Australian Government

Department of Health

Ratified PICO Confirmation

Application 1659

Catheter-based renal denervation for uncontrolled elevated systolic blood pressure

Summary of PICO/PPICO criteria to define the question(s) to be addressed in an Assessment Report to the Medical Services Advisory Committee (MSAC)

Component	Description
Patients	Adults ≥18 years of age with treatment-resistant hypertension confirmed by a specialist, with elevated systolic blood pressure ≥ 150 mm Hg and/or elevated diastolic blood pressure ≥110 mm Hg despite optimal medical management (using three or more antihypertensive drugs, including a diuretic, at optimal tolerated doses) and one or more of the following: • systolic blood pressure > 180 mm Hg • previous myocardial infarction • previous stroke or transient ischaemic attack (TIA) • diabetes mellitus • chronic kidney disease • atrial fibrillation • heart failure • peripheral arterial disease. Prior specialist consultation is required to confirm optimal medical management and verify treatment-resistant hypertension. Report the following sub-populations separately: • high-CVD-risk condition listed in eligibility options • age groups • baseline systolic or diastolic blood pressure strata.
Intervention	Renal denervation with radiofrequency ablation catheter (single electrode or multi-electrode catheters) plus optimal medical management Report the following sub-populations separately, where available: • bi-lateral vs unilateral denervation • single-electrode (first generation) device vs multi-electrode (second generation) device • device brand.
Comparator	Optimal medical management, with or without sham renal denervation.

Outcomes	**Efficacy outcomes**
	• incidence of cardiovascular disease – composite outcome and also reported separately for:
	  ○ new onset of end-stage renal disease
	  ○ new myocardial infarction
	  ○ new stroke or TIA
	  ○ new onset atrial fibrillation
	  ○ new onset heart failure
	  ○ new myocardial infarction

Component	Description
	• change in SBP (24-h ABPM and OBPM) • change in DBP (24-h ABPM and OBPM) • incidence of achieving target SBP or DBP (140 mm Hg) • incidence of achieving target DBP (90 mm Hg) • quality of life • cardiovascular mortality • all cause mortality. **Safety outcomes** • Incidence of major adverse events • Renal artery re-intervention (e.g. as a result of perforation or dissection) • Vascular complications • New stroke • Embolic event resulting in end-organ damage • New-onset of end-stage renal disease • Renal artery stenosis (>70%) • All-cause mortality (short-term only – long term mortality outcomes are captured as efficacy outcomes). **Healthcare resources** • Cost of catheter (the applicant intends to apply for listing on Part C of Prostheses List) • Cost of procedure (i.e. proposed service fee; anaesthetist services; theatre/admission costs, including consumables; amortised cost of generator) • Cost associated with changes in clinical management (e.g. radiographic imaging for renal stenosis; PBS-listed hypertension medications).

Abbreviations: ABPM = ambulatory blood pressure measurement; CVD = cardiovascular disease; DBP = diastolic blood pressure; mm Hg = millimetres of mercury; OBPM = office blood pressure measurement; PBS = Pharmaceutical Benefits schedule; SBP = systolic blood pressure; TIA = transient ischaemic attack

PICO or PPICO rationale for therapeutic and investigative medical services only

Context of application

In 2012, an application to MSAC was initiated by the applicant (Medtronic Australia) for catheter-based renal denervation for treatment-resistant hypertension (Application 1338[1]): the Decision Analytic Protocol (DAP) was finalised in September 2013, and an MSAC submission was lodged in October 2013. Four renal denervation systems were Therapeutic Goods Administration (TGA)-approved at the time of the 2013 MSAC submission: the first generation Medtronic Symplicity Flex device and three other radiofrequency devices (Table A2, Appendix).

After submission, results from the SYMPLICITY HTN-3 single-blind, randomised, sham-controlled clinical trial became available, which failed to confirm a significant beneficial effect of renal denervation on blood pressure compared to the sham procedure. According to the applicant, as a consequence of the outcome of the HTN-3 trial, the MSAC application for renal denervation was not evaluated, and many programs for the development of various renal denervation devices were halted or suspended. The applicant has noted the HTN-3 trial results may have been confounded by extensive changes to baseline medication regimens during follow up, and a potential 'trial effect', resulting in a large reduction in blood pressure in both the intervention and sham groups.

The applicant claims these and other issues were addressed in the design of the subsequent SPYRAL HTN global trial program, including objective measures of adherence to baseline medication regimens. On the basis of data from the SPRYRAL HTN trials, the applicant now wishes to recommence the MSAC application process to request the inclusion of catheter-based renal denervation as a funded item on the Medicare Benefits Schedule (MBS).

Currently only two renal denervation devices are listed on the Australian Register of Therapeutic Goods (ARTG): the applicant's second generation Symplicity Spyral catheter and the EnligHTN Ablation Catheter (Abbott Medical Australia Pty Ltd) (Table A1A, Appendix). It is the applicant's understanding that the EnligHTN catheter is not currently used in Australia – no renal denervation catheters are currently listed on the Prostheses List.

[1] http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1338-public

Population

Hypertension, or elevated blood pressure, is an established risk factor for cardiovascular disease (CVD), and is defined by the practice guidelines of the National Heart Foundation of Australia (NHFA 2016) as:

- systolic blood pressure of ≥140 mm Hg and/or
- diastolic blood pressure of ≥90 mm Hg.

There are three grades of hypertension (Grades 1 to 3), defined by blood pressure thresholds, and a fourth category – isolated systolic hypertension – in which systolic blood pressure exceeds 140 mm Hg but diastolic blood pressure is <90 mm Hg. Hypertension is a major risk factor and antecedent of cardiovascular and end organ damage: myocardial infarction; chronic kidney disease; ischaemic and haemorrhagic stroke; heart failure and premature death (NHFA 2016).

Lifestyle advice is recommended for all hypertensive patients. First-line anti-hypertensive drugs include angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), calcium channel blockers and thiazide diuretics, and some of these can be used in combination, or with beta-blockers (NHFA 2016). Among patients treated for hypertension, however, it is estimated that 20-30% have uncontrolled blood pressure. Treatment-resistant hypertension (i.e. where all therapy options have been optimised) has been estimated at 8-18% (NHFA 2016). Treatment-resistant hypertension is noted as particularly increasing the risk of developing left ventricular hypertrophy, microalbuminuria, kidney failure and coronary artery disease (NHFA 2016).

The proposed eligible population, adapted from the applicant's proposed population, is:

Adults ≥18 years of age with treatment-resistant hypertension confirmed by a specialist, with elevated systolic blood pressure ≥ 150 mm Hg or elevated diastolic blood pressure ≥110 mm Hg despite optimal medical management (using three or more antihypertensive drugs, including a diuretic, at optimal tolerated doses) and one or more of the following conditions:

- systolic blood pressure > 180mm Hg
- previous myocardial infarction
- previous stroke or transient ischaemic attack (TIA)
- diabetes
- chronic kidney disease
- atrial fibrillation
- heart failure
- peripheral arterial disease.

Rationale

While the proposed eligible population is similar to that described in the Application, patients with diastolic blood pressure ≥110 mm Hg (i.e. severe/Grade 3) have been added as this population is also considered at high risk of CVD and while much of the evidence for treatment targets is for systolic blood pressure, there is general support for diastolic blood pressure to be <90 mm Hg (NHFA 2016 guideline).

Table 1 Classification of clinical blood pressure levels in adults

Diagnostic category*	Systolic (mm Hg)		Diastolic (mm Hg)
Optimal	<120	and	<80
Normal	120-129	and/or	80-84
High-normal	130-139	and/or	85-89
Grade 1 (mild) hypertension	140-159	and/or	90-99
Grade 2 (moderate) hypertension	160-179	and/or	100-109
Grade 3 (severe) hypertension	≥180	and/or	≥110
Isolated systolic hypertension	>140	and	<90

*When a patient's systolic and diastolic blood pressure levels fall into different categories, the higher diagnostic category and recommended actions apply.
Reproduced with permission from the National Heart Foundation of Australia. Guideline for the diagnosis and management of hypertension in adults 2016. (Sourced from Table 2.1). © 2016 National Heart Foundation of Australia

The applicant did not use the term treatment resistant hypertension to define the eligible population in the application form – instead they define eligible patients with a description that avoids assessment of poor adherence to medications, on the basis that it is challenging to verify or address. However, in the 2013 finalised DAP for the prior application for renal denervation (Application 1338), PASC noted the following:

> *PASC acknowledges that it may be impossible to rule out non-compliance to specific aspects of previous treatment (such as weight loss or adherence to lifestyle changes). However, by the time that a patient is considered to be 'treatment resistant' in line with current guidelines they will have realistically failed all current therapy, and all possible causes of uncontrolled blood pressure should be addressed as part of the current hypertension management guidelines. In addition, PASC recognises that patients who are unable to adhere to medication due to intolerance or cognitive difficulties could also benefit from the proposed service.*

PASC also noted in 2013 that patients who are 'unable to adhere to medication due to intolerance or cognitive difficulties could also benefit from the proposed service'. However, consistent with the PASC considerations for the prior DAP, the proposed population for this PICO specifies that patients are to be confirmed as having treatment-resistant hypertension by a specialist.

A further addition to the proposed population is a requirement for specialist consultation to establish treatment resistance. The NHFA 2016 guideline suggests seeking specialist advice if hypertension remains uncontrolled after following the treatment recommendations in primary care, and while it is not mandated, specialist consultation is the typical path for these patients (clinical expert opinion from the applicant). The prerequisite was added, therefore, as it is consistent with current best practice, and it provides an opportunity for expert review to identify and address any alternative causes of hypertension prior to an invasive intervention.

The addition of previous TIA and peripheral arterial disease to the list of eligibility options was based on their inclusion in the NHFA 2016 guideline as patients at increased CVD risk for whom tailored advice is provided. This expands the proposed eligible population and was deemed appropriate by the clinical expert for the applicant.

Alignment of core eligibility requirements with populations in evidence base

The comparative evidence nominated in the Application as the key published research, or key research that may have results available in the near future, are all from the SPYRAL HTN global trial program i.e. sham-controlled randomised controlled trials (RCTs) using the applicant's second generation Symplicity Spyral device:

- SPYRAL HTN-Off MED Pivotal trial – a sham-controlled trial in which subjects were naïve to, or were prepared to cease all, anti-hypertensive medications – completed (n=331) and reported (Böhm et al, 2020a).

This trial does not match the population in the proposed PICO (i.e. patients under optimal medical management).

- SPYRAL HTN-ON MED Expansion trial – a sham-controlled trial in which subjects were taking 1 to 3 antihypertensive medications prescribed at ≥ 50% of the maximum manufacturer's dosage – expected to complete in October 2021 (protocol: Böhm et al, 2020b).2
- SPYRAL HTN-ON MED pilot study – used as a prior to establish a Bayesian analysis in the SPYRAL HTN-ON MED Expansion trial but has no powered endpoints – completed (n=80) and reported (Kandzari et al, 2018).

Treatment resistant hypertension is a core eligibility requirement for the proposed population. The degree to which the SPYRAL HTN-ON MED trial populations align with this core requirement is unclear. The Expansion trial protocol describes a lengthy and rigorous screening phase to establish a stable antihypertensive medication regimen. However, based on the description below, it seems patients could be eligible for inclusion if they had uncontrolled hypertension after attempting only one antihypertensive medication, which does not align with treatment resistance, or optimal medical management.

> For the SPYRAL HTN–ON MED Expansion trial, subjects must be taking 1–3 antihypertensive medications prescribed at ≥ 50% of the maximum manufacturer's dosage. Antihypertensive medication classes must include a thiazide-type diuretic, a dihydropyridine calcium channel blocker, an angiotensin-converting enzyme-I/ angiotensin-II receptor blocker, **and/or** a beta-blocker. Subjects must be on a stable dose of each medication for at least 6 weeks before the first screening visit and continuing until a confirmatory second screening visit.

The applicant developed assessment report (ADAR) should provide more clarity on the trial eligibility requirements.

Alignment of eligibility options with populations in evidence base

In order to target patients with greatest clinical need, the proposed population includes eligibility 'options' that restrict the service to patients with a heightened risk of CVD due to the presence of at

[2] On the assumption that data from this trial will likely be used to support the MSAC application in the ADAR, any discussions of the relationship between the PICO and the evidence base in this PICO confirmation have been informed by the cited protocol for the two large trials (i.e. differences between the protocols of the SPYRAL HTN-ON MED pilot study and the ensuing SPYRAL HTN-ON MED Expansion trial, if any, have not been taken into account).

least one of a list of conditions – this list of conditions was developed 'in consultation with local expert clinicians and are considered relevant to the Australian patient population and applicable in clinical practice'. As described earlier, this list has been broadened during PICO confirmation to include previous TIA and peripheral arterial disease.

While the use of CVD risk factors to restrict eligibility may be a pragmatic solution to limit what would otherwise be an exceptionally large number of eligible Australian patients, it will impact the applicability of the RCTs. The SPYRAL-HTN global trial program, in particular, excluded patients with systolic blood pressure ≥180 mm Hg, moderate to severe kidney disease, recent myocardial infarction or stroke, and recent atrial fibrillation or heart failure. Registry studies may supplement the RCTs to some degree in this regard.

Burden of disease and estimated prevalence

The applicant provided comprehensive information on the burden of disease and exploratory estimates of prevalence in Australia. These exploratory estimates will need to be modified in the ADAR to take into consideration the implications of changes to the proposed eligibility criteria (e.g. addition of previous TIA and peripheral arterial disease as eligibility options, any refinements to the severity of conditions listed as eligibility options, requirement for patients to be treatment resistant etc).

Hypertension is the worldwide leading preventable cause of death, primarily due to its strong association with increased risk for heart attack, stroke, heart failure, and kidney disease. It has been established that the risk of cardiovascular mortality rises linearly with increases above age-related targets in blood pressure - doubling for every 20 mm Hg (systolic) and 10 mm Hg (diastolic) increase above 115/75 mm Hg (Lewington et al 2002).

The National Heart Foundation HeartWatch Survey (2011) found that one third of Australians have been told by a doctor they have high blood pressure, but only half are reported to be taking their prescribed medication (NHFA 2016). With true treatment intolerance estimated at between 8-18% of treated patients (NHFA 2016), it would appear the population with hypertension due to treatment non-compliance is potentially large.

Based on measured data from the 2017–18 Australian Bureau of Statistics National Health Survey (AIHW, 2019a) about 1 in 3 people aged 18 and over (34%) were found to have high blood pressure, as defined by a blood pressure ≥140/90 mm Hg. This comprised 23% with uncontrolled high blood pressure; and 11% whose blood pressure was controlled using medication(s). Using various other Australian datasets and international studies, the applicant has estimated the number of eligible Australian patients with private health insurance who may elect to have the procedure to be approximately 28,000. The summary table is reproduced below, and the applicant notes the estimates are indicative only and will be explored further in the ADAR. However, the applicant proposes that catheter laboratory capacity constraints are expected to limit the number of patients treated in the first three years to under 17,000.

Table 2 Summary of applicant estimates

Filter	Number of individuals	Comment
Population Australia	~25.5 million	ABS, March 2020
Adults	~20 million	ABS, March 2020
Elevated BP (SBP/DBP ≥140/90 mm Hg)	~6.7 million	~ One third (34%) of adults have elevated BP ABS, 2017-18 Health Survey
Treated with one or more antihypertensive agent	~4.25 million	PBS data 2018 - Falser 2020
Treated with three or more antihypertensive agents	~620,000	~15% of all patients treated PBS data 2018 - Falster 2020
Uncontrolled HTN despite three or more antihypertensive agents	~450,000	~72.2% of all patients on 3 or more medications - Carey 2019
Uncontrolled HTN despite three or more antihypertensive agents and excluding pseudo-resistant HTN	~225,000	50% - Judd 2014
Patients with 1 or more comorbidities other than hypertension	~113,000	50% - Assumption based on Carcel 2019
Patients potentially seeking RDN treatment	~56,000	50% - Schmeider 2020
Patients with private health insurance	~28,000	50% - APRA, Private Health Insurance Annual Coverage Survey 2019

Source: Medtronic Application form for current Application #1659
ABS, Australian Bureau of Statistic, blood pressure; HTN, hypertension; mm Hg, millimetres of mercury; PBS, Pharmaceutical Benefits Schedule.

PASC noted the applicant's pre-PASC response requested broadening the PICO population from treatment-resistant hypertension to 'apparent' treatment-resistant hypertension. This deviation from the National Heart Foundation of Australia (NHFA) guideline definition of treatment-resistant hypertension was claimed to allow for the possibility that it may be impossible to rule out non-compliance to specific aspects of previous treatment (including weight loss or adherence to lifestyle changes, as well as medication therapy). Further, the pre-PASC response also requested to amend the clinical algorithm to replace the instruction to 'rule out poor compliance' with 'encourage adherence to medication using a guidelines-based approach'. PASC considered that the definition of 'apparent' treatment resistance was unclear and did not support this change. PASC considered that the population should be patients with treatment-resistant hypertension as defined in the NHFA guidelines.

PASC noted that the draft PICO included elevated diastolic blood pressure (≥110 mm Hg) as an eligibility criterion but that the applicant's pre-PASC response asserted that it is not appropriate to include isolated diastolic hypertension (IDH) claiming these patients are unlikely to be considered for renal denervation. The applicant claimed that while IDH is associated with future systolic hypertension, it is generally not associated with atherosclerotic cardiovascular disease outcomes

independently of baseline systolic blood pressure (McEvoy 2020), and there are no data to support use in this small population (<2% of hypertensive patients in the US). PASC noted advice from the applicant's clinical expert that an elevated systolic blood pressure is an important criterion but that does not mean an elevated diastolic blood pressure is not relevant. PASC acknowledged that focussing on patients with an elevated systolic blood pressure may be a pragmatic approach but given guidelines specify systolic and diastolic blood pressure criteria for defining hypertension, PASC considered that 'and/or an elevated diastolic blood pressure (≥110 mm Hg)' should be retained.

PASC noted that eligible patients must also be considered to be at high risk of cardiovascular disease based on one or more specified risk factors. However, PASC noted that patients with a number of these comorbidities were not represented in the patient population included in the SPYRAL HTN-ON MED trial. PASC advised that MSAC is likely to be concerned about the applicability of the trial evidence if the PICO population is vastly different to that for the trial producing the evidence of comparative effectiveness. PASC advised that the proposed population should be carefully defined and that a robust justification should be presented for extending the population beyond those in the key clinical trials.

PASC also noted that the SPYRAL HTN-ON MED trial included patients with mild to moderate hypertension who were on at least one antihypertensive agent, whereas the population specified in the PICO is quite different with treatment-resistant hypertension defined as on at least three antihypertensive agents. PASC noted that subgroup analysis of the patients on three or more antihypertensive agents would be required and was concerned that this would significantly reduce the data available.

PASC also noted the SPYRAL HTN-ON MED trial was conducted in a very highly selected population, i.e. only a small proportion of the patients screened were considered eligible for inclusion in the SPYRAL HTN-ON MED trial. PASC considered that the implications of this should be considered in the assessment report.

PASC noted a Home Medicines Review (HMR) for optimising medication may not be an appropriate requirement for the service as they are frequently declined by patients. The applicant noted appropriate alternatives to HMR include the pharmacy-based Medication Use Review (MedsCheck).

PASC noted there is a reasonable chance that patients resistant to antihypertensive drugs may also be resistant to any blood-pressure-lowering effects of renal denervation.

Intervention

The intervention is endovascular renal denervation with a radiofrequency ablation catheter.

The involvement of the renal afferent and efferent sympathetic nerves at the interface of blood pressure regulation, and the well acknowledged concept that renal sympathetic overactivity leads to the development and progression of hypertension provides the rationale for renal nerve ablation as an approach to poorly manageable cases of hypertension. Afferent fibres originating from the central nervous system target the kidney at different tissue levels enhancing sodium and water retention, increasing renin release and decreasing renal blood flow which ultimately leads to an increased circulating volume. Efferent fibres arising from the renal pelvis convey, in turn, sympatho-excitatory stimuli to autonomic regulatory nuclei in the midbrain leading to peripheral vasoconstriction and increased cardiac rate and output (Bolignano 2019).

Catheter-based renal denervation is a minimally invasive procedure using standard endovascular intervention techniques similar to those used in renal angioplasty or stenting. It is intended as a one-time treatment adjunct to existing standard-of-care medication therapy. An ablation catheter is localised via the femoral artery to the renal arteries and the efferent and afferent nerves adjacent to the artery are ablated through the arterial wall (see Figure 1 and Figure 2 supplied by the applicant).

The proposed medical service is an inpatient procedure in an appropriate catheterisation laboratory and takes approximately 1.5-2 hours – patients treated early in the day can be discharged later that day, and patients treated later in the day are required to stay overnight. It is typically performed under conscious sedation by a suitably qualified interventionist (interventional cardiologists, interventional radiologists, vascular surgeons and interventional nephrologists) with adequate experience in catheterisation and angioplasty of renal arteries as well as the necessary technical resources available for the management of any immediate complications that may occur.

The medical service is comprised of the following stages:

1. An initial aortogram/selective renal angiogram to determine patient suitability (including vessel calibre, length, diameter, angle of origin and the presence of atherosclerotic plaque).
2. If suitability is confirmed, sedation or analgesia is administered, and a catheter is percutaneously introduced via the femoral artery and positioned to the distal region of the renal artery under angiographic guidance and radiofrequency energy is delivered to the artery wall. Both renal arteries are treated.
3. At the end of the procedure, an angiogram of the renal arteries is performed to check for the presence of renal artery dissection or infarct.
4. The patient is observed for 2 hours post-procedure.

Following this service, optimal medical management should be continued.

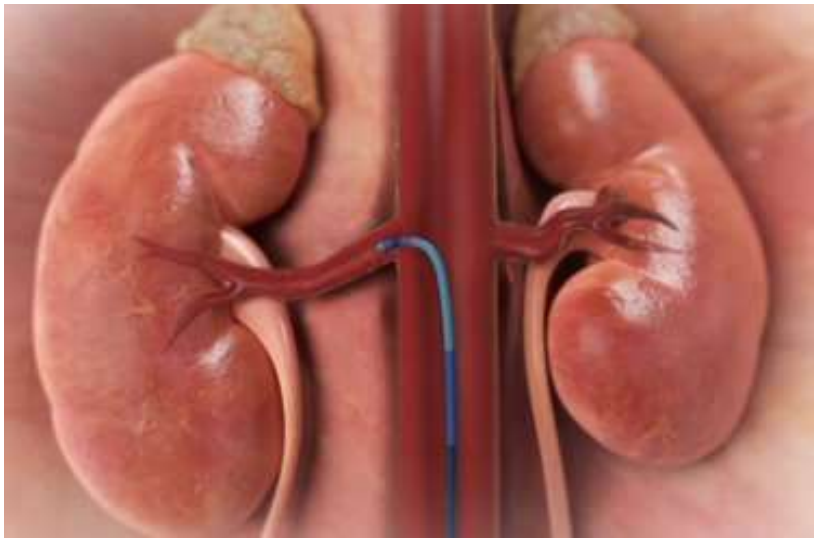

Figure 1 Guide in the renal artery

Source: Figure 12 of the Application

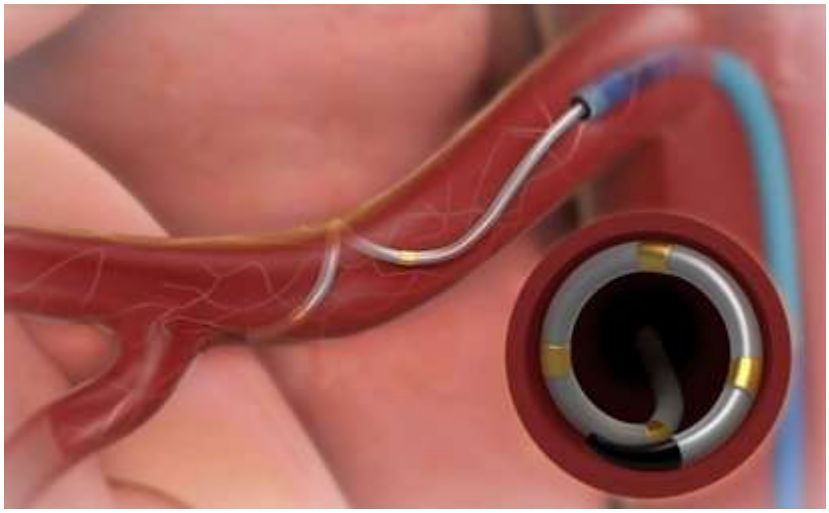

Figure 2 Positioning of catheter in the artery

Source: Figure 12 of the Application

The applicant notes that approximately 5% of patients in the clinical trials did not proceed past the renal angiogram to receive the renal denervation procedure due to anatomical contraindications, and claims that in clinical practice this is expected to be lower (2-5%). These estimates should be justified in the assessment, as the proportion of patients who are deemed ineligible after angiography may be more frequent in the proposed population (limited to patients with co-morbid conditions or Grade 3 hypertension) compared to patients in the trial population from which the estimate is derived.

Where a patient is not eligible to proceed to renal denervation, the medical service fees shown below would be charged.

Table 3 Medical service fees

MBS item #	Description	Fee	Benefit 75%	Benefit 85%
60027	Digital subtraction angiography, examination of abdomen – 4 to 6 data acquisition runs	$839.50	$629.65	$754.80
60075	Selective arteriography or selective venography by digital subtraction angiography technique – 2 vessels	$97.55	$73.20	$82.95
	Total	**$937.05**	**$702.85**	**$837.75**

Rationale

Alternative ablation technologies

The Symplicity Spyral device uses radiofrequency ablation, but devices using ultrasound or pharmacological ablation (e.g. local alcohol microinjection) are also in development. On pre-PASC departmental advice, the MBS item descriptor should be restricted to radiofrequency ablation. Only one other renal denervation device is currently registered on the ARTG (EnligHTN Ablation Catheter, Abbott Medical Australia Pty Ltd), and this also uses radiofrequency ablation. (The applicant notes that according to clinicaltrials.gov the EnligHTN clinical trial has been terminated,[3] and it is the applicant's understanding that this catheter is not currently used in Australia.)

The clinical evidence to be presented in the ADAR, therefore, should extend to any renal denervation catheters that use radiofrequency.

First and second generation devices

The previous, withdrawn MSAC submission was for the first generation Symplicity catheter, which is a single-electrode device (Symplicity Flex), but these have been superseded by a second generation, multi-electrode device (Symplicity Spyral). Trials of the first generation Symplicity Flex include HTN-3 – the sham-controlled RCT that failed to confirm a blood pressure reduction compared to the sham procedure and triggered withdrawal of the prior application. The applicant notes design improvements of the Symplicity Spyral catheter include improved vessel access and reduced procedural variability and treatment time, as well as an updated procedure protocol that treats both the main renal artery and the branches rather than just the renal artery. The prospective registry includes data for both devices.

On pre-PASC departmental advice, high-level evidence for both first and second generation devices should be presented in the ADAR.

PASC noted that in the current NHFA 2016 guidelines, percutaneous transluminal radiofrequency sympathetic denervation of the renal artery is currently not recommended for the clinical management of resistant hypertension or lower grades of hypertension. PASC noted that this may or may not change with new evidence.

PASC also noted that international guidelines do not mention the use of renal denervation in the management of hypertension.

[3] https://clinicaltrials.gov/ct2/show/NCT01903187?term=Enlightn&draw=2&rank=1

PASC noted that after performing the renal denervation procedure, the success of the procedure cannot be confirmed.

PASC noted there was uncertainty regarding the training, appropriate locations for providing this service and management of complications like vascular rupture and questioned whether these uncertainties would result in issues with equitable access and/or a learning curve effect. PASC noted that consultation feedback recommended renal denervation be performed by an interventional cardiologist or interventional radiologist suitability trained to perform the procedure, which could be performed in cardiac catheterisation laboratories and standard interventional radiology units.

Comparator

In the clinical setting, the appropriate comparator is no renal denervation while on optimal medical management.

In the trial setting, the appropriate comparator is no renal denervation, or sham procedure, while on optimal medical management.

Rationale

Renal denervation is intended as a one-time treatment adjunct, to be used in addition to current practice (optimal medical management), so it is not intended to replace or substitute current practice. As continued optimal medical management is currently the only treatment option for patients eligible for the service, not receiving the service is the only appropriate comparator. The comparator in the withdrawn 2013 MSAC submission was ongoing medical management, including pharmaceutical management with different classes of anti-hypertensive medication and ongoing monitoring.

PASC considered that the nominated comparator, optimal medical management without renal denervation treatment (or with sham procedure in the clinical trial setting), was appropriate.

Outcomes

Patient relevant

Clinical effectiveness outcomes

- **Incidence of cardiovascular disease**
    - These are the outcomes of primary relevance to patients and are the intended ultimate consequences of the procedure – they include, but are not limited to, new onset of stroke, TIA, myocardial infarction, heart failure or atrial fibrillation.
    - The ADAR should report CVD outcomes individually, as well as reporting as a composite outcome, noting the applicant's expectation that, due to insufficient sample size and duration of follow up in the nominated clinical evidence base, clinical outcomes, as well as mortality and quality of life, will likely be derived via economic modelling using systolic blood pressure as a surrogate.

- **Change from baseline in blood pressure measures: systolic and diastolic, measured by 24-h ABPM and OBPM**
    - Tt is noted that blood pressure is a surrogate endpoint for clinically relevant outcomes such as incidence of cardiovascular and renal disease and mortality; this approach is appropriate as hypertension is a well established risk factor for the development and progression of cardiovascular and renal disease, and for conditions that can put patients at an increased risk of these diseases, such as atrial fibrillation.
    - The applicant nominated two methods of blood pressure measurements, ambulatory blood pressure measurement (ABPM) and office blood pressure measurement (OBPM) – both measures are relevant:
        - ongoing monitoring of patients in the clinical setting is likely to use OBPM
        - the NHFA 2016 guideline notes that ambulatory measures are stronger predictors of cardiovascular events compared to office measures, with hazard ratios roughly double that of clinic blood pressure per 10 mm Hg increase, and that treatment decisions should be based on ABPM (or home BPM), where available[4].
    - The setting in which blood pressure is measured is to be captured.

- **Incidence of achieving target blood pressure (140/90 mm Hg)**
    - The NHFA 2016 guideline recommends a treatment target of <140/90 mm Hg for all patients requiring antihypertensive drugs (the guideline also notes that for patients at high risk of CVD, aiming for a systolic blood pressure target of <120 mm Hg is reasonable where tolerated and deemed safe on clinical grounds).

[4] Diagnostic thresholds for hypertension set by the NHFA 2016 guideline differ according to how they are measured: 24-h ABPM thresholds are ≥130/≥80 mm Hg; OBPM thresholds are ≥140/≥90 mm Hg.

- A diastolic blood pressure responder analysis was added in light of the adaptation of the proposed eligible population to include patients with diastolic blood pressure of 110 mm Hg.

- **Quality of life**
  - As noted earlier, quality of life will likely be derived via economic modelling using systolic blood pressure as a surrogate.

- **Cardiovascular mortality and all-cause mortality**
  - These outcomes will likely also be derived via economic modelling using systolic blood pressure as a surrogate.
  - Separation of cardiovascular mortality and all-cause mortality has been added as these outcomes may be available in registry studies or studies of other devices.

Safety outcomes

These should be reported both as procedure-related outcomes (short term follow up e.g. 1-3 months post-procedure) and as longer-term safety outcomes:

- Incidence of major adverse events
- Renal artery re-intervention (e.g. as a result of perforation or dissection)
- Vascular complications
- New stroke
- Embolic event resulting in end-organ damage
- New-onset of end-stage renal disease
- Renal artery stenosis (>70%)
- All-cause mortality *(short-term only – long term mortality outcomes are captured as efficacy outcomes)*

Healthcare system

The applicant has stated they will apply for the inclusion of the single use Symplicity Spyral renal denervation catheter on Part C of the Prostheses List (to be submitted May 2021 for consideration by PLAC at the November 2021 meeting). The applicant notes that while not meeting the criteria for inclusion on Part A of the Prostheses List (because it is not a permanent surgical implant), a listing on Part C would seem appropriate given that cardiac ablation catheters are listed on Part C.

Regarding blood pressure management costs, the applicant notes that since renal denervation is intended as an addition to ongoing optimal medical management, there would be minimal change in medical management costs. They also note that these patients would be expected to have a lower risk of experiencing cardiovascular health outcomes attributed to poorly controlled hypertension. As such, renal denervation would be expected to result in an overall reduction in healthcare resource utilisation associated with treating the long-term consequences of uncontrolled hypertension.

There is the potential for more patients to seek confirmation of treatment resistance in order to access the service – if this occurs, it would result in an increase in specialist referrals, medication use and investigations to rule out alternative causes of hypertension (e.g. radiographic imaging for renal stenosis).

PASC noted the applicant does not anticipate any data for cardiovascular endpoints will be available from the trials, and will likely be derived via economic modelling using systolic blood pressure as a surrogate outcome. This approach was queried as PASC was of the view that commonly used measured outcomes of cardiovascular morbidity and mortality are needed, and the effect of confounding of other risks for adverse cardiovascular outcomes should be addressed. The applicant claimed the evidence supporting most anti-hypertensive drugs do not have cardiovascular endpoints, and that the FDA accepts blood pressure reduction as a surrogate for cardiovascular outcomes.

PASC noted one of the concerns about a denervation procedure is that re-innervation may occur, and that MSAC would be interested in long-term evidence of the durability of effect.

Current clinical management algorithm for identified population

The diagnosis and onward management of patients with hypertension mainly takes place in the primary health care setting. Life-style advice, including not smoking, eating a nutritious diet and regular adequate exercise is recommended for all patients. The initiation of antihypertensive therapy takes into consideration the patient's baseline 5-year risk of CVD. The current clinical management algorithm for patients starting drug therapy for hypertension, according to NHFA 2016 guidelines, is shown in Figure 3.

There are a number of different classes of antihypertensive drugs available. The major classes include ACE inhibitors, ARBs, calcium channel blockers (CCBs), beta-blockers (BBs), diuretics. The class or classes of drug selected for a patient depends on the patient's age, presence of associated clinical conditions or end organ damage, potential interaction with other drugs and implications for adherence, cost and patient choice. Despite differences in mechanism, single drug therapy with first-line classes of thiazide diuretics, CCB, ACE inhibitors, or ARBs are considered similar in terms of efficacy. However, an ACE inhibitor plus CCB combination is superior to an ACE inhibitor plus diuretic combination or beta-blocker and diuretic combination.

Essentially patients are initiated with a low-moderate recommended dose of a first line drug, which if not tolerated, should be exchanged for a low-moderate dose of an antihypertensive drug of a different pharmacological class. If the target blood pressure is not achieved after 3 months, a second drug of a low-moderate dose of a different pharmacological class is added on to the first therapy.

Adding on the second drug is preferential to increasing the dose of the first in order to avoid side effects. If the target blood pressure is not achieved after 3 months and antihypertensive drugs have been well-tolerated by the patient, it is recommended that the dose of one of the drugs is increased incrementally to the maximum tolerated dose (excluding thiazide diuretics) before increasing the dose of the other drug. If the target blood pressure is not achieved after 3 months, despite maximum tolerated doses of at least two drugs, a third class of drug may be initiated, at a low-moderate dose.

At this stage it is recommended the patient is investigated, either by the GP or after referral to a specialist (hypertension specialist or a general cardiologist) to identify and then manage possible causes of suboptimal blood pressure control. Possible causes could include: pseudo-hypertension as a result of poor-adherence to therapy or hypertension only in a clinical setting; suboptimal drug therapy; secondary hypertension resulting from an undiagnosed underlying condition (e.g., sleep

apnoea; kidney disease, diabetes); hypertensive effects arising from other medications the patient may be taking; poor lifestyle (e.g., diet, exercise, smoking; undisclosed alcohol use, recreational drug use or high salt intake). Investigations could include a physical examination, urine and blood analysis, electrocardiogram (ECG), echocardiogram, ankle-brachial index (ABI), carotid Doppler and renal artery duplex ultrasound, renal nuclear medicine imaging, and/or CT angiography. Renal imaging as part of this routine care would be expected to identify patients with renal stenosis, thereby deeming them ineligible for renal denervation. Ambulatory blood pressure measurements can be used to rule out white-coat hypertension.

If blood pressure remains elevated above target after the addition of a third medication, then, consistent with the NHFA 2016 guidelines, and if not already done so, a GP should consider referring patients on to seek the advice of a specialist. If not already performed under the care of the GP, the hypertension specialist or general cardiologist will carry out the investigations described above, and instigate optimal medical management of the patient.

Currently, continued optimal medical management, usually involving care advice from a hypertension specialist or general cardiologist, remains the only option for these patients. The NHFA 2016 guidelines provide no specific recommendations regarding the onward management of patients at this stage, noting only that, under specialist advice, spironolactone many be used as an add-on drug in some patients.

PASC noted that the clinical algorithm positions renal denervation for treatment of patients with uncontrolled blood pressure despite of treatment with blood pressure lowering medication, with high risk for cardiovascular disease.

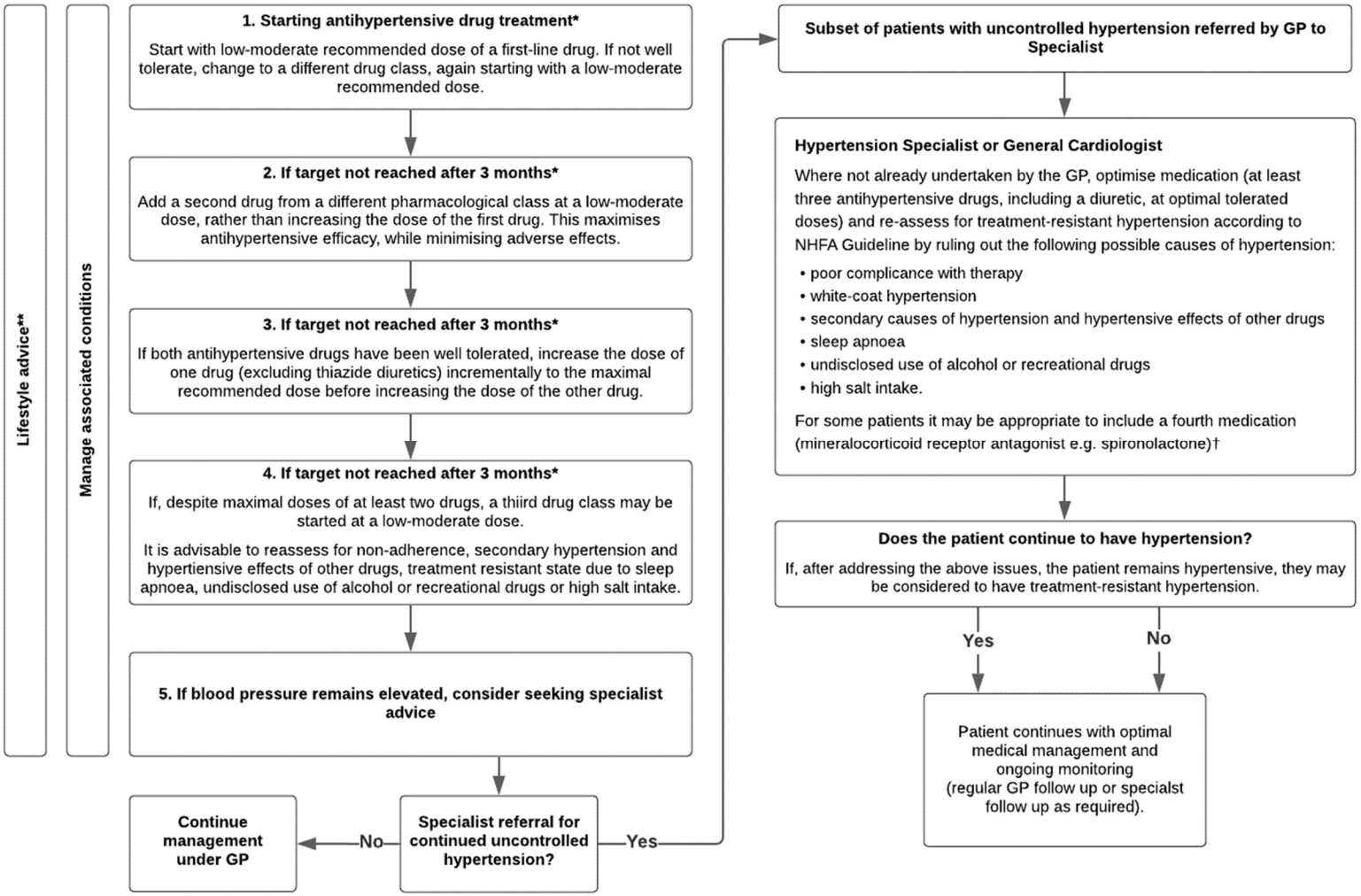

Figure 3 Current clinical management algorithm for patients starting drug treatment for hypertension

*Maximum effect of drug likely to be seen in 4-6 weeks. If baseline BP is severely elevated earlier reviews may be considered. For steps 1-4, review every 4-6 weeks for tolerance, efficacy and adverse effects. **All patients should receive lifestyle advice with follow-up based on clinical context. Abbreviations: CVD, cardiovascular disease; GP, general practitioner; NHF, National Heart Foundation. Adapted and reproduced with permission from the National Heart Foundation of Australia. Guideline for the diagnosis and management of hypertension in adults 2016. (Sourced from Fig.6.2 and Section 10.5). © 2016 National Heart Foundation of Australia.

Proposed clinical management algorithm for identified population

As described above, the NHFA 2016 guideline states that general practitioners (GPs) should consider seeking specialist advice for hypertensive patients who remain uncontrolled in primary care.

The proposed clinical management algorithm in Figure 4 applies to patients who are referred to a hypertension specialist or general cardiologist, which is a prerequisite for accessing the proposed service. If not already undertaken in primary care, the specialist explores potential reasons for hypertension and instigates optimal medical management. As described in the previous section for current clinical management, treatment resistance is established by excluding causes of hypertension such as white-coat and secondary causes and lifestyle factors. Poor compliance with medication regimens is also explored and adherence encouraged prior to confirming treatment resistance.

The application proposed that where a patient has confirmed treatment-resistant hypertension with elevated systolic blood pressure ≥ 150 mm Hg despite optimal medical management AND is at high risk for CVD (based on having one or more specified high-CVD risk conditions listed in the MBS item) **they would be a potential candidate for the proposed service and could be referred to an interventional cardiologist.**

Once the patient has been determined by the interventionist as provisionally suitable for renal denervation, and if the patient preference is to be treated by renal denervation, they would be booked in to receive the procedure. However, only after an aortogram and selective renal angiography is performed, immediately prior to the renal denervation procedure, can the patient's renal anatomy be confirmed as eligible for renal denervation.[5] **Confirmation of suitable renal anatomy is the point at which the patient can be considered eligible for the proposed medical service.**

If at any stage a patient is not eligible to proceed to renal denervation, they will continue with optimal medical management and ongoing monitoring with their GP or specialist. Patients who receive renal denervation will also continue with optimal medical management and ongoing monitoring with their GP or specialist after the procedure.

It is noted that if the proposed service is made available on the MBS, there may be a consequent increase in patients seeking diagnosis of treatment resistance, which could increase antihypertensive medication use and the frequency of specialist consultations.

[5]Renal anatomical characteristics that would preclude patients from renal denervation include arteries with a diameter less than 3 mm or greater than 8 mm; arteries with significant disease or with flow-limiting obstructions.

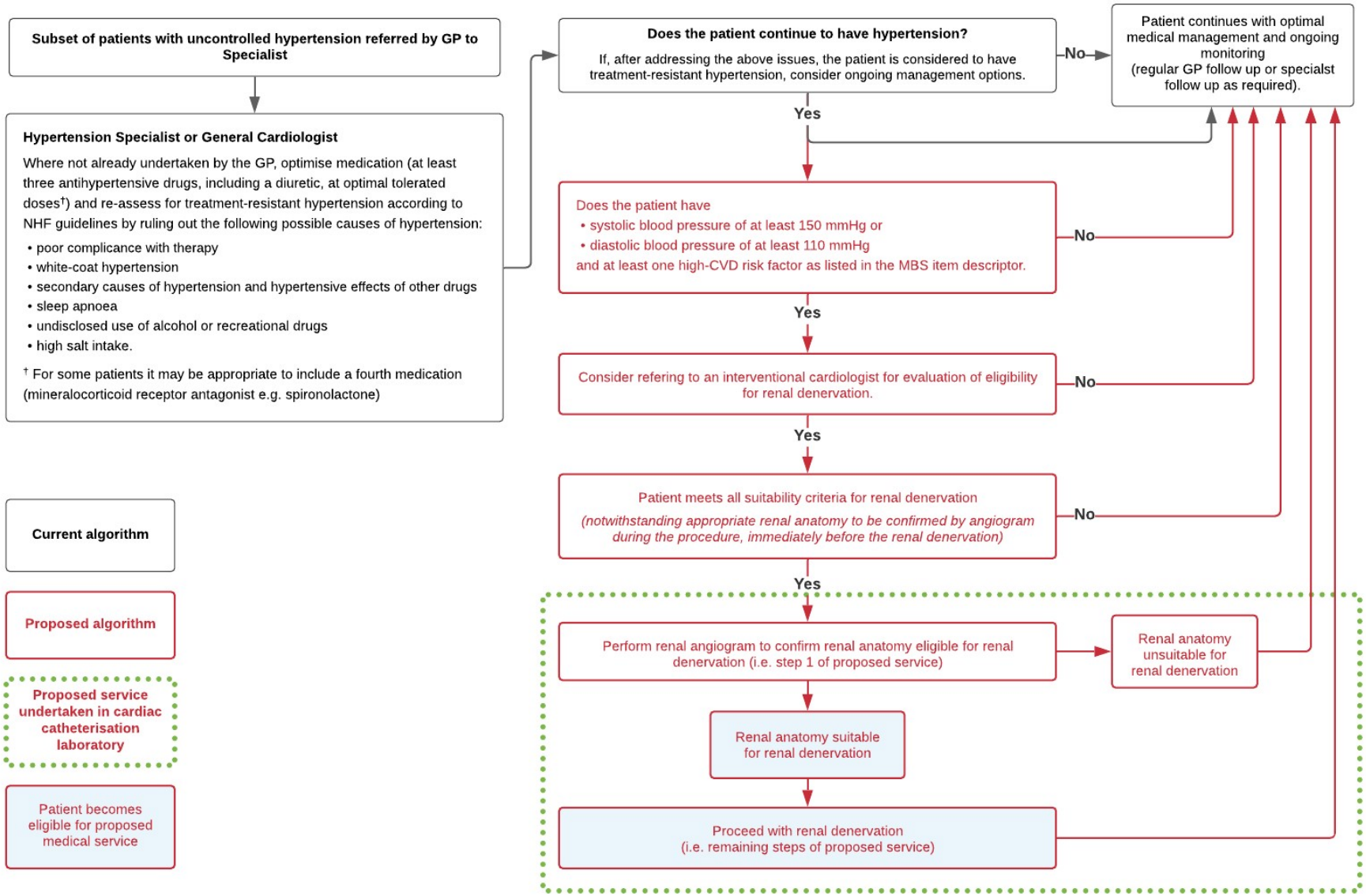

Figure 4 Proposed treatment management algorithm including renal denervation in selected patients

Abbreviations: CVD, cardiovascular disease; GP, general practitioner; mm Hg, millimetres of mercury; NHFA, National Heart Foundation Australia.

Proposed economic evaluation

The clinical claim is that renal denervation is clinically superior to medical management alone and has inferior safety. Therefore, based on table D1.1 of the MSAC guideline, the appropriate economic evaluation is a cost-utility analysis.

PASC noted that the applicant estimated ~28,000 patients with treatment-resistant hypertension would meet the proposed eligibility criteria for renal denervation. However, it is estimated only a small fraction (3,750 patients in year 1 increasing to 7,500 patients in year 3) would be able to access the service based on the estimated capacity of ~ 90 private catheter laboratories.

PASC noted that there may be a significant market waiting to be treated that hasn't been factored into the utilisation estimates.

PASC was concerned that utilisation estimates were uncertain and that there is likely a large number of patients who will not be able to access the service.

Proposed item descriptor

The proposed item descriptor presented in the Application is shown below, with red text to indicate proposed modifications to the applicant-proposed descriptor.

Category 3 – THERAPEUTIC PROCEDURES
MBS ### Endovascular radiofrequency ablation of renal sympathetic nerves under image guidance (angiography) in adults ≥18 years of age with treatment-resistant hypertension confirmed by a specialist, with elevated systolic blood pressure ≥ 150 mm Hg or elevated diastolic blood pressure ≥110 mm Hg despite optimal medical management (using three or more antihypertensive drugs, including a diuretic, at optimal tolerated doses) and one or more of the following conditions: • systolic blood pressure > 180mm Hg • previous myocardial infarction • previous stroke or TIA • diabetes • chronic kidney disease • atrial fibrillation • heart failure • peripheral arterial disease Includes angiography. One service only. (Anaes.) Fee: $### Benefit: 75% = $### 85% = $###

PASC noted inclusion of 'radiofrequency' in the item descriptor and that the descriptor is well defined but does not align with the trial population or NHFA 2016 guidelines as discussed under 'Population'.

Fee

A fee of $2,164.05 has been proposed. The applicant notes that the proposed fee for catheter-based renal denervation is guided by the MBS item 38287 [ABLATION OF ARRHYTHMIA CIRCUIT OR FOCUS or isolation procedure involving 1 atrial chamber -Fee $2164.05]. The applicant notes that this

procedure is considered a reasonable benchmark for procedure type (catheter-based ablation) and time taken.

Consultation feedback

Consultation feedback was received from three specialist organisations: Royal Australian and New Zealand College of Radiologists (RANZCR), Interventional Radiology Society of Australasia (IRSA) and Australian and New Zealand Society of Nephrology (ANZSN). Feedback from RANZCR was not supportive. RANZCR highlighted that the trials for renal denervation do not demonstrate a clinical benefit in terms of a reduction of adverse cardiovascular outcomes, which has been the standard for other therapeutic trials in hypertension that have shaped current clinical practice guidelines. RANZCR also noted that the clinical significance of a reduction in blood pressure of 1-6 mm Hg with renal denervation (e.g. impact of myocardial infarction, strokes) had not been demonstrated.

Feedback from the IRSA was supportive, and agreed with the proposed population, comparator and clinical claims for the proposed service. However, the IRSA considered that the population should be strictly for patients with treatment-resistant hypertension. The IRSA noted that the application proposed the procedure can be performed mainly by interventional cardiologists. However, the IRSA noted that renal interventions are predominantly performed by interventional radiologists who are trained in performing renal angioplasty, stenting, embolisation as well as a range of other renal interventions such as percutaneous ablation and percutaneous nephrostomy. IRSA considered that the procedure should be performed by an interventional specialist, which could include interventional cardiologists if suitably trained for renal interventions and able to perform renal angioplasty/stenting.

Feedback from the ANZSN noted benefits of the proposed service include lowering cardiovascular risk by lowering blood pressure and reducing the medication burden. However, ANZSN highlighted that patient selection is critical, noting the key trials included patients with systolic blood pressure between 150-180 mm Hg and diastolic blood pressure >90 mm Hg. ANZSN also noted that the efficacy of renal denervation in the proposed treatment-resistant hypertensive patients with high cardiovascular risk has not yet been proven as the SPYRAL HTN-ON MED trial is still ongoing. ANZSN highlighted that renal denervation may be less effective in patients with isolated systolic hypertension. ANZSN also noted that the efficacy of each individual treatment is difficult to measure as there is not tool to measure the success or otherwise of the procedure.

Both ANZSN and IRSA considered that all patients should be reviewed by a specialist/service dedicated to the treatment of resistant hypertension to ensure medications, lifestyle and other factors are optimised, and have 24hr ambulatory blood pressure monitoring to exclude the 'white coat effect', which may contribute to 1/3 of apparent treatment-resistant hypertension. The IRSA also suggested including a computerised tomography (CT) scan (CT angiography of the kidneys) as a pre-procedure assessment, along with pre and post-procedure renal function blood tests.

PASC noted the feedback from the three specialist organisations and agreed that the clinical significance of a change in blood pressure of 1-6 mm Hg had not been demonstrated. PASC also noted there was a lack of consumer engagement in this application and the trials lacked patient-centred outcomes.

Next steps

PASC noted concerns about the applicability of the evidentiary base and the apparent lack of long-term comparative data to establish durability of the antihypertensive effect and a reduction in adverse outcomes associated with hypertension. PASC advised that, upon ratification of the post-PASC PICO, the application can proceed to the Evaluation Sub-Committee (ESC) stage of the MSAC process. However, PASC advised the applicant should think carefully about the implications of these issues for the application moving forward.

PASC noted the applicant has elected to progress its application as an ADAR (applicant-developed assessment report).

Applicant Comments

Population

Medtronic advised it plans to address the applicability of the ON-MED trial with sub-group analysis from both the ON-MED trial and the Symplicity registry. For example, sub-group analyses demonstrating consistency of treatment effect by number of prior treatments will help provide support that catheter-based renal denervation (RDN) will have a similar level of effectiveness in the proposed treatment resistant population.

Intervention

The applicant commented that international hypertension guidelines were created before the availability of the more recent RDN evidence.

The applicant advised it has a comprehensive training program. Physicians will complete self-learning modules and familiarise themselves with the subject matter. Then, in a second step, they will attend a face-to-face RDN workshop or a virtual class to discuss the learnings of the self-learning modules and have a deep dive into the procedure with selected KOLs. Once these steps are completed, cases will be proctored by Medtronic personnel.

Consultation feedback

The applicant considered that the clinical significance of a change in blood pressure (BP) has been estimated in several publications from meta-analyses and RCTs that reported the cardiovascular benefit after BP reduction with oral anti-hypertensive medications:

- *In the largest meta-analysis comprising 613,815 patients from 122 studies, reduction of office BP by 10mmHg was associated with the reduction of cardiovascular events by 20%, overall mortality by 13%, coronary artery disease by 17%, strokes by 27% and heart failure by 28%, respectively[6].*
- *In a meta-analysis of 147 RCTs comprising 464,000 patients a reduction in 10mmHg systolic and 5mmHg diastolic office BP was related to a decrease of coronary heart disease and*

[6] Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016; 387:957–967.

stroke events by approximately 22 and 41%, respectively, depending on the age of the patient[7].

- *A 2018 position paper updating the European Society of Hypertension (ESH) guidelines concluded that "although not definitely proven by a prospective outcome trial, we can expect that the 10-mmHg decrease in office BP achieved in RDN trials, if maintained long term, would be associated with a reduction in cardiovascular events by roughly 25% (in particular with respect to heart failure and stroke).[8]"*
- *In the HOPE-3 study, patients with baseline office BP more than 143.5mmHg (mean 154mmHg) had a reduction of BP by 5.8/3.0mmHg (due to pharmacologic therapy) associated with a 28% lower incidence of cardiovascular events compared with the placebo group[9].*
- *A recent meta-analysis of 48 RCTs of BP lowering medication found that Hazard ratios (HR) associated with a reduction of systolic blood pressure by 5 mm Hg for a major cardiovascular event were 0·91 (95% CI 0·89–0·94) for participants without previous cardiovascular disease and 0·89 (0·86–0·92), for those with previous cardiovascular disease[10].*

The applicant considered that treatment-resistant hypertension patient population proposed for RDN have no other treatment options so any reduction in BP would be advantageous.

The applicant advised it is currently in the process of engaging consumers for this application.

The applicant advised it will be progressing this application as an ADAR. The applicant plans to address the applicability of the ON-MED trial with sub-group analysis from both the ON-MED trial and the Symplicity registry in the ADAR. The applicant will present long-term evidence of the durability of effect from the Symplicity registry in the ADAR.

[7] Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009; 338:b1665.

[8] Schmieder RE, Mahfoud F, Azizi M, Pathak A, Dimitriadis K, Kroon AA, Ott C, Scalise F, Mancia G, Tsioufis C; Members of the ESH Working Group on Interventional Treatment of Hypertension. European Society of Hypertension position paper on renal denervation 2018. J Hypertens. 2018 Oct;36(10):2042-2048. doi: 10.1097/HJH.0000000000001858. PMID: 30015759.

[9] Yusuf S, Lonn E, Pais P, Bosch J, Lopez-Jaramillo P, Zhu J, et al. Bloodpressure and cholesterol lowering in persons without cardiovascular disease. N Engl J Med 2016; 374:2032–2043.

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McEvoy JW, Daya N, Rahman F, Hoogeveen RC, Blumenthal RS, Shah AM, Ballantyne CM, Coresh J, Selvin E. Association of Isolated Diastolic Hypertension as Defined by the 2017 ACC/AHA Blood Pressure Guideline With Incident Cardiovascular Outcomes. JAMA. 2020 Jan 28;323(4):329-338. doi: 10.1001/jama.2019.21402. PMID: 31990314; PMCID: PMC6990938.

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Appendix

Table A1 Catheter-based renal denervation systems (catheters and generators) currently listed on the ARTG

ARTG ID	Type of therapeutic good	Product name	Indication/Intended purpose	Manufacturer's and/or Sponsor's name
Catheters				
343930	Medical Device Included Class IIb	Symplicity Spyral - Radio-frequency ablation system renal denervation catheter	The Symplicity Spyral multi-electrode renal denervation catheter is indicated for the treatment of uncontrolled hypertension.	Medtronic Inc/ Medtronic Australasia Pty Ltd
221818	Medical Device Included Class IIb	EnligHTN -Radio-frequency ablation system renal denervation catheter	The Ablation Catheter is designed to deliver radiofrequency (RF) energy to the renal nerves to achieve targeted denervation.	St Jude Medical/ Abbott Medical Australia Pty Ltd
Generators				
198986	Medical Device Included Class IIb	Symplicity system - generator, lesion, radio frequency	Symplicity Catheter System is intended to deliver low-level radiofrequency energy through the wall of the renal artery to denervate the human kidney. The System may consist of a generator (to deliver the controlled radiofrequency energy at specific power, temperature and time settings) with its power cord, a foot pedal and an extension cable.	Medtronic Inc/ Medtronic Australasia Pty Ltd
198878	Medical Device Included Class IIb	EnligHTN system Generator, lesion, radio frequency	The EnlightN system RF ablation generator is intended to deliver RF energy to the Renal Artery Ablation Catheter	St Jude Medical/ Abbott Medical Australia Pty Ltd

Table A2 Catheter-based renal denervation systems (catheters and generators) listed on the ARTG at the time of the subsequently withdrawn MSAC 2013 submission

ARTG no.	Sponsor	Item Description	Product Category
186730	Medtronic Australasia Pty Ltd	Ardian Symplicity® Catheter System is intended to deliver low-level radiofrequency energy **through the wall of the renal artery to denervate the human kidney**. The System may consist of a generator (to deliver the controlled radiofrequency energy at specific power, temperature and time settings) with its power cord, a foot pedal and an extension cable.	Medical Device Class IIb
198986	Medtronic Australasia Pty Ltd	Symplicity® Catheter System is intended to deliver low-level radiofrequency energy **through the wall of the renal artery to denervate the human kidney**. The System may consist of a generator (to deliver the controlled radiofrequency energy at specific power, temperature and time settings) with its power cord, a foot pedal and an extension cable.	Medical Device Class IIb
198985	Medtronic Australasia Pty Ltd	Symplicity® Catheter System is intended to deliver low-level radiofrequency energy **through the wall of the renal artery to denervate the human kidney**.	Medical Device Class IIb
170236	Medtronic Australasia Pty Ltd	The Symplicity® System is intended to deliver low-level radiofrequency energy **through the wall of the renal artery to denervate the human kidney**.	Medical Device Class IIb
200781	Covidien Pty Ltd	The generator delivers low-level radiofrequency energy **through the wall of the renal artery to denervate the human kidney**. The System may consist of a generator (to deliver the controlled radiofrequency energy) with its AC power cord.	Medical Devices Class I
201773	Covidien Pty Ltd	The generator delivers low-level radiofrequency energy **through the wall of the renal artery to denervate the human kidney**. The	Medical Devices Class IIb

ARTG no.	Sponsor	Item Description	Product Category
		System may consist of a generator (to deliver the controlled radiofrequency energy) with its AC power cord.	
198878	St Jude Medical Australia Pty Ltd	The RF Ablation Generator is intended to deliver RF energy to the **Renal Artery Ablation Catheter**	Medical Device Class IIb
197340	St Jude Medical Australia Pty Ltd	The ablation catheter is indicated **for use in renal denervation procedures for the treatment of hypertension**.	Medical Device Class IIb
200215	Pacific Clinical Research Group Pty Ltd	The Vessix Vascular V2 Renal Denervation System is intended to be used to treat patients with medication-resistant hypertension. The Vessix Vascular V2 Catheter is **NOT intended for use in any artery other than the renal artery** and is designed and intended to be used ONLY with the Vessix Vascular V2 Generator.	Medical Device Class IIb

Source: Table 2 in the Final DAP for the prior application in 2013 (Application 1338)
http://www.msac.gov.au/internet/msac/publishing.nsf/Content/60408107686574D0CA25801000123BD2/$File/1338-FinalDAP.pdf