Reimbursement claims analysis of outcomes with carvedilol and metoprolol
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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
The use of carvedilol and metoprolol, two beta-blockers, for the treatment of heart failure (HF).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with HF. The inclusion criteria specified patients aged between 18 and 64 years with the following:

two in- or outpatient medical claims with HF (International Classification of Disease, 9th Revision, ICD-9, 428) as the primary diagnosis, separated by at least 1 month or 1 medical claim for HF;
less than two medical claims for hypertension during the study period, and at least one pharmacy claim for a thiazide or loop diuretic within the study period;
at least one pharmacy claim for carvedilol or metoprolol (but not both); and
6 months or more of continuous enrolment in the health plan after the first claim for carvedilol or metoprolol was identified.

Setting
The setting was likely to have been secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from June 1997 to December 1998. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness analysis.
**Study sample**
The use of power calculations was not reported. A sample of 245 eligible patients was retrospectively identified from claims data. There were 139 patients in the carvedilol group and 106 in the metoprolol group. The patients in the carvedilol group had a mean age of 52 (+/- 8) years and 76% were men. The patients in the metoprolol group had a mean age of 54 (+/- 7) years and 56% were men.

**Study design**
This was a retrospective cohort study that was carried out in HMOs located in geographically diverse areas. The HMOs covered more than 2 million lives. The data were extracted retrospectively from patient claims. The length of follow-up was 6 months and all the patients had complete follow-up data.

**Analysis of effectiveness**
All of the patients included in the initial study sample were considered in the analysis of effectiveness. The outcome measures used were:

- the rates of total, HF-related and cardiac-related hospitalisations, and emergency department (ED), outpatient and home health hospitalisations;
- time-to-event, defined as the time from the first prescription for carvedilol or metoprolol to hospital admission (censoring for patients who were not hospitalised occurred at 180 days after the first prescription);
- the number of health care services (hospitalisations, ED visits, and outpatient visits) used per patient over the six-month period.

Time-to-event was calculated using the Kaplan-Meier approach. At baseline, the two groups were comparable in age and co-morbidity, as assessed using the Charlson index. However, there were significantly more women and fewer patients with ischaemic heart disease in the carvedilol group. A regression analysis was conducted to assess the effect of treatment and the impact of baseline factors such as gender, age, Charlson index and physician specialty.

**Effectiveness results**
The rate of total hospitalisations was 36% with carvedilol and 62.3% with metoprolol, (p<0.001).

The rate of HF-related hospitalisations was 7.9% with carvedilol and 14.2% with metoprolol, (p non significant).

The rates of cardiac-related hospitalisations were 15.1% (carvedilol) and 24.5% (metoprolol), (p non significant).

The rates of ED hospitalisations were 23.8% (carvedilol) and 42.5% (metoprolol), (p=0.002).

The rates of outpatient hospitalisations were 97.1% (carvedilol) and 100% (metoprolol), (p non significant).

The rates of home health hospitalisations were 19.4% (carvedilol) and 28.3% (metoprolol), (p non significant).

For time-to-event, a significantly higher proportion of patients in the carvedilol group did not require hospitalisation during the follow-up period (the data were only shown in a graph).

The regression analysis showed that carvedilol was significantly associated with a decrease in the risk of any hospitalisation (adjusted odds ratio 0.35; 95% confidence interval: 0.20 - 0.63; p<0.001).

The number of services used per patient over the 6-month period was:

- 0.8 with carvedilol and 1.9 with metoprolol for total hospitalisation, (p<0.05),
- 0.7 with carvedilol and 1.6 with metoprolol for ED visits, (p<0.05), and
Clinical conclusions
The effectiveness study showed that, compared with metoprolol, carvedilol led to significantly fewer hospitalisations but resulted in more outpatient visits.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used in the economic evaluation. In effect, a cost-consequences analysis was conducted.

Direct costs
Discounting was not relevant since the costs were incurred during 6 months. The unit costs and the quantities of resources used were not given separately. The health services included in the economic evaluation were all-cause hospitalisations, ED visits, outpatient visits and home health visits. Both pharmacy and medical costs were included. Pharmacy costs included the amount paid plus copayments. Medical costs included the amount paid, copayment, reserved and deducted. Only patients with full pharmacy benefits were considered. The cost/resource boundary of the HMO appears to have been used. Resource use was estimated for the same sample of patients as that used in the effectiveness study. The costs were estimated from patient claims. The price year was not reported.

Statistical analysis of costs
An analysis of covariance was used to analyse log-transformed medical and pharmacy costs. It predicted 6-month expenditures with 95% confidence interval, after adjusting for age, gender Charlson index, physician specialty and HMO plan.

Indirect Costs
The indirect costs were not included in the analysis of costs.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The pharmacy costs per patient were $1,677 with carvedilol and $1,322 with metoprolol, (p<0.001).

The medical costs per patient were $6,424 with carvedilol and $13,153 with metoprolol, (p<0.001), mainly due to the lower hospitalisation costs per patient ($4,563 and $10,685, respectively; p<0.005).

The total costs per patient over the 6-month period were $8,100 with carvedilol and $14,475 with metoprolol, (p<0.025).

Similar results were observed in the adjusted cost analysis.
Synthesis of costs and benefits
Not relevant since a cost-consequences approach was taken.

Authors' conclusions
Patients with heart failure (HF) who received carvedilol had lower costs, fewer hospitalisations, and a longer time to first hospitalisation than patients who received metoprolol.

CRD COMMENTARY - Selection of comparators
The authors stated that both carvedilol and metoprolol were two widely prescribed beta-blockers. However, the use of other comparable therapies was not investigated. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The basis of the effectiveness analysis was a retrospective cohort study, which had some limitations. Such limitations were related to not only the retrospective nature of the study, but also the potential role played by selection bias and confounding factors. The two groups were not well balanced at baseline. Statistical analyses were conducted to assess the impact of potential confounding factors on the effectiveness outcomes. The length of follow-up was stated, but it was unclear whether a longer follow-up period would have been more appropriate. However, as the authors noted, details of prior drug consumption were not available. The study sample was likely to have been representative of the study population since the patients were identified at different centres. The authors noted that the use of a financial database to gather clinical information might have introduced some bias due to errors, coding variations and incompleteness. Finally, the use of hospitalisation to assess the impact of the intervention on patient health was not particularly appropriate. The use of a prospective design and more valid effectiveness measures would have been helpful.

Validity of estimate of measure of benefit
No summary benefit measure was used because a cost-consequences analysis was conducted.

Validity of estimate of costs
The perspective of the study appears to have been that of the HMO. Accordingly, all the relevant categories of costs were included in the analysis. However, a detailed breakdown of the cost items was not reported. The unit costs and price years were not provided, thus limiting the possibility of replicating the study and carrying out reflation exercises in other settings. Statistical tests were conducted on the costs, but all the estimates were specific to the study setting. Sensitivity analyses were not performed. It was unclear whether charges were used.

Other issues
The authors compared their findings with those from other studies, and found similar results. With respect to the external validity of the study, the authors noted that their conclusions should be limited to a sample of relatively young patients, as only individuals younger than 65 years of age were enrolled. However, sensitivity analyses were not conducted. The authors noted some limitations to the validity of the analysis, which have been reported already.

Implications of the study
The authors suggested that future studies should be based on larger sample sizes and be of a prospective design.

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Other publications of related interest

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