Using simulation to estimate the cost effectiveness of improving ambulance and thrombolysis response times after 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 study examined two interventions to improve ambulance and thrombolysis response times for acute myocardial infarction (MI). The focus of the analysis was to improve the ambulance response time to 75% of calls reached within 8 minutes, and the hospital arrival to thrombolysis time interval to 75% receiving it within 30 minutes and 20 minutes.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients experiencing an acute MI.

Setting
The setting was an emergency department. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies published between 1991 and 2003. The resource use data and costs were estimated from sources published in 1996 and 2000, as well as from drug prices in 1999. The price year was 2000.

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

Modelling
A discrete event model was used to simulate the treatment of coronary heart disease (CHD) from the first onset of angina, or MI, to age 85 years or death. A further simulation to model interventions for the prevention of CHD was developed in parallel. Both simulations were used to test the cost, effect and overall cost-effectiveness of treatments and interventions over a 20-year timeframe. In particular, the model assessed the effect of faster access to treatment for MI in terms of faster ambulance arrival times and the effect of varying the provision of thrombolysis and the timing of thrombolysis (door-to-needle time, DTN). In the treatment model, simulated patients moved between stable and unstable angina, MI and sudden cardiac death. The transitions between events were based on risks such as age, severity of coronary artery disease and history of CHD. A graphical representation of the model was provided in the paper.

Five main scenarios were considered in the simulation:
scenario 1, 75% of "life-threatening" calls to receive an ambulance response within 8 minutes;

scenario 2, 75th percentile of distribution of DTN time for thrombolysis is 30 minutes (with the existing proportion of patients receiving thrombolysis);

scenario 3, 75th percentile of distribution of DTN time for thrombolysis is 20 minutes (with the existing proportion of patients receiving thrombolysis);

scenario 4, 75th percentile of distribution of DTN time for thrombolysis is 30 minutes (including the additional eligible patients (10% of the total) who currently fail to receive thrombolysis); and

scenario 5, a combination of scenarios 1 and 2.

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the probabilities of transitions across health states;
- the proportion of patients experiencing cardiac arrests or MIs;
- the percentage of patients discharged (survival rate to hospital discharge) given different ambulance response times;
- ambulance response time distributions (percentage of patients for each time interval) at baseline (actual situation) and in the case of achieving NSF targets;
- the proportion of patients at hospital arrival with a diagnosis of MI and receiving thrombolysis;
- thrombolysis efficacy; and
- the percentages of patients for each DTN time at baseline (actual situation) and in the case of achieving NSF targets.

Study designs and other criteria for inclusion in the review
The authors stated that a search was conducted to identify the best evidence with which to populate the decision model. However, few details of the review and the primary studies were reported. Much of the data were extracted from three datasets: Heartstart Scotland (1991-98), the United Kingdom Heart Attack Study (1994-95) and the West Midlands Thrombolysis Project (1995-98). Thrombolysis efficacy data came from a meta-analysis.

Sources searched to identify primary studies
MEDLINE, the Cochrane Library, EMBASE and grey literature were searched for relevant primary studies.

Criteria used to ensure the validity of primary studies
The use of large, national databases and a meta-analysis should improve the validity of the primary estimates.

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

Number of primary studies included
Five primary studies provided the clinical data.
Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The proportion of patients experiencing cardiac arrests or MIs was 61%.

The percentage of patients discharged (survival rate to hospital discharge) was 14.7% for an ambulance response time of 0 - 4 minutes, 9.2% for a response time of 4 - 8 minutes, 5.1% for a response time of 8 - 12 minutes, and 4.3% for a response time of at least 12 minutes.

The percentage of patients at baseline responded to in the time interval was 12.2% for an ambulance response time of 0 - 4 minutes, 42.9% for a response time of 4 - 8 minutes, 28.8% for a response time of 8 - 12 minutes, and 16.1% for a response time of at least 12 minutes.

The percentage of patients at each time interval achieving the NSF ambulance targets was 22.1% for an ambulance response time of 0 - 4 minutes, 52.9% for a response time of 4 - 8 minutes, 17.1% for a response time of 8 - 12 minutes, and 7.9% for a response time of at least 12 minutes.

The proportion of patients at hospital arrival with a diagnosis of MI and receiving thrombolysis was about 50%.

In terms of thrombolysis efficacy, a relative mortality risk of 0.70 was associated with a time interval (from onset of symptoms to administration of thrombolysis) of up to 1 hour. The relative mortality risk was 0.74 for a time interval of 2 - 3 hours, 0.79 for 4 - 6 hours, 0.85 for 7 - 12 hours, and 0.98 for more than 12 hours.

The percentage of patients reaching different DTN times at baseline was 29.8% for a time of 0 - 29 minutes, 33.7% for a time of 30 - 59 minutes, 24.9% for a time of 59 - 119 minutes, 8.8% for a time of 120 - 239 minutes, and 2.5% for a time of 240 minutes or longer.

The percentage of patients at each DTN time interval achieving the NSF thrombolysis targets was 75.3% for a time of 0 - 29 minutes, 18.1% for a time of 30 - 59 minutes, 4.9% for a time of 59 - 119 minutes, 1.1% for a time of 120 - 239 minutes, and 0.6% for a time of 240 minutes or longer.

Measure of benefits used in the economic analysis
The summary benefit measure was the number of CHD life-years saved with each intervention in comparison with standard care. This was obtained using a modelling approach. An annual discount rate of 3.5% was applied. The number of deaths prevented in each scenario was also reported.

Direct costs
The analysis of the costs was conducted from the perspective of the NHS. It included the costs associated with improving ambulance response time and the costs of thrombolytic drug treatment (streptokinase and alteplase). A breakdown of the cost items was not provided, and the unit costs and the quantities of resources used were not presented separately. The costs and resource use data for ambulance services were estimated using data from the Review of Ambulance Performance Standards, which estimated the cost associated with attaining a 75% ambulance response time within 8 minutes. These costs were compared with the actual costs spent by the Department of Health on improving ambulance response times. The costs of thrombolytic drug treatment were taken from the British National Formulary. Some assumptions were made to identify the optimal strategies to reduce time to thrombolysis. Discounting was relevant, as the costs were incurred during a 20-year timeframe, and an annual rate of 3.5% was applied. The price year was 2000.
Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the economic analysis.

Currency
UK pounds sterling ().

Sensitivity analysis
Sensitivity analyses were carried out to assess the robustness of cost-effectiveness ratios to variations in base-case scenarios. First, for the ambulance response (scenario 1), cardiac arrest survivors were assumed to have a similar in-hospital survival rate to those who did not experience an out of hospital cardiac arrest (scenario 6). Second, a best ambulance scenario was considered in which all response times were decreased by 2.4 minutes, unless they became negative in which case they were zero (scenario 7). Third, a worst ambulance scenario was also considered, in which the distribution for ambulance response times gave the same target response times but the response times were reduced by the minimal amount possible to achieve that target (scenario 8). Fourth, 90% of life-threatening calls received an ambulance response within 8 minutes and the distribution for ambulance response times was calculated in a similar way to that for scenario 1 (scenario 9). Fifth, higher relative risks for reducing mortality were considered and alternative estimates of relative mortality risk estimates were used (scenario 10).

Estimated benefits used in the economic analysis
The annual undiscounted CHD life-years saved per million population per year (+/- 95% confidence interval limits) were:

- 57 (+/- 3.9) with scenario 1 (ambulance 75% in 8 minutes),
- 15 (+/- 3.5) with scenario 2 (thrombolysis 30-minute target),
- 17 (+/- 3.8) with scenario 3 (thrombolysis 20-minute target),
- 36 (+/- 3.8) with scenario 4 (thrombolysis for all eligible patients and 30-minute target), and
- 70 (+/- 3.6) with scenario 5 (scenarios 1 and 2 combined).

The numbers of deaths prevented per million population per year with scenarios 1 to 5 were 5 (scenario 1), 2 (scenario 2), 2 (scenario 3), 4 (scenario 4) and 7 (scenario 5).

The sensitivity analysis showed that the CHD life-years saved per million population per year with scenarios 6 to 10 were 105 (scenario 6), 81 (scenario 7), 35 (scenario 8), 85 (scenario 9) and 24 (scenario 10). The corresponding deaths prevented per million population per year were 11 (scenario 6), 7 (scenario 7), 4 (scenario 8), 7 (scenario 9) and 3 (scenario 10).

Cost results
The marginal annual cost of achieving the 8-minute target was estimated to be 448,100 for a population of one million.

The annual cost of nurse-initiated thrombolysis to meet the 30-minute DTN time for thrombolysis was assumed to be between 135,000 and 752,500 per million population.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative strategies.

The estimated discounted incremental cost per life-year saved with the 8-minute ambulance response time target (scenario 1) in comparison with the mid-1990s standard of care was 8,540.

The discounted incremental cost per life-year saved with the 30-minute DTN time for thrombolysis (scenario 2) in comparison with the mid-1990s standard of care was between 10,150 and 54,230.

No cost-effectiveness ratios were presented for the other scenarios.

Authors' conclusions
The improvement of both ambulance response time and thrombolysis door-to-needle (DTN) time was a cost-effective strategy from the perspective of the UK National Health Service (NHS) since the cost-effectiveness ratios were well below the putative threshold set by UK standards. However, the absolute gain with improving ambulance response was much greater than that associated with further reducing DTN time for thrombolysis.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear as each intervention was compared with standard practice in the mid-1990s. Several scenarios were considered. You should decide whether any or all of these are valid health technologies in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from searches of the main clinical databases. The authors stated that the best evidence was selected, although details of the review of the literature were not reported clearly. Much of the data came from three main UK databases. Data came also from a meta-analysis, a type of study that usually has a high internal validity. The issue of homogeneity among the primary sources was not addressed, but alternative scenarios for the effectiveness of the interventions were considered in the sensitivity analysis. The approaches used to calculate the clinical impact of the interventions were explicitly described.

Validity of estimate of measure of benefit
The choice of the summary benefit measure was appropriate, not only because life-years are a relevant dimension of health for patients with acute MI, but also because they are comparable with the benefits of other health care interventions. The impact of the interventions on quality of life was not investigated, although it would have been interesting. Discounting was applied, even though undiscounted benefits were presented.

Validity of estimate of costs
The costs included were consistent with the perspective adopted in the study, thus only direct medical costs were considered. The sources of the data were reported, but information on unit costs and resource consumption was not provided. Consequently, a detailed breakdown of the cost items was not given, which limits the possibility of replicating the cost analysis in other settings. The cost estimates were specific to the study setting and sensitivity analyses were not performed. No statistical analyses were carried out either. The price year was reported, which enhances the possibility of carrying out reflation exercises in other time periods.

Other issues
The authors reported the results from other studies that had assessed the impact of the interventions on life-years saved. These findings were comparable to those achieved in the current analysis. In terms of the generalisability of the study results to other settings, the authors stated that the results of the current model could be applicable to other developed countries with similar emergency services. However, no sensitivity analyses of the costs were performed and the external validity of the study appears to have been low. The study results referred to a hypothetical population of
patients experiencing an acute MI and this was reflected in the authors' conclusions. The authors stated that some of the assumptions made were conservative (such as the exclusion of non-CHD lives saved or the use of an optimistic baseline time distribution) and that the benefits of the interventions may have been underestimated.

**Implications of the study**
The study results support the improvement of ambulance response and thrombolysis DTN times for patients experiencing an acute MI. The authors suggested that future studies should assess the impact of faster ambulance response on in-hospital mortality rates.

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