Cost-effectiveness of captopril therapy after 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
Captopril (angiotensin-converting enzyme inhibitor) therapy for survivors of myocardial infarction (MI) with an ejection fraction of 40% or less.

Type of intervention

Economic study type
Cost-effectiveness analysis.

Study population
A hypothetical cohort of 50 to 80 year old survivors of MI with an ejection fraction of 40% or less.

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

Dates to which data relate
The effectiveness and main resource use data were derived from a study published in 1992 (the Survival and Ventricular Enlargement (SAVE) trial). The price date used was 1991.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Costing was undertaken prospectively on a sub-sample of the clinical trial.

Study sample
The study sample was based on the SAVE randomised controlled trial of captopril therapy in 2,231 survivors of MI with an ejection fraction of 40% or less and of all ages. Of these, 1,116 patients were included in the 'placebo' group, and 1,115 were allocated to the intervention (captopril therapy).

Study design
Multi-centred randomised controlled trial. The number of sites was not reported. The duration of follow-up of the treatment cohort was 4 years. All the data pertinent to this analysis were collected and analysed in a blinded manner by the authors, without knowledge of treatment groups.
Analysis of effectiveness
The clinical study analysed the data using the intention to treat principle. A further retrospective analysis reported in the economic study (not presented here) excluded those patients aged under 40 due to "small sample size". The primary health outcome used in the analysis was survival rate at 4 years after MI. The placebo and captopril groups were comparable in age and prognostic features.

Effectiveness results
Captopril was found to improve survival by 19% at an average follow-up of 3.5 years.

Modelling
Decision-analytic models were used to estimate the costs and benefits of captopril therapy in 50-80 year old survivors of MI. One separate model was used for each age group within that age range (using age-specific effectiveness estimates as derived from the SAVE trial. Long-term survival (beyond the 4-year study period of the clinical trial) was estimated using a Markov model. Cox proportional hazard models were fitted into trial data to incorporate the effects of age and treatment, and the interaction of age with treatment, to yield survival estimates. The utilities, hospital stay and cardiac medication costs derived from patients’ follow-up at one centre were assumed to apply to the entire study cohort and stratified by whether they were receiving captopril or placebo.

Measure of benefits used in the economic analysis
The outcome measure used was quality-adjusted life-years (QALYs) gained. A decision-analytic model was used to assess the cost-effectiveness of captopril therapy. A Markov model was used to model the effectiveness of therapy on long-term prognosis by following a hypothetical cohort of patients (from the SAVE trial) through states of health and illness. The time trade-off valuation tool was used. During the course of the SAVE trial a sample of 82 study patients from one study site (Brigham and Women's Hospital in Boston) was used to assess time trade-off utilities.

Direct costs
Main quantities of resource use were analysed separately from the costs. Costs rather than charges were used in the analysis. All costs were converted to 1991 US dollars using the medical care component of the consumer price index (CPI). All costs were discounted. Costs estimates for the model were based on actual resource utilisation of trial patients after adjusting for protocol-driven costs associated with outpatient visits. Professional and hospital costs were calculated on the basis of average length of stay using the median reimbursement rates. The cost of captopril therapy was based on the average daily dose in mg of all SAVE patients assigned to captopril therapy and consisted of an acquisition cost for a full dose of 50mg three times daily, plus a dispensing cost per month supply. Costs of outpatients tests were assumed to be equal under both strategies and were thus not modelled explicitly.

Statistical analysis of costs
Costs were treated in a stochastic way. Standard deviations, mean values and a 95% confidence interval (CI) were reported.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out on all survival benefit, utility and cost estimates over wide ranges. Included in the analyses were the scenario of no survival benefit with costs being incurred beyond 4 years (‘limited-benefit’ scenario), additional benefits beside costs (‘persistent-benefit’ scenario) and a ‘worst-case’ scenario.
Estimated benefits used in the economic analysis
Under the 'limited-benefit' scenario, the average (discounted) QALYs ranged from 3.96 to 8.13 for the captopril strategy and from 3.44 to 8.10 for the no captopril strategy. The 'limited-benefit' scenario yielded corresponding ranges of 4.33 - 8.34 (captopril) and 3.44 -8.10 (no captopril). These estimated average benefits reflect discounting of benefits beyond 1 year at a 5% annual rate, and the lower bounds refer to 80 year old patients, with the upper range limits referring to 50 year olds.

Cost results
Under the 'limited-benefit' scenario, the total average costs for captopril ranged from $16,699, for 80 year old patients, to $32,098, for 50 year old patients; the no-captopril strategy had associated costs ranging from $14,844, for 80 year olds, to $30,369, for patients aged 50. The 'persistent-benefit' scenario yielded total average costs ranging from $14,844 to $30,369; the no captopril option had the same costs (and, therefore, cost range) as those reported for this strategy under the 'limited-benefit' scenario. All the cost figures are expressed in 1991 prices and reflect annual cost discounting at a 5% rate.

Synthesis of costs and benefits
In the 'limited-benefit' analyses, the incremental (discounted) cost per additional (discounted) quality-adjusted life-year (QALY) gained (ICER) of captopril therapy (relative to no captopril) ranged from $3,600/QALY for 80 year old patients to $60,800/QALY for 50 year old patients. In the 'persistent-benefit' analyses, the ICER ranged from $3,700 to $10,400/QALY, depending on age. In the 'worst-case' analysis, the ICER for captopril therapy remained favourable ($8,700 to $29,200/QALY) for 60 to 80 year old patients but was higher ($217,600/QALY) for 50 year old patients. In the limited-benefit analyses, patients aged 60 to 80 were not sensitive to changes in parameter values. If captopril cost 1,000/year, the ICER increased to $180,800/QALY. In the persistent-benefit analyses, increasing the cost of captopril therapy for the 50 year old patients to 1,000/year yields an ICER of $24,900/QALY. In the 'worst-case' scenario, with a 1% lower quality adjustment (utility), the cost-effectiveness of captopril therapy remained favourable in patients aged over 60. The ICER for 50 year old patients was $217,600/QALY. For 60 year old patients it was $29,200/QALY, and for the 70 and 80 year old patients it was $13,700/QALY and $8,700/QALY, respectively. These represent 1991 prices. A 5% discount rate was applied to both costs and benefits.

Authors' conclusions
The cost-effectiveness of captopril therapy for 50 to 80 year old survivors of MI with low ejection fraction compares favourably with other interventions for survivors of MI. It is not only effective for the survivors but also relatively cost-effective. Except when contraindicated, it should be added to the growing list of medical therapies for such patients.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator was not clearly stated. It may be that no captopril is not a relevant comparator to use in a study such as this since it may not reflect current general practice for treating patients with MI and low ejection fraction.

Validity of estimate of measure of benefit
The validity of the estimates of effectiveness may be weakened by the fact that the clinical trial used as a source of effectiveness data was not designed to address the questions of age-specific effectiveness implicit in the separate, age-specific economic models used in the economic study. In addition, part of the original clinical study sample (those aged under 40) was not considered in the economic models due to "low sample" considerations.

Validity of estimate of costs
On the other hand, the cost analysis seemed to cover all relevant issues likely to be present in a study such as this. Although limitations of applying costs obtained from a randomised, controlled trial to non-trial patients exist, the authors were able to show, through the sensitivity analyses performed, that the outcomes were not substantially altered, even with large changes in the base case cost estimates. The cost methodology was specified and costs were discounted.
Implications of the study
Further studies may be needed before clear implications can be derived from an economic study as to the efficiency of captopril therapy for MI survivors with a low ejection fraction.

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