Community screening for left ventricular systolic dysfunction using plasma and urinary natriuretic peptides

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
Community screening strategies for left ventricular systolic dysfunction (LVSD) were examined. The strategies used plasma and urinary natriuretic peptides.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised men aged between 45 and 80 years and women aged between 55 and 80 years who were undiagnosed for LVSD. Patients with a prior diagnosis of LVSD or heart failure were excluded, as were those for whom screening was considered inappropriate (e.g. housebound or terminally ill patients).

Setting
The level of care was the community. The economic study was undertaken in Leicester, UK.

Dates to which data relate
The effectiveness and resource use data were collected between September 1999 and May 2002. No price year was reported.

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

Link between effectiveness and cost data
The resource use data were derived prospectively from the same patient sample as that which provided the effectiveness evidence. The unit costs were derived from another study (see 'Direct Costs' field).

Study sample
No sample size or power calculations were reported. The study sample included randomly selected patients from 21 general practices in the former Leicester Health Authority area. A total of 2,392 people were invited to participate in the study. Of these, 1,360 patients accepted the screening invitations. Only participants with an analysable echocardiogram and available simultaneous blood and urine samples were included in the study. Thus, 1,308 individuals (43.3% women) were included in the sample. The mean age was 63 years (range: 45 - 80). The initial sample was
appropriate for the clinical question as it included patients in whom screening strategies may identify asymptomatic LVSD.

**Study design**
This was a diagnostic accuracy study that was carried out in 21 general practices. The patients underwent echocardiography scan and blood and urine sampling. One operator conducted the echocardiography scans. The authors did not report whether the test result evaluators were unaware of the results from the other tests.

**Analysis of effectiveness**
The primary health outcomes used in this study were the prevalence of LVSD in the study sample and the diagnostic performance of each screening strategy. Patients with a left ventricular wall motion index (LVWMI) score of at least 1.8 (equivalent to a left ventricular ejection fraction of 40%) were considered to have LVSD. The area under the curve for receiver operator characteristic curves (ROC-AUC) was estimated, along with the 95% confidence intervals. The authors also determined the independent predictive factors for LVSD, using a binary logistic regression analysis. Then, the product of the urinary and plasma N-BNP level was examined. The secondary outcome examined was the performance to detect other cardiac abnormalities in individuals with preserved systolic function.

The authors did report summary statistics for the study participants.

**Effectiveness results**
Twenty eight patients had LVSD.

The sensitivity, specificity, and positive and negative predictive values (PPV and NPV) were as follows:

- plasma N-BNP test, sensitivity 96.4%, specificity 41.0%, PPV 3.4% and NPV 99.8%;
- urinary N-BNP test, sensitivity 96.4%, specificity 67.2%, PPV 6.0% and NPV 99.9%;
- plasma and urinary N-BNP tests, sensitivity 96.4%, specificity 78.0%, PPV 8.7% and NPV 99.9%;
- sequential tests (urine and then plasma N-BNP), sensitivity 96.4%, specificity 41.2%, PPV 8.7% and NPV 99.5%;
- plasma N-BNP test in high-risk individuals, sensitivity 95.7%, specificity 42.8%, PPV 5.4% and NPV 99.7%;
- urinary N-BNP test in high-risk individuals, sensitivity 95.7%, specificity 70.0%, PPV 9.8% and NPV 99.8%; and
- plasma and urinary N-BNP tests in high-risk individuals, sensitivity 95.7%, specificity 79.1%, PPV 13.5% and NPV 99.8%.

Independent predictive factors for LVSD included plasma N-BNP, urinary N-BNP and male gender. These accounted for 41.4% of the variance (Nagelkerke $r^2$, p<0.0005).

The performance of the logistic model was sensitivity 96.4%, specificity 76.6%, PPV 8.3% and NPV 99.9%.

The receiver operator characteristic curves showed both plasma (ROC-AUC = 0.840) and urinary N-BNP (ROC-AUC = 0.831) to be as effective in excluding LVSD, irrespective of a correction for urinary creatinine.

The specificity and PPV of urinary N-BNP were higher than those of plasma N-BNP.

Both the logistic model and the product of the urinary and plasma N-BNP level yielded a higher ROC-AUC and specificity for the detection of LVSD than either plasma N-BNP or urinary N-BNP alone, while maintaining a high NPV.
Plasma N-BNP showed significant ROC-AUCs for the detection of atrial fibrillation and valvular abnormalities that were not replicated with urinary N-BNP. Neither test was clinically useful for the detection of left ventricular hypertrophy. For the detection of a combination of LVSD, atrial fibrillation or valvular abnormalities, both plasma and urinary N-BNP had significant ROC-AUCs, although plasma N-BNP performed better than urinary N-BNP.

**Clinical conclusions**
The authors concluded that both plasma and urinary N-BNP were effective at excluding the presence of LVSD, with urinary N-BNP exhibiting a higher specificity. The plasma and urinary N-BNP product further enhanced the specificity and PPV of LVSD diagnosis. Sequential testing (urine, followed by plasma N-BNP in the urine-positive cases) was likely to achieve similar specificity.

**Measure of benefits used in the economic analysis**
No summary measure of benefit was used. The study was therefore classified as a cost-consequences analysis.

**Direct costs**
The costs of undertaking laboratory tests were included in the analysis. The cost components were not reported. The costs of different screening strategies were based on another cost-effectiveness analysis (Heidenreich et al., see 'Other Publications of Related Interest' for bibliographic details). The unit costs were reported, but the resource quantities were not. Discounting was also not reported, but it would not have been relevant if the authors were interested only in the immediate screening costs. No price year was reported.

**Statistical analysis of costs**
The cost data were treated deterministically.

**Indirect Costs**
No indirect costs were included in this study.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was reported.

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

**Cost results**
The total cost and the cost to detect one case of LVSD were, respectively:

- for echocardiography scan, $549,360 and $15,555;
- for plasma N-BNP tests in all patients, $370,716 and $10,497;
- for urinary N-BNP tests in all patients, $229,596 and $6,501;
- for plasma and urinary N-BNP tests in all patients, $213,072 and $6,033;
for urinary N-BNP tests in all patients and plasma N-BNP in urine-positive cases, $179,756 and $5,089;

for echocardiography scan in all IHD patients and urinary N-BNP in the remainder, $264,100 and $7,478;

for echocardiography scan in all IHD, hypertensive and diabetic patients and urinary N-BNP in the remainder, $336,300 and $9,522;

for echocardiography scan in all patients with IHD, hypertension, diabetes, atrial fibrillation, left ventricular hypertrophy and valve lesions and urinary N-BNP in the remainder, $290,885 and $10,773.

Synthesis of costs and benefits
The costs and benefits were not combined as the study was, in effect, a cost-consequences analysis.

Authors' conclusions
Both plasma and urinary N-BNP N-terminal precursor of B-type natriuretic peptide) were effective at excluding the presence of left ventricular systolic dysfunction (LVSD), with urinary N-BNP exhibiting a higher specificity. Sequential testing (urine, followed by plasma N-BNP in the urine-positive cases) was likely to achieve similar specificity while limiting the number of echocardiograms and the total number of N-BNP measurements, thus reducing the echocardiographic burden in screening programmes.

CRD COMMENTARY - Selection of comparators
Although no one strategy was used as the comparator, the authors justified the choice of plasma N-BNP as it was the recommended screening test in Europe and the USA. It appears that all potential screening alternatives for LVSD have been assessed in the study. in addition, the choice of the risk factors examined for the selective screening strategies was based on the literature and a logistic regression analysis.

Validity of estimate of measure of effectiveness
The analysis was based on a diagnostic accuracy study, which was appropriate for the study question. Details of the study sample, such as demographics, were given to set the context for the reader and to enable an assessment of generalisability to other settings. The authors reported appropriate outcomes for a diagnostic yield study. The study sample appears to have been representative of the study population. The main drawback of the study was the lack of power calculations and subsequent small sample size. This meant that it was unclear whether or not the study sample was sufficiently large to accurately assess the diagnostic accuracy of the screening strategies.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefits. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
The authors did not explicitly report the study perspective adopted with regard to the costs. Thus it was not possible to assess whether all the relevant categories of costs were included in the analysis. The analysis appears to have focused on the immediate direct costs of screening patients. The cost-savings due to false positives and false negatives avoided were not included in the analysis. The unit costs and the quantities were not reported separately, which will hinder the generalisability of the results to other settings. It was unclear whether the overhead costs were incorporated in the unit cost estimates since the cost components were not reported. The unit costs were derived from a published study. No statistical or sensitivity analysis of the costs was carried out, and this limits the interpretation of the results. The failure to report a price year also limits any future reflation exercise. Discounting was not relevant and was not carried out.
Other issues
The authors compared their effectiveness results, but not their economic results, with those from other studies. The authors acknowledged that the validity of their findings in other populations remains to be established. In particular, the value of urinary and plasma N-BNP in larger groups of high-risk individuals, as well as in ethnic minorities, should be examined. In addition, they could not approach individuals who declined the offer of screening to examine reasons for their refusal. The conclusions were an accurate reflection of the scope of the analysis and the results presented. The authors reported no other limitations to their study.

Implications of the study
The authors made no specific recommendations for changes in policy or practice and/or the need for further research.

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Other publications of related interest

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