Population

Describe the population in which the proposed health technology is intended to be used: There are four stages of heart failure, at risk (A), pre heart failure (B), symptomatic heart failure (C) and advanced heart failure (D); see Table 1. Advanced, chronic heart failure (stage D) is characterised by persistent symptoms despite use of conventional guideline directed medical therapy, defined as per the criteria in the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) position statement (Crespo-Leiro 2018), see Table 2.

A systematic literature review showed that the prevalence of heart failure in Australia is 1–2%, with a higher prevalence observed in the elderly, the indigenous population and in females (Sahle 2016). Following age standardisation the prevalence of HF was 1.7 times higher in the indigenous population versus non-indigenous Australians (Woods 2012).

Given the rising prevalence of heart failure coupled with the ageing population, the prevalence of advanced heart failure is also increasing. The prognosis of advanced heart failure is poor, with one year survival estimated at 25–63% (Rose 2001; Estep 2015).

In Australia, advanced heart failure is the most common cause of hospitalisation and is associated with significant morbidity, mortality, and immense costs for the hospital system. The annual cost of managing heart failure in Australia has been estimated at $900 million and almost $2.7 billion when the cost of inpatient care is included (Chan 2016).

Table 1 Stages of heart failure

Stages	Definition and criteria
Stage A: at risk of HF	Patients at risk for HF but without current or prior symptoms or signs of HF and without structural cardiac changes or elevated biomarkers of heart disease.
Stage B: Pre-HF	Patients without current or prior symptoms or signs of HF with evidence of one of the following: Structural heart disease Abnormal cardiac function Elevated levels of BNPs or persistently elevated cardiac troponin
Stage C: Symptomatic HF	Patients with current or prior symptoms and/or signs of HF caused by a structural and / or functional cardiac abnormality
Stage D: Advanced HF	Severe symptoms and/or signs of HF at rest, recurrent hospitalisations despite attempts to optimise GDMT, refractory or intolerant to GDMT, requiring advanced therapies, transplantation, mechanical circulatory support or palliative care.

BNP, B-type natriuretic peptide; GDMT, guideline-directed medical therapy; HF, heart failure.

Source: https://www.acc.org/latest-in-cardiology/articles/2021/07/12/12/31/universal-definition-and-classification-of-heart-failure (accessed 3 March 2023)

Table 2 Advanced heart failure criteria as per the HFA ESC 2018 position statement (Crespo-Leiro 2018)

All the following criteria must be present despite optimal medical treatment:
1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].
2. Severe cardiac dysfunction defined by at least one of the following: • LVEF ≤ 30% • Isolated RV failure (e.g., ARVC) • Non-operable severe valve abnormalities • Persistently high (or increasing) BNP or NT-proBNP values and severe LV diastolic dysfunction or structural abnormalities (according to the definitions of HFpEF)
3. Episodes of pulmonary or systemic congestion requiring high-dose i.v. diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing > 1 unplanned visit or hospitalisation in the last 12 months
4. Severe impairment of exercise capacity with inability to exercise or low 6MWT distance (<300 m) or pVO2 <12 mL/kg/min or <50% predicted value, estimated to be of cardiac origin.

6MWT= 6-minute walk test; ARVC = arrhythmogenic right ventricular cardiomyopathy; BNP = B-type natriuretic peptide; HFpEF = heart failure with preserved ejection fraction; i.v. = intravenous; LV = left ventricular; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA =New York Heart Association; pVO2 = peak oxygen consumption; RV = right ventricular. Source: Crespo-Leiro (2018) table 3, adapted.

Durable ventricular assist device (VAD) eligibility considerations

Durable mechanical circulatory support (MCS) with a VAD is indicated in selected patients with advanced heart failure that have not recovered despite medical therapy or short-term durable MCS to keep patients alive until transplant (bridge to transplant [BTT]), to reverse contraindications to transplantation (bridge to candidacy [BTC]) or as destination therapy (DT), see Table 3. Of these, bridge to transplantation (BTT) and BTC are the only indications for which patients can access durable VADs on the MBS (MBS items 38615 and 38618). The purpose of the application is to expand the listing to patients who are not eligible for a transplant and in whom a VAD is used as a permanent life-sustaining intervention, a strategy referred to as DT. Bridge to recovery (BTR) refers to use of MCS, short-term or long-term, to keep a patient alive until cardiac function recovers sufficiently to remove MCS. BTR represents a rare situation. The AHA 2022 guidelines (Heidenreich 2022) recommend that in patients with advanced HF with reduced ejection fraction and hemodynamic compromise and shock, temporary MCS, including percutaneous and extracorporeal ventricular assist devices (such as ECMO), are reasonable as a "bridge to recovery" or "bridge to decision", hence durable VAD is not a suitable option in these patients.

Currently, approximately 30% of patients with chronic heart failure who are progressing, or worsening require durable VAD support as BTT in Australia (Australian and New Zealand Cardiothoracic Organ transplant registry 2018), with the proportion increasing over recent years, highlighting donor shortages and increasing waiting times for a transplant.

Table 3 Nomenclature describing indications for mechanical circulatory support

Term	Description
Bridge to decision (BTD) [or bridge to bridge (BTB)]	Use of short-term MCS (ECMO or Impella) in patients with cardiogenic shock until haemodynamics and end-organ perfusion are stabilised, contraindications for long-term MCS are excluded (brain damage after resuscitation) and additional therapeutic options including long-term VAD therapy or heart transplant can be evaluated.
Bridge to candidacy (BTC)	Use of MCS (usually LVAD) to improve end-organ function and/or to make an ineligible patient eligible for heart transplantation.
Bridge to transplantation (BTT)	Use of MCS (LVAD, BiVAD or TAH) to keep a patient alive who is otherwise at high risk of death before transplantation until a donor organ becomes available.
Bridge to recovery (BTR)	Use of MCS (short-term or long-term) to keep a patient alive until cardiac function recovers sufficiently to remove MCS.
Destination therapy (DT)	Long-term use of MCS (LVAD) as an alternative to transplantation in patients with end-stage HF ineligible for transplantation.

BiVAD, biventricular assist device; ECMO, extracorporeal membrane oxygenation; HF, heart failure; LVAD, left ventricular assist device; MCS, mechanical circulatory support; TAH, total artificial heart; VAD, ventricular assist device.

Source: McDonagh (2021)

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles classifies patients with heart failure based on clinical parameters and characteristics to identify those with a potential indication for durable MCS, see Table 4. Notably, there are three modifiers that if present may alter the phenotype of patients of a given INTERMACS.

Table 4 INTERMACS profiles

IM	Profile	Time frame for intervention
1	**Profile 1. Critical cardiogenic shock** Patient with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, often confirmed by worsening acidosis and/or lactate levels. "Crash and burn."	Definitive intervention needed within hours.
2	**Profile 2. Progressive decline** Patient with declining function despite i.v. inotropic support, may be manifest by worsening renal function, nutritional depletion, inability to restore volume balance. "Sliding on inotropes." Also describes declining status in patients unable to tolerate inotropic therapy.	Definitive intervention needed within few days.
3	**Profile 3. Stable on inotrope or inotrope-dependent** Patient with stable blood pressure, organ function, nutrition, and symptoms on continuous i.v. inotropic support (or a temporary circulatory support device or both) but demonstrating repeated failure to wean from support due to recurrent symptomatic hypotension or renal dysfunction. "Dependent stability."	Definitive intervention elective over a period of weeks to few months.
4	**Profile 4. Frequent Flyer** Patient can be stabilised close to normal volume status but experiences daily symptoms of congestion at rest or during activities of daily living. Doses of diuretics generally fluctuate at very high levels. More intensive management	Definitive intervention elective over a period of weeks to few months.

IM	Profile	Time frame for intervention
	and surveillance strategies should be considered, which may in some cases reveal poor compliance that would compromise outcomes with any therapy. Some patients may shuttle between 4 and 5[a].	
5	**Profile 5. Housebound** Comfortable at rest and with activities of daily living but unable to engage in any other activity, living predominantly within the house. Patients are comfortable at rest without congestive symptoms, but may have underlying refractory elevated volume status, often with renal dysfunction. If underlying nutritional status and organ function are marginal, patients may be more at risk than INTERMACS 4, and require definitive intervention	Variable urgency, depends upon maintenance of nutrition, organ function, and activity.
6	**Profile 6. Exertion limited** Patient without evidence of fluid overload, comfortable at rest and with activities of daily living and minor activities outside the home but fatigues after the first few minutes of any meaningful activity. Attribution to cardiac limitation requires careful measurement of peak oxygen consumption, in some cases with haemodynamic monitoring, to confirm severity of cardiac impairment. "Walking wounded."	Variable, depends upon maintenance of nutrition, organ function, and activity level.
7	**Profile 7. Advanced NYHA class III symptoms** Patient without current or recent episodes of unstable fluid balance, living comfortably with meaningful activity limited to mild physical exertion.	Heart transplantation or MCS may not be currently indicated.
	Modifiers for profiles	**Possible profiles that can be modified**
	Temporary MCS can modify profile only in hospitalised patients. They include IABP, ECMO, TandemHeart, LVAD, Impella.	1, 2, 3
	Arrhythmia can modify any profile. They include recurrent ventricular tachyarrhythmias that have recently contributed substantially to clinical compromise, frequent ICD shocks or requirement for external defibrillation, usually more than twice weekly.	1–7
	Frequent episodes of HF decompensation characterise patients requiring frequent emergency visits or hospitalisations for diuretics, ultrafiltration, or temporary i.v. vasoactive therapy. Frequent episodes may be considered as at least two emergency visits/admissions in the past 3 months or three in the past 6 months.	3 if at home, 4, 5, 6. Rarely for profile 7.

ECMO= extracorporeal membrane oxygenation; HF = heart failure; IABP = intra-aortic balloon pump; ICD = implantable cardioverter-defibrillator; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; i.v. = intravenous; LVAD = left ventricular assist device; MCS = mechanical circulatory support; NYHA= New York Heart Association.

a Note that the AHA HF guidelines describe the IM 4 as 'resting symptoms on oral therapy at homet' with the following features: "Patient who is at home on oral therapy but frequently has symptoms of congestion at rest or with activities of daily living (dressing or bathing). He or she may have orthopnea, shortness of breath during dressing or bathing, gastrointestinal symptoms (abdominal discomfort, nausea, poor appetite), disabling ascites, or severe lower extremity edema" (Heidenreich 2022).

B Note that the AHA HF guidelines describe the IM 5 as 'exertion intolerant' (Heidenreich 2022).

Source: McDonagh (2021)

Transplant eligibility

The proposed patient population for implantation of a durable VAD for use as destination therapy are patients who are not eligible for cardiac transplantation . Here follows a short summary of eligibility criteria for establishing cardiac transplant candidacy, noting that eligibility is not solely established based on cardiac function, rather comorbidity is also considered.

As per the Transplantation Society of Australia and New Zealand (TSANZ) clinical guidelines for organ transplantation (2021), in Australia, transplants are offered to patients with end-stage heart disease, who have exhausted all alternative treatment options and are expected to realise a survival benefit with a reasonable chance of returning to an active lifestyle (TSANZ 2021). End-stage heart disease may present as irreversible cardiogenic shock, intractable symptomatic heart failure (NYHA class III-IV) despite maximally tolerated guideline directed therapy, the need for durable support (MCS or artificial heart), frequent discharges from an AICD or recurrent ventricular arrythmias, intractable angina despite optimal medical management, interventions, or surgery.

Specifically, those with advanced systolic chronic heart failure are considered potential candidates for heart transplant if they meet the following criteria:

- Advanced CHF symptoms (NYHA 3 or 4) refractory to optimal treatment
- Severe left ventricular systolic or diastolic dysfunction
- VO2 max ≤12 mg/kg/min
- Heart Failure Survival Score of medium- to high-risk, or Seattle Heart Failure Model one-year estimated survival < 80%
- No contraindication to heart transplantation (including conditions that would result in an unacceptably high mortality risk from the transplant surgery, significantly and adversely affect post-transplant survival or prohibit appropriate rehabilitation post-transplant).

Inclusion/ exclusion criteria

The crucial indication for cardiac transplantation is the presence of end-stage heart disease for which no alternative therapy is available. In turn, end stage heart disease may be manifested as:

- Irreversible cardiogenic shock (e.g. complicating acute myocardial infarction)
- Intractable symptomatic heart failure (NYHA Class III-IV) despite maximally tolerated evidence-based medical therapy
- The need for permanent mechanical cardiac support, i.e. ventricular assist device (VAD) or total artificial heart
- Frequent discharges from an automatic implanted cardioverter defibrillator (AICD) or recurrent ventricular arrhythmias
- Intractable angina despite optimal medical, interventional and surgical treatment.

Patients on the transplant list have severely reduced quality of life and without the transplant have an expected survival of less than two years.

In 1984, the acceptable age range for referral to heart transplant was set arbitrarily between 5–50 years of age, however, owing to experience with cardiac transplantation over the last three decades has resulted in age range for recipient eligibility being widened (youngest 16 days vs oldest 73 years). Based on international experience, transplantation of patients over 70 years of age demonstrates poorer post-transplant survival relative to younger recipients. Patients with multiple comorbidities and/or advanced frailty in patients over 70 years of age is expected to exclude most elderly patients from consideration for heart transplantation.

Major exclusion criteria (absolute contraindications) include:

- active malignancy,
- complicated diabetes,
- obesity,
- infection,
- inability to comply with complex medical therapy/ non-adherence,
- substance abuse,
- irreversible degeneration / damage of other organ systems and acute medical conditions.

Relative contraindications include:

- uraemia with eGFR < 40 mL/min,
- hyperbilirubinemia > 50 mmol/L,
- intractable ascites with hypoalbuminemia,
- fixed pulmonary hypertension with transpulmonary gradient > 15 mmHg or pulmonary vascular resistance (PVR) >4 Woods units after pulmonary vasodilator challenge.

These relative contraindications represent patients with increased post-transplant mortality risk (TSANZ 2021).

Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the technology:
The proposed patient population include those in whom durable VAD is used as destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation.

Provide a rationale for the specifics of the eligible population:
Currently durable MCS using VAD is funded on the MBS for use as 'a bridge to cardiac transplantation in patients with refractory heart failure who are currently on a heart transplant waiting list' (BTT) or are 'expected to be suitable candidates for cardiac transplantation following a period of support on the ventricular assist device' (BTC), via items 38615 and 38618. The request to expand the population for access to VAD consists of patients with refractory heart failure who are ineligible for heart transplant, and in whom VAD is used as destination therapy (ie, final therapy). Patients who are not eligible for cardiac transplantation have no other option available to them then being managed on GDMT. Patients with an INTERMACS profile 1-4 will be eligible, consistent with the clinical evidence for which effectiveness of durable VAD is demonstrated (MOMENTUM 3 study), and in whom there is a high clinical need of a lifesaving treatment option.

It should be noted that INTERMACS profiles 5-7 represents <3% of the overall population based on the INTERMACS registry (Yuzefpolskaya 2023).

Are there any prerequisite tests?
No

Are the prerequisite tests MBS funded?
Not applicable

Please provide details to fund the prerequisite tests:
Not applicable

Intervention

Name of the proposed health technology:
The proposed medical service is the insertion of a durable ventricular assist device (VAD) capable of providing mechanical circulatory support (MCS) for at least 6 months.

Note. An alternate term used to describe durable VAD is left ventricular assist device (LVAD). However, durable VAD is favoured in this Application given right ventricular assist devices also exist. To note, clinical guidelines and clinical trials refer to the intervention as LVAD. To this end some interchangeability of use of VAD and LVAD is evident in this application.

'Durable' refers to an implanted VAD that is capable of providing mechanical circulatory support (MCS) for at least 6 months and in the context of destination therapy is considered permanent - i.e., for the lifetime of the patient.

Describe the key components and clinical steps involved in delivering the proposed health technology:
The most recent and current generation durable VAD available in Australia, and listed on the ARTG and PL, is a third generation, fully magnetically levitated centrifugal-flow VAD (HeartMate 3).

For completeness, an overview of durable VAD characteristics from first to third generation devices is provided in Table 5. To note, another third generation VAD is registered for use in Australia, HeartWare (ARTG 181875) which is a continuous flow VAD. This device has a centrifugal flow, however, is not fully magnetically levitated like the HeartMate 3. Whilst HeartWare is registered on the ARTG, it is no longer listed on the Prostheses List (PL) and no longer used globally. To this end, the nominated intervention in this Application is the insertion of a durable VAD using the HeartMate 3 system.

Table 5 Overview of durable VAD characteristics – first through third generation devices

	First generation	Second generation	Third generation	
Example	HeartMate XVE	HeartMate II	HeartWare	HeartMate 3
Flow type	Pulsatile	Axial-continuous	Centrifugal	Fully magnetically levitated centrifugal
Implant site	Abdomen	Abdomen/chest	Pericardium	Pericardium
Electrical source	Pneumatic	Electric	Electric	Electric

Source: Griffin & Katz (2014)

The HeartMate 3™ Left Ventricular Assist System (LVAS) is a set of equipment and materials that together comprise a medical device designed to provide therapeutic benefit to those affected with advanced heart failure. In service, the LVAS assumes some or all the workload of the left ventricle, thereby restoring the patient's systemic perfusion whilst palliating the underlying pathology. The LVAS features a Left Ventricular Assist Device (LVAD i.e., durable VAD), a blood pump intended for implantation in such patients, an extracorporeal controller, plus all the features, controls, attachments, interfaces, power sources, supporting equipment, labelling, and tools required to achieve the desired therapeutic benefit.

The VAD is implanted via an open chest procedure by a cardiothoracic surgeon in the operating theatre, either via median sternotomy or thoracotomy.

The HeartMate 3 is a fully magnetically levitated, continuous flow, centrifugal pump. The previous generation device, HeartMate II, is a continuous axial flow pump. These designations, axial vs centrifugal, refer to the way the blades rotate within the pump and transports blood through the pump. According to the MOMENTUM 3 trial, a randomised controlled, head-to-head comparison of the centrifugal pump, HeartMate 3, and the axial flow pump, HeartMate II – HeartMate 3 was associated with less frequent need for pump replacement than HeartMate II and was superior with respect to survival free of disabling stroke or reoperation to replace or remove a malfunctioning device (Mehra 2019). Given the superior outcomes with the most recent generation device, the Application is specific to the HeartMate 3.

Equipment and overview

As shown in Figure 2, the LVAS consist of the following main equipment:

1. **VAD** – The HeartMate 3™ Left Ventricular Assist Device is a centrifugal flow rotary heart pump that is connected in parallel to the native circulation, such that either can supply blood to the aorta, and is implanted in the thorax of patients with advanced heart failure. The inflow cannula of the LVAD attaches to the apex of the left ventricle. Its sealed outflow graft connects to the ascending aorta (Figure 2).
2. **Drive line**: which consists of two cables, the pump cable – that extends from the VAD through the skin, and the modular cable – which connects the pump cable to the system controller (Figure 2).
3. **System controller**: which is an extracorporeal interface device that receives power from the power module, the mobile power unit, or portable batteries, and appropriately delivers that power to the VAD. It is the primary user interface and has several important functions:
    - Operating condition display,
    - Source of audible and visible alarms,
    - Communication link for transferring event/period log and alarm information, and
    - Battery backup in the case of full power disconnection.

The VAD is powered through the system controller by one of three sources: 1) the power module 2) mobile power unit that is connected to an AC electrical outlet or 3) two HeartMate 14 Volt Lithium-Ion direct current batteries.

The emergency backup battery in the reserve backup system controller is charged every six months.

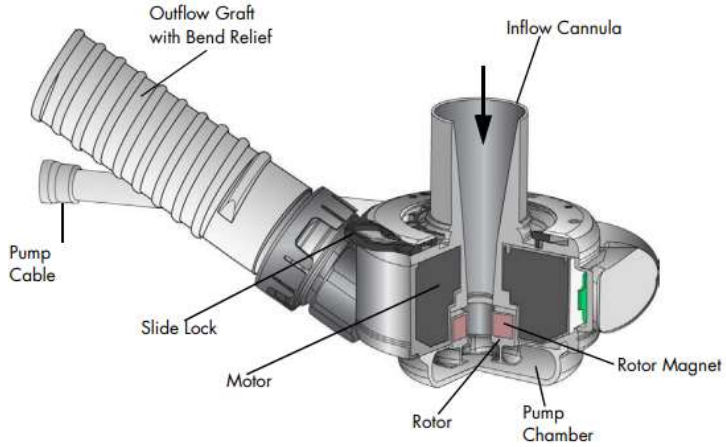

Figure 1 VAD components

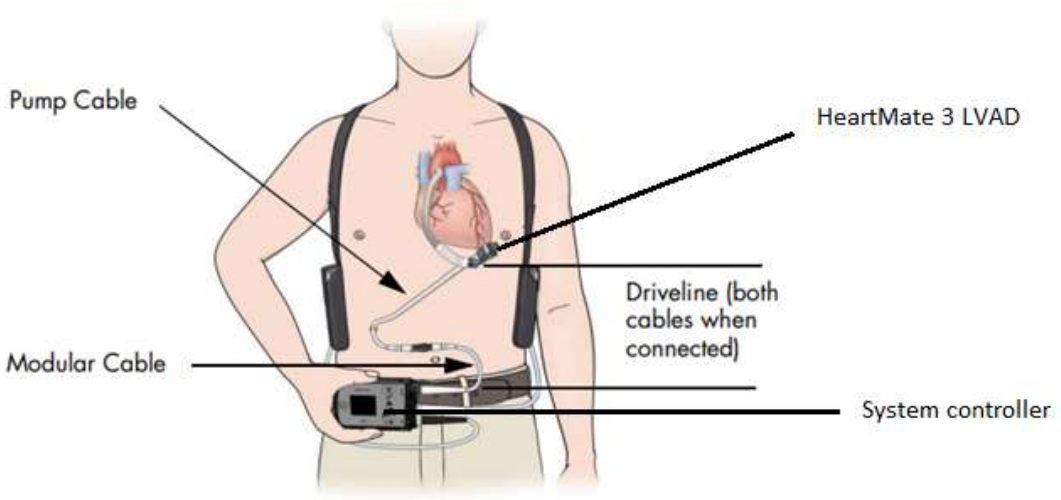

Figure 2 Overview of LVAS equipment

Function

The HeartMate 3 VAD uses a rotary blood pump to generate flow and assist the left ventricle. It is a centrifugally configured device so that the paths of the entering and exiting flow stream are perpendicular to the pump's axis. The device has only one moving part, the rotor assembly, which is fully (i.e., actively) magnetically levitated within the flow stream.

The pump is driven by an external power source via a Driveline (discussed below) and can generate a blood flow up to 10 litres per minute. Blood enters the pump from the left ventricle through an Inflow Cannula. Blades on the spinning rotor move the blood through the pump to an Outflow Cannula and ultimately to the native circulation.

Implant location and procedures

The proper orientation of the VAD is shown in Figure 3. The inflow cannula is placed utilising left ventricle apical cannulation with the pump placed within the pericardial space between the ventricular apex and the diaphragm. An abdominal pocket is not required for implantation; therefore, entry into the abdominal cavity will not be performed. The sealed outflow graft is anastomosed to the ascending aorta and the pump cable exits either the right or left upper quadrant of the abdomen and connects to the external equipment.

A midline chest incision is made not to extend below the xiphoid process. The pericardium is opened and reflected laterally to allow exposure of the LV apex.

In creating the driveline exit site, the tunnel created for the pump cable should be as long as possible to maximise ingrowth along the cable's polyester velour covering and to minimise the risk of exit site infection. The pump cable has been designed to allow for velour or silicone to cross the exit site. (It is recommended that the velour covered portion of the pump cable remains inside the patient and that only the silicon covered portion crosses the exit site to reduce exit site infection).

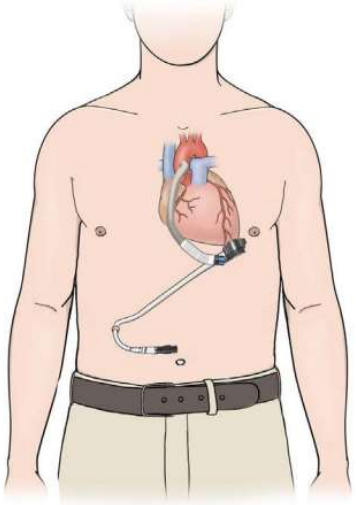

Figure 3 HeartMate 3 implant configuration

Implantation key steps:

- Opening the chest
- Creating the driveline exit site
- Attaching the sealed outflow graft to the aorta
- Preparing the ventricular apex site
- Inserting the pump in the ventricle
- Attaching the sealed outflow graft to the pump
- De-airing the pump (residual air must be evacuated)
- Securing the pump and connections

Post-implant procedures

- Transferring the patient out of the operating room
- Installing the backup battery in the system controller

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?
Yes

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:
It is not essential to have this trademark component in the MBS item as per current items, unless MSAC feels it is necessary to limit to HeartMate 3 given it is the device for which evidence exists.

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency): (please highlight your response)
Yes

Provide details and explain:
The implant procedure is expected to be performed once per patient and the service must be performed by a cardiothoracic surgeon at an implant centre. There are currently four quaternary hospitals that perform adult heart transplants and implant durable VADs in Australia. One additional hospital performs the same procedure in children. Therefore, access to durable VAD

in the proposed population is limited by capacity constraints due to the low number of implant centres in Australia.

If applicable, advise which health professionals will be needed to provide the proposed health technology:
The service will be delivered by cardiothoracic surgeons.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:
Not applicable.

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:
Not applicable.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?
Yes

Provide details and explain:
Education and training of cardiothoracic surgeons is coordinated by the Royal Australasian College of Surgeons (RACS) Board of Cardiothoracic Surgery.

Indicate the proposed setting(s) in which the proposed health technology will be delivered:
☐ Consulting rooms
☐ Day surgery centre
☐ Emergency Department
☒ Inpatient private hospital
☒ Inpatient public hospital
☐ Laboratory
☐ Outpatient clinic
☐ Patient's home
☐ Point of care testing
☐ Residential aged care facility
☐ Other (please specify)

The proposed service is provided in an in-patient setting, in the operating theatre.

Is the proposed health technology intended to be entirely rendered inside Australia?
Yes

Please provide additional details on the proposed health technology to be rendered outside of Australia:
Not applicable

Comparator

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:
The nominated comparator is guideline directed medical therapy (GDMT), also referred to as optimal medical management (OMM).

List any existing MBS item numbers that are relevant for the nominated comparators:
Not relevant

Please provide a rationale for why this is a comparator:
The nominated comparator to durable VAD in patients with advanced heart failure, who are not eligible for heart transplant (ie, in whom intent is destination therapy) is guideline directed medical therapy (GDMT). By definition, patients with advanced heart failure have continued to progress and present with severe symptoms despite maximum GDMT. Patients with advanced heart failure who are not eligible for a heart transplant have no alternate options than to continue managed with GDMT.

GDMT consists of renin-angiotensin system inhibition using angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), or angiotensin receptor II blocker - neprilysin inhibitor (ARNi); beta blockers, mineral corticoid receptor antagonists (MRAs), sodium-glucose contranspporter 2 inhibitors and hydralazine and isosorbide dinitrate. As a decongestion strategy, patients may also receive diuretics. (Heidenreich 2022; Section 7.3).

As first line therapy, inhibition of the renin-angiotensin system is recommended to reduce mortality and morbidity, with ARNi, ACEi or ARB. An ARNi consists of an ARB and an inhibitor of neprilysin, with sacubitril/valsartan an example. Neprilysin is an enzyme that degrades natriuretic peptides, bradykinin, adrenomedullin and other vasoactive peptides. Three beta-blockers have demonstrated effectiveness in heart failure in patients with reduced ejection fraction – bisoprolol, sustained-release metoprolol succinate and carvedilol (Heidenreich 2022), all of which are listed on the PBS for heart failure patients. Mineralocorticoid receptor antagonists (MRAs), also referred to as aldosterone antagonists or anti-mineralocorticoids, are recommended as part of GDMT in HF patients, including spironolactone or eplerenone, listed on the PBS. Sodium-glucose contranspporter 2 inhibitors, are recommended for patients with symptomatic chronic heart failure and reduced ejection fraction and have been shown to reduce heart failure hospitalisation (Heidenreich 2022). Dapagliflozin was recently listed on the PBS for heart failure patients irrespective of their diabetes status as recommended by the PBAC at their July 2021 meeting (Dapagliflozin heart failure public summary document [PSD], July 2021). In patients who, due to drug intolerance or renal insufficiency, cannot be treated with first line agents such as ARNi, ACEi or ARB, a combination of hydralazine and isosorbide dinitrate may be considered to reduce morbidity and mortality in symptomatic HF patients (Heidenreich 2022).

Patients with advanced heart failure may also need inotropic agents, either phosphodiesterase inhibitors, adrenergic agonists or vasopressors administered intravenously. The objective of treatment with inotropic agents is to improve haemodynamic compromise. Parenteral inotropes are an option for patients who are refractory to other therapies and are suffering from the consequences of end-organ hypoperfusion. There is a lack of evidence of one inotropic agent over another, hence agents are selected based on their effects and adverse effect profile and consideration to discontinuation and changing regimen with longer-term periods of support is considered regularly (Heidenreich 2022). An overview of intravenous inotropic agents used in the management of heart failure is provided in Table 6.

Table 6 Intravenous inotropic agents used in the management of heart failure

Agent	Dose (mcg/kg)		Effects				AEs	Cautions
	Bolus	Infusion (per min)	CO	HR	SVR	PVR		
Adrenergic agonist								
Dopamine	NA	5–10	↑	↑	↔	↔	T, HA, N, tissue necrosis	MAO-I
	NA	10–15	↑	↑	↑	↔		
Dobutamine	NA		↑	↑	↔	↔	↑/↓ BP, HA, T, N, F, hypersensitivity	MAO-I; CI; sulphite allergy
PDE 3 inhibitors								
Milrinone	NR	0.125 – 0.75	↑	↑	↓	↓	T, ↓BP	Accumulation may occur in setting of renal failure; monitor kidney function and LFTs
Vasopressors								
Epinephrine	NR	5–15 mcg/min	↑	↑	↑ (↓)	↔	HA, T	MAO-I
		15–20 mcg/min	↑	↑↑	↑↑	↔	HA, T	MAO-I
Nor-epinephrine	NR	0.5–30 mcg/min	↔	↑	↑↑	↔	↓ HR, tissue necrosis	MAO-I

AE, adverse events; BP, blood pressure; CI, contraindication; CO, cardiac output; F, fever; H, hepatic; HA, headache; HF, heart failure; HR, heart rate; LFT, liver function test; MAO-I, monoamine oxidase inhibitor; N, nausea; NA, not applicable; NR, not recommended; P, plasma; PDE, phosphodiesterase; PVR, pulmonary vascular resistance; R, renal; SVR, systemic vascular resistance; T, tachyarrhythmias.

Up arrow means increase. Side arrow means no change. Down arrow means decrease. Up/down arrow means either increase or decrease.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator? (please select your response)

☐ None *(used with the comparator)*
☐ Displaced *(comparator will likely be used following the proposed technology in some patients)*
☒ Partial *(in some cases, the proposed technology will replace the use of the comparator, but not in all cases)*
☐ Full (*subjects who receive the proposed intervention will not receive the comparator)*

Please outline and explain the extent to which the current comparator is expected to be substituted:
It is expected that patients will continue to use some medical management after the insertion of the VAD, although it is expected that medication use will be significantly reduced.

Outcomes

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): (please select your response)
The outcomes relevant to the assessment of VAD along with descriptions are provided in the table below.

Type	Outcome	Outcome claim
Health benefit	Mortality	VAD is expected to improve mortality relative to OMT
Health benefit	Stroke	VAD is expected to improve freedom from stroke relative to OMT
Health harm	Procedural complications / adverse events	Given OMT is not a procedure, insertion of VAD is expected to incur some procedural complications
Health harm	Device issues such as pump replacement / device malfunction /pump explanation or permanent deactivation (unless myocardial recovery)	Given OMT is not a procedure, insertion of VAD is expected to incur some device issues
Health benefit	Functional status (NYHA)	VAD is expected to improve functional status relative to OMT
Health benefit	Quality of life	VAD is expected to improve functional status relative to OMT
Health benefit / resources	Re-Hospitalisations	VAD is expected to reduce re-hospitalisations relative to OMT, hence providing both a health benefit to patients and reduction in resources

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:
Not applicable – VAD is not a test. For outcomes relevant to VAD see table above.

Proposed MBS items

How is the technology/service funded at present? (for example: research funding; State-based funding; self-funded by patients; no funding or payments):
Insertion of VAD is currently funded under MBS item codes 38615 and 38618. This application is seeking to expand the item codes to include patients who are ineligible for cardiac transplantation (and hence in whom therapy intent is destination therapy)

Please provide at least one proposed item with their descriptor and associated costs, for each population/Intervention:

MBS item number (where used as a template for the proposed item)	38615 and 38618
Category number	3
Category description	Therapeutic procedures
Proposed item descriptor	See below
Proposed MBS fee	Same as per 38615 and 38618, see below
Indicate the overall cost per patient of providing the proposed health technology	Refer to Cost breakdown attachment
Please specify any anticipated out of pocket expenses	The out-of-pocket expenses are expected to be the same as per the current codes; unknown what current co-pay is – this will depend on clinician fees.
Provide any further details and explain	Refer to Cost breakdown attachment

Details for the relevant amended MBS items for insertion of a left or right ventricular assist device (38615) and insertion of a left and right ventricular assist device (38618) are provided in Table 7.

Consistent with the proposed population, reflecting patients with refractory heart failure who are ineligible for cardiac transplantation with an INTERMACS profile of 1–4, an additional criterion is incorporated into the MBS items (see criteria (x)).

Based on consultation with four leading experts in the management of patients with refractory heart failure and VAD implantation / cardiac transplantation the following advice was received:

- To ensure appropriate patient selection for VAD implantation, it is proposed the decision is to be determined via a VAD Case Conference, and the terminology 'in a VAD patient be incorporated into the descriptors as defined in the notes. Currently, patient selection for VAD is tightly managed via four quaternary adult transplant centres in Australia. The clinicians felt that expanding durable VAD eligibility to those with 'destination therapy' intent as per criterion (x), warrants a decision be made by a multidisciplinary team. It is thus proposed a Case Conference for VAD (ie, currently not needed, but needed in the event the item code is expanded as proposed) be required to establish eligibility. This is modelled on the Transcatheter Aortic Valve Implantation (TAVI) case conference item codes (6080 and 6081) (See notes in Proposed MBS Descriptors).
- It was suggested that with the proposed expansion of the MBS descriptors to include destination therapy, insertion of VAD should be performed by accredited clinicians at accredited hospitals. Currently, provision of the proposed MBS items will be limited to quaternary centres, with a small eligible patient population due to capacity and capability constraints (see Utilisation attachment). The proposed expanded patient population is well defined, with well-defined clinical expertise in a multi-disciplinary team required to determine patients eligible for a VAD. Considering that VAD implantation and patient assessment is already well established for the current MBS

items (VAD for BTT or BTC), this raises the question of what would be appropriate accreditation for clinicians and hospitals for the additional destination therapy population. Continued liaison with local experts will determine the necessity for accreditations of centres and clinicians to ensure appropriate patient care in the expanded patient population.

- To ensure the proposed destination therapy patient population, those who are not eligible for cardiac transplant (new criterion (x)) reflects those with a high clinical need and who will benefit the most from VAD, use is limited to patients with INTERMACS profiles 1–4. This is also consistent with the evidence base of VAD (MOMENTUM 3).
- To ensure items 38615 and 38618 are purely used for long-term use of VAD (as opposed to temporary mechanical circulatory support) it is suggested that the term 'durable' be included along with the definition 'capable of providing mechanical circulatory support for at least 6 months'. Notably, the clinicians suggest that criteria (b) 'acute post cardiotomy support for failure to wean from cardiopulmonary transplantation' and (c) 'cardio-respiratory support for acute cardiac failure which is likely to recover with short term support of less than 6 weeks' may include use of temporary support (for example using ECMO). MSAC may wish to review the potential overlap of criteria (b) and (c) with existing MBS item codes for temporary circulatory support (eg, VA-ECMO may be claimed via item 13832 for use in intensive care unit). It is not clear whether the removal of these criteria from 38615/38618 would mean some patients will miss out on VAD whether durable or temporary. Furthermore, it is not clear what impact the inclusion of the term 'durable' in the MBS item descriptors will have on current patients qualifying for criteria (b) and (c). This is considered beyond the scope of the Application but highlighted for PASC/MSAC consideration.

Furthermore, whilst criterion (e) states that 'another item in this Schedule applies if the service described in the item is for the use of a ventricular assist device as destination therapy in the management of a patient with heart failure who is not expected to be a suitable candidate for cardiac transplantation' no such other item exists in the Schedule, hence should be removed (this criterion is essentially replaced with the new proposed (x) criterion).

Table 7 Amended MBS item codes – additions in green and deletions as strikethrough

38615	Insertion of a durable left or right ventricular assist device (VAD) capable of providing mechanical circulatory support for at least 6 months, in a VAD Patient for use as: (a) a bridge to cardiac transplantation in patients with refractory heart failure who are: (i) currently on a heart transplant waiting list, or (ii) expected to be suitable candidates for cardiac transplantation following a period of support on the ventricular assist device; or (x) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation; or (b) acute post cardiotomy support for failure to wean from cardiopulmonary transplantation; or (c) cardio-respiratory support for acute cardiac failure which is likely to recover with short term support of less than 6 weeks; or (d) item 11704, 11705, 11707, 11714, 18260, 33824, 38418, 38806 or 45503 applies~~;~~ ~~or~~ ~~(e) another item in this Schedule applies if the service described in the item is for the use of a ventricular assist device as destination therapy in the management of a patient with heart failure who is not expected to be a suitable candidate for cardiac transplantation~~
Notes	TN.8.67 Cardiac and Thoracic Surgical Items - (Items 38470 to 38766) Items 38470 to 38766 must be performed using open exposure or minimally invasive surgery which excludes percutaneous and transcatheter techniques unless otherwise stated in the item.
NEW	**VAD Patient** A VAD Patient means a patient who, as a result of a VAD Case Conference, has been assessed as suitable for VAD based on the following: a) bridge to cardiac transplantation in patients with refractory heart failure who are: (i) currently on a heart transplant waiting list, or (ii) expected to be suitable candidates for cardiac transplantation following a period of support on the ventricular assist device; or (x) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation; or (b) acute post cardiotomy support for failure to wean from cardiopulmonary transplantation; or (c) cardio-respiratory support for acute cardiac failure which is likely to recover with short term support of less than 6 weeks A VAD Case Conference is a process by which: (a) there is a team of 3 or more participants, where: (i) the first participant is a cardiothoracic surgeon (ii) the second participant is a specialist or consultant physician who does not perform a service described in items 38615 or 38618 for the patient being assessed; and (iii) the third participant is a specialist or consultant physician or VAD co-ordinator who does not perform a service described in items 38615 or 38618 for the patient being assessed; and (iv) the first participant will perform the VAD procedure

	(b) the team assesses a patient's risk and technical suitability to receive the service described in item 38615 or 38618, taking into account matters such as: (i) the patient's risk and technical suitability for a ventricular assist device implantation; and (ii) the patient's cognitive function and frailty; and (c) the result of the assessment is that the team makes a recommendation about whether or not the patient is suitable to receive the service described in item 38615 or 38618; and (d) the particulars of the assessment and recommendation are recorded in writing.
38618	Insertion of a durable left and right ventricular assist device (VAD) capable of providing mechanical circulatory support for at least 6 months, in a VAD Patient for use as: (a) a bridge to cardiac transplantation in patients with refractory heart failure who are: (i) currently on a heart transplant waiting list, or (ii) expected to be suitable candidates for cardiac transplantation following a period of support on the ventricular assist device; or (x) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation; or (b) acute post cardiotomy support for failure to wean from cardiopulmonary transplantation; or (c) cardio-respiratory support for acute cardiac failure which is likely to recover with short term support of less than 6 weeks; or (d) item 11704, 11705, 11707, 11714, 18260, 33824, 38418, 38806 or 45503 applies~~; or (e) another item in this Schedule applies if the service described in the item is for the use of a ventricular assist device as destination therapy in the management of a patient with heart failure who is not expected to be a suitable candidate for cardiac transplantation~~
Notes	TN.8.67 Cardiac and Thoracic Surgical Items - (Items 38470 to 38766) Items 38470 to 38766 must be performed using open exposure or minimally invasive surgery which excludes percutaneous and transcatheter techniques unless otherwise stated in the item.
	VAD Patient A VAD Patient means a patient who, as a result of a VAD Case Conference, has been assessed as suitable for VAD based on the following: a) bridge to cardiac transplantation in patients with refractory heart failure who are: (i) currently on a heart transplant waiting list, or (ii) expected to be suitable candidates for cardiac transplantation following a period of support on the ventricular assist device; or (x) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation; or (b) acute post cardiotomy support for failure to wean from cardiopulmonary transplantation; or (c) cardio-respiratory support for acute cardiac failure which is likely to recover with short term support of less than 6 weeks A VAD Case Conference is a process by which: (a) there is a team of 3 or more participants, where: (i) the first participant is a cardiothoracic surgeon

	(ii) the second participant is a specialist or consultant physician who does not perform a service described in items 38615 or 38618 for the patient being assessed; and (iii) the third participant is a specialist or consultant physician or VAD co-ordinator who does not perform a service described in items 38615 or 38618 for the patient being assessed; and (iv) the first participant will perform the VAD procedure (b) the team assesses a patient's risk and technical suitability to receive the service described in item 38615 or 38618, taking into account matters such as: (i) the patient's risk and technical suitability for a ventricular assist device implantation; and (ii) the patient's cognitive function and frailty; and (c) the result of the assessment is that the team makes a recommendation about whether or not the patient is suitable to receive the service described in item 38615 or 38618; and (d) the particulars of the assessment and recommendation are recorded in writing.

Algorithms

Preparation for using the health technology

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

Referral to HF specialist should be considered in patients with advanced HF as timely referral is crucial to optimise outcomes (Heidenreich 2022). The following acronym has been developed by Australian Clinicians to assist decision making to refer: (Baumwol 2017) to assist in decision making to refer:

I-Need-Help

I=Intravenous inotropes

N=NYHA class IIIb to IV or persistently elevated natriuretic peptides

E=End-organ dysfunction

E=EF≤35%

D=Defibrillator shocks

H=Hospitalisations >1

E=Edema despite escalating diuretics

L=Low SBP ≤90 mmHg, high heart rate

P=Prognostic medication, progressive intolerance or down-titration of GDMT

Patient evaluation and selection for durable MCS as a therapy for advanced HF involves consideration of multiple factors. Given the potential for adverse events and complications and high resource utilisation, it is imperative that patients with the opportunity for the greatest treatment effect are selected to target those with the highest benefit / risk ratio (Potapov 2019).

The AHA 2022 HF guidelines recommend long-term MCS with VAD be considered in selected patients with NYHA class IV symptoms who are dependent on IV inotropes or temporary MCS or

who have NYHA class IV symptoms despite GDMT (class of recommendation = 1; level of Evidence =A; Heidenreich 2022). These recommendations are irrespective of transplant eligibility. The ESC HF guidelines recommend long-term MCS be implemented in patients eligible for transplant and should be considered in those with advanced HF with reduced ejection fraction despite GDMT and who are not eligible for heart transplantation or other surgical options (ie, destination therapy) (McDonagh 2021).

In patients not expected to become eligible for transplant, the European Association for Cardio-Thoracic Surgery (EACTS) expert consensus statement on long-term mechanical circulatory support (Potapov 2019) state that LVAD should be considered in patients with NYHA class IIIB–IV, with ejection fraction ≤25% that also meet at least one of the following criteria: INTERMACS 2–4, inotrope dependence, progressive end-organ dysfunction, peak VO_2 <12 ml/kg/min and temporary MCS dependence.

Table 8 Recommendations for management of advanced heart failure patients as per AHA (2022) HF guidelines, ESC (2021) HF guidelines and EACTS consensus statement (2019) on long-term MCS

AHA 2022 (Heidenreich 2022)		
COR	**LOE**	**Recommendation**
1	A	In select patients with advanced HFrEF with NYHA class IV symptoms who are deemed to be dependent on continuous intravenous inotropes or temporary MCS, durable LVAD implantation is effective to improve functional status, QOL, and survival.
2a	B-R	In select patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS can be beneficial to improve symptoms, improve functional class, and reduce mortality.
2a	B-NR	In patients with advanced HFrEF and hemodynamic compromise and shock, temporary MCS, including percutaneous and extracorporeal ventricular assist devices, are reasonable as a "bridge to recovery" or "bridge to decision."
ESC 2021 (McDonagh 2021)		
I	C	Patients being considered for long-term MCS must have good compliance, appropriate capacity for device handling and psychosocial support
I	C	Heart transplantation is recommended for patients with advanced HF, refractory to medical / device therapy and who do not have absolute contraindications.
IIa	A	Long-term MCS should be considered in patients with advanced HFrEF despite optimal medical and device therapy, not eligible for heart transplantation or other surgical options, and without severe right ventricular dysfunction, to reduce the risk of death and improve symptoms.
IIa	B	Long-term MCS should be considered in patients with advanced HFrEF refractory to optimal medical and device therapy as a bridge to cardiac transplantation in order to improve symptoms, reduce the risk of HF hospitalisation and the risk of premature death.
IIa	C	Renal replacement therapy should be considered in patients with refractory volume overload and end-stage kidney failure.
IIb	C	Continuous inotropes and/or vasopressors may be considered in patients with low cardiac output and evidence of organ hypoperfusion as bridge to MCS or heart transplantation
IIb	C	Ultrafiltration may be considered in refractory volume overload unresponsive to diuretic treatment.

EACTS consensus on LT-MCS 2019 (Potapov 2019)		
I	B	It is recommended that reversible causes of heart failure are ruled out
IIa	B	LT-MCS implantation should be considered in patients with the following: • NYHA functional class IIIB–IV and • Ejection fraction ≤25% and At least one of the following criteria: o INTERMACS 2–4 o Inotrope dependence o Progressive end-organ dysfunction o Peak VO_2 <12 ml/kg/min o Temporary MCS dependence
IIb	B	LT-MCS implantation may be considered in patients with: • New York Heart Association functional class IIIB–IV and • Ejection fraction ≤25% and o To reverse elevated pulmonary vascular resistance or potentially reversible renal failure in potential heart transplant candidates o To allow time for transplant contraindications to be reversed such as recent cancer, obesity and recovering drug and alcohol dependence in potential heart transplant candidates

GDMT, guideline-directed medical therapy; HFrEF, failure with reduced ejection fraction; NYHA, New York Heart Association; LT-MCS, long-term mechanical circulatory support; MCS, mechanical circulatory support; LVAD, left ventricular assist device; QOL, quality of life

COR, class of recommendation (AHA):

Class 1=strong

Class 2a=moderate

COR, class of recommendation (ESC / EACTS):

Class I=recommended or indicated

Class IIa=conflicting evidence, but weight of evidence in favour, should be considered

Class IIb=conflicting evidence, usefulness/efficacy is well established by evidence/opinion, may be considered.

Class III=not recommended.

LOE, level of evidence (AHA):

Level A=high quality evidence from more than one randomised controlled trial (RCT);

Level B-R=moderate quality evidence form one or more RCTs;

Level B-NR; moderate quality evidence from one or more well designed non-randomised or observational studies.

LOE, level of evidence (ESC / EACTS):

Level A= multiple RCTs or meta-analyses

Level B=single RCT or large non-randomised studies

Level C=consensus of expert opinion and/or small studies, retrospective studies, registries.

Source: AHA 2022 guidelines (Heidenreich 2022), section 8.4. ESC guidelines (2021) (McDonagh 2021, pg 3642); EACTS Consensus (Potapov 2019, pg 233).

Specific indications and contraindications to MCS as per the ESC 2021 HF guidelines (McDonagh 2021) and the scientific statement from the AHA with recommendations for the use of MCS (Cook 2017) is provided in

Table 9 (note the AHA HF 2022 guidelines refer to indications / contraindications as per Cook 2017).

Table 9 Indications and contraindications to long-term MCS as per ESC HF guidelines (McDonagh 2021) and AHA scientific statement on MCS (Cook 2017)

AHA scientific statement on MCS (2017)	**ESC HF guidelines (2021)**
Indications (combinations of these)	**Indications**
Frequent hospitalizations for HF	Patients with persistence of severe symptoms despite optimal medical and device therapy, without severe right ventricular dysfunction and/or severe TR, with a stable psychosocial background and absence of major contraindications*, and who have at least one of the following: • LVEF <25% and unable to exercise for HF or, if able to perform cardiopulmonary exercise testing, with peak VO_2 < 12 mL/kg/min and/or < 50% predicted value. • ≥ 3 HF hospitalisations in previous 12 months without an obvious precipitating cause. • Dependence on i.v. inotropic therapy or temporary MCS. • Progressive end-organ dysfunction (worsening renal and/or hepatic function, type II pulmonary hypertension, cardiac cachexia) due to reduced perfusion and not to inadequately low ventricular filling pressure (PCWP ≥ 20 mmHg and SBP ≤ 90 mmHg or cardiac index ≤ 2 L/min/m2).
NYHA class IIIb to IV functional limitations despite maximal therapy	
Intolerance of neurohormonal antagonists	
Increasing diuretic requirement	
Symptomatic despite CRT	
Inotrope dependence	
Low peak VO_2 (<14–16)	
End-organ dysfunction attributable to low cardiac output	
Contraindications:	
Absolute	*Stable psychosocial background includes demonstrated understanding of the technology and patient living in the same household with a caregiver that will help the patient (i.e. living alone and poor psychosocial background is LVAD contraindication). Major contraindications include contraindication to long-term oral anticoagulation, infection, severe renal dysfunction, ventricular arrhythmias.
Irreversible hepatic disease	
Irreversible renal disease	
Irreversible neurological disease	
Medical nonadherence	
Severe psychosocial limitations	
Relative	
Age >80 y for destination therapy	
Obesity or malnutrition	
Musculoskeletal disease that impairs rehabilitation	
Active systemic infection or prolonged intubation	
Untreated malignancy	
Severe PVD	
Active substance abuse	
Impaired cognitive function	
Unmanaged psychiatric disorder	
Lack of social support	

CRT, cardiac resynchronisation therapy; DT, destination therapy; HF, heart failure; i.v, intravenous; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; NYHA, New York Heart Association; PCWP, pulmonary capillary wedge pressure; PVD, peripheral vascular disease; SBP, systolic blood pressure; TR, tricuspid regurgitation.

Source: AHA 2022 HF guidelines (Heidenreich 2022), table 19 & AHA Scientific statement on MCS Cook (2017) table 1 ; ESC 2021 HF guidelines (McDonagh 2021)

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?
Yes

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:
Not applicable.

Use of the health technology

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:
As discussed in the Cost Breakdown attachment, healthcare resources, reflecting direct costs, that will be delivered at the time of the proposed medical service include professional attendances, nursing care, consumables, laboratory/pathology tests, imaging procedures, dispensed pharmaceuticals, operating room time etc. Indirect costs are overhead costs such as cleaning, administrative staff support etc which cannot be directly allocated to individual patients but are necessary to support patient care. See Cost Breakdown attachment for further details or resource items used.

Explain what other healthcare resources are used in conjunction with the comparator health technology:
NA. The comparator is GDMT which is prescribed by the treating physician with ongoing management. No other healthcare resources are used in conjunction with the comparator.

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:
As per the healthcare resources used in conjunction with the proposed health technology.

Clinical management after the use of health technology

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the proposed health technology:
Post-operative care similar to open heart patient. Device Assessment and optimisation, a ramped speed ECHO study.

Ongoing Patient Assessment and Care through outpatient clinic visits to include Vital signs, peripheral circulation, mental status, level of consciousness, 12 lead EKG, ECHO, nutritional support, cardiac rehab, patient and caregiver education, anticoagulation management, device assessment and Driveline Exit site monitoring.

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the comparator health technology:
Variations dependant on clinical need. Ongoing Patient Assessment and Care, re-hospitalisations, adjustment of GDMT with tolerances, fluid state management, resources and tests related to symptom management and palliation.

Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:
Post operative care, device assessment, anticoagulation management and driveline exit site monitoring.

Algorithms

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:
The current clinical algorithm for the management of the proposed patient population, those who are not eligible for a heart transplant and in whom the therapy intent is destination therapy is provided in Figure 4. Currently in Australia, patients who are eligible for a heart transplant (BTT), or who are expected to be suitable candidates for cardiac transplantation following insertion of VAD (BTC), are eligible for VAD on the MBS via items 38615 and 38618. A discussion on transplant eligibility is provided above for context.

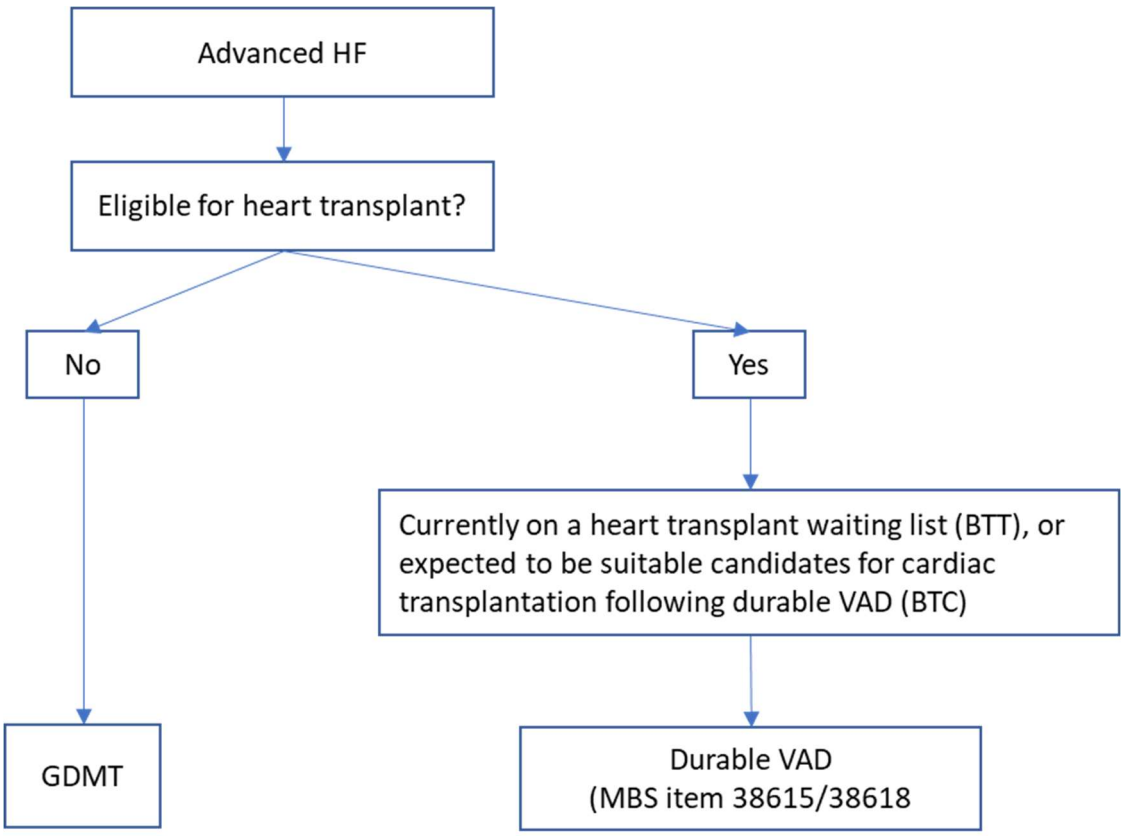

Figure 4 Current management algorithm of the proposed patient population, those who are not eligible for a heart transplant, or are not expected to be suitable candidates

The proposed clinical algorithm for the management of the proposed patient population, those who are not eligible for a heart transplant, or are not expected to be suitable candidates is provided in Figure 4. Listing durable VAD in the proposed population would provide these patients with a therapy option that is associated with superior survival and quality of life compared with GDMT (Mehra 2019; Estep 2015; Rose 2001).

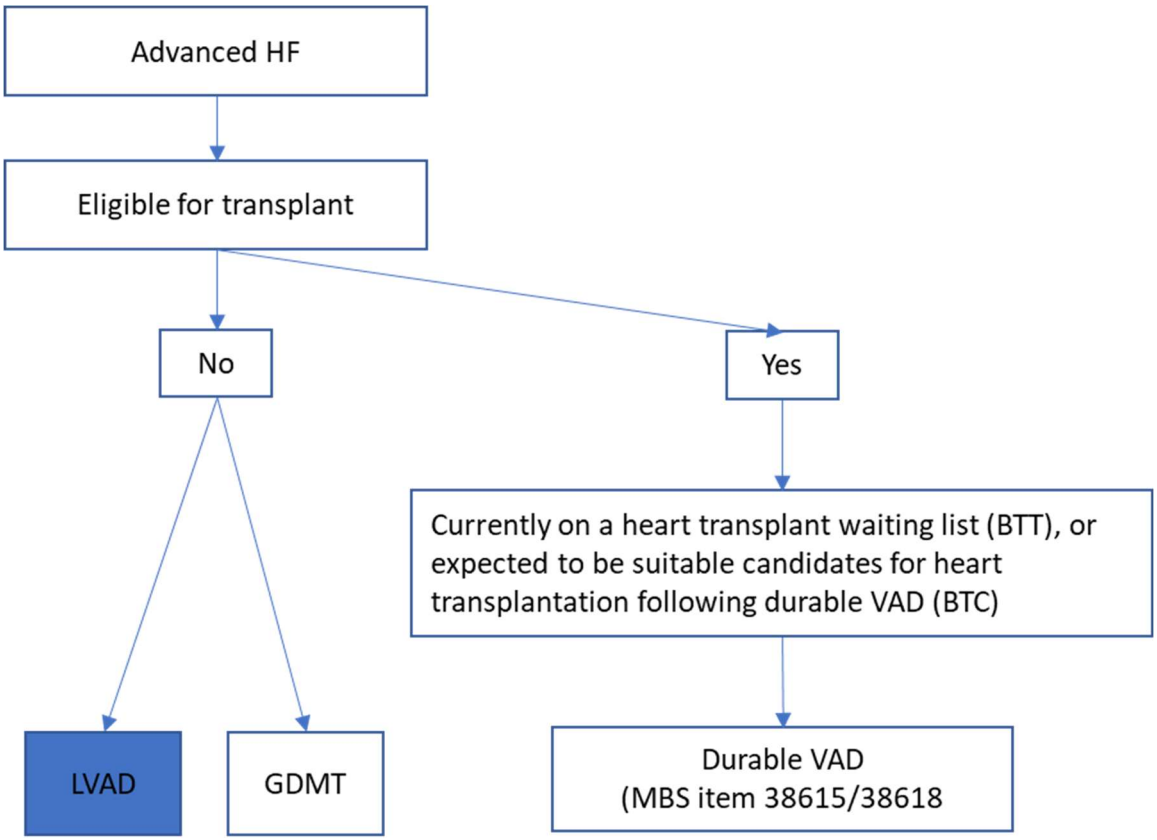

Figure 5 Proposed management algorithm of the proposed patient population, those who are not eligible for a heart transplant, or are not expected to be suitable candidates

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)? (please select your response)

☒ Superior
☐ Non-inferior
☐ Inferior

Please state what the overall claim is, and provide a rationale:

Insertion of durable VAD in patients who are not eligible for a heart transplant with the intention of destination therapy is associated with superior survival and quality of life relative to GDMT.

The results from the REMATCH study showed that a first-generation VAD (HeartMate vented electric device, Thoratec, Pleasanton, Calif) showed superior survival in patients ineligible for heart transplant versus optimal medical management (Rose 2011). The rates of survival at one year were 52 percent in the device group and 25 percent in the OMT group (P=0.002), and at two years were 23 percent and 8 percent (P=0.09), respectively.

As illustrated in Figure 6, survival has been shown to improve with later generation VADs, with HeartMate 3 having similar survival to that observed from heart transplant (Netuka 2020). Heartmate 3 is the current VAD that is used in Australian clinical practice.

MOMENTUM3 showed the HeartMate3 device to be associated with less frequent need for pump replacement than HeartMate II and was superior with respect t to survival free of disabling stroke or reoperation to replace or remove a malfunctioning device (Mehra 2019). These results confirm HeartMate3 to offer a superior device technology to that of HeartMate II.

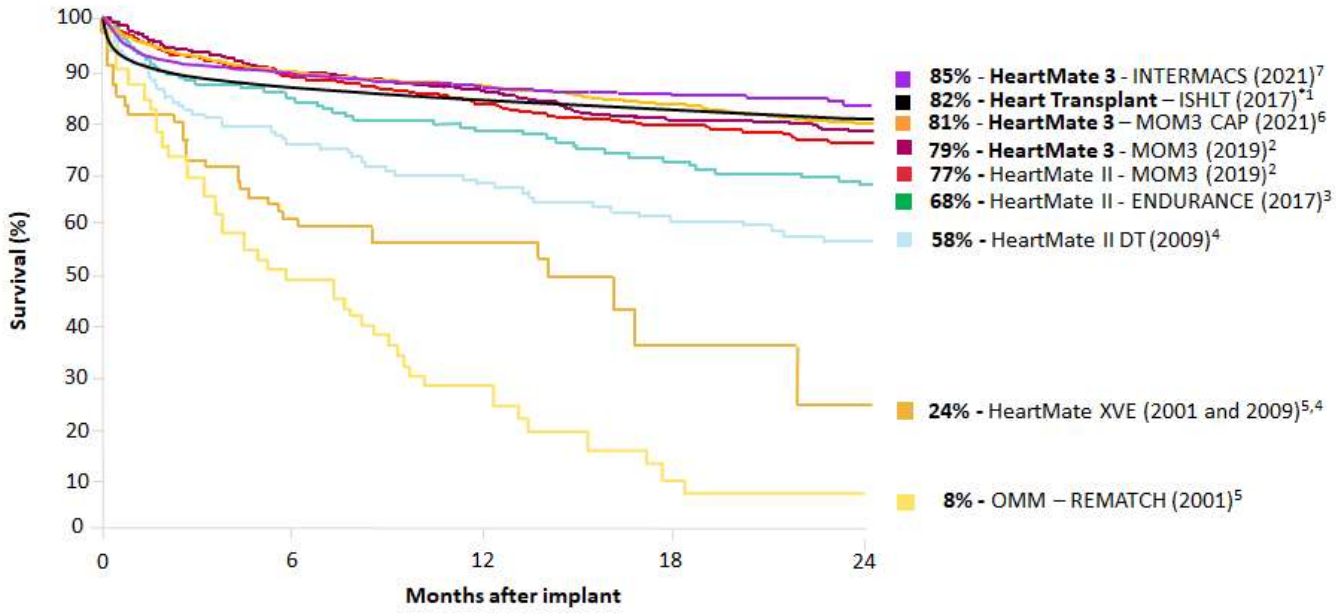

Figure 6 Comparisons of survival curves with HearMate 3 and II, transplant and optimal medical management

Note. Based on published data from multicenter experience and separate studies, which may involve different patient populations and other variables. Not a head-to-head comparison. Data presented for informational purposes only. *82% 2-year survival for adult heart transplants patients between 2009 and 20151

1. Khush KK, Cherikh WS, Chambers DC, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-fifth Adult Heart Transplant Report-2018; Focus Theme: Multiorgan Transplantation. J Heart Lung Transplant. 2018;37:1155-1168.

2. Mehra M, Uriel N, Naka Y, et al. A Fully Magnetically Levitated Ventricular Assist Device-Final Report. N Engl J Med. 2019;380:1618-1627.

3. Rogers JG, Pagani F, Tatooles A, et al. Intrapericardial left ventricular assist device for advanced heart failure. New Engl J Med. 2017;376:451-460.

4. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med. 2009;361:2241-2251.

5. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med. 2001 Nov 15;345(20):1435-43.

6. Mehra, Cleveland, Uriel, et al. Eur J Heart Failure 2021 (in press). 7. Pagani et al. Concordance of Treatment Effect: An Analysis of The Society of Thoracic Surgeons Intermacs Database. Ann Thorac Surg, 2021. https://doi.org/10.1016/j.athoracsur.2021.05.017

Note from Abbott.

LVAD as destination therapy for transplant ineligible patients has been shown to be cost-effective as an end-of-life therapy. In this cost-effectiveness analysis from the UK perspective, the authors noted: The base-case scenario showed an ICER of £47,361/QALY gained for LVAD vs OMM for patients who are ineligible for heart transplantation (Lim et al, 2021), which is below the end-of-life willingness-to-pay threshold of £50,000/QALY gained as generally accepted. The authors are referring here to the UK National Institute for Health and Care Excellence (NICE) approach whereby willingness-to-pay thresholds differ when therapies are end-of-life or for very rare conditions. The authors note that – "*[h]ere, the payer's willingness-to pay may be higher than the usually reported threshold of £20,000 to £30,000/QALY gain given the end-of-life nature of the therapy in the target population and be set at £50,000".* It would be reasonable to apply such an approach to inform decision making regarding durable VAD use for DT in the Australian context.

Considering that durable VAD as DT is a life-saving device, then there are parallels with the Australian Life Saving Drugs Program (LSDP). These medicines are typically very high cost and not cost effective enough to list on the Pharmaceutical Benefits Scheme (PBS). From an equity perspective and consistency across Australian HTA processes (for drugs and devices) it would be reasonable to expect that VADs for DT would be assessed similarly to life-saving drug therapies. Example incremental cost-effectiveness ratios (ICERs) for drugs on the LSDP:

- Avalglucosidase alfa (Enzyme replacement therapy for Pompe disease). The PBAC noted the base case ICER for late onset Pompe disease (LOPD) was > $1,055,000 per quality adjust life year (QALY) gained (with sensitivity analyses ranging from $855,000 to < $955,000/QALY to > $1,055,000/QALY) and for infantile-onset Pompe disease (IOPD) was $455,000 to < $555,000/ QALY (with sensitivity analyses ranging from $255,000 to < $355,000/ QALY to $555,000 to < $655,000/ QALY). (LSDP listed on 1-September-2022)
- Asfotase alfa (Enzyme replacement therapy for perinatal- and infantile-onset hypophosphatasia) …over $1 million per QALY gained….(LSDP listed on 1-May-2022)
- Cerliponase alfa (treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease). The redacted table shows ICERs in the ranges of $105,000/LYG - $200,000/LYG and more than $200,000/LYG; and $105,000/QALY - $200,000/QALY and more than $200,000/QALY gained. ICERs vary depending on different sensitivity analyses (LSDP listed 1-May -2022)

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

Not applicable – VAD is not an investigative test.

Identify how the proposed technology achieves the intended patient outcomes:

A durable VAD is a surgically implanted heart pump designed to provide mechanical circulatory support (MCS) to those with advanced heart failure who are refractory to standard medical therapy. The HeartMate 3 VAD is a fully magnetically levitated centrifugal pump, that assumes some or all of the workload of the ventricle, thereby restoring the patient's systemic perfusion while palliating the underlying pathology.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management?	N/A
A change in health outcome?	N/A
Other benefits?	N/A

Not Applicable – VAD is not a test

Please provide a rationale, and information on other benefits if relevant:
Not Applicable – VAD is not a test

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?
☒ More costly
☐ Same cost
☐ Less costly

Provide a brief rationale for the claim:
The proposed technology is a surgical procedure involving implantation of the prostheses (the pump) whereas the comparator consists of medication. Refer to the Cost Breakdown attachment for further discussion on cost of the proposed intervention.

Summary of Evidence

We are aware that the MSAC prefer direct evidence of a proposed service vs current care, ideally in the form of a randomised controlled trial (RCT). Rows 2 and 3 of the "*Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application*)" table below describe two RCTs which would provide direct evidence relevant to this application – the AMBUVAD and SweVAD studies. However, given the available evidence provided in the first table below, it is reasonable to claim that there is no clinical equipoise regarding the effectiveness of HeartMate 3 vs. medical therapy in patients ineligible for cardiac transplantation.

The SweVAD study started in June 2016 – if MOMENTUM 3 data was available at this time (published in 2019), such a study may not have gained ethics approval. We are also aware that there have been challenges recruiting for this RCT - indicating the difficulties in conducting RCTs in this patient population. The AMBUVAD study started in 2021 – it is somewhat concerning that this study had ethics approval. We are aware that the SweVAD study has had challenges enrolling patients, which is reflective of the difficulties of recruiting patients who may prefer a VAD based on available data or who may prefer medical management due to concerns about VAD implantation and living with a VAD.

Considering that durable VAD therapy is effectively an 'end-of-life' treatment option that addresses an unmet need – and that the number of patients who would be treated is very small – we are of the view that waiting for results of these RCTs would be unethical – as it would potentially delay access to patients who would benefit from durable VAD therapy (and these trials may never be completed).

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology.

	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.	RCT, OL, MC NCT02224755	MOMENTUM 3 A Fully Magnetically Levitated Left Ventricular Assist Device — Final Report Mehra (2019)	**Population:** BTT, BTC, DT **Comparison:** HM3 vs HM2 The study included 1028 subject, 516 randomised to HM3 and 512 to HM2. The results from the primary analysis, freedom from disabling stroke, or reoperation to replace or remove a malfunctioning device at 2 years, demonstrated superiority in favour of HM3 (HR=0.84; 95% CI: 0.78–0.91). Subgroup analyses by intended use consistent results across BTT, BTC and DT populations (p value for interaction = 0.62; supplement). Pump replacement was less common with HM3 than HM2 (2.3% vs 11.3%; RR=0.21; 95% CI: 0.11–0.38).	https://pubmed.ncbi.nlm.nih.gov/30883052/	2019
2.	Observational, 5 year follow up of MOMENTUM 3 NCT03982979	**MOMENTUM 3** – 5 year follow up Five-Year Outcomes in Patients With Fully Magnetically Levitated vs Axial-Flow Left Ventricular Assist Devices in the MOMENTUM 3 Randomized Trial Mehra (2022)	**Population:** BTT, BTC, DT **Comparison:** HM3 vs HM2 A total of 477 patients of 536 patients still receiving LVAD support at 2 years contributed to the extended-phase analysis. The 5-year Kaplan-Meier estimate of survival to transplant, recovery, or LVAD support free of debilitating stroke or reoperation to replace the pump in HM3 vs HM2 was 54.0% vs 29.7% (HR= 0.55; 95% CI: 0.45-0.67). Overall Kaplan-Meier survival was 58.4% vs 43.7% in the HM3 vs HM2 groups (HR= 0.72; 95% CI: 0.58-0.89) and SAEs of stroke, bleeding, and pump thrombosis were less frequent in the HM3 group.	https://pubmed.ncbi.nlm.nih.gov/36074476/	2022

	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, MC, observational study NCT01452802	ROADMAP Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients Results From the ROADMAP Study Estep (2015)	**Population:** DT, not dependent on inotropes (ie, IM 4-7) **Comparison:** HM2 vs OMM This prospective, observational study compared outcomes of HM2 (n=97) vs OMM (n=103). At baseline, the HM2 patients were more severely ill, as evidenced by more IM profile 4 (65% vs 34%). Despite this, a statistically significantly higher proportion of HM2 patients met the primary endpoint (survival and improvement ≥75 m in 6MWD at 12 months) than OMM patients (39% vs. 21%; OR=2.4; 95% CI: 1.2–4.8). AEs were higher with HM2 primarily due to bleeding events. HRQoL improved significantly more with HM2 vs OMM.	https://pubmed.ncbi.nlm.nih.gov/28396040/	2015
4.	RCT, OL, MC	REMATCH Long-term use of a left ventricular assist device for end-stage heart failure. Rose (2001)	**Population:** DT (BTT ineligible; 72% inotrope dependent) **Comparison:** HM XVE vs OMM A total of 129 patients were randomised to HM XVE (n=68) and OMM (n=61). The Kaplan Meier analysis for survival demonstrated a reduction of 48% int the risk of death with LVAD vs OMM (RR: 0.52; 95% CI: 0.34–0.78). SAE occurred 2.35 times more frequently in the LVAD group than OMM, mainly driven by infection, bleeding, and malfunction of the device (noting this is an older generation LVAD). QoL was significantly improved with LVAD vs OMM.	https://pubmed.ncbi.nlm.nih.gov/11794191/	2001

6MWT, 6 minute walk test; BTC, bridge to candidacy; BTT, bridge to transplant; DT, destination therapy; IM, INTERMACS; LVAD, left ventricular assist device; MC, multicentre; OL, open-label; OMM, optimal medical management; OR, odds ratio; RCT, randomised controlled trial; RR, relative risk; SAE, serious adverse advent.

Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application).

	Type of study design	Title of research	Short description of research	Website link to research	Date
1.	RCT	DOT HeartMate 3 Study [Direct Oral Anticoagulant Therapy with the HeartMate 3 LVAD: A Pilot Study DOT-HM3 Study]	Patients implanted with HM3 will be randomised to receive apixaban or control. Expected sample = 45	NCT04974684	Status: recruiting Expected completion: April 2023
2.	RCT	LVAD Versus GDMT in Ambulatory Advanced Heart Failure Patients (AMBU-VAD)	BTT, BTC or DT patients will be randomised to HM3 or OMM, and assessed 12 months post implantation. Expected sample = 92	NCT04768322	Status: recruiting Expected completion: February 2027
3.	RCT	Swedish Evaluation of Left Ventricular Assist Device as Permanent Treatment in End-stage Heart Failure (SweVAD)	The primary objective is to compare survival between HM3 as DT and OMM in a Swedish end stage HF population ineligible for cardiac transplantation. Expected sample = 80	NCT02592499	Status: recruiting Expected completion: December 2023
4.	RCT	Evaluation of the Hemocompatibility of the Direct Oral Anti-Coagulant Apixaban in Left Ventricular Assist Devices (DOAC LVAD)	Patients implanted with HM3 will be randomised to receive apixaban or warfarin. Expected sample = 40	NCT04865978	Status: recruiting Expected completion: May 2024
5.	RCT	Prospective Multi-Center Randomized Study for Evaluating the EVAHEART®2 Left Ventricular Assist System (COMPETENCE)	The objective of the study is to evaluate the safety and effectiveness of the EVA2 by demonstrating non-inferiority to HM3 when used for the treatment of refractory advanced heart failure. Expected sample = 399	NCT01187368	Status: recruiting Expected completion: March 2024
6.	RCT	Evaluation of the Jarvik 2000 Left Ventricular Assist System With Post-Auricular Connector--Destination Therapy Study	The MC study will be prospective, dual-armed, non-blinded (open-label) and randomised, comparing a treatment group receiving the Jarvik 2000 LVAD with post-auricular connector to HM2 for DT. Expected sample = 350	NCT01627821	Status: recruiting Expected completion: December 2023

BTC, bridge to candidacy; BTT, bridge to transplant; DT, destination therapy; LVAD, left ventricular assist device; MC, multicentre; OMM, optimal medical management; RCT, randomised controlled trial.