Tuberculosis (TB) was the world’s deadliest infectious disease in 2019. The burden of TB is disproportionately borne by vulnerable and marginalized communities, including Canadian Inuit, where it reflects colonization and persistent socioeconomic inequities. Overall, Canada has a low incidence of TB (defined as < 10 cases per 100 000 population annually), with an incidence rate of 4.9 per 100 000 in 2017. However, the overall incidence across Inuit communities was more than 40-fold higher. 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.

In 2019, the incidence of TB in Nunavik (in Northern Quebec) was 495 per 100 000. The Nunavik Regional Board of Health and Social Services (NRBHSS) implemented community-wide active screening for 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; the outbreaks in these villages have been much more extensive. With active screening, people with TB disease may be identified and receive treatment while minimally symptomatic and less contagious. People with LTBI may be identified and receive treatment before they develop active TB disease. 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.
pertinent to consider the benefits and costs of community-wide screening, within a TB elimination strategy that also addresses underlying health determinants.11,14 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 TB infection and disease.

**Epidemiologic parameters**

Epidemiologic parameters fell into 3 categories. The first included parameters related to TB pathogenesis and treatment.16,21 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 data22 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.
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
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 10000 model runs and sampled parameters from pre-specified 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. 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<sup>22</sup>         |
| a) Total cost of human resources                                          | 776             | NRBHSS<sup>22</sup>         |
| b) Total cost of lodging and transport                                    | 1102            | NRBHSS<sup>22</sup>         |
| c) Total cost of communication and mobilization                           | 5               | NRBHSS<sup>22</sup>         |
| d) Total cost of training and workshops                                   | 2               | NRBHSS<sup>22</sup>         |
| e) Total cost of supplies                                                 | 49              | NRBHSS<sup>22</sup>         |
| f) Total cost of amenities                                                | 18              | NRBHSS<sup>22</sup>         |
| **Cost related to management of active TB and LTBI**                      |                 |                             |
| Cost of medication for active TB                                          | 674             | RAMQ<sup>28</sup>           |
| Cost of medication for latent TB                                          | 114             | RAMQ<sup>28</sup>           |
| Cost of visits to manage active TB treatment                              | 436             | FIQ<sup>29</sup>, Alsdurf et al<sup>10</sup> |
| Cost of visits to manage LTBI treatment                                   | 42              | FIQ<sup>29</sup>, Alsdurf et al<sup>10</sup>, Campbell et al<sup>31</sup> |
| Cost of severe adverse event caused by active TB treatment                | 16 364          | Tan et al<sup>26</sup>       |
| Cost of adverse event during LTBI treatment                               | 782             | Campbell et al<sup>31</sup>  |
| Cost of medical evacuation                                                | 6713            | Banerji et al<sup>32</sup>   |
| Cost of hospital stay per day                                             | 2050            | NRBHSS<sup>22</sup>         |

Note: FIQ = Fédération Interprofessionnelle 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).
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.

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         | 6996027 (5647525 to 8975360)      | 90 (79 to 103)                       | 38 (33 to 45)                                    |
| A         | 7493340 (5927277 to 9748954)      | 103 (90 to 118)                      | 42 (36 to 48)                                    |

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 incident LTBI† | No. (95% uncertainty range) of TB-related deaths |
|-----------|------------------------------------------|-------------------------------------------------------------|-----------------------------------------------|--------------------------------------------------|
| B         | 14745984 (11715969 to 18606081)          | 249 (227 to 266)                                            | 87 (83 to 94)                                 | 1.5 (1.2 to 1.8)                                 |
| C         | 15691149 (13059608 to 18908752)          | 102 (90 to 117)                                            | 30 (28 to 35)                                 | 0.3 (0.2 to 0.3)                                 |
| A         | 16359259 (12846266 to 20772912)          | 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         | –                                                              | 6430 (–29131 to 13658)                                        | Dominant†                                                    |
| C         | 674 (–1427 to 2808)                                           | 6430 (–29131 to 13658)                                        | 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 avertting active TB cases, we considered them to be “dominant”, therefore, Strategy A was dominated.
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. Our study builds on previous work from Nunavut and Nunavik 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.

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. 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.

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 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.

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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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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