

## Research Report

Title: Getting cost-effective technologies into practice: the value of implementation. An application to B-type natriuretic peptide (BNP) testing in diagnosing chronic heart failure.

Authors: Whyte S, Dixon S, Faria R, Walker S, Palmer S, Sculpher M.

Correspondence to: Sophie Whyte, Health Economics and Decision Science, SCHARR, University of Sheffield, Firth Court, Western Bank. Sheffield, S10 2TN.

Email: [sophie.whyte@sheffield.ac.uk](mailto:sophie.whyte@sheffield.ac.uk)

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# **1 Executive Summary**

## **1.1 Aim**

In 2010 NICE released a clinical guideline recommending that natriuretic peptide (NP) testing in patients with suspected heart failure without previous myocardial infarction can accelerate diagnosis of heart failure and also avoid unnecessary echocardiography. A framework for the evaluation of the value of implementation activities is applied to this recommendation for NP testing.

## **1.2 Methods**

The following quantities were estimated: *expected value of perfect implementation* (the maximum the NHS can invest on implementation activities whilst still accruing some positive value from the intervention); *expected value of actual implementation* (the maximum the NHS can invest on implementation activities for specific increases in utilisation); and *value of the implementation activity* (the additional value of the specific implementation activity given its expected costs and effectiveness).

Data sources used to inform the model included: published data on disease incidence; cost-effectiveness data from a published Health Technology Assessment (HTA) which informed the clinical guidelines; cost and effectiveness evidence from an intervention designed to increase NP utilisation in London; data on utilisation and disease incidence from a clinical expert; audit data on NP testing utilisation; and a systematic review of implementation initiatives. Diffusion curves were estimated based on historic data to produce predictions of future utilisation. Incremental costs and quality-adjusted life years (QALYs) of N testing compared to 'do nothing' were estimated to be -£3.88 and 0.08 respectively. The annual suspected Heart Failure (HF) population in England and Wales was estimated to be 210,000. Current utilisation and optimal maximum utilisation of NP testing were estimated to be 4.4 and 8.6 per 1,000 population respectively. The implementation intervention was estimated to cost approximately £24K and assumed to result in an absolute increase in utilisation of 5%. Both a static population analysis and multi-period analysis were undertaken and results are presented for cost-effectiveness thresholds of £20,000 and £30,000 per QALY gained.

## **1.3 Results**

There appeared to be considerable value in additional implementation efforts directed towards encouraging the utilisation of NP testing for persons with suspected HF. At a threshold of £20,000 per QALY gained, additional investment in an activity that increases utilisation by 5% (absolute increase in utilisation rates) would generate an additional 799 QALYs (£16 million in terms of monetary equivalent) across England and Wales, compared to the use of these resources in other (health generating) National Health Service (NHS) activities. Scenario analyses demonstrated that value to the NHS was sensitive to uncertain model inputs such as the size of the eligible population and the efficacy of the implementation intervention. The analysis highlighted a lack of evidence on: cost effectiveness, effectiveness of implementation intervention, utilisation, and population size.

## 1.4 Conclusions

This framework can be applied to any existing cost effectiveness analysis, thus helping a decision maker to quantify the value of investing resources into increasing utilisation in a manner consistent with the value assessment of new interventions conducted by the National Institute for Health and Care Excellence (NICE). This case study provides a useful demonstration of the practical challenges faced in populating such a model. In particular, the importance of publishing incremental costs and QALYs related to clinical guidelines compared to current care is highlighted. Data on diffusion of utilisation is crucial for such evaluations.

## 2 Background

### 2.1 Diagnosing heart failure

The prevalence of heart failure (HF) is expected to rise in the future as a result of an ageing population, obesity, improved survival of people with ischaemic heart disease and more effective treatments for heart failure. Hospital episode statistics (HES) data show that the number of episodes with primary diagnosis of HF increased from 117,000 in 2010/2011 to 127,000 in 2012/2013; an increase of 4.2% per annum.<sup>1</sup>

B-type natriuretic peptides (B-type natriuretic peptide (BNP) or N-terminal pro-B type natriuretic peptide (NTproBNP)) referred to as NPs, are markers of heart failure. The NICE clinical guideline 108 (CG108) released in 2010 recommends that testing for NPs in patients with suspected heart failure without previous myocardial infarction (MI) can accelerate diagnosis of heart failure and also avoid unnecessary echocardiography. Figure 2.1 shows the HF pathway described in CG108.<sup>2</sup> If NP testing shows high levels (BNP>400pg/ml or NTproBNP>2000pg/ml) then the patient is referred directly to specialist assessment and echocardiogram within 2 weeks. If NP testing shows raised levels (BNP 100-400pg/ml or NTproBNP 400-2000pg/ml) then the patient is referred to specialist assessment and echocardiogram within 6 weeks. If NP testing shows normal levels (BNP<100pg/ml or NTproBNP<400pg/ml) heart failure is unlikely. For trusts which are not yet utilising NP testing in line with CG108, a NP test and/or Electrocardiography (ECG) are used to rule out HF in all patients regardless of MI history. This pathway is shown in Figure 2.1.

Figure 2.1A: Heart Failure Pathway described in NICE clinical guideline 108<sup>3</sup>

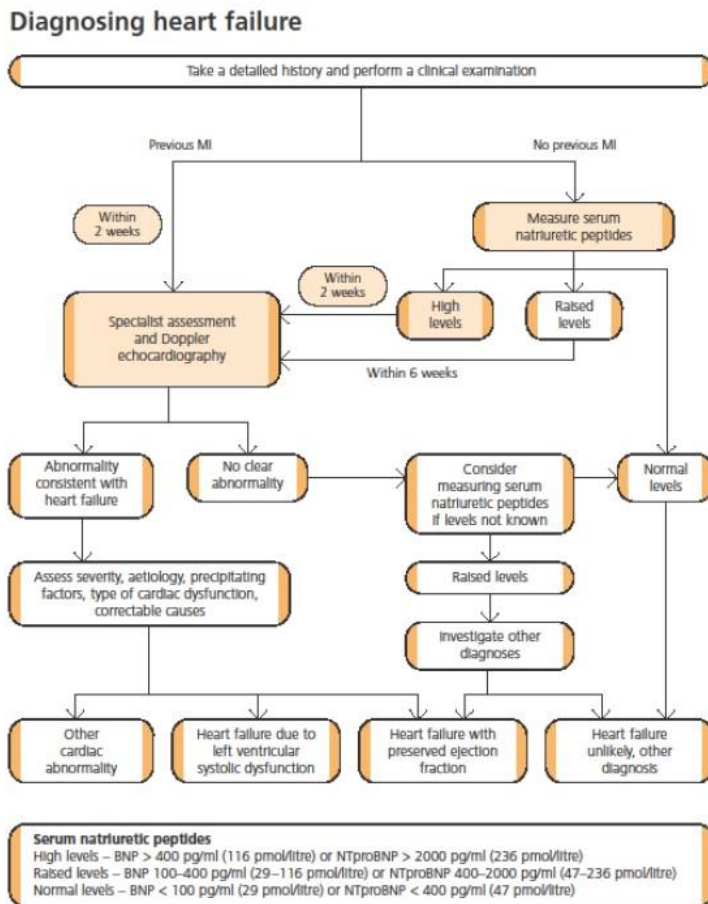
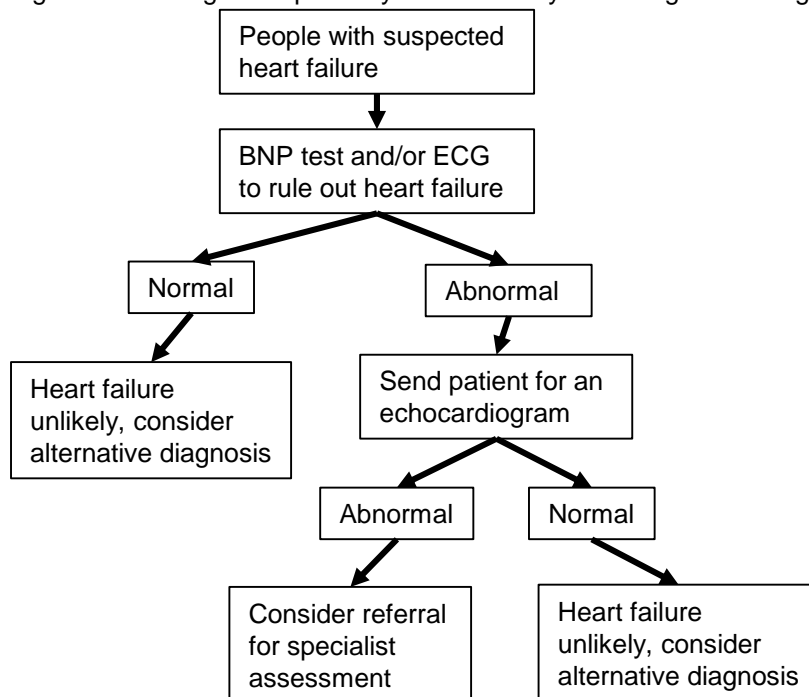


Figure 2.1B: Diagnostic pathway of trusts not yet utilising NP testing in line with CG108<sup>4</sup>





## 2.2 Barriers to consistent adoption of BNP testing in diagnosing chronic heart failure

In general terms utilisation can be increased via the following three routes: (1) Increasing the number of trusts who offer BNP testing, (2) Increasing the number of General Practitioners (GPs) who refer for BNP testing, (3) Increasing the number of patients who agree to undertake BNP testing. Although in general patients' acceptability of the intervention needs to be maximised, this is not relevant in the case of BNP testing. This report focuses increasing utilisation by addressing barriers to the adoption of NP testing by trusts.

The NICE implementation collaborative (NIC) identified the following barriers to adoption of NP testing:

- Cost impact uncertainties. While savings will be made via the reduction in echocardiograms, funding for the tests will be required by the NHS pathology departments
- Long term savings are often not prioritised over 'in year' spend. It can be difficult to get commissioners and providers to see the value of a diagnostic which can create long term savings
- Complexity of (partial) decommissioning of services within the NHS
- Failure to communicate heart failure strategy throughout the NHS
- Complexities involved in redesigning patient pathways to accommodate this technology.

## 3 Conceptual framework for valuing implementation initiatives

This case study applies the framework for valuing implementation initiatives described in "Getting cost-effective technologies into practice: the value of implementation- Draft report on framework for valuing implementation initiatives".<sup>5</sup>

The framework assesses the value to the NHS of investing in implementation activities to increase utilisation of interventions recommended by NICE. The *expected value of perfect implementation* represents the maximum the NHS can invest on implementation activities whilst still accruing some positive value from the intervention. The *expected value of actual implementation* represents the maximum the NHS can invest on implementation activities for specific increases in utilisation (i.e. for a specified % increase). All things equal, the expected value of actual implementation is larger for interventions with more favourable cost-effectiveness estimates (i.e. the degree of cost-effectiveness is potentially important), with larger patient populations and lower utilisation of the intervention (both in terms of existing levels of utilisation and/or low anticipated future uptake). The *value of the implementation activity* represents the additional value of the specific implementation activity given its expected costs and effectiveness. The value of the implementation activity is larger the smaller the costs and the larger the increase in utilisation (effectiveness).

## **4 Methods**

### **4.1 Net benefit. Is the technology of value to the NHS?**

The value of NP testing corresponds to the lifetime net benefit from using NP testing for the diagnosis heart failure, as described in NICE CG108, for the average patient presenting with suspected heart failure. The economics of the diagnostic section of the NICE CG108 was informed by the HTA report by Mant et al 2009.<sup>6</sup> (Note that the economic model in Appendix H of CG108 only relates to the treatment section of the guideline).

#### **4.1.1 Cost-effectiveness analysis by Mant et al.**

The HTA undertakes decision analysis to test the impact of plausible diagnostic strategies for the diagnosis of heart failure in primary care on costs and diagnostic yield in the UK setting. It determines cut-points (or diagnostic thresholds) for NP testing considering the costs of echo and the costs of missed diagnoses. The study established how much a diagnosed case of heart failure is worth, the willingness to pay (WTP). From the WTP, the study calculated the diagnostic threshold for NP testing which varies according to the pre-test probability (prevalence of heart failure, depends on MICE score) and diagnostic performance of NP testing. NP thresholds were calculated assuming that the cost-effective NP threshold is that at which the cost of echo matches the WTP.

Three alternatives were considered in the decision analysis: do nothing, perform NP test then echo depending on the result of NP, and perform echo for all. Patient groups were defined according to MICE (Male gender, history of myocardial Infarction, basal Crepitations, oEdema) score. The MICE rule allocates the following points: (male: 2 points, history of myocardial infarction: 6 points, crepitations: 5 points, ankle oedema: 3 points).<sup>7</sup> The base-case analysis only considers the costs to the NHS: costs of the tests, costs of hospitalisations avoided and costs of medication. Subsequent analyses include QALY gains from treatment following earlier diagnosis.

The WTP to diagnose one case of heart failure was estimated. The incremental cost-effectiveness ratios (ICERs) calculated related to additional cost per additional case detected and these were compared to the WTP thresholds. The survival benefit from early treatment vs late treatment (6 months later) was estimated using data from the Framingham study. Assuming that patients' EQ-5D throughout is 0.65, the overall QALY gain is 0.106 at 3 years, 0.161 at 5 years and 0.254 at 10 years' time horizon. The cost to the NHS of avoided hospitalisations less the cost of additional drug costs from early diagnosis is £270.

#### **4.1.2 Estimates of cost effectiveness used in this study**

There are several key differences between the economic analyses undertaken by Mant et al and the clinical guidelines.

- Mant et al suggest that a person's diagnostic pathway be determined by their MICE score and the cost-effectiveness of different diagnostic strategies are calculated for each MICE score. The NICE CG108 suggests different diagnostic pathways determined by whether the person has a history of MI.

- The Mant et al study applies different NP test thresholds for referral to echocardiography dependent on a person's MICE score. The NICE CG108 recommends a threshold of BNP>400pg/ml or NTproBNP>2000pg/ml for 2 week referral and BNP>400pg/ml or NTproBNP>2000pg/ml for 6 week referral to echocardiography.
- The Mant et al study compares a strategy of NP testing to 'do nothing' in which no further investigations are made. The 2003 NICE guidelines recommend that persons with suspected HF receive an ECG and/or NP test (where available). Hence it is suggested that ECG represents current care (where NP testing is not available) and that this should be the comparator. The study by Mant et al did include information on the effectiveness of ECG but ECG was not included as a comparator within the economic section. *"Electrocardiography (ECG), B-type natriuretic peptides (BNP) and N-terminal pro- B-type natriuretic peptides (NT-proBNP) all had high sensitivities (89%, 93% and 93% respectively). Chest X-ray was moderately specific (76–83%) but insensitive (67–68%). BNP was more accurate than ECG, with a relative diagnostic odds ratio of ECG/BNP of 0.32 (95% CI 0.12–0.87)."*<sup>6</sup>

For the purposes of this project the model and results from the Mant et al HTA was adapted to more closely represent the CG108. A diagnostic strategy dependent on previous MI is modelled with a NP testing threshold for referral of BNP>400pg/ml or NTproBNP>2000pg/ml, applied as in the NICE CG108. However, the comparator for this analysis remains 'do nothing' as data on the cost-effectiveness of ECG were not provided within the HTA, nor were available from the HTA authors. The value of incremental costs and QALYs compared to a comparator of ECG are likely to be considerably lower than for the comparator 'do nothing'. Estimates of the sensitivity and specificity of the BNP test were obtained from one of the HTA authors.<sup>8</sup> Table 4.1 presents a summary of this adaptation of the Mant et al HTA.

**Table 4.1: Adaptation of economic analyses from Mant et al HTA**

<b>Economic Analyses for CG108 based on data from Mant et al HTA</b>			
Rule: If previous MI then echo; If no previous MI then BNP test, echo if BNP >100 in line with CG108			
Cost echo	£	87	NICE costing template
Cost BNP	£	28	NICE costing template
Savings form reduced admissions less	£	270	Mant et al
QALY gain (10 year time horizon)		0.254	Mant et al
No previous MI		0.86	PC from Andrea Roalfe 14 April 2014
Pre-BNP probability of HF, No MI		0.29	PC from Andrea Roalfe 14 April 2014
Sensitivity		0.83	PC from Andrea Roalfe 14 April 2014
Specificity		0.67	PC from Andrea Roalfe 14 April 2014
BNP positivity		0.48	Calculated from above
Previous MI		0.14	Calculated from above
Probability of HF, previous MI		0.67	PC from Andrea Roalfe 14 April 2014
Additional cases		301	Calculated from above
<i>For 1,000 persons with suspected HF</i>			
Cost (CG108 versus nothing)	-£	3,881	Calculated from above
QALYs (CG108 versus nothing)		76.40	Calculated from above

#### **4.2 Current value. What is the value of the technology given current utilisation and population size?**

#### **4.2.1 Population size**

The population eligible for NP testing consists of persons presenting with suspected heart failure. The scope of this study is to produce predictions for England and Wales.

Estimates of the incidence of heart failure vary considerably between sources:

- An estimate of the annual incidence of heart failure based on General Practise Research Database (GPRD) data is 22,542 cases for England and Wales.<sup>9</sup>
- The Hillingdon Heart Failure Study used a combination of clinical assessment, echocardiography and radiography to diagnose heart failure in the study population and adhered to European Society of Cardiology guidelines for its definition of heart failure. The study found a crude incidence rate of 140/120 per 100,000 for men/women and estimated 59,000 cases annually in England and Wales.<sup>10</sup>
- A significant proportion of total incidence will present via a HF clinic and the remainder will be admitted to hospital. For Sheffield heart failure clinic an incidence of 98 per 100,000 was seen.<sup>11</sup> This is equivalent to 55,000 cases annually in England and Wales. We note that the Sheffield HF diagnostic clinic data was restricted to the patients well enough to attend the clinic and did not include patients who were admitted to hospital with acute heart failure during this period.
- A clinical expert estimates an annual incidence of 70,000 new cases in England and Wales.
- Data from Hospital Episode Statistics gives 121,000 inpatient episodes for heart failure per year in England and Wales.<sup>12</sup> Clinical opinion suggests that 20-35% of such episodes are new, indicating an annual incidence of 23,000-40,000 cases.<sup>11</sup>

Based on these data sources we will assume that the annual incidence of HF in England and Wales is 70,000 in the base case and 50,000 will be considered in a scenario analysis. Based on the Cowie et al study the prevalence of HF in persons presenting with suspected HF is 33%. Hence the population of persons presenting with suspected HF is of size 210,000 for the base case (3.7 per 1,000 population) and 150,000 in the scenario analysis.

#### **4.2.2 Current utilisation of NP testing**

Data on the current utilisation of NP testing was available from two sources: the NHS Atlas of variation in diagnostic services, and from an audit developed by the Healthcare scientists' innovation project.

##### *NHS Atlas of variation in diagnostic services*

The NHS Atlas of variation in diagnostic services was published in November 2013.<sup>13</sup> It provides data on the estimated annual rate of use for NP tests ordered by GPs per 1,000 practice population, by primary care trust (PCT), 2012. The data is a sample (23 days in June 2012) and has been gathered from the live e-Reporting Pathology Messaging Implementation Programme (PMIP) feed as part of an audit of the data quality within the messages. The data indicates wide variation in test usage possibly due to differences in clinical practice or variations in test availability, either because of local laboratory policy or funding restrictions. Data was available from 111 out of 151 PCTs (74%). The

average estimated annual rate was 4.43 per 1,000 weighted population (95 percentiles 0.10-11.38). However, as the GP testing information is based on a sample set only and reflects only 23 days of extraction from the PMIP system, the estimates should be used with caution.

The NHS Atlas of variation in diagnostic services also provides data on the rate of echocardiography activity per 1,000 weighted population, by PCT, 2012/13. Data quality and completeness of activity data should be good. However, given that data are only collected at an aggregate level (i.e. total counts by PCT/provider), it is not possible to do detailed standardisation to remove the effect of different population compositions. The average estimated annual rate was 21 per 1,000 practice population (95 percentiles 9-33).

Table 4.2: NP and echocardiography activity by PCT from the NHS atlas of variation in diagnostic services

	<b>BNP tests ordered by GPs</b>	<b>Echocardiography activity</b>
PCTs with available data	74%	100%
Estimated annual tests for PCT population		
Mean	1534	7289
Min	14	212
Max	6,114	47,370
Percentiles	(29 - 4,342)	(1,927 - 17,810)
	per 1,000 practice population	per 1,000 weighted population
Mean	4.4	21.0
Min	0.0	1.2
Max	14.4	42.0
Percentiles	(0.10 - 11.38)	(9 - 33)
per population of England and Wales		
Mean	248,565	1,179,336
Min	2,692	68,413
Max	805,699	2,356,309
Percentiles	(5,495 - 638,074)	(477,346 - 1,849,523)

#### *Healthcare scientists' innovation project*

The Healthcare Scientists innovation project developed an audit flowchart process 'Pipeline adoption scale' which describes 22 steps associated with the adoption of a new technology.<sup>14</sup> A total of 14 of these 22 steps were found to be completed by NHS healthcare scientists. A questionnaire was developed to use to undertake an audit of NTproBNP testing, see Figure 4.2A.

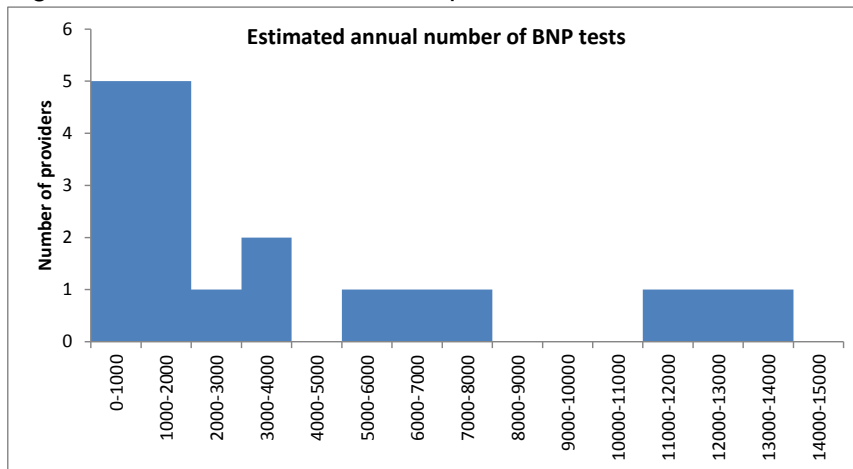
Figure 4.2A: Questions included within the audit.

**Questions**

- 1 Does your trust offer BNP testing?
- 2a Would your trust consider offering BNP testing?
- 3a What barriers are preventing successful adoption?
- 3b State reason for this
- 3c Where are you in introducing BNP testing?
- 2b Does your trust actively use BNP testing?
- 3d Are you in the post adoption phase for BNP?
- 4a Is BNP analysis performed in primary care as a POCT service?
- 4b Where are you in introducing BNP testing?
- 3e State the number of BNP tests performed?
- 4c State number of referrals following BNP testing?
- 5a State the number of echos following BNP testing?  
If applicable state what other organisations your Trust performs BNP
- 6a testing for eg PCTs/GP surgeries. Account for this in Qu 3e answer.
- 7a Are there other areas you could roll out to?

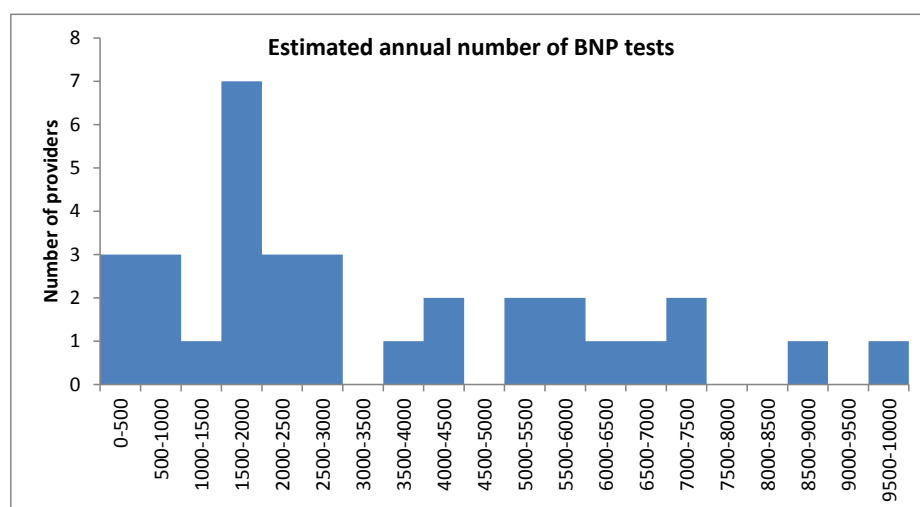
In December 2012, the 26 provider trusts in London were audited to determine which stage along the implementation pipeline they were at. A response was received from 24 trusts within a 2 week period. 20 Trusts were included in the study providing data on the number of NTproBNP tests completed in the previous 6 month period (late 2012). This data has been converted to an estimated annual number. Figure 4.2B shows that the majority of provider trusts were in the early stages of implementation of NP testing with less than 100 tests being performed annually.

Figure 4.2B: Estimated annual NTproBNP tests from audit of 26 London Provider trusts



A national audit (excluding London) was undertaken in October 2013. A total of 47 trusts responded to the questionnaire. Details of the questionnaire are shown in Figure 4.2C. The questionnaire showed that 43/47 (91%) of the trusts offer BNP testing. BNP testing appears to be offered universally in London the North East and much of the North.

Figure 4.2C: Estimated annual BNP test from national audit (excluding London)



The data from the London audit and the national (excluding London) audit are at provider hospital level. Each provider hospital may receive patients from more than one PCT (particularly if they are located near a PCT boundary); it is therefore not possible to have data on the population size served by each provider. This means that it is not possible to compare the estimates of BNP test usage between providers, as they serve populations of different and unknown sizes.

#### *BNP utilisation estimates*

As provider population sizes were not available, BNP testing rates could not be obtained from the audit data and the data cannot be compared to the data from the Atlas of variation in diagnostic services. Hence, data from the Atlas of variation in diagnostic services was used to inform BNP current utilisation estimates.

The estimates of population size suggest that the maximum annual number of tests should be 210,000 or 3.7 per 1,000 patient population. This estimate is not compatible with the data from the diagnostics Atlas. As there is considerable uncertainty surrounding the number of persons with suspected heart failure presenting for each one person with actual heart failure, the diagnostics atlas data will be used to estimate maximum utilisation.

We make the assumption that some PCTs within the diagnostics Atlas data set will have achieved maximum optimal utilisation. Maximum utilisation was 14.4 BNP tests per 1,000 practice population but this rate was only observed for one PCT. Clinical opinion suggests that additional NP testing is also undertaken, which is not in-line with CG108. This includes: GP's using NP as a screening test in the absence of symptoms, GPs using the test as a way to find access to cardiology opinion, and doing multiple tests on the same patient.<sup>11</sup> Hence, we suggest that the optimal maximum utilisation will be lower than the observed maximum rate of 14.4 tests per 1,000 population.

Examining the percentiles of the data shows that 10% of PCTs within the data set had a BNP utilisation rate of over 8.6 tests per 1,000 patient population and 20% a rate of over 7.1 tests per 1,000 patient population. Using 8.6 as maximum utilisation rate for base case analysis and 7.1 for scenario analysis, we see that current utilisation is at 51% (base case) or 63% (scenario analysis) of maximum utilisation.

### **4.3 Expected value of perfect implementation. What is the value of increasing utilisation so all eligible patients receive the test?**

#### **4.3.1 Diffusion curves for utilisation of NP testing**

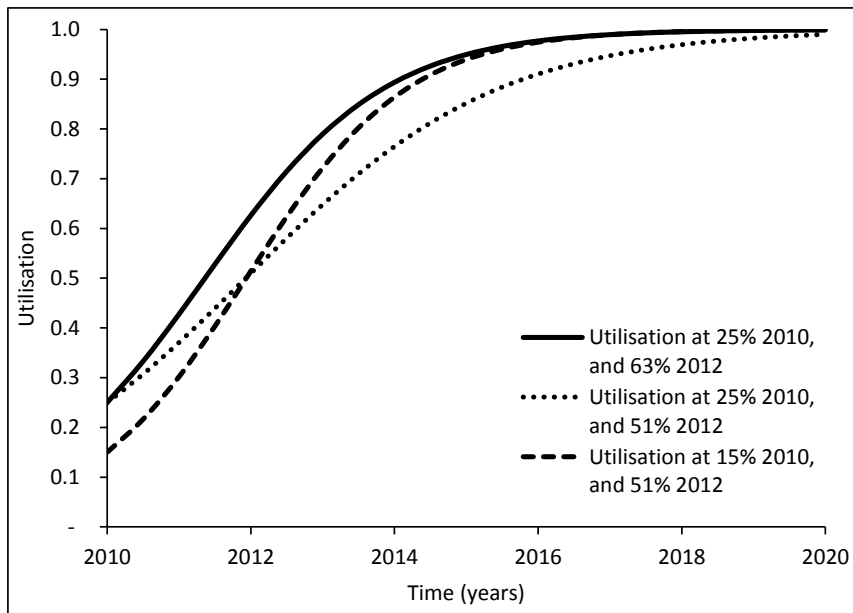
Diffusion theory suggests an S-shaped curve is appropriate to represent the total cumulative utilisation over a period of time.<sup>15</sup> This entails an exponential growth in early periods that levels off and declines later. However, it is difficult to know whether the utilisation of NP testing follows this pattern and, if so, in what stage of the curve is utilisation currently at. In addition diffusion models will be affected by the following: technology characteristics such as usability, benefit-risk profile and price; characteristics of the organisation; external environment; characteristics of the individual adopters, such as skills, motivation, acceptance and beliefs; available evidence; available resources.

The diffusion curve will be informed by the date which NP testing started to be used as a means of 'rule-out' for echocardiography. Section 4 of the NHS Improvement report indicates that several trusts undertook pilots and audits of NP testing in the period 2005-2007.<sup>16</sup> The NHS Improvement NP resource was published in 2008. The NICE CG108 and the NICE guidance costing template were released in August 2010. The NHS technology adoption centre (NTAC) adoption pack was produced in 2013.

A S shaped curve (of the form  $f(t)=1/(1+\exp(-at+k))$ ) was fitted to two data points for 2010 and 2012. Utilisation in 2012 was based on estimates from the Diagnostics Atlas data as described in a previous section. In the NICE costing template expert clinical opinion estimated that without the NICE CG108 approximately 30% of patients currently receive a BNP or NTproBNP test and approximately 90% currently receive an ECG.<sup>4</sup> These estimates reflect the situation in 2010. In the base case we assume that for these 30% utilisation was 50% of optimal maximum utilisation i.e. 15%. These diffusion curves are presented in Figure 4.3.

Figure 4.3: BNP utilisation diffusion curves





#### 4.4 Expected value of actual implementation. What is the value of increasing utilisation from current to achievable?

Utilisation may increase with implementation activities; however, it may not reach full (or perfect) implementation. The effectiveness of implementation activities is likely to vary with the type of activity and its particular context.

##### 4.4.1 Initiatives to increase implementation

The NIC have identified the following list of initiatives which could increase the implementation of CG108:

- Ensure that a known individual is accountable for the implementation of CG108 in each Clinical Commissioning Group
- Ensure that that individual is trained and aware of the business economics and patient outcome benefits of early diagnosis of heart failure enabled by CG108
- Develop a template communication package targeted at general practitioners, for use by clinical commissioning group (CCG) accountable individual
- Define a reporting mechanism to enable CCG to track usage in individual practitioners
- Input to discussion of 'aligning financial incentives' to reward adoption

##### 4.4.2 Resources designed to increase implementation

In November of 2010, the Innovative Technology Adoption Procurement Programme (iTAPP) was launched. This programme encourages NHS-wide adoption of high impact innovative medical technologies that can increase the quality of care provided to patients, whilst reducing the overall cost of care. Medical technology companies are invited to submit details of specific medical technologies that would fall under the remit of iTAPP. iTAPP is now being transitioned to the National Institute for Health and Clinical Excellence. An adoption pack is available for NP testing on the NTAC website.<sup>17</sup> This is useful, though it is poorly advertised so usage may be low.

NHS Improvement (now NHS Improving Quality (NHSIQ)) produced a resource 'Heart Improvement Programme: Brain-type Natriuretic Peptide (BNP): An Information Resource for Cardiac Networks' in 2008.<sup>16</sup> They also produced a tool for trusts to use to estimate the cost effectiveness of NP testing for their population, but there were insufficient funds to further develop this tool.

The 'Implementing NICE guidance costing template' which aims to help organisations in England, Wales and Northern Ireland plan for the financial implication of implementing the NICE clinical guideline on chronic heart failure. It produces estimates of the cost impact based on assumptions made about current practice and a prediction of how current practice may change following implementation.

#### **4.4.3 NHS London NP testing implementation initiative**

##### *Description of NHS London NTproBNP testing implementation initiative*

The first part of the initiative involved determining the barriers to implementation and the developing the pipeline adoption scale. This was organised by a project manager (Stefanie Radford) with input from one other (Fiona Carragher) and a small group of scientists.

An audit was undertaken in which 26 London provider trusts were asked to complete a question regarding their use of NTproBNP testing. 'Intervention trusts' were allocated on the basis of delivering the lowest numbers or no NTproBNP tests. The Intervention trusts were supported in a variety of ways including: peer support from London Scientific & Diagnostic Network, help with leadership, and commissioning problems. Activities includes: sharing resources and/or template documentation, networking and engagement among key stakeholders including manufacturers/suppliers. A two hour workshop was attended by 5 exemplar trusts and 3 Intervention trusts in February 2013. One or two persons from each trust attended. Knowledge, business plans and contact details were shared. The workshop may have led to trusts undertaking initiatives to allow implementation such as training.<sup>14;18</sup>

##### *Effectiveness of the NP London implementation initiative*

The 5 intervention trusts and 10 control trusts were re-engaged in November 2013 to obtain data on: (1) change in number of NTproBNP tests undertaken, and (2) movement along pipeline adoption scale (if appropriate). Data was available from 2 of the 5 intervention trusts and 3 of 10 control trusts. We note that implementation rates may vary between trusts for other reasons: resources, trained staff, and availability of echo facilities, use of NICE guidelines.

For the control trusts increases in NTproBNP testing of 19% and 35% were observed in 2 trusts in the 12 month period January 2013 to December 2013. The third control trust did not provide NTproBNP test figures but stated that they were still offering the same service.

For the interventions trusts, 1 provider trust went from not being on the pipeline adoption scale to the 'adoption' phase at step 10 on the pipeline adoption scale (sign off of business case). 1 provider trust remained at step 5 (only offer to inpatients, currently working on business case).

##### *Cost of NP pro BNP London implementation initiative*

An estimate of the cost of the workshop was developed by EEPRU and validated by S Radford. The estimate includes costs for staff time and consumables costs based on information from the workshop organiser.<sup>18</sup> It was assumed that the top and bottom 20% of trusts would be invited to the workshop. (With the top 20% acting as exemplar trusts and the bottom 20% intervention trusts). This corresponds with the uptake observed in the 20 London trusts who responded in the LSDN project. It was assumed that two members of staff from each trust would be invited in addition to three other experts. It was assumed that the workshop would be arranged and facilitated by a project manager. Unit costs for staff time were taken from the personal social services research unit costs of health and social care 2013.<sup>19</sup> The total cost was estimated to be £4,172 and Table 4.4A provides a breakdown of this cost.

Table 4.4A: Cost of London BNP Implementation Intervention

Cost of intervention		
Workshop organisation and facilitation time (days)	2	PC Stefanie Radford (Including: Arranging attendees via email, Room booking, Agenda planning, Printing, one-to-one meetings in advance (Identified suitable attendees from intervention/exemplar sites - visited them - follow up), Searched online for cardiac and stroke contacts)
Workshop consumables costs	£500	PC Stefanie Radford: Workshop venue was hosted by NHS London at MWB (used Arundel room), cost includes refreshments for 16 people.
Hospital radiographer (per hour)	£34	Unit costs of health and social care 2013
Workshop participants time (hours)	4	Assumes 2 hours meeting + 2 hours travel time
Number of trusts invited to workshop (per 25 trusts)	10	Assumes top and bottom 20% invited
Number of workshop participants (per 25 trusts)	23	Assumes two representatives from each trust attend plus three additional experts
Workshop participants time cost	£3,128	
Workshop organisation and facilitation cost	£1,044	
<b>Total cost of workshop</b>	<b>£4,172</b>	

#### 4.4.4 Implementation initiatives identified from the systematic review

Utilisation may increase with implementation activities; however, it may not reach full (or perfect) implementation. The effectiveness of implementation activities is likely to vary with the type of activity and its particular context. A systematic review was conducted to establish the effectiveness of implementation activities.<sup>20</sup> This review included 27 systematic reviews examining the effectiveness of activities to improve the implementation of guidelines. The following types of initiative are included.

Table 4.4B: Type of implementation initiatives included within the systematic review

Educational meetings	Leader
Computerised clinical decision support system	Educational outreach visits
Reminders	Facilitation
Organisational	Educational material
Financial	Audit and feedback
QI strategy	Electronic guideline
Local opinion	Multifaceted

For the NP case study it is suggested that ‘organisational, educational, opinion leader, educational outreach, facilitation’ are the most relevant initiative types. Two studies were identified by a systematic reviewer as being of the greatest relevance to the BNP case study, see Table 4.4C. Estimates of effect size from the O’Brien et al study were considered the most relevant.<sup>21</sup>

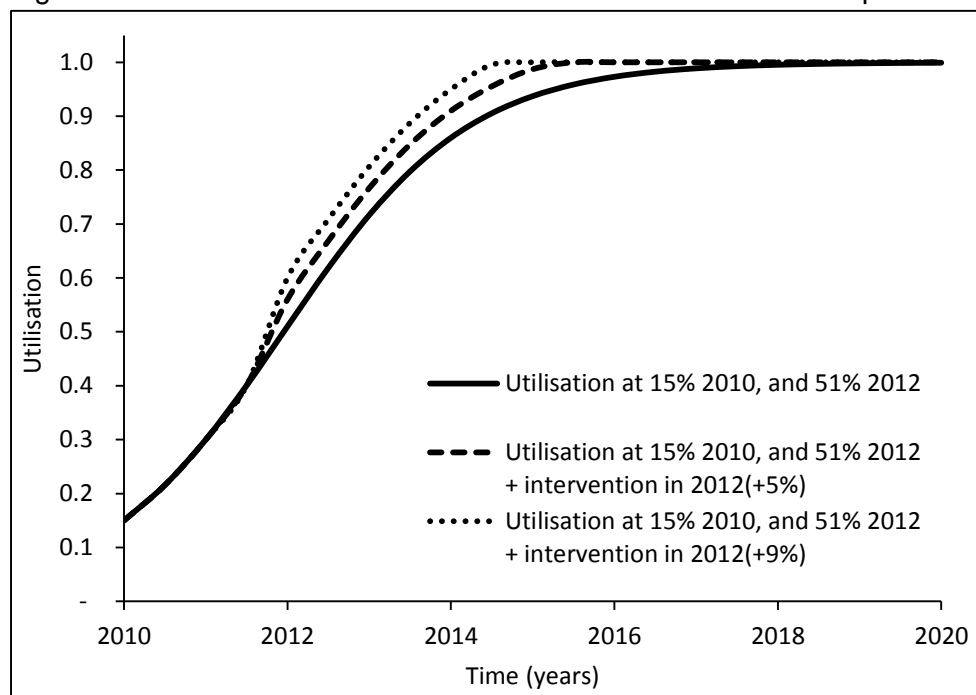
Table 4.4C: Studies reporting effectiveness of implementation activities selected from the systematic review

Study	Objective of the study	Results
Baskerville 2012	Overall effect size of practice facilitation studies that identified evidence-based guideline implementation within primary care practices as the outcome	<p>Some studies included looked at number of tests. Practice facilitation has a moderately robust effect on evidence based guideline adoption within primary care. Implementation fidelity factors, such as tailoring, the number of practices per facilitator, and the intensity of the intervention, have important resource implications.</p> <ul style="list-style-type: none"> <li>• An overall effect size of 0.56 (95% CI, 0.43-0.68) favoured practice facilitation (<math>z = 8.76</math>; <math>P &lt; .001</math>)</li> <li>• publication bias was evident</li> <li>• Primary care practices are 2.76 (95% CI, 2.18-3.43) times more likely to adopt evidence-based guidelines through practice facilitation.</li> </ul>
O’Brien et al, 2008 <sup>21</sup>	To assess the effects of education outreach visits on the practice of healthcare professionals or patient outcomes.	<p>Reports a large number of comparisons between education outreach visits, alone or in combination with other interventions, and no intervention on a variety of outcomes. Relevant results are those referring to the effect of the interventions on prescribing (reported as median adjusted risk difference and interquartile range):</p> <ul style="list-style-type: none"> <li>• Effect of multifaceted interventions: 8.8% (2.9%-12.7%)</li> <li>• Effect of education outreach visits alone: 5.0% (3.0-6.23%).</li> </ul>

#### 4.4.5 Estimates of effectiveness of implementation initiative used in the model

It was not possible to estimate the effectiveness of the London BNP initiative as data was only available from two trusts. Hence, estimates of effect size from the O’Brien et al study were used as these were considered the most relevant.<sup>21</sup> In the base case analysis an effect size of 5% was used and a scenario analysis applied an effect size of 9%. Figure 4.4 below shows the predicted diffusion of utilisation with and without the implementation intervention.

Figure 4.4: Predicted diffusion of utilisation with and without an implementation intervention



#### 4.5 Value of implementation activity. What is the value of specific implementation activities given their costs?

The value of the implementation activity is inversely related to its costs. The costs of the activity may include not only the development and roll out of the implementation activity itself, but also any costs related to service reconfiguration. It does not include the costs of the intervention and other costs included in the appraisal (e.g. costs of monitoring). The costs of an implementation initiative will be based on the estimated cost of the LSDN project, see Table 4.5.

Table 4.5: Costs of implementation activity used in the base case

<i>Cost of the initiative</i>	
Cost of initiative for 25 providers in London	£4,172 estimated cost of LSDN project
Cost of the initiative in England and Wales	£28,187 scaled by population size

#### 4.6 Multi-period analysis

A multi-period analysis was undertaken for 10 years from 2012. The multi-period analysis was started in 2012 as this was the time point for which utilisation data was available. Future costs and QALYs accrued were discounted at a rate of 3.5% in line with the NICE methods guide. This analysis assumes that the increase in utilisation of the intervention does not change the population size. However the population presenting with suspected HF was assumed to increase at a rate of 4.2% per annum, based on Hospital Episode Statistics data on the number of finished consultant episodes with a primary diagnosis of heart failure.<sup>1</sup> The total value of the implementation activity over the 10 year period was calculated.

## 4.7 Scenario analyses

The following scenario analyses were undertaken to explore the impact of key uncertainties on model results:

- Population size: annual rate of suspected HF 0.27% (population of 150,000)
- Current utilisation of BNP testing 63%
- Efficacy of the implementation intervention 9% increase.

In addition a generalizability analysis was undertaken. This indicates the minimum increase in utilisation for a given cost of an implementation activity that is still of value to the NHS and, conversely, the maximum cost for a given increase in utilisation for a threshold of £20,000 and £30,000 per QALY gained.

## 5 Results

### 5.1 Net benefit. Is the technology of value to the NHS?

NICE has recommended that testing for NPs in patients with suspected heart failure without previous MI can accelerate diagnosis of heart failure and also avoid unnecessary echocardiography.<sup>3</sup> The value of NP testing in patients without previous MI was estimated at £1,524 or 0.076 QALYs for a threshold of £20,000 per QALY gained and £2,288 or 0.076 QALYs for a threshold of £30,000 per QALY gained.

### 5.2 Current value. What is the value of the technology given current utilisation and population size?

Table 5.2 shows the current value of NP testing for the suspected HF population. The current value represents the benefit of NP testing to the NHS given the patient population currently receiving testing. The current value to the NHS is approximately £164 million or 8,230 QALYs for a threshold of £20,000 per QALY gained.

Table 5.2: Static population analysis with base case assumptions

Static population analysis	WTP=£20000		WTP=£30000	
	NMB	NHB	NMB	NHB
Net Benefit to the NHS	£1,524	0.076	£2,288	0.076
Current value of technology given current utilisation and population size. Population= 210000, current utilisation= 4.43	£164,594,517	8,230	£247,101,322	8,237
Expected Value of Perfect Implementation. Value of increasing utilisation from current to desirable maximum. Current utilisation=4.43, Desirable maximum=8.62	£155,486,060	7,774	£233,427,041	7,781
Expected Value of Actual Implementation. Value of increasing utilisation from current to achievable. Current utilisation=4.43, Achievable utilisation with intervention=4.86	£16,004,029	800	£24,026,418	801
Value of the implementation activity. Expected value of actual implementation minus cost of intervention (£28,187)	£15,975,842	799	£23,998,232	800

### 5.3 Expected value of perfect implementation. What is the value of increasing utilisation so all eligible patients receive the test?

Table 5.2 presents the expected value of perfect implementation of NP testing for the overall population with suspected HF. The expected value of perfect implementation represents the maximum amount that the NHS should invest in implementation activities whilst still accruing a non-negative value from NP testing. It corresponds to the value of NP testing in the eligible population currently not receiving testing. The expected value of perfect implementation is approximately £155million or 7,774 QALYs for the suspected HF population in England and Wales for a threshold of £20,000 per QALY gained.

### 5.4 Expected value of actual implementation. What is the value of increasing utilisation from current to achievable?

Table 5.2 shows the expected value of implementation assuming that the implementation activity increases utilisation by 5% (from 51% to 56%) for the base-case. The 5% increase in utilisation corresponds to the average effectiveness of educational outreach activities as reported in the literature.<sup>21</sup> The expected value of actual implementation is much smaller than the expected value of perfect implementation. For the overall population in England and Wales, the NHS could invest up to £16million for an activity that increases utilisation by 5% at a threshold of £20,000 (approximately £3million for a one percent increase in utilisation).

### 5.5 Value of implementation activity. What is the value of specific implementation activities given their costs?

Table 5.2 shows the value of an implementation activity costing an average of £4,172 per 25 providers (£28,187 for the whole England and Wales). As the implementation activity has a relatively low cost the value of the implementation activity is similar to the expected value of actual implementation providing additional value to the NHS at £16million or 799 QALYs for England and Wales at a threshold of £20,000 per QALY.

## 5.6 Multi-period analysis

The multi-period analysis demonstrates how the value of the implementation activity accrues over a 10 year period, see Table 5.6. The total value of the implementation activity over 10 years is £76million.

Table 5.6: Multi-period analysis with base case assumptions

Multi-period analysis: Predictions for 10 years, including discounting, WTP=£20000

Year	Population presenting with suspected HF*	Predicted utilisation without intervention	Predicted utilisation with intervention	Perfect Implementation	Current value	Expected Value of Actual Implementation	Expected Value of Perfect Implementation	Value of Implementation Activity
2012	210,000	51%	56%	100%	£163.2	£179.2	£320.1	£16.0
2013	218,820	72%	77%	100%	£230.9	£247.0	£322.2	£16.1
2014	228,010	86%	91%	100%	£279.0	£295.2	£324.4	£16.2
2015	237,587	94%	99%	100%	£306.1	£322.4	£326.6	£16.3
2016	247,566	97%	100%	100%	£320.0	£328.8	£328.8	£8.8
2017	257,963	99%	100%	100%	£327.3	£331.1	£331.1	£3.7
2018	268,798	100%	100%	100%	£331.7	£333.3	£333.3	£1.6
2019	280,087	100%	100%	100%	£334.9	£335.5	£335.5	£0.6
2020	291,851	100%	100%	100%	£337.5	£337.8	£337.8	£0.3
2021	304,109	100%	100%	100%	£340.0	£340.1	£340.1	£0.1
TOTAL					£2,971	£3,051	£3,300	£80

All costs are presented in £millions, all costs are discounted at an annual rate of 3.5% from 2013 onwards

\*Assumes HF incidence increasing by 4.2% per annum

## 5.7 Scenario analyses

A scenario analysis around the size of the eligible population was undertaken to explore the impact of the uncertainty in the size of the HF population. In this analysis the annual rate of suspected HF was assumed to be 0.27% (equivalent to an eligible population of 150,000). The results of this analysis are presented in Table 5.7A.



Table 5.7A: Scenario analysis – size of eligible population

Static population analysis	WTP=£20000		WTP=£30000	
	NMB	NHB	NMB	NHB
Net Benefit to the NHS	£1,524	0.076	£2,288	0.076
Current value of technology given current utilisation and population size. Population= 150000, current utilisation= 4.43	£117,567,512	5,878	£176,500,945	5,883
Expected Value of Perfect Implementation. Value of increasing utilisation from current to desirable maximum. Current utilisation=4.43, Desirable maximum=8.62	£111,061,471	5,553	£166,733,600	5,558
Expected Value of Actual Implementation. Value of increasing utilisation from current to achievable. Current utilisation=4.43, Achievable utilisation with intervention=4.86	£11,431,449	572	£17,161,727	572
Value of the implementation activity. Expected value of actual implementation minus cost of intervention (£28,187)	£11,403,263	570	£17,133,541	571

A scenario analysis around the current utilisation of BNP testing was undertaken to explore the impact of uncertainty in the maximum optimal utilisation rate for NP testing. In this analysis a current utilisation rate of 63% was assumed which is derived from a maximum optimum utilisation rate of 7.1 BNP tests per 1,000 GP population. The results of this analysis are presented in Table 5.7B.

Table 5.7B: Scenario analysis – maximum optimum utilisation rate

Static population analysis	WTP=£20000		WTP=£30000	
	NMB	NHB	NMB	NHB
Net Benefit to the NHS	£1,524	0.076	£2,288	0.076
Current value of technology given current utilisation and population size. Population= 210000, current utilisation= 4.43 (63%)	£200,396,149	10,020	£300,849,350	10,028
Expected Value of Perfect Implementation. Value of increasing utilisation from current to desirable maximum. Current utilisation=4.43, Desirable maximum=7.08 (100%)	£119,684,427	5,984	£179,679,013	5,989
Expected Value of Actual Implementation. Value of increasing utilisation from current to achievable. Current utilisation=4.43, Achievable utilisation with intervention=4.79 (68%)	£16,004,029	800	£24,026,418	801
Value of the implementation activity. Expected value of actual implementation minus cost of intervention (£28,187)	£15,975,842	799	£23,998,232	800

A scenario analysis around the current utilisation of BNP testing was undertaken to explore the impact of uncertainty in the efficacy of implementation intervention. In this analysis an increase in utilisation of 9% as a result of the intervention was assumed. The results of this analysis are presented in Table 5.7C.

Table 5.7C: Scenario analysis – efficacy of the implementation intervention

Static population analysis	WTP=£20000		WTP=£30000	
	NMB	NHB	NMB	NHB
Net Benefit to the NHS	£1,524	0.076	£2,288	0.076
Current value of technology given current utilisation and population size. Population= 210000, current utilisation= 4.43 (51%)	£164,594,517	8,230	£247,101,322	8,237
Expected Value of Perfect Implementation. Value of increasing utilisation from current to desirable maximum. Current utilisation=4.43, Desirable maximum=8.62 (100%)	£155,486,060	7,774	£233,427,041	7,781
Expected Value of Actual Implementation. Value of increasing utilisation from current to achievable. Current utilisation=4.43, Achievable utilisation with intervention=5.19 (60%)	£28,167,091	1,408	£42,286,496	1,410
Value of the implementation activity. Expected value of actual implementation minus cost of intervention (£28,187)	£28,138,904	1,407	£42,258,309	1,409

### Generalizability analysis

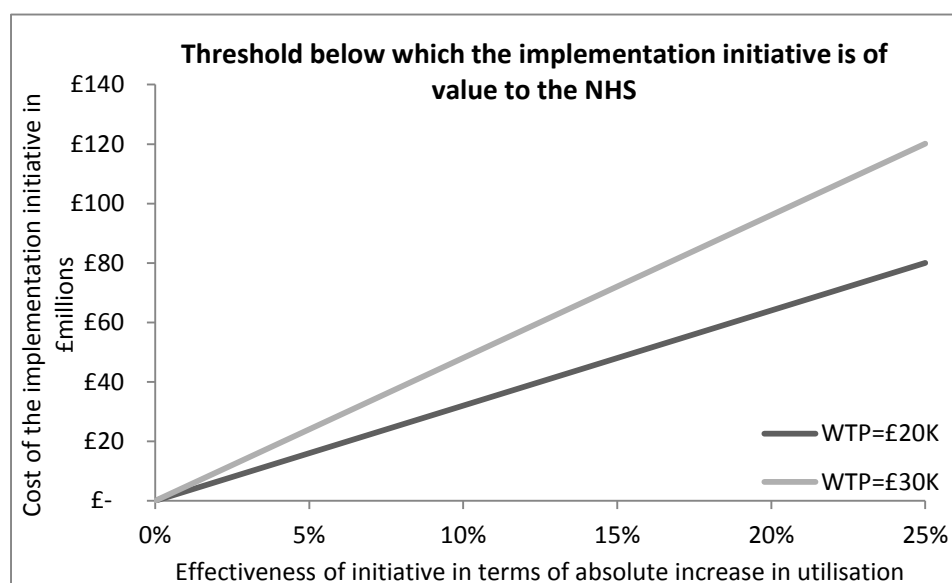
This indicates the minimum increase in utilisation for a given cost of an implementation activity that is still of value to the NHS and, conversely, the maximum cost for a given increase in utilisation for a threshold of £20,000 and £30,000 per QALY gained. The generalizability analysis provides indicative estimates of costs and effectiveness which could be applied to a broader range of implementation activities. The results of the generalizability analysis are presented in Table 5.7D and Figure 5.7. For an initiative resulting in a 5% absolute increase in utilisation there would be value to the NHS if the cost of the initiative was less than £16million (for a WTP threshold of £20,000).

Table 5.7D: Generalisability analysis

### Threshold below which the implementation initiative is of value to the NHS

Effectiveness of initiative in terms of absolute increase in utilisation	Cost of the implementation initiative in £millions	
	WTP=£20K	WTP=£30K
0%	£0	£0
5%	£16	£24
10%	£32	£48
15%	£48	£72
20%	£64	£96
25%	£80	£120

Figure 5.7: Generalisability analysis



## 6 Discussion

### 6.1 Conclusions

The value of the implementation activity depends on its costs and effectiveness in increasing utilisation. In this case study, there appears to be value in additional implementation efforts directed towards encouraging the utilisation of NP testing for persons with suspected HF without previous MI. At a threshold of £20,000 per QALY gained, additional investment in an activity that increases utilisation by 5% (absolute increase in utilisation rates) would generate an additional 799 QALYs (£16 million in terms of monetary equivalent) across England and Wales compared to the use of these resources in other (health generating) NHS activities. Scenario analyses demonstrated that value to the NHS was sensitive to uncertain model inputs such as the size of the eligible population and the efficacy of the implementation intervention.

### 6.2 Strengths

These analyses demonstrate a practical application of the implementation framework to a case study. They estimate the added value to the NHS of investing in activities that increase utilisation of recommended interventions. This framework can help the NHS in general and commissioners in particular in quantifying the value of investing resources in increasing utilisation in a manner consistent with the value assessment of new interventions conducted by NICE. Scenario analysis shows how changes in model parameters can affect the predicted value of implementation. This case study provides a useful demonstration of the practical challenges faced in populating such a model.

### 6.3 Limitations

The main limitations of the analysis are a lack of evidence on: cost effectiveness, effectiveness of implementation intervention, utilisation, and population size.

The lack of evidence on cost effectiveness was a key limitation. The clinical guidelines did not include an economic evaluation in relation to the use of NP testing for HF diagnosis. The HTA on which the clinical guideline development was based did include an economic model, however the diagnostic strategy recommended in the guidelines was not modelled. In addition the most relevant comparator (ECG) was not included within the economic evaluation; hence, estimates of incremental costs and QALYs are likely to be considerably overestimated by using the 'do nothing' comparator.

There was a lack of evidence on utilisation rates of NP testing. Although data on current rates of NP testing were available, obtaining an estimate of maximum optimal rates was very difficult. There was a disparity between estimated optimal rates based on the suspected heart failure population and rates observed in the diagnostics Atlas data set. Robust data on NP testing rates were only available for one time point so estimated diffusion curves were subject to considerable uncertainty.

There was a lack of evidence on the effectiveness of implementation initiatives. There was detailed evidence describing several initiatives specifically designed to increase utilisation of NP testing, however evidence of their efficacy was very limited. The literature on the effectiveness of more general implementation initiatives is of limited quality and difficult to generalise to this specific case study.

There was considerable uncertainty surrounding the evidence on population size. The differences in estimates of population size from different published data sources highlights the importance of validating data sources with clinical experts.

#### **6.4 Key uncertainties and areas for future research**

The key areas of uncertainty relates to a lack of evidence on cost effectiveness, population size and utilisation. These areas are detailed in the limitations section above and are key areas for future research.

Multi-period analysis requires an understanding of how the patient population will change over time. Predictions of changes in utilisation rates over time with and without an intervention are also required. Diffusion curve methodology can be used to predict how utilisation will change over time in the future but the generation of a diffusion curve is associated with considerable data requirements.

Parameter uncertainty could be quantified using probabilistic sensitivity analyses; however, this approach requires data on the variability of parameter inputs. Extending the analysis to incorporate this uncertainty in a probabilistic model of the value of implementation is an area for future research.

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