Cost-effectiveness of thrombolytic therapy for acute myocardial infarction

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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
Thrombolytic therapy for treatment of acute myocardial infarction (AMI) patients using either streptokinase or alteplase. This was compared with standard non-thrombolytic therapy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Adults with acute myocardial infarction or unstable angina.

Setting
The practice setting was hospitals. The economic study was carried out in Virginia, USA.

Dates to which data relate
The effectiveness analysis was based on a meta-analysis of all available clinical trials published between 1958-1990 and on a study using pooled results from 9 randomised trials which was published in 1994 (dates of the 9 trials were not given). Resource use and costs were based on studies published in 1992, 1995 and 1991. Costs were inflated to 1995 dollars.

Source of effectiveness data
Estimates of final outcomes were based on syntheses of previously completed studies.

Modelling
A decision tree model was used to integrate the probability of outcomes (mortality rates and adverse events) with values of outcomes and associated costs. Two identical cohorts of 29,300 patients were constructed for the analysis, containing 4 age groups. Differential parameters were used within these groups, where possible.

Outcomes assessed in the review
The outcomes assessed were survival rates at 35 days (hospital discharge), survival rates at 1 year and incidence of adverse events (bleeding, haemorrhagic strokes, occlusive strokes and reinfarctions).

Study designs and other criteria for inclusion in the review
Meta-analyses of controlled clinical trials that evaluated thrombolytic therapy in general, for patients with AMI or unstable angina. Studies with age-specific outcomes were included in the review. One meta-analysis was chosen for the heterogeneous nature of the study populations used.

**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**
Two meta-analyses were used to derive effectiveness data. The Fibrinolytic Therapy Trial (FTT) study pooled data from 9 unconfounded, randomised trials. The Grunewald meta-analysis used all available published clinical trials from 1958 - 1990.

**Methods of combining primary studies**
Results from the primary studies were combined using a decision tree model. The FTT study was used to derive group sizes, hospital mortality rates and incidence of adverse events. The Grunewald study was used to derive survival rates at 1 year.

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

**Results of the review**
The proportion of patients surviving to hospital discharge was 90.3% for the treatment cohort and 88.6% for the control group. When adjusted 1 year mortality rates were applied to patients discharged from hospital, 83.0% in the treatment group survived 1 year and 81.4% in the control group. The rate of bleeding was 1.02% in the intervention cohort and 0.31% in the control cohort. The rate of haemorrhagic strokes was 0.30% in the treatment group and 0.04% in the control group. The rate of occlusion was 0.62% in the treatment group and 0.58% in the control group. The reinfarction rate was 2.86% in the treatment group and 2.48% in the control group. Rates of adverse events were presented for the cohort as a whole and were also presented by age group.

**Measure of benefits used in the economic analysis**
The authors chose their end point as deaths averted at one year. Life years saved were also estimated using the Gompertz parametric survival functions, assuming a mean survival rate of 15.5 years.

**Direct costs**
Costs and quantities of the resources were reported separately. It is unclear whether costs were discounted. Total costs for the intervention and control groups were estimated using the decision tree model. The cost boundary adopted was that of the hospital. Direct health service costs included the cost of thrombolytic therapy, the cost of cardiac catheterization, the cost of adverse events and additional general medical care costs for the 1 year survivors. The cost of thrombolytic therapy was calculated by assuming 70% of cases used alteplase and 30% streptokinase, the current US market share of each drug. Drug prices were taken from the 1995 Physician's GenRx. All other costs were based on
published information from other studies. All costs were inflated to 1995 prices using the consumer price index. Costs common to all patients were not included in the analysis.

**Statistical analysis of costs**
A statistical analysis was not performed.

**Indirect Costs**
Indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Three one-way simple sensitivity analyses were carried out. To evaluate the effect of time to treatment on cost-effectiveness, patients were stratified in groups by time to treatment (0-6 hours, 7-12 hours and 13-24 hours) and weighting factors in the model were adjusted. This investigated the generalisability of results. Additional sensitivity analyses were conducted to model exclusive use of streptokinase or alteplase, and of variability in rates of angina after infarction.

**Estimated benefits used in the economic analysis**
The authors estimated that at 1 year, there would be 455 deaths averted (from a cohort of 29,300) due to thrombolytic therapy. Incremental life years gained were not reported.

**Cost results**
Total per patient costs (including adverse events) for the therapy cohort were $11,160 and for the control cohort $7,713.

**Synthesis of costs and benefits**
The marginal cost of thrombolytic therapy per death averted at 1 year was $222,344. The marginal cost per life-year saved was $14,438. For patients treated within 6 hours of acute myocardial infarction the marginal cost per life-year saved was $11,788. For those treated between 7 and 12 hours after infarction this ratio was $17,447, and for those treated between 13 and 24 hours after infarction the ratio was $338,397. With all patients treated with streptokinase, the marginal cost per year of life saved was $8,340, compared with $15,763 with exclusive use of alteplase. Post-infarction angina increased the ratio to $15,698.

**Authors' conclusions**
Thrombolytic therapy is significantly more cost-effective than many other cardiovascular interventions and compares favourably with other forms of medical therapy. Shortening the time to treatment has a critical impact on cost-effectiveness.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparator, standard non-thrombolytic therapy, is clear.

**Validity of estimate of measure of benefit**
The authors made selective use of two meta-analyses. The FTT study comprised a sub-group of all trials and it is
unknown how representative these studies are. The Grunewald study was comprehensive, but included evidence from non-randomised sources which could have introduced biases. The statistical significance of the differences between the key estimates used in the models was not reported and sensitivity analysis was not employed to investigate a range of parameter values.

Validity of estimate of costs
Details of the methods of cost estimation were not given, though the studies on which they were based were quoted. Costs and quantities were reported separately. The authors did not use sensitivity analysis to address possible variations in unit costs.

Other issues
A range of the estimates for mortality rates should have been explored in a sensitivity analysis, to determine whether the value chosen had an impact on the cost-effectiveness of thrombolytic therapy. Variations in costs were not investigated by either sensitivity or statistical analysis. The authors conclusions cannot therefore be justified by the evidence presented in this study.

Implications of the study
The authors assumed that streptokinase and alteplase are equally effective. They did not report the distribution of outcomes, in patients treated within 6 hours of AMI. Further research, employing both statistical and sensitivity analyses, is needed to investigate these issues, if the cost-effectiveness of thrombolytic therapies is to be determined.

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