Meta-analysis and stochastic simulation of mortality and cost savings outcomes among coronary patients treated with PTCA versus other treatments

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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
Coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA), stent, and antiplatelet medication (abciximab, eptifibatide, tirofiban) were examined. Three treatment scenarios, which created specific combinations of these therapies, were defined.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with acute coronary syndromes undergoing PTCA, CABG with and without stent, and antiplatelet medication.

Setting
The setting was secondary care. A specific clinical setting was not identified since the effectiveness data were derived from a review of completed studies. The local costs were estimated from Clarian Health Partners in Indianapolis, USA.

Dates to which data relate
The effectiveness data related to studies published between 1993 and 2001. The unit costs for 2000 and 2001 were collected and inflated to 2001 prices. The dates during which the resource use data were collected were unclear, but it is likely that the data were derived for the same period.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Outcomes assessed in the review
The outcomes assessed were all-cause mortality, acute myocardial infarctions (MIs), repeat PTCA and repeat CABG.

Study designs and other criteria for inclusion in the review
The review searched for placebo-controlled trials using a variety of keywords. The primary end point in the studies had to be a composite of death, MI and revascularisation procedures.
Sources searched to identify primary studies
MEDLINE, Current Contents and International Pharmaceutical Abstracts were searched. Secondary references were used to identify additional trials.

Criteria used to ensure the validity of primary studies
The initial search was refined according to the trial design, sample size, multicentre status and follow-up. Patients from the review were matched according to their demographic and health status characteristics.

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

Number of primary studies included
Eighteen primary studies were used in the review.

Methods of combining primary studies
The authors pooled data from the relevant studies and used meta-analysis techniques.

Investigation of differences between primary studies
Some differences between the primary studies were discussed. For example, the authors stated that the STRESS trial was excluded since it concerned moderate patients as in comparison with other trials included in the relevant part of the study. The authors summarised the characteristics of the patients in each of the trials relevant to the current study, but did not discuss any differences.

Results of the review
The number of deaths avoided per 1,000 severe patients undergoing CABG was 6 (95% confidence interval, CI: -17 - 5).

The number of deaths avoided per 1,000 severe patients undergoing PTCA with stent was 9 (95% CI: -1 - 18).

The authors did not provide summary results for acute MIs, repeat PTCA, or repeat CABG.

The number of deaths avoided per 1,000 moderate patients was 2 (95% CI: -10 - 13) with PTCA plus stent, 3 (95% CI: -7 - 13) with PTCA plus antiplatelet, and 5 (95% CI: -4 - 13) with PTCA, stent and antiplatelet.

The number of deaths avoided per 1,000 moderate patients was 6 (95% CI: 0 - 12) with eptifibatide, 3 (95% CI: -4 - 10) with tirofiban, and 1 (95% CI: -9 - 10) for abciximab.

Measure of benefits used in the economic analysis
The economic analysis used the number of lives saved per 1,000 patients.

Direct costs
The costing was carried out from the perspective of the third-party payer. The costs associated with all the technologies (both drugs and procedures) evaluated in the analysis were considered. The total costs for MI, PTCA and CABG were estimated from actual data at the local hospital (the Clariant Health Partners in Indianapolis). Nationwide equivalents were collected from published sources. The costs per patient were also estimated. The costs for each treatment were reported separately, but were not broken down into constituent parts. Specific drug dosages were considered, but the source of these data was not reported. No waste was assumed. The costs were measured in 2000 and 2001, then inflated...
to 2001 dollars using the Consumer Price Index. Discounting was not reported and, as the follow-up in the clinical study was only 30 days, it does not appear to have been relevant.

**Statistical analysis of costs**
Statistical analyses were used only for the effectiveness estimates. The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not reported.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and multi-way sensitivity analyses were used to explore the impact of the cost of drugs, the cost of restenotic events (from local to national level), the rate to inflate prices, mortality rates and restenotic event rates. A threshold analysis was used to estimate the switching probability between the treatment options based on the cost-saving per event avoided per patient. Stochastic meta-analyses were carried out using Monte Carlo simulations with 1,000 iterations.

**Estimated benefits used in the economic analysis**
See the 'Results of the Review' section.

**Cost results**
The net cost (intervention cost minus cost-saving) per severe patient was $49,649 for CABG and $20,820 for PTCA plus stent.

The net cost (intervention cost minus cost-saving) per moderate patient was $216 for PTCA plus stent, -$174 for PTCA plus antiplatelet, and $731 for PTCA, stent and antiplatelet.

The net cost (intervention cost minus cost-saving) per moderate patient was $726 for eptifibatide, $357 for tirofiban and -$135 for abciximab.

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the interventions evaluated in the analysis.

When the average cost-effectiveness ratio was used, PTCA with antiplatelet drugs cost $66,808 per life saved, PTCA with stent and antiplatelet drugs cost $156,114 per life saved, and PTCA with stent cost $124,834 per life saved.

In the incremental analysis, PTCA plus stent was reported to be dominated by PTCA plus antiplatelet. PTCA, stent and antiplatelet required an incremental cost of $174,463 per life saved in comparison with PTCA plus stent.

When comparing the three drugs in addition to PTCA in moderate patients, eptifibatide resulted in a $590 additional cost-saving per patient in comparison with abciximab, and it saved more lives per 1,000 patients (dominant). Tirofiban required $200,915 per life saved compared with abciximab.

**Authors’ conclusions**
In terms of cost-saving, coronary artery bypass graft (CABG) was the preferred treatment followed by percutaneous
transluminal coronary angioplasty (PTCA) with stent. However, in terms of mortality rates, PTCA was preferable for severe patients. For moderate patients, the authors concluded "patients should receive PTCA with the addition of eptifibatide".

CRD COMMENTARY - Selection of comparators

The authors compared a range of treatments for moderate and severe patients with CAD. The comparators were justified through a general discussion of the treatment of patients with CAD and possible treatments. Current practice was not evident from the discussion. You should decide whether they represent valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The authors did not state that a systematic review of the literature had been carried out. The methods and conduct of the review (e.g. sources searched, inclusion criteria) were reported. Estimates of effectiveness from primary studies were combined through meta-analysis techniques that considered the variety of information available. However, although the authors identified three primary outcomes to be obtained from the review, they failed to present results for all three outcomes. The reason for this was unclear. Patients from the review were matched to reduce the likelihood of systematic bias. Some studies were explicitly excluded due to expected differences between them. The authors did not discuss the impact of any remaining differences between the primary studies when estimating effectiveness, but did carry out some sensitivity analyses.

Validity of estimate of measure of benefit

The estimate of benefits (lives saved) was obtained directly from the effectiveness study. It seems to have been an appropriate measure. The authors suggested that a measure incorporating the value of life was beyond the scope of the analysis.

Validity of estimate of costs

The costs were estimated from the perspective of the third-party payer, although those included in the analysis seem to represent costs to the hospital rather than charges to the third party. Therefore, the extent to which the final results indicated the costs to the third-party payer was unclear. Also, the effect of premiums and co-payments paid by patients was not included in the analysis. It would have been helpful had the authors adopted a wider perspective. As CABG and PTCA treatments involve a stay in hospital, there are likely to be some productivity implications for the economy. These could have been measured using the patients’ wage as a proxy for productivity. Also, since the CIs for cost were not estimated, it was not possible to estimate whether small alterations in the cost would have affected the principle results of the study. However, extensive sensitivity analyses and stochastic tests were conducted on the estimated costs. The unit costs and the quantities were not reported separately, although the authors indicated the total cost for each specific treatment.

Other issues

The authors made appropriate comparisons of their findings with those from other studies, highlighting areas of similarity and difference. Where differences existed, potential reasons for those differences were discussed. The issue of generalisability to other settings was not addressed. However, as the study comprised published literature from a variety of settings, both local and national, and given that sensitivity analyses were carried out, the results may well be generalisable. The authors presented some of the results selectively. For instance, they explicitly stated that the results from the deterministic meta-analyses were not presented due to lower confidence in the results, and the results for some primary outcomes in the review were also not reported. A number of limitations to the study were presented. These included the use of all-cause mortality, rather than mortality from specific causes, in order to reduce confounding from co-morbidities.

Implications of the study

The authors recommended that moderate patients "should" be treated with PTCA plus eptifibatide. They stated that
decision-makers should use their conclusions when recommending treatment strategies for patients with CAD. However, they made no specific suggestions for further work.

**Source of funding**
None stated.

**Bibliographic details**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Angioplasty, Transluminal; Percutaneous Coronary; Clinical Trials as Topic; Coronary Artery Bypass; Coronary Disease /drug therapy /surgery; Coronary Restenosis /complications; Follow-Up Studies; Health Care Costs; Humans; Meta-Analysis; Platelet Aggregation Inhibitors /therapeutic use /economics; Stents; Treatment Outcome

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