Pharmacoeconomic modeling of nesiritide versus dobutamine for decompensated heart failure

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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 study examined two treatments, nesiritide (NES) and dobutamine (DOB), for patients with decompensated heart failure (DHF). NES was assumed to be administered at a rate of 0.015 or 0.030 microg/kg per minute, while DOB was administered at a rate of >=5 microg/kg per minute.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with acute DHF.

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

Dates to which data relate
The clinical data, as well as some information on resource use, were derived from studies published between 2000 and 2004. The price year was 2004.

Source of effectiveness data
The clinical data used in the economic evaluation were:

- the rates of readmissions (at 30 days for analyses 1 to 3; at 21 days for analysis 4),
- the 6-month mortality rates, and
- age- and gender-stratified life expectancy for patients alive 6 months after initial hospital admission.

Modelling
A decision tree model was constructed to simulate the clinical and economic impact of the two treatments under examination in a hypothetical cohort of patients with DHF. The structure of the decision tree was reported and was very simple. Patients could receive one of the two drugs under analysis followed by short-term readmission for heart failure or no readmission, and could be dead or alive after 6 months. The time horizon of the decision model was lifetime.
Sources searched to identify primary studies
Readmission rates and 6-month mortality rates were derived from the two published RCTs on NES, the Prospective Randomized Evaluation of Cardiac Ectopy with Dobutamine or Natrecor Therapy (PRECEDENT) trial and the Nesiritide Study Group (NSG). Some information on dosages and sample sizes were reported for both studies. Life expectancy was derived from US life tables.

Methods used to judge relevance and validity, and for extracting data
The primary studies were identified selectively in order to include the best evidence available. In effect, no systematic search for data was reported. Observational studies were not included since they are likely to provide less valid estimates of drug efficacy. Also, only the PRECEDENT trial was used in the base-case analysis, as possible confounding by indication was present in the NSG (the authors stated that patients in the DOB group were more severe than patients in the NES group at baseline).

Measure of benefits used in the economic analysis
The summary benefit measure was the number of life-years (LYs) after initial hospitalisation. The LYs were estimated using a modelling approach and life expectancy data from the general population. Discounting does not appear to have been performed.

Direct costs
The viewpoint of the third-party payer was presumably used in the analysis. The analysis included the costs of drugs and hospitalisations (both at initial admission and subsequent readmissions). The unit costs and resource quantities used were presented separately for the drugs only. In analyses 1 to 3, the costs associated with hospital readmissions were assumed to have been the same regardless of treatment arm. The costs of hospitalisations, which were included in analysis 4, came from Health Care Cost and Utilization Project records (charge-to-cost-adjusted costs for the initial hospitalisation dependent on age, gender and presence of clinical events reported in both RCTs used in the analysis of the clinical data). The drug costs were estimated from average wholesale prices using drug dosages from the clinical trials. Discounting was not performed as the costs were incurred during a short time. The price year was 2004.

Statistical analysis of costs
The economic data were assigned probabilistic distributions.

Indirect Costs
Productivity costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
The issue of uncertainty was addressed by running 51 consecutive Monte Carlo simulations for cohorts of 1,000 hypothetical patients for each of the four analyses. A description of the probabilistic distributions and reasons for the choice of the distributions were given. Analysis 1 incorporated a probabilistic sensitivity analysis in all model parameters. In analyses 2 to 4, a probabilistic sensitivity analysis was conducted on some parameters, while other parameters were considered fixed in order to represent best or worst scenarios.

Estimated benefits used in the economic analysis
The expected LYs with NES and DOB were, respectively:
4.68 (+/- 0.18) and 4.36 (+/- 0.22) (difference 0.33 +/- 0.22) in analysis 1;  
5.09 (+/- 0.05) and 3.90 (+/- 0.08) (difference 1.19 +/- 0.07) in analysis 2;  
4.25 (+/- 0.07) and 4.83 (+/- 0.05) (difference -0.57 +/- 0.05) in analysis 3; and  
4.73 (+/- 0.07) and 4.24 (+/- 0.08) (difference 0.48 +/- 0.05) in analysis 4.

**Cost results**  
The expected costs per patient with NES and DOB were, respectively:

- $12,225 (+/- 178) and $11,974 (+/- 249) (difference $251 +/- 290) in analysis 1;  
- $11,845 (+/- 31) and $12,579 (+/- 107) (difference -$734 +/- 106) in analysis 2;  
- $12,706 (+/- 98) and $11,464 (+/- 62) (difference $1,242 +/- 73) in analysis 3; and  
- $12,077 (+/- 50) and $12,153 (+/- 108) (difference -$77 +/- 87) in analysis 4.

**Synthesis of costs and benefits**  
Average and incremental cost-effectiveness ratios (ACERs and ICERs, respectively) were calculated in order to combine the total costs and LYs.

- The ACERs of NES and DOB were, respectively:  
  - $2,611 and $2,749 in analysis 1;  
  - $2,327 and $3,226 in analysis 2;  
  - $2,986 (no estimate for DOB) in analysis 3; and  
  - $2,555 and $2,864 in analysis 4.

The incremental analysis showed that the ICER with NES over DOB was $767 in analysis 1, while NES dominated DOB in analyses 2 and 4, DOB dominated NES in analysis 3. The authors stated that for analysis 1, the 95% confidence interval around the mean ICER spanned all four quadrants of the incremental cost-effectiveness scatter plot.

**Authors' conclusions**  
No robust conclusion about the cost-effectiveness of nesiritide (NES) versus dobutamine (DOB) for the treatment of decompensated heart failure (DHF) could be drawn, owing to the uncertain estimates obtained in the decision model.

**CRD COMMENTARY - Selection of comparators**  
The authors justified the choice of DOB as the main comparator of NES, despite a few differences in the pharmacological effects of these agents. Dosages for both drugs were reported. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**  
The clinical data used to populate the decision model were derived from selectively identified studies. Although a systematic review of the literature was not undertaken, the choice of the primary studies was appropriate as the authors' aim was to select the best evidence available. Some information on the primary studies was reported. In general, the use of RCTs ensures a high internal validity. The authors justified their use of the PRECEDEENT trial instead of the NSG trial for the base-case analysis, and this appears appropriate.
Validity of estimate of measure of benefit
The use of LYS as the summary benefit measure was appropriate as survival is the key outcome of a treatment for DHF. LYS have the further advantage of being comparable with the benefits of other health care interventions.

Validity of estimate of costs
The cost analysis was restricted to the direct medical costs, although the perspective of the analysis was not explicitly stated. Thus, it would appear that the viewpoint of a third-party payer has been adopted. The authors reported extensive information on the categories of costs included, their sources, the price year and the probabilistic distributions of economic inputs. However, little information on resource use was given. The impact of variations in the cost estimates was investigated in the probabilistic sensitivity analysis.

Other issues
The authors pointed out differences between their findings and those from the previous economic evaluation of NES versus DOB. The issue of the generalisability of the study results to other settings was not explicitly addressed, although the sensitivity analysis enhances the external validity of the study. Further, a full probabilistic analysis was appropriate to deal with the uncertainty surrounding both clinical and economic inputs of the model.

The authors noted some potential limitations of the analysis, which have already been highlighted, such as the choice of an appropriate comparator and the use of cost data from other studies. However, the authors' conclusions are subject to some doubts. For example, it is unclear why they did not present cost-effectiveness acceptability curves that would have provided information on the probability of NES being cost-effective given different willingness-to-pay thresholds. In fact, the ICER found in analysis 1 is very favourable to NES, and it was not clear why it was considered necessary for all the points in the 95% confidence interval to be in a unique quadrant. The authors seem to have used Bayesian techniques to assess uncertainty around key model parameters, but then drawn their conclusions on the basis of a frequentist statistical background.

Implications of the study
The study results do not indicate clearly which treatment is the best option for patients with DHF.

Source of funding
None stated.

Bibliographic details

PubMedID
16509026

Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
Cardiotonic Agents /adverse effects /economics /therapeutic use; Cost-Benefit Analysis; Decision Trees; Dobutamine /adverse effects /economics /therapeutic use; Follow-Up Studies; Heart Failure /drug therapy /economics /mortality; Hospitalization /statistics & numerical data; Humans; Models, Economic; Models, Statistical; Monte Carlo Method; Natriuretic Agents /adverse effects /economics /therapeutic use; Natriuretic Peptide, Brain /adverse effects /economics /therapeutic use

AccessionNumber
22006000298

Date bibliographic record published
31/12/2007

Date abstract record published
31/12/2007