

MSAC Application 1740

NT-proBNP to aid in the diagnosis of patients with suspected heart failure in the non-hospital setting

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable.

Please use this template, along with the associated [Application Form Instructions](#) to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted. The separate [MSAC Guidelines](#) should be used to guide health technology assessment (HTA) content of the Application Form

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au

Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):

Corporation name: Roche Diagnostics Australia Pty Limited

ABN: 29 003 001 205

Business trading name: Roche Diagnostics Australia

Primary contact name: **REDACTED**

Primary contact numbers

Business: **REDACTED**

Mobile: **REDACTED**

Email: **REDACTED**

Alternative contact name: **REDACTED**

Alternative contact numbers

Business: **REDACTED**

Mobile: **REDACTED**

Email: **REDACTED**

2. (a) Are you a consultant acting on behalf on an applicant?

Yes

No

(b) If yes what is the Applicant(s) name that you are acting on behalf of?

Not applicable

3. (a) Are you a lobbyist acting on behalf of an Applicant?

Yes

No

(b) If yes, are you listed on the Register of Lobbyists?

Yes

No

(c) Have you engaged a consultant on your behalf?

Yes

No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

NT-proBNP to aid in the diagnosis of patients with suspected heart failure in the non-hospital setting

5. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Heart failure (HF) is a complex clinical syndrome with typical symptoms and signs that generally occur on exertion. It is secondary to an abnormality of cardiac structure or function that impairs the ability of the heart to fill with blood or eject blood sufficient to fulfil the needs of the metabolising organs. The high incidence rate of HF in Australia warrants consideration; approximately 69 new cases per 10,000 adults aged 45 and over are diagnosed with HF each year (1). However, HF is difficult to definitively diagnose in non-acute primary care, as symptoms are non-specific and differential diagnosis is complex and patients often present with co-existing comorbidities. Signs and symptoms that are characteristic of HF are also common to other chronic diseases (COPD, obesity, myocardial ischaemia). The gold standard for diagnosing (or ruling out) HF is standard diagnostic workup including echocardiogram, however, it is expensive and associated with long wait times.

6. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

NT-proBNP is a protein released by the heart when the heart wall is stretched. When NT-proBNP levels in the blood are low, HF can be excluded. Raised NT-proBNP levels in the blood can indicate that someone has HF and levels tend to rise with disease severity. NT-proBNP testing involves a blood test to determine the level of cardiac neurohormone in the blood of a patient suspected of having HF. NT-proBNP acts as a counter-regulatory hormone to stabilise circulatory function. In an attempt to maintain cardiac output from a failing heart, the renin-angiotensin-aldosterone system is activated to enhance blood volume retention, circulatory vasoconstriction and ventricular remodelling in order to maintain ventricular pre-load. This physiological response to the failing heart actually increases the workload of the heart because of an increase in vascular resistance and after-load. The circulatory volume overload stretches cardiac myocytes which then release BNP and NT-proBNP (the hormonally inactive, more stable natriuretic peptide).

7. (a) Is this a request for MBS funding?

- Yes
 No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

- Amendment to existing MBS items)
 New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service/technology:

Not applicable

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

- An amendment to the way the service is clinically delivered under the existing item(s)
 An amendment to the patient population under the existing item(s)
 An amendment to the schedule fee of the existing item(s)
 An amendment to the time and complexity of an existing item(s)
 Access to an existing item(s) by a different health practitioner group
 Minor amendments to the item descriptor that does not affect how the service is delivered
 An amendment to an existing specific single consultation item

- An amendment to an existing global consultation item(s)
- Other (please describe below):

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

- A new item which also seeks to allow access to the MBS for a specific health practitioner group
- A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
- A new item for a specific single consultation item
- A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

- Yes
- No

(g) If yes, please advise:

Not applicable

8. What is the type of medical service/technology?

- Therapeutic medical service
- Investigative medical service
- Single consultation medical service
- Global consultation medical service
- Allied health service
- Co-dependent technology
- Hybrid health technology

9. For investigative services, advise the specific purpose of performing the service (which could be one or more of the following):

- To be used as a screening tool in asymptomatic populations
- Assists in establishing a diagnosis in symptomatic patients
- Provides information about prognosis
- Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
- Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

10. Does your service rely on another medical product to achieve or to enhance its intended effect?

- Pharmaceutical / Biological
- Prosthesis or device
- No

11. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

Not applicable

(b) If yes, please list the relevant PBS item code(s):

Not applicable

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

- Yes (please provide PBAC submission item number below)
- No

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Not applicable

12. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

- Yes
 No

(b) If yes, please provide the following information (where relevant):

Not applicable

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

- Yes
 No

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

- Yes
 No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

13. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables:

- Each NT-proBNP test is a discrete single use test, to be disposed of after use. Elecsys® proBNP II and proBNP II STAT assays come in kits of 100 and 300 tests per kit. NT-proBNP assays developed by other vendors may be used.

Multi-use consumables:

- **cobas e** 402, e 411, e 601, e 602, e 801 – instruments to run the tests

Reagents:

- Streptavidin-coated microparticles, 1 bottle, 12.4 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- Anti-NT-proBNP-Ab~biotin, 1 bottle, 21.0 mL:
Biotinylated monoclonal anti-NT-proBNP antibody (mouse)
1.1 µg/mL; phosphate buffer 40 mmol/L, pH 5.8; preservative.
- Anti-NT-proBNP-Ab~Ru(bpy), 1 bottle, 19.7mL:
Monoclonal anti-NT-proBNP antibody (sheep) labelled with ruthenium complex 1.1 µg/mL;
phosphate buffer 40 mmol/L, pH 5.8; preservative.

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

14. (a) If the proposed medical service involves use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer, or any other type of therapeutic good, please provide details

Type of therapeutic good: In-vitro diagnostic test

Manufacturer's name: Roche Diagnostics

Sponsor's name: Roche Diagnostics

Other commercially available tests include: Siemens Healthineers (Stratus® CS Acute Care™), BioMerieux (VIDAS NT-proBNP2), Abbott Alere NT-proBNP, Ortho VITROS® NT-proBNP II, Radiometer AQT90 FLEX NT-proBNP

- (b) Has it been listed on the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)? If the therapeutic good has been listed on the ARTG, please state the ARTG identification numbers, TGA-approved indication(s), and TGA-approved purpose(s).

Yes.

ARTG identification number: 200275

Product type: IVD Class 2

Global Medical Device Nomenclature (GMDN): CT974 Clinical chemistry-specific protein IVDs

Intended purpose: Products used for the qualitative/quantitative determination of specific proteins in biological samples

Specific conditions: No Specific Conditions included on Record

- (c) If a medical device is involved, has the medical device been classified by TGA as a Class III OR Active Implantable Medical Device (AIMD) under the TGA regulatory scheme for devices?

- Class III
 AIMD
 N/A

- (d) Is the therapeutic good classified by TGA for Research Use Only (RUO)?

No

15. (a) If not listed on the ARTG, is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

- Yes (If yes, please provide supporting documentation as an attachment to this application form)
 No

16. If the therapeutic good is not ARTG listed, is the therapeutic good in the process of being considered by TGA?

Not applicable

- (b) If the therapeutic good is NOT in the process of being considered by TGA, is an application to TGA being prepared?

- Yes (please provide details below)
 No

PART 4 – SUMMARY OF EVIDENCE

17. Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At ‘Application Form lodgement’, please do not attach full text articles; just provide a summary.

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
1.	Diagnostic accuracy study	Primary care REFerral for Echocardiogram (REFER) in heart failure: a diagnostic accuracy study ISRCTN17635379	Enrolled 304 participants presenting with HF symptoms. Study evaluated performance of a CDR, with or without NT-proBNP assay, for identifying heart failure. Reference standard was expert consensus from 3 cardiologists. At threshold of <125 pg/mL NT-proBNP alone was better than validated CDR+NT-proBNP at HF diagnosis. Sensitivity was 94.2% and specificity was 49.0%.	Primary care REFerral for Echocardiogram (REFER) in heart failure: a diagnostic accuracy study	February 2017
2.	Prospective diagnostic accuracy study	Rapid point-of-care NT-proBNP optimal cut-off point for heart failure diagnosis in primary care	220 patients referred by GPs to echocardiography with suspected HF were included. Patients received ECG, chest X-ray and NT-proBNP test. HF diagnosis was made by cardiologist blinded to NT-proBNP test value. Best cut-off for NT-proBNP test was 280 pg/mL (sensitivity 1, specificity 0.88), measurement of NT-proBNP would avoid 67% of requested ECGs.	https://pubmed.ncbi.nlm.nih.gov/22541282/	July 2012

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
3.	Prospective multicentre controlled trial (cluster randomised) including diagnostic accuracy study	Diagnostic accuracy of point-of-care testing for acute coronary syndromes, heart failure and thromboembolic events in primary care: a cluster randomised controlled trial. DRKS00000709	369 patients presenting to 68 primary care practices presenting with chest pain. Patients received POCT (measuring NT-proBNP and other markers) or conventional diagnosis based on best clinical practice. POCT showed high sensitivity, specificity and NPV for HF diagnosis. Working diagnosis were significantly more correct in POCT versus conventional.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3071323/	March 2011
4.	Meta-analysis	Meta-analysis: Effect of B-type Natriuretic peptide testing on clinical outcomes in patients with acute dyspnoea in the emergency room	A meta-analysis of five randomised controlled trials which compared BNP and/or NT-proBNP testing to diagnose HF with routine care in patients presenting with acute dyspnoea.	https://pubmed.ncbi.nlm.nih.gov/21135296/	December 7 th , 2010
5.	National Institute for Health and Care Excellence (NICE) guideline	Chronic heart failure in adults	A guideline which covers diagnosing and managing chronic HF in people aged 18 and over. It aims to improve diagnosis and treatment to increase the length and quality of life for people with HF. The guideline provides information on the use of NT-proBNP assays for the diagnosis of HF.	https://www.ncbi.nlm.nih.gov/books/NBK536075/	September 2018

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
6.	Diagnostic accuracy study	The diagnostic accuracy and utility of a B-type natriuretic peptide test in a community population of patients with suspected heart failure	297 patients HF symptoms were referred by GPs for BNP and NT-proBNP testing. The study measured sensitivity, specificity, NPV and PPV.38% of patients had LVDS. Using cut-offs of 40 pg/ml and 150 pg/ml for BNP and NT proBNP, could have prevented 24% and 25% of referrals to the clinic, respectively.	https://pubmed.ncbi.nlm.nih.gov/16638247/	May 2006
7.	RCT	B-type natriuretic peptide in the evaluation and management of dyspnoea in primary care	323 patients presenting with dyspnoea referred by 29 primary care physicians in Switzerland and Germany. Patients assigned in 1:1 ratio for diagnostic strategy with or without BNP testing. HF diagnosed in 34% patients. BNP testing increased diagnostic certainty as defined by need for further diagnostic work up (33% vs 45%).	https://pubmed.ncbi.nlm.nih.gov/22550938/	02 May 2012
8.	Meta-analysis of prospective studies	Diagnosing heart failure in primary care: individual patient data meta-analysis of two European prospective studies	Pooled data from 1073 participants with HF symptoms. Assessed the diagnostic accuracy of NT-proBNP and evaluated threshold levels in primary care patients. NT-proBNP was better at detecting HFrEF than HFpEF in a primary care setting. In persons >70 yrs, a threshold of 125 ng/L had NPV of 84.9% and PPV of 68.1%. A threshold of 400ng/L had an NPV of 74.7% and PPV of 81.8%.	https://pubmed.ncbi.nlm.nih.gov/33755352/	June 2021

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
9.	Community-based cohort study	Life expectancy for community-based patients with heart failure from time of diagnosis	Review of 733 patients with rapid access to HF diagnostic clinic b/w 2002 and 2012. 38.9% were diagnosed with HF, 63.8% of these patients were alive after 5 years. Prognosis following HF diagnosis was better than previously reported, owing to prompt diagnosis in the community setting.	https://pubmed.ncbi.nlm.nih.gov/25464268/	January 2015
10.	Cross sectional diagnostic accuracy study	The diagnostic value of physical examination and additional testing in primary care patients with suspected heart failure	721 patients suspected of new onset HF underwent diagnostic workup – chest X-ray, ECG, NT-proBNP assay and echocardiography in outpatient diagnostic HF clinic. HF diagnosis was determined by outcome panel using clinical data, blinded to biomarker data. 28.7% of patients had HF. The largest additional quantitative diagnostic contribution was NT-proBNP assay.	https://pubmed.ncbi.nlm.nih.gov/22104551/	December 2011

Abbreviations: BNP; brain natriuretic peptide, CDR; clinical decision rule, ECG; electrocardiogram, GP; general practitioner, HF; Heart failure, HFpEF; heart failure preserved ejection fraction. HFrEF; Heart failure reduced ejection fraction, LVSD; left ventricular systolic dysfunction, NPV; negative predictive value, NT-proBNP; N-terminal pro b-type natriuretic peptide, POCT; point-of-care test, PPV; positive predictive value, RCT; randomised controlled trial.

18. Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application). Do not attach full text articles; this is just a summary.

No yet-to-be-published relevant studies for NT-proBNP in the setting or population requested in this application were identified.

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. List all appropriate professional bodies/organisations representing the health professionals who provide the service. For **MBS-related applications** ONLY, please attach a brief 'Statement of Clinical Relevance' from the most relevant college/society.

Cardiac Society of Australia and New Zealand (CSANZ)

The Royal College of Pathologists of Australasia (RCPA)

20. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):

CSANZ

21. List the consumer organisations relevant to the proposed medical service (noting there is **NO NEED** to attach a support letter at the 'Application Lodgement' stage of the MSAC process):

National Heart Foundation of Australia

22. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:

Siemens Healthineers

BioMerieux

Abbott Diagnostics

Ortho Clinical Diagnostics

Radiometer

23. Nominate two experts that can be contacted about the proposed medical service, and current clinical management of the condition:

Name of expert 1: **REDACTED**

Telephone number(s): **REDACTED**

Email address: **REDACTED**

Justification of expertise: **REDACTED**

Name of expert 2: **REDACTED**

Telephone number(s): **REDACTED**

Email address: **REDACTED**

Justification of expertise: **REDACTED**

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease (in terms of both morbidity and mortality):

Heart failure (HF) is a complex clinical syndrome with typical symptoms and signs that generally occur on exertion but can also occur at rest. It is secondary to an abnormality of cardiac structure or function that impairs the ability of the heart to fill with blood or eject blood sufficient to fulfil the needs of the metabolising organs. HF is divided into two main types, HF with a reduced ejection fraction (HFrEF) and HF with a preserved ejection fraction (HFpEF). HFrEF is defined as clinical symptoms of heart failure and a measured left ventricular ejection fraction (LVEF) of less than 50%. HFpEF is defined as a clinical syndrome with or without symptoms of heart failure, a LVEF of at least 50%, and objective evidence of structural heart disease or diastolic dysfunction without an alternative cause (2).

The high incidence rate of HF in Australia warrants consideration; approximately 69 new cases per 10,000 adults aged 45 and over are diagnosed with HF each year(1), equating to approximately 73,620 newly diagnosed HF patients in 2022. However, HF is difficult to definitively diagnose in non-acute primary care, as symptoms are non-specific and differential diagnosis is complex. Further to this, chronic HF in particular is associated with a long-term apparition of symptoms and gradual disease progression. Patients with suspected chronic HF typically present at the primary care setting (i.e. GPs and cardiologists) for diagnosis and triage. General signs and symptoms of chronic HF as listed in Table 1 are also common in other diseases, such as COPD, acute coronary syndrome, myocarditis, valvular heart disease, hypertrophic cardiomyopathy, pulmonary hypertension, renal dysfunction, and stroke. Patients often present with co-existing comorbidities. Consequently, approximately 35% of people who present with HF symptoms actually have HF (3, 4).

Survival rates for chronic HF range from 81% to 91% at 1 year and 52% to 63% at 5 years (5, 6). Diagnosis of HF at the time of hospitalisation for HF has been associated with less improvement in survival, early identification of HF in primary care is needed to reduce hospitalisation and adverse outcomes (7). A systematic review of mortality and repeat hospitalisation rates for patients hospitalised with HF in Australia found 20% of patients are readmitted within 30-days of discharge, and 56% of patients within 1 year of discharge, with all-cause mortality rates of 8% and 25% respectively for these groups (8).

Appreciating the high rates of cardiovascular risk factors in Australia's Indigenous population, the age-standardised prevalence rates of HF in Indigenous Australians is 1.7 times higher than in non-Indigenous Australians (9). Furthermore, Indigenous people with HF have more comorbidities and higher mortality than those who are not Indigenous, and Indigenous Australians are 1.4 times more likely to die from HF than non-Indigenous Australians. Early detection and management of cardiac conditions is likely to reduce the risk of HF among Indigenous people and consequently, cardiovascular assessments are now recommended from 18 years of age in these groups (10). Rates of hospitalisation for HF are substantially higher in remote areas compared to non-remote areas. Individuals with a socioeconomic status (SES) of 1 (the lowest SES) had a HF rate of 353 per 100,000 people compared to a rate of 251 for individuals with the same SES in major cities (11).

The current gold standard test for confirming (or ruling out) a suspected HF diagnosis is standard HF diagnostic workup including echocardiography. However, long wait times and the location of centres providing echocardiography services means that access is limited, particularly for Aboriginal and Torres Strait Islander people and those living in rural, regional and remote areas. Consequently, there is a profound need for accurate and timely differential diagnosis to improve patient access to effective treatments and alleviate pressures on the healthcare system.

25. Specify the characteristics of patients with (or suspected of having) the medical condition, who would be eligible for the proposed medical service/technology (including details on how a patient would be investigated, managed and referred within the Australian health care system, in the lead up to being eligible for the service):

HF is a common clinical condition in older adults, the prevalence of HF increases with each decade of life from 3% in those aged 65-74 years to 7% in those aged 75-84 years, and over 10% in those aged ≥85 years (12). Additionally, HF is associated with significant multimorbidity. A study of patients in the Australian population aged ≥45 with a diagnosis of HF who presented to general practitioners showed less than 1% of patients had an isolated diagnosis of HF. Over 50% of patient presented with six or more comorbidities, with hypertension and osteoarthritis being the most prevalent (13). Patients with HF will also often present with cardiovascular diseases with similar aetiology, such as ischaemic heart disease which will require similar treatment strategies. HF has typical symptoms; however, these are often non-specific in nature. Dyspnoea is a core, yet non-specific symptom of HF, patients will often present to primary care with this breathlessness. Patients may also present with fatigue and palpitations. The symptoms of HF will initially present following exertion (physical and emotional), as the disease progresses the symptoms will manifest following lower levels of physical exertion, and potentially while at rest (14). Table 1 describes the typical and less typical signs and symptoms which may occur in a patient presenting with HF. Due to the prevalence of HF in older individuals and the multimorbidity patients will present with, the management and diagnosis of these patients is normally complex and requires input from a multidisciplinary team for appropriate clinical management.

Table 1: Typical and less typical signs and symptoms of HF.

More typical HF symptoms	More specific HF signs
Dyspnoea (usually following exertion)	Elevated jugular venous pressure
Orthopnoea	Hepatojugular reflux
Paroxysmal nocturnal dyspnoea	Third heart sound
Fatigue	Laterally displaced apex beat
Less typical HF symptoms	Less specific HF signs
Nocturnal cough	Weight gain (>2 kg/wk)
Wheeze	Weight loss (in advanced HF)
Abdominal bloating	Peripheral oedema (ankle, sacrum)
Anorexia	Pulmonary crackles
Confusion (elderly)	Pleural effusions
Depression	Cardiac murmur
Palpitations	Tachycardia
Dizziness	Tachypnoea
Syncope	Cheyne-Stokes respirations
Bendopnea (shortness of breath when leaning forward)	Ascites

Source: p. 1136, Table 1, National Heart Foundation of Australia and CSANZ: Guidelines for the Prevention, Detection, and Management of Heart Failure in Australia 2018

As previously described, patients with HF will most commonly present initially with dyspnoea. Dyspnoea may also be indicative of a broad range of different pathophysiological states besides HF. Consequently, patients presenting with dyspnoea to a primary care physician can present a clinical challenge to health care providers. Thus, approaches to further evaluation of the patient will differ according to the duration and severity of the dyspnoea, as well as patient age and general health status. The clinician will enquire about the presence of any additional signs and symptoms of HF (as listed in Table 1). A physical examination of the patient will then assess vital signs (heart rate and rhythm, blood pressure, respiratory rate, and temperature), peripheral perfusion, volume status (jugular venous pressure, peripheral and sacral oedema, ascites and hepatic congestion), cardiac palpitation, and auscultation (apex beat, gallop rhythm, and murmurs) and auscultation of lung fields (air entry, crackles and wheeze).

Further investigations in patients where HF is suspected to confirm the diagnosis are as follows:

- 12-Lead ECG

- to assess cardiac rhythm, QRS duration and presence of underlying conditions such as myocardial ischaemia or LV hypertrophy.
- Chest X-ray
 - Detect pulmonary congestion and identify alternative cardiac or non-cardiac causes for patient symptoms
- B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide
 - Recommended when diagnosis of HF is suspected but uncertain
- Transthoracic echocardiogram
 - Recommended to improve accuracy of HF diagnosis, assess cardiac structure, and function and assist in the classification of the HF diagnosis and therefore guide management of the condition.

An ECG is recommended to assess cardiac rhythm and identify potential underlying conditions such as myocardial ischaemia or arrhythmias but provides a low quality of evidence for a diagnosis of HF. While HF is unlikely to be the correct diagnosis if a patient has a normal ECG, abnormalities on an ECG may be associated with a diagnosis other than HF (15). Additionally, chest X-rays provide insufficient evidence to confirm a diagnosis of HF, an abnormal chest X-ray may be further suggestive of HF, but a normal chest X-ray cannot rule out HF diagnosis. The main utility of chest X-rays in this circumstance is to rule out other pathologies which may be responsible for the patients' symptoms. The current diagnosis of HF in a primary care setting follows a stepwise clinical algorithm (Figure 1). Where HF is suspected but the diagnosis uncertain the patient will be referred by the primary care physician for further investigation in the form of an echocardiogram. A serum NT-proBNP assay, which is the technology in focus for this application, provides an alternative to high-cost echocardiography at this stage in the clinical pathway (Figure 2). NT-proBNP is a peptide released by the myocardium in response to pressure overload. NT-proBNP assays such as the Elecsys® NT-proBNP II and Elecsys® NT-proBNP II STAT assays quantify the levels of the peptide in patient blood and serum samples. The NT-proBNP assay would be delivered in conjunction with the standard diagnostic workup described previously, prior to an echocardiogram. Elevated NT-proBNP is indicative of a diagnosis of HF, if patients are above threshold levels further investigation via echocardiography is recommended to confirm the diagnosis. If patients are below threshold values for NT-proBNP, a diagnosis of HF is rejected, and patients will not require an echocardiogram.

PART 6b – INFORMATION ABOUT THE INTERVENTION

26. Describe the key components and clinical steps involved in delivering the proposed medical service/technology:

The Elecsys® NT-proBNP II and Elecsys® NT-proBNP II STAT assay is a fully automated immunoassay for the detection and quantitation of NT-proBNP, the N-terminal fragment of BNP, in plasma and serum. The Elecsys® NT-proBNP II and Elecsys® NT-proBNP II STAT assays are intended for use on the cobas® e 402, e 601, e 602, or e 801 immunoassay analysers, respectively. The assay is conducted on patients' blood, collected through a standard blood test. The NT-proBNP assay will be requested by a cardiologist to rule out or support a diagnosis of HF in patients with uncertain or unconfirmed HF. The NT-proBNP assay will be delivered in conjunction with the standard diagnostic work up for investigating a diagnosis of HF. Investigation of a diagnosis of HF will follow a standard stepwise clinical pathway, the NT-proBNP assay is intended as an intervention prior to patients receiving an echocardiogram (Figure 2). NT-proBNP quantitation is already widely available in laboratories around Australia. An echocardiogram is labour-intensive and thus expensive in comparison with biochemical markers. To alleviate the cost of echocardiograms, a disease management strategy that utilises NT-proBNP to rule out HF prior to echocardiogram would be associated with significant cost-savings to the healthcare system (16).

The assay is based on the 'sandwich principle', a sandwich immunoassay is a method using two antibodies, which bind to different sites on the antigen or ligand. The capture antibody, which is highly specific for the antigen, is attached to a solid surface. The antigen is then added, followed by addition of a second antibody referred to as the detection antibody. The detection antibody binds the antigen at a different epitope than the capture antibody. As a result, the antigen is 'sandwiched' between the two antibodies (17). The Elecsys® NT-proBNP II assay is a two-step sandwich assay with an 18-minute incubation, while the Elecsys® NT-proBNP II STAT assay is a rapid one step sandwich assay with a 9-minute incubation.

Elecsys® NT-proBNP II assay:

- 1st incubation: Antigen in the sample (9 µL), a biotinylated monoclonal NT-proBNP-specific antibody, and a monoclonal NT-proBNP-specific antibody labelled with a ruthenium complex) form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.

Elecsys® NT-proBNP II STAT:

- During a 9-minute incubation, antigen in the sample (9 µL), a biotinylated monoclonal NT-proBNP-specific antibody, a monoclonal NT-proBNP-specific antibody labelled with a ruthenium complex and streptavidin-coated microparticles react to form a sandwich complex, which is bound to the solid phase.

For both assay applications:

- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode.
- Results are determined via a calibration curve which is instrument specifically generated by 2-point calibration and a master curve provided via the cobas® link.

27. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

The submission pertains to the cobas® e 402, e 601, e 602 and e 801 immunoassay analysers which are trademarked by Roche Diagnostics. The Elecsys® NT-proBNP and NT-proBNP STAT are also trademarked to Roche Diagnostics. Other NT-proBNP assays and analysers are available, which are trademarked by other sponsors. This application does not request a brand-specific item number and it is expected that other vendors of the NT-proBNP test will be able to claim under the proposed listing.

28. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

NT-proBNP assays are currently subsidised (MBS item 66830) for the quantitation of NT-proBNP for the diagnosis of HF in patients presenting with dyspnoea to a hospital emergency department. NT-proBNP assays are also endorsed in the clinical pathway for HF diagnosis by the National Heart Foundation of Australia and CSANZ: guideline. Consequently, NT-proBNP assays are not strictly novel. However, the focus of this application is the use of NT-proBNP assays in patients presenting to primary care (cardiologists) with a suspected or uncertain diagnosis of HF. The assay is to be included within the current diagnostic work up (i.e. clinical assessment, chest X-ray, ECG), prior to referring the patient for an echocardiogram, which is part of the current standard investigation where HF is suspected or uncertain.

29. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency)?

The proposed service can only be requested by cardiologists.

The proposed service only pertains to NT-proBNP laboratory tests.

Patients with a confirmed HF diagnosis are not eligible for the service.

Patients with unconfirmed HF are eligible for a maximum of 1 service in a 12-month period

30. If applicable, identify any healthcare resources or other medical services that would need to be delivered at the same time as the proposed medical service:

N/A

31. If applicable, advise which health professionals will primarily deliver the proposed service:

A referral request for NT-proBNP testing would come from the patient's managing cardiologist. It is proposed that only cardiologists will be able to request the test. NT-proBNP assays should be conducted in laboratories with the appropriate accreditation and registration for the diagnostic procedure and performed and interpreted by qualified and trained pathologists and laboratory technicians.

It is noted that there is a point-of-care NT-proBNP test device, however this application only seeks the reimbursement of the laboratory test for the diagnosis of HF requested by a cardiologist.

32. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

Not applicable

33. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

As described in question 31, only cardiologists will be able to request the proposed service and the diagnostic test can only be claimed by a National Association of Testing Authorities (NATA) accredited laboratory.

34. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

NT-proBNP assays should be conducted NATA-accredited laboratories by pathologists and laboratory assistants appropriately trained in conducting and interpreting the test.

35. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select ALL relevant settings):

- Inpatient private hospital (admitted patient)
- Inpatient public hospital (admitted patient)
- Private outpatient clinic
- Public outpatient clinic
- Emergency Department
- Private consulting rooms - GP
- Private consulting rooms – specialist
- Private consulting rooms – other health practitioner (nurse or allied health)
- Private day surgery clinic (admitted patient)
- Private day surgery clinic (non-admitted patient)
- Public day surgery clinic (admitted patient)
- Public day surgery clinic (non-admitted patient)
- Residential aged care facility
- Patient's home
- Laboratory
- Other – please specify below

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Not applicable

36. Is the proposed medical service intended to be entirely rendered in Australia?

- Yes
- No – please specify below

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

37. Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service):

Accurate diagnosis of HF requires a multifaceted, systematic approach. Therefore, the main comparator for NT-proBNP assays is standard HF diagnostic workup (Table 2). As specified in the CSANZ 2018 HF guidelines, this includes initial assessment (vital signs, cardiac enzymes, full blood count, liver function tests, ECG, chest X-ray) and echocardiography as a part of the standard clinical investigations (14). As described in question 25, patients presenting to primary care with symptoms suggestive of HF, most often dyspnoea, will be assessed. A physical examination will assess vital signs (heart rate/rhythm, blood pressure, respiratory rate and temperature), peripheral perfusion and volume status (jugular venous pressure, peripheral and sacral oedema, ascites and hepatic congestion), cardiac palpitations, and auscultation (apex best, gallop rhythm, and murmurs and auscultation of lung fields). If HF remains suspected, measurements of oxygen saturation, 12-lead ECG, chest X-ray and serum biochemistry (electrolytes, renal function and liver function) and full blood count will be conducted. At this stage, some patients may receive a HF diagnosis and receive an echocardiogram for characterisation/classification of HF. If a HF diagnosis is suspected but uncertain under the current clinical management paradigm, these patients will also be referred for an echocardiogram. For patients who do not have HF, waiting for an echocardiogram may delay the diagnosis of another condition. The standard HF diagnostic workup concludes when HF is diagnosed and characterised or HF is ultimately ruled out.

Table 2 Components of standard HF diagnostic workup

HF diagnosis component	HF diagnosis component
Cardiorespiratory physical examination (heart rate/rhythm, blood pressure, respiratory rate and temperature), peripheral perfusion and volume status (jugular venous pressure, peripheral and sacral oedema, ascites and hepatic congestion), cardiac palpitations, and auscultation (apex best, gallop rhythm, and murmurs and auscultation of lung fields)	12-lead ECG
Blood biochemistry (electrolytes, urea, creatinine, glucose)	Liver function tests
Full blood count	Thyroid function tests
Echocardiography	

Source: Adapted from CSANZ HF 2018 Guidelines; Page 1146
Abbreviations: ECG, electrocardiogram

38. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

- Yes (please list all relevant MBS item numbers below)
 No

-

Category 1 – Professional attendances
MBS 110

Professional attendance at consulting rooms or hospital, by a consultant physician in the practice of the consultant physician's speciality (other than psychiatry) following referral of the patient to the consultant physician by a referring practitioner-initial attendance in a single course of treatment

Fee: \$161.90

Category 2 – Diagnostic procedures and investigations

MBS 11704

Twelve-lead electrocardiography, trace and formal report, by a specialist or a consultant physician, if the service:

- a) is requested by a requesting practitioner; and
- b) is not associated with a service to which item 12203, 12204, 12205, 12207, 12208, 12210, 12213, 12215, 12217 or 12250 applies.

Note: the following are also requirements of the service:

- i. a formal report is completed; and
- ii. a copy of the formal report is provided to the requesting practitioner; and
- iii. the service is not provided to the patient as part of an episode of hospital treatment or hospital-substitute treatment; and
- iv. is not provided in association with an attendance item (Part 2 of the schedule); and
- v. the specialist or consultant physician who renders the service does not have a financial relationship with the requesting practitioner.

Fee: \$33.05

Category 5 – Diagnostic imaging services

MBS 55126

Initial real time transthoracic echocardiographic examination of the heart with real time colour flow mapping from at least 3 acoustic windows, with recordings on digital media, if the service:

(a) is for the investigation of any of the following:

- i. symptoms or signs of cardiac failure;
- ii. (ii) suspected or known ventricular hypertrophy or dysfunction;
- iii. (iii) pulmonary hypertension;
- iv. (iv) valvular, aortic, pericardial, thrombotic or embolic disease;
- v. (v) heart tumour;
- vi. (vi) symptoms or signs of congenital heart disease;
- vii. (vii) other rare indications; and

(b) is not associated with a service to which:

- i. another item in this Subgroup applies (except items 55137, 55141, 55143, 55145 and 55146); or
- ii. (ii) an item in Subgroup 2 applies (except items 55118 and 55130); or
- iii. (iii) an item in Subgroup 3 applies

Applicable not more than once in a 24 month period (R)

Fee: \$240.05

Category 6 – Pathology services

MBS 65070

Erythrocyte count, haematocrit, haemoglobin, calculation or measurement of red cell index or indices, platelet count, leucocyte count and manual or instrument generated differential count - not being a service where haemoglobin only is requested - one or more instrument generated sets of results from a single sample; and (if performed)

- a) a morphological assessment of a blood film;
- b) any service in item 65060 or 65072

Fee: \$16.95

Category 6- Pathology services

MBS 66509

4 tests described in item 66500

MBS 66500

Quantitation in serum, plasma, urine or other body fluid (except amniotic fluid), by any method except reagent tablet or reagent strip (with or without reflectance meter) of: acid phosphatase, alanine aminotransferase, albumin, alkaline phosphatase, ammonia, amylase, aspartate aminotransferase, bicarbonate, bilirubin (total), bilirubin (any fractions), C-reactive protein, calcium (total or corrected for albumin), chloride, creatine kinase, creatinine, gamma glutamyl transferase, globulin, glucose, lactate dehydrogenase, lipase, magnesium, phosphate, potassium, sodium, total protein, total cholesterol, triglycerides, urate or urea

Fee: \$15.65

Category 6- Pathology services

MBS 66719

Thyroid function tests (comprising the service described in item 66716 and either or both of a test for free thyroxine and a test for free T3) for a patient, if:

- a. the patient has a level of TSH that is outside the normal reference range for the particular method of assay used to determine the level; or
- b. the request from the requesting medical practitioner indicates that the tests are performed:
 - i. for the purpose of monitoring thyroid disease in the patient; or
 - ii. to investigate the sick euthyroid syndrome if the patient is an admitted patient; or
 - iii. to investigate dementia or psychiatric illness of the patient; or
 - iv. to investigate amenorrhoea or infertility of the patient; or
- c. the request from the requesting medical practitioner indicates that the medical practitioner suspects the patient has a pituitary dysfunction; or
- d. the request from the requesting medical practitioner indicates that the patient is on drugs that interfere with thyroid hormone metabolism or function

Fee: \$34.80

Category 6- Pathology services

MBS 73932

Initiation of a patient episode by collection of a specimen for 1 or more services (other than those services described in items 73922, 73924 or 73926) if the specimen is collected by an approved pathology practitioner or an employee of an approved pathology authority from a person in the place where the person was residing. Unless item 73933 applies

Fee: \$10.25

39. (a) Will the proposed medical service/technology be used in addition to, or instead of, the nominated comparator(s)?

- In addition to (i.e. it is an add-on service)
 Instead of (i.e. it is a replacement or alternative)

(b) If yes, please outline the extent to which the current service/comparator is expected to be substituted

The primary comparator is standard HF diagnostic workup, which includes multiple medical services as identified in the CSANZ HF Guidelines. NT-proBNP assays are expected to be used primarily for patients

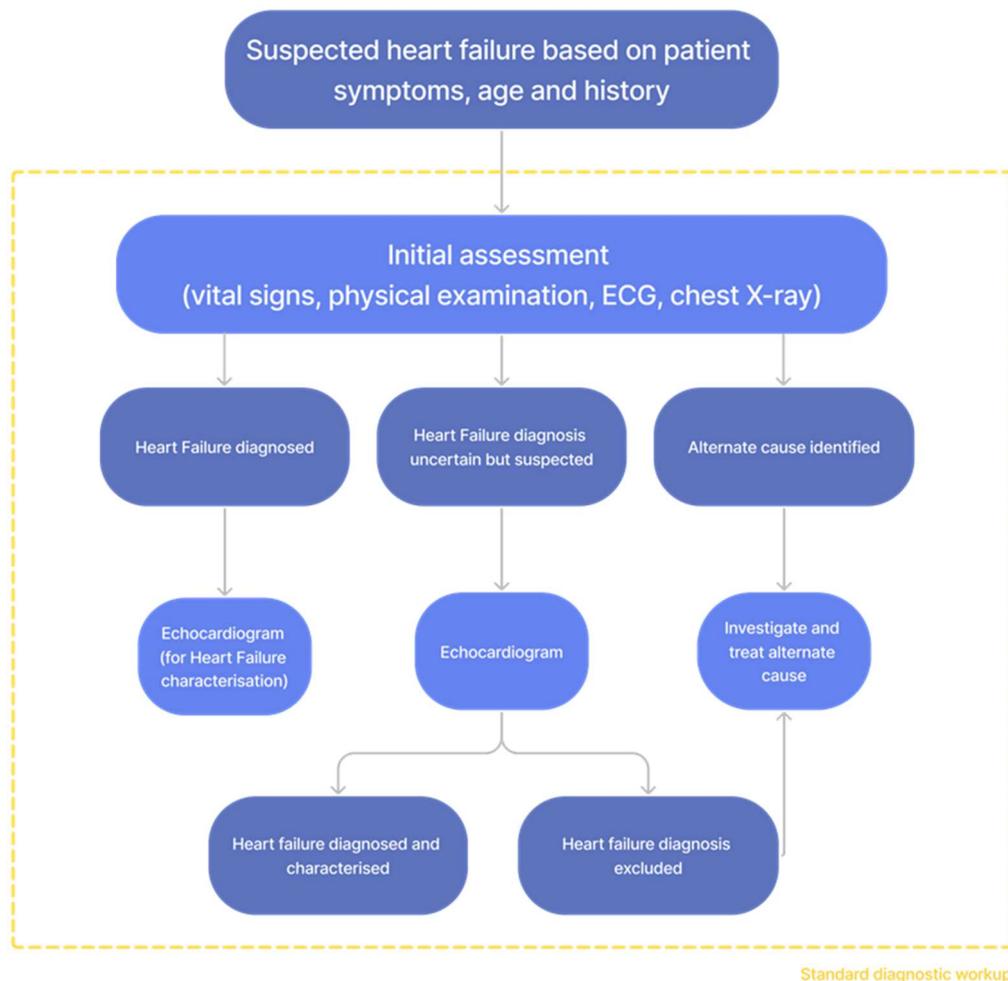
with a suspected or uncertain diagnosis of HF prior to echocardiography. Based on the proposed clinical management algorithm (Question 41), all patients will receive medical services associated with the initial assessment. For patients with an NT-proBNP above the rule out threshold, it is proposed that NT-proBNP will be used in addition to all services included in the standard diagnostic workup for HF (including echocardiography). For patients with an NT-proBNP below the rule out threshold, it is proposed that NT-proBNP will replace echocardiography, but still be used in addition to all other medical services included in the standard diagnostic workup. Given that the proportion of patients who present with HF symptoms that actually do not have HF is low (less than 35% (3, 4)), the number of echocardiogram services replaced by NT-proBNP is expected to be significant.

PART 6c CONTINUED – INFORMATION ABOUT ALGORITHMS (CLINICAL MANAGEMENT PATHWAYS)

- 40. Define and summarise the CURRENT clinical management pathway (algorithm) that patients follow when they receive the COMPARATOR service (i.e. the landscape before the proposed service is introduced). An easy-to-follow flowchart is preferred, depicting the current **clinical management pathway**), but dot-points would be acceptable. Please include health care resources used in the current landscape (e.g. pharmaceuticals, diagnostics and investigative services, etc.).**

There is no single diagnostic test for HF and as such, the standard diagnostic work up relies on clinical judgement based on a systematic combination of history, physical examination and appropriate investigations. Under the current clinical management pathway (Figure 1), standard diagnostic workup for patients who present to primary care (i.e. cardiologists) with symptoms indicative of HF will undergo initial assessments including vital signs, physical examination, ECG and chest X-ray. If these investigations do not result in a definitive diagnosis, patients will be referred to receive an echocardiogram to confirm or exclude a diagnosis of HF. The National Heart Foundation of Australia and CSANZ guidelines for the Prevention, Detection and Management of Heart Failure in Australia include NT-proBNP quantitation in the clinical management algorithm for diagnosing HF. However, as it is not listed on the MBS most patients do not receive an NT-proBNP test unless paying out-of-pocket. The indication proposed in this application will bring the MBS into line with the Australian guidelines for diagnosing HF in the non-hospital setting.

Figure 1: Current clinical management pathway for heart failure diagnosis.



Source: Adapted from CSANZ HF 2018 Guidelines; Figure 2, Page 1145(14)

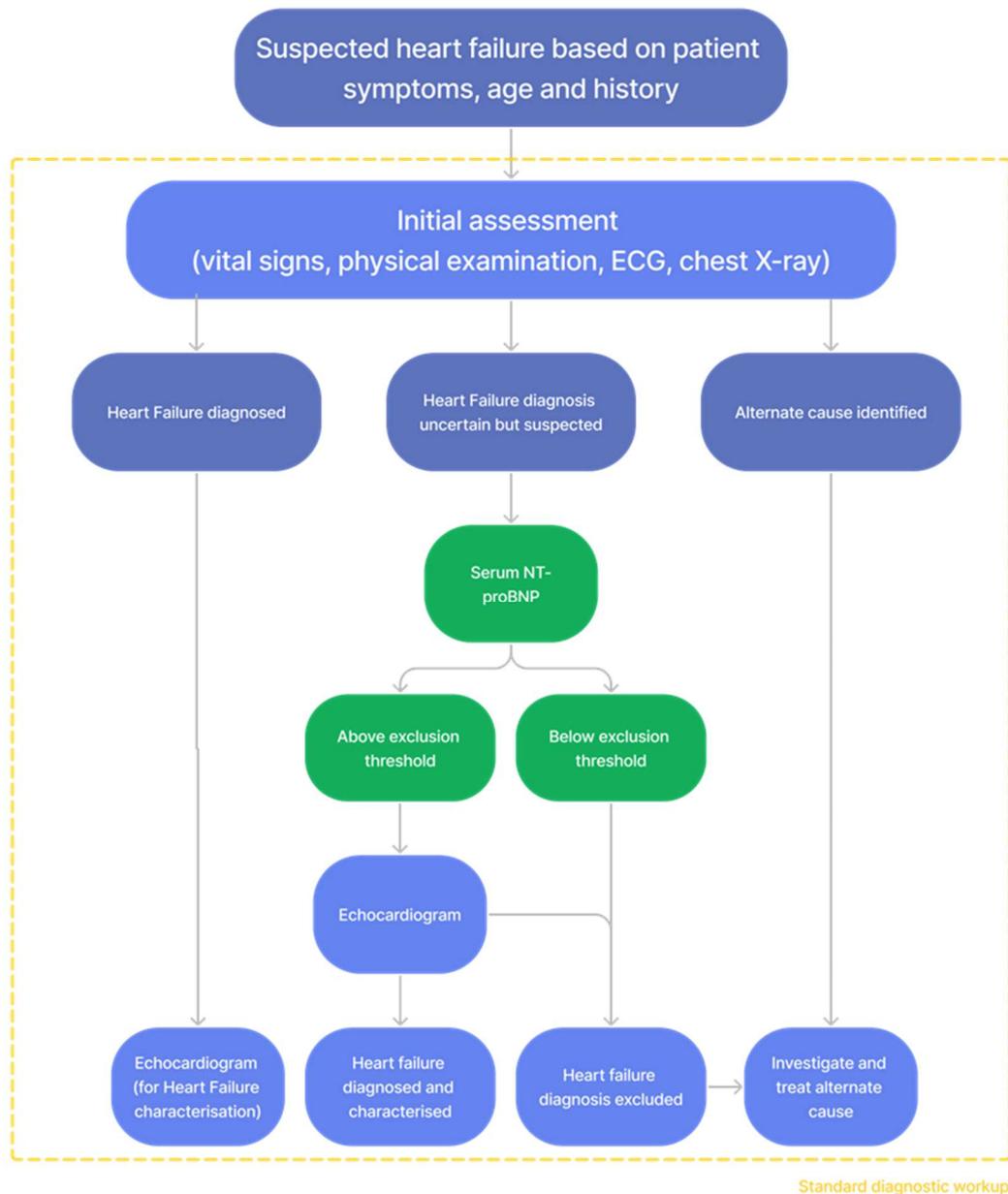
- 41. Define and summarise the PROPOSED clinical management pathway (algorithm) that patients would follow after the proposed service/technology is introduced, including variation in health care resources.**

Although the ECG is usually abnormal in patients with HF, the abnormalities are often non-specific. A chest X-ray may rule in the diagnosis of HF or identify an alternative cause for the patient's symptoms; however, a normal chest X-ray does not rule out HF (14). There is a clinical need for diagnostic tests which accurately exclude a diagnosis of HF, to reduce the number of unnecessary echocardiograms. In the proposed clinical management pathway (Figure 2), patients with suspected or uncertain diagnosis of HF will receive an NT-proBNP assay prior to receiving an echocardiogram.

In response to a pressure overload in the heart which precipitates stretching and damage of the myocardium, pre-proBNP is released, which is cleaved into pro-BNP and then subsequently cleaved into equimolar concentrations of inactive peptide NT-proBNP and the active peptide BNP, which can be detected in patient blood samples. Both NT-proBNP and BNP have utility as biomarkers for the detection of (or ruling out) HF. The focus of this application specifically is an assay of NT-proBNP levels as a diagnostic tool for the identification of, or exclusion of a diagnosis of HF in patients with suspected or uncertain HF. The hormonally inactive peptide NT-proBNP is more stable in serum samples, owing to its half-life of 120 min, compared to 20 min for BNP (18). As NT-proBNP is not a neprilysin substrate (compared to BNP which is), it is suitable for use in patients taking the ARNi class of HF drug (14) (CSANZ Guidelines page 1148 point number 5)

Cardiologists will be able to exclude a HF diagnosis in patients with an NT-proBNP level below the exclusion threshold, as the cause of the symptoms they are experiencing. These patients will not receive an echocardiogram and their alternate cause of symptoms will be explored. If the assay of NT-proBNP level is above the rule out threshold value, a diagnosis of HF is likely or cannot be ruled out, and patients will proceed to echocardiography for further investigation and characterisation of HF. The CSANZ HF Guidelines already include NT-proBNP in the clinical management pathway for diagnosing HF, however, the service is not publicly reimbursed. The proposed clinical management pathway also aligns with the 2021 European Society of Cardiology guidelines for the diagnosis and treatment of acute and chronic HF (Figure 1, page 3615) (19).

Figure 2: Proposed clinical management pathway for heart failure diagnosis.



Source: Adapted from CSANZ HF 2018 Guidelines; Figure 2, Page 1145(14)

PART 6d – INFORMATION ABOUT CLINICAL OUTCOMES

- 42. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):**

For patients with uncertain but suspected HF, NT-proBNP assays plus standard diagnostic workup is non-inferior compared to standard diagnostic workup alone in terms of diagnostic accuracy and superior in terms of efficient use of healthcare resources.

- 43. Please state what the overall clinical claim is:**

NT-proBNP testing is a safe and effective method for diagnosing or ruling out HF in patients who present in primary care (i.e. cardiologists), and is an efficient use of public resources when considering the time and cost associated with potentially redundant echocardiograms.

- 44. List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):**

- Test accuracy
 - Sensitivity
 - Specificity
 - Negative predictive value
 - Positive predictive value
- Change in management
 - Echocardiography avoided
 - Time to correct diagnosis
 - Time to appropriate treatment
 - Total medical cost
- Health outcomes
 - All-cause hospitalisation
 - Cardiac hospitalisation
 - Heart failure hospitalisation
 - All-cause mortality
 - HF-related death
- Safety
 - Adverse events

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

45. Estimate the prevalence and/or incidence of the condition in the proposed population:

The Study of Heart failure in the Australian Primary care setting (SHAPE) (20-22) is a retrospective cohort study of primary care data which examined the prevalence and annual incidence of HF in the Australian general community. Analysis of medical records for adult patients at participating general practices was undertaken. A total of 1.93 million patients over the age of 18 years were treated within the network of 43 GP practices over the five-year study period, of which 1.12 million adults visited the practice three or more times in a 24-month period ('active' patients). Of these 'active' patients, 20,219 were classified as having 'definite or probable HF'. From this, the age-standardised prevalence and annual incidence of HF in the 'active' population were calculated to be 2.20% (95% confidence interval [CI]: 2.17, 2.23) and 0.348% (95% CI: 0.342, 0.354). This is representative of the epidemiology of HF in the Australian community setting.

Given this application only pertains to the diagnosis of HF, patients with existing HF (i.e. prevalent patients) would not be eligible and thus are not considered. When the incidence rate is applied to the 2023 population of Australians who are 18 years or older, the number of incident HF patients who present to a general practitioner (GP) is estimated at 73,367. Previous health technology assessments have estimated that approximately 35% of people who present to a GP with suspected HF will actually have a confirmed diagnosis of HF (23), subsequently the number of patients with suspected HF who present to a GP is estimated to be 209,620 in 2023. The SHAPE study determined 45% of patients who present to a GP with probable or definite HF will be referred to a cardiologist, resulting in an estimated upper limit of 94,853 individuals who would be eligible for NT-proBNP testing. Based on the SHAPE study, it is expected that the patients who are not referred to a cardiologist would be referred to an endocrinologist, renal physician, hospital emergency department, or be lost to follow-up.

It is plausible that in practice, clinicians could confirm a HF diagnosis prior to requesting an NT-proBNP test. To estimate the lower limit of the population eligible for NT-proBNP testing, only the population of individuals with uncertain or probable HF as determined by their GP were considered (i.e. assuming those with definite HF are referred immediately for echocardiography). Based on the SHAPE study of people with definite or probable HF who present to a GP, an estimated 24% of those have a probable diagnosis of HF, equating to 49,267 patients in 2023. Assuming that 45% of these patients will be referred to a cardiologist as above, the estimated lower limit of patients eligible for NT-proBNP testing is approximately 22,293.

46. Subsequently, it is estimated that between 22,293–94,853 people would be eligible for an NT-proBNP test in 2023. How many years would the proposed medical service/technology be required for the patient?

This test is intended for the diagnosis of HF. Patients who have received a diagnosis of HF will not be eligible to receive a NT-proBNP test, meaning that HF monitoring and NT-proBNP guided treatment would not be reimbursed under the proposed listing. In addition, it is proposed that the service is not claimable more than once in a 12-month to further mitigate leakage into HF monitoring and NT-proBNP-guided treatment indications.

47. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

The number of people who will present with HF to a cardiologist in the first year (2023) and use the proposed services is estimated to be between 20,064–85,368.

NT-proBNP is already included in the CSANZ HF Guidelines and available through the MBS in the hospital emergency setting. Consequently, the uptake of NT-proBNP testing in the proposed population is expected to be approximately 90% in the first year. This is supported by estimated uptake rates from Ontario Health Technology Assessment of NT-proBNP testing in primary care (23). Applying this uptake rate to the population it is estimated between 20,064–85,368 tests will be claimed in the first year.

48. Estimate the anticipated uptake of the proposed medical service/technology over the next three years, factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors), as well as provide commentary on risk of 'leakage' to populations not targeted by the service.

The estimated uptake of NT-proBNP testing over the next three years is presented in Table 3. It is expected NT-proBNP testing will be adopted quickly once available, as CSANZ guidelines provide a strong recommendation for NT-proBNP quantitation for diagnosis in patients with suspected HF. The estimate assumes 90% uptake in year one and 100% from year two for patients presenting to cardiologists with suspected HF (23).

Table 3: Estimated uptake of NT-proBNP assay.

Year	2023	2024	2025
Australian population projection ≥18 years	21,082,471	21,411,852	21,744,502
HF incidence in patients who present to a GP (incidence 0.348%)	73,367	74,513	75,671
Patients with definite or probable [‡] or probable only [¶] HF who present to a GP	49,267–209,62	96,335–212,895	97,832–216,202
Patients referred to a cardiologist [~]	22,293–94,853	22,642–96,335	22,993–97,832
Estimated number of NT-proBNP tests [*]	20,064–85,368	22,642–96,335	22,993–97,832

[‡]Assuming 35% of patients who present to a GP have confirmed HF diagnosis

[¶] Assuming 35% of patients who present to a GP have confirmed HF diagnosis, and 24% of those with either probable or definite HF have an initial probable diagnosis of HF.

[~]Based on estimated 45% of patients who present to a GP with suspected HF being referred to a cardiologist.

^{*}Assuming 90% uptake in year 1, and 100% in year 2 (23).

PART 8 – COST INFORMATION

49. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The technology for testing NT-proBNP is already well established. The Elecsys® NT-proBNP II and Elecsys® NT-proBNP II STAT assay which are the focus of this application are identical to the NT-proBNP assay which is currently funded for the quantitation of BNP or NT-proBNP for the diagnosis of HF in patients presenting with dyspnoea to a hospital Emergency Department (MBS item 66830). Based on the current MBS listing for MBS item 66830, the estimated cost of providing NT-proBNP testing in a primary care setting is \$58.50.

50. Specify how long the proposed medical service/technology typically takes to perform:

The Elecsys® NT-proBNP II assay is a two-step sandwich assay with an 18-minute incubation, while the Elecsys® NT-proBNP II STAT assay is a rapid one step sandwich assay with a 9-minute incubation. Test results are typically available for clinical interpretation on the same day as the blood sample was taken.

51. Estimate the number of times the proposed medical service/technology would be delivered to a patient per year:

The NT-proBNP test is intended as a diagnostic test for HF. Patients would receive the test once, as required when presenting to a cardiologist when a diagnosis of HF is suspected but uncertain. Patients diagnosed with HF would not be eligible for more than one NT-proBNP assay under the MBS listing requested in this application. It is plausible that a patient without HF presents to a cardiologist and develops HF in later years. Such an individual would benefit from a second NT-proBNP. Once a patient receives a diagnosis of HF, they will no longer be eligible to receive NT-proBNP testing.

52. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and usage characteristics that defines eligibility for the medical service/technology.

Category 6 – Pathology services

Quantitation of NT-proBNP for diagnosis in patients with suspected heart failure, where all of the following apply:

- (a) Heart failure is suspected based on initial assessment
- (b) The service is requested by a specialist or consultant physician practicing as a specialist cardiologist
- (c) The patient does not have a confirmed heart failure diagnosis

Applicable not more than once in a 12-month period

Fee: \$58.50

53. If public funding is sought through an alternative (non-MBS) funding arrangement, please draft a service description to define the population and usage characteristics that defines eligibility for the service/technology.

Not applicable

References

1. Chan YK, Tuttle C, Ball J, Teng TK, Ahamed Y, Carrington MJ, et al. Current and projected burden of heart failure in the Australian adult population: a substantive but still ill-defined major health issue. *BMC Health Serv Res.* 2016;16(1):501.
2. Tan C, Dinh D, Brennan A, Hare DL, Kaye D, Lefkovits J, et al. Characteristics and Clinical Outcomes in Patients With Heart Failure With Preserved Ejection Fraction Compared to Heart Failure With Reduced Ejection Fraction: Insights From the VCOR Heart Failure Snapshot. *Heart, Lung and Circulation.* 2022;31(5):623-8.
3. Scott. M A, Price. C P, Cowie. M R, Buxton. M J. Cost-consequences analysis of natriuretic peptide assays to refute symptomatic heart failure in primary care. *The British Journal of Cardiology* 2008;15(6):199-204.
4. Burri E, Hochholzer K, Arenja N, Martin-Braschler H, Kaestner L, Gekeler H, et al. B-type natriuretic peptide in the evaluation and management of dyspnoea in primary care. *J Intern Med.* 2012;272(5):504-13.
5. Blackledge HM, Tomlinson J, Squire IB. Prognosis for patients newly admitted to hospital with heart failure: survival trends in 12 220 index admissions in Leicestershire 1993-2001. *Heart.* 2003;89(6):615-20.
6. Taylor CJ, Ryan R, Nichols L, Gale N, Hobbs FR, Marshall T. Survival following a diagnosis of heart failure in primary care. *Fam Pract.* 2017;34(2):161-8.
7. Zheng A, Cowan E, Mach L, Adam RD, Guha K, Cowburn PJ, et al. Characteristics and outcomes of patients with suspected heart failure referred in line with National Institute for Health and Care Excellence guidance. *Heart.* 2020;106(20):1579-85.
8. Al-Omary MS, Davies AJ, Evans T-J, Bastian B, Fletcher PJ, Attia J, et al. Mortality and Readmission Following Hospitalisation for Heart Failure in Australia: A Systematic Review and Meta-Analysis. *Heart, Lung and Circulation.* 2018;27(8):917-27.
9. Woods JA, Katzenellenbogen JM, Davidson PM, Thompson SC. Heart failure among Indigenous Australians: a systematic review. *BMC Cardiovasc Disord.* 2012;12:99.
10. Agostino JW, Wong D, Paige E, Wade V, Connell C, Davey ME, et al. Cardiovascular disease risk assessment for Aboriginal and Torres Strait Islander adults aged under 35 years: a consensus statement. *Medical Journal of Australia.* 2020;212(9):422-7.
11. Welfare ACoSaQiHCaAloHa. The Fourth Australian Atlas of Healthcare variation. Sydney: ACSQHC; 2021.
12. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. *Heart.* 2007;93(9):1137-46.
13. Taylor CJ, Harrison C, Britt H, Miller G, Hobbs FR. Heart Failure and Multimorbidity in Australian General Practice. *Journal of Comorbidity.* 2017;7(1):44-9.
14. Atherton JJ, Sindone A, De Pasquale CG, Driscoll A, MacDonald PS, Hopper I, et al. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Guidelines for the Prevention, Detection, and Management of Heart Failure in Australia 2018. *Heart Lung Circ.* 2018;27(10):1123-208.
15. Taylor C, Hobbs R. Diagnosing Heart Failure: Experience and 'Best Pathways'. *European Cardiology* 2010;6(3):10-2. 2010.
16. Ferrandis MJ, Ryden I, Lindahl TL, Larsson A. Ruling out cardiac failure: cost-benefit analysis of a sequential testing strategy with NT-proBNP before echocardiography. *Ups J Med Sci.* 2013;118(2):75-9.
17. Markossian S GA, Brimacombe K et al. *New in Assay Guidance Manual* Bethesda, Maryland: Eli Lilly & Company and the National Center for Advancing Translational Science; 2004- [Available from: <https://www.ncbi.nlm.nih.gov/books/NBK401307/>].
18. Weber M, Mitrovic V, Hamm C. B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide - Diagnostic role in stable coronary artery disease. *Exp Clin Cardiol.* 2006;11(2):99-101.

19. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42(36):3599-726.
20. Sindone AP, Haikerwal D, Audehm RG, Neville AM, Lim K, Parsons RW, et al. Clinical characteristics of people with heart failure in Australian general practice: results from a retrospective cohort study. *ESC Heart Failure*. 2021;8(6):4497-505.
21. Liew D, Audehm RG, Haikerwal D, Piazza P, Neville AM, Lim K, et al. Epidemiology of heart failure: Study of Heart failure in the Australian Primary care setting (SHAPE). *ESC Heart Failure*. 2020;7(6):3871-80.
22. Parsons RW, Liew D, Neville AM, Audehm RG, Haikerwal D, Piazza P, et al. The epidemiology of heart failure in the general Australian community - study of heart failure in the Australian primary care setting (SHAPE): methods. *BMC Public Health*. 2020;20(1).
23. Use of B-Type Natriuretic Peptide (BNP) and N-Terminal proBNP (NT-proBNP) as Diagnostic Tests in Adults With Suspected Heart Failure: A Health Technology Assessment. *Ont Health Technol Assess Ser*. 2021;21(2):1-125.
24. Audehm R, Neville A, Piazza P, Haikerwal D, Sindone A, Parsons R, et al. Healthcare services use by patients with heart failure in Australia: Findings from the SHAPE study. *Australian Journal for General Practitioners*. 2022;51:713-20.