Cost-effectiveness of LTBI treatment for TB contacts in British Columbia
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of latent tuberculosis infection treatment for hypothetical cohorts of tuberculosis contacts. The authors concluded that the current Canadian practice of treatment for contacts with a tuberculin skin test size of 5mm or more was cost-effective. However, a customised approach, which excluded low-risk groups from screening and provided treatment to high-risk groups without screening, was more economically attractive. The study was based on valid methodology, which should ensure the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of latent tuberculosis infection (LTBI) treatment for hypothetical cohorts of tuberculosis contacts defined by tuberculin skin test size and several known risk factors for progression to active tuberculosis.

Interventions
The interventions were no screening, which was not screening contacts and not offering preventive therapy; test-and-treat, which was testing contacts and treating those with a positive test, and treat-all, which was offering preventive therapy to all contacts in the subgroup without testing. Test-and-treat was compared with no screening and treat-all was compared with test-and-treat. Tuberculin skin test was positive when reaction was 5mm or more. Treatment was the standard, nine-month course of isoniazid.

These three strategies were analysed in different subgroups of individuals, such as household versus non-household contacts, prior history of Bacillus Calmette-Guerin (BCG) vaccination or not, age group (under 10 years versus older), and ethnicity (foreign-born, aboriginal, and Canadian-born non-aboriginal). The optimal strategy was determined for each of these subgroups and compared with the current strategy in the authors’ setting (test-and-treat) and with no screening.

Location/setting
Canada/community and primary care.

Methods
Analytical approach:
The analysis was based on a Markov model with a six-year time horizon. The authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical data came from a selection of known, relevant, published sources. Data on occurrence of tuberculosis in contacts (for each subgroup) were obtained from a large population-based provincial registry of tuberculosis contacts in British Columbia. The database covered a 12-year period (1990 to 2001). A proportional hazards (Cox) regression model was built to estimate the multivariate, adjusted hazard ratio of covariates on the risk of tuberculosis development. Few details on the other sources of data were reported. The key clinical endpoint was the risk of tuberculosis transmission.
Monetary benefit and utility valuations:
The utility valuations were derived from published sources. The key source used the Short Form (SF-6D) questionnaire. This questionnaire was given to 119 patients with LTBI, and 114 patients with active tuberculosis recruited through the British Columbia Centre for Disease Control (BCCDC) tuberculosis clinics.

Measure of benefit:
Quality-adjusted life-years (QALYs) and the number of active tuberculosis cases prevented were the summary benefit measures. Health outcomes were discounted at 3% per annum.

Cost data:
The economic analysis included the costs of physician visits, LTBI treatment, hospitalisations, diagnosis and management of contacts with active tuberculosis, contact investigations, and management of tuberculosis contacts with either LTBI or active tuberculosis. The unit costs and quantities were derived from the BCCDC and the British Columbian Medical Association 2004 Medical Services Plan payment schedule for medical practitioners. The hospital costs were obtained from a large tertiary referral hospital in Vancouver. All costs were discounted at an annual rate of 3%. The price year was 2003 and costs were in Canadian dollars (CAD).

Analysis of uncertainty:
A probabilistic second-order Monte Carlo simulation of 1,000 trials was undertaken using parameter distributions that were estimated from the literature; cost-effectiveness acceptability curves were generated. A third-party payer’s perspective that excluded the indirect costs was considered. A deterministic one-way sensitivity analysis was carried out on selected inputs, such as the time horizon, utility valuations (based on the Health Utilities Index, HUI-3, questionnaire), initial cohort age, discount rate, and compliance with LTBI therapy.

Results
Depending on the subgroups of contacts, the costs ranged from CAD 31 to CAD 5,586 with no screening, from CAD 44 to CAD 4,289 with test-and-treat, and from CAD 137 to CAD 4,259 with treat-all. The QALYs ranged from 4.5423 to 4.6334 with no screening, from 4.5665 to 4.6337 with test-and-treat, and from 4.5665 to 4.6336 with treat-all. The active tuberculosis cases ranged from 0.0029 to 0.5238 with no screening, from 0.0019 to 0.3964 with test-and-treat, and from 0.0019 to 0.3885 with treat-all.

When considering all contacts, the test-and-treat strategy dominated no screening, which means it was more effective and cheaper. Treat-all was not cost-effective in comparison with test-and-treat, which was dominant in terms of QALYs and the incremental cost per active tuberculosis case was CAD 94,552.

Test-and-treat was cost-effective (at a willingness-to-pay of CAD 50,000 per QALY) in most of the subgroups (approximately 60% of cases). The no screening option was the best option for the non-aboriginal Canadian-born, and for the foreign-born individuals, when both were non-household contacts older than 10 years. For the non-aboriginal Canadian-born household contacts aged under 10 years and without BCG vaccination, the treat-all intervention was the best option. Similar results were observed when using active tuberculosis cases avoided as the summary benefit measure.

The optimal policy was: to test and treat all contacts, except the non-household, non-aboriginal contacts aged over 10 years, for whom no screening or treatment was required, and to treat all household contacts aged under 10 years without screening.

The probabilistic sensitivity analysis showed that the current test-and treat policy in Canada was dominant in 74% of iterations with respect to no screening or treat-all. The optimal policy (that provided the most cost-effective alternative for each subgroup) had more than 90% chance of being the most cost-effective strategy at a threshold of CAD 50,000 per QALY. The sensitivity analysis showed that these base-case findings were robust to changes in assumptions. The most influential model inputs were the utility valuations for LTBI therapy.

Authors' conclusions
The authors concluded that the current Canadian practice of LTBI treatment for tuberculosis contacts with a tuberculin
skin test size of 5mm or more was cost-effective. However, a customised approach, which excluded low-risk groups from screening and provided treatment to high-risk groups without screening was more economically attractive.

**CRD commentary**

**Interventions:**
The selection of the comparators was appropriate as the available strategies for the management of tuberculosis contacts were examined, including the current policy implemented in Canada. These policies are also likely to be relevant for other health care settings.

**Effectiveness/benefits:**
The selective approach for sources was appropriate as country-specific evidence was used. A large database should provide sufficient data on long-term epidemiological estimates. Little information on the other sources of data was provided, which limits the possibility of making an objective judgement of the internal validity of the clinical data, but this issue was extensively investigated in the sensitivity analyses. The benefit measures were appropriate and of some importance for decision makers. In particular, QALYs are a generalisable benefit measure and capture the impact of the disease on patients’ health.

**Costs:**
The selection of a societal perspective suggests the inclusion of indirect costs, which were excluded in the third-party payer analysis, but the assessment of these costs was not described. The costs were often presented as macro-categories and were derived from a country-specific database. Some of the key assumptions made in the analysis were clearly described, and variations in cost estimates were considered in the sensitivity analysis. Other details of the analysis, such as the data sources, price year, use of discounting, and probability distributions were reported.

**Analysis and results:**
The costs and benefits were appropriately analysed using an incremental approach, which allowed the identification of the most economically attractive policy. All outcomes of the model were clearly presented. The analysis considered various patient populations, ensuring that the findings were relevant to different groups of individuals. The details of the decision model and key assumptions were provided. The issue of uncertainty was satisfactorily addressed using various approaches, which investigated different areas of variability.

**Concluding remarks:**
The study was based on valid methodology, which should have ensured the validity of the authors’ conclusions.

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