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Evaluation of TB elimination strategies in Canadian Inuit populations: Nunavut as a case study

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ABSTRACT

Tuberculosis (TB) continues to disproportionately affect Inuit populations in Canada with some communities having over 300 times higher rate of active TB than Canadian-born, non-Indigenous people. Inuit Tuberculosis Elimination Framework has set the goal of reducing active TB incidence by at least 50% by 2025, aiming to eliminate it by 2030. Whether these goals are achievable with available resources and treatment regimens currently in practice has not been evaluated. We developed an agent-based model of TB transmission to evaluate timelines and milestones attainable in Nunavut, Canada by including case findings, contact-tracing and testing, treatment of latent TB infection (LTBI), and the government investment on housing infrastructure to reduce the average household size. The model was calibrated to ten years of TB incidence data, and simulated for 20 years to project program outcomes. We found that, under a range of plausible scenarios with tracing and testing of 25%–100% of frequent contacts of detected active cases, the goal of 50% reduction in annual incidence by 2025 is not achievable. If active TB cases are identified rapidly within one week of becoming symptomatic, then the annual incidence would reduce below 100 per 100,000 population, with 50% reduction being met between 2025 and 2030. Eliminating TB from Inuit populations would require high rates of contact-tracing and would extend beyond 2030. The findings indicate that time-to-identification of active TB is a critical factor determining program effectiveness, suggesting that investment in resources for rapid case detection is fundamental to controlling TB.

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1. Introduction

Despite global efforts geared toward Tuberculosis (TB) elimination, it remains one of the leading causes of mortality among infectious diseases worldwide, with an estimated 1.4 million deaths in 2019 (WHOa). The End TB strategy aims to reduce the incidence of new TB infection or relapse by at least 90% compared with 2015 to less than 100 cases per 1 million population by 2035 (WHOa). For this purpose, and to achieve elimination in low-incidence countries, the World Health Organization (WHO) has established three strategy pillars of (i) patient oriented acts including early detection, treatment and prevention of TB disease; (ii) policies and systems that supports adequate resources, quality care, and social protection; and (iii) targeted research and development pertaining to new interventions such as vaccines and therapeutics (WHOa).

While Canada is placed among low-incidence countries on a global scale, TB remains a major public health concern, especially among First Nations and Inuit communities (o. Canada, 2014a). The incidence of TB in some Indigenous communities is several orders-of-magnitude higher than Canadian-born non-Indigenous populations (o. Canada, 2014b). Risk factors that contribute to such disproportionate rates of TB infection in these communities include the prevalence of comorbidities, high rates of diabetes and tobacco use, food insecurity and malnutrition, and overcrowded housing with poor ventilation and environmental conditions (P. H. A. o. Canada, 2014d; Orr, 2013; MacDonald et al., 2011). The Government of Canada, in joint efforts with Inuit Tapiriit Kanatami, has pledged to reduce the incidence of active TB by 50% (reduction from ~200 to no more than 100 cases per 100,000 population) by 2025, and eliminate the disease by 2030 in Inuit Nunangat (Canada, 2018; Filliter, 2018). This Arctic region is the home for 63.7% of the Inuit population in Canada (S. C. Government of Canada, 2018).

Consistent with the WHO pillars of the End TB strategy, Canada has formulated plans for contact investigations to identify latent TB infection (LTBI) for treatment based on the recommended regimens (WHOa; P. H. A. o. Canada, 2014a, 2014b, 2014c; P. H. A. o. Canada, 2014a, 2014b, 2014c; P. H. A. o. Canada, 2014a, 2014b, 2014c), in addition to investing $640 million over 10 years to address the housing need in Inuit communities (Filliter, 2018). However, these plans must also address factors hindering TB control such as inadequate treatment adherence and late identification of active pulmonary cases in the cascade of care.

Here, we evaluated whether TB elimination goals in Nunavut as part of the Inuit Nunangat region can be achieved under the standards for treatment regimens. For this evaluation, we developed a discrete-time agent-based simulation model to include TB control strategies including treatment of active cases and LTBI, contact-tracing and testing of close contacts in the cascade of care, as well as reduction of average household size.

2. Methods

2.1. Population study

Nunavut is the largest Canadian territory with a land-size of ~2.1 million km^2 in the Arctic region. It has a population of 38,780, mainly inhabited with (over 80%) Indigenous Inuit. The median age in Nunavut is 25 years, which is significantly younger than the median age of 42 years for Canada. The average household size is 3.8, representing at least 1.3 persons per household greater than the average household size in the Canadian general population (S. C. Government of Canada, 2018).

2.2. Model structure

To model the dynamics of TB infection, we considered both household and community transmission within an age-structured agent-based framework (McIntosh et al., 2017, 2019). Each agent, representing an individual, is characterized by a time-dependent vector of attributes, including demographic, health information, and time-dependent epidemiological statuses. To reflect the demographic composition of Nunavut, we distributed the total population to households of size 1, 2, 3, 4 and 5+ individuals and each agent was assigned an age based on the latest publicly available Canadian census data (S. C. Government of Canada, 2016; Nunavut Bureau of Statistics). For households with 5+ members, we set the maximum size to 15 persons per household and selected the exact household size randomly using a uniform distribution.

To include contact patterns in the population, we stratified the population into five age groups of 0–4, 5 to 19, 20 to 49, 50 to 64 and 65+ years old (S. C. Government of Canada, 2016). We relied on a population-based study of social contacts in Canada which included inter- and intra-age group daily number of contacts within and outside households (Table A1) (Drolet et al., 2022). These age-dependent contacts were sampled from a negative binomial distribution with the mean and standard deviation derived from the study. The proportion of contacts for daily activities outside households were approximately 60% for 0 to 4, 68% for 5 to 19, 76% for 20 to 49, 66% for 50 to 64, and 59% for 65+ years old (Table A.2) (Drolet et al., 2022).

We classified community (outside household) contacts of each individual into two types as “frequent” (e.g., repeated contacts with coworkers or classmates), and “casual” or infrequent with short duration (e.g., transportation, or other activities) (Yin et al., 2017). We then assigned 80% of community contacts for each individual as frequent, which may occur repeatedly with some individuals. The remaining contacts were casual and occurred randomly with individuals in the community during daily activities. We aggregated contacts according to the weekly time-step of the simulation model.

Each infected individual was assigned a lifetime risk of reactivation tuberculosis, taking into consideration the different risks of subsequent progression to active TB among different age groups (Horsburgh, 2004; Marais et al., 2004). The age stratification for including the risk of tuberculosis disease was 0–1, 1–2, 3–5, 6–10, 11–14 for children and 15–25, 26–35,

36–45, 46–55, 56–65 and 65+ for adolescents and adults (Horsburgh, 2004). We assumed a 3% case fatality rate for TB patients (Straetemans et al., 2011). Based on the life expectancy table, we additionally included the age-dependent probability of natural death for each individual (S. C. Government of Canada, 2022).

2.3. Natural history and transmission dynamics

We implemented the natural history of TB in the model by including baseline epidemiological statuses as susceptible, exposed and infected (i.e., latent and not infectious; referred to as LTBI), and active TB (infectious) (Fig. 1). Disease transmission occurred probabilistically as a result of contacts between susceptible individuals and active TB cases. If infection occurred, infected individuals entered the latent TB stage or developed active TB. For each infected individual in the LTBI stage, there is an age-dependent risk of progression to active TB disease (Table 1) during the remaining life expectancy (Marais et al., 2004; Horsburgh, 2004; WHOb). Without treatment, about 5%–10% of individuals with LTBI develop active TB during their lifetime (Fact Sheets, 2021). For those who ultimately develop active TB, the duration of LTBI varies from weeks (fast progression) to decades (slow progression) (Ragonnet et al., 2017). To account for this variability, we implemented a probability distribution for the duration of LTBI based on Kaplan-Meier tuberculosis-free survival probabilities (Borgdorff et al., 2011). The duration of LTBI for infected individuals who will develop active TB (determined by a Bernoulli random draw) was then sampled from this distribution with a probability of 45% within the first year, 62% within 2 years and 99% within 12 years of infection (Borgdorff et al., 2011).

2.4. Case-finding, isolation, and treatment of active TB

In the baseline scenario, the time-to-identification (ToI) of an active TB case was set to an average of four weeks from the onset of symptoms (Heffernan et al., 2021). For comparison purposes, we considered additional scenarios in which the average ToI was reduced to 3, 2, and 1 week from the onset of symptoms, and evaluated the effect of diagnosis delay on annual TB incidence (Patterson et al., 2018). For those who developed active TB, we assumed that a treatment regimen starts immediately after diagnosis.

Since the treatment rapidly diminishes the infectiousness (Ahmad & Morgan, 2000), we assumed a 50% reduction of infectivity after the first week of treatment. While treatment may continue for several weeks (depending on the regimen), we assumed that active TB cases become non-infectious after completing two weeks of treatment (Ahmad & Morgan, 2000). A successfully treated TB patient was assumed to regain susceptibility status with a probability that depends on the treatment regimen success rate (Menzies et al., 2009).

Consistent with the Canadian Tuberculosis Standards and the Nunavut Tuberculosis guidelines for home isolation, active TB patients were home-isolated for two weeks from the start of treatment after diagnosis. During the isolation period, daily contacts of TB patients were restricted to only those within the household (P. H. A. o. Canada, 2014a, 2014b, 2014c; Nunavut Tuberculosis Manual, 2018).

2.5. Contact-tracing and testing for LTBI

In order to identify and treat individuals with LTBI, the Canadian TB Standards classify contacts of active cases as high, medium, or low priority (P. H. A. o. Canada, 2014a, 2014b, 2014c). The high priority group includes household members and close non-household contacts who are at a greater risk of TB disease after infection, such as children under 5 years or individuals who are immunosuppressed. The medium priority is defined as daily or almost daily contacts, including frequent community contacts. The casual contacts fall under the low priority group (P. H. A. o. Canada, 2014a, 2014b, 2014c). Taking into account these priorities, we assumed that all household members of a diagnosed active TB case are tested by a Tuberculin Skin Test (TST). Aligned with the Nunavut Tuberculosis manual (Nunavut Tuberculosis Manual, 2018; P. H. A. o. Canada, 2014a,

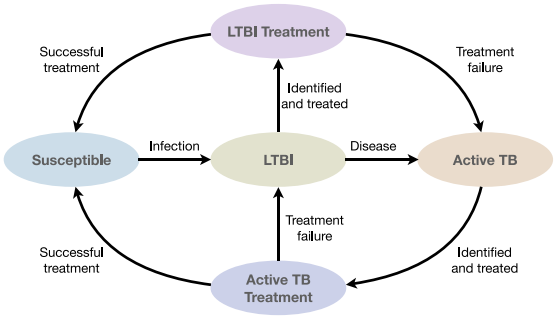

Fig. 1. Schematic structure of the model for the transmission dynamics and treatment of TB.

Table 1
Model parameters used for scenario simulations.

Description	Value	Source
Probability of TB transmission per contact	0.1750 (age >12) 0.0086 (age ≤ 12)	Calibrated
Risk of LTBI developing active TB without treatment[a]	0.02–0.4	[(Marais et al., 2004), (Horsburgh, 2004)]
Effectiveness of LTBI treatment	93%	[(Alvarez et al., 1758), (Martínez Alfaro et al., 1998), (P. H. A. o. Canada, 2014a, 2014b, 2014c)]
Probability of completing LTBI treatment regimen	0.95	[(Alvarez et al., 1758), (Pease et al., 2017)]
Success rate of active TB treatment	80.1% (age >15) 84.8% (age ≤ 15)	Torres et al. (2019)
Sensitivity of TST	77%	Pai et al. (2008)

[a] age-dependent.

2014b, 2014c), our scenario analyses expanded the contact-tracing to the medium priority group by considering frequent contacts with an active TB patient within the four weeks prior to identification. We then tested different proportions (i.e., 25%, 50%, 75%, and 100%) of frequent contacts that occurred with a diagnosed active TB case within the past four weeks. We assumed that the likelihood of identifying contacts of an active TB patient in backward contact-tracing decreases with time. We therefore set the probability of identifying an individual outside household among frequent contacts to be 100%, 75%, 50%, and 25% if the contact occurred during the first, second, third, and fourth week, respectively, before diagnosis of the active TB case.

In Nunavut, testing of LTBI with TST is the preferred method (Nunavut Tuberculosis Manual, 2018). While IGRA (Interferon-Gamma Release Assay) is a more sensitive test than TST, it is only used at the discretion of the patient's physician (Nunavut Tuberculosis Manual, 2018). In our model, we implemented TST as the only LTBI testing method, with an estimated mean sensitivity of 77%. (Pai et al., 2008). A false negative TST may occur if the infection has occurred in the past recent with insufficient time to react to the skin test (Anibarro et al., 2011; Nayak & Acharjya, 2012). We therefore considered the recommended eight-week window for conducting a second TST test for contacts of active active cases (P. H. A. o. Canada, 2014a, 2014b, 2014c). We assumed that the treatment of LTBI individuals will initiate upon positive TST, and that LTBI treatment reduces the risk of developing active TB by the estimated treatment efficacy.

2.6. Treatment regimens and success rates

The Canadian Tuberculosis Standards identify two treatment regimens for active TB. The first comprises of a 2-month daily (or 5 days per week) pyrazinamide (PZA), isoniazid (INH), rifampin (RMP), and ethambutol (EMB), continued with 4 months of daily (or 3 times per week) INH and RMP. The second regimen includes a 2-month daily (or 5 days per week) INH, RMP, and EMB with a 7-month follow-up of daily (or 3 times per week) INH and RMP (Table A.3). Since the second treatment regimen is mainly used for TB patients over 65 years of age and those with other risk factors, we performed the model analysis with the first, shorter treatment regimen. The success rates of active TB treatment for regaining susceptibility status (Table 1) is estimated to be 80.1% for adults and 84.8% for children (Torres et al., 2019).

The Canadian TB Standards also recommend several regimens for treatment of LTBI to reduce the risk of progression to active TB and subsequent transmission (Table A.4). The primary regimen includes 9 months of daily self-administered INH (9INH) (P. H. A. o. Canada, 2014a, 2014b, 2014c; Pease et al., 2019). With the aim of increasing the completion and acceptance rate of the treatment, an alternative regimen with a shorter duration of 3 months and similar efficacy to 9INH has also been approved (Alvarez et al., 1758; Pease et al., 2017). This regimen which includes the combination of INH and RMP dosed weekly for 3 months (3HP) is currently offered as directly observed treatment in Nunavut (Alvarez et al., 1758; Pease et al., 2017). In our comparative analysis, we included 3HP as the LTBI treatment regimen with 93% efficacy and 95% completion rate (Alvarez et al., 1758; Pease et al., 2017), assuming a relatively high compliance as a result of directly observed strategy (P. H. A. o. Canada, 2014a, 2014b, 2014c; Martínez Alfaro et al., 1998; Alvarez et al., 1758).

2.7. Reduction of household sizes

In addition to treatment and contact-tracing, we simulated the model when the average household size of 3.8 in the baseline scenario was reduced to 3.3 by increasing housing infrastructure. This was implemented in the model by distributing the population of households with 5 or more members to additional households using a Poisson distribution with the mean of 3.3. We assumed that the reduction in average household size is achieved by 2025.

2.8. Model calibration and simulation scenarios

Model calibration was performed with the baseline scenario in which active cases and LTBI individuals were treated, and all household members and 25% of frequent contacts of each active TB case were tested with TST. By minimising the sum of residuals using the least-squares fitting approach, we determined the transmission probability per contact through calibration to ten years of TB incidence data, from 2009 to 2018 in Nunavut (Secretariat and Secretariat, 2008). Since TB

transmission from children is rare (Starke, 2001), we assumed that the transmissibility of active TB cases among children under 12 years of age is reduced by 95% compared to adolescents and adults. We then implemented a combination of different control strategies to evaluate the reduction of annual TB incidence and the feasibility of achieving target goals outlined in TB elimination plans over a 20-year time-horizon of simulation with weekly time-step. In each scenario, we estimated the annual incidence of active TB by aggregating weekly outcomes, and calculated the percentage reduction of incidence from 2025 to 2040 by a 5-year increment, compared to the 2018 reported incidence. We used a bias-corrected and accelerated bootstrap method to derive the 95% credible intervals (CrI) from 500 Monte-Carlo simulations. The simulation code is available at: https://github.com/Ellie-Abdollahi/TB.

3. Results

3.1. Time-to-identification of active TB

For the baseline scenario with a 4-week ToI for active TB cases and 25% contact-tracing, we did not observe any significant change in the annual incidence during the 20-year simulation period compared to the calibration timelines (Fig. 2-A1, blue curve). As the contact-tracing increased to 50%, 75% and 100% of frequent contacts, the annual incidence reduced by 2.72%, 7.46% and 11.95% in 2025, and 6.42%, 16.59% and 23.79% in 2030, respectively (Fig. 2-A1, orange, purple, and green curves). These estimates suggest that the goal of 50% reduction in the annual incidence of TB by 2025 is not achievable (Fig. 2-A1). This goal would still not be attainable if ToI is greater than 2 weeks from the onset of active TB disease, even if 100% of frequent non-household contacts are traced and tested (Fig. 2, A1-2,B1-2).

Decreasing ToI to a maximum of 2 weeks would reduce TB incidence by at least 50% by 2035, if a minimum of 75% of frequent contacts are tested and those with LTBI are treated (Fig. 2, A3, B3). Further decrease in ToI to 1 week post-symptom onset would shorten the timelines of exceeding 50% reduction in TB incidence to between 2025 and 2030, even if only 25% of frequent non-household contacts are traced and tested. The magnitude of this reduction was estimated to be approximately 63.05% by 2030.

We found that as the ToI decreases, the effect of contact-tracing becomes less pronounced (Fig. 2, A1-A4). For instance, when the ToI is 4 weeks on average (i.e., the baseline scenario), increasing the proportion of frequent contacts who are traced and tested from 25% to 100% would result in approximately 36% reduction in the annual TB incidence by 2040 (Fig. 2, B1). However, the difference in incidence reduction between contact-tracing scenarios would be less than 2% at any time, when the ToI is not longer than 1 week (Fig. 2, B4). This effect results from early detection of active TB cases and a two-week isolation from the onset of treatment, which would eliminate transmission to frequent non-household contacts, thus

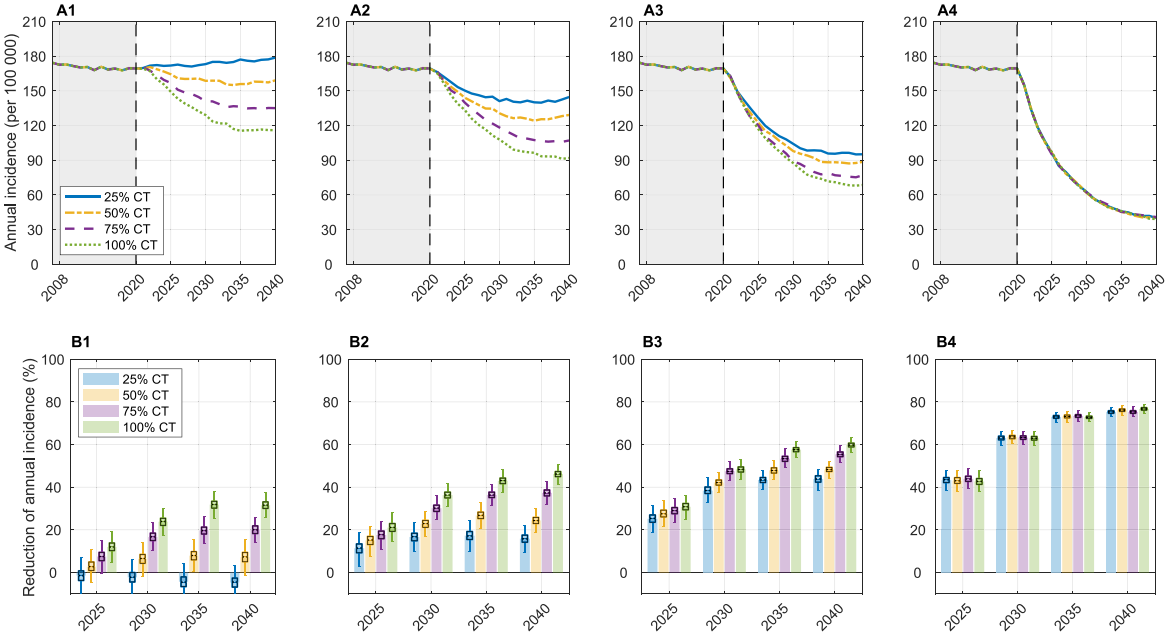

Fig. 2. Projected annual incidence of active TB per 100,000 population (A1-A4) and reduction of annual TB incidence (B1–B4) with different contact-tracing rates and an average household size of 3.8. ToI: 4 weeks (A1,B1), 3 weeks (A2,B2), 2 weeks (A3,B3), and 1 week (A4,B4). The treatment regimen for active TB was set as a combination of daily INH/RMP/EMB for 2 months followed by 4 months of INH/RMP. The treatment regimen for LTBI was set a combination of directly observed isoniazid and rifapentine for 3 months (3HP). CT: contact-tracing.

reducing the need for extensive contact-tracing. We also projected that, with rapid TB case findings (i.e., 1-week ToI) and a contact-tracing rate of at least 25%, the average reduction of TB incidence would be 62.97% by 2030, 72.77% by 2035, and 76.70% by 2040 (Fig. 2, B4).

3.2. Reduction of household sizes

We assumed that the government investment for housing infrastructure will lead to a lower average of persons per household, starting from 2025. We found that the reduction in average household size from 3.8 persons in the baseline scenario to 3.3 persons would decrease the annual TB incidence by less than 2% (Figure A1, Table A.7). This is consistent with previous studies, suggesting that the reduction in household sizes would have a minimal effect on the TB incidence rates (Grijalva et al., 2015; McCreesh & White, 2018; Tuite et al., 2017).

4. Discussion

The high burden of TB across Indigenous populations in Canada is a serious challenge in meeting the goals of TB elimination plans. Our results indicate that, while rapid identification of active TB patients is critically important to achieving a minimum 50% reduction in the annual incidence, this is not feasible by 2025 within a plausible range of scenarios simulated here. However, along with active case findings, wider availability of IGRA as a more sensitive test could help increase detection rates and lead to a higher reduction of TB incidence. The use of IGRA as a routine screening tool in remote communities is currently facing significant hurdles, including transfer of samples to a distant laboratory and lengthy turnaround times (Fact Sheets, 2020).

Our study highlights the need for enhanced access to the TB diagnosis and delivery of preventive treatment for LTBI. Despite current efforts for TB control in Nunavut, several challenges still hamper the effectiveness of the elimination program (Patterson et al., 2018). These include prolonged delay to case detection, limited access to diagnostic tools and services, and inadequate capacity for contact-tracing and rapid initiation of treatment. Given the importance of case findings, increasing the availability of more accurate diagnostic services and laboratory capacity is fundamental. Furthermore, improving housing infrastructure can contribute to the reduction of household transmission, albeit its impact on the overall TB incidence in the population appears limited. Molecular research indicates that only 8–19% of transmission occurs within households or between recognised social relationships (McCreesh & White, 2018). A possible explanation for this lower rate compared to community transmission of TB is that once a household contact has been infected, any future infectious encounters before recovery from disease are wasted. This is notwithstanding the occurrence of a significant number of daily contacts within households, especially in communities that are characterised by high-density living conditions.

Our results are consistent with previous work assessing the impact of interventions on the TB incidence in the northern Canadian Indigenous populations (Patterson et al., 2018; Tuite et al., 2017). However, our objective was to evaluate whether the goals of TB elimination in these settings can be attained within timelines indicated in the regional action plan (Nunavut's Regional Action Plan for, 2021). We found that, while a combination of strategies can reduce the incidence of TB, eliminating it from Inuit communities in Canada by 2030 is not achievable with currently available therapeutics.

Our study has several limitations that should be noted for interpretation of the results. For frequent contacts in the community, we assumed a cluster of peers (e.g., coworkers or classmates) for each individual and used the mean of their age-specific contact distribution (negative binomial distribution) to sample the members of the cluster randomly. We also assumed that 80% of community contacts occurs repeatedly within each cluster and the remaining were assigned as casual contacts. Due to the importance of contact patterns in TB transmission dynamics (Begun et al., 2013; Trauer et al., 2019), household and community data on individual interactions would improve our model parameterization. While we included only age-specific risks of disease activation, preexisting conditions such as diabetes, renal disease, cancer and smoking could substantially affect the rate of developing active TB. For example, the use of tobacco products among adolescents in Nunavut is about 6 times higher than the national average, with a two-fold higher risk of TB activation compared with never smokers (Lin et al., 2009; Rao et al., 2014; Wang et al., 2018). Despite these limitations, our quantitative projections provide actionable insights for TB elimination programs in Inuit populations.

5. Conclusion

Our study suggests that improving access to diagnostic tools for rapid identification of active TB patients constitutes an essential component of TB control programs. Contact-tracing and timely initiation of treatment of LTBI requires targeted efforts and significant investment towards achieving TB elimination goals. The findings here provide a quantitative

assessment of timelines within which milestones of TB control would be attainable, and should help policy makers and practitioners alike to improve TB intervention strategies in the absence of a life-long protection measure.

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Authors' contributions

EA and SMM conceived the study; EA developed the model, collected the data, performed simulations and statistical analysis; EA and SMM wrote the first draft of the paper; YK, PF, JB, and HS contributed to model design, providing contextual information, writing of the paper, and interpretation of the results.

Declaration of competing interest

None declared.

Appendix A

Table A.1
Contact matrix derived from empirical observations (Drolet et al., 2022). Daily number of contacts within and between these age groups were sampled from a negative binomial distribution and then aggregated to calculate weekly number of contacts.

Age group	0–4	5–19	20–49	50–65	65+	Mean number of daily contacts (SD)★
0–4	0.33	0.15	0.37	0.12	0.04	10.21 (3.99)
5–19	0.04	0.49	0.35	0.08	0.04	16.793 (5.78)
20–49	0.04	0.16	0.56	0.16	0.07	13.795 (8.93)
50–65	0.04	0.11	0.43	0.26	0.16	11.2669 (7.86)
65+	0.02	0.06	0.27	0.22	0.44	8.0027 (3.21)

★Standard deviation.

Table A.2
Age-stratified proportion of contacts occurring inside or outside of household.

Age group	% of contacts inside	% of contacts outside
0–4	40.45	59.55
5–19	31.91	68.09
20–49	24.04	75.96
50–65	33.58	66.42
65+	40.93	59.07

Table A.3
Standard regimens for treatment of active TB (P. H. A. o. Canada, 2014a, 2014b, 2014c).

Regimen	Initial phase	Schedule	Drug	Second phase	Schedule
PZA/INH/RMP/EMB	2 months	Daily	INH/RMP	4 months	3 times/week
INH/RMP/EMB	2 months	Daily	INH/RMP	7 months	3 times/week

Table A.4
Standard regimens for treatment of LTBI (P. H. A. o. Canada, 2014a, 2014b, 2014c).

Regimen	Duration	Schedule	Efficacy	Compliance	Source
INH/RMP	3 months	Twice weekly (DOT)	93%	95%	[(Alvarez et al., 1758), (Martínez Alfaro et al., 1998)]
INH	9 months	Daily	93%	86%	[(Spyridis et al., 2007), (Comstock, 1999)]
INH	6 months	Daily	68%	75%	Whalen et al. (1997)
INH/RPT	3 months	Once weekly	68%	96%	[(Whalen et al., 1997), (Martinson et al., 2011), (Schechter et al., 2006)]
RMP	4 months	Daily	63%	80%	[(A Double, 1992), (Menzies et al., 2008)]

Table A.5
Simulated scenarios.

Intervention	Scenario
Contact-tracing (CT)	25% of non-household repeated contacts★
	50% of non-household repeated contacts
	75% of non-household repeated contacts
	100% of non-household repeated contacts
Testing method (TM)	Tuberculin Skin Test (TST)★
Active treatment regimen (ATR)	Regimen 1★ (Table A3)
LTBI treatment regimen (LTR)	Regimen 1★ (Table A4)
Time-to-identification (ToI)	4 weeks delay between onset of symptoms to diagnosis
	3 weeks delay between onset of symptoms to diagnosis
	2 weeks delay between onset of symptoms to diagnosis
	1 week delay between onset of symptoms to diagnosis
Average household size (AHS)	3.8★ (most recent census data)
	3.3

★Baseline scenario.

Table A.6
Reduction of incidence (%) in each simulated scenario with different contact-tracing rates compared to the baseline scenario with average household size of 3.8. The treatment regimen for active TB was set a combination of daily INH/RMP/EMB for 2 months followed by 4 months of INH/RMP. The treatment regimen for LTBI was set a combination of directly observed isoniazid and rifapentine for 3 months (3HP). CT: contact-tracing.

ToI	CT	25%			50%			75%			100%		
	Year	Mean	95% CrI		Mean	95% CrI		Mean	95% CrI		Mean	95% CrI	
4 weeks	2025	−1.48	−8.17	4.93	2.72	−4.03	8.67	7.46	1.70	13.06	11.95	6.47	17.57
	2030	−2.29	−9.05	4.54	6.42	0.31	11.77	16.59	11.48	21.12	23.79	18.61	28.26
	2035	−4.36	−10.72	2.59	7.86	2.31	13.22	19.66	14.15	24.46	31.81	27.17	36.19
	2040	−4.72	−10.97	1.36	7.16	1.31	13.48	20.03	15.53	24.77	31.52	27.12	35.98
3 weeks	2025	11.36	5.42	16.86	15.03	9.40	20.61	17.58	12.23	22.72	21.05	15.73	25.94
	2030	16.65	10.89	22.52	22.84	18.26	27.40	30.13	25.71	34.27	36.29	31.86	40.53
	2035	17.25	11.80	22.57	26.70	21.61	31.43	36.36	32.59	40.39	42.99	39.07	46.71
	2040	15.81	10.61	20.72	24.38	19.87	29.06	37.32	33.31	41.24	46.15	42.69	49.56
2 weeks	2025	25.20	20.39	29.26	27.58	22.92	32.03	28.89	24.28	32.96	30.79	26.44	34.94
	2030	38.38	33.99	42.23	42.13	38.24	45.85	47.45	43.74	50.96	48.32	45.02	51.61
	2035	43.36	40.01	46.99	47.85	44.46	51.43	53.33	50.10	56.54	57.57	54.97	60.21
	2040	43.80	40.04	47.49	48.19	44.76	51.43	55.38	52.40	58.38	59.79	57.27	62.08
1 week	2025	43.29	39.29	46.46	43.03	39.59	46.56	43.88	39.98	47.32	42.67	38.84	46.31
	2030	63.05	60.49	65.38	63.50	60.92	65.96	63.22	60.68	65.51	62.97	60.65	65.39
	2035	72.96	71.26	74.73	73.15	71.07	75.01	73.40	71.61	75.21	72.77	70.91	74.57
	2040	75.22	73.14	76.91	76.06	74.01	77.65	75.27	73.47	77.02	76.70	74.88	78.38

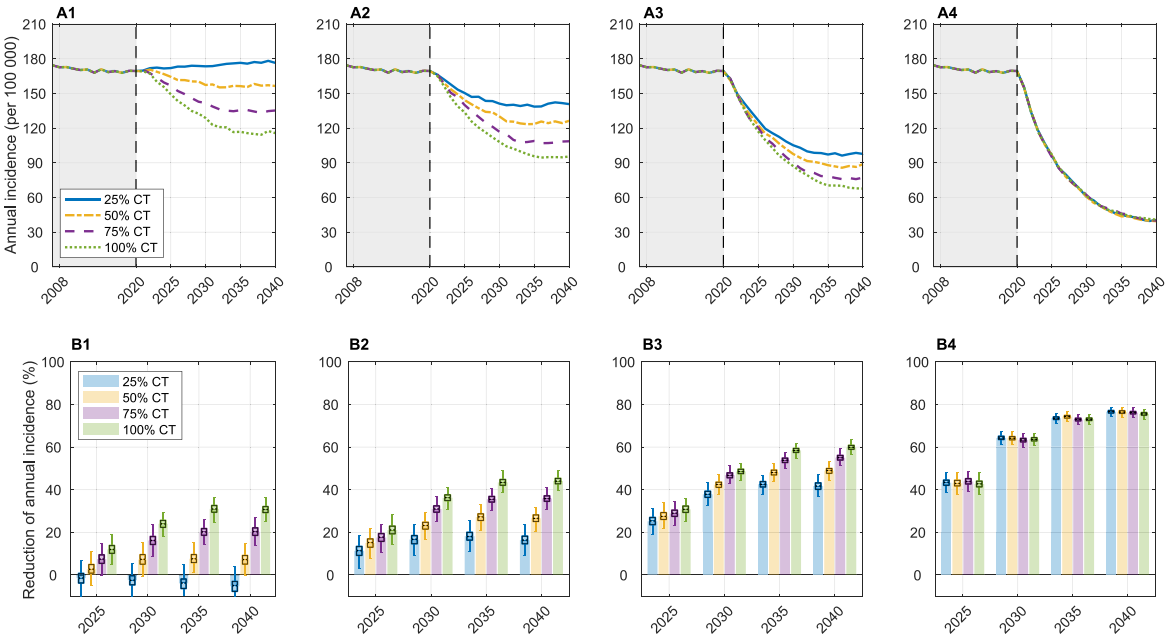

Fig. A.1. Projected annual incidence of active TB per 100,000 population (A1-A4) and reduction of annual TB incidence (B1–B4) when the average household size is reduces to 3.3 in 2025 from 3.8, with different contact-tracing rates. ToI: 4 weeks (A1,B1), 3 weeks (A2,B2), 2 weeks (A3,B3), and 1 week (A4,B4). The treatment regimen for active TB was set as a combination of daily INH/RMP/EMB for 2 months followed by 4 months of INH/RMP. The treatment regimen for LTBI was set a combination of directly observed isoniazid and rifapentine for 3 months (3HP). CT: contact-tracing.

Table A.7
Reduction of incidence (%) in each simulated scenario with different contact-tracing rates compared to the baseline scenario with average household size of 3.8 prior to 2025 and 3.3 from 2025 onward. The treatment regimen for active TB was set a combination of daily INH/RMP/EMB for 2 months followed by 4 months of INH/RMP. The treatment regimen for LTBI was set a combination of directly observed isoniazid and rifapentine for 3 months (3HP). CT: contact-tracing.

ToI	CT	25%			50%			75%			100%		
	Year	Mean	95% CrI		Mean	95% CrI		Mean	95% CrI		Mean	95% CrI	
4 weeks	2025	−1.48	−8.17	4.93	2.72	−4.03	8.67	7.46	1.70	13.06	11.95	6.47	17.57
	2030	−2.46	−9.36	4.15	7.23	1.51	12.93	16.14	10.86	21.01	24.01	19.36	28.43
	2035	−3.92	−10.39	3.17	7.60	2.32	13.35	20.17	15.30	24.74	31.00	26.26	35.49
	2040	−5.24	−11.79	0.79	7.20	1.23	13.08	20.31	15.73	25.31	30.65	26.35	35.31
3 weeks	2025	11.36	5.42	16.86	15.03	9.40	20.61	17.58	12.23	22.72	21.05	15.73	25.94
	2030	16.63	10.83	22.48	23.18	18.66	27.99	30.98	26.74	35.16	36.21	31.66	40.35
	2035	18.19	12.60	23.68	27.13	22.14	32.04	35.52	31.55	39.78	43.40	39.53	46.83
	2040	16.32	11.05	21.29	26.61	21.94	31.00	35.89	32.11	40.13	44.06	40.61	47.54
2 weeks	2025	25.20	20.39	29.26	27.58	22.92	32.03	28.89	24.28	32.96	30.79	26.44	34.94
	2030	37.83	33.50	41.80	42.34	38.35	46.06	46.79	43.14	50.44	48.54	45.37	51.95
	2035	42.54	39.03	45.91	48.08	44.66	51.73	53.77	50.63	56.66	58.43	55.84	61.19
	2040	41.72	37.81	45.32	48.91	45.59	52.20	55.01	51.98	57.87	59.89	57.29	62.51
1 week	2025	43.29	39.29	46.46	43.03	39.59	46.56	43.88	39.98	47.32	42.67	38.84	46.31
	2030	64.27	62.00	66.57	64.15	61.73	66.57	63.25	60.86	65.40	63.67	61.20	65.95
	2035	73.52	71.70	75.23	74.25	72.30	75.92	72.89	70.93	74.68	73.02	71.13	74.90
	2040	76.55	74.67	78.12	76.39	74.44	77.98	76.13	74.34	77.94	75.56	73.70	77.33

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