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Association between indicators of livestock farming intensity and hospitalization rate for acute gastroenteritis

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SUMMARY

To evaluate associations between indicators of livestock farming intensity (manure surplus and livestock density) and acute gastroenteritis hospitalization (AGH) rate, we conducted an ecological study on 306 selected agricultural municipalities of Quebec. We estimated the AGH rate for the period 2000–2004 from the Quebec hospital database. Multivariate Poisson regression was used to estimate the strength of association between the farming indicators and AGH with adjustment for confounders. The modifying effect of age and water source was also evaluated. Association between manure and AGH was observed in children, especially those aged 0–4 years for selected zoonotic infections [adjusted hospitalization rate ratio (aHRR) 1·93, 95% CI 1·21–3·09]. The risk ratio was higher for subjects using ground-water source. An increasing HRR trend with each additional level of poultry density was observed in children aged 0–4 years, especially for *Salmonella* infections. We conclude that livestock farming intensity may be linked to bacterial acute gastroenteritis in children.

Key words: Acute gastroenteritis, animal farming, livestock, waterborne diseases, zoonotic infections.

INTRODUCTION

Acute gastroenteritis is the second most common disease worldwide [1]. The prevalence of diarrhoea, a major symptom of gastroenteritis, in selected communities of Canada and the United States, was found to be the highest in several developed countries (Australia, Canada, Ireland, United States) [2]. A study in Hamilton (Ontario, Canada) estimated the mean annual cost per case of gastroenteritis at Can$1089. Although it might not be representative of Canada, those numbers highlight the importance of this illness and the need for prevention efforts [3].

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Manure is known for its benefit as a fertilizer. However, in livestock farming areas, it has also been considered an important environmental issue. Manure may carry a variety of bacterial and protozoan pathogens which can cause acute gastroenteritis in humans (also known as zoonoses) such as *Cryptosporidium parvum*, *Giardia* spp., *Campylobacter* spp., *Escherichia coli* O157:H7, and *Salmonella* spp. [4, 5]. Hutchison *et al*. [6] studied the levels of zoonotic pathogens in British livestock manure and found that over 30% of livestock manure examined contained at least one pathogen. When contaminated run-off from manure-applied fields reaches the drinking-water supply, it could be a threat to public health especially in the case of water-treatment deficiency or inadequate monitoring. In fact, a study in Ontario (Canada) identified that the application of manure to land was associated with endemic human Shiga toxin-producing *E. coli* infection [7].

A surplus occurs when manure produced on intensive livestock farms far exceeds agronomic requirements. A significant association between manure surplus and acute gastroenteritis hospitalization (AGH)-zoonotic has been shown in our previous study [standardized rate ratio 1·4, $P \leqslant 0{\cdot}01$] [8]. However, the relation of the disease with a specific type of animal production has not yet been investigated because the only indicator used was the phosphorus index, which is not an animal-specific indicator. Different animals might carry different pathogens. As the number of animals on a farm increase, the probability of pathogens being present in the manure will increase as well [4, 5, 9].

The 2001 Canadian Census of Agriculture has shown an increasing number of livestock in Canada compared with the previous census in 1996: cattle increased by 4·4%, pigs by 26·4% and sheep by 46%. There was also an increase of 5·5% on the total manure spread in Canada [10]. Therefore, it is important to improve our earlier study with more recent data by adding a more specific indicator, livestock density.

The main objective of the present study is to evaluate the association between manure surplus or livestock density indicators and human AGH. Furthermore, because the risk of gastroenteritis may vary according to water source [11] and subjects' age [12], we aimed to assess the modifying effects of water source and subjects' age.

METHODS

Study design

An ecological study design was used in Quebec agricultural municipalities. In this study, the exposure data was measured at municipal level but the analysis was carried out at an individual level by inferencing individual exposure from the municipal data. An agricultural municipality was defined as a municipality with at least 25% of its surface area used for agricultural purposes. The agricultural municipalities with intensive farming activities – manure surplus and high animal density – were selected and compared with those without intensive farming activities.

Study population

The study population consisted of subjects living in Quebec (Canada) agricultural municipalities which were classified into two groups based on the manure surplus status. The first group consisted of subjects living in municipalities in seven watersheds considered by the Ministère du Développement durable, de l'Environnement et des Parcs du Québec (MDDEP) to be in 'manure surplus' (the exposed group). These watersheds involve the following rivers: Chaudière, Etchemin, Boyer, L'Assomption, Bayonne, Yamaska and Nicolet. The second group consisted of subjects living in Quebec municipalities located outside the watersheds (the unexposed group). All Quebec agricultural municipalities ($n = 306$) out of 1476 Quebec municipalities were included in the study. Among them, 139 municipalities were considered to be exposed to manure, while 167 were unexposed.

Data sources

Cases

Cases of AGH were obtained from the Med-Echo database for the period January 2000–December 2004. Med-Echo is the only hospital database available in Quebec in which all hospitalizations are registered. The following variables were obtained from the database for each case: age, sex, municipality code, admission date, date of discharge, main diagnosis [according to Classification of Diseases, 9th revision (ICD-9) codes], 15 secondary diagnoses (ICD-9 codes) and encrypted health insurance number.

We used a modified list of ICD-9 codes for acute gastroenteritis previously used in a study of the association between water quality and gastro-intestinal illness in Vancouver (Canada) [13] to select gastroenteritis cases from the Med-Echo database (see Appendix). A hospital admission was counted as an acute gastroenteritis case if it fitted the appropriate ICD-9 code. We classified the codes into four categories:

(1) acute potentially zoonotic gastroenteritis,
(2) acute non-zoonotic gastroenteritis,
(3) acute gastroenteritis with unknown aetiology,
(4) various symptoms related to gastroenteritis.

The ICD-9 codes classified as acute potentially zoonotic gastroenteritis were the codes for infections which were considered by the World Health Organization experts as potentially zoonotic and possibly water-related [9].

The case definition in this study was also adapted from the Vancouver study [13]. A hospital admission for a case of gastroenteritis was defined as any individual from the studied municipality admitted to hospital with a main diagnosis of any of the ICD-9 codes from categories 1, 2 or 3 or with the main diagnosis of any of the ICD-9 codes from category 4 with at least one secondary diagnosis of any of the ICD-9 codes from category 1. A main diagnosis is a diagnosis determined by a physician based on clinical and/or laboratory testing, and considered as the leading cause of a hospitalization. A secondary diagnosis is another diagnosis which is not the leading cause of hospitalization, and for which a patient could have been diagnosed or received treatment during hospitalization [14].

Individuals who were admitted to and discharged from a hospital on the same day were excluded. In order to ensure that we included only incident cases, if the same individual was hospitalized more than once for the same diagnosis within 30 days from the date of discharge of the last hospitalization, only the first hospitalization was retained.

Risk factor variables

Two exposures as the indicators of livestock farming intensity were assessed: manure surplus and livestock density. Both indicators were measured at the municipal level.

The definition of 'manure surplus' was based on the phosphorus index used to assess the overproduction of manure in a municipality by the MDDEP. It is the soil-surface phosphorous balance resulting from the application of animal manure to farmland and its absorption by cultivated plants in a given municipality. The phosphorous index (kg/ha per year) was calculated as the quantity of phosphorus produced by farm animals in a municipality (kg/year), after subtracting the estimated quantity of phosphorous consumed by cultivated plants (kg/year) in the municipality, divided by the total cultivated area of the municipality (ha). If the phosphorous index was >0 kg/ha per year then it was considered a positive index, otherwise as a negative index [8]. The phosphorous index data for each selected municipality were obtained from the MDDEP.

Livestock density data of each municipality were obtained from the Ministère de l'Agriculture des Pêcheries et de l'Alimentation du Québec for the period 2000–2003. Livestock density was defined as the number of animal units relative to total cultivated area (a.u./ha) within a municipality. One animal unit is equivalent to ~ 500 kg of animal body weight [15]. Five variables of livestock density were developed: (1) total animal density, (2) dairy cattle density, (3) beef cattle density, (4) swine density, and (5) poultry density.

Municipality water-source data were obtained from the Drinking Water Database of MDDEP updated on October 2002. We used three categories of water source in analysis: (1) surface water, (2) ground water, and (3) private well. The term 'private well' was applied to the municipalities where there were no community waterworks or where community waterworks was supplied to $\leqslant 49\%$ of the population.

The deprivation index, developed by Pampalon & Raymond [16], was used as a socioeconomic level indicator. The index is based on the smallest geographic unit for which census data are available in Canada, namely the enumeration area (EA). One EA has ~ 750 persons. It is considered to be socioeconomically homogeneous. In the selected municipalities, the average number of EAs in each municipality was 3·02 (range 1–22). To estimate the deprivation level of AGH cases, EAs were linked to the postal code of each case, as recorded in the Med-Echo database. The index combines six indicators which are related to a large number of health and welfare determinants: the proportion of persons without a high-school diploma; the ratio of employment to population; average income and the proportion of persons who are separated, divorced, or widowed; the proportion of single-parent families; and the proportion of people living alone. The indicators represent two forms of deprivation represented by two variables: material and social deprivation variables. Each variable was classified according to quintiles, ranging from the least deprived (quintile 1) to the most deprived (quintile 5) segments of the Quebec population [16].

In addition, the changes of municipality codes during the study period were taken into account while gathering AGH cases. We used the 2001 Canadian census of population to estimate the size of population of each municipality by age and sex and to obtain the socioeconomic data of the population.

Statistical analysis

We compared the baseline characteristics between the exposed and unexposed study population groups. Binomial regression was used to compare the proportion of each baseline characteristic except for average income, to which a Student's *t* test was applied.

The AGH rate as outcome was defined as the number of AGH cases that occurred during the study period divided by the person-years over the study period [17]. The AGH rates were calculated for the 2000–2004 period: (1) by 5-year age groups, (2) by sex group, (3) for total AGH cases and by categories of acute gastroenteritis. All those rates were calculated separately using exposure groups except for the first one, where the rate was calculated for the whole population. Univariate Poisson regression was used to compare the hospitalization rate according to sex and age.

AGH events were discrete counts and rare events, which is a characteristic of a Poisson distribution [18]. The group-level data, either municipal or EA level, were assigned to each subject within the same group. Therefore, a Poisson regression model with the individual as the smallest unit of analysis was chosen to evaluate the association between AGH and farming indicators. Since each indicator of livestock farming intensity was a single variable measured on 'cluster' of subjects (municipality), we incorporated the generalized estimating equation approach into the regression model and we entered municipality as a repeated effect [19]. Exponentiation of the main effect coefficient in the Poisson models estimates the adjusted hospitalization rate ratio (aHRR) for the effect.

We assessed the association between the two farming indicators and AGH with cases retained from all four categories of AGH. Furthermore, associations between the farming indicators and AGH-zoonotic, with cases retained from the AGH potentially zoonotic category, were also assessed separately. The following variables were considered as potential confounders: age, sex, deprivation index, and water source. Age and water source were also considered as modifiers prior to evaluating their confounding effect.

To evaluate the association between AGH (or AGH-zoonotic) and manure surplus as well as the modifying effects of age and water source on the association, we created three models: (1) one model included manure surplus, age, sex and deprivation index variables, (2) one model included manure surplus, age, sex, deprivation index and an interaction term between manure surplus and age variables, (3) a third model included manure surplus, age, sex, deprivation index, water source and an interaction term between manure surplus and water-source variables. The modifying effects were tested using the Wald test for the interaction term included in the models. In the absence of the modifying effect, we assessed the possible confounding effects.

In order to evaluate the association between AGH and livestock density, the two groups of municipalities previously defined as 'exposed' and 'unexposed' to manure surplus were pooled. They were then classified according to quartile breaks for each livestock-density variable based on the number of municipalities under study. The lowest quartile (Q1) was chosen as the reference group. Variance inflation factors were calculated to assess the possibility of multicollinearity between livestock-density variables. Since we did not observe any multicollinearity, we placed all livestock-density variables into one model, except for the total animal-density variable which we ran in a separate model because, by nature, it is correlated with the other livestock-density variables. The trends of risk ratio across the quartiles of livestock-density variables were tested. We used the Wald statistic to test the trend by using the median of density in each quartile as a continuous variable in the model. Furthermore, effects of specific zoonotic pathogens were also evaluated for exploratory purposes. However, due to an insufficient number of cases, we were only able to assess the association between livestock density and *Salmonella*, *Campylobacter* and *E. coli* infections.

The variables entered in the models are shown in Table 1. Only the variables with significant and/or confounding effects were kept in the final model. A P value of $\leqslant 0{\cdot}05$ was considered statistically significant. A confounding effect was assessed by calculating the difference between the HRR before and after a selected variable was entered. If the difference was $\geqslant 10\%$, the variable was considered as a confounder. SAS statistical software version 9.1 was used for analysis [20].

RESULTS

Baseline characteristics of the study population

The 306 municipalities under study had a population of 1 135 790 in 2001 and represent about 16 % of the Quebec population (7 237 480 people). A total population of 521 630 (46 %) was considered to be exposed to manure while a population of 614 160 (54 %) was unexposed.

Table 1. *Distribution of the value of each variable included in the Poisson regression models used to evaluate the association between human acute gastroenteritis and both manure surplus* and livestock density in Quebec (Canada) agricultural municipalities†, 2000–2004*

Variables (variable type, level of measurement)	Categories§	No. of AGH cases	No. of municipalities
Manure surplus (discrete, municipal level)	Exposed	4581	139
	Unexposed	5612	167
Livestock density variables‡ (continuous, municipal level)			
Total animal density (a.u./ha)	Q1 = 0–0·43	3858	76
	Q2 = 0·43–0·68	2114	76
	Q3 = 0·68–1·18	2987	76
	Q4 = 1·18–6·15	1179	76
Dairy cow density (a.u./ha)	Q1 = 0–0·16	3514	76
	Q2 = 0·16–0·26	2807	76
	Q3 = 0·26–0·37	1956	76
	Q4 = 0·37–0·74	1856	76
Beef cattle density (a.u./ha)	Q1 = 0–0·05	3855	76
	Q2 = 0·05–0·13	2637	76
	Q3 = 0·13–0·25	2154	76
	Q4 = 0·25–1·07	1487	76
Swine density (a.u./ha)	Q1 = 0	2710	100
	Q2 = 0–0·09	3341	52
	Q3 = 0·09–0·52	2218	76
	Q4 = 0·52–4·98	1864	76
Poultry density (a.u./ha)	Q1 = 0–0·00002	1696	76
	Q2 = 0·00002–0·00173	1814	76
	Q3 = 0·00173–0·07042	3825	76
	Q4 = 0·07042–4·72408	2798	76
Water source (discrete, municipal level)	Ground water	2781	122
	Surface water	5477	50
	Private wells	1935	134
Deprivation index (discrete, enumeration area level)			
Material deprivation	Q1	1000	—
	Q2	1961	—
	Q3	2486	—
	Q4	2726	—
	Q5	1832	—
Social deprivation	Q1	2095	—
	Q2	2418	—
	Q3	2121	—
	Q4	1935	—
	Q5	1436	—
Age (discrete, individual level)	0–4 years	2791	—
	5–9 years	871	—
	10–19 years	584	—
	20–29 years	593	—
	30–54 years	1719	—
	55–64 years	844	—
	65–74 years	1089	—
	⩾75 years	1702	—
Sex (discrete, individual level)	Female	6014	—
	Male	4179	—

AGH, Acute gastroenteritis hospitalization; a.u./ha, animal unit/hectare.
* Manure surplus was indicated by a positive phosphorous index.
† An agricultural municipality was a municipality with at least 25% of its surface area used for agricultural purposes.
‡ Data for two municipalities were missing.
§ Q, Quartile or quintile.

Table 2. *Comparison of baseline characteristics of the exposed and the unexposed groups based on 2001 Canadian Census of Population (Statistics Canada)*

Variable*	Exposed† (n = 521 630)	Unexposed (n = 614 160)	P‡
Proportion of the population aged ⩾15 years (%)	78·9	78·8	0·31
Employment rate (%)	62·6	62·6	0·53
Participation rate§ (%)	66·7	67	<0·01
Unemployment rate (%)	6·1	6·7	<0·01
Proportion of persons without school degrees (all ages) (%)	37·2	33·5	<0·01
Proportion of persons aged 15–24 years without school degrees (%)	37·8	38	0·36
Proportion of persons who are separated, divorced or widowed (%)	15·1	14·2	<0·01
Proportion of single-parent families (%)	14·3	13·6	<0·01
Proportion of people living alone (%)	10·2	8·5	<0·01
Average income (Can$)	45 628	55 205	<0·01¶

* Terms rate and proportions were used instead of real numbers to ensure comparability between municipalities.
† Exposed group refers to subjects living in municipalities with a positive phosphorous index and at least 25% of their surface area used for agricultural purposes.
‡ Obtained from binomial regression model or Student's t test.
§ 'Participation rate in labour market activities refers to the labour force in the week (Sunday to Saturday) prior to Census Day (15 May 2001), expressed as a percentage of the population 15 years of age and over' [21].
¶ Student's t test.

The baseline characteristics of the study population are shown in Table 2. Most variables were statistically different between the exposed and unexposed groups ($P<0·01$), except for the proportion of the population aged ⩾15 years ($P=0·31$), the employment rate ($P=0·53$) and the proportion of persons aged 15–24 years without a school degree ($P=0·36$). All variables except for the proportion of the population aged ⩾15 years, participation rate, and unemployment rate are incorporated in the deprivation index.

Number of cases and AGH rate

A total of 10 457 cases of AGH for the study population was recorded in the Quebec hospital database for the period 2000–2004. Despite universal health insurance in Quebec, 264 cases did not have a health insurance number and were then excluded. Consequently, 10 193 cases were included in the study. The majority of the AGH cases (88%) were gastroenteritis of unknown aetiology. Of all cases, 526 were categorized as AGH-zoonotic. This included: 186 cases of *Salmonella* infections (other than typhoid and paratyphoid fever), 23 cases of *Giardia* infections, two cases of other specified protozoal intestinal diseases, 90 cases of *E. coli* infections (all strains), 220 cases of *Campylobacter* infections, and five cases of *Yersinia enterocolitica* infections.

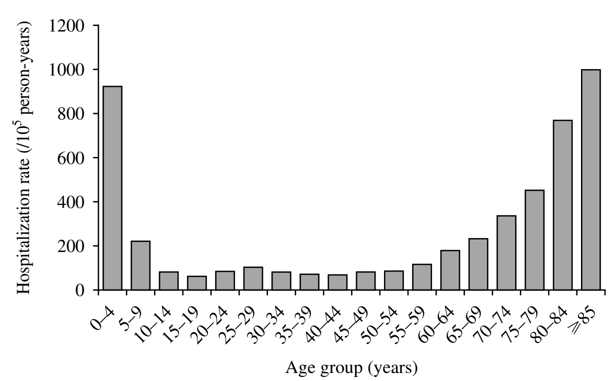

Fig. 1. Age-specific acute gastroenteritis hospitalization rates in Quebec (Canada) agricultural municipalities (municipalities with at least 25% of their surface areas used for agricultural purposes), 2000–2004.

AGH rate varies by age ($P<0·01$) with the highest rates occurring in the youngest (0–4 years) and the oldest (⩾85 years). In the older population, rates tended to increase by age group (Fig. 1). We also found that females had higher rates than males in both the exposed and unexposed groups ($P<0·01$) (Table 3). Of the four acute gastroenteritis categories, acute gastroenteritis with unknown aetiology had the highest rate, regardless of its exposure status (155·2/100 000 person-years for the exposed group and 161·7/100 000 person-years for the unexposed group) (Table 3).

Table 3. *Hospitalization rate for acute gastroenteritis* [*per 100 000 person-years* (*p-yr*)] *in the agricultural municipalities* exposed and unexposed to manure surplus†, Quebec, Canada, 2000–2004*

	Exposed‡			Unexposed		
Strata	*n*	Rate (10^{-5} p-yr)	95% CI§	*n*	Rate (10^{-5} p-yr)	95% CI§
All gastroenteritis	4581	175·6	170·5–180·7	5612	182·7	178·0–187·5
Female	2640	92·4	88·9–96·0	3374	118·1	114·2–122·1
Male	1941	68·7	65·7–71·8	2238	79·3	76·0–82·5
P¶		<0·01			<0·01	
Acute zoonotic gastroenteritis	251	9·6	8·4–10·8	275	8·9	8·0–10·0
Acute non-zoonotic gastroenteritis	8	0·3	0·1–0·5	15	0·5	0·2–0·7
Acute gastroenteritis with unknown aetiology	4049	155·2	150·5–160	4965	161·7	157·2–166·2
Various symptoms associated with gastroenteritis	273	10·5	9·2–11·7	357	11·6	10·4–12·8

* An agricultural municipality was a municipality with at least 25% of its surface area used for agricultural purposes.
† Manure surplus was indicated by a positive soil-surface phosphorous index.
‡ The population exposed to manure surplus.
§ Wald confidence interval.
¶ *P* value obtained from univariate analysis of sex variable by Poisson regression.

Association between AGH and surplus of manure

For analysis with cases retained from all four categories of AGH, the aHRR of AGH for the manure surplus indicator was 1·03 (95% CI 0·76–1·40). Furthermore, we observed that age modified the association between AGH and manure surplus (*P* for the interaction term <0·01). Risk ratio was higher for young children with a significant HRR for the 5–9 years age group (aHRR 1·45, 95% CI 1·02–2·05). An apparent protective effect was observed in adults aged ⩾20 years. However, the effect was only significant in age groups 55–64 and 65–74 years. Moreover, we observed a modifying effect of water source (*P* for the interaction term = 0·03). A significant risk ratio of manure surplus was observed in municipalities supplied by private wells and ground water (Table 4). Finally, since we found the modifying effect of subjects' age, we verified the age-specific effect for each water-source type. The significant risk ratio of manure surplus in municipalities supplied by private wells and ground water was especially observed in children aged 0–4 years (private wells: aHRR 1·81, 95% CI 1·30–2·54; ground water: aHRR 1·73, 95% CI 1·25–2·38).

For analysis with cases retained from the category of AGH potentially zoonotic, the aHRR of AGH-zoonotic for the manure surplus indicator was 1·06 (95% CI 0·86–1·31). However, we found a borderline significant effect modification of age (*P* for the interaction term = 0·06) with a significant risk ratio in children aged 0–4 years (HRR 1·93, 95% CI 1·21–3·09) (Table 5). Finally, we did not find any modifying or confounding effect of water source on the association between the manure surplus and AGH-zoonotic. Sex and deprivation index were finally excluded from this analysis because they did not have any significant or confounding effect on the association (data not shown).

Association between AGH and livestock density

Because the association between AGH and manure surplus was especially observed in children aged 0–9 years, we decided to evaluate the association between livestock density and AGH/AGH-zoonotic in this age group. Furthermore, pathogen-specific effects were assessed for the same age group.

In this age group, we observed a small increasing trend of HRR across the quartiles of all types of livestock density, except for beef cattle. However, in the AGH model, the trend was only significant for poultry density (*P* = 0·04). For the AGH-zoonotic model, the trend was significant for total animal density (*P* = 0·04) and swine density (*P* = 0·04) (Table 6). Further analysis was conducted for AGH-zoonotic in children aged 0–4 years and similar trends were observed in this age group without significant effect for total animal and swine density. However, we observed a significant increasing trend with an apparent

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Table 4. *Evaluation of modifying effect of subjects' age and water source on the association between hospitalization rate for acute gastroenteritis and manure surplus* in the Quebec (Canada) agricultural municipalities†, 2000–2004*

	Exposed		Unexposed				
Modifier/strata	*n*	Person-years	*n*	Person-years	aHRR‡	95% CI§	*P*
Age (yr)¶							
0–4	1383	136 600	1360	165 975	1·25	0·88–1·78	0·21
5–9	446	176 475	412	222 225	1·45	1·02–2·05	0·04
10–19	263	376 975	312	440 150	1·08	0·77–1·52	0·64
20–29	245	311 350	337	339 500	0·86	0·64–1·16	0·33
30–54	688	1 020 350	1018	1 243 600	0·85	0·65–1·11	0·22
55–64	310	274 825	518	319 200	0·72	0·53–0·98	0·04
65–74	407	185 050	653	205 775	0·73	0·53–0·99	0·04
⩾75	629	126 525	866	134 375	0·80	0·60–1·06	0·12
Water source‖							
Ground water	1896	988 200	747	492 375	1·35	1·00–1·83	0·05
Surface water	1933	1 222 750	3379	1 476 025	0·74	0·49–1·12	0·15
Private well#	542	397 200	1350	1 102 400	1·38	1·06–1·80	0·02

* Manure surplus was indicated by a positive soil-surface phosphorous index.
† An agricultural municipality was a municipality with at least 25% of its surface area used for agricultural purposes.
‡ aHRR, Adjusted hospitalization rate ratio of manure surplus for acute gastroenteritis. The modifying effect of age and water source was assessed in two separate models.
§ Confidence intervals were based on empirical standard error estimates.
¶ The model was adjusted for sex and deprivation index. There was a modifying effect of age on the association between AGH and manure surplus (*P* value of the interaction term $<0{\cdot}01$).
‖ The model was adjusted for age, sex, and deprivation index. There was a modifying effect of water source on the association (*P* value of the interaction term $=0{\cdot}03$).
The term 'private wells' was applied to the municipalities where there were no community waterworks or where community waterworks was supplied to ⩽49% of the population.

Table 5. *Evaluation of modifying effect of age on the association between hospitalization rate for acute potentially zoonotic gastroenteritis and manure surplus* in the Quebec (Canada) agricultural municipalities†, 2000–2004*

	Exposed		Unexposed				
Modifier/strata	*n*	Person-years	*n*	Person-years	HRR‡	95% CI§	*P* value
Age (yr)¶							
0–4	50	136 600	32	165 975	1·93	1·21–3·09	0·01
5–9	26	176 475	25	222 225	1·34	0·73–2·49	0·34
10–19	26	376 975	43	440 150	0·73	0·42–1·24	0·24
20–29	26	311 350	26	339 500	1·12	0·61–2·06	0·71
30–54	51	1 020 350	54	1 243 600	1·17	0·70–1·97	0·54
55–64	14	274 825	23	319 200	0·73	0·39–1·40	0·35
65–74	28	185 050	35	205 775	0·91	0·55–1·52	0·73
⩾75	24	126 525	34	134 375	0·77	0·46–1·28	0·31

* Manure surplus was indicated by a positive soil-surface phosphorous index.
† An agricultural municipality was a municipality with at least 25% of its surface area used for agricultural purposes.
‡ HRR, Hospitalization rate ratio of manure surplus for acute potentially zoonotic gastroenteritis.
§ Confidence intervals were based on empirical standard error estimates.
¶ The modifying effect of age on the association between AGH-zoonotic and manure surplus was borderline significant (*P* value of the interaction term $=0{\cdot}06$). Sex and deprivation index variables were excluded because they did not have significant or confounding effect.

Table 6. *Association between acute gastroenteritis hospitalization and livestock density [animal unit/hectare (a.u./ha)] [hospitalization rate ratio (HRR) and 95% confidence intervals (CI) obtained from multivariate Poisson regression model] in children aged 0–9 years, Quebec, Canada, 2000–2004*

		All gastroenteritis					Acute zoonotic gastroenteritis				
Livestock density variables*	Median density	*n*	Person-years	aHRR†	95% CI‡	*P*	*n*	Person-years	aHRR§	95% CI‡	*P*
Total animal¶ (a.u./ha)						0·32‖					0·04‖
Q1	0·30	1248	315 700	1			46	315 700	1		
Q2	0·55	652	102 175	1·22	0·62–2·43	0·56	13	102 175	0·76	0·41–1·38	0·11
Q3	0·86	1110	178 150	1·45	0·98–2·14	0·06	47	178 150	1·66	1·03–2·69	0·04
Q4	2·04	526	103 350	1·17	0·85–1·62	0·33	25	103 350	1·51	0·91–2·50	0·36
Dairy cow¶ (a.u./ha)						0·11‖					0·36‖
Q1	0·09	1140	275 650	1			37	275 650	1		
Q2	0·21	1008	198 250	1·08	0·83–1·42	0·56	42	198 250	1·34	0·84–2·13	0·22
Q3	0·32	733	113 475	1·14	0·77–1·68	0·50	30	113 475	1·66	0·91–3·03	0·10
Q4	0·46	691	112 000	1·22	0·86–1·69	0·22	22	112 000	1·22	0·65–2·30	0·53
Beef cattle¶ (a.u./ha)						0·06‖					0·38‖
Q1	0·02	1326	275 875	1			54	275 875	1		
Q2	0·09	942	172 050	1·12	0·81–1·54	0·50	25	172 050	0·76	0·48–1·23	0·27
Q3	0·18	784	140 875	0·95	0·73–1·25	0·74	30	140 875	0·80	0·47–1·36	0·42
Q4	0·34	520	110 575	0·79	0·56–1·11	0·17	22	110 575	0·79	0·49–1·27	0·33
Swine¶ (a.u./ha)						0·60‖					0·04‖
Q1	0	775	239 350	1			27	239 350	1		
Q2	0·001	1201	179 500	1·61	1·21–2·14	$<$0·01	33	179 500	1·35	0·80–223	0·26
Q3	0·24	801	143 425	1·27	0·90–1·79	0·17	30	143 425	1·37	0·67–2·81	0·39
Q4	1·07	795	137 100	1·22	0·85–1·74	0·28	41	137 100	2·00	1·04–3·82	0·04
Poultry¶ (a.u./ha)						0·04‖					0·54‖
Q1	0	566	130 675	1			15	130 675	1		
Q2	0·0001	570	150 425	0·89	0·66–1·20	0·46	21	150 425	1·13	0·59–2·15	0·71
Q3	0·03	1284	231 375	1·18	0·86–1·61	0·30	48	231 375	1·48	0·91–2·40	0·11
Q4	0·17	1152	186 900	1·32	0·93–1·87	0·12	47	186 900	1·36	0·76–2·43	0·31

* All livestock-density variables, except total animal density, were assessed in the same model.

† aHRR, Adjusted hospitalization rate ratio adjusted to the other livestock-density variables (except the total animal density), age, sex, and deprivation index.

‡ Confidence intervals were based on empirical standard error estimates.

§ aHRR, Adjusted hospitalization rate ratio adjusted to the other livestock-density variables (except the total animal density), age, and deprivation index.

¶ Categorized variable.

‖ *P* trend obtained by Wald statistics.

dose–response effect for poultry density (aHRR from Q1 to Q4 = 1, 2·33, 2·53, 2·98, respectively; $P = 0{\cdot}03$).

In children aged 0–9 years, increasing trends of HRR were observed between *Campylobacter* infections and dairy-cow density (aHRR from Q1 to Q4 = 1, 1·08, 2·90, 1·72, respectively; $P = 0{\cdot}05$), *E. coli* infections and swine density (aHRR from Q1 to Q4 = 1, 1·15, 4·32, 6·06, respectively; $P = 0{\cdot}03$). In children aged 0–4 years, a significant increasing trend of HRR of *Salmonella* infections was only observed in poultry density (aHRR from Q1 to Q4 = 1, 3·95, 5·20, 7·37, respectively; $P = 0{\cdot}05$).

DISCUSSION

Several studies have shown associations between livestock farming intensity and acute gastroenteritis incidence [7, 22, 23]. We found that the association between livestock farming intensity and AGH as well as AGH-zoonotic was modified by subjects' age and water source.

Morbidity from gastroenteritis mostly involves young children [1] and has been observed in several studies [12, 22, 24]. This may be due to lack of immunity because the immune system in children may not be well developed yet. Protective immunity resulting from repeated low-level exposure from infected persons or other sources including drinking water has recently been suggested as an important consideration for the lower risk in adults [24–26]. Persons exposed to contaminated water in their normal drinking water may also develop some protective immunity [27, 28].

Variation of risk of gastroenteritis according to water-source type has been shown in some studies. Birkhead & Vogt [11] observed higher risks of *Giardia* infections in municipalities supplied by ground water [relative risk (RR) 1·8, 95% CI 0·9–3·4], non-filtered surface water (RR 1·9, 95% CI 1·1–3·3), and private water supply (RR 2·2, 95% CI 1·3–3·6) compared to filtered surface water. Drinking water from a private supply has also been identified as a risk factor for gastroenteritis in children [24]. The higher probability of water contamination in municipalities receiving ground water but not surface water was also observed in a local study conducted on the seven watersheds exposed to manure surplus. In addition, all surface water in the exposed territories received complete treatment (filtration and disinfection) before distribution [29]. Therefore, lack of association between manure surplus and AGH in municipalities receiving surface water supply may be due to the high quality of drinking water provided by surface water systems. In contrast, not all waterworks distributing ground water used the treatment [29].

In our study, the association observed between livestock density and AGH-zoonotic in children should be interpreted with caution since only a small number of cases were available for analysis and some analyses were exploratory. Associations between livestock density, especially cattle, and acute gastroenteritis have been observed in previous studies in Canada and other countries [7, 22, 23, 30]. Valcour *et al*. [7] found a strong association between ratio of beef cattle number to human population and human Shiga toxin-producing *Escherichia coli* (STEC) infection in Ontario. Haus-Cheymol *et al*. [23] found that the paediatric incidence of haemolytic–uraemic syndrome (HUS) was associated with dairy-cattle density and the ratio of calves to children aged <15 years in France ($P<0{\cdot}01$). Nygard *et al*. [30] observed a significant association between ruminant density and *Campylobacter* incidence in Sweden [incidence rate ratio (IRR) 1·08, 95% CI 1·05–1·11]. Surprisingly, in the present study, the associations observed were mostly with swine and poultry density. Association with poultry density has been investigated by Potter *et al*. [22]. A higher incidence of *C. jejuni* enteritis in the counties with high poultry density than those with low poultry density was observed (IRR 1·31, 95% CI 1·21–1·42). In our study, the association observed between poultry density and AGH-zoonotic in children was mostly due to *Salmonella* infections. It is well known that poultry is a major source of *Salmonella* infections in humans, although cattle can also be an important reservoir [9]. The association with swine density may be due to the high production of pigs in Quebec as this province is the main producer of pigs in the country [10]. It is widely known that ruminants are considered to be the main reservoir for *E. coli* especially *E. coli* O157 [9]. However, our results may indicate that swine could be another reservoir, as observed in other countries and recently in the United States [31]. Above all, it is also possible that the observed associations were due to the multiple comparisons issue in which the null hypothesis is incorrectly rejected [32].

As already known, acute gastroenteric-causing pathogens have several routes of transmission. They may spread from person to person or may be transmitted by food or environmental vehicles or they may also result from exposure to animals [33]. In the present study, direct and indirect contact with farm animals or animal excreta may have been important routes of transmission. Contact with animal faeces: living on, working on, or visiting a farm has been found to be associated with gastroenteritis [34, 35].

Our study has several strengths. The AGH cases obtained from Med-Echo were clinically and/or laboratory confirmed and the database covers all hospitals in the province of Quebec that offers universal health insurance. Furthermore, we evaluated the modifying effect of age on the association between manure surplus and AGH and controlled for the confounding effect of sex. Both of these are important demographic determinants of acute gastroenteritis [12]. We also introduced a deprivation index because socioeconomic characteristics may influence host susceptibility. The importance of this index in health research has recently been demonstrated [36].

As an ecological study, our analysis was based on data at group level rather than an individual level. This has some limitations, particularly for the indicators of livestock farming intensity data which were measured at the municipal level. Individuals living in a municipality with manure surplus or with high animal density are not always exposed to the same level of manure pathogens. For example, individuals living where the manure is only spread 100 m from their residence may be more exposed than those where the manure is spread 1 km from their house. The water-source variable was also measured at the municipal level which may not reflect the water source consumed by individuals. The possibility of misclassification of exposure due to the use of these data measurements is not negligible. Moreover, we were unable to measure several potential confounders which were available only at the individual level, such as contact with farm animals, farm (where the manure was spread) to house distance, consumption of possibly contaminated food, water consumption, water treatment applied by individuals, travel history, etc. Despite limitations, ecological studies remain useful especially when the influence of environmental variables is difficult to measure at an individual basis. Additionally, they are inexpensive, take little time, and can cover a wide study area.

CONCLUSIONS

We have evaluated the association between livestock farming intensity and hospitalization for acute gastroenteritis. We noted a significant association between manure surplus and acute gastroenteritis as well as acute potentially zoonotic gastroenteritis in young children. Moreover, we found an increased trend of risk of hospitalization for acute potentially zoonotic gastroenteritis in children, especially *Salmonella* infections, with increasing levels of poultry density. Further study with more individual data on exposure and risk factors is needed to better explain the observed associations.

APPENDIX

List of ICD-9 codes for acute gastroenteritis (modified from Aramini *et al.* [13])

ICD-9 code	Description
Category 1: Acute potentially zoonotic gastroenteritis	
003[a]	Other *Salmonella* infections (other than typhoid and paratyphoid fever)
007.1	Giardiasis
007.4	Cryptosporidiosis
007.8	Other specified protozoal intestinal diseases
007.9	Unspecified protozoal intestinal disease
008.0[b]	Intestinal infections due to other organisms – *Escherichia coli* (*E. coli*)
008.43	*Campylobacter*
008.44	*Yersinia enterocolitica*
Category 2: Acute non-zoonotic gastroenteritis	
002[c]	Typhoid and paratyphoid fevers
004[d]	Shigellosis
006[e]	Amoebiasis
007.5	Cyclosporiasis
008.61	Rotavirus
008.62	Adenovirus
008.63	Norwalk virus, norwalk-like agent
008.64	Other small round viruses
008.65	Calicivirus
008.66	Astrovirus
070.0	Viral hepatitis A with hepatic coma
070.1	Viral hepatitis A without mention of hepatic coma
070.43	Hepatitis E with hepatic coma
070.53	Hepatitis E without mention of hepatic coma
Category 3: Acute gastroenteritis of unknown aetiology	
009.0	Infectious colitis, enteritis, and gastroenteritis
009.1	Colitis, enteritis, and gastroenteritis of presumed infectious origin
009.2	Infectious diarrhoea
009.3	Diarrhea of presumed infectious origin

APPENDIX (*cont.*)

ICD-9 code	Description
535.0	Gastritis and duodenitis – Acute gastritis
535.4	Gastritis and duodenitis – Other specified gastritis
535.5	Gastritis and duodenitis – Unspecified gastritis and gastroduodenitis
535.6	Gastritis and duodenitis – Duodenitis
558	Other noninfectious gastroenteritis
787.0	Nausea and vomiting
Category 4: Various symptoms associated with gastroenteritis	
276[f]	Disorders of fluid, electrolyte, and acid-base balance
283.11	Haemolytic–uraemic syndrome
446.6	Thrombotic thrombocytopenic purpura
578.1	Melaena
691.0	Diaper or napkin rash
780.6	Fever of unknown origin (FUO)
783.0	Anorexia
783.2	Abnormal loss of weight and underweight
787[g]	Symptoms involving digestive system
789.0	Other symptoms involving abdomen and pelvis – Abdominal pain

[a] Including subcategories: 003.0, 003.1, 003.2, 003.8, and 003.9.
[b] Including subcategories: 008.00, 008.01, 008.02, 008.03, 008.04, 008.09.
[c] Including subcategories: 002.0, 002.1, 002.2, 002.3, and 002.9.
[d] Including subcategories: 004.0, 004.1, 004.2, 004.3, 004.8, and 004.9.
[e] Including subcategories: 006.0, 006.2, 006.3, 006.8, and 006.9.
[f] Including all subcategories: from 276.0 to 276.9.
[g] Including all subcategories: from 787.1 to 787.9

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DECLARATION OF INTEREST

None.

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