CAN *Help*
WORKING GROUP

ISR (Tuktoyaktuk) *H. pylori* Project

Progress Report – August 2017

The ISR *H. pylori* Project arose from a collaborative effort of the Canadian North *Helicobacter pylori* (CAN*Help*) Working Group to investigate *H. pylori* infection in northern Canada with goals of addressing community concerns, improving clinical management, and reducing health risks.

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When you see a *, please refer to p.13 for a definition of the term

ISR (Tuktoyaktuk) *H. pylori* Project Timeline

Jan 2010 - Feb 2011

- Initial project planning

Feb 2011 - Apr 2012

- Recruitment, *H. pylori** screening* by breath test, questionnaires (health/participant/household)

Aug 2012

- Treatment

Mar 18-19, 2013

- Endoscopy*

May 2013

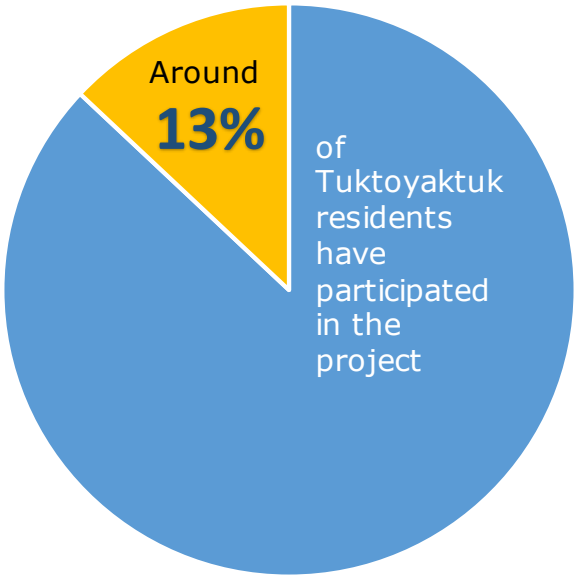
- Pathology*
- Pathology results reported to participants

Ongoing

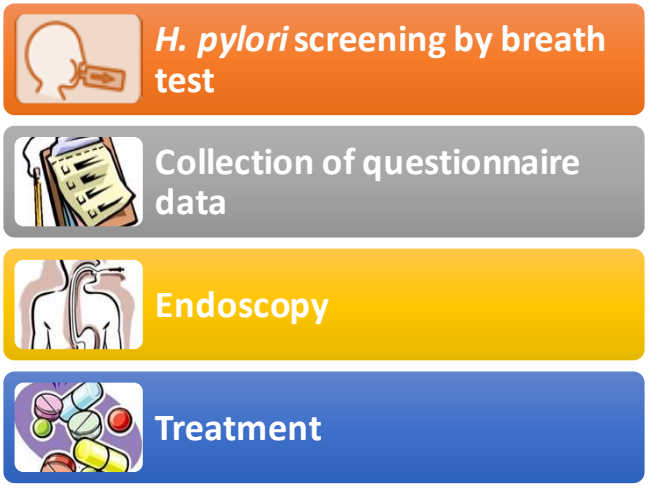
- Long-term treatment follow-up*
- Analysis of questionnaire data

Overview of the Findings

What has been done so far?



Completed components of the project include



What remains to be done?

- Analysis of questionnaire data: ongoing

What have we learned?

Two-thirds of those who had a scope test and whose stomach biopsies* revealed *H. pylori**, had severe chronic inflammation of the stomach.

The quadruple (4-drug) therapy seems to work better than the conventional 3-drug therapy or sequential therapy, although we need treatment follow-up data from more participants to be more certain about this. The 4-drug therapy regimen is complex and may be difficult for some people to take as prescribed. Available treatments for eliminating *H. pylori** infection are burdensome and more research is needed to find out how to make the treatments easier to take.

Most people who were initially free from *H. pylori** infection or successfully treated for the infection remained *H. pylori*-free for 2 years or longer.

57% of participants screened by breath test were positive for *H. pylori** infection.

Some of the people who tested negative after treatment, tested positive few years later.
The reasons why this might happen include:

- *After-treatment test results were false negative and they still had the infection.*
- *H. pylori** *reinfection*

The CAN*Help** Working Group research so far has not pinpointed an environmental source of *H. pylori** in ISR or other communities where *H. pylori* projects are being carried out; this is consistent with findings of research around the world: the evidence suggests that most people with *H. pylori* infection get it from direct contact with a person who has the infection.

Participation and Data Counts

108	•**Participants recruited**
105	•**Urea breath test screening* completed** (103 had a positive, negative, or borderline result)
91	•**Interviewer-administered health questionnaires completed**
79	•**Interviewer-administered participant questionnaires completed**
60	•**Interviewer-administered household questionnaires completed** (reporting household data for 237 individuals)
13	•**Participants completing endoscopy*** (13 participants consented to endoscopy)
13	•**Biopsies* available for *H. pylori** testing**
15	•**Participants enrolled in treatment trial** (31 participants consented to treatment, and 29 were assigned treatment)
18	•**Post-treatment breath tests* completed** (15 had positive/negative/borderline results)
2	•**Interviewer-administered post-treatment questionnaires completed**

Findings to Date

Proportion positive* on breath test	**57% (59/103)**
Endoscopic* findings from 13 Tuktoyaktuk residents	
Gastritis*	**8% (1/13)**
Gastric* erosions	**15% (2/13)**
Gastric ulcer	**0**
Duodenitis*	**8% (1/13)**
Duodenal* erosions	**0**
Duodenal ulcer	**0**
Esophagitis	**15% (2/13)**
Barrett's esophagus	**0**
Pathology* findings (Sydney classification) from 13 Tuktoyaktuk residents	
Chronic gastritis	**77% (10/13)**
Severe	**23% (3/13)**
Moderate	**31% (4/13)**
Mild	**23% (3/13)**
Atrophic* changes	**46% (6/13)**
Intestinal metaplasia*	**31% (4/13)**
***H. pylori** positive**	**62% (8/13)**
Chronic gastritis	**100% (8/8)**
• Severe gastritis	• 37.5% (3/8)
• Moderate gastritis	• 37.5% (3/8)
• Mild gastritis	• 25% (2/8)
Atrophic changes	**62.5% (5/8)**
Intestinal metaplasia	**37.5% (3/8)**
Microbiology* findings from 13 Tuktoyaktuk residents	
Culture* positive	**31% (4/13)**
Antibiotic susceptibility* tests performed on 4 isolates from culture	
Resistance* to any antibiotics tested	**100% (4/4)**
• Metronidazole:	• 50% (2/4)
• Clarithromycin	• 25% (1/4)
• Rifampicin	• 50% (2/4)
Resistance to multiple (2 or 3) antibiotics	**25% (1/4)**
Treatment success from treatment trial participants with a post-treatment breath test*	
Sequential therapy	**66% (2/3)**
Quadruple therapy	**100% (1/1)**

The breath test prevalence (proportion positive) of 57% is a better reflection of the prevalence of *H. pylori** infection in Tuktoyaktuk than the 62% positive by histopathology* (or the 31% positive by culture*) among those with biopsies* from endoscopy*. Since residents who were informed of positive breath test results were motivated to undergo endoscopy, there are proportionally more positives in the group with biopsies.

Summary of Project Activities

To categorize activities, we will be using the following symbols:

Community visit

Data collection

Dissemination and knowledge exchange

Physician's visit

Planning

Upcoming Activities

- None planned at this time

Previous Project Activities

2.1 Year 2010

January 2010: Initial Stages of Research Planning

After successful launch of the Aklavik *H. pylori* Project in 2007, news about the project spread and Lead Investigator Dr. Karen Goodman was asked to take the research to other Northwest Territories and Yukon communities.

In January 2010, the Inuvialuit Regional Corporation (IRC) asked Dr. Goodman to expand the research to five other Inuvialuit Settlement Region (ISR) communities.

A Memorandum of Agreement between the IRC and the University of Alberta was developed, and finalized in February 2011, and the ISR *H. pylori* Project was launched in Tuktoyaktuk.

2.2 Years 2011 and 2012

February to March 2011: First Wave of Data Collection

Project Coordinator Janis Geary and Fieldwork Coordinators Ashley Wynne and Maricon Hidalgo initiated data collection with a team of University of Alberta research assistants in Tuktoyaktuk in February 2011. This fieldwork team recruited participants using telephone and door-to-door outreach during the months of February and March 2011. During this time, project staff obtained informed consent and screened participants for *H. pylori** infection by breath test. They also interviewed participants using participant, household, and health questionnaires. The coordinators created a phone list and map of the community to track coverage of households. They also made regular radio announcements to encourage participation throughout the recruitment and data collection processes and to respond to commonly asked questions.

Initial recruitment efforts were met with a positive response from the community. Most residents contacted indicated a desire to participate. The biggest challenge was getting potential participants to follow through on scheduled appointments to complete the informed consents, breath tests, and questionnaires. Approaches that were effective in overcoming this challenge in other communities were less successful in Tuktoyaktuk, for reasons that were not clear.

March to April 2012: Continuation of Data Collection

Fieldwork Coordinator Moritz Schmidt traveled to Tuktoyaktuk in March 2012 to continue data collection through April 2012. He distributed breath test results to participants who had not yet received them.

Moritz also continued recruitment efforts through door-to-door visits, posters, TV bingo announcements, and presentations and discussions at community events such as the Beluga Jamboree. He attempted, in collaboration with the Tuktoyaktuk Community Corporation, to hire a local coordinator, but no applications were received. He had several conversations with the staff at the Rosie Ovayouk Health Centre, during which he clarified project activities, objectives, and planning goals, and addressed questions and concerns. During this time, he also enrolled new participants and screened them for *H. pylori** through urea breath tests.

May 2012: Physician's Visit

Dr. Sander van Zanten, Lead Gastroenterologist*, visited Tuktoyaktuk on May 8 and 9, 2012 to meet with residents who were concerned about their *H. pylori** breath test results and/or wanted more information about *H. pylori*. He also held information sessions on clinical guidelines for treatment of *H. pylori* infection for Tuktoyaktuk health centre staff on May 9, 2012 and Beaufort-Delta physicians in Inuvik on May 10, 2012.

August 2012: Treatment

Gastroenterologist* Dr. Sander van Zanten initiated the treatment phase of the project for Tuktoyaktuk participants in August 2012. He met with interested project participants one-on-one to evaluate their eligibility for the treatment trial and oversee the administration of treatment. Participants were offered the option of participating in the treatment trial only if the therapies were suitable for them. To date, consent for the treatment trial was obtained from 31 participants and 29 received medications, 15 as part of the trial, which was designed to compare sequential and quadruple therapies, two of the best available treatment regimens

for eliminating *H. pylori** infection. The duration of both therapies was 10 days. Sequential therapy consisted of a proton pump inhibitor and amoxicillin for days 1-5, followed by a proton pump inhibitor, clarithromycin and metronidazole for days 6-10. Quadruple therapy consisted of a proton pump inhibitor with bismuth, metronidazole, and tetracycline for days 1-10. Participation in the treatment trial has remained open.

2.3 Years 2013 and 2014

March to April 2013: Endoscopy* and Dissemination Activities

Lead Gastroenterologist* Dr. Sander van Zanten visited the Inuvik General Hospital on March 18 and 19, 2013 to offer endoscopy* to Tuktoyaktuk project participants. The gastroenterologist was assisted by experienced Inuvik Hospital staff, including nurses and service aids. Endoscopy protocols developed for the Aklavik *H. pylori* Project and Old Crow *H. pylori* Project were adapted for use in Inuvik. Study participants from Tuktoyaktuk 15+ years of age who wished to undergo endoscopy were eligible, as were children whose parents requested that they be included, at the gastroenterologist's discretion. During the 2 days, the team carried out 13 endoscopies and obtained biopsies* for culture* and histopathology* from all 13 participants. No adverse effects occurred during the endoscopy procedures.

Data Dissemination Lead and PhD student Emily Walker (previously Hastings) visited Tuktoyaktuk during March 31 to April 2, 2013 to meet with project participants and present results from her MSc thesis research on environmental exposures in relation to transmission of *H. pylori**. Emily gave a presentation to community members who were interested in hearing about updates from the project and findings to date. The following is a summary of results she presented to community members:

> Emily's thesis results indicate that *H. pylori** infection did not occur more frequently in individuals exposed to investigated environmental sources that could potentially be contaminated with the bacteria, relative to participants who were not exposed to these sources. This includes environmental exposures such as untreated water, sewage, cats and dogs. Since contamination of local water sources with the bacteria is a commonly expressed concern in communities across the north, continued analysis of the role of environmental exposures in transmission of *H. pylori* will include testing water samples from northern communities to determine whether living *H. pylori* organisms are in local water sources.
>
> Preliminary analysis of the effect of exposure to mice indicates that *H. pylori** infection was more frequent in individuals who reported having evidence of mice in their home, relative to those who did not report having evidence of mice in their home. Further research is needed to address whether there is a potential role for mice in transmission of *H. pylori* or if evidence of mice in the home is a marker for another source of transmission. It should be noted that a very small proportion of participants reported exposure to mice. Therefore, even if it is possible for mice to transmit the bacteria, it is not likely that this the usual route by which *H. pylori* spreads.

During this trip, Emily also completed follow-up breath tests with participants who had received treatment through the project to ensure that the infection was cleared. Individuals were then notified of their infection status and arrangements for further care were made for participants who were still positive.

May 2013: Pathology* Results Reporting

Safwat Girgis, team Pathologist*, completed pathologic assessment of the gastric* tissue biopsies* in May 2013. Later that month, Dr. Sander van Zanten, Community Projects Lead Laura McAlpine (previously Aplin), and Emily Walker contacted endoscopy* participants individually to report their pathology results to them.

April 2014: Dissemination Activities

In April 2014, CAN*Help** Working Group partner Evelyn Storr, Director of Community Development at the Inuvialuit Regional Corporation, requested that the CAN*Help* Working Group project staff accompany her on a tour of Inuvialuit Settlement Region (ISR) communities to share information on opportunities to participate in CAN*Help* Working Group activities.

May 2014: Chart Reviews – Antibiotic Use and Key Informant Interviews

MSc student Kate Williams traveled to Tuktoyaktuk May 2014 to collect antibiotic exposure histories from medical charts of participants who had *H. pylori** cultured from stomach biopsies* and tested for antibiotic susceptibility* and/or were treated and completed a post-treatment breath test*. For each of these participants, information was collected for the five-year period before project enrolment on: demographic factors; frequency of antibiotic prescriptions; type of antibiotics prescribed; and reason for prescription. Kate will use this information for her MSc thesis, to estimate associations of antibiotic exposures on two health outcomes: 1) the prevalence of antibiotic-resistant* *H. pylori* infection and 2) success of treatment to eliminate *H. pylori* infection.

Data Dissemination Lead and PhD student, Emily Walker, also travelled to Tuktoyaktuk May 2014 to conduct semi-structured qualitative interviews with key informants from the community to identify specific research questions that address predominantly-expressed community concerns about the health effects of regular exposure to environmental contaminants. Emily will use this information, along with information from similar interviews conducted in other communities, to focus her PhD dissertation work. She completed 3 interviews in Tuktoyaktuk, which were recorded, transcribed and analyzed to identify major themes. Some aspects of this analysis are ongoing.

October to November 2014: Dissemination Activities

Accompanied by Director of Community Development at the Inuvialuit Regional Corporation Evelyn Storr, Community Projects Lead Laura McAlpine, Research Agreements Lead Janis Geary, and Community Partnership Coordinator Sabrina Lakhani held community information sessions in Paulatuk, NT on October 16, 2014, Ulukhaktok, NT on November 24, 2014, and Sachs Harbour, NT on November 26, 2014. At the meetings, community members were enthusiastic about current participation opportunities. In Ulukhaktok and Sachs Harbour, attendees requested that project staff circulate a letter to all local organizations to see if there is a shared interest. Several individuals in Sachs Harbour also offered to form a planning committee to initiate plans for CAN*Help** Working Group activities in their community.

2.4 Year 2015

April 2015: Dissemination Activities

Community Projects Lead Laura McAlpine and Executive Director of Community Development Division of Inuvialuit Regional Corporation, Evelyn Storr, travelled to Tuktoyaktuk in April 2015 to hold a community information session. The community members of were informed of the CAN*Help** Working Group's research findings to date and share opportunities available through the group.

May 2015: Chart Reviews

In May 2015, undergraduate trainee Shelly Jun travelled to Tuktoyaktuk with Lab Manager Richelle Redekop to complete chart reviews. Shelly and Richelle extracted information on utilization of *H. pylori** -associated health care from participants of the Inuvialuit Settlement Region (ISR) *H. pylori* Project. Shelly was awarded a University of Alberta Undergraduate Research Initiative Stipend to carry out a research project during the summer of 2015. Using the chart review data collected in Tuktoyaktuk, Shelly completed a data analysis over the summer to estimate health care burden of *H. pylori*-related disease among participants in Canadian Arctic. Findings from the project will be used in the CAN*Help** Working Group's future policy analysis.

Definitions and Acronyms

Antibiotic resistance	Ability of a microorganism to withstand the effects of an antibiotic
Antibiotic susceptibility	Susceptibility/Sensitivity of bacteria to antibiotics
Atrophy	Wasting away and breakdown
Biopsy, of stomach	A tiny piece of stomach taken during endoscopy
CAN*Help*	Canadian North *Helicobacter pylori*
Culture	As bacteria are living organisms, they can be made to grow in laboratories under the right conditions. A culture test provides conditions that encourages bacteria to grow
Duodenal	Related to the duodenum (small intestine)
Duodenitis	Inflammation of the duodenum (small intestine)
Endoscopy, of stomach	Using a scope/tube to look inside the stomach
Gastric	Related to the stomach
Gastritis	Inflammation of the lining of stomach
Gastroenterologist	Stomach specialist
Histopathology	A test where biopsy material are made into slides so a pathologist can examine them under a microscope to see if *H. pylori* organisms are visible
H. pylori	*Helicobacter pylori*
Long-term follow-up	Includes both breath tests and endoscopy. It is done few years after treatment to estimate the incidence rate of *H. pylori* infection, and to examine the change in stomach lining
Metaplasia	Abnormal change in the nature of a tissue
Microbiology	Science that studies microscopic forms of life
Microbiologist	A scientist who specializes in microbiology
Pathology	Science that identifies diseases and conditions by studying tissues and organ biopsies
Pathologist	A scientist who specializes in pathology
Positive for *H. pylori*	Have the *H. pylori* infection
Post-treatment breath tests	Tests given after the participants complete their treatment
Screening	Testing
Short-term follow-up	Breath test given starting 8 weeks after treatment