

Chapter 3.4.

Gastric cancer prevention in Arctic North America (Alaska, Canada, and Greenland)

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Summary

- Indigenous people in Arctic North America have a higher burden of disease from *H. pylori* infection than non-Indigenous counterparts.
- This disease burden disparity is most striking when comparing gastric cancer frequencies in Indigenous groups with those in non-Indigenous residents of the same geographical region.
- Health jurisdictions in the region should prioritize the collection of accurate data on Indigenous identity and report gastric cancer frequencies specific to Indigenous groups.
- Although the disproportionately frequent occurrence of *H. pylori* infection and gastric cancer across Arctic communities has been observed for more than two decades, public health authorities in Arctic North America have not targeted this disparity in current cancer prevention strategies, nor have they implemented screen-and-treat programmes for gastric cancer prevention.
- A perceived obstacle to the implementation of gastric cancer prevention strategies is the lack of evidence of cost–effectiveness specific to Arctic Indigenous communities, given observations from treatment trials conducted in such communities of relatively frequent hesitancy to receive treatment, along with relatively frequent treatment failure and reinfection.
- In this setting, community-driven screen-and-treat projects offer the possibility of engaging high-risk communities in designing gastric cancer prevention activities that serve their goals and values and give them agency in public health initiatives.

3.4.1 Introduction

Alaska, Canada, and Greenland comprise the far northern region of North America and are dominated by vast Arctic landscapes that are sparsely populated by small Indigenous communities. The Indigenous Arctic coastal people, known as Inuit, established coastal communities across Alaska, Canada, and Greenland. Traditionally, other Indigenous North American groups, known as Alaska Natives in Alaska and First Nations in Canada, have lived in small Arctic communities that lie south of the tree line. Relatively large multiethnic urban populations of Alaska and Canada are concentrated near their southern borders.

Most Arctic Indigenous communities fare poorly on many health indicators compared with non-Indigenous counterparts, even though they live in high-resource countries [1]. According to the Indigenous-led Waapihk Research organization, the social determinants of Inuit health can be summarized as follows: (i) the geography and climate of the remote Arctic environment, with its extreme weather conditions, poses transportation barriers, induces a high cost of living, and limits access to health-care services and facilities; (ii) economic disparity, high unemployment, poverty, and inadequate housing are common, and limited access to education and employment exacerbates poverty; (iii) intergenerational trauma resulting from the legacy of colonial policies, such as forced relocations and cultural assimilation, has an impact on mental health, evidenced in higher rates of substance use, depression, and suicide; (iv) the loss of language, customs, and traditional knowledge and practices creates identity issues and a sense of cultural disconnect, which negatively affect mental health and well-being; and (v) inadequate health-care infrastructure, shortages of health-care professionals, high-cost medical services, and dependence on medical transportation to access treatment restrict health-care access [2]. These factors are now compounded by environmental deterioration caused by climate change. Although crisis conditions have been acknowledged internationally, the health and well-being of Arctic Indigenous communities has received insufficient attention at a global level [3].

In 1997, investigators affiliated with the United States Centers for Disease Control and Prevention (CDC) Arctic Investigations Program, based in Anchorage, Alaska, in collaboration with the Alaska Area Native Health Service, observed that the prevalence of *H. pylori* infection was 99% among 140 Yupik adults in three villages in western

Alaska, who also had a high prevalence of severe gastric mucosal abnormalities upon endoscopic examination [4]. Since then, accumulating evidence of the high prevalence of *H. pylori* infection and the corresponding gastric cancer risk among Indigenous populations of the circumpolar north has flagged this inequity as a major global health concern. In the ensuing years, gastric cancer prevention efforts in this region have focused on describing the burden of *H. pylori*-associated disease and generating evidence on the benefits of screen-and-treat strategies for Arctic Indigenous communities. In the meantime, public health authorities have left the responsibility for prevention and control of *H. pylori*-associated disease largely in the hands of primary care practitioners and gastroenterologists, with no systematic approach to reducing gastric cancer rates.

3.4.2 Descriptive epidemiology of gastric cancer in Arctic North America

In 1996, shortly before the first report on *H. pylori* infection prevalence in an Alaskan community, investigators from the Danish Cancer Registry, Statistics Canada, and the Alaska Area Native Health Service estimated standardized incidence ratios to compare cancer incidence rates in circumpolar Inuit with those in non-Indigenous comparison populations in Connecticut (USA), Canada, and Denmark [5]; the report revealed excess gastric cancer incidence in Inuit men.

In 2004, a report on cancer incidence in Greenlandic Inuit in 1973–1997, using data from the Danish Cancer Registry, described an increasing trend in gastric cancer incidence of 24% every 5 years in both sexes during the study period [6]. In 1988–1997, standardized gastric cancer incidence ratios comparing Greenlanders with the Danish population were 2.2 (95% confidence interval [CI], 1.4–3.4) for women and 2.9 (95% CI, 2.1–4.0) for men. Noting that gastric cancer incidence had decreased globally in the preceding decades, the authors stated that the increases observed in Greenland were unparalleled in industrialized countries. High levels of nitrosamine had been observed in the dried, unsalted fish preparations that are consumed in Greenland, but there was no indication of increased consumption of these traditional foods during a period in which the consumption of fruits and vegetables had increased. The authors stated that estimates of the seroprevalence of *H. pylori* in Greenland during the study period were not available. Similar increases in the rates of lung cancer incidence were not observed

in either sex in the study; therefore, increases in the prevalence of smoking were not likely to be responsible for the dramatic increases in gastric cancer incidence.

In 2008, an update using data from 1989–2003 was published by the Circumpolar Inuit Cancer Review Working Group [7]. This update showed that gastric cancer incidence rates in both Inuit men and Inuit women were about 4 times those in non-Indigenous comparison populations. A 2008 review summarized studies of Arctic Indigenous communities that estimated a consistently higher incidence of gastric ulcers relative to duodenal ulcers, as well as studies that estimated a consistently high prevalence of *H. pylori* infection [8]. Several data sources showed elevated gastric cancer rates among North American Indigenous populations compared with non-Indigenous counterparts [9–11].

A 2012 report analysed cancer patterns among Inuit across Canada in 1998–2007. Gastric cancer incidence rates were higher among Inuit men than among men in the rest of Canada [12].

In 2012, members of the Canadian *Helicobacter* Study Group assessed evidence on *H. pylori* infection in First Nations people and recent immigrants to Canada [13]. They noted that the prevalence of *H. pylori* infection had been decreasing across Canada and that this had changed the distribution of upper gastrointestinal diseases, including reduced frequency and severity of peptic ulcer disease. However, Indigenous people and recent immigrants in Canada continued to have high prevalence of *H. pylori* infection; thus, there remained an opportunity to investigate whether *H. pylori* infection is a treatable risk factor for malignancy in Canadian communities with high frequencies of both *H. pylori* infection and gastric cancer.

A 2014 systematic review of gastric cancer incidence, mortality, and survival in Indigenous populations worldwide revealed elevated rates of gastric cancer incidence and mortality in nearly all Indigenous Peoples compared with non-Indigenous counterparts in the same regions or countries, with increasing trends in incidence observed in some groups [14]. In populations for which there are data, the largest age-standardized incidence ratios were observed in Inuit residing in the circumpolar region, with age-standardized incidence ratios of 3.9 for men and 3.6 for women.

A retrospective cohort study used data from 1991–2014 to compare gastric cancer incidence in immigrants and non-immigrants living in the Canadian province of Ontario [15]. Investigators identified immigrants who were first eligible for the Ontario Health Insurance Plan at age ≥ 40 years and matched each of them to 5 non-immigrants by year of birth and sex. The study identified 415 gastric cancer cases in 209 843 immigrant women, 1872 cases in 1 049 215 non-immigrant women, 596 cases in 191 792 immigrant men, and 2998 cases in 958 960 non-immigrant men. Most of the immigrants came from the World Bank regions of East Asia and Pacific, South Asia, and Europe and Central Asia. The crude gastric cancer incidence rate was 22% higher in immigrant women than in non-immigrant women and 9% higher in immigrant men than in non-immigrant men. Adjusted hazard ratios were 1.29 (95% CI, 1.12–1.48) for women within 10 years of health insurance eligibility and 1.19 (95% CI, 1.01–1.40) beyond 10 years and 1.17 (95% CI, 1.04–1.31) for men within 10 years of health insurance eligibility and 1.00 (95% CI, 0.87–1.15) beyond 10 years. Female immigrants from the East Asia and Pacific region and the Europe and Central Asia region had the highest gastric cancer incidence rates compared with age-matched female non-immigrants, both before and after the 10-year mark. The same pattern was seen for male immigrants from the Europe and Central Asia region but not for male immigrants from the East Asia and Pacific region, in whom gastric cancer incidence rates were only higher compared with age-matched male non-immigrants during the first 10 years after health insurance eligibility.

The Alaska Cancer Registry reports statewide cancer statistics. Its most recent *Cancer in Alaska multi-year summary report*, published in 2017, reported incidence statistics for 2010–2014 and mortality statistics for 2005–2014 [16]. During this period, the diagnostic frequency rank of gastric cancer among all cancer sites was fourth among American Indian and Alaska Native men in Alaska and seventh among Alaska Native women in Alaska; gastric cancer was not in the top 10 most frequently diagnosed cancer sites among White men or women in Alaska. For cancer deaths, gastric cancer was the 11th most frequent cancer site among all men in Alaska and the ninth most frequent among all women in Alaska; it was third among Alaska Native men in Alaska and fourth among Alaska Native women in Alaska.

In 2017, a report using Yukon Cancer Registry data, *Cancer mortality trends, 1999–2013* [17], highlighted gastric cancer as the fourth most frequent cause of cancer death

in Yukon men and the fifth most frequent cause of death in Yukon women, even though gastric cancer is diagnosed much less frequently than many other cancers [18]. The report estimated the age-standardized mortality ratio, comparing gastric cancer mortality rates in Yukon in both sexes combined with those in Canada in 2008–2012, as 1.8 (95% CI, 1.1–2.6). However, according to the Yukon Government *Cancer incidence report, 2009–2016* [19], gastric cancer was the 14th most frequently diagnosed cancer among Yukon men and women combined, with incidence rates similar to those expected based on the rates in Canada. The report noted that the average gastric cancer incidence rates coupled with the higher-than-average gastric cancer mortality rates suggest that gastric cancer may be presenting relatively late in Yukon compared with the rest of Canada or that gastric cancer in Yukon is more aggressive. Given that Indigenous people are a minority in Yukon, comprising 22% of the territorial population [20], the lack of ethnicity-specific disease frequency estimates in the Yukon health statistics masks the burden of gastric cancer in the Indigenous population in Yukon.

In 2018–2021, published analyses of gastric cancer data from diverse Canadian cancer registries showed high age-standardized gastric cancer incidence rates in Indigenous residents of the western Canadian province of Alberta relative to non-Indigenous Albertans [21], in Indigenous residents of the Northwest Territories relative to non-Indigenous Canadians [22], and in low-income communities with a high concentration of Indigenous people, visible minorities, and immigrants [23]. Cancer registry data also revealed a younger age distribution of gastric cancer cases in the Northwest Territories and Yukon relative to Canada as a whole: the proportion of gastric cancer cases diagnosed in people aged < 60 years was 48% in the Northwest Territories in 1997–2015, > 40% in Yukon, and < 25% across Canada as a whole, during similar time periods [22]. Also, of the gastric cancer cases diagnosed in Indigenous residents of the Northwest Territories in 1997–2015, 16% occurred in people aged < 40 years, compared with < 2% across Canada as a whole [22].

In 2021, investigators affiliated with the CDC Arctic Investigations Program and the Alaska Native Tribal Health Consortium published a description of gastric cancer occurrence in 1990–2017 in Alaska Natives living in Alaska compared with the White population in the USA [24]. Greater proportions of gastric cancer cases in Alaska Natives were diagnosed at younger ages: 11% of cases in Alaska Natives and 3% of cases in White people in the USA ($P < 0.0001$) occurred in people aged < 40 years, and

37% of cases in Alaska Natives and 20% of cases in White people in the USA ($P < 0.0001$) occurred in people aged 40–59 years. Proportionally more gastric cancer diagnoses among Alaska Natives were distant-stage cancer (48% in Alaska Natives and 35% in White people in the USA; $P < 0.0001$). The age-adjusted gastric cancer incidence rate was substantially higher in the Alaska Native population (20.8 per 100 000 per year in Alaska Natives and 6.7 per 100 000 per year in White people in the USA; $P < 0.0001$). Although the gastric cancer incidence rate decreased in the White population in the USA during the study period, little change in incidence was seen in the Alaska Native population.

A 2021 article co-authored by health officials from across the circumpolar north described gastric cancer incidence and mortality trends using cancer incidence and mortality data for 1999–2016 from circumpolar cancer registries [25]. Only cancer registries in the USA enabled data to be stratified by ethnicity, although it should be noted that nearly 90% of the population of Greenland identifies as Inuit [26]. Among men, the highest age-standardized gastric cancer incidence rates were reported for Karelia, in the Russian Federation (40.8 per 100 000 per year), followed by Greenland (20.2 per 100 000 per year), which was slightly higher than the rate among Indigenous men in Alaska (18.6 per 100 000 per year) and nearly double the rate in North Jutland, in Denmark (11.5 per 100 000 per year). Among women, the highest age-standardized gastric cancer incidence rates were reported for Arkhangelsk, in the Russian Federation (17.7 per 100 000 per year), followed by Indigenous women in Alaska (10.3 per 100 000 per year), with Greenland in third place (8.8 per 100 000 per year). Standardized rate ratios were estimated by comparing age-adjusted incidence rates with those of the broader proximal geographical unit (Greenland compared with Nordic countries; Indigenous people in Alaska compared with White people in Alaska). Across circumpolar populations, the largest standardized rate ratios were reported for Alaska (men, 3.8; 95% CI, 2.7–5.4; women, 4.1; 95% CI, 2.6–6.4) followed by Greenland (men, 2.8; 95% CI, 1.9–4.6; women, 2.3; 95% CI, 1.3–4.8) for both men and women. The authors of this analysis concluded, “There is a need to address disparities observed among circumpolar subpopulations ... [and doing so] could benefit from coordinated international action” [25].

3.4.3 Gastric cancer prevention activities in Alaska

Alaskan public health researchers published the results of the earliest intervention studies that used treatment to eliminate *H. pylori* infection in Arctic Indigenous communities [8]. These studies revealed high prevalence of antibiotic resistance, high rates of treatment failure, and high rates of reinfection. These challenges, which are not generally encountered in high-income countries, led to a 2015 expert commentary by members of the Circumpolar *H. pylori* Working Group, which has held annual meetings since 2007, convened by the CDC Arctic Investigations Program and the Statens Serum Institut in Copenhagen, Denmark. These experts concluded that studies were needed to determine whether there were population subgroups for whom screening and treatment of *H. pylori* infection was cost-effective for gastric cancer prevention, highlighting the lack of community-based intervention studies [27].

In 2019, in response to calls from outsiders for a screen-and-treat initiative to be implemented in Alaska to reduce gastric cancer rates among Alaska Native communities, researchers affiliated with the CDC Arctic Investigations Program and the Alaska Native Tribal Health Consortium explained their position [28], emphasizing the collaborative partnership between these two agencies, which had facilitated *H. pylori* research conducted since the 1990s in Alaska. They summarized the substantial benefit for Alaska Natives of research that has yielded Alaska-specific descriptions of *H. pylori* infection and associated disease, including recognition of the high prevalence of *H. pylori* infection, documentation of associated health disparities, laboratory-based surveillance of antimicrobial resistance, assessments of the utility of *H. pylori* detection methods for Alaskan residents, treatment trials showing high rates of treatment failure, and estimates of high reinfection rates among rural Alaska Native residents.

The Alaskan public health experts noted that their investigations provided data to aid clinical decision-making to clinicians and health leaders, resulting in early adoption of more effective therapies prescribed to eliminate *H. pylori* infection. The experts explained that recent goals were to find a way to identify *H. pylori*-positive people at highest risk of gastric cancer to target for *H. pylori* treatment, to develop and test markers to detect gastric cancer at earlier stages, and to develop pilot studies for early gastric cancer screening. The Alaskan public health experts concluded by emphasizing that no one other than Alaska Native health leaders should decide whether a specific

prevention strategy should be adopted for Alaska Native communities. They noted that the role of health professionals is to inform such decisions based on empirical evidence of the risks, the benefits, and the alternatives, without presuming to know what is best for others [28].

In July 2019, a multiagency workgroup hosted a 2-day symposium in Anchorage, bringing together internationally recognized experts and local leaders to identify the best strategies to combat gastric cancer among Alaska Natives [29]. The symposium organizers aimed to identify goals and actions that were scientifically sound, feasible, and culturally acceptable. The symposium connected scientists with the relevant expertise, Alaskan health providers, Alaska Native community and tribal leaders, and public health officials. The symposium attendees identified the gaps in knowledge specific to the Alaska Native population for the following questions: (i) what are the genetic, dietary, environmental, and behavioural risk factors for gastric cancer; (ii) who would benefit from oesophago-gastro-duodenoscopy (OGD) screening for gastric cancer; (iii) what is the best way to detect diffuse gastric cancer in its early stages, and how effective is endoscopy at doing so; (iv) why do some people develop gastric cancer at a very young age; and (v) what is the current epidemiology of *H. pylori* infection. The symposium identified goals and actions, calling for support of:

- ongoing interventions that target gastric cancer risk factors:
 - protocols for care providers to emphasize early referral of high-risk patients;
 - a statewide upper endoscopy protocol for biopsy sampling;
 - specialized training for pathologists and endoscopists to improve gastric cancer detection;
 - updated local *H. pylori* clinical guidelines;
 - surveillance OGDs for first-degree relatives of patients with gastric cancer and people diagnosed with gastric intestinal metaplasia; and
 - education on gastric cancer prevention and screening for communities of new gastric cancer cases.
- scientific projects to enhance knowledge of gastric cancer in the Alaska Native population:

- continued collaboration with Canadian research teams on *H. pylori* genomics;
- further investigation of gastric cancer markers to optimize risk stratification;
- further descriptive research on *H. pylori* infection epidemiology in Alaska Native communities;
- assessment of the effectiveness of treatment of dental caries in concert with *H. pylori* treatment;
- enrolment of patients with newly diagnosed gastric cancer and their families in studies designed to identify risk factors.

The participants in the Alaska symposium concluded that broad *H. pylori* screening and treatment would not be beneficial, because of the high prevalence of *H. pylori* infection and antibiotic resistance, high reinfection rates, and logistic challenges. The participants also concluded that a statewide OGD screening programme, similar to those in Japan and the Republic of Korea, was logistically, economically, and culturally unrealistic; instead, individuals at highest risk should be prioritized for screening [29].

In addition to surveillance of cancer rates, the Alaska Department of Health regularly updates its Comprehensive Cancer Control Program. For 2021–2025, it aimed to address social determinants of health by approaching cancer control through a health equity framework [30], focusing key initiatives on primary prevention, early cancer detection, care for patients with cancer, and promotion of health equity. It does not specifically mention gastric cancer or *H. pylori* infection.

3.4.4 Gastric cancer prevention activities in Canada

The Canadian government defines the Arctic region loosely, acknowledging as stakeholders Indigenous Peoples in Canada along with the governments of the three northern territories (Nunavut, Northwest Territories, and Yukon) and the three provinces with Arctic regions (Newfoundland and Labrador, Quebec, and Manitoba) [31]. Canada's borders contain 25% of the global Arctic, which makes up more than 40% of Canada's land-mass [32].

In 1997, Canadian gastroenterologists formed the Canadian *Helicobacter* Study Group to offer guidelines for clinical management of *H. pylori* infection, which were first published in 1998 and subsequently updated [33–38]. In 2002, members of this Study

Group published a review of the risks and benefits of treatment to eliminate *H. pylori* infection [39]. The Study Group did not recommend widespread testing for *H. pylori* infection, because of insufficient research on the cost–benefit for gastric cancer prevention, potential increases in antibiotic resistance, and potential negative health effects of eliminating *H. pylori* infection. The Study Group recommended that the clinical management guidelines designed in Canada be applied, with *H. pylori* infection diagnosed and treated in appropriately selected patients [39].

In 2002, Cancer Care Ontario, the cancer adviser to the government of the most populous Canadian province, organized a workshop to determine whether there was sufficient evidence to consider the promotion of *H. pylori* treatment for the purpose of cancer prevention and to identify critical areas for research [40]. The workshop participants concluded that despite widespread acceptance of the safety of treatment to eliminate *H. pylori* infection, current evidence did not warrant the implementation of population screening for *H. pylori* infection in populations at average risk of gastric cancer. They called, instead, for a demonstration project to estimate prevalence of *H. pylori* infection, evaluate the merits of screening, measure patient and physician participation, develop education materials, and establish a registry for monitoring and evaluation.

A 2009 report described an economic evaluation of *H. pylori* screening strategies for the prevention of gastric cancer [41], based on a Markov model that compared the lifetime cost and effectiveness of four *H. pylori* screening strategies (no screening, serology-based testing, stool antigen testing, and ¹³C-urea breath testing) as part of a screen-and-treat initiative for gastric cancer prevention in a hypothetical cohort of 10 000 Canadian men aged 35 years with an *H. pylori* prevalence of 33% and a gastric cancer incidence rate of 6.6 per 100 000. Treatment consisted of the four-drug regimen recommended by the Canadian *Helicobacter* Study Group, with an estimated effectiveness of 87%. The estimated accuracy of each detection method was incorporated into the models; costs were valued in 2008 Canadian dollars. The analysis estimated incremental cost–effectiveness ratios per quality-adjusted life year of \$29 800 for stool antigen testing, \$33 000 for serology-based testing, and \$50 400 for ¹³C-urea breath testing. The report did not estimate the cost–effectiveness of screen-and-treat strategies for demographic groups in Canada with higher *H. pylori* prevalence, but it

would be reasonable to expect improved cost-effectiveness of these strategies in groups with relatively high gastric cancer incidence rates.

The 2014 Northwest Territories Health and Social Services report titled *Cancer in the Northwest Territories 2001–2010* did not include gastric cancer among the most frequent cancer sites for which estimated frequencies were reported [42]. However, a section on cancer prevention in this report focused on modifiable risk factors and mentioned tobacco smoking, consumption of red meat, and salt intake as risk factors for gastric cancer. This section included information on *H. pylori* infection, noting it as a major cause of gastric cancer and referencing ongoing research conducted by the Canadian North *Helicobacter pylori* (CANHelp) Working Group (see Section 3.4.6). The 2015 report *Charting our course: Northwest Territories cancer strategy 2015–2025* [43] emphasized three strategic priorities: strengthening initiatives that promote healthy lifestyles and behaviours, supporting programmes that aim to reduce the use of tobacco, alcohol, and other drugs, and supporting community-driven cancer awareness and prevention initiatives. The strategy did not include any specific mention of gastric cancer or *H. pylori* infection.

A section of Yukon *Cancer mortality trends, 1999–2013*, called “Avoiding cancer: infectious agents”, stated that *H. pylori* infection is the most important risk factor for gastric cancer, and that when *H. pylori* is present the risk of cancer is influenced by dietary factors, including an increased risk with a diet high in salt and a reduced risk with intake of fruits and vegetables. The report pointed out that treating *H. pylori* infection substantially reduces the risk of *H. pylori*-associated cancers. It emphasized that work done by the CANHelp Working Group identified *H. pylori* as a public health concern in the Canadian North and that this Working Group was collaborating with community members and decision-makers to identify ways to reduce the health risks associated with *H. pylori* infection (see Section 3.4.6) [17].

In 2022, the Government of Nunavut’s Department of Health published the report *Cancer in Nunavut: burden and trends, 2008–2017* [44]. The report described the cancer control interventions in Nunavut: the Tobacco Reduction Program, the Human Papillomavirus Immunization Program, and opportunistic screening for colorectal cancer and cervical cancer. It made no specific mention of gastric cancer or *H. pylori* infection.

Health Canada, the Canadian Ministry of Health, posts information on the health effects of tobacco, including its association with an increased risk of gastric cancer [45]. The Government of Canada's Action on Cancer [46] does not include information specific to gastric cancer, but it features *Cancer incidence in Canada: trends and projections (1983–2032)*, a website published by the Public Health Agency of Canada, which includes trends and projections for gastric cancer incidence [47]. This public information emphasizes that the overall gastric cancer incidence rate has been decreasing in Canada for decades; in fact, during 1998–2007, gastric cancer had the second most rapidly decreasing incidence rate of all cancers, after laryngeal cancer. The website does not mention demographic groups with above-average gastric cancer incidence or mortality rates. However, it does mention that *H. pylori* infection is a major risk factor for gastric cancer and lists additional gastric cancer risk factors, excluding ethnicity and place of birth: dietary habits, tobacco smoking, alcohol consumption, genetic factors, occupational exposure to dusty and high-temperature environments, exposure to radiation, and socioeconomic factors. It specifies that dietary risk factors include diets rich in starch, poor in protein quality, poor in fruits and vegetables, and high in salt and nitrate. This website explains decreases in gastric cancer incidence rates in Canada as follows: annual per capita consumption of fruits and vegetables in Canada has increased by more than 30% since the 1960s; the decrease in gastric cancer incidence rates may be due to decreased smoking, changes in diet, and, more recently, recognition and treatment of *H. pylori* infection.

3.4.5 Gastric cancer prevention activities in Greenland

In the published literature, there is little information of relevance to gastric cancer prevention in Greenland. A small number of studies focused on the descriptive epidemiology of gastric cancer or *H. pylori* infection. In addition to the gastric cancer data described above, reports published in 1997–2005 estimated prevalence of *H. pylori* infection at 61–77% in two small studies of dyspeptic adults, 47% in 71 population survey participants in Nuuk, and 58% in a population-based sample of 685 residents of Sisimiut [8]. The Greenland government contributes cancer data to NORDCAN [48]; NORDCAN tables show that age-standardized gastric cancer incidence rates in Greenland are 3.0 times the NORDCAN average rate in women and 4.4 times the NORDCAN average rate in men.

3.4.6 CANHelp Working Group community projects: community-driven gastric cancer prevention activities

Although Canada has no national or regional gastric cancer prevention programmes, a community-driven research programme with gastric cancer prevention goals shows how community-engaged research can be part of a multilevel approach to the development and implementation of effective gastric cancer prevention strategies for high-risk communities [49]. The CANHelp Working Group is an intersectoral research team of community partners in the Northwest Territories and Yukon (including community organizations, community leaders, government health officials, and health-care providers), health-technology industry representatives, and academic partners from diverse disciplines from the University of Alberta, which is the major academic centre closest to the Northwest Territories, in the southern province of Alberta, which shares a border with the Northwest Territories [50, 51]. The research programme was formed after leaders of Northwest Territories Indigenous communities voiced concerns about the cancer risk from *H. pylori* infection, which was being detected with high frequency among community members. Leaders of these communities advocated for research to reduce the cancer risk. In response, Northwest Territories health officials reached out to gastroenterologists at the University of Alberta for research support. These health officials sought information to improve health care for *H. pylori* infection, because public health physicians in the Northwest Territories were concerned about frequent treatment failure in patients treated for *H. pylori* infection. The health officials also recognized the need for information about the overall burden of disease from *H. pylori* in their jurisdictions.

Outreach from Northwest Territories health officials to gastroenterologists at the University of Alberta was facilitated by an agency called the Northern Health Services Network, which facilitates specialist care in Alberta for residents of northern territories. This infrastructure facilitated the development of community-driven gastric cancer prevention research projects that were supported by local, territorial, and out-of-territory health-care decision-makers and practitioners. The CANHelp community-driven projects were carried out in diverse Indigenous communities in the western Arctic region of Canada. These projects aimed to develop public health strategies for control of *H. pylori* infection, including strategies for the clinical management of *H. pylori* infection that are both cost-effective and culturally appropriate.

In 2007, the *CANHelp* Working Group launched its initial community project, the Aklavik *H. pylori* project [51], in Aklavik, Northwest Territories, a blended community of 500–600 predominantly Inuit and Gwich'in (Athabaskan) First Nations residents. After media reports of the successful project launch in Aklavik, leaders of the community of Old Crow, Yukon, approached the research team and requested that the research be extended to Old Crow, a Gwich'in (Athabaskan) First Nations community about 200 km north-west of Aklavik. The advocacy of Old Crow community leaders led to the inclusion of Yukon health officials in the *CANHelp* Working Group. Over the next decade, community-driven *H. pylori* projects were launched in four Northwest Territories communities and five Yukon communities.

Prevention research focused on gastric cancer end-points was not feasible, because of the small sizes of the territorial populations (the 2006 census population sizes were 41 000 in the Northwest Territories and 30 000 in Yukon) [52]. Furthermore, population-based data on the disease burden associated with *H. pylori* infection were not available for this region. Therefore, *CANHelp* projects focused on describing the *H. pylori*-associated disease burden and identifying effective treatments to eliminate *H. pylori* infection, and thus generated local evidence that was relevant to clinical decision-making about *H. pylori* infection for Arctic Indigenous communities [53, 54]. The projects included screening participants for *H. pylori* using ¹³C-urea breath testing and treatment trials, with University of Alberta gastroenterologists overseeing treatment. In seven communities, *CANHelp* projects offered upper gastrointestinal endoscopy with gastric biopsies for pathological and microbiological assessments. In five of these communities, endoscopic examinations were done in endoscopy clinics that were set up temporarily in community health centres by technical support personnel and that were staffed by visiting gastroenterologists, endoscopy nurses, and service aides; endoscopies were done at the Inuvik Regional Hospital for *CANHelp* project participants in two Northwest Territories communities (Tuktoyaktuk and Inuvik). University of Alberta gastroenterologists advised local practitioners on follow-up care for abnormal endoscopy findings.

Early findings of the *CANHelp* projects showed that participating communities had high prevalence of *H. pylori* infection (59% of Indigenous participants who were screened using the urea breath test in all nine projects tested positive for *H. pylori* infection) and severe chronic gastritis [53], as well as more frequent visible mucosal

lesions in the stomach than in the duodenum [54]. *CANHelp* treatment trials showed that the clarithromycin-based three-drug therapy, recommended by Canadian clinical guidelines before 2016, had poor effectiveness compared with four-drug regimens [55]. Information from *CANHelp* projects was shared with local practitioners as it became available. The lead *CANHelp* gastroenterologist presented annual updates, along with the latest recommendations for management of *H. pylori* infection, at grand rounds for physicians in the Northwest Territories and Yukon. The public health physician at the Inuvik Regional Hospital, whose catchment area included the four participating Northwest Territories communities and other outlying communities, checked regularly with the lead *CANHelp* gastroenterologist about recommended treatment regimens and updated pharmacies serving the region on an ongoing basis about which regimens should be prescribed for elimination of *H. pylori* infection. Through these channels, findings from the community research projects were translated into improved clinical management of *H. pylori* infection and benefited Northwest Territories and Yukon residents who sought health care for *H. pylori*-associated complaints, whether or not they had participated in *CANHelp* projects.

In 2018, when Alberta Health Services updated *H. pylori* treatment guidelines under the direction of the lead *CANHelp* gastroenterologist, the Northwest Territories Chief Public Health Officer, also a member of the *CANHelp* Working Group, sought input from fellow Working Group members about the relevance of this update for the Northwest Territories population, about half of which is Indigenous. By that time, *CANHelp* community projects had generated a substantial amount of relevant information, which was used to adapt the updated Alberta guidelines for northern and Indigenous populations in Canada. These guidelines included the recommendation of surveillance of gastric precancerous lesions (intestinal metaplasia or severe atrophy) detected during gastroscopy in patients with gastric cancer risk factors, including Indigenous ethnicity, immigration from a high-incidence region, family history of gastric cancer, or intestinal metaplasia that is extensive or of incomplete cell type [56]. The guidelines were approved for circulation to clinicians by both the Northwest Territories Chief Public Health Officer and the Yukon Chief Medical Officer of Health.

CANHelp projects in three communities included a component aimed at assessing the long-term impacts of treatment to eliminate *H. pylori* infection. Of 310 participants from three communities with baseline pathology data from gastroscopy with gastric

biopsies collected in 2008–2013, 69 had follow-up pathology data from repeat gastroscopy with gastric biopsies collected in 2017 [57]. Compared with baseline data, the prevalence of *H. pylori* infection and precancerous gastric pathology was substantially lower at follow-up. Most participants who were *H. pylori*-positive at baseline and *H. pylori*-negative at follow-up had reduced severity of active, chronic, and/or atrophic gastritis at follow-up. In multivariable models of the probability of improved chronic gastritis and improved active gastritis, this probability was greatest among individuals who had reduced *H. pylori* density at follow-up. For chronic gastritis, the next strongest predictor was completion of treatment to eliminate *H. pylori* before follow-up. For active gastritis, the next strongest predictor was *H. pylori* density at baseline. In multivariable models of the probability of progression of atrophic gastritis and/or intestinal metaplasia, the strongest predictors were detection of *H. pylori* in gastric biopsies at baseline or follow-up (positively associated with progression) and treatment to eliminate *H. pylori* before follow-up (inversely associated with progression), whether or not the treatment was successful.

Across the CANHelp projects, participation rates in *H. pylori* screening varied widely by community. More consistently, on average across communities, about one third of participants who tested positive for *H. pylori* infection declined treatment and, among those dispensed treatment, about one third did not participate in follow-up testing to confirm treatment success. The CANHelp projects revealed challenges in participation for initiatives aimed at preventing gastric cancer by eliminating *H. pylori* infection. Although the number of participants with gastric pathology follow-up data was small, the substantial differences in comparison groups yield evidence that *H. pylori* treatment has the potential to reduce the risk of gastric cancer in Arctic Indigenous communities. Based on the available data, it is likely that most *H. pylori*-positive community members who participated fully in the treatment component of CANHelp projects had a sustained reduction in risk indicators for gastric cancer. This suggests that screening and treatment for *H. pylori* infection targeted to high-risk communities has the potential to reduce gastric cancer risk.

3.4.7 Conclusions

Consistent evidence from settings across Arctic North America shows that Indigenous people in this region have a higher burden of disease from *H. pylori* infection than non-

Indigenous counterparts. The disparity is most striking when comparing gastric cancer frequencies in Indigenous groups with those in non-Indigenous residents of the same geographical region; this reflects the importance of prioritizing the collection of accurate data on Indigenous identity and incorporating these data into the descriptive epidemiology of gastric cancer in the Arctic. Although the disproportionately frequent occurrence of *H. pylori* infection and gastric cancer across Arctic communities has been observed for more than two decades, public health authorities in Arctic North America have not targeted this disparity in current cancer prevention strategies, nor have they implemented screen-and-treat programmes for gastric cancer prevention. A perceived obstacle to the implementation of such strategies is the lack of evidence of cost-effectiveness specific to Arctic Indigenous communities, given observations from treatment trials conducted in such communities of relatively frequent hesitancy to receive treatment, along with relatively frequent treatment failure and reinfection. In this setting, community-driven screen-and-treat projects offer the possibility of engaging high-risk communities in designing gastric cancer prevention activities that serve their goals and values and give them agency in public health initiatives.

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