	0	1
AE+CD+CP	1	0	0	1
AE+CP	2	1	0	3
AE+CP+CV	1	0	0	1
AE+CP+E7	1	0	0	1
AE+CP+RV	1	0	0	1
AE+CP+SA	1	0	1	2
AE+CP+SR	1	0	0	1
AS+CA+CP	1	0	0	1
AS+CP	3	0	0	3
CA+CP	15	0	0	15
CD+CP	3	0	0	3
CD+CP+E6+SR	1	0	0	1
CP	54	5	15	74
CP+CR	1	0	0	1
CP+CV	1	0	0	1
CP+CV+E4	1	0	0	1
CP+E1	1	0	0	1
CP+E2	0	1	0	1
CP+E4	3	0	1	4
CP+E6	3	0	0	3
CP+E7	2	0	0	2
CP+GI	1	0	0	1
CP+RV	5	1	1	7
CP+SR	2	1	0	3
Total	**114**	**9**	**18**	**141**

Table A2.22 Multiple organisms including *Cryptosporidium*

	GP CASE	COMM CASE	CONTROL	Total
AE+CR	2	0	0	2
CA+CR	1	0	0	1
CP+CR	1	0	0	1
CR	27	3	2	32
CR+E4+E6	1	0	0	1
CR+E5	1	0	0	1
CR+E5+GI	1	0	0	1
CR+E7	2	0	0	2
CR+GI	1	0	0	1
CR+SR	1	0	0	1
CR+YS	1	0	0	1
Total	**39**	**3**	**2**	**44**

Table A2.23 Multiple organisms including Calicivirus

	GP CASE	COMM CASE	CONTROL	Total
AD+CV	1	0	0	1
AE+CP+CV	1	0	0	1
AE+CV	0	1	0	1
CA+CV	2	0	0	2
CP+CV	1	0	0	1
CP+CV+E4	1	0	0	1
CV	28	6	4	38
CV+E4	3	1	0	4
CV+E6	2	0	0	2
CV+E7	0	0	1	1
CV+RV	1	0	0	1
Total	**40**	**8**	**5**	**53**

Table A2.24 Multiple organisms including Enterotoxigenic *E.coli*

	GP CASE	COMM CASE	Total
AE+E1	0	2	2
AE+E1+E6	1	0	1
CA+E1	2	0	2
CA+E1+E6	1	0	1
CP+E1	1	0	1
E1	34	8	42
E1+E4	1	0	1
E1+E6	5	1	6
E1+E6+SH	1	0	1
E1+E7	1	0	1
E1+GI	0	1	1
E1+SA+SH	1	0	1
E1+SH	4	0	4
Total	**52**	**12**	**64**

Table A2.25 Multiple organisms including Verocytotoxin producing *E.coli*

	GP CASE	COMM CASE	CONTROL	Total
AD+E2	1	0	0	1
CA+E2	1	0	0	1
CA+E2+E4	1	0	0	1
CP+E2	0	1	0	1
E2	1	1	13	15
E2+E4	0	1	0	1
E2+E7+YS	1	0	0	1
E2+RV	1	0	0	1
E2+YS	0	0	2	2
Total	**6**	**3**	**15**	**24**

Table A2.26 Multiple organisms including Attaching and Effacing *E.coli*

	GP CASE	COMM CASE	CONTROL	Total
AD+E4	4	0	0	4
AE+CA+E4	1	0	0	1
AE+E4	5	2	3	10
AE+E4+E7	1	0	0	1
AE+E4+SA	4	0	0	4
AS+E4	2	0	0	2
BA+E4	1	0	0	1
CA+E2+E4	1	0	0	1
CA+E4	4	0	1	5
CA+E4+GI	0	0	1	1
CD+E4	0	0	1	1
CP+CV+E4	1	0	0	1
CP+E4	3	0	1	4
CR+E4+E6	1	0	0	1
CV+E4	3	1	0	4
E1+E4	1	0	0	1
E2+E4	0	1	0	1
E4	58	15	62	135
E4+E5	0	0	1	1
E4+E6	7	1	1	9
E4+E7	1	0	1	2
E4+E7+SR	1	0	0	1
E4+GI	1	0	1	2
E4+GI+SA	1	0	0	1
E4+RV	4	0	0	4
E4+SA	3	0	0	3
E4+SH	1	0	0	1
E4+SR	9	3	1	13
E4+ST	1	0	0	1
E4+YS	0	0	3	3
Total	**119**	**23**	**77**	**219**

Table A2.27 Multiple organisms including Enteropathogenic *E.coli*

	GP CASE	COMM CASE	CONTROL	Total
CR+E5	1	0	0	1
CR+E5+GI	1	0	0	1
E4+E5	0	0	1	1
E5	2	1	7	10
Total	**4**	**1**	**8**	**13**

Table A2.28 Multiple organisms including Enteroaggregative *E.coli*

	GP CASE	COMM CASE	CONTROL	Total
AD+E6	1	0	0	1
AD+E6+SR	1	0	0	1
AE+CA+E6	1	0	0	1
AE+E1+E6	1	0	0	1
AE+E6	4	0	2	6
AE+E6+RV	1	0	0	1
AE+E6+SR	1	0	0	1
AS+E6	3	1	0	4
BA+E6+E7	0	0	1	1
CA+E1+E6	1	0	0	1
CA+E6	4	0	0	4
CA+E6+RV	1	0	0	1
CA+E6+YS	1	0	0	1
CD+CP+E6+SR	1	0	0	1
CD+E6	1	0	0	1
CD+E6+SR	1	0	0	1
CP+E6	3	0	0	3
CR+E4+E6	1	0	0	1
CV+E6	2	0	0	2
E1+E6	5	1	0	6
E1+E6+SH	1	0	0	1
E4+E6	7	1	1	9
E6	77	11	40	128
E6+E7	1	1	2	4
E6+E7+SA	1	0	0	1
E6+E7+SH+SR	1	0	0	1
E6+GI	2	0	0	2
E6+RV	4	1	0	5
E6+SA	3	1	1	5
E6+SH	5	0	0	5
E6+SR	5	4	0	9
Total	**141**	**21**	**47**	**209**

Table A2.29 Multiple organisms including Diffusely Adherent *E.coli*

	GP CASE	COMM CASE	CONTROL	Total
AD+AE+E7	1	0	0	1
AD+E7	2	0	0	2
AE+CA+CP+E7	1	0	0	1
AE+CA+E7	3	0	0	3
AE+CP+E7	1	0	0	1
AE+E4+E7	1	0	0	1
AE+E7	2	0	6	8
AE+E7+SA	1	0	0	1
AS+E7	4	1	0	5
BA+E6+E7	0	0	1	1
CA+E7	13	0	0	13
CA+E7+YS	1	0	0	1
CP+E7	2	0	0	2
CR+E7	2	0	0	2
CV+E7	0	0	1	1
E1+E7	1	0	0	1
E2+E7+YS	1	0	0	1
E4+E7	1	0	1	2
E4+E7+SR	1	0	0	1
E6+E7	1	1	2	4
E6+E7+SA	1	0	0	1
E6+E7+SH+SR	1	0	0	1
E7	44	18	90	152
E7+GI	0	0	1	1
E7+GI+SA	1	0	0	1
E7+RV	7	2	1	10
E7+SA	5	0	0	5
E7+SH	1	0	0	1
E7+SR	3	0	0	3
E7+SR+YS	0	1	0	1
E7+YS	1	0	3	4
Total	**103**	**23**	**106**	**232**

Table A2.30 Multiple organisms including *E.coli* O157

	GP CASE	Total
EC	3	3
Total	**3**	**3**

Table A2.31 Multiple organisms including *Giardia*

	GP CASE	COMM CASE	CONTROL	Total
CA+CD+GI	1	0	0	1
CA+E4+GI	0	0	1	1
CA+GI	1	0	0	1
CP+GI	1	0	0	1
CR+E5+GI	1	0	0	1
CR+GI	1	0	0	1
E1+GI	0	1	0	1
E4+GI	1	0	1	2
E4+GI+SA	1	0	0	1
E6+GI	2	0	0	2
E7+GI	0	0	1	1
E7+GI+SA	1	0	0	1
GI	17	1	10	28
GI+SR	1	1	0	2
Total	**28**	**3**	**13**	**44**

Table A2.32 Multiple organisms including Rotavirus group C

	GP CASE	COMM CASE	Total
RC	6	2	8
Total	**6**	**2**	**8**

Table A2.33 Multiple organisms including Rotavirus group A

	GP CASE	COMM CASE	CONTROL	Total
AE+CP+RV	1	0	0	1
AE+E6+RV	1	0	0	1
AE+RV	3	0	0	3
AS+RV	1	0	0	1
BA+RV	1	0	0	1
CA+E6+RV	1	0	0	1
CA+RV	1	0	0	1
CD+RV+YS	1	0	0	1
CP+RV	5	1	1	7
CV+RV	1	0	0	1
E2+RV	1	0	0	1
E4+RV	4	0	0	4
E6+RV	4	1	0	5
E7+RV	7	2	1	10
RV	171	25	6	202
RV+SR	3	0	0	3
RV+SR+YS	0	0	1	1
RV+YS	2	0	0	2
Total	**208**	**29**	**9**	**246**

Table A2.34 Multiple organisms including *Salmonella*

	GP CASE	COMM CASE	CONTROL	Total
AE+AS+SA	1	0	0	1
AE+CP+SA	1	0	1	2
AE+E4+SA	4	0	0	4
AE+E7+SA	1	0	0	1
AE+SA	7	0	0	7
AE+SA+ST	1	0	0	1
AS+SA	0	1	0	1
CA+SA	3	0	0	3
E1+SA+SH	1	0	0	1
E4+GI+SA	1	0	0	1
E4+SA	3	0	0	3
E6+E7+SA	1	0	0	1
E6+SA	3	1	1	5
E7+GI+SA	1	0	0	1
E7+SA	5	0	0	5
SA	109	6	9	124
SA+SR	3	0	0	3
SA+YS	1	0	1	2
Total	**146**	**8**	**12**	**166**

Table A2.35 Multiple organisms including *Shigella*

	GP CASE	COMM CASE	Total
AE+SH	1	0	1
E1+E6+SH	1	0	1
E1+SA+SH	1	0	1
E1+SH	4	0	4
E4+SH	1	0	1
E6+E7+SH+SR	1	0	1
E6+SH	5	0	5
E7+SH	1	0	1
SH	8	1	9
Total	**23**	**1**	**24**

Table A2.36 Multiple organisms including SRSV

	GP CASE	COMM CASE	CONTROL	Total
AD+E6+SR	1	0	0	1
AE+CP+SR	1	0	0	1
AE+E6+SR	1	0	0	1
AE+SR	6	3	0	9
AS+SR	1	0	0	1
BA+SR	1	0	0	1
CA+SR	1	1	0	2
CA+SR+YS	1	0	0	1
CD+CP+E6+SR	1	0	0	1
CD+E6+SR	1	0	0	1
CD+SR	1	0	0	1
CP+SR	2	1	0	3
CR+SR	1	0	0	1
E4+E7+SR	1	0	0	1
E4+SR	9	3	1	13
E6+E7+SH+SR	1	0	0	1
E6+SR	5	4	0	9
E7+SR	3	0	0	3
E7+SR+YS	0	1	0	1
GI+SR	1	1	0	2
RV+SR	3	0	0	3
RV+SR+YS	0	0	1	1
SA+SR	3	0	0	3
SR	122	34	7	163
SR+YS	2	2	0	4
Total	**169**	**50**	**9**	**228**

Table A2.37 Multiple organisms including *Staphylococcus aureus*

	GP CASE	COMM CASE	CONTROL	Total
AE+SA+ST	1	0	0	1
AE+ST	0	0	1	1
CA+ST	3	0	0	3
E4+ST	1	0	0	1
ST	5	1	5	11
Total	**10**	**1**	**6**	**17**

Table A2.38 Multiple organisms including *Vibrio*

	GP CASE	Total
VB	1	1
Total	**1**	**1**

Table A2.39 Multiple organisms including *Yersinia*

	GP CASE	COMM CASE	CONTROL	Total
AD+YS	1	0	0	1
AE+CA+YS	1	0	0	1
AE+CD+YS	1	0	0	1
AE+YS	0	3	2	5
AS+YS	2	0	0	2
CA+E6+YS	1	0	0	1
CA+E7+YS	1	0	0	1
CA+SR+YS	1	0	0	1
CA+YS	7	3	1	11
CD+RV+YS	1	0	0	1
CD+YS	1	0	0	1
CR+YS	1	0	0	1
E2+E7+YS	1	0	0	1
E2+YS	0	0	2	2
E4+YS	0	0	3	3
E7+SR+YS	0	1	0	1
E7+YS	1	0	3	4
RV+SR+YS	0	0	1	1
RV+YS	2	0	0	2
SA+YS	1	0	1	2
SR+YS	2	2	0	4
YS	26	17	59	102
Total	**51**	**26**	**72**	**149**

Appendix 3
Serotyping and toxin testing

Table A3.1 *Salmonella* serotypes

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
AMERSFOORT	**1**	**0**	**0**	**0**	**1**
ARECHAVALETA	**1**	**0**	**0**	**0**	**1**
BAREILLY	**1**	**0**	**0**	**0**	**1**
BOVIS-MORBIFICANS	**1**	**0**	**0**	**0**	**1**
BREDENEY	**1**	**0**	**0**	**0**	**1**
CERRO	**1**	**0**	**0**	**0**	**1**
CORVALLIS	**1**	**0**	**0**	**0**	**1**
DERBY	**1**	**0**	**0**	**0**	**1**
EBRIE	**0**	**1**	**0**	**0**	**1**
EIMSBUETTEL	**0**	**1**	**0**	**0**	**1**
ENTERITIDIS	**89**	**2**	**3**	**1**	**95**
PT1	1	0	0	0	1
PT4	72	2	2	1	77
PT5a	1	0	0	0	1
PT6	2	0	1	0	3
PT6b	1	0	0	0	1
PT7	2	0	0	0	2
PT8	1	0	0	0	1
PT11	2	0	0	0	2
PT24	1	0	0	0	1
PT34	2	0	0	0	2
PT69	2	0	0	0	2
RDNC	2	0	0	0	2
HAARDT	**1**	**0**	**0**	**0**	**1**
HADAR	**5**	**0**	**0**	**0**	**5**
PT2	3	0	0	0	3
PT14	1	0	0	0	1
PT18	1	0	0	0	1
HEIDELBERG	**1**	**0**	**0**	**0**	**1**
INDIANA	**0**	**1**	**0**	**0**	**1**
INFANTIS	**0**	**0**	**1**	**0**	**1**
JAVA PT DUNDEE	**1**	**0**	**0**	**0**	**1**
JAVIANA	**0**	**1**	**0**	**0**	**1**
KEDOUGOU	**0**	**0**	**0**	**1**	**1**
MONTEVIDEO	**1**	**0**	**0**	**0**	**1**
NEWPORT	**2**	**0**	**0**	**0**	**2**
PARATYPHI B PT 1	**0**	**1**	**0**	**0**	**1**
SCHWARZENGRUND	**1**	**0**	**0**	**0**	**1**
STANLEYVILLE	**1**	**0**	**0**	**0**	**1**
TYPHIMURIUM	**29**	**2**	**3**	**0**	**34**
DT10	1	0	0	0	1
DT104	13	1	2	0	16
DT104b	2	0	0	0	2
DT141	1	0	0	0	1
DT170	1	0	0	0	1
DT193	1	1	0	0	2
DT204c	0	0	1	0	1
DT208	7	0	0	0	7
RDNC	2	0	0	0	2
U285	1	0	0	0	1
VIRCHOW	**7**	**1**	**0**	**0**	**8**
PT8	1	0	0	0	1
PT26	3	1	0	0	4
PT45	1	0	0	0	1
PT45	1	0	0	0	1
PT53	1	0	0	0	1
WANGATA	**1**	**0**	**0**	**0**	**1**
WORTHINGTON	**0**	**0**	**1**	**0**	**1**
Total	**146**	**10**	**8**	**2**	**166**

Table A3.2 *Shigella* serotypes

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
BOYDII 2	1	0	0	0	1
FLEXNERI 4a	1	0	0	0	1
FLEXNERI 6	1	0	0	0	1
SONNEI	20	0	1	0	21
PT 2	5	0	0	0	5
PT3	5	0	0	0	5
PT6	5	0	1	0	6
PT23	1	0	0	0	1
PT67	1	0	0	0	1
PT L	1	0	0	0	1
RDNC	2	0	0	0	2
Total	**23**	**0**	**1**	**0**	**24**

Table A3.3 Enterovirulent *E. coli* serotypes

ENTEROTOXIGENIC EC	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
SINGLE ORGANISM					
O1	1	0	0	0	1
O 2	0	0	1	0	1
O6	15	0	1	0	16
O8	0	0	1	0	1
O62	1	0	0	0	1
O82	1	0	0	0	1
O114	1	0	0	0	1
O128ab	1	0	0	0	1
O128ac	1	0	0	0	1
O141	0	0	1	0	1
O151	1	0	0	0	1
O159	1	0	1	0	2
O166	1	0	0	0	1
O169	9	0	3	0	12
O Rough	3	0	0	0	3
O?	14	0	3	0	17
not typed	1	0	0	0	1
DOUBLE ORGANISM					
O114, O169	0	0	1	0	1
O148, O?	1	0	0	0	1
Total	**52**	**0**	**12**	**0**	**64**

VEROCYTOTOXIGENIC EC	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
SINGLE ORGANISM					
O26	0	0	1	0	1
O52	1	0	0	0	1
O82	0	1	0	0	1
O91	0	1	1	0	2
O115	0	0	0	1	1
O118	0	1	0	0	1
O128ab	0	2	0	1	3
O146	0	1	0	1	2
O157 PT2	1	0	0	0	1
O157 PT14	1	0	0	0	1
O157 PT32	1	0	0	0	1
O162	0	2	0	0	2
O Rough	1	0	1	0	2
O?	4	1	0	3	8
Total	**9**	**9**	**3**	**6**	**27**

Table A3.3 – *continued*

ATTACHING & EFFACING EC	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
SINGLE ORGANISM					
O2	2	1	0	1	4
O3	1	0	0	0	1
O4	2	0	0	0	2
O8	1	0	0	0	1
O9ab	0	0	0	1	1
O10	1	0	0	0	1
O11	1	0	0	0	1
O13	0	0	1	0	1
O21	2	1	0	0	3
O24	1	0	0	0	1
O26	0	0	2	1	3
O28ac	1	0	0	0	1
O32	1	0	0	0	1
O33	2	1	2	2	7
O45	0	1	0	0	1
O49	1	2	0	0	3
O63	1	0	0	0	1
O64	1	0	0	0	1
O70	3	3	0	0	6
O71	2	1	0	0	3
O76	1	1	0	0	2
O80	1	0	1	0	2
O82	1	0	0	0	1
O85	0	2	0	0	2
O89	0	1	0	0	1
O96	0	0	1	0	1
O98	1	0	0	0	1
O101	1	0	0	0	1
O103	3	0	0	0	3
O111ab	6	1	0	0	7
O113	2	0	0	0	2
O114	2	0	0	0	2
O121	1	0	0	0	1
O124	1	0	0	0	1
O125ac	1	0	0	1	2
O126	0	1	0	0	1
O127a	2	0	1	0	3
O127ab	1	0	0	0	1
O128ab	0	1	0	0	1
O129	1	0	1	0	2
O131	1	0	0	0	1
O132	1	1	0	0	2
O139	1	0	0	0	1
O142	1	1	0	0	2
O145	0	1	0	0	1
O156	0	0	1	0	1
O162	0	1	0	0	1
O165	0	1	0	0	1
O172	1	0	0	0	1
O Rough	8	4	0	0	12
O?	55	38	11	3	107
Not typed	1	0	0	1	2
DOUBLE ORGANISM					
O2, O?	1	0	0	0	1
O4, O137	0	1	0	0	1
O88, O?	0	0	1	0	1
O111ab, O Rough	0	0	1	0	1
O125ac, O?	1	0	0	0	1
O127ab, O?	0	1	0	0	1
O132, O?	0	1	0	0	1
Total	**119**	**67**	**23**	**10**	**219**

Table A3.3 – *continued*

ENTEROPATHOGENIC EC	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
SINGLE ORGANISM					
O7	1	2	0	0	3
O15	1	0	1	0	2
O23	0	1	0	0	1
O73	1	1	0	0	2
O Rough	1	0	0	0	1
O?	0	1	0	2	3
DOUBLE ORGANISM					
O127a, O?	0	1	0	0	1
Total	**4**	**6**	**1**	**2**	**13**

Table A3.3 – *continued*

ENTEROAGGREGATIVE EC	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
SINGLE ORGANISM					
O1	0	1	0	0	1
O2	1	0	0	0	1
O3	2	0	0	0	2
O4	3	2	0	0	5
O5	0	1	0	0	1
O6	3	1	1	0	5
O7	2	0	0	0	2
O8	2	0	0	0	2
O11	1	1	0	0	2
O15	0	1	0	0	1
O18ac	5	1	0	0	6
O19ab	0	1	0	0	1
O21	2	0	0	1	3
O33	1	0	0	0	1
O53	1	1	0	0	2
O62	3	0	0	0	3
O66	1	0	0	0	1
O73	1	0	0	0	1
O75	0	0	1	0	1
O77	1	0	0	0	1
O80	1	0	0	0	1
O81	0	0	2	0	2
O82	2	0	0	0	2
O86	6	0	0	0	6
O91	0	0	1	0	1
O106	1	0	0	0	1
O111ab	3	3	0	0	6
O113	1	0	0	0	1
O118	1	1	0	0	2
O119	1	0	0	0	1
O125ab	1	0	1	0	2
O128ac	0	1	0	0	1
O129	0	0	1	0	1
O130	0	4	2	0	6
O131	2	0	0	0	2
O134	5	2	0	0	7
O151	1	0	0	0	1
O162	1	0	0	0	1
O165	0	1	0	0	1
O169	1	0	0	0	1
O Rough	9	0	3	0	12
O?	65	20	9	3	97
Not typed	8	1	0	0	9
DOUBLE ORGANISM					
O73, O?	1	0	0	0	1
O86, O?	1	0	0	0	1
O Rough (two different H types)	1	0	0	0	1
Total	**141**	**43**	**21**	**4**	**209**

Table A3.3 – *continued*

DIFFUSELY ADHERENT EC	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
SINGLE ORGANISM					
O1	22	21	3	3	49
O2	8	8	1	1	18
O6	2	0	0	0	2
O7	2	0	0	1	3
O8	2	2	1	1	6
O9a	0	0	1	0	1
O10	0	1	0	0	1
O11	3	3	0	0	6
O12	3	3	1	0	7
O15	4	1	1	0	6
O19ab	2	4	0	0	6
O20	0	2	0	0	2
O21	4	5	4	0	13
O36	1	0	0	0	1
O73	1	0	0	0	1
O75	8	10	1	1	20
O83	1	0	1	0	2
O87	0	1	0	0	1
O95	0	0	1	0	1
O98	0	2	0	0	2
O101	0	0	1	0	1
O102	2	0	0	0	2
O119	1	0	0	0	1
O124	0	1	0	0	1
O127a	1	0	0	0	1
O157	2	1	0	1	4
O170	0	0	1	0	1
O Rough	2	0	1	0	3
O?	31	26	5	5	67
DOUBLE ORGANISM					
O1, O?	0	1	0	0	1
O148 H4, O Rough	0	1	0	0	1
O20, O20	1	0	0	0	1
Total	**103**	**93**	**23**	**13**	**232**

Table A3.4 *Campylobacter* serotypes

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
COLI	**30**	**2**	**2**	**1**	**35**
LI/P26	1	0	0	0	1
LI/P NT	3	2	0	0	5
LI/P1	0	0	0	1	1
LI/P2*	1	0	0	0	1
LI/P20	1	0	0	0	1
LI/P26	2	0	0	0	2
LI/P30	2	0	0	0	2
LI/P30*	1	0	0	0	1
LI/P46	8	0	1	0	9
LI/P53	1	0	0	0	1
LI/P54	7	0	0	0	7
LI/P54*	2	0	0	0	2
LII/P NT	0	0	1	0	1
LII/P30	1	0	0	0	1
FETUS	**1**	**0**	**0**	**0**	**1**
HYOINTESTINALIS	**1**	**0**	**0**	**0**	**1**
JEJUNI	**305**	**12**	**27**	**3**	**347**
LI/P1	17	2	1	2	22
LI/P1 10	1	0	0	0	1
LI/P1 12	0	0	1	0	1
LI/P2	5	0	1	0	6
LI/P2*	8	0	0	0	8
LI/P3	1	0	0	0	1
LI/P3*	1	0	0	0	1
LI/P5	1	0	0	0	1
LI/P5*	1	0	0	0	1
LI/P5 1	1	0	0	0	1
LI/P6*	1	0	0	0	1
LI/P7	1	0	0	0	1
LI/P7*	4	0	0	0	4
LI/P8	1	0	0	1	2
LI/P8*	2	0	0	0	2
LI/P10	4	0	0	0	4
LI/P10*	2	0	0	0	2
LI/P11	10	0	0	0	10
LI/P11*	1	0	0	0	1
LI/P12	2	0	0	0	2
LI/P12*	3	0	0	0	3
LI/P15	2	0	0	0	2
LI/P15*	1	0	0	0	1
LI/P16	1	0	0	0	1
LI/P16*	10	1	0	0	11
LI/P17	1	0	0	0	1
LI/P17*	2	1	0	0	3
LI/P18	8	2	0	0	10
LI/P19	3	0	0	0	3
LI/P19*	3	0	0	0	3
LI/P21	3	0	0	0	3
LI/P21*	3	0	0	0	3
LI/P23	1	0	0	0	1
LI/P23*	2	0	2	0	4
LI/P29	2	0	0	0	2
LI/P33	1	0	0	0	1
LI/P35	0	1	0	0	1
LI/P37	2	0	0	0	2
LI/P37*	2	0	0	0	2
LI/P38	1	0	0	0	1
LI/P38*	0	0	1	0	1
LI/P41	1	0	0	0	1
LI/P41*	0	0	1	0	1
LI/P42*	1	0	0	0	1
LI/P44	1	0	0	0	1
LI/P50*	4	0	1	0	5
LI/P53	5	0	0	0	5
LI/P55	1	0	0	0	1
LI/P57*	1	0	1	0	2

Table A3.4 – *continued*

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
LI/P60	1	0	0	0	1
LI/P63	1	0	0	0	1
LI/P64*	11	1	2	0	14
LI/P64 4	1	0	0	0	1
LI/P64 16	1	0	0	0	1
LI/P16 50 13 6	2	0	0	0	2
LI/P NT	5	0	1	0	6
LII/P1	11	1	2	0	14
LII/P1*	7	0	0	0	7
LII/P2	20	0	2	0	22
LII/P2*	9	0	1	0	10
LII/P3	1	0	1	0	2
LII/P3*	1	0	0	0	1
LII/P4*	1	0	0	0	1
LII/P5	3	1	0	0	4
LII/P5*	1	0	0	0	1
LII/P7*	0	0	2	0	2
LII/P8	1	0	0	0	1
LII/P8*	4	1	1	0	6
LII/P10	1	0	0	0	1
LII/P11	19	0	2	0	21
LII/P11*	3	0	0	0	3
LII/P12	3	0	0	0	3
LII/P12*	2	0	0	0	2
LII/P13	1	0	0	0	1
LII/P16*	5	0	0	0	5
LII/P17	3	0	0	0	3
LII/P17*	1	0	0	0	1
LII/P18	1	0	0	0	1
LII/P21*	1	0	0	0	1
LII/P23*	1	1	1	0	3
LII/P31	1	0	0	0	1
LII/P35	1	0	0	0	1
LII/P37	1	0	1	0	2
LII/P37*	1	0	0	0	1
LII/P42	1	0	0	0	1
LII/P44*	1	0	0	0	1
LII/P53	3	0	0	0	3
LII/P63	1	0	0	0	1
LII/P64	1	0	0	0	1
LII/P64*	12	0	1	0	13
LII/P65*	1	0	0	0	1
LII/P1 3	1	0	0	0	1
LII/P10 1	1	0	0	0	1
LII/P2 1	1	0	0	0	1
LII/P NT	10	0	1	0	11
LII/PII	1	0	0	0	1
LIII/P1 2	1	0	0	0	1
LIII/P7*	3	0	0	0	3
LIII/P9	1	0	0	0	1
LIIIP9 37	1	0	0	0	1
LIII/P19	1	0	0	0	1
LIII/P23 36	1	0	0	0	1
LIII/P38	2	0	0	0	2
LIII/P55	1	0	0	0	1
LIII/P57	1	0	0	0	1
LIV/P6*	1	0	0	0	1
LIV/P7 6 27	1	0	0	0	1
LIV/P27 7 6	1	0	0	0	1
LIV/P42	1	0	0	0	1
UPSALIENSIS	**2**	**2**	**2**	**0**	**6**
SPECIES	**14**	**0**	**1**	**0**	**15**
Total	**354**	**17**	**32**	**4**	**407**

LI Lior biotype I; **LII** Lior biotype II; **LIII** Lior biotype III; **LIV** Lior biotype IV
P Penner heat stable serotype
NT not typable
* the predominant serotype where there may be other lower titre cross reactions

Table A3.5 *Yersinia* serotypes

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
BERCOVIERI	**0**	**1**	**0**	**0**	**1**
ENTEROCOLITICA	**40**	**33**	**15**	**11**	**99**
O1, 2a, 3 BT1a	0	0	0	1	1
O3 BT4	1	0	0	0	1
O4, 32 BT1a	0	1	1	0	2
O5 BT1a	7	6	3	1	17
O6, 30 BT1a	3	1	0	0	4
O6, 31 BT1a	1	0	0	0	1
O7 BT1a	1	1	0	0	2
O9 BT3	3	0	4	1	8
O10, K1 BT1a	3	2	1	1	7
O11, 24 BT1a	0	1	0	0	1
O12, 26 BT1a	0	0	0	1	1
O13, 7 BT1a	1	0	0	0	1
O14 BT1a	0	1	0	0	1
O18 BT1a	1	0	0	0	1
O18 BT1b	0	1	0	0	1
O19, 8 BT1a	2	0	1	2	5
O19, 8 BT1b	1	0	0	0	1
O28 BT1a	1	0	0	0	1
O41, 43 BT1a	1	1	1	0	3
O47 BT1a	0	1	0	0	1
O48 BT1a	1	1	0	0	2
O? BT1a	11	13	3	4	31
O? BT1b	0	1	1	0	2
O Rough BT1a	2	2	0	0	4
FREDERIKSENII	**10**	**19**	**9**	**5**	**43**
O1, 2a, 3	1	0	0	0	1
O2a, 2b, 3	0	1	0	0	1
O11, 23	0	1	0	0	1
O16	0	0	0	1	1
O16, 29	2	1	0	0	3
O17	0	0	1	0	1
O36	0	0	2	0	2
O39	1	1	0	0	2
O40	0	2	0	0	2
O41, 42	0	1	0	0	1
O46	0	2	0	1	3
O48	1	1	0	0	2
O52	1	0	0	0	1
O?	4	8	6	2	20
O Rough	0	1	0	1	2
INTERMEDIA	**1**	**0**	**2**	**0**	**3**
O17	0	0	1	0	1
O40	0	0	1	0	1
O48	1	0	0	0	1
MOLLARETII	**0**	**1**	**0**	**0**	**1**
ROHDEI	**0**	**2**	**0**	**0**	**2**
Total	**51**	**56**	**26**	**16**	**149**

Table A3.6 *Aeromonas* serotypes

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
CAVIAE	**126**	**77**	**32**	**23**	**258**
O2	1	1	1	0	3
O3	4	3	2	1	10
O8	0	0	0	1	1
O11	3	1	0	0	4
O12	2	0	0	0	2
O13	1	0	0	0	1
O15	2	0	0	0	2
O16	2	0	0	1	3
O17	0	0	1	1	2
O22	0	2	0	0	2
O26	1	0	0	0	1
O27	0	0	1	0	1
O30	1	0	0	0	1
O31	0	0	0	1	1
O33	0	0	1	0	1
O37	0	2	0	0	2
O43	0	0	1	0	1
O44	3	1	1	0	5
O?	102	64	23	17	206
O Rough	4	3	1	1	9
HYDROPHILA	**31**	**14**	**9**	**3**	**57**
O3	0	1	0	0	1
O7	0	1	0	1	2
O11	1	0	0	0	1
O14	1	0	0	0	1
O30	0	0	1	0	1
O32	1	0	0	0	1
O33	1	0	0	0	1
O35	1	0	0	0	1
O37	0	0	0	1	1
O40	1	0	0	0	1
O?	25	11	8	1	45
O Rough	0	1	0	0	1
VERONII biotype sobria	**7**	**2**	**4**	**1**	**14**
O2	1	0	0	0	1
O3	1	0	0	0	1
O12	1	0	0	0	1
O37	1	0	0	0	1
O?	2	2	3	0	7
O Rough	1	0	1	1	3
SPECIES	**1**	**3**	**0**	**1**	**5**
Total	**165**	**96**	**45**	**28**	**334**

Table A3.7 Vibrio serotypes

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL	
CHOLERAE NON-O1		1	0	0	0	1
Total	1	0	0	0	1	

Table A3.8 Bacillus spp.

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
CEREUS	1	2	0	1	4
FIRMUS	1	0	0	0	1
LICHENFORMIS	0	1	0	0	1
PUMILUS	0	2	0	0	2
SUBTILIS	2	3	0	1	6
Total	4	8	0	2	14

Table A3.9 *Clostridium difficile* ribotypes

C. DIFFICILE PCR RIBOTYPE	TOXIN A	TOXIN B	ALL CASES	ALL CONTROLS	TOTAL
1	+	+	14	5	19
2	+	+	10	5	15
5	+	+	9	9	18
6	+	+	0	1	1
7	+	+	1	0	1
9	–	–	3	14	17
10	–	–	26	32	58
11	+	+	2	0	2
12	+	+	0	3	3
14	+	+	22	11	33
15	+	+	12	5	17
17	–	+	2	3	5
18	+	+	3	0	3
19	+	+	4	2	6
20	+	+	26	20	46
21	+	+	0	1	1
23	late	weak	3	3	6
26	variable	variable	9	10	19
31	–	–	13	4	17
32	–	–	1	1	2
35	–	–	4	1	5
37	+	+	0	1	1
38	–	–	1	2	3
39	–	–	5	0	5
45	+	+	1	1	2
46	+	+	1	0	1
50	+	+	4	0	4
54	+	+	3	1	4
56	+	+	8	5	13
57	+	+	0	1	1
62	+	+	1	0	1
66	–	–	0	1	1
67	–	–	1	0	1
76	+	+	0	2	2
77	+	+	0	1	1
78	late	+	0	1	1
79	–	–	1	0	1
82	–	–	1	0	1
83	+	+	1	1	2
84	–	–	2	1	3
85	–	–	2	0	2
86	+	+	1	1	2
87	+	+	1	1	2
88	–	–	1	0	1
89	–	–	1	0	1
90	+	+	0	1	1
91	–	–	1	0	1
92	+	+	2	0	2
93	+	+	1	0	1
94	+	+	3	0	3
95	+	+	1	0	1
96	+	+	1	0	1
97	+	+	1	0	1
98	+	+	1	1	2
99	–	–	1	0	1
100	–	–	1	0	1
103	+	+	2	1	3
104	+	+	0	1	1
Total			**215**	**154**	**369**

Table A3.10 *Clostridium perfringens* testing

	POSITIVE ELISA OR RPLA N = 141				NEGATIVE ELISA AND RPLA N = 1023			
	CASE		CONTROL		CASE		CONTROL	
NO. OF SEROTYPED SAMPLES PER PATIENT	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE
0	92	89	12	12	424	415	464	452
1	1	5	2	1	5	8	11	13
2	27	23	4	4	47	55	53	61
3	2	4	0	1	8	6	7	7
4	0	2	0	0	2	2	2	3
5	1	0	0	0	0	0	0	1
total	**123**	**123**	**18**	**18**	**486**	**486**	**537**	**537**

Table A3.11 *Clostridium perfringens* serotypes

	POSITIVE RESULT				NEGATIVE RESULT			
	CASE		CONTROL		CASE		CONTROL	
SEROTYPE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE
1	0	0	0	0	0	0	0	0
1,44	0	1	0	0	0	0	0	1
1,5,9,14	0	0	0	0	0	0	1	0
1,7,44	0	0	0	0	1	1	0	0
2,27	0	0	0	0	0	0	1	0
3	0	0	0	0	1	1	0	1
3,24	0	0	0	0	0	0	0	1
3,34	0	1	0	0	0	0	1	1
3,4	0	0	0	0	1	1	0	0
3,4,34	1	1	0	0	1	2	0	0
3,4,36	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
4,34	0	0	0	0	0	0	0	0
5	1	2	0	0	2	4	1	2
5, 43	0	0	0	0	0	0	0	0
5,14,31,43	0	0	0	0	0	0	0	1
5,14,42	0	0	0	0	0	0	0	1
5,41,43	0	0	0	0	0	0	0	1
5,7,9,70	0	0	0	0	1	0	0	0
5,9	0	0	0	0	0	0	1	0
6	1	0	0	0	1	0	0	0
6,50,74	0	0	0	0	0	0	1	1
7	0	0	0	0	1	3	1	1
7,11	0	0	0	0	0	0	0	1
7,11,13	0	1	0	0	0	2	0	0
7,11,13,18	0	0	0	0	0	1	0	0
7,11,13,67	0	0	0	0	1	1	0	0
7,18	0	0	0	0	1	1	0	0
7,36	0	0	0	0	1	1	0	0
7,44	0	0	0	0	1	0	0	0
7,9,41	0	0	0	0	0	0	0	1
7,9,43	0	0	0	0	1	1	0	0
8	0	0	0	0	0	0	2	1
8,19	0	0	0	0	1	0	0	0
8,29	0	0	0	0	1	0	0	0
8,44	0	0	0	0	0	1	0	0
9	0	1	0	0	1	0	0	0
9,57	0	0	0	0	0	1	0	0
10,11,13,18	0	0	0	0	1	0	0	0
10,55	0	0	0	0	0	0	0	0

Table A3.11 – *continued*

	POSITIVE RESULT				NEGATIVE RESULT			
	CASE		CONTROL		CASE		CONTROL	
SEROTYPE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE
11	0	0	0	0	2	2	0	0
11,13	1	1	0	0	0	0	0	0
11,56	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	1	0
12,27	0	0	0	0	0	0	0	0
14,43	0	0	0	0	0	0	0	1
15	0	2	0	0	0	2	0	0
17,52	0	0	0	0	0	0	1	1
18	0	0	0	0	0	2	0	3
19	0	0	0	0	0	0	0	0
20,39,50,74	0	1	0	0	0	0	0	0
22	0	0	0	0	1	0	0	0
23,27	0	0	0	1	0	0	0	1
24	0	0	0	0	0	0	0	0
24,34,62	0	0	0	0	0	0	0	1
25	0	0	0	0	1	0	3	4
25 (weak)	0	0	0	0	0	1	0	0
25,31,42	0	0	0	0	1	1	0	0
25,31,68	0	1	0	0	3	1	0	1
25,33,61,68	1	0	0	0	0	0	0	0
26,27	1	0	0	0	0	0	0	0
27	2	1	1	1	1	0	4	4
27,43,62	0	0	0	0	1	0	0	0
27,66,68	0	0	0	0	0	0	0	0
27,69,72	0	0	0	0	0	0	0	0
27,70,71	0	0	0	0	0	0	1	0
28	0	0	0	0	3	2	2	2
28,37	1	0	0	0	0	0	0	1
29	0	0	0	0	0	0	2	5
30	0	0	0	0	0	0	0	1
31	0	0	0	0	0	0	0	1
31,35,68	0	0	0	0	0	1	0	0
31,36	0	0	0	0	0	1	0	0
31,68	0	0	0	0	2	1	0	1
32	0	0	0	0	0	0	0	4
33	0	0	0	0	0	1	1	0
33,61	7	3	0	0	2	1	3	2
33,61,68	1	0	0	0	0	0	0	0
34	0	1	0	0	0	0	0	1
35	0	0	0	0	1	1	0	0
35,63,67	0	0	0	0	0	0	0	1
36	3	0	0	0	0	1	0	0
36,38	0	1	0	0	0	1	1	0
36,38,41,53,67	0	0	0	0	0	0	0	1
36,68	0	0	0	0	0	1	0	1
38	1	0	0	0	1	0	2	1
38,39,42	0	0	0	0	0	0	0	0
38,40	0	1	0	0	0	0	0	0
38,41	0	0	0	0	0	2	0	0
38,41,67	0	0	0	0	0	0	0	1
38,46,47	0	0	0	0	0	0	1	1
38,56,67	0	0	0	0	0	0	0	1
38,57,67	0	0	0	0	0	0	1	1
38,67	0	0	0	0	0	0	1	1
38,67,71	0	0	0	0	0	0	3	1
38,71	0	0	0	0	0	0	0	1
39	1	1	0	0	0	0	0	0
41	0	0	0	0	2	1	1	0
42	0	0	0	0	0	0	2	0
43	0	0	0	0	1	0	1	2
44	0	1	0	0	1	1	0	1
45	0	0	0	0	0	0	1	1

Table A3.11 – *continued*

	POSITIVE RESULT				NEGATIVE RESULT			
	CASE		CONTROL		CASE		CONTROL	
SEROTYPE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE
46	0	0	0	0	0	0	0	1
46,47	1	1	0	0	0	0	0	0
48	0	0	0	0	0	0	1	0
50	0	0	1	1	2	2	1	0
50,74	0	0	0	0	0	2	0	0
51	0	0	0	0	0	0	1	0
52	0	0	0	0	0	0	0	1
54	0	0	0	0	1	0	0	0
55	3	3	0	0	1	2	1	0
57	1	0	0	0	0	0	0	1
58	0	0	0	0	0	0	0	1
61	0	0	0	0	0	0	0	0
62	0	0	0	0	0	0	0	1
63	0	0	0	0	1	0	0	0
63,67	0	0	0	0	0	0	1	0
64	0	0	0	0	0	0	0	0
64, 68	0	0	0	0	0	0	0	0
65,69	0	0	0	0	1	0	1	1
65,69,71	0	0	0	0	0	0	0	0
65,69,72	1	1	0	0	1	3	0	1
66	1	1	0	0	1	0	0	0
67	0	0	0	0	0	0	1	2
68	1	0	1	1	1	2	1	1
69,72	0	0	0	0	0	1	0	1
70	0	0	0	0	0	0	1	1
71	0	0	0	0	4	4	1	3
72	0	0	0	0	0	0	0	0
73	0	0	0	0	1	0	0	0
74	0	0	0	0	0	0	0	1
75	0	0	0	0	3	1	3	0
PS20,PS60	0	0	0	0	0	0	1	0
PS21	0	0	0	0	1	1	1	0
PS28	0	0	0	0	0	0	1	1
PS28,PS56,PS59,PS62	0	0	0	0	0	0	0	0
PS30	0	1	0	0	0	0	0	2
PS30,PS40	0	0	0	0	1	1	0	0
PS35	0	0	0	0	0	1	1	1
PS35,PS56	0	0	0	0	0	0	1	1
PS39	0	0	0	0	1	1	0	0
PS40	0	0	0	0	0	0	1	0
PS40,PS73	0	0	0	1	0	0	0	0
PS41,PS43	0	0	0	0	0	0	0	0
PS47	0	0	0	0	0	0	2	0
PS56	0	0	0	0	0	1	0	1
PS56,PS59,PS62,PS68	0	0	0	0	0	0	1	1
PS56,PS59,PS62,PS74	0	0	0	0	0	0	0	1
PS59,PS62	0	0	0	0	0	1	0	0
PS60	1	0	0	0	1	1	2	1
PS68	0	0	0	0	0	1	0	0
PS68,PS80	0	1	0	0	0	0	2	1
PS69	1	1	0	0	0	0	0	0
PS73	0	0	1	0	1	0	2	1
PS74	0	0	0	0	0	1	0	0
PS79	0	0	0	0	0	0	0	0
PS80	0	0	0	0	1	0	0	0
TW16	0	0	0	0	0	0	0	0
TW16,TW40,PS67	0	0	0	0	1	1	0	0
TW17	0	0	1	1	0	1	0	0
TW18	0	0	0	0	0	1	0	0
TW18,PS25	0	0	0	0	0	0	1	0
TW18,PS35	0	0	0	0	1	1	0	0
TW19	0	0	0	0	2	1	2	2
TW22	0	0	0	0	0	0	0	1
TW23	1	0	0	0	1	1	1	1

Table A3.11 – *continued*

	POSITIVE RESULT				NEGATIVE RESULT			
	CASE		CONTROL		CASE		CONTROL	
SEROTYPE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE	SPORE	VIABLE
TW24	1	1	0	0	1	2	2	1
TW28	0	0	0	0	0	1	0	0
TW28,PS20	0	0	0	0	0	1	0	0
TW29,PS41,PS42,PS43	0	0	0	0	0	0	1	0
TW40,PS67	2	2	0	0	0	0	0	0
TW48	0	0	0	0	0	0	0	0
TW50	0	1	0	0	0	0	0	0
TW51	0	0	0	0	0	0	0	0
TW52	0	0	0	0	1	0	1	2
TW52,PS30	0	1	0	0	0	0	0	0
TW55	0	0	0	0	1	0	0	0
TW8	0	0	0	0	1	1	0	1
TW9	0	0	0	0	1	1	1	1
AA	0	0	0	1	0	0	1	0
NSA	0	0	0	0	1	2	2	0
NT	10	8	2	2	26	30	27	41
Total number of different organisms identified	25	29	6	8	60	63	59	75

Table A3.12 *Staphylococcus aureus* phage typing

	GP CASE	GP CONTROL	COMMUNITY CASE	COMMUNITY CONTROL	TOTAL
3A, 3C+-, 55, 71++	1	0	0	0	1
6, 42E, 47, 53, 54, 75, 77, 81++, 84, 85+	0	1	0	0	1
29++	0	1	0	0	1
29, 42E+, 52, 79, 80, 81++, 95	1	0	0	0	1
29, 42E+, 79	1	0	0	0	1
29, 42E+, 80+-, 95++	0	1	0	0	1
29, 52, 79, 80++	1	0	0	0	1
52. 52A, 79, 80, 95++	1	0	0	0	1
52+-, 80+	0	0	1	0	1
54+	1	0	0	0	1
94++	1	0	0	0	1
NT	3	1	0	1	5
Total	**10**	**5**	**1**	**1**	**17**

Appendix 4
Supplementary Results for Chapter 7

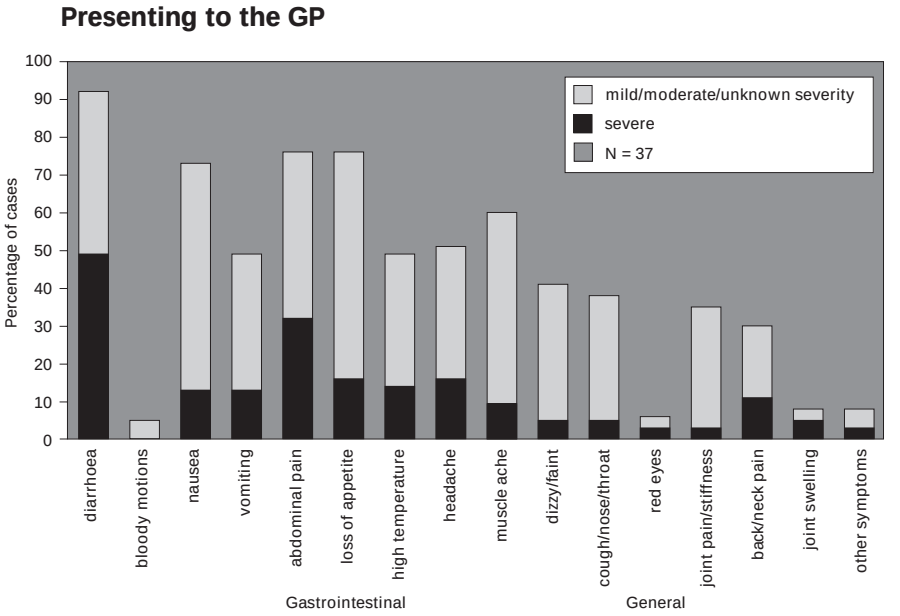
Table A4.1 Symptoms by study for adults and children

STUDY COMPONENT	COMMUNITY COHORT N = 555		COMMUNITY COHORT N = 296		COMMUNITY COHORT N = 221		ENUMERATION COMPONENT N = 2,182		ENUMERATION COMPONENT N = 1,299		ENUMERATION COMPONENT N = 871		GENERAL PRACTICE COMPONENT		GENERAL PRACTICE COMPONENT	GENERAL PRACTICE COMPONENT
SYMPTOMS	CASES	%	ADULTS	%	CHILDREN	%	CASES	%	ADULTS	%	CHILDREN	%	CASES	%	ADULTS %	CHILDREN %
Diarrhoea	102	18.38	49	16.55	36	16.29	828	37.95	507	39.03	317	36.39	462	27.97	29.40	25.40
Bloody diarrhoea	10	1.80	8	2.70	2	0.90	76	3.48	60	4.62	15	1.72	47	2.85	4.20	0.50
Vomiting	42	7.57	15	5.07	22	9.95	431	19.75	230	17.71	200	22.96	165	9.99	9.30	11.20
Abdo pain	101	18.20	59	19.93	32	14.48	737	33.78	488	37.57	246	28.24	417	25.24	30.30	16.40
Appetite	74	13.33	33	11.15	35	15.84	713	32.68	424	32.64	287	32.95	351	21.25	22.90	18.40
Weight loss	28	5.05	12	4.05	13	5.88	479	21.95	319	24.56	158	18.14	239	14.47	18.20	7.80
Flatuence	67	12.07	43	14.53	13	5.88	489	22.41	328	25.25	157	18.03	287	17.37	21.40	10.40
Urine	5	0.90	3	1.01	2	0.90	110	5.04	83	6.39	27	3.10	48	2.91	3.10	2.50
Discharge	8	1.44	5	1.69	2	0.90	60	2.75	46	3.54	14	1.61	44	2.66	3.60	1.00
Joint pain	38	6.85	27	9.12	8	3.62	259	11.87	217	16.71	39	4.48	172	10.41	14.30	3.50
Joint swelling	15	2.70	14	4.73	1	0.45	53	2.43	47	3.62	6	0.69	38	2.30	3.10	0.80
Back pain	43	7.75	30	10.14	11	4.98	260	11.92	224	17.24	35	4.02	187	11.32	15.20	4.50
Aching	37	6.67	30	10.14	6	2.71	307	14.07	248	19.09	57	6.54	214	12.95	16.90	6.00
Heel pain	13	2.34	12	4.05	1	0.45	54	2.47	46	3.54	6	0.69	26	1.57	2.50	0.00
Headache	55	9.91	34	11.49	17	7.69	429	19.66	311	23.94	116	13.32	264	15.98	19.50	9.80
Dizziness	22	3.96	15	5.07	2	0.90	228	10.45	178	13.70	49	5.63	130	7.87	10.70	2.80
Double vision	5	0.90	3	1.01	2	0.90	39	1.79	34	2.62	5	0.57	27	1.63	2.60	0.00
Clumsiness	11	1.98	11	3.72	17	7.69	86	3.94	73	5.62	13	1.49	51	3.09	4.40	0.80
Unsteadiness	13	2.34	8	2.70	4	1.81	142	6.51	93	7.16	48	5.51	50	3.03	4.20	1.00
Pins/needles	24	4.32	18	6.08	3	1.36	116	5.32	102	7.85	13	1.49	70	4.24	6.00	1.20
Hand weak	11	1.98	10	3.38	1	0.45	94	4.31	76	5.85	18	2.07	45	2.72	3.70	1.00
Leg weak	17	3.06	13	4.39	2	0.90	180	8.25	143	11.01	33	3.79	93	5.63	7.60	2.20
Faintness	6	1.08	6	2.03	0	0.00	39	1.79	34	2.62	5	0.57	33	2.00	2.50	1.20
Tiredness	101	18.20	67	22.64	26	11.76	762	34.92	553	42.57	205	23.54	482	29.18	36.60	16.20
Red eyes	11	1.98	6	2.03	5	2.26	107	4.90	74	5.70	33	3.79	74	4.48	5.20	3.20
Sleepy	67	12.07	38	12.84	24	10.86	579	26.54	401	30.87	176	20.21	292	17.68	22.00	10.00
Skin rash	6	1.08	2	0.68	4	1.81	114	5.22	54	4.16	60	6.89	80	4.84	3.20	7.70
Other	16	2.88	8	2.70	7	3.17	114	5.22	71	5.47	42	4.82	55	3.33	3.20	3.50

Table A4.2 Symptoms by organism for adults and children

ORGANISM	*SALMONELLA*				*CAMPYLOBACTER*				ENTEROAGGREGATIVE *E. COLI*					
SYMPTOM	ADULTS N	ADULTS %	CHILDREN N	CHILDREN %	ADULTS N	ADULTS %	CHILDREN N	CHILDREN %	CASES N	CASES %	ADULTS N	ADULTS %	CHILDREN N	CHILDREN %
Diarrhoea	15	22.73	7	32	51	32.48	3	9.38	16	24.62	12	27.91	3	10.34
Bloody diarrhoea	0	0.00	1	5	7	4.46	0	0.00	3	4.62	2	4.65	0	0.00
Vomiting	1	1.52	3	14	16	10.19	2	6.25	3	4.62	2	4.65	1	3.45
Abdo pain	19	28.79	6	27	57	36.31	5	15.63	11	16.92	9	20.93	3	10.34
Appetite	17	25.76	4	18	31	19.75	5	15.63	10	15.38	6	13.95	3	10.34
Weight loss	13	19.70	2	9	35	22.29	2	6.25	10	15.38	7	16.28	2	6.90
Flatuence	11	16.67	4	18	35	22.29	2	6.25	16	24.62	13	30.23	3	10.34
Urine	1	1.52	1	5	10	6.37	1	3.13	0	0.00	0	0.00	0	0.00
Discharge	2	3.03	0	0	5	3.18	0	0.00	1	1.54	0	0.00	1	3.45
Joint pain	12	18.18	2	9	25	15.92	0	0.00	3	4.62	2	4.65	2	6.90
Joint swelling	3	4.55	0	0	4	2.55	0	0.00	0	0.00	0	0.00	0	0.00
Back pain	9	13.64	1	5	26	16.56	0	0.00	6	9.23	5	11.63	2	6.90
Aching	15	22.73	1	5	34	21.66	0	0.00	6	9.23	5	11.63	2	6.90
Heel pain	2	3.03	0	0	3	1.91	0	0.00	0	0.00	0	0.00	0	0.00
Headache	10	15.15	3	14	28	17.83	1	3.13	6	9.23	5	11.63	2	6.90
Dizziness	8	12.12	2	9	20	12.74	0	0.00	3	4.62	2	4.65	1	3.45
Double vision	3	4.55	0	0	3	1.91	0	0.00	1	1.54	1	2.33	0	0.00
Clumsiness	1	1.52	0	0	2	1.27	1	3.13	2	3.08	1	2.33	1	3.45
Unsteadiness	4	6.06	0	0	7	4.46	0	0.00	2	3.08	1	2.33	2	6.90
Pins/needles	1	1.52	1	5	6	3.82	1	3.13	2	3.08	2	4.65	0	0.00
Hand weak	3	4.55	0	0	5	3.18	1	3.13	0	0.00	0	0.00	0	0.00
Leg weak	4	6.06	0	0	14	8.92	0	0.00	2	3.08	1	2.33	1	3.45
Faintness	0	0.00	0	0	8	5.10	0	0.00	0	0.00	0	0.00	0	0.00
Tiredness	33	50.00	4	18	64	40.76	6	18.75	19	29.23	14	32.56	6	20.69
Red eyes	2	3.03	0	0	7	4.46	0	0.00	2	3.08	2	4.65	0	0.00
Sleepy	18	27.27	4	18	40	25.48	3	9.38	13	20.00	7	16.28	5	17.24
Skin rash	1	1.52	2	9	6	3.82	2	6.25	2	3.08	1	2.33	1	3.45
Other	1	1.52	2	9	5	3.18	2	6.25	1	1.54	0	0.00	1	3.45

Fig. A4.1 Symptom profile of Aeromonas cases (adults)



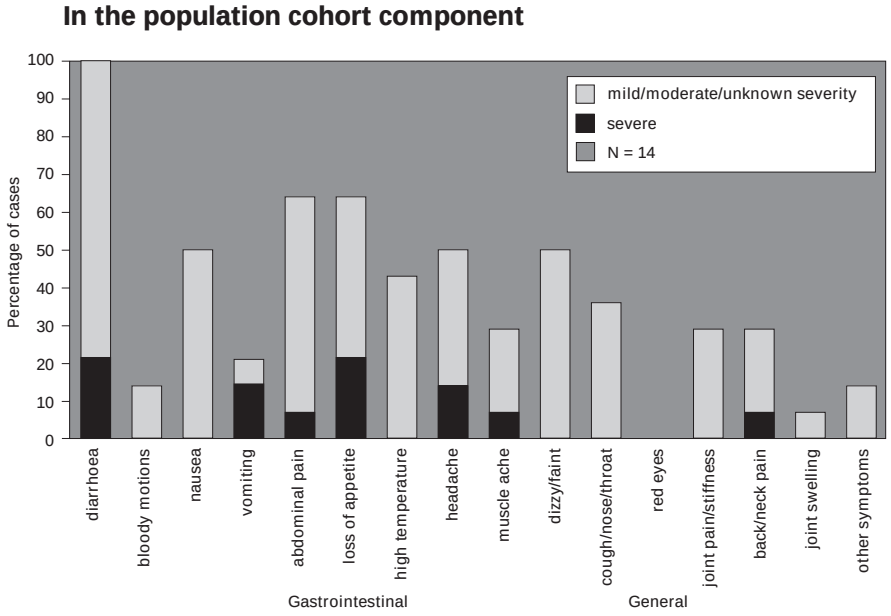
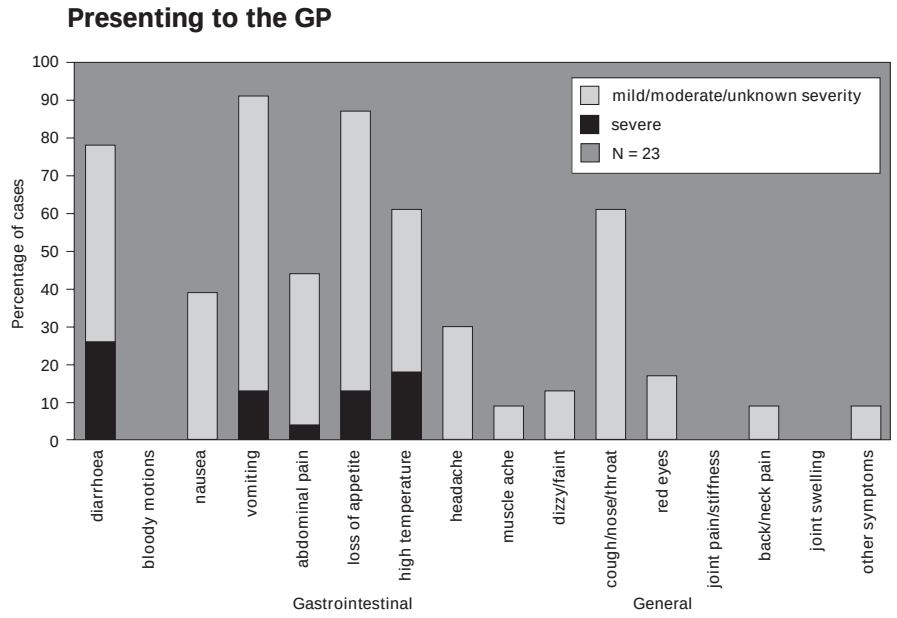


Fig. A4.2 Symptom profile of Aeromonas cases (children)



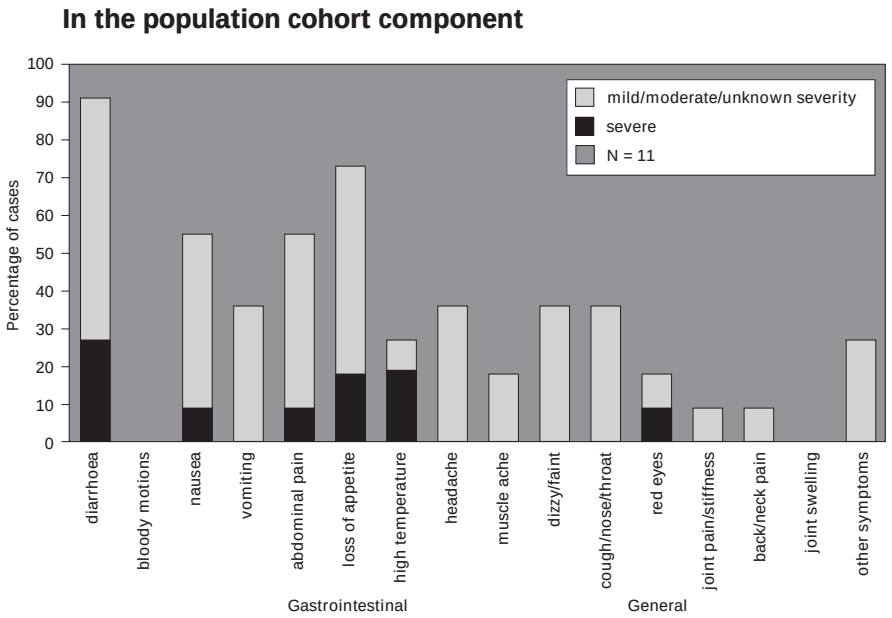
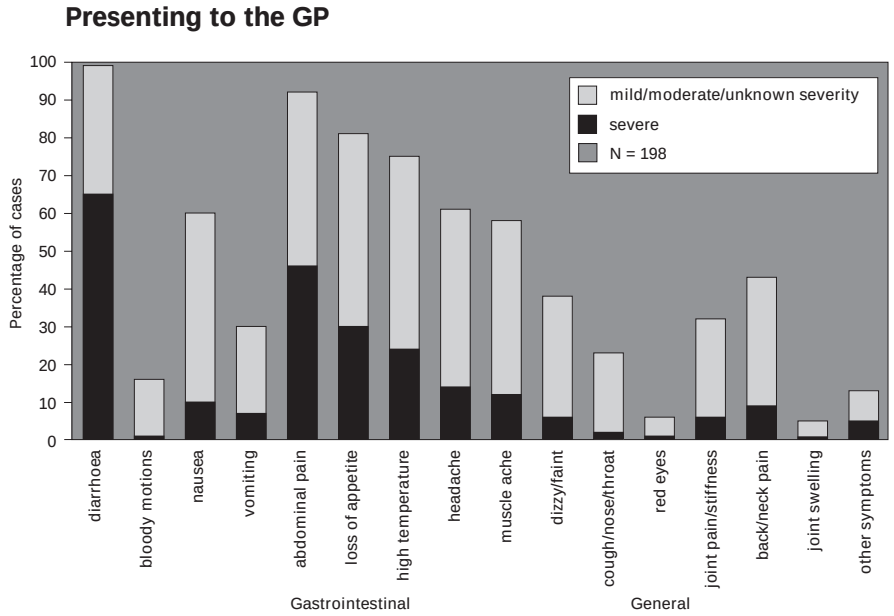


Fig. A4.3 Symptom profile of *Campylobacter* cases (adults)



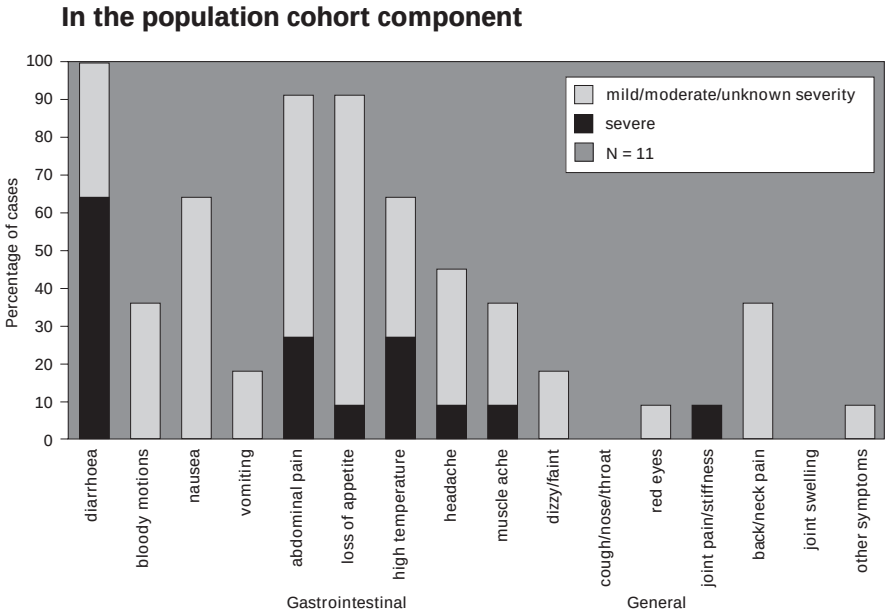
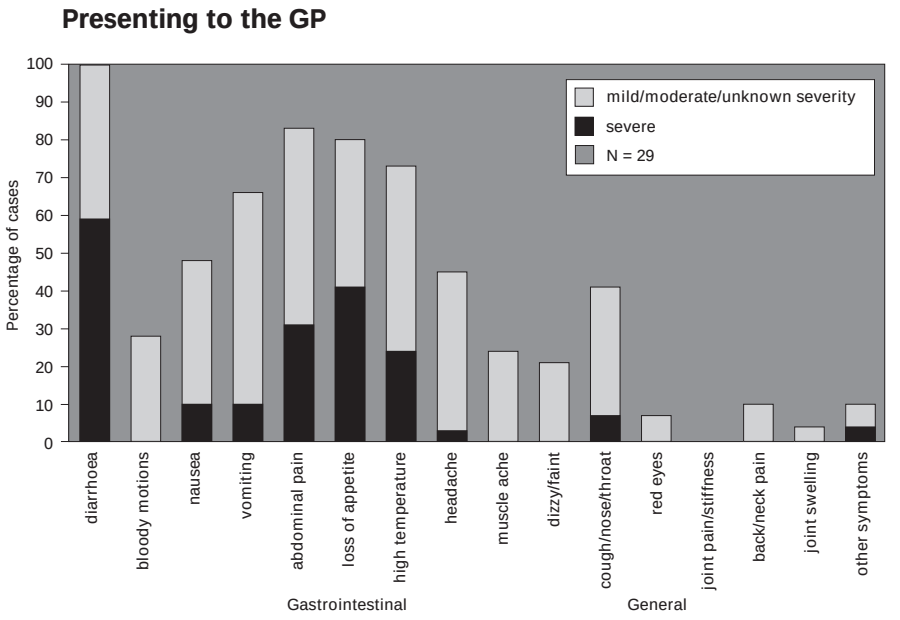


Fig. A4.4 Symptom profile of *Campylobacter* cases (children)



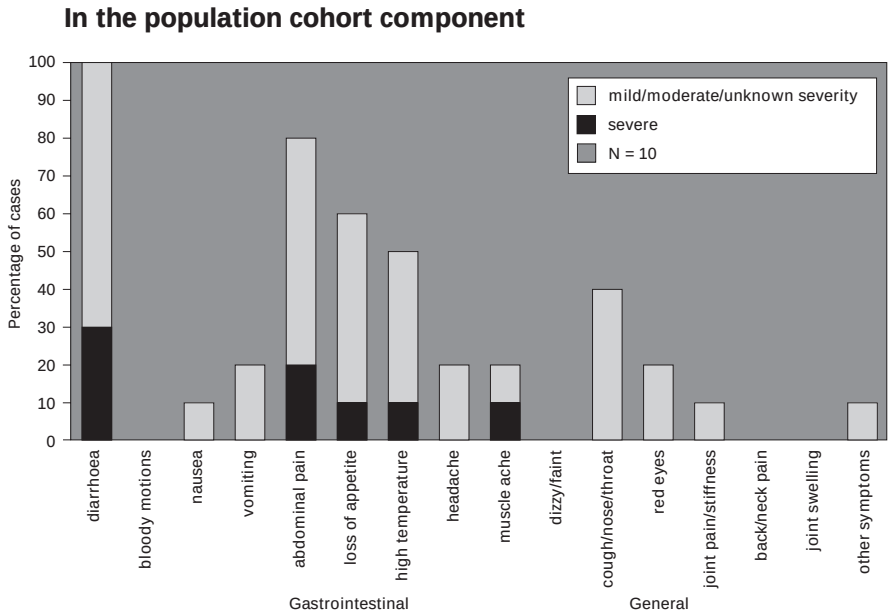


Fig. A4.5 Symptom profile of *C.perfringens* cases (adults)

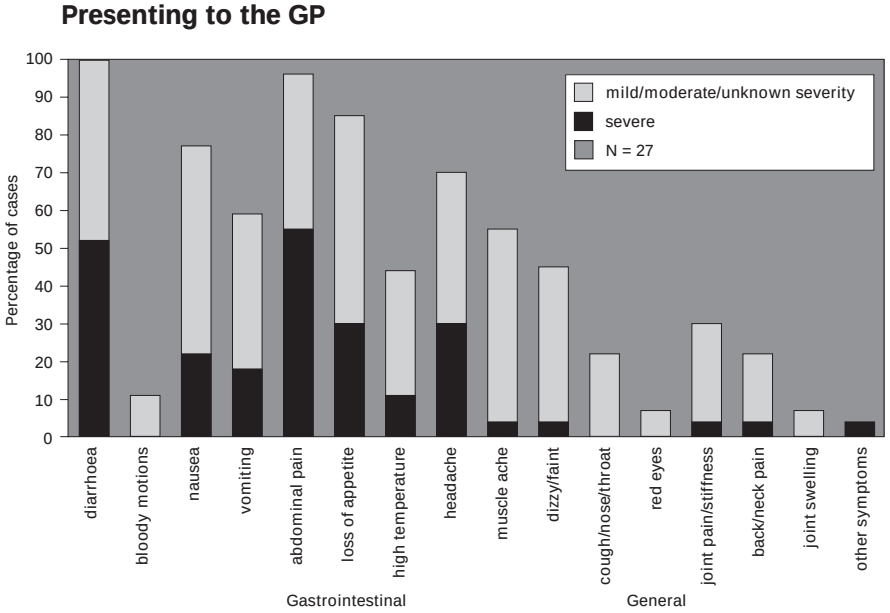


Fig. A4.6 Symptom profile of *C.perfringens* cases (children)

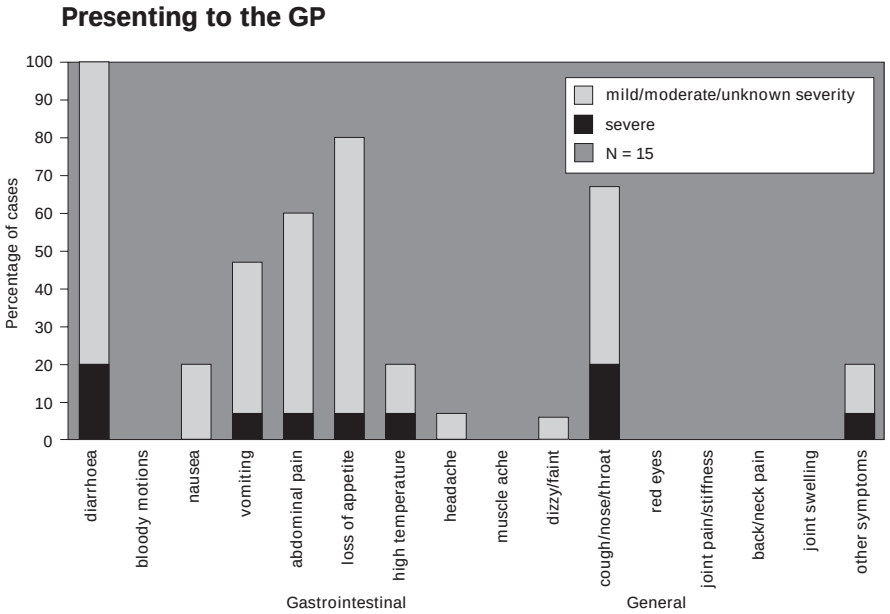


Fig. A4.7 Symptom profile of AEEC cases (adults)

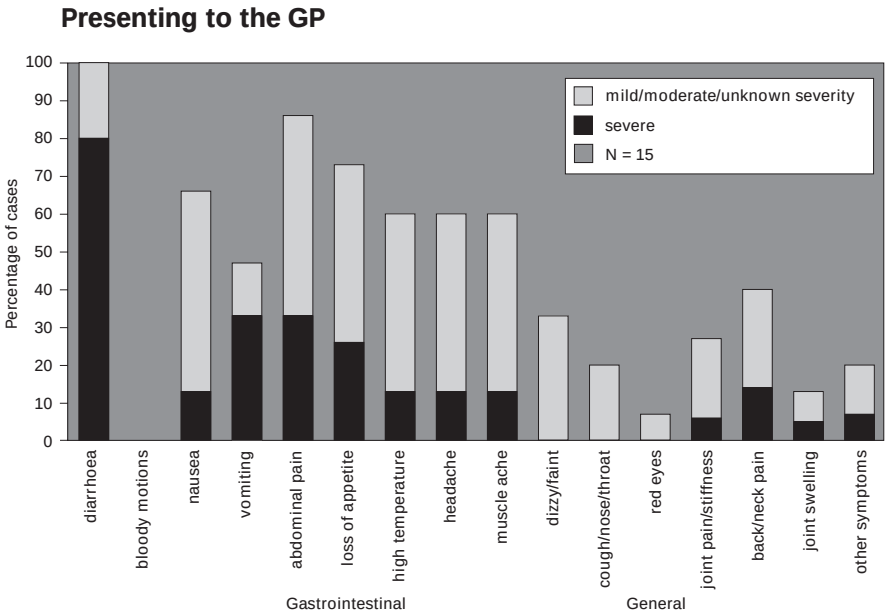


Fig. A4.8 Symptom profile of AEEC cases (children)

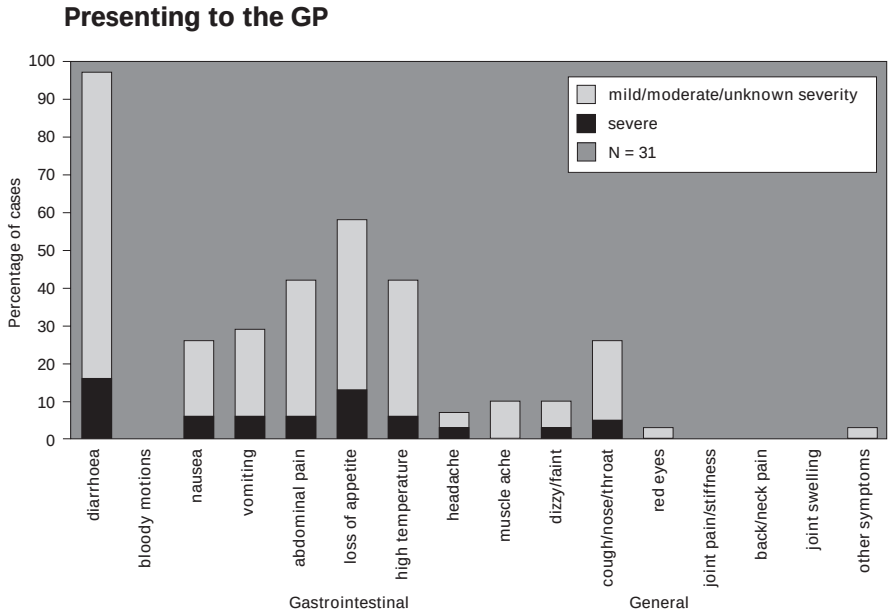


Fig. A4.9 Symptom profile of DAEC cases (adults)

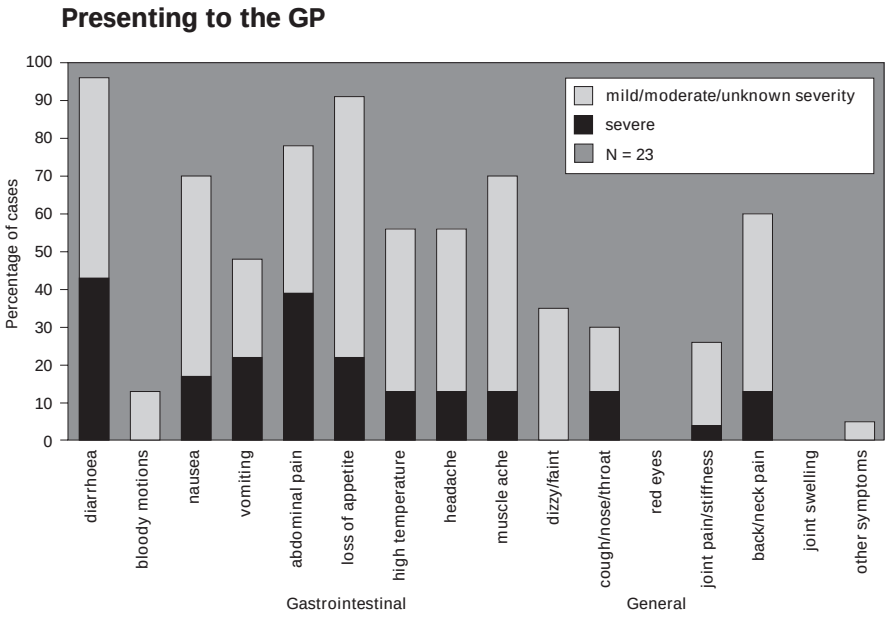


Fig. A4.10 Symptom profile of DAEC cases (children)

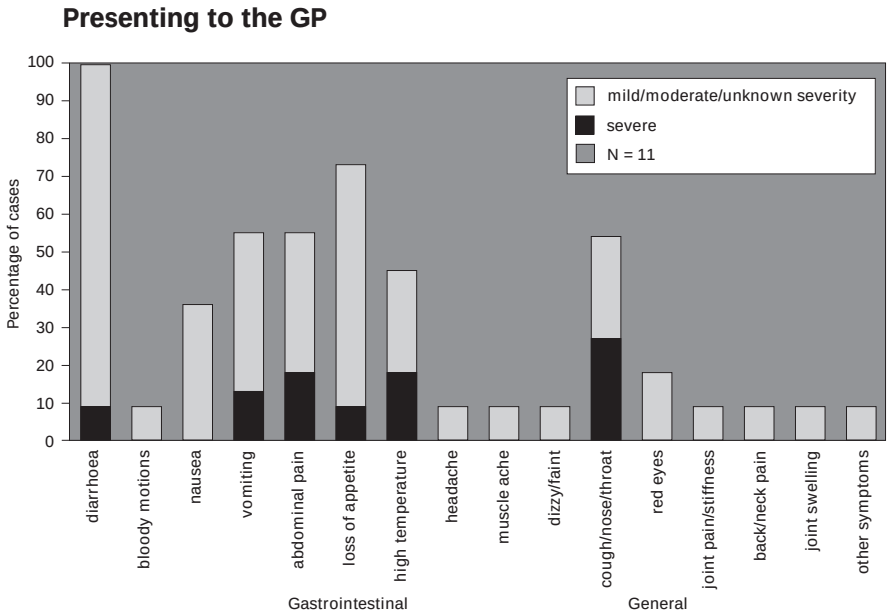


Fig. A4.11 Symptom profile of EAggEC cases (adults)

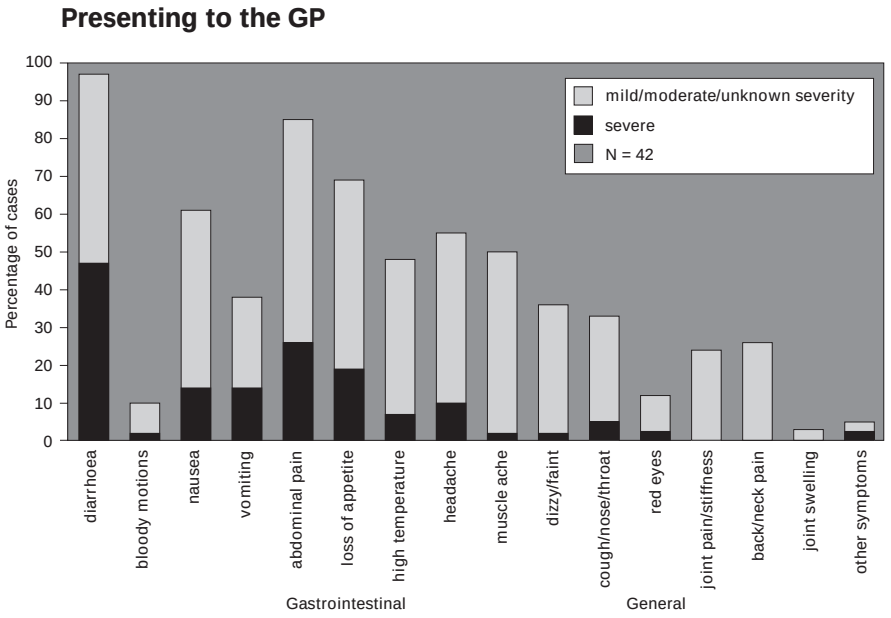


Fig. A4.12 Symptom profile of EAggEC cases (children)

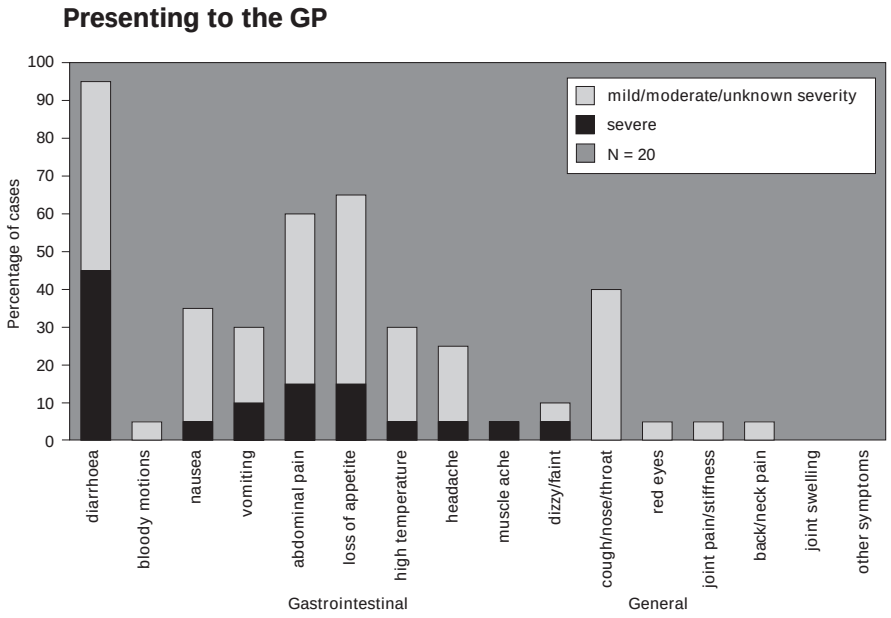


Fig. A4.13 Symptom profile of ETEC cases (adults)

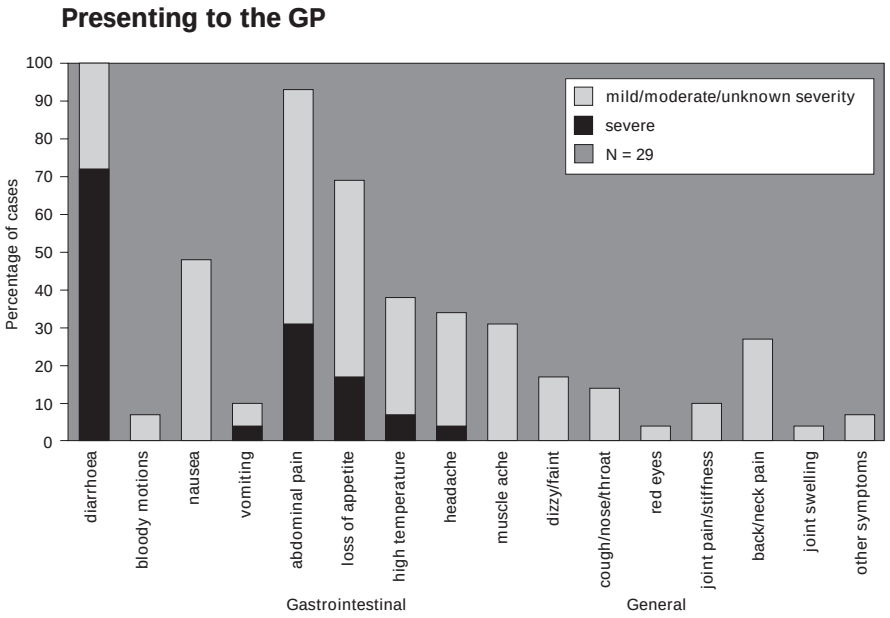


Fig. A4.14 Symptom profile of *Salmonella* cases (adults)

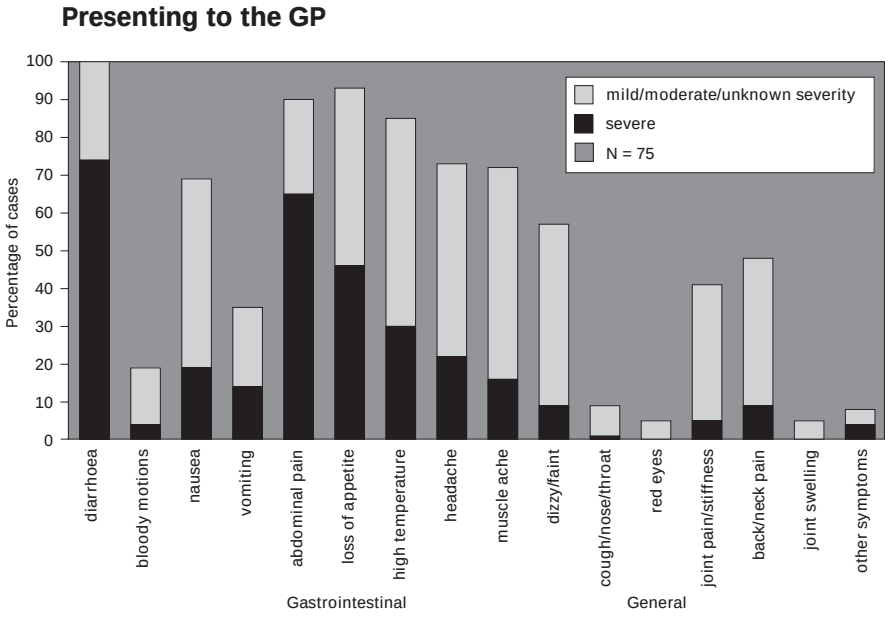


Fig. A4.15 Symptom profile of *Salmonella* cases (children)

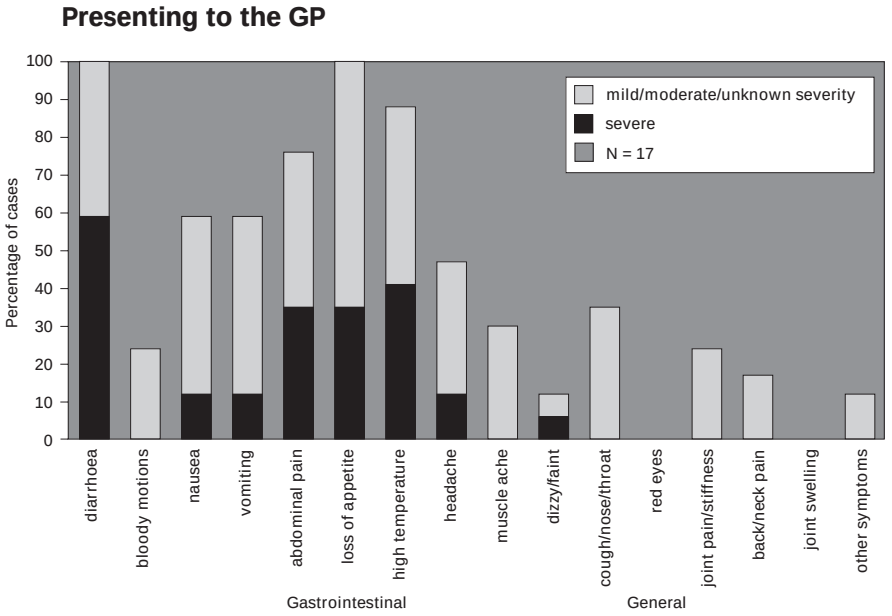


Fig. A4.16 Symptom profile of *Yersinia* cases (adults)

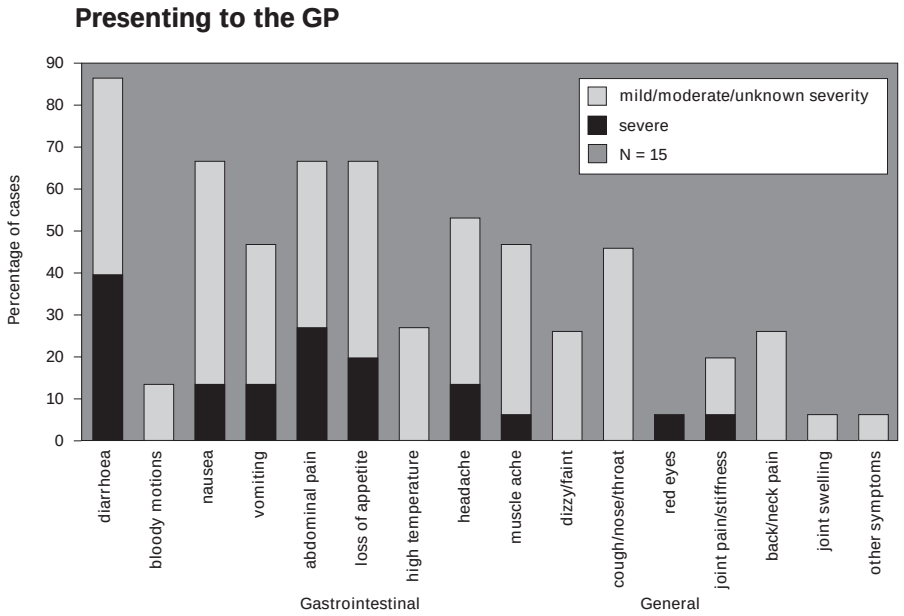


Fig. A4.17 Symptom profile of *Cryptosporidium* cases (children)

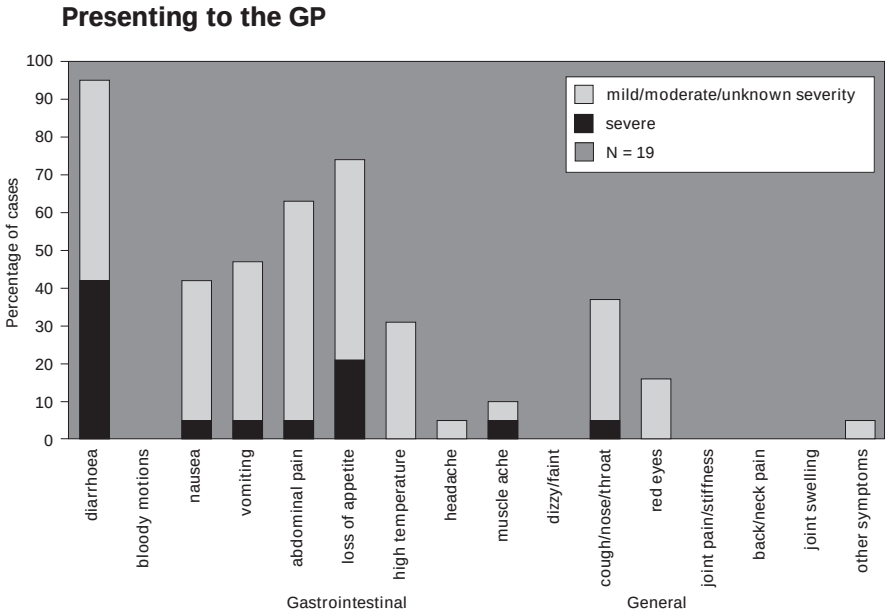


Fig. A4.18 Symptom profile of *Giardia* cases (adults)

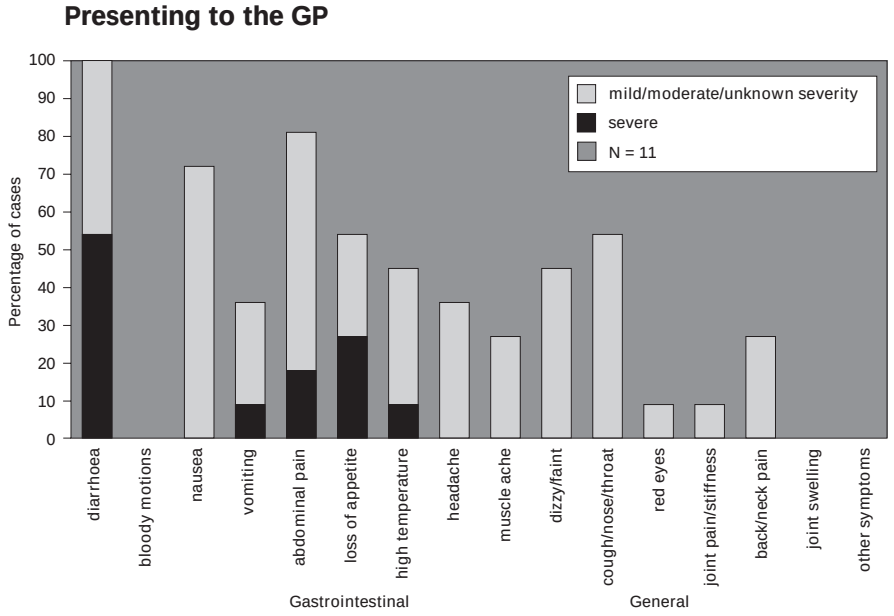
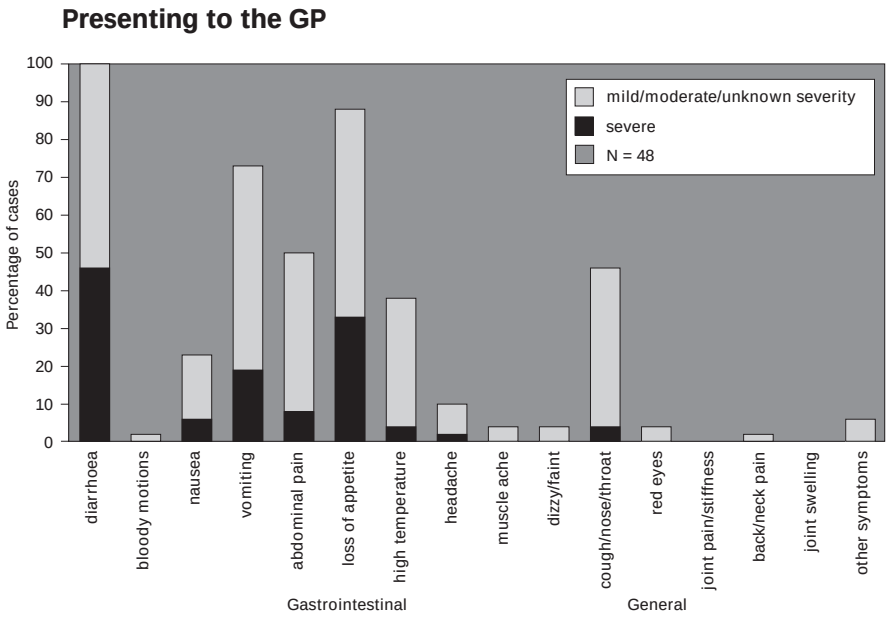


Fig. A4.19 Symptom profile of Adenovirus group F cases (children)



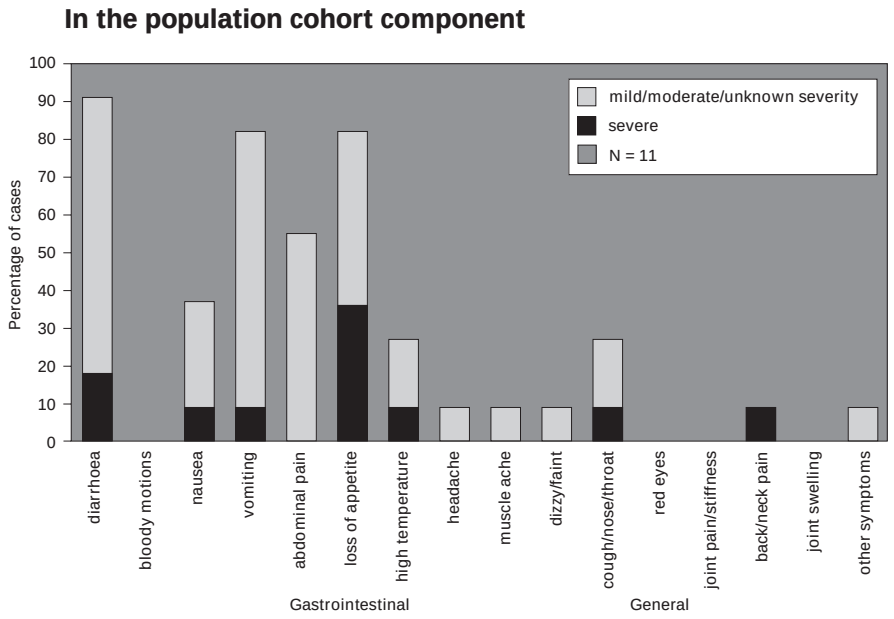


Fig. A4.20 Symptom profile of Astrovirus cases (adults)

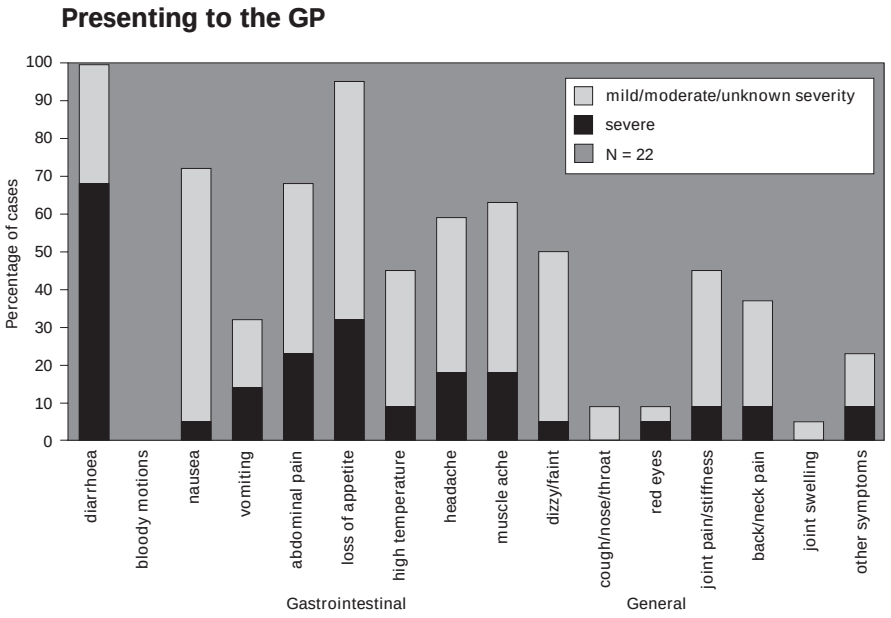


Fig. A4.21 Symptom profile of Astrovirus cases (children)

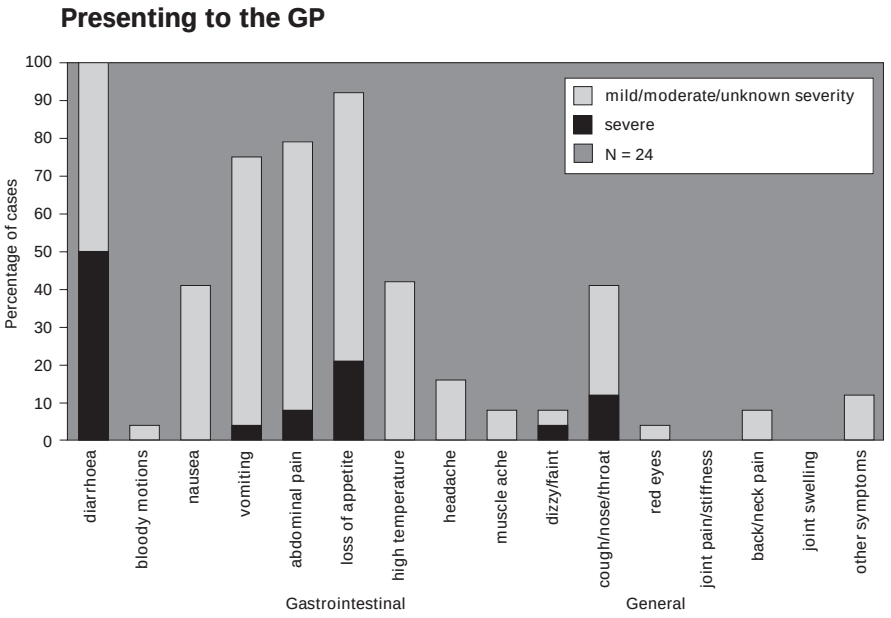


Fig. A4.22 Symptom profile of Calicivirus cases (children)

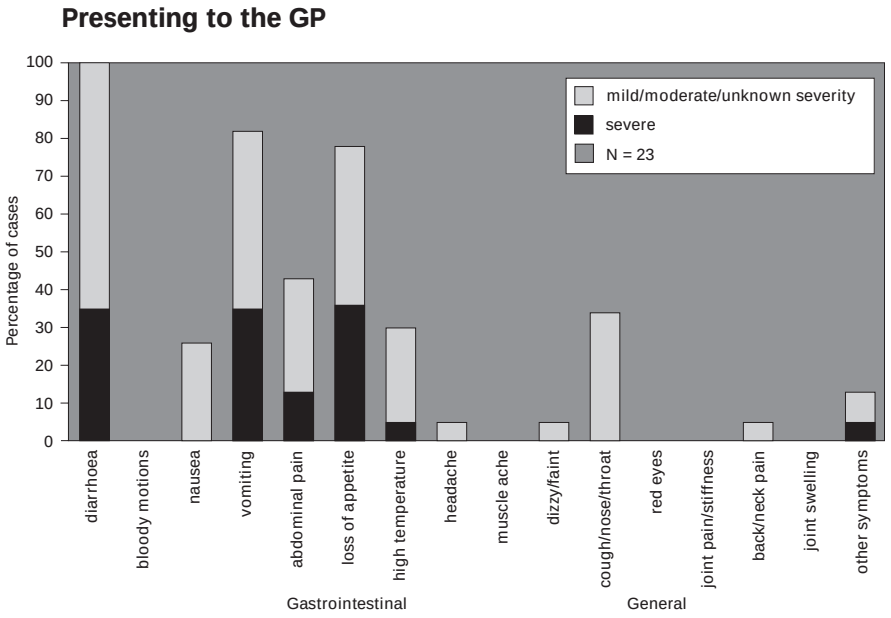


Fig. A4.23 Symptom profile of Rotavirus cases (adults)

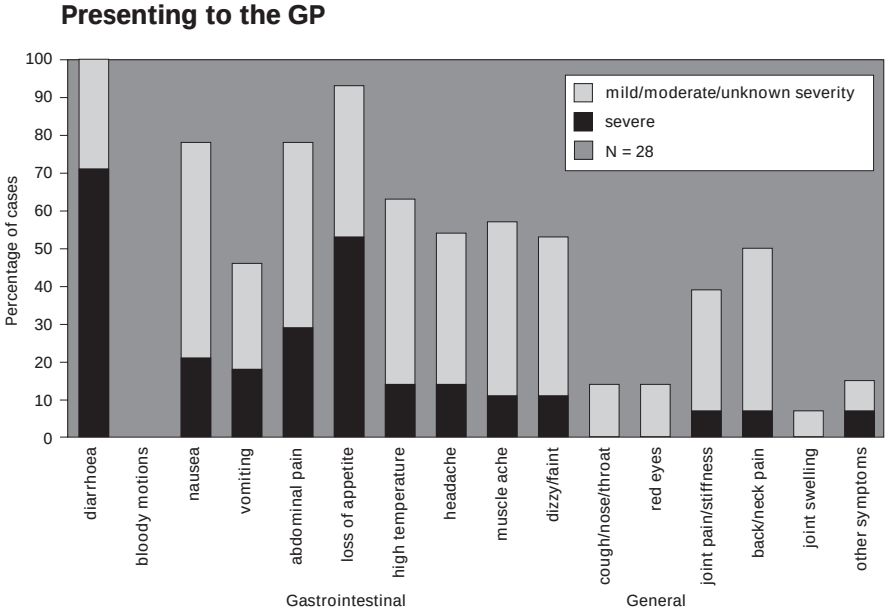
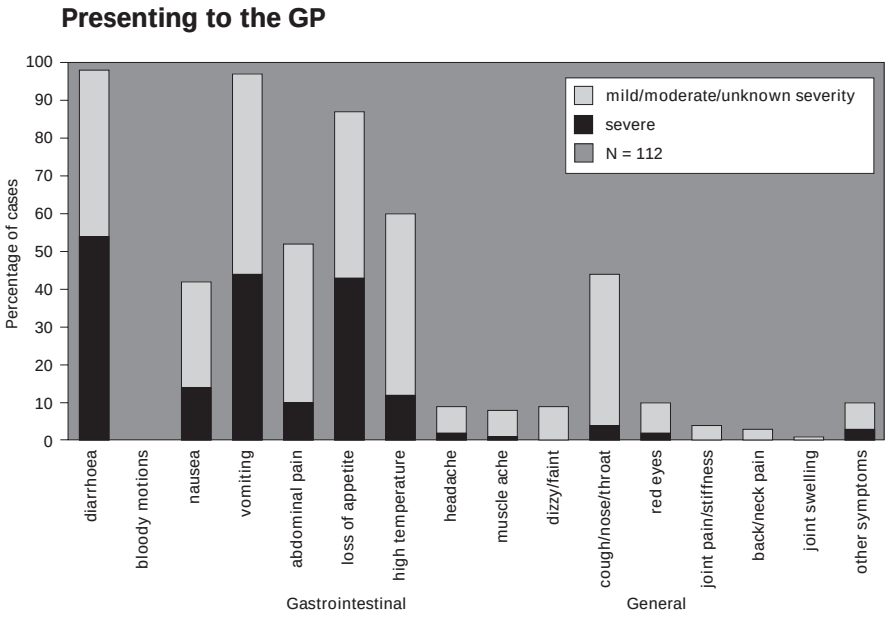


Fig. A4.24 Symptom profile of Rotavirus cases (children)



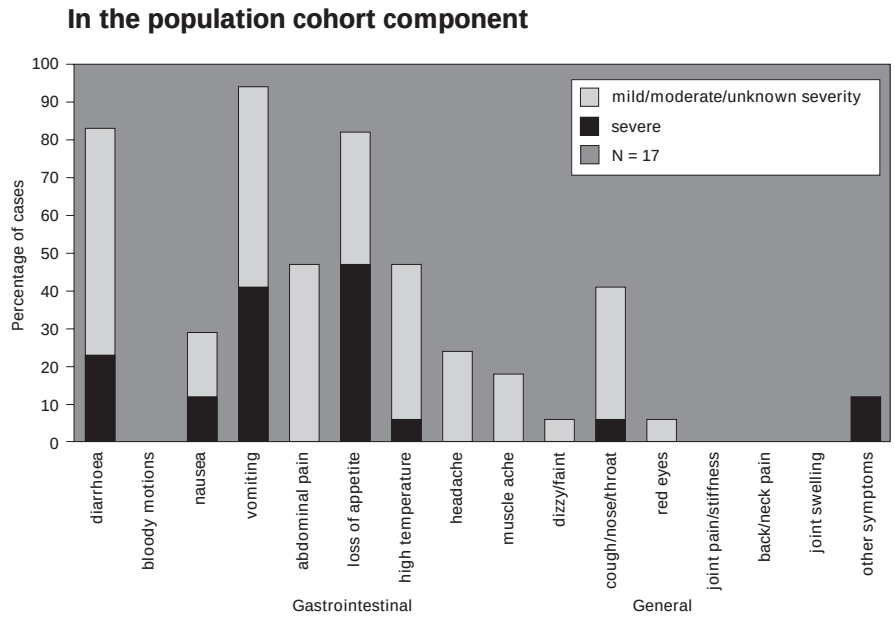
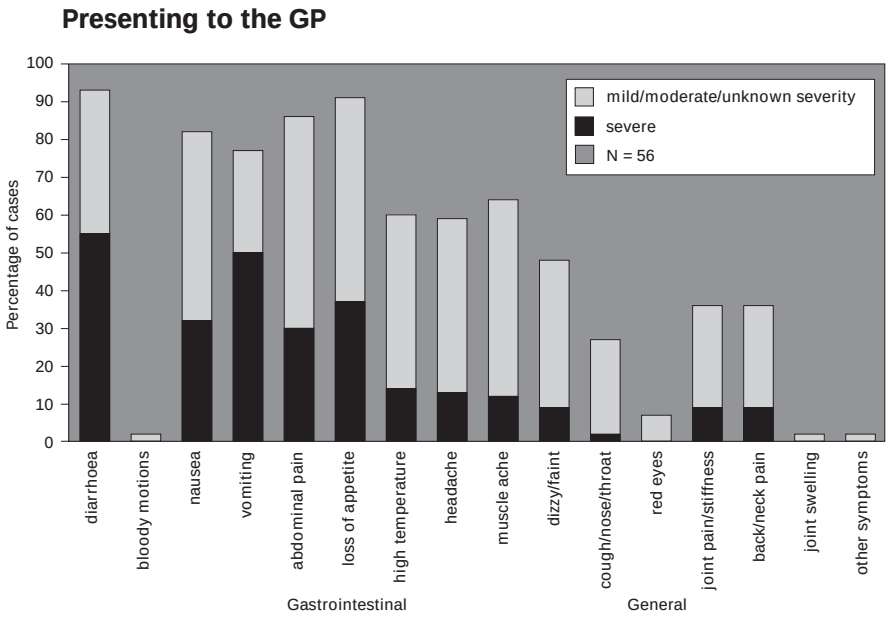


Fig. A4.25 Symptom profile of SRSV cases (adults)



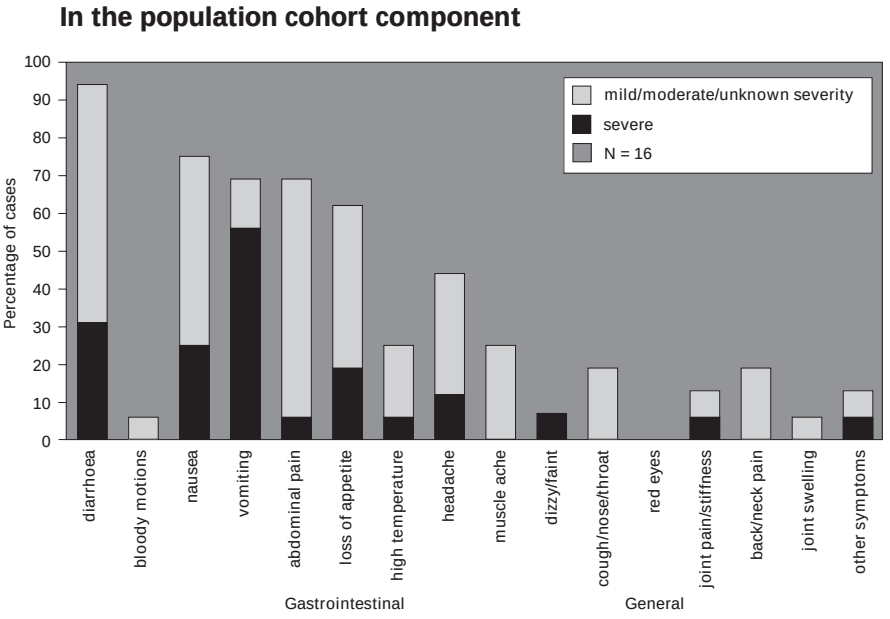
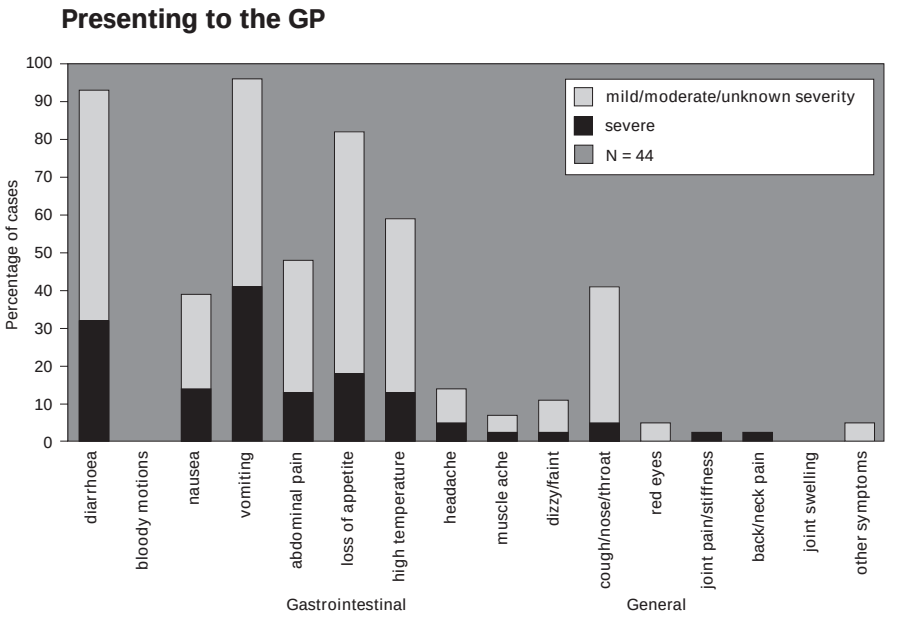


Fig. A4.26 Symptom profile of SRSV cases (children)



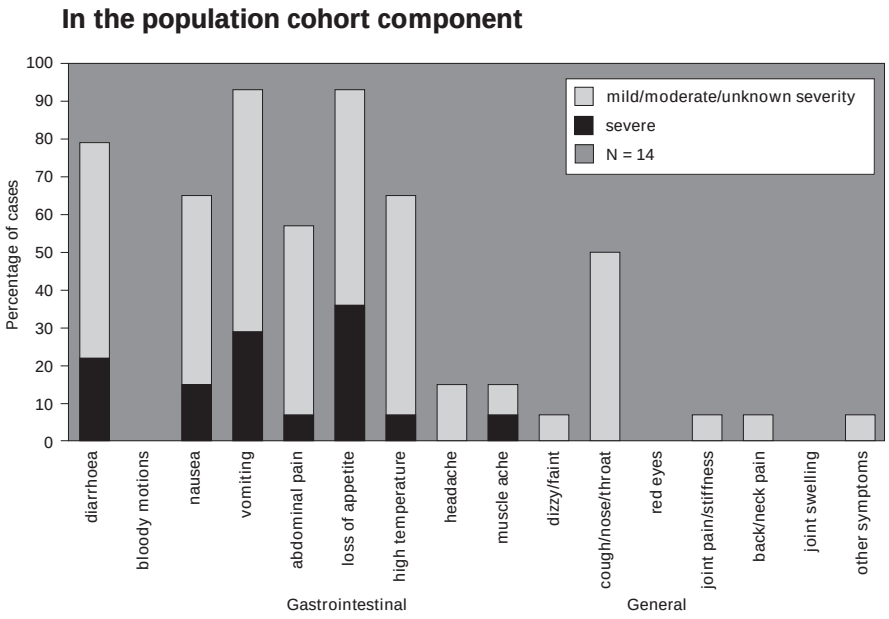
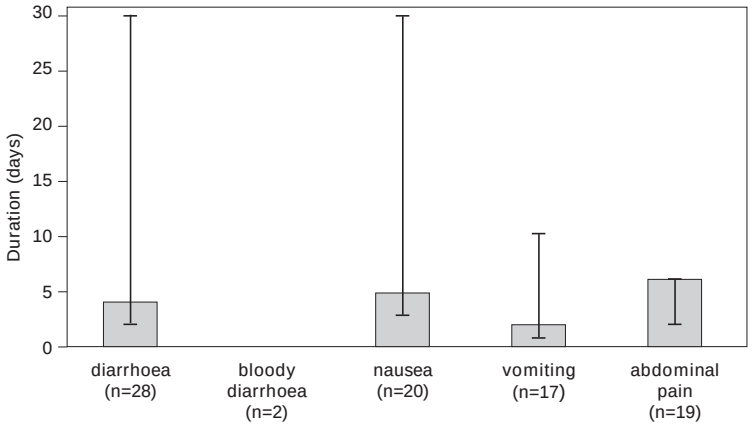


Figure A4.27 Duration of symptoms in cases positive for *Aeromonas* (adults)

Presenting to the GP



75 percentile figure for abdominal pain not included

In the population cohort component

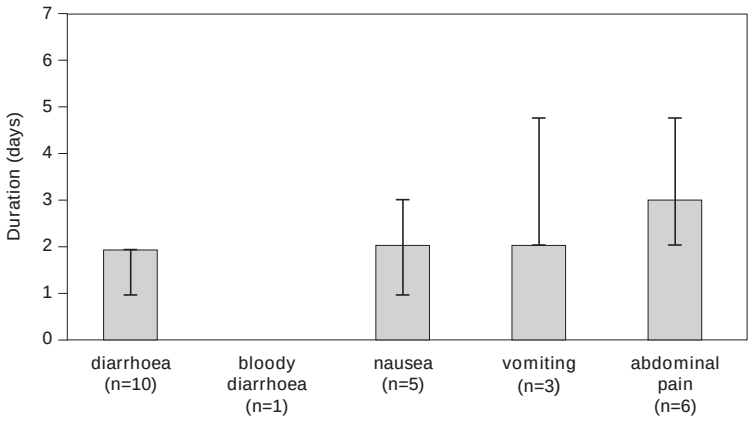


Figure A4.28 Duration of symptoms in cases positive for *Campylobacter* (adults)

Presenting to the GP

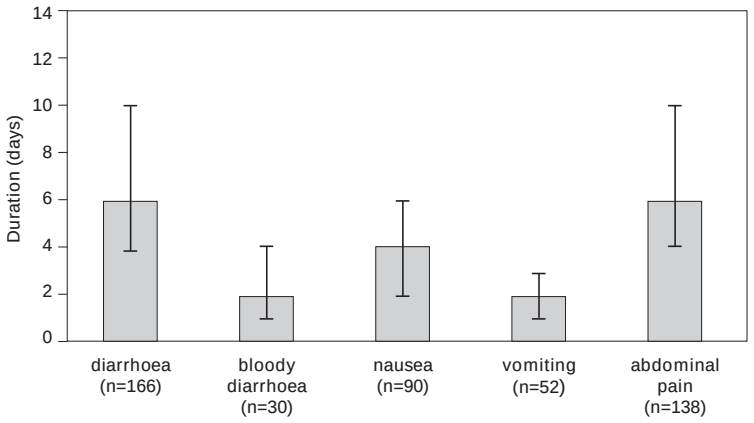


Figure A4.29 Duration of symptoms in cases positive for *Campylobacter* (children)

Presenting to the GP

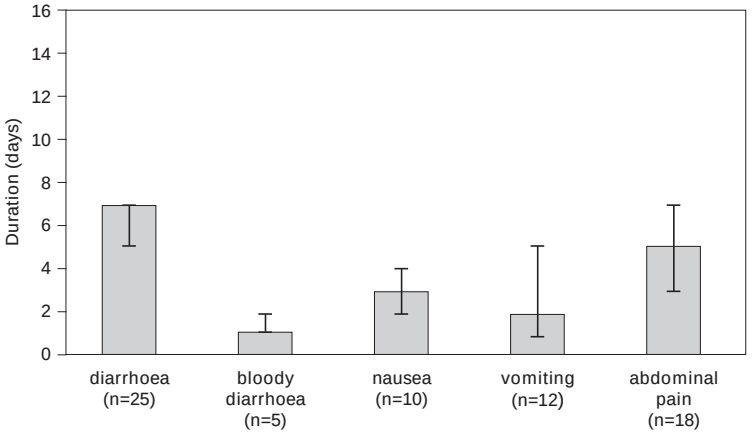
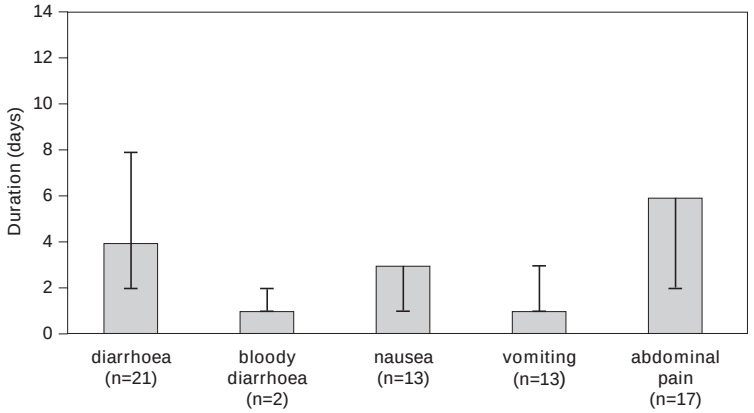


Figure A4.30 Duration of symptoms in cases positive for *Clostridium perfringens* (adults)

Presenting to the GP



75 percentile figure for nausea and abdominal pain not available

In the population cohort component

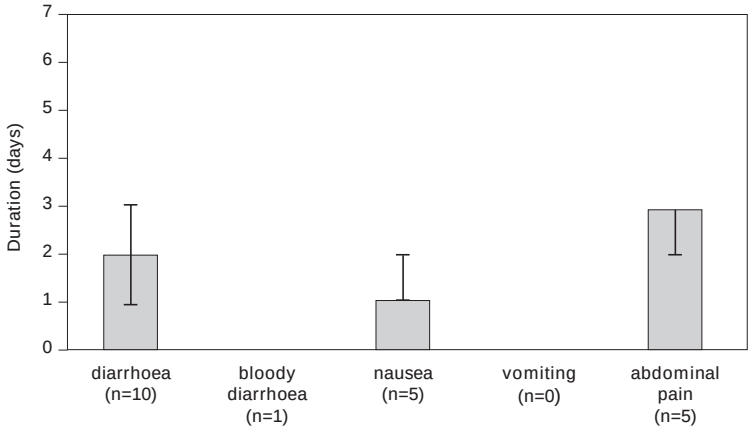
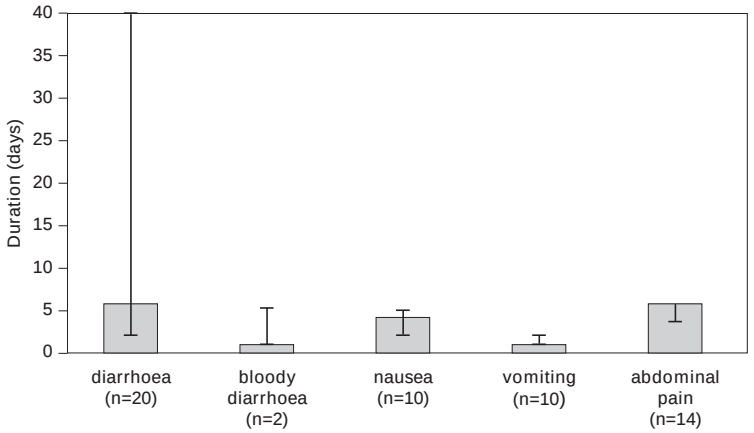


Figure A4.31 Duration of symptoms in cases positive for DAEC (adults)

Presenting to the GP



75 percentile figure for abdominal pain not available

Figure A4.32 Duration of symptoms in cases positive for EAggEC (adults)

Presenting to the GP

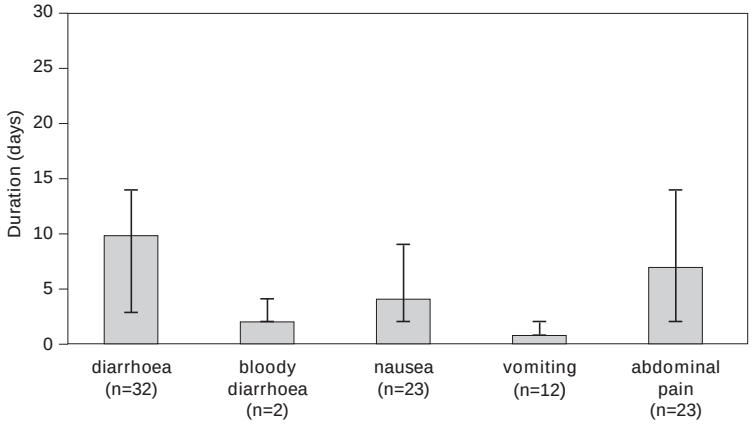
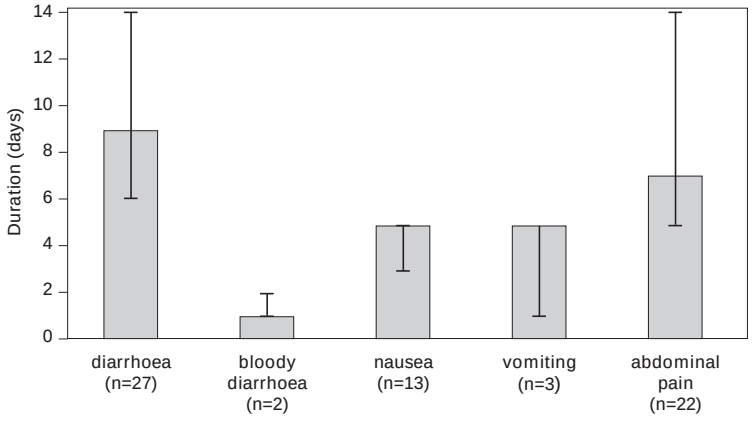


Figure A4.33 Duration of symptoms in cases positive for ETEC (adults)

Presenting to the GP



75 percentile figure for vomiting not available

Figure A4.34 Duration of symptoms in cases positive for *Salmonella* (adults)

Presenting to the GP

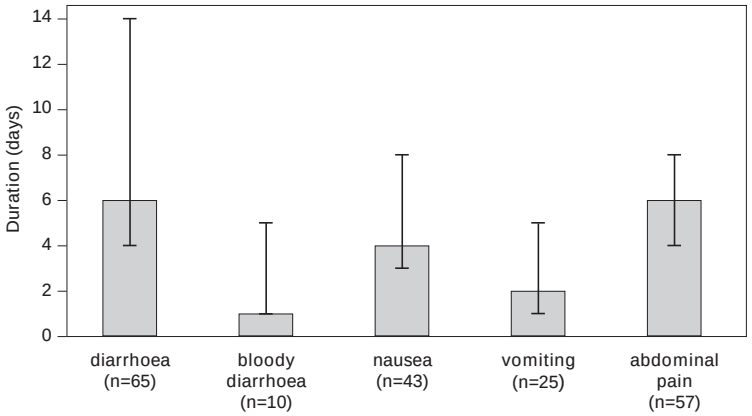


Figure A4.35 Duration of symptoms in cases positive for *Yersinia* (adults)

Presenting to the GP

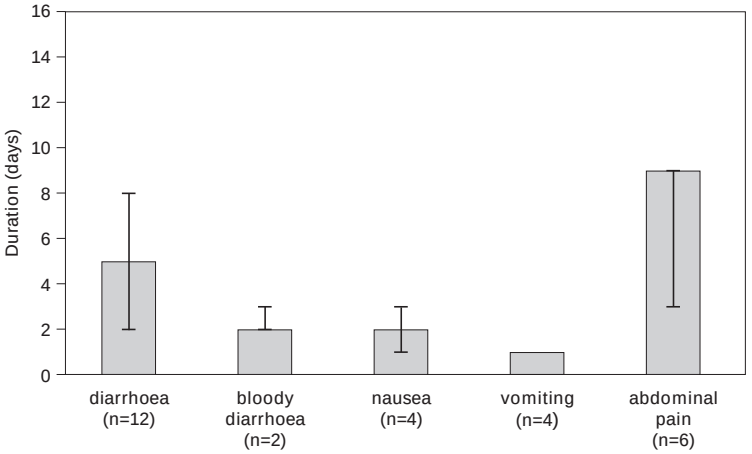
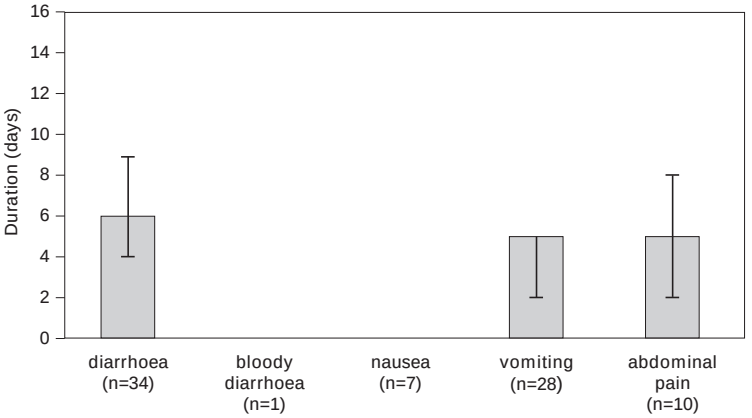


Figure A4.36 Duration of symptoms in cases positive for Adenovirus (children)

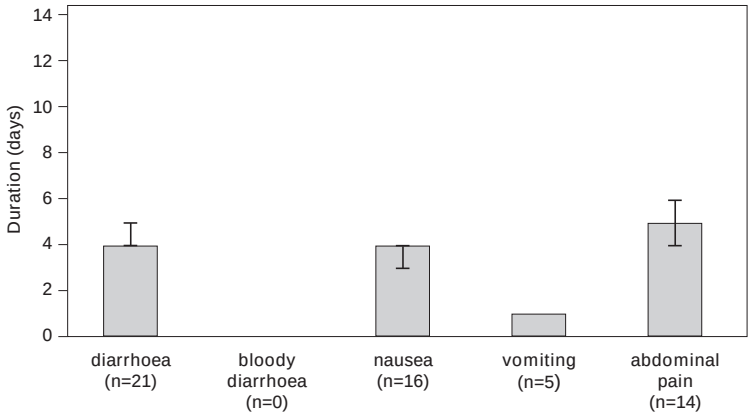
Presenting to the GP



median figure for nausea not available

Figure A4.37 Duration of symptoms in cases positive for Astrovirus (adults)

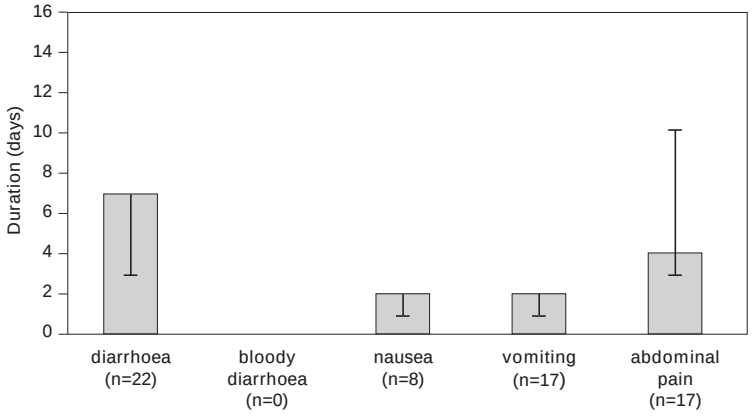
Presenting to the GP



75 percentile figure for nausea and vomiting not available

Figure A4.38 Duration of symptoms in cases positive for Astrovirus (children)

Presenting to the GP



75 percentile figure for diarrhoea not available

Figure A4.39 Duration of symptoms in cases positive for Rotavirus (adults)

Presenting to the GP

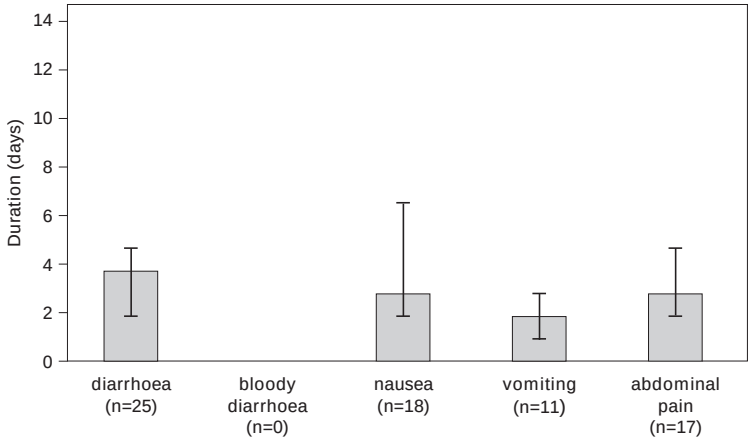


Figure A4.40 Duration of symptoms in cases positive for Rotavirus (children)

Presenting to the GP

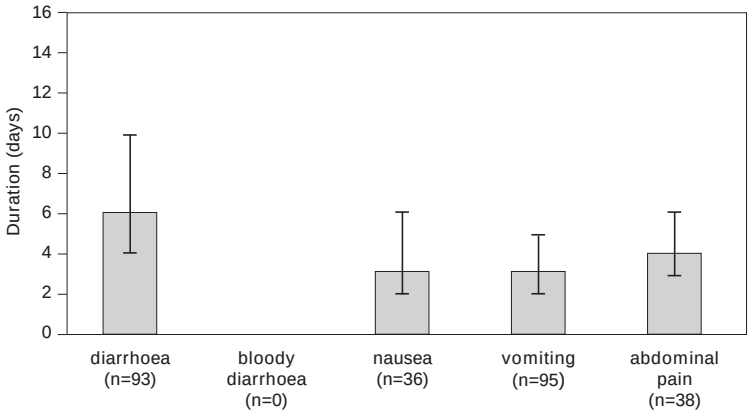
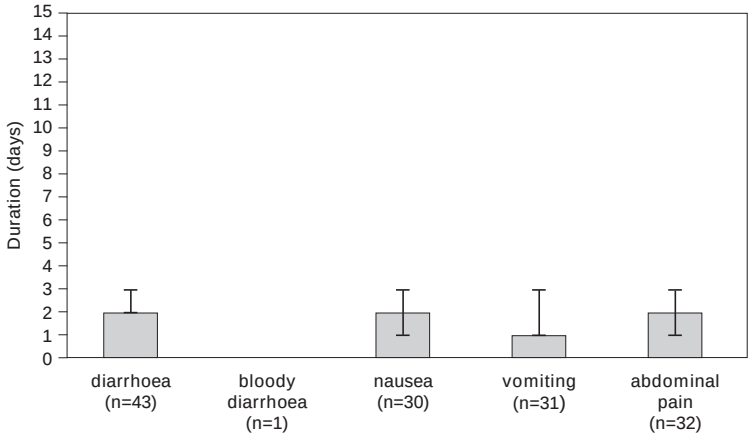


Figure A4.41 Duration of symptoms in cases positive for SRSV (adults)

Presenting to the GP



In the population cohort component

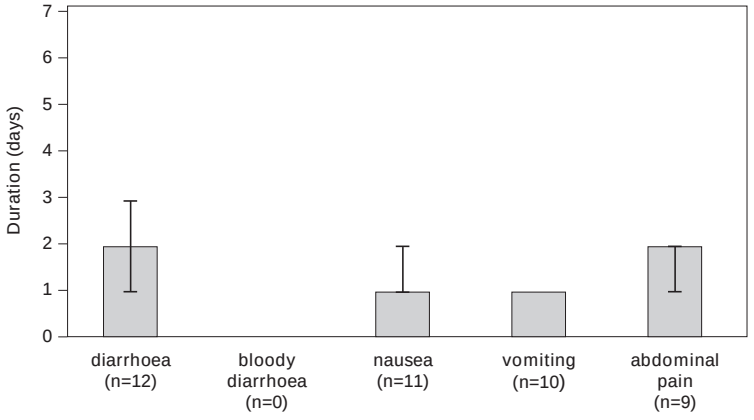


Figure A4.42 Duration of symptoms in cases positive for SRSV (children)

Presenting to the GP

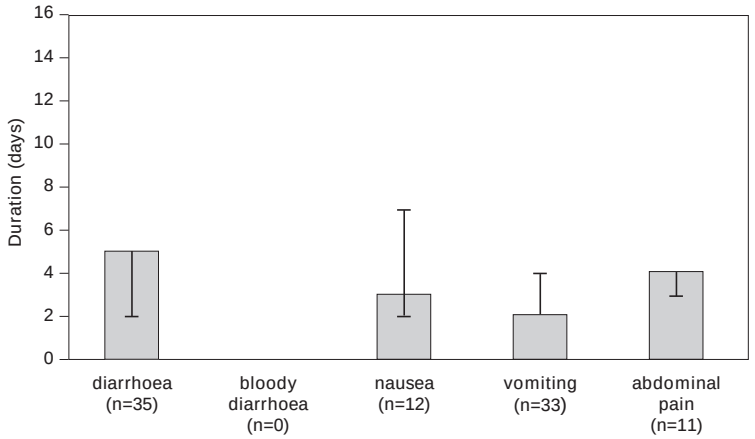


Figure A4.43 No. of days' illness: all cases

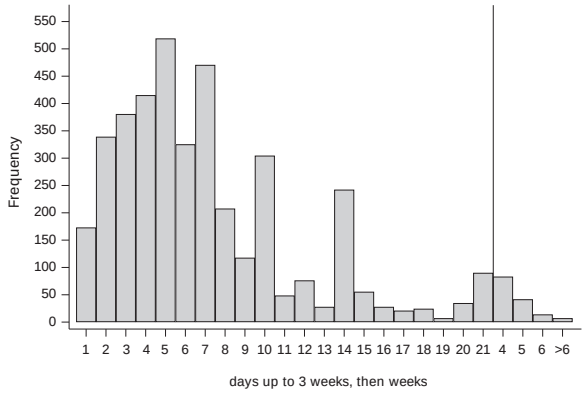


Figure A4.44 No. of days' illness: GP case-control study

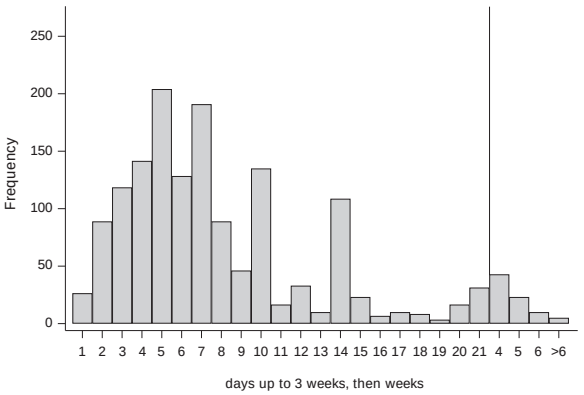


Figure A4.45 No. of days' illness: community case-control study

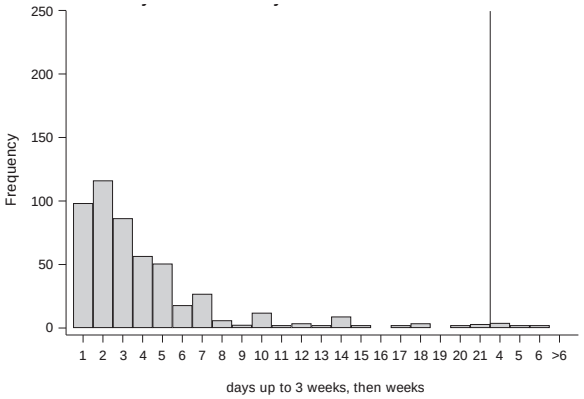


Figure A4.46 No. of days' illness: enumeration study

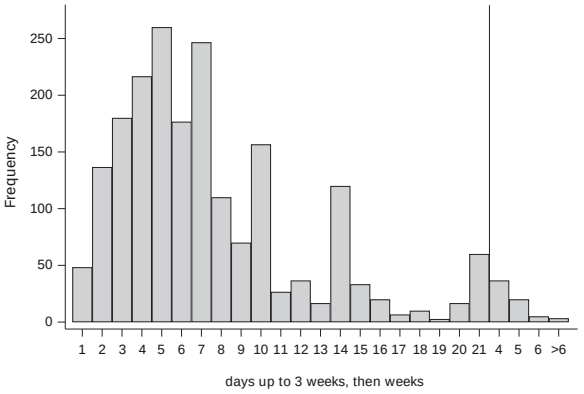


Figure A4.47 No. of days' illness: community case-control study, patient consulting GP

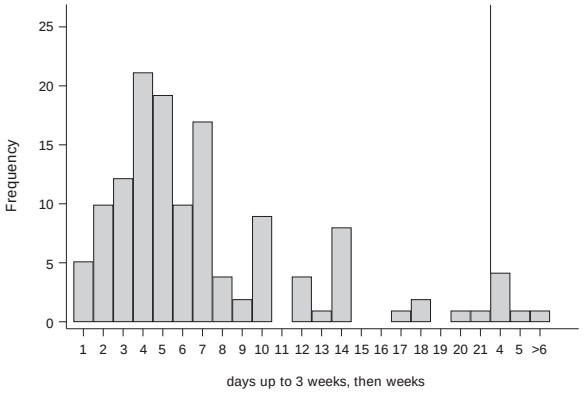


Figure A4.48 No. of days' illness: community case-control study, patient not consulting GP

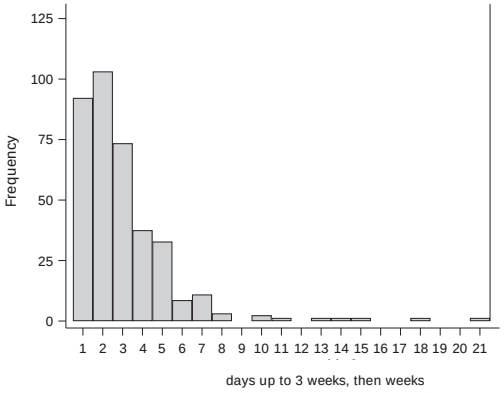


Figure A4.49 No. of days' illness, by study and target organism

No target organism

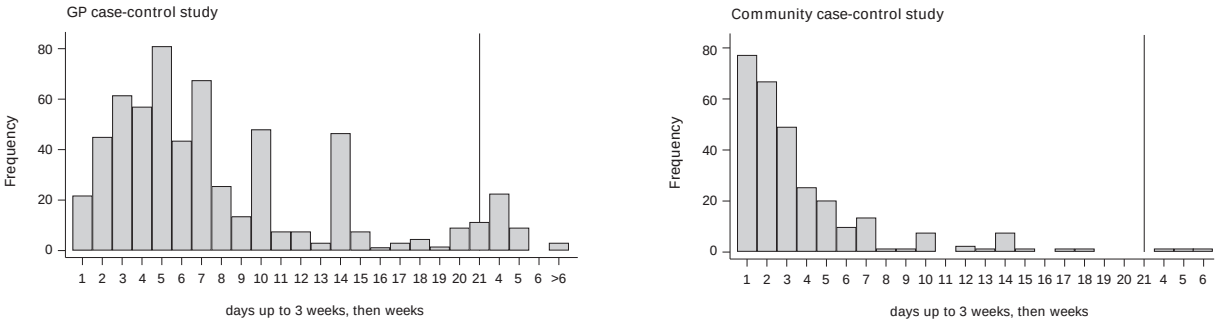


Figure A4.50

Salmonella spp.

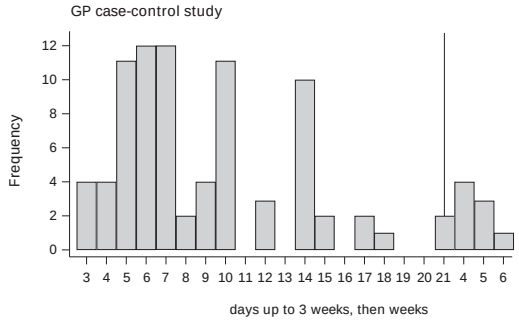


Figure A4.51

S. enteritidis

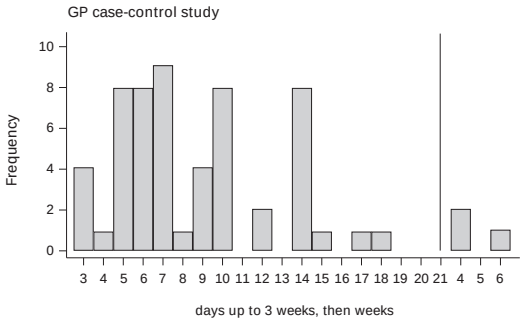


Figure A4.52

Campylobacter spp.

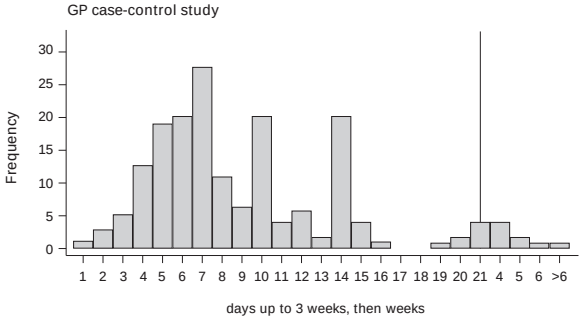


Figure A4.53

C. jejuni

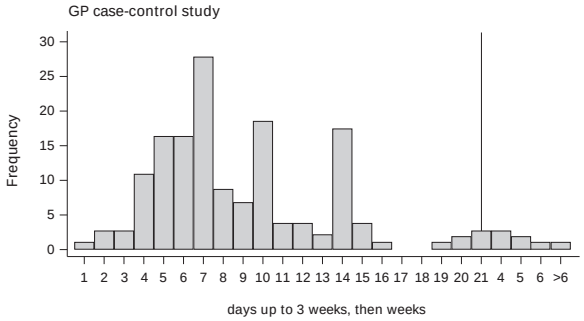
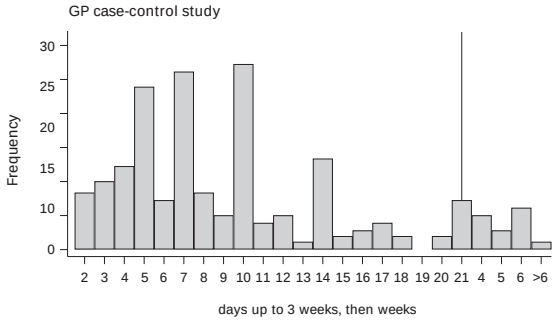


Figure A4.54

E. coli



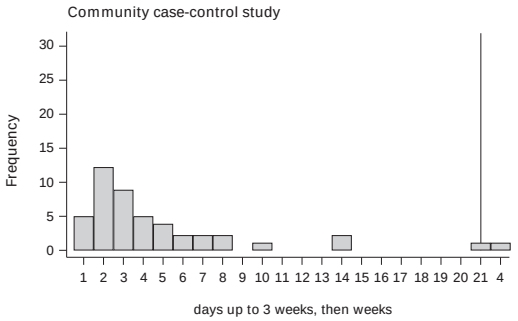
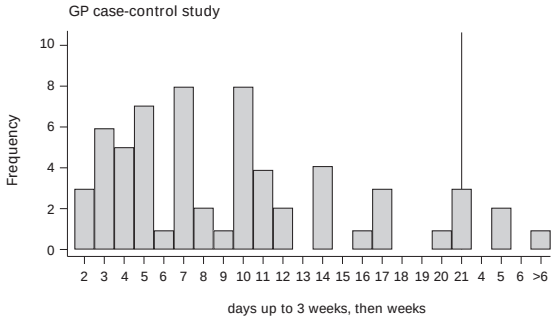


Figure A4.55

Enteroaggerative *E. coli*



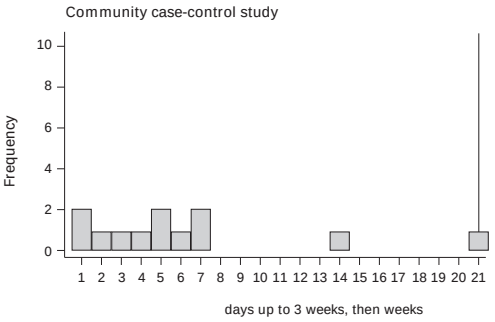


Figure A4.56

Cl.difficile

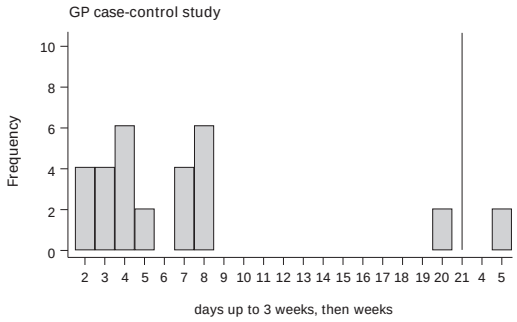


Figure A4.57

Rotavirus

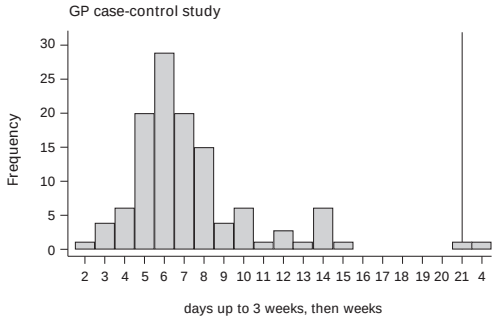


Figure A4.58

Rotavirus group A

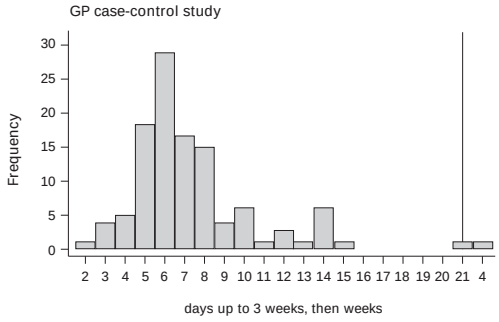
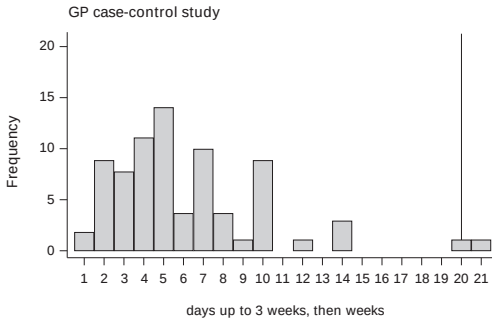
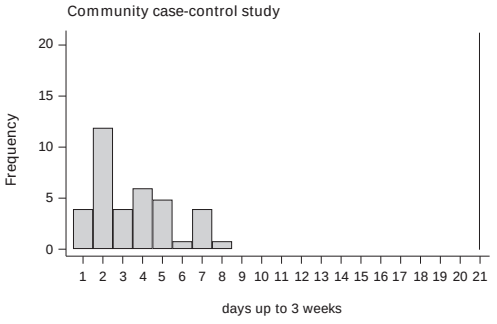


Figure A4.59

SRSV





Appendix 5
Supplementary Results for Chapter 8

Table A5.1 Socio-economic study structure by study and for all cases by size of household and estimated number institutionalised; cumulative percentages

	TYPE OF ACCOMMODATION					
	GP COMPONENT		COMMUNITY COMPONENT		ENUMERATION COMPONENT	
NUMBER IN HOUSEHOLD	NOT IN INSTITUTION	IN INSTITUTION	NOT IN INSTITUTION	IN INSTITUTION	NOT IN INSTITUTION	IN INSTITUTION
1–3	943 (57.9)*	4	255 (46.3)	1	1217 (56.1)	0
4–6	630 (38.7)	7	258 (46.8)	0	832 (38.4)	0
7+	21 (1.3)	8	12 (2.2)	1	44 (2.0)	7
missing	34 (2.1)	1	26 (4.7)	0	75 (3.5)	0
Total	1628 (100)	20	551 (100)	2	2168 (100)	7
Range	0–9	2–23	0–10	3–51	0–65	10–43

*number (%)

Table A5.2 Socio-economic study: household size and family structure, all cases by age

	CASE = <16YRS	CASE = >16YRS	TOTAL
No. in household = 2			
1 parent + child <16yrs	46	27	73
1 adult (not parent) + child <16yrs	2	0	2
2 adults (couple)	0	672	672
2 adults (not a couple)	0	122	122
Total	48	821	869
No. in household = 3			
1 parent + 2 children <16yrs	39	15	54
2 adults + 1 child <16yrs	375	177	552
3 adults (2 parents + 1 adult child)	0	220	220
3 adults (related)	0	36	36
3 adults (unrelated)	0	18	18
Total	414	466	880
No. in household = 4			
1 parent + 3 children <16yrs	9	4	13
2 parents + 2 children <16yrs	542	241	783
3 adults + 1 child <16yrs	9	2	11
1 parent + 3 children >16yrs	0	1	1
4 adults (2 parents + 2 adult children)	0	87	87
4 adults (related)	0	23	23
4 adults (unrelated)	0	10	10
Total	560	368	928
No. in household = 5			
1 adult + 4 children <16yrs	8	1	9
2 adults + 3 children <16 yrs	192	85	277
3 adults + 2 children <16yrs	14	28	42
4 adults + 1 child <16yrs	5	2	7
1 adult + 4 adult children	0	1	1
2 adults + 3 adult children	0	5	5
3 adults + 2 adult children	0	7	7
5 adults (related)	0	5	5
5 adults (unrelated)	0	7	7
Total	219	141	360
No. in household = 6			
1 adult + 5 children	3	1	4
2 adults + 4 children	52	17	69
3 adults + 3 children	1	3	4
4 adults + 2 children	6	2	8
5 adults + 1 child	2	5	7
6 adults (related)	0	4	4
6 adults (unrelated)	0	2	2
Total	64	34	98
No. in household = 7			
2 adults + 5 children	16	6	22
3 or more adults + children	3	1	4
7 adults (related and unrelated)	0	3	3
Total	19	10	29
No. in household = 8			
1 or 2 adults + children	7	0	7
3 or more adults + children	5	0	5
8 related adults	0	1	1
Total	12	1	13

Table A5.3 Household members ill; GP case-control study component

NO. ALSO SICK IN HOUSEHOLD	CHILD CASE					
	N	(%)	% CHILDREN	% MOTHER	% FATHER	% OTHER ADULT
0	366	(61)				
1	131	(21)	16.0	35.9	19.8	28.3
2	69	(11)	18.8	35.5	28.9	16.8
3	19	(3)	15.8	22.8	28.0	33.4
4	10	(2)	20.0	17.5	15.0	47.5
5	4	(1)	25.0	15.0	15.0	45.0
Total	599	(100)				

NO. ALSO SICK IN HOUSEHOLD	ADULT CASE					MISSING AGE			TOTAL	
	N	(%)	% CHILDREN	% SPOUSE	% OTHER ADULT	N	(%)	% CHILDREN	N	(%)
0	789	(81.5)				53	(61)		1208	(73)
1	125	(13)	15.2	50.4	34.4	18	(21)	33.3	274	(17)
2	36	(4)	30.6	22.2	47.2	10	(12)	20.0	115	(7)
3	11	(1)	21.2	27.2	51.6	3	(3)	22.0	33	(2)
4	5	(0.5)	20.0	0.0	80.0	3	(3)	0.0	18	(1)
5	0	(0)	0.0	0.0	0.0	0	(0)	0.0	4	(0.1)
Total	966	(100)				87	(100)		1652	(100)

Percentage of household that are sick

NO. SICK IN HOUSEHOLD	NO. IN HOUSEHOLD (INCLUDING CASE)								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**N**
1	100	84.6	68.3	64.8	62.9	63.0	63.6	30.8	**1171**
2		15.4	21.2	20.9	14.1	6.5	18.2	23.1	**272**
3			10.5	10.0	12.4	10.9	9.1	0.0	**113**
4				4.3	5.9	6.5	0.0	0.0	**31**
5					4.7	6.5	9.1	46.1	**18**
6						6.5	0.0	0.0	**3**
7							0.0	0.0	**0**
8								0.0	**0**
N	**117**	**410**	**420**	**421**	**170**	**46**	**11**	**13**	**1608**

Table A5.4 Household members ill; community component

NO. ALSO SICK IN HOUSEHOLD	CHILD CASE					
	N	(%)	% CHILDREN	% MOTHER	% FATHER	% OTHER ADULT
0	153	(59)				
1	35	(16)	20.0	31.4	17.1	31.5
2	17	(8)	29.4	29.4	20.6	20.6
3	10	(4)	10.0	26.7	16.7	46.6
4	6	(3)	25.0	12.5	12.5	50.0
5	0	(0)	0.0	0.0	0.0	0.0
Total	211	(100)				

NO. ALSO SICK IN HOUSEHOLD	ADULT CASE					MISSING AGE			TOTAL	
	N	(%)	% CHILDREN	% SPOUSE	% OTHER ADULT	N	(%)	% CHILDREN	N	(%)
0	248	(84)				26	(68)		427	(77)
1	30	(10)	33.3	40.0	26.7	8	(21)	37.5	73	(13)
2	13	(4)	38.5	30.8	30.7	3	(8)	16.7	33	(6)
3	3	(1)	55.6	33.3	11.1	1	(3)	66.6	14	(3)
4	1	(0.5)	50.0	25.0	25.0	0			7	(1)
5	1	(0.5)	50.0	16.7	33.3	0			1	(0.1)
Total	296	(100)				38	(100)		555	(100)

Percentage of household that are sick

NO. SICK IN HOUSEHOLD	NO. IN HOUSEHOLD (INCLUDING CASE)								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**N**
1	100	88.1	79.8	71.8	70.4	38.5	25.0	100	**402**
2		11.9	13.5	15.5	9.9	30.8	12.5	0.0	**68**
3			6.7	9.2	7.0	7.7	25.0	0.0	**32**
4				3.8	7.0	15.4	12.5	0.0	**14**
5					5.6	7.7	12.5	0.0	**6**
6						0.0	12.5	0.0	**1**
7							0.00	0.0	**0**
8								0.0	**0**
N	**28**	**109**	**119**	**174**	**71**	**13**	**8**	**1**	**523**

Table A5.5 Household members ill; enumeration component

NO. ALSO SICK IN HOUSEHOLD	CHILD CASE					
	N	(%)	% CHILDREN	% MOTHER	% FATHER	% OTHER ADULT
0	453	(52)				
1	209	(24)	16.7	35.4	19.1	28.8
2	132	(15)	18.6	31.1	28.0	22.3
3	64	(7)	20.3	26.6	22.4	30.7
4	8	(1)	25.0	15.6	18.8	40.6
5	4	(0.5)	10.0	10.0	10.0	70.0
	1	(0.1)	0.0	0.0	12.5	87.5
Total	871	(100)				

NO. ALSO SICK IN HOUSEHOLD	ADULT CASE					MISSING AGE		TOTAL	
	N	(%)	% CHILDREN	% SPOUSE	% OTHER ADULT	N	(%)	N	(%)
0	975	(75)				12	(100)	1440	(66)
1	226	(17)	16.8	52.7	30.5	0		435	(20)
2	67	(5)	35.1	20.9	44.0	0		199	(9)
3	22	(2)	22.7	25.8	51.5	0		86	(4)
4	7	(0.5)	32.1	14.3	53.6	0		15	(0.7)
5	2	(0.2)	20.0	20.0	60.0	0		6	(0.3)
6								0	(0)
7								0	(0)
8								1	(0)
Total	1299	(100)				12	(100)	2182	(100)

Percentage of household that are sick

NO. SICK IN HOUSEHOLD	NO. IN HOUSEHOLD (INCLUDING CASE)								
	1	2	3	4	5	6	7	8	N
1	100	77.2	62.3	52.3	54.3	52.9	54.6	55.6	**1357**
2		22.8	25.4	22.3	17.3	16.2	4.6	22.2	**424**
3			12.3	51.1	16.8	7.4	4.6	22.2	**194**
4				10.3	7.7	10.3	27.3	0.0	**86**
5					3.9	5.9	4.6	0.0	**13**
6						7.4	4.6	0.0	**6**
7							0.0	0.0	**0**
8								0.0	**0**
N	**183**	**491**	**543**	**556**	**208**	**68**	**22**	**9**	**2080**

Table A5.6 The effect of illness on the person who was ill; GP case-control component

N	OVERALL	RESPONDERS N	RESPONDERS (%)	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
1652	8.59				0–80	14169
In hospital and confined to bed						
	0.04	27	(1.6)	2.44	0 - 15	66
In hospital but able to get up						
	0.05	20	(1.2)	4.03	0–15	80.5
At home and confined to bed						
	1.15	635	(38.4)	2.98	0–50	1892
At home and able to get up but not able to do most normal activities						
	2.98	1101	(66.6)	4.47	0–75	4922
At home, but able to get up and do most normal activities						
	2.45	882	(53.4)	4.59	0–85	4051.5
Feeling ill but able to go to work/school/shops etc.						
	1.96	546	(33.1)	5.93	0–42	3235.5
If adult, no. of days paid employment lost						
966	2.44	407	(42.1)	5.79	0–80	2355
If a child/student, no. of days school/college lost						
627	1.42	190	(30.3)	4.70	0–31	892.5
Extra days barred from work/school/college after recovery because of infection						
1330	0.27	61	(4.6)	5.95	0–42	363
No. of days unable to perform normal household activities						
1652	1.99	639	(38.7)	5.16	0–55	3295.5
No. of days unable to take part in normal leisure activities						
1652	3.43	724	(43.8)	7.83	0–60	5671.5

Table A5.7 The effect of illness on the person who was ill; community component

N	OVERALL	RESPONDERS N	RESPONDERS (%)	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
555	3.92				0–40	2173
In hospital and confined to bed						
	0.01	2	(0.4)	2.75	0–5	5.5
In hospital but able to get up						
	0.02	4	(0.7)	2.88	0–7	11.5
At home and confined to bed						
	0.42	140	(25.2)	1.65	0–16	231.5
At home and able to get up but not able to do most normal activities						
	1.07	258	(46.5)	2.29	0–13	591
At home, but able to get up and do most normal activities						
	1.31	278	(50.1)	2.62	0–28	729
Feeling ill but able to go to work/school/shops etc.						
	1.05	201	(36.2)	2.91	0–18	584
If adult, no. of days paid employment lost						
296	0.46	60	(20.3)	2.25	0–8	135
If a child/student, no. of days school/college lost						
227	0.80	71	(31.3)	2.57	0–24	182.5
Extra days barred from work/school/college after recovery because of infection						
448	0.06	12	(2.7)	2.13	0–7	25.5
No. of days unable to perform normal household activities						
555	0.61	139	(25.0)	2.43	0–18	338
No. of days unable to take part in normal leisure activities						
555	1.34	192	(34.6)	3.87	0–22	742.5

Table A5.7a The effect of illness on the person who was ill; community component – for those presenting to a GP

N=149

		RESPONDERS				
N	OVERALL MEAN	N	(%)	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
149					0–40	1042
In hospital and confined to bed						
149	0.03	1	(0.7)	5	5	5
In hospital but able to get up						
149	0.08	4	(2.7)	2.88	0–7	11.5
At home and confined to bed						
149	0.84	52	(34.9)	2.39	0–16	124.5
At home and able to get up but not able to do most normal activities						
149	1.98	88	(59.1)	3.35	0–13	295
At home, but able to get up and do most normal activities						
149	2.38	77	(51.7)	4.61	0–28	355
Feeling ill but able to go to work/school/shops etc.						
149	1.40	49	(32.9)	4.27	0–18	209
If adult, no. of days paid employment lost						
62	1.16	23	(37.1)	3.13	0–8	72
If a child/student, no. of days school/college lost						
73	1.23	22	(30.1)	4.07	0–24	89.5
Extra days barred from work/school/college after recovery because of infection						
113	0.12	3	(2.7)	4.33	0–7	13
No. of days unable to perform normal household activities						
149	1.02	38	(25.5)	3.99	0–18	151.5
No. of days unable to take part in normal leisure activities						
149	2.23	53	(35.6)	6.28	0–22	333

Table A5.7b The effect of illness on the person who was ill; community component – for those who did not see a GP

N=406

		RESPONDERS				
N	OVERALL MEAN	N	(%)	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
406	2.79				0–21	1131
In hospital and confined to bed						
406	0.001	1	(0.3)	0.5	0.5	0.5
In hospital but able to get up						
406	0		0	0	0	0
At home and confined to bed						
406	0.26	88	(21.7)	1.22	0–4	107
At home and able to get up but not able to do most normal activities						
406	0.73	170	(41.9)	1.74	0–8	296
At home, but able to get up and do most normal activities						
406	0.92	201	(49.5)	1.86	0–21	374
Feeling ill but able to go to work/school/shops etc.						
406	0.92	152	(37.4)	2.47	0–17	375
If adult, no. of days paid employment lost						
234	0.27	37	(15.8)	1.70	0–4	63
If a child/student, no. of days school/college lost						
154	0.60	49	(31.8)	1.90	0–6	93
Extra days barred from work/school/college after recovery because of infection						
335	0.04	9	(2.7)	1.39	0–3	12.5
No. of days unable to perform normal household activities						
406	0.46	101	(24.9)	1.85	0–7	186.5
No. of days unable to take part in normal leisure activities						
406	1.01	139	(34.2)	2.95	0–14	409.5

Table A5.8 The effect of illness on the person who was ill; enumeration component

		RESPONDERS				
N	OVERALL	N	(%)	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
2181	7.90				0–80	17234.5
In hospital and confined to bed						
	0.10	66	(3.0)	3.27	0–21	216
In hospital but able to get up						
	0.09	56	(2.6)	3.59	0–21	201
At home and confined to bed						
	1.31	915	(41.9)	3.13	0–90	2860
At home and able to get up but not able to do most normal activities						
	2.90	1503	(68.9)	4.22	0–90	6336.5
At home, but able to get up and do most normal activities						
	2.05	1146	(52.5)	3.90	0–32	4466
Feeling ill but able to go to work/school/shops etc.						
	1.57	675	(30.9)	5.09	0–58	3435
If adult, no. of days paid employment lost						
1299	2.02	820	(40.0)	5.03	0–85	2618
If a child/student, no. of days school/college lost						
896	1.33	264	(29.5)	4.51	0–90	1189.5
Extra days barred from work/school/college after recovery because of infection						
1801	0.33	105	(5.8)	5.68	0–42	596
No. of days unable to perform normal household activities						
2182	2.11	896	(41.1)	5.13	0–48	4600.5
No. of days unable to take part in normal leisure activities						
2182	3.38	989	(45.3)	7.46	0–63	7374.5

Table A5.9 The effect of illness on the person who was ill; GP case-control component

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
No,. IID organism663	8.34				0–80	5522
Salmonella	90	10.90			2.5–42	981
S.enteritidis	59	9.59			2.5–42	566
Campylobacter	192	9.34			0–56	1792.5
C.jejuni	172	9.44			0–56	1624.5
Enterovir *E.coli*	198	11.07			0–74	2192.5
EAggEC	65	11.07			0–74	719.5
C.difficile	18	7.17			0–31	129
Rotavirus	122	7.12			0–27	868.5
Rotavirus gpA	119	7.12			0–27	847.5
SRSV	83	5.78			0–21	479.5
In hospital and confined to bed						
No IID organism	663	0.05	10	3.45	0–15	34.5
Salmonella	90	0.07	2	3	0–4	6
Campylobacter	192	0.18	3	1.17	0–2	35
C.jejuni	172	0.002	3	1.17	0–2	3.5
Enterovir *E.coli*	198	0.01	1	2	2	2
Rotavirus	122	0.01	1	1	1	1
Rotavirus gpA	119	0.008	1	1	0–1	1
SRSV	83	0.04	3	1.17	0–2	3.5
In hospital but able to get up						
No IID organism	663	0.07	9	4.89	0–15	44
Salmonella	90	0.18	2	8	0–4	6
Campylobacter	192	0.04	2	3.5	0–4	7
C.jejuni	172	0.002	1	4	0–4	4.0
Enterovir *E.coli*	198	0.07	1	14	14	14
Rotavirus	122	0.01	1	1	1	1
Rotavirus gpA	119	0.008	1	1	0–1	1
SRSV	83					
At home and confined to bed						
No IID organism	663	1.04	258	2.67	0–50	689.5
Salmonella	90	2.15	49	3.95	0–17	193.5
S.enteritidis	59	2.64	38	4.10	0–17	156
Campylobacter	192	1.88	99	3.65	0–17	361.5
C.jejuni	172	1.78	88	3.48	0–13	306.5
Enterovir *E.coli*	198	1.10	69	3.16	0–15	218
EAggEC	65	1.65	30	3.57	0–14	107
C.difficile	18	0.67	7	1.71	0–4	12
Rotavirus	122	1.06	37	3.5	0–10	129.5
Rotavirus gpA	119	1.07	36	3.54	0–10	127.5
SRSV	83	0.78	31	2.08	0–7	64.5
At home and able to get up but not able to do most normal activities						
No IID organism	663	2.76	420	4.36	0–75	1830
Salmonella	90	3.55	68	4.70	0–21	319.5
S.enteritidis	59	2.93	46	3.76	0–10	173
Campylobacter	192	3.59	145	4.75	0–20	688.5
C.jejuni	172	3.63	132	4.72	0–20	623.5
Enterovir *E.coli*	198	3.15	128	4.87	0–44	623
EAggEC	65	4.12	46	5.83	0–44	268
C.difficile	18	3.25	10	5.85	0–14	58.5
Rotavirus	122	3.39	94	4.40	0–14	414
Rotavirus gpA	119	3.39	91	4.44	0–14	404
SRSV	83	2.41	58	3.45	0 - 11	200

Table A5.9 The effect of illness on the person who was ill; GP case-control component *continued*

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
At home, but able to get up and do most normal activities						
No IID organism	663	2.34	325	4.78	0–85	1553.5
Salmonella	90	3.01	49	5.52	0–24	270.5
S.enteritidis	59	2.47	32	4.55	0–18	145.5
Campylobacter	192	2.45	116	4.05	0–42	469.5
C.jejuni	172	2.39	103	3.99	0–42	410.5
Enterovir *E.coli*	198	3.54	116	6.03	0–42	700
EAggEC	65	3.09	41	4.90	0–21	201
C.difficile	18	1.58	7	4.07	0–13	28.5
Rotavirus	122	1.86	69	3.30	0–19	227.5
Rotavirus gpA	119	1.89	68	3.30	0–10	224.5
SRSV	83	1.80	41	3.65	0–20	149.5
Feeling ill but able to go to work/school/shops etc.						
No IID organism	663	2.21	232	6.30	0–30	1462
Salmonella	90	2.41	35	6.2	0–24	217
S.enteritidis	59	1.85	22	4.95	0–22	109
Campylobacter	192	1.80	68	5.09	0–24	346
C.jejuni	172	1.84	63	5.02	0–24	316
Enterovir *E.coli*	198	3.06	77	7.86	0–42	605.5
EAggEC	65	2.74	27	6.59	0–21	178
C.difficile	18	0.44	2	4.00	0–4	8
Rotavirus	122	0.52	20	3.18	0–7	63.5
Rotavirus gpA	119	0.51	19	3.18	0–7	60.5
SRSV	83	0.42	10	3.50	0–10	35

Table A5.10 No. of days of employment/school/college/other activities lost because of illness

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
If adult, no. of days paid employment lost						
No IID organism	448	2.02	183	4.94	0–80	904.5
Salmonella	66	4.83	34	9.38	0–28	319
S.enteritidis	43	3.48	20	7.48	0–24	149.5
Campylobacter	157	2.93	71	6.48	0–21	460
C.jejuni	140	2.93	66	6.21	0–21	410
Enterovir *E.coli*	112	1.74	41	4.74	0–15	194.5
EAggEC	38	1.62	14	4.39	0–10	61.5
C.difficile	9	3.78	3	11.33	0–25	34
Rotavirus	24	133	9	3.56	0–5	32
Rotavirus gpA 23	1.30	8	3.75	0–5	30	
SRSV	38	1.32	16	3.13	0–7	50
If a child/student, no. of days school/college lost						
No IID organism	198	1.55	66	4.65	0–25	307
Salmonella	26	2.31	14	4.29	0–8	60
S.enteritidis	19	2.47	11	4.27	0–8	47
Campylobacter	39	2.44	24	3.96	0–10	95
Entero *E.coli*	80	2.02	22	7.34	0–31	161.5
EAggEC	22	2.82	8	7.75	0–17	62
Rotavirus	91	0.71	15	4.3	0–10	64.5
Rotavirus gpA	90	0.67	14	4.32	0–10	60.5
SRSV	42	0.40	6	2.83	0–5	17
Extra days barred from work/school/college after recovery because of infection						
No IID organism child	189	0.14	6	4.5	0–14	27
No IID organism adult	342	0.23	14	5.54	0–28	77.5
Salmonella child	22	0.34	3	2.5	0–3	7.5
Salmonella adult	54	1.52	5	16.4	0–42	82
S.enteritidis	15	0.5	3	2.5	0–3	7.5
S.enteritidis	35	1.89	3	22	0–8	66

Table A5.10 No. of days of employment/school/college/other activities lost because of illness *continued*

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
Campylobacter adult	118	0.37	6	7.3	0–14	44
C.jejuni	106	0.30	5	6.4	0–14	32
Entero E.coli child	77	0.27	4	5.25	0–14	21
adult	84	0.52	4	11	0–14	44
EAggEC	22	0.09	2	1	0–1	2
EAggEC	28	0.64	2	9	0–17	18
Rotavirus child90	0.01	1	1	1	1	
Rotavirus gpA	89	0.01	1	1	0–1	1
SRSV child	42	0.24	3	3.33	0–5	10
SRSV adult	20	0.3	2	3	0–3	6
No. of days unable to perform normal household activities						
No IID organism	663	1.97	268	4.87	0–55	1304.5
Salmonella	90	3.56	45	7.11	0–21	320
S.enteritidis	59	3.53	31	6.73	0–21	208.5
Campylobacter	192	3.38	111	5.84	0–21	648.5
C.jejuni	172	3.28	102	5.53	0–18	564.5
E.coli	198	1.95	75	5.14	0–15	385.5
E.coli entero	65	2.38	29	5.33	0–15	154.5
C.difficile	18	0.97	7	2.50	0–7	17.5
Rotavirus	122	1.00	27	4.54	0–15	122.5
Rota gpA	119	1.00	26	4.56	0–15	118.5
SRSV	83	1.11	32	2.89	0–10	92.5
No. of days unable to take part in normal leisure activities						
No IID organism	663	3.14	287	7.26	0–60	2082.5
Salmonella	90	6.46	53	10.96	0–35	581
S.enteritidis	59	6.17	37	9.84	0–28	364
Campylobacter	192	5.76	56	8.84	0–56	1105.5
C.jejuni	172	5.73	114	8.64	0–56	985.5
Entero *E.coli*	198	4.02	93	8.55	0–28	795.5
EAggEC	65	5.18	35	9.63	0–28	337
C.difficile	18	4.22	9	8.44	0–31	76
Rotavirus	122	1.74	32	6.63	0–21	212
Rota gpA	119	1.68	31	6.45	0–21	200
SRSV	83	1.76	28	5.21	0–21	146

Table A5.11 The effect of illness on the person who was ill; community component

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
No IID organism	321	3.55			0–40	1138.5
Salmonella	4	7.75			0–14	31
S.enteritidis	2	11.25			8.5–14	22.5
Campylobacter	23	6.52			0–28	150
C.jejuni	18	6.11			2–28	110
Entero *E.coli*	49	4.5			0–28	220.5
EAgg EC	12	6.25			0.5–21	75
C.difficile	5	3.20			0–7	16
Rotavirus	21	4.83			0–7	16
Rotavirus gpA	19	4.87			0.5–11	92.5
SRSV	38	3.32			0–8	126
In hospital and confined to bed						
No IID organism	321	0.002	1	0.5	0–0.5	0.5
Entero *E.coli*	49	0.10	1	5	5	5
In hospital but able to get up						
No IID organism	321	0.003	1	1	0–1	1.0
Campylobacter	23	0.30	1	7	7	7
Entero *E.coli*	49	0.06	1	3	3	3
At home and confined to bed						
No IID organism	321	0.36	71	1.61	0–7	114.5
Salmonella	4	0.88	1	3.5	0–5	3.5
S.enteritidis	2	1.75	1	3.50	0–3.5	3.50
Campylobacter	23	0.46	7	1.5	0–3	10.5
C.jejuni	18	0.58	7	1.50	0–3	10.5
Entero *E.coli*	49	0.43	12	1.75	0–6	21
EAggEC	12	0.46	4	1.38	0–3	5.50
C.difficile	5					
Rotavirus	21	0.69	6	2.42	0–4	14.5
Rotavirus gpA	19	0.71	5	2.70	0–4	13.50
SRSV	38	0.58	21	1.05	0–3	22
At home and able to get up but not able to do most normal activities						
No IID organism	321	0.91	135	2.16	0–12	291
Salmonella	4	0.75	1	3	3	3
S.enteritidis	2	1.50	1	3.00	0–3	3.00
Campylobacter	23	2.5	15	3.83	0–13	57.5
C.jejuni	18	2.08	13	2.88	0–9	37.5
Entero *E.coli*	49	0.85	20	2.08	0–7	41.5
EAggEC	12	1.17	6	2.33	0–7	14.0
C.difficile	5	1.00	2	2.50	0–3	5.0
Rotavirus	21	2.4	16	3.16	0–7	50.5
Rotavirus gpA	19	2.39	14	3.25	0–7	45.5
SRSV	38	1.28	27	1.80	0–7	48.5
At home, but able to get up and do most normal activities						
No IID organism	321	1.22	152	2.58	0–28	392
Salmonella	4	4.13	3	5.5	0–14	16.5
S.enteritidis	2	7.50	2	7.50	0–14	15.0
Campylobacter	23	2.13	14	3.5	0–19	49
C.jejuni	18	2.44	13	3.38	0–19	44.0
Entero *E.coli*	49	1.98	31	3.13	0–21	97
EAggEC	2	3.88	8	5.81	0–21	46.5
C.difficile	5	1.60	2	4.00	0–7	8.0
Rotavirus	21	1.12	9	2.61	0–7	23.5
Rota gpA	19	1.08	8	2.56	0–7	1.0
SRSV	38	0.57	16	1.34	0–4	21.5

Table A5.11 The effect of illness on the person who was ill; community component *continued*

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
Feeling ill but able to go to work/school/shops etc.						
No IID organism	321	1.01	116	2.81	0–18	325.5
Salmonella	4	2	3	2.67	0–5	8
S.enteritidis	2	0.50	1	1.00	0–1	1.0
Campylobacter	23	0.91	6	3.5	0–5	21
C.jejuni	18	0.44	3	2.67	0–3	8.0
Entero *E.coli*	49	1.59	25	3.12	0–14	78
EAggEC	12	1.58	5	3.80	0–7	19.0
C.difficile	5	0.20	1	1.00	0–1	1.0
Rotavirus	21	0.62	4	3.25	0–7	13
Rotavirus gpA	19	0.68	4	3.25	0–7	13.0
SRSV	38	0.66	15	1.67	0–5	25.0

Table A5.12 No. of days of employment/school/college/other activities lost because of illness

ORGANISM	N	OVERALL MEAN	RESPONDERS N	RESPONDERS MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
If adult, no. of days paid employment lost						
No IID organism	196	0.49	40	2.39	0–8	95.5
Salmonella	2	0.5	1	1	1	1
Campylobacter	11	0.82	3	3	0–5	9
C.jejuni	10	0.9	3	3	0–5	9
Entero *E.coli*	23	0.26	3	2	2	6
EAggEC	5	0.4	1	2	0–2	2
SRSV	18	0.33	5	1.2	0–2	6
If a child/student, no. of days school/college lost						
No IID organism	105	0.73	36	2.13	0–7	76.5
Campylobacter	11	1.27	3	4.67	0–5	14
Entero *E.coli*	23	0.37	4	2.13	0–4	8.5
EAggEC	7	0.57	1	4.0	0–4	4
Rotavirus	17	0.76	4	3.25	0–7	13
Rotavirus gpA	15	0.87	4	3.25	0–7	13
SRSV	19	0.21	4	1.0	0–1.5	4
Extra days barred from work/school/college after recovery because of infection						
No IID organism	101	0.04	3	1.5	0–2.5	4.5
Entero *E.coli*	23	0.04	1	1	1	1
SRSV	15	0.07	1	1	0–1	1
No. of days unable to perform normal household activities						
No IID organism	321	0.61	88	2.23	0–11	196.5
Campylobacter	23	0.85	7	2.79	0–5	19.5
C.jejuni	18	0.81	6	2.42	0–5	14.5
Entero *E.coli*	23	0.72	8	4.44	0–10	35.5
EAggEC	12	0.83	2	5.0	0–6	10
Rotavirus	21	0.52	3	3.67	0–6	11
Rotavirus gpA	19	0.58	3	3.67	0–6	11
SRSV	38	0.62	13	1.81	0–5	23.5
No. of days unable to take part in normal leisure activities						
No IID organism	321	1.32	116	3.66	0–14	424.5
Salmonella	4	3.38	2	6.75	0–8.5	13.5
S.enteritidis	2	4.25	1	8.5	0–8.5	8.5
Campylobacter	23	4.70	12	5.75	0–20	108
C.jejuni	18	2.39	9	4.78	0–12	43
Entero *E.coli*	49	1.32	14	4.61	0.–22	64.5
EAggEC	12	1.33	5	3.2	0–7	16
Rotavirus	21	0.86	4	4.5	0–7	18
Rotavirus gpA	19	0.95	4	4.5	0–7	18
SRSV	38	1.24	18	2.61	0–7	47

Table A5.13 The effect of illness on the person who was ill by sex; No. of days of illness GP case-control component

N = 1652

			RESPONDERS			
	N	OVERALL MEAN	N	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
Male	681	8.55			0–56	5823
Female	873	8.55			0–80	7463
In hospital and confined to bed						
Male	682	0.03	15	1.57	0–5	23.5
Female	873	0.03	10	2.55	0–7	25.5
In hospital but able to get up						
Male	682	0.06	10	4.1	0–14	41
Female	873	0.045	10	3.95	0–15	39.5
At home and confined to bed						
Male		0.93	216	2.94	0–50	635.5
Female		1.33	386	3.02	0–28	1164
At home and able to get up but not able to do most normal activities						
Male		2.93	435	4.59	0–75	1996
Female		3.05	608	4.38	0–70	2661.5
At home, but able to get up and do most normal activities						
Male		2.73	375	4.96	0–85	1859
Female		2.21	451	4.28	0–80	1932.5
Feeling ill but able to go to work/school/shops etc.						
Male		2.09	220	6.47	0–42	1424
Female		1.85	293	5.50	0–30	1611
If adult, no. of days paid employment lost						
Male	360	3.11	178	6.30	0–56	1121
Female	93	2.06	226	5.42	0–80	1224
If a child/student, no. of days school/college lost						
Male	330	1.35	93	4.80	0–22	446
Female	296	1.51	97	4.60	0–31	446.5
Extra days barred from work/school/college after recovery because of infection						
Male	592	0.26	23	6.61	0–19	152
Female	729	0.29	38	5.55	0–42	211
No. of days unable to perform normal household activities						
Male	682	1.35	179	5.13	0–50	918
Female	873	2.55	429	5.20	0–55	2229.5
No. of days unable to take part in normal leisure activities						
Male	682	3.32	288	7.86	0–56	2263
Female	873	3.63	407	7.79	0–60	3169.5

Table A5.14 The effect of illness on the person who was ill by sex; No. of days of illness; Community case-control study

N = 555

			RESPONDERS			
	N	OVERALL MEAN	N	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
Male	243	3.33			0–40	810
Female	271	4.41			0–35	1196
In hospital and confined to bed						
Male	243	0.02	1	5	0–5	5
Female	271	0.002	1	0.5	0–0.5	0.5
In hospital but able to get up						
Male	243	0.01	1	3	0–3	3
Female		0.03	2	4	0–7	8
At home and confined to bed						
Male		0.33	59	1.35	0–4	79.5
Female		0.48	67	1.93	0–16	129
At home and able to get up but not able to do most normal activities						
Male		0.91	108	2.05	0–7	221
Female		1.18	129	2.49	0–13	321
At home, but able to get up and do most normal activities						
Male		0.95	114	2.04	0–17	232
Female		1.63	142	3.11	0–28	441
Feeling ill but able to go to work/school/shops etc.						
Male		0.87	81	2.60	0–14	210.5
Female		1.26	107	3.19	0–18	341
If adult, no. of days paid employment lost						
Male	129	0.40	21	2.43	0–6	51
Female	167	0.50	39	2.15	0–8	84
If a child/student, no. of days school/college lost						
Male	118	1.02	40	3.84	0–24	154
Female	106	0.58	30	2.07	0–7	62
Extra days barred from work/school/college after recovery because of infection						
Male	202	0.06	7	1.79	0–4	12.5
Female	243	0.05	5	2.6	0–7	13
No. of days unable to perform normal household activities						
Male	243	0.31	32	2.38	0–10	76
Female	271	0.88	96	2.48	0–18	238.5
No. of days unable to take part in normal leisure activities						
Male	243	1.07	70	3.72	0–14	260.5
Female	271	1.53	103	4.02	0–22	414

Table A5.15 The effect of illness on the person who was ill by sex ; No. of days of illness Enumeration study

N = 2182

			RESPONDERS			
	N	OVERALL MEAN	N	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
No IID organism	321	3.55			0–40	1138.5
No. of days of illness						
Male	969	8.01			0–58	7757.5
Female	1210	7.82			0–80	9467.5
In hospital and confined to bed						
Male	969	0.11	34	3.09	0–21	105
Female		0.09	32	3.47	0–17	111
In hospital but able to get up						
Male	969	0.07	25	2.80	0–17	70
Female		0.11	31	4.23	0–21	131
At home and confined to bed						
Male		1.16	385	2.93	0–17	1127
Female		1.43	529	3.27	0–90	1731
At home and able to get up but not able to do most normal activities						
Male		2.80	667	4.07	0–42	2714
Female		2.99	834	4.34	0–90	3620.5
At home, but able to get up and do most normal activities						
Male		2.16	526	3.97	0–32	2089.5
Female		1.96	618	3.84	0–28	2372.5
Feeling ill but able to go to work/school/shops etc.						
Male		1.58	295	5.21	0–58	1535.5
Female		1.57	379	5.00	0–42	1896.5
If adult, no. of days paid employment lost						
Male	508	2.34	248	4.78	0–22	1186.5
Female	790	1.81	272	5.26	0–85	1431.5
If a child/student, no. of days school/college lost						
Male	459	1.14	122	4.27	0–15	521
Female	436	1.53	141	4.72	0–90	665.5
Extra days barred from work/school/college after recovery because of infection						
Male	820	0.23	37	5.04	0–21	186.5
Female	979	0.42	68	6.02	0–42	409.5
No. of days unable to perform normal household activities						
Male	969	1.44	306	4.55	0–30	1393.5
Female	1211	2.65	590	5.44	0–48	3207.0
No. of days unable to take part in normal leisure activities						
Male	969	5.27	443	7.16	0–63	3172.5
Female	1211	3.47	545	7.71	0–60	4201

Table A5.16 The effect of illness on the person who was ill by age; No. of days of illness GP case-control study

N = 1652

			RESPONDERS			
N	AGE	OVERALL MEAN	N	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
143	<1	7.47			0–27	1067.5
319	1-4	7.68			0–42	2449
137	5–15	6.95			0–28	952
730	16–60	9.54			0–80	6963.5
235	>60	8.22			0–70	1931
87	Missing	9.26			0–30	806
In hospital and confined to bed						
143	<1	0.01	2	0.75	0–1	1.5
319	1–4	0.02	5	1.3	0–2	6.5
137	5–15	0.007	1	1	0–1	1.0
730	16–60	0.03	9	2.72	0–5	24.5
235	>60	0.07	8	1.94	0–7	15.5
87	Missing	0.10	2	8.5	0–15	17
In hospital but able to get up						
143	<1	0.14	5	3.9	0–14	19.5
319	1–4	0.03	5	1.6	0–2	8
137	5–15	0.01	1	2	0–2	2
730	16–60	0.03	6	3.67	0–7	22
235	>60	0.12	3	9.67	0–15	29
87	Missing	-	-	-	-	-
At home and confined to bed						
143	<1	0.43	17	3.65	0–15	62
319	1–4	0.46	56	2.63	0–14	147.5
137	5–15	1.29	63	2.80	0–10	176.5
730	16–60	1.58	384	3.02	0–50	1158.5
235	>60	1.15	88	3.07	0–17	270
87	Missing	0.89	27	2.87	0–15	77.5
At home and able to get up but not able to do most normal activities						
143	<1	2.18	64	4.875	0–21	312
319	1–4	2.78	211	4.21	0–14	887.5
137	5–15	2.65	103	3.52	0–18	363
730	16–60	3.22	528	4.45	0–75	2351.5
235	>60	3.25	143	5.34	0–70	763.5
87	Missing	2.81	52	4.70	0–21	244.5
At home, but able to get up and do most normal activities						
143	<1	2.49	68	5.24	0–18	356
319	1–4	3.08	191	5.15	0–42	984
137	5–15	1.68	80	2.87	0–14	229.5
730	16–60	2.22	372	4.36	0–85	1623
235	>60	2.58	118	5.14	0–42	607
87	Missing	2.90	53	4.75	0–19	252
Feeling ill but able to go to work/school/shops etc.						
143	<1	0.55	16	4.94	0–15	79
319	1–4	1.02	64	5.09	0–28	325.5
137	5–15	1.77	41	5.93	0–28	243
730	16–60	2.87	340	6.16	0–42	2095.5
235	>60	1.4	56	5.88	0–30	329
87	Missing	1.88	29	5.64	0–23	163.5

Table A5.17 The effect of illness on the person who was ill by age; No. of days of illness
Community case-control study
N = 555

			RESPONDERS			
N	AGE	OVERALL MEAN	N	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
17	<1	9.82			0–35	167
114	1–4	4.89			0–28	558
90	5–15	2.89			0–14	260
227	16–60	3.93			0–40	891
69	>60	2.78			0–17	192
38	Missing	4.03			0–12	153
In hospital and confined to bed						
17	<1	-	-	-	-	-
114	1–4	-	-	-	-	-
90	5–15	-	-	-	-	-
227	16–60	0.02	2	2.75	0–5	5.5
69	>60	-	-	-	-	-
38	Missing	-	-	-	-	-
In hospital but able to get up						
17	<1	-	-	-	-	-
114	1–4	0.06	1	7	0–7	7
90	5–15	0.01	1	1	0–1	1
227	16–60	0.01	1	3	0–3	3
69	>60	-	-	-	-	-
38	Missing	0.01	1	0.5	0–0.5	0.5
At home and confined to bed						
17	<1	0.18	1	3	0–3	3
114	1–4	0.30	20	1.7	0–4	34
90	5–15	0.46	29	1.41	0–3.5	41
227	16–60	0.47	59	1.81	0–16	107
69	>60	0.34	17	1.38	0–3.5	23.5
38	Missing	0.60	14	1.64	0–4	23
At home and able to get up but not able to do most normal activities						
17	<1	1.47	6	4.17	0–12	25
114	1–4	1.57	58	3.09	0–13	179
90	5–15	1.09	49	1.61	0–8	79
227	16–60	0.79	97	1.85	0–8	179
69	>60	0.93	28	2.29	0–6	64
38	Missing	1.21	20	2.3	0–7	46
At home, but able to get up and do most normal activities						
17	<1	2.88	7	7	0–28	49
114	1–4	2.01	76	3.01	0–19	229
90	5–15	0.62	42	1.33	0–5	56
227	16–60	1.09	94	2.63	0–28	247
69	>60	1.42	39	2.51	0–17	98
38	Missing	1.32	20	2.5	0–12	50
Feeling ill but able to go to work/school/shops etc.						
17	<1	0.47	4	2	0–4	8
114	1–4	0.88	27	3.70	0–14	100
90	5–15	0.44	21	1.90	0–5	40
227	16–60	1.69	124	3.08	0–18	382.5
69	>60	0.30	12	1.75	0–4	21
38	Missing	0.86	13	2.5	0–5	32.5

Table A5.18 The effect of illness on the person who was ill by age; No. of days of illness Enumeration study

N = 2182

			RESPONDERS			
N	AGE	OVERALL MEAN	N	MEAN	OVERALL RANGE	TOTAL NO. OF DAYS
No. of days of illness						
213	<1	8.65			0–40	1841.5
426	1–4	7.33			0–42	3122
232	5–15	6.97			0–80	1617
929	16–60	8.22			0–58	7641
369	>60	7.94			0–40	2931
12	Missing	6.83			0–14	82
In hospital and confined to bed						
213	<1	0.16	16	2.13	0–6	34
426	1–4	0.07	12	2.46	0–5	29.5
232	5–15	0.09	8	2.75	0–8	22
929	16–60	0.06	18	2.92	0–8	52.5
369	>60	0.21	12	6.5	0–21	78
12	Missing	-	-	-	-	-
In hospital but able to get up						
213	<1	0.05	7	1.5	0–2	10.5
426	1–4	0.08	15	2.2	0–7	33
232	5–15	0.08	6	3	0–6	18
929	16–60	0.04	16	2.44	0–7	39
369	>60	0.27	12	8.38	0–21	100.5
12	Missing	-	-	-	-	-
At home and confined to bed						
213	<1	0.82	44	3.98	0–28	175
426	1–4	0.62	83	3.16	0–14	262
232	5–15	1.34	107	2.91	0–20	311.5
929	16–60	1.63	515	2.95	0–90	1517.5
369	>60	1.56	160	3.61	0–22	577
12	Missing	1.38	6	2.75	0–4.5	16.5
At home and able to get up but not able to do most normal activities						
213	<1	2.58	115	4.78	0–28	549.5
426	1–4	2.69	278	4.12	0–28	1145
232	5–15	2.58	181	3.30	0–20	597.5
929	16–60	2.94	691	3.95	0–90	2732.5
369	>60	3.47	227	5.65	0–25	1282
12	Missing	2.46	11	2.68	0–6	29.5
At home, but able to get up and do most normal activities						
213	<1	2.08	98	4.52	0–20	443
426	1–4	2.81	269	4.45	0–28	1198
232	5–15	1.53	129	2.74	0–14	354
929	16–60	1.78	485	3.41	0–28	1654
369	>60	2.14	155	5.09	0–32	789
12	Missing	2.33	10	2.8	0–8	28
Feeling ill but able to go to work/school/shops etc.						
213	<1	0.90	28	6.82	0–30	191
426	1–4	0.85	85	4.26	0–42	362
232	5–15	1.36	82	3.85	0–30	315.5
929	16–60	2.43	418	5.41	0–58	2263
369	>60	0.79	57	5.10	0–21	291
12	Missing	1.04	5	2.5	0–7	12.5

Table A5.19 Hospital admission
No. of days in hospital, by study (All cases)

NO OF DAYS IN HOSPITAL	TOTAL NO. OF CASES	GP COMPONENT N	COMMUNITY COMPONENT N	ENUMERATION COMPONENT N	TOTAL NO. OF DAYS IN HOSPITAL
0.5	7	2	1	4	3.5
1	19	6	2	11	19
1.5	14	3	0	11	21
2	12	5	0	7	24
2.5	2	1	0	1	5
3	13	2	0	11	39
3.5	2	1	0	1	7
4	8	0	0	8	32
4.5	3	1	0	2	13.5
5	7	2	1	4	35
5.5	1	0	0	1	5.5
6	4	1	0	3	24
7	8	1	1	6	56
8	1	0	0	1	8
10	2	1	0	1	20
14	3	1	0	2	42
15	2	2	0	0	30
18	2	0	1	1	36
21	2	0	0	2	42
Total	112	29	6	77	462.5

2 cases - missing data

Table A5.20 Admission to hospital, by study and age (All cases)

	GP COMPONENT			COMMUNITY COMPONENT			ENUMERATION COMPONENT		
AGE	N	N	(%)	N	N	(%)	N	N	(%)
<1yr	143	5	(3.5)	17	0	(0.0)	213	17	(8.0)
1–4yrs	319	7	(2.2)	114	1	(0.9)	426	19	(4.5)
5–15 yrs	137	1	(0.7)	90	1	(1.1)	232	10	(4.3)
16–60yrs	731	11	(1.5)	227	2	(0.9)	930	19	(2.0)
>60yrs	235	3	(1.3)	69	1	(1.4)	369	14	(3.8)
Missing	87	2	(2.3)	38	1	(2.6)	12	0	(0.0)
Total	1652	29	(1.8)	555	6	(1.1)	2182	79	(3.6)

Table A5.21 Attending a Hosptial outpatient department, by study and age

	GP COMPONENT			COMMUNITY COMPONENT			ENUMERATION COMPONENT		
AGE	N	N	(%)	N	N	(%)	N	N	(%)
<1yr	143	3	(2.1)	17	0	(0.0)	213	8	(3.8)
1–4yrs	319	1	(0.3)	114	1	(0.9)	426	6	(1.4)
5–15 yrs	137	0	(0.0)	90	0	(0.0)	232	5	(2.2)
16–60yrs	731	10	(1.5)	227	3	(1.3)	930	22	(2.4)
>60yrs	235	3	(1.3)	69	2	(2.9)	369	16	(4.3)
Missing	87	3	(3.4)	38	1	(2.6)	12	0	(0.0)
Total	1652	20	(1.2)	555	7	(1.3)	2182	57	(2.6)

Table A5.22 Visit to Hospital Accident and Emergency (A&E) (Casualty) Department as a result of IID

	GP COMPONENT						COMMUNITY COMPONENT						ENUMERATION COMPONENT					
		VISIT		ADMISSION				VISIT		ADMISSION				VISIT		ADMISSION		
AGE	N	N (%)		N (%)		% ADMITTED	N	N(%)		N (%)		% ADMITTED	N	N (%)		N (%)		% ADMITTED
<1yr	143	3	(2.1)	3	(2.1)	100	17	0	(0)	0	(0)	-	213	15	(7.0)	6	(2.8)	40
1–4yrs	319	6	(1.9)	1	(0.3)	17	114	2	(1.8)	1	(0.9)	50	426	22	(5.2)	12	(2.8)	55
5–15yrs	137	1	(0.7)	0	(0)	0	90	1	(1.1)	1	(1.1)	100	232	5	(2.2)	2	(0.9)	40
16–60yrs	731	9	(1.2)	3	(0.4)	33	227	3	(1.3)	2	(0.9)	67	930	23	(3.2)	9	(1.0)	39
>60yrs	235	1	(0.4)	1	(0.4)	100	69	0	(0)	0	(0)	-	369	7	(1.9)	6	(1.6)	86
Missing	87	3	(3.4)	1	(1.1)	33	38	0	(0)	0	(0)	-	12	0	(0)	0	(0)	0
Total	1652	23	(1.4)	9	(0.5)	39	555	6	(1.1)	4	(0.7)	67	2182	72	(3.3)	35	(1.6)	49

Table A5.23 Use of GP services; GP case-control component

RANGE AGE	NO. OF CONTACT TIMES	GP HOME VISIT 0–10 N (% TOTAL)		NO. OF VISITS	VISIT GP AT SURGERY 0–25 N (% TOTAL)		NO. OF VISITS
	0	118	(83.1)	0	5	(3.5)	0
< 1 yr	1	19	(13.4)	19	87	(61.3)	87
N = 142	2 or more	5	(3.5)	10	50	(35.2)	114
	total			29			201
	0-	233	(79.5)	0	32	(10.9)	0
1–4 yrs	1	50	(17.1)	50	191	(65.2)	191
N = 293	2 or more	10	(3.4)	21	70	(23.9)	168
	total			71			359
	0	105	(82.7)	0	15	(11.8)	0
5–15 yrs	1	16	(12.6)	16	92	(72.4)	92
N = 127	2 or more	6	(4.7)	13	20	(15.8)	46
	total			29			138
	0	538	(78.8)	0	89	(13.0)	0
16–60 yrs	1	116	(17.0)	116	435	(63.7)	435
N = 683	2 or more	29	(4.3)	72	159	(23.3)	420
	total			188			855
	0	126	(59.7)	0	59	(28.0)	0
> 60 yrs	1	69	(32.7)	69	115	(54.5)	115
N = 211	2 or more	16	(7.6)	46	37	(17.5)	117
	total			115			232
	0	63	(79.8)	0	6	(7.6)	0
Missing	1	11	(13.9)	11	48	(60.8)	48
N = 79	2 or more	5	(6.3)	14	25	(31.7)	68
	total			25			116
	0	1300	(78.7)	0	206	(13.4)	0
Total	1	281	(18.3)	281	968	(63.1)	968
N = 1535	2 or more	71	(4.6)	176	361	(23.5)	933
	total			457			1901

117 cases — missing data

Table A5.24 Use of GP services by those presenting to a GP in the community component

RANGE AGE	NO. OF CONTACT TIMES	GP HOME VISIT 0–5 N (% TOTAL)		NO. OF VISITS	VISIT GP AT SURGERY 0–5 N (% TOTAL)		NO. OF VISITS
	0	6	(75.0)	0	0		0
< 1 yr	1	2	(25.0)	2	6	(75.0)	6
N = 8	2 or more	0		0	2	(25.0)	6
	total			2			12
	0	39	(81.2)	0	6	(12.5)	0
1–4 yrs	1	9	(18.8)	9	28	(58.3)	28
N = 48	2 or more	0		0	14	(29.2)	31
	total			9			59
	0	7	(53.8)	0	4	(30.8)	0
5–15 yrs	1	3	(23.1)	3	7	(53.9)	7
N = 13	2 or more	3	(23.1)	6	2	(15.3)	4
	total			9			11
	0	35	(85.4)	0	3	(7.3)	0
16–60 yrs	1	4	(9.8)	4	31	(75.6)	31
N = 41	2 or more	2	(4.9)	4	7	(17.1)	20
	total			8			51
	0	9	(52.9)	0	6	(35.3)	0
> 60 yrs	1	6	(35.3)	6	7	(41.2)	7
N = 17	2 or more	2	(11.8)	4	4	(23.5)	10
	total			10			17
	0	6	(37.5)	0	9	(56.3)	0
Missing	1	8	(50.0)	8	5	(31.2)	5
N = 16	2 or more	2	(12.5)	7	2	(12.5)	7
	total			15			12
	0	514	(92.6)	0	28	(19.6)	0
Total	1	32	(22.3)	32	84	(58.7)	84
N = 143	2 or more	9	(6.3)	21	31	(21.7)	78
	total			53			162

6 cases — missing data

Table A5.25 Use of GP services; enumeration study

RANGE AGE	NO. OF CONTACT TIMES	GP HOME VISIT 0–7 N (% TOTAL)		NO. OF VISITS	VISIT GP AT SURGERY 0–30 N (% TOTAL)		NO. OF VISITS
	0	141	(70.9)	0	14	(7.0)	0
< 1 yr	1	39	(19.6)	39	100	(50.3)	100
N = 199	2 or more	19	(9.5)	42	85	(42.7)	229
	total			81			329
	0	302	(76.8)	0	48	(12.2)	0
1–4 yrs	1	69	(17.6)	69	233	(59.3)	233
N = 393	2 or more	22	(5.6)	56	112	(28.5)	256
	total			125			489
	0	149	(71.0)	0	37	(17.6)	0
5–15 yrs	1	53	(25.2)	53	134	(63.8)	134
N = 210	2 or more	8	(3.8)	20	39	(18.6)	86
	total			73			220
	0	622	(75.0)	0	142	(17.1)	0
16–60 yrs	1	161	(19.4)	161	515	(62.1)	515
N = 829	2 or more	46	(5.6)	122	172	(20.8)	456
	total			283			971
	0	152	(48.3)	0	133	(42.2)	0
> 60 yrs	1	114	(36.2)	114	140	(44.4)	140
N = 315	2 or more	49	(15.5)	130	42	(13.3)	97
	total			244			237
	0	8	(80.0)	0	2	(20.0)	0
Missing	1	2	(20.0)	2	6	(60.0)	6
N = 10	2 or more	0		0	2	(20.0)	4
	total			2			10
	0	1600	(73.3)	0	376	(19.2)	0
Total	1	438	(22.4)	438	1128	(57.7)	1128
N = 1956	2 or more	144	(7.4)	370	452	(23.1)	1128
	total			808			2256

226 cases — missing data

Table A5.26 Use of phone and nurse services; GP case-control component

RANGE AGE	NO. OF CONTACT TIMES	PHONE GP 0–5 N (% TOTAL)		PHONE GP 0–5 NO. OF VISITS	NURSE HOME VISIT 0–7 N (% TOTAL)		NURSE HOME VISIT 0–7 NO. OF VISITS
	0	89	(62.7)	0	129	(90.9)	0
< 1 yr	1	41	(28.9)	41	10	(7.0)	10
N = 142	2 or more	12	(8.4)	28	3	(2.1)	7
	total			69			17
	0	210	(69.1)	0	303	(99.7)	0
1–4 yrs	1	55	(18.1)	55	1	(0.3)	1
N = 304	2 or more	39	(12.8)	94	0		0
	total			149			1
	0	96	(73.9)	0	125	(96.1)	0
5–15 yrs	1	25	(19.2)	25	4	(3.1)	4
N = 130	2 or more	9	(6.9)	22	1	(0.8)	2
	total			47			6
	0	532	(75.7)	0	686	(94.1)	0
16–60 yrs	1	122	(17.4)	122	10	(4.5)	10
N = 703	2 or more	49	(7.0)	119	3	(1.4)	20
	total			241			30
	0	172	(77.8)	0	208	(94.1)	0
> 60 yrs	1	35	(15.8)	35	10	(4.5)	10
N = 221	2 or more	14	(6.3)	39	3	(1.4)	11
	total			74			21
	0	62	(77.5)	0	76	(95.0)	0
Missing	1	10	(12.5)	10	4	(5.0)	4
N = 80	2 or more	8	(10.0)	18	0		0
	total			28			4
	0	1161	(73.5)	0	1527	(96.7)	0
Total	1	288	(18.2)	288	40	(2.5)	39
N = 1580	2 or more	131	(8.3)	320	13	(0.8)	40
	total			608			79

82 cases — missing data

Table A5.27 Use of phone and nurse services by those presenting to a GP in the community component

RANGE AGE	NO. OF CONTACT TIMES	PHONE GP 0–3 N (% TOTAL)	PHONE GP 0–3 NO. OF VISITS	NURSE HOME VISIT 0–1 N (% TOTAL)	NURSE HOME VISIT 0–1 NO. OF VISITS
	0	6 (75.0)	0	8 (100)	0
< 1 yr	1	2 (25.0)	2	0	0
N = 8	2 or more	0	0	0	0
	total		2		0
	0	40 (81.6)	0	49 (100)	0
1–4 yrs	1	6 (12.2)	6	0	0
N = 49	2 or more	3 (6.2)	7	0	0
	total		13		0
	0	6 (42.9)	0	13 (92.9)	0
5–15 yrs	1	6 (42.8)	6	1 (7.1)	1
N = 14	2 or more	2 (14.2)	5	0	0
	total		11		1
	0	40 (95.2)	0	42 (100)	0
16–60 yrs	1	2 (4.8)	2	0	0
N = 42	2 or more	0	0	0	0
	total		2		0
	0	13 (65.0)	0	19 (95.0)	0
> 60 yrs	1	6 (30.0)	6	1 (5.0)	1
N = 20	2 or more	1 (5.0)	2	0	0
	total		8		1
	0	10 (62.5)	0	15 (93.8)	0
Missing	1	4 (25.0)	4	1 (6.2)	1
N = 16	2 or more	2 (12.5)	5	0	0
	total		9		1
	0	115 (79.2)	0	146 (98.0)	0
Total	1	26 (17.5)	26	3 (2.0)	3
N = 149	2 or more	8 (5.3)	19	0	0
	total		45		3

Table A5.28 Use of phone and nurse services; enumeration study

RANGE AGE	NO. OF CONTACT TIMES	PHONE GP 0–10 N (% TOTAL)		PHONE GP 0–10 NO. OF VISITS	NURSE HOME VISIT 0–21 N (% TOTAL)		NURSE HOME VISIT 0–21 NO. OF VISITS
	0	6	(75.0)	0	8	(100)	0
< 1 yr	1	2	(25.0)	2	0		0
N = 203	2 or more	18	(8.8)	44	2	(1.0)	4
	total			107			14
	0	276	(67.8)	0	397	(97.5)	0
1–4 yrs	1	105	(25.8)	105	8	(2.0)	8
N = 407	2 or more	26	(6.4)	74	2	(0.5)	5
	total			179			13
	0	166	(74.8)	0	219	(98.6)	0
5–15 yrs	1	44	(19.8)	44	3	(1.4)	3
N = 222	2 or more	12	(5.4)	28	0		0
	total			72			3
	0	656	(74.9)	0	863	(98.3)	0
16–60 yrs	1	161	(18.3)	161	12	(1.4)	12
N = 878	2 or more59	(6.7)	143	3	(0.3)	9	
	total			304			21
	0	264	(72.4)	0	313	(92.9)	0
> 60 yrs	1	64	(19.0)	65	16	(4.7)	16
N = 337	2 or more	29	(8.6)	74	8	(2.4)	39
	total			139			55
	0	7	(63.6)	0	11	(100)	0
Missing	1	4	(36.4)	4	0		0
N = 11	2 or more	0		0	0		0
	total			4			0
	0	1473	(71.6)	0	1994	(96.9)	0
Total	1	441	(21.4)	442	49	(2.4)	49
N = 2058	2 or more	144	(7.0)	363	15	(0.7)	57
	total			805			106

124 cases — missing data

Table A5.29 Use of Laboratory services

Data entered for those completing section 3 of the economic questionnaire

Stool tests

	GP CASE CONTROL STUDY N = 1580			COMMUNITY CASE CONTROL STUDY N = 149			ENUMERATION STUDY N = 2058		
RANGE	0–10			0–4			0–6		
NO. OF	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS
0	145	(9.2)	0	0		0	1384	(67.2)	0
1	1321	(83.6)	1321	97	(65.1)	97	564	(27.4)	564
2 or more	114	(7.2)	282	27	(18.1)	60	110	(5.4)	274
Total			1603			157			838

Blood tests

RANGE	0–10			0–4			0–10		
NO. OF	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS
0	1520	(96.8)	0	143	(96.0)	0	1970	(95.7)	0
1	38	(2.4)	38	2	(2.0)	3	73	(3.6)	73
2 or more	22	(1.4)	57	3	(2.0)	8	15	(0.7)	48
Total			95			11			121

Urine tests

RANGE	0–4			0–4			0–10		
NO. OF	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS
0	1498	(94.8)	0	140	(94.0)	0	1926	(93.6)	0
1	67	(4.2)	67	9	(6.0)	9	119	(5.8)	119
2 or more	15	(1.0)	35	0		0	13	(0.6)	29
Total			102			9			148

Other tests

RANGE	0–2			0–1			0–1		
NO. OF	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS	N	(%)	NO. OF TESTS
0	1576	(99.8)	0	148	(99.3)	0	2052	(99.7)	0
1	3	(0.2)	3	1	(0.7)	1	6	(0.3)	6
2 or more	1	(0.0)	2	0		0	0		0
Total			5			1			6

Table A5.30 Prescription medicines; GP case-control Component

EXEMPTION		EXEMPT N = 403				NOT EXEMPT N = 267				MISSING N = 25			
NO. OF PRESCRIPTIONS PER PATIENT		1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS	1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS	1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS
AGE	N												
< 1yr	141	51	7	8	103								
1–4 yrs	317	73	16	6	129								
5–15 yrs	137	35	6	2	53								
16–60 yrs	731	41	21	12	140	170	47	26	360	12	5	2	29
> 60 yrs	235	71	25	8	147	10	2	1	19	1	1	0	3
missing	87	17	79	0	25	9	1	1	14	4	0	0	4
total no. of patients		288	154	36		189	50	28		17	6	2	
total no. of prescriptions					597				393				36

Table A5.31 Prescription medicines; community component

EXEMPTION		EXEMPT N = 403				NOT EXEMPT N = 267				MISSING N = 25			
NO. OF PRESCRIPTIONS PER PATIENT		1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS	1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS	1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS
AGE	N												
< 1yr	16	1	2	0	4								
1–4 yrs	113	8	4	3	25								
5–15 yrs	90	5	0	0	5								
16–60 yrs	227	3	0	0	3	13	4	2	27	1	0	0	1
> 60 yrs	69	10	1	2	20	0	0	0	0	0	0	0	0
missing	38	4	2	1	13	1	0	0	1	1	0	0	1
total no. of patients		31	9	6		14	4	2		2	0	0	
total no. of prescriptions					70				28				2

Table A5.32 Prescription medicines; enumeration component

EXEMPTION		EXEMPT N = 403				NOT EXEMPT N = 267				MISSING N = 25			
NO. OF PRESCRIPTIONS PER PATIENT		1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS	1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS	1	2	3 OR MORE	TOTAL NO. OF PRESCRIPTIONS
AGE	N												
< 1yr	212	78	29	8	165								
1–4 yrs	421	136	36	14	260								
5–15 yrs	231	53	20	5	109								
16–60 yrs	930	78	22	10	170	207	64	16	326	12	5	0	22
> 60 yrs	369	111	40	13	242	11	3	0	17	0	0	0	0
missing	12	4	1	0	6	3	0	0	3	0	0	0	0
total no. of patients		460	148	51		221	67	16		12	5	0	
total no. of prescriptions					952				346				22

Table A5.33 Relationship of first carer at home or first person accompanying case to GP, hospital, etc.

	GP COMPONENT		COMMUNITY COMPONENT		ENUMERATION COMPONENT	
Visit to GP						
Relationship						
Mother	368	(65.4)	40	(74.1)	472	(63.8)
Father	51	(9.1)	7	(13)	65	(8.8)
Female partner	30	(5.3)	2	(3.7)	40	(5.4)
Male partner	59	(10.5)	4	(7.4)	76	(10.3)
Female grandparent					17	(2.3)
Male grandparent					9	(1.2)
Other	55	(9.7)	1	(1.9)	61	(8.2)
Total	563		54	(100)	740	(100)
Visit to casualty (A&E)						
Relationship						
Mother	7	(36.8)	2		19	(35.8)
Father	4	(21.1)			9	(17)
Female partner	1	(5.3)			3	(5.7)
Male partner	3	(15.8)	1		3	(5.7)
Other	4	(21.1)			19	(35.8)
Total	19		2		53	(100)
Stayed in hospital						
Relationship						
Mother	8	(80.0)	2		31	(83.8)
Father	1	(10.0)			5	(13.5)
Grandparent	1	(10.0)			1	(2.7)
Total	10		2		37	(100)
Visit to Out-patient departments (OPD)						
Relationship						
Mother	2	(18.2)			9	(27.3)
Father					2	(6.1)
Female partner			1		4	(12.1)
Male partner	4	(36.4)	2		2	(6.1)
Other	5	(45.4)			16	(48.5)
Total	11		3		33	(100)
Caring for case at home						
Relationship						
Parent	411	(58)	134	(64)	518	(52)
Partner	220	(31)	61	(29	320	(33)
Grand parent	20	(3)	3	(1)	41	(4)
Relative	18	(3)	9	(4)	46	(5)
Other	37	(5)	4	(2)	59	(6)
Total	706	(100)	211	(100)	984	(100)
No. of days caring for case at home						
Total	5364.5		990		7674	

Table A5.34 Other expenses due to illness

GP case-control component
N = 1652

ITEM	N (%) WITH ADDITIONAL EXPENSES		OVERALL MEAN (£)	RANGE (£)	% OF TOTAL COST	TOTAL COST (£)
Medicine	418	(25.3)	1.25	0–50	11.6	2063.50
Telephone	810	(49.0)	0.62	0–20	5.7	1023.60
Food	460	(27.8)	1.56	0–200	14.5	2584.70
Leisure:						
Books	215	(13.0)	0.40	0–12	3.7	661.00
Video	70	(4.2)	0.27	0–36	2.5	440.50
Toys	38	(2.3)	0.19	0–100	1.8	313.20
Other	12	(0.7)	0.04	0–15	0.4	66.00
New clothing	34	(2.1)	0.24	0–100	2.2	398.80
New bedding	23	(1.4)	0.21	0–50	1.9	340.00
Cleaning:						
Bleach	373	(22.6)	0.49	0–20	4.5	812.50
Nappies	257	(15.6)	1.23	0–100	11.3	2025.20
Washing powder	308	(18.6)	0.55	0–25	5.1	907.30
Other	5	(0.3)	0.14	0–47	1.3	235.00
Travel	57	(3.5)	0.61	0–300	5.6	1006.90
Cancelled passes	33	(2.0)	0.34	0–104	3.2	568.00
Pre-paid fees	119	(7.2)	1.93	0–400	17.8	3193.60
Pre-paid leisure	83	(5.0)	0.66	0–160	6.1	1085.50
Fuel	1	(0.1)	0.03	0–45	0.3	45.00
Care of child	2	(0.1)	0.06	0–46	0.5	92.00
Total						**17862.30**

Table A5.35 Other expenses due to illness

Community case-control component
N = 555

ITEM	N (%) WITH ADDITIONAL EXPENSES		OVERALL MEAN (£)	RANGE (£)	% OF TOTAL COST	TOTAL COST (£)
Medicine	96	(17.3)	0.67	0–15	13.2	372.00
Telephone	149	(26.8)	0.29	0–40	5.8	161.90
Food	83	(15.0)	0.63	0–42	12.5	351.50
Leisure:						
Books	41	(7.4)	0.22	0–21	4.3	121.60
Video	13	(2.3)	0.12	0–13	2.4	67.50
Toys	9	(1.6)	0.08	0–10	1.5	43.50
Other	2	(0.4)	0.03	0–15	0.7	18.50
New clothing	7	(1.3)	0.34	0–60	6.6	186.00
New bedding	4	(0.7)	0.16	0–50	3.2	89.00
Cleaning:						
Bleach	89	(16.0)	0.30	0–10	5.9	164.80
Nappies	45	(8.1)	0.42	0–15	8.2	231.20
Washing powder	73	(13.2)	0.38	0–50	7.5	210.10
Other	2	(0.4)	0.17	0–47	3.3	94.00
Travel	12	(2.2)	0.34	0–100	6.7	188.00
Cancelled passes	1	(0.2)	0.01	0–5	0.2	5.00
Pre-paid fees	23	(4.1)	0.52	0–60	10.3	289.00
Pre-paid leisure	27	(4.9)	0.31	0–58	6.2	174.60
Fuel	0					
Care of child	1	(0.2)	0.08	0–46	1.6	46
Total						**2815.00**

Table A5.36 Other expenses due to illness

Enumeration component
N = 2182

ITEM	N (%) WITH ADDITIONAL EXPENSES		OVERALL MEAN (£)	RANGE (£)	% OF TOTAL COST	TOTAL COST (£)
Medicine	418	(25.3)	1.25	0–50	11.6	2063.50
Medicine	550	(25.2)	1.25	0–50	12.2	2732.80
Telephone	1029	(47.2)	0.60	0–40	5.9	1317.80
Food	580	(26.6)	1.27	0–52	12.4	2772.50
Leisure:						
Books	281	(12.9)	0.41	0–70	4.0	901.60
Video	116	(5.3)	0.34	0–22	3.3	734.40
Toys	64	(2.9)	0.22	0–65	2.1	472.30
Other	17	(0.8)	0.04	0–15	0.4	89.50
New clothing	56	(2.6)	0.31	0–45	3.0	669.00
New bedding	57	(2.6)	0.45	0–100	4.4	982.20
Cleaning:						
Bleach	449	(20.6)	0.46	0–15.2	4.5	1010.50
Nappies	329	(15.1)	1.14	0–100	11.1	2491.50
Washing powder	408	(18.7)	0.57	0–50	5.5	1239.20
Other	8	(0.4)	0.17	0–47	1.7	376.00
Travel	97	(4.4)	0.64	0–180	6.2	1393.30
Cancelled passes	27	(1.2)	0.23	0–135	2.3	507.50
Pre-paid fees	115	(5.3)	1.40	0–400	13.6	3044.20
Pre-paid leisure	107	(4.9)	0.65	0–225	6.4	1428.20
Fuel	5	(0.2)	0.10	0–45	1.0	225.00
Care of child	0					
Total						**22387.50**

Table A5.37 Total cost to patient, by study component

	GP CASE CONTROL N = 1652	ENUMERATION N = 2182
Phone GP	609	805
Prescriptions	2040.50	2143.50
Additional costs:		
In hospital	213	1040.7
At OPD	12	34
On holiday when ill	1781.70	1138.40
At home when ill	17862.30	22437.50
Transport:		
To GP	1647.18	2119.67
To hospital	994.93	1048.32
To laboratory	44.73	231.15
TOTAL	**25205.34**	**30998.24**

Table A5.38 Total cost to patient, by study component Community case-control component

	THOSE WHO REPORTED SEEING A DOCTOR N = 149	ALL THOSE IN THE COMMUNITY CASE CONTROL COMPONENT N = 555
Phone GP	45	45
Prescriptions	146.50	146.50
Additional costs:		
In hospital	22	22
At OPD	1.5	1.5
On holiday when ill	69	76
At home when ill	1341.70	2814.80
Transport:		
To GP	199.93	199.93
To hospital	78.35	78.35
To laboratory	6.45	6.45
TOTAL	**1910.43**	**3390.53**

For those who reported not seeing a doctor:
Additional costs: on holiday when ill — £7
at home when ill — £1473.10

Table A5.39 Average personal costs to patient, by study component

	GP CASE CONTROL N = 1652	ENUMERATION N = 2182
Phone GP	0.38	0.39
Prescriptions	1.29	1.04
Additional costs:		
In hospital	0.13	0.48
At OPD	0.01	0.02
On holiday when ill	1.08	0.52
At home when ill	10.81	10.28
Transport:		
To GP	1.00	0.97
To hospital	0.48	0.57
To laboratory	0.03	0.11
TOTAL	**15.33**	**14.29**

Costs dependent on having seen a GP e.g. prescription costs, only attributed to those who saw a GP

Table A5.40 Average personal costs to patient, by study component Community case-control component

	THOSE WHO REPORTED SEEING A DOCTOR N = 149	ALL THOSE IN THE CASE COMMUNITY COMPONENT N = 555
Phone GP	0.30	0.08
Prescriptions	0.98	0.26
Additional costs:		
In hospital	0.15	0.04
At OPD	0.01	0.003
On holiday when ill	0.46	0.14
At home when ill	9.00	5.07
Transport:		
To GP	1.3	0.36
To hospital	0.53	0.14
To laboratory	0.04	0.01
TOTAL	**12.77**	**6.11**

For those who reported not seeing a doctor:
Average additional costs: on holiday when ill — £0.02
at home when ill — £3.7

Table A5.41 Total cost to patient, by organism and study component

GP case control component

	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
Phone GP	193	56	39	97	83	55	18	8	80	79	26
Prescriptions	797.90	224.75	161.60	409.75	353.50	209.75	70.7	25.25	14.75	15.15	45.45
Additional costs:											
In hospital	89.50	28	0	14	9	4	0	0	0	0	2
At OPD	6	0	0	0	0	6	0	0	0	0	0
On holiday when ill	159.50	224	125	789.50	779.50	454.20	193	10	10	5	20
At home when ill	6021	1601.60	1236	1933	1808	2283.20	729.30	289.70	1864.40	1772.40	855.60
Transport:											
To GP	600.22	181.68	132.54	156.96	129.86	224.52	66.77	21.42	107.68	103.48	53.99
To hospital	214.58	553.50	0	3.85	2.8	554.90	1.4	0	6	6	0.98
To laboratory	14.85	0	7.70	13.6	5.6	0.7	0	0	0	0	0.70
TOTAL	**8096.55**	2869.53	**1701.84**	3417.66	**3171.26**	3792.27	**1079.87**	**354.37**	2082.83	**1981.03**	**1004.72**

Table A5.42 Average personal cost per case, by organism and study component

GP case control component

	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
Phone GP	0.29	0.62	0.66	0.51	0.48	0.28	0.28	0.44	0.66	0.66	0.31
Prescriptions	1.20	2.50	2.74	2.13	2.06	1.06	1.09	1.40	0.12	0.13	0.55
Additional costs:											
In hospital	0.13	0.31	0	0.07	0.05	0.02	0	0	0	0	0.02
At OPD	0.01	0	0	0	0	0.03	0	0	0	0	0
On holiday when ill	0.24	2.49	2.12	4.11	4.53	2.31	2.98	0.56	0.08	0.04	0.24
At home when ill	9.08	17.80	20.95	10.07	10.51	11.59	11.22	16.09	15.28	14.89	10.31
Transport:											
To GP	0.91	2.02	2.25	0.82	0.76	1.14	1.03	1.19	0.88	0.87	0.65
To hospital	0.32	6.15	0	0.02	0.02	2.82	0.02	0	0.05	0.05	0.01
To laboratory	0.02	0	0.13	0.07	0.03	0	0	0	0	0	0.01
TOTAL	**12.21**	31.89	**28.84**	17.80	**18.44**	19.25	**16.61**	**19.69**	17.07	**16.65**	**12.11**

Table A5.43 Total cost to patient, by organism and study component

Community component

	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
Phone GP	193	56	39	97	83	55	18	8	80	79	26
Phone GP	21	1	1	6	4	1	1	0	2	2	2
Prescriptions	101	0	0	16	15.15	0	0	0	0	0	0
Additional costs:											
In hospital	2	0	0	9.5	0	0	0	0	0	0	0
At OPD	1.5	0	0	0	0	0	0	0	0	0	0
On holiday when ill	51	0	0	0	0	20	2	0	5	0	0
At home when ill	1435.20	31	23.50	195.30	155.60	237.30	97.30	43.50	129.60	120.40	240.60
Transport:											
To GP	129.93	1.05	0	16.31	12.25	4.39	0.56	1.65	7.07	7.07	9.97
To hospital	29.8	0	0	0	0	3.5	0	0	0	0	0.38
To laboratory	5.6	0	0	0	0	0	0	0	0	0	0.38
TOTAL	**1777.03**	33.05	**24.50**	243.11	**187**	266.19	**100.86**	**45.15**	143.67	**129.47**	**253.27**

Table A5.44 Average personal cost per case, by organism and study commponent

Community component

	NO IID ORGANISM	*SALMONELLA* SPP.	*S.ENTERITIDIS*	*CAMPYLOBACTER* SPP.	*C.JEJUNI*	ENTEROVIR *E.COLI*	EAGGEC	*C.DIFFICILE*	ROTAVIRUS	ROTAVIRUS GP 3	SRSV
Phone GP	0.07	0.25	0.5	0.26	0.22	0.02	0.08	0	0.10	0.11	0.05
Prescriptions	0.31	0	0	0.70	0.84	0	0	0	0	0	0
Additional costs:											
In hospital	0.006	0	0	0.41	0	0	0	0	0	0	0
At OPD	0.005	0	0	0	0	0	0	0	0	0	0
On holiday when ill	0.16	0	0	0	0	0.42	0.17	0	0.24	0	0
At home when ill	4.47	7.75	11.75	8.49	8.64	4.94	8.11	8.7	6.17	6.34	6.33
Transport:											
To GP	0.40	0.26	0	0.71	0.68	0.09	0.05	0.33	0.34	0.37	0.26
To hospital	0.09	0	0	0	0	0.07	0	0	0	0	0.01
To laboratory	0.02	0	0	0	0	0	0	0	0	0	0.01
TOTAL	**5.54**	8.26	**12.25**	10.57	**10.39**	5.54	**8.41**	**9.03**	6.85	**6.81**	**6.67**

Table A5.45 Costs of days of lost employment, by study and sex, for cases

	N	N (% OF TOTAL)		TOTAL COST (£)	AVERAGE COST (£)
GP case control component					
Overall	1652	476	(28.8)	231230.60	139.97
Male	682	203	(29.8)	116296.70	170.52
Female	873	249	(28.5)	93473.84	107.07
Missing	97	24	(24.7)	10706.60	110.38
Overall — adjusted for sex				220475.92	133.46
Community case control component					
Overall	555	83	(15.0)	14781.50	26.63
Male	243	29	(11.9)	5846.07	24.06
Female	271	45	(16.6)	6543.81	24.15
Missing	41	9	(22.0)	1398.25	34.10
Overall — adjusted for sex				13788.13	24.84
Enumeration component					
Overall	2182	597	(27.4)	265507.70	121.68
Male	969	282	(29.1)	125579.00	129.60
Female	1211	315	(26.0)	122921.00	101.50
Missing	2	0		0	0
Overall — adjusted for sex				248500.00	113.89

Table A5.46 Average costs of days of lost employment, by study and sex, for cases, carers and accompanying persons

	GPCC	CCCC	ENUMERATION COMPONENT
Cases			
overall	139.97	26.63	121.68
adjusted for sex	133.46	24.84	113.89
adjusted for social class	138.20	26.20	
adjusted for sex & social class	130.78	24.97	
Carers			
overall	21.62	15.48	27.68
adjusted for social class of carer	22.22	17.39	23.88
Accompanying person			
overall	14.36	1.87	12.77

Table A5.47 Costs of days of lost employment for cases, adjusted for social class

GP case-control component

OVERALL	N = 1652					
SOCIAL CLASS	**N**	**N**	**(%)**	**NO. OF DAYS**	**TOTAL COST (£)**	**AVERAGE COST PER CASE**
1	102	28	(27.5)	108.5	12680.40	124.32
2	445	129	(29.0)	768	84971.50	190.95
3a	295	125	(42.4)	658	47935.29	162.49
3b	270	74	(27.4)	532.5	30783.83	114.01
4	183	73	(39.9)	549	32769.81	179.07
5	40	16	(40.0)	118	6572.60	164.32
Other	139	8	(5.8)	29	2317.10	16.67
Missing	178	23	(12.9)	131	10466.90	58.80
Total					228497.43	138.2
MALES	**N = 682**					
SOCIAL CLASS	**N**	**N**	**(%)**	**NO. OF DAYS**	**TOTAL COST (£)**	**AVERAGE COST PER CASE**
1	62	17	(27.4)	73	9338.89	150.63
2	211	61	(28.9)	359	42688.70	202.32
3a	101	37	(36.6)	220.5	16980.71	168.13
3b	163	54	(33.1)	370.5	23771.28	145.84
4	69	24	(34.8)	231.5	16320.75	236.53
5	14	6	(42.9)	40.5	2417.44	172.67
Other	31	3	(9.7)	6	535.50	17.27
Missing	31	1	(3.2)	2	178.50	5.76
Total					112231.77	164.56
FEMALES	**N = 873**					
SOCIAL CLASS	**N**	**N**	**(%)**	**NO. OF DAYS**	**TOTAL COST (£)**	**AVERAGE COST PER CASE**
1	39	11	(28.2)	35.5	3109.09	79.72
2	229	68	(29.7)	409	39734.34	173.51
3a	190	85	(44.7)	427.5	19468.35	102.47
3b	106	20	(18.9)	162	8871.12	83.69
4	113	49	(43.4)	317.5	14998.70	132.73
5	26	10	(38.5)	77.5	3151.15	121.20
Other	107	5	(4.7)	23	1475.68	13.79
Missing	63	1	(1.6)	5	320.80	5.09
Total					91129.23	104.39

Total cost — adjusted for sex & sclass — 203361 (average cost per case = 130.78)

Table A5.48 Costs of days of lost employment of cases adjusted for social class

Community case-control component

OVERALL	N = 555					
SOCIAL CLASS	**N**	**N**	**(%)**	**NO. OF DAYS**	**TOTAL COST (£)**	**AVERAGE COST PER CASE**
1	18	2	(11.1)	3	350.61	19.48
2	135	22	(16.3)	49.5	5476.68	40.57
3a	69	15	(21.7)	23.5	1711.97	24.81
3b	49	12	(24.5)	37.5	2167.88	44.24
4	45	14	(31.1)	40.5	2417.45	53.72
5	3	1	(33.3)	2.5	139.25	46.42
Other	23	2	(8.7)	5	399.50	17.37
Missing	213	15	(7.0)	23.5	1877.65	8.82
Total					14540.99	26.20
MALES	**N = 243**					
SOCIAL CLASS	**N**	**N**	**(%)**	**NO. OF DAYS**	**TOTAL COST (£)**	**AVERAGE COST PER CASE**
1	15	1	(6.7)	1	127.93	8.53
2	65	9	(13.8)	15.5	1843.10	28.36
3a	20	2	(10.0)	4	308.04	15.40
3b	33	10	(30.3)	32.5	2085.20	63.19
4	17	3	(17.6)	7	493.05	29.03
5	1	0		0	0	0
Other	5	1	(20.0)	1	89.25	17.85
Missing	87	3	(3.4)	4.5	401.62	4.62
Total					5348.19	22.01
FEMALES	**N = 271**					
SOCIAL CLASS	**N**	**N**	**(%)**	**NO. OF DAYS**	**TOTAL COST (£)**	**AVERAGE COST PER CASE**
1	3	1	(33.3)	2	175.16	58.39
2	70	13	(18.6)	34	3303.10	47.19
3a	49	13	(26.5)	19.5	888.03	18.12
3b	16	2	(12.5)	5	273.80	17.11
4	28	11	(39.3)	33.5	1582.54	56.52
5	1	0		0	0	0
Other	18	1	(5.6)	4	256.64	14.26
Missing	86	4	(4.7)	4	256.64	2.98
Total					6735.98	24.86

Total cost — adjusted for sex & sclass — 12084.17 (average cost per case = 24.97)

Table A5.49 Costs of days of lost employment for carers

GP case-control component

	N	N	(%)	NO. OF DAYS	TOTAL COST (£)	AVERAGE COST PER CASE
Overall	1652	180		447	35715.30	21.62
Social class						
1	36	20	(55.5)	34	3973.58	
2	112	51	(45.5)	116	12834.24	
3a	125	62	(49.6)	146	10636.10	
3b	60	31	(51.6)	73.5	4249.03	
4	60	15	(25.0)	45.5	2715.89	
5	2	1	(50.0)	1	55.70	
Other	5	0		0	0	
Missing	15	7	(46.7)	28	2237.20	
Total	415				36701.74	

Community case-control component

	N	N	(%)	NO. OF DAYS	TOTAL COST (£)	AVERAGE COST PER CASE
Overall	555	51		107.5	8589.25	15.48
Social class						
1	6	2	(33.3)	2.5	292.18	
2	44	16	(36.4)	54	5974.56	
3a	38	17	(44.7)	24.5	1784.83	
3b	17	8	(47.1)	14	809.34	
4	13	5	(38.5)	9	537.21	
5	4	1	(25.0)	1	55.70	
Other	4	0		0	0	
Missing	7	3	(42.9)	2.5	199.75	
Total	133				9653.57	

Enumeration component

	N	N	(%)	NO. OF DAYS	TOTAL COST (£)	AVERAGE COST PER CASE
Overall	2182	253		756	60404.39	27.68
Social class						
1	27	20	(74.1)	47	5492.89	
2	147	69	(46.9)	189.5	20966.28	
3a	162	78	(48.1)	191	13914.35	
3b	97	54	(55.7)	167.5	968.32	
4	75	28	(37.3)	87	5193	
5	9	3	(33.3)	4	218.20	
Other	18	2	(11.1)	2.5	199.75	
Missing	39	17	(43.6)	64.5	5153.55	
Total	574				52106.34	

Table A5.50 Costs of days of lost employment, for accompanying person

	N	N	(%)	NO. OF DAYS	TOTAL COST (£)	AVERAGE COST PER CASE
GP component	1652	117	(7.1)	297	23722.31	14.36
Community component	555	6	(1.1)	13	1038.70	1.87
Enumeration component	2182	149	(6.8)	349	27869.11	12.77

Table A5.51 Food safety and how it affects the choices you make

Person completing

By Study

PERSON COMPLETING QUESTIONNAIRE	GP COMPONENT		COMMUNITY COMPONENT		ENUMERATION COMPONENT	
	N	%	N	%	N	%
Person who was ill	954	57.7	311	56.0	1214	55.6
Adult for child who was ill	624	37.8	230	41.4	847	38.8
Adult for another adult who was ill	20	1.2	3	0.5	39	1.8
Missing	53	3.2	0	0.0	82	3.8
Total	1652	100	555	100	2182	100

Table A5.52 If your illness was shown to have been caused by a food item which had been eaten, how much, for every £100 you earn (after tax) would you be willing to pay (once only) to avoid this illness again?

By Study component and Age

	GPCC						COMMUNITY CC						ENUMERATION COMPONENT					
AGE	0–4YRS		5–16YRS		ADULT		0–4YRS		5–16YRS		ADULT		0–4YRS		5–16YRS		ADULT	
AMOUNT (£)	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Up to 1	51	11.0	13	9.5	120	12.4	17	13	14	15.6	51	17.2	48	7.5	22	9.5	160	12.3
1.01–5	38	8.2	14	10.2	117	12.1	15	11.5	9	10.0	33	11.1	59	9.2	29	12.5	139	10.7
5.01–10	49	10.6	16	11.7	86	8.9	22	16.8	13	14.4	34	11.5	71	11.1	30	12.9	106	8.2
10.01–25	22	4.8	7	5.1	51	5.3	9	6.9	2	2.2	18	6.1	29	4.5	12	5.2	53	4.1
25.01–50	16	3.5	5	3.7	36	3.7	6	4.6	3	3.3	15	5.1	19	3.0	12	5.2	47	3.6
50.01–100	35	7.6	8	5.8	60	6.2	6	4.6	2	2.2	11	3.7	53	8.3	13	5.6	66	5.1
more than 100	16	3.5	8	5.8	38	3.9	2	1.5	3	3.3	18	6.1	31	4.9	5	2.2	63	4.8
missing	235	50.9	66	48.2	458	47.4	54	41.2	44	48.9	116	39.2	329	51.5	109	47.0	665	51.2
Total	462	100	137	100	966	100	131	100	90	100	296	100	639	51.5	232	100	1299	100

Table A5.53 Amount spent on food each month by those willing to pay extra

	GP COMPONENT		COMMUNITY COMPONENT		ENUMERATION COMPONENT	
AMOUNT (£)	N	%	N	%	N	%
Up to 100	166	15.8	50	13.6	266	20.0
101–200	367	34.9	107	29.2	428	32.2
201–300	329	31.2	127	34.6	397	29.8
301–400	111	10.5	54	14.7	139	10.4
401–500	56	5.3	20	5.5	66	5.0
more than 500 [600–1000]	9	0.9	5	1.4	8	0.6
missing	15	1.4	4	1.1	27	2.0
Total	1053	100	367	100	1331	100

Table A5.54 If you were offered poultry meat which had been irradiated and could be guaranteed 99% free of salmonella, would you be prepared to buy it in preference to non-irradiated poultry if any of the following applied?

GP case-control component

		n	%	AMOUNT (p)	n	%
It cost a few pence more	yes	848	51.3	Up to 5	86	10.1
				6–25	239	28.2
				26–50	328	38.7
				more than 50 [55–500]	173	20.4
				missing	22	2.6
				Total	848	100
It was the same price	yes	223	13.5			
It was a few pence less	yes	109	6.6	Up to 5	26	23.9
				6–25	24	22.0
				26–50	24	22.0
				more than 50 [75–150]	14	12.8
				missing	21	19.3
				Total	109	100
Not at any price	yes	338	20.5			
Missing		134	8.1			
Total		1652	100			

Table A5.55 If you were offered poultry meat which had been irradiated and could be guaranteed 99% free of salmonella, would you be prepared to buy it in preference to non-irradiated poultry if any of the following applied?

Community component

		N	%	AMOUNT (P)	N	%
It cost a few pence more	yes	267	48.1	Up to 5	30	11.2
				6–25	91	34.1
				26–50	93	34.8
				more than 50 [50–500]	41	15.4
				missing	12	4.5
				Total	267	100
It was the same price	yes	72	13.0			
It was a few pence less	yes	32	5.8	Up to 5	7	21.9
				6–25	4	12.5
				26–50	7	21.9
				more than 50 [75–150]	4	12.5
				missing	10	31.2
				Total	32	100
Not at any price	yes	136	24.5			
Missing		48	8.6			
Total		555	100			

Table A5.56 If you were offered poultry meat which had been irradiated and could be guaranteed 99% free of salmonella, would you be prepared to buy it in preference to non-irradiated poultry if any of the following applied?

Enumeration component

		N	%	AMOUNT (P)	N	%
It cost a few pence more	yes	1137	52.1	Up to 5	110	
				6–25	362	
				26–50	427	
				more than 50 [55–500]	213	
				missing	25	
				Total	1137	
It was the same price	yes	305	14.0			
It was a few pence less	yes	155	7.1	Up to 5	30	19.4
				6–25	39	25.2
				26–50	36	23.2
				more than 50 [60–150]	24	15.5
				missing	26	16.8
				Total	155	100
Not at any price	yes	379	17.4			
Missing		206	9.4			
Total		2182	100			

Table A5.57 Which category in the above table would have been ticked if you could be assured that irradiated meat is absolutely safe and tastes the same as non-irradiated meat?

GP case-control component

	N	%	AMOUNT (P)	N	%
It cost a few pence more	812	49.2	Up to 5	62	7.6
			6–25	204	25.1
			26–50	358	44.1
			more than 50 [60–550]	66	8.1
			missing	122	15.0
			Total	812	100
It was the same price	216	13.1			
It was a few pence less	43	2.6	Up to 5	6	14.0
			6–25	12	27.9
			26–50	20	46.5
			more than 50 [75–150]	1	2.3
			missing	4	9.3
			Total	43	100
Not at any price	129	7.8			
Missing	452	27.4			
Total	1652	100			

Table A5.58 Which category in the above table would have been ticked if you could be assured that irradiated meat is absolutely safe and tastes the same as non-irradiated meat?

Community component

	N	%	AMOUNT (P)	N	%
It cost a few pence more	247	49.4	Up to 5	20	7.3
			6–25	80	29.2
			26–50	125	45.6
			more than 50	18	6.6
			[75- 10]		
			missing	116	42.3
			Total	274	100
It was the same price	100	18.0			
It was a few pence less	14	2.5	Up to 5	1	7.1
			6–25	6	42.9
			26–50	4	28.6
			more than 50	0	0
			[75–150]		
			missing	3	21.4
			Total	14	100
Not at any price	47	8.5			
Missing	120	43.8			
Total	555	100			

Table A5.59 Which category in the above table would have been ticked if you could be assured that irradiated meat is absolutely safe and tastes the same as non-irradiated meat?

Enumeration component

	N	%	AMOUNT (P)	N	%
It cost a few pence more	986	45.2	Up to 5	71	7.2
			6 - 25	263	26.7
			26 - 50	445	45.1
			more than 50	59	6.0
			[55 - 500]		
			missing	148	15.0
			Total	986	100
It was the same price	346	15.9			
It was a few pence less	83	3.8	Up to 5	9	10.8
			6 - 25	15	18.1
			26 - 50	36	43.4
			more than 50	3	3.6
			[75 - 150]		
			missing	20	24.1
			Total	83	100
Not at any price	137	6.3			
Missing	630	28.8			
Total	2182	100			

Table A5.60 Responsibility for safety of food

GP CASE CONTROL COMPONENT	RANK					
	1 %	2 %	3 %	4 %	5 %	6 %
National Government	33.8	7.4	11.4	12.9	16.4	18.1
Food manufacturers	26.9	37.7	21.8	10.0	2.7	0.9
Food producers	22.2	27.2	22.8	15.3	8.6	3.9
Customer	10.6	3.0	6.1	17.6	11.5	51.3
Food retailer	5.0	14.4	30.3	26.1	21.4	2.8
Local Authority	1.5	10.3	7.6	18.1	39.5	23.0
COMMUNITY COMPONENT	**RANK**					
	1 %	2 %	3 %	4 %	5 %	6 %
National Government	31.9	8.2	11.8	13.3	14.3	20.5
Food manufacturers	25.6	34.1	28.5	8.2	3.1	0.5
Food producers	23.7	25.9	22.2	15.7	8.7	3.9
Customer	14.3	4.8	4.8	19.3	13.8	43.0
Food retailer	3.1	16.9	28.5	28.5	20.1	2.9
Local Authority	1.5	10.1	4.1	10.5	40.1	29.2
ENUMERATION COMPONENT	**RANK**					
	1 %	2 %	3 %	4 %	5 %	6 %
National Government	36.6	7.8	10.6	12.2	15.7	17.2
Food manufacturers	26.3	35.0	24.5	10.5	2.6	1.0
Food producers	21.3	27.7	23.3	15.9	9.2	2.6
Customer	10.0	2.6	6.1	13.7	10.4	57.3
Food retailer	4.6	14.9	26.6	25.6	25.7	2.6
Local Authority	1.3	12.0	9.0	22.0	36.3	19.5

Table A5.61 Responsibility for safety of food

By organisms

S.enteritidis **N=45**	**RANK**					
	1 %	**2 %**	**3 %**	**4 %**	**5 %**	**6 %**
National Government	26.7	15.6	13.3	13.3	13.3	17.8
Food manufacturers	40.0	33.3	13.3	11.11	0.0	2.2
Food producers	15.6	33.3	26.7	8.9	11.11	4.4
Customer	8.9	0.0	8.9	17.8	6.7	57.8
Food retailer	6.7	15.6	31.1	24.4	20.0	2.2
Local Authority	2.2	2.2	6.7	24.4	48.9	15.6
C.jejuni **N=128**	**RANK**					
	1 %	**2 %**	**3 %**	**4 %**	**5 %**	**6 %**
National Government	29.7	6.3	9.4	17.2	18.8	18.8
Food manufacturers	26.6	44.5	17.2	10.2	0.8	0.8
Food producers	27.3	21.1	27.3	13.3	9.4	1.6
Customer	7.8	3.1	3.1	25.0	10.9	50.0
Food retailer	6.3	15.6	36.7	19.5	18.8	5.1
Local Authority	2.3	9.4	6.3	14.8	41.4	25.8
EAggEC **N=53**	**RANK**					
	1 %	**2 %**	**3 %**	**4 %**	**5 %**	**6 %**
National Government	45.3	3.8	11.3	17.0	7.6	15.1
Food manufacturers	26.4	41.5	22.6	3.8	3.8	1.9
Food producers	17.0	26.4	26.4	11.3	9.4	9.4
Customer	9.4	0.0	7.6	15.1	13.2	54.7
Food retailer	1.9	17.0	24.5	35.9	18.9	1.9
Local Authority	0.0	11.3	7.6	17.0	47.2	17.0
C.difficile **N=18**	**RANK**					
	1 %	**2 %**	**3 %**	**4 %**	**5 %**	**6 %**
National Government	38.9	0.0	11.1	11.1	16.7	22.2
Food manufacturers	38.9	16.7	44.4	0.0	0.0	0.0
Food producers	5.6	50.0	5.6	22.2	11.1	5.6
Customer	11.1	5.6	11.11	16.7	22.2	33.3
Food retailer	5.6	22.2	22.2	27.8	16.7	5.6
Local Authority	0.0	5.6	5.6	22.2	33.3	33.3
Rotavirus Gp A **N=98**	**RANK**					
	1 %	**2 %**	**3 %**	**4 %**	**5 %**	**6 %**
National Government	38.8	5.1	11.2	6.1	20.4	18.4
Food manufacturers	18.4	31.6	34.7	11.2	2.0	2.0
Food producers	19.4	34.7	20.4	15.3	7.1	3.1
Customer	17.4	3.1	7.1	11.2	17.4	43.9
Food retailer	6.1	14.3	20.4	39.8	17.4	2.0
Local Authority	0.0	11.2	6.1	16.3	35.7	30.6

Table A5.61 – *continued*

By organisms

SRSV N=83	RANK					
	1 %	2 %	3 %	4 %	5 %	6 %
National Government	25.3	7.2	14.5	12.1	14.5	26.5
Food manufacturers	36.1	31.3	21.7	8.4	2.4	0.0
Food producers	21.7	33.7	19.3	14.5	7.2	3.6
Customer	10.8	1.2	8.4	25.3	9.6	44.6
Food retailer	3.6	20.5	31.3	21.7	21.7	1.2
Local Authority	2.4	6.0	4.8	18.1	44.6	24.1
No IID organism N=670	**RANK**					
	1 %	2 %	3 %	4 %	5 %	6 %
National Government	35.5	8.8	12.2	11.8	14.3	17.3
Food manufacturers	23.4	36.3	27.0	9.6	2.8	0.9
Food producers	23.7	25.7	21.6	16.0	8.8	4.2
Customer	11.5	3.4	4.9	17.0	12.8	50.3
Food retailer	4.6	14.5	27.3	28.4	22.1	3.1
Local Authority	1.2	11.3	6.9	17.3	39.1	24.2

Appendix 6
Case-control study questionnaires

A6.1 LIST OF SYMPTOMS INCLUDED IN THE CASE QUESTIONNAIRES

A6.1.1 Acute phase

- Diarrhoea (loose, watery motions)
- Blood in motions
- Nausea (feeling sick)
- Vomiting (being sick)
- Abdominal (tummy) pain
- Loss of appetite
- High temperature (shivering/sweating)
- Cough, running/blocked nose, sore throat
- Headache
- Aching muscles
- Joint pains/stiffness
- Back or neck pains/stiffness
- Joint swelling
- Painful red eyes
- Dizziness/faintness
- Other (please specify)

A6.1.2 Three weeks after onset

- Diarrhoea (loose, watery motions)
- Blood in motions
- Nausea (feeling sick)
- Vomiting (being sick)
- Abdominal (tummy) pain
- Loss of appetite
- Loss of weight
- Excessive flatulence (breaking wind)
- Discomfort in passing urine
- Discharge from vagina or penis
- Joint pains/stiffness or limping
- Joint swelling
- Back or neck pains/stiffness
- Aching muscles
- Pain in heels
- Headaches
- Dizzy spells
- Seeing double
- Clumsiness of hands (e.g. dropping things)
- Unsteady walking (e.g. falling over)
- Pins and needles
- Weakness of hands (e.g. difficulty gripping things)
- Weakness of legs (e.g. difficulty walking or rising)
- Faintness or fits

- Feeling tired
- Painful red eye (s)
- Desire to sleep more than usual
- Skin rash
- Other

IN CONFIDENCE

GE Q1.1

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

PLEASE ENTER STUDY NUMBER.

PLEASE READ THIS PAGE FIRST

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this study following your recent episode of gastroenteritis. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

SECTION 1 THIS SECTION CONFIRMS DETAILS OF THE AGE AND SEX OF THE PERSON WHO WAS ILL AND WHO IS NAMED IN THE ACCOMPANYING LETTER

Please state:

1.1 Today's date: ...../...../.....
day month year

1.2 Your date of birth: ...../...../.....
day month year

1.3 Sex: Male ☐ Female ☐

SECTION 2 THIS SECTION ASKS ABOUT THE SYMPTOMS YOU EXPERIENCED DURING YOUR ILLNESS

2.1 On what date did your symptoms start? ...../...../.....
day month year

2.2 On what date did you first see your GP about these symptoms? ...../...../.....
day month year

2.3 Did your illness incapacitate you? ***(i.e. prevent you going about your normal daily activities)***

Yes ☐ No ☐ Not sure ☐

2.4 Do you suffer from any long-standing illness or disability?

Yes ☐ No ☐

If "**Yes**", ***please specify***: .....
.....
.....
.....

MRC use only

2.5 Did you have any of the following symptoms?

If **"YES"**, in your opinion how severe were they and how many days did they last?

(tick ALL appropriate boxes or LEAVE BLANK IF YOU DID NOT HAVE THE SYMPTOM)

An EXAMPLE is given on how to enter if you had mild diarrhoea that lasted for 3 days and is still present.

Symptom	Yes	Mild	Moderate	Severe	Total days	Still present
e.g. Diarrhoea	✓	✓			03	✓
Diarrhoea (loose watery motions)						
Blood in motions						
Nausea (feeling sick)						
Vomiting (being sick)						
Abdominal (tummy) pain						
Loss of appetite						
High temperature (shivering/ sweating)						
Cough, runny/ blocked nose, sore throat						
Headache						
Aching muscles						
Joint pains/ stiffness						
Back or neck pain/stiffness						
Joint swelling						
Painful red eyes						
Dizziness/ faintness						
Other						

If "Other", ***please specify***: .....

MRC use only

2.6 If you answered "**Yes**" to diarrhoea in ***Question 2.5***, what was the greatest number of times you went to the lavatory with diarrhoea in any 24-hour period?

Number of times ☐☐ Not sure ☐ ☐☐

2.7 If you answered "**Yes**" to vomiting in ***Question 2.5***, what was the greatest number of times you vomited (were sick) in any 24-hour period?

Number of times ☐☐ Not sure ☐ ☐☐

2.8 If you answered "**Yes**" to joint swelling in ***Question 2.5***, which of your joints were swollen? ***(e.g. left knee, both knees, etc.)***

..... Not sure ☐ ☐☐

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH A SIMILAR ILLNESS

3.1 How many different people ***(excluding you)*** lived or spent a night in your household ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***? ..... people ☐

Please fill in the following details for all of these people, EXCLUDING YOURSELF: their age and sex, whether they are a permanent member of the household or a visitor, and whether they were ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED.

The example on how to enter is for a female member of the household aged 43, who was ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure
	43	F	✓		✓		
Person 1:							
Person 2:							
Person 3:							
Person 4:							
Person 5:							
Person 6:							
Person 7:							
Person 8:							

MRC use only

3.2 Were you the first person in the household to be ill? Yes ☐ No ☐ Not sure ☐

If "No", please give the **PERSON NUMBER** ***(from Question 3.1)*** of the first person to be ill: Person .....

3.3 Did you have contact ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", how many people? .....

3.4 If "**Yes**" to ***Question 3.3***, where did this contact occur? ***(tick all boxes that apply)***

Pre-school child group ***(e.g. nursery, toddlers group)*** ☐ School ☐

Workplace ☐ Social occasion ***(e.g. friend's house, meal out)*** ☐

Other ☐

If "Other", ***please specify***: .....

SECTION 4 THIS SECTION ASKS ABOUT YOUR TRAVEL AND LEISURE ACTIVITY IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED

4.1 During this time, did you spend one or more nights away from home? ***(exclude shift work)***

Yes ☐ ↓ No ☐ → If "**No**", please go to **QUESTION 4.6**

If "**Yes**", please continue:

4.2 Were you away?: On holiday ☐ On business ☐ Other ☐

4.3 Were you staying?: In the UK ☐ Abroad ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: .....

MRC use only

4.4 What was the main resort/town stayed at? .....

4.5 Where did you **EAT** most of your meals? ***(tick one box)***

Hotel/guest house ☐ Self-catering in an apartment, villa, etc. ☐

Camping ☐ Restaurant, café, etc. ☐

Private house ☐ Other ☐

If "Other", ***please specify***: .....

4.6 Did you go swimming or join in water sports ***(e.g. sailing, water skiing)*** in the UK or abroad?

Yes ☐ ↓ No ☐ → If "**No**", please go to **SECTION 5**

If "**Yes**", ***please specify*** type(s) of activity: .....

.....

.....

4.7 Where did this activity take place? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

If "Other", ***please specify***: .....

4.8 Did you swallow any water in any of the following? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

If "Other", ***please specify***: .....

MRC use only

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ No ☐ → If "No", please go to **QUESTION 5.6** ☐

If "**Yes**", ***please indicate*** which pet(s) ***(tick all boxes that apply)***

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐☐

If "Other", ***please specify***: .....

5.2 Did you clean up any pet's motions (mess) or clean out the cage/ aquarium/litter tray, etc. of any of your pets ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which pet(s): ..... ☐☐

5.3 Did any of your pets, where relevant, have diarrhoea ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which pet(s): ..... ☐☐

5.4 Do you feed your pet(s) with any of the following?: ***(tick all that apply)***

Raw meat/fish	☐	☐
Cooked meat/fish from a shop	☐	☐
Meat/fish cooked at home	☐	☐
Canned meat/fish	☐	☐

MRC use only

5.5 If you have a cat or dog, where do you normally feed it? ***(please tick one box)***

In the kitchen (on the floor)	☐
In the kitchen (on a worktop/table)	☐
Outside	☐
Other	☐

If "Other", ***please specify***: ..... ☐☐

5.6 Were you in close contact with any other animals ***(e.g. zoo, farm, other people's pets) IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which animal(s): ..... ☐☐

..... ☐

Please specify where ***(e.g. zoo, farm, etc.)***: ..... ☐

SECTION 6 THIS SECTION ASKS ABOUT YOUR FOOD AND WATER CONSUMPTION

6.1 Did you eat ***ANY OF THE FOLLOWING FOODS IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

Meat:	Yes	Not sure	
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc.)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE 10 DAYS BEFORE YOU WERE ILL*** did you eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐ ☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐ ☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Meals-on-wheels	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

MRC use only

The following questions ask for more details about particular foods.

6.3 If you ate chicken ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, was this?: ***(tick all boxes that apply)***

- Bought raw fresh, cooked and eaten at home
- Bought raw frozen, cooked and eaten at home
- Pre-cooked, eaten at home hot (include ready-made dinners)
- Pre-cooked, eaten at home cold
- In a hot or cold take-away meal (include sandwiches)
- In a hot or cold meal not at home (e.g. restaurant/canteen)
- Barbecued chicken

6.4 How many times **IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED** did you eat chicken? ***(tick one box)***

Never ☐ Once ☐ More than once ☐ ---> how many times? .....

6.5 ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, did you **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐

6.6 If you bought chicken, was this?: ***(tick all that apply)***

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐

6.7 If you ate cold, shop-sliced meats ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, where were they bought? ***(tick all that apply)***

	Butcher	Delicatessen	Supermarket	Other shop
Pork/ham	☐	☐	☐	☐
Chicken/turkey	☐	☐	☐	☐
Beef	☐	☐	☐	☐
Corned beef	☐	☐	☐	☐
Tongue	☐	☐	☐	☐
Other	☐	☐	☐	☐

If "Other", ***(please specify)***: .....

MRC use only

6.8 Did you eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

6.9 Did you eat any of the following milk and dairy products ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***? ***(tick all that apply)***

	Pasteurised	Unpasteurised	Not sure if pasteurised
Goats'/sheep's milk	☐	☐	☐
Soft cheese	☐	☐	☐
Fromage frais	☐	☐	☐
Yoghurt	☐	☐	☐
Ice cream	☐	☐	☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐

6.10 Are you a vegetarian?

- No
- Partial vegetarian (don't eat meat, but eat fish)
- Strict vegetarian (don't eat meat or fish)
- Vegan (don't eat meat, fish or dairy products)

6.11 Did you take any antibiotics prescribed by your doctor ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

6.12 Did you take indigestion medicines, bought over the counter or prescribed by your doctor, ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

MRC use only

6.13 Did you take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by your doctor, ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

Drinking cold water

6.14 ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, how many glasses (a glass holds about ¼ pint) of the following types of **UNBOILED WATER** did you drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE, LEAVE BLANK)

	Approximate number of glasses per day	
	In the UK	Abroad
Mains water	☐☐	☐☐
Bottled water: fizzy, sparkling	☐☐	☐☐
Bottled water: still	☐☐	☐☐
Non-mains water (e.g. borehole, well, spring)	☐☐	☐☐
Water dispenser	☐☐	☐☐

6.15 During this period did you have any ice in drinks?

In the UK: Yes ☐ No ☐

Abroad: Yes ☐ No ☐

6.16 Do you filter your water? Yes ☐ No ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐

MRC use only

SECTION 7 **THIS SECTION ASKS FOR SOME BASIC INFORMATION ABOUT YOU, i.e. THE PERSON WHO WAS ILL AND WHO IS NAMED IN THE ACCOMPANYING LETTER**

7.1 Current marital status:

Married ***(or living as)*** ☐ Single ***(never married)*** ☐

Divorced, separated ☐ Widowed ☐ ☐

7.2 Current paid employment status ***(tick one box)***:

Working full-time ***(30 or more hours per week)*** ☐

Working part-time ***(under 30 hours per week)*** ☐

Unemployed, seeking work ☐

Waiting to start a job ☐

Out of work due to temporary sickness ☐

Unable to work because of permanent disability or illness ☐

Retired from paid work ☐

Full-time student ☐

Not seeking work ***(e.g. caring for home or family)*** ☐

Other ☐ ☐☐

If "Other", ***please specify***: .....

.....

7.3 What is your occupation? ***(if unemployed, what was your most recent occupation; if retired, what was your main occupation?)*** ☐

Job title: .....

What do/did you actually do?: ☐☐☐

.....

In which industry/business is this?: .....

7.4 What is/was your position? ***(tick one box)***

Manager ☐ Supervisor or foreman ☐

Self-employed ☐ Employee ***(i.e. none of the above)*** ☐

MRC use only

7.5 If you are unemployed, how long is it since you were in paid employment?
Under 12 months ☐
12 months or over ☐

7.6 How old were you when you first left full-time education *(school, college, university)*? *(tick one box)*

Under 16 years ☐ 16 years ☐ 17 years ☐
18 years ☐ 19 years or over ☐ Still in full-time education ☐

7.7 To which ethnic group do you consider that you belong? *(tick one box)*

White (UK) ☐ White (other) ☐
Black (Caribbean) ☐ Black (African) ☐
Black (other) ☐ Indian ☐
Pakistani ☐ Bangladeshi ☐
Chinese ☐ Other ☐

If "Other", *please specify*: .....

7.8 What is the occupation of your spouse, or partner if applicable? *(If unemployed, what was his/her most recent occupation; if retired, what was his/her main occupation?)*

Job title: .....

What does/did he/she actually do?: .....

.....

In which industry/business is this?: .....

7.9 What is/was his/her position? *(tick one box)*

Manager ☐ Supervisor or foreman ☐
Self-employed ☐ Employee *(i.e. none of the above)* ☐

MRC use only

SECTION 8 THIS SECTION ASKS ABOUT THE DETAILS OF YOUR HOUSEHOLD'S ACCOMMODATION

8.1 Please state the type of accommodation in which you live:

Detached/semi-detached *(including bungalow)* ☐
Terraced *(including end of terrace)* ☐
Purpose-built flat/ maisonette in a block ☐
Self-contained flat in a converted house ☐
Rooms in a converted house, not self-contained ☐
Caravan/houseboat/mobile home ☐
Institutional home *(e.g. nursing home, boarding school, etc.)* ☐
Other ☐

If "other", *please specify*: .....

8.2 Does any other household share the bathroom and/or WC with you? Yes ☐ No ☐

8.3 Does any other household share the kitchen with you? Yes ☐ No ☐

8.4 Is the accommodation?:

Owned/mortgaged by you or your family ☐
Rented from a private landlord ☐
Rented from a council, new town, housing association or charitable trust ☐
Other ☐

If "other", *please specify*: .....

8.5 How many rooms does your household have? *(exclude WC/toilet, hall and landing)* ..... rooms

SECTION 9 This section asks about your kitchen and food shopping and preparation in your household. Please ask THE PERSON WHO USUALLY HAS THE MAIN RESPONSIBILITY FOR FOOD SHOPPING AND PREPARATION in your household to complete this section.

Your kitchen:

9.1 What is the narrowest width of your kitchen? *(tick one box only)* (1 metre is about 3 feet)

Less than 2 metres ☐ 2-3 metres ☐
More than 3 metres ☐ Not sure ☐

MRC use only

9.2 What is the total length of work surface you can use when preparing food? ***(tick one box only)***

Less than 1 metre ☐ 1-2 metres ☐
More than 2 metres ☐ Not sure ☐

9.3 Does your household have regular use of the following?: ***(tick all boxes that apply)***

Fridge ☐ Freezer (include fridge/freezer) ☐
Microwave oven ☐ Slow cooker ☐
Gas/electric cooker ☐ Dishwasher ☐
Food mixer/blender ☐ Combi-oven ☐

9.4 Do you use a thermometer to check the storage temperature of your fridge? Yes ☐ No ☐

If "**Yes**", what is the temperature now? .... °C

9.5 Do you use a food thermometer to check the cooking temperature of food in the oven? Yes ☐ No ☐

9.6 Do you have a baby still in nappies? Yes ☐ No ☐

If "**No**", please go to **QUESTION 9.7**

If "**Yes**", do you ever use cloth nappies? Yes ☐ No ☐

If "**Yes**", where do you **USUALLY** soak/wash soiled nappies? ***(tick one box)***

Bucket in kitchen ☐ Bucket in bathroom ☐
Sink in kitchen ☐ Sink in bathroom ☐
Bucket outside ☐ Other ☐

If "Other", ***please specify***: .....

Your usual food shopping procedures:

9.7 How often is your household's main food shopping done? ***(tick one box only)***

More than once a week ☐ Once a week ☐ Once a fortnight ☐
Once a month ☐ Less often ☐ Not sure ☐

MRC use only

9.8 If you normally do the shopping, how do the following statements apply to you? ***(tick one box for each statement)***

	Always	Sometimes	Never	Not sure
I check the "Use by" or "Best before" date	☐	☐	☐	☐
I follow the storage instructions	☐	☐	☐	☐
I check the packaging for damage when shopping	☐	☐	☐	☐
I pack frozen foods together in a cool container for transport	☐	☐	☐	☐
I check the appearance of the product when shopping	☐	☐	☐	☐

9.9 How much time usually passes between buying frozen or chilled items and putting them in the fridge or freezer? ***(tick one box only)***

Up to 1 hour ☐ Up to 2 hours ☐
Up to 3 hours ☐ More than 3 hours ☐

9.10 Where do you usually store the following items in your fridge? ***(tick a box for each item)***

	Top/middle shelf	Bottom shelf	Salad drawer	In the door	Wherever there is room	N/A*
Raw meat	☐	☐	☐	☐	☐	☐
Unwashed raw salad	☐	☐	☐	☐	☐	☐
Cooked food	☐	☐	☐	☐	☐	☐
Sandwiches	☐	☐	☐	☐	☐	☐

* N/A = not applicable

Your usual food practices:

9.11 Where would you normally defrost a frozen chicken? ***(tick one box only)***

In the fridge ☐ On kitchen work surface ☐
In the microwave ☐ In the oven ☐
In a bowl of warm water ☐ In a bowl of cold water ☐
In the kitchen sink ☐ Other ***(please specify)***: ☐
Not applicable ☐

.....

9.12 How long would you thaw an average sized (3lb) chicken by this method? .... hours Not applicable ☐

MRC use only

9.13 Do you use separate chopping boards for raw meats and cooked meats? Yes ☐ No ☐ Not sure ☐ ☐

9.14 Do you use separate chopping boards for other raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.15 Do you clean your chopping board between use for raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.16 What material is your main chopping board made from? ***(please tick one box)***

Wood ☐ Plastic ☐ Other ***(please specify)*** ☐ ☐☐

.....

9.17 Do you use the same cloth for wiping all surfaces in your kitchen? Yes ☐ No ☐ Not sure ☐ ☐

9.18 Where do you normally cool foods or leftovers to be eaten later (reheated or cold)? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐☐

9.19 Where do you normally store leftovers or foods prepared for eating later? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐☐

9.20 How do you usually reheat leftovers or foods prepared in the home? ***(tick any that apply)***

In a normal oven ☐ In a microwave oven ☐

In a saucepan on the hob ☐ Other ☐

Not sure ☐

If "Other", ***please describe***: ..... ☐☐

MRC use only

9.21 Please indicate whether you think the following list of statements is true or false ***(tick one box for each statement)***:

	Agree	Disagree	Don't know	
Food poisoning is caused by germs	☐	☐	☐	☐
Pets should not be allowed on kitchen work tops	☐	☐	☐	☐
Food poisoning germs are killed by proper cooking	☐	☐	☐	☐
Most germs do not grow in a fridge	☐	☐	☐	☐
The drip (blood, etc.) from raw meat and chicken can contain germs	☐	☐	☐	☐
It doesn't matter how long food is kept as long as it is stored cold	☐	☐	☐	☐
It doesn't matter whether you wash your hands or not before handling food	☐	☐	☐	☐
Contaminated food always looks or smells bad	☐	☐	☐	☐
Once a food is cooked and cooled it can be kept for a day at room temperature before it is eaten	☐	☐	☐	☐
One food can contaminate another by touching it	☐	☐	☐	☐

SECTION 10 Finally, what do you think was responsible for your illness? ***(please give details below)***:

.....

.....

..... ☐☐☐

.....

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q1.2

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

PLEASE ENTER STUDY NUMBER.

PLEASE READ THIS PAGE FIRST

Dear Parent/Guardian,

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this study following your child's recent episode of gastroenteritis. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

SECTION 1 THIS SECTION CONFIRMS DETAILS OF THE AGE AND SEX OF THE CHILD WHO WAS ILL AND WHO IS NAMED IN THE ACCOMPANYING LETTER

Please state:

1.1 Today's date: ...../...../.....
day month year

1.2 Your child's date of birth: ...../...../.....
day month year

1.3 Your child's sex: Male ☐ Female ☐

SECTION 2 THIS SECTION ASKS ABOUT THE SYMPTOMS YOUR CHILD EXPERIENCED DURING HIS/HER ILLNESS

2.1 On what date did your child's symptoms start? ...../...../.....
day month year

2.2 On what date did he/she first see your GP about these symptoms? ...../...../.....
day month year

2.3 Did your child's illness incapacitate him/her? ***(i.e. prevent him/her going about his/her normal daily activities)***

Yes ☐ No ☐ Not sure ☐

2.4 Does your child suffer from any long-standing illness or disability?

Yes ☐ No ☐

If "**Yes**", ***please specify***: .....
.....
.....
.....

MRC use only

2.5 Did your child have any of the following symptoms?

If **"YES"**, in your opinion how severe were they and how many days did they last?

(tick ALL appropriate boxes or LEAVE BLANK IF HE/SHE DID NOT HAVE THE SYMPTOM, OR YOU ARE UNSURE)

An EXAMPLE is given on how to enter if your child had mild diarrhoea that lasted for 3 days and is still present.

Symptom	Yes	Mild	Moderate	Severe	Total days	Still present
e.g. Diarrhoea	✓	✓			0 3	✓
Diarrhoea (loose watery motions)						
Blood in motions						
Nausea (feeling sick)						
Vomiting (being sick)						
Abdominal (tummy) pain						
Loss of appetite						
High temperature (shivering/ sweating)						
Cough, runny/ blocked nose, sore throat						
Headache						
Aching muscles						
Joint pains/ stiffness/ limping						
Back or neck pain/stiffness						
Joint swelling						
Painful red eyes						
Dizziness/ faintness						
Other						

If "Other", ***please specify***: .....

MRC use only

2.6 If you answered **"Yes"** to diarrhoea in ***Question 2.5***, what was the greatest number of times your child went to the lavatory with diarrhoea in any 24-hour period?

Number of times ☐☐ Not sure ☐

2.7 If you answered **"Yes"** to vomiting in ***Question 2.5***, what was the greatest number of times he/she vomited (was sick) in any 24-hour period?

Number of times ☐☐ Not sure ☐

2.8 If you answered **"Yes"** to joint swelling in ***Question 2.5***, which of your child's joints were swollen?
(e.g. left knee, both knees, etc.)

..... Not sure ☐

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH A SIMILAR ILLNESS

3.1 How many different people ***(excluding the child who was ill)*** lived or spent a night in your household ***IN THE 10 DAYS BEFORE THIS CHILD'S ILLNESS STARTED***? ..... people

Please fill in the following details for all of these people, EXCLUDING THE SICK CHILD: their age and sex, whether they are a permanent member of the household or a visitor, and whether they were ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED.

The example on how to enter is for a female member of the household aged 43, who was ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE YOUR CHILD'S ILLNESS STARTED.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure
	43	F	✓		✓		
Person 1:							
Person 2:							
Person 3:							
Person 4:							
Person 5:							
Person 6:							
Person 7:							
Person 8:							

MRC use only

3.2 Was the sick child the first person in the household to be ill? Yes ☐ No ☐ Not sure ☐ ☐

If "**No**", please give the **PERSON NUMBER** ***(from Question 3.1)*** of the first person to be ill: Person ..... ☐☐

3.3 Did your child have contact ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", how many people? ..... ☐☐

3.4 If "**Yes**" to ***Question 3.3***, where did this contact occur? ***(tick all boxes that apply)***

Pre-school child group ***(e.g. nursery, toddlers group)*** ☐ School ☐

Social occasion ***(e.g. friend's house, meal out)*** ☐ *Other* ☐

*If "Other", **please specify**:* ..... ☐☐

SECTION 4 THIS SECTION CONCERNS YOUR CHILD'S TRAVEL AND LEISURE ACTIVITY IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED

4.1 During this time, did your child spend one or more nights away from home?

Yes ☐ ↓ No ☐ → If "**No**", please go to **QUESTION 4.6** ☐

If "**Yes**", please continue:

4.2 Was he/she away?: On holiday ☐ Other ☐ ☐

4.3 Was he/she staying?: In the UK ☐ Abroad ☐ ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: ..... ☐☐

MRC use only

4.4 What was the main resort/town stayed at? ..... ☐☐

4.5 Where did your child **EAT** most of his/her meals? ***(tick one box)***

Hotel/guest house ☐ Self-catering in an apartment, villa, etc. ☐

Camping ☐ Restaurant, café, etc. ☐

Private house ☐ Other ☐ ☐

If "Other", ***please specify***: .....

4.6 Did your child go swimming or join in water sports ***(e.g. sailing, water skiing)*** in the UK or abroad?

Yes ☐ ↓ No ☐ → If "**No**", please go to **SECTION 5** ☐

If "**Yes**", ***please specify*** type(s) of activity: .....

..... ☐☐

.....

4.7 Where did this activity take place? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other	
UK	☐	☐	☐	☐	☐	
Abroad	☐	☐	☐	☐	☐	☐☐

If "Other", ***please specify***: .....

4.8 Did he/she swallow any water in any of the following? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other	
UK	☐	☐	☐	☐	☐	
Abroad	☐	☐	☐	☐	☐	☐☐

If "Other", ***please specify***: .....

MRC use only

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND YOUR CHILD'S CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ No ☐ → If "No", please go to **QUESTION 5.6** ☐

If "**Yes**", ***please indicate*** which pet(s) ***(tick all boxes that apply)***

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐☐

If "Other", ***please specify***: .....

5.2 Did your child clean up any pet's motions (mess) or clean out the cage/aquarium/litter tray, etc. of any of your pets ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which pet(s): ..... ☐☐

5.3 Did any of your pets, where relevant, have diarrhoea ***IN THE 10 DAYS BEFORE YOUR CHILD'S ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which pet(s): ..... ☐☐

5.4 Do you feed your pet(s) with any of the following?: ***(tick all that apply)***

Raw meat/fish	☐	☐
Cooked meat/fish from a shop	☐	☐
Meat/fish cooked at home	☐	☐
Canned meat/fish	☐	☐

MRC use only

5.5 If you have a cat or dog, where is it normally fed? ***(please tick one box)***

In the kitchen (on the floor)	☐
In the kitchen (on a worktop/table)	☐
Outside	☐
Other	☐

If "Other", ***please specify***: ..... ☐☐

5.6 Was the sick child in close contact with any other animals ***(e.g. zoo, farm, other people's pets) IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which animal(s): ..... ☐☐

..... ☐

Please specify where ***(e.g. zoo, farm, etc.)***: .....

SECTION 6 THIS SECTION ASKS ABOUT YOUR CHILD'S FOOD AND WATER CONSUMPTION

6.1 Did your child eat ***ANY OF THE FOLLOWING FOODS IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

	Yes	Not sure	
Meat:			
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc.)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE 10 DAYS BEFORE YOUR CHILD WAS ILL*** did he/she eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐ ☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐ ☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Meals-on-wheels	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

MRC use only

The following questions ask for more details about particular foods.

6.3 If your child ate chicken ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***, was this?: ***(tick all boxes that apply)***

- Bought raw fresh, cooked and eaten at home
- Bought raw frozen, cooked and eaten at home
- Pre-cooked, eaten at home hot (include ready-made dinners)
- Pre-cooked, eaten at home cold
- In a hot or cold take-away meal (include sandwiches)
- In a hot or cold meal not at home (e.g. restaurant/canteen)
- Barbecued chicken

6.4 How many times **IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED** did your child eat chicken? ***(tick one box)***

Never ☐ Once ☐ More than once ☐ ---> how many times? .....

6.5 ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***, did he/she help **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐

6.6 If you bought chicken, was this?: ***(tick all that apply)***

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐

6.7 If your child ate cold, shop-sliced meats ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***, where were they bought? ***(tick all that apply)***

	Butcher	Delicatessen	Supermarket	Other shop
Pork/ham	☐	☐	☐	☐
Chicken/turkey	☐	☐	☐	☐
Beef	☐	☐	☐	☐
Corned beef	☐	☐	☐	☐
Tongue	☐	☐	☐	☐
Other	☐	☐	☐	☐

If "Other", ***(please specify)***: .....

MRC use only

6.8 Did your child eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

6.9 Did he/she eat any of the following milk and dairy products ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***? ***(tick all that apply)***

	Pasteurised	Unpasteurised	Not sure if pasteurised
Goats'/sheep's milk	☐	☐	☐
Soft cheese	☐	☐	☐
Fromage frais	☐	☐	☐
Yoghurt	☐	☐	☐
Ice cream	☐	☐	☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐

6.10 Are you and the child who was ill vegetarians?

	You	Your child
No	☐	☐
Partial vegetarian (don't eat meat, but eat fish)	☐	☐
Strict vegetarian (don't eat meat or fish)	☐	☐
Vegan (don't eat meat, fish or dairy products)	☐	☐

6.11 Did your child take any antibiotics prescribed by a doctor ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

6.12 Did he/she take indigestion medicines, bought over the counter or prescribed by a doctor, ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

MRC use only

6.13 Did your child take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by a doctor, ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

Drinking cold water

6.14 ***IN THE 10 DAYS BEFORE YOUR CHILD'S ILLNESS STARTED***, how many glasses (a glass holds about ¼ pint) of the following types of **UNBOILED WATER** did he/she drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE OR UNSURE FOR ANY TYPE OF WATER, LEAVE BLANK)

	Approximate number of glasses per day	
	In the UK	Abroad
Mains water	☐☐	☐☐
Bottled water: fizzy, sparkling	☐☐	☐☐
Bottled water: still	☐☐	☐☐
Non-mains water (e.g. borehole, well, spring)	☐☐	☐☐
Water dispenser	☐☐	☐☐

6.15 During this period did he/she have any ice in drinks?

In the UK: Yes ☐ No ☐

Abroad: Yes ☐ No ☐

6.16 Do you filter your water? Yes ☐ No ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐

MRC use only

Is your child less than 1 year old?

Yes ☐ No ☐ → If "**No**", please go to **SECTION 7**

If "**Yes**", please continue:

6.17 How is your baby currently being fed milk? ***(please tick one box)***

Breast feed only ☐ Mixed breast/bottle feed ☐

Bottle feed only ☐ Other ☐

6.18 Have you started weaning your baby onto solids?

Yes ☐ No ☐

6.19 If not currently breast feeding, has your baby ever been breast fed?

Yes ☐ No ☐

If "**Yes**", how old (in months) was your baby when this was stopped? ☐☐

6.20 If your baby is being bottle fed, how do you sterilise the bottles/teats, etc.?

Cold water with chemicals ☐ Boiling water ☐

Steam ☐ Other ☐

If "Other", ***please specify***: .....

6.21 If your baby is being bottle fed, do you usually boil water to make the feed?

Yes ☐ No ☐

MRC use only

6.22 How do you store the baby's bottled milk before feeding?

In the fridge ☐
At room temperature ☐
Other ☐

If "Other", ***please specify***: .....

6.23 Do you give your baby water to drink? Yes ☐ No ☐

If "**Yes**", is it boiled first? Yes ☐ No ☐

SECTION 7 **THIS SECTION ASKS FOR SOME BASIC INFORMATION ABOUT YOUR CHILD, WHO IS NAMED IN THE ACCOMPANYING LETTER, AND OTHER MEMBERS OF YOUR HOUSEHOLD**

7.1 Does your child attend any of the following?:
(tick any boxes that apply)

Day nursery/creche ☐
Toddlers play group ☐
Child minder ☐
Nursery school or class ☐
Local Authority school ☐
Private school ☐
Other ☐

If "Other", ***please specify***: .....

7.2 To which ethnic group do you consider that your child belongs?
(tick one box)

White (UK) ☐
Black (Caribbean) ☐
Black (other) ☐
Pakistani ☐
Chinese ☐
White (other) ☐
Black (African) ☐
Indian ☐
Bangladeshi ☐
Other ☐

If "Other", ***please specify***: .....

MRC use only

The following questions ask about the main wage earner in your household. If there is more than one wage earner, please enter one person's details.

7.3 What is the occupation of the main wage earner in the household?
(If currently unemployed, what was his/her most recent occupation; if retired, what was his/her main occupation?)

Job title: .....

What does/did he/she actually do?: .....

.....

In which industry/business is this?: .....

7.4 What is/was the main wage earner's position? ***(tick one box)***

Manager ☐
Self-employed ☐
Supervisor or foreman ☐
Employee ***(i.e. none of the above)*** ☐

7.5 What is the current marital status of the main wage earner?

Married ***(or living as)*** ☐
Divorced, separated ☐
Single ***(never married)*** ☐
Widowed ☐

7.6 How old was the main wage earner when he/she first left full-time education ***(school, college, university)***? ***(tick one box)***

Under 16 years ☐
16 years ☐
17 years ☐
18 years ☐
19 years or over ☐
Still in full-time education ☐

MRC use only

SECTION 8 THIS SECTION ASKS ABOUT THE DETAILS OF YOUR HOUSEHOLD'S ACCOMMODATION

8.1 Please state the type of accommodation in which you live:

- Detached/semi-detached *(including bungalow)*
- Terraced *(including end of terrace)*
- Purpose-built flat/ maisonette in a block
- Self-contained flat in a converted house
- Rooms in a converted house, not self-contained
- Caravan/houseboat/mobile home
- Institutional home *(e.g. nursing home, boarding school, etc.)*
- Other

If "other", ***please specify***: .....

8.2 Does any other household share the bathroom and/or WC with you? Yes / No

8.3 Does any other household share the kitchen with you? Yes / No

8.4 Is the accommodation?:

- Owned/mortgaged by you or your family
- Rented from a private landlord
- Rented from a council, new town, housing association or charitable trust
- Other

If "other", ***please specify***: .....

8.5 How many rooms does your household have? *(exclude WC/toilet, hall and landing)* ..... rooms

SECTION 9 This section asks about your kitchen and food shopping and preparation in your household. Please ask THE PERSON WHO USUALLY HAS THE MAIN RESPONSIBILITY FOR FOOD SHOPPING AND PREPARATION in your household to complete this section.

Your kitchen:

9.1 What is the narrowest width of your kitchen? *(tick one box only)* (1 metre is about 3 feet)

- Less than 2 metres
- 2-3 metres
- More than 3 metres
- Not sure

MRC use only

9.2 What is the total length of work surface you can use when preparing food? *(tick one box only)*

- Less than 1 metre
- 1-2 metres
- More than 2 metres
- Not sure

9.3 Does your household have regular use of the following?: *(tick all boxes that apply)*

- Fridge
- Freezer (include fridge/ freezer)
- Microwave oven
- Slow cooker
- Gas/electric cooker
- Dishwasher
- Food mixer/blender
- Combi-oven

9.4 Do you use a thermometer to check the storage temperature of your fridge? Yes / No

If "**Yes**", what is the temperature now? .... °C

9.5 Do you use a food thermometer to check the cooking temperature of food in the oven? Yes / No

9.6 Do you have a baby still in nappies? Yes / No

If "**No**", please go to **QUESTION 9.7**

If "**Yes**", do you ever use cloth nappies? Yes / No

If "**Yes**", where do you **USUALLY** soak/wash soiled nappies? *(tick one box)*

- Bucket in kitchen
- Sink in kitchen
- Bucket outside
- Bucket in bathroom
- Sink in bathroom
- Other

If "Other", ***please specify***: .....

Your usual food shopping procedures:

9.7 How often is your household's main food shopping done? *(tick one box only)*

- More than once a week
- Once a week
- Once a fortnight
- Once a month
- Less often
- Not sure

MRC use only

9.8 If you normally do the shopping, how do the following statements apply to you? ***(tick one box for each statement)***

	Always	Sometimes	Never	Not sure	
I check the "Use by" or "Best before" date	☐	☐	☐	☐	☐
I follow the storage instructions	☐	☐	☐	☐	☐
I check the packaging for damage when shopping	☐	☐	☐	☐	☐
I pack frozen foods together in a cool container for transport	☐	☐	☐	☐	☐
I check the appearance of the product when shopping	☐	☐	☐	☐	☐

9.9 How much time usually passes between buying frozen or chilled items and putting them in the fridge or freezer? ***(tick one box only)***

Up to 1 hour ☐ Up to 2 hours ☐

Up to 3 hours ☐ More than 3 hours ☐ ☐

9.10 Where do you usually store the following items in your fridge? ***(tick a box for each item)***

	Top/middle shelf	Bottom shelf	Salad drawer	In the door	Wherever there is room	N/A*	
Raw meat	☐	☐	☐	☐	☐	☐	☐
Unwashed raw salad	☐	☐	☐	☐	☐	☐	☐
Cooked food	☐	☐	☐	☐	☐	☐	☐
Sandwiches	☐	☐	☐	☐	☐	☐	☐

* N/A = not applicable

Your usual food practices:

9.11 Where would you normally defrost a frozen chicken? ***(tick one box only)***

In the fridge ☐ On kitchen work surface ☐

In the microwave ☐ In the oven ☐

In a bowl of warm water ☐ In a bowl of cold water ☐

In the kitchen sink ☐ Other ***(please specify)***: ☐ ☐

Not applicable ☐ .....

9.12 How long would you thaw an average sized (3lb) chicken by this method? .... hours Not applicable ☐ ☐ ☐

MRC use only

9.13 Do you use separate chopping boards for raw meats and cooked meats? Yes ☐ No ☐ Not sure ☐ ☐

9.14 Do you use separate chopping boards for other raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.15 Do you clean your chopping board between use for raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.16 What material is your main chopping board made from? ***(please tick one box)***

Wood ☐ Plastic ☐ Other ***(please specify)*** ☐ ☐ ☐

.....

9.17 Do you use the same cloth for wiping all surfaces in your kitchen? Yes ☐ No ☐ Not sure ☐ ☐

9.18 Where do you normally cool foods or leftovers to be eaten later (reheated or cold)? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.19 Where do you normally store leftovers or foods prepared for eating later? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.20 How do you usually reheat leftovers or foods prepared in the home? ***(tick any that apply)***

In a normal oven ☐ In a microwave oven ☐

In a saucepan on the hob ☐ Other ☐

Not sure ☐

If "Other", ***please describe***: ..... ☐ ☐

MRC use only

9.21 Please indicate whether you think the following list of statements is true or false *(**tick one box for each statement**)*:

	Agree	Disagree	Don't know	
Food poisoning is caused by germs	☐	☐	☐	☐
Pets should not be allowed on kitchen work tops	☐	☐	☐	☐
Food poisoning germs are killed by proper cooking	☐	☐	☐	☐
Most germs do not grow in a fridge	☐	☐	☐	☐
The drip (blood, etc.) from raw meat and chicken can contain germs	☐	☐	☐	☐
It doesn't matter how long food is kept as long as it is stored cold	☐	☐	☐	☐
It doesn't matter whether you wash your hands or not before handling food	☐	☐	☐	☐
Contaminated food always looks or smells bad	☐	☐	☐	☐
Once a food is cooked and cooled it can be kept for a day at room temperature before it is eaten	☐	☐	☐	☐
One food can contaminate another by touching it	☐	☐	☐	☐

SECTION 10 **Finally, what do you think was responsible for your child's illness?** *(please give details below)*:

.....

.....

..... ☐☐☐

.....

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q1.4

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

PLEASE ENTER STUDY NUMBER.

PLEASE READ THIS PAGE FIRST

Dear Parent/Guardian,

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing for your child to participate in this study as a control for comparison. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

SECTION 1 THIS SECTION CONFIRMS DETAILS OF THE AGE AND SEX OF THE CHILD ACTING AS A CONTROL AND WHO IS NAMED IN THE ACCOMPANYING LETTER

Please state:

1.1 Today's date: ...../...../.....
day month year

1.2 Your child's date of birth: ...../...../.....
day month year

1.3 Your child's sex: Male ☐ Female ☐

SECTION 2 THIS SECTION ASKS ABOUT ANY SYMPTOMS YOUR CHILD MAY HAVE EXPERIENCED RECENTLY

2.1 *IN THE LAST 10 DAYS*, did your child have any diarrhoea or vomiting?

Yes ☐ No ☐

If "Yes", you do not need to complete any more questions. Please return the questionnaire in the stamped, addressed envelope provided.

If "**No**", please continue:

2.2 Does your child suffer from any long-standing illness or disability?

Yes ☐ No ☐

If "**Yes**", ***please specify***: .....
.....
.....
.....

MRC use only

2.3 ***DURING THE LAST 3 WEEKS*** has your child had any of the symptoms listed below? ***(tick all boxes that apply)***

Diarrhoea	☐	Headaches	☐	☐	☐
Blood in motions	☐	Dizzy spells	☐	☐	☐
Vomiting	☐	Seeing double	☐	☐	☐
Abdominal (tummy) pain	☐	Clumsiness of hands (dropping things)	☐	☐	☐
Loss of appetite	☐	Unsteady walking (falling over)	☐	☐	☐
Loss of weight	☐	Pins and needles	☐	☐	☐
Excessive flatulence (breaking wind)	☐	Weakness of hands (difficulty gripping things)	☐	☐	☐
Discomfort in passing urine	☐	Weakness of legs (e.g. difficulty walking or rising)	☐	☐	☐
Cough/runny nose/ sore throat	☐	Faintness or fits	☐	☐	☐
Joint pains/stiffness limping	☐	Feeling tired	☐	☐	☐
Joint swelling	☐	Painful red eye(s)	☐	☐	☐
Back or neck pain/ stiffness	☐	Greater desire to sleep	☐	☐	☐
Aching muscles	☐	Skin rash	☐	☐	☐
Pain in heels	☐	Other	☐	☐	☐

If "Other", ***please specify***: .....

MRC use only

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH A SIMILAR ILLNESS

3.1 How many different people ***(excluding the child named in the accompanying letter)*** lived or spent a night in your household ***IN THE LAST 10 DAYS*** ?

..... *people* ☐

Please fill in the following details for all of these people, EXCLUDING THE CHILD CONCERNED: their age and sex, whether they are a permanent member of the household or a visitor, and whether they were ill with diarrhoea or vomiting IN THE LAST 10 DAYS.

The example on how to enter is for a female member of the household aged 43, who was ill with diarrhoea or vomiting IN THE LAST 10 DAYS.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure
	43	F	✓		✓		
Person 1:	☐	☐	☐	☐	☐	☐	☐
Person 2:	☐	☐	☐	☐	☐	☐	☐
Person 3:	☐	☐	☐	☐	☐	☐	☐
Person 4:	☐	☐	☐	☐	☐	☐	☐
Person 5:	☐	☐	☐	☐	☐	☐	☐
Person 6:	☐	☐	☐	☐	☐	☐	☐
Person 7:	☐	☐	☐	☐	☐	☐	☐
Person 8:	☐	☐	☐	☐	☐	☐	☐

(Please note: question 3.2 not relevant to this questionnaire)

3.3 Did your child have contact ***IN THE LAST 10 DAYS*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", how many people? ..... ☐☐

MRC use only

3.4 *If "Yes" to Question 3.3, where did this contact occur? (tick all boxes that apply)*

Pre-school child group *(e.g. nursery, toddlers group)* ☐ School ☐

Social occasion (e.g. friend's house, meal out) ☐ *Other* ☐

If "Other", ***please specify***: .....

SECTION 4 THIS SECTION CONCERNS YOUR CHILD'S TRAVEL AND LEISURE ACTIVITY IN THE LAST 10 DAYS

4.1 During this time, did your child spend one or more nights away from home?

Yes ☐ ↓ No ☐ → If "**No**", please go to **QUESTION 4.6**

If "**Yes**", please continue:

4.2 Was he/she away?: On holiday ☐ Other ☐

4.3 Was he/she staying?: In the UK ☐ Abroad ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: .....

4.4 What was the main resort/town stayed at? .....

4.5 Where did your child **EAT** most of his/her meals? ***(tick one box)***

Hotel/guest house ☐ Self-catering in an apartment, villa, etc. ☐

Camping ☐ Restaurant, café, etc. ☐

Private house ☐ Other ☐

If "Other", ***please specify***: .....

MRC use only

4.6 Did your child go swimming or join in water sports *(e.g. sailing, water skiing)* in the UK or abroad?

Yes ☐ ↓ No ☐ → If "**No**", please go to **SECTION 5**

If "**Yes**", ***please specify*** type(s) of activity: .....

.....

.....

4.7 Where did this activity take place? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

If "Other", ***please specify***: .....

4.8 Did he/she swallow any water in any of the following? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

If "Other", ***please specify***: .....

MRC use only

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND YOUR CHILD'S CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ No ☐ → If "No", please go to **QUESTION 5.6** ☐

If "Yes", *please indicate* which pet(s) *(tick all boxes that apply)*

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐

If "Other", *please specify*: .....

5.2 Did your child clean up any pet's motions (mess) or clean out the cage/aquarium/litter tray, etc. of any of your pets *IN THE LAST 10 DAYS*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which pet(s): ..... ☐ ☐

5.3 Did any of your pets, where relevant, have diarrhoea *IN THE LAST 10 DAYS*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which pet(s): ..... ☐ ☐

5.4 Do you feed your pet(s) with any of the following?: *(tick all that apply)*

Raw meat/fish	☐	☐
Cooked meat/fish from a shop	☐	☐
Meat/fish cooked at home	☐	☐
Canned meat/fish	☐	☐

MRC use only

5.5 If you have a cat or dog, where is it normally fed? *(please tick one box)*

In the kitchen (on the floor)	☐
In the kitchen (on a worktop/table)	☐
Outside	☐
Other	☐

If "Other", *please specify*: ..... ☐ ☐

5.6 Was your child in close contact with any other animals *(e.g. zoo, farm, other people's pets) IN THE LAST 10 DAYS*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which animal(s): .....

..... ☐ ☐

Please specify where *(e.g. zoo, farm, etc.)*: ..... ☐

SECTION 6 THIS SECTION ASKS ABOUT YOUR CHILD'S FOOD AND WATER CONSUMPTION

6.1 Did your child eat *ANY OF THE FOLLOWING FOODS IN THE LAST 10 DAYS*?

(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

	Yes	Not sure	
Meat:			
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc.)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE LAST 10 DAYS*** did he/she eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Meals-on-wheels	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

MRC use only

The following questions ask for more details about particular foods.

6.3 If your child ate chicken ***IN THE LAST 10 DAYS***, was this?: ***(tick all boxes that apply)***

- Bought raw fresh, cooked and eaten at home
- Bought raw frozen, cooked and eaten at home
- Pre-cooked, eaten at home hot (include ready-made dinners)
- Pre-cooked, eaten at home cold
- In a hot or cold take-away meal (include sandwiches)
- In a hot or cold meal not at home (e.g. restaurant/canteen)
- Barbecued chicken

6.4 How many times **IN THE LAST 10 DAYS** did your child eat chicken? ***(tick one box)***

Never ☐ Once ☐ More than once ☐ ---> how many times? .....

6.5 ***IN THE LAST 10 DAYS***, did he/she help **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐

6.6 If you bought chicken, was this?: ***(tick all that apply)***

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐

6.7 If your child ate cold, shop-sliced meats ***IN THE LAST 10 DAYS***, where were they bought? ***(tick all that apply)***

	Butcher	Delicatessen	Supermarket	Other shop
Pork/ham	☐	☐	☐	☐
Chicken/turkey	☐	☐	☐	☐
Beef	☐	☐	☐	☐
Corned beef	☐	☐	☐	☐
Tongue	☐	☐	☐	☐
Other	☐	☐	☐	☐

If "Other", ***(please specify)***: .....

MRC use only

6.8 Did your child eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

6.9 Did he/she eat any of the following milk and dairy products ***IN THE LAST 10 DAYS***? ***(tick all that apply)***

	Pasteurised	Unpasteurised	Not sure if pasteurised
Goats'/sheep's milk	☐	☐	☐
Soft cheese	☐	☐	☐
Fromage frais	☐	☐	☐
Yoghurt	☐	☐	☐
Ice cream	☐	☐	☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐

6.10 Are you and your child vegetarians?

	You	Your child
No	☐	☐
Partial vegetarian (don't eat meat, but eat fish)	☐	☐
Strict vegetarian (don't eat meat or fish)	☐	☐
Vegan (don't eat meat, fish or dairy products)	☐	☐

6.11 Did your child take any antibiotics prescribed by a doctor ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

6.12 Did he/she take indigestion medicines, bought over the counter or prescribed by a doctor, ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

MRC use only

6.13 Did your child take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by a doctor, ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

Drinking cold water

6.14 ***IN THE LAST 10 DAYS***, how many glasses (a glass holds about ½ pint) of the following types of **UNBOILED WATER** did he/she drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE OR UNSURE FOR ANY TYPE OF WATER, LEAVE BLANK)

	Approximate number of glasses per day	
	In the UK	Abroad
Mains water	☐☐	☐☐
Bottled water: fizzy, sparkling	☐☐	☐☐
Bottled water: still	☐☐	☐☐
Non-mains water (e.g. borehole, well, spring)	☐☐	☐☐
Water dispenser	☐☐	☐☐

6.15 During this period did he/she have any ice in drinks?

In the UK: Yes ☐ No ☐

Abroad: Yes ☐ No ☐

6.16 Do you filter your water? Yes ☐ No ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐

MRC use only

Is the child who was ill less than 1 year old?

Yes ☐ No ☐ → If "**No**", please go to **SECTION 7**

If "**Yes**", please continue:

6.17 How is your baby currently being fed milk? ***(please tick one box)***

Breast feed only ☐ Mixed breast/bottle feed ☐

Bottle feed only ☐ Other ☐

6.18 Have you started weaning your baby onto solids?

Yes ☐ No ☐

6.19 If not currently breast feeding, has your baby ever been breast fed?

Yes ☐ No ☐

If "**Yes**", how old (in months) was your baby when this was stopped? ☐☐

6.20 If your baby is being bottle fed, how do you sterilise the bottles/teats, etc.?

Cold water with chemicals ☐ Boiling water ☐

Steam ☐ Other ☐

If "Other", ***please specify***: .....

6.21 If your baby is being bottle fed, do you usually boil water to make the feed?

Yes ☐ No ☐

MRC use only

6.22 How do you store the baby's bottled milk before feeding?

In the fridge ☐
At room temperature ☐
Other ☐

If "Other", ***please specify***: .....

6.23 Do you give your baby water to drink? Yes ☐ No ☐

If "**Yes**", is it boiled first? Yes ☐ No ☐

SECTION 7 **THIS SECTION ASKS FOR SOME BASIC INFORMATION ABOUT YOUR CHILD, WHO IS NAMED IN THE ACCOMPANYING LETTER, AND OTHER MEMBERS OF YOUR HOUSEHOLD**

7.1 Does your child attend any of the following?:
(tick any boxes that apply)

Day nursery/creche ☐
Toddlers play group ☐
Child minder ☐
Nursery school or class ☐
Local Authority school ☐
Private school ☐
Other ☐

If "Other", ***please specify***: .....

7.2 To which ethnic group do you consider that your child belongs?
(tick one box)

White (UK) ☐
Black (Caribbean) ☐
Black (other) ☐
Pakistani ☐
Chinese ☐
White (other) ☐
Black (African) ☐
Indian ☐
Bangladeshi ☐
Other ☐

If "Other", ***please specify***: .....

MRC use only

The following questions ask about the main wage earner in your household. If there is more than one wage earner, please enter one person's details.

7.3 What is the occupation of the main wage earner in the household?
(If currently unemployed, what was his/her most recent occupation; if retired, what was his/her main occupation?)

Job title: .....

What does/did he/she actually do?: .....

.....

In which industry/business is this?: .....

7.4 What is/was the main wage earner's position? ***(tick one box)***

Manager ☐
Self-employed ☐
Supervisor or foreman ☐
Employee ***(i.e. none of the above)*** ☐

7.5 What is the current marital status of the main wage earner?

Married ***(or living as)*** ☐
Divorced, separated ☐
Single ***(never married)*** ☐
Widowed ☐

7.6 How old was the main wage earner when he/she first left full-time education ***(school, college, university)***? ***(tick one box)***

Under 16 years ☐
16 years ☐
17 years ☐
18 years ☐
19 years or over ☐
Still in full-time education ☐

MRC use only

SECTION 8 THIS SECTION ASKS ABOUT THE DETAILS OF YOUR HOUSEHOLD'S ACCOMMODATION

8.1 Please state the type of accommodation in which you live:

- Detached/semi-detached *(including bungalow)*
- Terraced *(including end of terrace)*
- Purpose-built flat/ maisonette in a block
- Self-contained flat in a converted house
- Rooms in a converted house, not self-contained
- Caravan/houseboat/mobile home
- Institutional home *(e.g. nursing home, boarding school, etc.)*
- Other

If "other", *please specify*: .....

8.2 Does any other household share the bathroom and/or WC with you? Yes ☐ No ☐

8.3 Does any other household share the kitchen with you? Yes ☐ No ☐

8.4 Is the accommodation?:

- Owned/mortgaged by you or your family
- Rented from a council, new town, housing association or charitable trust
- Rented from a private landlord
- Other

If "other", *please specify*: .....

8.5 How many rooms does your household have? *(exclude WC/toilet, hall and landing)* ..... rooms

SECTION 9 This section asks about your kitchen and food shopping and preparation in your household. Please ask THE PERSON WHO USUALLY HAS THE MAIN RESPONSIBILITY FOR FOOD SHOPPING AND PREPARATION in your household to complete this section.

Your kitchen:

9.1 What is the narrowest width of your kitchen? *(tick one box only)* (1 metre is about 3 feet)

- Less than 2 metres ☐
- 2-3 metres ☐
- More than 3 metres ☐
- Not sure ☐

MRC use only

9.2 What is the total length of work surface you can use when preparing food? *(tick one box only)*

- Less than 1 metre ☐
- 1-2 metres ☐
- More than 2 metres ☐
- Not sure ☐

9.3 Does your household have regular use of the following?: *(tick all boxes that apply)*

- Fridge ☐
- Freezer (include fridge/ freezer) ☐ ☐
- Microwave oven ☐
- Slow cooker ☐ ☐
- Gas/electric cooker ☐
- Dishwasher ☐ ☐
- Food mixer/blender ☐
- Combi-oven ☐ ☐

9.4 Do you use a thermometer to check the storage temperature of your fridge? Yes ☐ No ☐ ☐

If "**Yes**", what is the temperature now? .... °C ☐

9.5 Do you use a food thermometer to check the cooking temperature of food in the oven? Yes ☐ No ☐ ☐

9.6 Do you have a baby still in nappies? Yes ☐ No ☐ ☐

If "**No**", please go to **QUESTION 9.7**

If "**Yes**", do you ever use cloth nappies? Yes ☐ No ☐ ☐

If "**Yes**", where do you **USUALLY** soak/wash soiled nappies? *(tick one box)*

- Bucket in kitchen ☐
- Bucket in bathroom ☐
- Sink in kitchen ☐
- Sink in bathroom ☐
- Bucket outside ☐
- Other ☐

If "Other", *please specify*: ..... ☐☐

Your usual food shopping procedures:

9.7 How often is your household's main food shopping done? *(tick one box only)*

- More than once a week ☐
- Once a week ☐
- Once a fortnight ☐
- Once a month ☐
- Less often ☐
- Not sure ☐ ☐

MRC use only

9.8 If you normally do the shopping, how do the following statements apply to you? ***(tick one box for each statement)***

	Always	Sometimes	Never	Not sure	
I check the "Use by" or "Best before" date	☐	☐	☐	☐	☐
I follow the storage instructions	☐	☐	☐	☐	☐
I check the packaging for damage when shopping	☐	☐	☐	☐	☐
I pack frozen foods together in a cool container for transport	☐	☐	☐	☐	☐
I check the appearance of the product when shopping	☐	☐	☐	☐	☐

9.9 How much time usually passes between buying frozen or chilled items and putting them in the fridge or freezer? ***(tick one box only)***

Up to 1 hour ☐ Up to 2 hours ☐

Up to 3 hours ☐ More than 3 hours ☐ ☐

9.10 Where do you usually store the following items in your fridge? ***(tick a box for each item)***

	Top/middle shelf	Bottom shelf	Salad drawer	In the door	Wherever there is room	N/A*	
Raw meat	☐	☐	☐	☐	☐	☐	☐
Unwashed raw salad	☐	☐	☐	☐	☐	☐	☐
Cooked food	☐	☐	☐	☐	☐	☐	☐
Sandwiches	☐	☐	☐	☐	☐	☐	☐

* N/A = not applicable

Your usual food practices:

9.11 Where would you normally defrost a frozen chicken? ***(tick one box only)***

In the fridge ☐ On kitchen work surface ☐

In the microwave ☐ In the oven ☐

In a bowl of warm water ☐ In a bowl of cold water ☐

In the kitchen sink ☐ Other ***(please specify)***: ☐ ☐

Not applicable ☐ .....

9.12 How long would you thaw an average sized (3lb) chicken by this method? .... hours Not applicable ☐ ☐ ☐

MRC use only

9.13 Do you use separate chopping boards for raw meats and cooked meats? Yes ☐ No ☐ Not sure ☐ ☐

9.14 Do you use separate chopping boards for other raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.15 Do you clean your chopping board between use for raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.16 What material is your main chopping board made from? ***(please tick one box)***

Wood ☐ Plastic ☐ Other ***(please specify)*** ☐ ☐ ☐

.....

9.17 Do you use the same cloth for wiping all surfaces in your kitchen? Yes ☐ No ☐ Not sure ☐ ☐

9.18 Where do you normally cool foods or leftovers to be eaten later (reheated or cold)? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.19 Where do you normally store leftovers or foods prepared for eating later? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.20 How do you usually reheat leftovers or foods prepared in the home? ***(tick any that apply)***

In a normal oven ☐ In a microwave oven ☐

In a saucepan on the hob ☐ Other ☐

Not sure ☐

If "Other", ***please describe***: ..... ☐ ☐

MRC use only

9.21 Please indicate whether you think the following list of statements is true or false *(tick one box for each statement)*:

	Agree	Disagree	Don't know	
Food poisoning is caused by germs	☐	☐	☐	☐
Pets should not be allowed on kitchen work tops	☐	☐	☐	☐
Food poisoning germs are killed by proper cooking	☐	☐	☐	☐
Most germs do not grow in a fridge	☐	☐	☐	☐
The drip (blood, etc.) from raw meat and chicken can contain germs	☐	☐	☐	☐
It doesn't matter how long food is kept as long as it is stored cold	☐	☐	☐	☐
It doesn't matter whether you wash your hands or not before handling food	☐	☐	☐	☐
Contaminated food always looks or smells bad	☐	☐	☐	☐
Once a food is cooked and cooled it can be kept for a day at room temperature before it is eaten	☐	☐	☐	☐
One food can contaminate another by touching it	☐	☐	☐	☐

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q2.1

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

Study type [2]

Practice number [ ][ ][ ]

Study number [ ][ ][ ]

PLEASE READ THIS PAGE FIRST

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this study. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

SECTION 1 **THIS SECTION CONFIRMS DETAILS OF THE AGE AND SEX OF THE PERSON WHO IS NAMED IN THE ACCOMPANYING LETTER**

Please state:

1.1 Today's date: ...../...../.....
day month year

1.2 Your date of birth: ...../...../.....
day month year

1.3 Sex: Male [ ] Female [ ]

1.4 During the last month, ie. since this date last month, have you suffered from diarrhoea (3 or more loose bowel movements in any 24-hour period) ?

Yes [ ] No [ ] Don't know [ ]

If "Yes", were you asked to provide a bowel movement sample to be analysed by a doctor or laboratory?

Yes [ ] No [ ]

(Please note: Sections 2 to 6 are not relevant to this questionnaire)

MRC use only

SECTION 7 **THIS SECTION ASKS FOR SOME BASIC INFORMATION ABOUT YOU, i.e. THE PERSON WHO IS NAMED IN THE ACCOMPANYING LETTER**

7.1 Current marital status:

- Married *(or living as)*
- Single *(never married)*
- Divorced, separated
- Widowed

7.2 Current paid employment status *(tick one box)*:

- Working full-time *(30 or more hours per week)*
- Working part-time *(under 30 hours per week)*
- Unemployed, seeking work
- Waiting to start a job
- Out of work due to temporary sickness
- Unable to work because of permanent disability or illness
- Retired from paid work
- Full-time student
- Not seeking work *(e.g. caring for home or family)*
- Other

If "Other", *please specify*: .....

.....

7.3 What is your occupation? *(if unemployed, what was your most recent occupation; if retired, what was your main occupation?)*

Job title: .....

What do/did you actually do?: .....

.....

In which industry/business is this?: .....

7.4 What is/was your position? *(tick one box)*

- Manager
- Supervisor or foreman
- Self-employed
- Employee *(i.e. none of the above)*

MRC use only

7.5 If you are unemployed, how long is it since you were in paid employment?

- Under 12 months
- 12 months or over

7.6 How old were you when you first left full-time education *(school, college, university)*? *(tick one box)*

- Under 16 years
- 16 years
- 17 years
- 18 years
- 19 years or over
- Still in full-time education

7.7 To which ethnic group do you consider that you belong? *(tick one box)*

- White (UK)
- White (other)
- Black (Caribbean)
- Black (African)
- Black (other)
- Indian
- Pakistani
- Bangladeshi
- Chinese
- Other

If "Other", *please specify*: .....

7.8 What is the occupation of your spouse, or partner if applicable? *(If unemployed, what was his/her most recent occupation; if retired, what was his/her main occupation?)*

Job title: .....

What does/did he/she actually do?: .....

.....

In which industry/business is this?: .....

7.9 What is/was his/her position? *(tick one box)*

- Manager
- Supervisor or foreman
- Self-employed
- Employee *(i.e. none of the above)*

7.10 How many people (excluding yourself) are permanent members of your household?

....people

MRC use only

SECTION 8 THIS SECTION ASKS ABOUT THE DETAILS OF YOUR HOUSEHOLD'S ACCOMMODATION

8.1 Please state the type of accommodation in which you live:

- Detached/semi-detached *(including bungalow)*
- Terraced *(including end of terrace)*
- Purpose-built flat/ maisonette in a block
- Self-contained flat in a converted house
- Rooms in a converted house, not self-contained
- Caravan/houseboat/mobile home
- Institutional home *(e.g. nursing home, boarding school, etc.)*
- Other

If "other", *please specify*: .....

8.2 Does any other household share the bathroom and/or WC with you? Yes / No

8.3 Does any other household share the kitchen with you? Yes / No

8.4 Is the accommodation?:

- Owned/mortgaged by you or your family
- Rented from a private landlord
- Rented from a council, new town, housing association or charitable trust
- Other

If "other", *please specify*: .....

8.5 How many rooms does your household have? *(exclude WC/toilet, hall and landing)* ..... rooms

SECTION 9 This section asks about your kitchen and food shopping and preparation in your household. Please ask THE PERSON WHO USUALLY HAS THE MAIN RESPONSIBILITY FOR FOOD SHOPPING AND PREPARATION in your household to complete this section.

Your kitchen:

9.1 What is the narrowest width of your kitchen? *(tick one box only)* (1 metre is about 3 feet)

- Less than 2 metres
- 2-3 metres
- More than 3 metres
- Not sure

MRC use only

9.2 What is the total length of work surface you can use when preparing food? *(tick one box only)*

- Less than 1 metre
- 1-2 metres
- More than 2 metres
- Not sure

9.3 Does your household have regular use of the following?: *(tick all boxes that apply)*

- Fridge
- Freezer (include fridge/ freezer)
- Microwave oven
- Slow cooker
- Gas/electric cooker
- Dishwasher
- Food mixer/blender
- Combi-oven

9.4 Do you use a thermometer to check the storage temperature of your fridge? Yes / No

If "**Yes**", what is the temperature now? .... °C

9.5 Do you use a food thermometer to check the cooking temperature of food in the oven? Yes / No

9.6 Do you have a baby still in nappies? Yes / No

If "**No**", please go to **QUESTION 9.7**

If "**Yes**", do you ever use cloth nappies? Yes / No

If "**Yes**", where do you **USUALLY** soak/wash soiled nappies? *(tick one box)*

- Bucket in kitchen
- Sink in kitchen
- Bucket outside
- Bucket in bathroom
- Sink in bathroom
- Other

If "Other", *please specify*: .....

Your usual food shopping procedures:

9.7 How often is your household's main food shopping done? *(tick one box only)*

- More than once a week
- Once a week
- Once a fortnight
- Once a month
- Less often
- Not sure

MRC use only

9.8 If you normally do the shopping, how do the following statements apply to you? ***(tick one box for each statement)***

	Always	Sometimes	Never	Not sure	
I check the "Use by" or "Best before" date	☐	☐	☐	☐	☐
I follow the storage instructions	☐	☐	☐	☐	☐
I check the packaging for damage when shopping	☐	☐	☐	☐	☐
I pack frozen foods together in a cool container for transport	☐	☐	☐	☐	☐
I check the appearance of the product when shopping	☐	☐	☐	☐	☐

9.9 How much time usually passes between buying frozen or chilled items and putting them in the fridge or freezer? ***(tick one box only)***

Up to 1 hour ☐ Up to 2 hours ☐

Up to 3 hours ☐ More than 3 hours ☐ ☐

9.10 Where do you usually store the following items in your fridge? ***(tick a box for each item)***

	Top/middle shelf	Bottom shelf	Salad drawer	In the door	Wherever there is room	N/A*	
Raw meat	☐	☐	☐	☐	☐	☐	☐
Unwashed raw salad	☐	☐	☐	☐	☐	☐	☐
Cooked food	☐	☐	☐	☐	☐	☐	☐
Sandwiches	☐	☐	☐	☐	☐	☐	☐

* N/A = not applicable

Your usual food practices:

9.11 Where would you normally defrost a frozen chicken? ***(tick one box only)***

In the fridge ☐ On kitchen work surface ☐

In the microwave ☐ In the oven ☐

In a bowl of warm water ☐ In a bowl of cold water ☐

In the kitchen sink ☐ Other ***(please specify)***: ☐ ☐

Not applicable ☐ .....

9.12 How long would you thaw an average sized (3lb) chicken by this method? .... hours Not applicable ☐ ☐ ☐

MRC use only

9.13 Do you use separate chopping boards for raw meats and cooked meats? Yes ☐ No ☐ Not sure ☐ ☐

9.14 Do you use separate chopping boards for other raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.15 Do you clean your chopping board between use for raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.16 What material is your main chopping board made from? ***(please tick one box)***

Wood ☐ Plastic ☐ Other ***(please specify)*** ☐ ☐ ☐

.....

9.17 Do you use the same cloth for wiping all surfaces in your kitchen? Yes ☐ No ☐ Not sure ☐ ☐

9.18 Where do you normally cool foods or leftovers to be eaten later (reheated or cold)? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.19 Where do you normally store leftovers or foods prepared for eating later? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.20 How do you usually reheat leftovers or foods prepared in the home? ***(tick any that apply)***

In a normal oven ☐ In a microwave oven ☐

In a saucepan on the hob ☐ Other ☐

Not sure ☐

If "Other", ***please describe***: ..... ☐ ☐

MRC use only

9.21 Please indicate whether you think the following list of statements is true or false *(tick one box for each statement)*:

	Agree	Disagree	Don't know	
Food poisoning is caused by germs	☐	☐	☐	☐
Pets should not be allowed on kitchen work tops	☐	☐	☐	☐
Food poisoning germs are killed by proper cooking	☐	☐	☐	☐
Most germs do not grow in a fridge	☐	☐	☐	☐
The drip (blood, etc.) from raw meat and chicken can contain germs	☐	☐	☐	☐
It doesn't matter how long food is kept as long as it is stored cold	☐	☐	☐	☐
It doesn't matter whether you wash your hands or not before handling food	☐	☐	☐	☐
Contaminated food always looks or smells bad	☐	☐	☐	☐
Once a food is cooked and cooled it can be kept for a day at room temperature before it is eaten	☐	☐	☐	☐
One food can contaminate another by touching it	☐	☐	☐	☐

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q2.2

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

Study type [2]

Practice number [ ][ ][ ]

Study number [ ][ ][ ]

PLEASE READ THIS PAGE FIRST

Dear Parent/Guardian,

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this study. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

SECTION 1 **THIS SECTION CONFIRMS DETAILS OF THE AGE AND SEX OF THE CHILD WHO IS NAMED IN THE ACCOMPANYING LETTER**

Please state:

1.1 Today's date: ...../...../..... [ ]
day month year

1.2 Your child's date of birth: ...../...../..... [ ]
day month year

1.3 Your child's sex: Male [ ] Female [ ] [ ]

1.4 During the last month, ie. since this date last month, has your child suffered from diarrhoea (3 or more loose bowel movements in any 24-hour period) ?

Yes [ ] No [ ] Don't know [ ] [ ]

If "Yes", was he/she asked to provide a bowel movement sample to be analysed by a doctor or laboratory?

Yes [ ] No [ ] [ ]

(Please note: Sections 2 to 6 are not relevant to this questionnaire)

MRC use only

SECTION 7 THIS SECTION ASKS FOR SOME BASIC INFORMATION ABOUT YOUR CHILD, WHO IS NAMED IN THE ACCOMPANYING LETTER, AND OTHER MEMBERS OF YOUR HOUSEHOLD

7.1 Does your child attend any of the following?:
(tick any boxes that apply)

- Day nursery/creche ☐
- Toddlers play group ☐
- Child minder ☐
- Nursery school or class ☐
- Local Authority school ☐
- Private school ☐
- Other ☐

☐☐

If "Other", ***please specify***: .....

7.2 To which ethnic group do you consider that your child belongs?
(tick one box)

- White (UK) ☐
- White (other) ☐
- Black (Caribbean) ☐
- Black (African) ☐
- Black (other) ☐
- Indian ☐
- Pakistani ☐
- Bangladeshi ☐
- Chinese ☐
- Other ☐

☐☐

If "Other", ***please specify***: .....

MRC use only

The following questions ask about the main wage earner in your household. If there is more than one wage earner, please enter one person's details.

7.3 What is the occupation of the main wage earner in the household?
(if currently unemployed, what was his/her most recent occupation; if retired, what was his/her main occupation?)

Job title: ..... ☐

What does/did he/she actually do?: ..... ☐☐☐

.....

In which industry/business is this?: .....

7.4 What is/was the main wage earner's position? ***(tick one box)***

- Manager ☐
- Supervisor or foreman ☐
- Self-employed ☐
- Employee ***(i.e. none of the above)*** ☐

7.5 *What is the current marital status of the main wage earner?*

- *Married **(or living as)*** ☐
- Single ***(never married)*** ☐
- Divorced, separated ☐
- Widowed ☐ ☐

7.6 How old was the main wage earner when he/she first left full-time education ***(school, college, university)***? ***(tick one box)***

- Under 16 years ☐
- 16 years ☐
- 17 years ☐
- 18 years ☐
- 19 years or over ☐
- Still in full-time education ☐ ☐

7.7 How many people (excluding yourself) are permanent members of your household?

..... people ☐

MRC use only

SECTION 8 **THIS SECTION ASKS ABOUT THE DETAILS OF YOUR HOUSEHOLD'S ACCOMMODATION**

8.1 Please state the type of accommodation in which you live:

- Detached/semi-detached *(including bungalow)* ☐
- Terraced *(including end of terrace)* ☐
- Purpose-built flat/ maisonette in a block ☐
- Self-contained flat in a converted house ☐
- Rooms in a converted house, not self-contained ☐
- Caravan/houseboat/mobile home ☐
- Institutional home *(e.g. nursing home, boarding school, etc.)* ☐
- Other ☐

If "other", *please specify*: .....

8.2 Does any other household share the bathroom and/or WC with you? Yes ☐ No ☐

8.3 Does any other household share the kitchen with you? Yes ☐ No ☐

8.4 Is the accommodation?:

- Owned/mortgaged by you or your family ☐
- Rented from a private landlord ☐
- Rented from a council, new town, housing association or charitable trust ☐
- Other ☐

If "other", *please specify*: .....

8.5 How many rooms does your household have? *(exclude WC/toilet, hall and landing)* ..... rooms

SECTION 9 **This section asks about your kitchen and food shopping and preparation in your household. Please ask THE PERSON WHO USUALLY HAS THE MAIN RESPONSIBILITY FOR FOOD SHOPPING AND PREPARATION in your household to complete this section.**

Your kitchen:

9.1 What is the narrowest width of your kitchen? *(tick one box only)* (1 metre is about 3 feet)

- Less than 2 metres ☐
- 2-3 metres ☐
- More than 3 metres ☐
- Not sure ☐

MRC use only

9.2 What is the total length of work surface you can use when preparing food? *(tick one box only)*

- Less than 1 metre ☐
- 1-2 metres ☐
- More than 2 metres ☐
- Not sure ☐

9.3 Does your household have regular use of the following?: *(tick all boxes that apply)*

- Fridge ☐
- Freezer (include fridge/ freezer) ☐ ☐
- Microwave oven ☐
- Slow cooker ☐ ☐
- Gas/electric cooker ☐
- Dishwasher ☐ ☐
- Food mixer/blender ☐
- Combi-oven ☐ ☐

9.4 Do you use a thermometer to check the storage temperature of your fridge? Yes ☐ No ☐ ☐

If "**Yes**", what is the temperature now? .... °C ☐

9.5 Do you use a food thermometer to check the cooking temperature of food in the oven? Yes ☐ No ☐ ☐

9.6 Do you have a baby still in nappies? Yes ☐ No ☐ ☐

If "**No**", please go to **QUESTION 9.7**

If "**Yes**", do you ever use cloth nappies? Yes ☐ No ☐ ☐

If "**Yes**", where do you **USUALLY** soak/wash soiled nappies? *(tick one box)*

- Bucket in kitchen ☐
- Bucket in bathroom ☐
- Sink in kitchen ☐
- Sink in bathroom ☐
- Bucket outside ☐
- Other ☐

If "Other", *please specify*: ..... ☐

Your usual food shopping procedures:

9.7 How often is your household's main food shopping done? *(tick one box only)*

- More than once a week ☐
- Once a week ☐
- Once a fortnight ☐
- Once a month ☐
- Less often ☐
- Not sure ☐ ☐

MRC use only

9.8 If you normally do the shopping, how do the following statements apply to you? ***(tick one box for each statement)***

	Always	Sometimes	Never	Not sure	
I check the "Use by" or "Best before" date	☐	☐	☐	☐	☐
I follow the storage instructions	☐	☐	☐	☐	☐
I check the packaging for damage when shopping	☐	☐	☐	☐	☐
I pack frozen foods together in a cool container for transport	☐	☐	☐	☐	☐
I check the appearance of the product when shopping	☐	☐	☐	☐	☐

9.9 How much time usually passes between buying frozen or chilled items and putting them in the fridge or freezer? ***(tick one box only)***

Up to 1 hour ☐ Up to 2 hours ☐

Up to 3 hours ☐ More than 3 hours ☐ ☐

9.10 Where do you usually store the following items in your fridge? ***(tick a box for each item)***

	Top/middle shelf	Bottom shelf	Salad drawer	In the door	Wherever there is room	N/A*	
Raw meat	☐	☐	☐	☐	☐	☐	☐
Unwashed raw salad	☐	☐	☐	☐	☐	☐	☐
Cooked food	☐	☐	☐	☐	☐	☐	☐
Sandwiches	☐	☐	☐	☐	☐	☐	☐

* N/A = not applicable

Your usual food practices:

9.11 Where would you normally defrost a frozen chicken? ***(tick one box only)***

In the fridge ☐ On kitchen work surface ☐

In the microwave ☐ In the oven ☐

In a bowl of warm water ☐ In a bowl of cold water ☐

In the kitchen sink ☐ Other ***(please specify)***: ☐ ☐

Not applicable ☐

.....

9.12 How long would you thaw an average sized (3lb) chicken by this method? .... hours Not applicable ☐ ☐ ☐

MRC use only

9.13 Do you use separate chopping boards for raw meats and cooked meats? Yes ☐ No ☐ Not sure ☐ ☐

9.14 Do you use separate chopping boards for other raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.15 Do you clean your chopping board between use for raw and cooked foods? Yes ☐ No ☐ Not sure ☐ ☐

9.16 What material is your main chopping board made from? ***(please tick one box)***

Wood ☐ Plastic ☐ Other ***(please specify)*** ☐ ☐ ☐

.....

9.17 Do you use the same cloth for wiping all surfaces in your kitchen? Yes ☐ No ☐ Not sure ☐ ☐

9.18 Where do you normally cool foods or leftovers to be eaten later (reheated or cold)? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.19 Where do you normally store leftovers or foods prepared for eating later? ***(tick one box only)***

	Covered	Uncovered
In the fridge	☐	☐
In the larder (pantry)	☐	☐
On a work surface	☐	☐
Other	☐	☐

If "Other", ***please describe***: ..... ☐ ☐

9.20 How do you usually reheat leftovers or foods prepared in the home? ***(tick any that apply)***

In a normal oven ☐ In a microwave oven ☐

In a saucepan on the hob ☐ Other ☐

Not sure ☐

If "Other", ***please describe***: ..... ☐ ☐

MRC use only

9.21 Please indicate whether you think the following list of statements is true or false *(tick one box for each statement)*:

	Agree	Disagree	Don't know	
Food poisoning is caused by germs	☐	☐	☐	☐
Pets should not be allowed on kitchen work tops	☐	☐	☐	☐
Food poisoning germs are killed by proper cooking	☐	☐	☐	☐
Most germs do not grow in a fridge	☐	☐	☐	☐
The drip (blood, etc.) from raw meat and chicken can contain germs	☐	☐	☐	☐
It doesn't matter how long food is kept as long as it is stored cold	☐	☐	☐	☐
It doesn't matter whether you wash your hands or not before handling food	☐	☐	☐	☐
Contaminated food always looks or smells bad	☐	☐	☐	☐
Once a food is cooked and cooled it can be kept for a day at room temperature before it is eaten	☐	☐	☐	☐
One food can contaminate another by touching it	☐	☐	☐	☐

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q2.3

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

Study type	2
Practice number	
Study number	
Case/control	1
Case/control number	

PLEASE READ THIS PAGE FIRST

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this part of the study following your recent episode of gastroenteritis. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

(Please note: Section 1 is not relevant to this questionnaire.)

SECTION 2 THIS SECTION ASKS ABOUT THE SYMPTOMS YOU EXPERIENCED DURING YOUR ILLNESS

2.1 On what date did your symptoms start? ...../...../..... (day month year)

2.2 Have you seen your GP about these symptoms?

Yes ☐ No ☐

If "yes", on what date did you first see your GP? ...../...../..... (day month year)

2.3 Did your illness incapacitate you? ***(i.e. prevent you going about your normal daily activities)***

Yes ☐ No ☐ Not sure ☐

2.4 Do you suffer from any long-standing illness or disability?

Yes ☐ No ☐

If "**Yes**", ***please specify***: .....
.....
.....
.....

MRC use only

2.5 Did you have any of the following symptoms?

If **"YES"**, in your opinion how severe were they and how many days did they last?

(tick ALL appropriate boxes or LEAVE BLANK IF YOU DID NOT HAVE THE SYMPTOM)

An EXAMPLE is given on how to enter if you had mild diarrhoea that lasted for 3 days and is still present.

Symptom	Yes	Mild	Moderate	Severe	Total days	Still present
e.g. Diarrhoea	✓	✓			0 3	✓
Diarrhoea (loose watery motions)						
Blood in motions						
Nausea (feeling sick)						
Vomiting (being sick)						
Abdominal (tummy) pain						
Loss of appetite						
High temperature (shivering/ sweating)						
Cough, runny/ blocked nose, sore throat						
Headache						
Aching muscles						
Joint pains/ stiffness						
Back or neck pain/stiffness						
Joint swelling						
Painful red eyes						
Dizziness/ faintness						
Other						

If "Other", ***please specify***: .....

MRC use only

2.6 If you answered **"Yes"** to diarrhoea in ***Question 2.5***, what was the greatest number of times you went to the lavatory with diarrhoea in any 24-hour period?

Number of times ☐☐ Not sure ☐ ☐☐

2.7 If you answered **"Yes"** to vomiting in ***Question 2.5***, what was the greatest number of times you vomited (were sick) in any 24-hour period?

Number of times ☐☐ Not sure ☐ ☐☐

2.8 If you answered **"Yes"** to joint swelling in ***Question 2.5***, which of your joints were swollen? ***(e.g. left knee, both knees, etc.)***

..... Not sure ☐ ☐☐

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH A SIMILAR ILLNESS

3.1 How many different people ***(excluding you)*** lived or spent a night in your household ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***? ..... people ☐

Please fill in the following details for all of these people, EXCLUDING YOURSELF: their age and sex, whether they are a permanent member of the household or a visitor, and whether they were ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED.

The example on how to enter is for a female member of the household aged 43, who was ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure
	43	F	✓		✓		
Person 1:							
Person 2:							
Person 3:							
Person 4:							
Person 5:							
Person 6:							
Person 7:							
Person 8:							

MRC use only

3.2 Were you the first person in the household to be ill? Yes ☐ No ☐ Not sure ☐

If "No", please give the **PERSON NUMBER** *(from Question 3.1)* of the first person to be ill: Person .....

3.3 Did you have contact ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", how many people? .....

3.4 If "**Yes**" to *Question 3.3*, where did this contact occur? *(tick all boxes that apply)*

- Pre-school child group *(e.g. nursery, toddlers group)* ☐
- School ☐
- Workplace ☐
- Social occasion *(e.g. friend's house, meal out)* ☐
- Other ☐
- Not applicable ☐

If "Other", *please specify*: .....

SECTION 4 THIS SECTION ASKS ABOUT YOUR TRAVEL AND LEISURE ACTIVITY IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED

4.1 During this time, did you spend one or more nights away from home? *(exclude shift work)*

Yes ☐ ↓ No ☐ → If "**No**", please go to **QUESTION 4.6**

If "**Yes**", please continue:

4.2 Were you away?: On holiday ☐ On business ☐ Other ☐

4.3 Were you staying?: In the UK ☐ Abroad ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: .....

MRC use only

4.4 What was the main resort/town stayed at? .....

4.5 Where did you **EAT** most of your meals? *(tick one box)*

- Hotel/guest house ☐
- Self-catering in an apartment, villa, etc. ☐
- Camping ☐
- Restaurant, café, etc. ☐
- Private house ☐
- Other ☐

If "Other", *please specify*: .....

4.6 Did you go swimming or join in water sports *(e.g. sailing, water skiing)* in the UK or abroad?

Yes ☐ ↓ No ☐ → If "**No**", please go to **SECTION 5**

If "**Yes**", *please specify* type(s) of activity: .....

.....

.....

4.7 Where did this activity take place? *(tick all that apply)*

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

If "Other", *please specify*: .....

4.8 Did you swallow any water in any of the following? *(tick all that apply)*

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

If "Other", *please specify*: .....

MRC use only

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ No ☐ → If "No", please go to **QUESTION 5.6** ☐

If "Yes", *please indicate* which pet(s) *(tick all boxes that apply)*

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐☐

If "Other", *please specify*: .....

5.2 Did you clean up any pet's motions (mess) or clean out the cage/ aquarium/litter tray, etc. of any of your pets *IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which pet(s): ..... ☐☐

5.3 Did any of your pets, where relevant, have diarrhoea *IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which pet(s): ..... ☐☐

5.4 Do you feed your pet(s) with any of the following?: *(tick all that apply)*

Raw meat/fish	☐	☐
Cooked meat/fish from a shop	☐	☐
Meat/fish cooked at home	☐	☐
Canned meat/fish	☐	☐

MRC use only

5.5 If you have a cat or dog, where do you normally feed it? *(please tick one box)*

In the kitchen (on the floor)	☐
In the kitchen (on a worktop/table)	☐
Outside	☐
Other	☐

If "Other", *please specify*: ..... ☐☐

5.6 Were you in close contact with any other animals *(e.g. zoo, farm, other people's pets) IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which animal(s): ..... ☐☐

..... ☐

Please specify where *(e.g. zoo, farm, etc.)*: .....

SECTION 6 THIS SECTION ASKS ABOUT YOUR FOOD AND WATER CONSUMPTION

6.1 Did you eat *ANY OF THE FOLLOWING FOODS IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED*?

(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

	Yes	Not sure	
Meat:			
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc.)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE 10 DAYS BEFORE YOU WERE ILL*** did you eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Meals-on-wheels	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

MRC use only

The following questions ask for more details about particular foods.

6.3 If you ate chicken ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, was this?: ***(tick all boxes that apply)***

- Bought raw fresh, cooked and eaten at home
- Bought raw frozen, cooked and eaten at home
- Pre-cooked, eaten at home hot (include ready-made dinners)
- Pre-cooked, eaten at home cold
- In a hot or cold take-away meal (include sandwiches)
- In a hot or cold meal not at home (e.g. restaurant/canteen)
- Barbecued chicken

6.4 How many times **IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED** did you eat chicken? ***(tick one box)***

Never ☐ Once ☐ More than once ☐ ---> how many times? .....

6.5 ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, did you **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐

6.6 If you bought chicken, was this?: ***(tick all that apply)***

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐

6.7 If you ate cold, shop-sliced meats ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, where were they bought? ***(tick all that apply)***

	Butcher	Delicatessen	Supermarket	Other shop
Pork/ham	☐	☐	☐	☐
Chicken/turkey	☐	☐	☐	☐
Beef	☐	☐	☐	☐
Corned beef	☐	☐	☐	☐
Tongue	☐	☐	☐	☐
Other	☐	☐	☐	☐

If "Other", ***(please specify)***: .....

MRC use only

6.8 Did you eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

6.9 Did you eat any of the following milk and dairy products ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***? ***(tick all that apply)***

	Pasteurised	Unpasteurised	Not sure if pasteurised
Goats'/sheep's milk	☐	☐	☐
Soft cheese	☐	☐	☐
Fromage frais	☐	☐	☐
Yoghurt	☐	☐	☐
Ice cream	☐	☐	☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐

6.10 Are you a vegetarian?

- No ☐
- Partial vegetarian (don't eat meat, but eat fish) ☐
- Strict vegetarian (don't eat meat or fish) ☐
- Vegan (don't eat meat, fish or dairy products) ☐

6.11 Did you take any antibiotics prescribed by your doctor ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

6.12 Did you take indigestion medicines, bought over the counter or prescribed by your doctor, ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

MRC use only

6.13 Did you take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by your doctor, ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", please give the **NAME** of each if possible: .....

..... ☐☐☐

.....

Drinking cold water

6.14 ***IN THE 10 DAYS BEFORE YOUR ILLNESS STARTED***, how many glasses (a glass holds about ½ pint) of the following types of **UNBOILED WATER** did you drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE, LEAVE BLANK)

	Approximate number of glasses per day		
	In the UK	Abroad	
Mains water	☐☐	☐☐	☐☐ ☐☐
Bottled water: fizzy, sparkling	☐☐	☐☐	☐☐ ☐☐
Bottled water: still	☐☐	☐☐	☐☐ ☐☐
Non-mains water (e.g. borehole, well, spring)	☐☐	☐☐	☐☐ ☐☐
Water dispenser	☐☐	☐☐	☐☐ ☐☐

6.15 During this period did you have any ice in drinks?

In the UK: Yes ☐ No ☐ ☐

Abroad: Yes ☐ No ☐ ☐

6.16 Do you filter your water? Yes ☐ No ☐ ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐ ☐

MRC use only

(Please note: Sections 7, 8 and 9 not relevant to this questionnaire)

SECTION 10 **Finally, what do you think was responsible for your illness?** ***(please give details below):***

.....

.....

..... ☐☐☐

.....

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q2.4

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

Study type [2]

Practice number [ ][ ][ ]

Study number [ ][ ][ ]

Case/control [1]

Case/control number [ ][ ]

PLEASE READ THIS PAGE FIRST

Dear Parent/Guardian,

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this part of the study following your child's recent episode of gastroenteritis. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

(Please note: Section 1 is not relevant to this questionnaire)

SECTION 2 THIS SECTION ASKS ABOUT THE SYMPTOMS YOUR CHILD EXPERIENCED DURING HIS/HER ILLNESS

2.1 On what date did your child's symptoms start? ...../...../..... day month year

2.2 Did your child see a GP about these symptoms?

Yes [ ] No [ ]

If "Yes" on what date did he/she first see the GP? ...../...../..... day month year

2.3 Did your child's illness incapacitate him/her? ***(i.e. prevent him/her going about his/her normal daily activities)***

Yes [ ] No [ ] Not sure [ ]

2.4 Does your child suffer from any long-standing illness or disability?

Yes [ ] No [ ]

If "**Yes**", ***please specify***: .....

.....

.....

.....

MRC use only

2.5 Did your child have any of the following symptoms?

If **"YES"**, in your opinion how severe were they and how many days did they last?

(tick ALL appropriate boxes or LEAVE BLANK IF HE/SHE DID NOT HAVE THE SYMPTOM, OR YOU ARE UNSURE)

An EXAMPLE is given on how to enter if your child had mild diarrhoea that lasted for 3 days and is still present.

Symptom	Yes	Mild	Moderate	Severe	Total days	Still present
e.g. Diarrhoea	✓	✓			0 3	✓
Diarrhoea (loose watery motions)						
Blood in motions						
Nausea (feeling sick)						
Vomiting (being sick)						
Abdominal (tummy) pain						
Loss of appetite						
High temperature (shivering/ sweating)						
Cough, runny/ blocked nose, sore throat						
Headache						
Aching muscles						
Joint pains/ stiffness/ limping						
Back or neck pain/stiffness						
Joint swelling						
Painful red eyes						
Dizziness/ faintness						
Other						

If "Other", ***please specify***: .....

MRC use only

2.6 If you answered "**Yes**" to diarrhoea in ***Question 2.5***, what was the greatest number of times your child went to the lavatory with diarrhoea in any 24-hour period?

Number of times ☐☐ Not sure ☐

2.7 If you answered "**Yes**" to vomiting in ***Question 2.5***, what was the greatest number of times he/she vomited (was sick) in any 24-hour period?

Number of times ☐☐ Not sure ☐

2.8 If you answered "**Yes**" to joint swelling in ***Question 2.5***, which of your child's joints were swollen?
(e.g. left knee, both knees, etc.)

..... Not sure ☐

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH A SIMILAR ILLNESS

3.1 How many different people ***(excluding the child who was ill)*** lived or spent a night in your household ***IN THE 10 DAYS BEFORE THIS CHILD'S ILLNESS STARTED***? ..... people

Please fill in the following details for all of these people, EXCLUDING THE SICK CHILD: their age and sex, whether they are a permanent member of the household or a visitor, and whether they were ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED.

The example on how to enter is for a female member of the household aged 43, who was ill with diarrhoea or vomiting IN THE 10 DAYS BEFORE YOUR CHILD'S ILLNESS STARTED.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure
	43	F	✓		✓		
Person 1:							
Person 2:							
Person 3:							
Person 4:							
Person 5:							
Person 6:							
Person 7:							
Person 8:							

MRC use only

3.2 Was the sick child the first person in the household to be ill? Yes ☐ No ☐ Not sure ☐ ☐

If "**No**", please give the **PERSON NUMBER** ***(from Question 3.1)*** of the first person to be ill: Person ..... ☐☐

3.3 Did your child have contact ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", how many people? ..... ☐☐

3.4 If "**Yes**" to ***Question 3.3***, where did this contact occur? ***(tick all boxes that apply)***

Pre-school child group ***(e.g. nursery, toddlers group)*** ☐ School ☐

Social occasion ***(e.g. friend's house, meal out)*** ☐ *Other* ☐

*If "Other", **please specify**:* ..... ☐☐

SECTION 4 THIS SECTION CONCERNS YOUR CHILD'S TRAVEL AND LEISURE ACTIVITY IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED

4.1 During this time, did your child spend one or more nights away from home?

Yes ☐ ↓ No ☐ → If "**No**", please go to **QUESTION 4.6** ☐

If "**Yes**", please continue:

4.2 Was he/she away?: On holiday ☐ Other ☐ ☐

4.3 Was he/she staying?: In the UK ☐ Abroad ☐ ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: ..... ☐☐

MRC use only

4.4 What was the main resort/town stayed at? ..... ☐☐

4.5 Where did your child **EAT** most of his/her meals? ***(tick one box)***

Hotel/guest house	☐	Self-catering in an apartment, villa, etc.	☐
Camping	☐	Restaurant, café, etc.	☐
Private house	☐	Other	☐

If "Other", ***please specify***: ..... ☐☐

4.6 Did your child go swimming or join in water sports ***(e.g. sailing, water skiing)*** in the UK or abroad?

Yes ☐ ↓ No ☐ → If "**No**", please go to **SECTION 5** ☐

If "**Yes**", ***please specify*** type(s) of activity: .....

..... ☐☐

.....

4.7 Where did this activity take place? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

☐☐

If "Other", ***please specify***: .....

4.8 Did he/she swallow any water in any of the following? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other
UK	☐	☐	☐	☐	☐
Abroad	☐	☐	☐	☐	☐

☐☐

If "Other", ***please specify***: .....

MRC use only

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND YOUR CHILD'S CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ No ☐ → If "No", please go to **QUESTION 5.6** ☐

If "**Yes**", ***please indicate*** which pet(s) ***(tick all boxes that apply)***

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐

If "Other", ***please specify***: .....

5.2 Did your child clean up any pet's motions (mess) or clean out the cage/aquarium/litter tray, etc. of any of your pets ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which pet(s): ..... ☐ ☐

5.3 Did any of your pets, where relevant, have diarrhoea ***IN THE 10 DAYS BEFORE YOUR CHILD'S ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which pet(s): ..... ☐ ☐

5.4 Do you feed your pet(s) with any of the following?: ***(tick all that apply)***

Raw meat/fish	☐	☐
Cooked meat/fish from a shop	☐	☐
Meat/fish cooked at home	☐	☐
Canned meat/fish	☐	☐

MRC use only

5.5 If you have a cat or dog, where is it normally fed? ***(please tick one box)***

In the kitchen (on the floor)	☐
In the kitchen (on a worktop/table)	☐
Outside	☐
Other	☐

If "Other", ***please specify***: ..... ☐ ☐

5.6 Was the sick child in close contact with any other animals ***(e.g. zoo, farm, other people's pets) IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", ***please specify*** which animal(s): ..... ☐ ☐

..... ☐ ☐

Please specify where ***(e.g. zoo, farm, etc.)***: ..... ☐ ☐

SECTION 6 THIS SECTION ASKS ABOUT YOUR CHILD'S FOOD AND WATER CONSUMPTION

6.1 Did your child eat ***ANY OF THE FOLLOWING FOODS IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

	Yes	Not sure	
Meat:			
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc.)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE 10 DAYS BEFORE YOUR CHILD WAS ILL*** did he/she eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

MRC use only

The following questions ask for more details about particular foods.

6.3 If your child ate chicken ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***, was this?: ***(tick all boxes that apply)***

- Bought raw fresh, cooked and eaten at home
- Bought raw frozen, cooked and eaten at home
- Pre-cooked, eaten at home hot (include ready-made dinners)
- Pre-cooked, eaten at home cold
- In a hot or cold take-away meal (include sandwiches)
- In a hot or cold meal not at home (e.g. restaurant/canteen)
- Barbecued chicken

6.4 How many times **IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED** did your child eat chicken? ***(tick one box)***

Never ☐ Once ☐ More than once ☐ ---> how many times? .....

6.5 ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***, did he/she help **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐

6.6 If you bought chicken, was this?: ***(tick all that apply)***

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐

6.7 If your child ate cold, shop-sliced meats ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***, where were they bought? ***(tick all that apply)***

	Butcher	Delicatessen	Supermarket	Other shop
Pork/ham	☐	☐	☐	☐
Chicken/turkey	☐	☐	☐	☐
Beef	☐	☐	☐	☐
Corned beef	☐	☐	☐	☐
Tongue	☐	☐	☐	☐
Other	☐	☐	☐	☐

If "Other", ***(please specify)***: .....

MRC use only

6.8 Did your child eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

6.9 Did he/she eat any of the following milk and dairy products ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***? ***(tick all that apply)***

	Pasteurised	Unpasteurised	Not sure if pasteurised
Goats'/sheep's milk	☐	☐	☐
Soft cheese	☐	☐	☐
Fromage frais	☐	☐	☐
Yoghurt	☐	☐	☐
Ice cream	☐	☐	☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐

6.10 Are you and the child who was ill vegetarians?

	You	Your child
No	☐	☐
Partial vegetarian (don't eat meat, but eat fish)	☐	☐
Strict vegetarian (don't eat meat or fish)	☐	☐
Vegan (don't eat meat, fish or dairy products)	☐	☐

6.11 Did your child take any antibiotics prescribed by a doctor ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

6.12 Did he/she take indigestion medicines, bought over the counter or prescribed by a doctor, ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

MRC use only

6.13 Did your child take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by a doctor, ***IN THE 10 DAYS BEFORE HIS/HER ILLNESS STARTED***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

Drinking cold water

6.14 ***IN THE 10 DAYS BEFORE YOUR CHILD'S ILLNESS STARTED***, how many glasses (a glass holds about ¼ pint) of the following types of **UNBOILED WATER** did he/she drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE OR UNSURE FOR ANY TYPE OF WATER, LEAVE BLANK)

	Approximate number of glasses per day	
	In the UK	Abroad
Mains water	☐☐	☐☐
Bottled water: fizzy, sparkling	☐☐	☐☐
Bottled water: still	☐☐	☐☐
Non-mains water (e.g. borehole, well, spring)	☐☐	☐☐
Water dispenser	☐☐	☐☐

6.15 During this period did he/she have any ice in drinks?

In the UK: Yes ☐ No ☐

Abroad: Yes ☐ No ☐

6.16 Do you filter your water? Yes ☐ No ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐

MRC use only

Is the child who was ill less than 1 year old?

Yes ☐ No ☐ → If "**No**", please go to **SECTION 7**

If "**Yes**", please continue:

6.17 How is your baby currently being fed milk? ***(please tick one box)***

Breast feed only ☐ Mixed breast/bottle feed ☐

Bottle feed only ☐ Other ☐

6.18 Have you started weaning your baby onto solids?

Yes ☐ No ☐

6.19 If not currently breast feeding, has your baby ever been breast fed?

Yes ☐ No ☐

If "**Yes**", how old (in months) was your baby when this was stopped? ☐☐

6.20 If your baby is being bottle fed, how do you sterilise the bottles/teats, etc.?

Cold water with chemicals ☐ Boiling water ☐

Steam ☐ Other ☐

If "Other", ***please specify***: .....

6.21 If your baby is being bottle fed, do you usually boil water to make the feed?

Yes ☐ No ☐

MRC use only

6.22 How do you store the baby's bottled milk before feeding?

In the fridge ☐
At room temperature ☐
Other ☐ ☐

If "Other", ***please specify***: .....

6.23 Do you give your baby water to drink? Yes ☐ No ☐ ☐

If "**Yes**", is it boiled first? Yes ☐ No ☐ ☐

(Please note: Sections 7, 8 and 9 are not relevant to this questionnaire)

SECTION 10 **Finally, what do you think was responsible for your child's illness?** ***(please give details below):***

.....
.....
..... ☐☐☐
.....

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q2.5

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NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

Study type	2
Practice number	
Study number	
Case/control	0
Case/control number	

PLEASE READ THIS PAGE FIRST

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing to participate in this part of the study as a control for comparison. The answers you give will help us to discover ways of preventing these types of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

(Please note: Section 1 is not relevant to this questionnaire)

SECTION 2 THIS SECTION ASKS ABOUT ANY SYMPTOMS YOU MAY HAVE EXPERIENCED RECENTLY

2.1 ***IN THE LAST 10 DAYS***, did you have any diarrhoea or vomiting?

Yes ☐ No ☐

If "Yes", you do not need to complete any more questions. Please return the questionnaire in the stamped, addressed envelope provided.

If "**No**", please continue:

2.2 Do you suffer from any long-standing illness or disability?

Yes ☐ No ☐

If "**Yes**", ***please specify***: .....

.....

.....

.....

MRC use only

2.3 ***DURING THE LAST 3 WEEKS*** have you had any of the symptoms listed below? ***(tick all boxes that apply)***

Diarrhoea	☐	Headaches	☐	☐☐
Blood in motions	☐	Dizzy spells	☐	☐☐
Vomiting	☐	Seeing double	☐	☐☐
Abdominal (tummy) pain	☐	Clumsiness of hands (eg. dropping things)	☐	☐☐
Loss of appetite	☐	Unsteady walking (eg. falling over)	☐	☐☐
Loss of weight	☐	Pins and needles	☐	☐☐
Excessive Flatulence (breaking wind)	☐	Weakness of hands (eg. difficulty gripping things)	☐	☐☐
Discomfort in passing urine	☐	Weakness of legs (eg. difficulty walking or rising)	☐	☐☐
Discharge from vagina or penis	☐	Faintness or fits	☐	☐☐
Joint pains or stiffness	☐	Feeling tired	☐	☐☐
Joint swelling	☐	Painful red eye(s)	☐	☐☐
Back or neck pain/ stiffness	☐	Greater desire to sleep	☐	☐☐
Aching muscles	☐	Skin rash	☐	☐☐
Pain in heels	☐	Other	☐	☐☐

If "Other", ***please specify***: ..... ☐☐

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH DIARRHOEA OR VOMITING

3.1 How many different people ***(excluding you)*** lived or spent a night in your household ***IN THE LAST 10 DAYS***? ..... people ☐

MRC use only

Please fill in the following details for all of these people, EXCLUDING YOURSELF: their age and sex, whether they are a permanent member of the household or a visitor, and whether they have been ill with diarrhoea or vomiting IN THE LAST 10 DAYS.

The example on how to enter is for a female member of the household aged 43, who has been ill with diarrhoea or vomiting IN THE 10 LAST DAYS.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure	
	43	F	✓		✓			
Person 1:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 2:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 3:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 4:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 5:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 6:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 7:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐
Person 8:	☐	☐	☐	☐	☐	☐	☐	☐☐☐☐☐

(Please note: question 3.2 not relevant to this questionnaire)

3.3 Did you have contact ***IN THE LAST 10 DAYS*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", how many people? ..... ☐☐

3.4 If "**Yes**" to ***Question 3.3***, where did this contact occur? ***(tick all boxes that apply)***

Pre-school child group ***(e.g. nursery, toddlers group)***	☐	School	☐
Workplace	☐	Social occasion ***(e.g. friend's house, meal out)***	☐
Other	☐	Not applicable	☐

If "Other", ***please specify***: ..... ☐☐

MRC use only

SECTION 4 THIS SECTION ASKS ABOUT YOUR TRAVEL AND LEISURE ACTIVITY IN THE LAST 10 DAYS

4.1 During this time, did you spend one or more nights away from home? *(exclude shift work)*

Yes ☐ ↓ No ☐ → If "No", please go to **QUESTION 4.6** ☐

If "**Yes**", please continue:

4.2 Were you away?: On holiday ☐ On business ☐ Other ☐ ☐

4.3 Were you staying?: In the UK ☐ Abroad ☐ ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: ..... ☐☐

4.4 What was the main resort/town stayed at? ..... ☐☐

4.5 Where did you **EAT** most of your meals? *(tick one box)*

Hotel/guest house	☐	Self-catering in an apartment, villa, etc.	☐
Camping	☐	Restaurant, café, etc.	☐
Private house	☐	Other	☐ ☐☐

If "Other", ***please specify***: .....

4.6 Did you go swimming or join in water sports *(e.g. sailing, water skiing)* in the UK or abroad?

Yes ☐ ↓ No ☐ → If "No", please go to **SECTION 5** ☐

If "**Yes**", ***please specify*** type(s) of activity: .....

..... ☐☐

.....

MRC use only

4.7 Where did this activity take place? *(tick all that apply)*

	Swimming pool	Sea	River	Lake	Other	
UK	☐	☐	☐	☐	☐	☐☐
Abroad	☐	☐	☐	☐	☐	

If "Other", ***please specify***: .....

4.8 Did you swallow any water in any of the following? *(tick all that apply)*

	Swimming pool	Sea	River	Lake	Other	
UK	☐	☐	☐	☐	☐	☐☐
Abroad	☐	☐	☐	☐	☐	

If "Other", ***please specify***: .....

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ ↓ No ☐ → If "No", please go to **QUESTION 5.6** ☐

If "**Yes**", ***please indicate*** which pet(s) *(tick all boxes that apply)*

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐☐

If "Other", ***please specify***: .....

MRC use only

5.2 Did you clean up any pet's motions (mess) or clean out the cage/aquarium/litter tray, etc. of any of your pets ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", ***please specify*** which pet(s): .....

5.3 Did any of your pets, where relevant, have diarrhoea ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", ***please specify*** which pet(s): .....

5.4 Do you feed your pet(s) with any of the following?: ***(tick all that apply)***

- Raw meat/fish ☐
- Cooked meat/fish from a shop ☐
- Meat/fish cooked at home ☐
- Canned meat/fish ☐

5.5 If you have a cat or dog, where do you normally feed it? ***(please tick one box)***

- In the kitchen (on the floor) ☐
- In the kitchen (on a worktop/table) ☐
- Outside ☐
- Other ☐

If "Other", ***please specify***: .....

5.6 Have you been in close contact with any other animals ***(e.g. zoo, farm, other people's pets) IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", ***please specify*** which animal(s): .....

.....

Please specify where ***(e.g. zoo, farm, etc.)***: .....

MRC use only

SECTION 6 THIS SECTION ASKS ABOUT YOUR FOOD AND WATER CONSUMPTION

6.1 Have you eaten ***ANY OF THE FOLLOWING FOODS IN THE LAST 10 DAYS***?
(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

	Yes	Not sure	
Meat:			
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE LAST 10 DAYS*** did you eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Meals-on-wheels	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

The following questions ask for more details about particular foods.

6.3 If you have eaten chicken ***IN THE LAST 10 DAYS***, was this?: ***(tick all boxes that apply)***

Bought raw fresh, cooked and eaten at home	☐
Bought raw frozen, cooked and eaten at home	☐
Pre-cooked, eaten at home hot (include ready-made dinners)	☐
Pre-cooked, eaten at home cold	☐
In a hot or cold take-away meal (include sandwiches)	☐
In a hot or cold meal not at home (e.g. restaurant/canteen)	☐
Barbecued chicken	☐ ☐☐

6.4 How many times **IN THE LAST 10 DAYS** did you eat chicken? ***(tick one box)***

Never ☐ Once ☐ More than once ☐ ---> how many times? ..... ☐

MRC use only

6.5 ***IN THE LAST 10 DAYS***, did you **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐ ☐

6.6 If you bought chicken, was this?:
(tick all that apply)

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐ ☐☐

6.7 If you ate cold, shop-sliced meats ***IN THE LAST 10 DAYS***, where were they bought? ***(tick all that apply)***

	Butcher	Delicatessen	Supermarket	Other shop	
Pork/ham	☐	☐	☐	☐	
Chicken/turkey	☐	☐	☐	☐	
Beef	☐	☐	☐	☐	
Corned beef	☐	☐	☐	☐	
Tongue	☐	☐	☐	☐	
Other	☐	☐	☐	☐	☐☐

If "Other", ***(please specify)***: ..... ☐☐

6.8 Did you eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐ ☐

6.9 Did you eat any of the following milk and dairy products ***IN THE LAST 10 DAYS***? ***(tick all that apply)***

	Pasteurised	Unpasteurised	Not sure if pasteurised	
Goats'/sheep's milk	☐	☐	☐	
Soft cheese	☐	☐	☐	
Fromage frais	☐	☐	☐	
Yoghurt	☐	☐	☐	
Ice cream	☐	☐	☐	☐☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐ ☐

MRC use only

6.10 Are you a vegetarian?

No	☐	
Partial vegetarian (don't eat meat, but eat fish)	☐	
Strict vegetarian (don't eat meat or fish)	☐	
Vegan (don't eat meat, fish or dairy products)	☐	☐☐

6.11 Did you take any antibiotics prescribed by your doctor ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", please give the **NAME** of each if possible: .....

..... ☐☐☐

.....

6.12 Did you take indigestion medicines, bought over the counter or prescribed by your doctor, ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", please give the **NAME** of each if possible: .....

..... ☐☐☐

.....

6.13 Did you take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by your doctor, ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐ ☐

If "**Yes**", please give the **NAME** of each if possible: .....

..... ☐☐☐

.....

MRC use only

Drinking cold water

6.14 ***IN THE LAST 10 DAYS***, how many glasses (a glass holds about ½ pint) of the following types of **UNBOILED WATER** did you drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE, LEAVE BLANK)

	Approximate number of glasses per day		
	In the UK	Abroad	
Mains water	☐	☐	☐☐☐☐
Bottled water: fizzy, sparkling	☐	☐	☐☐☐☐
Bottled water: still	☐	☐	☐☐☐☐
Non-mains water (e.g. borehole, well, spring)	☐	☐	☐☐☐☐
Water dispenser	☐	☐	☐☐☐☐

6.15 During this period did you have any ice in drinks?

In the UK:	Yes ☐	No ☐	☐
Abroad:	Yes ☐	No ☐	☐

6.16 Do you filter your water? Yes ☐ No ☐ ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐ ☐

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q2.6

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE:

Study type [2]

Practice number [ ][ ][ ]

Study number [ ][ ][ ]

Case/control [0]

Case/control number [ ][ ]

PLEASE READ THIS PAGE FIRST

Dear Parent/Guardian,

The Medical Research Council would like to find out more about the occurrence of gastroenteritis (stomach upsets) and has set up this study to try to learn more about its causes. Thank you for agreeing for your child to participate in this part of the study as a control for comparison. The answers you give will help us to discover ways of preventing this type of illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

(Please note: Section 1 is not relevant to this questionnaire)

SECTION 2 THIS SECTION ASKS ABOUT ANY SYMPTOMS YOUR CHILD MAY HAVE EXPERIENCED RECENTLY

2.1 ***IN THE LAST 10 DAYS***, did your child have any diarrhoea or vomiting?

Yes ☐ No ☐ ☐

If "Yes", you do not need to complete any more questions. Please return the questionnaire in the stamped, addressed envelope provided.

If "No", please continue:

2.2 Does your child suffer from any long-standing illness or disability?

Yes ☐ No ☐ ☐

If "Yes", ***please specify***: .....

.....

.....

..... ☐☐

MRC use only

2.3 ***DURING THE LAST 3 WEEKS*** has your child had any of the symptoms listed below? ***(tick all boxes that apply)***

Diarrhoea	☐	Headaches	☐
Blood in motions	☐	Dizzy spells	☐
Vomiting	☐	Seeing double	☐
Abdominal (tummy) pain	☐	Clumsiness of hands (eg. dropping things)	☐
Loss of appetite	☐	Unsteady walking (eg. falling over)	☐
Loss of weight	☐	Pins and needles	☐
Excessive Flatulence (breaking wind)	☐	Weakness of hands (eg. difficulty gripping things)	☐
Discomfort in passing urine	☐	Weakness of legs (eg. difficulty walking or rising)	☐
Cough/runny nose/ sore throat	☐	Faintness or fits	☐
Joint pains/stiffness Limping	☐	Feeling tired	☐
Joint swelling	☐	Painful red eye(s)	☐
Back or neck pain/ stiffness	☐	Greater desire to sleep	☐
Aching muscles	☐	Skin rash	☐
Pain in heels	☐	Other	☐

If "Other", ***please specify***: .....

MRC use only

SECTION 3 THIS SECTION ASKS ABOUT OTHER MEMBERS OF YOUR HOUSEHOLD AND WHETHER THEY WERE AFFECTED WITH A SIMILAR ILLNESS

3.1 How many different people ***(excluding the child named in the accompanying letter)*** lived or spent a night in your household ***IN THE LAST 10 DAYS*** ?

..... *people*

Please fill in the following details for all of these people, EXCLUDING THE CHILD CONCERNED: their age and sex, whether they are a permanent member of the household or a visitor, and whether they were ill with diarrhoea or vomiting IN THE LAST 10 DAYS.

The example on how to enter is for a female member of the household aged 43, who was ill with diarrhoea or vomiting IN THE LAST 10 DAYS.

Person number	Age (years)	Sex M/F	Permanent member	Visitor	Illness present: Yes	Illness present: No	Illness present: Not sure
	43	F	✓		✓		
Person 1:							
Person 2:							
Person 3:							
Person 4:							
Person 5:							
Person 6:							
Person 7:							
Person 8:							

(**Please note**: Question 3.2 not relevant to this questionnaire)

3.3 Did your child have contact ***IN THE LAST 10 DAYS*** with any other people outside the household who you know were suffering with diarrhoea or vomiting?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", how many people? .....

MRC use only

3.4 If "**Yes**" to ***Question 3.3***, where did this contact occur? *(tick all boxes that apply)*

Pre-school child group *(e.g. nursery, toddlers group)* ☐ School ☐

Social occasion *(e.g. friend's house, meal out)* ☐ other ☐

If "Other", ***please specify***: ..... ☐☐

SECTION 4 THIS SECTION CONCERNS YOUR CHILD'S TRAVEL AND LEISURE ACTIVITY IN THE LAST 10 DAYS

4.1 During this time, did your child spend one or more nights away from home?

Yes ☐ ↓ No ☐ → If "**No**", please go to **QUESTION 4.6** ☐

If "**Yes**", please continue:

4.2 Was he/she away?: On holiday ☐ Other ☐ ☐

4.3 Was he/she staying?: In the UK ☐ Abroad ☐ ☐

The UK includes England, Wales, Scotland, Northern Ireland, the Isle of Man and the Channel Islands

If not the UK, please state which country: ..... ☐☐

MRC use only

4.4 What was the main resort/town stayed at? ..... ☐☐

4.5 Where did your child **EAT** most of his/her meals? ***(tick one box)***

Hotel/guest house ☐ Self-catering in an apartment, villa, etc. ☐

Camping ☐ Restaurant, café, etc. ☐

Private house ☐ Other ☐ ☐

If "Other", ***please specify***: .....

4.6 Did your child go swimming or join in water sports ***(e.g. sailing, water skiing)*** in the UK or abroad?

Yes ☐ ↓ No ☐ → If "**No**", please go to **SECTION 5** ☐

If "**Yes**", ***please specify*** type(s) of activity: .....

..... ☐☐

.....

4.7 Where did this activity take place? ***(tick all that apply)***

	Swimming pool	Sea	River	Lake	Other	
UK	☐	☐	☐	☐	☐	
Abroad	☐	☐	☐	☐	☐	☐☐

If "Other", ***please specify***: .....

4.8 Did he/she swallow any water in any of the following? *(tick all that apply)*

	Swimming pool	Sea	River	Lake	Other	
UK	☐	☐	☐	☐	☐	
Abroad	☐	☐	☐	☐	☐	☐☐

If "Other", ***please specify***: .....

MRC use only

SECTION 5 THIS SECTION ASKS ABOUT YOUR PETS AND YOUR CHILD'S CONTACT WITH OTHER ANIMALS

5.1 Do you have any pets?

Yes ☐ No ☐ → If "No", please go to QUESTION 5.6 ☐

If "Yes", *please indicate* which pet(s) *(tick all boxes that apply)*

Dogs, adult	☐	Lizards/snakes	☐
Puppies (up to 1 year)	☐	Tortoise	☐
Cats/kittens	☐	Terrapins	☐
Rabbits/guinea pigs/ gerbils/hamsters	☐	Fish in aquarium/bowl	☐
Horses/ponies	☐	Fish in pond	☐
Birds	☐	Other	☐ ☐☐

If "Other", *please specify*: .....

5.2 Did your child clean up any pet's motions (mess) or clean out the cage/aquarium/litter tray, etc. of any of your pets *IN THE LAST 10 DAYS*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which pet(s): ..... ☐☐

5.3 Did any of your pets, where relevant, have diarrhoea *IN THE LAST 10 DAYS*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which pet(s): ..... ☐☐

5.4 Do you feed your pet(s) with any of the following?: *(tick all that apply)*

Raw meat/fish	☐	☐
Cooked meat/fish from a shop	☐	☐
Meat/fish cooked at home	☐	☐
Canned meat/fish	☐	☐

MRC use only

5.5 If you have a cat or dog, where is it normally fed? *(please tick one box)*

In the kitchen (on the floor)	☐
In the kitchen (on a worktop/table)	☐
Outside	☐
Other	☐

If "Other", *please specify*: ..... ☐☐

5.6 Was your child in close contact with any other animals *(e.g. zoo, farm, other people's pets) IN THE LAST 10 DAYS*?

Yes ☐ No ☐ Not sure ☐ ☐

If "Yes", *please specify* which animal(s): ..... ☐☐

..... ☐☐

Please specify where *(e.g. zoo, farm, etc.)*: ..... ☐

SECTION 6 THIS SECTION ASKS ABOUT YOUR CHILD'S FOOD AND WATER CONSUMPTION

6.1 Did your child eat *ANY OF THE FOLLOWING FOODS IN THE LAST 10 DAYS*?

(Please tick "Yes" [or "Not sure"] for each food listed, or LEAVE BLANK IF NOT EATEN)

	Yes	Not sure	
Meat:			
Chicken	☐	☐	☐
Other poultry (turkey, duck, etc.)	☐	☐	☐
Beef	☐	☐	☐
Lamb/mutton	☐	☐	☐
Pork/ham	☐	☐	☐
Offal products (liver, kidney, tripe, etc.)	☐	☐	☐
Meat pies/pasties	☐	☐	☐
Meat pâté	☐	☐	☐
Sausages	☐	☐	☐
Burgers	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Fish or shellfish:			
Oily fish (e.g. mackerel, herring, tuna)	☐	☐	☐
Non-oily fish (e.g. cod, haddock, plaice)	☐	☐	☐
Oysters	☐	☐	☐
Cockles, mussels, clams	☐	☐	☐
Whelks, winkles	☐	☐	☐
Crab, lobster	☐	☐	☐
Prawns, shrimps	☐	☐	☐
Salads/vegetables/fruit eaten raw:			
Raw salad/vegetable/coleslaw prepared at home	☐	☐	☐
Prepared raw salad/vegetable/coleslaw from a shop	☐	☐	☐
Raw salad/vegetable/coleslaw eaten at a restaurant	☐	☐	☐
Pulse vegetables (lentils, beans etc.)	☐	☐	☐
Tofu (bean curd)	☐	☐	☐
Cold rice salad	☐	☐	☐
Apple/pear/peach/nectarine/grapes	☐	☐	☐
Orange/tangerine/clementine/banana/kiwi fruit	☐	☐	☐
Other tropical fruit (e.g. mango, starfruit, etc.)	☐	☐	☐
Melon	☐	☐	☐
Dried fruits (raisins, sultanas, apricots, etc.)	☐	☐	☐
Desiccated coconut	☐	☐	☐
Cooked rice:			
Boiled rice, eaten immediately	☐	☐	☐
Boiled rice, reheated	☐	☐	☐
Fried rice	☐	☐	☐
Milk products:			
Pasteurised milk (carton or silver, red, gold top bottle)	☐	☐	☐
Unpasteurised milk (carton or green top bottle)	☐	☐	☐
Bottled milk which had the top pecked by birds	☐	☐	☐
Bakery products:			
Fresh cream cakes or tarts	☐	☐	☐
Artificial cream cakes, custard or vanilla slices	☐	☐	☐

continued .....

MRC use only

	Yes	Not sure	
Egg or egg products:			
Runny egg (boiled, scrambled, fried, poached, etc.)	☐	☐	☐
Well-cooked egg (boiled, scrambled, etc.)	☐	☐	☐
Raw egg (egg-nog, etc.)	☐	☐	☐
Home-made sauce (e.g. mayonnaise, etc.)	☐	☐	☐
Home-made sweet/pudding (mousse, Tiramisu, etc.)	☐	☐	☐

6.2 ***IN THE LAST 10 DAYS*** did he/she eat any of the following meals prepared outside the home?

	Yes	Not sure	
Fast food: Chicken	☐	☐	☐
Fast food: Beef/hamburger	☐	☐	☐
Fast food: Doner kebab	☐	☐	☐
Take-away or home delivery meal:			
Sandwich bar	☐	☐	☐
Fish and chips	☐	☐	☐
Pizza	☐	☐	☐
Chinese food	☐	☐	☐
Indian food	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Restaurant meal:			
English (include Public House)	☐	☐	☐
Chinese	☐	☐	☐
Indian	☐	☐	☐
Other nationality ***(please specify)***:	☐	☐	☐☐
Canteen (work, school, hospital, etc.)	☐	☐	☐
Reception/party (e.g. wedding, etc.)	☐	☐	☐

MRC use only

The following questions ask for more details about particular foods.

6.3 If your child ate chicken ***IN THE LAST 10 DAYS*** was this?:
(tick all boxes that apply)

- Bought raw fresh, cooked and eaten at home
- Bought raw frozen, cooked and eaten at home
- Pre-cooked, eaten at home hot (include ready-made dinners)
- Pre-cooked, eaten at home cold
- In a hot or cold take-away meal (include sandwiches)
- In a hot or cold meal not at home (e.g. restaurant/canteen)
- Barbecued chicken

6.4 How many times **IN THE LAST 10 DAYS** did your child eat chicken?
(tick one box)

Never ☐ Once ☐ More than once ☐ ---> how many times? .....

6.5 ***IN THE LAST 10 DAYS***, did he/she help **PREPARE** fresh chicken for eating?

Yes ☐ No ☐ Not sure ☐

6.6 If you bought chicken, was this?:
(tick all that apply)

	Fresh	Frozen
Ready gutted, with giblets	☐	☐
Ready gutted, without giblets	☐	☐
Ungutted	☐	☐
Kosher	☐	☐
Halal	☐	☐

6.7 If your child ate cold, shop-sliced meats ***IN THE LAST 10 DAYS***, where were they bought?
(tick all that apply)

	Butcher	Delicatessen	Supermarket	Other shop
Pork/ham	☐	☐	☐	☐
Chicken/turkey	☐	☐	☐	☐
Beef	☐	☐	☐	☐
Corned beef	☐	☐	☐	☐
Tongue	☐	☐	☐	☐
Other	☐	☐	☐	☐

If "Other", ***(please specify)***: .....

MRC use only

6.8 Did your child eat any other foods from a delicatessen or supermarket delicatessen counter ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

6.9 Did he/she eat any of the following milk and dairy products ***IN THE LAST 10 DAYS***?
(tick all that apply)

	Pasteurised	Unpasteurised	Not sure if pasteurised
Goats'/sheep's milk	☐	☐	☐
Soft cheese	☐	☐	☐
Fromage frais	☐	☐	☐
Yoghurt	☐	☐	☐
Ice cream	☐	☐	☐

Were any of the products ticked above made abroad?

Yes ☐ No ☐ Not sure ☐

6.10 Are you and your child vegetarians?

	You	Your child
No	☐	☐
Partial vegetarian (don't eat meat, but eat fish)	☐	☐
Strict vegetarian (don't eat meat or fish)	☐	☐
Vegan (don't eat meat, fish or dairy products)	☐	☐

6.11 Did your child take any antibiotics prescribed by a doctor ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....
.....
.....

6.12 Did he/she take indigestion medicines, bought over the counter or prescribed by a doctor, ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....
.....
.....

MRC use only

6.13 Did your child take any other medicines (tablets, pills, liquids, etc.), bought over the counter or prescribed by a doctor, ***IN THE LAST 10 DAYS***?

Yes ☐ No ☐ Not sure ☐

If "**Yes**", please give the **NAME** of each if possible: .....

.....

.....

Drinking cold water

6.14 ***IN THE LAST 10 DAYS***, how many glasses (a glass holds about ¼ pint) of the following types of **UNBOILED WATER** did he/she drink **PER DAY** on average (include diluted drinks)?

(enter number of glasses for all that apply; IF NONE OR UNSURE FOR ANY TYPE OF WATER, LEAVE BLANK)

	Approximate number of glasses per day	
	In the UK	Abroad
Mains water	☐☐	☐☐
Bottled water: fizzy, sparkling	☐☐	☐☐
Bottled water: still	☐☐	☐☐
Non-mains water (e.g. borehole, well, spring)	☐☐	☐☐
Water dispenser	☐☐	☐☐

6.15 During this period did he/she have any ice in drinks?

In the UK: Yes ☐ No ☐

Abroad: Yes ☐ No ☐

6.16 Do you filter your water? Yes ☐ No ☐

If "**Yes**", what method do you use?

Jug ☐ Plumbed-in filter ☐ Other ☐

MRC use only

Is your child less than 1 year old?

Yes ☐ No ☐ → If "No", please go to **SECTION 7**

If "**Yes**", please continue:

6.17 How is your baby currently being fed milk ? ***(please tick one box)***

Breast feed only ☐ Mixed breast/bottle feed ☐

Bottle feed only ☐ Other ☐

6.18 Have you started weaning your baby onto solids?

Yes ☐ No ☐

6.19 If not currently breast feeding, has your baby ever been breast fed?

Yes ☐ No ☐

If "**Yes**", how old (in months) was your baby when this was stopped? ☐☐

6.20 If your baby is being bottle fed, how do you sterilise the bottles/teats, etc.?

Cold water with chemicals ☐ Boiling water ☐

Steam ☐ Other ☐

If "Other", ***please specify***: .....

6.21 If your baby is being bottle fed, do you usually boil water to make the feed?

Yes ☐ No ☐

MRC use only

6.22 How do you store the baby's bottled milk before feeding?

In the fridge ☐
At room temperature ☐
Other ☐ ☐

If "Other", *please specify*: .....

6.23 Do you give your baby water to drink? Yes ☐ No ☐ ☐

If "Yes", is it boiled first? Yes ☐ No ☐ ☐

THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE. PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN IT AS SOON AS POSSIBLE USING THE STAMPED, ADDRESSED ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE PASSED OUTSIDE OF THIS STUDY WITHOUT YOUR PERMISSION.

IN CONFIDENCE

GE Q4B

MRC USE ONLY

NATIONAL GASTROENTERITIS STUDY

TO BE COMPLETED BY THE TRIAL NURSE

PLEASE ENTER APPROPRIATE STUDY NUMBER:

GP case/control ☐☐☐☐☐☐☐☐

Cohort nested case/control ☐☐☐☐☐☐☐☐☐☐

Enumeration ☐☐☐☐☐☐☐

PLEASE READ THIS PAGE FIRST

This questionnaire has been designed to find out about how gastroenteritis affected the person who was ill and their family. Thank you for agreeing to participate in this study following your recent episode of gastroenteritis. It should be filled in by you, or by a parent or guardian if you are a child (under 16 years). Your answers will help us to evaluate ways of preventing such illness.

Please read each question carefully before you answer it and try to answer every section. Questions should be answered by putting a tick in the appropriate box(es) or writing in the space provided.
PLEASE DO NOT WRITE IN THE MARGIN.

When you have completed the questionnaire please return it in the pre-paid envelope supplied. If any questions are not clear, please contact:

Nurse .....

(telephone number: .....***)***

The information you give will be treated in strict confidence.

IID STUDY
IN ENGLAND

MRC use only

SECTION 1 THIS SECTION ASKS FOR SOME BASIC INFORMATION ABOUT THE PERSON WHO WAS ILL (THE PERSON NAMED IN THE ACCOMPANYING LETTER) AND THEIR HOUSEHOLD

1.1 When did your (or your child's) illness start? ...../...../..... day month year ☐

1.2 What is today's date? ...../...../..... day month year ☐

1.3 How many people, including yourself, normally live in your household? ..... people ☐

1.4 Please list the members of your household below (excluding the person who was ill): ***(TICK THOSE WHO HAD A SIMILAR ILLNESS IN THE 10 DAYS BEFORE OR AFTER YOUR/YOUR CHILD'S ILLNESS AND ENTER ANY TIME TAKEN AWAY FROM NORMAL ACTIVITY)***

Relationship to you	Sex	Age (yrs)	Occupation (state rank: e.g. foreman)	Had a similar illness	Days off normal activity
e.g. Husband	(M)/F	26	Car mechanic, employee	✓	5
	M/F				
	M/F				
	M/F				
	M/F				
	M/F				
	M/F				
	M/F				
	M/F				

☐☐☐
☐☐☐
☐☐☐
☐☐☐
☐☐☐
☐☐☐
☐☐☐
☐☐☐

1.5 Since your/your child's gastroenteritis started, have you/your child developed and continued to have any of the following symptoms? Do not include any long-term symptoms you had before the gastroenteritis. ***(tick all boxes that apply)***:

Diarrhoea	☐	Loss of weight	☐	☐	☐
Blood in motions	☐	Excessive flatulence (breaking wind)	☐	☐	☐
Vomiting (being sick)	☐	Discomfort in passing urine	☐	☐	☐
Abdominal (tummy) pain	☐	Discharge from vagina or penis	☐	☐	☐
Loss of appetite	☐	Joint pains/stiffness or limping	☐	☐	☐

continued .....

MRC use only

Joint swelling	☐	Pins and needles	☐
Back or neck pain/ stiffness	☐	Weakness of hands (e.g. difficulty gripping things)	☐
Aching muscles	☐	Weakness of legs (e.g. difficulty walking or rising)	☐
Pain in heels	☐	Faintness or fits	☐
Headaches	☐	Feeling tired	☐
Dizzy spells	☐	Painful red eye(s)	☐
Seeing double	☐	Desire to sleep more than usual	☐
Clumsiness of hands (e.g. dropping things)	☐	Skin rash	☐
Unsteady walking (e.g. falling over)	☐	Other	☐

If "Other", ***please specify***: .....

1.6 If you/your child had joint pain/swelling, please state which joints were affected:

.....

SECTION 2 THE QUESTIONS IN THIS SECTION ARE TO FIND OUT ABOUT THE EFFECTS OF ILLNESS ON THE PERSON WHO WAS ILL.

2.1 For how many days and half days, ***in total***, were you (or your child) unwell? ..... days

PLEASE ANSWER EACH PART OF QUESTION 2.2, PUTTING 0 IF NONE. THE NUMBERS SHOULD ADD UP TO THE TOTAL DAYS OF ILLNESS GIVEN IN REPLY TO QUESTION 2.1.

2.2 How many of these days and half days were you/your child:

a. In hospital and confined to bed? ..... days
b. In hospital but able to get up? ..... days
c. At home and confined to bed? ..... days
d. At home and able to get up but not able to do normal activities? ..... days
e. At home, but able to get up and do most normal activities? ..... days
f. Feeling ill but able to go to work/school, shops, etc. ..... days

MRC use only

2.3 If adult, how many days and half days paid employment ***(full- or part-time)*** did you miss because of illness? ..... days

2.4 If the ill person is a schoolchild or student, how many days and half days at school/college were missed? ..... days

2.5 How many extra days and half days were you/your child barred from work/school after recovery because of the infection? ..... days

2.6 How many days and half days were you unable to perform normal household activities (e.g. cooking, cleaning, etc.)? ..... days

2.7 For how many days and half days were you unable to take part in your normal leisure activities (e.g. sports, visits to the pub, attending clubs, etc.)? ..... days

2.8 If you were absent from full or part-time paid employment because of your illness, how did this affect your work? ***(please tick appropriate box)***

- It would have to wait until you returned ☐
- It would be done by a colleague ☐
- Your employer paid temporary staff to do your work ☐
- Other ***(please describe)***: ☐

.....

SECTION 3 DID YOU OR YOUR CHILD (i.e. THE PERSON ILL) SEE A DOCTOR (GP) BECAUSE OF THIS ILLNESS?

Yes ☐ No ☐ → If "No", please go to **SECTION 4**

↓

If "**Yes**", please indicate below how many times:
(answer every question)

3.1 Your GP visited you/your child at home ..... times

3.2 You/your child saw your doctor at the surgery ..... times

3.3 You consulted your doctor by telephone ..... times

3.4 You/your child were visited by a nurse/health visitor ..... times

MRC use only

3.5 How many of the following types of specimen were taken from you/ your child and tested? ***(DO NOT INCLUDE THOSE TAKEN IN HOSPITAL)***

stool (faeces) ..... blood ..... urine ..... other ....

3.6 How many visits did you/your child make ***only*** *to deliver specimens to the surgery?* ***(DO NOT COUNT VISITS WHEN A DOCTOR WAS ALSO CONSULTED)*** ..... visits

3.7 How many visits did you/your child make to deliver specimens to a laboratory or environmental health department? ..... visits

3.8 How many times were specimens collected from you/ your child by an Environmental Health Officer? ..... times

3.9 How many specimens were sent by post? ..... specimens

3.10 How long, in hours and half hours ***(from leaving to returning home)***, does a visit to the doctor usually take? ..... hours

3.11 Did someone go with you (or your child) to the doctor's surgery?

Yes ☐ No ☐ → If "No", please go to **Question 3.15**

↓

3.12 Please give details below of any adult (over 16 years) who accompanied you/your child when consulting the doctor:

Relationship to the person ill	Main occupation* (e.g. motor mechanic)	Number of visits made to the doctor's surgery with you/your child
e.g. Mother	Housewife	2

* please state if housewife, unemployed or retired

3.13 What arrangements did the accompanying person(s) have to make? ***(Please tick appropriate box(es):***

None ☐ Time off work ☐

Babysitter or carer for someone they look after ☐ Time off school/college ☐

Cancel planned arrangements ☐ Other ***(please describe)***: ☐

Not known ☐ .....

.....

MRC use only

3.14 If the accompanying person(s) took time off work, how many days and half days were they away in total? ..... days

3.15 Did you (or your child) receive medicines on prescription for this illness?

Yes ☐ No ☐ → If "No", please go to **SECTION 4**

↓

If "Yes", how many items altogether? ..... items

3.16 Is the person who was ill exempt from prescription charges? ***(under 16, retired, pregnant, etc.)***

Yes ☐ No ☐

SECTION 4 AS A RESULT OF THIS ILLNESS DID YOU OR YOUR CHILD (i.e. THE PERSON ILL) GO TO A HOSPITAL ACCIDENT AND EMERGENCY (CASUALTY) DEPARTMENT?

Yes ☐ No ☐ → If "No", please go to **SECTION 5**

↓

If "Yes", how may times? ..... times

4.1 Were you (or your child) admitted to hospital from the Casualty Department? Yes ☐ No ☐

4.2 If not admitted, how long, in total ***(in hours and half hours)***, did your/your child's visit take from leaving to returning home? ..... hours

4.3 Did someone go with you (or your child) to Casualty?

Yes ☐ No ☐ → If "No", please go to **SECTION 5**

↓

4.4 Please give details below of any adult (over 16 years) who accompanied you/your child to the Casualty Department:

Relationship to the person ill	Main occupation* (e.g. motor mechanic)	Number of visits made to the Casualty Dept. with you/your child

* please state if housewife, unemployed or retired

MRC use only

4.5 What arrangements did the accompanying person(s) have to make? *(Please tick appropriate box(es):*

None	☐	Time off work	☐
Babysitter or carer for someone they look after	☐	Time off school/college	☐
Cancel planned arrangements	☐	Other *(please describe)*:	☐
Not known	☐		

4.6 If the accompanying person(s) took time off work, how many days and half days were they away in total? ..... days

SECTION 5 WERE YOU OR YOUR CHILD (i.e. THE PERSON ILL) ADMITTED TO HOSPITAL?

Yes ☐ ↓ No ☐ → If "No", please go to **SECTION 6**

5.1 How many days and half days were you/your child in hospital? ..... days

5.2 On average, how many visitors did you/your child have each day? ..... visitors

5.3 During your (or your child's) hospital stay, how much do you think was spent on?:

Clothes (i.e. night clothes), toilet articles	£.....
Newspapers, books, telephone calls	£.....
Food, sweets, juice, etc.	£.....
Other *(please specify)*	£.....

5.4 If the patient was a child, did any adult(s) stay in hospital with the child?

Yes ☐ ↓ No ☐ → If "No", please go to **SECTION 6**

5.5 Please give details below of any adult (over 16 years) who stayed in hospital with the child:

Relationship to the child	Main occupation* (e.g. motor mechanic)	Number of days and half days spent in hospital

* please state if housewife, unemployed or retired

MRC use only

5.6 What arrangements did the accompanying person(s) have to make? *(Please tick appropriate box(es):*

None	☐	Time off work	☐
Babysitter or carer for someone they look after	☐	Time off school/college	☐
Cancel planned arrangements	☐	Other *(please describe)*:	☐
Not known	☐		

5.7 If the accompanying person(s) took time off work, how many days and half days were they away in total? ..... days

SECTION 6 DID YOU OR YOUR CHILD (i.e. THE PERSON ILL) ATTEND A HOSPITAL OUTPATIENT DEPARTMENT?

Yes ☐ ↓ No ☐ → If "No", please go to **SECTION 7**

6.1 How many times did you/your child go to the Outpatient Department? ..... times

6.2 How long on average, in hours, did each visit take? *(from leaving home to returning home)* ..... hours

6.3 Did someone go with you/your child to the Outpatient Department?

Yes ☐ ↓ No ☐ → If "No", please go to **SECTION 7**

6.4 Please give details below of any adult (over 16 years) who accompanied you/your child to the Outpatient Department:

Relationship to the person ill	Main occupation* (e.g. motor mechanic)	Number of visits made to the Outpatient Dept. with you/your child

* please state if housewife, unemployed or retired

6.5 On average, how much did you/your child *(and the accompanying person)* spend on food/drink on each visit? £.....

MRC use only

6.6 What arrangements did the accompanying person(s) have to make? ***(Please tick appropriate box(es):***

None	☐	Time off work	☐
Babysitter or carer for someone they look after	☐	Time off school/college	☐
Cancel planned arrangements	☐	Other ***(please describe)***:	☐
Not known	☐	.....	

☐☐

6.7 If the accompanying person(s) took time off work, how many days and half days were they away in total? ..... days ☐

SECTION 7 TRAVEL RELATED TO YOUR/YOUR CHILD'S (i.e. THE ILL PERSON'S) ILLNESS

7.1 Please give the number of journeys you or your child ***(the ill person)***, or someone on your behalf, made to see your doctor, attend hospital or deliver specimens. Please indicate how many journeys were by ambulance, car, public transport, etc. ***(Write in the spaces and count both the outward and homeward journeys to the doctor, hospital, etc. – i.e. 1 visit to the doctor's surgery by bus each way equals 2 journeys by public transport)***

		Number of journeys
Journeys by ambulance:	Doctor's surgery	.....
	Hospital (including Casualty & Outpatient Departments)	.....
Journeys by private car:	Doctor's surgery	.....
	Hospital	.....
	Laboratory	.....
	Environmental Health Dept.	.....
Journeys by public transport: (e.g. bus, train, underground)	Doctor's surgery	.....
	Hospital	.....
	Laboratory	.....
	Environmental Health Dept.	.....
Journeys by cab/taxi:	Doctor's surgery	.....
	Hospital	.....
	Laboratory	.....
	Environmental Health Dept.	.....

☐

MRC use only

7.2 If your (or your child's) journeys were made by any other means of transport, please list them below ***(the example is a person who walked to their doctor's surgery once)***:

Other Means of travel	Numbers of journeys to: Doctor's surgery	Hospital: Casualty/Out-patient Dept.	Laboratory	Environmental Health Dept.
e.g. Walking	2	-	-	-
1.				
2.				
3.				

☐☐☐

7.3. How far ***(in miles)*** is your home from:

a. Your doctor's surgery? ..... miles

b. The hospital you/your child attended? ..... miles

c. The laboratory you delivered specimens to? ..... miles

d. Your local Environmental Health Department? ..... miles

☐

SECTION 8 TIME SPENT BY FAMILY AND FRIENDS CARING FOR YOU (OR YOUR CHILD)

8.1 Please give details below of any person ***(family relative or friend)*** who spent time looking after you/your child at home:

(DO NOT INCLUDE TIME SPENT ACCOMPANYING YOU/YOUR CHILD TO THE DOCTOR OR HOSPITAL)

The example is for a part-time working mother who was absent from her employment for 5 days

Relationship to the person ill	Occupation* (e.g. motor mechanic)	Number of days: Caring for you/ your child	Away from paid employment
e.g. Mother	Housewife/p.t. secretary	10	5

☐☐☐☐

* please state if housewife, unemployed or retired

MRC use only

SECTION 9 DID YOU/YOUR CHILD (i.e. THE PERSON ILL) BECOME ILL WHILE ON HOLIDAY OR VISITING AWAY FROM HOME?

Yes ☐ No ☐ → If "No", please go to **SECTION 10**

If "Yes", please continue below:

9.1 Were you (or your child) away: ***(please tick the appropriate box)***

in the UK ☐ abroad ☐

9.2 How long ***(in days)*** was your/your child's holiday? ..... days

9.3 For how many days and half days of the holiday ***(in total)***, were you/your child unwell? ..... days

PLEASE ANSWER EACH PART OF QUESTION 9.4, PUTTING 0 IF NONE. THE NUMBERS SHOULD ADD UP TO THE TOTAL DAYS OF ILLNESS GIVEN IN REPLY TO QUESTION 9.3.

9.4 How many days and half days of the illness ***(your reply to Question 9.3)*** were you (or your child):

a. Confined to bed? ..... days

b. Up, but unable to leave the hotel/residence? ..... days

c. Able to get about but feeling unwell? ..... days

9.5 If your (or your child's) illness started while on holiday, how many days after the first day of the holiday did you/your child begin to feel unwell? ..... days

9.6 Please list other members of your group who stayed with or looked after you (or your child) during the illness:

Relationship to you/your child	Number of days + half days caring for you/your child
e.g. Friend	3½ days

9.7 If you were on holiday abroad, how much did you spend on medicines/medical care? £.....

MRC use only

9.8 Did you/your child stay longer (in the UK or abroad) because of illness?

Yes ☐ No ☐ → If "No", please go to **Question 9.10**

9.9 How many extra days did you/your child stay? ..... days

9.10 About how much extra did this cost? £.....

9.11 Did you/your child go home early because of illness?

Yes ☐ No ☐ → If "No", please go to **Question 9.13**

If "Yes", how many days of the holiday were lost? ..... days

9.12 About how much extra did this cost? £.....

9.13 Did you claim back any costs of illness on your insurance?

Total cost ☐ Some cost ☐ None ☐

9.14 Please give details and amounts of any other costs relating to your/your child's illness while on holiday abroad ***(e.g. telephone calls)***:

.....

.....

.....

SECTION 10 OTHER EXPENDITURE DUE TO ILLNESS

PLEASE ITEMISE OTHER OR ADDITIONAL COSTS NOT COVERED BY PREVIOUS SECTIONS, WHICH RESULTED FROM YOUR OR YOUR CHILD'S ILLNESS. (COSTS INCURRED IN THE UK ONLY; PLEASE EXCLUDE MONEY SPENT ABROAD).

As far as possible, please itemise only those costs which resulted directly from your (or your child's) illness.

10.1 Medicines, ointments, tablets bought from a chemist: ***(DO NOT INCLUDE MONEY PAID FOR DOCTORS' PRESCRIPTIONS)*** £.....

10.2 Telephone calls resulting from the illness: £.....

MRC use only

10.3 Special foods or drink: £.....

10.4 Leisure items: books/magazines £.....
videos £.....
toys/games £.....
other £.....

10.5 New clothing: £.....

10.6 New bedding: £.....

10.7 Cleaning/hygiene materials: bleach/disinfectant £.....
(extra to normal use)
nappies/absorbent pads £.....
washing powders/liquids £.....

10.8 Travel *(other than visits to a doctor or hospital)*: £.....

10.9 Cancelled or unused bus or train passes: £.....

10.10 Pre-paid playschool, school or college fees: £.....

10.11 Pre-paid leisure activities (e.g. outings, concerts, clubs etc.): £.....

10.12 Please describe any other costs, including cancelled arrangements, which you feel resulted from your/ your child's illness:

i ..... £.....
ii ..... £.....
iii ..... £.....
iv ..... £.....
v ..... £.....

10.13 **If you feel we have not covered all the costs you had, financial or otherwise, please describe items you feel have been missed and, if possible, give the costs:**

.....
.....
.....
.....
.....

MRC use only

SECTION 11 INCOME DETAILS

THIS INFORMATION IS FOR MEDICAL COSTINGS ONLY AND WILL BE TREATED AS STRICTLY CONFIDENTIAL

To help assess the financial impact of your (or your child's) illness, it is necessary to ask for details of your household's income. Would you please indicate your household's total annual income (after the deduction of tax and National Insurance) by ticking the appropriate box below. **(Equivalent monthly totals are shown in brackets).**

(This information will be treated in the strictest confidence. If, however, you are unwilling to disclose these particulars, this is understood and we would like to express our thanks for the time taken in completing the questionnaire).

Up to ... £2,500 (£208 per month) ☐	£25,001 - £30,000 (£2,084 - £2,500 per month) ☐
£2,501 - £5,000 (£209 - £417 per month) ☐	£30,001 - £35,000 (£2,501 - £2,917 per month) ☐
£5,001 - £10,000 (£418 - £833 per month) ☐	£35,001 - £40,000 (£2,918 - £3,333 per month) ☐
£10,001 - £15,000 (£834 - £1,250 per month) ☐	£40,001 - £45,000 (£3,334 - £3,750 per month) ☐
£15,001 - £20,000 (£1,251 - £1,667 per month) ☐	£45,001 - £50,000 (£3,751 - £4,167 per month) ☐
£20,001 - £25,000 (£1,668 - £2,083 per month) ☐	Over .... £50,000 (£4,167 per month) ☐

If over £50,000 (£4,167 per month), please give amount to nearest £5,000: £ ..... ☐☐

SECTION 12 THIS SECTION ASKS FOR YOUR OPINIONS ABOUT FOOD SAFETY AND HOW THIS AFFECTS THE CHOICES YOU MAKE

12.1 Are you the person who was ill? Yes ☐ No ☐ ☐
(named in the accompanying letter)

If "No", are you completing this questionnaire?: for a child ☐ for another adult ☐ ☐

12.2 If your (or your child's) illness was shown to have been caused by a food item which had been eaten, how much, for every £100 you earn (after tax and other deductions) would you be willing to pay (**once only**) to avoid this illness again?
(please tick one box only)

£1 ☐ £5 ☐ £10 ☐ £25 ☐ £50 ☐ £100 ☐ other/ more ☐

If "other/more", please indicate how much: £..... ☐

MRC use only

12.3 ***Over 60,000 cases of food poisoning were notified last year. Most of these people had a relatively mild illness, but some were more seriously ill and a small number required treatment in hospital. About 40-60 people a year are reported to have died with a salmonella infection or other foodborne disease.***

Would you be willing to pay more on your food bill for measures to reduce the risk to yourself and other people?

Yes ☐ ↓ No ☐ → If "No", please go to Question 12.7

12.4 Please state the approximate amount you spend on food per month:

Up to £100	☐	£201-300	☐	£401-500	☐
£101-200	☐	£301-400	☐	Over £500	☐

If over £500, please indicate to the nearest £100: £.....

12.5 Please indicate how much extra you would be willing to pay, for every £1 you spend on your regular monthly food bill, to ensure that it has the lowest possible risk of causing food poisoning: ***(please tick one box)***

Extra pence per £1 spent on monthly food bill

1p	5p	10p	25p	50p	Other or more (how much)
☐	☐	☐	☐	☐	..... p

12.6 ***Some foods appear to have a greater chance of causing food poisoning than others. For example, "poultry" meat is believed to be a common source of some types of illness caused by food, such as salmonella food poisoning.***

If a fresh chicken (weight about 3lb) normally costs about £2.50, how much more would you be willing to pay for a chicken which had been treated to reduce the chance of it having salmonella food poisoning bacteria on it? ***(tick a box for a or b or write in the space provided)***

	1p	5p	10p	25p	50p	Other or more (how much)
a) If all chickens were free of bacteria, making the risk of infection negligible	☐	☐	☐	☐	☐	..... p
b) If the proportion of contaminated chickens was halved, reducing the risk of infection by half	☐	☐	☐	☐	☐	..... p

MRC use only

12.7 Surveys indicate that up to a half of chicken carcases may have salmonella on them. If you were offered poultry (chicken) meat which had been irradiated and could be guaranteed 99% free of salmonella, would you be prepared to buy it in preference to non-irradiated poultry if any of the following applied?: ***(choose one option)***

		Up to 5p	Up to 25p	Up to 50p	Over 50p
a) It cost a few pence more	☐ If ticked, how much?	☐	☐	☐	☐
If over 50p, how much?					
b) It was the same price	☐				
c) It was a few pence cheaper	☐ If ticked, how much?	☐	☐	☐	☐
If over 50p, how much?					
d) Not at any price	☐				

12.8 Which category (a, b, c, d) ***in Question 12.7*** would you have ticked if you could be assured that irradiated meat is absolutely safe and tastes the same as non-irradiated meat? ***(please circle appropriate letter)***

a b c d

If category a or c was circled, which amount would you have selected?: Up to ..... p

12.9 ***Improving food safety is likely to be costly but could save many people from an unpleasant illness and could prevent sickness absence from work, school, etc.***

Who do you think should have responsibility for the safety of the food we eat? Please put the following in order of importance, in your opinion, by numbering them 1-6, i.e. number 1 is the most important and number 6 the least important. Leave blank if you don't know.

National government	☐	Local authority	☐
Food manufacturers	☐	Food retailers (supermarkets, shops, etc.)	☐
Food producers, e.g. the farmer	☐	You - the consumer	☐

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE.
PLEASE CHECK THAT YOU HAVE FILLED IN ALL SECTIONS AND RETURN AS SOON AS POSSIBLE IN THE ENVELOPE SUPPLIED.

THIS INFORMATION WILL BE ENTERED ONTO COMPUTERISED RECORDS AND IS COVERED BY THE DATA PROTECTION ACT. NO INFORMATION WILL BE CONVEYED OUTSIDE THIS STUDY WITHOUT YOUR PERMISSION.

Appendix 7
Stool Voiding Instructions and Microbiological Methods

A7.1 STOOL VOIDING INSTRUCTIONS

NATIONAL GASTROENTERITIS STUDY

HOW TO COLLECT AND POST A STOOL SAMPLE (MOTION)

Use a clean toilet which has been well flushed. Do not allow toilet cleaners or disinfectants to come into contact with the stool sample.

1. IN CASE OF DIARRHOEA (LOOSE STOOLS/MOTIONS)

Line the inside of the bottom of the toilet bowl with a sheet of greaseproof paper if you have it. If not, use toilet paper. Pass the stool (motion) into the toilet. With the spoon provided scoop enough to fill the pot to the line, if possible (about half full). Flush the paper away.

2. IF THE MOTION IS NOT LOOSE

It may be easier to sit on the toilet and collect a piece of formed stool on toilet paper as it leaves the body. With the spoon provided scoop enough to fill the pot to the line, if possible (about half full).

3. FROM A NAPPY

With the spoon provided scoop enough stool (motion) directly from the nappy to fill the pot to the line, if possible (about half full).

Once the stool has been taken, place the spoon in the pot and screw on the cap tightly. Write your name, (or your child's), the time and date of passing the stool, on the label on the pot and on the laboratory form.

Wrap the pot in the wadding and place in the plastic bag and then in the cardboard box. Ensure that the laboratory form is placed inside the box.

Wash your hands thoroughly, using soap and running water, then dry well.

Moisten the stamped addressed label with tap water and use to seal the box.

Post into a postbox as soon as possible on the same day. If you are unable to post the same day, store in a cold place (but not your fridge or freezer) and post first thing next day.

If you have any queries please ring the study nurse.

IID Study in England

Stool Request Form

NATIONAL GASTROENTERITIS STUDY Faeces (stool) specimen	PUBLIC HEALTH LABORATORY Bridle Path, York Road, Leeds, LS15 7TR Tel: 0532 645011 Fax: 0532 603655
Practice name and address Telephone number: ..... Name of reporting doctor:	Study Number: ☐☐☐☐☐☐☐☐ Surname: Forenames: Address: Post code: ..... Date of birth: ...../...../..... Sex: M/F*
Clinical details, comments:	PLEASE COMPLETE ALL ENTRIES BELOW Date of onset of illness: ...../...../..... am/pm* (leave a blank if you are a 'control') Date stool specimen taken ...../...../..... am/pm*
Leeds PHL Lab. No:	* delete as appropriate

PLEASE ENSURE THAT THE SPECIMEN IS LABELLED CORRECTLY
AND THAT THE CAP IS TIGHTLY CLOSED

A7.2 MICROBIOLOGICAL METHODS

Stool specimens from participants in the IID Study were received at the Leeds Public Health Laboratory by First Class Post. Details of the patient and specimen were entered into the laboratory tracking system (Telepath, incorporating bar code readers). The specimen was then subjected to a range of tests according to a standard protocol (the priority list, Table A7.1), dependent on the amount of specimen available, estimated by weight; approximately 10g was required to complete all tests and to archive material for subsequent study (Table A7.2). A wide range of 'Target Organisms' was sought using a range of test procedures, including bacteriological culture (with enrichment and enumeration where appropriate), bacterial toxin detection, enterovirulent *E.coli* detection by DNA methods, microscopy for protozoa and helminth ova, and electron microscopy and enzyme immunoassay for viruses. Figure A7.1 summarises the flowsheet for various tests performed.

Bacterial isolates were confirmed using standard phenotypic tests. Where appropriate, isolates were transferred, in batches, to Public Health Laboratory Service (PHLS) reference laboratories for confirmation and typing. Isolates were stored frozen with archived stool for subsequent studies.

A7.2.1 Bacteriological culture and microscopy

There are no international or national standard methods for the isolation and identification of enteric pathogens from faecal specimens. In the absence of such standards, the Leeds Public Health Laboratory and other laboratories undertaking analyses for the IID Study used only methods and materials that: were acceptable to the majority of microbiologists within the PHLS and the NHS and have a 'track record' of successful application in these diagnostic services.

Many of the methods were taken from 'Methods for use in Microbiological Surveillance' published by the Department of Health Steering Group on the Microbiological Safety of Food (DoH 1994).

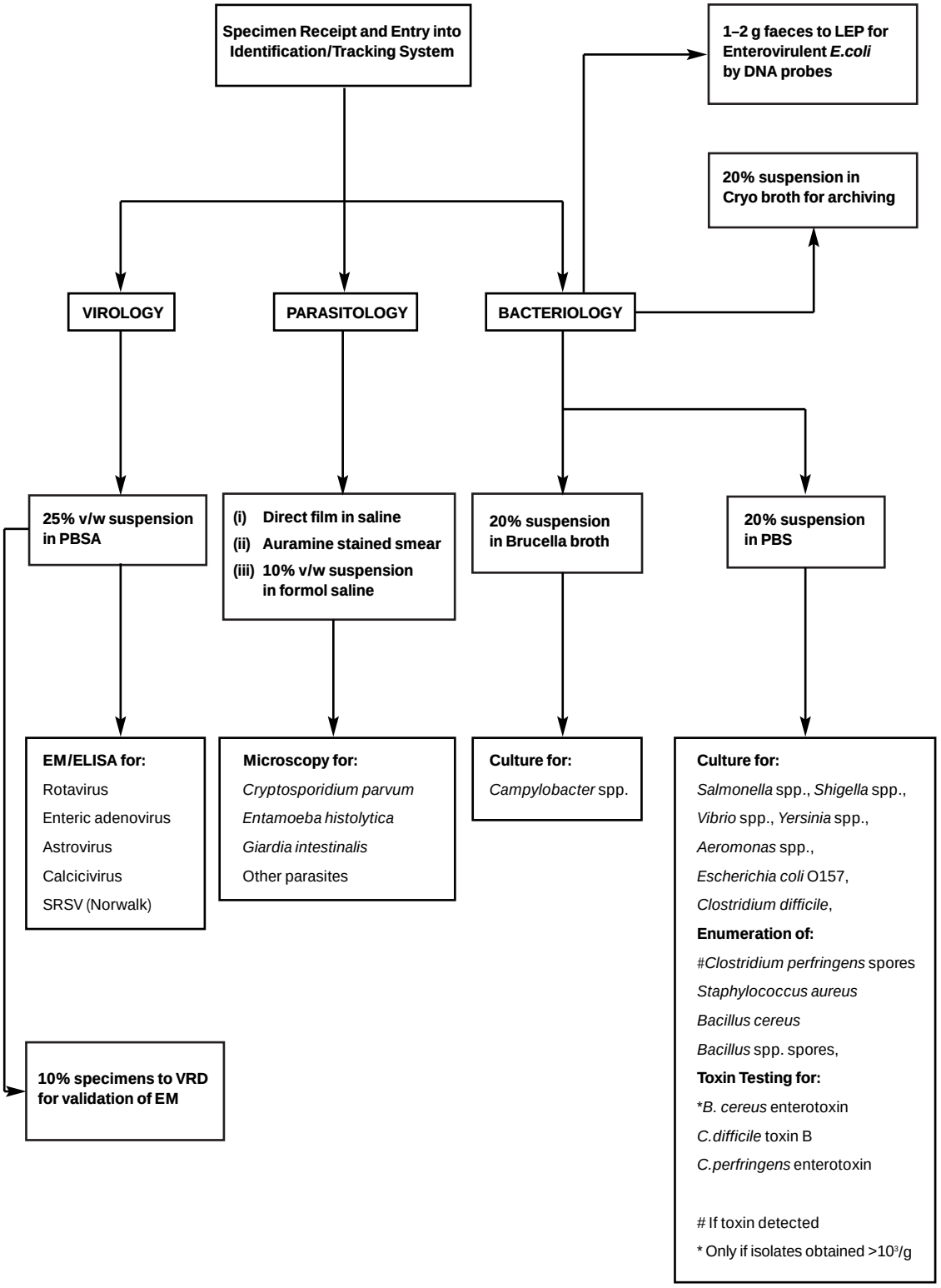
Table A7.1 Priority list for laboratory investigations

	PROCEDURE	PRINCIPAL PATHOGENS SOUGHT
Stage 1	Bacteriological culture	*Campylobacter*
Stage 2	Bacteriological culture	*Aeromonas, Bacillus, Clostridium difficile, Salmonella, Shigella, Staphylococcus aureus, Vibrio, Yersinia*
Stage 3	Bacteriological Culture	*Escherichia coli* O157
	Direct microscopy	*intestinals*
Stage 4	1-2g faeces to LEP (DNA probes)	Enterovirulent *Escherichia coli*
	Direct microscopy	*Giardia lamblia, Cryptosporidium parvum*
Stage 5	Virology (EM and ELISA)	Adenovirus, Astrovirus, Calicivirus, Rotavirus, SRSV (Norwalk-like)
Stage 6	Toxin tests; culture counts for vegetative cells and spores	*Clostridium difficile, Clostridium perfringens, Bacillus cereus, Staphylococcus aureus*
Stage 7	Concentration & Microscopy for ova, cysts and parasites	Protozoa and helminths
Stage 8	20% frozen suspension	Archival strorage at CAMR

Table A7.2 Priority and testing scheme based on specimen weight

WEIGHT (g)	PROCEDURE	PROCESSED TO STAGE
<1.5	Do not process. Request repeat specimen.	
1.5–2.49	0.5g in 2ml Brucella broth (culture for *Campylobacter* spp.) 1.0g in 4ml PBS (culture for other enteric pathogens) Direct Smear (*Giardia* spp.)	**2**
2.5–3.49	As above and 1-2g faeces to LEP (enterovirulent *Escherichia coli*) Direct Smear (*Giardia* spp. and *Cryptosporidium parvum*)	**4**
3.5–4.49	As above and 0.5g in 1.5ml PBSA (virology)	**5**
4.5–5.49	As above but 2.0g in 8ml PBS (culture for other enteric pathogens)	**5**
5.5–7.49	As above and additional 1.0g in 4ml PBS (*Clostridium perfingens* enterotoxin & counts)	**6**
7.5–8.49	As above and additional 2.0g in 8ml PBS (*Clostridium difficile* cytotoxin)	**6**
8.5–9.49	As above and 1.0g in 9ml formol saline (ova, cysts and parasites)	**7**
9.5–10.49	As above and 1.0g in 4ml Cryo broth (archiving at CAMR)	**8**
>10.5	As above but 1.0g in 4ml Brucella broth (culture for *Campylobacter*)	**8**

Figure A7.1 Summary flowsheet of testing procedures



LEP: Laboratory of Enteric Pathogens, Central Public Health Laboratory

VRD: Virus Reference Division, Central Public Health Library

The methods for each microorganism are described in outline as they are intended to be used by competent microbiological staff who will be familiar with the techniques involved. Media are referred to throughout by their generic names and the formulae for selective media are listed separately. This is in accordance with their intended use by experienced microbiological staff. It is not recommended that selective media are made up from the formulae as commercially available media from reputable suppliers are likely to be more consistent and of an assured quality. For the IID Study, batches of media used at Leeds PHL were quality controlled to assure consistent performance.

The isolation methods used for bacterial target organisms, confirmatory tests and typing methods applied to isolates are summarised in Table A7.3 and are detailed in section 7.3. Methods for toxin detection and microscopy for protozoa etc. are given in Tables A7.4 and A7.5, respectively.

A7.2.2 **Enterovirulent *E.coli* detection by DNA methods**

An aliquot of stool specimen was despatched immediately to the Laboratory of Enteric pathogens, Central Public Health Laboratory (LEP) for detection and isolation of enterovirulent *E.coli* by DNA hybridisation procedures. These methods are not in routine use in pathology laboratories, but have been developed and validated by LEP and were available on a referral basis. The methods used are detailed in 7.5.

A7.2.3 **Virology methods**

Initial plans to examine only specimens which had been collected within 5 days of onset of IID symptoms were abandoned and all specimens were examined by electron microscopy (EM) and enzyme immunoassay (EIA) for a range of enteric viruses. The methods used are summarised in Table A7.6 and detailed in section 7.6. A quality control programme for EM was included on a sample of the specimens. Similarly, the use of PCR for Small Round Structured Virus (SRSV, Norwalk-like virus) was investigated as a subsidiary study.

Table A7.3 Media for the detection of bacteria

	DIRECT PLATING AGAR	ENRICHMENT MEDIA	TYPING METHOD
Salmonella spp. and *Shigella* spp.	(i) Desoxycholate Citrate agar (DCA) (ii) Xylose Lactose Desoxycholate (XLD) agar	(i) Rappaport-Vassiliadis broth (ii) Selenite Cysteine broth	serotyping, phage-typing genotyping for virulence determinants including toxins and adhesins
Campylobacter spp.	(i) Charcoal, Cefoperazone Desoxycholate agar (CCDA) (ii) Skirrow's medium (iii) Blood agar with membrane filter	Exeter broth	Penner serotyping Lior biotyping
Vibrio spp.	(i) Thiosulphate Citrate Bile Sucrose agar	Alkaline Peptone Water	serotyping
Aeromonas spp.	(i) Aeromonas agar (Ryan)	Alkaline Peptone Water	serotyping
Yersinia spp.	(i) Cefsulodin, Irgasan, Novobiocin agar	Phosphate Buffered Saline (4°C)	serotyping
Staphylococcus aureus	(i) Baird Parker agar		phage-typing
Bacillus spp.	(i) Bacillus cereus selective agar (ii) Blood agar (after ethanol shock)		serotyping
Clostridium perfingens	(i) Neomycin Blood agar (ii) Blood agar (after ethanol shock)		serotyping
Clostridium difficile	(i) Cefoxitin, Cycloserine Fructose, Egg Yolk agar		toxin A assay PCR ribotyping
Escherichia coli O157	(i) Sorbitol MacConkey agar with cefixime and rhamnose (CR-SMAC)		serotyping phage-typing verocytotoxin-typing

Table A7.4 Tests for bacterial toxins

C.perfringens enterotoxin	Faecal extract	RPLA (Unipath) In-house ELISA
C.difficile toxins	Faecal suspension Isolates	Toxin B cytotoxin assay (Vero cells) Toxin A ELISA (Techlab)
B.cereus enterotoxin	Faecal extract	RPLA (Unipath)

Table A7.5 Tests for protozoon parasites

Cryptosporidium parvum	Auramine phenol stain and Fluorescence microscopy
Entamoeba listolytica	Formol/ether concentration Microscopy of iodine-stained deposit
Giardia intestinalis	Formol/ether concentration Microscopy of iodine-stained deposit
Other protozoa	Formol/ether concentration Microscopy of iodine-stained deposit

Table A7.6 Tests for enteric viruses

VIRUS	ELECTRON MICROSCOPY	ANTIGEN-CAPTURE ELISA	TYPING TESTS
Adenovirus types 40,41	Yes	Yes	
Rotavirus	Yes	Yes	Electrophoresis if EM positive but ELISA negative
SRSV (Norwalk-like)	Yes	No	
Calicivirus	Yes	No	
Astrovirus	Yes	No	

A7.2.4 **Archived stool**

Where sufficient stool was available, an aliquot (~0.2g) was stored at -70°C in Cryo protective broth for subsequent studies. A validation study was instigated to follow loss of viability of common enteric pathogens during storage by this method.

A7.3 STANDARD BACTERIOLOGICAL METHODS

Methods and media are taken from the SGMSF Methods for use in Microbiological Surveillance (DoH, 1994) except *E.coli* O157 (section A7.3.6) and are presented alphabetically for the main target organisms, as follows:

A7.3.1 Detection and enumeration of *Aeromonas hydrophila*
A7.3.2 Detection and enumeration of *Bacillus cereus*
A7.3.3 Detection and enumeration of *Campylobacter* spp.
A7.3.4 Detection and enumeration of *Clostridium difficile*
A7.3.5 Detection and enumeration of *Clostridium perfringens*
A7.3.6 Detection and enumeration of *Escherichia coli* O157
A7.3.7 Detection and enumeration of *Salmonella* spp. and *Shigella* spp.
A7.3.8 Detection and enumeration of *Staphylococcus aureus*
A7.3.9 Detection and enumeration of *Vibrio* spp.
A7.3.10 Detection and enumeration of *Yersinia* spp.

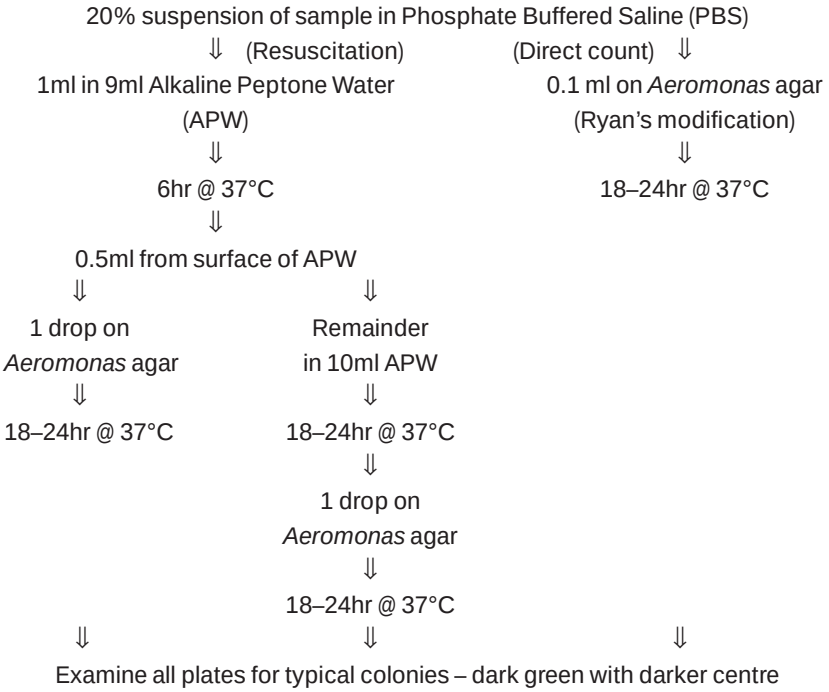
A7.3.1 Detection and enumeration of *Aeromonas hydrophila*

(Atkinson 1986; Rahim *et al.* 1984; Furniss *et al.* 1978)

Introduction

This method uses the same procedure as the method for *Vibrio* (2.9), except that *Aeromonas* agar (Ryan's modification) is substituted as the selective medium.

Procedure



Screen all typical colonies by oxidase (+ve) and urease (-ve) tests. Confirm all presumptive positives by a range of biochemical tests (see Table A7.7) and refer confirmed positives to reference laboratory.

Table A7.7 Preliminary identification of *Vibrio* spp. and *Aeromonas* spp.
(Barrow and Feltham 1993)

	1	2	3	4	5
Growth at 37°C	+	+	+	+	+
Motility	+	+	+	+	d
Oxidase	+	+	-	+	+
Nitrate reduced	+	+	-	+	+
Gas in glucose	-	d	-	-	d
Arginine decarboxylase	-	+	+	-	+
Lysine decarboxylase	+	d	d	-	d
Ornithine decarboxylase	d	-	-	-	-
O/129 Resistance (10 μg)	d	d	-	d	+
O/129 Resistance (150 μg)	-	-*	-	d	+
Growth with 6% NaCl	d	d	+	+	-

1 *Vibrio* spp. including *V.cholerae, V.mimicus, V.vulnificus, V.parahaemolyticus, V.alginolyticus, V.harveyi, V.cincinnatiensis*
2 *Vibrio* spp. including *V.fluvialis, V.furnissii, V.anguillarum, V.damsela*
3 *Vibrio* spp. including *V.metschnikovii*
4 *Vibrio* spp. including *V.hollisae, V.natriegens*
5 *Aeromonas* spp.
* Some resistant isolates
d 16–84% strains positive
0/129: Vibriostatic agent 2-4-diamino-6,7-diisopropylpteridine

Selective medium

Aeromonas agar (Ryan)

Proteose peptone	5.0 g/l	Bile salts	3.0 g/l
Yeast extract	3.0 g/l	Sodium thiosulphate	10.67 g/l
L-lysine monohydrochloride	3.5 g/l	Sodium chloride	5.0 g/l
L-arginine monohydrochloride	2.0 g/l	Ferric ammonium citrate	0.8 g/l
Inositol	2.5 g/l	Bromothymol blue	0.04 g/l
Lactose	1.5 g/l	Thymol blue	0.04 g/l
Sorbitol	3.0 g/l	Agar	12.5 g/l
Xylose	3.75 g/l	Adjusted to pH 8.0± 0.1	
		Supplemented with Ampicillin	5.0 mg/l

A7.3.2 Detection and enumeration of *Bacillus cereus*

(Holbrook and Anderson 1980; Karansky *et al*. 1978; Mossel *et al.* 1967; Barrow and Feltham 1993; Collee *et al.* 1989; Anon. 1990)

Introduction

This method is designed to detect and quantify the presence of *B.cereus* in faecal samples, both as spores and as total viable cells. The rapid staining technique is essential to distinguish *B.cereus* from *B.thuringiensis*, which has identical colonial characteristics on this medium.

Viable Cells

20% suspension in
Phosphate Buffered Saline (PBS)
⇓
1:200 dilution in Peptone Water (PW)
for 10^{-3}
⇓
Decimal dilution to 10^{-5}
⇓
Plate 0.1 ml of 10^{-3} and 10^{-5} dilutions
on *Bacillus cereus* selective agar
⇓
Incubate for 24hr @ 37°C

Spores

20% suspension in PBS
⇓
1:1 suspension in 95% ethanol
30 minutes @ room temperature
⇓
Dilute 1:100 in PW (i.e. to 10^{-3})
⇓
Decimal dilution to 10^{-5} in PW
⇓
Plate 0.1 ml of 10^{-3} and 10^{-5} dilutions
on *Bacillus cereus* selective agar and
on blood agar
⇓
Incubate for 24hr @ 37°C

Examine all plates for typical colonies: 5mm, blue, with blue precipitation zone.

Confirm all presumptive positives by testing 5 typical colonies using a rapid staining procedure:
1. Prepare microscope slide film from either centre of 24hr or from edge of 48hr colony
2. Air dry the film and fix with minimal flaming.
3. Place the slide over boiling water and flood with 5% w/v malachite green for 2 minutes.
4. Wash and blot the slide dry
5. Stain with 0.3% w/v sudan black in 70% ethyl alcohol for l5 minutes.
6. Wash with xylene for 5 seconds and blot dry.
7. Counterstain with 0.5% w/v safranin for 20 seconds.
8. Wash and examine under microscope.

B.cereus cells are 4.5 μm long by 1-1.5 μm wide with square ends and rounded corners. Spores are stained pale to mid-green, central to para-central and do not swell the sporangium. Lipid globules are black and vegetative cytoplasm red.

Estimate the numbers of *B.cereus* viable organisms and spores per gram of the original sample from the numbers of positives in the 10^{-3} and 10^{-5} dilutions.

Toxin assay

Where the total *B.cereus* count exceeds 10^3 cfu/g, the stool sample should be tested for the presence of diarrhoeal enterotoxin using a commercially available kit (e.g. BCET–RPLA, Oxoid Diagnostics) following the manufacturer's instructions

Selective medium

***Bacillus cereus* Selective Agar Base**

Peptone	1 g/1
Mannitol	10 g/l
Sodium chloride	2 g/l
Magnesium sulphate	0.1 g/l
Disodium hydrogen phosphate	2.5 g/l
Potassium dihydrogen phosphate	0.25 g/l
Bromothymol blue	0.12 g/l
Sodium pyruvate	10 g/l
Agar	14 g/l
Adjusted to pH 7.2±0.2	
Supplemented with:	
l:5 egg-yolk emulsion in water	50 ml/l
Polymyxin B	100,000 IU/l

A7.3.3 **Detection and enumeration of *Campylobacter* spp.**

(Albert *et al.* 1993; Botton and Robertson 1982; Hutchinson and Bolton 1983; Griffiths and Park 1990; Penner 1988; Skirrow and Benjamin 1982)

Introduction

Three methods are indicated, which should be carried out in parallel. All three methods start with a 20% suspension of the sample in Brucella broth. The direct method is intended to indicate the approximate number of organisms present in more highly contaminated samples, while the enrichment method is designed to detect lower numbers of organisms and the membrane filtration method to detect a wider variety of strains, including antibiotic sensitive strains. All incubation for this micro-organism is carried out under microaerobic conditions (approx. 10% v/v CO_2, 6% v/v O_2, 2% v/v H_2, 82% v/v CO_2) either in a suitable incubator or using a commercial gas generating pack.

Isolation on selective media

20% suspension of sample in Brucella broth

⇓	⇓	⇓
0.1ml each on Charcoal Cefoperazone Desoxycholate agar (CCDA) and Skirrow's Blood Agar Medium (Skirrow)	0.1ml on 0.45u filter on blood agar	0.1ml in 10ml Exeter broth
⇓	⇓	⇓
48hr @ 37°C	30min @ 37°C	4hr @ 37°C
⇓	⇓	⇓
Examine for typical colonies	Remove filter then 48hr @ 37°C	30-44hr @ 42–43°C
	⇓	⇓
	Examine for typical colonies	0.1 ml on Exeter agar
		⇓
		48hr @ 42–43°C
		⇓
		Examine for typical colonies

Colonial morphology

C.jejuni – grey, moist, flat spreading colonies after 42hr on CCDA and Skirrow, some strains have green hue or dry appearance;
C.coli – cream-grey, moist, raised, discrete colonies on CCDA and Skirrow;
C.lari – variable some as above, some as grey discrete colonies on CCDA and Skirrow.

Colonial morphology on Exeter agar is variable, the only appearance common to *Campylobacter* species being a shiny surface.

Confirmation and speciation

Any suspect colonies should have Gram films made from them and counter-stained using 0.l% carbol fuchsin. They should display typical 'gullwing' morphology but do often present as small coccal forms. These atypical growths will revert to normal morphology when repeat films are made from overnight blood agar plates. Biochemical confirmation and identification of the commonest species are detailed in Table A7.8.

Table A7.8 Differential reactions and characteristics for *Campylobacter* spp. (adapted from Penner 1998)

Species	Catalase	H_2S (TSI)	Hippurate	Growth at			Susceptibility to		Indoxyl Acetate Hydrolysis
				25°C	37°C	42°C	Naladixic	Cephalothin	
C.fetus	+	-	-	+	+	(-)	R	S	-
C.hyointestinalis	+	+	-	(+)	+	+	R	S	-
C.jejuni	+	-	+	-	+	+	S	R	+
C.coli	+	-	-	-	+	+	S	R	+
C.lari	+	-	-	-	+	+	R	R	-
C.upsaliensis	(-)	-	-	-	+	+	S	S	+

Key

+ = Positive reaction; (+) = most strains positive but some negative;
- = Negative reaction; (-) = most strains negative but some positive.

Selective media

Charcoal Cefoperazone Desoxycholate agar (CCDA)

Nutrient Broth No.2	25.0 g/l
Bacteriological charcoal	4.0 g/l
Casein Hydrolysate	3.0 g/l
Sodium desoxycholate	0.25 g/l
Ferrous sulphate	0.25 g/l
Sodium pyruvate	0.25 g/l
Agar	12.0 g/l
Supplemented with:	
Cefoperazone	8 mg/l

Skirrow Blood Agar Medium

Blood agar	
Supplemented with:	
Vancomycin	5 mg/l
Polymixin	1250 IU/l
Trimethoprim	2.5 mg/l

Exeter Medium

Nutrient broth	1000 ml
Lysed Horse Blood	50 ml
Rifampicin	10 mg
Trimethoprim	10 mg
Polymyxin B	4 mg
Amphotericin	2 mg
Cefoperazone	15 mg
Ferrous sulphate	200 mg
Sodium pyruvate	200 mg
Sodium metabisulphite	200 mg
For solid medium:	
Agar	15 g/l

A7.3.4 **Detection and enumeration of *Clostridium difficile***

(Burdon 1982; Bowman *et al*. 1986; Edelstein 1988; Haslam *et. al.* 1986; Lance *et al.* 1979; Molby *et al.* 1980; Pedlar and Orr 1990; Anon. 1990)

Introduction

This test is divided into three parts: a standard culture for detection of viable organisms, a tissue culture test for presence of toxin and titration of toxin levels, where the presence of toxin is detected.

Viable cells

0.1 ml 20% suspension in Phosphate Buffered Saline (PBS)

⇓

Inoculate directly on to a Cefoxitin, Cycloserine, Fructose, egg yolk agar (CCFA) plate IMMEDIATELY

Place in anaerobic cabinet and incubate for 4 days at 37°C, examining at 48 hour intervals

⇓

Examine for typical colonies –
yellow, 'ground glass' with serrated edge
Gram film shows slender Gram-positive rods

⇓

Confirm presumptive positives using commercially available latex kit

⇓

Sub-culture positive isolates in Cooked Meat Medium for referral or storage

Toxin assay

Add 0.2ml (10g/l) kanamycin solution to 9.8ml of 20% suspension of sample in PBS

⇓

Centrifuge for 5 minutes at 3,000 rpm

⇓

Dilute 0.1 ml supernatant in 0.9ml PBS to make 10^{-2} dilution

⇓

Add 0.1 ml of this to duplicate tissue culture tube (use Vero or HeLa or HEp2 cells)

⇓

Incubate overnight with positive and negative controls
Examine for any toxic effects, typically 'rounding up' of culture cells

Toxin titration

a) Add 0.2ml of *C.sordellii* antitoxin (diluted 4×10^{-1}) to one row of four tissue culture tubes.
b) Make dilutions of 1×10^{-2} to 1×10^{-4} and add 0.1 ml of each dilution to a tube in the row with antitoxin and add 0.1 ml of each dilution to a row of tubes without antitoxin.
c) Incubate overnight and examine for neutralising effect in the tubes containing antitoxin.

Selective medium

Cycloserine cefoxitin fructose agar (CCFA):

Proteose peptone	40.0 g/l
Disodium hydrogen phosphate	5.0 g/l
Potassium dihydrogen phosphate	1.0 g/l
Magnesium sulphate	0.1 g/l
Sodium chloride	2.0 g/l
Fructose	6.0 g/l
Agar	15.0 g/l
Adjusted to pH 7.4 ±0 2	
Supplemented with	
1:5 egg yolk emulsion in water	50 ml/l
D-cycloserine	500 mg/l
Cefoxitin	16 mg/l

A7.3.5 **Detection and enumeration of *Clostridium perfringens***

(Brett *et al.* 1992; Handford 1979; Harmon and Kautter 1987; Willis and Phillips 1998; Anon. 1990)

Introduction

This method combines a spore count and a total estimation of the number of a *Cl.perfringens* in the sample, using a selective blood agar, for those samples where the presence of toxin has been detected.

Procedure

Toxin assay

All samples should be tested for presence of *Cl.perfringens* enterotoxin using a commercially available kit (e.g. PET-RPLA kit, Oxoid Diagnostics) following the manufacturer's instructions.

If the toxin assay is positive, the following tests should then follow.

Viable cells

20% suspension in
Phosphate Buffered Saline (PBS)
⇓
1:200 dilution in Peptone Water (PW)
for 10^{-3}
⇓
Decimal dilution to 10^{-5}
⇓
Plate 0.1 ml of 10^{-3} and 10^{-5} dilutions
on Neomycin blood agar
⇓
Incubate anaerobically 24hr @ 37°C

Spores

20% suspension in PBS
⇓
1:1 suspension in 95% ethanol
30 minutes @ room temperature
⇓
Dilute 1:100 in PW (i.e. to 10^{-3})
⇓
Decimal dilution to 10^{-5} in PW
⇓
Plate 0.1 ml of 10^{-3} and 10^{-5} dilutions
on Neomycin blood agar
⇓
Incubate anaerobically 24hr @ 37°C

Examine all plates for typical colonies – large, regular, convex, shiny, often haemolytic.

Confirm presumptive positives by tests for motility (-ve), Nagler reaction (+ve), lactose and sucrose utilisation (both +ve).

Estimate and report the numbers of spores and total viable *Cl.perfringens* per gram of the original sample, from the 10^{-3} and 10^{-5} dilutions.

Selective medium

Neomycin blood agar

Blood agar base no.2	40 g/l
Defibrinated horse blood	66 ml/l
Neomycin sulphate	70 mg/l

A7.3.6 Detection and enumeration of *Escherichia coli* O157

(Chapman *et al.* 1991; Smith and Scotland 1993)

Introduction

This method is based on the selective detection of viable organisms of *E.coli* O157 differentiated by an inability to ferment sorbitol or rhamnose incorporated in a formulation of MacConkey's agar made additionally selective by the inclusion of cefixime.

Procedure

0.1 ml 20% suspension in Phosphate Buffered Saline (PBS)
⇓
Inoculate directly on to a Sorbitol MacConkey with cefixime and rhamnose (CR-SMAC) plate
⇓
Incubate for 24h at 37°C (no longer)
⇓
Examine for colourless colonies
⇓
Confirm presumptive positives by aglutination with O157 antiserum
⇓
Sub-culture positive isolates for referral or storage

Selective medium

Sorbitol MacConkey cefixime rhamnose agar (CR-SMAC):

Peptone	20.0 g/l
Sorbitol	10.0 g/l
Bile salts No.3	1.5 g/l
Sodium chloride	5.0 g/l
Neutral red	0.03 g/l
Crystal violet	0.001 g/l
Agar	15.0 g/l
Adjusted to pH 7.1 ±0 2	
Supplemented with	
Rhamnose	5.0 g/l
Cefixime	0.5 mg/l

A7.3.7 **Detection and enumeration of *Salmonella* and *Shigella* spp.**
(Rappaport *et al.* 1956; Fricker 1987; van Schothorst and Renaud 1983; AOAC 1978; Barrow and Feltham 1993; Anon. 1990)

Introduction

The methods for detection and enumeration of these bacteria are described in three phases - isolation on selective media; presumptive identification by first stage biochemical and serological tests; and confirmation by second stage biochemical and serological tests. The appropriate clinical action should be taken if a presumptive positive *Salmonella* is identified.

Isolation on selective media

20% suspension of sample in Phosphate Buffered Saline (PBS)

⇓

1ml into Rappaport Vassialidis (RV) *and* Selenite Cysteine (SC) broths

⇓

Incubate 24hr @ 37°C (SC) or 24hr @ 41.5±0.5°C (RV)

⇓

Inoculate on XLD and on DCA

⇓

24hr @ 37°C

⇓

AND

⇓

0.1ml Direct Inoculation on Desoxycholate Citrate (Hynes) agar (DCA) *and* on Xylose Lactose Desoxycholate agar (XLD)

⇓

24hr @ 37°C

⇓

Identify positive colonies by colonial morphology

Colonial morphology

Organism	Medium	Colonial appearance
Salmonella, *Edwardsiella*	XLD	Red with black centre.
Shigella, *Providencia* H_2S -ve *Salmonella*	XLD	Red.
E.coli	DCA	Most strains inhibited, few strains produce pink umbilicated colonies 1-2mm diam. possibly with zone of precipitation.

Shigella sonnei	DCA	1mm at 18h to 2mm at 38h; smooth, initially colourless turning pink.
Shigella flexneri	DCA	Colourless, similar to *Sh.sonnei*, but with narrow plane periphery around central dome.
Escherichia, *Enterobacter* *Klebsiella*, *Citrobacter* *Proteus*, *Serratia*	XLD	Yellow, opaque
S.paratyphi B	DCA	1mm at 18h, 2-4mm on 2nd day. Slightly opaque, dome-shaped with central black dot
S.typhi	DCA	0.25-1 mm at 18h, pale pink; 2mm on 2nd day. Flat, conical, colourless, slightly opaque with central grey dot
Other salmonellae	DCA	Similar to *S.paratyphi* B. Non-pathogenic, non-lactose fermenters, such as *Proteus* and *Pseudomonas* spp., grow on the medium and may produce colonies which closely simulate those of the salmonellae or shigellae; *Proteus* colonies are often glossy (more translucent than those of the pathogens), with a large central black dot and a 'fishy' odour

Presumptive identification

1) Subculture 5 typical colonies from XLD or DCA into urea broth and triple sugar iron agar (TSI) and onto nutrient agar (single colony picks).
2) Discard all urease positive cultures and red TSI slopes
3) Test urease negative cultures as indicated in Table 2.6A

Table A7.9

TSI REACTIONS				SLIDE AGGLUTINATION TESTS (FROM CULTURES ON NON-SELECTIVE MEDIA)
BUTT	**SLOPE**	**GAS**	**GROWTH**	
Yellow	Pink	None	Non-spreading	Polyvalent *Salmonella* 'O' Polyvalent *Salmonella* 'H' *Salmonella* 'Vi' *Shigella sonnei* (phases 1 and 2) Polyvalent *Shigella flexneri* Polyvalent *Shigella dysenteriae* Polyvalent *Shigella boydii* (1, 2 & 3)
Yellow	Pink	+/-	Non-spreading	Polyvalent *Shigella boydii* (1, 2 & 3) Polyvalent *Shigella flexneri*
Black or Yellow	Pink or Yellow	+/- or +	Non-spreading	Polyvalent *Salmonella* 'O' Polyvalent *Salmonella* 'H' *Salmonella* 'Vi'

Refer to LEP all cultures which are biochemically identified as *Salmonella* or *Shigella* but which show negative serology.

Positive results should be quantified at this stage, from the initial dilutions on selective media. Cultures showing agglutination with *Salmonella* polyvalent 'O' antiserum, and polyvalent 'H' antiserum should be investigated to determine the specific 'O' antigens.

Selective media

Desoxycholate citrate agar (Hynes)(DCA)

'Lab Lemco' powder	5.0 g/l
Peptone	5.0 g/l
Lactose	10.0 g/l
Sodium citrate	8.5 g/l
Sodium thiosulphate	5.4 g/l
Ferric citrate	1.0 g/l
Sodium desoxycholate	5.0 g/l
Neutral red	0.02 g/l
Agar	12.0 g/l
pH 7.3±0.2	

Rappaport Vassialidis medium (RV)

Soya Peptone	5.0 g
Sodium chloride	8.0 g
Potassium dihydrogen phosphate	1.6 g
Magnesium chloride.$6H_2O$	40 g
Malachite green	0.04 g
Adjusted to pH 5.2±0.2	

Selenite cystine broth(SC)

Tryptone	5.0 g/l
Lactose	4.0 g/l
Disodium phosphate	10.0 g/l
L-cystine	0.1 g/l
Adjusted to pH 7.0±0.2	

Xylose lysine desoxycholate agar (XLD)

Yeast extract	3.0 g/l
L-lysine HCl	5.0 g/l
Xylose	3.75 g/l
Lactose	7.5 g/l
Sucrose	7.5 g/l
Sodium desoxycholate	1.0 g/l
Sodium chloride	5.0 g/l
Sodium thiosulphate	6.8 g/l
Ferric ammonium citrate	0.8 g/l
Phenol red	0.08 g/l
Agar	12.5 g/l
Adjusted to pH 7.4±0.2	

N.B. These quantities are for 1110 ml medium, which is the final volume after additions. Commercially available media usually give directions for reconstituting 1 litre of medium

Confirmation of *Salmonella* and *Shigella* species

The presence of *Salmonella* is confirmed by identification of a specific 'H' antigen. Presumptive positive *Shigella* cultures are confirmed by slide agglutination tests against all the components of the polyvalent sera that gave a positive reaction, followed by a set of biochemical tests.

Salmonella species – serological confirmation

The 'H' phase of salmonellae may be changed by passing through a Craigie tube containing 0.2ml of the appropriate antiserum. Poorly motile cultures benefit from moist slopes or Craigie tubes.

Tube agglutination must be done to obtain diagnostic titre (5×10^{-1}) with the specific 'H' antiserum. The antigen is prepared from an overnight growth in peptone water by adding 3–5 drops of 40% formaldehyde. Incubate in 50°C waterbath for 2 hours for *Salmonella* 'H' titrations (flagellar antigens).

Inoculate a nutrient agar slope for 'O' antigen production if necessary. Antigen is prepared from growth on nutrient agar slope washed off into 5ml peptone water and boiled for 30 minutes. Dilute, if needed, to workable concentration. Incubate in 50°C waterbath overnight before reading for *Salmonella* 'O' antigens.

Table A7.10 Tube agglutination of diagnostic titres

TUBE NO.	1	2	3	4	CONTROLS
Saline (drops)	0	5	8	9	10
Anti-serum (1 in 10) (drops)	10	5	2	1	0
Bacterial suspension (drops)	15	15	15	15	15
Final dilution	2×10^{-1}	5×10^{-1}	1.25×10^{-2}	2.5×10^{-2}	0

Shigella and *Salmonella* – biochemical confirmation

The following biochemical tests should be carried out for confirmation of all serologically positive *Shigella* species (except *Sh.sonnei*) and suspect isolates of *Salmonella* giving doubtful serological results. Urease and TSI reactions are usually sufficient to identify *Sh.sonnei*.

Table A7.11 Biochemical tests for identifying *Salmonella* and *Shigella* isolates
(Barrow and Feltham 1993)

	Salm	*S.typhi*	*Sh.flex*	*Sh.sonn*	*Sh.boyd*	*Sh.dys I*	*Sh.dys*
Glucose (acid & gas)	+	A	A g	A	A g	A	A
Lactose	-	-	-	(A)	-	-	-
Sucrose	-	-	-	(A)	-	-	-
Dulcitol		(d)	(d)	-	-	-	-
Mannitol	+	+	+	+	+	-	-
Salicin	-	-	-	-	-	-	-
Urea	-	-	-	-	-	-	-
Indole (from peptone)	-	-	d	-	d	-	d
ONPG	-	-	-	+	-	+	d
Malonate	-	-	-	-	-	-	-
Lysine	+	+	-	-	-	-	-
Ornithine	+	-	-	+	-	-	-
Arginine	(+)	(d)	(d)	-	d	-	-
Citrate (Koser's)	+	+	-	-	-	-	-

Key
+ = 85-100% strains +ve; d = 16-84% strains +ve; - = 0-15% strains +ve;
( ) = delayed reaction in test; A = acid only produced; g = some strains produce gas

A7.3.8 Detection and enumeration of *Staphylococcus aureus*

(Baird-Parker 1962; Chopin *et al.* 1985; Barrow and Feltham 1993; Collee *et al.* 1989; Anon. 1990)

Introduction

This method uses direct inoculation of a dilution series onto Baird Parker agar

Procedure

20% suspension of sample in Phosphate Buffered Saline (PBS)
⇓
1:200 (10-3) dilution in 0.1% Peptone Water (PW)

⇓	⇓
dilution in PW (10-5)	Plate 0.1ml on
⇓	Baird Parker (BP) agar
Plate 0.1ml on	⇓
Baird Parker (BP) agar	48hr @ 37°C
⇓	
Inoculate on XLD and on DCA	
⇓	
48hr @ 37°C	

Examine all plates for *Staph.aureus* colonies – 1–3mm, grey-black, shiny, convex, with 2–5mm zone of clearing

Confirm all presumptive positives by testing 5 typical colonies for coagulase (tube method; +ve), DNase (+ve) and mannitol fermentation (+ve).

Selective medium

Baird-Parker agar (BP):

Tryptone	10 0 g/l
'Lab-Lemco' powder	10.0 g/l
Yeast extract	1.0 g/l
Sodium pyruvate	10.0 g/l
Glycine	12.0 g/l
Lithium chloride	5.0 g/l
Agar	20.0 g/l

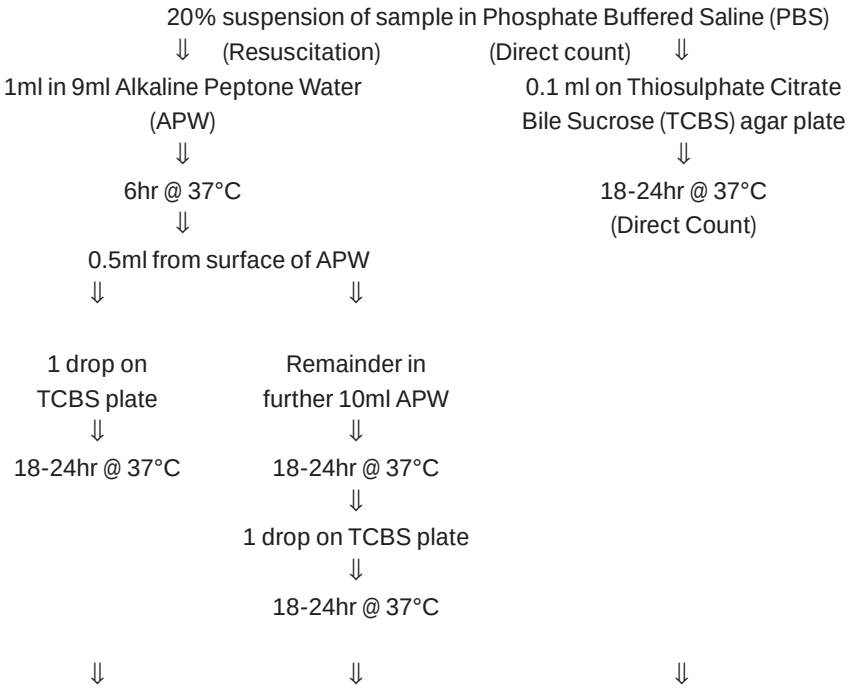
Adjusted to pH 6 9 ± O.1
Supplemented with
1:5 egg-yolk emulsion in water at 50 ml/l
and potassium tellurite to a final concentration of 10 mg/l

A7.3.9 **Detection and enumeration of *Vibrio* spp.**
(Furniss *et al.* 1978; Gerbaud *et al.* 1985; WHO 1980)

Introduction

The selective medium in this method is quoted in WHO guidelines for detecting *Vibrio* in faecal samples. The method combines direct inoculation, for quantitative assessment of higher numbers, with resuscitation/enrichment in alkaline peptone water (APW), for lower numbers and/or stressed organisms.

Procedure



Examine all plates for typical colonies: 2-5 mm diameter, yellow or blue-green.

Confirmation

Confirm all presumptive positive colonies by a range of standard biochemical tests as shown in Table 7.12.

Table A7.12 Preliminary identification of *Vibrio* and *Aeromonas* spp.
(Barrow and Feltham 1993)

	1	2	3	4	5
Growth at 37˚C	+	+	+	+	+
Motility	+-	+	+	+	d
Oxidase	+	+	-	+	+
Nitrate reduced	+	+	-	+	+
Gas in glucose	-	d	-	-	d
Arginine decarboxylase	-	+	+	-	+
Lysine decarboxylase	+	d	d	-	d
Ornithine decarboxylase	d	-	-	-	-
O/129 resistance (10 g)	d	d	-	d	+
O/129 resistance (150 g)	-	-*	-	d	+
Growth in 6% NaCl	d	d	+	+	-

1 *Vibrio* spp. including *V.cholerae, V.mimicus, V.vulnificus, V.parahaemolyticus, V.alginolyticus, V.harveyi, V.cincinnatiensis*
2 *Vibrio* spp. including *V.fluvialis, V.furnissii, V.anguillarum, V.damseli*
3 *Vibrio* spp. including *V.metschnikovii*
4 *Vibrio* spp. including *V.hollisae, V.natriegens*
5 *Aeromonas* spp.
* Some resistant isolates
d 16–84% strains positive
O/129 Vibriostatic agent 2-4-diamino-6,7-diisopropylpteridine

Selective medium

Thiosulphate-citrate-bile-sucrose agar (TCBS)

Yeast extract	5 0 g/l	Sodium chloride	10.0 g/l
Bacteriological peptone	10.0 g/l	Ferric citrate	1.0 g/l
Sodium thiosulphate	10.0 g/l	Bromothymol blue	0.04 g/l
Sodium citrate	10.0 g/l	Thymol blue	0.04 g/l
Oxbile	8.0 g/l	Agar	14.0 g/l
Sucrose	20.0 g/l	Adjusted to pH 8.6 ± 0.2	

A7.3.10 Detection of *Yersinia* spp.

(Schiemann 1979; Swaminathan *et al.* 1982; Barrow and Feltham 1993; Anon. 1990)

Introduction

This method combines direct inoculation onto CIN (Cefsulodin/Irgasan/Novobiocin) agar, to enumerate more highly contaminated samples, with cold enrichment, for samples where *Yersinia* may be present in smaller numbers or at a competitive disadvantage.

Procedure

20% suspension of sample in Phosphate Buffered Saline (PBS)

⇓ (Resuscitation) (Direct count) ⇓

1ml in 9ml PBS — 0.1 ml on CIN agar plate

⇓ ⇓

7 days @ 4°C — 48hr @ 30°C

⇓

Inoculate on CIN agar plate

⇓

48hr @ 30°C

⇓ ⇓

Examine plates for typical colonies: 'bull's eye' appearance, i.e. pale periphery and red centre

Test all suspect colonies in urea broth (urease +ve) and TSI (yellow butt and slope, no gas)

Carry out standard biochemical confirmatory tests on all presumptive colonies, using commercially available test kits if preferred; characteristics of *Yersinia* spp. are: growth at 4°C on nutrient/MacConkey agars; motility at 22°C; urease +ve; ornithine decarboxylase +ve; acid production from sucrose, cellobiose, amygdalin, rhamnose, raffinose; no acid production from melibiose

Selective medium

CIN agar (Cefsulodin/Irgasan/Novobiocin)

Special peptone	20.0 g/l	Crystal violet	0.001 g/l
Yeast extract	2 0 g/l	Agar	12.5 g/l
Mannitol	20.0 g/l	Adjusted to pH 8.6 ± 0.2	
Sodium pyruvate	2.0 g/l	Supplemented with:	
Sodium chloride	10.0 g/l	Cefsulodin	15 mg/l
Magnesium sulphate	0.01 g/l	Irgasan	4 mg/l
Sodium desoxycholate	0.5 g/l	Novobiocin	2.5 mg/l
Neutral red	0.03 g/l		

A7.4 PARASITOLOGICAL METHODS

(Casemore 1991; Jeffrey 1991; Ridley and Hawgood 1956)

A7.4.1 Examination for cryptosporidia

Make a reasonably thin film of undiluted stool specimen on a glass slide and allow to dry at room temperature

A7.4.1.1 Screening stain

Stain dried film with the following:

Auramine/Phenol solution	5 minutes
Wash	5 minutes
Carbol Fuchsin (0.5%)	15 seconds
Wash	5 minutes

Drain and dry on hot-plate
Examine by UV light microscopy for characteristic fluorescing ‘polo-mint’ rings.

A7.4.1.2 Confirmatory stain

A preparation of a known positive is included as a control
Stain dried film with the following solutions:

Carbol Fuchsin (0.5%)	15 minutes
Wash	5 minutes
1% HCl in methanol	10 seconds
Wash	5 minutes
malachite Green (0.4%)	30 seconds
Wash	5 minutes

Drain and dry on hot-plate
Examine by light microscopy for characteristic oocysts stained red (or unstained) against green background.

A7.4.2 Examination for *Entamoeba histolytica* and *Giardia intestinalis* ova and cysts

Add ~1g stool to 10ml formol saline in an universal bottle.
Mix well and leave at room temperature overnight.
Mix well and filter through gauze into a clean glass universal bottle
Add 3ml diethyl ether and shake vigorously

Centrifuge at 1,500 rpm for one minute
Discard supernatant
Add one drop of deposit to one drop 10% iodine solution on a glass microscope slide
Add coverslip and examine by light microscopy
Scan whole of area covered by coverslip with ×10 objective
Check suspect bodies with ×40 objective, comparing with examples given in parasitology atlas

A7.5 METHODS USED IN THE PHLS LABORATORY OF ENTERIC PATHOGENS (LEP)

A7.5.1 **Summary of Studies**
A7.5.1.1 Enterovirulent (Diarrhoeagenic) *E.coli*.
A7.5.1.2 Characterization of other organisms.
A7.5.1.3 Laboratory protocol for examination of faecal samples.

A7.5.2 **Procedures for isolation of enterovirulent *E.coli*.**
A7.5.2.1 Preparation of membranes for DNA hybridization tests using faecal specimens.
A7.5.2.2 Preparation of membranes using broth cultures.
A7.5.2.3 Treatment of membranes with spotted faeces or cultures.
A7.5.2.4 Hybridization with fluorescein-labelled probes.
A7.5.2.5 Detection of fluorescein-labelled hybrids.
A7.5.2.6 Preparation of fluorescein-labelled probes.
A7.5.2.7 Examination of faecal plating for probe-positive colonies.
A7.5.2.8 Tissue culture tests for adhesion.

A7.5.3 **Typing of organisms in the LEP**
A7.5.3.1 Identification and serotyping of *Aeromonas, E.coli, Plesiomonas, Shigella, V.cholerae & Yersinia*.
A7.5.3.2 Phage typing of *E.coli* O157 and *Shigella sonnei*.
A7.5.3.3 *Salmonella* identification and typing.

A7.5.4. **Reporting of isolates and faecal specimens during the IID study**

(Ahmed *et al.* 1987; Anderson and Williams 1956; Bentley *et al.* 1996; Callow 1959; Chambers *et al.* 1987 De Sa *et al.* 1980; Ewing 1986; Frost *et al.* 1989; Gross and Rowe 1985; Shipp and Rowe 1980; Ward *et al.* 1987.)

A7.5.1 Summary of studies

A7.5.1.1 Enterovirulent *Escherichia coli*

The Laboratory of Enteric Pathogens (LEP) examined faecal specimens for the presence of enterovirulent (diarrhoeagenic) *Escherichia coli*. Specimens were tested with DNA probes directed against different groups of pathogenic or potentially pathogenic *E.coli*. The following seven groups were studied:

- Enteropathogenic *E.coli* (EPEC); identified with the EPEC adherence factor probe (EAF).
- Enterotoxigenic *E.coli* (ETEC); identified with probes for the heat stable and heat-labile enterotoxin genes (ST and LT).

- Verocytotoxin-producing *E.coli* (VTEC); identified with probes for the Vero cytotoxin (VT) genes, VT1 and VT2 .
- Enteroinvasive *E.coli* (EIEC), hybridizing with the EIEC probe for intestinal invasion genes.
- Enteroaggregative *E.coli* (EAggEC); identified with the AA probe for aggregative adhesion.
- Attaching and effacing *E.coli* (AEEC); these hybridized with the eae probe for attaching and effacing ability.
- Diffusely adherent *E.coli* (DAEC); identified with the DA probe for diffuse adhesion.

Faeces were examined by the protocols given below. Colonies identified as positive with any of the probes were characterized biochemically and fully serotyped. Strains hybridizing with the EAF, AA, eae or DA probes were also tested for adhesion to cultured cells *in vitro* (see below).

A7.5.1.2 **Characterization of other organisms**

Cultures of *Aeromonas*, *E.coli* O157, *Plesiomonas*, *Salmonella*, *Shigella* and *V.cholerae* and *Yersinia* isolated by Leeds PHL during the study were submitted to the LEP for identification and typing.

A7.5.1.3 **Protocol for examination of faecal specimens for enterovirulent *E.coli.***

The following is a summary of the laboratory protocol for the examination of specimens. Details of the individual procedures are given.

Faecal samples received were given a unique laboratory number. A loopful of faecal material, appropriately resuspended in phosphate buffered saline if necessary, is streaked around a MacConkey agar plate to obtain single colonies. Plates were incubated at 37°C overnight and stored at 4°C.

Faecal samples were grouped in batches of 10 and inoculated onto nylon membranes supported on MacConkey agar plates without indicator. Strains of *E.coli* that were positive with the DNA probes used and a negative control were included on each membrane. Seven copies of each membrane were prepared.

After incubation at 37°C overnight, membranes were prepared for DNA hybridization as described in section A7.5.3.

As a back-up to the direct testing of faeces, a sweep of coliform growth from the plates generated in A7.4.1 above was inoculated into 2.5ml of nutrient broth and grown overnight. Broth cultures were grouped in batches of 40 and spotted, together with control strains, on to nylon membranes supported on MacConkey agar (section A7.5.2.2). Seven copies of each membrane were prepared. The membranes were prepared for colony hybridization as in section A7.5.2.3.

The DNA probes used and the groups of *E. coli* that they detect were as listed above. Each sample was tested with 7 probes, mixed EAF + LT, mixed STA1 + STA2, mixed VT1 + VT2, EIEC, AA, *eae* and DA.

Fluorescein-labelled probes (Fl-dUTP) were prepared by the procedures described in section A7.5.2.6. These probes were EAF, ST (comprising STA1 and STA2 sequences), LT, VT (comprising VT1 and VT 2), EIEC, AA, *eae* and DA. Details of the probes are given in Table A7.13.

Batches of membranes were hybridized with the DNA probes. The methods are described in sections A7.5.2.4 and A7.5.2.5.

All faecal specimens or enrichments of coliform growth from faecal specimens that give a positive or possibly positive result in the initial screening with any probe were identified. On the basis of the pilot study, this will represent about 15% of the total samples received. The appropriate plates from section A7.5.1.3 above were selected for testing with the specific probe or probes of interest. Growth from the master plate was replica-plated onto a nylon membrane supported on a nutrient agar (section A7.5.2.7) and after growth for about 5h at 37°C, the membranes were prepared as described in section A7.5.2.3.

Membranes were hybridized with the appropriate probe. Two replica plates were prepared for the EAF + LT positive samples. Colonies that appear to be probe-positive were identified by comparing growth on the master plates with the X-ray films. Five such colonies were picked from each plate and subcultured in 2.5ml of nutrient broth. These cultures were then spotted out for colony hybridization to check their reaction with the appropriate probe.

Two confirmed probe-positive colonies from each specimen were streaked out for purity on MacConkey agar. From one of these plates a single colony was selected for serological and biochemical identification.

Colonies from DNA probe tests were assigned unique 'E' numbers and serotyped with antisera to O-antigens 1 to 173 and H-antigens 1 to 55 (see section A7.5.3.1). The same cultures were also identified biochemically.

These characterized cultures were retested by colony hybridization with the appropriate probes. For these tests, individual probes for VT1, VT2, EAF and LT were used rather than the mixed probes employed before (see section A7.5.1.3).

Strains that were confirmed as positive with the EAF, *eae*, AA or DA probes were tested for patterns of adherence to tissue culture cells that have been associated with these probes. The AA and DA positive strains were tested for attachment to Hep2 cells in culture and the EAF and *eae* positive strains were examined for their ability to cause attachment and effacement of the cell surface assayed by the fluorescein actin staining (FAS) test (see section A7.5.2.8).

A7.5.2 Procedures for isolation of enterovirulent *E. coli*

A7.5.2.1 Preparation of membranes for DNA hybridization tests using faecal specimens

Prepare a 'standard' faecal suspension by adding a known volume of PBS to a known weight of faeces and mix well. e.g. 1 gram faeces + 4mls PBS.

Leave the suspension to settle (15 mins) and centrifuge 1ml of suspension in a microcentrifuge. Resuspend the pellet in 200µl PBS. Liquid faeces do not require this treatment. Mark up 7 membranes (Hybond N, Amersham International) with a unique IID number followed by the suffix 1 to 7. The numbers 1 to 7 determine which probes will be used for hybridization.

Spot a known volume of suspension on a membrane (up to 10 samples per membrane). Positive and negative controls are included on each membrane. The membranes are placed on MacConkey plates without dye and incubated overnight at 37°C. Process the membranes as usual ensuring that the lysis is complete. Ensure that the book is updated with the list of samples spotted.

A7.5.2.2 **Preparation of membranes using broth cultures**

Use broth cultures grown overnight at 37°C. One drop of each culture (about 0.01ml) is spotted on nylon membranes that have been placed on MacConkey agar plates. Up to fifty spots can be put on a membrane in a grid pattern. Control cultures are also spotted at the bottom of each membrane. The plates with membranes are incubated at 37°C for 5-6 hours.

Control strains
These strains are grown overnight in nutrient broth and spotted on each membrane.

E3787	*E. coli* O26.H11	VT1 +ve
E32511	*E. coli* O157.H-	VT2 +ve
E2347	*E. coli* O127.H6	EAF +ve, *eae* +ve
E60725	*E. coli* O92:H33	AA +ve
E66438	*E. coli* O75:H-	DA +ve
E7476	*E. coli* O166:H27	ST +ve
E5798	*E. coli* O7:H18	LT +ve
E35990	*E. coli* O143:H-	EIEC +ve
14R519	*E. coli* K12	negative control

A7.5.2.3 **Treatment of membranes spotted with faeces or cultures**

Prepare four trays with sheets of Whatman 3MM paper (or similar). Saturate the first sheet with 10% SDS and then place the membranes colony side up on the SDS saturated paper for 5 minutes. For steps 2 to 5 take care not to cover the upper side of the membranes with any of the solutions. Between each step the membranes were blotted on sheets of paper towel.

Transfer the membranes to the second sheet saturated with denaturing solution (0.5M NaOH, 1.5M NaCl). Leave for 10 minutes.

Transfer the membranes to the third sheet saturated with neutralising solution (1.5M NaCl, 0.5M Tris, pH8). Leave for 5 minutes.

Transfer the membranes to the fourth sheet saturated with 2×SSPE, pH 7.4. Leave for 5 minutes. (To prepare 2×SSPE: 17.4g NaCl, 3.1g $NaH_2PO_4.2H_2O$, 0.74g EDTA per litre, pH 7.4).

Allow the membranes to dry at room temperature. Binding of the released DNA to the membrane can be performed by either of the following methods.

a) Wrap the membranes in cling film and place on a UV transilluminator (colony side down) for 4 minutes.
b) Place the membrane between sheets of 3MM paper and bake for 2h at 80°C.

The membranes are then ready for use in hybridization tests. Store in bags until required.

A7.5.2.4 **Hybridization with fluorescein-labelled probes**

Refer to the booklet provided by Amersham for details and background of the ECL system. Procedures for labelling probes using PCR or random primer methods are described in separate protocols (section A7.5.2.6).

Pre-heat the hybridization oven to 68°C according to the manufacturer's instructions.

Make a list of membranes to be tested and which probes were to be used. Wet the membranes in a small volume of 5×SSC in a plastic box. Depending on the number of membranes for a particular probe, decide whether to use small or medium bottles. For guidance, do not put more than about the equivalent of about ten membranes in a medium bottle because there may be problems with the probe reaching its target. Wet the appropriate sized meshes in a tray of 5×SSC.

Place the membranes on the mesh so they do not overlap. Put a second layer of mesh on top if necessary. Roll up the mesh loosely and put into the bottle.

Add 5×SSC, warmed to 68°C, to fill about 1/4 of the bottle. Roll gently to unwind the membranes and put into the oven with balance tubes if necessary. Rotate for about 1 hour.

Remove and take meshes apart in a shallow tray containing a small amount of 5×SSC. Wipe membranes with damp tissue to remove cellular debris. Re-assemble the meshes and replace in the bottles.

Add the ECL hybridization solution – about 20ml for a small bottle and about 30ml for a medium one. Freshly boiled salmon DNA should be added to the bottles with the hybridization solution at the rate of 0.1ml per 10 ml of solution.

Pre-hybridize for at least 2 hours at 68°C in the oven.

Thaw out the probe solution which will have been diluted in between 5ml and 10ml of ECL hybridization solution (see protocol on probe preparation, section A7.5.2.6).

Pour off the pre-hybridization mixture, removing as much as possible with a Pasteur pipette.

Boil the probe solution for at least 5 minutes, cool rapidly on ice and add all of it to the appropriate bottle. Rotate the bottle to check all membranes were in contact with the solution.

Hybridize overnight at 68°C.

Carefully remove as much probe as possible and return it to the original container and store in the freezer.

With the membranes still in the bottle wash at room temperature, preferably in a second hybridization oven, for two periods of 10 minutes in 2×SSC/0.1% SDS. Conditions for subsequent washes depend on the probe being used and are listed below. Note that for any washes not at 68°C, membranes will have to be removed from the bottle and incubated in a plastic box or bag in a shaking water bath at the appropriate temperature.

Mixed VT *eae*, EAF, LT	0.1×SSC/0.1% SDS 2×15 minutes at 68°C
AA, Mixed ST	5×SSC/0.1% SDS 2×15 minutes at 54°C 2×SSC/0.1%SDS 30 sec at RT
DA, EIEC	0.5×SSC/0.1% SDS 2×15 minutes at 68°C

Finally, rinse briefly in ECL buffer 1 and go on to the detection step (section A7.5.2.5). Keep the membranes damp at all times.

A7.5.2.5 **Detection of fluorescein-labelled hybrids**

The procedure is similar to that described in the Amersham booklet but smaller volumes of reagents can be used to make it more economical.

Transfer the hybridized membranes to plastic bags. Arrange them so that they are 'back to back' with the DNA sides facing outwards and not overlapping. Eight complete membranes can be put into a bag but extras can be accommodated if needed. Try to keep the number of bags to a minimum.

Prepare blocking reagent (0.5% blocker in ECL buffer 1). Each full bag of membranes will need 25 to 30 ml of blocking solution. To make the solution, weigh out the powder, add ECL buffer 1 and heat very gently in the microwave on low power until it dissolves when stirred. Do not overheat or it will form lumps. Cool to room temperature and add appropriate volumes to the bags. Seal so as to leave plenty of space around the membranes but excluding as much air as possible. Shake for 1h at room temperature.

Cut off part of top of bag and pour out blocker as completely as possible. Add into the bag some ECL buffer 1 and gently agitate manually. Pour off wash solution and smooth out bag on a paper towel to remove as much liquid as you can.

Conjugate is made up in ECL buffer 1 containing 0.5% bovine serum albumen. The stock conjugate is diluted 1/1000. For a full bag, you will need 20ml of diluted conjugate but for smaller numbers of membranes, reduce the amount used. Reseal bag and shake at room temperature for 1h.

Remove membranes to a plastic box and wash at room temperature in ECL buffer 1 containing Tween 20. Wash for 2×10 minutes followed by 2×5 minutes. Keep the membranes damp.

Make up a minimal volume of substrate by mixing equal volumes of the two reagents taking care not to cross contaminate the two solutions. For a whole membrane you need about 4ml but the membranes will not be treated at the same time and the substrate can be reused for two sets of membranes.

In the dark room assemble white plastic trays, cling film taped to paper backing, timers, substrate, pipette, tracker tape tabs and document wallets. Switch off room lights and put the safelight on. Load cassettes with film noting that up to six full membranes go on a film. Some types of membrane, e.g. those membranes with spotted faeces may be exposed to film for longer than the standard time and should be put on the same sheet of film.

With the lights on, arrange the membranes DNA side up on trays. Pipette substrate solution on surface of batches of membranes and leave for 1 minute. Blot the membranes on paper towel and reclaim the substrate for the next lot of membranes. Arrange the membranes on cling film/paper sheet and cover with other half of the cling film sandwich and insert the parcel into a plastic document wallet. Put tracker tape marker on if required. Repeat with further lots of membranes.

With the safelight on, put the film onto the wallets and expose in cassettes for appropriate times. This is usually 7 minutes for some membranes but up to 20 minutes for membranes spotted with faeces.

With safelight on, develop film in the processor according to the manufacturer's instructions. Overlay the film and the membranes and score results. Note that it may

be possible to re-probe membranes if they are removed from the cling film and kept damp.

A7.5.2.6 Preparation of fluorescein-labelled probes

Probes are labelled with the dUTP which has a fluorescein attached to it at position 11 or 12. dUTP becomes incorporated into the DNA probe in place of dTTP but in practice probe labelling takes place with a mixture of dUTP and dTTP; the ratio of the two can affect the degree of probe labelling. Two methods are used for the preparation of labelled probes. Labelling the probe in the PCR reaction gives a product that avoids the possibility of contamination with vector but is only possible if there are primers corresponding to the ends of the probe sequence. There tends to be rather a lot of variation in the yield of product labelled by PCR. It has been found that a more reliable method is to amplify the probe fragment by PCR without the presence of fluorescein-labelled dUTP. The unlabelled fragment can be purified, stored and then labelled by random priming. Any DNA fragment can be labelled by the random primer method.

A7.5.2.6.1 PCR labelling

PCR amplification can be done at present for the VT1, VT2, LT, AA, DA, EAF, *eae* and EIEC probes. Table A7.13 shows the strains that are used in the PCR. Before using any of these strains they should be streaked out on selective medium (L-agar or nutrient agar containing ampicillin (Ap), since the success of the method depends on the presence of the probe DNA fragment cloned in a vector coding for Ap resistance.

One tube of PCR labelling mix is made up as follows in the clean cabinet:

5 µl of PCR buffer
1.5 µl of MgCl2
5 µl of 20 uM upstream primer } diluted from stock
5 µl of 20 uM downstream primer } diluted from stock
2 µl 1/10 dilution of Taq polymerase
9 µl sterile water
1 drop (about 30 µl) of oil

These mixtures can be stored frozen if several labellings using the same primer sets are planned.

Immediately before you want to start, make up the following nucleotide mixture in a separate tube:

5 µl each of 3 mM dATP, dCTP and dGTP
5 µl of Flu-dUTP
2.5 µl of dTTP

Add this 22.5 µl mixture to the 27.5 µl reaction mix prepared above. If you want to scale up the amount of probe to be made on one occasion, make up two labelling tubes, rather than doubling the volumes in one tube.

If you are simply preparing unlabelled fragment for use in random priming, then make up PCR tubes in the normal way with dATP, dCTP, dGTP and dTTP.

Take the PCR tube(s) to the location you are using to add the DNA template (see general protocols on PCR). Here add 2 µl of a broth culture of the strain containing the appropriate probe sequence. As quickly as possible take the PCR tubes to the machine and start the amplification according to the predetermined programme (Table A7.14).

After the amplification retrieve the tubes and fridge. (See Tables A7.13 and A7.14 on page 572.)

A7.5.2.6.2 Purification of PCR-labelled probe or unlabelled fragment

The required fragment is purified by running it on an agarose gel and extracting the DNA from the band.

Prepare an agarose gel in Tris borate buffer using the midi horizontal apparatus. The concentration of agarose depends on the size of fragment to be purified (Table A7.13). Make up mixtures to run on the gel. The 50 µl PCR mix is run in two halves in separate tracks. Always run a track containing a molecular weight marker - usually the molecular weight marker VIII and/or a *Hind*III-*Eco*RI digest of lambda DNA. The gel is run at 100 volts until the dye is near the end and then stained in ethidium bromide. The gel is examined under long wavelength UV in the cabinet but not photographed or viewed with the transilluminator.

If the desired fragment (labelled or not) is in the correct position the band is cut out with clean scalpel into pre-weighed Eppendorf tubes. The gel can now be photographed to preserve a record that the right fragment was used. The DNA is purified from the gel slices according to the protocol for the use of Qiaex II resin. This product will work with gels in Tris borate whereas earlier versions or other products do not. The final eluates are pooled and from two slices you should get 80 (l of final product. Label the tubes and store in the freezer.

A7.5.2.6.3 Dilution of the probe for hybridization

The probe is usually diluted at the rate of 1 to 2 µl of labelled stock per 1 ml of ECL hybridization mixture. Take the appropriate amount of stock probe and add it to 100 µl of TE buffer in an Eppendorf tube. Boil this in a plastic rack for 7 minutes and chill rapidly on ice. Spin to bring all the solution to the bottom of the tube. Add all this to the required amount of ECL hybridization solution that has been pre-heated to 68˚C and to which has been added 10µl per ml of freshly boiled salmon DNA. Scintillation vials with plastic caps are used to contain the diluted probe. After the probe has been used the first time it may be clear that the probe concentration is too low. If this is the case more boiled stock probe can be added in to the vial. Record the new dilution factor for making up the next batch. Keep a record of all uses of each probe.

Add the probe to the bottles containing the pre-hybridized membranes, ensuring that as much of the pre-hybridization solution as possible is drained off first so that the probe will not be diluted. After the hybridization period recover the probe as completely as possible with a Pasteur pipette and return to the vial.

Used probes are stored in the freezer. Probe solutions can be used at least 4 times making sure that the vial is boiled each time for at least 5 minutes.

A7.5.2.6.4 Random primer labelling of probes

This method is used if primers corresponding to the ends of the required probe are not known or not available. It is a very reliable method to label fragments generated by PCR. It can be used to label any double stranded DNA molecule, including complex mixtures such as plasmid or phage digests. The method used is basically as in the Amersham ECL kit instructions.

The DNA fragment to be labelled is previously purified and concentrated with Qiaex resin and should have been checked on a gel to verify that it is the right fragment and to get some estimate of its approximate concentration.

The labelling mix contains in the following order:

water to make final volume of 50 µl
10 µl nucleotide mixture
5 µl primers (random nonamers)
20 µl boiled probe fragment (about 100 ng)*
1 µl Klenow polymerase

*Take a volume of purified fragment containing about 100 ng of DNA and dilute it with TE buffer to 20 µl. The rough concentration of the fragment can be estimated by comparing the intensity of the fragment band on an agarose gel with a known amount of digested lambda DNA. The 20 µl of diluted probe is boiled for 5 minutes, quick-chilled and spun down before adding to the labelling mixture above.

The reaction goes on for 4 hours at 37°C or overnight at room temperature, preferably in the dark. The reaction is stopped by adding 4 µl 0.25 M EDTA and the product is stored frozen. It can be use directly as a stock probe solution without further purification.

The probe is denatured and diluted into hybridization mixture as described above for PCR-labelled probes. The dilution factor is either 1 µl or 2 µl per ml hybridization buffer.

A7.5.2.7 **Examination of faecal platings for probe-positive colonies**

A7.5.2.7.1 Replica plating on to nylon membrane:

A MacConkey agar plate containing streaked out growth from a faecal sample is given a set of orientation marks. Complementary marks are made on a nylon membrane which is then placed on a nutrient agar plate. Growth from the master plate is transferred on to a velvet pad held in a replica-plating block by gently pressing the surface of the plate on the velvet. In the same orientation, the nylon filter is then pressed on to the velvet and growth is transferred to the membrane surface. Both master and replica plate are incubated at 37°C for about 4–6 hours. The master plates are stored at 4°C and membranes are prepared for DNA hybridization as described in section A7.5.2.3.

If a replicated plate from a faeces shows positive colonies by probe these should be marked on the master plate and numbered. Mark two well separated colonies. Pick as cleanly as possible with a straight wire and streak out on MacConkey agar. Keep the replicated plate, seal it with tape and store at 4°C.

After the streaked out colonies have grown, pick into broth up to five colonies representing the colony types present. Spot out on gridded membranes in the usual way for confirmatory probe tests.

If probe-positive colonies have been obtained, Dorset eggs should be made from the broth culture by streaking out on MacConkey plates first. Keep two colonies from a sample on Dorset egg. Label with the IID number of the specimen and pick number. If none of the colonies is probe positive, go back to the master plate and start again.

Dorset eggs are retained until batches can be serotyped and tested further.

A7.5.2.8 **Tissue culture tests for adhesion**

A7.5.2.8.1 Attachment to Hep-2 cells:

Strains positive with the AA or DA probes were tested for adhesion to Hep-2 cells. The method tests the ability of bacteria to adhere to monolayers of Hep-2 cells. D-mannose (1% w/v) is present during the test to prevent attachment to the tissue culture cells or other surfaces due to type 1 fimbriae, which may be expressed by the bacteria.

Monolayers of HEp-2 cells grown for 2 to 3 days on glass coverslips in 12 well plates are prepared in the absence of antibiotics. The bacterial strains to be tested are grown overnight without shaking at 37°C in peptone water. Before the test the HEp-2 monolayers are washed twice with Earle's balanced salts solution (EBSS). 1.5 mL of attachment medium of BME medium without antibiotics and containing D-mannose (1% w/v) is added to each dish. 25 µl of the overnight bacterial culture are added to each dish to give about 10^7 to 10^8 bacteria and the dishes reincubated at 37°C for 3 hours. The monolayers are then washed three times with EBSS and 1.5 ml of the attachment medium is added. After a further 3 hours incubation period the monolayers are washed thoroughly three times with EBSS, covered with methanol and left for 5–10 min. The monolayers on glass coverslips are then prepared for viewing under oil immersion at ×1000 magnification. The methanol is removed and replaced with newly prepared Giemsa stain (10% v/v in phosphate buffer) for 30–45 minutes. The coverslips are then removed, washed twice with Giemsa diluent and mounted on glass slides with Depex after passing through two lots of acetone, acetone-xylene (50/50 v/v), acetone-xylene (33/66 v/v) and, finally, xylene. Appropriate controls were included in each batch of tests.

The pattern of attachment should then be assessed by examining at least 200 cells over a number of fields. Arrangements noted are:

1 **Localised.** Bacteria appear in clusters that may range from five to over 100 bacteria and the percentage of cells with clusters may range from 0.5% to 100%.
2 **Diffuse.** Bacteria are arranged fairly evenly over the surface of the cells, and attachment to all cells is similar. In good attachment the whole surface is covered with over 100 bacteria. Poor attachment may also be seen with bacterial numbers of less than 20.
3 **Aggregative.** Bacteria are arranged in irregular masses and attach to the glass as well as cells in some cases.

A7.5.2.8.2 Maintenance of Hep-2 cells:

Cell line Hep-2, carcinoma of larynx, ATCC No. CCL23
Growth medium: basal medium eagle with Hanks salts. To 100ml add:
15ml foetal bovine serum
2ml penicillin-streptomycin (5000 units/ml)
0.5ml glutamine (200 mM)
Amphotericin B (Fungizone) (250 µg/ml) may also be added (see below).

All reagents obtained from Flow Laboratories Ltd., Rickmansworth, England.

Monolayers are washed twice with 5 ml Dulbecco's phosphate-buffered saline without calcium and magnesium (DPBS). Five ml 0.25% (w/v) trypsin are added and poured off after 1 minute. The monolayers are then incubated at 37°C until cells begin to detach (*c*. 5 minutes). Five ml basal medium eagle (BME) growth medium

are then added and the cells resuspended. A 2 ml portion of suspended cells is then added to 12 ml growth medium in a tissue culture flask (75 cm^2) containing 0.15 ml amphotericin B (250 μg/ml) and incubated at 37˚C. This procedure is repeated twice weekly.

Two days before a test, a monolayer of Hep-2 cells which has been growing for 3 days is resuspended after trypsin treatment in BME growth medium without antibiotics. A portion is used for further cultures. For the Hep-2 adhesion test some of the remaining suspended cells are diluted in the complete tissue culture growth medium without antibiotics to obtain a final concentration of *c*.10^6 cells/ml (a dilution of 1/20 is usually satisfactory). For tests performed in petri dishes 2 ml of this diluted suspension are distributed into each 4 cm petri dish (tissue culture grade) containing a 22 mm sterile square glass coverslip. Alternatively, 1.5 ml of cell suspension are distributed in wells of a 12 well cluster plate (Costar) each containing a 13 mm sterile round glass coverslip. The dishes are gassed with 95% air–5% CO_2 and incubated at 37˚C for 48 hours.

A7.5.2.8.3 Fluorescence actin staining (FAS) test:

3h or 6h adhesion tests are performed by the procedure described. After the final washing in EBSS, the cells/bacteria are fixed by treating with 8% formalin in EBSS for 10 min at room temperature. After further washing three times in EBSS the cells are treated with 0.1% Triton X-100 in EBSS for 4 minutes at room temperature to permeabilize the cell membrane. The coverslips are washed again three times and after the final wash the liquid remaining in the well is carefully removed.

225μl EBSS are added to a vial of stored FITC-phalloidin (50 μg/ml) to give a 5 μl/ml solution and protected from light. Phalloidin is toxic and should be handled and made up with great care. Ten microlitres of this solution are added to each coverslip. The plates are covered with the lids and protected from the light. To avoid drying, a square piece of filter paper, moistened in water, is inserted in the lid of the plate. After 30 minutes, the coverslips are washed with EBSS (three washes of 10 minutes each). The washings are discarded into a pipette jar, reserved for this purpose, and disposed of appropriately.

The coverslips are drained, mounted on glass slides using 8 μl of Aquamount and viewed by incident light fluorescence microscopy for the presence of fluorescent areas. These are correlated with the presence of attached bacteria visualised by phase microscopy.

A7.5.3 Typing of organisms in the Laboratory of Enteric Pathogens

A7.5.3.1 Serotyping of *Aeromonas*, *E. coli*, *Shigella, Yersinia* and *V. cholerae*

The methods are described by Gross and Rowe (1985). Incubation temperatures for broth cultures are as follows:

E.coli, Shigella, Vibrio	37˚C
Aeromonas	30˚C
Yersinia	28˚C

All organisms are grown overnight in a Hedley Wright broth at the given incubation temperature.

The methodology for serotyping is the same for all organisms. The O-antisera used are listed below:

E. coli	O1–O173
Sh. dysenteriae	1–12
Sh. flexneri	I–VI
Sh. boydii	O1–18
Yersinia	O1–O57
Aeromonas	O1–O45
Vibrio	O1–O83 and O139

A7.5.3.2 Phage typing of *E. coli* O157 and *Shigella sonnei*

Phage typing of *E.coli* O157 is performed as described by Frost *et al*. (1989) using the scheme of Ahmed *et al.* (1987) developed in Canada. Strains of *Sh. sonnei* were phage typed using the scheme of Hammerström as described by Bentley *et al.* (1996).

A7.5.3.3 *Salmonella* identification and typing

The *Salmonella* strains are identified according to the procedures described by Ewing (1986).

Salmonella phage typing is carried out by the techniques described by Anderson and Williams (1956). Strains of the following serotypes are phage typed: *S. enteritidis*, *S. typhimurium*, *S. virchow* and *S. hadar* (Callow, 1959; Chambers *et al.* 1987, De Sa *et al.* 1980; Ward *et al.* 1987).

A7.5.4 Reporting of isolates and specimens during the IID Study

It is essential that all isolates and specimens received as part of the IID survey can be identified as such, and not included in routine surveillance.

All parcels came via LEEDS PHL.

Faecal specimens for probing:

Specimens were accompanied by SURVEY FORM A.

Any organisms isolated from positive faeces were referred for typing and given an E/S/P number.

Faeces results, list of probes and result +/-, and any organisms isolated by LEP, were sent to LSHTM only.

Cultures from Leeds PHL for identification and typing.

Cultures were accompanied by SURVEY FORM B. Cultures were given an E/S/P number with sending laboratory address = IID SURVEY (ZZ000000).

Reports for cultures isolated by Leeds PHL were sent to LEEDS PHL addressed to IID survey. A copy of the report was sent to the IID survey microbiologist for entry onto the IID database.

All data for faeces and cultures were entered on project PC system Epi Info using IID survey number as identifier.

Table A7.13 Preparation of ECL-labelled probes by PCR

PROBE	STRAIN FOR PCR	DRUG RESISTANCE	SIZE OF AMPLIFIED PRODUCT (KB)	% GEL FOR PURIFICATION*	PRIMER SYSTEM
VT1	62R720	Ap	0.75	1.0	T3, T7
VT2	62R738	Ap	0.85	1.0	T3,T7
eae	62R731	Ap	1.0	1.0	T3,T7
EAF	62R729	Ap	1.0	1.0	T3,T7
AA	62R734	Ap	1.0	1.0	T3,T7
DA	62R736	Ap	0.37	1.2	T3,T7
EIEC	62R748	Ap	1.0	1.0	T3,T7
Salmonella	62R750	Ap	0.43	1.2	S11,S15
ail	62R755	Ap	0.7	1.0	T3,T7
inv	62R753	Ap	0.57	1.2	YC1,YC2
LT	62R764	Ap	1.3	1.0	T3,T7
STA1	58R285	Ap	0.147	3.0**	est A1/L, est A1/R
STA2	58R287	Tc	0.147	3.0**	STA/L, STA/R

* Optimum concentration. When running several different products, use the % that will retain the smallest size.
** For ST use Nusieve agarose and standard agarose in the ratio 3:1.

Table A7.14 Conditions for preparation of PCR-labelled probes (ECL, digoxigenin)
1st cycle: 94˚C, 1.5 min; Annealing temp, 2 min; 72˚C, 3min.
Then 35 cycles of 94˚C, 1 min; Annealing temp, 2 min; 72˚C 3 min.

PRIMER SYSTEM	PROBES	ANNEALING TEMP.
T3, T7	VT1, VT2, *eae*, EAF, DA, AA, EIEC, *ail*, LT	55˚C
S11, S15	*Salmonella*	57˚C
YC1, YC2	*inv*	65˚C
est A1/R	STA1	55˚C
STA/L STA/R	STA2	55˚C

A7.6 VIROLOGICAL METHODS

(Barrett and Ogra 1985; Beards *et al.* 1984; Beards 1990; Bellamy *et al.* 1983; Brandt *et al.* 1981; Brandt *et al.* 1983; Bridger and Brown 1984; Coulson and Holmes 1984; Cukor and Blacklow 1984; Cukor *et al.* 1984; Davies 1982; Herman *et al.* 1985; Hermann *et al.* 1987; Johansson *et al.* 1980; Kapikian *et al.* 1980; Martin and Follett 1987; Sanders 1985; Sarkkinen *et al.* 1980; Wigand *et al.* 1983; Yolken and Leister 1981; Yolken and Leister 1982; Yolken *et al.* 1977; Yolken 1982)

A7.6.1 Introduction

The methods for virological analysis fall broadly onto two categories:

- Electron microscopy (EM)
- Immunological methods.

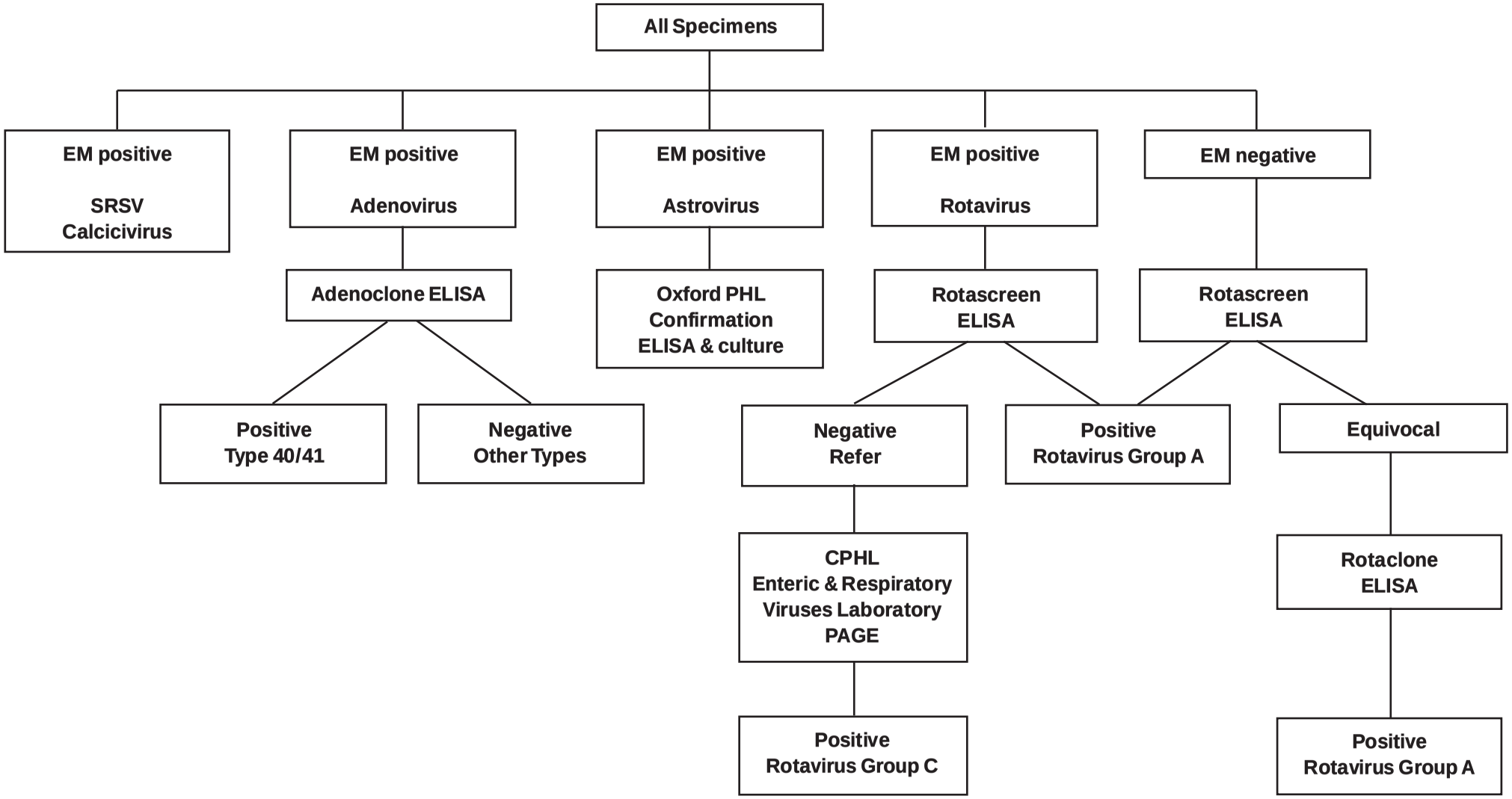
The quality control system for the EM methods is described. The immunological methods used in the IID Study were commercially available detection and assay systems, although the original references on which they are based are given. The flowsheet for virological examinations is given in Figure A7.2.

A7.6.2 Quality control procedures

The aims of this method are:

- To control the quality of grids and stain used in the EM preparation and their effect on sensitivity.
- To control the performance of the EM operator and ELISA systems

Figure A7.2 Flowsheet for electron microscopy for vruses and rotavirus & adenovirus screening by ELISA



The first aim is necessary because of grids vary in surface quality which affects their ability to bind virus or to produce optimum staining. In order to test the quality of the grids and stain, stock preparations of both rotavirus and adenovirus are tested against batches of grids at 2-weekly intervals and counts per unit area are made. Batches of grids which produce counts less than 50% of the previously established mean counts are rejected.

The second aim will be met by a system of internal quality control measures. These consist of a panel of positive specimens for all five enteric viruses which are run through the system under code ('blind') by the EM operator. The results are compared to the previously obtained result. This is done at 3 monthly intervals and allows the EM operators to assess their own performance and instrument resolution. External quality control of the EM operator performance is also monitored by sending 10% of the original specimens to be checked (by Dr Hazel Appleton) at the Enteric and Respiratory Virus Laboratory, Central Public Health Laboratory. These quality controls are every tenth specimen regardless of EM result.

The enzyme immunoassay (ELISA) tests are internally controlled using strong and weak positives for each run of rotavirus antigen detection and for each adenovirus antigen detection kit. Specimens found to contain astrovirus are confirmed by an 'in house' antigen detection ELISA using an astrovirus group-reactive antibody (obtained from CDC Atlanta by Dr D Brown) or by astrovirus culture and confirmation by immunofluorescence (Oxford PHL).

A7.6.3 Preparation of grids for electron microscopy

Make a 25% extract of faeces in PBS A and add 1 ml Arklone (trichlortrifluoroethane)

Vortex for 20 seconds and then centrifuge at 2,500 × g for 30 minutes.

Take 1 ml of clear supernatant and add to 1.5 ml polyallomer tube. Inject 100 µl of 30% sucrose (wt/vol) in PBS A into the bottom of the tube so as to form a separate layer.

Centrifuge at 45,000 × g for 1 hour (Beckman Optima TL centrifuge).

Remove the supernatant including the sucrose layer.

Re-suspend the pellet in 50µl PBS A by repeated pipetting and vortexing.

Clarify the re-suspended pellet by centrifuging for 10 minutes at 2,500 × g.

Place 25 µl of supernatant on a pre-marked Petri dish and place a grid, coated surface down, on the drop.

Allow to stand at room temperature for 1 to 2 hours. Pick up the grid and blot off excess specimen with clean filter paper. Place the grid face down on 1 drop of 2% phosphotungstic acid, pH 6.6

Immediately (within 10 - 60 seconds) pick up the grid and blot off the excess stain. Place the grid face up on clean filter paper to dry. Store the grid in a pre-labelled gelatin capsule before examination in the electron microscope (5 minutes at ×50,000)

Precautions
The grids should be handled only with the same pair of forceps throughout. After use the forceps are cleaned by immersion in Cidex (2h) followed by 5% Lysol and water rinse.

A7.6.4 Screening for presence of rotavirus

This method is based on use of a commercially available ELISA kit (Rotascreen , Mercia Diagnostics). Other commercially available products may be equally suitable.

A7.6.4.1 Protocol

Dilute 25% suspension in PBS A to 10% by mixing 0.25 ml with 0.75 ml of PBS A.

Allow all reagents to reach room temperature before use.

The positive control will be included in every assay.

The negative control (PBS A) will be included in duplicate in every assay.

Select sufficient fresh microwell strips to accommodate all test samples and controls. Fit the strips into the plastic holding frame.

Dispense 100 µl positive or negative control into the designated wells. Dispense 100 µl of the faecal suspensions into appropriately labelled wells. Seal the strips in one of the re-sealable plastic bags provided. Incubate at 37˚C for 60 minutes.

During the last 10 minutes of the 37˚C incubation prepare the tracer in a clean tube.

For each row of eight wells in use mix in the following order:

1 µl dilution buffer
10 µl conjugate
10 µl antibody

Do not mix more than is necessary for immediate requirements. Cover the tube and leave the tracer at room temperature until ready for use.

Aspirate and rinse the wells using the automatic plate washer set for five complete consecutive washes. Ensure that there is no residual wash buffer in the wells on completion of the washing cycle.

Dispense 100 µl of the prepared tracer into each well. Seal the strips in the plastic bag. Incubate at 37˚C for 60 minutes. Discard the unused tracer.

During the last 10 minutes of the incubation period prepare sufficient working strength substrate for immediate requirements only. For each row of eight wells in use mix 10 µl TMB Chromogen with 1 ml substrate solution. Protect the dilute substrate from the light.

Aspirate and rinse the wells

Immediately dispense 100 µl of substrate into all wells, using a multi-channel pipette and incubate at room temperature for 30 minutes. Discard any unused substrate.

Stop the reaction by adding 25 µl of 1N H_2SO_4 to each well. Gently mix the well contents until the colour in the wells has changed from blue to a uniform yellow.

Ensure that the underside of the wells is dry and that there are no bubbles in the well contents. Read the absorbance at 450 mm using a plate reader blanked on air.

A7.6.4.2 Assay validation

The positive control absorbance is >0.6 OD_{450} units.
The mean absorbance of the negative controls is <0.25 OD_{450} units

A7.6.4.3 Analysis of results

The cut off is defined as three times the mean absorbance of the negative controls.

Stool specimens giving absorbance values within 10% of the cut off value are considered to give an equivocal result and should be tested by ELISA (section A7.6.5).

A positive result is indicated when the absorbance value of a test sample is outside the equivocal range, greater than the cut-off value and greater than 1 OD_{450} unit.

A negative result is indicated when the absorbance value of a test sample is outside the equivocal range and less than the cut off value.

A7.6.5 Confirmation of rotavirus by ELISA

This method is based on use of the commercially available 'Rotaclone' kit (Cambridge Biotech Corp). Other commercially available products may be equally suitable.

A7.6.5.1 Protocol

Allow all reagents to reach room temperature before use.

Use the 10% suspension previously made for the rotavirus screening assay.

Snap off a sufficient number of wells for samples and the controls and insert into the microwell holder. Record sample position.

Add 100 µl of 10% sample, negative control (sample diluent) or positive control to the bottom of separate microwells.

Add 100 µl of enzyme conjugate to each microwell. Mix by gently swirling on table top.

Incubate at room temperature for 60 ± 5 minutes.

Aspirate and rinse the wells with deionised water using the automatic plate washer set for five complete consecutive washes. Ensure there is no residual water in the microwells.

Add 100 µl of substrate A (urea peroxide) solution to each microwell.

Add 100 µl of substrate B (TMB) solution to each microwell.

Incubate at room temperature for 10 minutes.

Add 100 µl of stop solution (IN H_2SO_4) to each microwell

Read the absorbance of each microwell at 450 nm against an air blank within 60 minutes.

A7.6.5.2 **Assay validation**

A positive control well should have an OD_{450} of >0.30 units
A negative control well should have an OD_{450} of <0.15 units
A precipitate may form in strong positive samples. This will not affect the results.

A7.6.5.3 **Analysis of results**

Specimens with an OD_{450} of ≥0.150 are considered positive
Specimens with an OD_{450} of <0.150 are considered negative

A7.6.6 **Detection of adenovirus serotype 40, 41**

This method is based on use of a 'Adenoclone' kit available from Cambridge Biotech Corporation. Other commercially available products may be equally suitable.

A7.6.6.1 **Protocol**

Allow all reagents to reach room temperature before use.

Use the 10% suspension previously made for the rotavirus screening assay.

Snap off a sufficient number of wells for samples and the controls and insert into the microwell holder. Record sample position.

Add 100 µl of 10% sample, negative control (sample diluent) or positive control to the bottom of separate microwells.

Add 100 µl of enzyme conjugate to each microwell. Mix by gently swirling on table top.

Incubate at room temperature for 60 ± 5 minutes.

Aspirate and rinse the wells with de-ionised water using the automatic plate washer set for five complete consecutive washes. Ensure there is no residual water in the microwells.

Add 100 µl of substrate A (urea peroxide) solution to each microwell.

Add 100 µl of substrate B (TMB) solution to each microwell.

Incubate at room temperature for 10 minutes.

Add 100 µl of stop solution (IN 1N H_2SO_4 to each microwell

Read the absorbance of each microwell at 450 nm against an air blank within 60 minutes.

A7.6.6.2 Assay validation

A positive control well should have an OD_{450} of >0.30 units
A negative control well should have an OD_{450} of <0.15 units
A precipitate may form in strong positive samples. This will not affect the results.

A7.6.6.3 Analysis of results

Specimens with an OD_{450} of >0.150 are considered positive
Specimens with an OD_{450} of <0.150 are considered negative

A7.7 ARCHIVE PRESERVATION OF SAMPLES BY FREEZING

A7.7.1 Introduction

The method is based on those of Crowther (1971) and Hudson *et al*. (1984) in which faecal bacteria are preserved qualitatively and quantitatively for extended periods by rapid freezing in a bacteriological nutrient broth containing glycerol as cryoprotectant (cryo broth). There are some reductions in the total counts and counts of some genera but these are small compared to losses on storage or freezing in the absence of cryoprotectant.

A7.7.2 Method

- A 20% suspension of faecal sample is made in cryo broth in a 2 ml polypropylene vial. The vial is then labelled with sample identification data using an indelible felt tip marker.
- The vial is then snap-frozen in a -70˚C freezer
- Store samples at or below -70˚C and transfer between laboratories on dry ice
- Store unused vials of cryo broth at room temperature or at 4˚C. Discard after 6–8 months or if obviously contaminated.

A7.7.3 Precautions

- Avoid spilling cryoprotectant or diluted sample from the vial and check that the cap is screwed tightly.
- Freezing in a domestic type freezer (at -20˚C) is not ideal as considerable losses of flora can occur.

A7.7.4 Medium

Cryoprotective broth (Cryo broth)

Lab-Lemco powder	10g
Glycerol	100 ml
Distilled water	900 ml

Adjust to pH 7.3
Fill as 4.5 ml in 7 ml bijoux bottle or as 50 ml in medical flat
Sterilise by autoclaving at 115˚C for 20 minutes

A7.7.5 **Validation studies**

Multiple aliquots of 20% suspensions of faeces in cryoprotective broth from three cases each of *Salmonella* spp., *Campylobacter* spp., and verocytotoxigenic *E.coli* O157 (VTEC) infection were prepared using specimens obtained from a routine diagnostic laboratory (Salisbury PHL). Aliquots were cultured at time intervals to confirm the suitability of the storage method. Some of these aliquots were then refrozen to assess loss of viability after a thaw/refreeze cycle. Sufficient numbers of aliquots of frozen suspension have been stored for viability to be assessed monthly to 3 months, then at 6 months, and annually for the first five years and then finally at 10 years.

Analysis of aliquots of each of the specimens after two year's storage are presented here; the results for the specimens containing salmonella are depicted Figure A7.3(a), and the effect of refreezing for 2 months following thawing at 3, 6, 12 and 24 months are given in Figure A7.3(b); comparable data for specimens containing campylobacters are presented in Figures A7.4(a) and A7.4(b).

For specimens containing salmonella, loss of viability during storage (Figure A7.3a) was very slight, irrespective of whether the specimen contained heavy or light growth initially; in addition, refreezing caused surprisingly little loss of viability (Figure A7.3b).

Figure A7.3(a) *Salmonella* survival

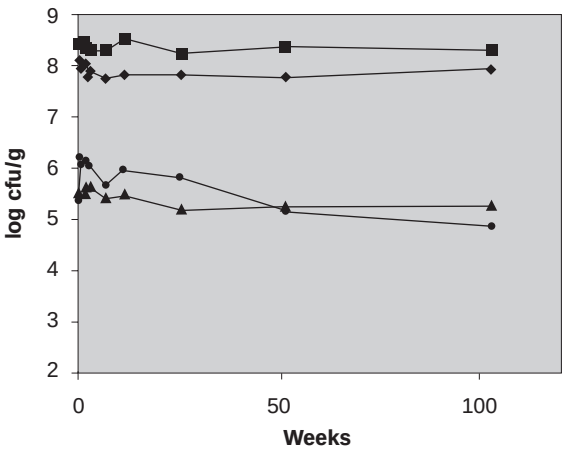


Figure A7.3(b) *Salmonella* viability; effect of thaw-refreeze cycle

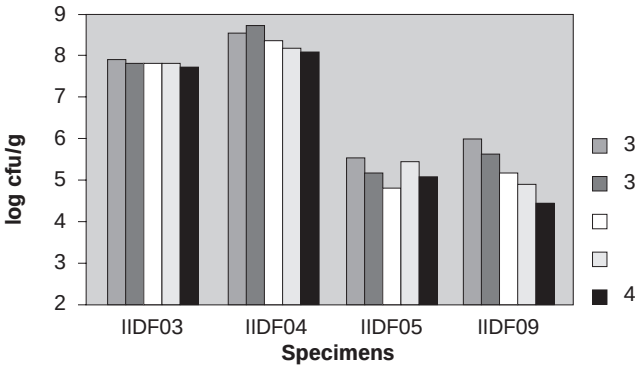


Figure A7.4(a) *Campylobacter* survival

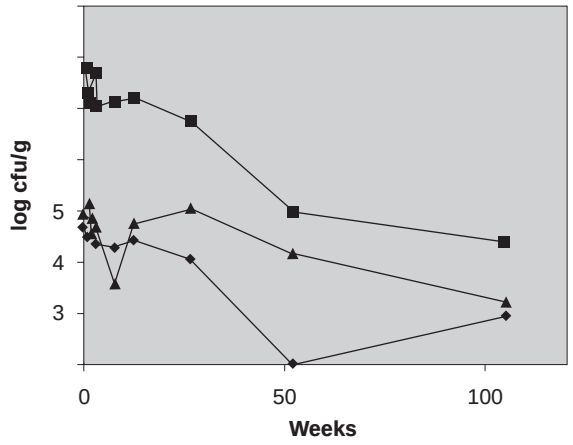
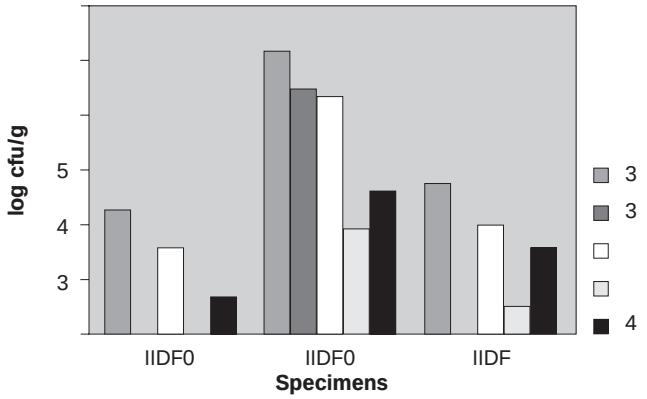


Figure A7.4(b) *Campylobacter* viability; effect of thaw-refreeze cycle



In contrast, the corresponding data for the specimens containing *campylobacters* reveal a gradual loss of viability during storage (Figure A7.4(a)). An apparent complete loss of viability in two of three specimens after refreezing at 3 months was not apparent at 6 months and after (Figure A7.4(b)); we suspect that the batch of medium used for the 3 months experiment may have been inhibitory to sub-lethally damaged cells. However, the general trend over two years was for a steady decline in viability, both in frozen samples and thawed–refrozen samples.

Results with *E.coli* O157 containing specimens gave recovery rates intermediate between the campylobacter and salmonella specimens (data not shown).

The loss of viability of campylobacters over just two years is of concern with respect to future culture studies using the archived stool material, although it is likely that this will use predominantly non-culture probe techniques, such as PCR.

These early data confirm that freeze–thaw–refreeze–thaw cycles may cause some loss of viability, particularly of ‘fragile’ bacteria such as campylobacters, even in the presence of glycerol as a cryoprotectant. We have proposed, therefore, that culture studies for novel pathogens from the frozen faecal suspensions will probably need to be performed in one laboratory only. A possible alternative strategy would be to scrape sufficient of the frozen suspension from the surface for culture, as is used in many laboratories to recover stock cultures. However, for this to be successful the detection methods would need to be very sensitive, and the homogeneity of faeces within the suspension cannot be assumed.

Probably the most material efficient approach will be to perform all of the culture studies required in one session in one laboratory, and to distribute the remaining faecal suspension on a number of membranes. These can be stored frozen for later use with DNA methods for the identification of novel pathogens, similar to the strategy employed by CPHL Laboratory of Enteric Pathogens (LEP) for the determination of enterovirulent E.coli in the main IID microbiological investigations; LEP have recently applied such approaches to identify non-culturable campylobacters in faeces (J. Stanley, personal communication). A general method is being devised by the microbiologists on the IID Executive Committee that will allow the efficient recovery of all DNA and RNA species (bacterial, viral, fungal and protozooal) to enable specific and sensitive genetic methods of detection to be applied.

Glossary

This glossary is intended as an aid to reading the main text and is not intended to be definitive.

ACID BARRIER OF THE STOMACH: The normal stomach is an acid environment and some microorganisms will not survive the level of acidity. Thus the stomach can act as a barrier preventing some microorganisms from passing any further down into the intestines.

AETIOLOGY: The cause or origin of a disease.

AGGLUTINATION: The clumping together of antigens by antibodies so that a visible agglutinate is formed.

ANAEMIA: The lack of red cells, or of their haemoglobin (the oxygen-carrying substance) in blood.

ANAEROBIC: Refers to the absence of oxygen.

ANTIBODY: A protein formed in direct response to the introduction into an individual of a foreign substance (antigen). Antibodies can combine with their specific antigens e.g. to neutralise toxins or destroy bacteria.

ANTIGEN: A foreign substance which specifically binds to antibody or T-cell receptors.

ANTISERUM: A fluid that contains antibodies.

ASCERTAINMENT: The process of determining what is happening in a population or study group, eg family and household composition, occurrence of cases of specific diseases; the latter is also known as case finding.

ASYMPTOMATIC CARRIER: A person in whom a particular micro-organism is present but who does not suffer any resulting symptoms or disease.

ASYMPTOMATIC INFECTION: An infection with a micro-organism where the person infected does not suffer any resulting symptoms or disease.

ATTACHING AND EFFACING : The ability to attach to and efface intestinal epithelial cells. Enterovirulent or diarrhoeagenic strains of *Escherichia coli* that attach to and efface the intestinal epithelium

ATTRIBUTABLE (OR ABSOLUTE) RISK: The incidence of the disease among those exposed to a risk factor over and above the incidence among those not exposed assuming the relationship between exposure and disease is causal.

BACTERAEMIA: The presence of bacteria in the blood.

BACTERICIDAL: Able to kill at least some types of bacteria.

BACTERIOPHAGE TYPING: A method for distinguishing varieties of bacteria ('phage types) within a particular species on the basis of their susceptibilities to a range of bacteriophages (bacterial viruses).

BACTERIUM: A microscopic organism with a rigid cell wall; unicellular and multiplying by splitting in two.

BIOASSAY: Any quantitative procedure in which a given organsim is used for assay purposes.

BIOTYPE: A variant of a bacterium which exhibits specific, defined biological properties.

BIOTYPING: A method for distinguishing varieties of bacteria by metabolic and/or physiological properties.

BLOOD CULTURE: A procedure for detecting the presence of viable bacteria in blood.

CASE: A person in the population identified as having a particular disease.

CASE-CONTROL STUDIES: Studies in which a group of people with a particular disease (the cases) are compared with a group of people without the disease (the controls), to determine whether the cases have been exposed more or less often to a specific factor than the controls.

CHI-SQUARED TEST: See significance tests.

CHOLERA-LIKE TOXIN: An enterotoxin which has similar effects to that produced by strains of *Vibrio cholerae* responsible for the symptoms of cholera, which include a profuse dehydrating diarrhoea.

COHORT (LONGITUDINAL) STUDIES: In a prospective cohort people are identified and grouped on the basis of their exposure to a specific factor and are then followed up over time to determine whether the incidence of a particular disease is different in the different exposure groups. In a population based cohort e.g. a group of people born in the same year, people are identified prior to exposure and followed up over time to investigate the development of a variety of conditions. In a retrospective (historical) cohort people are identified and investigated after the exposure and outcomes have occurred.

COLONISATION: The phenomenon of a community of micro-organisms becoming established in a certain environment (especially in the intestinal tract of humans or animals) without necessarily giving rise to disease.

COLONY IMMUNOBLOTTING: A serological technique for detecting specific micro-organisms.

COMMENSAL: An organism which derives benefit from living in close physical association with another organisms, the host, which derives neither benefit nor harm from its relationship with the commensal.

COMPETITIVE EXCLUSION: Growth of two different bacterial species in competition with each other which results in decline of one species and increase in the other.

CONFIDENCE INTERVALS: The range of values that will be expected to include the true value. A 95% confidence interval of between 10 and 14 means that the true value will lie within the interval 10 to 14 (inclusive) 95 times if the same experiment were repeated 100 times.

CONFOUNDING FACTOR: A factor that is associated both with the disease and with the study factor, e.g. social class is associated with both coronary heart disease and diet.

CONTROL: A person without the particular disease being studied selected for the purposes of comparison with a case.

COST BENEFIT ANALYSIS: Analysis of the costs of a particular course of action and its benefits to an individual and to the society at large.

COST EFFECTIVENESS ANALYSIS: Analysis of the costs of a treatment or course of action and the effectiveness of that intervention.

CROSS-SECTIONAL STUDIES: Studies in which a defined population or a sample of that population is surveyed and their disease and exposure status determined at one point in time.

CROSSOVER TRIALS: Trials in which patients are assigned randomly to one of two interventions and then after a set time transferred to the other intervention, sometimes after a washout period. The patients thus act as their own controls.

CRYOPROTECTIVE BROTH: A broth in which organisms are suspended before being frozen. The broth helps to preserve the viability of frozen cells.

CULTURABLE/NON-CULTURABLE: Refers to an organism which can/cannot currently be grown on a culture medium.

CULTURE MEDIUM: A liquid or solid medium which is capable of supporting the growth of micro-organisms.

D-VALUE: The time required at a given temperature to reduce the number of viable cells or spores of a given micro-organism to 10% of the initial number, usually quoted in minutes.

DEPURATION: The removal of microorganisms from bivalve molluscs by placing them in less polluted waters.

DIARRHOEAGENIC: Giving rise to diarrhoea.

DIFFERENTIAL MEDIUM: A medium that assists in the preliminary identification of a microorganism, for example, by a colour reaction.

DIFFUSELY ADHERENT: Strains of *E. coli* that adhere diffusely to the intestinal epithelium.

DISEASE: A term used to describe any state of an individual characterised as a deviation from the condition regarded as normal or healthy.

DNA HYBRIDISATION: The matching of a DNA fragment (e.g. a DNA probe) to a target DNA sequence in a microorganism. This can be used to detect or identify the organism.

DNA PROBE: A DNA fragment that has been labelled with a marker to indicate when DNA hybridisation has occurred.

DOUBLE BLIND: A double blind trial is one in which neither the patient nor the observer know to which of the treatment regimes any patient in the trial is allocated.

DYSENTERY: A disease characterised by inflammation of the intestine producing abdominal pain with the frequent passage of fluid stools, leading to dehydration.

***E. coli* O157:** A serogroup of *Escherichia coli* that is commonly associated with intestinal disease, often characterised by bloody diarrhoea and more serious systemic illness, including haemolytic uraemic syndrome (HUS). The symptoms are due to verocytotoxins and other virulence factors. Many (but not all) strains of *E.coli* O157 produce verocytotoxins and other virulence factors, and are classified as VTEC (q.v.)

EFFACE: Cause the loss of microvilli from the surface of epithelial cells in the intestine. A property of several enterovirulent *Escherichia coli* (q.v.) including AEEC, EPEC and VTEC.

EFFECTIVENESS: The extent to which a specific intervention produces a beneficial effect in a defined population when used in normal practice.

EFFICACY: The extent to which a specific intervention produces a beneficial result under ideal conditions e.g. during a randomised controlled trial.

ELISA (Enzyme-Linked Immunosorbent Assay): A serological test which uses enzyme reactions as indicators.

ENDOTHELIAL CELLS: Cells which form the layer (the endothelium) lining the inner surface of blood and lymph vessels and the heart.

ENRICHMENT CULTURE: Growth of microorganisms in a medium that assists the growth of damaged cells.

ENTERITIS: Inflammation of the intestine.

ENTEROAGGREGATIVE: Strains of *E. coli* that adhere to cultured intestinal cell monolayers and cause them to aggregate.

ENTEROHAEMORRHAGIC: Strains of *E. coli* that give rise to bloody diarrhoea, possibly with progression to Haemolytic Uraemic Syndrome (HUS) as a result of toxic damage to the cells lining the intestine.

ENTEROINVASIVE: Strains of *E. coli* that cause an inflammatory disease of the intestinal tract which closely resembles bacterial dysentery and in which the bacteria penetrate the gut wall.

ENTEROPATHOGEN: A pathogen that can cause disease in the intestines.

ENTEROPATHOGENIC: Strains of *E. coli* that cause a form of diarrhoea generally associated with infants, with transmission mainly being via the oral-faecal route.

ENTEROTOXIGENIC: Strains of *E. coli* that produce an enterotoxin, giving rise to loss of water and salt, and profuse watery diarrhoea.

ENTEROTOXIN: A toxin, usually produced by a bacterium, that causes gastroenteritis, by altering the absorptive or secretory properties of the intestinal epithelium, or by causing the death of the epithelial cells.

ENTEROVIRULENT: Causing intestinal disease. Specifically, the term 'Enterovirulent *Escherichia coli*' is used as a descriptive term for all of the various types of *Escherichia coli* thought to cause intestinal disease, including AEEC, DAEC, EAggEC, EIEC, EPEC, and VTEC (q.v.). The terms enterovirulent *E.coli* and diarrhoeagenic *E.coli* are synonymous.

ENUMERATION: A descriptive study to quantify (count) events of interest, in this case, numbers of subjects presenting to GPs.

EPIDEMIC: The condition in which a disease spreads rapidly through a community in which that disease is not normally present or is present at a low level.

EPIDEMIOLOGY: The study of factors affecting health and disease in populations and the application of this study to the control and prevention of disease.

EPITHELIAL CELLS: Cells which form the layer (the epithelium) lining the inner surface of the intestines.

EXOTOXINS: Toxins that are secreted by the bacterial cell, and which can cause illness in the absence of bacteria.

EXTRA-INTESTINAL: Outside or beyond the intestine.

FACTORIAL TRIALS: Trials in which two (or more) treatments are used either alone or in combination to allow evaluation of the combined as well as the single effects of the different treatments.

FLAGELLAR ANTIGEN: Part of the bacterial flagellum that gives rise to antibody formation. Flagellar antigens are known as 'H' antigens.

FLAGELLUM: A long hair-like appendage on the surface of the cell whose movement is used for cellular locomotion.

GASTROENTERITIS: Inflammation of the lining of the stomach and the small intestine, characterised by diarrhoea and/or vomiting.

GENOTYPING: Distinguishing and grouping organisms by their content of genetic information, either in total or with respect to particular factors, regardless of whether or not the information in the genetic material is expressed in the characteristics of the organism.

GENUS: A sub-class of organisms which have natural affinities or similarities. A genus is subdivided into species.

GNOTOBIOTIC: Describing germ-free conditions or a germ-free animal that can be used to study the response to a defined organism or organisms.

GRAM NEGATIVE: A colour reaction to a staining procedure used as an initial step in the identification of bacteria.

GUILLAIN-BARRÉ SYNDROME: A disorder characterised by acute onset of weakness in the distal muscles of the legs which spreads upwards over the course of a few days to involve the trunk, arms and sometimes the cranial nerves.

H ANTIGEN: The flagellar antigen of bacteria

HAEMOLYTIC URAEMIC SYNDROME (HUS): A clinical condition which may arise from a variety of causes, and which is characterised by anaemia and kidney failure.

HAEMORRHAGIC COLITIS (HC): Inflammation and bleeding from the large bowel that may be caused by an infectious agent.

HAZARD: The disposition of a thing, a condition or a situation to produce injury; or an event, sequence of events or combination of circumstances that could potentially have adverse consequences.

HELMINTHS: A term often applied to parasitic flatworms but also applicable to nematodes (roundworms).

HORIZONTAL TRANSMISSION: The transfer of a disease or parasite via close contact (c.f. vertical transmission).

HUMECTANT: A substance which absorbs moisture.

IgA, IgG, IgM: Different types of immunoglobulin (antibody) found in body fluids.

IMMUNE STATUS: State of immunity or resistance to infection of an individual to a particular pathogen, or to microorganisms in general.

IMMUNOASSAY: Any test which uses the specificity of the antigen-antibody reaction to quantify substances.

IMMUNOCOMPETENT: An individual who is able to mount a normal immune response.

IMMUNOCOMPROMISED: An individual who is unable to mount a normal immune response.

IMMUNOGLOBULINS: A class of proteins which are antibodies and are found in body fluids. They are very specific to a particular antigen and are an important part of the immune system.

IMMUNOLOGICAL TESTS: Tests based on antigen-antibody reactions.

IMMUNOMAGNETIC SEPARATION (IMS): A technique for isolating a particular microorganism using magnetic beads coated with antibodies to that organism.

***IN VITRO*:** Literally "in glass" i.e. in a test tube, plate etc. Used to describe biological processes made to happen in laboratory apparatus, outside a living organism.

INCIDENCE: The number of new cases of a disease that arise in a defined population over a specified time period.

INCIDENCE RATE: The rate at which new events occur in a population. The numerator is the number of new events that occur in a defined period; the denominator is the population at risk of experiencing the event during this period, sometimes expressed as person-time.

INCUBATION PERIOD: The time interval between the initial entry of a pathogen into a host, and the appearance of the first symptoms of disease.

INDEX CASE: The first case in an outbreak of infectious disease.

INFECTION: The situation in which an agent, such as a virus or bacterium, has been transmitted to a host and is able to replicate within that host. There may, or may not be outward signs of disease; it is possible to be infected with an agent without suffering symptoms of the disease commonly associated with that agent (although disease may develop at a later time).

INFECTIOUS DISEASE: A disease caused by an infectious agent.

INFECTIOUS DOSE: The amount of infectious material, e.g. number of bacteria, necessary to produce an infection.

INFECTIOUS INTESTINAL DISEASE: Disease producing gastrointestinal symptoms due to infectious agents.

INTENTION-TO-TREAT ANALYSIS: An analysis which includes all the persons randomized into a clinical trial in the group to which they were originally allocated, whether or not they complied with, or completed, the regimen under study (see also On treatment analysis, below).

INTESTINAL FLORA: Commensal organisms living in the intestine.

ISOENZYME TYPING: A method used to distinguish organisms on the basis of differences between their isoenzymes. Isoenzymes are proteins which catalyse the same reactions but differ from each other in some way.

ISOLATE: Bacterial growth obtained as the result of culturing a sample.

JARMAN SCORE: A composite index to describe the deprivation of a community, It is based on Census data; the items reflect GPs perception of workload and include measures of disadvantage (eg overcrowding) as well socio-demographic factors affecting primary care (e.g. the proportion of the population over 65).

LATEX AGGLUTINATION: An agglutination reaction in which the test antigen or antibody is bound to latex particles so that clumping is visible to the naked eye.

LIPOPOLYSACCHARIDE (LPS): That part of the outer membrane of Gram negative bacterial cells which functions as the 'O' antigen. (See Somatic antigen).

MASTITIS: Inflammation of the mammary gland.

MATERNAL IMMUNITY: Immunity in newborn mammals which is derived from the acquisition of circulating antibodies from the mother.

MENINGES: Membranous lining of the brain and spinal cord.

MICROAEROPHILIC: Refers to a gaseous environment in which oxygen is present but is at a concentration (partial pressure) significantly lower than in air. A microaerophilic organism prefers or can only survive in such an environment.

MICROFLORA: The microbial population of an area such as the gastro-intestinal tract.

MINIMUM INFECTIVE DOSE: The lowest number of organisms capable of causing infection.

MOLECULAR FINGERPRINTING: Genetic characterisation of an organism which allows it to be compared with other isolates.

MOTILE BACTERIA: Bacteria that can move independently, usually by flagella (q.v.).

NEONATAL SEPSIS: The condition in which a new born baby has symptoms associated with microbial infection.

NEONATE: A new born baby, up to four weeks of age.

NESTED CASE CONTROL STUDY: A case control study in which cases and controls are drawn from the population in a cohort study. As some data are available about both cases and controls, the effects of some potential confounding variables are reduced or eliminated. In this type of case control study, a set of controls is selected from subjects at risk at the time of occurrence of each case that arises in a cohort, thus allowing for the confounding effects of time in the analysis.

NEUROLOGICAL COMPLICATIONS: Symptoms which occur in the nervous system as a complication of a disease which primarily affects another part of the body.

NORWALK-LIKE VIRUS: Small round structured viruses which infect humans.

NOSOCOMIAL INFECTION: An infection acquired whilst in hospital.

NOTIFIABLE DISEASE: A disease that, by statutory requirements, a medical practitioner must report to the public health authority. In England, the recipient of the notification is the proper officer of the Local Authority, generally the local Consultant in Communicable Disease Control (CCDC).

OBSERVATIONAL STUDIES: Studies in which certain features (past, present or future) are observed in groups of individuals without any intervention being introduced other than the gathering of information. Observational studies can be used to investigate the diagnosis, causes and natural history of disease, to assess the accuracy of diagnostic methods and to evaluate the process of care.

ON-TREATMENT ANALYSIS: An analysis in which events occuring during a trialare realted to the treatment being received.

OPPORTUNITY COSTS: Non-monetary costs reflecting the use of time and other resources and hence their non-availability for other uses.

OUTBREAK: Two or more linked cases of disease linked to a common source.

PROBABILITY (P) VALUE: An indication of the strength of the evidence for a true treatment effect. The smaller the p-value the smaller the probability that the difference between treatment groups could have arisen by chance. P-values of 0.05 and lower, meaning that there is a 1 in 20 likelihood or less that an event arose by chance, are usually accepted as indicating significant differences.

PARALLEL GROUP TRIALS: Trials in which patients are assigned randomly to one of two (or more) interventions to try to achieve a fair, unbiased comparison through groups that are identical in all respects apart from the intervention.

PASTEURISATION: A form of heat treatment that kills vegetative pathogens and spoilage bacteria in milk and other foods.

PATHOGEN: Any biological agent that can cause disease.

PATHOGENESIS: The mechanism(s) whereby disease is brought about.

PATHOGENIC: Capable of causing disease.

PATHOGENICITY: Ability to behave as a pathogen.

pH: An index used as a measure of acidity or alkalinity.

PHAGE TYPE: ‘phage type; see Bacteriophage typing

PHENOTYPING: Distinguishing and grouping organisms by their appearance and/or physiological properties.

PLASMA: The fluid part of the blood in which the cells are suspended.

PLATELETS: Specialised blood cells involved in clotting.

POLYMERASE CHAIN REACTION (PCR): A technique which enable multiple copies of a DNA fragment to be generated by amplification.

POWER: The probability that a trial can detect a true difference between the intervention group and control group, if one exists. 80% or above is usually acceptable for a clinical trial. (See Type II error).

PRECISION: Good repeatability.

PREVALENCE: The percentage of a population affected by a particular disease at a given time.

PRODROMAL: Relating to the period of time following the incubation period when the first non-specific symptoms of illness appear, but before the development of the main symptoms that characterise the disease.

PROTOZOA: Unicellular organisms that are distinguished from bacteria by several important features, most importantly the presence of a membrane-bound nucleus and eukaryotic ribosomes. Protozoa can be free-living or parasitic for man and animals, e.g. the malaria parasite and *Cryptosporidium parvum.*

R-TYPE: Antibiotic resistance type.

RANDOMISED CONTROLLED CLINICAL TRIALS: Experiments in which interventions are evaluated for efficacy and safety in patients either with a specific disease or at risk of developing a specific disease. Patients are randomly allocated to received either the intervention or to be in a control group (i.e. to receive no treatment or placebo or an existing standard intervention).

RANDOM ERROR: The variation of observed values from a true value which is due to chance alone. A large random error implies imprecision or poor repeatability. When random error occurs the estimate is equally likely to be above or below the true value.

REACTIVE ARTHRITIS: A non-infective arthritis which may be secondary to an episode of infection elsewhere in the body.

REGRESSION ANALYSES: Statistical techniques, e.g. multiple logistic regression, to assess effects of a factor independent of its association with other factors.

RELATIVE RISK: The incidence or prevalence of the disease among exposed persons divided by the incidence of the disease among unexposed persons.

REPEATABILITY: Ability to get the same answer if the measurement is repeated under the same conditions.

RISK: The probability that a specific hazard will be realised.

RISK ANALYSIS: The structured approach to the reduction of risk. It includes risk assessment, risk management, risk communication and risk monitoring.

RISK ASSESSMENT: Determining the risk associated with a particular hazard.

RISK COMMUNICATION: Communication of information about risk and options for managing risk.

RISK FACTOR: An aspect of personal behaviour or life-style, an environmental exposure, or an inborn or inherited characteristic, which on the basis of epidemiologic evidence is known to be associated with disease.

RISK MANAGEMENT: Selection and implementation of a course of action designed to eliminate or minimise risks.

RISK MONITORING: The assessment of the effectiveness of control measures.

SECRETORY IgA: A form of IgA which is resistant to enzymic breakdown and is found on mucosal surfaces e.g. the intestinal epithelium.

SELECTIVE MEDIA: Types of culture media which use selective agents such as dyes and antibiotics to inhibit the growth of some types of bacteria and allow the growth of others.

SENTINEL PRACTICE: A general practice which collaborates in regular monitoring surveillance of diagnoses, including IID, in patients presenting to primary care.

SENTINEL PRACTICE SCHEME: The Royal College of General Practitioners Research Unit's reporting scheme for a wide range of clinical diagnoses including IID.

SEQUELAE: A condition which follows the occurrence of a disease e.g. late complications, permanent ill effects.

SERO-CONVERSION: The development of antibodies not previously present as the result of a primary infection or immunisation.

SERODIAGNOSIS: Identification of a micro-organism by means of serological tests.

SEROGROUP: A group of organisms related by their response to an antibody. Serogroups Provide a broad grouping which can be further broken down into serotypes.

SEROLOGY: The investigation of disease by tests for the presence of antibodies or the examination of antigen-antibody reactions *in vitro.*

SEROTYPE: An antigenically distinct variant of an organism

SEROTYPING: A method of distinguishing varieties of bacteria (serotypes) within a single species by defining their antigenic properties on the basis of their reaction to known antisera. A number of serotypes may constitute a serogroup.

SEROVAR: See serotype.

SERUM ANTIBODIES: Antibodies found in the fluid fraction of coagulated blood.

SHIGA-LIKE TOXIN (SLT): A term used synonymously with Verocytotoxin (VT) because VTs have an almost identical biological profile to the toxin produced by the 'Shiga bacillus' (*Shigella dysenteriae* type 1).

SHIGELLOSIS: See dysentery.

SIGNIFICANCE LEVEL: Probability that an observed difference could have arisen by chance (i.e. a false positive result). Usually 0.05 or below (a 1 in 20 chance or lower) is acceptable for a clinical trial. (See probability value).

SIGNIFICANCE TESTS : Statistical tests to decide whether differences seen, e.g. between treatments, are true, or could have arisen by chance.

- Chi-squared (test) - Used to test for a difference between proportions. The larger the value of chi-squared , the smaller the probability, p, that the difference could have arisen by chance
- t-test. The two-sample or unpaired t-test is used to test whether the difference between two means obtained from two different groups of individuals is significant. The larger the value of t, the smaller the probability, p, that the difference could have arisen by chance. The paired t-test is used to compare means of two measurements obtained on the same individual, e.g. as in a crossover trial.
- Analysis of variance (F). Used to compare several means or two means after adjusting for other variables. The larger the value of F, the smaller the probability, p, that the difference could have arisen by chance.
- Wilcoxon test. A test based on ranking values which can be used to test whether the difference between two medians obtained from two different groups of individuals is significant. Unlike the t-test, the Wilcoxon test can be used on data which are very skewed or based on few patients. The larger the value of z the smaller the probability (p) that the difference could have arisen by chance

SLTEC: Shiga-like toxin-producing *Escherichia coli*; synonymous with VTEC (Verocytotoxin-producing *Escherichia coli*) (q.v).

SOCIO-DEMOGRAPHIC FACTORS: The basic characteristics of a population including the age sex structure and ethnic minority proportions.

SOCIO-ECONOMIC BURDEN: Financial and other costs including effects on quality of life, as a result of disease.

SOMATIC ANTIGEN: The antigen on the cell wall known as the "O" antigen. (See lipopolysaccharide).

SORBITOL MACCONKEY AGAR: A selective and differential medium for the detection of *Escherichia coli* O157:H7.

SPECIES: A sub-class of organisms within a genus on the basis of their similarities. It can be further sub-divided into sub-species.

SPECIFIC IMMUNE RESPONSE: Any form of immune response which is specific to a given antigen.

SPORADIC CASE: A single case of disease apparently unrelated to other cases.

SPORE: Environmentally resistant form of an organism in which growth does not occur. (See vegetative cells).

SPORING/NON-SPORING: Refers to the potential/lack of potential of an organism to produce an environmentally resistant form called a spore.

STANDARDIZED MORTALITY RATIO: The ratio of the observed number of deaths to the expected number of deaths in a study population, multiplied by 100.

STRAIN: A sub-grouping of organisms within a species, characterised by some particular quality.

SUB-SPECIES: A classification of organisms within a species on the basis of their similarities.

SUB-TYPE: A taxonomic rank below species that is used to differentiate organisms further.

SUB-TYPING: Any method used to distinguish between species or sub-species or strains.

SUSCEPTIBLE INDIVIDUAL: An individual who has no pre-existing immunity or resistance to infection who is therefore liable to become infected.

SYSTEMATIC ERROR: A systematic error implies bias, meaning the measurements are inaccurate even if precise and repeatable. When systematic error occurs the estimate is more likely to be consistently above or below the true value. Three sources of systematic error (bias) are:

- confounding - the estimate of the association between an exposure/intervention and disease is mixed up with the real effect of another exposure on the same disease when the two exposures are correlated. (See confounding factor).
- information bias - misclassification of patients with regard to disease status, exposure or both - often due to inaccurate recall;
- selection bias - cases or controls are included in or excluded from observational studies on the basis of criteria related to the factor under investigation e.g. women taking HRT in the 70s were likely to be at a lower risk of coronary heart disease (CHD) than women not taking HRT because of the early (false) analogies made between HRT and oral contraceptives - so studies of HRT and CHD involving these women are biased.

T-TEST: See significance tests.

THERMOPHILIC CAMPYLOBACTERS: Refers to those campylobacters which grow well at 42°C and 37°C, but not at 25°C.

THROMBOTIC THROMBOCYTOPAENIA PURPURA (TTP): A clinical condition resulting from the aggregation of platelets in various organs, characterised by fever with skin and central nervous involvement, anaemia and kidney failure.

TOXIN: Any poisonous substance, including those produced by microorganisms.

TYPE II ERROR: The failure to detect a real difference between two values (i.e. a false negative result). Detection of a difference where one does not exist (i.e. a false positive result) is a type I error.

TYPING: Any method used to distinguish between closely related microorganisms.

UNDER-ASCERTAINMENT: Incomplete identification of cases or collection of data. (See ascertainment).

UNTYPABLE: Refers to an organism which does not give a recognised reaction or pattern of reactions when a particular typing method is used.

VALIDITY: Ability to measure what is claimed by the technique used.

VEGETATIVE CELLS: Bacterial cells in which nutrition and growth predominate (c.f. spore).

VEROCYTOTOXIN: A protein produced by *E.coli* that is toxic to Vero (monkey kidney) cells and other cells in culture. There are several closely related verocytotoxins (VTs) and they are related to the Shiga toxin of *Shigella dysenteriae* type 1. It is thought to be the major virulence factor of VTEC such as *E.coli* O157.

VEROCYTOTOXIN PRODUCING *Escherichia coli* (VTEC): A particular sub-species of *E. coli,* often of the serogroup O157 which is associated with Haemorrhagic Colitis and Haemolytic Uraemic Syndrome.

VERTICAL TRANSMISSION: The transmission of a disease or parasite from a parent to its offspring via the egg, via the placenta, or by genetic inheritance (c.f. horizontal transmission). In mammals, it may also occur during birth.

VIABLE: Refers in microbiology to an organism capable of growth and reproduction under appropriate conditions.

VIRULENCE: Virulence is defined broadly in terms of the severity of the symptoms in the host. Thus a highly virulent strain may cause severe symptoms in a susceptible individual, while a less virulent strain would produce relatively less severe symptoms in the same individual.

VIRULENCE FACTOR: A factor affecting the ability of an organism to cause disease, and the severity of the disease thus caused.

VIRULENT FACTORS: Those characteristics of an organism responsible for the pathogenicity or severity of disease.

WATER ACTIVITY(A_W): A measure of the available water in a substance, where pure water is assigned a value of 1.0.

WILCOXON-TEST: See significance tests.

WILLINGNESS TO PAY: An economic study in which subjects are asked how much they would be willing to pay for some measure which might or would prevent disease.

Z-VALUE: The temperature coefficient of thermal destruction. It is the change in temperature (°C) which alters the D-value by a factor of 10.

ZOONOSIS: An infection transmitted from animals to humans. In the animal host, the organism may cause disease or it may be commensal.

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