



Tuberculosis

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REVIEW

A systematic review of economic models used to assess the cost-effectiveness of strategies for identifying latent tuberculosis in high-risk groups



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ARTICLE INFO

Article history:

Received 11 December 2015

Received in revised form

30 March 2016

Accepted 12 April 2016

Keywords:

Systematic review

Latent tuberculosis

Decision-analytical modelling

Cost-effectiveness

SUMMARY

Background: Timely diagnosis and treatment of latent tuberculosis infection (LTBI) through screening remains a key public health priority. Although globally it is recommended to screen people at high risk of developing TB, the economic evidence underpinning these recommendations is limited. This review critically appraised studies that had used a decision-analytical modelling framework to estimate the cost-effectiveness of interferon gamma release assays (IGRAs) compared to tuberculin skin test (TST) for detecting LTBI in high risk populations.

Methods: A comprehensive search of MEDLINE, EMBASE, NHS-EED was undertaken from 2009 up to June 2015. Studies were screened and extracted by independent reviewers. The study quality was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) and the Philips' checklist, respectively. A narrative synthesis of the included studies was undertaken.

Results: Ten studies were included in this review. Two economic evaluations were conducted in a child population, six in an immunocompromised population and two in a recently arrived population from a country with a high incidence of TB. Most studies ($n = 7$) used a decision tree structure with Markov nodes. In general, all models were clearly described in terms of reporting quality, but were subject to limitations to structure and model inputs. Models have not elaborated on their setting or the perspective of the studies was not consistent with their analyses. Other concerns were related to derivation of prevalence, test accuracy and transition probabilities.

Conclusion: Current methods available highlight limitations in the clinical effectiveness literature, model structures and assumptions, which impact on the robustness of the cost-effectiveness results. These models available are useful, but limited on the information that can be used to inform on future cost-effectiveness analysis. Until consideration is given on deriving the performance of tests used to identify LTBI that progresses to active TB, and the development of more comprehensive models, the economic benefit of LTBI testing with TST/IGRAs in high risk populations will remain unanswered.

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1. Background

Diagnosis and treatment of latent Tuberculosis infection (LTBI) through screening remains a key public health priority in the elimination of tuberculosis. For over a century, the tuberculin skin test (TST) has been used to diagnose LTBI, despite its many limitations. These include being neither very sensitive, due to anergy in an immunocompromised population, nor specific, due to cross-reactivity in people who are Bacilli Calmette-Guérin (BCG) vaccinated and those who are infected with non-tubercular mycobacteria (NTM) [1]. Furthermore, TST requires people to return to have their results read, and there is the possibility of error when measuring the size of the induration of the skin reaction. This has led to the development of new *in vitro* interferon-gamma release assays (IGRAs) aimed at improving the diagnosis for LTBI.

Currently, two IGRAs are commercially available for the diagnosis of LTBI, QuantiFERON Gold In-tube (QFT-GIT) (Cellestis Ltd., Carnegie, Australia) and T-SPOT.TB (Oxford Immunotec Ltd, Oxford, UK). IGRAs do not boost responses due to repeated testing, and people are not required to make a second visit to have the results read [2]. These tests offer alternatives for the diagnosis of LTBI, but are more expensive. In the UK, current guidelines recommend the use of IGRAs and/or TST for the diagnosis of LTBI in high risk populations which include children, people who are immunocompromised or at risk of immunosuppression and people from countries with a high incidence of TB [3]. The health economic modelling which underpin these recommendations are based on ‘what-if’ analyses/scenarios rather than empirical screening evidence [4] and this offers little insight on which diagnostic strategy is the most cost-effective.

Decision makers, such as the National Institute for Health and Care Excellence (NICE), often rely on mathematical modelling to aid in decision making processes, as they are constantly faced with questions on what interventions should be funded. The purpose of modelling is to structure evidence on clinical and economic outcomes in a form that can be used to inform decisions on clinical practices and allocation of resources in order to achieve maximum benefits for health care [5]. Since the introduction of IGRAs, many

studies have estimated the cost-effectiveness of various strategies for the diagnosis of LTBI using economic modelling in a decision analytical context. A previous clinical guideline [3] which included a systematic review highlighted that no published studies were identified in these high risk groups. Hence, in this review, the aim is to identify from recent literature the suitability of existing cost-effectiveness models that compared different diagnostic strategies for identifying LTBI in children, immunocompromised or at risk of immunosuppression and people from countries with a high incidence of TB.

2. Methods

2.1. Study eligibility criteria

Citations retrieved were screened by two reviewers (PA and AT) and included in the review if they met the following criteria: Children (immunocompetent), people who are immunocompromised or at risk from immunosuppression (e.g. transplant recipients or HIV) and recent arrivals from countries with a high incidence of TB (≥ 40 cases per 100,000), and comprising a formal economic evaluation involving direct comparison between IGRAs (QFT-G, QFT-GIT or T-SPOT.TB) and TST, and included a decision analytic model.

2.2. Search strategy

A search of the literature for published economic evaluations was performed for the purpose of identifying the suitability of existing cost-effectiveness models and their model design.

The cost-effectiveness search was developed and conducted as part of a wider systematic review that aimed to compare both the clinical effectiveness and cost-effectiveness of screening tests (IGRAs and TST) for LTBI in high risk groups [6]. Electronic databases were searched, applying the search strategy to the following databases: MEDLINE, MEDLINE In-Process Citations and Daily Update, Embase, NHS Economic Evaluation Database (NHS EED), Health Economics Evaluation Database (HEED), Science Citation Index, Research Papers in Economics (RePEC) and Cost-effectiveness

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