

Association between environmental risk factors and campylobacter infections in Sweden

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SUMMARY

Campylobacter sp. is the most common cause of acute bacterial gastroenteritis in Sweden and the incidence has been increasing. Case-control studies to identify risk factors have been conducted in several countries, but much remains unexplained. The geographical distribution of campylobacter infections varies substantially, and many environmental factors may influence the observed pattern. Geographical Information Systems (GIS) offer an opportunity to use routinely available surveillance data to explore associations between potential environmental risk factors showing a geographical pattern and disease incidence, complementing traditional approaches for investigating risk factors for disease. We investigated associations between campylobacter incidence and environmental factors related to water and livestock in Sweden. Poisson regression was used to estimate the strength of the associations. Positive associations were found between campylobacter incidence and average water-pipe length per person, ruminant density, and a negative association with the percentage of the population receiving water from a public water supply. This indicates that drinking water and contamination from livestock may be important factors in explaining sporadic human campylobacteriosis in Sweden, and that contamination occurring in the water distribution system might be more important than previously considered.

BACKGROUND

Campylobacter sp. is nowadays the most common cause of acute bacterial gastroenteritis in Sweden, as in many other industrialized countries. The predominant species causing disease in humans is *Campylobacter jejuni*, responsible for more than 90% of reported cases in Europe [1]. Risk factors for campylobacter infections have been studied in several case-control studies [2–4]. Some frequently identified risk factors in these studies include eating chicken,

drinking unpasteurized milk, visiting/living on a farm, contact with pets and drinking unprocessed water.

Compared to the situation in many other countries, the prevalence of campylobacter in broilers in Sweden is low [5]. A voluntary control programme has been running since 1991, and the prevalence of campylobacter-infected flocks has decreased to under 10% [6]. It was anticipated that this, combined with raising people's awareness of the importance of preparing chicken properly, would lead to a decrease in human campylobacter infections. However, during the 1990s the incidence in humans increased steadily [6].

Water has been incriminated as the source of infection in several outbreaks of campylobacter

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infections, and in Sweden campylobacter has been the most commonly identified pathogen in waterborne outbreaks [7]. For sporadic infections however, the role of water in transmission is not yet fully understood. Campylobacter can survive for longer periods in water sources during winter, but is sensitive to UV light and higher temperatures, and is therefore rapidly decimated during the summer [8, 9]. During this period, animals and birds may act as reservoirs for re-contamination of water sources. In several studies different farm animals have been shown to be asymptomatic carriers of *Campylobacter* sp. [10–13] and have also been suspected of being the source of contamination of the water supply in waterborne outbreaks. *Campylobacter jejuni* is the predominant species found in ruminants and poultry, and *Campylobacter coli* in swine [14]. Transmission from animals and birds to water can occur either through direct contamination, or indirectly by contamination of the catchment area with subsequent drainage into water reservoirs. In a study in United Kingdom, cattle were found to have contaminated a ground-water source [15], and in Finland cattle were shown to act as a reservoir for campylobacter during summer, and a water–animal–water cycle was suggested as a model for maintaining the water contamination [16].

In Sweden, approximately 90% of the Swedish population are supplied with water from public water companies, and the remaining 10% have their own private water supply serving a few households. Altogether approximately 50% of those connected to a public supply are supplied from surface water, 25% by artificially infiltrated surface water and 25% by ground water [17]. Nearly all surface water is disinfected before distribution, while this is done for only half of the artificially infiltrated water, and for approximately one quarter of the ground water. Surface water is more prone to contamination from livestock and other sources than ground water, but since ground water is often distributed without any treatment, even a small amount of contamination can give rise to infections in humans and animals.

Looking at the geographical distribution of diseases was one of the first methods used in epidemiology to study sources of transmission and rate of spread of disease, exemplified by the work on cholera in London by John Snow [18]. The logic behind using geography to study risk factors for disease is to explore the correlation between potential risk factors having a spatial pattern and disease occurrence. Risk factors can include either physical and environmental

factors, social, cultural and economic factors, or genetic factors. In infectious diseases, such an ecological design has mainly been applied for vector-borne diseases, but recently this approach has also been used to study risk factors for EHEC infections in Canada and Sweden [19, 20] or tuberculosis in Germany [21].

In the present study we combined geographic, climatic, agricultural, water-supply and disease data to describe the geographical distribution of campylobacter infections in Sweden, and to evaluate the geographical association between these factors and disease incidence. This was done in order to generate research hypotheses and provide a background for planning more targeted microbiological and epidemiological studies.

MATERIALS AND METHODS

Campylobacteriosis is a mandatory notifiable disease in Sweden, and both physicians and laboratories are required to notify. Between 5000 and 7000 cases have been notified annually during the 1990s, approximately 30–40% of which have been infected in Sweden, the remainder being acquired abroad [22]. The treating physician writes the probable place of infection on the notification form, based on travel history and incubation period. In this study we included all domestic cases notified to the Swedish Institute for Infectious Disease Control (SMI) during the three years 1998–2000.

Information on agricultural variables and water supply was obtained for each of Sweden's 289 municipalities. Livestock density was defined as number of animals/km² for cattle, small ruminants, swine and poultry [23]. Water distribution and supply data included was: (1) proportion of people in the municipality receiving water from a public water supply, e.g. receiving water from a water company as opposed to having a private well, (2) proportion of the distributed water obtained from surface-water sources, and (3) average water-pipe length measured in metres per person (calculated as total length of the water distribution network in the municipality divided by number of people receiving public water supply) [24]. Data on water distribution and supply was not available for all municipalities, and was missing for 11, 26 and 15 of the 289 municipalities respectively for the three above-mentioned water-related variables. The municipalities for which the data was not available were omitted from the multivariable analysis.

A north–south gradient for campylobacter incidence with a lower incidence in the north has previously been described in the Nordic countries [25]. Different factors have been suggested to explain this gradient, including climatic factors and factors relating to agriculture and lifestyle. To correct for possible climatic variations due to large differences between north and south, we included a variable for average annual temperature and average annual precipitation measured at ten weather stations throughout Sweden during the period 1998–2000. This information was obtained from a climatic database [26].

To correct for other major confounders that might be associated with urban or rural living conditions, especially concerning differences in food habits and lifestyle, we also included a variable for municipality class. In the official classification defined by the Swedish Association of Local Authorities nine categories are defined [27]. They are classified according to various structural characteristics, including population size, degree of urbanization and production sector, ranging from sparsely populated municipalities to large cities. For the analysis these categories were divided into rural (categories 1–3), towns (categories 4–6) and large cities and suburbs (categories 7–9).

GEOGRAPHICAL DATA PROCESSING

The infectious disease control in Sweden is administered at the county level, of which there are 21 in Sweden. The statistics for the water-supply data and the agricultural data is recorded at the level of the municipalities, of which there are 289. We therefore needed to break down the data from the infectious disease register to the administrative level of the municipalities to be able to perform the correlation analysis. We therefore imported the data from the infectious disease register into a geographical information systems (GIS) package (ArcView®) and mapped the individual cases based on their place of residence. If a place of infection different from the place of residence was written on the notification form, this place was preferred for the mapping. The geocoding procedure in ArcView was used to allocate the cases on the map. A map of the municipalities was then superimposed on the map of the cases, and by using the ‘point-in-polygon’ procedure in ArcView the cases were assigned to a municipality. The rate in each municipality was calculated as an average of the annual rates in the study period 1998–2000.

Population data for each year were obtained from Statistics Sweden [28]. For the climatic data we used the geoprocessing procedure in ArcView to assign the values for the weather stations located closest to the geographical centre of the municipalities to each municipality.

Statistical analysis

The correlation between the explanatory variables was examined by Pearson correlation in a correlation matrix. If strong correlation was found between two variables, they were either merged or the most biologically plausible variable was selected for inclusion in further analyses.

Univariate and multivariable Poisson regression were used to estimate the relative risk of campylobacter infection associated with the environmental risk factors investigated. The number of cases in each municipality was used as outcomes in the Poisson regression. In the model the expected number of cases occurring in a municipality was assumed to be proportional to the population size and the exponential of a linear combination of the environmental variables included in the analysis. Municipal classification was included in the regression model as nominal variables. Stata Statistical Software was used for the analysis [29].

A second model excluding the three largest cities in Sweden (category ‘large city’ according to the Swedish official classification of the municipalities) was also investigated, since there are reasons to believe that the aetiological fractions explained by the different sources might be different in the largest cities compared to the rest of the country.

RESULTS

There were 23 481 campylobacter infections notified to the national register in the three years 1998–2000. Of these 13 715 (58%) were reported as acquired abroad, 7280 (31%) were reported as acquired in Sweden and for 2486 (11%) this information was missing. We only included cases acquired in Sweden in this study. In total 7007 of the 7280 cases (96%) could be assigned to a municipality. For 1205 cases (17%) the probable place of infection differed from the home address. This difference was highest in August, when 337 of 1456 cases (23%) had a probable place of infection different from their home address.

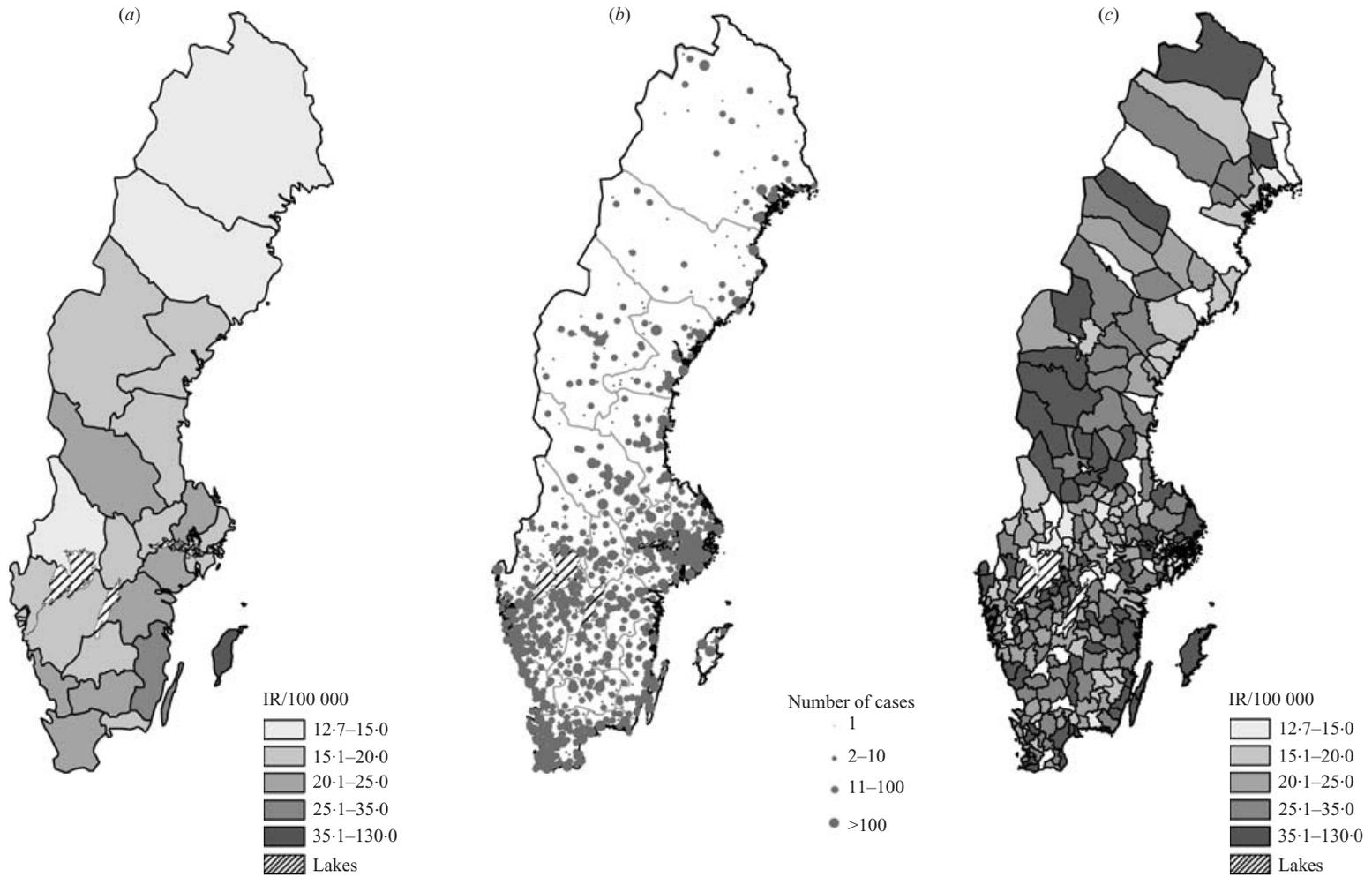


Fig. Geographical distribution of campylobacter infections in Sweden 1998–2000. Average annual incidence rate per 100 000 population by (a) county; (b) dot map of cases based on place of infection or address of residence; and (c) average annual incidence by municipality.

Table 1. *Distribution of variables included in the study. Average during the three years 1998–2000 in Sweden, and range in the municipalities*

	Sweden	Range in municipalities	<i>n</i> *
Population	8 876 000	2800–739 600	289
Campylobacter cases†	7007	0–770	289
Campylobacter annual IR/100 000	26.3	0–122	289
Cattle/km ²	4.2	0–50.5	289
Small ruminant/km ²	1.1	0–20.0	289
Poultry/km ²	19.1	0–1100	289
Swine/km ²	5.2	0–185	289
Per cent public water supply	85.7	39.6–100	278
Per cent surface water	49.9	0–100	252
Water-pipe length (m/person)	8.5	1.8–80.2	274
Mean monthly precipitation (cm)‡	6.3	4.7–8.5	10
Mean annual temperature‡	4.9	–1.2–8.1	10

IR, Incidence rate.

* Number of municipalities where this information was available.

† Sum for the three years 1998–2000.

‡ As measured 1998–2000 on 10 weather stations distributed throughout Sweden.

The overall annual incidence rate of domestic campylobacter infections during the study period 1998–2000 was 26.3/100 000 population, with a range in the municipalities from 0 to 122/100 000 population (Fig., Table 1). The total number of cases over the 3-year period reported in each municipality varied from 0 to 770 (mean 20.5, median 11).

Several of the explanatory variables were correlated (Table 2). Since there was a strong correlation between cattle and small ruminant density, i.e. sheep, it was not possible to analyse the effects separately. We therefore combined these in a single variable – ruminant density – which was calculated based on their representative livestock units [30]. Swine density was correlated with cattle density, but since these animals normally carry different serotypes, we kept both for the analysis. The latitude was strongly correlated with the mean annual temperature, and was therefore excluded from further analysis.

In univariate Poisson regression analysis, living in rural area, ruminant, swine and poultry density, water-pipe length and mean annual temperature were significantly related to increased campylobacter incidence. The proportion having a public water supply was significantly related to a decreased incidence (Table 3).

Multivariable Poisson regression analysis identified ruminant density [incidence rate ratio (IRR) 1.08, 95% CI 1.05–1.11], water-pipe length (IRR 1.12, 95% CI 1.08–1.16) and mean annual temperature (IRR 1.05, 95% CI 1.03–1.07) as independent risk

factors related to an increased campylobacter incidence (Table 3, Model 1). After exclusion of the three largest cities (accounting for 1377 cases), the IRRs for ruminant density and water-pipe length increased, and the proportion having public water supply were significantly related to a decreased incidence (Table 3, Model 2).

DISCUSSION

An urban–rural gradient for campylobacter infections has been described for several countries [31–33], but few studies have tried to investigate the reason for a geographical variation in incidence. Most studies investigating risk factors for sporadic campylobacter infections have been case-control studies, primarily focusing on identifying risk factors for foodborne infections. In rural areas in Sweden, dairy production, and swine and poultry farming are important agricultural industries, and contamination of water is possible, especially when manure is used as fertilizer. The influence of this is difficult to assess in individually based studies, where cases and controls are often matched on geographical location. In the present analysis we used disease mapping to assess factors that may have a more indirect influence on the risk of infection, through contamination of water or the general environment.

Our results suggest an association between living in an area with high ruminant density and an increased incidence of campylobacter infections. The univariate

Table 2. Degree of correlation between the explanatory variables studied. Correlation matrix (pairwise Pearson correlation coefficients). Significant values in bold at the 0.05 significance level (two-tailed test)

	Public water supply	% surface water	Pipe length (m/person)	Municipal category	Cattle density	Poultry density	Sheep density	Swine density	Mean annual temp.	Mean monthly precip.	x-coord.	y-coord.
Public water supply	1	0.25	-0.29	0.47	-0.24	-0.05	-0.20	-0.05	-0.02	-0.25	0.29	0.11
% surface water	0.25	1	-0.32	0.35	-0.10	0.02	-0.06	-0.06	0.15	-0.05	0.00	-0.02
Pipe length (m/person)	-0.29	-0.32	1	-0.59	0.12	-0.01	0.08	0.03	-0.37	-0.01	0.07	0.23
Municipal category	0.47	0.35	-0.59	1	-0.05	0.02	-0.01	0.02	0.42	-0.03	0.03	-0.26
Cattle density	-0.24	-0.10	0.12	-0.05	1	0.29	0.64	0.57	0.24	0.33	-0.33	-0.55
Poultry density	-0.05	0.02	-0.01	-0.02	0.29	1	0.19	0.58	0.09	0.19	-0.19	-0.29
Sheep density	-0.20	-0.06	0.08	-0.01	0.64	0.19	1	0.31	0.31	0.11	-0.19	-0.46
Swine density	-0.05	-0.06	0.03	0.02	0.57	0.58	0.31	1	0.12	0.30	-0.29	-0.41
Mean annual temp.	-0.02	0.15	-0.37	0.42	0.24	0.09	0.31	0.12	1	0.07	-0.44	-0.73
Mean monthly precip.	-0.25	-0.05	-0.01	-0.03	0.33	0.19	0.11	0.30	0.07	1	-0.70	-0.46
x-coordinate	0.29	0.00	0.07	0.03	-0.33	-0.19	-0.19	-0.29	-0.44	-0.70	1	0.66
y-coordinate	0.11	-0.02	0.23	-0.26	-0.55	-0.29	-0.46	-0.41	-0.73	-0.46	0.66	1

analysis identified an association between living in a rural area and an increased risk of campylobacter infections. However, when this variable was included in the multivariable analyses together with water-pipe length and ruminant density, living in a rural area did not show any significant independent effect. Seepage from cattle manure used as fertilizer to ground-water wells has previously been incriminated in waterborne outbreaks [34], and since sheep and cattle are regularly let out in the fields for grazing in Sweden during summer, there is a high risk for contamination of drinking-water sources. However, the increased risk in municipalities with a high density of ruminants can also be explained by a higher direct transmission from cattle and small ruminants. The relative importance of indirect transmission from farm animals through water and the environment is difficult to measure, and the next step to investigate this would be to conduct a multi-level study incorporating data from individual based studies with the data on environmental factors.

An increased risk with longer water distribution pipelines indicates that contamination occurring during distribution from the waterworks to the households may be more important than previously thought. There are several factors that may contribute to increased risk of contamination in the distribution network. In Sweden it is estimated that approximately 20% of all water produced is lost through leakage [35], and this predisposes for contamination during periods with low pressure in the distribution system. In sparsely populated areas, long pipelines with little flow can lead to unstable water pressure. A study conducted in Norway found a higher risk of gastroenteritis in households experiencing episodes of low pressure in the water distribution network than in households without low-pressure episodes [36]. This was explained by higher risk of contamination from the surroundings during low-pressure episodes. The risk for cross contamination is also increased, since water and sewage pipelines are often placed in close proximity to each other for practical reasons. Fewer resources for maintenance and control of breakage and leaks in more sparsely populated areas may additionally contribute to poorer water quality at household level. Since the level of chlorination in Sweden is low compared to many other countries, the residual effect within the distribution network is also very low. Protection zones are established around drinking-water sources, however, there is no regulation regarding placement of water pipelines.

Table 3. *Univariate and multivariable (Mult) association of environmental factors and campylobacter incidence in municipalities of Sweden, 1998–2000*

Variable	n*	IRR†	95% CI	Mult.	95% CI	Mult.	95% CI
				IRR† Model 1 (n=274)	Model 1 (n=274)	IRR† Model 2 (n=271)	Model 2‡ (n=271)
Ruminant density§	289	1.12	1.09–1.14	1.08	1.05–1.11	1.12	1.09–1.15
Swine density	289	1.02	1.01–1.03				
Poultry density	289	1.03	1.01–1.05				
Per cent public water supply	278	0.93	0.91–0.95			0.93	0.90–0.95
Per cent surface water	263	0.99	0.99–1.00				
Water-pipe length per person	274	1.11	1.08–1.15	1.12	1.08–1.16	1.13	1.09–1.17
Mean monthly precipitation (cm)	289	1.00	0.99–1.02				
Mean temperature	289	1.03	1.01–1.04	1.05	1.03–1.07	1.02	1.01–1.04
Rural municipality	289	1.17	1.10–1.25				

* n, Number of municipalities where information was available; IRR, Incidence rate ratio; CI, confidence interval.

† IRR of an increase in animal density of 10 ruminant or swine per km² or 100 poultry per km², per 10% increase in public water supply or proportion supplied with surface water, and per 10 m increase in average water-pipe length per person.

‡ In Model 2 the three largest cities in Sweden are excluded.

§ Combined variable for cattle and small ruminants.

We did not find any significant association to the proportion of water taken from surface water sources compared to ground water. One possible explanation for this is that, in principle, all waterworks distributing surface water use some form of treatment and disinfection before distribution (e.g. chlorination) thus reducing any increased risk of contamination of the raw water. Ground water is often distributed without any treatment.

Our results also showed that having a public water supply instead of a private supply seemed to confer protection, which can be explained by less regulation and follow-up on control of contamination of small private wells.

The present analysis is based on data aggregated for populations rather than data on individuals. Findings from ecological analyses do not necessarily reflect associations at the individual level. One major limitation is described as the ‘ecological fallacy’, where an association found between a potential risk factor and the outcome at the aggregated level does not reflect the biological effect at the individual level, due to within-group differences in exposure level and covariates [37]. Although ecological studies may have several methodological problems, the influence of environmental variables can often be difficult to assess on an individual basis, and an ecological study may be one way to investigate the exposure effect. This method has become more available now, as the use of geographical information systems has made it

easier to analyse routinely available surveillance data on a more detailed geographical level. This reduces the risk of finding spurious correlation due to data aggregated over large levels. As can be seen in the Figure, a different pattern emerges when data is broken down from county level to municipality level.

The transmission routes of campylobacter infections can be divided in three categories; waterborne, foodborne or direct contact with carriers. While this study mainly focuses on risk factors related to non-foodborne infections, we have included all domestic cases notified to the infectious disease register in Sweden – which involve all routes of transmission. This may dilute the results of the analyses and thus weaken the observed associations. A stronger influence of non-foodborne transmission in rural areas is supported by our results, showing a stronger association for the environmental factors related to water supply and ruminants when the three largest cities in Sweden are excluded from the analysis.

CONCLUSION

The importance of water in explaining sporadic campylobacter infections has not been thoroughly investigated. A great effort has been made in Sweden to reduce transmission through food products, e.g. poultry products, however the incidence among humans has not decreased during the same time period. This ecological study indicates that water might be an

important route of transmission for campylobacter infections in Sweden, and that contamination of the water distribution network may be an important factor. Ecological studies such as this are easy to conduct, and can help to assess possible risks associated with environmental factors. This study utilizes data already available from disease surveillance and from different national databases and is therefore a resource-effective method for a preliminary assessment on environmental risk factors. However, this is a new approach and few such studies have been conducted so far for campylobacter, therefore the results need to be interpreted with caution. They should now be used as a starting point for further microbiological and epidemiological studies focused on water and water contamination.

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