



Old Crow *H. pylori* Project Progress Report

1 Apr 2015



The Old Crow 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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Overview of Project Timeline and Findings

What has been done so far?

- Around 80% of Old Crow residents have participated in this project.
- Completed components of the project include *H. pylori* screening by breath test, collection of questionnaire data, endoscopy, and treatment.

What remains to be done?

- Short-term treatment follow-up is ongoing, as is analysis of questionnaire data and reporting research results back to the community.
- Long-term follow-up will be carried out over the next several years.

What have we learned?

- Of participants screened by breath test, 68% were positive for *H. pylori* infection.
- Of those who had a scope test and whose stomach biopsies revealed *H. pylori* when examined by a pathologist, around two-thirds had severe chronic inflammation of the stomach; this frequency of 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 Old Crow 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.



Old Crow *H. pylori* Project Timeline

- Wave 1 data collection
 - Recruitment, *H. pylori* screening by breath test, questionnaires (health/participant/household) Dec 2010 to Feb 2011
- Endoscopy and treatment Jan 20 to 23 2012
- Pathology Feb to Mar 2012
- Pathology results reported to participants Mar 26 to 30 2012
- Short-term treatment follow-up Ongoing
- Research results reported to community Ongoing

Participation and Data Counts

- Participants recruited: 202
- Urea breath tests completed: 194 (189 have a positive, negative, or borderline result)
- Interviewer-administered health questionnaires completed: 138
- Interviewer-administered participant questionnaires completed:
 - 138 individual respondents
 - 86 household respondents (reporting household data for 141 individuals)
- Participants consenting to endoscopy: 66
- Participants completing endoscopy: 64 (63 with biopsies)
- Biopsies available for *H. pylori* testing: 63
- Participants consenting to treatment: 91
- Participants assigned treatment: 82
- Participants enrolled in treatment trial: 71
- Post-treatment breath tests completed: 52 (50 have a positive, negative, or borderline result)
- Interviewer-administered post-treatment questionnaires completed: 49

Findings to Date

- Proportion positive on breath test: 68% (128/189)
- Endoscopic findings from 63 Old Crow residents:
 - Gastritis: 13% (8/63)
 - Gastric erosions: 3% (2/63)
 - Gastric ulcer: 2% (1/63)
 - Duodenitis: 5% (3/63)
 - Duodenal erosions: 0
 - Duodenal ulcer: 5% (3/63)
 - Esophagitis: 3% (2/63)
 - Barrett's esophagus: 3% (2/63)

- Pathology findings (Sydney classification) from 63 Old Crow residents:
 - Chronic gastritis: 92% (58/63)
 - Severe: 59% (37/63)
 - Moderate: 29% (18/63)
 - Mild: 5% (3/63)
 - Atrophic changes: 67% (42/63)
 - Intestinal metaplasia: 33% (21/63)
 - *H. pylori* positive: 90% (57/63)
 - Among 57 *H. pylori* positive participants:
 - Chronic gastritis: 100% (57/57)
 - Severe gastritis: 65% (37/57)
 - Moderate gastritis: 32% (18/57)
 - Mild gastritis: 4% (2/57)
 - Atrophic changes: 74% (42/57)
 - Intestinal metaplasia: 35% (20/57)
- Microbiology findings from 63 Old Crow residents:
 - Culture positive: 89% (56/63)
 - Antibiotic susceptibility tests were performed on 53 isolates obtained from culture:
 - Resistance to any antibiotics tested: 51% (27/53)
 - Metronidazole: 42% (22/53)
 - Clarithromycin: 25% (13/53)
 - Ciprofloxacin: 8% (4/53)
 - Tetracycline: 2% (1/53)
 - Amoxicillin, nitrofurantoin, rifampicin: 0
 - Resistance to multiple (2 or 3) antibiotics: 21% (11/53)
 - Metronidazole and Clarithromycin: 15% (8/53)
 - Metronidazole, Clarithromycin and Ciprofloxacin: 4% (2/53)
- Treatment success among 43 treatment trial participants with a post-treatment breath test:
 - Sequential therapy: 60% (12/20)
 - Quadruple therapy: 91% (21/23)

The breath test prevalence (proportion positive) of 68% is a better reflection of the prevalence of *H. pylori* infection in Old Crow than the 90% positive by histopathology (or the 89% 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 Proposed Project Activities

On-going Project Activities

1.1 Recent Activities

Emily Hastings, PhD student and Data Dissemination Lead, and Laura Aplin, Community Projects Lead, travelled to Old Crow during July 20-25, 2014, for the Biennial Gwich'in Gathering. During the trip they set up an information booth in the local arena, where the events of the gathering were held, and provided information about CANHelp Working Group community projects, preliminary findings, future directions, and how additional communities can obtain more information or get involved.

MSc student Kate Williams traveled to Old Crow in June 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 also travelled to Old Crow June 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 7 interviews in Old Crow, which were recorded, transcribed and analyzed to identify major themes. Some aspects of this analysis are ongoing.

1.2 Current & Upcoming Activities

Student intern Alice Wang will be in Old Crow during Feb to Apr 2015 to offer repeat breath testing to project participants for long-term follow-up. The purpose of follow-up breath testing is to find out if participants have been re-infected with *H. pylori* since the treatment trial began in Jan 2012. Alice will also offer repeat testing to participants who were negative for *H. pylori* when they were first tested as part of the project to make sure they are still *H. pylori*-negative. Project staff will travel to Old Crow throughout 2015 as needed to follow-up with project participants.

Members of the Old Crow *H. pylori* Project planning committee requested that a community information session be held to update residents on project activities and findings to date. This is tentatively scheduled to take place some time during spring or summer 2015.

Previous Project Activities

2.1 First Wave of Data Collection (Dec 2010 – Feb 2011)

Field Research Coordinator Laura Aplin and Community Coordinator Christine Creyke initiated data collection in Old Crow in December 2010. Recruitment of participants took place by telephone and door-to-door outreach from December 2010 to February 2011. During this time, informed consent was obtained and participants were screened for *H. pylori* infection by breath test. Project staff also interviewed participants using participant (individual and household) risk factor questionnaires and health questionnaires. The coordinators created a phone list and map of the community to track coverage of households. Regular radio announcements on the Yukon radio station CHON FM were used to encourage participation throughout the recruitment and data collection processes and to respond to commonly asked questions. In December 2010, the first set of breath test results were reported to project participants. The last group of breath-test screened participants received their test results in March 2011.

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.

2.3 Physician's Visit (Aug 2011)

Dr. Sander van Zanten, Lead Gastroenterologist, traveled to Old Crow during August 8 to 11, 2011 to meet with residents who were concerned about their breath test results and/or wanted more information about *H. pylori*. On Tuesday August 9, the Old Crow *H. pylori* Project hosted a community dinner. At this dinner, Sander van Zanten spoke about what the project had accomplished so far and the upcoming endoscopy and treatment phases. He also answered questions posed by community members. Throughout the remainder of the week he met with community members one-on-one to answer their questions and address their concerns.

2.4 Endoscopy and Treatment (Jan 20-23, 2012)

The endoscopy and treatment phases of the Old Crow *H. pylori* Project took place during Friday, January 20 through Monday, January 23, 2012. Participants were primarily recruited through sign-up sheets posted at the Vuntut Gwitchin First Nation Main Reception, the John Tizya Centre, and the Old Crow Health Centre.

A community information session and meet-and-greet with the endoscopy and treatment team was held at the Old Crow Community Hall on Thursday, January 19. Dr. Sander van Zanten gave a short presentation on endoscopy and treatment, and community members posed questions. Overall, the event was well attended and the audience was very enthusiastic about the upcoming components.

For the endoscopy phase of the Old Crow project, gastroenterologists Amy Morse, John Morse, and Sander van Zanten performed unsedated transoral gastrointestinal endoscopy at the Old Crow Health Centre in temporary endoscopy units equipped with rented endoscopy towers and gastroscopes, with technical support from Olympus Canada. Experienced Alberta Health Services endoscopy nurses and service workers assisted the gastroenterologists. Endoscopy protocols developed for the Aklavik *H. pylori* Project were adapted for use in Old Crow. Study participants 15+ years of age who wished to undergo endoscopy were eligible, as were children whose parents request that they be included, at the gastroenterologist's discretion. Over 4 days, the team performed 64 endoscopies; 1 participant attempted but was unable to complete the procedure, and biopsies for culture and histopathology were obtained from 63. No adverse effects occurred during the endoscopy procedures. Of the 63 individuals who completed the procedure, 57 completed an interviewer-administered post-endoscopy satisfaction survey, with 96% indicating they would be willing to have the procedure again if needed.

During this time, for participants who consented to treatment, gastroenterologists Amy Morse, John Morse, and Sander van Zanten evaluated eligibility for the project treatment trial and oversaw the administration of therapy. Participants who were not eligible for the trial were prescribed treatment outside the trial protocol as appropriate. Consent for the treatment trial was obtained from 77 participants and 69 received medications, 61 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; to date, 91 participants have consented to treatment and 71 have participated in the trial.

Project staff Emily Hastings and Laura Aplin coordinated treatment follow-up activities at the Old Crow Health Centre. This included phone reminders to participants during the course of treatment as well as collection of bubble packs to count unused medication and interviews of participants using a post-therapy questionnaire.

2.5 Biopsy Data

Dr. Safwat Girgis, the team Pathologist, completed pathologic assessment of the gastric tissue biopsies in March 2012. Later that month, Laura Aplin returned to Old Crow to report the pathology findings to endoscopy participants individually. Old Crow Health Centre staff assisted gastroenterologists Sander van Zanten and Amy Morse with making arrangements for any participants who required a follow-up endoscopy.



Dr. Monika Keelan's microbiology lab processed biopsies for culture. Preliminary identification of *H. pylori* was performed with biochemical testing. Antibiotic susceptibility testing was finalized July 2012. The results of the antibiotic susceptibility analyses were taken into account for any treatment participants who required a second-line therapy for *H. pylori*.

2.6 Chart Review - General

Ashley Wynne carried out chart reviews at the Old Crow Health Center in April 2012. The chart review collected information for each participant for the 5 years preceding project enrolment on digestive complaints as well as testing and treatment for *H. pylori* infection. The chart review information will enhance the completeness of the health questionnaires and help the project better estimate the burden of digestive diseases among residents of Old Crow.

2.7 Treatment Follow-up

Fieldwork Lead Laura Aplin visited Old Crow during March 26 to 30, 2012 and again during August 16 to 24, 2012 to collect remaining bubble packs and administer additional post-therapy questionnaires. She also carried out follow-up breath testing with participants who had completed treatment, at least 4 weeks prior, to see if their therapy was successful. Those who still tested positive by breath test were prescribed a second treatment by one of the project physicians. At least 2 weeks before each visit, community members were informed of the upcoming trip through flyers and radio announcements on CHON FM's Cool Country Morning and Vuntut Gwich'in Ginjik Nekall radio programs.

Dr. Sander van Zanten traveled to Old Crow on August 16, 2012 to host a community information session and dinner at the Old Crow Community Hall. At this forum, he provided an update of project progress and shared preliminary findings from the endoscopy and treatment components. Overall, the information session was well attended, particularly by elders in the community.

2.8 Dissemination Activities

Emily Hastings, Data Dissemination Lead, visited Old Crow during March 25 to 31, 2013 to 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.