Dual skin testing for latent tuberculosis infection: a decision 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 use of a dual skin test (DST) for the detection of latent tuberculosis infection (LTBI). The intervention consisted of two tests. The Mycobacterium tuberculosis (MTB) purified protein derivative (PPD) test aimed to identify tuberculosis, while the Mycobacterium avium sensitin (MAS) test aimed to detect non-tuberculosis mycobacteria (NMT). The second test (MAS) was included so that positive PPD reactions due to LTBI could be distinguished from reactions due to Mycobacterium avium complex and other NMT.

All individuals received PPD and those with results of less than 10 mm were not treated for LTBI. PPD results of at least 10 mm were sub-divided into 10 to 14 mm and at least 15 mm. Individuals with results of at least 15 mm were treated for LTBI, while the 10- to 14-mm group received the second test with MAS. When the MAS induration exceeded PPD by at least 5 mm (MAS dominant), then treatment for LTBI was not offered and the PPD reaction was ascribed to NTM. Treatment for LTBI was offered to all other individuals.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical population in the USA consisting of adults at risk of LTBI. This included health care workers and residents or employees of congregate settings such as nursing homes or jails, but excluded immigrants from high-prevalence countries.

Setting
The setting was the community. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1990 and 2002. No explicit dates for the resource use data were reported. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies.

Modelling
A decision tree model was constructed to assess the clinical and economic outcomes of SST versus DST in a hypothetical cohort of 100,000 individuals. The structure of the tree was illustrated. The time horizon was that...
necessary to perform the different tests and to obtain the test results.

**Outcomes assessed in the review**
The outcomes assessed were:

- LTBI prevalence,
- the sensitivity and specificity of PPD at 10 and 15 mm,
- the sensitivity and specificity of MAS, and
- the prevalence of NMT in 10 to 14 mm.

**Study designs and other criteria for inclusion in the review**
A review of the literature does not appear to have been conducted. The design of the primary studies was not reported.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
The effectiveness data used in the model were derived from 8 primary studies.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
LTBI prevalence was 0.05.

The sensitivity of PPD at 10 mm was 0.94 and the specificity was 0.98.

The sensitivity of PPD at 15 mm was 0.59 and the specificity was 0.99.

The sensitivity of MAS was 0.73 and the specificity was 0.97.

The prevalence of NMT in 10 to 14 mm was 0.40.

**Measure of benefits used in the economic analysis**
The model outputs considered were:

the rates of individuals treated for LTBI, unnecessary LTBI treatments, and undetected cases of LTBI; and

the overall LTBI sensitivity and specificity.

However, such outputs were not used as summary benefit measures in the economic analysis.

**Direct costs**
Discounting was not relevant since the costs were incurred during a short time. The unit costs were not presented separately from the quantities of resources used. The health services used in the economic evaluation were tests, treatment for LTBI, and missed LTBI. The cost/resource boundary of the health care system was adopted in the study. The costs were estimated from published studies and using charges obtained from the authors' institution. Such charges were then converted into costs using centre-specific cost-to-charge ratios. The source of the resource use data was unclear. The costs were presented in 2000 values.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and threshold sensitivity analyses were conducted to address the issue of robustness of the estimated costs to variations in the model inputs. The choice of the ranges of values was based on data derived from the literature and authors' assumptions.

**Estimated benefits used in the economic analysis**
The rate of individuals treated for LTBI was 6% with SST and 5% with DST.

The rate of unnecessary LTBI treatments was 23% with SST and 9% with DST.

The rate of undetected cases of LTBI was 6% with SST and 7% with DST.

The overall LTBI sensitivity and specificity were, respectively, 94% and 98% with SST, and 93% and greater than 99% with DST.

Given the hypothetical cohort considered in the model, DST reduced the number of unnecessary LTBI treatments by 921 individuals per 100,000 tested. However, it increased the number of undetected cases of LTBI by 47 per 100,000 tested.

**Cost results**
The total costs per person were $45 with SST and $42 with DST. Therefore, DST led to a saving of $3 per person.

The estimated costs were quite robust to variations in the model inputs.
In general, wide variations were required before SST became the cheapest strategy. For example, when the cost of LTBI treatment was lowered from $404 (used in the base-case), DST remained favourable for all values until a threshold of $132. When the cost of MAS was increased from $20 (base-case), DST was favourable until a threshold of $105. Also, when the prevalence of LTBI was increased from 0.05 (base-case), DST remained favourable up to a threshold of 0.19. Finally, when the prevalence of NTM among individuals with 10- to 14-mm PPD was decreased from 0.40 (base-case), DST remained favourable until a threshold of 0.14.

**Synthesis of costs and benefits**

A synthesis of the costs and benefits was not actually conducted. A cost-consequences analysis appears to have been carried out.

**Authors’ conclusions**

The dual skin test (DST) was a promising approach for the detection of latent tuberculosis infection (LTBI) because it improved the specificity associated with the traditional single skin test (SST), thus reducing unnecessary drug treatments and overall costs from the perspective of the US health care payer.

**CRD COMMENTARY - Selection of comparators**

The authors justified their selection of the comparator (SST), which was considered to be current practice. The authors highlighted that recent diagnostic tests (e.g. in vitro tests) may represent alternatives with the benefit of minimising the practical limitations associated with skin testing. However, concerns exist about the costs and the diagnostic accuracy of in vitro tests. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness estimates were derived from published studies. A review of the literature was presumably not undertaken and the primary estimates were identified selectively. No information on the primary studies was provided, thus it was unclear whether valid sources were used. The methods used to extract and then combine the primary estimates were not reported. Most of the probability values were varied in the sensitivity analysis to investigate the issue of uncertainty.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the analysis since a cost-consequences analysis was conducted.

**Validity of estimate of costs**

The authors stated explicitly which perspective was adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. However, a detailed breakdown of the cost items was not provided, and details on the methods used to calculate the costs were not given because the costs were estimated from published studies. This reduces the possibility of replicating the study in other settings. The costs were treated deterministically but some cost estimates were varied in the sensitivity analysis. The price year was reported, which makes reflation exercises in other settings easy.

**Other issues**

The authors made few comparisons of their findings with those from other studies. They did not address the issue of generalisability of the study results to other settings. However, some sensitivity analyses were conducted, which improved in part the external validity of the analysis. The authors noted some limitations of their analysis, which were mainly related to the use of uncertain probability values (e.g. those pertaining to MAS). However, the results were robust under a wide range of parameter variations. It was also noted that the prevalence of LTBI was a key model input and the cost-effectiveness of either test depended on this parameter.
Implications of the study
The study results suggested that further studies should evaluate the cost-effectiveness of DST for populations (e.g. health care workers) in which targeted PPD testing is advised, where resources are limited, where large numbers of individuals may be tested, and where the prevalence of LTBI may be relatively low.

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Other publications of related interest
Lee E, Holzman RS. Evolution and current use of the tuberculin test. Clinical Infectious Diseases 2002;34:365-70.


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