Cost and cost-effectiveness of an early invasive vs conservative strategy for the treatment of unstable angina and non-ST-segment elevation myocardial infarction


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 health interventions examined in the study were two strategies for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction (UA-NSTEMI): early invasive strategy (including catheterisation within 4 to 48 hours and revascularisation as appropriate) versus conservative strategy (including catheterisation performed only because of recurrent ischemia or a positive stress test). Patients in both groups were treated with aspirin, heparin, and the glycoprotein (Gp IIb/IIIa) inhibitor tirofiban.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis; cost-utility analysis.

Study population
The study population comprised patients with UA-NSTEMI.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from a study published in 1998 and 2001. The price year was 2000.

Source of effectiveness data
The effectiveness evidence came from a single study (see 'Other Publications of Related Interest' below).

Link between effectiveness and cost data
The costing was conducted prospectively on a sub-sample of patients included in the effectiveness study (in particular, only subjects recruited in US non-VA Hospitals were considered).

Study sample
Power calculations were not reported. The main details of the study had been previously published. Overall, a sample of 2,220 patients was enrolled: 1,114 were assigned to the early invasive group and 1,106 were included in the conservative group. Those participating in US non-VA Hospitals were 863 (mean age: 63 +/- 12 years; 44% were aged 65 years or older; 38% women) in the early invasive group and 859 (mean age: 63 +/- 12 years; 44% were aged 65 years
or older; 37% women) in the conservative group. Other details on the methods of sample selection were not given.

**Study design**
This was a randomised clinical trial. Limited information on the design was provided. The length of follow-up was 6 months after hospital discharge. Information on loss to follow-up and methods for assessment was not reported.

**Analysis of effectiveness**
It was not stated whether the analysis of the clinical study was based on intention to treat. The primary endpoint used in the analysis was the proportion of patients experiencing death, myocardial infarction (MI), or re-hospitalisation for acute coronary syndrome (ACS). Secondary outcomes were the proportions of patients experiencing single endpoints, such as death or MI, death, MI, or re-hospitalisations due to ACS. Odds ratios (ORs) were calculated both in the whole sample of patients and in the sub-sample of patients participating in US-non-VA Hospitals. Six-month average life-years and utility values were also calculated. Study groups appear to have been comparable at baseline with respect to demographic and clinical characteristics.

**Effectiveness results**
In the whole sample, the proportion of patients experiencing the primary endpoint was 15.9% in the early invasive group and 19.4% in the early conservative group (OR: 0.78; 95% confidence interval (CI): 0.62 - 0.97; p=0.03).

The proportions of patients experiencing single endpoints in the early invasive and early conservative groups were 7.3% versus 9.5% (OR: 0.74; 95%CI: 0.54 - 1; p=0.05) for death or MI; 3.3% versus 3.5% (OR: 0.93; 95%CI: 0.58 - 1.47; p=0.74) for death; 4.8% versus 6.9% (OR: 0.67; 95%CI: 0.46 - 0.96; p=0.03) for MI; and 11% versus 13.7% (OR: 0.78; 95%CI: 0.60 - 1; p=0.05) for re-hospitalisations due to ACS.

Six-month average life-years were 0.486 versus 0.488, (p=0.75).

Average utility was not statistically significantly different between the groups. Similar results were obtained for the sub-sample of patients participating in US non-VA Hospitals.

**Clinical conclusions**
The effectiveness study showed that an early invasive strategy led to fewer cardiovascular events than a conservative approach. However, 6-month average life-years were comparable.

**Measure of benefits used in the economic analysis**
The main summary benefit measures used in the economic analyses were survival and quality-adjusted life-years (QALYs). However, most of the results were presented in terms of cost per life-year gained. They were calculated in two different time frames: the trial observation period (6 months) and lifetime. The extrapolation of survival and QALYs to a lifetime horizon was carried out using two alternative sources: the Framingham Heart Study and the PURSUIT trial. Details of the two approaches were described.

**Direct costs**
Discounting was not relevant as costs were incurred over a period of 6 months. Unit costs and quantities of resources used were not presented separately. The health services included in the economic evaluation were hospitalisations, emergency department visits, outpatient visits and procedures, nursing home and rehabilitation stays, and cardiac medications. The cost/resource boundary of the third party payer appears to have been adopted. The estimation of resource use was based on actual data derived from a sub-sample of patients included in the clinical trial used as the source of effectiveness evidence. Costs were estimated from Medicare reimbursement rates, which were converted into costs using the cost/charge ratio obtained from the hospital's annual Medicare Cost Report. Medication costs came from average wholesale prices. All costs were presented in 2000 values using the medical care component of the consumer price index.
price index.

**Statistical analysis of costs**
The Wilcoxon rank-sum test was used to compare initial length of hospitalisation and the number of re-hospitalisations. Logistic regression was used to analyse the economic endpoints and an intention to treat basis was used when differences in mean costs were estimated. Confidence intervals were calculated using bootstrapping methods. Statistical tests were also used to deal with missing cost data.

**Indirect Costs**
Indirect costs were estimated as a societal perspective was adopted. Discounting was not relevant as the time frame of the study was 6 months. The unit cost was not provided separately from quantities of resources used. Productivity losses were estimated separately for men and women for six age categories derived from the US Bureau of Labor, and were derived from annual wages. Days of missed work were derived from a sub-sample of patients included in the clinical trial. The price year was 2000.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not conducted but several alternative scenarios were considered, including higher discount rate, use of Framingham Heart Study or PURSUIT data, exclusion of productivity costs, use of the overall TACTICS-TIMI 18 population or the subgroup of US non-VA patients, and consideration of non-significant statistical difference in survival at 6 months.

**Estimated benefits used in the economic analysis**
Six-month average QALYs gained were 0.345 in the early invasive group and 0.35 in the conservative group, \( p=0.83 \).

Six-month average life-years were 0.486 versus 0.488, \( p=0.75 \).

The undiscounted survival advantage of invasive over conservative strategy was 0.068 years using Framingham estimates and 0.070 using PURSUIT estimates.

**Cost results**
Initial hospitalisation costs per patient were $15,714 for early invasive strategy and $14,047 for conservative strategy (cost difference: $1,667; 95% CI: $387 - $3,091).

Six-month follow-up costs after discharge, per patient, were $6,098 for early invasive strategy and $7,180 for conservative strategy (cost difference: -$1,082; 95% CI: -$2,051 to -$76).

Total 6-month costs per patient were $21,813 for early invasive strategy and $21,227 for conservative strategy (cost difference: $586; 95% CI: -$1,087 - $2,486). Therefore, no difference in costs was observed.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio was calculated to combine costs and benefits of the two strategies under evaluation.

When the analysis was restricted to the trial period (6 months), the invasive strategy was dominant since it was both more effective (more QALYs) and less costly.
When a long-term horizon was used, the discounted incremental cost per life-year gained with invasive over conservative strategy was $12,739 using Framingham estimates and $13,022 using PURSUIT estimates. The values of the cost-effectiveness ratios ranged from $8,371 to $25,769, depending on the underlying assumptions. These results held over a variety of assumptions.

Authors' conclusions
The authors stated that clinical benefits, namely reductions in major cardiovascular events, could be achieved with a small increase in costs in patients treated with an early invasive approach rather than a conservative strategy.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The two alternative approaches were selected because they represented the technologies under evaluation in the primary clinical trial used as the source of effectiveness evidence. The two strategies represent widely used approaches for the management of UA-NSTEMI patients. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a randomised clinical trial, which was appropriate for the study question. Limited information on the primary study was provided since most of the details on design and results had been published in a separate article. Therefore it is difficult to assess the internal validity of the study, although it appears to have been high due to the robust design, the large sample size, and the baseline comparability of the two groups.

Validity of estimate of measure of benefit
The choice of the summary benefit measures appears to have been appropriate as both reflected the impact of the intervention on patient health. Furthermore, both survival and QALYs can easily be compared with the benefits of other health care interventions. Short- and long-term benefits were estimated. Alternative approaches were used to extrapolate long-term benefits and the methods used were described in detail. Discounting was applied and the impact of an alternative rate was investigated in the sensitivity analysis.

Validity of estimate of costs
The perspective of society was adopted and it appears that all relevant categories of costs were included in the analysis. An alternative scenario in which indirect costs were not included was also considered. The approach used to estimate costs and resource use was reported. Statistical tests were conducted to deal with the issue of missing data and descriptive statistics were used to present data. The source of cost data was reported for each item. A cost/charge ratio was applied to assess true costs. The price year was given, which would facilitate reflation exercises in other settings. However, unit costs were not presented separately from quantities of resources used, and all estimates were specific to the study setting as no sensitivity analyses were conducted. The authors noted that costs were estimated over a 6-month period, which represents a limitation of the study.

Other issues
The authors compared their findings with those from other published studies and discussed the possible explanations for the differences in the economic results. However, the issue of the generalisability of the study results to other settings was not addressed and only limited sensitivity analyses were conducted. Therefore, the external validity of the analysis was low. The study referred to UA-NSTEMI patients and this was reflected in the conclusions of the analysis.

Implications of the study
The study results support the use of an early invasive approach for the management of UA-NSTEMI patients.
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Other publications of related interest


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