Long-term cost-effectiveness analysis of nebivolol compared with standard care in elderly patients with heart failure: an individual patient-based simulation model

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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.

CRD summary
The objective was to examine the cost-effectiveness of nebivolol in comparison with standard care for the treatment of chronic heart failure (CHF) in patients aged 70 years and over. The authors concluded that nebivolol was a cost-effective treatment for CHF in elderly patients. The study was well conducted and satisfactorily reported. The issue of uncertainty was well addressed. The authors' conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of nebivolol in comparison with standard care for the treatment of chronic heart failure (CHF) in elderly patients aged 70 years and over.

Interventions
Nebivolol (target dose of 10mg once daily after a maximum of 16 weeks titration period starting with 1.25mg daily) was compared with standard care, which covered several drugs but excluded β-blockers.

Location/setting
UK/primary and secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model with individual patient-based simulations. The model was populated with data obtained from a single study, and a lifetime horizon was considered. The authors stated that the analysis was carried out from the perspective of the UK National Health Service (NHS).

Effectiveness data:
Clinical inputs for the model (treatment effect and transition probabilities) were derived from the Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors with Heart Failure (SENIORS), a randomised, double-blind, parallel-group, multicentre, international trial (RCT). A sample of 2,135 patients was enrolled from 11 countries and 2,128 patients (1,067 in the nebivolol group and 1,061 in the standard care group) were followed. Mean age was 76.1 years in both groups, and follow-up was for a minimum of 12 months and a maximum of 40 months. All-cause mortality was based on UK official statistics. The primary clinical outcome was mortality or cardiovascular (CV) admission.

Monetary benefit and utility valuations:
Utility valuations were not available from the SENIORS study and were derived from another RCT, namely the Cardiac Resynchronization – Heart Failure (CARE-HF) trial, which made a distinction among health states defined by New York Heart Association (NYHA) classes.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure. A 3.5% annual discount rate was applied to QALYs accrued after the first year.
Cost data:
The economic analysis included drugs, general practitioner (GP) visits, outpatient specialist visits, and CV-related hospitalisations. Resource use was derived from the SENIORS study, except for some assumptions on the number of specialist visits. Drug costs were taken from the British National Formulary. Hospitalisation costs were based on the national schedule of reference costs, while other health service costs came from Unit Costs of Health and Social Care. Costs were in Euros (EUR). The price year was 2006. Future costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
Both deterministic and probabilistic sensitivity analyses were carried out. In the former, alternative assumptions on age of starting treatment, discount rates, and number of outpatient specialist visits were made on the basis of authors' opinions. In the latter, probabilistic distributions were assigned to model inputs in order to provide confidence intervals (CIs) around the mean values for cost-effectiveness and cost-utility ratios, and to generate cost-effectiveness acceptability curves (CEACs).

Results
The expected costs were EUR 6,740 with standard treatment and EUR 9,288 with nebivolol. The expected LYs were 7.547 with standard treatment and 8.378 with nebivolol. The expected QALYs were 5.194, with standard treatment and 5.843 with nebivolol.

The incremental cost per LY gained with nebivolol over standard care was EUR 3,066 (95% CI: EUR 2,877, EUR 3,277). The incremental cost per QALY gained with nebivolol over standard care was EUR 3,926 (95% CI: EUR 3,731, EUR 4,159).

The CEAC showed that, at an NHS willingness to pay of EUR 4,434 per QALY, the probability of nebivolol being cost-effective approached 100%.

The deterministic sensitivity analysis indicated that, even if patients started treatment at 80 years (the oldest cohort), the incremental cost per QALY was EUR 5,291, well below commonly quoted thresholds.

Authors' conclusions
The authors concluded that nebivolol was a cost-effective treatment for CHF in elderly patients.

CRD commentary
Interventions:
The selection of the two comparators was appropriate in that a new treatment was compared with the usual approach for this patient population. The authors justified the exclusion of β-blocker drugs given the lack of head-to-head comparisons.

Effectiveness/benefits:
The clinical evidence came from a RCT, which is generally considered to be a valid source of evidence. Further strengths of this study were the multi-centre design, the large patient sample, and the use of double-blinding. The statistical approaches used in the derivation of clinical endpoints were described. Some key details on the patient profiles were given. More information may be available in the primary publication of the SENIORS trial. Both QALYs and LYs gained were used as benefit measures and the source for the utility weights was given. QALYs are appropriate given the impact of the disease on the quality of life. QALYs and LYs gained have the further advantage of being comparable with the benefits of other health care interventions.

Costs:
The analysis of costs was consistent with the perspective. A breakdown of cost items was provided and unit costs were presented. Other details of the analysis such as the price year, use of discounting, sources of data, and statistical analyses were reported. Overall, the economic study was well conducted and reported, which enhances the transparency of the analysis. This will help if replicating the economic study in other settings and time periods.
The use of an incremental analysis to combine the costs and benefits was appropriate given the higher benefits and higher costs of nebivolol. The sensitivity analysis investigated areas of uncertainty both in individual model inputs (univariate sensitivity analysis), and in simultaneous simulations (probabilistic analysis). The authors provided a clear description of the decision model in terms of health states and the patterns of transition. One strength of the model was the use of individual patient-based simulations which allowed the use of time-dependent transition probabilities. The results of the study were clearly presented and discussed.

Concluding remarks:
On the whole, the study was well conducted and satisfactorily reported. The issue of uncertainty was well addressed. The authors’ conclusions appear to be valid.

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Other publications of related interest


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