Economic implications of extended-release metoprolol succinate for heart failure in the MERIT-HF trial: a US perspective of the MERIT-HF trial


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 study examined once-daily extended-release (ER) metoprolol added to standard treatment for patients with heart failure (HF). Standard treatment consisted of a diuretic, an angiotensin-converting enzyme inhibitor and, if required, digitalis. Dosages were not explicitly reported, but the authors stated that titration up to a maximum of 200 mg daily was allowed and could be varied on the basis of the patient’s characteristics.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with HF from left ventricular systolic dysfunction.

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 studies published between 1995 and 2000. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A discrete event simulation model was constructed to simulate the treatment of patients with HF from left ventricular systolic dysfunction. Each patient was assigned attributes such as age and gender (which help determine specific event risks) and was then exposed to these risks over time. The model consisted of 5 modules, specifically, start, events, hospitalisation, management and end. At the start, hypothetical patients with HF were created and assigned baseline characteristics. Weekly cycles were considered. Thus, every week the patients experienced a determined probability of hospitalisation from exacerbated HF, hospitalisation for other cardiovascular disease and for causes other than cardiovascular disease, death from cardiovascular disease, and death from other causes. The time horizon of the model was 2 years. Ten thousand patients were simulated each time the model was run, and the analyses were replicated 1,500 times. The structure of the model was depicted in the paper.
Outcomes assessed in the review
The outcomes estimated from the literature were:

the characteristics of the patient population,
the probabilities of events with standard therapy,
the ER metoprolol relative risk (RR) of events, and
the non-compliance rate.

Study designs and other criteria for inclusion in the review
The clinical data used in the model were all derived from different publications of the MERIT-HF trial. Moreover, the authors reported details of the estimates of clinical data in the appendix.

Sources searched to identify primary studies
Not applicable.

Criteria used to ensure the validity of primary studies
The validity of the primary studies was ensured by the use of data derived from a clinical trial.

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

Number of primary studies included
Four publications of the MERIT-HF trial provided the clinical data.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not applicable as data from the same patient sample were used.

Results of the review
In terms of the patient characteristics of the MERIT-HF trial, males accounted for 77.5% of the population. The age distribution was 10.7% aged 40 to 49 years, 22.9% aged 50 to 59 years, 35.3% aged 60 to 69 years, 30.6% aged 70 to 79 years, and 0.5% aged 80 to 81 years, with a mean of 63.7 years.

With standard therapy, the weekly probability values were as follows:

- cardiovascular death, 0.197%;
- other death, 0.014%;
- first hospitalisation for HF, 0.353%;
- subsequent hospitalisation for HF, if readmitted, 5.502%;
first hospitalisation for other cause, 0.516%; and

subsequent hospitalisation for other cause, if readmitted, 3.893%.

The ER metoprolol RR was as follows:

- cardiovascular death, 0.62;
- other death, 1.00;
- hospitalisation because of HF, 0.65; and
- other hospitalisations, 1.00.

The weekly rate of non-compliance was 0.267%.

Measure of benefits used in the economic analysis

The summary benefit measure used was the number of life-years (LYs) associated with the two treatments. This was estimated through a decision modelling approach. No discounting was applied as the benefit was estimated over a 2-year time horizon. Other model outputs (events such as deaths and hospitalisations) were also reported.

Direct costs

The analysis of the costs was carried out from the perspective of a third-party payer. It included the costs associated with office visits, hospitalisations, medications, and resources associated with death. The unit costs were not presented separately from the quantities of resources used since most costs were reported as macro-categories. Most resource use data were derived from the different publications of the MERIT-HF trial. Inpatient resource use data and costs were derived from all-payer 1999 acute care hospital discharge databases from five US states. The costs of office visits came from the national Medicare physician fee schedule, while drug costs came from the Red Book. Charges were adjusted to costs by means of a cost-to-charge ratio of 0.61, whenever relevant. The costs incurred in the second year were discounted at an annual rate of 3%. The price year was 2001. When 2001 values were not available, the costs were updated using appropriate Medical Care Inflation Indexes.

Statistical analysis of costs

Bootstrapped means and standard deviations were calculated for the costs.

Indirect Costs

The indirect costs were not included in the economic evaluation.

Currency

US dollars ($).

Sensitivity analysis

A univariate sensitivity analysis was carried out to assess the robustness of base-case costs and benefits to variations in the rates of death and hospitalisations, the time horizon and the discount rate. Alternative values were derived from the literature or were fixed by the authors. Acceptability curves were presented, based on the results of the model simulations.

Estimated benefits used in the economic analysis

Over a 2-year period, with standard therapy, patients survived on average 1.8 (+/- 0.004) years. ER metoprolol averted
death in 6.7 (+/- 1.1) per 100 patients. This effect translated into 7.1 (+/- 1.2) LYs gained per 100 patients over the 2
years of the model.

In addition, 14.4 (+/- 2.6) fewer hospitalisations due to heart failure per 100 patients were predicted for ER metoprolol
over 2 years, compared with usual treatment, and 10.9 (+/- 2.7) fewer all-cause hospitalisations per 100 patients.

Cost results
Over 2 years, the total cost per patient was $23,246 with metoprolol and $23,641 with standard treatment. The cost-
difference was -$395 (+/- 297).

The additional cost of ER metoprolol was more than offset by the reduction in costs associated with hospitalisations.

Synthesis of costs and benefits
An incremental analysis was carried out to combine the costs and benefits. However, in the base-case, an incremental
cost-effectiveness ratio was not calculated as metoprolol was a dominant strategy (both more effective and less
expensive).

The probabilistic analysis revealed that ER metoprolol was dominant in 90% of the 1,500 replications of the analysis.

The cost per LY gained with ER metoprolol over standard care never exceeded $4,200, and 98% of the time, the results
were either cost-saving or the ratios were below $2,000 per LY gained.

The results of the sensitivity analysis suggested that the model was somewhat sensitive to the use of a longer time
horizon, owing to the cost of the drug which continued to accrue. However, the incremental cost per LY gained was
always relatively low. The costs and benefits were minimally affected by changes in probabilities and the discount rate.

Authors’ conclusions
The use of extended-release (ER) metoprolol added to current treatment for patients with heart failure (HF) from left
ventricular systolic dysfunction prevented deaths and hospitalisations while reducing the cost of care from the
perspective of the third-party payer.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was appropriate as it reflected the current treatment used for patients with HF from left
ventricular systolic dysfunction. The dosages depended on the initial severity of disease and the readers were referred to
the original trial for more details. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from different publications of the same clinical trial, which was chosen because of the
large sample size. The use of data from a clinical trial should ensure a high internal validity, given the robustness of the
primary design. Extensive information on the estimation of clinical data was provided in the appendix, together with the
methods used to obtain weekly probabilities from the results of the trial. In general, the methodology applied appears to
have been appropriate. The impact of variations in some key clinical estimates was investigated in the sensitivity
analysis.

Validity of estimate of measure of benefit
The summary benefit measure was appropriate and is comparable with the benefits of other health care interventions.
Discounting was not performed, which was appropriate given the short timeframe of the analysis. The impact of the
intervention on other aspects of health, such as quality of life, was not investigated, although this would have been
helpful.
Validity of estimate of costs
The costs included were consistent with the perspective adopted in the study. A detailed breakdown of the costs was not provided, as most costs were presented as macro-categories. This may limit the possibility of replicating the analysis in other settings. The sources of the data were reported for all costs. When charges were used, a cost-to-charge ratio was applied. Discounting was relevant for costs accrued in the second year. The price year was reported, which will facilitate reflation exercises in other time periods. The costs were treated stochastically.

Other issues
The authors stated that comparisons with the findings from other studies were difficult, owing to the underlying differences in assumptions, data sources and populations. Further, a wide range of results has been published, although there appears to be some consistency in the cost-effectiveness of beta-blockers. In terms of the issue of the generalisability of the study results, the authors stated that clinical data were obtained from a multi-country study (although the analysis has the typical limitations of a controlled trial carried out in a non-natural context) and the costs were derived from several US payers, thus the external validity of the study should be high. The authors noted that the analysis was restricted to the time horizon of the trial, and extrapolations to longer time periods were uncertain. Thus, the current results are limited by the implicit assumption that the clinical probabilities remain constant over time. A further limitation was the applicability of the study conclusions to patients with very severe or very mild HF, which were insufficiently represented in the MERIT-HF study.

Implications of the study
The study results suggest that ER metoprolol is an effective and economically attractive treatment for patients with HF from left ventricular systolic dysfunction.

Source of funding
Supported in part by AstraZeneca.

Bibliographic details

PubMedID
16360958

DOI
10.1016/j.cardfail.2005.06.433

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adrenergic beta-Antagonists /administration & dosage /economics /therapeutic use; Adult; Aged; Aged, 80 and over; Cost-Benefit Analysis; Delayed-Action Preparations; Female; Heart Failure /drug therapy /economics /mortality; Hospital Costs; Hospital Mortality; Hospitalization /economics /statistics & numerical data; Humans; Male; Metoprolol /administration & dosage /analogues & derivatives /economics /therapeutic use; Middle Aged; Models, Econometric; Prospective Studies; Randomized Controlled Trials as Topic; Reproducibility of Results; Survival Analysis; Treatment Outcome; United States

AccessionNumber
22006000184

Date bibliographic record published
31/12/2006

Date abstract record published
31/12/2006