
Interferon-gamma release assays and TB screening in high-income countries: a cost-effectiveness analysis

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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.

Health technology

The study examined several screening strategies for tuberculosis (TB). Specifically, chest radiograph screening (CXR), tuberculin skin test (TST), an interferon-gamma release assay (IGRA), namely QuantiFERON-TB Gold (QFT), and a sequential strategy consisting of TST followed by QFT if TST-positive. A strategy of no screening was also considered as comparator. QFT was chosen as the IGRA given its lower costs in comparison with the other ex vivo test commercially available (T-Spot). All strategies were described in detail. For each strategy, a different patient management was assumed on the basis of the test results.

Type of intervention

Screening.

Economic study type

Cost-effectiveness analysis

Study population

The study population comprised three hypothetical cohorts of individuals from countries with low, intermediate or high prevalence of TB. Individuals were also grouped depending on the bacille Calmette-Guerin (BCG) vaccination status (none, infant, older). The three different groups of individuals finally considered were immigrants, close contacts and casual contacts.

Setting

The setting appears to have been primary care, although this was not explicitly stated. The economic study was carried out in Canada.

Dates to which data relate

The clinical data were derived from studies published between 1960 and 2006. The economic data were obtained from studies published between 1995 and 2006. The price year was 2004.

Modelling

A decision model was constructed to simulate the impact of the alternative screening strategies in different patient populations. The time horizon of the model was 20 years. The structure of the decision model was not reported but health states and transition patterns were described. Typical TB health states were considered: non-infected, recent latent TB infection (LTBI), long-standing LTBI and active TB disease.

Study designs and other criteria for inclusion in the review

The clinical data used in the analysis were:

the incidence of smear-positive TB,

the annual risk of infection in country of origin,

the prevalence of LTBI,

the prevalence of active TB,

the prevalence of underlying multidrug resistance,

the prevalence of underlying isoniazid resistance,

the sensitivity and specificity of the different screening tests, and

other probabilities such as isoniazid-induced hepatitis, hospitalisation if hepatitis develops, treatment acceptance and cure rates.

All epidemiological data were obtained for countries with low, intermediate and high incidence of TB.

Sources searched to identify primary studies

Much of the clinical and epidemiological data were based on published studies. Rates of incidence of smear-positive TB were taken from publications by the World Health Organization. Treatment outcomes came from large-scale screening programmes. Rates of development of active TB were derived from cohort studies and randomised controlled trials, while outcomes of undiagnosed active TB were obtained from studies referring to the pre-antibiotic era. Age-specific all-cause mortality came from Canadian life tables. Some assumptions about the size and age of immigrant cohorts were also made.

Methods used to derive estimates of effectiveness

Some published literature reviews were selected as primary sources of data, but some studies appear to have been identified selectively.

Measure of benefits used in the economic analysis

The summary benefit measure used was the number of future active TB cases prevented with the screening strategies in comparison with no screening. This benefit measure was estimated using the decision model and was discounted at an annual rate of 3%.

Direct costs

The viewpoint of the health care system and the patient was adopted. The categories of costs considered were screening tests (including medical evaluation), out-of-pocket expenditures, treatment of LTBI and treatment of active TB (making a distinction between active TB cases picked up by screening and those diagnosed passively). QFT screening included the manufacturer's current unit costs, plus costs for clinical personnel, transportation, laboratory personnel and reporting. A breakdown of the cost items was not reported and, apart for screening tests, the unit costs were not presented separately from the quantities of resources used. The quantities and the costs were derived from earlier micro-costing studies and patient expenditures from earlier patient surveys. Discounting was relevant as 10-year costs were considered, and an annual discount rate of 3% was applied to costs incurred after the first year. The price year was 2004. Costs from previous years were inflated to 2004 values using appropriate inflation indices.

Statistical analysis of costs

The costs and quantities were treated deterministically.

Indirect Costs

Productivity costs were not considered.

Currency

Canadian dollars (CAD). One US dollar was equivalent to CAD 1.30 in 2004 (average exchange rate).

Sensitivity analysis

A deterministic sensitivity analysis was undertaken in order to address the issue of uncertainty in key model inputs, especially epidemiological and clinical data. Alternative estimates were derived from ranges of values available from the published literature. Several scenarios were also considered.

Estimated benefits used in the economic analysis

Without screening, the number of future active TB cases over 20 years was 0.5 per 1,000 immigrants for countries of origin with low incidence of smear-positive TB, 9.8 for countries with intermediate incidence, and 15.7 for countries with high incidence.

The future active TB cases prevented by screening were 0.02, 0.5 and 0.8 with CXR, depending on the incidence of disease (low, intermediate and high, respectively), and 0.05, 1.3 and 2.1 with the QFT assay or TST.

Cost results

Without screening, the total costs over 20 years in a cohort of 1,000 immigrants were CAD 8,810 for countries with a low incidence of disease, CAD 204,510 for countries with intermediate incidence, and CAD 327,490 for countries with high incidence.

With CXR screening, the total costs over 20 years in a cohort of 1,000 immigrants were CAD 52,553, CAD 219,850 and CAD 328,190 depending on the incidence of disease (low, intermediate and high, respectively).

With QFT screening, the total costs over 20 years in a cohort of 1,000 immigrants were CAD 64,920, CAD 303,020 and CAD 459,040 depending on the incidence of disease.

With TST screening, alternative assumptions were made with respect to specificity and BCG coverage. Thus, the total costs over 20 years in a cohort of 1,000 individuals ranged from CAD 30,320 to CAD 129,660, from CAD 267,250 to CAD 332,520, and from CAD 423,250 to CAD 465,260 depending on the incidence of disease.

Synthesis of costs and benefits

Incremental cost-effectiveness ratios (ICERs; i.e. the incremental cost per case prevented) were calculated in order to combine the costs and benefits of the alternative strategies.

When only immigrants were considered, the ICER with CXR over no screening was CAD 2,187,167, CAD 30,680 and CAD 875 depending on the incidence of disease (low, intermediate and high incidence countries, respectively).

The ICER with QFT over no screening was CAD 1,122,200, CAD 75,777 and CAD 62,643 depending on the incidence of disease.

Considering alternative assumptions with respect to specificity and BCG coverage, the ICER with TST relative to no screening ranged from CAD 430,200 to CAD 2,417,000, from CAD 48,262 to CAD 100,050, and from CAD 45,600 to CAD 65,605 depending on the incidence of disease.

Given the similar benefits achieved with TST and QFT, a cost-minimisation analysis was performed. When considering alternative assumptions with respect to specificity and BCG coverage, TST was cost-saving in two scenarios: no BCG and TST specificity at 98%; and BCG in infancy and TST specificity at 92%. QFT was cost-saving in the other two scenarios: BCG older and TST specificity at 60%; mixture of BCG and TST specificity at 85%.

However, different results were obtained when close contacts or casual contacts were considered. In the case of screening for close contacts, QFT and TST were both dominant compared with no screening. Similarly, TST and QFT were dominant for casual contacts in the case of immigrants from countries with low TB incidence, while they were associated with high ICERs for countries with intermediate or high incidence. QFT was more cost-effective than TST in close and casual contacts who had received BCG vaccination after infancy because of reduced TST specificity. In general, TST would be more cost-effective than QFT unless TST sensitivity was less than 90% and risk of reactivation was very high. Finally, sequential testing was a cost-saving strategy in populations with a low prevalence of true TB infection or a high likelihood of false-positive TST due to BCG.

Authors' conclusions

The authors concluded that, despite considerable costs associated with the implementation of tuberculin skin test (TST)

or QuantiFERON -TB Gold (QFT) screening of immigrants at entry for tuberculosis (TB), few cases would be prevented in comparison with the conventional strategy of chest radiograph (CXR), which remained the most cost-effective strategy. Screening with TST or QFT would be cost-effective in scenarios where the risk of disease was high. In general, TST has the potential for higher cost-effectiveness, although QFT might be less costly in cohorts where bacille Calmette-Guerin (BCG) is given after infancy. However, both TST and QFT screening would be the preferred strategies for close contacts and in some circumstances for casual contacts.

CRD COMMENTARY - Selection of comparators

The authors justified their choice of the comparators, which were appropriately selected and described. Several strategies were considered, including some combinations of screening tests. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The clinical data used to populate the model were derived from published studies. However, they were presumably identified selectively as no details of a systematic review of the literature were reported; instead, published reviews of the literature were used as sources of some data. Other estimates came from World Health Organization reports or cross-sectional studies, which are usually considered to be a weak source of data. Key clinical inputs were varied in alternative scenarios. The authors did not discuss the implications of using sources which might not be homogeneous and comparable in terms of patient populations and methodological aspects.

Validity of estimate of measure of benefit

The benefit measure was specific to the interventions under examination and cannot be compared with the benefits of other health strategies. However, cases prevented represents a widely used end point of screening programmes. Discounting was appropriately performed.

Validity of estimate of costs

The economic analysis was consistent with the authors' stated perspective. Accordingly, all relevant categories of costs appear to have been included. A breakdown of the cost items was not reported and the costs were presented as macro-categories. This might reduce the possibility of replicating the analysis in other settings. All economic data were derived from other published studies, details of which were not provided. Statistical analyses of the costs were not performed and the impact of variation in economic inputs was not investigated. The price year was reported, which will facilitate reflation exercises in other time periods.

Other issues

The findings were not compared with those from other studies. The issue of the generalisability of the study results to other settings was not addressed, although the consideration of different populations might increase the external validity of the analysis. The authors stated that the strengths of the analysis lay in the multiple scenarios considered, in which alternative assumptions about previous vaccination policies and different epidemiological backgrounds were taken into account. It was noted that estimates of test accuracy might vary over time, with the result that current findings may not be applicable in future time periods. A further limitation of the analysis was that the model did not account for infection with the human immunodeficiency virus. Overall, there was little information on the clinical and economic data used in the model, as most of these details were presumably reported in a separate appendix.

Implications of the study

The key finding of the study is that the optimal screening strategy depends strongly on the country of origin of immigrants and the BCG status of these populations. Screening of contacts could also be considered to be a generally cost-effective strategy.

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None stated.

Bibliographic details

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Dasgupta K, Schwartzman K, Marchand R, et al. Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. *Am J Respir Crit Care Med* 2000;162:2079-86.

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Pai M, Riley LW, Colford JM Jr. Interferon-gamma assays in the immunodiagnosis of tuberculosis: a systematic review. *Lancet Infect Dis* 2004;4:761-76.

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