Health and economic benefits of increased beta-blocker use following 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
Increased use of beta-blockers after myocardial infarction (MI). The study was based on the most commonly used beta-blockers, atenolol (100 mg once a day) and metoprolol (100 mg twice a day).

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
A hypothetical cohort of survivors of MI aged 35 to 84 years, who had no absolute contraindications (i.e., atrioventricular block greater than first degree, heart rate less than 60/min, asthma, or allergy/intolerance) for beta-blocker use.

Setting
The study setting was hospital. The economic analysis was carried out in the USA.

Dates to which data relate
Effectiveness, cost and utility data were obtained mainly from literature cited in a 1997 publication describing the model and from sources published between 1994 and 1999. One study from 1977 was also used to estimate quality of life. The price year was 1999-2000.

Source of effectiveness data
The evidence for the final outcomes were based on a literature review and assumptions made by the authors.

Modelling
The study used the Coronary Heart Disease (CHD) Policy Model, a computer-simulation Markov model of CHD in the US population. The costs and effects of the adopted strategies were estimated based on two cohorts of patients. The 'single-cohort' model: a cohort of MI survivors discharged in 2000 and followed up for 20 years; and the 'multicohort' model: treating 20 successive annual cohorts of patients with a first MI, starting in 2000. It was reported that the CHD Policy Model has been used for numerous studies for more than a decade and has been extensively validated by comparing its output with published statistics.

Outcomes assessed in the review
The outcomes obtained from the literature were as follows: CHD event rate reduction with beta-blocker use including
MI, sudden death from cardiac arrest, mortality, and effectiveness; quality-adjusted life-year (QALY) reductions due to beta-blockers. Other parameters used in the model were: beta-blocker eligibility; beta-blocker current use rate; withdrawal rates among patients with no relative contraindications and among those with relative contraindications.

Study designs and other criteria for inclusion in the review
It was reported that the primary data sources of this study for treatment effectiveness were meta-analyses of clinical trials and data from the National Cooperative Cardiovascular Project (CCP). The current use in 2000 was estimated by examining trends from 1990-98.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

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

Number of primary studies included
A total of 15 studies were referenced as the sources for the inputs incorporated in the model; including two meta-analyses.

Methods of combining primary studies
Meta-analyses and narrative methods were used to combine studies.

Investigation of differences between primary studies
Not reported.

Results of the review
The baseline values (range for sensitivity analyses) for the outcomes were as follows:

- beta-blocker eligibility, 92% (lower limit, 60%);
- beta-blocker current use rate, 44% (upper limit, 59%);
- withdrawal rates among patients with no relative contraindications and among those with relative contraindications, 12% and 30% (upper limit, 50%), respectively;
- CHD event rate reductions with beta-blocker use including MI 27%, sudden death from cardiac arrest 32%, mortality 22%, and duration of effectiveness (3 year full benefits, then 3 year reduced (7%), then 1% rate reduction for 14 years).
- QALY reduction due to beta-blockers was estimated to be 0% in the base estimate (upper limit, 1%).

Methods used to derive estimates of effectiveness
Assumptions made by the authors.
Estimates of effectiveness and key assumptions
The authors made the conservative assumption that all patients who withdrew from treatment would do so in the first year and hence experience none of the benefits of beta-blocker treatment. It was assumed that the beneficial effect of beta-blockers was independent of other medications.

Measure of benefits used in the economic analysis
Prevented MIs, CHD mortality, life-years gained, and QALYs gained in the time horizon of 2000-2020.

Direct costs
Costs were discounted. Cost items were reported separately. The perspective adopted in the cost analysis was stated to be that of society. The estimates for the drug costs were based on the 1998 average wholesale prices and assumed maximum dose for 20 years. The price year was 2000. All costs were adjusted to year 2000 using the 1999 Medical Services Consumer price Index and the assumption of a continued inflation rate of 3% for 1999-2000. The cost analysis did not cover the costs of the following: adverse effects due to beta-blockers since serious sequelae are infrequent and would not add significantly to the costs; the incremental costs of office visits, laboratory tests, and pharmacy costs that may be associated with beta-blocker use because these would be minimal; and the possible increased costs due to substitution of higher cost or less effective treatments. Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A series of one-way sensitivity analyses was performed on the main parameters of the model. Threshold values for the sensitive parameters were reported.

Estimated benefits used in the economic analysis
Changing beta-blocker use from 44% to all MI survivors except those with absolute contraindications in 2000 and continuing treatment for 20 years would result in 4,300 fewer CHD deaths, 3,500 MIs prevented, 45,000 life-years gained, and 35,000 QALYs gained compared with current use. If the increase in beta-blockers use were implemented in all first-MI survivors annually over 20 years, beta-blockers would result in 72,000 fewer CHD deaths, 62,000 MIs prevented, and 447,000 life-years gained. Benefits were discounted at 3% (range: 0%-10%).

Cost results
Increasing beta-blocker use in the Single-Cohort model would result in an incremental cost of $158,000,000 compared with current use. Costs were discounted at 3% (range: 0%-10%).

Synthesis of costs and benefits
The incremental cost-utility ratio of the strategy of increased use of beta-blockers compared with the current use was $4,500 in the Single-Cohort model. In the 'multicohort' model, increasing beta-blocker use from current to target levels would be cost-effective each year until 2010 and would approach a steady state of cost per QALY gained of $5,400 in 2020. Sensitivity analyses demonstrated that the cost-utility of beta-blocker therapy would always be less than $11,000 per QALY gained, even under unfavourable assumptions, and may even be cost saving. Restricting beta-blockers only to ideal patients (those without absolute and relative contraindications) would reduce the epidemiological impact of beta-blocker therapy by about 60%.

Authors’ conclusions
This study simulation indicates that increased use of beta-blockers after MI would lead to impressive gains in health and
would be potentially cost saving.

CRD COMMENTARY - Selection of comparators
Using current level of use and no use as the comparators allowed the active value of the interventional strategy to be evaluated.

Validity of estimate of measure of benefit
Internal validity would have been improved by information on the methods of literature review and combination of results used to derive the estimates.

Validity of estimate of measure of benefit:
The estimation of benefits was modelled. The instrument used to derive a measure of health benefit (Markov model), appears to have been appropriate.

Validity of estimate of costs
Some positive aspects of the cost analysis were as follows: adequate details of methods of cost estimation were given; the price year and perspective adopted in the cost analysis were specified; and sensitivity analysis was performed on cost data. However, it is not clear whether the cost calculations were based on true costs or charges; it appears that all important direct cost elements may not have been included in the cost analysis, as, for some reason, a group of cost components was excluded; the effects of alternative procedures on indirect costs were not addressed, thus reducing the validity of any evidence of net benefit to society.

Other issues
The authors’ conclusions are strengthened by the sensitivity analysis, although this was only a one-way sensitivity analysis. The issue of generalisability to other settings or countries was not explicitly addressed; and it is not clear whether the range of values adopted in the sensitivity analyses were meant to enhance the generalisability of the study results to other settings or countries. Appropriate comparisons were made with other studies.

Implications of the study
Although clinical trials would need to be conducted to conclusively demonstrate the efficacy of beta-blockers in patients with relative contraindications (e.g., diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, and congestive heart failure), the latest evidence and this analysis suggest that these patients can derive substantial benefits from beta-blocker use at a reasonable cost.

More extensive efforts will be required to encourage beta-blocker use. This will require multiple strategies and the involvement of physicians, pharmacists and other health care providers, policymakers, and patients.

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