Active screening for tuberculosis in high-incidence Inuit communities in Canada: a cost-effectiveness analysis

Aashna Uppal MScPH, Ntwali Placide Nsengiyumva MSc, Céline Signor MSc, Frantz Jean-Louis MPH, Marie Rochette MD MSc, Hilda Snowball, Sandra Etok, David Annanack, Julie Ikey, Faiz Ahmad Khan MD MPH, Kevin Schwartzman MD MPH

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Abstract

Background: Active screening for tuberculosis (TB) involves systematic detection of previously undiagnosed TB disease or latent TB infection (LTBI). It may be an important step toward elimination of TB among Inuit in Canada. We aimed to evaluate the cost-effectiveness of community-wide active screening for TB infection and disease in 2 Inuit communities in Nunavik.

Methods: We incorporated screening data from the 2 communities into a decision analysis model. We predicted TB-related health outcomes over a 20-year time frame, beginning in 2019. We assessed the cost-effectiveness of active screening in the presence of varying outbreak frequency and intensity. We also considered scenarios involving variation in timing, impact and uptake of screening programs.

Results: Given a single large outbreak in 2019, we estimated that 1 round of active screening reduced TB disease by 13% (95% uncertainty range –3% to 27%) and was cost saving compared with no screening, over 20 years. In the presence of simulated large outbreaks every 3 years thereafter, a single round of active screening was cost saving, as was biennial active screening. Compared with a single round, we also determined that biennial active screening reduced TB disease by 59% (95% uncertainty range 52% to 63%) and was estimated to cost Can$6430 (95% uncertainty range –$29 131 to $13 658 in 2019 Can$) per additional active TB case prevented. With smaller outbreaks or improved rates of treatment initiation and completion for people with LTBI, we determined that biennial active screening remained reasonably cost-effective compared with no active screening.

Interpretation: Active screening is a potentially cost-saving approach to reducing disease burden in Inuit communities that have frequent TB outbreaks.

Tuberculosis (TB) was the world's deadliest infectious disease in 2019.[1] The burden of TB is disproportionately borne by vulnerable and marginalized communities, including Canadian Inuit,[2] where it reflects colonization and persistent socioeconomic inequities.[3] Overall, Canada has a low incidence of TB (defined as < 10 cases per 100 000 population annually),[4] with an incidence rate of 4.9 per 100 000 in 2017.[5] However, the overall incidence across Inuit communities was more than 40-fold higher.[5] In 2018, Inuit Tapiriit Kanatami (the national representative organization for Inuit in Canada) and the Government of Canada announced their goal to eliminate TB from Inuit regions by 2030.[3]

In 2019, the incidence of TB in Nunavik (in Northern Quebec) was 495 per 100 000.[6] The Nunavik Regional Board of Health and Social Services (NRBHSS) implemented community-wide active screening for active TB and latent tuberculosis infection (LTBI) in 2 villages where repeated outbreaks were common. Outbreaks are considered to occur when either 2 or more contacts of a person with active TB are also diagnosed with active TB, or 2 or more people who develop active TB within 1 year are epidemiologically linked;[7] the outbreaks in these villages have been much more extensive.[8] With active screening, people with TB disease may be identified and receive treatment while minimally symptomatic and less contagious.[9] People with LTBI may be identified and receive treatment before they develop active TB disease.[10,11] Active screening is most often undertaken when other practices appear insufficient to interrupt transmission and reduce morbidity, and may be particularly relevant in remote settings.[12] It is

pertinent to consider the benefits and costs of community-wide screening, within a TB elimination strategy that also addresses underlying health determinants.[13,14] We used decision analysis modelling to project health outcomes and costs associated with active screening in these villages over a 20-year time frame. Our objectives were to evaluate the cost-effectiveness of the 2019 screening activities and to assess potential cost-effectiveness of future screening.

Methods

In 2019, the NRBHSS led community-wide active-screening campaigns in Village 1 (population about 1000) and Village 2 (population about 1500). These campaigns targeted anyone who was not already known to have active TB or LTBI, without age restrictions. Consequently, about 60% of the inhabitants were eligible for screening in Village 1 and about 70% were eligible in Village 2. People without a history of LTBI and without symptoms suggestive of active TB underwent tuberculin skin testing (TST). People with a TST result of at least 5 mm or who had a history of LTBI or active TB underwent chest radiography.[15] The NRBHSS worked with local staff as well as staff flown in to the villages to organize these screening campaigns. Additional details are provided in the Screening campaigns section of Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.210447/tab-related-content.

To simulate these campaigns, we incorporated summary public health and cost data into a decision analysis model using TreeAge Pro software (2019). Using simulated population cohorts that reflected the inhabitants of these villages, the model predicted TB-related health outcomes: persons with active TB, latent TB infection, and TB-related deaths, over a 20-year time frame, from 2019. The model also predicted direct cost to the health system, including those of managing active and latent TB, and of screening. We considered open cohorts,[16] and used an annual discount rate of 1.5% for future outcomes and costs.[17]

Figure 1 shows a simplified depiction of the model structure. We simulated an active screening campaign in 2019 (reflecting the campaigns that had actually occurred). The counterfactual scenario with no active screening shared the same model structure, but with lower probabilities for diagnosis and treatment of TB infection and disease.

We simulated secondary transmission, using observed data.[8,18,19] We used a ratio of 1.82 secondary active TB cases per index TB case in Village 1, which reflected pooled data from outbreak and nonoutbreak years.[18] A ratio of 0.67 people with new LTBI per index case was used.[8,19] The relatively low number of persons with incident LTBI reflects the high proportion already infected at baseline (48% in Village 1 and 33% in Village 2) versus those susceptible to infection (49% in Village 1 and 66% in Village 2) (Appendix 1, Supplementary Table S1). During simulated outbreaks, we increased the probabilities of progression, reactivation and transmission as observed in these villages (see the Simulating outbreaks section of Appendix 1 for details).

Epidemiologic parameters

Epidemiologic parameters fell into 3 categories. The first included parameters related to TB pathogenesis and treatment.[20,21] These came from published literature. The second category included parameters related to the LTBI or active TB treatment cascade. These parameters came from the Nunavik TB program data[22] and were vetted by regional experts and community members. Active screening was considered to increase diagnosis and treatment initiation among people with LTBI and to increase diagnosis among people with active TB.[22] The specific impact of active screening on these parameters reflected program data from both communities in 2019; details are provided in Appendix 1, Supplementary Table S2. The third category included other parameters, such as duration of hospital admission for TB disease. These were informed primarily by local data.[18] Table 1 outlines key epidemiologic parameters and their data sources.

Cost parameters

All costs were considered from the perspective of the health system and adjusted to 2019 Canadian dollars.[27] Cost inputs fell into 2 categories. The first category included costs related to active screening. These costs came from the Nunavik program data and reflected the steps needed to conduct active-screening activities in both communities in 2019.[22] All screening campaign costs were incurred by the health system, including lodging and transportation costs for staff who had to be flown into the villages. The second category included costs related to standard TB care. Wherever possible, these costs came from Nunavik, or Nunavut when necessary. Where such information was unavailable, costs came from published literature but were confirmed with regional experts. Table 2 highlights key cost parameters, which are further described in Appendix 1, Supplementary Table S1.

Screening strategies

We simulated 3 screening strategies, given a single outbreak in 2019, with no subsequent outbreaks.

No active screening (Strategy A)

We estimated what most likely would have occurred had no active screening been introduced in 2019. We used background rates of diagnosis, treatment initiation and treatment completion for TB disease and LTBI, informed by community data during 2017 and 2018, when there was no active screening. Screening close contacts of persons with TB disease is standard practice.

Community-wide active screening in 2019 only (Strategy B)

Village 1 and Village 2 had active community-based screening programs in 2019. This strategy incorporated program data to reflect increased rates of diagnosis, treatment initiation and treatment completion compared with Strategy A.

We then simulated an outbreak in 2019 and every 3 years thereafter, because these villages have had TB outbreaks every 2–3 years since 2011.[18] We considered an additional strategy in this context.

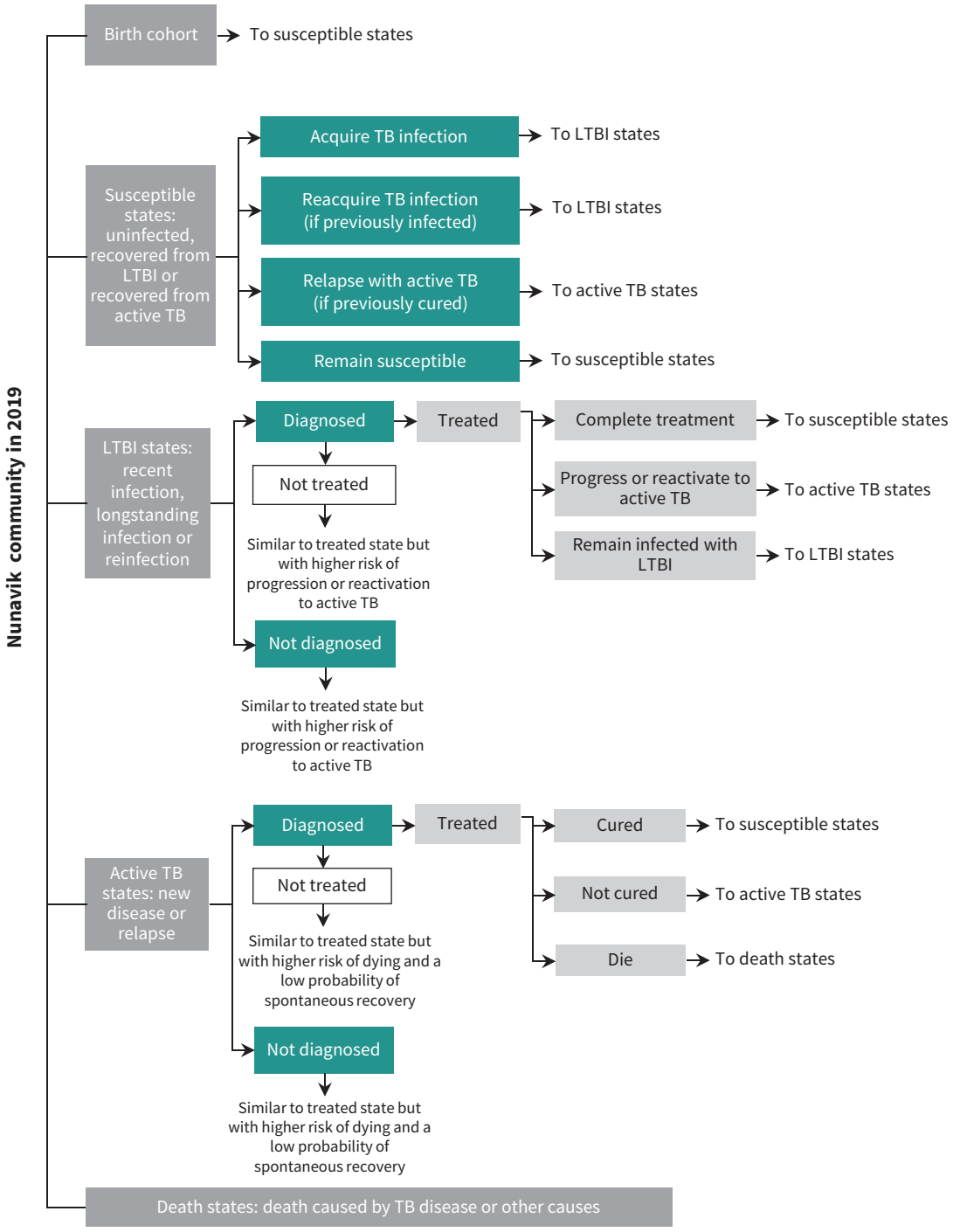

Figure 1: Simplified depiction of the decision analysis model. Transitions between health states are experienced by cohort members in each cycle. For example, each cycle, a number of newborns enter the susceptible states. Here, they may acquire or reacquire infection, relapse with active tuberculosis (TB), or remain susceptible. If infected or reinfected, cohort members move to the latent tuberculosis infection (LTBI) states, where the clinical pathway entails diagnosis and treatment. Probabilities of diagnosis and treatment are lower in strategies where there is no active screening. The clinical pathway for active TB states resembles that of LTBI states. Similarly, probabilities of diagnosis and treatment are lower in strategies where there is no active screening. Finally, there are death states, which include death caused by TB or other causes (i.e., background mortality).

Community-wide active screening every 2 years for 20 years (Strategy C)

Local public health authorities did not think annual screening was feasible but wished to consider biennial screening.

Secondary analyses

We considered additional strategies, involving variations in screening frequency and target groups. We also considered several scenarios to explore variations in key model parameters: increased

Table 1: Key epidemiologic parameters used in the decision analysis model

Epidemiologic parameter	Value	Source
Related to TB pathogenesis		
Probability of progression to active TB after recent infection	0.05–0.265‡	N'Diaye et al.[13]
Probability of reactivation to active TB after remote infection	0.0005–0.075‡	N'Diaye et al.,[13] Behr et al.[23]
Annual risk of infection	0.0095	N'Diaye et al.[13]
Probability of cure after complete active TB treatment	0.928	Gallant et al.[24]
Probability of cure after complete LTBI treatment	0.9	Ditkowsky and Schwartzman[25]
Probability of dying of untreated TB if smear was negative	0.02	Tiemersma et al.[26]
Probability of dying of untreated TB if smear was positive	0.07	Tiemersma et al.[26]
Probability of adverse event during active TB treatment	0.051	Tan et al.[20]
Probability of adverse event during LTBI treatment	0.003	Smith et al.[21]
Average number of new LTBI per index TB case	0.67	Khan et al.,[8] Inuit Tapiriit Kanatami[19]
Average number of secondary active TB cases per index TB case	1.82	NRBHSS[18]
Other		
Annual birth rate	0.019–0.023§	Institut de la statistique du Québec,[16]
Probability of non-TB–related death (background mortality)	0.014–0.021§	Institut de la statistique du Québec,[16] Inuit Tapiriit Kanatami[19]
Number of days in hospital if smear was negative*	14	NRBHSS[18]
Number of days in hospital if smear was positive*	60	NRBHSS[18]
TB cascade parameters in the absence of active screening†		
Active TB		
Proportion of people with active TB who were diagnosed	0.82¶	Calculated
Proportion of people who were diagnosed and started treatment	1	NRBHSS[22]
Proportion of people who started treatment and completed it	0.99	NRBHSS[22]
LTBI		
Proportion of people with LTBI who were diagnosed	0.83¶	Calculated
Proportion of people who were diagnosed and started treatment	0.70¶	NRBHSS[22]
Proportion of people who started treatment and completed it	0.75	NRBHSS[22]

Note: LTBI = latent tuberculosis infection, NRBHSS = Nunavik Regional Board of Health and Social Services, TB = tuberculosis.
*Standard TB management in the region requires all persons with active pulmonary TB to be admitted to hospital.[18]
†These cascade parameters are specific to Village 1. Those pertaining to Village 2 are provided in Appendix 1, Supplementary Table S2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.210447/tab-related-content.
‡The probabilities of progression and reactivation changed over time in the model, starting at their high values (0.265 and 0.075, respectively) and declining over time. This reflected the presence of an outbreak at the beginning of the model, with a subsequent decline in transmission. In scenarios where repeated outbreaks were simulated, we adjusted these parameters accordingly (in addition to the annual risk of infection parameter). This process is described in detail in the Simulating outbreaks section of Appendix 1.
§These values change year over year in the model to reflect changing birth and death rates in the region.
¶The value of these cascade parameters increases when active screening is added.

rates of LTBI treatment initiation and completion, decreased rates of LTBI diagnosis, use of local staff (to decrease lodging and transportation costs), reduced adherence to active screening and variations in outbreak intensity. Varying outbreak intensity involved lower peaks for the progression and reactivation parameters during outbreaks. Detailed descriptions are available in the Incorporation of additional strategies and Scenario analyses sections in Appendix 1.

Finally, we used one-way sensitivity analyses and probabilistic sensitivity analysis to assess the impact of variation in input parameters on predicted outcomes. The probabilistic sensitivity analysis involved 10 000 model runs and sampled parameters from prespecified ranges (listed in Appendix 1, Supplementary Table S1).

Ethics approval

Because the analysis was initiated by the NRBHSS and used only aggregate program data, ethics review board approval was not required. However, results were first shared with community members of the NRBHSS, and community leaders' and members' approval of this manuscript was obtained before submission.

Results

The 2019 active screening campaigns took place in the 2 villages over 6–11 weeks. They found 52 people with previously unknown LTBI and 13 with previously undiagnosed active TB.[22] For simplicity, we focus on results for Village 1, which had more extensive outbreaks.

Table 2: Key cost parameters used in the decision analysis model

Parameter	Value, 2019 Can$	Source
Cost related to active screening*		
Total cost of active screening per person (in 2019†)	1952	NRBHSS[22]
a) Total cost of human resources	776	NRBHSS[22]
b) Total cost of lodging and transport	1102	NRBHSS[22]
c) Total cost of communication and mobilization	5	NRBHSS[22]
d) Total cost of training and workshops	2	NRBHSS[22]
e) Total cost of supplies	49	NRBHSS[22]
f) Total cost of amenities	18	NRBHSS[22]
Cost related to management of active TB and LTBI		
Cost of medication for active TB	674	RAMQ[28]
Cost of medication for latent TB	114	RAMQ[28]
Cost of visits to manage active TB treatment	436	FIQ,[29] Alsdurf et al.[30]
Cost of visits to manage LTBI treatment	42	FIQ,[29] Alsdurf et al.,[30] Campbell et al.[31]
Cost of severe adverse event caused by active TB treatment	16 364	Tan et al.[20]
Cost of adverse event during LTBI treatment	782	Campbell et al.[31]
Cost of medical evacuation	6713	Banerji et al.[32]
Cost of hospital stay per day	2050	NRBHSS[33]

Note: FIQ = Fédération Interprofessionelle de la santé du Québec, LTBI = latent tuberculosis infection, NRBHSS = Nunavik Regional Board of Health and Social Services, RAMQ = Régie de l'assurance maladie du Québec, TB = tuberculosis.
*These costs are specific to Village 1 (there were 604 people screened in Village 1). Costs pertaining to Village 2 are provided in Appendix 1, Supplementary Table S1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.210447/tab-related-content.
†Construction costs are included in the lodging and transport costs. The village required an extra structure to be built to accommodate screening activities, which is what comprises the construction costs. In subsequent years, if active screening was repeated, we removed costs related to construction so the cost of active screening per person was cheaper. The total cost of active screening is equal to the sum of a, b, c, d, e and f.

Given a single outbreak in 2019

Results are summarized in Table 3, with strategies ordered from least to most expensive. Compared with no active screening, adding community-wide active screening in 2019 was estimated to reduce the number of people with active TB by 13% (95% uncertainty range –3% to 27%) over 20 years, and was less expensive (dominant), saving $355 (95% uncertainty range –$273 to $1055) per person.

Given an outbreak in 2019 and every 3 years thereafter

The results for Strategies A, B and C, in the presence of an outbreak every 3 years, are shown in Table 4 and Table 5. Compared with no active screening, Strategies B and C substantially reduced the number of active TB cases. Strategy C, in which community-wide active screening occurs every 2 years from 2019 to 2039, had the largest impact on TB morbidity and mortality, reducing active TB cases by 63% (95% uncertainty range 57% to 67%) compared with Strategy A. Strategies B and C were cost saving compared with Strategy A.

Compared with no active screening, Strategies B and C were both dominant. Strategy C was more effective but likely more expensive than Strategy B.

Village 2

In Village 2, active screening in 2019 alone was reasonably cost-effective ($22 134 per active TB case averted) but not cost saving compared with no active screening. Biennial active screening also was reasonably cost-effective, given outbreaks every 3 years ($22 292 per active TB case averted), compared with no active screening. However, 95% uncertainty ranges were wide. Detailed results are provided in Appendix 1, Supplementary Tables S4–S7.

Scenario analyses

With a strengthened LTBI cascade, a single round of active screening remained cost saving compared with no active screening in the presence of a single outbreak and in the presence of an outbreak every 3 years. Biennial active screening, however, was no longer cost saving in the presence of an outbreak every 3 years; the incremental cost per person, compared with no screening, was $392 (95% uncertainty range –$2584 to $5297).

When the intensity of future outbreaks was reduced by 25% (peaks in progression and reactivation parameters reduced by 25%), Strategy B remained cost saving compared with Strategy A, but Strategy C became more expensive than Strategy A. The incremental cost per person of biennial active screening, compared with no active screening, was $577 (95% uncertainty range –$2825 to $5981). The same pattern was observed when the intensity of future outbreaks was reduced to a greater degree (see Appendix 1, Supplementary Table S8 and Supplementary Figures S1 and S2 for further details on all scenario analyses).

Table 3: Outcomes over 20 years in Village 1, given a single outbreak in 2019

Strategy*	Cost, $ (95% uncertainty range)	No. of cases (95% uncertainty range)		No. (95% uncertainty range) of TB-related deaths
		Incident active TB†	Incident LTBI†	
B	6 996 027 (5 647 525 to 8 975 360)	90 (79 to 103)	38 (33 to 45)	0.6 (0.4 to 0.7)
A	7 493 340 (5 927 277 to 9 748 954)	103 (90 to 118)	42 (36 to 48)	0.9 (0.7 to 1.0)

Note: LTBI = latent tuberculosis infection, TB = tuberculosis.
*Strategy A: no active screening. Strategy B: community-wide active screening in 2019.
†Incident LTBI includes new infections and reinfections. Incident active TB similarly includes cases due to primary progression or reactivation, as well as relapse. Both incident LTBI and incident active TB include secondary infections and active TB cases. Results in Appendix 1 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.210447/tab-related-content) present secondary infections and secondary active TB cases separately.

Table 4: Outcomes over 20 years in Village 1 given an outbreak every 3 years, starting in 2019

Strategy*	Cost, $	No. (95% uncertainty range) of cases of incident active TB†	No. (95% uncertainty range) of cases of incident LTBI†	No. (95% uncertainty range) of TB-related deaths
B	14 745 984 (11 715 969 to 18 606 081)	249 (227 to 266)	87 (83 to 94)	1.5 (1.2 to 1.8)
C	15 691 149 (13 059 608 to 18 908 752)	102 (90 to 117)	30 (28 to 35)	0.3 (0.2 to 0.3)
A	16 359 259 (12 846 266 to 20 772 912)	276 (252 to 294)	94 (89 to 101)	1.9 (1.6 to 2.3)

Note: LTBI = latent tuberculosis infection, TB = tuberculosis.
*Strategy A: no active screening. Strategy B: community-wide active screening in 2019. Strategy C: community-wide active screening every 2 years from 2019 to 2039.
†Incident LTBI includes new infections, reinfections and secondary infections. Incident active TB similarly includes cases due to primary progression or reactivation, relapse and secondary cases. Results in Appendix 1 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.210447/tab-related-content) present secondary infections and secondary active TB cases separately.

Table 5: Incremental cost per case of active tuberculosis averted in Village 1, given an outbreak every 3 years, starting in 2019

Strategy*	Incremental cost per person compared with preceding strategy, $ (95% uncertainty range)	Incremental cost per active TB case averted† compared with preceding strategy, $ (95% uncertainty range)	Incremental cost per active TB case averted compared with Strategy A
B	–	–	Dominant‡
C	674 (–1427 to 2808)	6430 (–29 131 to 13 658)	Dominant‡
A	477 (–1827 to 2865)	Dominated†	–

Note: TB = tuberculosis.
*Strategy A: no active screening. Strategy B: community-wide active screening in 2019. Strategy C: community-wide active screening every 2 years from 2019 to 2039.
†Incremental cost per active TB case averted is the difference in costs divided by the difference in active TB cases between 2 strategies. The population of Village 1 at the end of the simulation was 1402.
‡Because Strategies B and C were less costly and more effective than Strategy A at averting active TB cases, we considered them to be "dominant", therefore, Strategy A was dominated.

Sensitivity analyses

We found that one-way sensitivity analysis suggested that per diem costs of hospital admission for active TB, duration of hospital admission if smear positive, the probability of progression to active TB and the probability of cure following incomplete LTBI treatment were the most influential drivers of cost-effectiveness. We also found that variations in these parameters changed the incremental savings per active TB case averted but did not change conclusions (Appendix 1, Supplementary Figures S3–S6).

We used probabilistic sensitivity analyses to derive the 95% uncertainty ranges in the previously mentioned tables; these analyses are shown in Appendix 1, Supplementary Figures S7–S10. These analyses showed that, with a single outbreak, active screening averted more active TB cases than no active screening in 94% of simulations for Village 1. Active screening was cost saving (as well as effective) in 86% of simulations. Therefore, active screening was the dominant strategy in most simulations. With outbreaks every 3 years, biennial active screening was more effective (and more expensive) than a single round of screening in 75% of simulations. We determined that biennial active screening averted more TB disease than no active screening and one-time screening in all simulations.

Interpretation

In Inuit communities with high TB incidence, we found that active screening is likely to be reasonably cost-effective and potentially cost saving. Historically, community-wide screening has been implemented after outbreaks. The ideal screening program will prevent future outbreaks, but it is impossible to predict exactly when an outbreak will occur. The high cost of care for TB in Canada's North makes preventive interventions more cost-effective. Although there is no absolute threshold that defines cost-effectiveness in terms of cost per TB case averted, we projected active screening to be cost saving compared with no active screening in Village 1, given repeated large outbreaks. In Village 2, active screening was likely cost-effective but not cost saving, which reflected a lower TB burden and screening yield (the 2019 screening campaign detected fewer people with active TB than in Village 1, despite having a larger population).

The Inuit Tuberculosis Elimination Framework highlights key knowledge gaps with respect to active screening.[3] Our study builds on previous work from Nunavut and Nunavik[15,34] by projecting potential costs and cost savings, as well as health benefits. Emerging literature suggests that active TB screening in such diverse settings as Cambodia, India, China, South Africa, Pakistan and the South Pacific is effective and cost-effective — particularly if repeated over the longer term.[12,35–37]

It is essential that all TB care and prevention activities engage and mobilize communities in a culturally safe and appropriate manner. To that end, the NRBHSS has partnered with communities to develop and implement a regional plan for TB elimination, within the TB Elimination Framework created by Inuit Tapiriit Kanatami. This framework acknowledges the importance of strengthening local capacity and of the social determinants of health, including housing and food security.[2,3] We focused on community-wide screening as a stand-alone intervention; we did not address these fundamental upstream determinants herein, but previous publications have explored them in the Nunavut context.[13,14]

Limitations

We made several key assumptions. We assumed that costs related to construction would not recur and that only operational costs would recur. We initially assumed that adherence to repeated cycles of community-wide screening was 100%, although this was varied in scenario analysis. We also assumed that people with LTBI who were identified by community screening would not otherwise have been found, and people with active TB who were found by active screening would have otherwise been diagnosed at a later, more infectious stage. In addition, the model was not stratified by age, so we could not assess whether benefits of active screening were higher in specific age groups — recognizing that the average age in Inuit communities is much younger than in Southern Canada.[19]

Another limitation was the lack of region-specific data for certain model parameters. Wherever possible, we then used data from other Inuit regions. This was the case for estimating secondary transmission, for which we used both program and published data. When such data were not available, we used data from other settings (for the probability of treatment toxicity, for example), whereas epidemiologic parameters were vetted by the local public health authority.

Conclusion

Tuberculosis continues to exact a large and disproportionate burden on many Inuit communities across Canada's North. We anticipate that community-based screening, supported by prompt and effective treatment of both active TB disease and latent infection, can play an important role in communities with the highest incidence.

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Affiliations: Montreal Chest Institute (Uppal, Khan, Schwartzman); Respiratory Epidemiology and Clinical Research Unit, Centre for Outcomes Research and Evaluation (Uppal, Nsengiyumva, Khan, Schwartzman), Research Institute of McGill University Health Centre; McGill International Tuberculosis Centre (Uppal, Nsengiyumva, Khan, Schwartzman), Montréal, Que.; Régie régionale de la santé et des services sociaux du Nunavik (Signor, Jean-Louis, Rochette); Kativik Regional Government (Snowball); Ulluriaq School (Etok), Kangiqsualujjuaq; Northern Village of Kangiqsualujjuaq (Annanack); Salluit Birth Center, Salluit (Ikey), Québec, Que.

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Data-sharing: The authors confirm that the most relevant data are provided in the main text or Appendix 1. In addition, there is a publicly available summary of epidemiologic data related to the screening programs (https://bc.lung.ca/sites/default/files/Jean%20Louis.pdf) and the decision analysis model has been posted online (https://www.mcgill.ca/tb/projects). Both the summary and the model protect the identity of the 2 villages considered in the study. Some specific data pertaining to the financial details of the screening campaigns have been withheld to maintain confidentiality of those involved. However, additional information may be made available upon reasonable request to the corresponding author.

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Correspondence to: Kevin Schwartzman, kevin.schwartzman@mcgill.ca