



ISR *H. pylori* Project Progress Report

1 Apr 2015

The ISR *H. pylori* Project arose from a collaborative effort of the Canadian North *Helicobacter pylori* (CANHelp) 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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Table of Contents

Overview of Project Timeline and Findings	3
ISR <i>H. pylori</i> Project Timeline	4
Participation and Data Counts.....	4
Findings to Date.....	4
Summary of On-going and Previous Project Activities	5
1. On-going Project Activities	5
1.1 Recent Activities	5
1.2 Upcoming Activities	6
2. Previous Project Work.....	6
2.1 First Wave of Data Collection (Feb – Mar 2011).....	6
2.2 Community Response to Initial Recruitment Efforts	7
2.3 Continued Data Collection (Mar – Apr 2012)	7
2.4 Physician’s Visit (May 2012)	7
2.5 Treatment.....	7
2.6 Endoscopy (Mar 18-19, 2013)	8
2.7 Biopsy Data	8
2.8 Dissemination Activities and Treatment Follow-up.....	8

Overview of Project Timeline and Findings

What has been done so far?

- Completed components of the project include *H. pylori* screening by breath test, collection of questionnaire data, endoscopy, and treatment.

What remains to be done?

- Long-term follow-up is ongoing, as is analysis of questionnaire data and reporting research results to the community.

What have we learned?

- Of participants screened by breath test, 57% were positive for *H. pylori* infection.
- 75% those who had a scope test and whose stomach biopsies revealed *H. pylori* when examined by a pathologist had moderate to severe chronic inflammation of the stomach; this frequency of moderate to severe chronic inflammation is consistent with an increased risk of stomach cancer in this community.
- Of treatments investigated in Aklavik, Old Crow, and Fort McPherson, early results show that a 4-drug regimen is much better than the 3-drug regimen most commonly used in Canada to treat *H. pylori* infection (HP-Pac), but we need more data to be sure about this.
- Available treatments for eliminating *H. pylori* infection are burdensome and more research is needed to find out how to make them more effective.
- Follow-up *H. pylori* testing in Aklavik suggests that most people who were successfully treated remained *H. pylori*-free for 2 years or longer.
- CANHelp Working Group research so far has not pinpointed an environmental source of *H. pylori* in Tuktoyaktuk 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.

ISR *H. pylori* Project Timeline

- Wave 1 data collection
 - Pilot work initiated Feb to Mar 2011
 - Recruitment, *H. pylori* screening by breath test, questionnaires (health, participant, household) Mar to Apr 2012
 - Treatment Aug 2012
 - Endoscopy Mar 18-19, 2013
 - Pathology May 2013
 - Pathology results reported to participants May 2013
 - Short-term treatment follow-up Ongoing
 - Research results reported to community Ongoing

Participation and Data Counts

- Participants recruited: 107
- Interviewer-administered health questionnaires completed: 91
- Breath tests completed: 104 (102 have a positive, negative, or borderline result)
- Tuktoyaktuk residents consenting to endoscopy: 13
- Tuktoyaktuk residents completing endoscopy: 13 (all 13 with biopsies)
- Biopsies available for *H. pylori* testing: 13
- Interviewer-administered participant questionnaires completed:
 - 79 individual respondents
 - 60 household respondents (reporting household data for 84 individuals)
- Participants consenting to treatment: 31
- Participants assigned treatment: 29
- Treatment trial participants: 15
- Post-treatment breath tests completed: 14 (13 have a positive, negative, or borderline result)
- Interviewer-administered post-treatment questionnaires completed: 2

Findings to Date

- Proportion positive on breath test: 57% (58/102)
- Endoscopic findings from 13 Tuktoyaktuk participants:
 - 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 participants:
 - 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)
 - Among 8 *H. pylori*-positive participants:
 - Chronic gastritis: 8/8
 - Severe: 3/8
 - Moderate: 3/8
 - Mild: 2/8
 - Atrophic changes: 5/8
 - Intestinal metaplasia: 3/8

- Microbiology findings from 13 Tuktoyaktuk residents:
 - Culture positive: 31% (4/13)
 - Antibiotic resistance from 4 Tuktoyaktuk isolates:
 - Antibiotic resistance to any antibiotics tested: 4/4
 - Metronidazole: 2/4
 - Clarithromycin: 1/4
 - Resistance to multiple (2 or 3) antibiotics: 1/4

- Treatment success from treatment trial participants with post-treatment breath test results:
 - Sequential therapy: 1/2
 - Quadruple therapy: 1/1

Summary of On-going and Previous Project Activities

1. On-going Project Activities

1.1 Recent Activities

In spring 2014, CANHelp Working Group partner Evelyn Storr, Director of Community Development at the Inuvialuit Regional Corporation, requested that project staff accompany her on a tour of Inuvialuit Settlement Region (ISR) communities to share information on opportunities to participate in CANHelp Working Group activities. Accompanied by Evelyn Storr, Community Projects Lead Laura Aplin, Research Agreements Lead Janis Geary, and Community Partnership Coordinator Sabrina Lakhani held community information sessions in Paulatuk, NT

(October 16, 2014), Ulukhaktok, NT (November 24, 2014), and Sachs Harbour, NT (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 CANHelp Working Group activities in their community.

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.

Emily Hastings, PhD student and Data Dissemination Lead, 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.

1.2 Upcoming Activities

The tour to remaining ISR communities (Aklavik, Inuvik, and Tuktoyaktuk) with Evelyn Storr will continue throughout 2015.

Additional trips will be made throughout 2015 to offer post-treatment breath tests to participants who had treatment to eliminate *H. pylori*, and to develop and implement additional knowledge exchange activities to inform community members of study progress and findings.

2. Previous Project Work

2.1 First Wave of Data Collection (Feb – Mar 2011)

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 2011. This fieldwork team recruited participants using telephone and door-to-

door outreach during 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.

2.2 Community Response to Initial Recruitment Efforts

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 surveys. Approaches that were effective in overcoming this challenge in other communities were less successful in Tuktoyaktuk, for reasons that were not clear.

2.3 Continued Data Collection (Mar – Apr 2012)

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. He 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.

2.4 Physician's Visit (May 2012)

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 and Beaufort-Delta physicians in Inuvik on May 10.

2.5 Treatment

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.

2.6 Endoscopy (Mar 18-19, 2013)

University of Alberta gastroenterologist Dr. Sander van Zanten visited the Inuvik General Hospital on March 18 and 19, 2013 to offer endoscopy to Tuktoyaktuk project participants. The gastroenterologists were 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.

2.7 Biopsy Data

Safwat Girgis, team Pathologist, completed pathologic assessment of the gastric tissue biopsies in May 2013. Later that month, Sander van Zanten, Laura Aplin, and Emily Hastings contacted endoscopy participants individually to report their pathology results to them.

2.8 Dissemination Activities and Treatment Follow-up

Emily Hastings, Data Dissemination Lead, 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.