Identifying antistreptokinase antibodies: economic impact of point-of-care testing in the setting of prior 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
The use of thrombolytic strategies in patients with acute myocardial infarction (AMI) who had been treated with streptokinase (SK). The strategies examined were:

- retreatment with SK and aspirin;
- de novo treatment with tissue plasminogen activator (tPA) and aspirin;
- selective use of tPA and aspirin among those patients resistant to SK, as determined by antibody testing (using a point-of-care testing kit); and
- retreatment with SK and aspirin if resistance were not detected.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with AMI who had been treated with SK.

Setting
The setting was tertiary care. The study was performed in Ontario, Canada.

Dates to which data relate
The effectiveness data were collected from studies published between 1988 and 1998. The cost data were collected from studies published between 1990 and 1999. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a non-systematic review of published studies and author's assumptions.

Modelling
A decision tree model (Massel, see Other Publications of Related Interest) was used to estimate the costs and effectiveness of the alternative treatments considered at analysis.
Outcomes assessed in the review
The following parameters were assessed in the short term (5 to 6 weeks):

- the mortality rate with placebo;
- the relative risk reduction in mortality for patients treated with aspirin, compared with placebo;
- the relative risk reduction in mortality for patients treated with aspirin plus SK;
- the absolute risk reduction in mortality when tPA was administered, compared with SK;
- the probability of stroke with SK and with tPA; and
- the utility associated with nonfatal stroke.

Compliance rates do not seem to have been considered, although the model took complications related to the thrombolytic agents into account.

Study designs and other criteria for inclusion in the review
The author did not report the criteria used to include studies in the review. At least one randomised controlled trial (RCT), one review of published RCTs, and a meta-analysis were included in the review.

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
Not reported.

Number of primary studies included
At least 6 studies seem to have been included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
The differences between the primary studies do not appear to have been investigated.

Results of the review
The mortality rate with placebo was 14.0%.

Compared with placebo, there was a 20% relative risk reduction in mortality for patients treated with aspirin.

Compared with placebo, there was a 40% relative risk reduction in mortality for patients treated with aspirin plus SK.

Compared with SK, there was a 1.9% absolute risk reduction in mortality when tPA was administered.
The probability of stroke was 0.5% with SK and 0.6% with tPA.

The utility associated with nonfatal stroke ranged from 0 to 0.79.

**Methods used to derive estimates of effectiveness**
The author made several assumptions to derive some of the estimates of effectiveness.

**Estimates of effectiveness and key assumptions**
The author assumed the following:

SK would be ineffective when administered to those patients in whom SK resistance was present, while tPA would be effective whether or not there was any resistance to SK;

in the base-case analysis, the sensitivity of point-of-care testing was 100% and the specificity was 31%;

50% of patients who had had prior treatment with SK were resistant to SK.

**Measure of benefits used in the economic analysis**
The summary measure of benefit used in the economic analysis was the number of lives saved per 1,000 treated patients. This was derived directly from the non-systematic review. This measure was only reported for the comparison between 'tPA for all' versus SK.

**Direct costs**
The resource quantities and the costs were not reported separately. The direct costs in the economic analysis were those incurred by the third-party payer. The author stated that these costs were for the treatment of AMI, in particular, the drugs, cardiac procedures (e.g. angiography, PTCA and bypass surgery) and hospitalisation. The costs were obtained from published studies and the 1991 Ontario Health Insurance Plan Fee Schedule. Therefore, the costs were estimated from actual data. The economic analysis appears to have considered a short-term period (5 to 6 weeks). The price year was 1999. Discounting was not performed, which was appropriate since the period considered at analysis was shorter than 2 years. Marginal costs may have been estimated, although this is an assumption since the author did not present the results of the cost data separately, but only the results of the combined costs and effectiveness estimations.

**Statistical analysis of costs**
No statistical analyses of the costs were reported.

**Indirect Costs**
No indirect costs were reported.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
One- and two-way sensitivity analyses were performed to assess the robustness of the results to variations in several parameters and estimators. For example, the levels of resistance to SK, the antibody test characteristics, the cost of the test kit, the cost of treating an AMI with tPA, and the absolute benefit of tPA over SK. A threshold analysis was also performed to determine the most preferred strategy when the effect per cost was considered, assuming a threshold of Can$50,000. The area of uncertainty investigated in the sensitivity analyses was, therefore, variability in the data.
Estimated benefits used in the economic analysis
The absolute risk reduction in mortality was 1.9% when tPA was compared with SK. Thus, the total number of lives saved per 1,000 patients treated with tPA, compared with SK, was 19 (see Results of the Review).

Cost results
The total cost results were not reported separately (see Synthesis of Costs and Benefits). The authors did report the unit costs of all major cost items included in the analysis.

Synthesis of costs and benefits
The estimated costs and benefits were combined by calculating incremental cost-effectiveness ratios (ICERs). These measured the incremental costs per short-term survivor with tPA in comparison with the other strategies. Although unclear, the baseline result appears to have been an ICER of Can$97,484 per additional short-term survivor when ‘tPA for all’ was compared with SK.

From the sensitivity analyses, the ICERs for ‘tPA for all’ in comparison with SK varied as follows:

from Can$153,922 per short-term survivor (0% SK resistance rate) to Can$82,381 (75% SK resistance rate), assuming that ‘tPA for all’ would save 19 lives;

from Can$292,452 per short-term survivor (0% SK resistance rate) to Can$110,359 (75% SK resistance rate), assuming that ‘tPA for all’ would save 10 lives;

from Can$584,904 per short-term survivor (0% SK resistance rate) to Can$82,381 (75% SK resistance rate), assuming that ‘tPA for all’ would save 5 lives.

The threshold analysis showed that, considering a threshold of Can$50,000, the preferred strategy was SK when SK resistance was lower than 60%. ‘Selective tPA’ was preferred when SK resistance was greater than 60% but less than 95%, and ‘tPA for all’ was preferred when SK resistance was greater than 95%.

The ranges of the ICER results for the comparisons between ‘tPA for all’ and selective tPA were reported. However, the values of the measures of benefits that were used to estimate these ICERs were unclear.

Authors’ conclusions
When compared with the currently used streptokinase (SK), tissue plasminogen activator (tPA) for all was the most effective strategy, while ‘selective tPA’ presented the most favourable incremental cost-effectiveness ratio (ICER), for the treatment of patients with acute myocardial infarction (AMI) and resistance to SK.

CRD COMMENTARY - Selection of comparators
The comparator chosen was SK, as this was the health technology used in the author's setting to treat AMI patients. The author commented that, elsewhere, other strategies (such as PTCA) may be used to treat AMI patients. You must decide whether SK is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The author did not state that a systematic review of the literature had been undertaken. Data from the available studies appear to have been used selectively. The differences between the primary studies do not appear to have been considered when estimating the effectiveness. Some important assumptions were formulated to derive estimates of effectiveness. However, not all of these assumptions were explicitly justified with reference to the medical literature. It was unclear why the author reported some effectiveness parameters (e.g. utilities associated with nonfatal stroke), but not others that were more relevant for the analysis (e.g. absolute risk reduction in mortality between ‘tPA for all’ and
selectively tPA’, or between ‘selectively tPA’ and SK). Adverse events associated with the interventions were not considered when estimating the effectiveness of the strategies analysed, although the author stated that this would not influence the results since these adverse events are very rare. Sensitivity analyses were performed to account for some of the uncertainty surrounding the results. The values used were justified with reference to the medical literature.

Validity of estimate of measure of benefit
The summary measure of benefit (number of short-term survivals) was derived directly from the review. Quality of life was not considered, which may have been relevant. A long-term measure of benefit was only discussed, and was not taken into account in the analysis.

Validity of estimate of costs
The perspective adopted was that of a Canadian provincial Ministry of Health, and productivity losses were not considered in the economic analysis for this reason. The reporting on the costs was very brief. Moreover, no total costs were reported, but only the results for the estimation of the ICERs. The resource quantities and the costs were not reported separately, which would hinder reflation exercises to other settings. The price year was reported. Discounting was not performed, but was not relevant since the time period considered at analysis was very short. A longer period would have been appropriate; the discussion of this issue was limited. Sensitivity analyses, to account for uncertainty surrounding the cost results, were reported.

Other issues
The author did not appear to make appropriate comparisons of the findings with those from other studies. The issue of the generalisability of the results to other settings was not addressed. The results were reported selectively, and some important results were not reported (e.g. the base-case comparisons between ‘tPA for all’ and tPA administered selectively).

Implications of the study
There is some confusion due to the selective reporting of effectiveness and costs estimations, which makes the conclusions of the study uncertain.

Source of funding
None stated.

Bibliographic details

PubMedID
12014660

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM
MeSH
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