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Cost-effectiveness analysis of 3 months of weekly rifapentine and isoniazid compared to isoniazid monotherapy in a Canadian arctic setting

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ABSTRACT

Objective To assess the cost effectiveness of once weekly rifapentine and isoniazid for 12 weeks (3HP) to the current standard care for latent tuberculosis (TB) infection (LTBI) in Iqaluit, Nunavut.

Design A cost-effectiveness analysis using a Markov model reflecting local practices for LTBI treatment.

Setting A remote Canadian arctic community with a high incidence of TB.

Participants Hypothetical patients with LTBI.

Interventions The cost effectiveness of 3HP was compared with the existing standard of care in the study region which consists of 9 months of twice weekly isoniazid (9H) given by directly observed therapy.

Outcome measures Effectiveness was measured in quality-adjusted life years (QALYs) with model parameters were derived from historical programmatic data, a local implementation study of 3HP and published literature. Costs from the perspective of the Nunavut healthcare system were measured in 2019 US dollars and were obtained primarily from local, empirically collected data. Secondary health outcomes included estimated TB cases and TB deaths averted using 3HP versus 9H. One way and probabilistic sensitivity analyses were performed.

Results The 3HP regimen was dominant over 9H: costs were lower (US$628 vs US$924/person) and health outcomes slightly improved (20.14 vs 20.13 QALYs/person). In comparison to 9H, 3HP treatment resulted in fewer TB cases (27.89 vs 30.16/1000 persons) and TB deaths (2.29 vs 2.48/1000 persons). 3HP completion, initiation and risk of fatal adverse events were the primary drivers of cost effectiveness.

Conclusion In a remote Canadian arctic setting, using 3HP instead of 9H for LTBI treatment may result in cost savings and similar or improved health outcomes.

Strengths and limitations of this study

- This cost-effectiveness analysis of weekly rifapentine and isoniazid focuses on a remote, high tuberculosis (TB) incidence setting.
- This is the first cost-effectiveness analysis of this treatment in Canada and the first in an Arctic region anywhere in the world.
- Local data were used to obtain most key costs and epidemiological parameters.
- The impact of treatment for latent TB infection on TB transmission was not accounted for in this study.
- Although direct costs of diagnosis and treatment were included in this study, additional costs to patients such as lost wages were not included.

INTRODUCTION

Canadian Inuit face high rates of tuberculosis (TB) despite Canada's low overall incidence of TB disease. In 2017, the incidence of active TB among Inuit was 205.8/100 000 compared with only 0.5/100 000 among Canadian-born non-indigenous people.[1]

The Government of Canada and Inuit Tapariit Kanatami (Inuit National Organisation) announced goals to eliminate TB across Inuit Nunangat (Inuit homeland) by 2030.[2] However, challenges persist since Inuit in Arctic communities face geographic isolation and difficult climatic conditions resulting in high costs and limited availability of human and material resources.[3]

Treatment of latent TB infection (LTBI) is critical to achieving TB elimination[4 5] and reduces future risk of developing active TB by over 90%[6] but is hindered by lengthy treatment, traditionally involving 9 months of twice weekly isoniazid (9H). Recently, regimens with a shorter duration have been developed, including once weekly rifapentine and isoniazid for 12 weeks (3HP). In a large randomised controlled trial and subsequent meta-analysis, 3HP demonstrated comparable efficacy, higher completion rates and similar safety profiles to 9H[7–9]. Although not approved in Canada

for general use, rifapentine can be obtained under urgent public health need criteria.[10]

Shorter LTBI treatments are of particular interest in the Inuit Nunangat because all LTBI treatment in this region is given in person by directly observed therapy (DOT). This is especially relevant in light of the COVID-19 pandemic since minimising such interactions could reduce opportunities for COVID-19 transmission as well as conserving supplies of personal protective equipment.

Our group recently conducted an implementation study of 3HP for LTBI treatment in Iqaluit, Nunavut. We demonstrated the feasibility of implementing 3HP and found increased (non-statistically significant) completion rates compared with historical 9H data.[11]

While studies have found 3HP to be cost effective in American, Taiwanese and other settings,[12–16] no data on 3HP cost effectiveness in Canadian or Arctic settings exist. Unique challenges delivering healthcare in this remote region make generalisations from other settings difficult. An understanding of the cost effectiveness of 3HP in Nunavut would provide critical evidence to support decision-makers across the Inuit Nunangat in allocating healthcare resources efficiently.

The objective of this work was to assess the cost effectiveness of 3HP for the treatment of LTBI in comparison to 9H in Iqaluit, Nunavut, over a 30-year time horizon.

METHODS

Study setting

Iqaluit is the capital of Nunavut (7740 residents, 55.1% of whom identify as Inuit[17] and its largest community). Throughout most of the year, access is only by air with sea access possible during the brief summer. Between 2010 and 2016, 178 cases of active TB were reported in Iqaluit (median: 26 cases/year, range: 9–50 cases/year)[18] representing 36% of all cases in Nunavut.[18]

Testing and treatment for LTBI and active TB in Iqaluit are coordinated by Iqaluit Public Health. Testing is performed for contacts of active TB cases, employment screening (eg, healthcare workers) and in other high risk individuals.[19] All persons with a positive tuberculin skin test or interferon gamma release assay are assessed by a physician and may be offered LTBI treatment. Standard LTBI treatment has been of 9 months of twice weekly isoniazid via DOT.[19]

Markov model overview

A Markov model was developed reflecting local practices for LTBI treatment using TreeAge Pro (V.2019; TreeAge Software, Williamstown, Massachusetts, USA). This was used to assess the cost effectiveness of LTBI treatment with 3HP compared with 9H treatment. The primary outcome was the incremental cost-effectiveness ratio (ICER). The primary health outcome was quality-adjusted life years (QALYs). Costs were calculated in 2019 US dollars from the perspective of the Nunavut healthcare system. Secondary health outcomes included estimated TB cases and TB deaths averted using 3HP versus 9H. A simplified schematic of the model structure is shown in figures 1 and 2.

The target model population included all persons with LTBI who were offered treatment. A mean age of 25 years was assumed based on local historical data (Iqaluit LTBI programme data, 2010–2016, unpublished). A cohort of LTBI patients offered treatment during the first modelled year were followed over a 30-year time horizon to allow sufficient time for reactivation of LTBI. Markov cycle length was 1 year with half cycle correction applied. Future costs and effectiveness were discounted at a rate of 3%.[20 21]

In both 3HP and 9H arms, LTBI patients could initiate or decline treatment. Declining treatment resulted in a period of surveillance involving biannual clinical

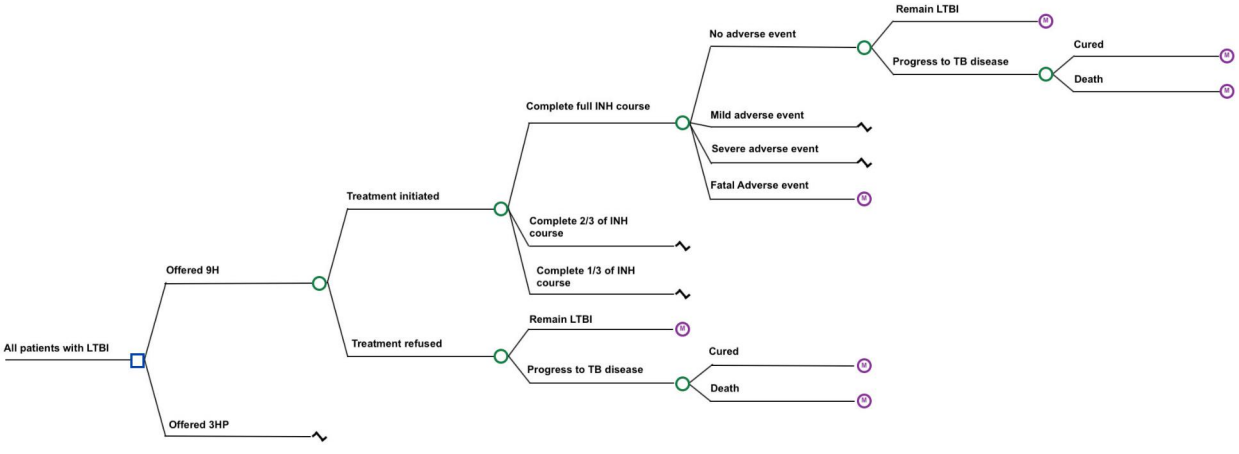

Figure 1 Simplified model decision structure. Two strategies were compared: treating LTBIwith 9H vs 3HP. Schematically these strategies are separated by a square representing a decisionnode. Green circles represent chance nodes where patients may experience one of severalpossible events shown on subsequent lines. The probabilities of developing each event are listedin Table 1. Jagged lines represent model structure omitted for simplicity. In all cases, thisomitted structure parallels that shown. The "M" symbol represents transition to the Markovportion of the model (shown in Figure 2). 9H = 9 months of twice weekly isoniazid; 3HP = 12weeks of once weekly rifapentine and isoniazid; LTBI = latent tuberculosis infection; TB =tuberculosis.

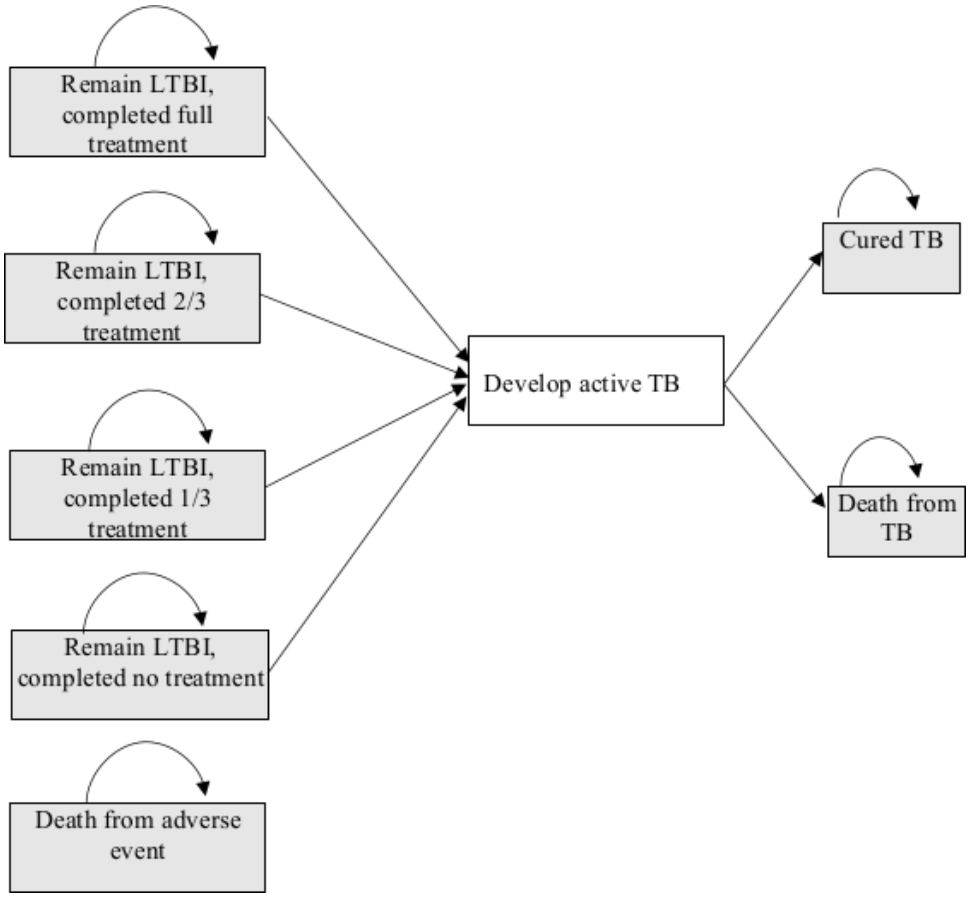

Figure 2 Schematic representation of Markov states. Patients enter this portion of the model in a Markov state (grey boxes) and may remain in that state (curved arrows) or, in some cases, transition to a different one (straight arrows). Patients in all states apart from cured TB disease and death have the possibility to develop active TB with the probability of doing so dependent on the duration of LTBI treatment completed. If active TB develops, it is either cured or results in death within that cycle. LTBI, latent tuberculosis infection; TB, tuberculosis.

assessments, chest X-rays and sputum testing for 2 years among those ≥13 years and quarterly clinical assessments without additional investigations among those <13 years.[19] If initiated, treatment could be partially completed (<1/3, 1/3 or 2/3 of complete treatment duration) or fully completed (12-week duration for 3HP, 9-month duration for 9H). Patients in both arms could experience adverse events (AEs) of varying severity (none, mild, severe and fatal), which might or might not result in stopping treatment. Active TB disease could occur at varying rates depending on LTBI treatment duration. All active TB was assumed to be diagnosed and treated, and patients could either be cured or die.

Key model assumptions

The rates of treatment initiation, fatal AEs and reduction in LTBI reactivation risk (based on a large non-inferiority trial[7]) were assumed to be equal between 3HP and 9H in base case analysis, but all variables were varied independently in sensitivity analyses. No fatal AEs related to 3HP have been reported among several randomised trials[22] yet long-term data comparable to 9H are not available; therefore, we assumed equal fatal toxicity risk between regimens, consistent with previous cost-effectiveness studies.[13 16 23]

The risk of AEs and the reduction in LTBI reactivation risk were assumed to be directly proportional to the treatment duration with no risk of AEs or reduction in reactivation risk among those completing less than one-third of the treatment.

Definitions

Treatment initiation was defined as taking ≥1 dose of medication. Mild AEs included grade 1–2 events and severe AEs included grade 3–4 events as defined by the Common Terminology Criteria for Adverse Events.[24]

Epidemiologic parameters

Model epidemiologic parameters are provided in table 1. Where possible, model parameters were based on historical data from Iqaluit and from a recent 3HP implementation study done in Iqaluit.[11 18]

Cost parameters

The cost parameters were derived from local unit costs with the exception of TB treatment cost, which was derived from total TB treatment costs in Iqaluit divided

Table 1 Epidemiologic parameter estimates

Parameter	Base case estimate	Univariable analysis range	Reference(s)
Initiation rate			Iqaluit LTBI program[11 28]
9H	0.79	0.72–0.80	
3HP	0.79[1]	0.72–0.80*	
Completion rates			
9H			Iqaluit LTBI programme
Probability of stopping isoniazid before 3 months among all those who initiated treatment	0.103	0.077–1.37	
Probability of stopping isoniazid at 3 months among all those who completed at least 3 months of treatment	0.088	0.063–0.122	
Probability of stopping isoniazid at 6 months among all those who completed at least 6 months of treatment	0.078	0.054–0.112	
Probability of completing 9 months of treatment among all persons who initiated treatment†	0.750		
3HP			11
Probability of stopping 3HP before 4 weeks among all those who initiated treatment	0.082	0.038–0.168	
Probability of stopping 3HP at 4 weeks among all those who completed at least 4 weeks of treatment	0.075	0.032–0.163	
Probability of stopping 3HP at 8 weeks among all those who completed at least 8 weeks of treatment	0.032	0.009–0.110	
Probability of completing 12 weeks of treatment among all persons who initiated treatment†	0.820		
Mild AE‡‡			7
9H	0.091	0.082–0.100	
3HP	0.077	0.069–0.085	
Severe AEs‡‡			7
9H	0.065	0.058–0.073	
3HP	0.057	0.050–0.064	
Fatal AEs‡			6 31
9H	0.00014	0.00004–0.00057	
3HP	0.00014[1]	0.00004–0.00057[1]	
Risk of reactivation of LTBI			16 32 33
First 2 years	0.025	0.01–0.05	
Subsequent years	0.001	0–0.0016	
Reduction in risk of TB disease‡			6 34
9H	0.93	–	
3HP	0.93[1]	–	
Risk of death following TB disease diagnosis	0.082	0.070–0.094	35–43
Health Utilities (QALYs)			
LTBI without treatment	1	–	Assumed
LTBI treatment	1	0.99–1	44
Mild AE	1	0.99–1	45
Severe AE	0.75	0.65–0.85	23
TB disease	0.88	0.86–0.90	44
Death	0	–	Assumed

Iqaluit LTBI programme: retrospective data from the Iqaluit LTBI programme, 2010–2016, unpublished.
*Assumed identical values for 9H and 3HP in base case analysis.
†Overall completion rates among initiators are given for reference. Only the component probabilities provide were used in the model.
‡Values for partially completed regimens were interpolated assuming a linear relationship between duration of treatment and parameter values.
AEs, adverse events; 9H, 9 months of twice weekly isoniazid; 3HP, once weekly rifapentine and isoniazid for 12 weeks; LTBI, latent tuberculosis infection; QALYs, quality-adjusted life years; TB, tuberculosis.

Table 2 Cost parameter estimates. Costs are in 2019 US dollars

Parameter	Base case estimate	Univariable analysis range	Reference(s)
Complete 9H treatment	$806	$489–$1207	IPH, NMH[25]
Drug costs	$5		
DOT costs	$500		
Other clinician costs	$173		
Chest X-ray	$55		
Sputum testing	$64		
Liver function testing	$9		
Partial isoniazid treatment			
3 months	$388	$271–$543	IPH, NMH[25]
6 months	$597	$389–$874	IPH, NMH[25]
Complete 3HP treatment	$383	$296–$492	IPH, NMH[25]
Drug costs	$87		
DOT costs	$77		
Other clinician costs	$96		
Chest X-ray	$55		
Sputum testing	$64		
Liver function testing	$5		
Partial isoniazid+rifapentine treatment			
4 weeks	$126	$103–$159	IPH, NMH[25]
8 weeks	$194	$151–$253	IPH, NMH[25]
Mild AE	$13	$0–$197	IPH[13]
Nursing costs	$13		
Severe AE	$2584	$1379–$6614	IPH, NMH[13 25]
Hospitalisation in Iqaluit×1.2 days*	$2411		
Outpatient clinician assessment	$156		
Laboratory monitoring	$17		
Fatal AEs	$65 737	$41 365–$75 725	IPH[25 46]
Hospitalisation in Iqaluit×7 days	$14 059		
Medical evacuation	$19 951		
Hospitalisation in Ottawa x 7 days	$7366		
Intensive care unit in Ottawa×7 days	$24 359		
Cured TB disease	$1517	$1214–$28 841	IPH[25]
Fatal TB disease	$66 495	$41 365–$76 635	IPH[25 46]
TB treatment costs×6 months	$759		
Hospitalisation in Iqaluit×7 days	$14 059		
Medical evacuation	$19 952		
Hospitalisation in Ottawa×7 days	$7366		
Intensive care unit in Ottawa×7 days	$24 359		
Surveillance for those <13 years old	$54	$50–$65	IPH, NMH
Nursing costs	$54		
Surveillance for those ≥13 years old	$531	$431–$638	IPH, NMH
Nursing costs	$54		
Chest X-ray×4	$220		
Sputum testing×4	$257		

IPH: data from Iqaluit Public Health, 2019, unpublished.
NMH: data from Nunavut Ministry of Health, 2019, unpublished.
*The number of days of hospitalisation was used assuming that, as in Sterling *et al*, 17% of these patients would have a grade 4 AE and all those with a grade 4 AE would require 7 days of hospitalisation.
AEs, adverse events; DOT, directly observed therapy; 9H, 9 months of twice weekly isoniazid; 3HP, once weekly rifapentine and isoniazid for 12 weeks.

by the number of persons treated (table 2). Estimates of personnel time were determined by direct onsite observation of TB activities supplemented by interviews with local personnel. Local unit costs of medications, consumables and salaries were obtained from Iqaluit Public Health and the Government of Nunavut Department of Health. Local unit costs of diagnostics, hospitalisation and medical transport were obtained from published literature.[25] All costs were adjusted to 2019 Canadian dollars using the Canadian Consumer Price Index,[26] then converted to US dollars using the average 2019 exchange rate.[27]

Sensitivity and scenario analyses

One-way (univariable) sensitivity analyses were conducted across all model parameters, time horizon (10–50 years) and discounting rate (0%–5%). Probabilistic sensitivity analysis was also performed by specifying underlying distributions for model parameters and using Monte Carlo simulation with 10 000 iterations to generate 95% uncertainty ranges (95% UR) around model outputs. Probability distributions for model parameters are provided in online supplemental e-Appendix. Finally, scenario analyses were performed to more comprehensively explore the impact of select model parameters. Scenario analyses included variation in the initiation and overall completion rates of 3HP±10% versus 9 hours, increasing risk of 3HP severe AEs to twice that of 9H and varying annual LTBI reactivation from 0.1% to 10% for the first 2 years. The impact on cost of self-administration of both regimens was also assessed.

Budget impact analysis

A budget impact analysis was performed over 1-year, 2-year and 5-year horizons estimating the total difference in healthcare cost of 3HP compared with 9H. Average per patient incremental costs for the relevant year(s) was determined from the model and multiplied by the average annual number of patients initiating LTBI treatment in Iqaluit between 2010 and 2016, which was 69 (Iqaluit LTBI programme data, 2010–2016, unpublished).

Patient and public involvement

Patient input informed the development of the research question by expressing a desire for implementation of a feasibility effective but short treatment regimen for LTBI. Patients were not directly involved in the design or conduct of the study. Key local stakeholders have been informed of the study results through a series of in-person and teleconferenced meetings. A plain language summary of the study will be made available to the public via the Taima TB research group website.

RESULTS

3HP dominated 9H with cost savings ($628 vs $924 per person) and slight improvement in health outcome (20.14 vs 20.13 QALYs per person) (table 3). This resulted in a negative ICER.

Table 3 Base case cost-effectiveness model outcomes

	9H	3HP
Clinical outcomes		
Overall effectiveness (QALYs)	20.13	20.14
TB cases per 1000 LTBI cases	30.16	27.89
TB deaths per 1000 LTBI cases	2.48	2.29
Cost outcomes (2019 US$)		
Total cost	$924	$628
Costs of LTBI treatment	$535	$260
Costs of AEs	$116	$108
Costs of TB disease treatment	$182	$168
Surveillance costs	$92	$92

Costs are in 2019 US dollars.
AEs, adverse events; 9H, 9 months of twice weekly isoniazid; 3HP, once weekly rifapentine and isoniazid for 12 weeks; LTBI, latent tuberculosis infection; QALY, quality-adjusted life years; TB, tuberculosis.

Cost savings were driven by fewer visits required to deliver 3HP (12 doses) compared with 9H (78 doses). Cost savings also resulted from fewer AEs with 3HP and fewer TB cases (27.89 vs 30.16 per 1000 LTBI cases) due to its higher completion rate (table 3). The improvement in health outcomes was driven primarily by higher completion rates for 3HP, resulting in fewer TB cases (noted above) and TB deaths (2.29 vs 2.48 per 1000 LTBI) in the 3HP arm.

In budget impact analysis, 3HP resulted in cumulative savings of $19 888 over 1 year, $40 122 over 2 years and $100 904 over 5 years compared with 9 hours, assuming a constant annual rate of LTBI treatment initiation.

Sensitivity analyses

In one-way sensitivity analyses, the model was most sensitive to variables related to 3HP completion and initiation and fatal AEs during 3HP treatment. These were the only variables with the potential to result in worsened health outcomes in the 3HP arm compared with 9H (online supplemental e-appendix, e-figures 1 and 2). 3HP remained dominant despite varying discounting rate (0%–5% per year), time horizon (10–50 years) and all other variables (online supplemental e-appendix, e-tables 3 and 4).

In the probabilistic sensitivity analysis, the probability of 3HP being dominant over 9H was 94.1% (figure 3). The median cost per LTBI case was $614 (95% UR: $487–$1005) for 3HP versus $888 (95% UR: $662–$1335) for 9H and the median QALYs per LTBI case were 20.13 (20.10–20.16) for 3HP versus 20.13 (20.09–20.15) for 9H. The probability of 3HP being less costly than 9H was 99.9% and the probability of 3HP being more effective than 9H was 94.2%.

Scenario analyses

When 3HP initiation and completion rates were varied ±10%, 3HP remained cost saving (online supplemental

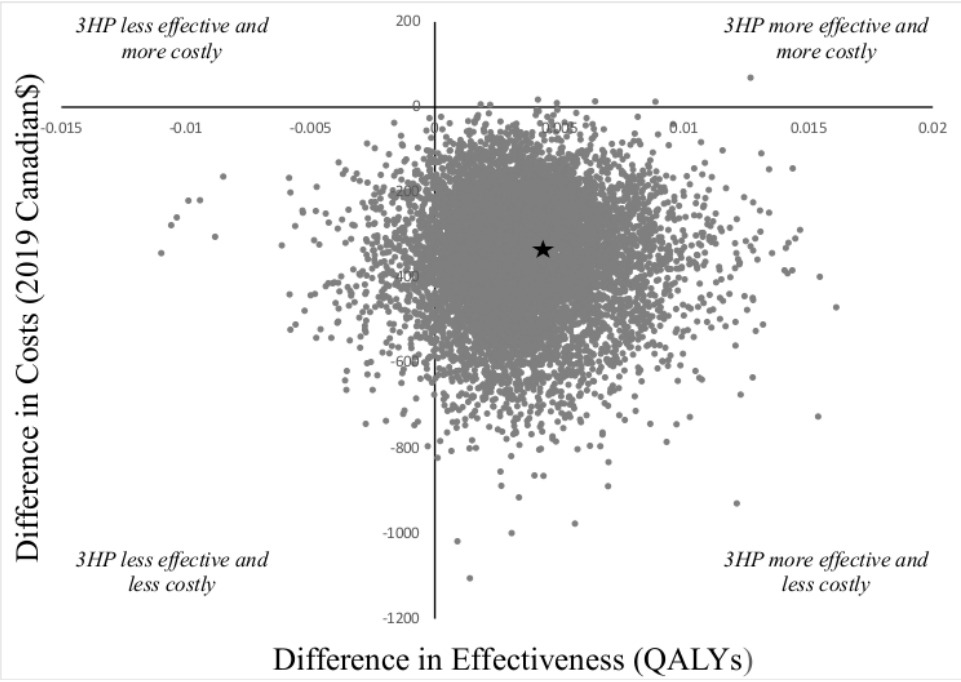

Figure 3 Cost-effectiveness plane showing the differences in costs and QALYs of using 3HP compared with using 9H from 10 000 simulations. The star represents the base case scenario. 3HP, once weekly rifapentine and isoniazid for 12 weeks; 9H, 9 months of twice weekly isoniazid; QALYs, quality-adjusted life years.

e-appendix, e-table 5a), but 3HP was no longer dominant over 9H when the 3HP initiation rate was <73.4% (vs 79.0% for 9H) and when the 3HP completion rate was <74.4% (vs 75% for 9H and 82.0% in the base case analysis) due to worsened health outcome (figure 4A). If the severe AE rate of 3HP increased to >7.4% (5.6% in base case analysis), 3HP also resulted in worsened health outcome compared with 9H (figure 4B) but remained cost saving (online supplemental e-appendix, e-table 5b). 3HP remained dominant over 9H across a broad range of LTBI reactivation rates (figure 4b and c; online supplemental e-appendix, e-tables 5b and c). If both 3HP and 9H were self-administered, 3HP remained dominant (online supplemental e-appendix, e-table 6). Cost savings were reduced, but 9H cost remained above 3HP because higher medication cost was offset by additional clinical visits during the longer 9H regimen and slightly higher costs from more active TB cases and AEs in the 9H arm.

DISCUSSION

Using a Markov model of LTBI treatment in a Canadian Arctic setting, our study suggests that the 3HP regimen will be superior to 9H (both cost saving and slightly more effective) across a range of assumptions. Both TB cases and TB deaths were projected to be lower with the use of this regimen.

The finding of cost savings with the 3HP regimen was very robust across a broad range of sensitivity and scenario analyses. As such, it is highly likely that implementation of 3HP would result in reduced costs for the Iqaluit TB programme and likely other similar settings as well. In budget impact analysis, the total savings were estimated at over $19 000 annually assuming that LTBI diagnosis and treatment continue at a similar pace. The primary driver of 3HP cost savings was the lower number of DOT visits due to shorter treatment duration. Additional savings accrued from fewer AEs and fewer active TB cases in 3HP arm meaning that modest cost savings were maintained even when both regimens were self-administered.

While 3HP results in a slightly improved health outcome compared with 9H in most sensitivity analyses, extreme values of 3 key parameters (3HP initiation <73.4%, 3HP completion <74.4% and 3HP fatal AE rate >0.00042) resulted in 3HP producing a worsened health outcome compared with 9H. A substantial decrease in 3HP initiation compared with 9H was modelled to evaluate the robustness of our findings but is unlikely to occur: the 3HP initiation rate was similar to the historical rate during a recent community rollout in Nunavut (80% with 3HP vs 79% historically)[11] and a recent study in an urban setting found stable initiation rates following the introduction of 3HP (78% with 3HP vs 79% historically).[28]

Another key influence on the relative effectiveness of the two regimens was the 3HP completion rate. When 3HP completion dropped below 74.4% (vs 82% in base case), 3HP resulted in a worsened health outcome compared with 9H. Previous studies have demonstrated consistently higher completion for 3HP than 9H suggesting such a scenario is unlikely.[7 8] However, unlike many settings, 9H is delivered via DOT in Iqaluit resulting in higher

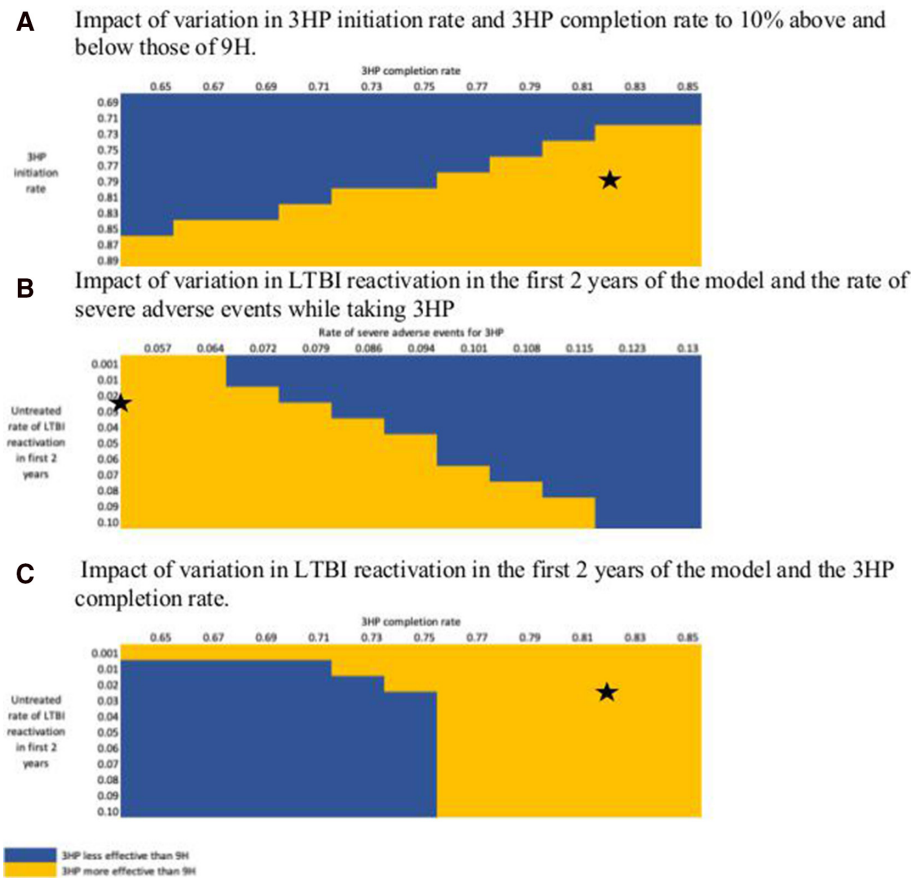

Figure 4 Influence on the relative effectiveness of 3HP versus 9H of variation in a variety of parameters to extreme values. Blue areas indicate that 3HP is less effective than 9H, while orange areas indicate that 3HP is more effective than 9H. The stars represent the values in the base case. (A) Impact of variation in 3HP initiation rate and 3HP completion rate to 10% above and below those of 9H. (B) Impact of variation in LTBI reactivation in the first 2 years of the model and the rate of severe adverse events while taking 3HP. (C) Impact of variation in LTBI reactivation in the first 2 years of the model and the 3HP completion rate. 3HP, once weekly rifapentine and isoniazid for 12 weeks; 9H, 9 months of twice weekly isoniazid; LTBI, latent tuberculosis infection.

9H completion rates compared with other settings.[18] Despite this, within the recent 3HP implementation trial in Iqaluit, there was a non-statistically significant trend to improved completion among those taking 3HP versus historical rates (82% vs 73%).[11] Furthermore, even if 3HP completion was modestly overestimated in our model, 3HP would remain cost saving.

As mentioned, given the absence of reported fatal AEs associated with 3HP,[22] the assumption of equal risk of fatal toxicity between 3HP and 9H is likely quite conservative. In sensitivity analysis, only when risk of fatal AEs associated with 3HP was 3.5 times higher than 9H (0.00042 vs 0.00012) was 3HP associated with a worse health outcome compared with 9H. Such an increase seems unlikely.

The most recent Canadian Tuberculosis Standards note concern regarding potential AEs associated with 3HP.[29] In scenario analysis, the rate of severe AEs related to 3HP would need to rise to 7.4% for 3HP to be associated with a worse health outcome than 9H. This is substantially higher than the 5.6% observed in a large clinical trial of 3HP.[7]

While the current study focused on 9H and 3HP, several other LTBI treatment regimens are used in other settings.[29] This includes rifampin given daily for 4 months (4R), which has recently been shown to be non-inferior to 9 months of daily isoniazid in a large randomised controlled trial.[30] 4R was not considered in the current study since all LTBI treatment in Nunavut is given by DOT and use of 4R would require an increase in the number of DOT visits from 78 doses with the current standard of twice weekly isoniazid to 120 doses with 4R. This was not felt to be feasible given the limited resources of the local TB programme.

This study has a number of strengths. First, it is the first study of cost effectiveness of 3HP in Canada and the first in an Arctic region. This regimen has been of particular interest since the onset of the COVID-19 pandemic since it requires the fewest doses of any currently recommended LTBI treatment.[29] Because all LTBI treatment in Nunavut is given in person by DOT, reducing LTBI treatment doses minimises opportunities for viral transmission and conserves personal protective equipment. Second,

local data were used to obtain most key costs and epidemiologic parameters.

Study limitations include an inability to account for TB transmission, which would have greatly increased model complexity. However, including transmission in the model would likely have favoured 3HP since this strategy resulted in fewer active TB cases and thus 3HP would be expected to remain the dominant strategy. Second, societal costs, including costs borne by patients, were not included. Inclusion would again likely favour 3HP given its shorter duration and lower burden of AEs compared with 9H. Third, the costs associated with the implementation and scale-up of 3HP such as additional staff training were not included. Fourth, we did not include the probability of death from causes other than TB and treatment-related AEs in our model. However, this factor would not differ between the two treatment arms in our study and thus would not be expected to have an important impact on incremental cost or effectiveness. Finally, reinfection with TB was not modelled but would be unlikely to substantially change the relative standing of 3HP and 9H since reinfection risk is not related to previous treatment regimen.

CONCLUSION

The findings of the present study suggest that in a remote Canadian arctic setting, 3HP is likely to offer cost savings and slightly improved health outcomes compared with 9 hour driven by higher anticipated completion rates. This would support the implementation of 3HP as standard therapy for LTBI treatment in Nunavut and other similar settings.

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Contributors GA, MP, SF and AZ conceived the study. The study was designed by AZ, CP and GA. SF and EK collected data. Data analysis was performed by CP with assistance from AZ. CP, AZ and GA interpreted the data with assistance from KS, RM, SM, MP, SF, EK and YH. CP drafted the initial manuscript, which was revised and approved by all authors. CP takes responsibility for the integrity of the data and accuracy of the data analysis.

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