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# HEDS Discussion Paper 05/06

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## **Health Economics and Decision Science**

**Discussion Paper Series**

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**Economic Evaluation of the Routine Use of Echocardiography versus Natriuretic Peptide and ECG-Targeted Echocardiography in the Diagnosis of Heart Failure.**

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This series is intended to promote discussion and to provide information about work in progress. The views expressed are those of the authors, and should not be quoted without their permission. The authors welcome your comments.

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## **Abstract**

- **Objectives** -To investigate the most efficient use of echocardiography and natriuretic peptide testing in the diagnosis of heart failure.
- **Design** - An economic model comparing two strategies: (A) provide echocardiography and electrocardiogram (ECG) for all individuals who present to a GP with symptoms that may be due to heart failure; (B) carry out B-type natriuretic peptide (BNP) blood test and ECG on all such individuals and provide echocardiography only where an abnormality is detected in one of more of these tests.
- **Setting** - Primary care in the UK NHS.
- **Subjects** - Individuals who present to a GP with new symptoms of heart failure.
- **Main outcome measures** - Cost per life year gained.
- **Results** – Baseline cost per life year gained by strategy A compared with strategy B is £3,987.
- **Conclusions** – Immediate echocardiography is the most cost-effective option. Where echocardiography is a scarce resource, efficient use can be obtained by using BNP and ECG tests to identify patients most likely to have heart failure.

## **Introduction**

Around 900 000 people in the UK today have heart failure.<sup>1</sup> The condition has a poor prognosis: just under 40% of patients diagnosed with heart failure die within a year – but thereafter the mortality is less than 10% per year<sup>2</sup>. Heart failure accounts for 2% of all NHS inpatient bed-days and 5% of all emergency medical admissions to hospital.<sup>1,3</sup>

The mainstay of treatment of heart failure is drug therapy – typically with diuretics, ACE inhibitors and beta-blockers, in addition to various lifestyle measures such as avoiding salty foods, taking regular exercise, and monitoring any weight gain that might suggest fluid retention. Such treatment lengthens life, improves symptoms, and reduces the need for emergency hospitalisation.<sup>4,5</sup> Access to these treatments requires efficient diagnosis of the condition. There is no ‘gold standard’ for the diagnosis of heart failure, which is a constellation of different symptoms due to underlying cardiac dysfunction. Many studies have reported that the accuracy of the diagnosis of heart failure is poor in primary care, particularly when there is low usage of echocardiography, which can confirm the presence of underlying cardiac dysfunction.

Echocardiography is a limited resource in the UK, chiefly because of lack of trained echocardiographers. Heart failure is very unlikely in a patient with a normal 12-lead electrocardiogram ECG<sup>6,7,8</sup> or low plasma B-type natriuretic peptide (BNP) concentration, given the high sensitivity of these tests.<sup>9,10,11,12,13,14</sup> Normal results may, therefore, be useful in guiding the doctor to consider other diagnoses and investigations. This paper investigates the cost-effectiveness of routine echocardiography and ECG for all patients presenting to a GP with suspected heart failure (strategy A), compared with a filtering strategy of initial testing by measurement of plasma BNP concentration and ECG, followed by an echocardiogram only when an abnormality is suggested by one or more of the tests (strategy B), as recommended by the National Institute for Clinical Excellence (NICE) in the chronic heart failure guideline published in 2003.<sup>4</sup>

## **Methods**

Our cost effectiveness analysis is based on a model that traces a hypothetical cohort of 100 adults who present to the GP with possible symptoms of heart failure. The two strategies previously defined are compared in terms of the direct NHS costs and patient outcomes over a period of five years from diagnosis.

A model schematic is shown in Figure 1, illustrating the basic structure and key parameters at each stage. Table 1 provides the baseline values and data sources for the key parameters, as well as the values used in sensitivity analysis.

#### *Prevalence of heart failure in this population*

This is an estimate of the proportion of people referred for testing by a GP who receive a diagnosis of heart failure after further investigation. The baseline estimate of 29% comes from the Hillingdon Heart Failure study, where 81 GPs referred all suspected new cases of heart failure to a rapid access study clinic.<sup>9,15</sup> The GPs in the Hillingdon study may have had higher than average awareness of the condition: for sensitivity analysis our lower estimate (18%) is taken from a study of an open access echocardiography service,<sup>16</sup> and our upper estimate (34%) comes from other empirical studies of diagnosing heart failure in patients referred from primary care.<sup>17,18</sup>

#### *Sensitivity and specificity of tests*

Echocardiography is assumed to be the diagnostic 'gold standard' – we assume that after such investigation all patients are correctly diagnosed as heart failure or not. This is obviously an oversimplification, although in practice most diagnostic services function so that history, clinical examination, and echocardiography are all that is required to confirm or refute a diagnosis of heart failure. Such an assumption implies that echocardiography is both 100% sensitive and specific. Hence in the model, there are no false positives because any abnormality detected by BNP or ECG will be referred for echocardiogram and as this is assumed to give a definitive diagnosis it will pick up any false positives from the first stage. The sensitivity of BNP and ECG will determine the number of missed cases and we assume that missed diagnoses are not re-diagnosed within the five year period considered.

The baseline figures for sensitivity and specificity of BNP plus ECG (0.94 and 0.44 respectively) are taken from the recently published UK BNP study.<sup>17</sup> These figures were found using a decision cut-point for plasma BNP level of 65 pg/ml and any abnormality on the resting ECG. The upper and lower 95% confidence intervals, calculated from the raw data were used in the sensitivity analyses.

In the base case strategy B requires 67.02 echocardiographs, 27.26 in patients with heart failure and 39.76 in patients without heart failure. This represents 94% and 56% of the relevant population respectively.

#### *Costs*

All costs are reported in 2003 Sterling. Costs of each strategy include the costs of the tests, costs of drug treatment for heart failure and the hospitalisation costs for heart failure admissions. The costs for 12 lead ECG and echocardiogram were obtained from NHS Reference Costs 2003<sup>19</sup>. The range of values for these costs are particularly uncertain and vary substantially according to whether the tests are carried out as an outpatient appointment or via a direct access arrangement. The baseline costs are the average of the direct access and outpatient costs. For the sensitivity analysis the lower limit is zero and the upper limit is twice the baseline. The cost of a BNP test was obtained from the manufacturers. The average cost of an inpatient bed day for heart failure and average length of stay for heart failure are taken from NHS Reference Costs 2003.

Costs of treatment with ACE inhibitors and beta-blockers are calculated from the British National Formulary according to target doses recommended in the NICE guideline.<sup>4</sup> Baseline costs are for mid price brands and sensitivity analysis considers the lowest cost generics and the most expensive brands. We also include the costs of tests carried out during initiation and titration of treatment, assuming this involves an average of three blood biochemistry tests.<sup>19</sup> Since both beta-blockers and ACE inhibitors are increasingly used to treat other conditions, we assume that a proportion of the cohort will already be taking these drugs prior to a heart failure diagnosis.

#### *Outcomes*

Outcomes are expressed in terms of life years gained from treatment, assuming that a diagnosis of heart failure means access to treatment that is not available to people who do not have a confirmed diagnosis. For simplicity it is assumed that everyone who has a diagnosis of heart failure is eligible for treatment with an ACE inhibitor and beta-blocker. Treatment with these agents is known to have a beneficial effect in terms of life expectancy and reduced hospitalisation in randomised clinical trials, and this benefit is assumed to continue over the five-year period considered. Whilst it is possible that treatment has benefits in terms of quality of life, another metric of cost-effectiveness, these are not considered here due to a lack of available data.

The Hillingdon cohort provides cumulative survival probabilities for people with heart failure who are treated with ACE inhibitors.<sup>15</sup> Beta-blocker treatment was rare in this cohort, due to the timing of the study. Treatment benefits from ACE inhibitors and beta-blockers in terms of life years gained and hospitalisation are taken from meta-analyses of randomised controlled trials. Since these trials generally include patients who have already had a diagnosis of heart failure for around 12 to 18 months prior to the trial start, we use data from trials of patients who receive ACE inhibitors for the treatment of heart failure after MI to estimate treatment benefits in the first year following diagnosis.<sup>20,21,22</sup> This information is used to adjust the Hillingdon probabilities so that we estimate outcomes for an untreated cohort and for treatment with the combination of ACE inhibitors and beta-blockers. Cumulative survival probabilities for people who present with possible symptoms but who do not receive a diagnosis of heart failure after further investigation are also taken from the Hillingdon study.

### *Discounting*

As the costs and outcomes in this model accrue over 5 years, discounting is used to give less weight to those that occur in the future compared with those that occur in the present. In keeping with recommendations from NICE<sup>23</sup> we discount both costs and benefits at 3.5% and investigate the sensitivity of the results to discount rates of 0% and 6%.

## **Results**

Using the baseline values reported in Table 1, the estimated total cost over 5 years for a cohort of 100 patients is £90,239 for strategy A and £87,360 for strategy B. The life years gained from each strategy are 256.47 and 255.73 respectively. This gives a cost per life year gained of immediate echocardiography of £3,897.

This result is based on a large number of estimated parameter values and the point estimate is particularly sensitive to changes in some of the key parameters. The last two columns of Table 1 report one-way sensitivity analysis using the lower and upper limits of each parameter. Of these estimates only one, using the lower limit for treatment benefits, is more than £6,500, and this value is still below the likely cost-effectiveness threshold cited in the NICE Technology Appraisal Guidance.<sup>27</sup>

Sensitivity analyses were undertaken assuming that patients with heart failure who were mistakenly 'ruled out' using the BNP and ECG filter tests would, if still alive, return to their GP

(or be admitted to hospital) and receive ECG and an echocardiograph in due course when, and if, their symptoms deteriorated. If it is assumed that this would take place at 1 year after the initial tests the cost per QALY of immediate echocardiography rises to £8,250, rising to £16,750 if this occurred by 6 months after the initial tests. These calculations have conservatively assumed that patients whose symptoms deteriorated would have a similar prognosis to those treated at first presentation.

## **Discussion**

The baseline estimate of cost per life year gained suggests that immediate echocardiography is cost effective. However, echocardiography facilities in the UK are currently in limited supply and appropriate and speedy referral for testing is a key issue. If the proportion of people being sent for tests that actually turn out to have heart failure is low, then immediate use of echocardiography becomes less cost effective, and waiting times will increase yet further. An advantage of both ECG and BNP testing is that they can be performed rapidly in a primary care setting, with results available within 20 minutes when using a near-patient testing assay, or next day from the local hospital biochemistry department. Therefore the use of these tests to filter out people who do not require an echocardiogram because of the very low likelihood of abnormality, can result in more efficient use of limited echocardiography facilities. ECG interpretation is now usually computerized, and need only be at the level of determining whether the trace is completely normal or not. Such targeted echocardiography has been recommended by NICE,<sup>4</sup> after taking into consideration the current strain on echocardiographic facilities in the UK. Our analysis suggests that the economics support the clinical drive for greater availability of echocardiography for patients with suspected heart failure.

Some qualifying remarks on the modelling assumptions are warranted. Firstly, we assume that the only value of echocardiography is in diagnosing heart failure. In fact echocardiography may provide information on underlying structural abnormalities of the heart that may not be the cause of symptoms but require further assessment or ongoing follow-up e.g. mild aortic stenosis. These additional benefits would increase the cost effectiveness of immediate echocardiography.

Secondly, the model assumes that everyone who has a diagnosis of heart failure is eligible for treatment with ACE inhibitors and beta blockers. In reality even at the most specialised centres

only around 70% of patients will be able to tolerate a beta-blocker, and not all at the target doses used in clinical trials. This reduction in potential treatment benefits will reduce the cost effectiveness of immediate echocardiography. however, even with lower estimates of treatment effects this strategy is still cost-effective.

**Figure 1: Cost effectiveness schematic for 5 year period model**

	<b>Events</b>		<b>Important parameters</b>
1	GP suspects HF & requests tests (Two options A v B)		'prevalence': the proportion of people sent for tests who actually have HF
2	<i>Strategy A</i> Echo and ECG for all	<i>Strategy B</i> ECG and BNP for all then ... Echo if BNP <u>or</u> ECG are T+	costs of tests sensitivity and specificity
3	<i>Test results*</i> HF diagnosis (T+, D+ and T+ D-) No HF diagnosis (T-, D+ and T- D-)		False positives Missed cases
4	Treatment (ACE inhibitors & $\beta$ -blockers) for T+		Costs: initiation and treatment Outcomes: survival and hospitalisation

\* D+(-): positive (negative) for disease, T+(-): positive (negative) test

**Table 1: Key parameters: baseline values, sensitivity analysis and data sources**

Parameter	Baseline estimate	Data source	Sensitivity analysis			
			Parameter Lower	Parameter Upper	C/ LYG (£) Lower	C/ LYG (£) Upper
Prevalence	29%	Hillingdon <sup>9</sup>	18%	34%	6,430	3,288
<i>Diagnostic accuracy</i>						
<i>Echocardiography</i>						
Sensitivity & Specificity BNP & ECG	100%	Gold standard	N/A	N/A		
Sensitivity	94%	UK NP <sup>17</sup>	88	97	2,671	6,349
Specificity	44%		37	51	3,238	4,556
<i>Costs of tests (£)</i>						
Echocardiography	98	Ref Costs	0	196	-477	7,736
12 lead ECG	65	Ref Costs	N/A	N/A		
BNP	12.5	Manufacturer	0	25	5,589	2,205
<i>Costs of drugs (£/ year)</i>						
ACE inhibitor	163	BNF	53	339	3,298	4,857
Beta blocker	125	BNF	112	327	3,826	4,998
Initiation and titration (£)	30	Ref Costs	0	100	3,841	4,029
<i>Hosp cost (£/ bed day)</i>	158	Ref Costs	122	193	3,991	3,806
<i>Treatment benefits</i>						
% reduction in odds of death (yrs 0,1,2,3,4)	Yr 0: 20 Yrs 1-4: 40	Meta analyses (see text)	Yr 0: 0 Yrs 1-4: 10	Yr 0: 30 Yrs 1-4: 50	16,012	3,133
% reduction in hosp. rate	18		0	30	4,974	3,179
% reduction in length of stay	5	Meta analyses (see text)	0	20	4,155	3,123
% already on ACE	20	UK NP <sup>17</sup>	0	30	4,133	3,779
% already on $\beta$ blocker	20	UK NP <sup>17</sup>	0	30	4,068	3,812
<i>Discount rate</i>						
Costs	3.5	NICE	0	6	3,994	3,836
Benefits	3.5	NICE	0	6	3,564	4,143

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