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The Epidemiology Of Tuberculosis In Nunavut

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HANDBOOK

The Epidemiology of Tuberculosis in Nunavut

an Investigative Thesis and Special Project

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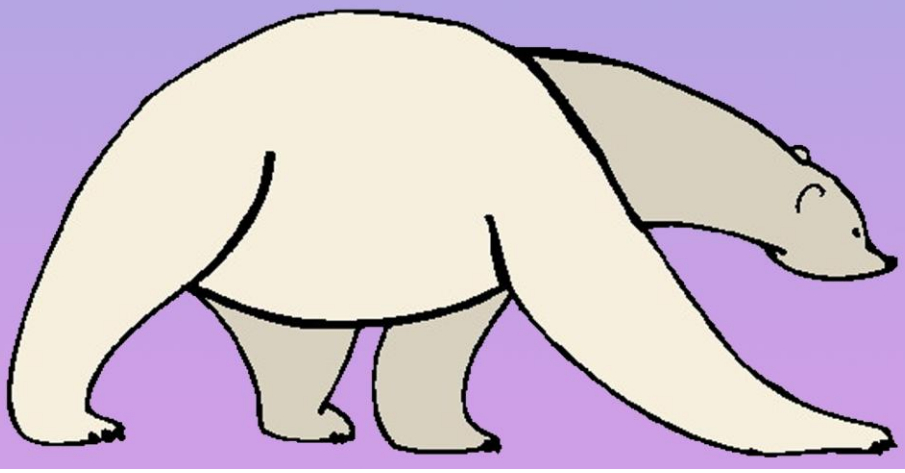

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Addressed To

A shortened version of this thesis has been sent to Canada's Northern Strategy, the Canadian Tuberculosis Reporting System (CTBRS) and Nunavut Department of Health and Social Services in the hope that it increases the feelings of accountability currently lacking with regard to the TB situation in Nunavut.

Acknowledgments

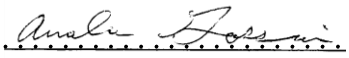
I would like to thank my family and professors.

Conflict of Interest

None found.

Yale Statement of Integrity

I have not given, received, or witnessed inappropriate exchange of information on this thesis, and I certify that this is my own original work. I have also appropriately quoted and cited all sources included in this assignment, including those from web sites.

Signed by Anala Gossai . .  . .

ABSTRACT

Despite the high level of control Canada exerts over tuberculosis (TB) at the national level, the people of Nunavut suffer from extraordinarily high rates of TB [Figure x], resulting in a disproportionate level of morbidity due to this contagious disease in the territory. Almost all cases of TB occur in Canadian Aboriginal peoples, and Nunavut may be experiencing an ongoing TB outbreak. The factors contributing to high TB rates in Nunavut have not been documented at length. This paper presents a novel look at TB in Nunavut, with a focus on the Inuit who comprise approximately 85% of the population. Using data collected by Statistics Canada, the United States CDC, the Greenlander government, and previous literature on the subject amongst the Inuit and comparable populations in Greenland and the United States (specifically Alaskan natives), the incidence of TB was revealed to be greatest in Nunavut. Results show the high rates of TB in Nunavut are most likely due to a failure in TB control with socioeconomic conditions compounding the serious situation. The work presented here has direct implications for the implementation of targeted control programs in Nunavut that may help solve the severe TB problem and improve Inuit health.

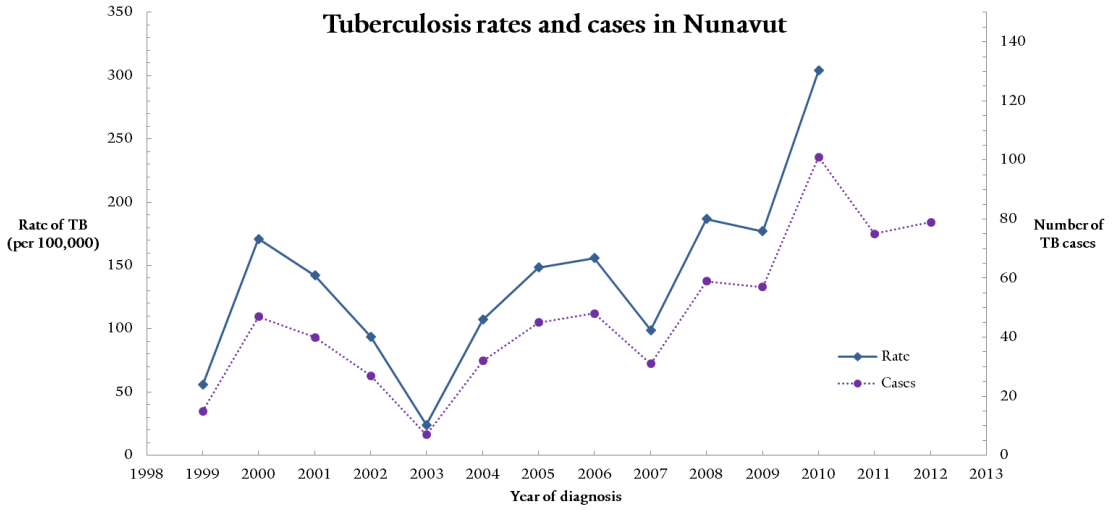


Figure x. Incidence and number of TB cases in Nunavut

An increase in the reported new and re-treatment TB cases and TB incidence rate is observed for the territory of Nunavut in Canada since its formation in the year 1999.

Source: Statistics Canada

Keywords: tuberculosis, Nunavut, Inuit, circumpolar health

Introduction

Welcome to Nunavut, Canada

Nunavut is Canada's youngest and largest northern territory, home to a substantial portion of Canadian Aboriginal peoples (First Nations, Mé tis and Inuit) settled sparsely across the land with a population of approximately 31,906 people in the year 2011 and with an estimated population of 33,761 for April 2012.[1] Nunavut officially separated from the Northwest Territories in the year 1999 through the *Nunavut Act* and the *Nunavut Land Claims Agreement*. Though the statistics available from Nunavut must be used with caution due to low response rates, it is estimated that 85% of the population is of an Aboriginal identity, many claiming Inuktitut as their conversational language, with 99% of those being of Inuit ancestry, and 1% being of First Nations or Mé tis ancestry.[1]

In Canada, public health requires that tuberculosis is reported, surveyed and managed at the federal, provincial and territorial levels. Health services in Nunavut are delivered by the Government of Nunavut Department of Health and Social Services. The three administrative regions are Qikiqtaaluk, Kivalliq and Kitikmeot. Legislation governing tuberculosis is defined in the Nunavut Public Health Act and Disease Registries Act, and the management or control of the disease is under the authority of the Office of the Chief Medical Officer of Health, with interdisciplinary teams providing support at the regional level.

The disparities between Nunavut and other Canadians are not restricted to health alone, as Nunavut experiences higher birth and emigration rates, in addition to higher proportions of uneducated, unemployed, and poverty-stricken individuals in relation to the rest of Canada.[1] Nunavut expended only 3,583,000 Canadian dollars on their populations' health in the year 2009, accounting for hospital care, medical care, and preventive care, as well as social services.[1] In comparison, the neighbouring Northwest Territories with a populace (many of whom claim Aboriginal heritage) in excess of Nunavut by only about 12,000 individuals, expended 238,907,000 dollars for healthcare and social services during the same year.[1]

Overview of tuberculosis

Tuberculosis is an ancient disease, with bacterial traces recovered from Egyptian mummies dating to 4,000 BC.[2] The causative organism of tuberculosis (TB) – the "white plague",[3] is *Mycobacterium tuberculosis* or tubercle bacillus.[2] The tubercle bacillus is a gram positive, intracellular pathogen possessing the distinctive staining property called acid-fastness (due to the cell wall component mycolic acid) and is notorious for its slow growth[4] during culture.[5] The morphology of TB resembles straight or slightly curved rods, 1 to 4 μm in length.[4] A single aerosolised droplet can contain 1 to 400 bacilli that travel to the alveoli of the lungs,[4] where they begin to grow and participate in the early haematogenous spread of TB to the rest of the body. The immune system begins to encapsulate the *M. tuberculosis* organisms in granulomas[4, 6] through an aggregation of activated macrophages, called tubercles,[5] to prevent further damage to the lungs and other organs until an event occurs to reduce host resistance.[2] Unfortunately, *M. tuberculosis* grows and persists within phagocytic cells and macrophages, thereby inhibiting this path of attack by the immune system and hiding during an ongoing immune response.[5] Within a phagosome in the macrophage,

M. tuberculosis nullifies the oxidative stress produced by the cell to destroy the bacteria using a survival factor coded within the genome of tubercle bacillus.[7] However, not all persons infected with the bacteria develop the symptoms of TB, and differences in resistance or susceptibility may be genetically determined.[8] An active pulmonary infection in a period of low immune resistance leads to extensive destruction of lung tissue which facilitates dissemination of *M. tuberculosis* organisms to neighbouring cells,[9] the spread of bacteria throughout the body, the replacement of healthy lung tissue with fibrotic tissue, and death.[5]

The primary reservoir for *M. tuberculosis* is humans.[2] The basic reproductive rate of an infection represents the number of secondary diseased cases that may be generated from a primary case in a susceptible population, and is an indicator of epidemic potential.[10] The reproductive rate of TB had been modelled mathematically to be $R_o = 5.16 \pm 2.82$ [11] (yet some calculations result in a range of $1.10 < R_o < 31.26$),[10] with an incubation period of 4 to 12 weeks (quite long compared with those for other infectious diseases)[2, 8] and a dose response relationship to disease severity compounded by length of continued contact over time.[8] TB is communicable for as long as the infected individual spews sputum containing the bacilli.[2]

Tuberculosis is an airborne disease typically transmitted through inhalation of droplets containing the bacilli.[2] The respiratory route of transmission makes even the act of conversation an opportunity of spread.[5] Thus, TB is primarily a disease of the lungs.[2] Prolonged exposure and direct or indirect contact with persons carrying active pulmonary lesions is necessary for infection, although TB is difficult to contract with respect to other communicable diseases.[2]

The severity of a TB infection depends upon the host's immune response to invasion, the dosage of bacterium, and the length of infection.[8] The risk of infection remains low (even among close contacts of the TB patient) and is reported to be < 30%.[12] Upon initial infection with TB, no symptoms may occur, except for the possible fatigue, anorexia, weight loss and light fever usually unnoticed by patients.[2] Only 5 to 10% of individuals initially infected with TB progress to primary[13] pulmonary TB, and have the opportunity to be actively found by health professionals, and receive treatment.[14] A period of latent TB ensues[13] if no treatment is provided for the initial infection in the remaining 90 to 95% of infected persons, during which the patient displays no clinical, microbiological or imaging evidence of the disease.[14, 15] Between 10 to 40% of patients lose containment of *M. tuberculosis* in the lungs over the period of a lifetime and experience TB reactivation.[14] Patients diagnosed with tuberculosis of the lungs following reactivation[6] of TB later in life during immune system compromisation often acutely present with a cough producing sputum containing mucus and pus, chest pains and occasionally bloody sputum, with these symptoms appearing chronically.[2] Some studies have suggested that individuals reinfected with TB, while possessing a latent TB infection, may be protected against progressive disease.[13] The pathological signs of tuberculosis coincide with highest risk of transmission. Outbreaks often result because of common exposure to a source of the bacteria – usually an untreated or undiagnosed TB patient who is highly infectious with a disease that has gone unchecked for an extended period of time. The majority of TB cases will progress within 12 months of infection, and by the end of 2 years, most complications associated with TB will have occurred.[8] Although the fatality rate attributed to

tuberculosis is generally low in the developed world, unpleasant long term effects from the disease may result in mild to severe disablement of the patient.

The diagnosis of TB may be confirmed by chest radiography[5, 16] performed in a hospital setting to detect the remnants of necrotic granulomas,[4] from sputum smear testing positive for TB,[8] during a tuberculin skin test, an interferon gamma release assay,[12] or other mycobacterial culture methods using appropriate samples.[16] A productive cough is the most important diagnostic symptom in a TB patient.[8] However, only sputum-positive TB cases transmit disease since TB is spread by droplet infection.[8] The tuberculin skin test is based upon the principle of delayed-type hypersensitivity to *M. tuberculosis*. This protective cellular immune response is observed 24 to 48 hours after tuberculin antigens (proteins extracted from *M. tuberculosis*) have been injected subcutaneously into a person previously infected with TB.[5] A positive tuberculin test indicates prior exposure to *M. tuberculosis*.

If an infection with active TB is left untreated, the patient has a prolonged period of infectiousness until diagnosed and treated, permitting transmission to many other persons.[8] This reinforces the importance of prevention regarding a TB infection. Chemotherapy for TB patients had originally been used to control the disease[5] as a clinical trial conducted with Inuit participants followed for a decade demonstrated that long term protection against TB was provided by the treatment.[17] Presently, TB patients may be treated with isoniazid combined with rifampin or other antitubercular drugs such as streptomycin, thiacetazone, pyrazinamide and ethambutol.[2, 8, 18, 19] Isoniazid is a growth factor analog of mycolic acid capable of interfering with cell wall synthesis in the bacilli,[18] and effective only against *M. tuberculosis*.[5] Isoniazid is the single most potent drug used for the control and treatment of TB.[5] However, a multidrug therapy is normally used to discourage the evolution of resistant organisms. Nine months of therapy usually resolves an active TB case;[2] but in those where uncertainty in the cure is present, therapy can continue for a further 6 months.[8] Unfortunately, a patient who has begun to feel well following treatment may default and not complete the course of therapy. This could lead to a relapse in the patient, and the patient may proceed to infect other community contacts.[8] Incomplete treatment also promotes the development of drug-resistant *M. tuberculosis*.[8]

Antibiotic-resistant strains of TB have been increasing in prevalence.[3] Those at risk of acquiring antibiotic-resistant *M. tuberculosis* isolates include patients who have already been treated for TB, failed in TB treatment, or suffer from chronic TB.[20] Anti-TB drugs apply selective pressure upon *M. tuberculosis*, allowing for random mutations which confer drug resistance to emerge as the dominant strain as drug-susceptible bacilli are removed.[21] Multidrug resistant (MDR) TB is defined as an *M. tuberculosis* bacillus at least resistant to isoniazid and rifampin.[12] Extremely or extensively drug resistant (XDR) strains of TB[4] are also resistant to fluoroquinolone and at least one second line injectable drug,[20] such as amikacin, kanamycin, and capreomycin.[12] MDR-TB is difficult to treat, requiring 12 to 24 months of therapy and second line drugs.[12] XDR-TB is even more difficult to treat, with a 30 to 40% cure rate.[12, 22] Additionally, both MDR- and XDR-TB patients are subject to high rates of mortality, and surgical resection of the lung may be recommended.[21, 22] Patients carrying antibiotic-resistant strains of *M. tuberculosis* are generally put on a treatment regimen of at least 4

drugs to which the bacilli are susceptible.[22] The concept of incurable TB (that is, TB organisms that resist all forms of treatment) has begun to be referred to in the clinical setting.[22]

The Bacille Calmette-Gué rin (BCG) vaccine exists to aide in TB control, although its efficacy is limited and uncertain (reinforcing the need for preventative and curative treatments). An attenuated strain of *M. tuberculosis*, *M. bovis*,[4] is contained within the vaccine.[5] The BCG vaccine induces cellular immunity to *M. tuberculosis*, but does not generate humoral immunity to elicit antibody formation.[8] The protection induced by the vaccine is high in children, but adults experience variable efficacy possibly due to faults in immunological memory as age progresses or pathogenic coinfections erupt.[3, 4] Protection against TB from the BCG vaccine has been found to last approximately 50 years.[3] Once the BCG vaccine has been administered, a primary TB infection may still take place, but the progression or dissemination of the infection will be reduced.[8] When the BCG vaccine is given intradermally, scarification results.[8] New, safer TB vaccines charged with providing longer lasting protection are in the process of development and trials, including DNA vaccines containing genetic sequences encoding TB antigens to induce CD4 and CD8 T cell responses, recombinant BCG vaccines, subunit vaccines containing immunodominant TB antigens targeted by the T cell response, and live attenuated vaccines.[3, 23]

Tuberculosis may be found all over the world and amongst people from all socioeconomic divisions, but tends to be endemic in underdeveloped regions, especially where sanitary conditions are poor and care facilities are outmoded. Although typically characterised as a disease of the developing world,[8] the prominence of TB infections in the history of the currently developed world imply TB was once (and still may be) prevalent in locales where it is currently present at low levels due to improved sanitary and social conditions, as well as public educational campaigns on TB prevention to increase TB awareness concerning the risks of TB, encourage the seeking of diagnosis, and alert to potential transmission mechanisms. In the year 1900, one of every 500 Americans died of TB, with only the enforcement of preventative and control measures leading to a reduction in case rate.[2] Similarly, the decline of TB in England and Wales was only achieved following a rise in living standards and fewer people to a room.[8] Control of TB has included rapidly finding and treating TB patients, investigating the source and network of contacts in outbreaks, application of chemotherapeutic methods, frequent community skin testing surveys and xray examinations, and public health education concerning TB.[2]

While TB is typically not a fatal disease in the young and healthy for developed countries if promptly diagnosed and treated, significant health consequences and death may be the result of TB amongst the HIV-infected, males, elderly, infants and Canadian Aboriginal peoples.[2] Delay in seeking a TB diagnosis will lead to death. The urban poor living in crowded conditions also experience higher TB rates than those in rural areas.[2] The majority of cases are survivable rather than fatal, but disease severity increases with age. These vulnerable portions of the population can only be addressed by public health action, as medical science has already devised an effective treatment regimen and BCG vaccine with some efficacy to combat the bacterium. TB is a reportable disease in many countries, although the instances of under-reporting suggest the burden and distribution of disease may be underestimated, but could be clarified with increased data acquisition.

Research questions

This thesis primarily attempts to address two questions: **1.** What is the current tuberculosis situation in Nunavut, and **2.** Is the incidence of tuberculosis in Nunavut different than those observed in comparable populations? The answers to these questions will hopefully lead to an answer for the question: Why does tuberculosis afflict Nunavut so harshly when compared to the rest of Canada?

Objectives of this investigation

Tuberculosis is present at high rates in the Northern regions of Canada. This thesis takes an in-depth, analytical look at the specific health problem of TB in the territory of Nunavut. A description of the epidemiology of TB in Nunavut is of public health importance. The problem of TB in Nunavut will be illustrated, evidence supporting possible reasons for the problem will be presented, and potential solutions to the problem will be provided. Lessons learnt from similar populations regarding efforts to decrease the rate of TB will be investigated. It is hoped that this thesis will be useful for the department of public health in Nunavut when targeting their TB control programs, and assist in their understanding of why TB continues to occur at such high incidences amongst their people.

It is hypothesised that TB prevalence may be linked to an inadequate or low level of TB control and the low socioeconomic conditions of the territory, exacerbating known risk factors for TB. The residents of Nunavut will be characterized and potentially linked to known TB risk factors. This thesis aims to demonstrate that remote peoples may be dealt with effectively in the context of TB prevention and rate reduction, and may serve as an inspiration for other infectious disease control efforts in similarly removed populations.

Research Design

Research methodology

An environmental scan and informed review of the literature pertaining to TB in Nunavut was undertaken to seek information on factors that may influence the rates of TB in a region, and data from Statistics Canada and the *Canadian Tuberculosis Reporting System* (*CTBRS*) were obtained. Correspondence with the *Centre for Communicable Diseases and Infection Control/Centre de la lutte contre les maladies transmissibles et les infections, Public Health Agency of Canada/Agence de santé publique du Canada* during November 2012 resulted in the amassing of data collected by CTBRS and Statistics Canada for the years 1999 to 2010 (as the data for years 2011 and 2012 had not yet been processed and published in Statistics Canada publications, but were available from brief updates on the situation). Detailed data tables were procured for the years 1999 to 2008, but only preliminary data tables were freely available for the years 2009 and 2010. The published literature on the topic was defined by a targeted search in Google Scholar and the website for Statistics Canada (www.statcan.gc.ca) throughout the academic year 2012 to 2013. When searching the peer-reviewed literature through Google Scholar, the search terms used consisted of a combination of: Nunavut, "Alaskan natives",

Greenland, "Native Americans", Inuit and/or tuberculosis (defined methodology exists in the appendix). Statistics Canada offers the public freely available data on many demographic and health topics, and regularly updates their data. For transparency, it must be acknowledged that response rates in Nunavut are often low, and thus data collected in this territory may not always accurately represent the past or present status of the situation. The online databases for the United States *Centers for Disease Control and Prevention* (CDC) and the Greenlander government were also accessed for TB data pertaining to their respective populations.

While literature exists on the topic of TB within the population of Nunavut, a concise approach to qualifying and quantifying the status of TB in the territory has not been attempted in recent years. The serious issue of TB warrants revisiting, and the compilation of new and old information carried in this thesis has the potential to rectify the TB outbreak if built upon.

Method of analysis

Knowledge on the subject of TB was summarized and related to the people of Nunavut. Where knowledge was lacking, similar populations such as Alaskan natives or other Northern populations were used to derive results related to those in Nunavut. The ecologic level data amassed was presented in the context of other Canadian and ostensibly comparable populations to assist with the formulation of tentative answers to the research questions.

Historical Perspectives on Tuberculosis

The history accompanying the people of northern Canada and health outcomes is a snarled web of social, political and economic factors that vary by both time and author.[24] Prior to European contact, the pool of infectious diseases afflicting the northern people was limited due to the cold climate, and only highly contested evidence exists to support the occurrence of upper respiratory infections during those early centuries.[24] The Inuit were the last of the Canadian Aboriginal peoples to encounter European explorers, and first contact situations were infrequent and lasted only short periods of time.[25] Following the fraternization with European settlers in the seventeenth century, documents indicate a change in the nature and impact of infectious diseases among northern Canadian Aboriginals, with repeated epidemics of highly transmittable diseases such as tuberculosis.[24] The severity of tuberculosis outbreaks was thought to be exacerbated by the nutritional stress and emotional anxiety accompanying the trading policies of forced labour, resettlement, overcrowding, and hunting violations.[24]

A century after the introduction of TB into the Canadian Arctic by Europeans in the 1800s, the Canadian government decided to address the desperate correspondences reporting hundreds of Inuit deaths due to TB following World War II.[26] The beginning of the 20th century was heralded by a collapse of the whaling industry and excessive fur trapping, and substantially undermined the traditional Inuit lifestyle.[25] Unemployment and disease reduced the virility of the Inuit population, and TB epidemics continually raged through the small communities.[25] The 1950s were marked by the highest incidence rates for TB ever observed in the Inuit populations of Alaska, Canada and Greenland,[27] and death from TB was reported in 7 of every 1,000 Inuit inhabitants.[17] Fortunately, by

the 1960s, the average death rate for TB within these Inuit regions had declined > 10 fold, as had the prevalence of reactions to tuberculin amongst children under five years of age.[17] It was decided that all presenting with active TB must be sent south for treatment, indirectly resulting in their unwanted isolation from their families.[26] Geography and SES were deemed barriers to effective public health practice in Nunavut.[28]

Once the Canadian government acknowledged the influence the entanglement of Aboriginal and European relationships had on current Aboriginal health, scientific studies were conducted to quantify the epidemiologic transition. Contrary to the health situations in most developed countries, in which chronic, non-communicable diseases appeared with higher prevalence as the society industrialised, infectious diseases were observed to still play a major role in the health profiles of northern people; rates of those diseases, such as tuberculosis, remain persistently high up north in the fully modernised country of Canada today.[24]

Review of Studies Relevant to Tuberculosis in Nunavut

While studies conducted in Nunavut specifically regarding TB within the population are rare, it is proposed that other Arctic peoples, such as the Greenland Inuit and Alaskan natives, as well as other Native American populations, are comparable to those in Nunavut [Figure 1, 2]. It has been estimated that 167,000 Inuit people exist today in the world.[29] The largest Inuit populations reside in Greenland (50,000 Inuit), Alaska (44,000 Inuit) and Northern Canada (50,000 Inuit),[29] but the history of TB in Native American tribes may also provide information of interest. Moreover, the Inuit from Alaska, Greenland and Northern Canada display striking linguistic homogeneity and cultural similarities reflecting their shared heritage,[30] thereby supporting their comparison in the context of TB and the health of circumpolar peoples. Thus, studies conducted within these communities may have findings of relevance for the problem of TB in Nunavut.

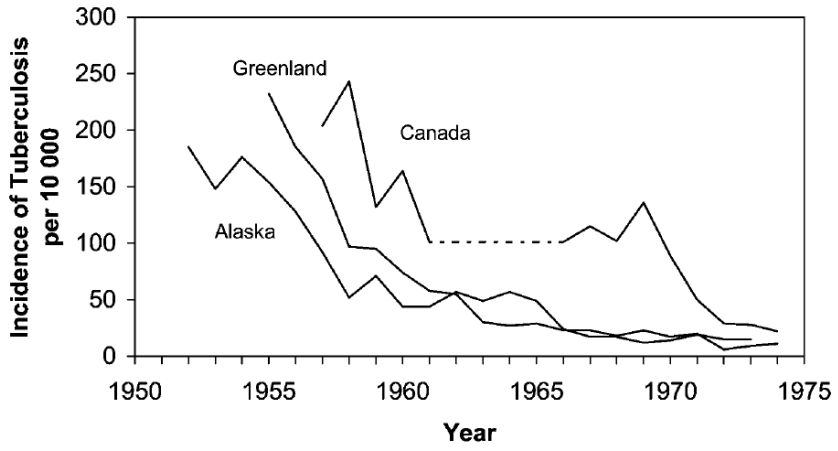


Figure 1. Decline in the incidence of TB amongst Alaska natives, Canadian Inuit and Greenlanders

It is observed that Canadian Inuit consistently maintain higher incidences of TB throughout the years when compared with other predominantly Inuit populations in history.

Adapted from: Bjerregaard *et al*, 2004

At one point in time, it was worried that TB was threatening the continued existence of First Nation and Native American peoples.[31] Collectively, the Inuit have experienced a steep decline in infectious diseases (including TB), but the level of TB has still remained above that of national populations.[29] The 19th and 20th centuries saw many Inuit die from TB, and the critical situation forced

many governments caring for the Inuit populations to implement measures in the 1940s and 1950s to combat the disease.[29] Xray surveys, evacuation, preventative therapy, vaccination, and general improvement of health services and community factors were enacted.[29] Despite this, the Inuit remain at higher risk for most infectious diseases and sporadic TB outbreaks still occur.[29]

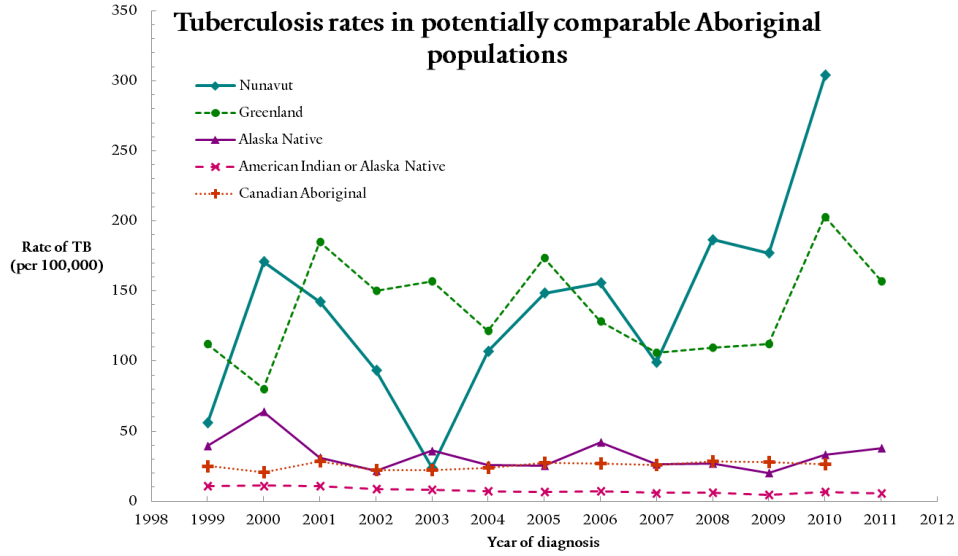


Figure 2. Incidence of TB in Nunavut with respect to comparable Aboriginal populations
The incidence of TB in Nunavut is compared to the incidence amongst Greenlanders, Alaska natives, American Indians and Canadian Aboriginal peoples. Nunavut has, in recent years, had the highest TB rates of all groups.

Source: Statistics Canada, United States CDC and Government of Greenland's *National TB strategi*

Nunavut

In the early 1900s, TB was seen as a serious illness, gathering attention in medical journals and among Canadian health workers.[28] TB epidemics had ravaged the Inuit people of northern Canada following war, reduced trading opportunities, impoverishment and appalling living conditions.[25] The realisation that many Arctic species were on the verge of extinction lead to the imposition of hunting regulations on Northern Canada's Aboriginal peoples, and contributed to malnourishment of the Inuit.[32] Seaborne medical teams arrived in Nunavut[33] to discover $^{1}/_{3}$ of the Inuit were suffering from TB.[34] Ships procured by the RCMP[35] began arriving in the 1950s during a TB epidemic to collect supposedly infected children and adults and take them south for treatment in sanatoriums; although families report many of those who boarded the ships were never heard of again.[36] It is believed that many died while under treatment for TB.[28] By the late 1960s, it is estimated that 30% of the population had been sent to southern sanitoria for TB treatment or schools.[37] The stress colonialism[26] had placed on the social system of the North had manifested in the high occurrence of communicable disease such as TB.[32] In the intervening decades between the 1960s and 1980s, the region which would become Nunavut had their greatest decline in case notification rates in patients aged < 25 years.[17] This decline had been attributed to the introduction of systematic case

finding (using chest radiography, sputum bacteriology and tuberculin skin testing) and treatment early in the 1960s.[17] In the 1960s, treatment consisted of 24 months of isoniazid and para-amino salicylic acid (replaced with ethambutol in the 1970s) with streptomycin supplied for the first 2 months of treatment.[17] The 1960s also saw a change from institutional (18 month stay) to domiciliary (< 3 month hospital visit) treatment.[17] Following the 1970s to the 1980s, many patients previously diagnosed with TB were provided preventative chemotherapy supplemented with antibiotics, as it had been observed that the highest rates of TB were in the strata of the population who had already been diagnosed with the disease.[17] Following this intervention, it was immediately observed over the subsequent few years that new cases primarily arose from those who had not been subjected to preventative chemotherapy.[17] Overall, the high rates of TB quantified in the Inuit community in the 1950s had a very rapid decline over the next three decades as a direct result of community-based interventions including population-wide screening and aggressive case management, as well as lowered transmission of TB due to chemotherapy.[17] This decline in incidence was one of the fastest ever demonstrated in any community at the time.[17] However, it has also been pointed out that TB rates had already begun their decline in those decades without the assistance of medical interventions.[17] The success in TB control in Nunavut lead to a reduction in the funding of TB programs in the early 1980s; although immediately following the cutback, an increase in the number of active TB cases was noted in the statistics collected.[38]

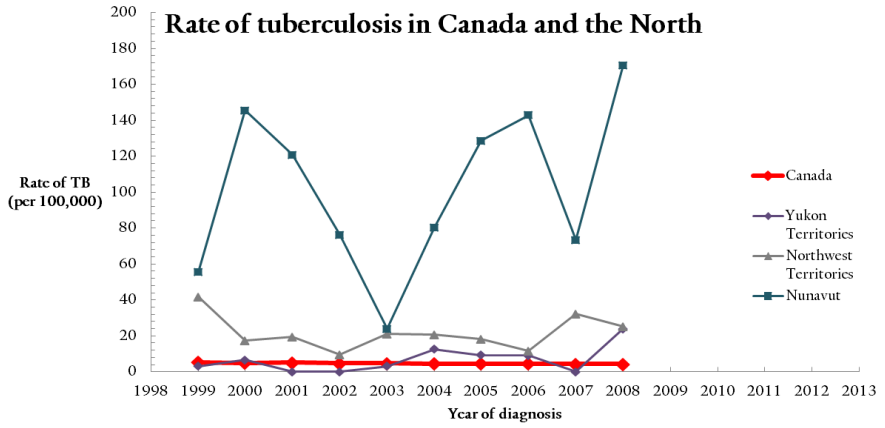


Figure 3. Incidence of TB in Nunavut and the north
The reported new, active TB incidence rates are compared across Canada's three northern territories: the Northwest territories, the Yukon territory and Nunavut. It can be seen that even in Canada's north, Nunavut has the highest TB rates of the region.

Source: Statistics Canada

When the new territory was formed in the year 1999, health professionals were aware of the continued TB outbreaks which had plagued the region, and relied heavily upon Nunavut's one hospital and primary care nurses placed in 26 health centres around the territory (nurse recruitment was difficult).[39] The health care delivery system remained largely unchanged.[39] The reversion following the steady decline in TB levels observed between the years 1950 to 1980 was concerning to health officials,[26] and measures were taken to address the increasing rates of TB [Figure 3]. It was

recognised that delayed diagnosis assisted the increase in TB incidence.[39] To lower the levels of TB in Nunavut, public health measures were put in to place (for example, childhood BCG vaccination and screening of high risk populations), but were allocated too few resources.[28] It was realised that the misguided strategy of forced deportation to the south following positive screen outcomes without familial consent had resulted in a loss of trust between the residents of the territory and the Canadian government.[28] One study in Nunavut was undertaken to attempt to discover how the Inuit participants contemplated TB.[26] It was found that the shift from traditional Inuit treatment methods to Euro-Canadian healthcare made the people feel as if they had lost control, and were reluctant to be examined for TB, finish their TB treatment regimens or continue with their prophylactic measures.[26] Despite this discovery, highly infectious TB patients were still sent south for isolation (for approximately one month depending on seriousness of disease)[38] until less infectious, then were followed with biweekly medication administered in their community.[26] Patients who were less infectious were allowed to stay within the community during treatment, but were asked to limit their social activities.[26, 38] School children and high risk facilities (such as prisons and homeless shelters) are periodically screened with relative success in comparison to the rest of the population of Nunavut.[28] Young people with limited medical contact are extremely difficult to screen for TB.[28] However, if an individual under the age of 35 years was found to be harbouring a latent TB infection, they were offered 9 months of biweekly prophylactic treatment.[26] To ensure high treatment completion rates, directly observed therapy (under a health professional or designated person)[26] is used for active TB cases and voluntary prophylactic treatment; but if a patient with active TB misses several drug doses in succession the risk of recurrent disease, contagiousness or MDR-TB developing is severe enough to lead to apprehension by the police in Nunavut.[38] The intense labour and resources required for contact tracing for people with active TB makes this practice unfavourable[28] – despite its recommended usage in the territory's TB manual.[26] The additional possibility of the absence of the health professional or designated person to directly observe the TB patient's therapy made treatment adherence problematic.[26]

While the rest of Canada has had a respite from the suffering caused by TB over the past years, Nunavut may currently be experiencing a large outbreak of TB.[28] Inuit infants in Baffin Island were found to be at increased risk of lower respiratory tract infections if their indoor air quality was poor and had limited circulation or significant levels of cigarette smoke contaminants.[40] Similarly, the children of Baffin Island contributed a disproportionate amount of TB cases (35% of TB disease diagnoses) between the years 1998 to 2008.[41] TB survivors and past epidemics provide a large pool of latent TB infection for the Inuit people to fuel transmission and the occurrence of new infections.[41] The Inuit population of Canada is at significantly greater risk of TB than any other ethnic group in the nation, with TB rates 185.8-fold higher than non-Aboriginal Canadians, as well as higher than other Aboriginal groups in Canada.[34] TB programs have once again become the focus of control for Nunavut, with territorial and regional TB coordinators hired and intensified surveillance promoted.[38] Contact tracing is expected to occur immediately following disease diagnosis and three months after, school aged children are screened for TB, and infants are given the BCG vaccine at birth.[38]

Greenland Inuit

Northern Europe is home to many traditional Inuit, with the population of Greenland (under the rule of Denmark) comprised of 89% of individuals reporting Inuit ancestry. The roughly 56,000 Greenlanders are concentrated in the country's capital, but also spread across 15 towns and smaller settlements.[42] A local hospital is found in each town.[42]

The Greenlandic peoples have experienced repeated TB epidemics, with the rate of TB reaching a maximum in the year 1952 at 2200 cases per 100,000 population.[27, 42] It was determined that a remarkable public health effort was required to prevent further escalation of the epidemic, and the National Tuberculosis Programme (NTP) was instituted.[43] Consequently, a screening and treatment campaign covering the entire nation was implemented along with routine BCG vaccination for all infants,[44] and resulted in a dramatic > 10% decline in the annual incidence of TB.[27, 42] A substantial decrease in mortality due to TB was also achieved due to improved living conditions, earlier diagnosis and TB treatment.[30] Over the course of a decade with marked NTP action, a 90% reduction of notified TB cases was accomplished.[43] Vaccine coverage among children under the age of 2 years in Greenland was impressively high (even in isolated and sparsely populated regions), and the success was partly attributed to the vaccination model which incorporated the offering of free vaccines administered by health visitors and the systematic calling of children at scheduled times.[45] Migration was associated with not receiving the vaccine.[45] The rate of TB reached a level comparable to western Europe in the 1980s[27] (the minimum TB incidence rate was reached at 25 cases per 100,000 population in the year 1985),[43, 46] and preventative efforts – routine neonatal BCG vaccination for instance, were abruptly abandoned by Greenlandic authorities in the year 1991.[27, 42, 44] This reduction in TB control activities heralded in a revival of the TB epidemic, and the incidence rate of TB once again began to rise [Figure 4].[42]

The intervening time period between 1991 and 1997 was marked by a doubling of the TB incidence since the rate reducing efforts were discarded,[43] and it was observed that a large portion of the afflicted were children under the age of 15 years.[27, 43] The increase was attributed to a series of micro-epidemics in small, isolated settlements characterised by local transmission, with a large disease burden placed upon the young.[43] The prominence of the young in the epidemic's distribution in the population of Greenland was indicative of recent transmission.[43] The Greenlandic peoples most

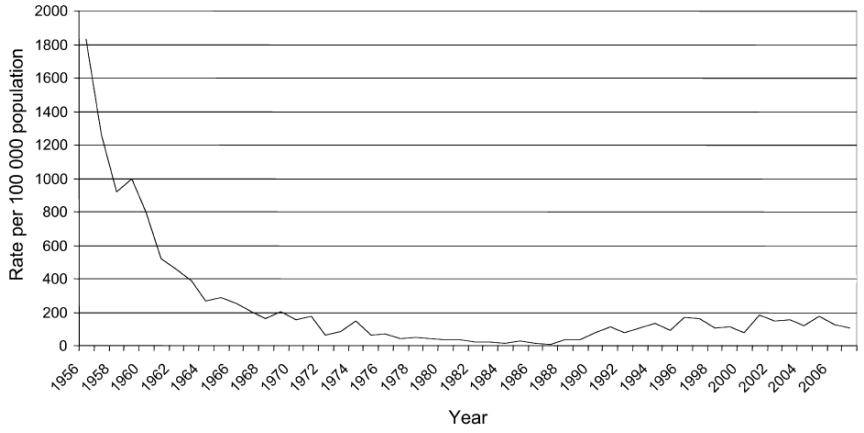


Figure 4. Incidence of TB in Greenland
The incidence of TB in Greenland has declined over time primarily due to control measures implemented by public health agencies. A rise in incidence was experienced following the stoppage of TB control efforts in 1991.

Adapted from: Ladefoged *et al*, 2011

affected by the TB epidemic in the 1990s were the circumpolar Inuit who had limited access to primary healthcare centres, medical personnel and diagnostic facilities,[46] and typically were only reachable by boat or helicopter.[43] The poor surveillance for TB further weakened case finding, case treatment, therapy with compliance, and control in disease spread.[43] A diagnosis of TB was difficult to reach due to the high prevalence of smoking and related long term coughs or bronchial abnormalities.[43] TB was not often suspected as the reason a patient presented with a chronic cough. Reactivation cases of TB were more likely to occur in the elderly, and it was put forth that a large reservoir of the bacilli was carried by 55 to 68% of the Inuit population born prior to the 1950s.[43] The increasingly positive HIV status of the population was also noted as a problem which could expand the spread of the TB epidemic.[43] To reduce the levels of TB in Greenland (an incidence rate of 172 TB cases per 100,000 population was reported for the year 1997),[43] the country's National Board of Health reintroduced mass BCG vaccinations of neonates into the population in the year 1997 to no apparent effect on TB rates,[27] accompanied by a complex system of surveillance, diagnostics, prophylactic treatment, notification, contact tracing protocols, TB education, and supervision of TB patients.[42, 46] Special nurses were assigned to monitor the epidemic in remote settlements.[46]

Nevertheless, Greenland has had a high TB rate in present times, averaging 131 cases per 100,000 population between the years 1998 and 2007[42], and still remains at 130 cases per 100,000 population as reported in the year 2010 [Figure 5].[47] TB transmission to Greenlandic children is high, with a 13.4% cumulative risk of infection by the time the child turned 18 years of age, for the year 2010.[27] Unfortunately, Inuit children had a significant risk of TB transmission > 4 times greater than that for children of other ethnicities, and the source contact from whom the child acquired the TB infection was predominantly someone from the same household as the child.[27, 47] The increased incidence is unrelated to any change in case definition,[43] deteriorating SES or living conditions, but could be an artifact of increased awareness of the disease, identification of prevalent cases infected decades earlier,[27] or improved diagnostic procedures.[42] A recent case-control study found that those with Inuit ethnicity had a 15.3 increased odds of TB compared to those who were not a member of the Greenlandic Inuit community.[42] Also at increased risk of TB were those who were unemployed, lived in small settlements, lacked access to water and hygienic facilities, suffered from malnutrition, or frequently used alcohol and tobacco products.[42] It was cited that access to health care from inaccessible settlements lead to delays in treatment and thereby higher infectious disease burden in these communities.[42] The occurrence of crowding in the residence or number of household members was not found to be a factor implicated in an increased risk of TB contraction in Greenland.[42] This finding was hypothesised to be reflective of the fact that persons per room did not reflect the cultural practice of congregating in a single room – irrespective of space.[42] However, when the Greenlandic Inuit population was inspected in particular, crowding was found to increase the risk of TB infection.[47] HIV infection[47] and diabetes were also unable to explain the high frequency of TB in Greenland overall,[42] yet diabetes was established as a risk factor for TB amongst the Greenlandic Inuit peoples.[48] The prevalence of diabetes within the Inuit community is high (10% of the population in the year 2012) and increasing, and the Greenlander's TB prevention efforts have been criticised with overlooking the association between TB and diabetes among the Inuit.[48] MDR-TB is uncommon in Greenland and thus, therapy is highly effective.[46, 47] That TB followed the trend of lowered social class

and hygienic standards led to the recommendation that public health interventions focus on improving lifestyle factors to indirectly lower the number of patients presenting with TB.[42]

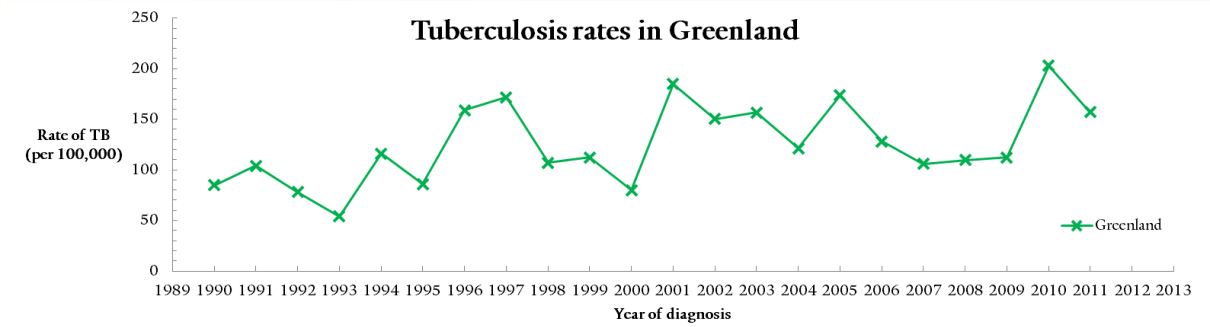


Figure 5. Incidence of TB in Greenland
A gradual increase in the TB incidence rate is observed in Greenland due to the stoppage of TB control efforts.
Source: Government of Greenland's *National TB strategi* and Soborg *et al*, 2001

The theory of the Inuit peoples being at higher risk for TB infection due to a factor endogenous to their ethnicity was explored in a study conducted by researchers concerning the cytokine response to *M. tuberculosis*.[49] It was found that cytokine patterns from the Greenlandic Inuit matched those of immune competent populations following PPD (purified protein derivative) TB antigen stimulation, suggesting the Inuit may not inherently be at greater risk of infection due to an impaired immune response.[49]

Alaska Natives

Alaska is home to many Inuit (or Eskimo) peoples as well as Alaskan Indians and Aleuts, and approximately 14.9% of the state's population claimed Inuit heritage to the United States Census Bureau in the year 2011. Alaska natives have a health care system both federally funded and tribally administered in the recognition that the native peoples of Alaska have different needs than those who are not of native heritage.[50] Alaska also instituted village-based community health aides in regional centres.[50] Most researchers have argued that TB was not present in Alaska until it was introduced by Europeans in the 18th century,[51] but some dubious skeletal remains from prehistoric men in the regions and early historical accounts support the view that TB was present (if not common) in the northern regions of the New World before European contact.[52] Generally, it has been concluded that the immunological naiveté of the native population combined with detrimental lifestyle changes and (anecdotally) the abandonment of traditional curing practices[53] lead to the TB pattern seen over the years.[52]

At the turn of the 19th century, almost every Inuit child born in the Yukon and Kuskokwim area of Alaska had a reaction to intradermally-introduced tuberculin by five years of age.[17] In the year 1910, some reports determined that the death rate due to TB was approaching 1000 per 100,000 population.[52] By the 1930s, it was noted that more death certificates cited TB as the cause of death than any other disease amongst the native peoples of Alaska despite the placement of nurses in large Indian villages by the Bureau of Indian Affairs.[54] For the year 1934, 655 per 100,000 deaths in Alaska were attributed to TB[55] in the native Indian and Inuit population with an upward trend, and the

disease was estimated to constitute 35% of all deaths.[31, 54] It was readily known that the native peoples of Alaska contributed most to the high TB death rate, and that TB was the leading cause of death in the state.[56] For example, in the year 1936, the death rate for Alaska natives due to TB was 794 per 10,000 population, compared to just 63 per 100,000 population for Europeans.[56] However, these numbers could slightly misrepresent the problem at the time, as many Europeans left Alaska for TB treatment, while the native Alaskans often attributed TB as the cause of most obscure deaths.[56] The health department was recommended to identify every individual in the state harbouring TB using xrays, to segregate active cases in sanitoria to prevent transmission and inactivate them using treatment or surgery, to trace the contacts of the TB patient, and educate the members of the population on precautions to take to guard against TB acquisition.[56] By the 1950s, it was said that 1 in every 4 infants was infected with the TB bacterium within the first year of life.[57] Alaska was undoubtedly suffering through a TB epidemic;[58] but despite the availability of control measures, none were used.[31] Isolation of individuals with active TB in hospitals or sanatoriums was the prime prevention and treatment strategy used before World War II, but bed space was limited.[51] TB was the scourge of Alaska,[57] and the layers of permafrost covering the land was acknowledged as a major barrier to providing care.[31]

The high prevalence of TB in Alaska came to the attention of the United States Centres for Disease Control and Prevention (CDC) following the second world war, and emergency action was taken[57] to control the epidemic through the authorisation of a TB Control Program.[31] The Alaska Department of Public Health aggressively supported and instituted TB case finding, education, BCG immunisation, outpatient treatment, chest xrays, ambulatory chemotherapy (especially for patients living in remote regions who were waiting for a hospital bed)[57] and patient hospitalisation or isolation.[31] Drug trials performed by the United States Department of Public Health and the CDC as well as a placebo-controlled BCG trial among Alaska natives informed treatment decisions.[59] Isoniazid chemoprophylaxis was utilised extensively in Alaska, and the drug was prescribed to people at risk of contracting TB (such as those with positive skin tests but negative chest radiographs) as a form of preventative treatment.[51] Urban-dwelling children in first and seventh grade were skin tested to ascertain risk of TB.[51] Despite the promotion of the BCG vaccine in Alaska and a mass vaccination campaign between the years 1949 and 1951,[58] use was limited and sporadic due to a scarce supply of personnel and difficulty administering the vaccine in remote regions before it was outdated, and attempts to implement immunisation against TB were essentially stopped by the year 1953.[51] Therefore, since only a small proportion of the population was immunised, success in reducing the rate of TB cannot be attributed to the BCG vaccine. Individuals infected with TB were carefully graded by the severity of their illness and treated accordingly to minimise further spread of the infection to other members of the community.[57] Those on treatment were assigned community health aides (CHAs) to supervise and support the patient.[51] When screening the population for TB, it was recognised early on that elderly family members were the likely source of their children's and grandchildren's infections, and thus were particularly encouraged to have a chest xray performed.[57] The substantial supply of personnel and facilities to the culturally-sensitive program ensured its success, and treatment resulted in a dramatic decrease of the death rate due to TB[57] to 8.5 per 100,000 population by the year 1964.[31] The risk of becoming infected with the tubercle bacilli was also

lessened, the number of new infections was markedly decreased,[58] and only 1 in every 100 infant was infected with the bacterium during the first year of life.[57] Indeed, children became rare patients for TB facilities in Alaska.[51] It was felt that the problem of TB was becoming concentrated within those who were previously infected.[58] The great success experienced in Alaska was credited to the uncommonly high cooperation[51] between the government and the Indian groups who took great interest in the health of their people and were eager to become involved in the TB program.[31] Unfortunately, TB continued to be the main medical problem in Alaska with respect to the rest of the United States, and caused much morbidity although the disease was being identified and treated at an earlier stage than in the past.[31] Between the 1950s and 1970s, the TB disease pattern observed amongst Alaskan natives was remarkably similar to the population of Greenland for the same time period [Figure 6].[51]

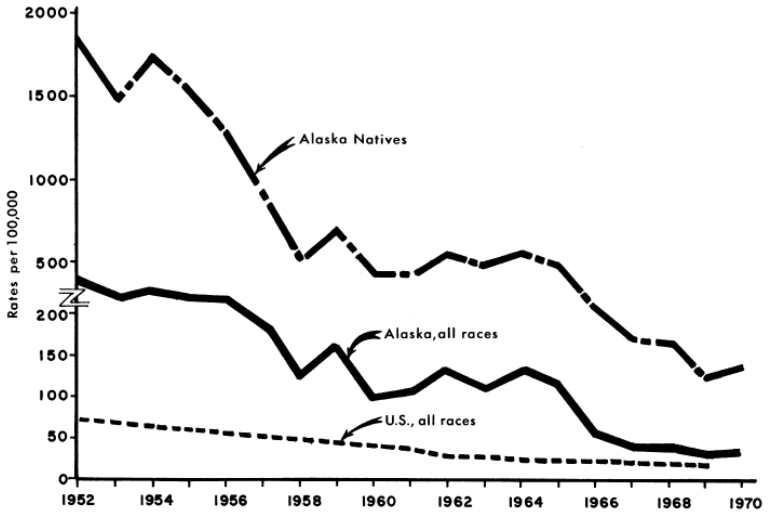


Figure 6. Incidence of TB in Alaska
It is observed that historically, Alaskan natives consistently maintained higher incidences of TB in the past when compared to state and national rates.
Adapted from: Johnson, 1973

Currently, the control obtained over TB by the 1960s has been maintained by the Indian Health Service and Alaska Department of Public Health, but Alaska natives still have higher rates of TB with higher levels of attributable morbidity[60] compared to other Alaskans [Figure 7], experience the smallest decrease in TB incidence with respect to other American-born ethnic groups,[61] and village outbreaks are still a threat.[55] This health disparity[60, 62] is not believed to be diminishing[63] due to disadvantages in income and education[64] manifesting in overcrowding,[56] cigarette smoking, heavy alcohol use,[65] high rates of diabetes and a deterioration of the public health infrastructure.[60] Interestingly, disparate rates of TB exist even after controlling for socioeconomic factors typically associated with TB, hinting that the Alaska natives may have some biogenetic predisposition to the disease.[64] Early in the epidemic, it was commented that the native peoples must have some natural resistance to the disease, as so few had an active form of TB despite such a high prevalence of infection.[56] Contact investigation has been maintained (despite the need for a public health nurse to

often fly to different rural villages during lulls in snowstorms), and the proportion of contacts adequately tested increased from 51% to 75% between the years 2000 and 2003.[55] The importance of contact investigation is readily understood when a case study discovered that one case patient diagnosed with infectious TB in the year 2000 involved eight Alaskan villages, 26 additional persons with TB were found, and 48 people with newly positive TB skin tests were examined.[55] Most village elders are infected with TB and go undetected for significant periods of time.[55] The crowded dwellings, limited air circulation, and frequent travel from village to village facilitates TB transmission.[55] To make the TB program more culturally appropriate, representatives from the Alaska natives peoples and regions were placed on the boards, and non-native employees were made to understand the cultural values of the people they serve.[53]

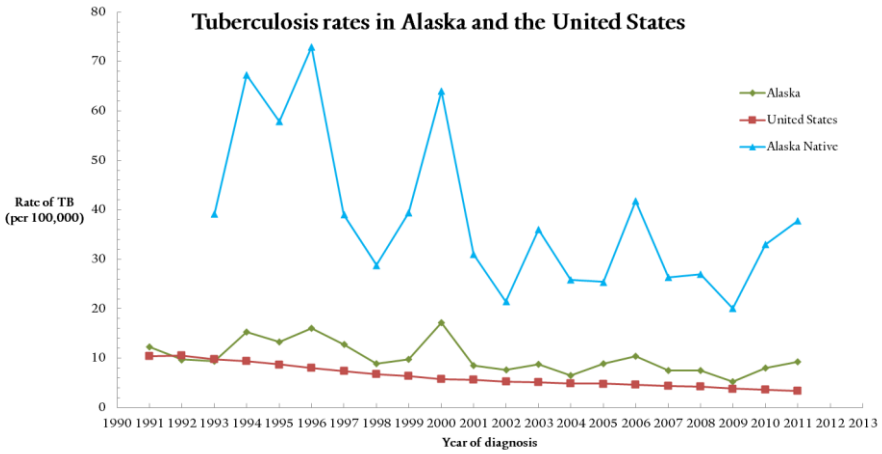


Figure 7. Incidence of TB in Alaska
It is observed that currently, Alaskan natives consistently maintain higher incidences of TB when compared to state and national rates.

Source: United States CDC

Native Americans

The population of the United States has a 1.2% proportion of Native Americans (including Alaskan natives) as of the year 2011 according to the United States Census Bureau. The occurrence of TB within Native American tribes pre-colonialism has been debated, although it has been put forth that with the original migration of peoples to the Americas, TB was brought and persisted at a low level of endemnicity in small, nomadic populations.[66] This low level of TB escalated into an epidemic with the onset of overcrowding, poor nutrition, alcohol abuse, and other general TB risk factors in the native populations.[67] However, the fact that most native peoples in America were immunologically naive to TB makes the previous statement difficult to support[66] and suggests a lack of ancestral experience with the disease.[68] Many native tribes believed that invisible enemies (that is, bacteria, viruses and other microorganisms) continually put their population at risk, and had traditional healing methods to deal with them.[69] Tuberculosis became a dreaded disease often highly stigmatised.[70]

The trail between Native American tribes, TB and contact with different cultures is a confusing, indecipherable maze. TB began to become a major problem for tribes with increased population density and cultural changes brought on by contact with European civilization, as well as their eventual relocation to reservations and deteriorating living conditions. [71] Prior to settlement on reservations in the 1880s, only sporadic cases of TB were observed amongst the Indians.[68] The reservation system in the United States created poor living conditions, sporting inadequate sanitation, traditional diets, housing, medical care and health education.[69] It was noticed that whenever Native Americans were forcibly confined to a compound, prison or reservation, an outbreak of TB would develop.[68] Depression due to their changed way of life and weakness in the mind, as well as body weakness through malnourishment or ill health, were both said to allow the tubercle bacteria to become active and cause TB.[69] In the year 1886, the death rate due to TB in Native Americans had reached 9,000 per 100,000 population – much higher than anything observed anywhere in the world at that time.[68] The first TB cases on a reservation or in a native community were often from non-native visitors who carried the bacteria into the population.[69] As time passed, farms, railroads, and especially schools facilitated greater contact between Native Americans and the TB bacilli.[69] From the 1920s to 1940s, those who perished from TB were mostly teenagers and young adults.[69] TB control was hampered by lack of a specific treatment, and only dissipated by the breakthrough of ambulatory chemotherapy in the early 1950s.[71] Some risk of noncompliance and mistrust of non-traditional treatment methods contributed to the difficulty in lowering the rate of TB amongst Native Americans.[71]

As TB within Native American groups grew to a prominent cause of morbidity and mortality, it was decided that public health efforts must be made. Field nurses, doctors and teachers educated Indian elders, who in turn taught children about the causes, transmission, treatment and prevention of TB in a manner understandable to their community.[69] As a result, the incidence rate of TB and deaths due to TB amongst Native Americans dropped dramatically by the 1940s,[69] even in the absence of widespread BCG vaccination or treatment.

In general, contemporary Native Americans face less threat from TB than in the past and have been experiencing reduced mortality due to TB and incidence of active disease since the 1950s [Figure 8].[72] Making TB a notifiable disease made the quality of data collected by the Indian Health Service higher.[72] However, lowered SES indicators – specifically crowding, income, poverty, public assistance, unemployment and education, were shown to increase the relative risk of TB.[73] Unfortunately, American Indians and Alaska natives are 5-fold more likely to die of TB than what the national average of the United States has been calculated as, and the link to HIV infection has been made (but HIV infection as a risk factor of TB is of more importance within other ethnic groups).[61] Drug resistant forms of TB do not account for many cases, with just 2.4% of cases reported being resistant to first line drugs such as isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin.[61] The relevance of preventative TB treatment was shown in a case-control study showing that subclinically-infected TB patients who had received adequate isoniazid chemoprophylaxis were significantly less likely to develop TB disease than those who did not receive prophylactic treatment.[74] The case-control study also emphasised the implementation of TB control programs with a focus on prevention within high risk groups, such as those with diabetes and

chronic renal failure.[74] However, one study concluded that the rate at which a response to a newly identified Native American TB patient was initiated was unsatisfactory, and onward referrals were only completed 67% of the time (below the expected average) – a result primarily attributed to the homelessness, alcoholism and low rate of return (to visit the community nurse following diagnosis) of the population.[75] Adjusting for SES between the years 1987 and 1993 accounted for approximately half the increased risk of TB associated with being Native American,[73] suggesting that TB is mainly a function of SES in the United States at the current time and TB is not merely a ' racial' disease.[72] It was found that TB had the highest index of disparity (170.3%) when compared across all races or ethnicities in the United States for the year 1998;[76] yet, native elders in the older age group remain to be disparately affected by TB even within Aboriginal groups (negatively compounded by chronic malnutrition, smoking and alcohol).[77] The United States aims to at least reduce the incidence of TB to < 1 per million population, which requires that latent TB prevalence be < 1%.[78] Native Americans presently residing in the United States are treated by a health department which has believed for decades that TB is both preventable and curable, with the elimination[78] of TB from Indian reservations an achievable outcome if concerted effort and cooperation is applied.[71] This attitude, as well as the acknowledgment that historical trauma must be addressed through the employment of culturally appropriate TB strategies, is essential when fighting TB within aboriginal communities.[79]

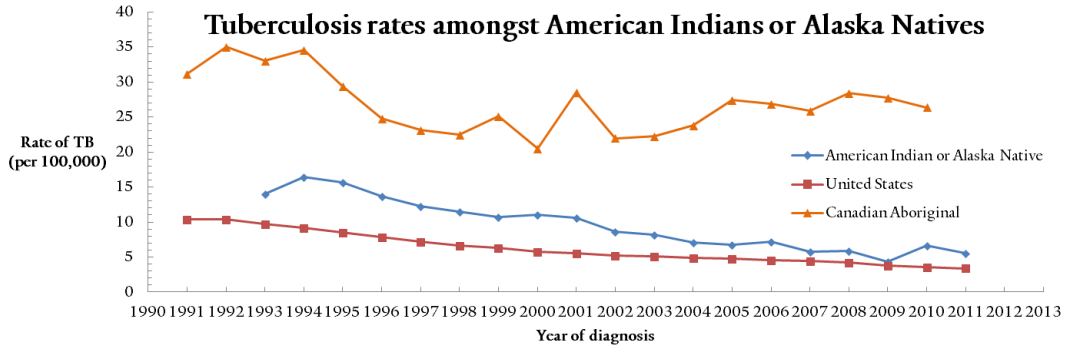


Figure 8. Incidence of TB amongst Native Americans in the United States
It is observed the TB rate of Native Americans (including American Indians and Alaskan Natives) has been approaching that of the nation over time. Canadian Aboriginal rates, however, remain higher than Native American Indians in the United States.

Source: Statistics Canada and United States CDC

Presentation and Analysis of Findings in Nunavut

Statistics Canada was accessed and data tables for risk factors were drawn. Risk factors for TB[80] in the population of Nunavut were inspected and assessed for a possible level of influence on the rate of TB in the territory. A possible explanation to the overall dramatic increase in TB since the year 1999, and consistently higher TB rate in Nunavut with respect to Canada and other comparable populations, was developed. The extraordinary penetration of TB in remote communities of the Canadian north is noted, but Nunavut appears to be disparately afflicted.

Tuberculosis control

Nunavut has some of the higher TB rates in the world,[81] and TB transmission is greater amongst the native peoples of a country and those locally born.[80, 82] The pattern of the TB outbreak in Nunavut appears to either be characteristic of a population lacking in TB control measures, or one whose control effort policies are ineffective at the population level. When compared to other Canadian provinces and territories, Nunavut clearly has TB incidences far above those reported for other regions and Canada overall – even when compared to other northern territories [Figure 9a, 9b].[1] However, it is interesting to remark that Nunavut and the Northwest Territories (the region from which Nunavut split) initially had comparable rates of TB in the year 1999 immediately following Nunavut's independence,[1] suggesting that some change in health service administration or organisation with the new governmental order may have influenced the subsequent rise in TB rates. The percentage of TB cases in Canada attributed to the territory of Nunavut[1] has also changed over the years [Figure 10] supporting the belief that Nunavut has been subject to TB outbreaks as opposed to TB affecting the region at an endemic level. Although TB may take hold in a population due to socioeconomic status struggles, the rates of TB may arguably be best lowered through intense efforts to control TB. TB control in the past was most effectively achieved through initial isolation of TB patients until noninfectious, case treatment until therapy is complete, early case identification, and the identification and treatment of those who were in contact with the TB patient.

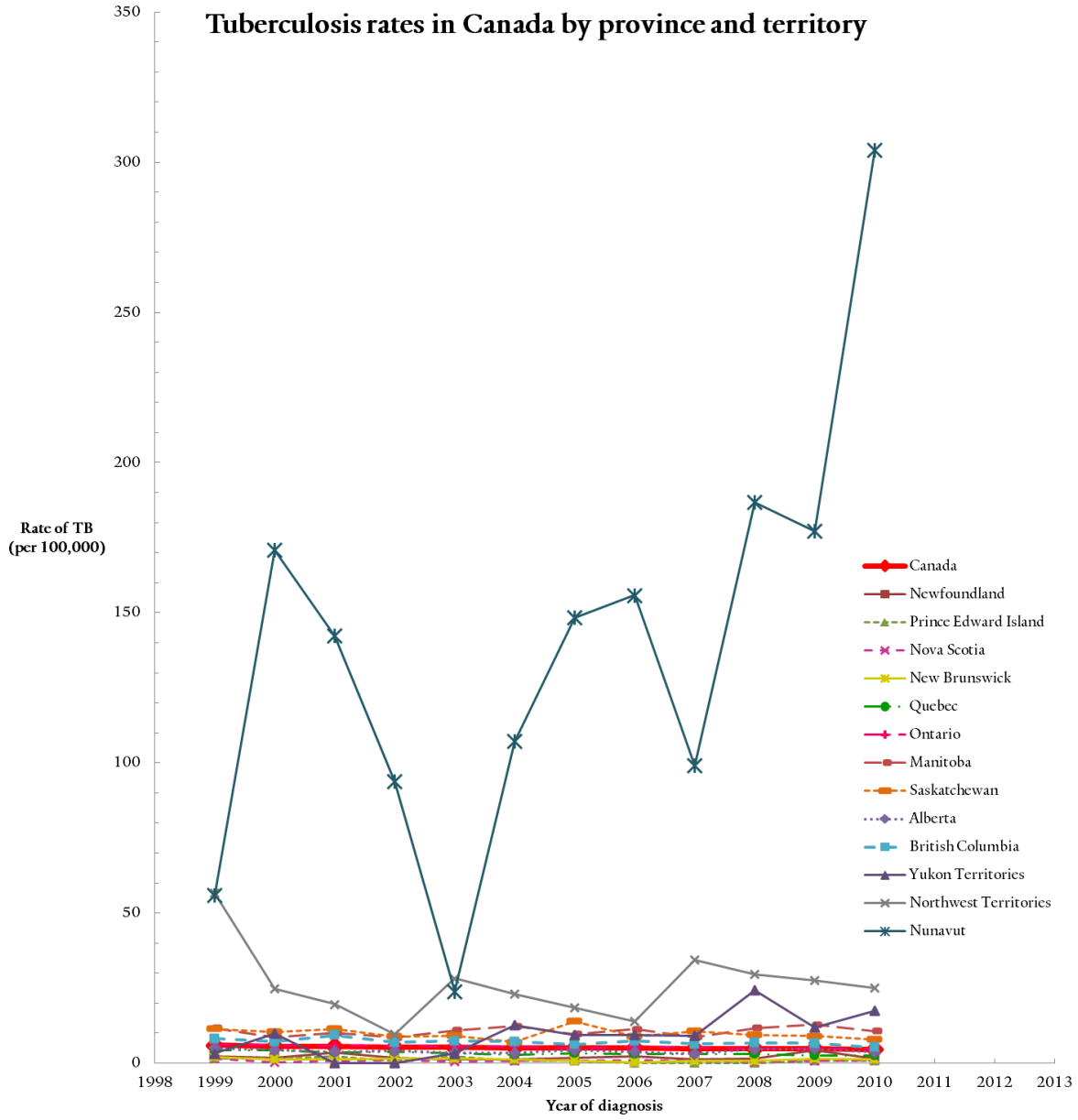


Figure 9a. Incidence of TB in Canadian provinces and territories

When the incidence of TB in other Canadian provinces and territories are compared to those reported in Nunavut over time, it is apparent Nunavut has a disproportionately high TB rate with respect to the rest of Canada.

Source: Statistics Canada

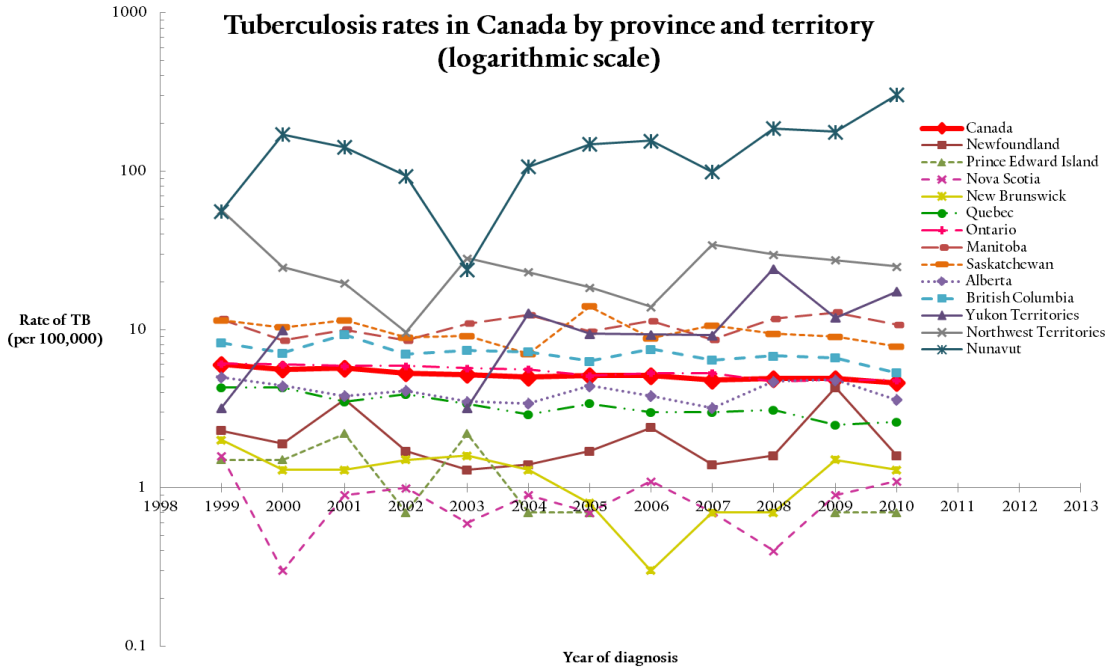


Figure 9b. Incidence of TB in Canadian provinces and territories

When the incidence of TB in other Canadian provinces and territories are compared to those reported in Nunavut over time, it becomes obvious that Nunavut has a disproportionately high TB rate with respect to the rest of Canada.

Source: Statistics Canada

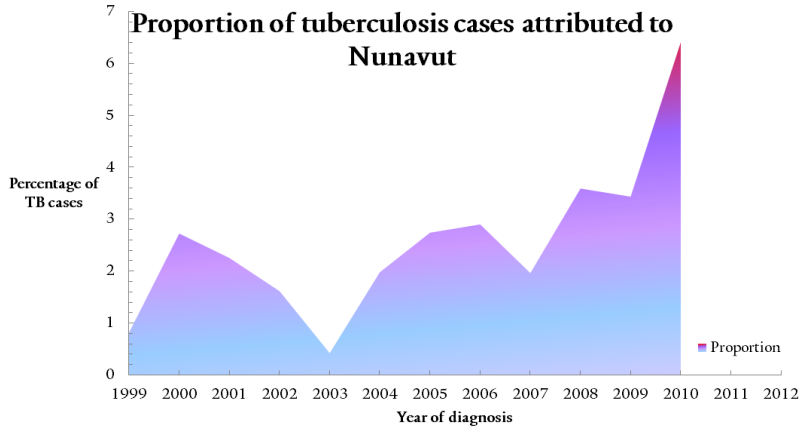


Figure 10. Percentage of TB cases in Canada attributed to Nunavut
The proportion of TB cases attributed to Nunavut patients for the total number of TB cases in Canada has changed over time.

Source: Statistics Canada

When compared to Aboriginal and Inuit populations in Canada, Greenland and the United States, Nunavut still fares worse than all other groups [Figure 11] – especially when the average incidence since the year 1999 for each group is calculated [Figure 12].[1] The pattern of TB in Nunavut appears to be most closely correlated with Greenland, and many common risk factors are found between both populations; although wider variation in incidence rates is observed in the Canadian territory. The similar rates of TB between the Nunavut and Greenland populations for the past decade was unexpected. The wide variation in TB incidence in Nunavut may be used as further indication that Nunavut is suffering from repeated TB outbreaks, as opposed to merely having a high endemic level of TB in the territory. However, large variation in incidence would naturally be observed in a small population such as that in Nunavut, as small fluctuations in case numbers would have great influence over the calculations for incidence. Correspondingly, the standard deviation in Greenland would be smaller due to their larger population size.

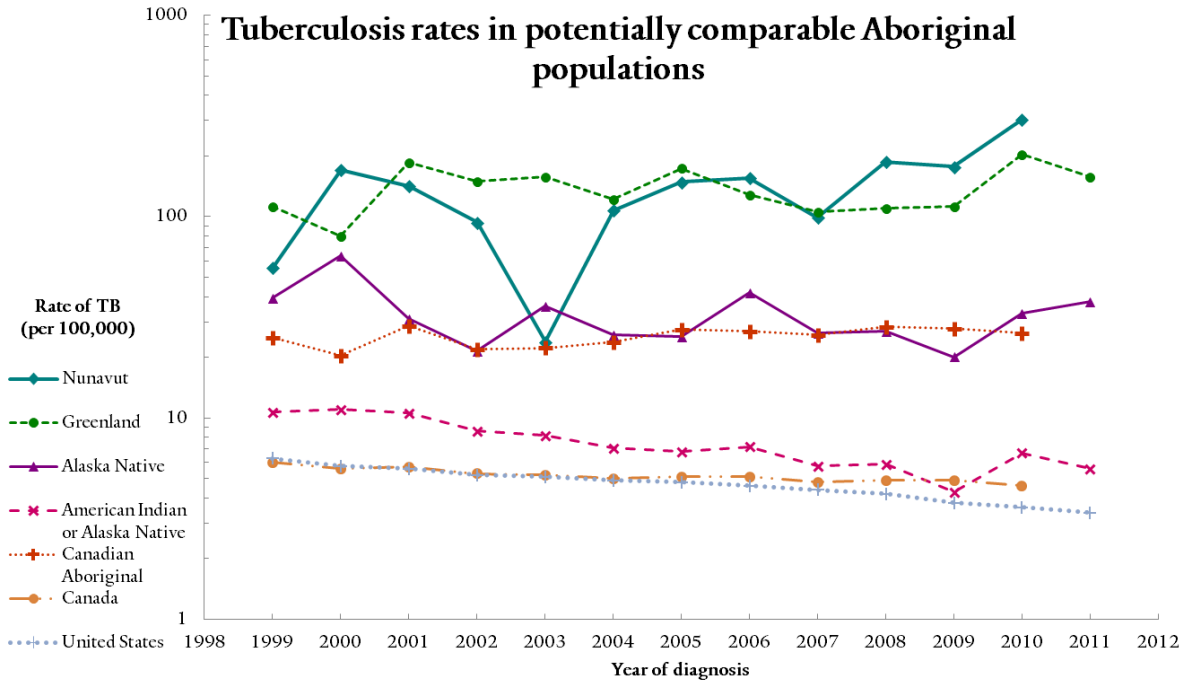


Figure 11. Incidence of TB in Nunavut with respect to comparable populations

The incidence of TB in Nunavut is compared to the incidence amongst Greenlanders, Alaska natives, American Indians and Canadian Aboriginal peoples. Nunavut has, in recent years, had the highest TB rates of all groups. Canadian rates of TB and the rate of TB in the United States are comparable and much lower than the TB rates reported for their indigenous populations.

Source: Statistics Canada, United States CDC and Government of Greenland's *National TB strategi*

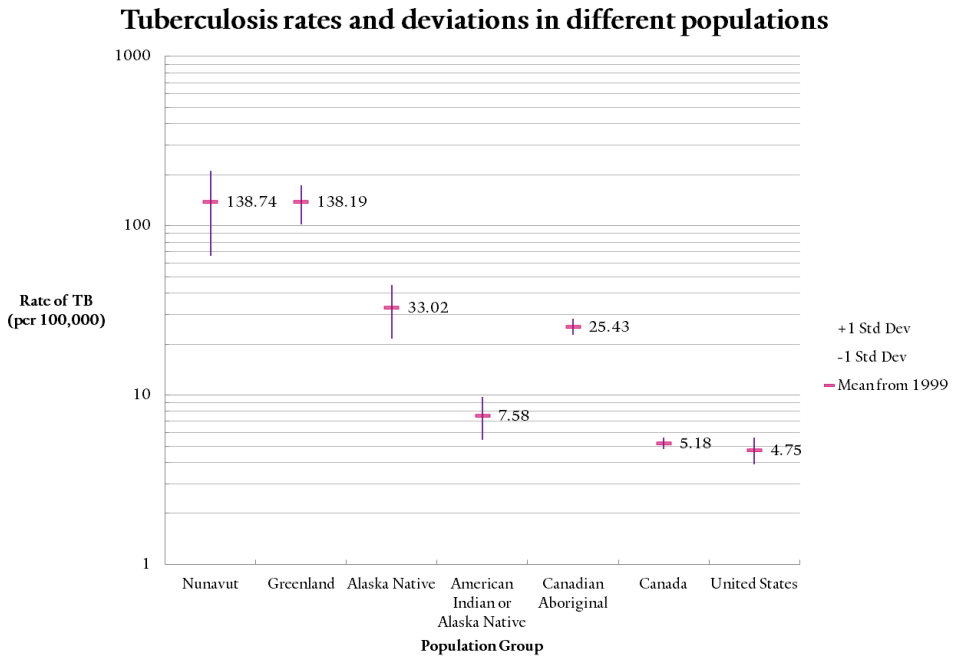


Figure 12. Mean incidence of TB in Nunavut and comparable populations since the year 1999
The incidence of TB in Nunavut is compared to the incidence amongst Greenlanders, Alaska natives, American Indians and Canadian Aboriginal peoples. Nunavut has, in recent years, had the highest TB rates of all groups (although Greenlander rates are comparable) and also has the largest standard deviation – supporting the suggestion that Nunavut is experiencing an outbreak of TB. Canadian rates of TB and the rate of TB in the United States are comparable and much lower than the TB rates reported for their indigenous populations, and also have smaller standard deviations.
Source: Statistics Canada, United States CDC and Government of Greenland's *National TB strategi*

The pattern of the TB outbreak in Nunavut is suggestive of much new transmission, resulting in new cases. This would imply that the background rate of TB does not need to be high. From the current trend of TB, it may be estimated that one-third to one-half of the population is infected with the bacterium, and either presents with active TB or is a latent carrier. The fluctuating incidence of TB was reported to have been observed in Nunavut in the 1990s, and thus it is ascertained that the recent fluctuation in TB rates is not a new trend.[83] The cause of this fluctuation is difficult to determine, but could be simply ascribed to having changes in case numbers in a small population.

The age at which risk of TB is maximal depends upon the prevalence of active infection within the population.[8] When many open cases of TB appear, even small children are at risk of infection; but, in a community where cases appear in the elderly with greater frequency, the age group at highest risk is adolescence.[8] The data provides evidence that new infections are occurring within Inuit communities, as pediatric TB is an indicator of ongoing TB transmission.[41] In general, it may be said that the younger the cases of TB, the more intense the transmission.[41] The involvement

of a large portion of adolescents and young adults in the outbreak presents a pattern suggestive of active community transmission within the regions of Nunavut [Figure 13].[1, 28]

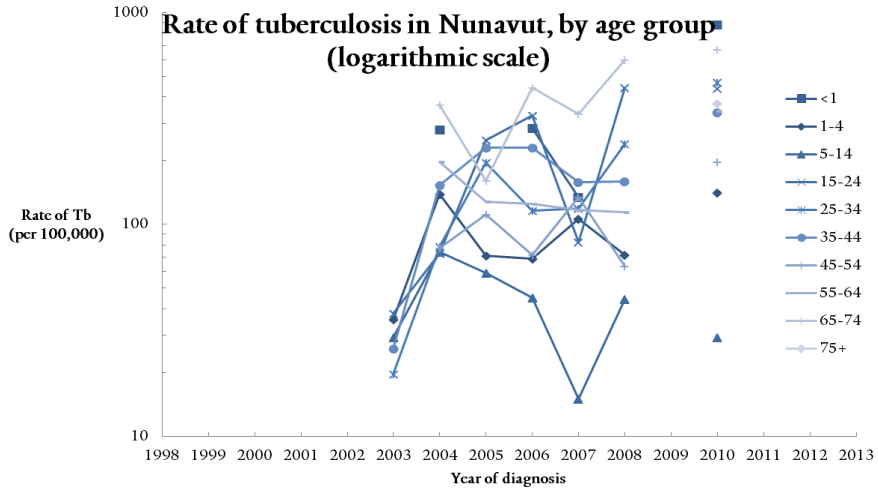


Figure 13. Incidence of TB in Nunavut stratified by age group
The appearance of a high rate of TB amongst children and young adults in Nunavut is suggestive of active TB transmission. When data are plotted on a log scale, values of zero and below are not plotted, and the province or territory displaying no data may merely have an incidence rate of zero.

Source: Statistics Canada

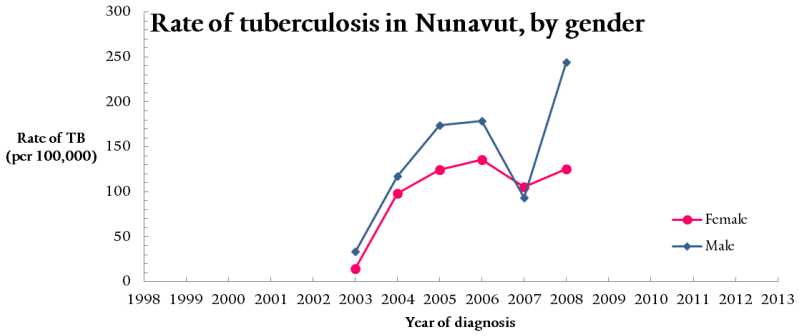


Figure 14. Incidence of TB in Nunavut stratified by gender
Males in Nunavut report higher TB rates than females. Prior to the year 2003, data was collected under "the North", and thus was excluded from analysis due to possible territorial differences.

Source: Statistics Canada

Nunavut displays the commonly observed gender disparity, with males reporting higher incidences of TB than females [Figure 14].[1]

Many indicators from Statistics Canada reported values based on provinces and "the North": a term encompassing the Yukon, the Northwest Territories, and Nunavut.[1] Although administratively

desirable, using "the North" conceals possible variation in TB and associated TB measures in these three territories.

Human immunodeficiency virus

HIV-infected individuals have an increased risk of developing TB upon infection.[80, 84] Resistance to TB provided by the immune system may be reduced due to infection with the human immunodeficiency virus (HIV).[8] Reduced host immune responses facilitate the increase in susceptibility and allow for reactivation or reinfection with *M. tuberculosis* to occur. The granulomas located in the lungs have suboptimal immunologic function when a TB patient is co-infected with HIV, and are unable to contain or eliminate the TB bacilli, leading to bacterial dissemination and active disease.[85, 86] This may be due to increased HIV replication at sites of TB infection where an abundance of immune cells are present, the induction of $CD4^+$ T cells near TB bacterium, or inhibition of the macrophage killing function by HIV.[85] No significant evidence has been presented to suggest that HIV-positive TB patients are more infectious.

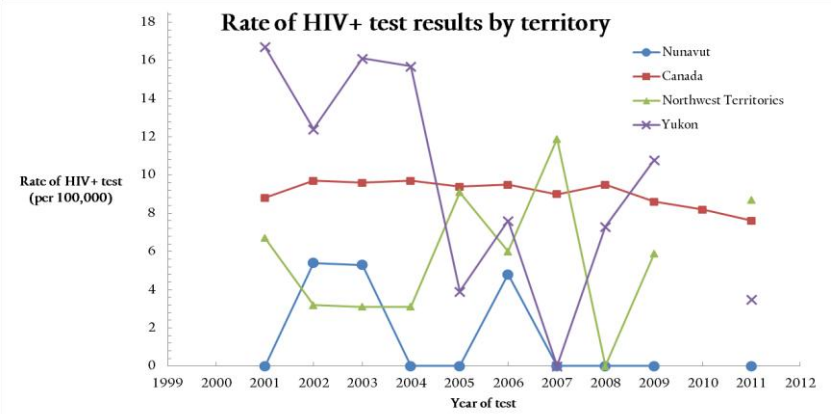


Figure 15. Rate of HIV-positive test results in Canada's North
The rate at which positive HIV test results are reported by adults > 15 years of age appears to be lowest in Nunavut compared to other northern territories, but this results may be due to underreporting and inadequate HIV testing in Nunavut. HIV is a risk factor for TB.

Source: Statistics Canada

The people of Nunavut have a higher risk of HIV infection due to the appearance of certain risk factors for HIV such as transience and injection drug use, but HIV does not appear to be a common coinfection with TB amongst those patients who consented to being tested for HIV [Table 1]; nor does HIV appear highly prevalent in Canada's north (although this result could be attributed to poor HIV testing and reporting for the region) [Figure 15].[1] It is proposed that the appearance of HIV in the population of Nunavut is not driving the increase in TB infections as has been observed in other populations in the world, such as with Native Americans in the United States.

Table 1. Reported new active and relapsed tuberculosis cases by HIV status in Nunavut

Year	HIV+	HIV-	Unknown	Notes
1999	1	16	22	the North
2000	1	38	22	the North
2001	0	25	22	the North
2002	0	18	13	the North
2003	0	4	3	
2004	0	16	16	
2005	0	34	11	
2006	0	42	6	
2007	0	24	7	
2008	0	43	16	
2009				
2010				
Total	2	260	138	
% of Total	0.76	99.24		

Source: Statistics Canada; Percent of total calculated from known HIV status only

Diabetes mellitus

Recent studies have provided evidence supporting the centuries of observations purporting that individuals with diabetes mellitus are more likely to progress to active TB, and those patients afflicted with both TB and diabetes are at an increased risk of treatment failure and death.[87] The link between diabetes and TB appears to be illogical, as the hyperglycemia indicative of diabetes stimulates NADPH oxidase – an enzyme involved in the respiratory burst generated by macrophages and monocytes when destroying *M. tuberculosis*.[7] It has been put forth that diabetes is not contrary to the survival of *M. tuberculosis* because diabetic patients inhibit macrophage

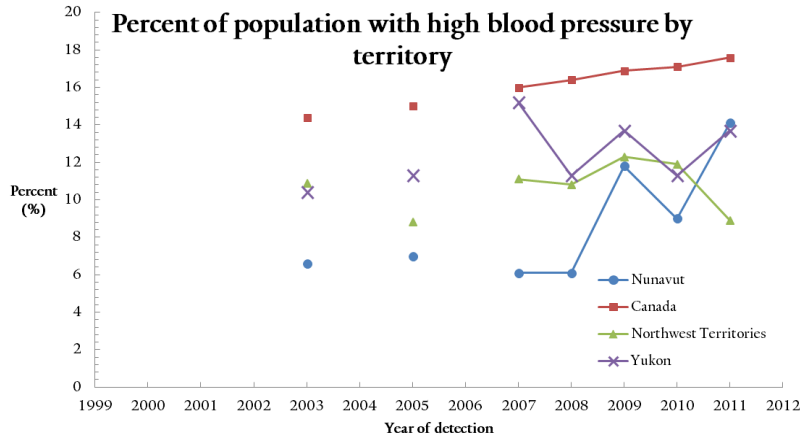


Figure 16. Proportion of the population with high blood pressure in Canada's north
Nunavut appears to have the lowest percentage of the population with high blood pressure compared to the rest of the Canadian north, but this could be a result of misreporting or inadequate testing. High blood pressure is a risk factor for diabetes, which is a risk factor for TB.

Source: Statistics Canada

NADPH oxidase through glycation of enzyme subunits during chronic exposure to high levels of glucose, allowing the *M. tuberculosis* to live freely within the cell.[7]

First Nations, Mé tis and Inuit peoples are at greater risk of diabetes than other Canadian ethnicities and races, but data concerning the prevalence of diabetes cases in Nunavut is too poor to be reported.[1] However, the proportion of the population with high blood pressure has been measured (if unreliably), and it would appear Nunavut residents have lower blood pressure than other Canadian residents or northern territories [Figure 16].[1] It is difficult to ascribe any meaning to these results in the context of TB due to the poorness of the data, as although high blood pressure is a risk factor for diabetes; and in turn, diabetes is a risk factor for TB, diabetes may still have some influence over the increasing incidence of TB in Nunavut as the percentage of the population with high blood pressure may be trending upward. However, it is concluded that the contribution of diabetes to the increased TB rates in Nunavut is low as no evidence exists to support diabetes as a risk factor for TB in Nunavut.

Bacterium

Drug resistance, especially to the antibiotic isoniazid, is of great concern in areas where the prevalence of TB is high.[14] In the northern regions of Canada, the appearance of antibiotic resistant TB is limited. MDR-TB isolates are rarely observed in Nunavut,[1] suggesting that treatment regimens are adhered to by patients. The only MDR-TB found in Nunavut occurred in one patient in the year 2001, with all years following reporting only susceptible isolates.[1] However, resistance to one or more drugs was observed recently in the years 2009 and 2010,[1] prefacing the beginning of what may become widespread multidrug resistance. The assertion that MDR-TB is not yet a major problem in Nunavut is also supported by evidence showing few patients defect from the TB treatment regimen.[1]

Whether an infected individual has the TB disease or latent TB (as evidenced by skin tests) determines the shape of the epidemic in the population. However, data on latent TB within Nunavut was not found and no evidence of mass TB skin testing has been recorded.

Poverty

TB has been labelled a disease of poverty, as TB follows the social gradient – increasing in prevalence in poorer areas and within poorer households.[88] Certainly, TB is primarily seen in the most socioeconomically deprived regions.[89] Under this interpretation of a social disease, social, economic and environmental conditions have been targeted for TB control efforts and studies as risk factors for disease acquisition.[42] Nunavut residents suffer high levels of poverty,[28] as well as many of its associated hazards; social factors have frequently been blamed for the large TB outbreak in Nunavut which has occurred over the last decade.[90] The standard of living in Nunavut is lower than the Canadian average and the territory's residents experience poorer general health.[26] In general, the First Nations people have been deemed the most disadvantaged group in Canada.[90]

Arctic homes are often described as small, cramped, damp and polluted with tobacco smoke.[29] Unsafe housing conditions may impact the health of residents, and thus healthy housing recommendations are presided over by many regional Departments of Public Health.[91] Overcrowded housing with poor ventilation[40] is typical for many households in Nunavut,[28, 92] thereby enhancing

the transmission of airborne pathogens, such as those which cause TB.[93] The high reproductive rate of TB[10, 11] also fuels transmission in overcrowded settlements. Census data from Statistics Canada has revealed that 39% of the Inuit population in Nunavut lived in a crowded dwelling in the year 2006 – a reduction from the 43% of Inuit living in overcrowded conditions 10 years prior, in the year 1996.[91] However, estimates from the Aboriginal Peoples Survey conducted in the year 2001 claim 54% of Inuit in Nunavut live in overcrowded residences.[92] In addition, 26% of Inuit peoples reported living in dwellings requiring major repair in the year 2006 – a proportion which had increased from the 21% reporting poor construction in the year 1996.[91] Poor housing conditions have been closely associated with the transmission of contagious diseases, such as TB, and it has been demonstrated that the quantity of persons sharing a dwelling may be an indicator for repeated respiratory infections.[91] In Nunavut, up to 18 people may share a small house, with beds used in shifts.[93] Inuit children have been especially affected by infections of the lower respiratory tract (of which TB is one), and the inadequate quantity and quality of living space in Nunavut has been blamed.[92] Similar findings have been documented in Inuit communities in Greenland and Alaska.[92]

Migration [Figure 17], especially through trucking or the transient drifting of homeless between territory and provinces, may import new TB cases into Nunavut as occurred on Native American reservations in the United States. Migration may also lead to the missing of the scheduled TB vaccination or screenings for Nunavut residents, thus weakening an already faltering control program. Migration is seen in Nunavut, as nontrivial proportions of the small population travel in and out of the territory.

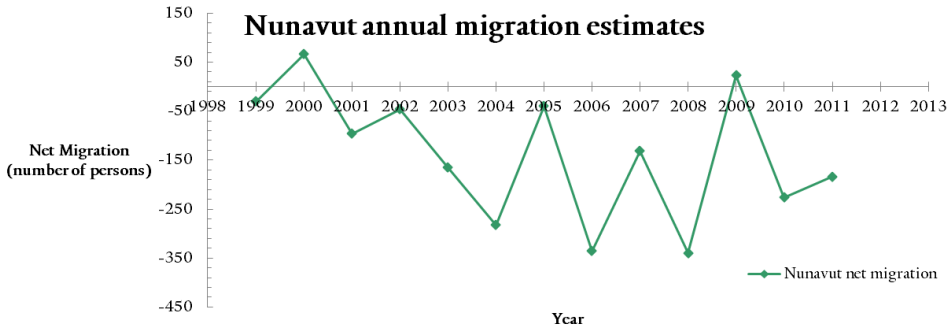


Figure 17. Nunavut's net migration per year
Nunavut appears to have a significant proportion of the population migrating in and out of the territory. Migration may import TB into the region, or make TB screening and BCG vaccination more difficult.

Source: Statistics Canada

Malnutrition is still highly prevalent among northern Canada's Aboriginal peoples [Figure 18].[93] Had the adolescents and young adults primarily infected with TB been healthy, their immune response would have been able to suppress the infection.[94] The protection Inuit peoples may have gained from their diet rich in marine mammals and fish, in conjunction with the vigorous physical activity needed to capture the food, has been lost in many Inuit regions of the world.[29] TB has been known to be a nutrition-sensitive disease, particularly affecting those deficient in nutrients.[95]

Nunavut's population suffers from severe food insecurity when compared to other northern regions of Canada, and this likely contributes to the high incidence of TB in Nunavut.

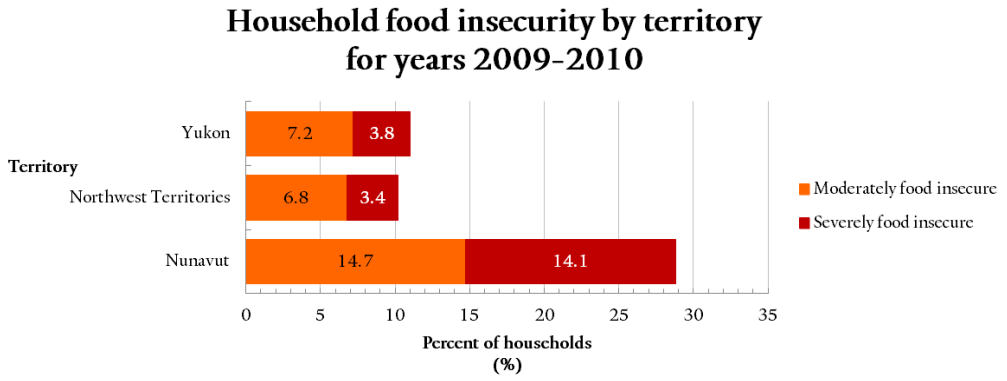


Figure 18. Food insecurity in households across Canada's north in the years 2009 to 2010
Almost 30% of Nunavut households report food insecurity, which is over double the percentage of households reporting food insecurity in either of Canada's two other northern territories. Poor nutrition may put Nunavut residents at greater risk of TB.

Source: Statistics Canada

Malnutrition and poor nutritional content in foods lowers immune resistance to TB.[8, 96] In particular, vitamin D deficiency from a lack of the substance in the diet or the minimal exposure to the sun has been suggested as a risk factor for TB.[97] In the past, vitamin D-rich cod liver oil capsules and sunlight[98] were administered to improve the health of TB sufferers, but this knowledge waned with the advent of antibiotics.[96, 97] Vitamin D may act as an immunomodulator, regulating the adaptive and innate immune system through a receptor[96] found upon many immune cells which, when bound, leads to the production of antimicrobial peptides.[97] In situations of low vitamin D, ligation of Toll-like receptors on the surface of macrophages leads to an upregulation of the vitamin D receptor, but when no vitamin D is bound, production of the antimicrobial peptides is not initiated.[96, 97] Thus, in the absence of vitamin D, the first line of defense against TB (that is, antimicrobial peptides) is hampered.[96] Vitamin D may also support other immune responses against TB, such as autophagy and cytokine production[97] and have antiproliferative effects against the bacillus.[96] Studies conducted on vitamin D supplementation to ward off or treat TB have been inconclusive.[97]

The peoples living above the Arctic Circle, including those living in Nunavut, are at high risk of vitamin D deficiency due limited ultraviolet B exposure and dietary intake as a consequence of their high latitude and decreased consumption of traditional foods, respectively.[98] The fatty fish and marine animals rich in vitamin D are no longer standard fare during meals, and ultraviolet B radiation (considered the principle source of vitamin D) has limited reach to the inhabitants as a function of the angle at which the solar rays hits the earth's surface up north.[98] A meta-analysis found that TB patients from Nunavut had lower levels of the circulating vitamin D metabolite, 25(OH)D, than appropriately matched controls.[98] A case-control study in Greenland (in which 81.5% of the participants were of Inuit origin) mimicked the findings in Nunavut, although it was ascertained that

a U-shaped association was present, as individuals with both low or high serum vitamin D concentrations had higher risk for active TB.[99] Furthermore, Nunavut adults were found to intake less than a quarter of the recommended dietary allowance (RDA) for vitamin D in the United States and Canada.[98] The change in diet from traditional to imported, low nutrient value foods has coincided with the resurgence of chronic and infectious diseases within northerly Aboriginal populations.[98] It could be suggested that the population of Nunavut is collectively immunocompromised due to their low vitamin D status.

Alcoholism, including heavy alcohol use and alcohol use disorders, has been supported epidemiologically as a risk factor for incident TB[80] and reinfections.[82, 88] Sustained, heavy drinking impairs the immune system, leading to an increased risk of TB infection, reinfection, or reactivation of a latent infection, as well as an increased risk of adverse outcomes during treatment.[88] In this immunocompromised state, the severity of the TB infection is greater than that for those who abstain from alcohol.[88] Intracellular survival and growth of *M. tuberculosis* within alveolar macrophages (the agents of the immune system generally tasked with destroying the bacilli) is enhanced in the presence of alcohol due to the suppression of antimycobacterial defense mechanisms typically employed by macrophages, such as mobilisation, adherence, phagocytosis, antigen presentation to lymphocytes, and superoxide production.[88] Alcohol use may also result in defective lung granuloma formation.[88] Chronic exposure to alcohol may suppress cytokine production and thus break cellular communication between immune cells.[88] The stigma associated with alcoholics, as well as their propensity for homelessness, imprisonment and malnutrition[88] may delay access to care for a TB infection. First Nations people have been plagued by alcoholism since colonial times, and this problem likely exacerbates the transmission of TB in Nunavut.

The smoking of cigarettes independently increases the risk of infection with *M. tuberculosis*, the development of severe TB and death from TB in a strong dose response pattern, whereby the greater the duration and quantity of smoke, the greater the risk of TB.[100] Smoking is hypothesised to manipulate the structure of the lungs and the immune system unfavourably with respect to TB.[100] Many Nunavut residents smoke indoors or are exposed to high concentrations of second hand smoke in the home.[28] Amongst Inuit infants on Baffin Island, a higher risk of lower respiratory tract infections was associated with cigarette smoke present in the domicile, and approximately 90% of the residences surveyed in the study contained a smoker.[40] Chronic lung diseases such as asthma and chronic obstructive pulmonary disorder increase the risk of presenting with TB. However, asthma is not frequently diagnosed by physicians in Nunavut, but the data on this illness is unreliable [Table 2]. Susceptibility to TB may be exacerbated by mining fumes and dust.[8] The mining activities in Northern Canada and Alaska have been detrimental to Inuit health due to pollution.[29]

Table 2. Population > 12 years of age diagnosed by a health professional as having asthma in rates per 100,000 (self-reported)

Year	Canada	Yukon Territories	Northwest Territories	Nunavut
2003	8.4	9.1	7.9	4
2004				
2005	8.3	8.7	8.7	4.3
2006				
2007	8.1	8.6	5.4	4
2008	8.4	8.2	6.5	4
2009	8.1	10.4	6.4	3.5
2010	8.5	10.5	6.8	
2011	8.6	10.1	6.6	
2012				

Source: Statistics Canada; Nunavut data to be used with caution due to unreliability of self-reporting

Most of the described risk factors are present in some combination in Nunavut residents,[101] weakening the population's collective immune system, and thereby weakening their body's ability to control the bacterium.

Lack of access to health care

The government of Nunavut provides primary health care services maintained through the Nunavut Department of Health and Social Services,[41] but access to many of these health services has been reported to be poorer than access in the rest of Canada.[26] Nunavut's total health expenditures have gradually been rising over the years at a fairly constant rate comparable to other territories and Canada since the territory's formation, but is still low when compared to recent costs expended for health by the Northwest Territories [Figure 19a, 19b]. However, given the size of the population and the trend Canadian provinces and territories follow when allocating health care spending, Nunavut appears to spend about what would be expected on health care for their number of residents [Figure 20]. Inadequate resources are still cited as a major barrier to controlling TB.[34]

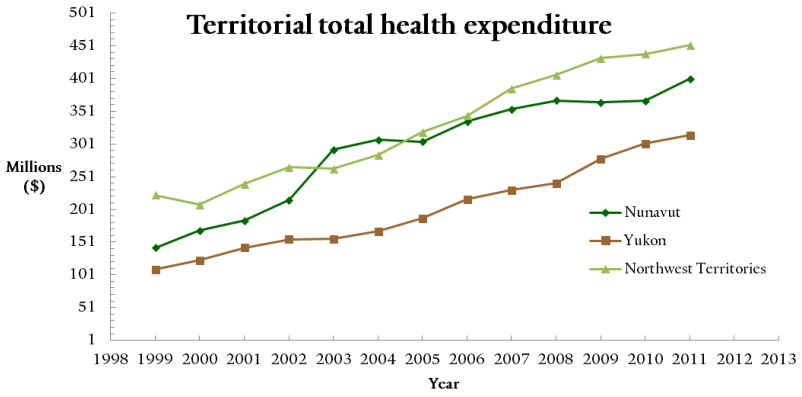


Figure 19a. Total health expenditure in Canada's northern territories
The health expenditure of Nunavut is less than that of the Northwest territories, despite being only a slightly smaller population. Health Expenditures include any type of expenditure for which the primary objective is to improve or prevent the deterioration of health status. This includes administration, capital, drugs, hospitals, other health institutions (such as residential care, mental facilities), physicians, public health, and other health professionals.

Source: Statistics Canada

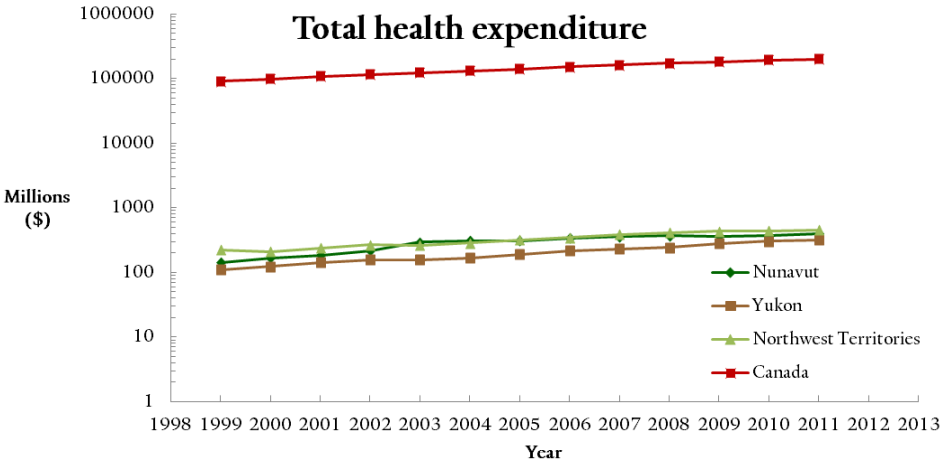


Figure 19b. Total health expenditure in Canada's northern territories
The health expenditure of Nunavut is less than that of the Northwest territories, despite being only a slightly smaller population. However, the trajectory of spending follows that of the nation and appears to be increasing at the same rate of spending as the rest of the territories.

Source: Statistics Canada

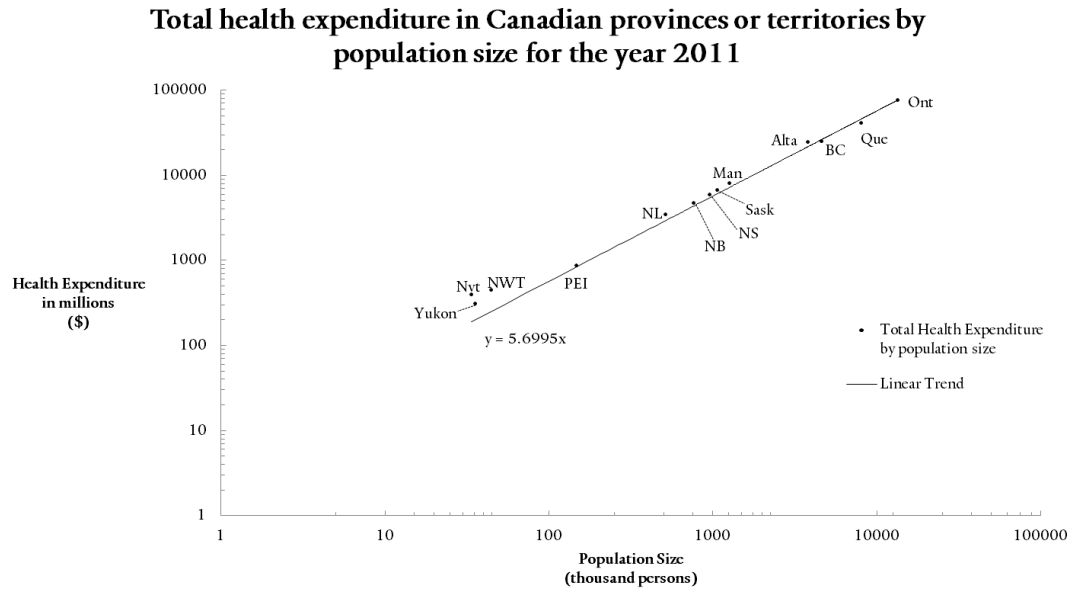


Figure 20. Total health expenditure in Canadian provinces and territories by population size for the year 2011
Health care spending in Canada appears to be directly correlated with the size of the population. The more people the province or territory has, the greater spent on health care. Nunavut appears to follow this linear trend with some deviation suggesting more is spent on health in Nunavut than would be based on their population size. Thus, the allocation of resources in Nunavut may leave insufficient funds to maintain the TB control program.

Source: Statistics Canada

TB treatment is mainly provided by local nursing stations.[26] The risk of being infected with the bacilli as estimated by the tuberculin skin test corresponds to the region's economic and health resources.[102] Adherence to treatment and successful treatment outcome is crucial when attempting to control the TB disease.[103] Adherence to TB therapy in Nunavut may be difficult due to the occurrence of unexpected side effects from the drugs, migration, or other health factors which reduce adherence such as alcoholism or mental disorders.[26] Treating latent TB also hinges on the completion of the drugs provided.[103] Having active TB may lead to exclusion and a deterioration of the social environment, which in turn can delay seeking assistance from a health professional regarding their disease.[88] Treatment is most effective with high nutritional quality not always available to an infected individual in Nunavut attempting to recover from TB. Despite these difficulties, Nunavut appears to have success in treating their TB patients, with few individuals absconding from treatment or remaining TB-positive after treatment [Table 3].

Table 3. Treatment outcomes for TB patients in Nunavut

Year	Total cases followed	Treatment completed (with or without cure negative culture)	Failed treatment (with or without positive culture)	Absconded from treatment	Unknown or other (died, transferred, ongoing treatment)	Notes
1999	39	35	0	0	4	the North
2000	85	27	24	1	33	the North
2001	47	44	0	0	3	the North
2002	27	25	0	0	2	
2003	7	6	0	0	1	
2004	32	30	0	0	2	
2005	45	43	0	0	2	
2006	48	44	0	3	1	
2007	31	29	0	1	1	
2008						
Total	361	283	24	5	49	
% of Total	100	78.4	6.6	1.4	13.6	

Source: Statistics Canada; Some columns combined from original data source for simplicity

Although education on TB has often been suggested as a strategy to reduce the incidence of disease, it was documented that many Inuit in Nunavut did not recall seeing or hearing information about TB in their community – even in communities where TB initiatives had occurred.[26] The Inuit gathered most of their knowledge from historical familiarity with the disease.[34] Recently, knowledge on the subject of TB has been disseminated through workshops, periodic radio shows, nurse presentations, written materials and brochures (with attempted translation in the regional language), and school presentations.[34] When a Nunavut resident did remember having heard or seen information on TB, they stated that it was not valuable to them as they did not have the symptoms described, they would have preferred an oral presentation instead of textual facts, or would have liked to hear personal stories instead of data.[26] This lack of culturally-appropriate communication suggests that attempts to educate Nunavut on TB must take in to consideration the preferred Inuit learning method, which includes oral transmission in the context of moral and practical knowledge.[26] Radio shows with an aspect of resident call-ins[34] to discuss the disease with nurses and community health workers in Nunavut has become an interesting option to connect the population to the disease in what is hoped to be a method more inclined to the Inuit culture.

Distrust of health offered by the Canadian government rooted in historic occurrences is undoubtedly present in Nunavut.[28] Satisfaction with all aspects of the health care system is lowest in the country amongst the residents of Nunavut.[32] Nunavut health care is often serviced from regional centres on Ontario, and it has been suggested that the Inuit peoples would fare better if their health

providers collaborated with those in Greenland to find practices most applicable to the population of Nunavut.[50] A collaboration with Greenland to reduce TB rates is supported due to the similarity between the Canadian Inuit and Greenlander Inuit disease patterns and risk factors (a likeness stronger than that observed between Alaska natives and the Canadian Inuit).

Cause for Negligence

TB has been closely linked to standards of living, social networks and hygienic conditions. This suggests that regions where TB persists may be deemed as having unimproved standards and face persecution, discrimination and shame for their diseased status.[8] This stigma associated with a TB diagnosis,[26] as well as the mistrust of physicians and Canadian public health by the inhabitants of the territory, may hamper TB control efforts and have contributed to the current outbreak situation.[28] A case study in Nunavut investigating Inuit perceptions of TB suggested that it was not socially acceptable to discuss bad experiences or poor health with others, and worried that TB was brought upon them due to their transgression of social conventions or break of moral conduct.[26] Following this sentiment, the Inuit of Nunavut dislike recounting experiences of which they are not entirely certain, and are more likely to deny knowledge of TB if they are not sure they understand the disease.[104] Tales of dying alone in TB sanatoria may discourage any inclination for TB treatment.[94]

The remoteness of Nunavut and perceived isolation of the territory's residents from the rest of Canada[28] has lead to the common misconception that problems in the region cannot be helped nor avoided, and the Inuit themselves are apathetic to their condition.[33] These allegations are erroneous, as the success seen with the native groups of Alaska and Greenlander Inuit (in equally, if not more remote regions of the world) has proven even the most distant peoples are capable of receiving TB treatment and reducing disease rates; and the Inuit display profound awareness of the wreckage TB has created of their population and show great interest in rectifying the situation. Inadequacy in the TB surveillance system in Nunavut may also have lead to outbreak conditions as timely information on cases may be challenging to obtain in isolated communities or remote regions due to delayed diagnosis.[93]

Finally, the struggles associated with daily living in Nunavut overshadow concerns about TB.[26] When faced with high suicide rates, depression, failed promises from the Canadian government, and an inability to trust even the safety of the water they must drink, a lingering cough may not warrant a special trip to the doctor.[90]

Summary of Findings

Nunavut has achieved some control over TB when compared to the TB rates reported in the past, with current rates only a tenth of the rates reported over half a century ago. However, little has improved in the incidence of TB over the past few decades and TB rates are high and increasing. The rate of TB in Nunavut does not differ significantly from rates reported in Greenland over the past decade, but is higher than TB incidence rates reported by other Native American groups in Alaska, the United States and Canada. The high completion rates for TB treatment and lack of MDR-TB are

significant accomplishments achieved by the territory. It also appears that educational efforts are underway in Nunavut and Inuit perceptions of TB are being studied. The challenges Nunavut faces contribute to the high incidence rates of TB reported. In particular, poverty-induced overcrowding, alcoholism, poor nutrition, and cigarette smoking increase the risk of the Nunavut population for TB.

At the time of writing, current TB control efforts in Nunavut include the recommendation for infant BCG vaccination, screening school children and other high risk populations with tuberculin skin tests, directly observed therapy for TB patients, and contact investigation with treatment supplied upon request. Although case finding and contact tracing is believed to occur to an extent, it is unknown the level to which this is implemented as no data on the subject could be found. Targeting school children, prisoners and the homeless for TB screening is wise but statistics on the process were not available. It is also recommended that contacts are provided with preventative treatment, but whether this is done is not clear. Information on the level of BCG vaccination or the percent of the population immunised against TB is unavailable.

Suggestions for Tuberculosis Control Efforts in Nunavut

It is hoped that the Public Health division of Nunavut Department of Health and Social Services will find this document of use. From it, a cohesive, culturally sensitive, campaign between both the Canadian government and Nunavut's leaders may be implemented to increase TB awareness and protection in Nunavut. Program development for TB and existing TB control programs may benefit from this dissertation due to the identification of those in the territory most susceptible to TB, and therefore will gain the most advantage from interventions for TB. This thesis has shown that when an intensive, culturally-appropriate community campaign addressing historical prejudices against TB has been attempted, the morbidity and mortality of the disease has been significantly lowered.[56]

The control of TB may be approached in three phases: the immediate, the intermediate and the long term.[8] Immediate action to reduce the rate of TB in a population may be tackled through case finding, the treatment of all cases, and contact tracing.[8] While some TB cases may present themselves for therapy, health professionals must actively search for other cases and systematically identify all contacts of the cases as they work through settlements or selected groups from the population.[8] Intermediate control of TB can be attempted through widespread BCG immunisation near the time of a child's birth,[8] as well as the implementation of general TB preventative measures.[105] Finally, long term reduction in disease will require more resources, improved hygiene, better social standards, increased nutritional uptake, and less crowded living conditions.[8] It has been observed repeatedly that even in the absence of TB treatment, the simple act of improving living standards lowered the rate of TB infection in the population. Nunavut may be in a state of ongoing TB outbreaks and would benefit from TB control efforts targeting all three phases stated.

From other populations, it may be extrapolated that the withdrawal of control efforts invariably results in an increase in the incidence of TB. Thus, a strong and continuous TB program employing dedicated health professionals who can commit a few years to the task would be desirable

– especially as the loss of a single, driven individual in a small TB control program can have negative effects on TB rates for the entire territory. Despite the harshness of the sanitoria in which TB patients were isolated from the larger population, the resulting shortened infectious period due to constant supervision heavily contributed to reduced TB transmission. The same effect may be derived from strict adherence to drug regimens and the widespread use of preventative treatment (such as isoniazid preventative treatment) as developed in Alaska.

TB is able to remain endemic at low levels even within small populations.[71] It has been argued that TB epidemics have a duration of 300 to 400 years, only ending with the development of herd immunity.[66] Therefore, the generation of herd immunity through treatment and vaccination could be attempted in Nunavut to ensure the current poorly controlled TB situation does not remain a problem in the territory for centuries to come.

Formal program review

To clearly ascertain the scope of the TB problem in Nunavut and have a new perspective on the situation, it is recommended that a formal program review be instigated to inspect current TB control efforts in Nunavut. A group of individuals consisting of a TB specialist, an Inuit representative, an employee from Health Canada, representatives from the TB control programs in Alaska and Greenland, and an individual experienced with financing health care may be asked to volunteer in the review committee. The review committee will be tasked with going to Nunavut and looking at current TB control measures and reviewing the data collected on TB by the territory. Data on TB cases, monetary allocations for TB control efforts, or steps followed when a TB case is identified (such as how contact tracing is approached or if BCG vaccinations are provided) can be inspected by the review committee and improved upon.

Vaccine use

The BCG vaccine is offered to all newborn infants in Nunavut[34] due to their eligibility according to the 7th edition of the Canadian Immunisation Guide published in the year 2006. However, statistics regarding the uptake rate of the vaccine were not found. Early protection given by immunisation at birth, followed by repeated doses upon entry to school, is effective in reducing the risk of TB contraction in a large family setting where the mixing of old and young is standard.[8] BCG vaccination in young children is also effective at preventing the most serious forms of TB, in addition to providing some immunity against infection. The vaccine is also most effective in the young (whereas less efficacy is observed amongst adults), and therefore BCG immunisation for all Inuit children is a reasonable request. Administration of the BCG vaccine also provides a readily identifiable scar (easily differentiated from other body markings with limited training) which indicates a degree of immunity to TB.[78]

Having a high proportion of immunised individuals against TB in Nunavut would increase herd immunity and hinder the transmission of TB amongst community residents. It must be noted that Alaska achieved a lowering of their TB rates despite the lack of widespread BCG vaccination, but the use of the BCG vaccine in Greenland resulted in dramatically lowered TB incidence – although this drop in TB rates was not sustained, supporting the need for more than BCG vaccination when

combating TB. As Nunavut appears to have more similarities with the Greenlander Inuit, it is suggested that the territory maintain their BCG immunisation program and continue the extensive use of the vaccine on all infants. The usefulness of the BCG vaccine varies directly with the infection rate,[58] and the efficacy of the BCG vaccine admittedly varies for unknown reasons.[106] Thus, BCG immunisation will only begin to diminish in importance once the rate of TB has been lowered in Nunavut and the source of future TB cases is confined to those who are already infected with TB and for whom the BCG vaccine has nothing to offer.

Screening

Children in Nunavut are screened for TB while in Kindergarten, Grade 6 and Grade 9;[34] or in high risk environments such as homeless shelters and prisons[28] – thus some members of the population may be not receive TB screening as adults. The transience and large net migration could also impede screening efforts, as children moving with their families could easily miss all screening opportunities offered through the school program. It is proposed that despite the resource intensive structure of the suggestion, yearly screening for those enrolled in Nunavut schools be implemented. It is unlikely yearly screening in itself will cause more than momentary discomfort to the children, and identification of a positive skin test in a child could lead to the discovery of active TB patients in the child's family if contact tracing is employed when a positive skin test is reported by the school to the health department. Screening is a powerful tool in lowering the rates of TB in a population. If possible, mass population screening should be attempted to determine the burden of TB in Nunavut.

Contact tracing

The TB control program in Nunavut could dramatically lower the rates of TB through contact investigation by screening those who have had interactions with the TB patient. Although this method of prevention and intervention has been noted as laborious, difficult[55] and resource intensive for the territory, the cost effectiveness and capacity to reduce TB rates has been shown in other populations.[28] Alaska also granted that contact investigations were labour intensive, but realised that for TB control, it was the best option – except for the detection and treatment of active TB.[55] It would be expected that about 5% of close contacts for the active TB case would also have active TB, and 20% or more would have latent TB. Unresolved cases of TB could set a family up for the trans-generational transmission of TB – from sick family member to uninfected family member, repeated over time.

Latent TB infections significantly contribute to the development of TB cases later on – especially in regions of high TB prevalence, and are easily screened for[14] using a tuberculin skin test. However, the tuberculin test suffers from poor specificity, primarily due to the false positive results displayed by those who had received the BCG vaccine (up to 15 years before test taking) caused by antigenic cross-reactivity with the BCG held within the vaccine and the PPD detected by the test.[105] Furthermore, most Nunavut residents should have been immunised against TB due to childhood vaccination requirements, and some agencies no longer recommend performing tuberculin skin tests on BCG-vaccinated adults with recent TB exposure.[105] Interferon-Gamma Release Assays (IGRA), such as the ELISPOT (T-Spot) assay and the QuantiFERON test, are more useful when testing for

TB prevalence in a region where the BCG vaccine is in use since they are antigen-specific TB tests.[107] This avoids the difficulty of a false positive skin test due to interaction with the BCG vaccine or the dismissal of a positive skin test in a vaccinated individual (who may in fact have a latent TB infection). For example, an ELISPOT assay has been adapted to detect antigens secreted by the TB bacilli which are absent from BCG using a blood sample (thereby eliminating the need for a patient to return for a skin test reading).[105] The 96% sensitivity of the ELISPOT assay is significantly higher than the 69% for the skin test, ELISPOT has high specificity, and its resistance to false negative results in patients with disseminated TB makes it clinically useful.[105] Despite a test result, exposure history of the patient must always be taken in to account. One paper proposes that to eliminate TB or at least reduce the incidence to < 1 per million population (in the United States), latent TB infection prevalence must be < 1% and continue to decrease.[78] A tuberculin skin test measurement > 10 mm is commonly said to be indicative of a latent infection.[78]

It is recommended that time be spent on characterising all Nunavut residents with respect to their TB status using screening with the QuantiFERON test or the new ELISPOT assay, as the proportion of active and latent TB infections present will determine the direction of the TB control program to be implemented in the region.

Treatment

Assigning a nurse or outreach worker to handle each TB case directly may increase the probability of treatment completion through increased adherence. Directly observed therapy (DOT) is used in Nunavut, with success marked by high completion rates in the region for TB treatment for active cases.[28] DOT is believed to lower the prevalence and incidence of TB if enough patients are managed.[108] Whether DOT is used for all TB cases identified in Nunavut (both latent and active, adult and children) is unknown, but is highly recommended. Appropriate treatment of cases for the full duration of therapy is extremely important for TB control. To ensure treatment success, Nunavut employs the use of incentives to encourage adherence to treatment regimens, and a budget is allocated for community clinics to assist individual TB patients (for example, with gift certificates or taxi ride vouchers).[34] It should also be considered whether local or Inuit community members could be trained to provide most TB treatments and care as this would increase the acceptability of TB regimens to Aboriginal patients in Nunavut.

For patients who are not adherent to therapy, or for whom social, mental or medical conditions inhibit compliance to the treatment regimen, long-term hospitalisation may be necessary to reduce the public health threat they pose and control the TB outbreak.[109] It may be less of a personal violation on the patient if the patient has demonstratively failed outpatient TB treatment, and if the treatment of the nonadherent patient was combined with psychosocial support.[109] Such action may even have the potential to reduce the number of involuntary hospital admissions for TB.[109] Determining when to end hospitalisation may be the most difficult aspect to determine, but discharge 2 weeks following apparently successful therapy is common practice.[110] Where the patient will be discharged too also is of concern, as if the patient is simply returning to their previous living conditions, waiting until the sputum has been shown to be culture negative for TB may be the more wise choice.[110]

The detection and subsequent treatment of latent infections within contacts of TB patients is often an important step in the control of an ongoing TB epidemic since the diagnosis and treatment of active TB disease is usually effectively accomplished in developed countries.[105] Prophylactic treatment of latent TB prevents the development of active TB in most patients.[105] Contact investigation is difficult to perform, but active cases may have a few contacts already infectious and displaying active TB, and another 5 to 10% of contacts may become cases in 1 to 2 years. Once a TB patient has been identified, extensive contact tracing, screening and treatment of contacts is supposed to be immediately initiated.[34] However, the lack of control the health department has over the rates of TB in Nunavut would suggest that contact tracing and treatment of contacts may not be occurring with as high performance as necessary to lower TB incidence, since the completion of treatment appears to be in good standing with TB patients, and it is hoped that infants are receiving their scheduled BCG vaccine (despite no literature or data found to corroborate this).

Evaluation

Any implemented TB control program will require evaluation. An ongoing system to monitor the incidence and recurrence of TB, the regions covered by the program, as well as treatment status (cured, died, absconded or failed) must be implemented alongside the TB control program.[111] Indicators which can be used to determine the influence the TB control efforts have on the rate of infection in a population include inspection of the incident rate of new TB cases diagnosed, the rate of sputum-positive cases, the proportion of children under 5 years diagnosed, the rate of BCG scars upon survey, the relapse rate, and the rate of patients lost to follow up.[8]

Benefits

TB is a costly disease and resource intensive, and may be viewed as an economic burden upon Nunavut.[89] Treatment per TB case is over $70,000 – twice as high as what treatment would cost for a TB case in Qué bec.[83] The costs of TB may be attributed to the patient's long term antibiotic prescription and accompanying nutritional support, as well as the use of health personnel to monitor the patient's response to the overall TB therapy.[89] Lowering the incidence of TB will reduce the cost the health department accumulates due to TB; and Nunavut will have a happier, healthier, more productive population.

Conclusions

Executive summary

Tuberculosis (TB) is a serious problem in Nunavut that has gone unchecked since the territory was first created in the year 1999. When compared to rates occurring in other northern territories in Canada, it becomes apparent that the incidence rate of this contagious disease in Nunavut is far above those reported in the Yukon and Northwest territories. Almost all cases of TB in Nunavut occur in Canadian Aboriginal peoples, and Nunavut may be experiencing an ongoing TB outbreak. The factors contributing to high TB rates in Nunavut have not been well documented, and it was decided that a novel look at TB in Nunavut, with a focus on the Inuit who comprise a

significant proportion of the population, was warranted. Overall, control of TB in Nunavut appears to be lacking.

Several nearby countries - Greenland and the United States (state of Alaska), also have large Inuit and Aboriginal or native populations. Examining their experience with efforts to control TB may be instructive when investigating TB control efforts in Nunavut. Using data collected by Statistics Canada, previous literature on the subject of TB amongst the Inuit, and information from the United States CDC and Greenlander government, the incidence of TB was revealed to be greatest in Nunavut when averaged over the years since the territory was formed. The rate of TB amongst Alaska natives was once much higher than rates reported in Nunavut, and was lowered through culturally sensitive TB control efforts, active case finding and treatment, and active contact investigation followed by the prophylactic treatment of contacts. The BCG vaccine did not play a role in the decline of TB in Alaska, which has been sustained to present times. In Greenland (which also had very high TB rates historically), it was believed that the source of many infections was a pool of elderly community members who harboured the TB bacilli in active and latent infections. Thus, the entire population was screened for TB, followed by the treatment of identified cases. In contrast to Alaska, prophylaxis was not emphasised in Greenland. Rather, the Greenlander Inuit underwent mass BCG vaccination campaigns, TB skin testing, and TB education. While this strategy initially worked to lower TB rates, the rate of TB in Greenland for the past 10 years has been as high as that in Nunavut. From Alaska, the importance of cooperation and sensitivity to the traditions of Aboriginal peoples when discussing TB may be learnt. However, Nunavut has a population resembling that of Greenland and thus the mass vaccination, contact tracing and treatment, combined with a screening strategy may be more applicable. It is also interesting to note that immediately following the stoppage of TB control efforts in Greenland, TB rates rebounded to levels as high as those reported in Nunavut. This exemplifies the need for continuity when instituting a control program for TB.

The large deviation in TB incidence rates reported over the years supports the assertion that Nunavut is experiencing repeated TB outbreaks, as opposed to background endemnicity of TB. In Nunavut, the occurrence of TB cases in children and young adults is indicative of active transmission. The reason for the oscillation in TB rates each year could not be determined by this study. Results show the high rates of TB in Nunavut are most likely due to failure in TB control, with socioeconomic conditions compounding the difficult situation. The high and increasing incidence of TB resembles that of Greenland, but differs from other Native American and Aboriginal groups. However, rates have been reduced to about a tenth of their historical highs – an accomplishment to not be overlooked. It merely appears that no progress has been made in recent decades in reducing the rates of TB in Nunavut. TB patients in Nunavut have a high rate of treatment completion, with few patients absconding from treatment. Contact tracing and treatment is an important aspect of TB control for which no data has been found.

In addition, Nunavut's population experiences some challenges that increase susceptibility and transmission of TB. Coinfection with HIV in TB patients does not appear to be common in Nunavut, although very few residents are tested for HIV. Whether diabetes is increasing the risk of TB amongst the Inuit is also difficult to determine due to inadequate data. Thankfully, multidrug resistant (MDR) TB has not been reported in the territory since the year 2001. This indicates that

Nunavut's TB patients have high compliance with treatment regimens; indeed, few patients have absconded from their TB treatment in the past. However, some resistant TB strains have been isolated in recent years, suggesting that MDR-TB may eventually become a concern in Nunavut. Food insecurity is reported by approximately 30% of Nunavut's households and may contribute to malnutrition, which in turn leaves an individual more susceptible to TB. Overcrowded Arctic homes with poor ventilation, the prevalence of alcoholism and indoor smoking, limited access to health care, and migration are also risk factors for TB displayed by some Nunavut residents. Whether the Inuit have a higher biogenetic susceptibility to TB remains to be supported. Nunavut's total health expenditure appears to be what is expected in Canada for their population size, implying that the lack of resources often cited as a difficulty in the TB control efforts for the region may be an issue of allocation rather than insufficient funds.

Nunavut requires a TB control program tailored to the specific context in which TB occurs in the territory, and is sensitive to the specific needs and beliefs of the Inuit who are mainly diagnosed with the disease. To improve the TB situation and lower the incidence of TB in Nunavut, it is recommended that a strong and supported TB control program be instituted involving the following components:

- Instigation of a formal program review
- Screening attempted for every Nunavut resident using IGRAs
- Aggressive contact tracing and treatment
- Improvement in the social and living conditions of Nunavut residents
- Collaboration with Greenland and Alaska's TB control program managers

Limitations of findings and of the study

When researching solutions for the research questions, it must be remembered that the solutions presented (though plausible) may have limited accuracy due to a number of factors. First, the exhaustive surveillance of TB in remote regions may come under suspicion since case reporting may become erratic due to difficulties in tracking TB patients and contacts. This unavoidable error could have lead to a misrepresentation of the TB pattern in Nunavut when the data is inspected. In addition to these mistakes, interpretation errors while reviewing the available data and literature, the limited public availability of data for a given time period, and the lack of fine classification of variables of interest would all have a negative impact on support for the proposed answers to the research questions.

Recommendations for further research

The propensity of Inuit peoples for TB infections even when SES conditions are controlled for supports the assumption that predisposing genetic factors exist within the Inuit population. This theory may be tested with further case-control studies and whole genome linkage scans, and has not yet been explored specifically in the context of Inuit origin. Discovering the reason behind the oscillation in TB rates over the years in Nunavut would also be a feat not yet accomplished in the literature.

Appendix

Literature review methodology

A search of the Google Scholar database for the exact phrase "Nunavut" and tuberculosis (not including patents, legal documents or citations) anywhere in the article was conducted. The search was run between November and December, 2012. A total of 1,040 results were returned, all potentially relevant. Results were ordered based on relevance. Review of the results began with the first, and continued until it was felt enough literature had been amassed to satisfy the need of the literature review required for the thesis. Some articles were obtained individually through investigation of article bibliographies and searches for commonly mentioned topics. All searches were performed while in the United States of America or Canada. Thus, results generated had a North American focus automatically when Google Scholar was used.

Three separate searches were conducted following the aforementioned search, using the same approach outlined. The Google Scholar database was searched for:

1. The exact phrase "Alaskan natives" and tuberculosis
2. Greenland and Inuit and tuberculosis
3. The exact phrase "Native Americans" and tuberculosis.

The publications produced by the Government of Canada, Health Canada, and Statistics Canada, and filed on their websites www.statcan.gc.ca and www.publications.gc.ca, were also searched for the term tuberculosis to contribute valuable data and literature to the thesis.

Selected data tables

Table I. Reported new active and re-treatment tuberculosis cases and TB incidence rate per 100,000 for each year in the territory of Nunavut

Year	Number of Cases	Rate (per 100,000)
1999	15	55.9
2000	47	170.9
2001	40	142.2
2002	27	93.7
2003	7	23.9
2004	32	107.2
2005	45	148.4
2006	48	155.8
2007	31	99.1
2008	59	186.7
2009	57	177.1
2010	101	304
2011	75	
2012	79	

Source: Statistics Canada

Table II. Incidence rate of TB per 100,000 amongst Alaskan natives, in the state of Alaska and in the United States

Year	Alaska Natives	Alaska	United States
1991		12.3	10.4
1992		9.7	10.5
1993	39.2	9.4	9.8
1994	67.3	15.3	9.4
1995	57.9	13.3	8.7
1996	72.9	16	8
1997	39	12.8	7.4
1998	28.8	8.9	6.8
1999	39.4	9.8	6.4
2000	64	17.2	5.8
2001	31	8.5	5.6
2002	21.5	7.6	5.2
2003	36	8.8	5.1
2004	25.9	6.5	4.9
2005	25.4	8.9	4.8
2006	41.8	10.4	4.6
2007	26.3	7.5	4.4
2008	27	7.5	4.2
2009	20.1	5.3	3.8
2010	33	8	3.6
2011	37.8	9.3	3.4
2012			

Source: United States CDC Publications

Table III. TB incidence rate per 100,000 for each year in Greenland

Year	Rate (per 100,000)	Source
1990	85	Soborg *et al*, 2001
1991	104	Soborg *et al*, 2001
1992	78	Soborg *et al*, 2001
1993	54	Soborg *et al*, 2001
1994	116	Soborg *et al*, 2001
1995	86	Soborg *et al*, 2001
1996	159	Soborg *et al*, 2001

1997	172	Soborg *et al*, 2001
1998	107	Soborg *et al*, 2001
1999	112.4	*National TB strategi*
2000	80.2	*National TB strategi*
2001	185	Soborg *et al*, 2001
2002	150.3	*National TB strategi*
2003	157	*National TB strategi*
2004	121.4	*National TB strategi*
2005	173.8	*National TB strategi*
2006	128.3	*National TB strategi*
2007	105.9	*National TB strategi*
2008	109.8	*National TB strategi*
2009	112.2	Soborg *et al*, 2001
2010	203	*National TB strategi*
2011	157.2	*National TB strategi*
2012		

Source: Government of Greenland

Table IV. Incidence rate of TB per 100,000 amongst American Indians (including Alaskan natives) in the United States and Canadian Aboriginal peoples

Year	American Indian	Canadian Aboriginal
1990		
1991		31.2
1992		35
1993	14	33.1
1994	16.4	34.6
1995	15.7	29.4
1996	13.7	24.8
1997	12.3	23.2
1998	11.5	22.5
1999	10.7	25.1
2000	11	20.5
2001	10.6	28.6
2002	8.6	22
2003	8.2	22.3
2004	7.1	23.8
2005	6.8	27.5

2006	7.2	26.9
2007	5.8	25.9
2008	5.9	28.4
2009	4.3	27.8
2010	6.7	26.4
2011	5.6	
2012		

Source: Statistics Canada and United States CDC Publications

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