Research articles

RISK FACTORS FOR SPORADIC *CAMPYLOBACTER* INFECTION: AN ALL-IRELAND CASE-CONTROL STUDY

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We report the findings of the first case-control study conducted in both the Republic of Ireland and Northern Ireland to determine risk factors for sporadic *Campylobacter* infections. A total of 197 cases and 296 case-nominated controls matched for age, were included. Based on Population Attributable Fraction (PAF), the most important risk factors were consuming chicken [adjusted matched (am) OR 6.8; 95%CI 2.1-21.9], consuming lettuce (amOR 3.3; 95%CI 1.5-7.1) and eating in takeaways (amOR=3.1; 95%CI 1.4-6.6). Contact with sheep (amOR=11; 95%CI 1.6-78), peptic ulcer (amOR=19; 95%CI 3.8-93.7), hiatus hernia (amOR=20.3; 95%CI 2.3-183.3), lower bowel problems (amOR=4.5; 95%CI 1.2-16.8) were also independently associated with infection. Mains water supply showed protective effect (amOR=0.2; 95 CI 0.1-0.9). The findings highlight the continued need for consumer food safety education and further control measures throughout the food chain on the island of Ireland.

Introduction

In line with many western countries, *Campylobacter* is the most common cause of laboratory confirmed bacterial gastrointestinal disease in both the Republic of Ireland (ROI) and Northern Ireland (NI). Between 1999 and 2006 over 20,000 laboratory-confirmed cases were reported in the two jurisdictions, giving a mean incidence rate of 47 per 100,000 population per year and representing about two thirds of all acute reported gastroenteritis [1,2].

Campylobacter infection is of important public health concern as it can cause considerable illness and loss of productivity and may be associated with sequelae, such as reactive arthritis and Guillain Barré syndrome [3-7]. Different risk factors have been reported in various studies conducted in several developed countries, with the most common ones being: consumption and handling of chicken, and in particular undercooked chicken or commercially prepared chicken; unpasteurised milk and dairy products; consumption of untreated water; contact with domestic pets like dogs and cats; contact with farm animals; travel abroad [7-14]. However, differences between risk factors across studies may reflect either different study methodologies or variations in the sources of infection across different countries [6,8]. In addition, epidemiological studies conducted in the United Kingdom (UK)

have suggested that there may be even regional differences in the contributing risk factors for infection [15].

Although the population health burden from *Campylobacter* is considerable, there have not been any analytical studies conducted in Ireland on the epidemiology of the disease in humans. This paper describes the first case-control study that was conducted in both ROI and NI, to identify risk and protective factors for sporadic *Campylobacter* infection on the island of Ireland and estimate the proportion of the risk attributable to the identified factors, in order to guide prevention efforts.

Methods

Study design

A prospective matched case-control study was conducted in all four Health Board areas in NI and the Health Service Executive (HSE) Eastern region in ROI (which includes the greater Dublin area and represents 36% of the ROI population). Data were collected over a 12-month period (from December 2003 to December 2004).

Two controls were nominated by each case matched for age group (0-5, 6-10, 11-20, 21-34, 35-49, 50-64 and 65+ years). Age was chosen as a matching variable because (i) potential high-risk exposures (e.g. food habits, leisure activities) vary considerably among different age groups and (ii) the age profile of campylobacteriosis in Ireland, both ROI and NI, peaks in some age groups, namely 0-4 and 20-34 years.

Cases

A case was defined as a person of any age (living or visiting the study area) whose laboratory confirmed *Campylobacter* spp. infection was reported through the routine surveillance systems in the participating health authorities, during the 12-month study period. Cases were excluded if (i) they were associated with an outbreak reported to the health authority or the national surveillance centre or (ii) at least one matched control could not be identified.

Controls

Cases (or adult respondents, in case of children patients aged less than 16 years) were asked to hand the questionnaires to

two controls matched for age group (such as neighbours, work colleagues, friends or schoolmates, but not household members).

Controls were excluded (i) if they had gastrointestinal symptoms in the 14 days prior to the completion of the questionnaire (ii) if they lived in the same household as the case or (iii) if the completed questionnaire of the matched case was not available.

Sample size

To detect an association with a matched odds ratio (mOR) of 2 at the 5% significance level, with 80% power and a case-control ratio of 1:2, a sample size of 186 case-control sets (i.e. a case with at least one matched control) was required, assuming 70% chicken consumption among controls, as reported in the North/South Ireland Consumption Survey [16]. The calculation was performed by a software written by the Statistics Unit of the Health Protection Agency (HPA) [17].

Study questionnaire

Information on exposures of the cases and their matched nominated controls was collected using a self-administered postal questionnaire. This gathered demographic data (age, gender, employment status, occupation), clinical details of cases (date of onset, duration and symptoms of the disease, if hospitalisation was required), and information on household contacts.

The 86 considered exposures were grouped into five categories:

- Food and drink history, including drinking water (type of water supply, bottled water, other sources), meat (beef, pork, lamb, sausage, ham, salami), fish, chicken, vegetables, fruit, milk and dairy products and eating out (type of restaurant or takeaway);
- Foreign travel (outside the island of Ireland);
- Contact with animals (pets and farm animals);
- Leisure activities (including swimming, gardening, visits to parks or farms, fishing and other sports);
- Medical history and medication (antacids, H2-receptor antagonists, antibiotics).

Dose-responses of the food and drink exposures (frequency of consumption) were investigated. All questions related to exposures in the seven days before the onset of symptoms for cases and seven days before the completion of the questionnaire for controls, except for medication (one month before illness onset/completion of questionnaire) and foreign travel (14 days before). Adult family members were asked to complete the questionnaires on behalf of children under the age of 16. The questionnaire was validated during a pilot study conducted in ROI that involved 20 cases. To increase the response rate, a reminder letter was sent to the cases that had not responded within 14 days.

The study received ethical approval by two Ethics Committees; the Faculty of Public Health Medicine Research Ethics Committee in ROI and the Queen's University of Belfast Research Ethics Committee in NI.

Statistical analysis

Data were entered in a database designed using EpiInfo2003 software (version 3; Centers for Disease Control and Prevention) and were checked for mistakes and inconsistencies (consistency and range checks). Food/drink exposures were treated as dichotomous variables, whereas frequencies of food/drink consumptions were analysed as continuous variables. Age was grouped into the following age bands: 0-5, 6-10, 11-20, 21-34, 35-49, 50-64 and 65+ years. Initial univariate matched analysis was carried out

to calculate age-group adjusted matched OR (mOR) and their 95% confidence intervals (95%CI). Age adjustment was performed to control for the potential residual confounding of age, as matching for age had not been successful in some young cases. Dose-response relationships were also examined between frequencies of food/drink consumptions and the disease.

Multiple conditional logistic regression models were constructed with Stata software (version 8, Stata Corporation, Texas). The initial regression model was developed including age, gender and all other variables for which (i) the p-value (for the OR) was less than 0.05, or (ii) the OR was more than 1.5 or less than 0.67 in the univariate analysis. These cut-off values were considered

TABLE 1

Socio-demographic characteristics of cases and controls included in the final analysis. All-Ireland Campylobacter infection case-control study, 2004

	Cases (n=197) n (%)	Controls (n=296) n (%)
Sex		
Males	91 (46.4)	101 (34.4)
Age group		
0-5 years	26 (13.3)	23* (8.0)
6-10 years	9 (4.6)	9* (3.1)
11-19 years	25 (12.8)	37 (12.9)
20-34 years	46 (23.4)	78 (27.2)
35-49 years	47 (23.9)	61 (21.3)
50-64 years	31 (15.8)	58 (20.2)
65+ years	13 (6.6)	21 (7.3)
Employment status		
Employed	98 (52.7)	175 (61.8)
Unemployed	8 (4.3)	16 (5.7)
Student	34 (18.3)	48 (17)
Retired	19 (10.2)	22 (7.8)
Other (housewife, baby, etc.)	27 (14.5)	22 (7.9)
Food-handler	13 (13.3)†	28 (16.0)‡
Contact with animals (as job)	3 (3.1)	7 (4.0)
Place of residence		
City/town	40 (90.9)	62 (89.9)
Village/rural area	4 (9.1)	7 (10.1)
Type of house		
Apartment	14 (7.7)	18 (6.8)
House	163 (89.6)	238 (90.5)
Farm	5 (2.7)	7 (2.7)
Household contacts		
Mean number of people in household (standard deviation)	3.5 (1.5)	3.8 (2.2)
Child < 5 years in household	44 (22.6)	68 (23.1)
Mean number of children <5 years in household (standard deviation)	0.31 (0.6)	0.31 (0.7)

* Five cases aged 0-5 years and five cases aged 6-10 years nominated controls that were older than 5 and 10 years, respectively

† Among the 98 employed cases

‡ Among the 175 employed controls

important for the specific exposures and the disease. To simplify the model, variables were removed one at a time depending on the significance testing ($p < 0.05$) by the likelihood ratio (LR) test or the alteration of OR. Because of several missing values, frequency of food/drink consumption variables were not included in the models and food/drink items as dichotomous variables were included instead. Potential interactions among all variables in the final model, age and country (ROI vs NI) were also examined. The population-attributable fractions (PAF) for all risk factors in the final model were calculated, using the following formula for matched case-control studies: $PAF = [P' * (amOR - 1) / amOR]$, where P' is

the proportion of cases exposed and amOR is the adjusted matched OR which was derived from the final conditional regression model.

Results

Response rate

A total of 978 persons fulfilling the case definition were contacted and 402 (41.1%) (215; 37.7% in ROI and 187; 45.7% in NI) returned a completed questionnaire. Of these, 197 (49%; 52.5% in ROI and 44.9% in NI) had at least one control that responded. The final analysis was made up of 197 cases (113 in ROI and 84 in NI) and 296 controls (172 in ROI and 124 in NI). Of the 197

TABLE 2

Univariate analysis of risk and protective factors (travel, eating out, poultry, meat and fish, vegetables and fruit consumption) for campylobacteriosis. All-Ireland Campylobacter infection case-control study, 2004.

Exposure	Cases (n=197) † n (%)	Controls (n=296) † n (%)	Crude OR * (95% CI)	P-value
Male	91 (46.4)	101 (34.4)	2.0 (1.2-3.2)	0.005
Foreign travel				
Foreign travel (outside the island of Ireland)	41 (20.8)	22 (7.5)	3.5 (1.7-7.3)	<0.001
Travel to United Kingdom	7 (3.6)	8 (2.7)	1.8 (0.6-5.7)	0.34
Travel to Europe	29 (14.7)	20 (6.8)	2.8 (1.4-5.8)	0.005
Travel to places outside Europe	12 (6.1)	2 (0.7)	17.8 (2.2-143)	0.007
Poultry and poultry products				
Chicken	181 (92.3)	251 (85.1)	3.0 (1.5-6.1)	0.002
Undercooked chicken	13 (6.7)	2 (0.7)	9.5 (2.1-43.5)	0.004
Duck	10 (5.1)	12 (4.1)	2.0 (0.7-5.6)	0.18
Turkey	11 (5.6)	44 (14.9)	0.3 (0.1-0.6)	0.002
Handle raw chicken bought from butchers	9 (4.6)	34 (11.5)	0.4 (0.2-0.9)	0.02
Meat and fish				
Any meat and fish	189 (95.9)	290 (98)	0.4 (0.1-1.5)	0.15
Beef (including mince)	143 (73)	244 (82.7)	0.6 (0.4-1)	0.03
Sausages	114 (58.5)	196 (60.2)	0.6 (0.4-1)	0.03
Pate	12 (6.1)	13 (4.4)	1.9 (0.7-4.8)	0.25
Salami	17 (8.7)	33 (11.2)	0.6 (0.3-1.2)	0.14
Fresh fish	40 (20.5)	84 (28.5)	0.5 (0.3-0.9)	0.02
Frozen fish	42 (21.5)	89 (30.2)	0.6 (0.4-1)	0.07
Any meat cooked rare	17 (8.8)	14 (4.7)	1.6 (0.7-3.6)	0.26
Handle raw meat	73 (37.4)	144 (49.5)	0.6 (0.4-1)	0.05
Vegetables and fruit	178 (90.4)	281 (94.9)	0.5 (0.2-1.1)	0.07
Lettuce	124 (63.6)	181 (61.4)	1.6 (1.0-2.6)	0.06
Prepared salad - other than lettuce, e.g. coleslaw	71 (36.4)	147 (50.1)	0.6 (0.4-0.9)	0.01
Milk and dairy products	187 (94.9)	283 (95.9)	0.9 (0.4-2.3)	0.88
Cold milk	87 (44.4)	171 (58.2)	0.5 (0.3-0.8)	0.00
Ice-cream	86 (44.3)	166 (56.5)	0.6 (0.4-0.9)	0.02
Yoghurt	99 (50.8)	184 (62.8)	0.6 (0.4-0.9)	0.01
Eating out	143 (73)	204 (69.2)	1.4 (0.9-2.2)	0.13
Fish and Chip shop	24 (12.2)	64 (21.7)	0.5 (0.3-0.9)	0.03
Indian Restaurant/ /takeaway	12 (6.1)	14 (4.7)	1.3 (0.5-3.1)	0.61
Chinese Restaurant/ /takeaway	61 (31.1)	89 (30.2)	1.1 (0.7-1.8)	0.55
Other Restaurant/takeaway	54 (27.6)	46 (15.6)	2.6 (1.5-4.4)	<0.001
Plane	19 (9.7)	5 (1.7)	7.8 (2.2-27.1)	0.001

* Matched odds ratio adjusted for age † For several variables answers were not available from all participants (denominators in percentages vary).

case-control sets, 101 cases were matched to one control each, 93 cases to two controls each, and three cases to three controls each (as these three cases handed questionnaires to three controls instead of two).

The participant (n=197) and non-participant cases did not differ significantly in terms of gender (p=0.24) and age group (p=0.13). In addition, the response rate of cases was similar in each season, suggesting that the number of participant cases by season reflected

the seasonal distribution of reported campylobacteriosis cases (data not shown).

Cases and controls

The main socio-demographic characteristics of cases and controls are shown in Table 1. The median age (32 years; range 0-76) of cases did not differ significantly from the median age (33 years; range 0-81) of controls (p=0.253). Regarding gender, 46.4% of cases and 34.4% of controls were male.

TABLE 3

Univariate analysis of risk and protective factors (alcohol and drinking water, contact with animals, leisure activities, medical history) for campylobacteriosis. All-Ireland Campylobacter infection case-control study, 2004.

Exposure	Cases (n=197) † n (%)	Controls (n=296) † n (%)	Crude OR* (95% CI)	P-value
Alcohol	98 (50.5)	174 (59.4)	0.7 (0.4-1.2)	0.15
Alcohol during meals	59 (30.3)	73 (24.9)	1.8 (1-3.2)	0.04
Drinking water				
Mains water supply	184 (93.4)	268 (96.3)	0.4 (0.2-1.0)	0.06
Well	4 (2.0)	3 (1.0)	2.4 (0.5-11.0)	0.27
Group water scheme	2 (1.0)	2 (0.7)	1.5 (0.2-12.0)	0.70
Tap water	151 (77.0)	245 (83.6)	0.8 (0.5-1.3)	0.37
Own pet(s)				
Own any pet	5 (2.5)	5 (1.7)	1.8 (0.5-7.1)	0.38
Dog (as pet)	16 (8.1)	36 (12.2)	0.5 (0.2-1.1)	0.08
Cat (as pet)	4 (2.0)	11 (3.7)	0.6 (0.2-2.1)	0.46
Fish (as pet)	4 (2.0)	10 (3.4)	0.3 (0.1-1.4)	0.12
Pet ill with diarrhoea	57 (28.9)	110 (37.4)	0.7 (0.4-1.1)	0.09
Contact with animals (other than pets)				
Other dogs	39 (19.3)	93 (31.6)	0.5 (0.3-0.8)	0.01
Horses	4 (2.0)	7 (2.4)	0.5 (0.1-2.6)	0.39
Sheep or lambs	8 (4.1)	5 (1.7)	3.8 (0.7-19)	0.11
Outdoor and leisure activities				
Swimming or water sports in the sea	10 (5.1)	8 (2.7)	2.4 (0.7-8.6)	0.18
Running/Jogging/Athletics	18 (9.2)	38 (12.9)	0.6 (0.3-1.1)	0.12
Play in a garden or park	42 (21.4)	90 (30.6)	0.4 (0.2-0.7)	0.00
Own a garden	175 (89.7)	262 (89.4)	1.4 (0.7-3.1)	0.35
Using manure in the garden	6 (3.1)	7 (2.4)	1.4 (0.4-4.6)	0.55
Health and medical history				
Any of the following health problems	73 (37.1)	63 (21.3)	2.3 (1.42-3.6)	0.00
Stomach ulcer	23 (11.7)	8 (2.7)	5.4 (2-14.7)	<0.001
Gall stones or liver disease	5 (2.6)	2 (0.7)	4.3 (0.8-24)	0.10
Hiatus hernia	18 (9.2)	4 (1.4)	11.9 (2.7-52)	0.00
Lower bowel problems	23 (11.7)	14 (4.8)	4.2 (1.8-9.6)	<0.001
Lower bowel problems	8(4.1)	6 (2)	2.7 (0.8-9.2)	0.11
Lower bowel problems	12 (6.2)	5 (1.7)	3.8 (1.2-11.3)	0.03
Any of the following drugs in the month before	47 (24)	52 (17.7)	1.4 (0.8-2.3)	0.21
Antacid medicines	21 (10.8)	34 (11.6)	0.9 (0.5-1.7)	0.70
Ulcer medicines	21 (10.8)	4 (1.4)	10.3 (3-35.7)	<0.001
Steroid tablets	4 (2.1)	4 (1.4)	1.7 (0.4-7.2)	0.47
Antibiotics	17 (8.7)	15 (5.1)	1.4 (0.7-3)	0.39

* Matched odds ratio adjusted for age † For several variables answers were not available from all participants (denominators in percentages vary).

Information on place of residence (city/village/rural area) was only available for 38.3% of the respondents. Of those, the majority (90.9% of cases and 89.9% of controls) reported living in a town or city.

There were no significant differences in the employment status between cases and controls (Pearson $\chi^2 = 8.1712$; $p = 0.086$). Among employed cases and controls, 13.3% and 16.0% respectively reported handling food as part of their occupation.

The median number of people living in the same household as the cases was three (range 1-8) compared to four (range 1-9) people living in the same household as controls ($p = 0.35$). Of the cases, 22.6%, and of the controls, 23.1% had at least one child under five years of age in their household ($p = 0.47$).

Clinical features of cases

The main symptoms reported by the 197 cases were diarrhoea (99.1%) (including bloody diarrhoea reported by 39.1%), abdominal pain (89.3%) and fever (63.8%). Almost a fifth of cases were admitted to hospital, with the median duration of hospitalisation being four days (range 1-14 days).

Univariate and multivariate analysis of risk factors

The results of the univariate analysis for selected risk and protective factors are shown in Table 2 and Table 3. Cases were more likely than controls to have consumed chicken, and undercooked chicken in particular, duck, lettuce, to have eaten in a takeaway restaurant, to have eaten in a plane, to have travelled outside Ireland, to have drunk from a well, to have had contact with a sheep or lamb and to have swum in the sea. Cases were also more likely than controls to suffer from peptic ulcer, hiatus hernia or lower bowel problems.

In the final conditional logistic regression model, seven variables remained significant independent risk factors for *Campylobacter* infection (consuming chicken, consuming lettuce, eating in a takeaway, contact with sheep, suffering from peptic ulcer, suffering from hiatus hernia and suffering from lower bowel problems) and six were protective factors (consuming turkey, consuming beef, consuming salad other than lettuce, having mains water supply at home, contact with dog other than one's own and playing in a park) (Table 4).

Eating chicken was the only risk factor that showed a dose-response relationship, as more frequent consumption of chicken increased the risk of infection by 20% per time of consumption (amOR 1.2 ; 95%CI: 1-1.4). When we stratified the results by country (ROI versus NI), country-specific ORs were not found significantly different. However, the numbers in the strata were not large enough to allow safe conclusions and the corresponding 95% CIs were wide (data not shown).

Discussion

Risk factors for transmission of infection

This study identified some independent risk factors for *Campylobacter* infection that could account for the majority of sporadic cases on the island of Ireland. The most important, based on PAF, was eating chicken, consuming lettuce and eating from a restaurant takeaway (other than Chinese or Indian) in the seven days before onset of illness. The other risk factors identified were: contact with sheep, suffering from stomach ulcer, peptic ulcer or gastritis, suffering from hiatus hernia, suffering from lower bowel problems.

Our study showed an increased risk associated with chicken consumption in general, and an even (three times) higher risk associated with undercooked chicken consumption. This finding, which was also supported by an observed dose-response relationship, was not unexpected as chicken and, in particular, undercooked chicken has been the most consistent finding in studies of risk factors for campylobacteriosis [4,5,7,8,11,12,15,18,19,20]. However, the PAF suggests that the consumption of chicken may account for an unusually high proportion (i.e. the majority) of sporadic cases that occur in Ireland, both ROI and NI. Given that chicken consumption exceeds 70% among the Irish population, this finding receives more importance [16]. Recent microbiological studies of raw poultry conducted in NI and ROI have shown that 50%-70% of raw chickens tested at retail level, were contaminated with *Campylobacter* [21-26]. Those contamination rates were consistently the highest among all food items examined. Furthermore, the genotypic characterisation by Pulsed Field Gel Electrophoresis (PFGE) of both clinical and food isolates and comparative cluster analysis during a recent all-Ireland study, has revealed that a high proportion of indistinguishable *Campylobacter* isolates found in poultry products were also found in human cases [21], re-emphasising the significant role that chicken plays in the epidemiology of human *Campylobacter* infection in Ireland.

Although, in line with several other studies, our study has found negative associations with salad vegetables, lettuce was identified as an important risk factor for infection. Lettuce consumption has previously been described in association with outbreaks [27-29], but, to our knowledge, it has never been identified as a risk factor for sporadic cases. The consumption of lettuce was implicated as the likely vehicle of infection in a recent large *Salmonella* Newport outbreak in NI [30]. Lettuce could be contaminated

TABLE 4

Final conditional logistic regression model. All-Ireland *Campylobacter* infection case control study, 2004.

Risk and protective factor	Crude OR* (n=457)	Adjusted OR* (n=457)	PAF †
Chicken	2.8 (1.4-5.7)	5.6 (1.8-15.6)	83.2
Lettuce	1.5 (0.9-2.5)	2.6 (1.3-5.2)	58.5
Other restaurant/takeaway	2.6 (1.5-4.4)	3.1 (1.4-6.6)	24.7
Hiatus hernia	11.9 (2.7-52.4)	20.3 (2.3-183.3)	21.6
Peptic ulcer	5.4 (2-14.7)	19.0 (3.8-93.7)	32.7
Lower bowel problems	4.2 (1.8-9.6)	4.5 (1.2-16.8)	14.4
Contact with sheep	3.8 (0.7-19.1)	11.0 (1.6-78)	14.5
Turkey	0.7 (0.5-1.1)	0.2 (0.1-0.5)	--
Beef	0.6 (0.4-1)	0.4 (0.2-0.8)	--
Salad (other than lettuce)	0.6 (0.4-0.9)	0.4 (0.2-0.8)	--
Mains water supply	0.4 (0.2-1)	0.2 (0.1-0.9)	--
Contact with a dog other than one's own	0.5 (0.3-0.8)	0.4 (0.2-0.8)	--
Playing in a park	0.4 (0.2-0.7)	0.3 (0.1-0.7)	--
Male	2.0 (1.2-3.2)	2.4 (1.2-4.7)	--

* Crude and adjusted matched odds ratios (ORs) are calculated based on 457 subjects, due to missing values in some variables

† Population-attributable fraction

with *Campylobacter* before or after the point of sale. Contamination at source could occur through the presence of contaminated soil, the use of contaminated water during harvesting or even flies [31]. During food preparation, fresh lettuce may also be cross-contaminated by kitchen tools or surfaces already contaminated from previous contact with other food [32]. Cross-contamination was the most frequent contributory factor identified in a review of foodborne outbreaks in England and Wales (including five due to *Campylobacter*) linked with lettuce and other salad vegetables and fruit [28,29]. A recent study in ROI, in common with several other studies, has demonstrated that *Campylobacter* can easily spread from fresh food, mainly chicken, to domestic kitchen surfaces and tools and subsequently to lettuce and other salad vegetables [33]. This suggests that cross-contamination of fresh products is very likely to happen in kitchens, particularly through poor handling or storage practices.

Consumption of food from takeaways (other than Chinese or Indian) was an important risk factor, based on PAF (PAF=25). This association suggests that food-hygiene preparation practices in these settings may be poor. Several other studies have implicated exposure to food (most often poultry) prepared outside the home to be associated with campylobacteriosis [7,18,34]. However, it was not possible in this study to identify specific food items associated with infection, bought from takeaways. Further attention to sources of food and food-handling practices in these restaurants in Ireland are needed. Cross-contamination of ready-to eat foods may be an important source of infection, given evidence from experimental studies suggesting that *Campylobacter* is frequently present in a variety of foods and has a low infectious dose (ranging from 500-10,000 cells) [22,35].

A small proportion of cases could be explained by contact with sheep. This association, though apparently uncommon, is entirely plausible. Sheep are known to be carriers [36], excrete *Campylobacter* and therefore may transmit infection to humans. Previously, occupational contact with animal faeces, living on a farm and contact with cattle have all been described as risk factors for *Campylobacter* infection [15].

The association between campylobacteriosis and suffering from peptic ulcer or hiatus hernia yielded the highest aMOR among all risk factors identified, although this factor explained a small percentage of cases, overall. Many of the patients who suffer from these gastrointestinal diseases may be receiving long-term treatment with acid suppressants, such as proton pump inhibitors (omeprazole) and H2 antagonists. These drugs have been previously reported to increase risk for *Campylobacter* infection probably by increasing gastric PH and therefore making the stomach a much less hostile environment for bacteria [37].

To our knowledge, the independent association between lower bowel problems and campylobacteriosis has not been previously reported. The biological plausibility of this finding is unclear, particularly, as data were not collected on specific diseases of the lower bowel. It is possible that some conditions or their treatment may lead to a prolonged gastrointestinal transit time and slow clearance of the organism. Alternatively, this finding may be due to a bias, as the case ascertainment for campylobacteriosis may have been higher for patients with pre-morbid bowel problems who may be more likely to submit a faecal stool sample. This bias may also apply to the previously mentioned diseases, i.e. peptic ulcer or hiatus hernia. However, more research is needed to clarify this apparent effect and the mechanisms behind it.

Protective factors

The role of mains water supply as a protective factor is interesting. It has been previously reported that inadequately treated water may cause *Campylobacter* infection in humans and this pathogen was implicated in several waterborne outbreaks in some countries [38-42]. In addition, a recent ecological study in Sweden indicated that water might be an important route of transmission for *Campylobacter* infection [43]. Water can be contaminated through animal faeces [44] and sewage and some *Campylobacter* strains can survive for long in untreated water sources [45]. In this study, cases were twice more likely to drink water from a source other than the mains water supply (e.g. wells or other water schemes). This association, however, was not statistically significant probably because this exposure was uncommon (reported only by 13 cases and 7 controls). It is possible that the protective effect of the public water supply reflects the association of infection with sources of untreated water.

Many of the other protective factors (mainly food items such as beef, turkey and salad vegetables other than lettuce) might indirectly confirm the association with chicken and lettuce as our data suggest that controls, who ate chicken or lettuce less frequently than cases, were more likely to replace those food items with another kind of meat (including poultry) or salad vegetable respectively.

The protective effect of playing in the park and of having contact with a dog other than one's own is less clear. It is possible that these individuals may have a healthier life-style and therefore be less prone to infections or may have engaged in some practices, not evaluated in the study, which protect them from *Campylobacter* infection.

Limitations of the study

The study only involved campylobacteriosis cases reported through the routine surveillance system, that constitute a subset of all cases occurring in the community. Epidemiological studies in the UK have shown that only one in eight cases of *Campylobacter* infections occurring in the community is reported through routine surveillance [15]. In addition, due to the relatively low response rate and the matched design of the study, cases that were included in the analysis may have not been representative of all reported cases. However, the available demographic data (age and gender), suggest that there were no statistically significant differences between participant and non-participant campylobacteriosis cases reported to the health authorities.

All *Campylobacter* species were included in the case-definition and no information on speciation was collected. It is possible that risk factors vary according to campylobacter species. Approximately 90-95% human infections are due to *C. jejuni* in the developed world [38], and sporadically available typing data suggest that Ireland has a similar distribution [1].

Controls were not randomly selected from the source population, which would have assured their representativeness in terms of the exposures, but were case-nominated. Choosing controls among friends, work colleagues and neighbours might lead to over-matching, as cases and controls may be similarly exposed to common risk factors (especially food). In addition, some of the controls may have come from the same household as the cases. This could have increased the risk of over-matching even more. This effect, however, may have only reduced the strength of

any association. We excluded those cases and controls from the analysis, whenever this was evident.

As in all case-control studies, cases as a result of their illness may be more able to recall exposures than controls, which may result in recall bias. However, cases that received their questionnaire long after their onset of symptoms in this study (median delay 16 days), may have reported a list of food preferences rather than their definite food exposures. This may have been less of a problem for controls, as exposure period referred to the week prior to their completing the questionnaire, i.e. a more recent period.

Information on place of residence was limited in this study, as only 38.3% of the respondents answered the relevant question. Surveillance data have shown increased incidence of *Campylobacter* infection in rural areas compared to urban areas and studies have suggested that exposure to risk factors may be different for people living in rural compared to those in urban areas [46]. Accurate knowledge of the geographical distribution of cases and controls would have been of added value, and it could have potentially resulted in different guidelines for rural and urban areas.

Conclusion and recommendations

The study suggests that consumption of chicken, lettuce and food from takeaways accounts for the majority of *Campylobacter* infections in the island of Ireland, both ROI and NI. All these factors could be prevented using basic food-hygiene measures. The findings of this study therefore, highlight the need for an improved and more efficient approach to basic food-hygiene measures to prevent campylobacteriosis and other infectious gastrointestinal illnesses in the community. Further measures are needed throughout the food chain from production, transport, retail and catering to reduce the risk of contamination and cross-contamination. Improved catering practice, whether in the domestic or commercial setting, is an important last line of defense in reducing exposure to potentially *Campylobacter*-contaminated products. In addition, it is essential to raise awareness in the population of the importance of good basic food-hygiene practices, using means of communication easily and readily accessible. Further efforts are needed to identify the defective points in the food chain and enable appropriate measures to reduce the overall burden of this infection in the Irish community. Linkage of epidemiological data with *Campylobacter* speciation and the development of new molecular diagnostic tests will also provide a greater understanding of *Campylobacter* infection.

Acknowledgements

In memory of Massimiliano Di Renzi, one of the main researchers of this study, who died tragically in a car accident. We would also like to thank the Food Safety Promotion Board – SafeFood that commissioned and supported financially this study; Alain Moren, Arnold Bosman, James Stuart (EPIET coordinators) and Lelia Thornton (SpPHM – HPSC) for their scientific advice; Tom Nichols (CDSC-Colindale, London) for statistical advice; Biagio Pedalino (EPIET Alumnus) for his support in the study protocol development; the Environmental Health Officers (EHOs) in the HSE Eastern Region: Catherine Cosgrove, Gavin McDonald, Sue Codd, Gemma O'Sullivan, Claire Wilde; Ian Daly (Principal EHO in Wicklow) and his team; Mary Conlon, Senior Area Medical Officer (SAMO) in Kildare) and her Area Medical Officers (AMOs) team; Sinead Tiernan, Eimear Brennan, Christiana Onafue, Aileen O'Brien, Patricia Mannion and Piaras O' Lorcain, in the Department of Public Health, Dr. Steevens Hospital, HSE Eastern Region, Patricia Garvey, Sarah Jackson, Ciara Carr, Fiona Cloak,

Marshall Cox, Aibheann O'Malley, Natasha Sheehan, Kathryn Walsh in the HPSC; Richard Hanna, Gavin Marshall, John Farrell, Maire Gorman, Paula O'Neill, Sinead Crossan, Kyle Carrick, Alison Briggs, Niall Currie, Kenny Shields, Cathy McVeigh, Ruth Liggett, Trevor Harrison, Monica Magennis, Sheena Donaghy, Aisling McCaughey, Shane Campbell, John Farrell, Paul O'Donoghue, Adrian Fitzsimons and Declan McQuaid, EHOs in the SHSSB; Andrew Taylor, Colin Magill, Gail McEwen, Richard Harvey, Hazel McKee, Heather Moore, Robert Lamont, Mark Sloan, Pauline Mullan, Steve Cooper, S. McCaig, Cathy Mc Veigh, Gavin Marshall EHOs in the other health board areas of Northern Ireland, all participating EHOs in the WHSSB of Northern Ireland and EHOs from the Northern Group Environmental Systems for their role in following up individual cases with campylobacter; Audrey McClune, Larry Dargan, Hilary Byrne and John McKee (Principal EHOs); Philip Donaghy and Richard Smithson (CCDCs) for facilitating the implementation of the study in their area; Rosin Brogan, Nicola Cunningham, Caroline Irwin, Martina McNulty (administrative and IT staff in HSSBs) for regularly forwarding information on notifications to the research team; Eileen Corey (administrative staff in CDSC-NI) for her valuable administrative and data entry support in NI; Marie Laffoy (Director of Public Health in the HSE Eastern Region) and Darina O'Flanagan (Director of the HPSC) for facilitating and supporting the study.

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This article was published on 19 February 2009.

Citation style for this article: Danis K, Di Renzi M, O'Neill W, Smyth B, McKeown P, Foley B, Tohani V, Devine M. Risk factors for sporadic *Campylobacter* infection: an all-Ireland case-control study. *Euro Surveill.* 2009;14(7):pii=19123. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19123>