The economics of TRACE: a cost-effectiveness analysis of trandolapril in postinfarction patients with left ventricular dysfunction

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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
Trandolapril in postinfarction patients with congestive heart failure (CHF). After a 0.5mg test dose the initial dose was 1mg once daily increased to 2mg after 2 days and to 4mg after 4 weeks.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with recent myocardial infarction (MI) who were confirmed to have left ventricular dysfunction.

Setting
Community. The economic study was carried out in France.

Dates to which data relate
The patients for the effectiveness study were enrolled between May 1990 and July 1992. The effectiveness and cost analysis was based on data collected between 1992 and 1995. 1996 prices were used.

Source of effectiveness data
The effectiveness data were based on a single study reported separately (Kober, 1995).

Link between effectiveness and cost data
Costing was partly undertaken on the same patient sample as that used in the effectiveness study and was carried out prospectively.

Study sample
A total of 6,676 patients were screened for the confirmation of left ventricular dysfunction through an echocardiographic examination, eligibility for inclusion being determined as Wall-Motion Index less than or equal to 1.2. Of 2,606 found eligible 859 were excluded due to mandatory ACE inhibition, cardiogenic shock or death during screening. 1,749 patients were randomised into the intervention (n=876) and control (n=873) groups. Mean age was 67.7 years and 67.3 years, proportion of males 72% and 71%, and body mass index 25.8kg/m?2 and 25.6kg/m?2 in intervention and control groups, respectively. Mean time after MI was 4.5 days in both groups. No power calculations were reported.
Study design
This was a randomised controlled trial based in 27 centres in Denmark. Treatment was continued for at least 2 years and the follow-up period was 3 years. The design was double blinded.

Analysis of effectiveness
The analysis was based on intention to treat. The primary health outcomes were overall mortality, cardiovascular death, sudden death, progression to severe heart failure, recurrent MI and change in ejection fraction (Wall-Motion Index). No significant differences were found in any baseline characteristics between intervention and control groups.

Effectiveness results
The observed overall mortality was 34.7% in the intervention group and 42.3% in the placebo group, which was found to be statistically significant (p=0.001) using Log-Rank test. Relative risk in the active group compared to placebo was 0.78 with 95% confidence interval of 0.67 to 0.91. Risk of death from other causes was also found to be reduced in the intervention group. Risk of recurrent MI was not significantly reduced.

Measure of benefits used in the economic analysis
The benefit measure was life years gained. A Kaplan-Meier survival model was used to estimate differences in life-expectancy. No adjustment to quality of life was carried out.

Direct costs
Direct costs consisted of treatment costs, concomitant treatment costs, and cost savings from prevented hospitalisations. Treatment costs and concomitant treatment costs were based on actual data from the clinical study. Hospitalisation costs were based on mean cost for diagnosis related group (DRG). Resource quantities were not reported separately from costs. The cost boundary adopted was that of the hospital. Costs were discounted. 1996 prices were used.

Statistical analysis of costs
Costs were compared using the Kruskal-Wallis nonparametric test.

Currency
French francs (Ffr).

Sensitivity analysis
The effect of the choice of discount rate was analysed using one-way simple sensitivity analysis. Bootstrapping simulation was used to analyse the distribution of the cost-effectiveness ratio.

Estimated benefits used in the economic analysis
The number of lives saved (undiscounted) by the intervention treatment was estimated to be 65. Life years gained were based on mean life expectancy of 3.54 years (discounted at 5%) multiplied by number of lives saved. Undiscounted life expectancy was estimated to be 5.52 years. Side effects of the treatment were not taken into account.

Cost results
The total undiscounted programme cost was Ffr22,080,500 for the intervention group and Ffr20,317,300 in the control group resulting in a difference of Ffr1,763,200 (undiscounted). Discounted by 5% the cost difference was Ffr1,599,274. The treatment cost of possible adverse effects of intervention were not reported.
Synthesis of costs and benefits
Costs and benefits were combined as cost per life year gained. The cost effectiveness ratio, when discounting both costs and benefits by 5%, was Ffr6,950 per life year gained. The lowest cost effectiveness ratio, Ffr4,250 was obtained when benefits were not discounted and costs were discounted by 7.5%. In contrast the highest cost effectiveness ratio, Ffr8,830, was based on discounting benefits by 7.5% and cost by 0%. Using a discount rate of 5% for both costs and benefits, the bootstrapping estimate of the mean cost per life year gained was Ffr8,410, (95% CI: Ffr7,990 to Ffr8,840).

Authors' conclusions
Trandolapril treatment can be considered a highly cost-effective strategy from a third-party payer perspective.

CRD COMMENTARY - Selection of comparators
The comparator was stated to be the "standard therapy only" but its precise nature was not specified nor was any justification given for its choice.

Validity of estimate of measure of benefit
The estimate of the measure of benefit was based on a large randomised, double-blinded trial, and hence, is likely to be internally valid. Given the strict inclusion criteria and, in particular, the high number of exclusions of eligible patients, the generalisability (external validity) of the results to typical patient populations should be assessed with care. As the authors noted, this is, however, a common problem with economic analyses closely based on controlled trials.

Validity of estimate of costs
Estimation of cost was limited to the treatment and concomitant treatment data collected as part of the trial and the mean cost of hospitalisations saved due to the reduced rate of medical events. It was not clear whether the costs of treating the side effects of drug therapy were included. Costs and resources used were not reported separately.

Other issues
The authors' conclusions appear to be justified given the limitations arising from the study design. The results were compared with other similar studies, but comparability with most current studies would require modelling the costs and outcomes beyond the 3-year study period. Also, results are specific to French settings and may be difficult to generalise to other countries due to possible differences in clinical practices. There is no evidence that data were used selectively.

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Other publications of related interest

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