

BMJ Open Disease manifestations of *Helicobacter pylori* infection in Arctic Canada: using epidemiology to address community concerns

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ABSTRACT

Objectives: *Helicobacter pylori* infection, linked to gastric cancer, is responsible for a large worldwide disease burden. *H pylori* prevalence and gastric cancer rates are elevated among indigenous Arctic communities, but implementation of prevention strategies is hampered by insufficient information. Some communities in northern Canada have advocated for *H pylori* prevention research. As a first step, community-driven research was undertaken to describe the *H pylori*-associated disease burden in concerned communities.

Design: Participants in this cross-sectional study completed a clinical interview and gastroscopy with gastric biopsies taken for histopathological examination in February 2008.

Setting: Study procedures were carried out at the health centre in Aklavik, Northwest Territories, Canada (population ~600).

Participants: All residents of Aklavik were invited to complete a clinical interview and gastroscopy; 194 (58% female participants; 91% Aboriginal; age range 10–80 years) completed gastroscopy and had gastric biopsies taken.

Primary and secondary outcome measures:

This analysis estimates the prevalence of gastric abnormalities detected by endoscopy and histopathology, and associations of demographic and clinical variables with *H pylori* prevalence.

Results: Among 194 participants with evaluable gastric biopsies, 66% were *H pylori*-positive on histology. Among *H pylori*-positive participants, prevalence was 94% for acute gastritis, 100% for chronic gastritis, 21% for gastric atrophy and 11% for intestinal metaplasia of the gastric mucosa, while chronic inflammation severity was mild in 9%, moderate in 47% and severe in 43%. In a multivariable model, *H pylori* prevalence was inversely associated with previous gastroscopy, previous *H pylori* therapy and aspirin use, and was positively associated with alcohol consumption.

Conclusions: In this population, *H pylori*-associated gastric histopathology shows a pattern compatible with elevated risk of gastric cancer. These findings

Strengths and limitations of this study

- This study is unique in yielding evidence of the effects of *Helicobacter pylori* infection on gastric histopathology in a community setting where the study population is not restricted to individuals seeking medical care for symptoms.
- It describes the *H pylori*-associated disease burden in a community in northern Canada.
- It provides an example of how multidisciplinary research can address health concerns identified by communities.
- The cross-sectional design limits inferences about determinants of severe gastritis and pre-cancerous gastric conditions in this population.

demonstrate that local concern about health risks from *H pylori* is warranted and provide an example of how epidemiological research can address health priorities identified by communities.

INTRODUCTION

Since the identification of *Helicobacter pylori* infection in 1983, research has revealed its associations with digestive diseases such as gastritis, peptic ulcer and gastric cancer,^{1–5} responsible for a large worldwide disease burden.^{6–7} Disease prevention strategies based on elimination of *H pylori* have not been widely implemented, however, and it is not fully clear whether specific infection control strategies are likely to result in net benefits to particular populations at risk. Since the late 1990s, a few reports, primarily from Alaska, Greenland and Canada, have shown *H pylori* prevalence and gastric cancer rates to be high among Arctic Indigenous communities, relative to elsewhere in North America and northern Europe,⁸ and similar

to much of the developing world. Given that clinical guidelines recommend a test and treat approach for primary care patients presenting with dyspeptic symptoms,^{9 10} public awareness of *H pylori* infection and its link to gastric cancer has emerged in high-prevalence communities. In northern Canada, some communities and health officials have sought *H pylori* prevention research, calling attention to the scant evidence on the impact of *H pylori* among Arctic Canadians.

Reported estimates of *H pylori* seroprevalence in Canada vary between 21% and 95%, with prevalence of 50% or more estimated exclusively in Aboriginal communities.⁸ Beyond these seroprevalence studies, little evidence of the *H pylori*-associated disease burden in Canada has been reported. Furthermore, seroprevalence is not an optimal measure of current prevalence, given that serological testing for *H pylori* does not distinguish between past and current infection¹¹; due to widespread treatment of *H pylori* infection in recent decades, many seropositive Canadians will not have an active infection. As harm from chronic *H pylori* infection is often silent until serious disease such as a bleeding ulcer or invasive cancer occurs, full elucidation of the *H pylori*-associated disease burden at the community level requires screening people who do not seek healthcare for digestive symptoms. Active *H pylori* infection can be detected non-invasively with breath or stool testing, but use of upper gastrointestinal endoscopy is required to detect disease manifestations of this infection. Endoscopy permits detection of visible abnormalities such as gastric ulcers and collection of gastric biopsies for histological examination to grade the density of *H pylori* and the severity of gastric mucosal pathology.

H pylori-induced gastric carcinogenesis starts with chronic *H pylori* infection accompanied by chronic gastritis.^{12 13} Superficial inflammation of the gastric mucosa can persist with or without symptoms or complications. In some cases, peptic ulcers develop, and with varied frequency depending on population characteristics, chronic gastritis can progress to atrophic gastritis, which involves loss of gastric glands. Subsequent stages in disease progression include intestinal metaplasia and dysplasia, conditions associated with a high risk of carcinoma. Progression through these steps is influenced by host susceptibility, virulence of infecting *H pylori* strains and environmental exposures.^{12 13}

The Aklavik *H pylori* Project is an ongoing research endeavour conducted in a Northwest Territories (NT) hamlet, where residents and healthcare providers have advocated for research to address concerns about cancer risks from *H pylori* infection. In Canada's NT (2006 population ~41 000),¹⁴ 50% of the population is Aboriginal, including Inuit, First Nations and Metis peoples.¹⁵ The objectives of this analysis were to estimate the prevalence of *H pylori* infection and associated gastrointestinal pathology, as well as associations between prevalent *H pylori* and selected social and clinical factors, in a northern Canadian Aboriginal community.

METHODS

This study analyses data from the initial components of the community-based participatory Aklavik *H pylori* Project previously described.¹⁶ Study participants were residents of Aklavik, NT, a primarily Aboriginal hamlet of ~600 people in Arctic Canada, with an ethnic distribution of ~55% Inuvialuit (western Canadian Inuit), ~35% Gwich'in Dene (Athabaskan First Nations), ~2% other Aboriginal and ~8% non-Aboriginal Euro-Canadian. Aklavik is located in the Mackenzie River delta, ~100 km south of the Arctic coast, 60 km east of the Yukon border and 676 km east of Fairbanks, Alaska. For eligibility purposes, 'resident' was defined broadly as being present in Aklavik during the study period (and included 3 temporary visitors and 22 people who resided across the river in Inuvik but had relatives residing in Aklavik). All Aklavik residents were invited to undergo non-invasive screening for *H pylori* infection by 13C-urea breath test¹⁷ and complete a structured questionnaire-based clinical interview (November 2007–February 2008). For the endoscopy component (February 2008), all Aklavik residents aged 15 years and older were encouraged to participate; younger children were included on parental request at the discretion of the endoscopists. Inclusion required written informed consent for the survey and endoscopy components; assent and parental consent were required for children under 17 years of age. Individuals were excluded if they had severe cardiovascular disease, uncontrolled hypertension or were unable or unwilling to complete the endoscopy procedure.

In accordance with community-based participatory research methods, the research goals and protocols were developed with input from a community project planning committee; the clinical questionnaire, in particular, was reviewed and modified by the planning committee to ensure local understanding and appropriateness. English was used for the questionnaire, as none of the participants preferred to respond in another language. Questionnaires were administered by trained interviewers. The interviewer team included Aklavik residents and University of Alberta graduate students, and the participants were offered their choice of interviewer. Interviews were conducted at the local health centre or participants' homes or place of work, with the location decided by the participant.

Transnasal gastroscopy (or transoral when the transnasal approach was contraindicated) was performed in temporary endoscopy units at the Aklavik Health Centre by seven physicians experienced in upper gastrointestinal endoscopy and with prior training in transnasal gastroscopy.^{18 19} The participants underwent unsedated endoscopy using Olympus GIF-N180 (Olympus, Tokyo, Japan) 4.9 mm diameter endoscopes with a working length of 110 cm and a 2 mm single instrument channel, after administration of topical anaesthetics as described previously.¹⁹ Five gastric biopsies (from antrum close to the pylorus, antrum greater curvature, antrum lesser curvature adjacent to the incisura

angularis, corpus lesser curvature and corpus greater curvature) were taken for histopathology and evaluated according to the updated Sydney protocol^{20 21} by a single tertiary-care centre gastrointestinal pathologist (SG), blinded to endoscopic findings. Sections were stained with H&E for regular histology and with Giemsa to detect *H pylori*. Histopathological assessment graded the severity (normal/absent, mild, moderate, severe) of acute and chronic inflammation by stomach subsite (antrum, body), as well as glandular atrophy, intestinal metaplasia, other neoplasias and *H pylori* density.

To compare the *H pylori*-associated disease burden in the Aklavik population with that of the southern Canadian metropolitan area that provides advanced healthcare for NT residents, we searched the University of Alberta Hospital (Edmonton, Alberta) pathology department computerised database to identify gastric biopsy evaluations of patients examined during one 12-month period from 1 April 2010 through 31 March 2011. We identified reports that stated relevant pathological diagnoses, restricting the denominator of prevalence estimates to reports that explicitly mentioned assessment for the relevant diagnostic category; we also excluded duplicate reports for the same individual.

Frequency distributions of demographic and clinical variables were summarised in tables, along with the proportion of participants in each category that were *H pylori* positive. Prevalence of each endoscopic and histopathological diagnosis was estimated by dividing the number with the diagnosis by the total number of participants who had biopsies examined; 95% CIs were calculated for these prevalence proportions; prevalence estimates were also calculated for subgroups stratified by *H pylori* status. To estimate the association between *H pylori* prevalence and variables selected based on clinical or sociodemographic relevance, ORs and 95% CIs were estimated from multivariable logistic regression as an appropriate measure of association for cross-sectional data.^{22 23} The set of adjustment variables was selected using a change-in-estimates approach, beginning with all of the preselected variables in the full model and excluding each one at a time. Likelihood ratio tests were performed to compare the model with each variable missing to the full model. For each estimated OR, we excluded from the set of adjustment variables those for which exclusion did not result in a greater than 10% change in the OR compared with the estimate from the full model. Likelihood ratio tests were used to select the optimal functional form for continuous variables (age, years of education) and care was taken to collapse categories only when this did not alter the dose-response pattern. The number of participants with data for particular variables is indicated in table notes. Participants with data missing from variables included in the multivariable logistic regression model were excluded from the analysis that estimated unadjusted and adjusted ORs. Statistical analysis was performed using STATA/IC V.10 statistical software (StataCorp, USA).

RESULTS

Of 379 participants in the Aklavik *H pylori* Project, 332 had results from breath tests to detect *H pylori* and 58% were positive. Among 200 individuals who consented to endoscopy, 4 could not tolerate the procedure and 2 were taking anticoagulant coumadin which precluded biopsy. Thus, 194 participants completed gastroscopy with biopsies (including 2 temporary visitors and 7 residents of Inuvik). The participants' ages ranged from 10 to 80 years; 91% were Aboriginal (114 Inuvialuit, 54 Gwich'in and 8 other), and 58% were women. Table 1 shows the distribution of sociodemographic and clinical variables among endoscopy participants. Table 2 shows the distribution of age, sex, ethnicity and education comparing endoscopy participants, all project participants and Aklavik census participants captured by Statistics Canada.²⁴ Small variations are noted in the distributions of these variables, with the major difference being an over-representation of older residents among endoscopy participants (it should be noted that the census data were missing education status for a large proportion of the population). Table 3 compares endoscopy participants and project participants who did not undergo endoscopy on the prevalence of chronic dyspepsia and other health-related factors among participants with data on these factors.²⁵ The prevalence of two or more chronic dyspepsia symptoms was 43% among project participants who participated in endoscopy and 41% among those who did not, while the proportion with no symptoms was 37% in the endoscopy group and 41% in the group that did not undergo endoscopy. Modestly higher proportions of endoscopy participants had a family history of *H pylori* infection or gastric cancer, had been tested for *H pylori* before enrolling in the Aklavik *H pylori* Project or were taking medications for stomach upset.

H pylori prevalence and associated demographic and clinical factors

The pathologist's assessment of gastric biopsies classified 66% of endoscoped participants as having *H pylori*. From the set of variables selected a priori for multivariable regression, selection criteria retained age, ethnicity, previous gastroscopy, previous antibiotic treatment for *H pylori*, aspirin use and alcohol use; each of these variables had likelihood ratio test p values <0.17 and the exclusion of each from the full model resulted in >10% change in estimates of at least four variables in the model. All variables excluded from the adjustment set used in all models had likelihood ratio p values >0.48. The change-in-estimates criterion identified two additional adjustment variables for ethnicity (smoking and education) and one additional adjustment variable for aspirin use (education; table 4). Regression results show lower prevalence odds among individuals of non-Aboriginal ethnicity compared with individuals of Aboriginal ethnicity (OR 0.07, CI 0.02 to 0.33) and among those reporting previous gastroscopy, *H pylori* therapy or aspirin use (OR 0.25, CI 0.09 to 0.65;

Table 1 *Helicobacter pylori* prevalence, as detected by histopathology, stratified by sociodemographic and clinical factors, among 194 Aklavik *H pylori* Project participants with gastric biopsies, Northwest Territories, Canada, 2008

	All participants (n)	<i>H pylori</i> + Per cent
Total	194	66.5
Age in years—mean (±SD), 40.3 (±17.1)		
10–19	29	72.4
20–29	32	87.5
30–39	33	75.8
40–49	42	57.1
50–80	58	53.4
Sex		
Female	112	67.0
Male	82	65.9
Ethnicity		
Non-Aboriginal	18	22.2
Aboriginal	176	71.0
Inuvialuit	114	70.2
Gwich'in	54	70.4
Metis	4	*
Gwich'in/Inuvialuit	2	*
Gwich'in/Metis	1	*
Other Aboriginal	1	*
Education (number of years completed)†—mean (±SD), 10.6 (±3.3)		
<7	17	58.8
7–9	46	69.6
10–12	86	73.3
More than 12	42	52.4
Family history of stomach cancer‡		
Yes	60	60.0
Yes, cancer, unsure of location	32	81.3
No	88	63.6
Unsure	13	76.9
Previous antibiotic treatment for <i>H pylori</i> ‡		
Yes	28	39.3
No	163	71.8
Unsure	1	*
Previous gastroscopy†		
Yes	38	31.6
No	155	74.8
Medications for stomach disorder		
One or more	52	61.5
None	142	68.3
Antacids		
Any	21	66.7
None	173	66.5
H ₂ blocker		
Any	7	57.1
None	187	66.8
Proton pump inhibitor		
Any	22	50.0
None	172	68.6
Other		
Any	9	66.7
None	185	66.5

Continued

Table 1 Continued

	All participants (n)	<i>H pylori</i> + Per cent
NSAID use excluding aspirin†		
Any	45	64.4
None	147	68.0
Aspirin use		
Any	31	45.2
None	161	71.4
Unsure	1	*
Alcohol use		
Any	117	73.5
None	77	55.8
Current smoker		
Any	110	73.6
None	84	57.1

*Proportions not presented for groups with less than five observations.

†Numbers of participants with missing data: education (3), family history of stomach cancer (1), previous antibiotic treatment (2), previous gastroscopy (1), NSAID use (2) and aspirin use (1).
H₂ blocker, histamine H₂ receptor antagonist; NSAID, non-steroidal anti-inflammatory drug.

OR 0.20, CI 0.07 to 0.56 and OR 0.35, CI 0.13 to 0.99, respectively), while higher odds were observed among the current consumers of alcohol compared with non-drinkers (OR 2.4, CI 1.1 to 5.0). Of individuals reporting previous *H pylori* therapy and gastroscopy, 39% (11/28) and 32% (12/38), respectively, were still positive for *H pylori* (14 individuals with previous gastroscopy also had previous *H pylori* therapy). Weak and imprecise adjusted ORs were observed for sex, family history of stomach cancer, stomach medication use and non-steroidal anti-inflammatory drug use. The OR for smoking reduced from 2.4 to 1.2 on adjustment; the adjustment variables with the largest impact on the change in this estimate were ethnicity, aspirin use and alcohol consumption. The adjusted OR for education shows odds of infection decreasing by 5% with each increasing year of education (OR 0.95, CI 0.83 to 1.1); this estimate, however, is imprecise, and it should be noted that only 22% of participants had more than 12 years of education, so it may not be accurate for effects beyond 12 years (although 16 of the 18 (89%) non-Aboriginal participants had more than 12 years of education, the adjusted OR for education does not appear to contain residual confounding by ethnicity given that the adjusted OR within the subgroup of Aboriginal participants was nearly identical (0.95 (CI 0.82 to 1.1)) to that of the total study population). To assess whether the effect of education might be mediated by clinical or substance use variables, we removed these variables from the model for the effect of education, but did not note that the estimated effect of education strengthened on doing so. *H pylori* prevalence did not increase monotonically with age in this population, unlike what has been reported elsewhere. This agrees with the age-

Table 2 Sociodemographic characteristics of endoscopy participants, all Aklavik *Helicobacter pylori* Project participants, and Aklavik residents captured by Statistics Canada 2006 census, Northwest Territories, Canada

	Aklavik <i>H pylori</i> Project				Statistics Canada 2006 Census*	
	Endoscopy participants		All participants		Aklavik residents ²⁴	
	n	Per cent	n	Per cent	n	Per cent
Total†	194	100	354	100	595	100
Age in years						
10–19	29	14.9	58	16.4	110	18.5
20–29	32	16.5	57	16.1	100	16.8
30–39	33	17.0	43	12.1	75	12.6
40–49	42	21.6	65	18.4	80	13.4
50+‡	58	29.9	90	25.4	130	21.8
Sex						
Female	112	57.7	189	53.4	275	46.2
Male	82	42.3	165	46.6	315	52.9
Ethnicity						
Non-Aboriginal	18	9.3	43	12.1	40	6.8
Aboriginal	176	90.7	309	87.3	545	92.4
Education§						
Less than high school	112	57.7	206	58.2	233	61.3
High school or equivalent	31	16.1	45	12.7	52	13.7
Post-high school training	48	24.9	70	19.8	91	23.9

*Per cents do not total to 100% due to rounding.

†Missing data: sex missing for 5 individuals from Statistics Canada; ethnicity missing for 2 Aklavik participants and 10 individuals from Statistics Canada; education missing for 33 Aklavik participants, 3 Aklavik endoscopy participants and 219 from Statistics Canada.

‡Maximum age in Aklavik is 80 years; maximum age in Statistics Canada is unspecified.

§Levels do not correspond precisely to a standard number of years of education, given diverse Canadian options for trade certification without completing high school.

specific prevalence pattern observed in the 332 project participants with breath test results: 54% in children under 20 years, 72% in 20–39-year-olds and 52% in people aged 40 or older. Of note, among participants aged 40 or older, 18% reported previous *H pylori* therapy, compared with 11% in participants under 40.

Endoscopic findings

The most frequent endoscopic abnormalities were gastritis (14%), esophagitis (10%), gastric erosions (6.2%) and gastric ulcer (3.1%) with duodenal lesions occurring much less frequently (table 5); frequencies of these endoscopic diagnoses were similar in the subpopulation

Table 3 Self-reported health history among 194 Aklavik *Helicobacter pylori* Project participants who underwent endoscopy and 115 who did not, Northwest Territories, Canada, 2008

	Endoscopy n=194		No endoscopy n=115	
	Per cent	95% CI	Per cent	95% CI
Stomach problems*†				
None	37	30 to 44	41	32 to 51
One	20	15 to 27	18	11 to 26
Two or more	43	36 to 50	41	32 to 51
Family history†				
<i>H pylori</i> infection	25	19 to 32	20	13 to 28
Stomach cancer	31	25 to 38	23	16 to 32
Medical history†				
Tested for <i>H pylori</i> before enrolment in Aklavik <i>H pylori</i> Project‡	21	15 to 27	12	7 to 20
Taking stomach medication‡	27	21 to 34	19	12 to 28

*Includes difficulty swallowing food, unexplained weight loss, recurrent vomiting, upper abdominal symptoms, epigastric pain, epigastric discomfort, epigastric burning, postprandial fullness, early satiety, heartburn, acid regurgitation, upper abdominal bloating, excessive belching and nausea.

†Missing data: stomach problems in five individuals who underwent endoscopy and one who did not; family history variables in one individual who underwent endoscopy, previous *H pylori* test in one individual who underwent endoscopy.

‡Includes any medication taken for stomach discomforts or heartburn.

Table 4 Unadjusted and adjusted ORs for the association of sociodemographic and clinical variables with *Helicobacter pylori* positivity, as classified by histopathology, among 189 Aklavik *H pylori* Project participants with gastric biopsies and complete data on presented variables, Northwest Territories, Canada, 2008

	Unadjusted		Adjusted*	
	OR	95% CI	OR	95% CI
Age in years				
10–19	1.0		1.0	
20–39	1.8	0.63 to 5.0	3.4	1.0 to 11
40–80	0.51	0.21 to 1.3	2.0	0.67 to 6.1
Sex				
Female (vs male)	1.1	0.62 to 2.1	1.3	0.61 to 2.8
Ethnicity				
Non-Aboriginal (vs Aboriginal)	0.11	0.03 to 0.36	0.07	0.02 to 0.33
Education				
Per year increase	0.93	0.84 to 1.0	0.95	0.83 to 1.1
Family history of stomach cancer				
Yes (vs no or unsure)	0.65	0.34 to 1.2	0.74	0.33 to 1.7
Previous antibiotic treatment for <i>H pylori</i>				
Yes (vs no or unsure)	0.25	0.11 to 0.58	0.20	0.07 to 0.56
Previous gastroscopy				
Yes (vs no or unsure)	0.18	0.08 to 0.39	0.25	0.09 to 0.65
Medications for stomach disorder				
H ₂ blocker or PPI (vs neither)	0.47	0.20 to 1.1	0.75	0.24 to 2.4
Aspirin use				
Any (vs none or unsure)	0.33	0.15 to 0.72	0.35	0.13 to 0.99
NSAID use excluding aspirin				
Any (vs none)	0.81	0.40 to 1.6	0.95	0.39 to 2.3
Current alcohol use				
Any (vs none)	2.3	1.2 to 4.3	2.4	1.1 to 5.0
Current smoking				
Any (vs none)	2.4	1.3 to 4.5	1.2	0.53 to 2.7

*Adjusted for age (categorised as in table), ethnicity, previous antibiotic treatment for *H pylori*, previous gastroscopy, aspirin use and alcohol use; ethnicity was additionally adjusted for education (in years) and smoking; aspirin use was additionally adjusted for education (in years). H₂ blocker, histamine H₂ receptor antagonist; NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor.

of *H pylori*-positive participants. There were no cases of duodenal ulcer or gastric cancer.

Histopathology

Among 176 participants with biopsies from both the gastric antrum and body, acute antral gastritis and acute pangastritis were seen in 25% and 37%, respectively. Chronic antral gastritis and chronic pangastritis were seen in 9.7% and 57%, respectively (table 6). Among

the 194 endoscoped participants, the prevalence of acute and chronic gastritis was 63% and 68%, respectively, and nearly all individuals with either form of gastritis were *H pylori*-positive (94% and 100%, respectively; table 7). There were no cases of gastric dysplasia or adenocarcinoma. Among *H pylori*-positive participants, prevalence was 21% for gastric atrophy and 11% for intestinal metaplasia, while chronic inflammation severity was mild in 9%, moderate in 47% and severe in 43%.

Table 5 Endoscopic findings among 194 Aklavik *Helicobacter pylori* Project participants with gastric biopsies, Northwest Territories, Canada, 2008

	Total		129 <i>H pylori</i> + participants		65 <i>H pylori</i> - participants	
	n	Per cent	n	Per cent	n	Per cent
Esophagitis	20	10.3	11	8.5	9	13.8
Gastric erosions	12	6.2	8	6.2	4	6.2
Gastritis	27	13.9	19	14.7	8	12.3
Gastric ulcer	6	3.1	4	3.1	2	3.1
Duodenal erosion	1	0.5	1	0.8	0	0
Duodenal ulcer	0	0	0	0	0	0
Gastric cancer	0	0	0	0	0	0

Table 6 Prevalence of acute and chronic gastritis by location in stomach among 176 Aklavik *Helicobacter pylori* Project participants with gastric biopsies sampled from antrum and body, Northwest Territories, Canada, 2008

	176 Participants with data		115 <i>H pylori</i> +		61 <i>H pylori</i> -	
	n	Per cent	n	Per cent	n	Per cent
Acute gastritis						
Antral only	44	25.0	44	38.3	0	0
Body only	1	0.6	1	0.9	0	0
Pangastritis	65	36.9	65	56.5	0	0
Chronic gastritis						
Antral only	17	9.7	15	13.0	2	3.3
Body only	1	0.6	0	0.0	1	1.6
Pangastritis	100	56.8	100	87.0	0	0

The percentage with *H pylori* infection was 100% for atrophy, 88% for intestinal metaplasia, 100% for severe inflammation, 100% for moderate inflammation and 77% for mild inflammation. Online supplementary figures S1–3 show magnified views of histological sections from a participant with severe chronic and acute inflammation and high *H pylori* density; all three views are from the same individual.

Table 7 compares the frequency of gastric histopathology diagnoses among Aklavik research participants with those of University of Alberta Hospital patients assessed for the same conditions. Of 3845 patient reports matching search terms 'gastric' or '*Helicobacter pylori*', 413 (10.7%) were classified as positive for *H pylori*. Excluding 815 records with no mention of *H pylori*, the prevalence of *H pylori*-positive diagnoses was 13.6% (413/3030; 2612 were explicitly classified as *H pylori*-negative and 5 were classified as *H pylori* uncertain). The 413 *H pylori*-positive diagnoses corresponded to 401 individual patients. Of the 401 individuals, 98.8% were diagnosed with gastritis. Of 390 that specified whether the gastritis was acute or chronic, 89.2% were specified as chronic only, 1% as acute only and 9.7%

had acute and chronic gastritis. Of 282 patients whose gastric inflammation was graded, 40.4% were graded mild, 55% were graded as mild-moderate or moderate and 4.6% of the patients were graded as moderate-severe or severe. All of the 401 *H pylori*-positive patients were assessed for glandular atrophy and intestinal metaplasia: 2.2% were diagnosed with atrophy and 15% with intestinal metaplasia. Thus, relative to University of Alberta Hospital patients assessed for relevant conditions, Aklavik residents have a much higher prevalence of *H pylori* (greater than four-fold), and *H pylori*-positive Aklavik residents have a much higher prevalence of severe gastric inflammation and gastric atrophy.

DISCUSSION

This study describes a high prevalence of active *H pylori* infection and associated gastric pathology among participants in the Aklavik *H pylori* Project. The pattern of endoscopically visible lesions occurring more frequently in the gastric body relative to the duodenum, along with the high prevalence of severe inflammation and gastric

Table 7 Prevalence of *Helicobacter pylori*-associated histopathology in individuals with evaluated gastric biopsies, comparing Aklavik *H pylori* Project participants (Northwest Territories, Canada) and University of Alberta Hospital patients (Edmonton, Alberta, Canada)

	Aklavik project participants (<i>H pylori</i> prevalence=66%) 129 <i>H pylori</i> + participants†		University of Alberta Hospital patients (<i>H pylori</i> prevalence=14%*) 401 <i>H pylori</i> + patients assessed	
	Per cent		Per cent	Explicitly assessed for condition (n)
Gastritis	100		99	401
Acute	94		11	390
Chronic	100		99	390
Mild	9		40	282
Moderate‡	47		55	282
Severe§	43		5	282
Atrophy	21		2	401
Intestinal metaplasia	11		15	401

*413 *H pylori*-positive diagnoses (in 401 unique patients) among 3030 pathology reports that mentioned *H pylori*.

†Missing data: Two from acute gastritis, one from atrophy and one from intestinal metaplasia.

‡Includes mild-moderate.

§Includes moderate-severe.



atrophy diagnosed in a project that screened community members not seeking healthcare for dyspeptic symptoms, is consistent with an elevated risk of gastric cancer in this community.

This research arose from public perception of a greater than expected number of gastric cancer cases in Aklavik in recent years. As the population of this hamlet is so small, this perception cannot be verified with official statistics, given that the NT cancer registry does not make public community-specific cancer frequencies when case counts are low to protect confidentiality. Statistics Canada suppresses the yearly number of gastric cancer cases diagnosed across the NT (2006 population ~41 000) for the same reason.¹⁴ NT Health and Social Services reported, however, for the time period 1992–2000, that the age-adjusted gastric cancer incidence rate among men in outlying areas of the territory was ~3 times the rate in men across Canada,²⁶ and that gastric cancer was the second most frequently diagnosed cancer in Inuit men and third most frequently diagnosed cancer in Dene First Nations men compared with 10th in men across Canada. (These statistics are not reported for NT women due to small numbers.)

Using histological assessment, a large Canadian multi-centre study reported a *H pylori* prevalence of 30% in patients with dyspepsia.²⁷ The Aklavik *H pylori* Project used two methods to estimate prevalence of active *H pylori* infection; prevalence estimates were 58% in the breath-test screened sample and 67% in the sample that underwent endoscopy. The *H pylori* prevalence estimates observed in this study is in the range of other reported prevalence estimates for northern Aboriginal communities in Canada (51–95%), Alaska (80%) and Greenland (58%).⁸

Systematic searches of the literature yield little information on *H pylori*-associated histopathology in North American Aboriginal communities. In 1997, Yip *et al*²⁸ reported that *H pylori* infection in an Alaska Native population with elevated faecal haemoglobin levels was accompanied by a high prevalence of grossly abnormal gastric mucosa with erythema and mucosal thickening, diffuse intraepithelial haemorrhages, gastric ulcers and multiple erosions (inflammation severity, gastric atrophy and intestinal metaplasia were not mentioned), while only 1% had duodenal ulcers. To place our findings in perspective, we performed a systematic literature search to locate studies of *H pylori*-associated histopathology frequencies for other populations. This search did not identify any other population-based studies. Nearly all studies identified were based on series of patients undergoing diagnostic evaluation, thus it is difficult to put the frequencies observed in Aklavik in perspective. Among 1040 patients investigated endoscopically for dyspepsia across Canada (*H pylori* prevalence=30%), the reported prevalence among *H pylori*-positive patients was 5.7% for gastric ulcer, 10.6% for gastric erosions, 6.6% for duodenal ulcer and 5.6% for duodenal erosions;²⁷ this report did not include histopathology frequencies.

Large studies conducted in Japan,²⁹ Taiwan³⁰ and China³¹ revealed high prevalence of atrophy and metaplasia among *H pylori*-positive patients, though reports did not mention the severity of chronic inflammation. A few smaller studies of patients undergoing medical care in diverse locations reported prevalence for subsets of the endoscopic and histopathological outcomes of interest,^{32–42} however, the diverse selection criteria across these studies impede meaningful summarisation of data patterns. An important limitation for comparing the frequencies observed in Aklavik to those reported in the literature is the much younger age distribution of the Aklavik population, given the mean age of 40 years compared with mean ages over 50 years in the published reports. Another limitation of comparisons across studies is the suboptimal degree of interobserver agreement on histopathological assessment of gastric biopsies, even among expert pathologists adhering to the Sydney system.^{43 44}

Although the prevalence of peptic ulcer disease in Aklavik *H pylori* Project participants did not appear to be elevated compared with the multicentre Canadian dyspepsia study,²⁷ it should be noted that a quarter of Aklavik participants reported taking antisecretory therapy, which provides protection against peptic ulcer disease. The low occurrence of duodenal lesions relative to gastric lesions in the Aklavik population is noteworthy, given that a relatively high ratio of gastric to duodenal ulcer is typical of populations with increased risk of gastric carcinoma.⁴⁵ Our comparison of *H pylori*-positive NT research participants with *H pylori*-positive patients receiving care at a university hospital in Alberta provides evidence of a much higher prevalence of histopathology indicating an increased risk of gastric carcinoma in the northern Aboriginal community. While the Alberta hospital pathology data did not result from systematic assessment of gastric biopsies for relevant conditions, restricting the prevalence estimates to patients who were explicitly assessed for relevant conditions would not likely have underestimated the prevalence of these conditions, because it does not seem plausible that individuals who were less likely to have these conditions were more likely to be assessed for them.

Reasons for the high prevalence of *H pylori* infection in this and other northern Aboriginal populations remain unclear, though it should be noted that *H pylori* prevalence is equally high in many of the world's developing regions,⁴⁶ as well as specific communities in developed regions: for example, immigrants to Canada from high-prevalence areas.⁴⁷ In a large national survey of the USA, elevated prevalence was observed in immigrants as well as Mexican-American and African Americans, and among sociodemographic subgroups defined by poverty, high household density, low education levels and rural residence.⁴⁸ Potentially important socioenvironmental factors unique to northern populations may include dispersed settlement that impedes access to organised social resources such as healthcare, geographical and

climate challenges for sanitation and water supply, and increased concentration of people in indoor spaces. Multiple lines of evidence suggest that *H pylori* infection may have been ubiquitous in humans in earlier eras and that it has declined in modernised and affluent settings. Thus, the question about why *H pylori* prevalence is high in particular communities can be reframed as why it has not declined in these settings as it has elsewhere. In the Aklavik population, factors clearly associated with lower odds of *H pylori* infection were previous *H pylori* therapy, previous gastroscopy, aspirin use and non-Aboriginal ethnicity, which in this community equates with not having grown up in a small hamlet in Arctic Canada.

These results from the Aklavik *H pylori* Project demonstrate that *H pylori* is highly endemic in this community, and severe inflammation and precancerous lesions of the gastric mucosa are highly prevalent. Motivated by worries among Aklavik residents over cancer risk from *H pylori* infection, this analysis shows that community concern is justified and provides an example of how epidemiological research can address health priorities identified by communities. The reasons for a more severe course of infection in this and similar communities have become a major focus of the community-driven research carried out by the Canadian North *Helicobacter pylori* (CANHelp) Working Group, which now includes *H pylori* projects in additional Yukon and NT communities. These projects are unique in yielding evidence of the effects of *H pylori* infection on gastric histopathology in a community setting where the study population is not restricted to individuals seeking medical care for symptoms. Future analyses will focus on identifying determinants of gastritis severity, such as dietary factors, exposure to environmental contaminants and bacterial genotypes. Such determinants would be potential modifiers of gastric cancer risk among individuals with *H pylori* infection and may suggest effective cancer prevention strategies. Driven by the desire of residents of the participating communities to reduce health risks from *H pylori* infection, the CANHelp Working Group's community *H pylori* projects are also assessing the short-term and long-term effectiveness of available *H pylori* treatment regimens to generate information for use in policy analysis that will aid regional health officials in identifying optimal strategies for control of this infection.

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Contributors JC designed the endoscopy component of this research, performed endoscopic assessment of participants, analysed the gastric biopsy data and drafted the manuscript. KJG is the primary investigator of the CANHelp (Canadian North *Helicobacter pylori*) Working Group research programme; she designed and directed the Aklavik *H pylori* project, supervised JC's research methodology and edited the manuscript. SG designed the histopathology methods and carried out the assessment of gastric biopsies. RB supervised the design of the endoscopy methodology and performed endoscopic assessment of participants. JM supervised the implementation of the endoscopy project and performed endoscopic assessment of participants. RNF provided key input in the overall research design and implementation and performed endoscopic assessment of participants. JG designed the data management methods that supported the analysis. KF-G conducted the analysis of the University of Alberta pathology data, verified all of the analyses and the accuracy of the data presentation, and assisted with manuscript preparation. SVVZ supervised the overall clinical methodology of the research and performed endoscopic assessment of participants. All authors reviewed and approved the manuscript.

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Ethics approval The study was approved by the University of Alberta Health Research Ethics Board, the Aurora Research Institute (Northwest Territories research licensing agency), the Aklavik Health Committee, the Hamlet of Aklavik council, the Aklavik Community Corporation (Inuvialuit governance) and the Ehditait Gwich'in Council.

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