Cost-effectiveness of B-type natriuretic peptide testing in patients with acute dyspnea

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
A diagnostic strategy that involved B-type natriuretic peptide (BNP) testing in patients presenting with acute dyspnoea was studied.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study was concerned with patients presenting to the hospital emergency department with acute dyspnoea. The exclusion criteria included trauma, severe renal disease and cardiogenic shock.

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

Dates to which data relate
The effectiveness evidence and resource use data were collected during the BASEL study (Mueller et al. 2004, see 'Other Publications of Related Interest' for bibliographic details). The resource use prices dated from 2002 and 2003.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
A total of 665 patients were screened, of which 213 were ineligible or did not give consent. Thus, 452 patients were enrolled in the study. The sample consisted of consecutive patients. Power calculations were not described in this paper. Two hundred and twenty-five patients were assigned to the BNP strategy group and 227 to the conventional strategy group.

Study design
The BASEL study was a randomised, controlled, single-blind trial. Groups were assigned, with the use of a computer-
generated randomisation scheme, in a 1:1 ratio without stratification. The duration of follow-up was 180 days; patients were contacted by telephone interview 6 months after initial presentation. One patient in the BNP group was lost to follow-up (99.8% complete). Physicians who were not involved in patient care assessed all end points in a blinded fashion, using all patient medical records. Further details of the study design are reported elsewhere (Mueller et al. 2004).

Analysis of effectiveness
The baseline demographic and clinical characteristics were well matched between the two treatment groups. The analysis of the clinical study was conducted on an intention to treat basis (i.e. all randomised patients). The primary outcome was all-cause mortality.

Effectiveness results
The outcomes were assessed at the initial hospital visit, and at 90 and 180 days.

At 180 days, all-cause mortality was 20% in the BNP group and 23% in the conventional group, (p=0.42). BNP patients spent significantly fewer total days in hospital than control patients, a median of 10 days (interquartile range, IQR: 2 to 24) compared with 14 days (IQR: 6 to 27), (p=0.05).

During the initial presentation, 75% of the BNP group and 85% of the conventional group were hospitalised, (p=0.008) and 15% (BNP group) and 24% (conventional group), respectively, were admitted to intensive care, (p=0.01). BNP patients spent significantly fewer days in hospital than the controls, a median of 8 days (IQR: 1 to 16) versus 10 days (IQR to 18), (p=0.02).

Clinical conclusions
The authors concluded that BNP testing reduced the rate of hospital admission, the rate of admission to intensive care and the time to discharge.

Measure of benefits used in the economic analysis
The benefit measure was the reduction in all-cause mortality rate at 180 days. This was derived directly from the trial.

Direct costs
Discounting was not required because of the short follow-up. The costs and most quantities were reported separately. The analysis included hospital costs (primarily determined by intensity and length of care) and cardiovascular and pulmonary medications. It was stated that other medications were not included because differences would be more likely due to baseline conditions than related to BNP testing. The estimation was based on BASEL data collected prospectively. Hospital charges were used as the most appropriate estimate of true costs. These were standardised according to the rates for patients with general insurance living in Basel, Switzerland. Medication costs dated from 2003 and BNP testing was priced from 2002. The cost of days in hospital and treatment included all hospitalisations during the follow-up period.

Statistical analysis of costs
A non-parametric bootstrap analysis was used to estimate the 95% confidence intervals for differences in mean costs and to assess the shape of the joint sampling distribution of the differences in mean individual costs and effects between the two treatment groups. A statistical significance level of 0.05 was used and all hypothesis testing was two-tailed. The costs were compared using bootstrap t-tests.

Indirect Costs
No indirect costs were included.
Currency
Swiss francs (CHF). Swiss francs were converted to US dollars ($) using the average, actual currency conversion rate during the trial period (not reported).

Sensitivity analysis
Uncertainty surrounding the cost-effectiveness estimate was represented by 95% and 50% confidence ellipses on the cost-effectiveness plane. Sensitivity analyses were performed for changes in the duration of initial hospitalisation, costs of hospital stays, expense for BNP testing, time in the intensive care unit, the cost of long-term medication and re-hospitalisation with BNP guidance. Ranges were selected conveniently (e.g. duration -10%, -20% and -30%) rather than based on actual data.

Estimated benefits used in the economic analysis
All-cause mortality at 180 days was 20% in the BNP group and 23% in the conventional group, (p=0.42).

Cost results
The mean total treatment cost at 180 days was significantly lower in the BNP group than in the control group, $7,930 (standard deviation, SD=8,805) per patient versus $10,503 (SD=10,176) per patient, (p=0.004).

Synthesis of costs and benefits
The incremental cost-effectiveness ratio was calculated via 5,000 bootstrap replications and was represented on a cost-effectiveness plane.

The point estimate was not reported directly, but it could be deduced from the centre point of the confidence ellipses that BNP testing dominated the conventional strategy.

In 80.6% of bootstrap replications, BNP guidance was less expensive and resulted in lower mortality (i.e. it dominated the conventional diagnostic strategy). In 19.3% of replications, it was less expensive and resulted in higher mortality.

In less than 0.1% of replications, BNP guidance was associated with higher costs and higher or lower mortality.

The cost-effectiveness of BNP guidance was robust to changes in several variables, but was sensitive to changes in re-hospitalisation days with BNP guidance.

A sub-group analysis showed that the benefit of BNP testing to reduce total treatment cost at 180 days was particularly evident in patients with a history of coronary artery disease ($8,566 versus $12,194 in the control group; p=0.005) and in patients with a history of pulmonary disease ($8,876 versus $12,408 in the control group; p=0.01).

Authors’ conclusions
The major finding was that B-type natriuretic peptide (BNP) testing is cost-effective. This finding was driven by significantly fewer total days in hospital, first seen at initial presentation and fully maintained at the 180-day follow-up.

CRD COMMENTARY - Selection of comparators
The conventional diagnostic strategy was fully described and was justified as best practice according to the most recent clinical guidelines in the authors’ setting. You should decide whether it represents current practice in your own setting. Given that the comparators differed only in BNP testing, the study may still be useful to estimate the incremental value of adding BNP testing to any baseline diagnostic strategy.
Validity of estimate of measure of effectiveness
The analysis was based on a randomised controlled trial, which was appropriate for the study question. The study sample was shown to be representative of the study population in terms of its demographics and clinical characteristics. The patient groups were comparable at baseline. The analysis of effectiveness was handled credibly, using intention to treat for all data. Appropriate statistical tests were undertaken.

Validity of estimate of measure of benefit
The measure of health benefit was obtained directly from the effectiveness analysis and measured quantity but not quality of life. The choice of estimate was not justified. It is possible, though unlikely, that BNP testing could have an impact on the patient's experience and hence quality of life, which would not be measured by the outcome. The cost-effectiveness analysis was handled thoroughly and credibly.

Validity of estimate of costs
The perspective was not stated but it appears to have been that of the health insurance provider, as hospital charges were standardised according to reimbursement rates for patients with general insurance. It is therefore possible that categories of costs relevant to this perspective were excluded (e.g. patients might be able to claim for time off work). Even if the perspective was intended to be that of the health care provider, it is likely that some direct costs were omitted since only hospitalisation costs (not, for example, general practitioner visits) were collected during the period post-discharge from hospital after initial presentation. The authors included only medication costs, which were considered to be related to BNP testing. It is unclear whether these omissions would have had a substantial effect on the authors’ conclusions.

The costs and the quantities were reported separately but the breakdown of ward stay during hospitalisation was not described in sufficient detail for the analysis to be reproduced. The quantities and costs were compared using appropriate statistical tests. The costs were drawn from hospital charges adjusted to avoid imbalance due to differences in reimbursement or charges associated with different types or classes of insurance. Prices of medications were given as standard rates; the source was not provided. The dates were not fully reported and the conversion rate was not given.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other countries was addressed, with the authors stating that extrapolation to North America and Europe seems justified given that disease prevalence, patient characteristics, treatment strategies and treatment costs are similar (citations given). The authors did not present their results selectively. The conclusions reflected the scope of the analysis and the patient population enrolled. The authors reported three limitations to their study. First, resource use was limited to items collected in the BASEL study. Second, the results are generalisable only to patients presenting in the emergency room. Finally, it is possible that different BNP cut-off values would be appropriate for patients with renal disease or obesity.

Implications of the study
The authors found that this long-term follow-up study confirms the benefits of BNP testing against some recent criticism of its value in clinical medicine. They suggested that the effects of BNP testing in patients presenting to physicians in private practice should be confirmed.

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**Other publications of related interest**

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