

## ***BNP health technology assessment: questions and issues***

### **A. Pathways**

Four diagnostic pathways will be considered for use in primary care; all will require clinical assessment, patient history, chest X-ray, blood tests and respiratory measures. The relevant diagnostic options are:

- BNP or NT Pro-BNP only then if positive echo
- BNP or NT Pro-BNP and ECG – if either positive then echo
- ECG only and if positive echo
- Echo only with referral based on clinical judgement.

The present pathway is considered to be closest to option 3. However, important to note that many patients in the community have not had their diagnosis confirmed by an echo. Of this group 50% could be mis-diagnosed.

Following implementation of the incentives in the GP contract, virtually all, new patients with symptoms suggestive of heart failure who are able to attend for an outpatient appointment should get an echo. This could further increase waiting times for an echo, with the main constraints being availability of skilled technicians and experts to interpret the scans.

All patients will be prescribed drugs on the basis of clinical judgement. However, for drug naïve patients the assessment will assume GPs take bloods to send to laboratories before commencing treatment to avoid the effect of the drug masking BNP or NT Pro-BNP.

For patients in the community who are being treated for heart failure but where the diagnosis is not confirmed by echo (because no echo has been requested rather than where an echo view has proven to be un-interpretable), then we will seek evidence on the clinical effectiveness of using BNP or NT Pro-BNP and a recommendation will be whether such patients should all be echoed without waiting for a BNP/NT Pro-BNP; or whether the diagnostic pathway should be BNP/NT Pro-BNP then echo.

The same evidence will be interpreted for the group of patients in the community who are being treated for another related disease such as hypertension and who also receiving drugs that could affect BNP or NT Pro-BNP levels

As it is possible that BNP or NT Pro-BNP may identify some patients who are negative on echocardiography but have essentially the same aetiology, outcomes and therapy as heart failure, these pathways may need to be amended on the basis of the answer to question 1 of the clinical effectiveness section.

Main issues are anticipated to be:

- sensitivity of interpretative and fixed ECGs ( equipment and variability by operator )
- sensitivity of mobile and fixed echos

- it is estimated that in about 5% of patients no clear echo assessment is available. What other diagnostic test could be used? Is fixed radionuclide ventriculography useful in this circumstance?
- are patients with raised BNP or NT Pro-BNP and normal echos considered to heart failure ?
- benefits to secondary care of better risk stratification in the community- should positive BNP or NT Pro-BNP results imply direct access to echo?
- use of BNP or NT Pro-BNP in the emergency setting.

Data requirements include:

- existing and forecast demand for and capacity of echo services at outpatients and waiting times
- how many Scottish hospitals/primary care settings are currently using BNP or NT Pro-BNP routinely and for what purpose?
- number of GPs and primary care teams with access to various types of ECG machines
- variability in operators' interpretation of ECGs
- annual incidence and prevalence of heart failure

## **B. Clinical effectiveness questions**

These questions refer to patients with signs and symptoms suggestive of heart failure but without confirmed disease.

Because of differences in the prevalence of both disease and presenting symptoms analyses will consider primary care and hospital presentation separately.

### Question 1

Does raised BNP or NT Pro-BNP identify some patients with a high risk of death or morbidity who are not identified by echocardiography? (We might alternatively phrase this as: 'are patients with raised BNP or NT Pro-BNP but normal echocardiography at increased risk of death or morbidity?').

### Question 2

Assuming a primary care setting, which of the four possible pathways outlined above is most clinically effective?

### Question 3

Which pathway is most clinically effective for patients arriving at an emergency setting?

### Important issues to consider in the assessment

1. Are there differences in performance between BNP and NT Pro-BNP? If so, is it possible to conclude that any of them should not be used for the purposes covered in this assessment?
2. Do the commercially available BNP and NT Pro-BNP assays have similar precision and repeatability?
3. What is required to ensure usable blood is delivered from general practices to laboratories?
4. Should diagnostic or prognostic cut-offs vary with age, sex, ethnicity or other identifiable patient characteristics?
5. Are BNP or NT Pro-BNP assays subject to false-positive results due to interference?
6. Is BNP or NT Pro-BNP superior to ECG for diagnosis, risk stratification and management of patients with suspected HF who are not taking drugs that may affect the activation of natriuretic peptides?
7. Is BNP or NT Pro-BNP superior to ECG for diagnosis, risk stratification and management of patients with suspected HF who are taking drugs that may affect the activation of natriuretic peptides?
8. Is diastolic heart failure different from left ventricular systolic dysfunction for use of BNP or NT Pro-BNP for diagnostic and prognostic purposes?
9. Does prognosis change with BNP or NT Pro-BNP concentration and, if so, can this help determine treatment?
10. Does prognosis change with timeliness of diagnosis (i.e. how effective are therapies at prolonging life if disease is diagnosed earlier)?
11. Can BNP or NT Pro-BNP be raised for other reasons, for example end stage renal failure?
12. Does literature support point of care tests in the emergency setting if laboratory turnaround times are say longer than 2 hours?

Note this assumes the assessment does not consider differences in the clinical effectiveness of mobile and fixed echos- rather this is a patient and consultant preference issue.

### Methodology

Literature review, pooling where necessary and show results in evidence tables

## **Economic and budget impact questions:**

### Question 4

Assuming a primary care setting, which of the four possible pathways outlined above is most clinically and cost effective?

### Question 5

Which pathway is most clinically and cost effective for patients arriving at the emergency setting?

### Question 6 Budget impact

What are the estimated changes in resources use, costs and patients outcomes from moving from the current diagnostic testing regime to the most clinically and cost effective option? Analysis will show separately cash costs and savings from use of other resources, which are costed on an opportunity cost basis.

Primary outcomes anticipated being:

- net cash flow from implementing the clinically and cost effective pathway; and
- cost per QALY gained from implementation (note need to quantify clinical benefit as well as utility per life year gained).

Main costs likely to be costs of tests (number and cost of each test), costs of mis-diagnosis- primarily drugs, costs of hospitalisation (inpatients and out patients).

Main benefits likely to be clinical outcome benefits, to include survival benefits and related utilities

Main drivers expected to be: proportion of patients referred for echo for each pathway; % mis-diagnosed under each pathway; prevalence of heart failure in people presenting with symptoms and variability across settings; volume of test per site and whether tests are laboratory or point of care tests

### Methodology

Evidence for cost and benefit data from manufacturers, ISD and others, supported by literature review, and combine with clinical effectiveness data in a model to inform decisions on most model clinical and cost effective pathways.

## **Organisational issues**

(Note the short HTA can only consider organisational issues that impact on clinical or cost effectiveness)

- i. Current access to echo and forecast referral rates for echo vs. capacity (staff-technicians and cardiologists, and equipment).

- ii. Different skills to undertake and interpret different tests.
- iii. How could BNP or NT Pro-BNP affect processes at out-patients eg use of BNP may improve risk stratification so fewer people without heart failure are referred to heart failure clinics allowing clinicians to focus on the more seriously ill?
- iv. How could BNP or NT Pro-BNP affect the emergency setting and in-patient processes?
  - v. What are implications of a 24-hour blood life for GPs?
- vi. Barriers to implementation – funding, training, the technology?
- vii. Need to pilot?

## **Patient issues**

(Note the short HTA can only consider organisational issues that impact on clinical or cost effectiveness)

- i. There is some work by NICE using focus groups that highlight the importance of patients receiving a timely and correct diagnosis – with clinicians getting it right first time.
- ii. Avoidance of harmful drugs if mis-diagnosed.
- iii. What is the importance of the estimated 50% currently diagnosed with heart failure but who do not have it?

## **Exclusions**

The following areas are excluded from the short HTA:

- i. Only treatment effect is effect of earlier/better diagnosis for those who are positive and negative for heart failure. The short HTA will examine clinical benefit from having an early diagnosis but will not investigate psychosocial aspects such as benefits of improved information on diagnosis.
- ii. Screening of asymptomatic people
- iii. No organisational/setting aspects other than where incidence of disease likely to vary
- iv. Use of BNP or NT Pro-BNP for monitoring purposes
- v. Use of BNP or NT Pro-BNP in patients with symptoms suggestive of ACS