Latent tuberculosis infection in children: a call for revised treatment guidelines

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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 various treatments for latent tuberculosis in immigrant children, considering isoniazid resistance. The authors concluded that rifampin should be the preferred treatment for children with latent tuberculosis infection, who were from countries with over 11% isoniazid resistance. The analysis was based on standard methods, but some sources of the clinical data were not fully reported. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of various treatments for latent tuberculosis (TB) in immigrant children, considering isoniazid resistance.

Interventions
The strategies were: isoniazid for nine months; rifampin for six months; combination treatment with isoniazid for nine months and rifampin for six months; and no treatment. A regimen of three months of combined isoniazid and rifampin was also considered separately.

Location/setting
USA/community setting.

Methods
Analytical approach:
The analysis was based on a decision tree model. The time horizon was not clear, but appeared to be short-term. The authors stated that the perspective of society was taken.

Effectiveness data:
The clinical data came from studies that were selected on the basis of their quality and similarity between the study conditions and the base case assumptions of the model. The key input to the model was the rate of resistance to isoniazid, which was taken from a study by the World Health Organization (WHO) in a Russian area. The drug efficacy was based on data from a randomised controlled trial that compared the two drugs in adults. Some assumptions were also needed.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The number of cases of TB prevented was the summary benefit measure.

Cost data:
The economic analysis included the cost of medications, visits to the health department, lost parental work, travel expenses, treatment of reactivated pulmonary TB, and treatment of liver failure. These costs were derived from average wholesale prices for drugs, Medicare reimbursement rates for nurse visits, average hourly salary in the state of Indiana for productivity losses, official mileage reimbursement for travel costs, and published studies for the treatment of both...
reactivated pulmonary TB and liver failure. All costs were in US dollars ($) and the price year was 2007.

**Analysis of uncertainty:**
One- and two-way sensitivity analyses were carried out by varying the model inputs across ranges of values that were based on published estimates. Several threshold analyses were performed and an alternative scenario considered the child’s Bacillus Calmette-Guerin (BCG) immunisation status.

**Results**
The average costs were $1,173 with rifampin, $1,235 with isoniazid, $1,364 with both, and $1,413 with neither. The probability that a TB reactivation did not occur was 0.94489 with rifampin, 0.93503 with isoniazid, 0.94504 with both, and 0.87 with neither.

The incremental analysis showed that isoniazid and no treatment were dominated, since they were less effective and more expensive than at least one other treatment. Rifampin was the reference strategy and the incremental cost per TB reactivation prevented with both drugs was $1,313,917.

The key finding from the sensitivity analysis was that for an area with an isoniazid-resistance rate of 11% or higher, rifampin was the least costly regimen. A similar result was found when considering the BCG status. The findings were sensitive to variations in the TB reactivation rate, rifampin resistance given isoniazid resistance, and the effectiveness or cost of rifampin and isoniazid.

The three-month regimen of isoniazid and rifampin was the least costly for all cases from areas with an isoniazid resistance of under 80%, as long as the regimen's efficacy was over 50%, but rifampin for six months remained the most effective strategy.

**Authors’ conclusions**
The authors concluded that rifampin should be the preferred treatment for children with latent tuberculosis infection originating from countries with over 11% isoniazid resistance.

**CRD commentary**

**Interventions:**
A justification for the selection of the comparators was provided; isoniazid was the most commonly recommended treatment, rifampin was recommended for patients exposed to isoniazid-resistant TB, and the combined strategy was used by some clinicians on the basis that the pathogen would be susceptible to at least one of the two drugs. No treatment was included as a baseline comparator.

**Effectiveness/benefits:**
The clinical data were from sources chosen on the basis of their quality and similarity. Treatment effectiveness was from a randomised controlled trial, which should ensure a high internal validity, but the trial was published in 1962. The data on drug resistance were from Russian children, who appropriately represented the immigrant population. The details of the other studies were not given, which makes it difficult to fully assess the suitability of the data. A disease-specific benefit measure was used and this does not allow a comparison of the results of this study with those of studies of other diseases.

**Costs:**
The categories of costs reflected the study viewpoint. The sources of data were generally described and appear to have been appropriate. The resource use and unit costs were not reported separately, as is common when Medicare or published sources are used. The price year was reported, but it was not stated whether future costs were discounted. The time horizon was not explicitly stated and so it is unclear if discounting was necessary. Some costs were varied in the sensitivity analysis.

**Analysis and results:**
The results were clearly presented and both the cost and effectiveness findings were reported separately. An incremental analysis was appropriately conducted. Only deterministic sensitivity analyses were performed, but the
inclusion of all parameters and the extensive use of threshold values increased the reliability of the findings. The authors stated that the main limitation of their study was the low quality of some of the published clinical sources used to obtain the model parameters.

Concluding remarks:
The analysis was based on standard methods, but some sources of the clinical data were not fully reported. The authors’ conclusions appear to be robust.

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