Comparing contact investigations of tuberculosis cases among the Canadian Born Aboriginal and non-Aboriginal population in Alberta, Canada

by

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Abstract

It is well established that the rates of tuberculosis (TB) among Aboriginal Peoples in Alberta are disproportionately higher than those in the Canadian-born 'other' population group (Jensen, Lau, Langlois-Klassen, et al., 2012). In addition, Aboriginal Peoples living on-reserve have higher rates still than those Aboriginal Peoples living off-reserve. Multiple factors likely contribute to this ongoing disparity. One possible reason for the difference in rates between these population groups is the relative success of contact investigations (CI) for source cases from these groups. This possibility has not been addressed systematically in the literature. A contact investigation is the activity undertaken to find and assess individuals who have come into contact with an infectious or potentially infectious TB case. The aim of CI is to identify secondary cases as well as those latently infected individuals who have not yet progressed to disease and in whom disease may be prevented. There are multiple types of contact investigations, including the concentric circle approach which has been used in the Province of Alberta, Canada. Contact investigation is widely accepted as a high-priority activity for TB programs in low incidence areas. Herein I describe a 10-year retrospective study of the contact investigation activities of adult (>14 yrs), Canadian-born, culture positive pulmonary TB cases in Alberta to identify: 1) differences in the outcomes of those activities among Aboriginal Peoples living on and off-reserve, as compared to Canadian-born 'others'. It is anticipated that any differences found between these groups will shed light on the potential for improvement of contact investigation in Alberta specific to the population group of the source case, and 2) to determine predictors of successful CI in each population group. This knowledge has the potential to provide guidance for TB programs based on those predictors.

Preface

This thesis is an original work by Lisa Eisenbeis. The research project, of which this thesis is part, received research ethics approval from the University of Alberta Research Ethics Board, Project Name "TB contact investigations outcomes in Alberta", Pro00035275, 06Feb2013.

DEDICATION:

The decision to undertake my graduate work was not without consideration of my family; my husband Steve and our daughters, Karrah and Kyana. This thesis represents time away from them but also their support and their frequently tested patience.

However, this endeavor sought to show myself that returning to school at the dawn of middle age was possible.

I hope this will provide my daughters with inspiration and a demonstration that anything is possible if you just push yourself to jump in.

Hoppípolla

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Table of Contents

Chapter 1: Introduction

Background.....1

TB and Aboriginal Peoples in Canada.....2

Historical Impact.....2

Social Determinants of Health.....3

Personal Health.....4

Aboriginal Peoples Living off-reserve.....4

TB Control Programs and the Role of Contact Investigation.....5

TB Prevention and Control in Alberta.....8

Goals and Objectives.....10

Literature Review.....11

Chapter 2: Research Process

Methods.....20

Exclusion.....24

Results.....24

Source Case.....24

Contact Investigation Composition.....26

Smear positive source case.....26

Smear negative source case.....28

Contact Profile.....28

Contact Screening Activities.....30

Timeliness of Assessment.....31

Time to first TST.....31

Time to first CXR.....32

Vulnerable Contacts.....33

Screening Outcomes.....34

Preventive Therapy for contacts aged 5 and up.....34

Preventive Therapy for vulnerable contacts.....35

Evidence of Transmission.....36

Predictors of Converters and Cases.....38

Predictors of Successful Contact Investigations.....38

Completion of required 8 week TST.....39

Completion Chest X-Ray within 6 months for positive reactors

.....39

Acceptance of preventive therapy when offered.....39

Completion of preventive therapy when accepted.....40

Chapter 3: Conclusions and Recommendations

Discussion.....43

Limitations of Study.....54

iPHIS.....54

Creation and documentation of contact lists.....55

Reliance on Quantitative Data.....55

Program variance.....56

Summary of Recommendations and Areas for Future Research.....57

Conclusion.....58

References.....59

Appendices

Appendix A: Data Points – Cases.....69

Appendix B: Data points – Contacts.....72

Appendix C: Data points – SAS descriptors.....77

Appendix D: Age & sex of contacts by source case population group & smear status

.....79

Appendix E: Contact screening activities (all ages) smear negative cases

.....80

Appendix F: Preventive therapy outcomes aged 5 and up smear negative cases

.....81

List of Tables

Table 1 Source case characteristics by population group.....25

Table 2 Contact characteristics by case population group and smear status

.....27

Table 3 Average age of contacts by case population group.....28

Table 4 Contacts' age group by source case population group.....29

Table 5 Contact screening activities (all ages) for smear positive source cases

.....31

Table 6 Timeliness of assessment for contacts ages ≥5 of smear positive source cases

.....32

Table 7 Timeliness of assessment close contacts ages <5 of smear positive source cases

.....33

Table 8 Preventive therapy outcomes for contacts ages≥5 for smear positive source cases.....34

Table 9 Vulnerable close contacts (ages <5) of smear positive source cases

.....36

Table 10a Transmission events (cases and converters) for smear positive source cases

.....37

Table 10b Type 1&2 secondary case type diagnosis by population group over time

.....37

Table 11 Predictors of converters and cases (type 1&2) found during contact investigation.....39

Table 12a Predictors of completion of 8 week TST 40

Table 12b Predictors of completion of Chest X-ray within 6 months for positive reactors (new or historic).....,,,,,,,,,,,,,,,.....41

Table 12c Predictors of acceptance of offered preventive therapy.....41

Table 12d Predictors of completion of accepted preventive therapy.....42

List of Figures

Figure 1 Concentric Circle Model.....6

Figure 2 Province of Alberta including designation of treaty zones and First Nations Communities.....9

Figure 3 Coding Process for cases identified as contacts.....23

Figure 4 Risk factors for development of active TB disease.....47

List of symbols, nomenclature or abbreviations

TB – tuberculosis

LTBI – latent tuberculosis infection

ABO – Aboriginal persons residing on reserve

ABN – Aboriginal persons not residing on reserve

CBO – Canadian-born 'others'

TST – tuberculin skin test

IGRA – interferon gamma release assays

RFLP – restriction fragment length polymorphism

AB – Alberta

CI – contact investigation

HIV – human immunodeficiency virus

CCA- concentric circle approach

PT – preventive therapy

S+ - smear positive

S- - smear negative

DOT – Directly Observed Therapy

DOPT – Directly Observed Preventive Therapy

FN – First Nations

LTBI – latent tuberculosis infection

HH – household (referencing relationship to source case)

Chapter 1: Introduction

Background

It is estimated that Aboriginal Peoples (First Nations Status and non-Status Indians, Métis and Inuit) constitute 5.8% of the population of Alberta (Long et al, 2013). Between 2005-2009, the rate of TB in Alberta among First Nations was 15.1/100000, as compared to only 0.8/100,000 among Canadian-born 'others' (Alberta Health and Wellness, 2013). Among Aboriginal Peoples on reserve rates and off-reserve were similar in the time periods 2000 - 2004 and 2005-2009 (Alberta Health and Wellness, 2005 & 2009). However, the crude rate for Status Indians between the years 1999-2008 is estimated at 17.5 versus 0.8 per 100 000 in the CBO population with higher rates on reserve versus off (20.2 & 12.6 respectively), indicating a clear sustained disparity between groups (Jensen et al, 2012). In addition, inconsistency in rate reporting for Aboriginal Peoples as a whole reflects the challenge of lacking definitive census information on this population. Ongoing diagnoses of pediatric TB and increased clustering of cases among Aboriginal Peoples in Canada (relative to Canadian-born 'others') may indicate that ongoing transmission is a barrier to TB elimination in this population (Alberta Health and Wellness, 2007 & 2012; Kunimoto et al, 2004). On-going transmission can be interrupted through good TB programming including successful and high yield contact investigation activities. This highlights the importance of determining the success of contact investigations as a strategy for TB control among Aboriginal Peoples in Alberta, which has not previously been systematically assessed. This analysis can determine if CI can substantially impact prevalence of infection among Aboriginal Peoples and thus contribute to TB elimination (Clark & Cameron, 2009) In what follows, I provide a systematic analysis of contact investigation activities in the Canadian-born to determine 1) whether there are population specific differences in the success

of CIs, and 2) whether any predictors of successful CIs can be identified that might strengthen or provide support to current CI methods.

TB and Aboriginal Peoples in Canada

Historical Impact. When considering investigation into TB outcomes among Aboriginal Peoples in Alberta, it is important to understand the historical context. Public health research as a whole can benefit from the consideration and understanding of history affecting the people under study (Hackett, 2005). In a larger context, the arrival of the European settlers to North America and the subsequent colonialism, assimilation efforts and discrimination have had devastating direct and indirect effect on the health of Aboriginal Peoples.

As noted in the Report of the Royal Commission on Aboriginal Peoples (1996), many infectious diseases, including tuberculosis, were introduced to the Indigenous Peoples of North America with catastrophic effects. Estimates of population decrease of up to 80% have been put forth based upon census information prior to 1871. Dobyns (1966, as cited in The Health of Native Americans, 1994, page 25) has implicated epidemic disease is the key element to the 'depopulation' of Aboriginal Peoples after European contact. It has been shown that the movement of TB across Canada was very much in parallel with the expansion of the fur trade (Pepperel, Granka, Alexander et al, 2011). The continued ongoing incidence of TB in Aboriginal Peoples is legacy of this history.

Indirect impacts of European settlement and subsequent colonialism-based government policy and action has also contributed negatively to social conditions among Aboriginal Peoples, which has subversively contributed to TB incidence. Some of this past has been acknowledged by present day Canadian Government, although it failed to directly acknowledge the dark history of the residential school era (King, 2012, page 122) and the management of TB in the pre-chemotherapeutic era when sanatoriums became increasingly prevalent across Canada.

During this time, many Aboriginal Peoples were taken from their communities and isolated in sanatoria, some never to return. This coupled with the mandated residential school attendance by children living on reserve and subsequent abuses in that setting has contributed to the negative "*collective memory*"[i] (Canadian Thoracic Society, 2014, p 347) of Aboriginal peoples. Further, it has interfered with any efforts to reconcile (Minister of Indian Affairs and Northern Development, 1997) or make progress against TB elimination efforts.

Social Determinants of Health. The historical mistreatment and discrimination, along with disparity of living and social conditions among Aboriginal Peoples continues and impacts the high incidence of TB. As noted by Adelson, (2005) in reference to the Aboriginal Peoples of Canada, the existing health disparity is a reflection of more widespread inequality. Factors such as housing, employment and income are, on average, lower in standard than that of Canadian-born "others" (The Canadian Encyclopedia, 2014, www.thecanadianencyclopedia.ca/en/article/native-people-social-conditions/). These factors are inter-related; poverty is linked to lower health status and educational attainment which affects quality of living conditions (Centre for Social Justice Foundation, 2002). Collectively, these are referred to as the "Social Determinants of Health" by the World Health Organization (WHO) (2014). The determinenets have been implicated in the ongoing battle against TB in Aboriginal Peoples. They have been recognizes and important by Health Canada (2012) in Aboriginal Peoples residing on reserve and by The Canada West Foundation (2001) in Aboriginal Peoples living off-reserve.

On reserve, the status of housing on many levels is dramatically lower than Canadian-Born "others" (Statistics Canada, 2008). Tuberculosis requires close extended contact for transmission and the crowding in reserve housing is well documented (Canada Mortgage and Housing Corporation, 2001) and contributes to TB transmission (Clark, Riben & Nowgesic, 2002). The lack of adequate space per person is compounded by poorly constructed homes,

evidenced by the proportion requiring major repairs (National Collaborating Centre for Aboriginal Health, 2009). This can lead to homes with inadequate ventilation which is implicated in TB transmission and development (CCDR, 2007).

Personal Health. In current times, other health conditions are affecting Aboriginal Peoples and their risk for TB and vulnerability to it. Unfortunately, in comparison to Canadian-Born "others", Aboriginal Peoples have disproportionate rates and incidence of HIV infection, diabetes and end-stage renal disease (Health Canada, 2012). Further, tobacco use is higher among Aboriginal Peoples and Aboriginal youth have been shown to have higher rates of binge drinking (CSJ Foundation for Research and Education, 2002). All of these diseases and behaviors are well documented to be risk factors for TB reactivation (Canadian Thoracic Society, 2014 p 127).

Aboriginal Peoples living off-reserve. Aboriginal Peoples living off-reserve have higher levels of many chronic health conditions compared to Canadian-Born "others" as well as similar harmful health practices (Statistics Canada, 2010). Socio-economic challenges are also affecting Aboriginal peoples living off reserve. They also have lower educational attainment and higher unemployment rates compared to Canadian-Born "others". The shared history and 'collective memory' does not restrict itself geographically, and those that live off reserve struggle with similar issues as those faced by those residing on reserve. Aboriginal Peoples residing off reserve and those that move between urban centres and their home communities pose a challenge. They are what the Royal Commission on Aboriginal Peoples called a 'policy vacuum" (1996:542), in that the programs and services afforded those living on reserve, are not available to them. They may also have difficulty accessing provincial programs and struggle with the cultural insensitivity of existing programs (Canada West Foundation, 2001).

The troubling history and current challenges facing Aboriginal Peoples present many challenges. Thus, despite having curative medication, efforts to impact TB rates must also address multiple factors that are affecting the health of Aboriginal Peoples.

TB Control Programs and the Role of Contact Investigation

The control of TB revolves around 3 basic tenets; identify disease, interrupt transmission and treat those latently infected to reduce the pool of individuals who may later progress to active disease. With the progress made in effective curative chemo therapeutics for TB in the latter part of the 20th century, more attention could be paid to the prevention of transmission and reduction in future cases. This is especially so for areas of low incidence, where resources may be more readily available for preventive measures. It is widely acknowledged the role CI can have on preventing additional cases in international standards (TB Care, 2014). However, areas of high incidence often lack the resources to undertake extensive CI (Kliner et al, 2013). This highlights the advantage of high income countries to control TB but also provides impetuses to ensure CI are evaluated to ensure successful use of resources to achieve its goals.

In Alberta, contact investigation has been undertaken using the 'concentric circle approach' (CCA). **See Figure 1** Information about a source case, such as onset of symptoms, where they spend their time, coupled with bacteriological and radiological information help determine the contacts that need follow-up activities. Contacts with new positive tuberculin skin Test (TST) or who convert their skin tests from negative to positive following contact with a case may represent transmission events. If there is an indication of transmission above the expected baseline of latent TB prevalence within the close contact circle, the circle is expanded by degrees to casual and community contacts, respectively, until no evidence of transmission is found (Alberta Health and Wellness, 2007). The persons who are '*household or equivalent who share same breathing space on a regular basis'* with a source case are deemed 'close', while casual

contacts are those who spent less time with the case or in a more open environment. No specific duration of contact was outlined in the Alberta or Canadian guidelines of this era.

Figure 1 Concentric Circle Model

The effectiveness of CI has not been examined by population-group. Specifically, there have been no population-based analyses of contact investigations in Canada that would help to understand how population specific factors such as environment, jurisdiction over program delivery, beliefs, and/or attitudes could influence the contact investigation itself. Further, published data from TB programs across Canada is limited. For First Nations Peoples, reported CI data was lacking from 6/7 provinces and areas in Canada in a report on the Epidemiology of TB (2012). An annual report by BCCDC (2013) provided limited information on CI by reporting the number, type and population groups of contacts, but no outcomes. They do provide a LTBI completion rate of 71.5% for 2010, but it is not broken down by population group or reason. The

national data from other provincial and territorial health departments is limited on this subject (Government of Saskatchewan, 2013; Inuit Tapiriit Kanatami, 2011; Winnipeg Regional Health Authority, 2012) making comparisons impossible.

Limitations do exist with the CCA (Daley & Kawamura, 2003; Reichler et al, 2002).The primary source of information is the index patient themselves, who may be limited in their willingness to divulge contacts or may not know detailed information about them such as full name or date of birth. This would certainly be an issue with the under-housed as they may rely on several temporary housing options with multiple contacts (Malejczyk et al, 2014). This would impact the thoroughness of the subsequent public health actions, perhaps missing key contacts. Further, the construction of the contact lists requires public health personnel to interview the index patient and they may have varying skill and knowledge based upon experience and training, which can also affect quality of information. Capturing geographic location information about the source case is not typical of CCA (Gardy et al, 2011) and is seen as a limitation as it fails to identify sites where transmission may have occurred. However, in Alberta, locations have often been critical elements of CI involving highly infectious cases and especially those living in the inner city. In these situations, the creation of the contact list is often reliant upon external agencies such as a class list for a high school or nightly census for a shelter serving the under-housed. These efforts may provide detailed lists but may not necessarily reflect the true exposure of the people named.

The conventional epidemiologic approach to contact investigation (identifying and assessing contacts named by the source case) has more recently been augmented with the use of molecular epidemiological tools (DNA fingerprinting of the disease-causing agent) to confirm transmission between cases. Occasionally, molecular epidemiology will link two cases where conventional epidemiologic investigation did not establish a connection. These instances may be shedding light on the shortcomings of contact investigation based on conventional epidemiology

alone. Furthermore, differences in identified number of contacts who complete recommended investigations, preventive therapy and follow-up between different population-groups may reflect factors related to differences between populations or to differences in TB program delivery based on population group.

A strong TB control program, which is successful in its CI activities, can have major cost savings. In 2004, preventive therapy for latently infected contacts that were at risk of progression to active disease cost approximately one thousand dollars to treat versus approximately forty-seven thousand dollars to treat an active case of TB disease (Menzies, Lewis & Oxlade, 2008). These costs do not include the human cost of lost wages and the toll a TB diagnosis can take on families and individuals. The importance of preventing cases is noted nationally by Health Canada in their report, Tuberculosis' Prevention and Control in Canada; a Federal Framework for Action (2014). CI is identified as a priority along with diagnosis and treatment of active cases in this framework. However, little specific guidance is provided in this document. Rather, the Canadian TB Standards serve to identify appropriate research based approaches. These form the basis for the TB programs across Canada, including AB.

TB Prevention and Control in Alberta

In Alberta (**see Figure 2**), tuberculosis prevention and control is undertaken by dedicated public health clinics in the larger centres of Edmonton and Calgary, which each serving its own geographical area and a Provincial 'virtual clinic' which serves all other residents of the province (primarily rural). For rural patients who live in non-reserve communities (including Aboriginal Peoples residing off-reserve), TB services are provided by Public Health Nurses under the direction of the central Provincial clinic. For those patients living on-reserve, Alberta Health Services TB Services is contracted by First Nations and Inuit Health Branch

(FNIHB) - Alberta Region, to direct care for their residents. Community Health nurses and other health centre staff operationalize the program within the community itself. In addition, FNIHB Alberta employs 2 specialty nurses who work under the mandate of TB Control with the province who primary focus on coordination of care, management and screening.

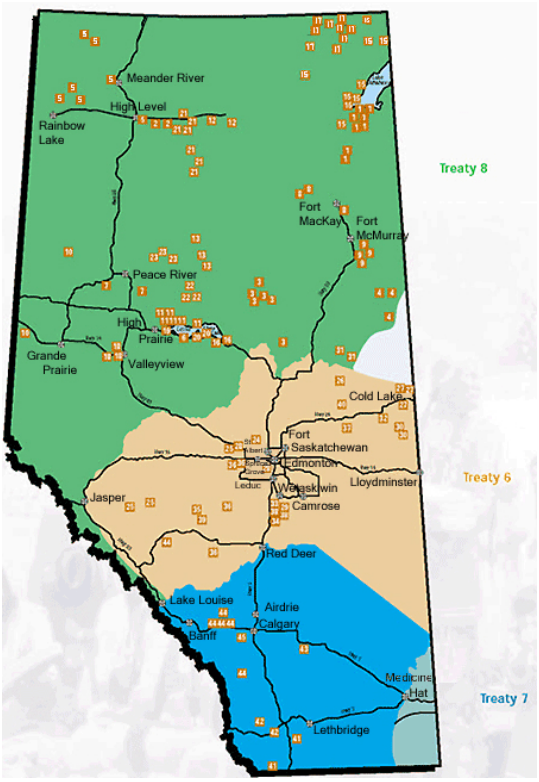

Figure 2 Province of Alberta including designation of treaty zones and First Nations Communities

The AB TB control manuals for 2002 and 2006, whose direction predominated during this study period, identified the same goals and guidelines for CI. Emphasis was placed upon priority contacts (notably children) and information gathering regarding several aspects of the case. With regard to contacts, information of past TSTs or TB history, along with risk factors and current symptoms should ideally be documented. Additionally, an evaluation of the CI event should ideally be undertaken to ensure program resources are sufficient.

In the USA, the CDC's 2005 guidelines have many similarities to Canada's. However, additional contact information is sought; race/ethnicity and amount of exposure time. They too, also encourage evaluation of the CI event itself and put emphasis on the management of data to meet this end.

Although Alberta's TB program outline is generally understood to be performing well, with regard to CI, no specific targets were set prior to 2005; rather a general target of LTBI completion was set at 75%. This was not achieved in subsequent years. The numbers of positive reactors and converters completing preventive therapy were even lower than number accepting preventive therapy. However, outcomes with regards to number of contacts, converters and secondary cases for S+ and S- pulmonary cases were reported. Conversely, for 2005-2009, a specific LTBI treatment completion rate for contacts who accept LTBI treatment was set at 80% which was, again, not achieved.

Between 2005 and 2009, the rates of active TB for First Nations Peoples living on-reserve were similar to the rate of those living off-reserve in Alberta; 14.9 and 15.4 respectively (Alberta Health and Wellness, 2012). Almost 20% of FN cases in Alberta are found through CI (Health Canada, 2012), which is universally lower than other reporting provinces and may reflect needed changes to current contact investigations practices.

Goals and Objectives

There is one primary and two secondary objectives of this study. Overall I aim to systematically assess (over a 10 year period) the relative success of the contact investigations undertaken in the Province of Alberta, and to 1) determine population specific differences in CIs, if they exist, 2) predictors of successful CI outcomes, if they exist by population group. In

particular I am interested in knowing whether jurisdictional division of the provision of care for Aboriginal Peoples living on and off-reserve confounds the CI activities in Alberta, as compared to Canadian-born 'others '. It is hypothesized that there will be differences in the number of contacts identified and the number of contacts who complete follow-up between Aboriginal Peoples on (ABO), and off reserve (ABN) and Canadian-born 'others'(CBO). It is anticipated that contact investigations for ABN may have lower numbers of contacts who complete investigations and treatment, which may be due to increased population mobility and larger numbers of casual contacts from inner city or shared residential settings. We further hypothesize that, on average, more contacts are identified for ABO as compared to the other groups due to larger household size, closer knit communities, and crowded living conditions. Given the co-involvement of provincial and federal health agencies to oversee and deliver TB care to Aboriginal Peoples living on reserve only, we anticipate that their CI outcomes will be superior to that of ABN across measurements of success; number of contacts completing screening, follow up and preventive therapy. It is further anticipated that time to screening and completion of follow up may be superior in CBO versus ABO given their geographical proximity to diagnostic services.

Literature Review

Once effective treatment was established for TB disease and the mechanisms of its transmission were well understood, efforts to prevent disease began to flourish. This is most notably found in the literature from low incidence countries. The development of the Mantoux skin test in the early part of the 20th century was the only test by which latent TB infection could be determined. Despite its high sensitivity, its specificity was low, particularly in light of broad use of BCG vaccine which created false positive results. However, as the only tool available it

was used in an effort to identify those people who may have been infected with the TB bacilli through exposure to an active case. Thereafter began contact tracing activities.

Contact tracing plays a substantial role in low incidence countries' TB control programs. As their active TB cases are minimal in comparison to other nations and can be adequately treated, the goal of prevention can be undertaken. Most recently, a European consensus paper published policy recommendations for contact tracing (Erkens et al, 2010). These recommendations were based upon the review of existing guidelines, literature review along with consultation with TB experts. Of interest is the detailed explanation, including duration of exposure, of how to label contacts. It suggests an ambitious timeline of 7 days from diagnosis of a S+ pulmonary case to initial communication or assessment with exposed individuals. This most certainly would be a challenging timeline, even in low incidence countries, given that this information would likely come by interviewing the case to obtain the names and then have prompt success in reaching those contacts named. Further, in light of more prevalent use of BCG in Europe, different cut points of TST are suggested in those vaccinated and to limit screening to a one time test at 8 weeks post contact. This may have limited relevance to populations of Aboriginal Peoples in Alberta, as BCG is in use in only 3 communities in the province (Jacobs et al, 2007). However, the availability of Interferon Gamma Release Assays[ii] in Alberta in the latter part of the study period have begun to alleviate the concerns about specificity conventional TST testing.

Erkens' paper does discuss 2 models of CI; 1) risk group approach and 2) stone in pond approach (a term used to refer to the concentric circle approach); however they do not recommend one over the other. The risk group approach would limit screening to those only considered 'high priority' and would only expand to other contacts if they had a risk factor for progression to disease. In CCA, high priority contacts are identified for prompt screening, with those considered at additional risk for progression being prioritized first. Goals for several CI

outcomes are suggested. For evaluation of high priority contacts, a goal of 90% is suggested and 75% for completion of LTBI treatment. The importance of evaluation of CI activities is promoted to provide information on efficacy of their efforts and ensure resource use is appropriate.

The United States relies upon the MMWR document (CDC, 2005), which provides comprehensive guidelines for investigation of contacts based upon an extensive review of the literature. It provides direction on several aspects of CI ranging from priority setting, treatment, media, data management and training among others. Of note is the information about the contact that should be routinely collected and documented; including medical risk factors, mental health disorders, ethnicity and country of birth in addition to TST and TB history. Many of these factors contribute to information that allows public health officials to prioritize contacts who are at highest risk for infection and development of disease. The latter includes those contacts that would benefit from "window period" prophylaxis, a key strategy to halt progression to disease in the most vulnerable contacts by providing two drug preventive therapy prior to the 8 week testing limit for TST. The capacity to identify and initiate window prophylaxis would be possible only in CI that have rapid response from public health and cooperation of contacts; which could reflect effective program management and resources. The concentric circle approach (CCA) is recommended by the CDC in this document. Although they identify some disadvantages to this approach, it does applaud the *"simplicity and intuitive appeal"* and acknowledges that alternatives such as social network analysis require additional research before being adopted or applyied within TB control programs.

In Canada, guidelines for contact tracing are outlined in the Canadian Tuberculosis Standards, which is developed in collaboration with the Canadian Thoracic Society and the Public Health Agency of Canada. Multiple editions reflected the typical standards of care based upon the science at that time. In turn, each province and territory interprets these standards to meet the needs and respect the capacity of their respective health departments. In Alberta, the

most recent provincial guidelines were released in 2010; however, previous versions from 2002 and 2006 will be referenced as the benchmark against which to measure the data in this thesis (Alberta Health and Wellness, 2002 & 2007).

Marks et al (2000) did an extensive review of the close contacts of smear positive pulmonary cases over 1 year (1996-1997) in urban areas of the United States. This study provided additional suggestions for measures of a successful CI, including LTBI treatment completion rates but also percentage of contacts that underwent TST testing and completion of CXRs. These features of "success" have been used as measures of successful CIs in this thesis in the context of the relative success of traditional concentric circle approach to CI. Marks further address characteristics of a '*good program*'. The knowledge of pre-existing immunosuppressive conditions and BCG status in contacts assists with prioritizing contacts and interpreting TST. This requires systematic collection and recording of that information, which is not routinely conducted in Alberta's provincial program. Of additional interest is the comparison of US vs. foreign born, which reflects an interest in epidemiological risk of different populations in the US. However Aboriginal Peoples in the US are included within the US born group and thus, the paper does not identify the possible differences of CI success among aboriginal versus non-Aboriginal US-born cases.

A similar study has been done by Jereb, Etkind, Joglar, Moore & Taylor (2003) which included a much larger geographic area of the US and more CIs. They also included all cases (US and FB) and focused their analysis on individuals who completed LTBI treatment but used the number of resultant active cases as their markers of success. Of interest is that the designation of 'evaluated' was only assigned to a contact once the second TST (if indicated) was completed and the decision not to include previous positives in their analysis which overlooks additional evaluation successes. However, they did include all forms of TB which would provide a more comprehensive look at success yield in cases not considered to be as infectious (smear negative

pulmonary, other sites). This may help to determine priorities for staff or shed light on cost-effectiveness of CI activity for less infectious cases.

Using the concentric circle or 'stone in pond' approach to CI, Borraccino et al, (2014) determined the yield of their investigations for pulmonary TB cases. Of particular interest is the low incidence setting parallel between Italy (7/100 000) and Canada (5/100 000) both essentially stable since 2009 (Worldbank, 2013, table 1). They looked at their pulmonary cases over a 7 year period (2002-2008) and the degree to which the identified contacts were assessed; this is not explicitly stated but inferred to indicate a TST plant and read after 10 weeks. Additionally, they determined the yield of positive reactors, those identified with LTBI and active disease. These numbers were in line with findings elsewhere (Jereb et al, 2003; Mulder et al, 2009), indicating a consistent expectation from this approach. A relatively small average number of contacts were identified per case; 5.7. However, these were mainly close contacts as investigation of occasional/casual contacts was only undertaken in a minority of cases (22/833). In the findings presented in this study, close contact was identified by persons who had >4 hours of close proximity contact vs. 12 hours in the Borraccino study, likely accounting for their smaller average. It may also reflect a different social and cultural setting for each geographical area of study. Borraccino included FB cases in their study. Surprisingly, in their comparison of S+ and S- cases, the number of secondary cases was not statistically significant. For this reason, it indicates that CI for S- culture positive cases is warranted in that setting or their definition for close contact was too restrictive.

Notably absent from the literature on CI is the Canadian perspective in particular, and experience for the Canadian-born population. A 1975 paper by Grzybowski, Barnett & Styblo looked at several questions related to CI and outcomes among Aboriginal and '*white*'[iii]/CBO persons over a 5 year period; however an on or off reserve distinction was not made. Given the date of study, it can be assumed the majority of the 'Indians' were living on-reserve, as this era

struggled with discriminatory legislation and assimilation programs which deterred Aboriginal peoples from leaving reserves and being subject to potentially more inequity (The University of British Columbia, 2009, para 13 & 14). Of particular relevance as well is the distinction between 'intimate' contacts that are comparable to close contacts in modern terms, as well as casual contacts. The populations of interest were in British Columbia and Saskatchewan where the significance of the TST measurement were different; 6mm and 10 mm respectively. '*White*' S+ cases tended to have on average more casual contacts vs. intimate (5.0 vs. 2.5) whereas Indians S+ cases had more intimate than casual contacts (5.0 vs. 3.4). The incidence of active disease in intimate contacts was higher when Indians were the source case vs. '*whites*' in all age groups except 30+, where the rate was equivalent. Rates of disease among intimate vs. casual contacts, where the source were S+ or S-, was observed more so in Indians, however, no discussion of the differences between ethnicities was undertaken in this paper. Unfortunately, a discussion of the completeness of CI was not included either though they did indicate what proportion of contacts were TST +.

A recent study from the United Kingdom (Saunders, Koh, Small & Dedicoat, 2014) undertook an extensive retrospective analysis of CI over a 21 year period. They sought to identify predictors of contact assessment completion for all types TB cases. Defining completion of assessment entailed the contact attending a screening appointment, completing diagnostic tests and subsequent notification appointment. This definition of completion was dependent upon age of the contact with 35 years defining a cutoff for TST use. For contacts over 35 years, screening entailed assessment for active disease and a CXR. The division by age makes direct comparison difficult as previous disease or documentation of prior infection are the only reasons to forgo a TST according to Canadian standards. Incomplete assessment was associated with 'working age' and being male and there were also some ethnic differences involving FB population in United Kingdom. For positive screening outcomes, they found that children were more likely to be identified as infected, which indicates the future potential burden of TB due to

ongoing transmission. However, their limitation of TST/IGRA use would skew this finding. It further highlights the importance of completing preventative therapy.

With regards to casual contacts and yield of investigations, specifically the TST result and hours of exposure, Greenaway, Palayew & Menzies (2003) looked at all populations in Canada and USA, but did not differentiate persons of Aboriginal descent pointedly. Their four population groups were divided by prevalence of LTBI, sensitization to NTM and BCG vaccination; none of which reflected Aboriginal persons in Canada, but did differentiate between immigrants of Eastern Europe, Asia and Africa and Canadian or US born. Their investigation did support the limiting of TSTs among casual contacts to a single test 8 weeks post contact to avoid a possible boosting effect of a baseline test. However, the effects of this phenomenon differed between their 4 population groups.

For many years Alberta's TB control guidelines have recommended the use of CCA, but other models exist. Pisu, Gerald, Shamiyeh, Bailey & Gerald (2009) compared CCA to a contact priority model (CPM) in a simulated scenario. Excluding high risk contacts (young children, immunosuppressed); CPM describes a model in which TST is only provided to contacts with close or prolonged exposure to cavitary S+. This method was more cost effective, although slightly less effective at diagnosing LTBI in casual contacts. However, there is no capacity within the CPM to expand assessment to low risk contacts. This is the main distinction between the models as CCA does indicate expansion of screening if the infection rate among close contacts is higher than expected for that population. Although the contact risk assessment is based upon sound evidence reflecting the associated transmission potential, it fails to acknowledge transmission events that have occurred in the absence of these factors. Also, this model is based upon the use of TST alone, whereas in the latter part of this thesis' study period, IGRA use began to affect CI in Alberta. Cost effectiveness cited by CPM could be less

pronounced if all contacts had access to IGRA; which has already demonstrated its own cost effectiveness by limiting unnecessary LTBI treatment and follow-up (Kunimoto et al, 2009).

The usefulness of CI in close household contacts was tested by a simulation modelwhich found that, in a moderate burden setting, effective reduction in TB incidence could be achieved with broad coverage of assessment and completion of LTBI medication (Kassaie, Andrews, Kelton & Dowdy, 2013). Although Alberta is considered a low burden setting, case rates among Aboriginal persons does identify some Aboriginal communities as higher risk, disproportionate to CBO, thus becoming relevant to this model. Kassaie's findings support the value of CI among household contacts, especially if LTBI treatment completion is achieved in reducing the burden of TB in the population. For Aboriginal Communities, greater uptake of LTBI treatment above its current rate could result in a reduction in case rates in subsequent years.

Number of contacts named per case was found to be 15.2 in a recent retrospective analysis from Amsterdam (Sloot, van der Loeff, Kouw & Borgdorff, 2014 & in press). In the Netherlands, the 3 year average case rate is 9/100 000, higher than Canada and Alberta. In this study, they looked at 10 years of CI and its outcomes. They had low rates of preventive therapy uptake among eligible contacts (45%). During a 3 year part of this study period, LTBI treatment completion was 91%. They also found that close contacts were more likely to than casual contacts to start treatment of LTBI and contacts of S- cases were less likely to complete assessment. They did differentiate between those that were Netherlands-born and those that were not and found no difference in the acceptance of LTBI treatment. The five year risk of TB among contacts with untreated LTBI was 2.4% and they question the utility of expanding LTBI treatment. However, given the very low uptake of LTBI treatment, it may not be sufficient to determine if it would impact the 5 year risk rate as no baseline can be determined.

The prevalence of TB often has an inverse relationship with a country's relative wealth; where areas of low TB incidence are considered high income on a global stage. In these settings,

CI is a standard element of TB programs and subsequently assessed and studied. However, the literature available suffers from several limitations; 1) inconsistency or unknown definitions of 'assessment' 2) varying indicators of CI "success" 3) inconsistent definition of contact type 4) limited consideration of population group. Further, within the range of service delivery methods in the TB control programs discussed, there is no reference to the unique history and epidemiology of Aboriginal Peoples whose care model is influenced by residence.

Chapter 2: Research Process

Methods

Data were extracted from the Integrated Public Health Information System (iPHIS) and affiliated quality assurance report system for all adult (>14yrs) Canadian-born, culture confirmed pulmonary cases of TB in Alberta from 2001 to 2010. Drug susceptibility test results for the isolate of *Mycobacterium tuberculosis* were not considered as there were only 8 cases in the study period with isolates that showed resistance of any kind. The data were first sorted according to population group: Aboriginal (First Nations Registered, First Nations not Registered, Metis, Inuit and Canadian-Born non-Aboriginal) disease type (ICD9 codes 11.0-11.9 and 12.3 to reflect pulmonary cases only). If multiple sites of disease were reported, one of which was a pulmonary site, they were included in this study. From that list of adult Canadian-born pulmonary cases only those with positive cultures from a respiratory tract specimen were included.

Once all eligible source cases were confirmed, an excel database was developed and cases were placed in order of diagnosis date by year. In the Province of Alberta, the date of diagnosis is the start date of treatment, or, in the case of death, the date of death. Each case received a unique code reflecting the year of diagnosis and case number indicating their position in the diagnosis date sequence. i.e. 01-01 year 2001 and first case diagnosed. This code was then used as part of the unique code attributed to contacts of each case, as described below. This system of coding ensured that contacts were properly attributed to the source case with whom they had been named as exposed. Additional data were collected from the Public Health Agency of Canada (PHAC) case reporting form generated by iPHIS; and for all cases diagnosed prior to 2004, additional data were obtained on an individual basis by accessing each client chart in

iPHIS and manually entering the data. (See Appendices A, B & C for a more comprehensive list and source of data elements)

A second database of all contacts identified in iPHIS was constructed for each eligible case as outlined above. This data set included contact demographics, tuberculin skin test converters, and number of contacts who completed their recommended follow up. Several data elements of the contacts could be summarized from the iPHIS QR in an excel format. (This platform is used by the TB Program in Alberta to generate standard reports, which are then used by the program for reporting and quality assurance.) The resulting line lists were alphabetically organized by contact last name and it was used to generate the final list of contacts. Each list may have had several lines of data for one contact, for example each instance of a TST or IGRA test[iv] was listed in a separate line. This format required summarizing the TST/IGRA history into one line; a process of individually assessing each line to move the appropriate data into new columns associated with the contact. The TST/IGRAs that were done in context of the contact investigation of the source case in the study period were included; and temporally listed as TST1 and TST2 using date of contact to indicate first in the episode. For TST/IGRA performed after the date of contact indicated and documented by the TB Program but within 8 weeks minus a day of that date were labelled TST1. Designations of TST2 were for those results a minimum of 56 days after date of contact but within the context of that CI. If a TST/IGRA was performed a year later but for a different reason i.e. another episode of TB exposure, it was not included as it and its related outcomes and actions were not in the context of the CI in question. In addition, the most recent TST/IGRA result prior to the event was included in order to determine any conversions in the context of the CI of interest. Previous positive TSTs (a prior history of disease were considered as “previous positive TST”) were noted and coded to indicate that no TST/IGRA was warranted in this contact investigation, so as to not under report this field in our outcome analysis. Several elements (DOB, history of LTBI and disease with associated treatment

completion, BCG, number of times named as a contact in Alberta) required individual location of the client's file in iPHIS and manual extraction to find the elements not provided as an electronic output by iPHIS. Subsequently, these data elements required manual entry into the database.

Chest X-ray dates provided in the iPHIS QR excel printouts did not necessarily reflect the contact episode under study. This information was relevant for contacts that had had more than 2 Chest X-rays or mulitple episodes of TB within the Province of Alberta. Therefore, manual interrogation, extraction and documenting of results from iPHIS were required. The first CXR completed after the date of contact documented was deemed CXR1 and the last completed for the contact event (within 36 months) was CXR2.

The contacts were assigned a similar coding system to the cases, although they were listed alphabetically and subsequently numbered in that order. The source case assigned identifier was the prefix for each corresponding contact, such that the identifier was (YY-##-##, e.g. 01-01-01 is contact one of source case one diagnosed in 2001). Calculation of 'time to' for both TSTs and CXRs was calculated by determining number of calendar days from contact date to diagnostic event in question using standard excel formula functions.

The unique, system-generated TB registry number of each contact was interrogated in the TB registry to determine whether there was any documentation of disease diagnosed after the date of contact and up to December 2013. For contacts of cases identified in the earlier list of cases, their subsequent period of time to determine if disease developed was longer. i.e. contact from 2001 had 11-12 years of post contact surveillance. Cases that were identified during and after the contact investigation period following source diagnosis were categorized into 6 groups; those linked by DNA fingerprinting data (IS6110 RFLP patterns), those clinical cases linked by epidemiology only (named on contact list) and those who were named as contacts, who had

culture confirmed disease but whose RFLP pattern was discordant to that of the source case and whether diagnosis occurred within or outside set time boundaries of 6, 12 and 36 months. **See Figure 3**

	Concordant RFLP pattern	Epidemiological link	Discordant RFLP pattern
Diagnosed ≤36 months post contact	1	2	3
Diagnosed >36 months post contact	4	5	6

Figure 3 Coding Process for Cases identified as contacts

Once the contact information for all source cases for each study year was finalized, additional fields of data were added to reflect and connect their outcomes to source case features (population group, smear status, gender, age, HIV status). These lists were then combined into a master list reflecting cases and their contacts' features and outcomes for the study period.

The master list was prepared for transfer into SAS. For descriptive analyses count/frequency and Mean/STD for different population groups were reported, respectively. The differences in frequencies and means were tested by chi square test and t-test, respectively. Fisher exact test was used when the expected number of counts was less than 5. Outcomes of CI were compared for TB cases among ABO, ABN and CBO based upon smear status.

In development of the prediction model, logistic regression analyses were used to determine the significant factors associated with outcomes of contact investigation in the univariate analysis. All of the factors that were significant at a 20% level in the univariate analysis were considered for multivariate analysis. A purposeful selection method was used to determine important factors in the multivariate regression. SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) was used for the statistical analysis.

Exclusion

TB cases found in Foreign Born persons are not included in this study. Firstly, there is evidence of little transmission to Canadian-born persons (Kunimoto, Sutherland, Wooldrage, et al., 2004) and thus, this population does not contribute significantly to the presence of TB in Canadian-born persons. Secondly, the research question is focused on the epidemiology of TB in the First Nations Peoples of Canada and the ongoing transmission variance among those on- and off-reserve. Finally, Aboriginal Peoples in Canada have a very different history of TB than Foreign Born persons, who are predominantly infected outside of Canada. The incidence of active TB disease among FB persons in Canada is as likely to be influenced by CI practices, it is more likely to be influenced by other screening and treatment efforts as suggested elsewhere (Varghese, Langlois-Klassen, Long, et al., 2014)

Results

Source Cases. There were a total of 171 source cases identified using the eligibility criteria discussed above. **See Table 1**. Of these, 49 were of Aboriginal descent and lived on reserve (ABO), including 1 Métis and 48 Registered First Nations Registered, 62 were of Aboriginal descent but living off-reserve (ABN); of these 30 were registered FN, 24 Métis, 3 Inuit, 5 non-registered FN, finally there were 60 Canadian-born other persons (no Aboriginal descent); representing 29, 36 and 35% of the total cases in the study period respectively. The preponderance of cases of Aboriginal descent versus CBO is reflective of the higher incidence rate among this group. Further, 29 of the ABN were associated with homelessness or the inner city of Edmonton, whereas only 8 of the CBO were.

Table 1

Source Case Characteristics by Population Group

	Aboriginal On Reserve n(%)	Aboriginal Off Reserve n(%)	Canadian - Born "other" n(%)	p value
Number assessed	49(29)	62(36)	60(35)	
Average Age (years ±SD)	45(19)	49(16)	55(18)	**0.01**
Age Group (years) 15-44	26(53)	25(40)	16(27)	**0.02**
45-64	15(31)	26(42)	28(47)	**0.22**
65+	8(16)	11(18)	16(27)	**0.33**
Sex Male	32(65)	33(53)	47(78)	**(0.01)**
Female	17(35)	29(47)	13(22)	
Smear Status				
Pos	28(57)	40(65)	31(52)	**(0.35)**
Neg	21(43)	22(35)	29(48)	
HIV status Pos	4(8)	8(13)	1(2)	**(0.18)**
Neg	38(78)	48(77)	51(85)	
Unknown/not done	7(14)	6(10)	8(13)	

The average age of the cases was significantly different across population groups being 45 years for ABO, 49 for ABN and 55 for CBO. Distribution of the cases into age categories varied between groups. For ABO, the majority of their cases were young adults in the 15-44 age group (p=0.02). Distribution of the cases into the older age categories did not demonstrate a

significant difference between groups. However, the majority of cases for ABN and CBO were in the 45-64 age group.

Male was the predominant sex across all populations groups, however, the largest majority was in CBO with 78%, which was significantly different from other cases (P=0.01). There was a fairly even distribution of sex in the ABN with females accounting for 47% of cases.

Smear status did not differ between population groups (p=0.35), although ABN had a stronger majority of cases that were positive at time of diagnosis. There was also no difference between population groups with known HIV positivity or those whose status was unknown (p=0.18).

Contact Investigation Composition. A summary of the size of the contact lists for each group is summarized in **Table 2**.

Smear Positive Source Case. The most statistically significant difference seen between groups was for the average number and median number of close contacts (p=0.01 and <0.001) respectively. Between each measure, CBO had the lowest average number and median number of named close contacts with 15.3 and 7 respectively. For ABN, the average and median number were 17.3 and 11.5 respectively. ABO had the highest average and median number of close contacts with 32.1 and 28 respectively. Only the average number of other contacts was marginally significant (p=0.048) between groups with ABN having the highest at 82 and ABO the lowest at 31 CBO falling in the middle with 36. The lack of statistical difference between median numbers of contacts among other contact types is likely due to several ABN source cases, who's CIs were quite extensive involving approximately 250-750 contacts, hence this use of median number. Of note is the difference (p<0.001 and 0.002) between population groups in the median number of close and other contacts per case that had a history of having been recommended for treatment of latent or active disease, with both Aboriginal groups having contacts with this medical history.

Table 2

Contact Characteristics by Case Population Group and Smear Status of Source Case

		Smear positive				Smear Negative			
		Aboriginal On Reserve n	Aboriginal Off Reserve n	Canadian-Born "other" n	P value	Aboriginal On Reserve n	Aboriginal Off Reserve n	Canadian-Born "other" n	P value
Total number contacts		1766	3952	1600		281	125	234	
Contact type	**Close**	898	690	474		226	113	163	
	Other	868	3262	1126		55	12	71	
Average number contacts per case by contact type	**Close**	32.1	17.3	15.3	**0.01**	10.8	5.1	5.6	**0.04**
	Other	31	82	36	**0.048**	2.6	0.5	2.4	**0.09**
Median number contacts per case by contact type	**Close**	28	11.5	7	**<0.01**	10	3	3	**0.02**
	Other	23.5	28	10	**0.26**	1	0	1	**0.03**
Median number history TB infection/disease per case by contact type	**Close**	3	1	0	**<0.01**	1	0	0	**0.017**
	Other	2.5	1	0	**0.002**	0	0	0	**0.03**

Smear Negative Source Case. Within the Province of Alberta, CI activities for smear-negative cases (who are less likely to be infectious) are not as aggressively pursued as with smear-positive source cases. As such, while there were some notable differences among the contacts of smear-negative cases, the numbers tended to be quite a bit lower (the yield being lower due to there being less of an effort by the program to find contacts outside of the initial "close" circle). Among smear negative cases, similar significant differences were noted as with smear positive source cases; although the average and median number of contacts per case was lower overall for the reasons provided above. As seen with S+ ABO cases, S- cases had higher average and median number of close contacts. In contrast to S+ cases, CBO had the second highest average and median number of close contacts while ABN had the lowest. Average and median number of close contacts for ABN were consistently approximately half that for average number and a third that for median number when compared to ABO.

Contact Profile. Other than contact type, sex and age were the most consistent descriptors of the contacts documented in iPHIS and included for study. **Table 3** indicates the average age of contacts in all categories by source case smear status and population group.

Table 3

Average Age of Contacts (years)

	Smear Positive			**P value**	**Smear Negative**			**P value**
	ABO	ABN	CBO		ABO	ABN	CBO	
Average age of contacts	30	40	46	<0.01	30	37	46	0.002

Among smear positive cases, the average age of the contacts within ABO, ABN and CBO population groups were 30, 40 and 46 years respectively, which represents a difference between the groups (P<0.001).

A more detailed summary of contact age group and sex with respect to source case population group and smear status is included in **Table 4** and **Appendix D**. The observation of

younger average age of contacts for ABO was also seen in the contact group of smear negative cases (0.002). Except for the male S+ cases in ABN and CBO, the 15-44 age groups is the predominant age of contacts, which reflects its broad age inclusion in a low mortality peer group. In addition, contacts within the 0-14 age group was higher among ABO as compared with Canadian-born others and ABN. With respect to gender, similar proportions of age groups are observed more commonly between all S- cases, which is likely a reflection of the smaller contact list size and of S- CIs including more being close contacts, thus providing a proxy or representation of the structure of the source case's household. Whereas, among S+ cases, more casual contacts are named, representing a more heterogeneous group depending upon the cases' employment or social circumstances. Among S+ cases, similar proportions of age groups in each gender group are noted with ABO; the same is noted for ABO smear negative cases. However, more imbalances of proportions in age groups between genders are seen for ABN and CBO smear positive cases. For the ABN S+ cases, there is a fairly equal distribution of contacts in the age groups 15-44 and 45-65 for male source cases; likely a reflection of the several cases being associated with the inner city and subsequently large contact lists involving shelters, which tend to be male dominated.

Table 4

Contact's Age Group by Source Case Population Group

	ABO S+	**ABN S+**	**CBO S+**	**ABO S-**	**ABN S-**	**CBO S-**
Contact age group	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
0-14	407(23)	199(5)	166(10.4)	67(23.8)	22(17.6)	17(7.3)
15-44	911(51.6)	1913(48.4)	683(42.7)	122(43.4)	68(54.4)	122(52.1)
45-64	364(20.6)	1618(40.9)	516(32.3)	61(17.6)	22(17.6)	71(30.3)
65+	84(4.8)	222(5.6)	235(14.7)	31(10.4)	13(10.4)	24(10.3)
TOTAL	**1766**	**3952**	**1600**	**281**	**125**	**234**

Contact Screening Activities. It was anticipated that the proportion of close contacts receiving a baseline skin test would be higher than other contacts, given the concentric circle approach. This was observed consistently for S+ source cases' contacts; however a reverse trend was observed for contacts of S- cases, where baseline testing completion rates for other contacts rates surpassed that of close contacts (**see Table 5** and **Appendix E**). The proportion of S+ close contacts who required and completed a baseline TST was highest with CBO source cases at 84.2%, followed by ABO at 73.8% and ABN with the lowest proportion at 69.4% (p=<0.01). However, the proportion of S+ close contacts with a positive TST (new or historical) who completed the subsequent CXR within 6 months was highest among ABO with 83.8%, followed by CBO and ABN with 77.5% and 73.9% respectively (p=0.02). Corresponding rates for S- contacts were lower than S+ counterparts, although no statistically significant difference between population groups was noted. Completion of a second TST a minimum of eight weeks past contact for eligible contacts was often higher than baseline across population groups with the exception of CBO, indicating better completion of assessment. Comparing population groups with the same smear status for completion of 8 week TST close and other contacts demonstrated no difference (p=0.27/0.20) in S- cases. However a difference was seen with both types of contacts of S+ cases (<0.001) with ABN demonstrating dramatically lower completion rates when compared to ABO and CBO.

Table 5

Contact Screening Activities (all ages) for Smear Positive Source Cases

		ABO n(%)	ABN n(%)	CBO n(%)	p value
total number contacts	Close	898	690	474	
	Other	868	3262	1126	
# without previous + TST documented at baseline	Close	709	558	436	
	Other	673	2815	1031	
# TST done at baseline	Close	523 (73.8)	387 (69.4)	367 (84.2)	**<0.01**
	Other	396 (58.8)	890 (31.6)	630 (61.1)	**<0.01**
# without previous + TST documented at 8 week	Close	582	476	392	
	Other	621	2700	926	
# with Second TST after 8 weeks	Close	475 (81.6)	293 (61.6)	334 (85.2)	**<0.001**
	Other	459 (73.9)	879 (32.6)	670 (72.4)	**<0.001**
# TST+ CXR within 6 m	Close	275 (83.8)	167 (73.9)	69 (77.5)	**0.02**
	other	201 (74.2)	307 (50.2)	181 (82.6)	**<0.01**

Timeliness of Assessment

Time to First TST. For contacts over the age of 4, time to assessment is an important indicator of efficiency of the CI. **See Table 6**. Average and median time to first TST between populations groups was predictably longer for other contacts; however the CBO S+ contacts had the smallest difference between close and other contacts. Only contacts of Aboriginal S+ cases had time to first TST long enough on average for other contacts to reflect the expected delay before extending the CI; but this was not observed with the median time. Between population groups, differences were noted when considering time to first TST for both close and other

contacts (P=0.03/ <0.01). Close contacts of S+ ABN cases had the longest average and median time to first TST; CBO and ABO had relatively similar times to first TST. However, for other contacts of S+ ABO cases had the longest average and median time to first TST compared to ABN and CBO (p<0.01/p<0.01).

Table 6

Timeliness of Assessment for Contacts Ages ≥5 of Smear Positive Source Cases

	Contact type	ABO	ABN	CBO	P value
number of first TSTs done baseline	Close	444	352	314	
	other	367	872	625	
Time to first TST (average/median)	Close	39/9	44/17	30/8	**0.03/<0.01**
	other	61/29	57/25	39/16.5	**<0.01/<0.01**
Number of initial CXRs done	Close	448	236	113	
	other	310	567	237	
Time to first CXR (average/median)	Close	73/12	96/25.5	97/14	**0.16/<0.01**
	other	108/34	166/72	79/34	**<0.01/<0.01**

Time to CXR. Another measurement of timeliness of assessment is time to first CXR which is a vital component of assessment for TST+ contacts. The time to first CXR ought to be longer than time to first TST and this was observed across all population groups. Median time to first CXR

was lowest for S+ ABO close contacts (Put time in days here) ($p<0.01$). This contrasted to other contacts of CBO S+ cases who were assessed sooner than other population groups ($p<0.01$).

Vulnerable Contacts, For close contacts under the age of 5, differences were noted between population groups for both average and median time to first TST and first CXR. **See Table 7** Average and median time to the first TST differed significantly between groups ($p=0.01$) with CBO contacts obtaining their first TST much faster after exposure compared to other groups. For CXR, CBO had the shortest time and ABN being longest time to completion. Comparatively, all less than 4 years of age time measurements were less than their over 5 year counterparts.

Table 7

Timeliness of Assessment Close Contacts Ages <5 of Smear Positive Source Cases

	Contact type	ABO	ABN	CBO	P value
Number identified	Close	101	44	56	
Number of first TSTs done	Close	79	32	50	
Time to first TST (average/median)	Close	28/7	23/10	4.7/3	**0.01** **<0.01**
Number of initial CXRs done	Close	87	31	52	
Time to first CXR (average/median)	Close	19/8	31/20	4.4/1	**<0.01** **<0.01**

Screening Outcomes

Preventive Therapy for Contacts Ages 5 and Up. There was great variability in the acceptance of preventative therapy among contacts of S+ cases across population groups. **See Table 8 and Appendix F** Among contacts of S+ cases, the close contacts of ABO had the highest acceptance rate at 72.7% which was significantly different than the rate for CBO and ABN (p=0.04). For those that accepted preventative therapy, the highest rate of completion of treatment was also observed among close contacts to S+ ABO cases at 73.7%, which was again different than ABN and CBO (P=0.045). If the rate of completion of treatment among all contacts offered preventative therapy is observed, only close contacts of S+ ABO had a rate over 50% (53.6%). In absolute numbers, 826 contacts of S+ Canadian-born cases were offered LTBI treatment and of those, 329 or 39.8% completed over a 10 year period; which is about 32.9/year. Of these, 149 were contacts to ABO, 113 to ABN and 67 to CBO.

Table 8

Preventive Therapy Outcomes ages ≥5 for Smear Positive Source Cases

		ABO n(%)	ABN n(%)	CBO n(%)	P value
# recommended	Close	209	120	68	
	other	125	189	115	
# accepted	Close	152 (72.7%)	71 (59.2%)	46 (67.6%)	**0.04**
	other	56 (44.8%)	109 (57.7%)	72 (62.6%)	**0.01**
# completed	Close	112 (73.7%)	49 (69.0%)	25 (54.3%)	**0.045**
	other	37 (66.1%)	64 (58.7%)	42 58.3%)	**0.60**
% completed / offered	Close	53.6%	40.8%	36.8%	**0.02**
	other	29.6%	33.9%	36.5%	**0.51**

Preventive Therapy for Vulnerable Contacts. A priority of CIs is to identify and prioritize the most vulnerable contacts for screening and assessment, given a higher risk of progression to disease and negative outcomes among those contacts. Vulnerable contacts benefit from 'window prophylaxis', which provides immediate chemotherapeutic protection against progression to disease during the first 8 weeks post final contact with the source case when it is not always feasible to know whether infection has or has not occurred. However, given that the information on underlying medical conditions was not systematically collected on contacts during the study years, the program and this analysis are both limited in determining the relative success of strategies for prioritizing potentially vulnerable contacts. In this analysis we did use age as a proxy for "vulnerability", with the understanding that any close contacts of S+ cases who were less than 5 years of age would have been prioritized by the program.

A summary of the assessment and management of these vulnerable contacts (<5 years, close contact of S+ case) is found in **Table 9**. A total of 201 vulnerable contacts were identified using these criteria. Of these, 101 were contacts to ABO, 44 for ABN and 56 for CBO. Of importance in this group overall is timely assessment and initiation of window prophylaxis. One concern was highlighted by this analysis, was that the rate at which contacts of Aboriginal cases on and off reserve was offered window prophylaxis. Only 50% of the off-reserve and 58.4% of the on-reserve vulnerable Aboriginal contacts were offered window prophylaxis, as compared to 91.1% of the vulnerable contacts of CBO cases ($P<0.01$). Another concern is the documented acceptance rate of prophylaxis among contacts to ABN cases of only about 50%,. Contacts of ABO and CBO cases accepted at a rate of 76.3 and 88.2% respectively ($p<0.01$) indicating a significant difference. However, of those who were required to complete the prophylaxis based upon their 8 week TST result, all of the ABN contacts completed the medication, followed by ABO with 92.3 and none of the CBO contacts ($P<0.01$).

Table 9

Vulnerable Close Contacts (ages <5) of Smear Positive Source Cases

	ABO	ABN	CBO	P value
# contacts	101	44	56	
Offer ltbi	59 (58.4%)	22 (50%)	51 (91.%)	**<0.01**
accept	45 (76.3%)	11 (50%)	45 (88.2%)	**<0.01**
Repeat neg	32	4	42	
infected	13	7	3	
Completed	12 (92.3%)	7 (100%)	0 (0%)	**<0.01**

Evidence of Transmission

Transmission events, including documented converters and cases, are represented in **Table 10a**. A total of 143 transmission events were noted for all cases, with 30 of these being diagnosed as cases within 6 months. With the exception of 1, all of these aforementioned cases were contacts to S+ cases. Of these, 20 were culture confirmed and had a matching RFLP pattern to the source case (type 1 case). The remaining 10 were clinical cases (no culture to fingerprint) with epidemiological links to the source case; typically seen in children from whom getting culture confirmation is challenging (type 2 case). Extending the period of surveillance to 12 months post source case diagnosis unmasked an additional 2 secondary cases with a matching fingerprint (RFLP). Further extending the surveillance window to 36 months post diagnosis of the source case yielded 4 more secondary cases; 2 with matching RFLPs and 2 with epidemiological links. (**See Table 10b**) The secondary cases found in 36 months were not listed on any additional subsequent contact list before their diagnosis, suggesting they are secondary cases to the source case whose CI was under review in this study. When the surveillance period was extended beyond 36 months, 3 more secondary cases confirmed by RFLP to a source case whose CI was under review were found.

Table 10a

Transmission Events (cases and converters) for Smear Positive Source Cases

		Smear Positive				p value
		ABO n(%)	ABN n(%)	CBO n(%)	total	
Transmission Events	Close	33 (4.7)	19 (3.4%)	10 (2.3)	62	**0.11**
	Other	18 (2.7)	33 (1.2)	22 (2.1)	73	**<0.01**
		Smear Negative				**p value**
		ABO n(%)	ABN n(%)	CBO n(%)	total	
Transmission Events	Close	4 (2.1%)	2 (2.2%)	2 (1.4%)	8	**0.81**
	Other	0	0	0	0	-

Table 10b

Type 1 and 2 Secondary Case Type Diagnosis by Population Group Over Time

Time from contact	ABO		ABN		CBO		total	
	Type 1	**Type 2**	**Type 1**	**Type 2**	**Type 1**	**Type 2**	**Type 1**	**Type 2**
6 months	14	5	5	4	1	1	**20**	**10**
12 months	1	1	-	-	-	-	**1**	**1**
24 months			1	1		1	**1**	**2**
36 months	-	-	1	-	-	-	**1**	**-**
total	**15**	**6**	**7**	**5**	**1**	**2**	**23**	**13**

Unexpected case finding also occurred during the course of CI activities. Twelve confirmed secondary cases were identified in the 36 month period after the date of diagnosis of the source case, but whose RFLP did not match that of the source case. Similarly, 7 more

secondary cases were found after the 36 month surveillance period, also with un-matched RFLP patterns, however the diagnoses of these 7 secondary cases was not associated with the CI itself.

In addition to these screening outcomes, 5 cases found during the CI were children under age 5; 3 had ABO as a source case and were all ABO also, 1 had an ABN source case and was also ABN and the final was a CBO child also with corresponding source case. Of the 5 children <5 years of age who were cases, 2 were found to be TST + at baseline at 1 and 5 days from date of contact, both ABO. Another ABO child was found to be a converter with the second TST occurring 66 days from contact. The other 2 cases, ABN and CBO did not receive TSTs but CXRs were completed 125 and 46 days from contact respectively. All of these cases were clinically diagnosed with no confirming culture and thus fingerprint confirmation. With the exception of the ABN, the children were all close contacts. For the ABN child, the CXR delay appears appropriate given their contact status as other and assessment would have been initiated later than close contacts, however, for the ABO child who's CXR did not occur until 186 days post contact, the delay does not fit with the expected timeline, suggesting perhaps another delay lack of or access to CXR facilities or poor compliance. The concordance of source case population group with that of their secondary cases demonstrates transmission staying within population groups almost exclusively as previously found (Kunimoto et al., 2004).

Predictors of Converters and Cases (type 1/2) Found During Course of CI Table 11

Logistic regression analysis demonstrated significant predictors of finding converters and cases either linked by RFLP or by conventional epidemiology within a 36 month period of time following source case identification. Smear status of the source cases was a strong predictor with S+ cases being 7.5 times more likely to have converters and cases found during CI ($p=0.006$). The age category of the source case was also a predictor of this outcome ($p=0.01$) with the younger age group of 15-44 years being 3.4 times more likely to have this outcome in their contacts. Further, being a close contact was a strong predictor ($p<0.001$) of this outcome.

Neither the population group nor HIV status of the source case was a significant predictor of this outcome.

Table 11

Predictors of Transmission Events

Predictor	Detail	OR	p value
Smear status of source case	POS	7.5	**0.006**
	NEG	1	
Reserve Status of source case	Aboriginal ON	4.7	0.08
	Aboriginal OFF	1.8	0.51
	CBO – N/A	1	
Age category of source case	15-44	3.4	**0.01**
	45-64	1	0.77
	65+	1.2	
Contact type	Close	5.5	**<.001**
	Other	1	
HIV status of Source case	Positive	3.1	0.11
	Status unknown	2.0	0.28
	Negative	1	

Predictors of successful CI

Completion of a Required 8 week TST Table 12a. Population group of the source case was a predictor of this outcome with ABO and CBO 17.7 and 15.0 times more likely to complete a required 8 week TST, respectively (p=0.0031 and 0.0123). Compared to CBO, ABN were 15 times less likely to complete the 8 week TST (p=0.0123). Female gender of the source case was a predictor with contacts of female cases being 11 times more likely to complete (p=0.0358) than male cases, however, gender of the contact was not significant. The age category of the source case and the type of contact (close, other) were not significant in predicting this outcome.

Completion of CXR Within 6 months for Positive Reactors (new or historic) Table 12b. Source case population group was a predictor of this outcome with ABO being 5.5 times more likely to complete the CXR (p=0.0015) when compared to ABN, and 11.5 times more likely than CBO (0.0006). Contacts of smear positive cases are 19.8 times more likely to complete this outcome (p=0.0005), whereas contact type, close or other, was not. Gender and age category of

the source case was not a predictor of this outcome. However, contacts that had a history of treatment of TB disease or LTBI who were recommended or completed treatment were 2.7 times more likely to complete their CXR than those without such a history (0=0.0011).

Acceptance of Preventative Therapy When Offered Table 12c. The only predictor of this outcome was the smear status of the source case; with contacts of smear positive case being 16.6 times more likely to accept (p=0.0129). Gender of the contact was not a predictor of this outcome. Age of the contact at time of assessment was significant, but unlikely to have any clinical impact given the very small differences between age groups (overpowered) (p=0.0305). Unfortunately, very little about the contacts themselves had any predictable impact on this outcome.

Completion of Accepted Preventative Therapy Table 12d. Compared to CBO, contacts of ABO were 20.8 times more likely to complete prophylaxis (0.0064). Contacts of smear positive cases were 24.8 times more likely to complete prophylaxis (p=0.0001). Contact type was not associated with completing prophylaxis nor was gender and age of contact.

Table 12a

Predictors of Completion of 8 week TST

Predictor	detail	Estimate	p value	Estimate	p value
Reserve status	CBO – N/A	15.0	**0.0123**	0.0	
	Aboriginal ON	17.7	**0.0031**	2.6	0.6337
	Aboriginal OFF	0.0	.	-15.0	**0.0123**
Gender of source case	F	11.0	**0.0358**		
	M	0.0	.		
Smear status of source case	NEG	0.7	0.8841		
	POS	0.0	.		
Age category of source case	15-44	-4.2	0.4794		
	45-64	-11.3	0.0681		
	65+	0.0	.		
Gender of contact	F	0.0	0.4055		
	M	0.0	.		
Contact type	Close	0.0	0.7997		
	Other	0.0	.		

Table 12b

Predictors of Completion of CXR Within 6 months for Positive Reactors (new or historic)

Predictor	detail	Estimate	p value	Estimate	p value
Reserve status	CBO – N/A	-6.0	0.0717	0.0	
	Aboriginal ON	5.5	**0.0015**	11.5	**0.0006**
	Aboriginal OFF	0.0	.	6.0	0.0717
Gender of source case	F	0.8	0.7176		
	M	0.0	.		
Smear status of source case	NEG	-19.8	**0.0005**		
	POS	0.0	.		
Age category of source case	15-44	3.8	0.1801		
	45-64	1.9	0.5673		
	65+	0.0	.		
Contact type	Close	-1.5	0.3591		
	Other	0.0	.		
History of TB treatment or recommendation(latent/active)	NO	-2.7	0.0011		
	YES	0.0	.		

Table 12c

Predictors of Acceptance of Offered Preventative Therapy

Predictor	detail	Estimate	p value	Estimate	p value
Reserve status	CBO – N/A	-2.0	0.7933	0.00	
	Aboriginal ON	9.5	0.1979	11.53	0.1377
	Aboriginal OFF	0.0	.	2.01	0.7933
Gender of source case	F	-0.9	0.8914		
	M	0.0	.		
Smear status of source case	NEG	-16.6	**0.0129**		
	POS	0.0	.		
Age category of source case	15-44	2.0	0.8153		
	45-64	-2.9	0.7381		
	65+	0.0	.		
Contact type	Close	0.0	**0.0289**		
	Other	0.0	.		
Gender of contact	F	0.0	**0.157**		
	M	0.0	.		
Age of contact		0.0	**0.0305**		

Table 12d

Predictors of Completion of Accepted Preventative Therapy

Predictor	detail	Estimate	p value	Estimate	p value
Reserve status	CBO – N/A	-13.2	0.0566	0.0	
	Aboriginal ON	8.9	0.1826	20.8	**0.0064**
	Aboriginal OFF	0.0	.	10.7	0.166
Gender of source case	F	7.5	0.2101		
	M	0.0	.		
Smear status of source case	NEG	-24.8	**0.0001**		
	POS	0.0	.		
Age category of source case	15-44	-3.7	0.6494		
	45-64	-4.1	0.6126		
	65+	0.0	.		
Contact type	Close	0.0	0.6287		
	Other	0.0	.		
Gender of contact	F	0.0	0.0958		
	M	0.0			
Age of contact		0.0	0.3011		

Chapter 3: Conclusions and Recommendations

Discussion

International standards for tuberculosis care include recommendations on the public health follow up of contacts by TB CARE (2014). Emphasis is placed upon the highest risk contacts based upon age, immune-competency, symptoms and those exposed to drug resistant TB. This is especially relevant in resource poor high incidence settings. As seen in the data presented in this thesis, a high income and low incidence area like Alberta benefits from resources that allow for more extensive CI for patients of all ages and type of exposure. However, how fruitful those extensive investigations have proven to be important to determine if public health funds are being utilized at the best efficiency.

Our examination of contact investigations for Canadian-born tuberculosis cases highlighted significant differences across Canadian-born population groups. Aboriginal source cases both on and off reserve are, on average, younger. The majority of ABO cases were found in an age group more associated with child bearing years and thus, higher likelihood of pediatric exposures. In support, it was noted that both S+ and S- ABO cases, had larger proportions of contacts in the 0-14 age group and also had higher average numbers of close contacts per case. Completion of LTBI treatment for contacts aged 5 and up was higher for ABO close contacts compared to ABN and CBO. The same marker for under aged 5 close contacts was in excess of the provincial performance target of 80% for both Aboriginal groups. Overall, despite variance across groups on several markers of contact assessment and care, CI for ABO S+ cases had more favorable outcomes when compared to ABN and CBO. Although ABN were anticipated to have poorer outcomes; the superiority of CI in ABO cases compared to ABN and CBO was unexpected due to assumed health access barriers for those living on reserve.

The number of close contacts per case in this study (notably for S+ cases) was on average, larger across all population groups than noted in most reviews of CI in the literature. BCCDC (2013) reported an average number of 19.8 contacts per case but it was not delineated by contact type or by population group. Despite the larger numbers of contacts requiring assessment, ABO and CBO S+ cases had respectable success in completion of TSTs at baseline and at 8 weeks. In a recent systematic review by Fox, Barry, Britton & Marks (2013), the prevalence of active disease for all contacts in high income countries was 1.4%, and increased to 1.9 % for close contacts and decreased to 0.4% for casual contacts of S+ cases, including FB persons. In this thesis, it was found that the proportion of transmission events (cases and converters) was not different between population groups for close contacts of S+ and S- cases (range 2.3- 4.7 S+, 1.4-2.1% S-). This suggests that the efficiency of the CI in finding and preventing secondary cases among close contacts was similar for all three groups.

The contact investigation data points to inequalities of health determinants between population groups. In particular, the higher housing density in First Nations reserve communities compared to off reserve Aboriginal and 'other' Canadian-Born is well documented (Health Co-Management Secretariat, 2010 & National Collaborating Centre for Aboriginal Health, 2010) and is reflected by some of the findings. ABO cases had the highest number of close contacts named, likely reflecting this increased density and/or a more communal living environment. Further, proximity to contacts may contribute to disproportionate rates of TB between population groups, as increasing TB incidence has been linked to the number of persons per room (Clark, Riben & Nowgesic, 2002). However, ABO ethnicity did not predict transmission events nor were differences noted between groups ($p=0.08$). This suggests sufficient CI effort and success for ABO. The disproportionate rates of disease between CBO and Aboriginal Peoples are not necessarily dependent upon CI inefficiencies.

The average age of contacts between S+ population groups likely represent different social structure and family composition. For ABO, ongoing transmission in the communities will impact the younger age groups and thus future cases, whereas among CBO, the cases are generally older and thus would have contacts in a similar age group to themselves which is beyond a typical age group associated with childbearing years. Families with younger children appear to be more impacted in the CIs of ABO cases. However, for contacts of Aboriginal cases in general, the picture is one of potential TB transmission to the pediatric and child bearing age group. It is most critical then, that despite strong LTBI treatment completion rates in the less than 5 age group, the lower rate of offering window prophylaxis for both Aboriginal groups needs to be improved.

Several potentially important pieces of information were unfortunately, not included among the information routinely collected. It demonstrates a need for more consistent and expanded information gathering and documentation for contacts. The CDC guidelines (2005) has indicated several that could be a value and such information, had it been collected, might have influenced outcomes of CI or predictors. This includes information on ethnicity, country of birth, and more exposure information regarding time and location detail and any medical risk factors that put the infected contact at risk for active disease (**See Figure 4**). Although population group of the source case is known for all included in this study, the population group of the contact is not routinely entered unless they become cases or suspect cases themselves. The exception is the frequent completion of the ethnicity field in iPHIS for peoples living on reserve as their band name is captured. There is difficulty in the inconsistent documentation of population group and thus, the limited capacity to investigate CBO or ABN for epidemiological risks or predictors.

More detailed information regarding contacts would also assist with prioritizing them for follow up and assessment. Identification of persons with immune-compromising conditions

allows for interventions that could interrupt transmission or disease development in these vulnerable contacts. Several factors are well documented as being associated with higher risk for TB disease as outlined in the 7th edition of the Canadian TB standards (2014) **See Figure 4**. However, the contact lists are often constructed using the assistance of the case themselves who may not be privy to the health status of contacts or may not feel it appropriate to divulge. More effort on interviewing contacts in a timely fashion and obtaining this information is a function of human resources and skill. Areas with low incidence, this skill is not practiced sufficiently to influence quality and often, training or skill development for interviewing and constructing a contact list may not be prioritized within the Public Health program. However, in areas of higher incidence, the skill may be more available given the frequency with which is it required. For follow up of cases in reserve communities, this skill is commonly used given the higher rates of disease and availability of TB specific resources and personnel with TB experience and knowledge. Whether this did impact timeliness of CI for ABO cannot be quantified beyond young children, the only vulnerable group examined. Further, the presence of a Community Health Representative (CHR) in FN communities provides additional connection to the community and often knowledge of the residents and their families. Whereas for cases residing off reserve, the Aboriginal population does not have a definitive infrastructure serving their health needs. Rather, their TB care falls under either of the outpatient clinics or the Provincial Clinic depending upon their location in the province.

Table 1. Risk factors for the development of active tuberculosis among people with a positive tuberculin skin test (presumed infected with *Mycobacterium tuberculosis*)

Risk factor	Estimated risk for TB relative to people with no known risk factor	Reference number
High risk		
Acquired immunodeficiency syndrome	110 - 170	5
Human immunodeficiency virus infection	50 - 110	6, 7
Transplantation (related to immune-suppressant therapy)	20 - 74	8 - 12
Silicosis	30	13, 14
Chronic renal failure requiring hemodialysis	7 - 50	15 – 18, 46, 47
Carcinoma of head and neck	11.6	19
Recent TB infection (≤2 years)	15.0	20, 21
Abnormal chest x-ray – fibronodular disease	6 - 19	22 - 24
Moderate risk		
Tumour necrosis factor alpha inhibitors	1.5 - 5.8	25, 26, 43
Diabetes mellitus (all types)	2 - 3.6	27 - 29
Treatment with glucocorticoids (≥15mg/d prednisone)	4.9	30
Young age when infected (0-4 years)	2.2 - 5	31
Slightly increased risk		
Heavy alcohol consumption (≥3 drinks/day)	3 - 4	32, 33
Underweight (<90% ideal body weight; for most people, this is a body mass index ≤20)	2 - 3	34
Cigarette smoker (1 pack/day)	1.8 - 3.5	35 - 38
Abnormal chest x-ray – granuloma	2	24, 39
Low risk		
Person with positive TST, no known risk factor, normal chest x-ray ("low risk reactor")	1	40
Very low risk		
Person with positive two-step TST (booster), no other known risk factor and normal chest x-ray	0.5	Extrapolated from 40 and 1

Taken from Canadian TB Standards, 7th Edition, 2014 pg 127

Figure 4 Risk factors for development of active TB disease

One priority in CI is to always identify the highest risk contacts at risk for advancement to disease for priority screening and assessment, given the higher risk of advancement to disease and negative outcomes. These contacts benefit from 'window prophylaxis', which provides chemotherapeutic protection against advancement to or negative outcomes of disease until such time as infection can be ruled out at 8 weeks with a TST. However, given that information on the medical status of contact was not routinely collected limited the ability to analyze relative success of priority screening. However, identifying a vulnerable group in this analysis was possible utilizing age of contact and analyzing those being less than 5 yrs of age and close contacts to S+ cases.

Completion of screening and assessment during a CI is shown to be more successful for ABO than for ABN, however CBO almost exclusively demonstrate better completion of TST in the context of a CI. With respect to the completion of CXR following a positive TST, a critical follow up requirement of contacts who do not take prophylaxis, the reverse of this occurred. This suggests that despite having lower TST completions overall when compared to CBO, ABO complete follow up at a higher rate. Currently, no performance target is identified for either of these measurements within Alberta or noted elsewhere in the literature. However the differences shown can be used to identify service gaps and used as markers for improvement to nullify the differences between population groups.

Regarding the timeliness of screening assessments differences were noted in the time to first TST. Among CBO S+ cases, their other contacts over age 5 had an average time to first TST of 39 days, well under the typical 8 week time period in which a decision to expand the circle would have been determined. Of concern, is that this time period was the same for ABO S+ close contacts who are at higher risk based upon exposure history. This could be a function of sheer volume as CBO had smaller numbers of close contacts per case, thus making completion of TST easier; which may also account for faster completion of other contacts as well. However, given that most secondary cases found during CI are close contacts, this screening of other contacts may be superfluous and not cost effective or even useful. These are potential resources that could be redirected into other aspects of CI. This is echoed with ABN, where time to other contacts' baseline TST suggested premature screening of this group and where the success of timely screening of close contacts was the poorest among the 3 population groups.

Despite geographical access and resource barriers to chest radiography for many FN communities (Andrea Warman, FNIHB, personal communication 14Oct2014), close contacts that were ≥5 years and ABO had the shortest median time to CXR. Longer times to CXR delay a recommendation for LTBI treatment, which may account for the lower offering of window

prophylaxis for ABO S+ close contacts under 5 which was less than half when compared to ABN. In addition, Provincial Clinic procedure requires the agreement of the patient's local physician which can also contribute to delay. Of concern, however, was the contrasting finding for contacts under age 5, where CBO were notably faster in time to TST and CXR (0.01/<0.01). Additional investigation into the low offering of window prophylaxis to the under 5 ABO group is warranted to determine if additional intervention is needed. Further, a standard for window prophylaxis offered should be set or a more standardized 'fast tracking' of these patients may be warranted.

Overall, rates of LTBI treatment acceptance and completion rates were higher for ABO S+ close contacts over age 5 than ABN, despite higher numbers of contacts. It suggests that despite a slower start to screening in ABO communities, the CI process is more effective at achieving LTBI treatment success. However, given that even these rates are below the performance marker set by Alberta Health and Wellness, additional efforts must be made to improve this, not only for ABO but for all Canadian Born populations. Barriers to completion of LTBI treatment medication in these groups may differ, so a range of strategies may be needed.

Timeliness of contact assessments is not a performance target for Alberta Health and Wellness; however, the CDC does outline acceptable time frames for this activity (2005). One measure is time to 'face to face' initial contact encounter with public health once named and the other is days from that meeting to completion of medical evaluation. Lacking in the current data collected for TB in AB are the dates needed to calculate these markers. However, when considering timeliness of first TST, the median times for ABO and CBO close contacts of all ages are within the total 12 days allotted by CDC guidelines. The time frames suggested for lower risk contacts cannot be applied to Alberta data for comparison as they indicate a time frame that falls within the 8 week window period; a critical mark for CCA and consideration of expansion of investigation. Provincial targets should be set for Alberta.

The relatively poorer CI outcomes for ABN are reflective of the frequent association of these cases to the inner city population of Edmonton. A difficult group for follow up regardless of health issue, the dynamic nature and instability of the cases' circumstances could make follow up challenging. Frequently, in transient or inner city populations, the source case rely upon contact list construction will be locations based, for example shelters. It suggests that the conventional CCA may not be the most appropriate or effective approach. This has been explored by researchers with specific focus on Aboriginal populations (Cook, Shah, Gardy & Bourgeois, 2012; Case et al, 2013). Social Network Analysis (SNA) has demonstrated usefulness in response to the syphilis resurgence and AIDS epidemic (Klovdahl, 1985). This combined with genomic advances in fingerprinting *M. tuberculosis* complex has the ability to better understand how dynamics within these unique settings can influence transmission by identifying unknown contacts (Rothenberg, McElroy, Wilce & Muth, 2003; Andre et al, 2007).

Alternate approaches to CI have been suggested in Canada. Cook et al (2012) and Cook et al (2007) have suggested exploring the use of SNA, geographic information systems and genomics for enhancing TB contact investigations. However, a comprehensive analysis produced little evidence of the relative success or failure of current methods of CI with and without SNA in Canada. The primary population discussed in this work is Aboriginal Peoples in British Columbia. However, the heterogeneity of this population group varies greatly across Canada and can be directly impacted by the different approaches taken by each province or territory's TB Control Program Policies and guidelines.

Social Network Analysis evolved out of the syphilis outbreak that emerged in the last 25 years (Rothenberg et al, 1998). The approach by health officials to contain this public health threat focused on locations where infected patients frequented, thus suggesting potential contact or similar lifestyle to that of the patient. However, syphilis is primarily transmitted through sexual and by direct skin to skin/rash/chancre contact. This of course is dramatically different

than the most common method of transmission of TB which is inhaled droplet. While some aspect of social settings plays a role in identifying TB contacts, it is about shared air space, not physical contact that puts them at risk, which can be independent of lifestyle influences. This is not to say that it may not be useful and perhaps used to some extent for certain TB cases, notably those who may be associated with the inner city setting and exposures in shelters but that, the relative success of current practices are not well understood.

The CI for a highly infectious case in Finland recently utilized genomics and Social Network Analysis to assist in the post investigation assessment of the CI process (Smit et al, 2014). However, the real time use of genomics is not currently available and may come at great cost. Further, use of these strategies requires identification of secondary cases that are confirmed by culture in order to make the link to the index case. This in itself confirms transmission and the failure of CI to prevent transmission. However, they may provide retrospective assistance in assessing outbreaks to determine the true index case and related factors as it did for Gardy et al (2011). They concluded that there was more than one source case and that the outbreak was precipitated by an increase in crack cocaine use in the community and locations of highest transmission. Perhaps the role of these new approaches will become clearer with better appreciation of the often overlooked TB guideline of recommending systematic CI assessment and evaluation to identify failure to prevent transmission. However routine use of these methods could utilize fiscal resources that might better serve other TB prevention efforts.

Lower successes among unique populations could suggest that alternate methods may be more successful and use resources more efficiently. For example, the transient and inner city populations of urban centres may benefit from a more risk oriented model or enhanced surveillance activities. A risk model may also be the most appropriate for contacts of less infectious cases of TB, given the low indicators for transmission events.

Comparing completion rates found in this thesis to those reported by AB TB program between 2000-2004 demonstrate that, where population group of the case is concerned, ABO perform above average rates for positive reactors and converters and all persons on prophylaxis. This was markably improved in the years 2005-2009 where completion rates for all contacts accepting prophylaxis was 78.8%. Given the much lower proportions found for contacts aged 5 and up in their study, it can be assumed that contacts of Foreign Born cases had much higher completion rates to compensate and create this high overall proportion average. However, a similar assessment of CI involving FB cases should be undertaken to identify weaknesses and strengths unique to that population group. Differences between the two periods of time may reflect the technological changes in data management by a conversion to iPHIS as well as increased nursing education as the development of the TB Nurses Working Group occurred in the latter half of the study period and allowed better knowledge transfer.

LTBI treatment completion is a primary outcome measure of a successful CI. The AB TB program should focus more efforts on LTBI treatment acceptance and completion for contacts of ABN cases, where rates are far from the $\geq$80% target set out by Alberta Health and Wellness (2012). Contacts of ABO also have acceptance and completion rates below the performance target although they remain the highest across population groups. The universal use of directly observed preventive therapy (DOPT) for persons residing in reserve communities undoubtedly had an effect on the higher rates of completion. Other strategies to improve LTBI treatment success need to be considered to meet target. Use of enablers has been utilized in these circumstances but additional efforts are needed. The advent of proposed shorter course regimens of LTBI treatment could provide some assistance in these scenarios as 9 months of Isoniazid has been associated with lower completion rates than shorter regimens (4 months of Rifampin)(Menzies et al, 2008; Fiske et al., 2014; Marks et al, 2000). Shorter course therapies could then also have a cost saving effect; requiring less human resource time for DOPT on reserve. However, other findings (Malejczyk et al, 2014) did not find the drug used for LTBI

treatment affected completion, rather stable housing was key to success. This may help to explain the lower completion rates among contacts to ABN cases many of which were associated with homelessness and inner city residence.

When considering predictors of favorable CI outcomes, individual contact details of gender, age and contact type were not helpful in determining success. Rather, source case factors were the only reliable predictor of several outcomes: completion of 8 week TST, CXR after TST, and acceptance and completion of LTBI prophylaxis. The key factors that predicted success for all these performance markers was smear positive status of the source case and if the source case was ABO. Higher priority is given to CI for S+ cases due to perceived risk, which may explain greater success of the CI. With respect to better LTBI treatment completion rates in contacts of ABO cases, one likely contributor is the unique program organization and partners involved in the care of peoples residing on reserve in Alberta. The collaborative partnership between FNIHB, AHS and their respective staff is likely the key to that success. Despite indications of lower assessment completion in some aspects, their overall success in LTBI treatment cannot be underestimated. Further, their program policy of DOPT for LTBI treatment appears helpful in achieving higher completion rates.

Case finding is also an important part of CI goals and much of this is dependent upon several diagnostic performance markers previously discussed. Completion of TSTs in children can be helpful in diagnosing active disease but also prompts the need for a CXR, another useful diagnostic in children as well as adults. Submission of sputa for acid fast bacilli smear and culture is routine for symptomatic or TST positive contacts with an abnormal CXR, which can confirm bacteriological disease. Given that there was no difference between groups for transmission events for close contacts suggest equivalent effort and success in screening. However, the difference found among other contacts for S+ cases suggest higher transmission

rates or mislabeling of contacts that were in fact close. This highlights the need to standardize definitions or qualifications for contact type.

An encouraging finding in this study was the timely discovery of secondary cases in the ABO group (all were discovered within 12 months; none were discovered between 12 and 36 months). Given that screening and LTBI outcomes for ABO were consistently higher than other population groups, this finding is likely associated. In support of this, is the continued case finding found for ABN and CBO between 12 and 36 months post contact. More emphasis on completion of assessments for contacts with within specific targets may benefit CI guidelines.

Limitations of Study

Several limitations of the study exist and were considered during the completion of this analysis.

iPHIS. With the exception of TB lab results from the Provincial Laboratory being directly downloaded into iPHIS, all data in this system is manually entered from a variety of sources. Relying on the iPHIS system for all data points includes inherent risks of human data entry error, inadequate completion of fields and the conversion of data from 2001-2003 into iPHIS from the previously used repository for TB cases diagnosed in the Province of Alberta. It is also possible that in the context of some CI, additional contacts were identified but not included in the iPHIS documentation. The transfer or interpretation of the material that was entered into iPHIS is vulnerable to human error at multiple stages. This is also true of the several data elements for both the source cases and their contacts that were individually located in iPHIS, manually noted on paper, and then transferred into the appropriate database by manual entry. This highlights the general lack of consistency of data gathering and documentation of contact

details that can be retrieved via the iPHIS reports, as much of the additional information of interest, is noted in a physician or health care provider narrative as opposed to a single variable.

Reliance on Quantitative Data. The exclusive use of quantitative data limited interpretation of the results and subsequent recommendations. It would be valuable to understand how TB is perceived by TB cases, regardless of population groups. Knowledge and beliefs about TB could impact the relative importance as a health issue and impact behavior. Of particular interest would be the perception from Aboriginal Peoples given their painful history with the disease and the impact on their population. Further, perceptions from the health care workers who serve the Aboriginal communities would provide further insight into potential barriers to CI. The lack of qualitative data did illuminate several areas that would benefit from further investigation.

Creation and Documentation of Contact Lists. With regard to the contact list, the original list is generated by public health staff (or acute care staff in some instances) using the patient and/or family members to identify persons who were considered contacts of the source case. The person constructing the list may or may not have experience or comfort in eliciting this list, which can influence its accuracy and completeness. In some rural areas of Alberta this may be the public health nurse's first experience with active TB in their area, in turn making the interview process for a contact list influenced by a lack of experience, training and/or direction.

In addition, it is possible that additional contact lists were generated manually but were not entered into iPHIS, notably among cases who were in acute or long-term care facilities. This is due to involvement of internal workplace health and safety or occupational health departments representing staff at facilities where an exposure may have taken place. The consistency of contact list generation by the frontline public health staff requires consideration as well as the individual case management preferences of the attending TB physician.

Finally, determination of what constitutes a person labeled as a close or casual contact is often based on limited or assumed information and subject to interpretation or differing

definitions. The inclusion of a sub-category of cases being identified as household or non household or by other contextual clues may help provide a clearer picture of the representation of where the exposure had occurred. Unfortunately, these details were not documented with sufficient consistency to analyze. These inconsistencies in data reflect variation in TB program approaches, clinical preferences and judgment within the province and demonstrate the need for systematic procedures for documentation of contact data.

Program Variance. The medical direction for CI was generally stable for the rural and Aboriginal on reserve cases during the majority of time for this study period. This was due to the ongoing consistent appointment and management of the provincial TB program by a single physician for the vast majority of the period of study (Jensen et al, 2012). However, the balance of cases from the Edmonton and Calgary Metro area were managed through outpatient clinics by numerous TB physicians. Decisions as to the breadth of the CI could differ under these circumstances; thus some CI lists could be shorter or longer than the length of a CI list another physician may deem appropriate. Direction on who is considered at risk is most often originating from the responsible TB physician. Their assessment of risk, although based upon the Alberta TB Guidelines, is also influenced by their experience and level of expertise.

Changes in supervisory direction regarding what data is entered are also subject to inconsistency given staff turnover and management changes. This was noted and quite apparent in the collection of the 2010 data, when the contact lists were clearly truncated. This was due to a decision (of unknown origin) to only enter contact information on patients who had completed some form of follow up (personal communication, 11Mar2014, Rhonda Fur, Provincial TB Manager).

Summary of Program Recommendations and Areas for Future Research

- **Development and adherence to provincial guidelines**
    - Guidelines for timeliness of assessments for close contacts
    - Clearer guidelines for necessity and timeliness of casual contact assessment
    - Clearer definitions for identification and categorization of contacts
    - Staff training and education for interviewing to obtain detailed and relevant contact lists

- **Documentation**
    - Contact information in a format which permits data abstraction and analysis
    - Collection of expanded contact information to include; ethnicity, exposure time and immune-compromising conditions
- **Research**
    - Identify barriers to successful contact investigations for population groups
        - Interview contacts who are offered LTBI treatment regarding their perceptions, views and beliefs as it relates to their acceptance and completion of medication as well as completion of Chest X-rays (parents interviewed as proxy for children)
        - Interview public health staff who serve all population groups to gain insight into their perceptions of barriers and enablers to CI success
    - Retrospective analysis of contact investigation data for all population groups using alternate models (i.e. Social Network Analysis and genomics) to determine if additional insight can be gained to support different CI methods between population groups and settings

Conclusion

Despite numerous outcomes that provided an assessment of the relative success of CI activities in Alberta, this work also highlighted several data deficiencies regarding contact information and context of the CI. In this study, only age and gender were the most consistently populated fields with regards to their demographics. Consideration of standardized, expanded information gathering and documentation around contacts is warranted. As outlined in the AB guidelines and elsewhere, other data should be documented such as; ethnic origin, co-existing medical conditions that increase risk for TB disease, HIV status and exposure time. A comprehensive and standard evaluations process for all CI should be integrated into the AB TB Control program and subject to review.

This study succeeded in delineating that differences between population groups do exist with regards to relative success of TB contact investigations. By analyzing CI outcomes by population group, differences highlighted unique features of each group that may require more tailored approaches to achieve objectives. However, to determine these, more work is required on the part of researchers. A more qualitative approach could extract valuable information from contacts and health care workers regarding the day to day challenges of participating in a CI. This information could be used to address issues through education, programming or ensuring other practical matters are dealt with. In the case of not completing a chest X-ray, it could be as simple as needing transportation, however this is as yet unknown until the question is asked.

A key element that is impossible for TB Control Programs to address on its own is the clear disparity between population groups; multiple partners will be needed to achieve this. Access to health services is not necessarily equal for all residents of Alberta. Addressing these inequalities to ensure all Albertans have basic elements that are connected to their well-being is a larger problem. Until this time, advocacy must continue if this shameful disparity is to be nullified.

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Appendix A

Contact investigation Data points –cases

Data point	Source	Coding info	comments
study id	Assigned to case by researcher		Sequential numbering 04- year (2004) 01 – 1st case that year
client DOB	EXCEL report		
ethnicity	EXCEL report		
on reserve	Manual entry from case's Case Report Form box 6	1-yes 2-no If CBO, 0	
On reserve	Manual entry from FNIHB report		
gender	EXCEL report		
age Dx	Formula Date of Dx – date of birth		
PHN	EXCEL		
TB file number	EXCEL		
diagnosis stage	EXCEL	i.e. new active, relapsed	
disease code	EXCEL		Pulmonary designations
disease code (3 columns)	Manual entry from case's Case report Form box 8		
Diagnosis date	EXCEL		Start date of treatment, or if deceased (no treatment started), date of first lab
diagnosis status	EXCEL		Should all read culture to ensure eligibility
episode detection method	EXCEL	i.e. symptoms compatible, contact, other	
episode outcome	EXCEL	i.e. fatal, treatment completed	
TB file number	Copied from column H		For visual connect to case during data

			entry
HIV	Inserted from another EXCEL file		If done previously, date will not show here, required manual confirmation if no date found in excel file
HIV	Inserted from another EXCEL file		No relevance
result	Inserted from another EXCEL file	NEG/POS	
CXR	Manual entry from case's Case Report Form box 9	Cavitary – 1 Non cavitary - 2	Cavitary status only
smear status	Manual entry from case's Case Report Form box 10	POS NEG 0 – if from surgical specimen	Of relevance to diagnosis
postal code	Manual entry from case's Case Report Form box 6 or by manual search and enter from individual iPHIS chart		If homeless, will be no fixed address (NFA)
# address changes	Manual search and entry in individual iPHIS chart		Number of times residence changed as entered in iPHIS demographics during treatment
risk factors	Manual entry from case's Case Report Form box 20	Coding as sequentially listed on PHAC form	
RFLP	Manual search and entry in individual iPHIS chart		
# in cluster	Manual search and entry in individual iPHIS chart	#/#	# in cluster up to end of study 2010/# to end 2012
previous episode	Manual search and entry in individual iPHIS chart		Number of times that individual has had an episode with TBS (including current)
year	Manual search and entry in individual iPHIS chart		Year of most recent previous episode
previous details	Manual search and entry in individual iPHIS chart	0 – no 1 – contact	Details of AD

		2 – LTBI 3 –other 4 – case	
Outcome		Coding: 0 – incomplete 1 – completed	
year	Manual search and entry in individual iPHIS chart		Year of most recent previous episode
previous details	Manual search and entry in individual iPHIS chart	0 – no 1 – contact 2 – LTBI 3 – other 4 – case	Details of AF
outcome		0 – incomplete 1 – completed	
year	Manual search and entry in individual iPHIS chart		Year of most recent previous episode
previous details	Manual search and entry in individual iPHIS chart	0 – no 1 – contact 2 – LTBI 3 – other 4 –case	Details of AH
Outcome		0 – incomplete 1 – completed	

EXCEL files are reports created by AHS TB Services upon request. For cases, the number of data points needed do not fit into 1 report, (rather 3), thus a merge of these files is required for complete information.
Case report forms are generated on individual basis from iPHIS reports in PDF format
Manual – individual chart search in iPHIS for subject and navigating through online chart for data points and confirmation of data.

Year is formatted in yyyy/mm/dd for all date data points

Appendix B

Contact investigation Data points – Contacts

Data point	Source	Coding info	comments
Source id	Assigned to source case by student researcher		Sequential numbering 04- year (2004) 01 – 1st case that year
study id (contact)	Assigned to contact by student researcher		Sequential numbering with 04-01 source id and 01- first listing on contact list (alphabetical)
postal code	Extracted from Excel dump, or manually searched and entered		
gender	Excel dump		As entered in iPHIS
DOB	Manual entry from iPHIS contact summary report		Generated case by case in PDF format
Age at time of contact	Excel formula (DOB, date of contact)		
PHN	Excel dump		
TB file #	Excel dump		
contact type	Excel dump	Will only be noting casual (not casual medium, low risk)	Close or casual only, unknown to be included with casual in 'other' category
Contact relation	Excel dump	NH – non household	
Contact event	Excel dump		If associated with specific location/event during contact investigation
contact date	Excel dump		if not listed, use date of diagnosis of source case
sputum date	Excel dump		Most recent sputa date
sputa done	Manual entry	y/n response	
# samples	Manual entry from viewing of iPHIS contact summary	Total number submitted for this contact episode	Within 36 months of date of contact

	report and corroboration with contact's iPHIS chart		
Xray date (w/I 36 m)	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart	most recent with relation to this event	
CXR date	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart	Other CXR	First in this episode
Status	Excel dump	Not of relevance currently	Collapsed column
status date	Excel dump	Not of relevance currently	Collapsed column
treatment recommended date	Excel dump		Indication of LTBI treatment offered if populated
treatment accepted	Excel dump	y/n	
treatment end date	Excel dump		When treatment ended or was closed
Reason end	Excel dump	Coding from AHS	Reason for treatment end i.e. complete, side effects, refusal
BCG (iPHIS)	Manual search and entry from contact's iPHIS chart	y/n/?	
Year (iPHIS)	Manual search and entry from contact's iPHIS chart		If entered in iPHIS
BCG (FNIHB)	Manual entry from FNIHB report	For FNP only	
Year (FNIHB)	Manual entry from FNIHB report	For FNP only	
Positive reactor	Excel dump	Limited relevance	Supplemental confirmation of TST reactions
recent positive	Excel dump	Not of relevance currently (accuracy)	Collapsed column
1st test negative	Excel dump	Not of relevance currently	Collapsed column

		(accuracy)	
previous positive	Excel dump	Not of relevance currently (accuracy)	Collapsed column
8 week negative	Excel dump	Not of relevance currently (accuracy)	Collapsed column
converter	Excel dump	y/n	Questionable accuracy - may allow for comparison to AX
most recent skin test date	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart		Last TST done in relation to this event
result type	Excel dump	POS, Significant or non significant	In reference to AH
reaction size	Excel dump	Number (mm)	In reference to AH
8 wk reference date	Formula – date of contact + 56 days		To allow determination of baseline and 8 week TSTs
8 week done	Manual decision and entry	0 – no 1 – yes 2 – NA – (past +)	Was a TST done min 56 days after date of contact, in relation to this event
past TST this episode date	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart		
result	Excel dump	POS, Significant or non significant	In reference to AM
reaction size	Excel dump	Number (mm)	In reference to AM
baseline done	Manual decision and entry	0 – no 1 – yes 2 – NA – (past +)	Was a TST done within 56 days, but after date of contact
converter	Manual decision and entry	y/n	
outcome	Excel dump	AHS coding	

past TST date	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart		TSTs done prior to event, most recent here
result	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart	POS/Significant/non significant	In relation to BA
reaction size	Combination – excel, iPHIS contact summary report and corroboration with contact's iPHIS chart	POS, significant or not significant	In relation to BA
QFT recent positive	Excel dump		
QFT previous positive	Excel dump		
QFT recent negative	Excel dump		
QFT recent indeterminate	Excel dump		
QFT date	Excel dump		
QFT result	Excel dump		
QFT value	Excel dump		
# x contact	Combination of iPHIS contact summary report and corroboration with contact's iPHIS chart		Number of times client has been named as a contact 2010 and prior
hx TBS	Combination of iPHIS contact summary report and corroboration with contact's iPHIS chart	0 – no 1 – contact 2 – LTBI 3 – other 4 – case	If previous contact resulted in treatment, will be coded as LTBI (2)
LTBI outcome	Combination of iPHIS contact summary report and corroboration with contact's	0 – incomplete 1 – completed	For those coded as 2 in BJ, was therapy considered adequate as entered in iPHIS?

	iPHIS chart		
hx TBS	Combination of iPHIS contact summary report and corroboration with contact's iPHIS chart	0 – no 1 – contact 2 – LTBI 3 – other 4 – case	If previous contact resulted in treatment, will be coded as LTBI (2)
LTBI outcome	Combination of iPHIS contact summary report and corroboration with contact's iPHIS chart	0 – incomplete 1 – completed	For those coded as 2 in BK, was therapy considered adequate as entered in iPHIS?
hx TBS	Combination of iPHIS contact summary report and corroboration with contact's iPHIS chart	0 – no 1 – contact 2 – LTBI 3 – other 4 – case	If previous contact resulted in treatment, will be coded as LTBI (2)
LTBI outcome	Combination of iPHIS contact summary report and corroboration with contact's iPHIS chart	0 – incomplete 1 – completed	For those coded as 2 in BK, was therapy considered adequate as entered in iPHIS?

EXCEL dump – from iPHIS QR reports, I can generate and download a contact listing for each case in excel format. This forms the base of the final database

iPHIS contact summary report – from iPHIS, I can generate and print a PDF document which provides a summary of the contacts and details for each source case. Contains elements not in the EXCEL dump.

Manual – individual chart search in iPHIS for subject and navigating through online chart for data points and confirmation of data.

All dates will be formatted in a yyyy/mm/dd format

Appendix C

Data points SAS

Red – case variables black – contact variables

source	Identifier for source case XX-yy XX indicates year of dx – yy sequential numbering
ethn	as per reporting form – CBO, FN registered, FN not registered, Inuit, Metis,
reserve	Applicable to Aboriginal population only 1-yes 2-no 3N/A (for CBO)
Cgender	Case M or F
Cage	Age at diagnosis rounded to whole number
Ccat	Case Age category 15-44-A, 45-64-B, 65+-C
HIV	Case HIV status POS NEG or NONE (if not done)
smear	Case smear status of sputa, as per reporting form
Study id	Identifier for contact XX-yy-zzz XX-yy is source case id and zzz is sequential numbering of all contacts for that case
age	Age at time of contact
age grp	Age grouped into standard age groups (see coding notes)
gender	M,F or U (unknown)
type	Contact type 1-close 2-casual 3-unknown
timeCXR2	Time in days to last CXR in episode (36 months from contact date)
timeCXR1	Time in days to first CXR in episode from contact date
accept	If offered LTBI, Y for accepted N for not
reason	Reason treatment ended by iPHIS code (only for those who accepted treatment)
bcg	Bcg status if known (used only for <5 in this study)
TST2time	Time in days to second TST in episode (min 56 days after contact date)
TST2result	For the second TST, result i.e. POS or NEG
8wk	Coded if a TST was done after 56 days from contact date 1-yes, 0-no, 2-prev test positive
TST1time	Time in days to first TST in episode from contact date. *note, if only an 8 wk TST was done, time in days will show here to capture time efficiency to first assessment
TST1result	For the first TST, result i.e. POS or NEG
baseline	Coded if a baseline TST was done within 56 days of contact 1-yes, 0-no, 2-prev test positive
convert	Coded if TSTs done within context of CI demonstrated conversion y or n
QFT	Result of QFT testing if done (POS-F or NEG)
Loutcome	If contact had been offered and completed proph in past 1-yes 0-no
Coutcome	If contact was a case in the past and was treated 1-yes 0-no/incomplete
outcome	Indicates secondary cases by code (see coding notes)

Coding notes

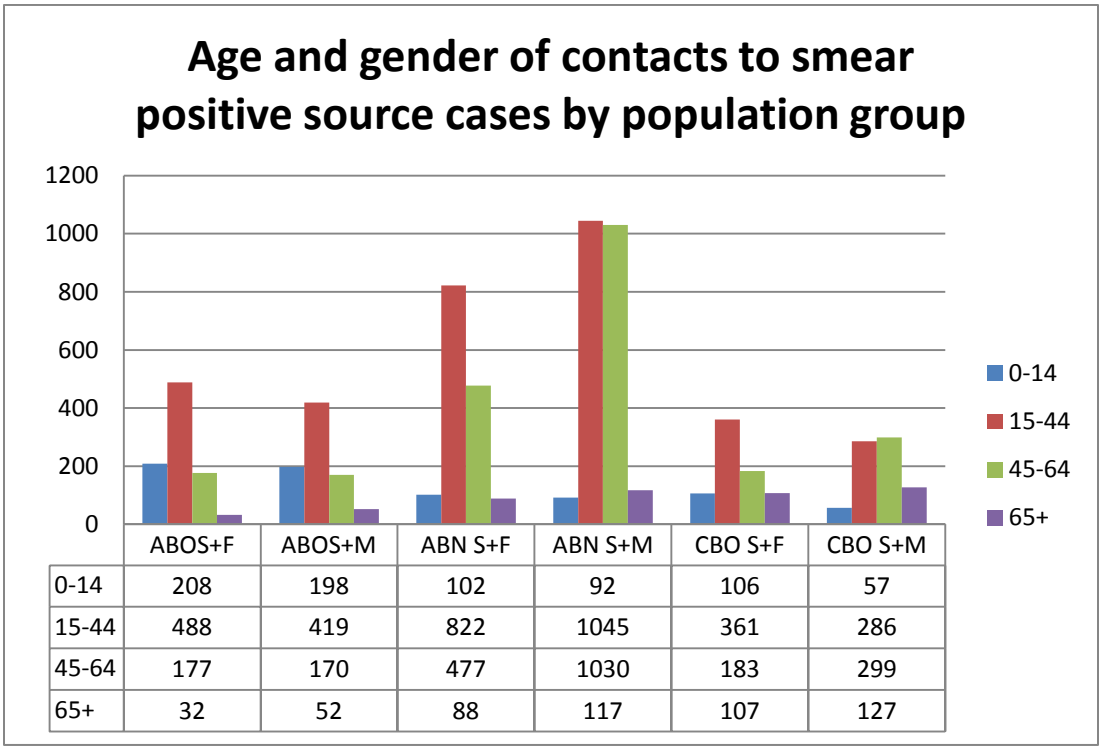
Case age categories:
15-44 – *A*
45-64 – *B*
65+ - *C*

Age groups for contacts:
Unknown – *0*
0-4 – *1*
5-14 – *2*
15-24 – *3*
25-34 – *4*
35-44 – *5*
45-54 – *6*
55-64 – *7*
65-74 – *8*
75+ - *9*

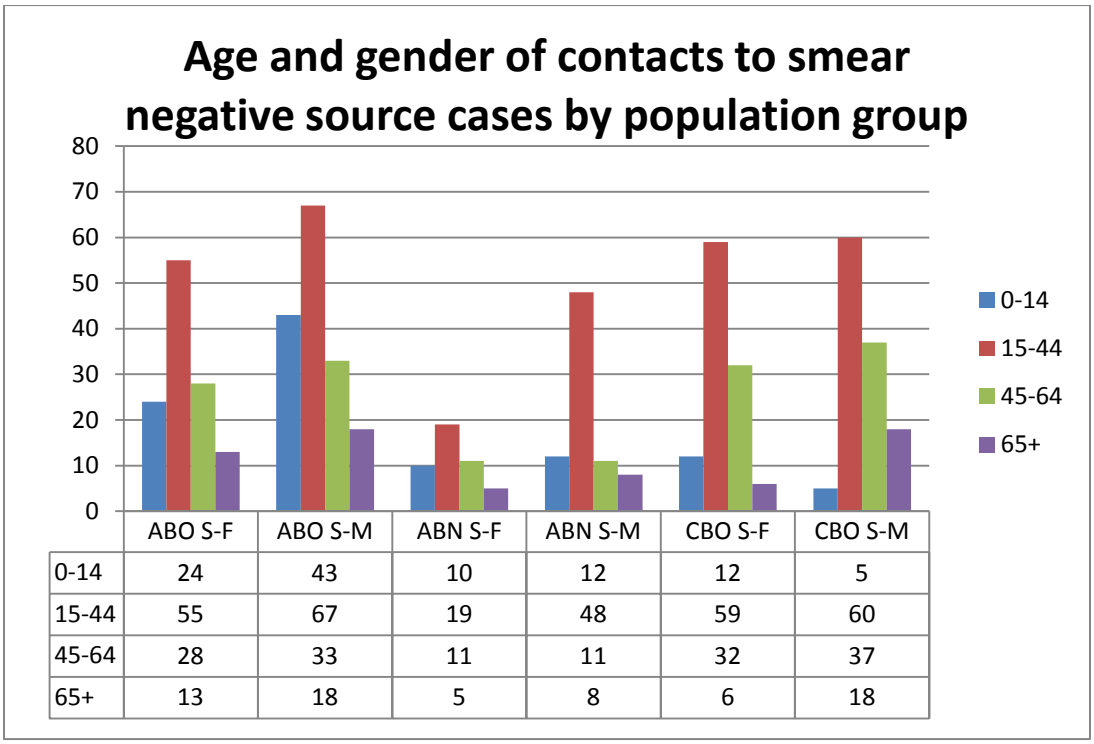
Outcome – case types
Secondary case linked by rflp within 36 months – *1*
Secondary case linked by epidemiology within 36 months – *2*
Secondary case identified during CI but RFLP does not match within 36 months – *3*
Case identified after 36 months and rflp match – *4*
Case identified after 36 months and no rflp to match but epi link – *5*
Case identified after 36 months and rflp does not match source case – *6*

Reason – LTBI outcomes
Case – *2*
Complete – *3*
Repeat test negative – *8*
All others, lumped as 'incomplete'

Appendix D



	ABOS+F	ABOS+M	ABN S+F	ABN S+M	CBO S+F	CBO S+M
0-14	208	198	102	92	106	57
15-44	488	419	822	1045	361	286
45-64	177	170	477	1030	183	299
65+	32	52	88	117	107	127



	ABO S-F	ABO S-M	ABN S-F	ABN S-M	CBO S-F	CBO S-M
0-14	24	43	10	12	12	5
15-44	55	67	19	48	59	60
45-64	28	33	11	11	32	37
65+	13	18	5	8	6	18

Appendix E

Contact screening activities (all ages) Smear Negative Source Case

		ABO n(%)	ABN n(%)	CBO n(%)	P value
total number contacts	Close	226	113	163	
	Other	55	12	71	
# without previous + TST documented	Close	187	90	142	
	Other	31	11	67	
# TST done at baseline	Close	94 (50)	48 (53.3)	104 (73.2)	**<0.01**
	Other	20 (64.5)	7 (63.6)	50 (74.6)	**0.51**
# eligible for a TST at 8 weeks	Close	172	72	128	
	Other	30	11	63	
# with Second TST	Close	127 (73.8%)	57 (79.2%)	88 (68.8%)	**0.27**
	Other	24 (80.0%)	8 (72.7%)	39 (61.9%)	**0.20**
# TST+ CXR within 6 m	Close	45 (69.2%)	21 (56.8%)	23 (63.9%)	**0.45**
	other	17 (63.0%)	1 (50.0%)	10 (90.9%)	**0.20**

Appendix F

Preventative Therapy outcomes (ages 5 and up) Smear Negative Source Case

		ABO n(%)	ABN n(%)	CBO n(%)	P value
# recommended	Close	25	15	14	
	other	11	2	4	
# accepted	Close	17 (68.0%)	11 (73.3%)	9 (64.3%)	**0.93**
	other	2 (18.2%)	1 (50.0%)	2 (50.0%)	**0.41**
# completed	Close	11 (64.7%)	11 (100%)	5 (55.6%)	**0.03**
	other	0 (.)	0 (.)	0 (.)	.
% completed / recommended	Close	44.0%	73.3%	35.7%	**0.09**
	other	.	.	.	.

[i] As summarized in the 2014 Edition of the Canadian Tuberculosis Standards page 347 "*The story of the TB epidemic in First Nations and Inuit populations speaks of transgenerational loss and suffering. Families and communities were disrupted as children, parents and grandchildren were sent to sanatoria throughout southern Canada for long periods of time, sometimes never to return. Survival was often accompanied by a legacy of emotional, psychological and physical 'scars'. Those who work in prevention and care in the 21st Century must be aware of the existence of a 'collective memory' of the suffering associated with the TB epidemic in these populations".*

[ii] IGRA use in contact investigations is deemed appropriate by the CCDR in 2008 with 3 caveats, of which, CI in Alberta adhere to. Where a confirmatory IGRA was performed and was discordant with the TST, the IGRA result was treated as the definitive TST, reducing the report of positive TST results. This affected data in the years 2004-2010. For 239 contacts that underwent IGRA testing, only 35 had concordant positive results to TST.

[iii] The term '*white*' is utilized as it reflects the original wording of the work and may reflect the perception of division/discrimination at the time. In current times, the term 'Caucasian' would be utilized however it does not suggest that discrimination is no longer an issue affecting Aboriginal Peoples in Alberta.