Cost-effectiveness of directly observed versus self-administered therapy for tuberculosis
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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
(1) Directly observed drug therapy (DOT) using: Isoniazid 300 mg per day at 15 days and 900 mg twice weekly from 1.5 months onwards; Rifampin 600 mg per day at 15 days and 600 mg twice weekly from 1.5 months onwards, Ethambutol 2.4 gm per day at 15 days and 4.8 gm twice weekly at 1.5 months; Pyrazinamide 2.0 gm per day at 15 days and 4.0 gm twice weekly at 1.5 months.

(2) Self-administered fixed dose combination drug therapy using: Rifater 6 tablets per day at 15 days and 1.5 months; Rifamate 2 tablets per day from 4 months onwards; Ethambutol 2.4 gm per day at 15 days and 1.5 months.

(3) Self-administered conventional individual drug therapy using: Isoniazid 300 mg per day; Rifampin 600 mg per day; Ethambutol 2.4 gm per day at 15 days and 1.5 months; Pyrazinamide 2.0 gm per day at 15 days and 1.5 months.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Hypothetical cohort of patients with drug-sensitive TB.

Setting
Hospital/primary care. The study was carried out in Baltimore, Maryland, USA.

Dates to which data relate
The data for the effectiveness analysis were obtained mainly from studies published in 1990, 1991, 1994 and 1995. The unit cost data were obtained from 1992-1993 hospital charge data, adjusted to 1994 prices and the remainder were from 1994.

Source of effectiveness data
Based on a review of previously completed studies.

Modelling
A decision tree was used in order to estimate benefits and costs.

Outcomes assessed in the review
Outcomes assessed were the rate of completion of therapy, rate of cure, rate of relapse, and mortality rate.

**Study designs and other criteria for inclusion in the review**
Nine controlled clinical trials were reported. No other details were provided.

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

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

**Methods used to judge relevance and validity, and for extracting data**
The methods used to judge relevance and validity were not reported. Extracting of data was by means of summary statistics for the relevant outcomes.

**Number of primary studies included**
Twenty primary studies were included.

**Methods of combining primary studies**
Primary studies were not combined. The authors chose baseline values by assumption in addition to a "reasonable" range of values.

**Investigation of differences between primary studies**
Differences were not investigated.

**Results of the review**
The rates of therapy completion for the three strategies were as follows (ranges in brackets):

- DOT 0.90 (0.75,0.90);
- fixed-dose combination therapy 0.75 (0.60,0.90);
- conventional therapy 0.60 (0.60, 0.70).

The rates of cure for therapy-completed cases were (range in brackets):

- DOT 0.985 (0.96,0.99);
- fixed-dose combination therapy 0.965 (0.96, 0.99);
- conventional therapy 0.965 (0.96,0.99).

The rates of relapse were DOT 0.015 (0.01,0.04); fixed-dose combination therapy 0.035 (0.01,0.04); conventional therapy 0.035 (0.01, 0.04).

The mortality rates for those who did not complete therapy (as well as for those relapsing with non-drug resistant (non-DR) TB) was 0.02 (range 0.01, 0.03) for all therapies. The mortality rate for those with DR TB relapse was 0.20 (0.15, 0.25) for all therapies.
Measure of benefits used in the economic analysis
The outcome measures used in the analysis were the expected number of patients having relapse with non-DR TB and DR TB and the expected overall number of deaths per 1,000 patients treated for each therapy. A decision tree was used in order to obtain values for these measures.

Direct costs
Generally, costs and quantities were reported separately. Costs were discounted for relapses beyond 1 year of therapy (relapses beyond 2 years were not assessed). Quantities were assumed based on the experience in the authors’ institution. The costs measured were operational costs, overhead costs, cost of follow up and complications, and travel costs for outreach visits. The boundary adopted related to hospital and patient. The unitary costs were mainly based on actual data obtained from the Maryland Health Service Cost Review Commission in 1992-1993. These were adjusted for inflation to 1994 prices. Drug costs were based on 1994 contractual costs to the Baltimore City Health Department. Costs of tests and blood counts were based on average national payments using 1994 Resource Based Relative Value Units for American Medical Association current practice terminology (CUT) codes. The overhead costs were based on the 1994 Baltimore City facility annual rate. The estimation of travel unitary costs was based on a guess. The price data appear to relate to 1994 (but this was not specifically reported).

Currency
US dollars ($).

Sensitivity analysis
The parameters used for sensitivity analyses were as follows: completion rate for fixed dose combination therapy, the DR TB rate for fixed-dose combination therapy, and the cure rate for DOT when therapy is not completed. Also, the cost of relapse with DR TB, relapse with non-DR TB and “direct” cost of TB were used for one way simple sensitivity analyses.

Estimated benefits used in the economic analysis
The number of relapse cases per 1,000 patients treated for non-DR TB were estimated at 30, 94 and 128 for DOT, fixed-dose combination therapy and conventional therapy respectively. The corresponding figures for DR-TB were 1, 2 and 5 whilst the overall mortality figures were 3, 8 and 13 patients respectively. These results were for a 6 month therapy regimen which was assumed to be accomplished within that period by 80% of treatment completers. The other 20% was assumed to finish therapy at 1 year.

Cost results
The total costs per person treated were: DOT $13,925, fixed-dose combination therapy $13,959, conventional therapy (single drug) $15,003. The discount rate used for relapses beyond 1 year was 4%.

Synthesis of costs and benefits
The cost per relapse averted and the cost per life saved were the two cost-effectiveness ratios calculated for each strategy. The costs per relapse averted were: DOT $14,378, fixed-dose combination therapy $15,446, conventional therapy $17,305. The costs per life saved were: DOT $13,966, fixed-dose combination therapy $14,068, conventional treatment $15,200. The results were sensitive to variability in the probability of relapse with incomplete DOT, the threshold value for the cost per life saved being 0.27 for DOT and the fixed-dose combination therapy. The results were sensitive to the probability of relapse with DR TB for fixed-dose combination therapy, the threshold value for the cost per life saved outcome being 0.0016 (again, for DOT and the fixed-dose combination therapy). The threshold for the relapse-averted outcome in terms of direct costs of DOT was $14,500. The corresponding value for the cost per life saved was $13,600, for the same pair of strategies as before.
Authors' conclusions
The authors concluded that the decision analysis of the cost-effectiveness of DOT and two forms of self-administered therapy indicated that, from an urban health department perspective, both DOT and fixed-dose combination therapy were more effective and less costly than conventional self-administered therapy for treatment of TB with DOT being the most cost-effective.

CRD Commentary
The study, in general terms, was well conducted, the main weakness being the way in which the previously published information was obtained. The search of sources does not seem to have been carried out systematically, and no discussion was included regarding differences between studies from which the final baseline parameter values were obtained. The way the study was designed corresponds to the chosen viewpoint, which is that of an urban public health department and, whilst the external validity is weakened by the points noted above, the internal validity is strong. The sensitivity analysis in the synthesis section appears to lend support to the final results.

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