Priorities for screening and treatment of latent tuberculosis infection in the United States
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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 assessed the cost-effectiveness of screening for latent tuberculosis infection in different risk groups, using the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs). The authors concluded that guidelines should prioritise the screening of close contacts, those infected with HIV, and those born abroad; the IGRA was more cost-effective than the TST. The cost-effectiveness methods were robust, but the sources were not fully described. The uncertainty was investigated and the conclusions seem valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of screening for latent tuberculosis infection in different risk groups, using the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs).

Interventions
The two options were the TST or IGRAs. No screening was the background comparator.

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon, for four broad risk groups: patients at high risk of reactivation (close contacts and those living with HIV infection), people born abroad (recent immigrants or those living in the USA for more than five years), vulnerable people (homeless, injection drug users, and former prisoners), and people with chronic medical conditions, such as diabetes or end-stage renal disease. The authors did not explicitly state the perspective.

Effectiveness data:
The clinical inputs were from a selection of relevant studies. Some epidemiological data were from the Centers for Disease Control and Prevention (CDC) and the National Health and Nutrition Examination Survey. The accuracy of the screening tests was a key input for the model. Some algorithms were used to estimate the risk of tuberculosis reactivation, as no US prospective observational data were found.

Monetary benefit and utility valuations:
The utility values were published estimates, collected using the Short Form (SF-36) health survey and the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of screening (tests, visits, and chest radiographs), isoniazid treatment (drug, visits, and management of adverse events), and the treatment of active tuberculosis (including death costs). The health
care costs not related to latent tuberculosis infection, by risk group, were from the Medical Expenditure Panel Survey and published reports. Some unit costs and resource quantities were given. The costs were in US dollars ($) and were discounted at an annual rate of 3%. The price year was 2011.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on selected inputs, using published and assumed ranges of values. The TST characteristics and IGRA costs were varied simultaneously.

Results
Compared with no screening, TST screening led to a gain of 0.00 to 0.13 quality-adjusted life-months at an incremental cost ranging from $50 to $140, depending on the risk group.

Compared with the TST, IGRA screening led to a gain of 0.00 to 0.008 quality-adjusted life-months at an incremental cost ranging from -$10 (a saving) to $20, depending on the risk group.

In patients at high risk of reactivation, the incremental cost per QALY gained was less than $50,000 with the TST over no screening, and with the IGRA over the TST.

In people born abroad, the IGRA dominated the TST, as the IGRA was more effective and cheaper. This was due to a lower loss to follow-up and better specificity. The incremental cost per QALY for the IGRA over no screening was less than $100,000, for all subgroups, up to the age of 45 years.

In vulnerable populations, the incremental cost per QALY gained with the TST over no screening was $95,000 for the homeless, $104,600 for injection drug users, and $147,600 for former prisoners. For the IGRA over the TST it was $194,300 for the homeless and over $200,000 for injection drug users and former prisoners.

In patients with chronic conditions, neither screening was cost-effective; the cost-utility ratio for the TST over no screening was $129,000 for patients taking immunosuppressive medications.

The sensitivity analysis showed that the cost-utility estimates were sensitive to variations in the rate of reactivation tuberculosis. Assuming that all patients returned for their TST results, the TST dominated the IGRA in adults with close contacts. Variations in the patient's age and the quality-of-life adjustments also altered the findings.

Authors' conclusions
The authors concluded that guidelines for screening for latent tuberculosis infection should prioritise the screening of close contacts, those infected with HIV, and those born abroad, regardless of the time spent living in the USA. The IGRA was more cost-effective than the TST, for these groups.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the authors considered guidelines that recommended the TST or IGRAs for groups of people at risk, as defined by the CDC.

Effectiveness/benefits:
Little information was given on the sources for the clinical inputs. Most of the epidemiological data were from well known US studies or databases, but the details for the sources of other key data, such as screening accuracy, were not reported. The authors acknowledged the need for assumptions, given a lack of valid data for some model inputs. Sensitivity analysis was conducted on the most uncertain parameters. QALYs were a valid benefit measure and they capture the impact of the disease on the patients' health. Appropriate instruments were used to elicit the preferences for health conditions, but the data sources were not described and it was unclear whose preferences were assessed and their relevance for the patient population.

Costs:
The authors did not state the perspective, but those costs relevant to the health care system appear to have been considered. They stated that the costs of expanding screening programmes were not included as they assumed that the
screening populations were already identified and managed by existing resources. Limited unit costs and resource quantities were provided, reducing the transparency of the analysis. Most of the economic data were from published sources, but their methods were not presented. From the references, it seems that most of them were official US sources, such as Medicare and the US Department of Labor. Reflation exercises will be possible as the price year was clearly stated. The impact of variations in selected economic inputs was investigated.

**Analysis and results:**
The results were extensively presented for each patient group. An incremental approach was used to synthesise the costs and benefits of the alternative strategies. A deterministic approach was used to investigate the uncertainty, and this focused on selected inputs. The authors acknowledged some limitations of their analysis, which were mainly due to the lack of good US data for tuberculosis reactivation and the need for assumptions. The analysis should be considered to be specific to the USA and the results will be difficult to transfer to other countries.

**Concluding remarks:**
The cost-effectiveness methods were robust, but the data sources were not fully described. The uncertainty was investigated and the authors’ conclusions appear to be valid.

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