Australian Government

Department of Health

RATIFIED PICO

Application 1635:

Transcatheter aortic valve implantation (TAVI) via transfemoral delivery using the balloon-expandable valve (BEV) system for patients at low risk for surgery.

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	Persons with symptomatic severe aortic stenosis determined at low risk for surgical aortic valve replacement by a Heart Team, which low risk is defined as fulfilling all of the following criteria: • Society of Thoracic Surgeons' Predicted Risk Of Mortality (STS-PROM)< 4% **AND** • No significant frailty (as determined by the Heart Team) **AND** • No procedure specific impediments.
Intervention	Transcatheter aortic valve implantation (TAVI) via transfemoral delivery using the SAPIEN 3 balloon-expandable valve (BEV) system.
Comparator	*Main comparator:* Surgical aortic valve replacement (SAVR) with a bioprosthesis or mechanical aortic valve. *Secondary, or potential 'near market comparator': TAVI with self- expandable valve[a] (SEV) system.*

Outcomes	• Safety, including any potential risk of harm to patient:
	  ○ Life-threatening / disabling, or major bleeding
	  ○ Major vascular complications
	  ○ Myocardial infarction
	  ○ New left bundle branch Block
	  ○ New permanent pacemaker
	  ○ New onset atrial fibrillation
	  ○ *Paravalvular leak rate*
	  ○ *Aortic valve reintervention*
	  ○ *Acute kidney injury.*
	• Efficacy / effectiveness including, but not limited to, patient-relevant outcomes:
	  ○ Composite of death, stroke or rehospitalisation
	  ○ Death; *Overall survival*
	  ○ Stroke
	  ○ Rehospitalisation
	  ○ Health-related quality of life, *using a disease specific tool (e.g. KCQS) and/or standardised tools (e.g. EQ-5D and/or SF-36).*
	• Healthcare resources
	  ○ Cost of valvular prosthesis
	  ○ Cost associated with changes in clinical management (testing required before the procedure, length of stay, post-discharge rehabilitation).
	• Cost-effectiveness:
	  ○ Cost per life-year gained
	  ○ Cost per quality-adjusted life year (QALY) gained.

Component	Description
	• Total Australian Government healthcare costs: ○ Total cost to the Medical Benefits Schedule (MBS) ○ *Total cost to other Government health budgets (e.g. Pharmaceutical Benefits Scheme [PBS], State and Territory Government health budgets, including public hospitals).*

Abbreviations: ACC = American College of Cardiology; AHA = American Heart Association; EQ-5D = EuroQol- five dimension tool; KCCQ = Kansas City Cardiomyopathy Questionnaire [KCCQ]; SF-36 = Short-Form-36 questionnaire
Italicised represents added in during preparation of the PICO.

PICO or PPICO rationale for therapeutic and investigative medical services only

POPULATION

PASC noted this application for TAVI BEV was for the low-risk population, but that this proposal would effectively broaden the proposed MBS population for TAVI to all levels of surgical risk. PASC noted this was the preference of the applicant, given the central role of the multi-disciplinary 'Heart Team' for patient selection, and that the audit data and accreditation requirements are established as per the high risk MBS listing, and would also apply for other TAVI risk populations, including low risk in this application. PASC also discussed the issues of supplier-induced/initiated demand, the independence of the multi-disciplinary 'Heart Team', and noted that this assessment was even perhaps more critical for the low-risk population.

PASC noted that the applicant proposed some changes to the description of the proposed population to better align with the eligibility criteria of the pivotal clinical trial PARTNER3. PASC agreed with the inclusion of "significant frailty (as determined by the Heart Team)" and removal of "No comorbidity", but noted that the exclusion criteria of the pivotal trial (PARTNER 3; see Table 3) were far more comprehensive then the proposed population. To address this potential applicability concern, PASC considered that the key exclusion criteria from pivotal trial(s) should be made clear in the proposed population (e.g. bicuspid valves, rheumatic valves, congenital AS or other anatomical features that increased risk of complications were excluded). PASC noted the applicant's advice that excluding bicuspid valves from low risk population would not be clinically appropriate as even elderly patients can present with this disease (noting also that bicuspid valves more prevalent in the younger population who would generally be better suited to surgery). PASC also noted that the multi-disciplinary Heart Team would decide on patient eligibility, but still considered that defining low risk-population should be as specific as possible, where it was reasonable to do so.

PASC noted the applicant's advice that the proposed population should not include an age cut-off. PASC also noted the applicant's concern for the suitability of TAVI in young patients, as there are currently limited follow-up data on TAVI durability.

The patient population for whom public funding for transcatheter aortic valve implantation (TAVI) (or transcatheter aortic valve replacement; TAVR) via transfemoral delivery using the SAPIEN 3 balloon-expandable valve (BEV) is intended are:

Patients with symptomatic severe aortic stenosis (AS)[1] determined at low risk for surgical aortic valve replacement (SAVR) by a Heart Team, which low risk is defined as fulfilling all of the following criteria:

- Society of Thoracic Surgeons' Predicted Risk of Mortality (STS-PROM) score < 4% **AND**
- No significant frailty (as determined by the Heart Team) **AND**
- No procedure specific impediments.

[1] AS: Stage D, patients who have developed symptoms as a result of valvular heart disease (Otto, Kumbhani et al .2017)

The STS-PROM score is an accepted tool to predict the 30-day risk of SAVR and serves as a starting point for risk assessment in TAVR candidates (1).

The 2014 American Heart Association (AHA); American College of Cardiology (ACC) guidelines (2) for the management of patients with valvular heart disease define: *no frailty*, as the presence of none of the seven frailty indices of Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting, urinary continence, and independence in ambulation i.e. no walking aid required or 5-meter walk in <6 seconds). Other frailty scoring systems may be applied as well (2).

As noted in the 2017 ACC Expert Consensus guidelines (1), algorithms for TAVR assessment assume that patients are adults with calcific valvular AS, given that TAVR for congenital AS, rheumatic valve disease and isolated aortic regurgitation has not been studied in clinical trials.

The proposed low-risk population sufficiently aligns to the definition of low risk in the 2014 AHA/ACC and 2017 ACC guidelines (1, 2) [Table 1]. For context, the adjacent intermediate risk population, which by definition is mutually exclusive to the low-risk population, was also included in Table 1.

PASC noted the applicant's advice that clinical guidelines for low risk patients with symptomatic severe AS are being updated in many jurisdictions. PASC considered it most important to ensure the agreed target population be aligned with any updated clinical guidelines.

The applicant further clarified that the Cardiac Society of Australia and New Zealand (CSANZ) and the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) are soon to publish a consensus statement about TAVIs. The applicant (Edwards Lifesciences) has been informed by authors of the statement that it will recommend that eligibility for TAVI be extended to patients traditionally defined as being at low surgical risk, at the discretion of a Heart Team. The applicant confirmed it will submit the published CSANZ/ANZSCTS consensus statement as soon as this is becomes available.

Table 1 Overall procedural risk as assessed by 2014 AHA/ACC and ACC Consensus Guidelines

-	2014 AHA/ACC Guideline	2017 ACC Consensus Guideline	
-	**Low risk**	**Low risk**	**Intermediate risk**
Criterion/Criteria	Must meet all criteria in this column:	*Must meet all criteria in this column (by definition)*	Any 1 Criterion in this column
STS PROM[a]	<4% **AND**	<4% **AND**	4%-8% **OR**
Frailty[b]	None **AND**	No frailty **AND**	Mild frailty **OR**
Major organ system compromise not to be improved postoperatively[c]	None **AND**	No comorbidity **AND**	1 major organ system compromise not to be improved postoperatively **OR**
Procedure-specific impediments[d]	None.	No procedure specific impediments.	A possible procedure specific impediments.

Source: *Compiled from* 1635 Application Form, 2014 AHA/ACC Guidelines (2) and 2017 ACC Consensus Guidelines (1)
Abbreviations: ACC = American College of Cardiology; AHA = American Heart Association; CVA = cerebral vascular accident; CKD = chronic kidney disease; $CLCO_2$ = diffusion capacity for carbon dioxide; INR = international normalised ratio; FEV1 = forced expiratory volume in 1 second LV = left ventricular PROM = Predicted Risk of Mortality; RV = right ventricular; STS = Society of Thoracic Surgeons; VKS = vitamin K antagonist
[a] Use of the STS PROM to predict risk in a given institution with reasonable reliability is appropriate only if institutional outcomes are within 1 standard deviation of STS average observed/expected ratio for the procedure in question; 2014 AHA/ACC Guideline
[b] Seven frailty indices: Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting, and urinary continence) and independence in ambulation (no walking aid or assist required or 5-meter walk in <6 s). Other scoring systems can be applied to calculate no, mild-, or moderate-to-severe frailty; 2014 AHA/ACC Guideline (2)

[c] Examples of major organ system compromise: Cardiac—severe LV systolic or diastolic dysfunction or RV dysfunction, fixed pulmonary hypertension; CKD stage 3 or worse; pulmonary dysfunction with FEV1 <50% or DLCO2 <50% of predicted; CNS dysfunction (dementia, Alzheimer's disease, Parkinson's disease, CVA with persistent physical limitation); GI dysfunction—Crohn's disease, ulcerative colitis, nutritional impairment, or serum albumin <3.0; cancer—active malignancy; and liver—any history of cirrhosis, variceal bleeding, or elevated INR in the absence of VKA therapy; ; 2014 AHA/ACC Guideline (2)
[d] Examples: tracheostomy present, heavily calcified ascending aorta, chest malformation, arterial coronary graft adherent to posterior chest wall, or radiation damage; 2014 AHA/ACC Guidelines (2)
Shaded grey indicates the adjacent intermediate risk population, which by definition is mutually exclusive to the low-risk population

Background

AS is one of the most common and serious valve diseases. It is characterised by a narrowing of the aortic valve opening, which restricts blood flow from the left ventricle to the aorta and causes pressure build-up in the left ventricle and consequent hypertrophy. Furthermore, stenotic aortic valves may not close fully, resulting in regurgitation back into the left ventricle.

The most common cause of AS is age-related calcification of the aortic valve. Less common causes are congenital bicuspid aortic valves and rheumatic heart disease. Other than calcification, the pathophysiological features of AS are inflammation, lipid accumulation and subendothelial thickening (3).

AS is a progressive disease that is asymptomatic until late stages. Symptomatic severe AS is classified as Stage D AS, and has the following features: symptoms (see below); calcified valve leaflets with reduced opening; jet velocity (Vmax) ≥4 m/s; and mean gradient ≥40 mm Hg. Variations in valve haemodynamics and the presence of symptoms are used to further subclassify symptomatic severe AS (2). Symptoms of AS include exertional dyspnoea, decreased exercise tolerance, exertional angina and exertional syncope or presyncope. Left untreated, patients will progress to heart failure.

Patients are then at high risk for sudden death. Prognosis is poor once there is a mean aortic valve gradient greater than 40 mm Hg. Severe AS is associated with survival of 38%, 32% and 18% at one, five years and ten years, respectively (4). Without aortic valve replacement (AVR), survival is lower.

Prevalence and/or incidence

The prevalence of aortic stenosis (AS) is age-dependent. A large population-based study from the National Health, Lung, and Blood Institute in the United States estimated the prevalence of moderate or severe AS from a low of 0.02% in those aged 18-44 years to a high of 2.8% in persons aged over 75 years. Similar findings are noted in other economically developed nations (3). Osnabrugge et al. (2013) (5) estimated that 12.4% of the population aged over 75 years have AS, and 3.4% have severe AS. Of those with severe AS, 75.6% are symptomatic. The authors further estimated that 79.1% of patients with symptomatic severe AS are at low surgical risk. Thourani et al. (2015) (6) estimated from the Society of Thoracic Surgeons (STS) dataset that 79.9% (113,377/141,905 classified as STS PROM <4%) of patients who underwent SAVR were of low surgical risk.

Utilisation estimates

The application estimated the number of patients that would be eligible for the proposed service using a market share approach. The applicant estimated that the total patients eligible for aortic valve repair procedures in 2018 would comprise of: the number of SAVR procedures performed on the MBS (items 38488, 38489); and the number of TAVI procedures performed from Australian Institute of Health and Welfare (AIHW) data, as the SAVR population would have decreased following the listing of TAVI for high-risk population in November 2017. *Forward estimates were derived by applying population growth from Australian Bureau of Statistics (ABS) data to the MBS utilisation data, and assuming the same proportional use of TAVI performed in AIHW hospital data. It was noted that this method does not consider the potential for the proposed intervention to grow the market for the treatment of patients with symptomatic severe AS who might currently refuse SAVR and now choose TAVI).* Regarding the AIHW hospital data for TAVI, the application considered the possibility that some patients would have been treated in private hospitals were the option available. To avoid underestimation of the population, the application assumed that all such patients would have been treated in the private sector if TAVI had been available.

Of these total patients eligible for aortic valve repair procedures in Australia, the application estimated that the majority (79.9%) would represent the surgical low-risk subpopulation (6). The application considered it unlikely that all patients would access TAVI, estimating that 80% of the eligible low-risk population would receive TAVI, deriving this from the proportion of high risk/inoperable patients eligible for TAVI receiving the procedure (5) [Table 2]. *Although the estimate taken from Osnabrugge et al. 2013* (5) *might be reasonable, it was noted this estimate was taken from patients at high operative risk (rather than low risk), thus raising applicability concerns. Sensitivity analysis of this estimate should be undertaken in the assessment phase.*

Table 2 Estimated eligible patient population

-	-	-	Year (t-2)	Year (t-1)	Current	Year 1	Year 2	Year 3	Year 4
-	**Parameter**	**Source/method**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
A	Australian population ≥ 65 yrs.	ABS 3222.0 Series B (7)	3,909,104	4,026,056	4,145,275	4,271,505	4,397,463	4,526,677	4,656,293
B	Market share: SAVR procedures	MBS items 38488, 34489 2016-18 (8)	2,775[a]	2,858	*2,944*	3,032	3,122	*3,216*	*3,312*
C	Market share: TAVI procedures	AIHW data 2017-18 (9)	1,884[b]	1,940	1,998	*2,058*	*2,120*	*2,183*	*2,249*
D	Total AVR population	B + C	4,659	*4,798*	*4,942*	*5,090*	*5,242*	*5,399*	*5,560*
E	Low risk group	Thourani et al. 2015 (79.9%) (6)	3,723	3,834	*3,949*	4,067	4,188	*4,314*	*4,443*
F	Eligible low risk group	Osnabrugge et al. 2013 80% (5)	*2,978*	*3,067*	*3,159*	*3,253*	*3,351*	*3,451*	*3,554*

Source: *Compiled from Table 7.2, p22; and Table 7.3, p23 of the 1635 Application Form*
Abbreviations: ABS = Australian Bureau of Statistics; AIHW = Australian Institute of Health and Welfare; AVR = aortic valve replacement; MBS = Medicare Benefits Schedule; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation
[a] *Forward estimates appeared to be calculated by applying population growth from row A (2.99%) to the average utilisation for 38488, 38489 (average = 2,775) from 2016/17 (2,751) and 2017/18 (2800); For example in Year 2019: 2,775 * 1.0299 = 2,858 (rounded)*
[b] *Forward estimates appeared to be calculated by assuming the same proportion of TAVI procedures performed from AIHW data (1,827 in 2017-18) and SAVR procedures performed from MBS data in 2018; 1,884/2,775 = 68%. For example in Year 2019: 2,858 * 0.68 = 1,940*
Italicised represents calculated values performed by Assessment Group performing the PICO or values not presented in the 1635 Application Form

Rationale

Patients with severe AS are typically elderly, although patients with congenital malformations of the aortic valve often present at younger ages. Diagnoses are made following the onset of symptoms (such as dyspnoea, angina or syncope) or incidentally. Regardless of presentation, an echocardiograph is needed to confirm a diagnosis of AS, and Doppler echocardiography is the preferred technique for assessing severity. Echocardiographic criteria for the definition of severe AS are as follows (10):

- Valve area <1.0 cm^2
- Indexed valve area <0.6 cm^2/m^2 body surface area (BSA)
- Mean pressure gradient >40 mm Hg (in patients with normal cardiac output/transvalvular flow)
- Maximum jet velocity >4.0 m/s
- Velocity ratio <0.25.

Transthoracic echocardiography (TTE) is usually sufficient, but occasionally transoesophageal echocardiography (TOE) may be required. Other relevant investigations include cardiac magnetic resonance imaging, multi-slice computed tomography, coronary angiography and peripheral vascular assessment. Valvular regurgitation is also assessed. Functional status is assessed by the New York Heart Association (NYHA) functional class system.

At present, patients with symptomatic severe AS at low surgical risk are managed expectantly, but much more often undergo SAVR. Medical management consists of pharmacological treatment to alleviate symptoms; however, does not alter the disease course or improve survival.

For patients who opt for SAVR, referral is made to a multi-disciplinary 'Heart Team' to determine their suitability for surgery. This assessment is based on clinical information (major cardiovascular and non-cardiovascular comorbidities, risk score assessment), functional assessment (frailty, physical and cognitive function), surgical risk assessment, and shared goals of care (benefit-risk discussion with the patient and family, patient-centred and meaningful goals, expectations and outcomes, likelihood of symptom relief and improved survival, possible complications, expected recovery process) (1). The application also stated that in contemporary Australian practice, although the classification of surgical risk into 'low', 'intermediate' and 'high' categories is undertaken, many other factors, including patient choice, must be considered by the Heart Team when it determines optimal management pathways for patients. The 2017 ACC Guidelines also highlight that patient management relies upon a 'shared decision making' approach based on a comprehensive understanding of the risk-benefit ratio of different treatment strategies and integration of patient preferences and values (1).

The present application pertains to patients who are determined to be at low risk for surgery by a Heart Team.

Pivotal trial population

The eligibility criteria of the pivotal randomised controlled trial (RCT) [PARTNER 3; Mack et al. (2019) (11)] are summarised in Table 3. Patients were eligible for inclusion as follows: severe calcific AS and considered at low surgical risk (n=950), according to the results of clinical and anatomical assessment, including a STS-PROM score of less than 4% (on this scale scores range from 0 to 100%, with higher scores indicating a greater risk of death within 30 days after the procedure), and agreement by the site Heart Team and the trial case review committee. Patients had to be eligible for TAVR with transfemoral placement of the balloon expandable SAPIEN 3 system (Edwards Lifesciences). Importantly, patients with clinical frailty (as determined by the Heart Team), bicuspid aortic valves, or other anatomical features that increased the risk of complications associated with either TAVR or surgery were excluded.

Although the inclusion criteria of the PARTNER 3 trial were broadly similar with the proposed population, its exclusion criteria were far more detailed and extensive (see Table 3 below) compared with this Application's proposed population, which uses the 'no comorbidities' criterion as per 2017 ACC Guidelines to restrict the patient population.

During preparation of the PICO, the applicant advised that the Heart Team should decide on the best course of action for each patient. The key clinical decision would be based on comorbidities and the STS score. In addition, the applicant also indicated that an updated Australian New Zealand (ANZ) TAVI consensus statement will be published, and the applicant which will be submitted to the Department when it became available. The applicant also highlighted that the Australasian Cardiac Outcomes Registry (ACOR) oversees governance (12).

Table 3 Trial eligibility criteria of the pivotal trial (PARTNER 3)

Inclusion criteria	Exclusion criteria

- Severe, calcific aortic stenosis, meeting the following criteria:
  - AVA ≤1 cm^2 or AVA index ≤0.6 cm^2/m^2 AND
  - NYHA Functional Class ≥ 2 OR
  - Exercise tolerance test that demonstrates a limited exercise capacity, abnormal BP response or arrhythmia
  - Asymptomatic with LVEF <50%
- Heart Team agrees the patient has a low risk of operative mortality and an STS<4
- Patient has been informed of the nature of study , agrees to its provisions and has provided written informed consent.
	- Native aortic annulus size unsuitable for sizes 20, 23, 26, or 29mm THV based on 3D imaging analysis
	- Iliofemoral vessel characteristics that would preclude safe passage of the introducer sheath
	- Evidence of an acute myocardial infarction ≤ 1 month (30 days) before randomization
	- Aortic valve is unicuspid, bicuspid, or non-calcified
	- Severe aortic regurgitation (>3+)
	- Severe mitral regurgitation (>3+) or ≥ moderate stenosis
	- Pre-existing mechanical or bioprosthetic valve in any position. (Note: mitral ring is not an exclusion)
	- Complex coronary artery disease:
	  - Unprotected left main coronary artery
	  - Syntax score > 32 (in the absence of prior revascularization)
	  - Heart Team assessment that optimal revascularization cannot be performed
	  - Symptomatic carotid or vertebral artery disease or successful treatment of carotid stenosis within 30 days of randomisation
	- Leukopenia (WBC < 3000 cell/mL), anemia (Hgb < 9 g/dL), Thrombocytopenia (Plt < 50,000 cell/mL), history of bleeding diathesis or coagulopathy, or hypercoagulable states

Inclusion criteria	Exclusion criteria
	- Hemodynamic or respiratory instability requiring inotropic support, mechanical ventilation or mechanical heart assistance within 30 days of randomization - Hypertrophic cardiomyopathy with obstruction (HOCM) - Ventricular dysfunction with LVEF < 30% - Cardiac imaging (echo, CT, and/or MRI) evidence of intracardiac mass, thrombus or Vegetation - Inability to tolerate, or condition precluding treatment with, antithrombotic/anticoagulation therapy during or after the valve implant procedure - Stroke or transient ischemic attack (TIA) within 90 days of randomization Renal insufficiency (eGFR < 30 ml/min per the Cockcroft-Gault formula) and/or renal - replacement therapy at the time of screening - Active bacterial endocarditis within 180 days of randomization - Severe lung disease (FEV1 < 50% predicted) or currently on home oxygen - Severe pulmonary hypertension (e.g., PA systolic pressure ≥ 2/3 systemic pressure) - History of cirrhosis or any active liver disease - Significant frailty as determined by the Heart Team (after objective assessment of frailty parameters) - Significant abdominal or thoracic aortic disease (such as porcelain aorta, aneurysm, severe calcification, aortic coarctation, etc.) that would preclude safe passage of the delivery system or cannulation and aortotomy for surgical AVR - Hostile chest or conditions or complications from prior surgery that would preclude safe reoperation (i.e., mediastinitis, radiation damage, abnormal chest wall, adhesion of aorta or IMA to sternum, etc.) - Patient refuses blood products - BMI > 50 kg/m^2 - Estimated life expectancy < 24 months

Source: Supplementary Appendix of Nishimura et al. 2014 (2)
Abbreviations: AVA = Aortic valve area; AVR = aortic valve repair; BMI = body mass index; BP = blood pressure; CT = computed tomography; eGFR = estimated glomerular filtration rate; FEV1 = forced expiratory volume 1; IMA = inferior mesenteric artery; LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; NYHA = New York Heart Association; PA = pulmonary aorta STS = Society of Thoracic Surgeons; THV = transcatheter heart valve

Other TAVI related applications in different TAVI populations

There are two MSAC applications for TAVI for the adjacent 'intermediate' risk population:

- **REDACTED**
- Application 1603: TAVI via transfemoral delivery using the SAPIEN 3 balloon expandable valve (BEV) system for patient at intermediate risk for surgery (1603 Ratified PICO confirmation). *Note, this application is specific to TAVI BEV. The applicant's rationale for this was that the PARTNER II trial showed BEVs have different clinical and economic outcomes in intermediate-risk patients. PASC advised that these "different clinical & economic outcomes" should be clarified during the assessment phase, including what they were compared to. This application is expected to go to November MSAC 2020.*

Preceding these applications were the MSAC applications for TAVI for high risk/non operable population:

- Application 1361, 1361.1 and 1361.2: At its at March 2016 meeting, MSAC supported MBS listing of the TAVI procedure for use in patients who are symptomatic with severe aortic stenosis and who are determined to be at high risk for SAVR or to be non-operable (Public Summary Document [PSD] 1361.2). MBS item 38495 (see Table 1 in Appendix) for TAVI implantation and case conference items (MBS items: 6080, 6081) were listed on 01 November 2017. *Note, earlier at its April 2015 MSAC meeting, MSAC supported the item to be agnostic to TAVI device, "MSAC preferred not to specify any particular TAVI device, for example by brand name or by specifying any particular device characteristic, such as a balloon-expandable device (to signal a preference for the applicant's SAPIEN device) or a self-expandable device (to signal a preference for Medtronic's CoreValve device). As noted below, the existing evidence does not justify discriminating against any particular device on clinical grounds, and there was no reason to inhibit price competition across device alternatives [1361 PSD, p2].*

Another TAVI-related MSAC application is Application 1605- Transradial delivery of a dual filter cerebral embolic protection (CEP) system, performed as an adjunct during TAVI. *It was noted: the TGA indication for CEP is not specific to TAVI; the proposed population from Application 1605 was not based on patient risk (as per applicant's request), and was expanded to include intermediate-risk patients (together with the originally-requested high-risk patients). The PASC confirmed population was: "patients with symptomatic severe aortic stenosis who meet MBS eligibility criteria for transcatheter aortic valve implantation (TAVI)" [1605 Ratified PICO confirmation, p3]; and the proposed MBS item descriptor for CEP [1605 Ratified PICO confirmation, p13] would not preclude the use of this device in TAVI patients determined at low surgical risk by the Heart Team.*

REDACTED

INTERVENTION

PASC confirmed the intervention, noting the application was for a device specific application with TAVI balloon expandable valves (BEVs). PASC recalled that a similar TAVI device specific application in the intermediate risk population (MSAC application 1603) was considered at the December 2019 PSAC meeting.

PASC noted the applicant's rationale for the TAVI device specific application relied upon differential claims against SAVR from the pivotal trials which used different primary endpoints and which PASC considered will be reviewed during the MSAC assessment phase:

- *TAVI BEV is the only TAVI that has demonstrated superiority to SAVR with respect to the composite endpoint of death, stroke or rehospitalisation at 12 months (PARTNER 3; Mack et al 2019)*

- *TAVI self-expanding valve (SEV) has demonstrated non-inferiority to SAVR with respect to the composite endpoint of death or disabling stroke at 24 months (Evolut low risk trial; Popma et al 2019).*

In Australia, TAVI is performed in a cardiac catheterisation or an operating room. TAVI is performed under general anaesthesia or local anaesthesia with sedation. For transfemoral delivery (relevant to this application), the latter is often sufficient. The procedure is performed without cardio-pulmonary bypass.

TAVI is usually performed under the guidance of fluoroscopy and TOE. Aortography may also be used. A percutaneous sheath is inserted into the femoral artery with a guide wire that is pushed passed the aortic valve. The aortic valve is predilated via balloon valvuloplasty while the heart is rapidly paced. The TAVI BEV valve is mounted on a balloon catheter and is inserted percutaneously over the guidewire until it crosses the aortic valve. Optimum positioning is confirmed by fluoroscopy. Once the correct position is confirmed, the heart is again rapidly paced and the balloon is expanded until the device meets the native annular walls. The balloon is then deflated and the catheter and guidewire are removed.

The procedure is estimated to take 1 to 1.5 hours.

The application stated that as the intervention is usually performed late in life, it is anticipated that the service would only be delivered once per patient. *It was noted the mean age of patients with symptomatic severe AS treated with SAPIEN 3 TAVI BEV was 73.3 ± 5.8 years in the PARTNER 3 trial (11).*

Immediately following the procedure, aortography and TOE are again performed to assess the location and the degree of any aortic regurgitation, and the functioning of the coronary arteries.

Patients are then transferred for monitoring to either a coronary care, high dependency or intensive care unit.

PASC noted the applicant's advice which indicated the procedure typically involves one night hospitalisation, and many are discharged from hospital the next day.

PASC discussed the experience of TAVI proceduralists in clinical trials and how that would be generalisable to Australia more broadly. The applicant advised that there is appropriate TAVI training and also that experienced TAVI proceduralists do visit other sites to upskill less experienced centres.

Rationale

The application considered that there are two main categories of transcatheter aortic valve prostheses: balloon-expandable (SAPIEN 3 [third-generation], Edwards Lifesciences [the Applicant]) and self-expanding (Evolut R, Medtronic CoreValve and Portico, Abbott). *It was also noted that there is another self-expanding valve (ACURATE neo™, Boston Scientific) used as an investigational device, and a new next-generation controlled expansion valve (LOTUS Edge™, Boston Scientific) (13).*

The application stated that other TAVI devices (sponsored by St Jude Medical Australia and Medtronic Australasia) do not involve BEVs; rather, they involve SEVs. The application also indicated that a TGA variation to ARTG 284496 to include the low risk indication is currently underway. *During preparation of the PICO, the applicant indicated that SAPIEN 3 TAVI BEV was approved for the low-risk population by the TGA in May 2020:*

> Intended purpose: The Edwards SAPIEN 3 Transcatheter Heart Valve System is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a Heart Team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

Consistent with the ARTG 284496 for TAVI BEV (Edwards), PASC noted TAVI SEVs are also currently TGA-approved for all TAVI risk levels (e.g. ARTG 284003, 319850).

The 2017 ACC Guidelines (1) state that the choice of valve depends on two key factors: 1) whether a balloon-expandable, self-expanding, or other type of valve is preferred for anatomic reasons or other considerations; and 2) the available valve sizes (1). The 2017 ACC Guidelines also provide situations where one valve platform might be preferred over the other:

- TAVI BEV preferred to SEV:
    - Patients with a dilated ascending (>43 mm) or severely angulated aorta (aortoventricular angle >70°, particularly for transfemoral access)
    - Only option in patients needing a transapical approach (e.g. those with a significant aortic calcification and peripheral vascular disease)
- TAVI SEV preferred to BEV:
    - Patients with severe calcification patients with severe calcification of the aortic annulus/LV outflow tract with an attendant risk of rupture, patients with an extremely oval-shaped annulus, or for transfemoral access when femoral artery diameter is between 5.0 mm and 5.5 mm
    - Also, the newer generation of self-expanding valves (CoreValve Evolut R, Medtronic) can be recaptured and repositioned prior to full deployment, offering the advantage of reducing complications from malpositioning. This has a potential benefit in patients with low coronary ostia as well (1).

The 2017 ACC Guidelines also state in patients who are eligible for either prosthesis, the choice generally comes down to operator and/or institutional preference and experience (1).

During preparation of the PICO, the applicant indicated that the rationale for the device specific application is that SAPIEN3 TAVI BEV is the only TAVI that has demonstrated superiority vs. current standard of care (SAVR) in the low-risk population. The hazard ratio for the primary endpoint composite of death, stroke or rehospitalisation was 0.54 (95% CI: 037 – 0.79, p-value=0.0001) at one year in the pivotal trial (11). The applicant also noted that TAVI SEV has only demonstrated non-inferiority to SAVR with respect to the composite endpoint of death or disabling stroke at 24 months (14).

The applicant noted that TAVI with balloon-expandable valves (BEV) is currently included on the MBS for patients with symptomatic severe AS who are at *high risk* for SAVR or who would otherwise be inoperable (MBS item 38495). TAVI with BEV in the *intermediate risk* population is currently under consideration to be added to the MBS (Application 1603). The present application seeks a new MBS item for the *TAVI with the SAPIEN 3 BEV* system, and for patients at *low* risk for surgery.

In order to attract a Medicare benefit under MBS item 38495, the patient's eligibility for TAVI BEV must be approved through a TAVI Case Conference, and the service must be performed by a TAVI practitioner in a hospital that is considered clinically accepted as suitable for the provision of TAVI services. The present application seeks the same conditions for the proposed new MBS item.

A TAVI practitioner is an interventional cardiologist with Fellowship of the Royal Australasian College of Physicians with specialty training in cardiology or a cardiothoracic surgeon with Fellowship of the Royal Australasian College of Surgeons with specialty training in cardiothoracic surgery, and has been accredited through Cardiac Accreditation Services Limited (CASL; http://tavi.org.au). CASL is a national body comprising representatives from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) and the Cardiac Society of Australia and New Zealand (CSANZ).

When gaining accreditation, a TAVI practitioner must also seek accreditation for a specific hospital/s. The hospital must be able to demonstrate to CASL that it meets the relevant requirements to be considered "clinically acceptable" (15).

At present, prior to receiving a Medicare-eligible TAVI procedure, a TAVI patient must have been assessed at a TAVI Case Conference (by a TAVI 'Heart Team') as having an unacceptably high risk for surgical aortic valve replacement and suitable to receive the TAVI procedure. There is an MBS item for coordination (item 6080) and participation in the conference (6081). The present application seeks to have these same 'accompanying' MBS items for the proposed new MBS item. The service may be provided in either a public or private hospital, as long as it's accredited.

The 1635 Application Form indicated that the SAPIEN 3 TAVI BEV system cost $**REDACTED** and provided costing information related to the proposed service (Table 10 in Appendix). For context, the current items listed on the publicly available Prosthesis List Part A are provided in Table 4.

REDACTED

Table 4 Summary of TAVI devices on Prosthesis List-Part A- July 2020

Sponsor	Product name	Description	Size	ARTG number	Benefit
Edwards Lifesciences Pty Ltd	Edwards SAPIEN 3 Transcatheter Heart Valve	Transcatheter, balloon expanded aortic heart valve with Commander Delivery System	20mm, 23mm, 26mm and 29mm	284496	$22,932
Medtronic Australasia Pty Ltd	Medtronic CoreValve™ Evolut™ R transcatheter aortic valve	Transcatheter aortic valve, self-expanding, re-sheath and/or complete recapture after partial	23mm-34mm	284003	$22,932

Sponsor	Product name	Description	Size	ARTG number	Benefit
		deployment and redeployment			
Medtronic Australasia Pty Ltd	Medtronic CoreValve™ Evolut™ PRO transcatheter aortic valve	Transcatheter aortic valve, self-expanding, re-sheath and/or complete recapture after partial deployment and redeployment	23mm-29mm	319850	$22,932
ABBOTT MEDICAL AUSTRALIA PTY LTD.	Portico transcatheter aortic valve	Self-expanding transcatheter aortic tissue valve, nitinol stent, bovine valve	23-29	254835	$22,932

Source: *Compiled from* July 2020 Prostheses List – Part A
Abbreviations: ARTG = Australian Register of Therapeutic Goods; TAVI = transcatheter aortic valve implantation.

COMPARATOR

PASC agreed with the draft PICO which considered SAVR is the primary comparator, and SEV is the secondary (or 'near market') comparator. PASC considered that the superiority claim of TAVI BEV vs. SAVR from direct evidence and the superiority claim of TAVI BEV vs. SEV from indirect evidence would need rigorous assessment.

The application considered the comparator is SAVR, the current gold standard for treating symptomatic severe AS in patients with low surgical risk. SAVR is an open-heart surgical procedure to repair or remove the narrowed aortic valve and replace it with a bioprosthestic or mechanical aortic valve. A SAVR procedure requires general anaesthetic and extracorporeal circulation, with access via a sternotomy or a less invasive transthoracic approach all of which require a bypass machine.

Rationale

The application considered that aortic valve replacement is the only effective therapy for patients with symptomatic severe AS who are at low or intermediate surgical risk (4).

SAVR can only be undertaken by cardiothoracic surgeons who have completed the Cardiothoracic Surgery Program and be eligible to be a Fellow of the Royal Australasian College of Surgeons or otherwise qualified to practise cardiothoracic surgery in Australia.

SAVR has two exiting MBS items (38488, 38489; see Table 8, Table 9 in Appendix).

Given the application is specific for TAVI BEV, a 'secondary' comparator, or could also be termed a 'near-market comparator', would be TAVI SEV. The precedent for this is that PASC requested that TAVI SEV be included as a secondary comparator in the similar device specific application for TAVI BEV in the intermediate-risk population (Ratified PICO confirmation 1603, p7).

For context, the assessment group considered it might also be useful to highlight the outcomes associated with low-risk patients who might refuse SAVR. It is presumed that these patients would be managed with best medical therapy. This was similarly requested by PASC in Application 1603 for the intermediate-risk patients (see Ratified PICO confirmation 1603, p7). It was noted in the pivotal trial that 43/497 (8.7%) randomly assigned patients did not undergo SAVR. The most common reason to withdrawal from the trial (in 41 patients) was owing to the decision not to undergo surgery or the preference to undergo surgery at a nontrial site (11).

OUTCOMES

PASC confirmed the outcomes, agreeing with the applicant's request for the removal of 'symptoms of heart failure', 'recovery time', and 'pain' from the draft PICO as they are outcomes included in the quality of life data. PASC also noted that the applicant requested the removal of "valve performance" as this was ill-defined and was not a specified endpoint in PARTNER 3.

PASC noted the applicant's advice that typically antiplatelet therapy was required post TAVI rather than anticoagulation therapy.

Safety outcomes:

- Life-threatening / disabling, or major bleeding
- Major vascular complications
- Myocardial infarction
- New left bundle branch block
- New permanent pacemaker
- New onset atrial fibrillation
- *Paravalvular leak rate*
- *Aortic valve reintervention*
- *Acute kidney injury.*

Efficacy/ effectiveness outcomes including, but not limited to, patient-relevant outcomes:

- *Overall survival*
- Composite of death, stroke or rehospitalisation (primary outcome of PARTNER 3 trial)
- Death
- Stroke
- Rehospitalisation
- Health-related quality of life.

The application did not specify if health status would be measured with a disease specific tool and/or standardised tool. A study included in the Application Form (Baron et al. 2019; (16)) reported health status using the disease specific tool, Kansas City Cardiomyopathy Questionnaire [KCCQ[2]] and standardised tools: EuroQol-five dimension tool (EQ-5D) and Short-Form-36 (SF-36) questionnaire.

[2] The KCCQ evaluates 5 domains of health status (physical function, social function, symptoms, quality of life, and self-efficacy/knowledge) in patients with heart failure and is scored from 0 to 100, with higher scores

Healthcare system

Cost-effectiveness:

- Cost per life-year gained
- Cost per quality-adjusted life year (QALY) gained.

Healthcare resources:

- Cost of valvular prosthesis
- Cost associated with changes in clinical management (testing required before the procedure, length of stay, post-discharge rehabilitation).

Total Australian Government Healthcare costs:

- Total cost to the Medical Benefits Schedule (MBS)
- *Total cost to other Government health budgets (e.g. Pharmaceutical Benefits Scheme [PBS], State and Territory Government health budgets, including public hospitals).*

The applicant considered that it is possible that there will be capacity restraints if there are insufficient facilities and trained staff to meet demand. It is likely that capacity will increase in coming years.

TAVI BEV vs. SAVR

On the basis of the primary endpoint at 1 year from the PARTNER 3 trial (11), the application considered that TAVI with the SAPIEN 3 BEV is superior to SAVR in patients with symptomatic severe AS at low risk for surgery in terms of death, stroke or rehospitalisation.

The PARTNER 3 trial (11) demonstrated that TAVI with the SAPIEN 3 BEV also results in significantly lower incidence of life-threatening/disabling, or major bleeding and new onset of atrial fibrillation compared to SAVR. However, as indicated in the Application Form (p19), TAVI patients had higher rates of major vascular complications, new left bundle branch block and new permanent pacemaker than SAVR.

The application also considered that TAVI with the SAPIEN 3 BEV would involve a shorter hospital stay, including shorter ICU/high-dependency unit time, and shorter recovery time.

A systematic review and meta-analysis of TAVI *vs.* SAVR in patients with severe AS at low and intermediate risk highlighted that two patients participating in a clinical guideline panel for TAVI BEV uniquely identified recovery time and pain as critical to decision making, *although the authors were unable to find direct evidence for these outcomes in the RCTs (17)*.

indicating better health status. The KCCQ has been shown to be a reliable and valid instrument in patients with AS and has been used to assess patient-reported outcomes in multiple prior studies comparing TAVR and SAVR

The application considered one of the major uncertainties, of particular relevance to younger patients, is the long-term durability of TAVI with the SAPIEN 3 BEV (as identified in a clinical practice guideline in patients with severe AS at low to intermediate risk (18)), and possible need for future revision procedures. *The authors of this clinical practice guideline considered that "future recommendations and guidelines would benefit from the following research questions:*

- *Qualitative or survey study. What are the values and preferences of patients deciding between TAVI and SAVR, particularly with respect to uncertain durability of TAVI devices, the desire to avoid open heart surgery, and post-procedure pain and recovery time?*
- *What is the durability of the TAVI valves beyond five years*?" (18)).

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The applicant also indicated supportive evidence from long term follow-up in intermediate risk patients is available.

TAVI: BEV vs. SEV

During preparation of the PICO, the applicant confirmed that there are no head-to-head clinical trials comparing TAVI BEV vs. TAVI SEV. Therefore, indirect comparisons using SAVR as common comparator will be necessary in order to perform the secondary comparison.

PASC noted the applicant was concerned about the inclusion of Elgendy et al. 2020 in the draft PICO because there appeared to be several errors in the low risk subgroup analysis. PASC agreed to remove this study from the draft PICO on the basis that the applicant stated it would perform a transparent systematic review as part of the ADAR which will include balanced critiques of any published meta-analysis.

Current and proposed clinical management algorithms

PASC confirmed the algorithms. PASC noted the applicant's advice that only SAVR would be performed in the setting of repeat aortic valve repair. PASC considered that this should be reflected in the proposed algorithm.

Current clinical management algorithm for identified population

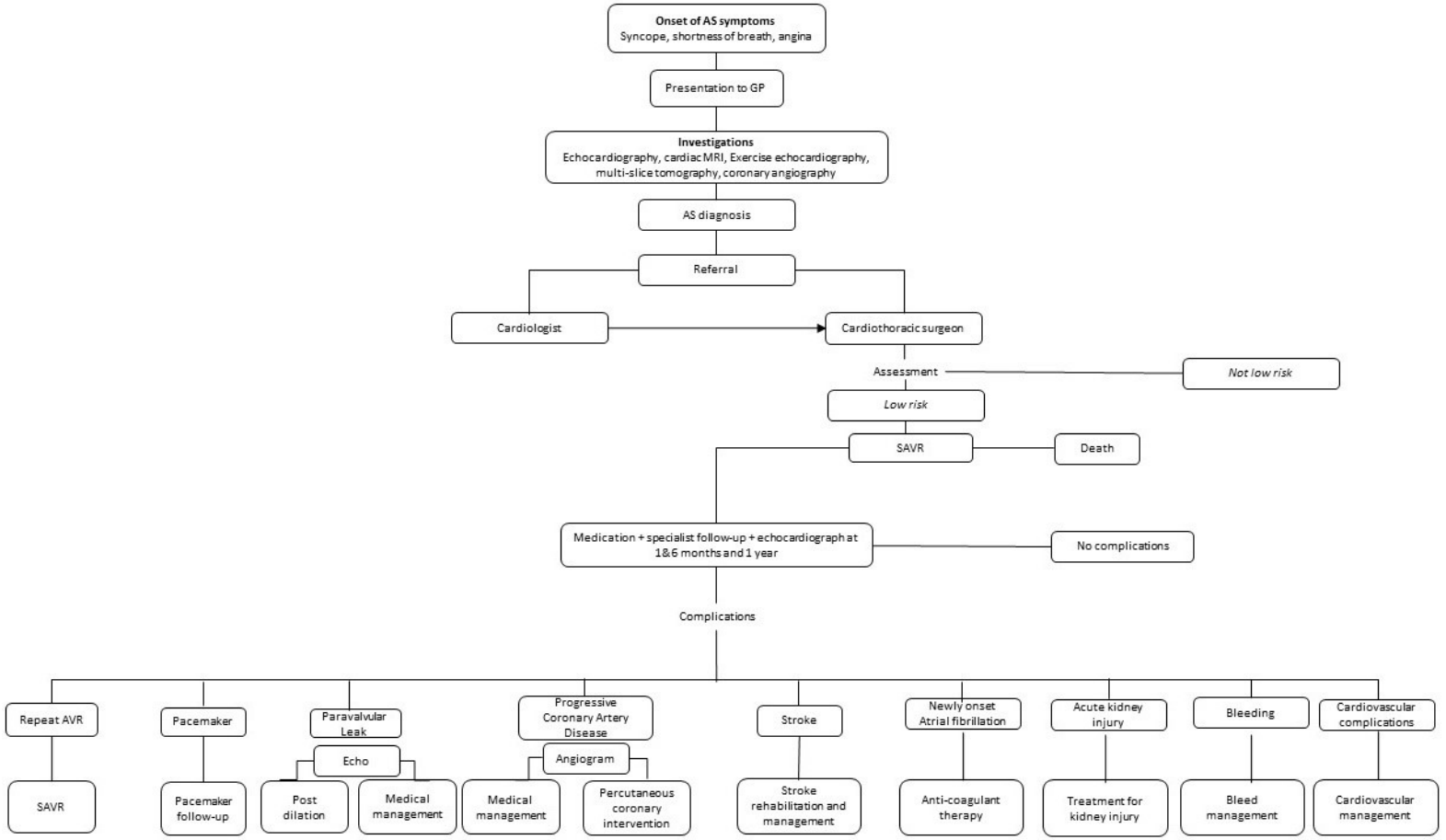

Figure 1 Current clinical management algorithm of patients with symptomatic severe AS categorised as low-risk for SAVR

Source: Compiled during preparation of PICO from Attachment 1 of 1635 Application Form
Abbreviations: AS = aortic stenosis; GP = general practitioner; MRI = magnetic resonance imaging; SAVR = surgical aortic valve repair; Echo = echocardiogram
Italicised represents added in during preparation of the PICO

Proposed clinical management algorithm for identified population

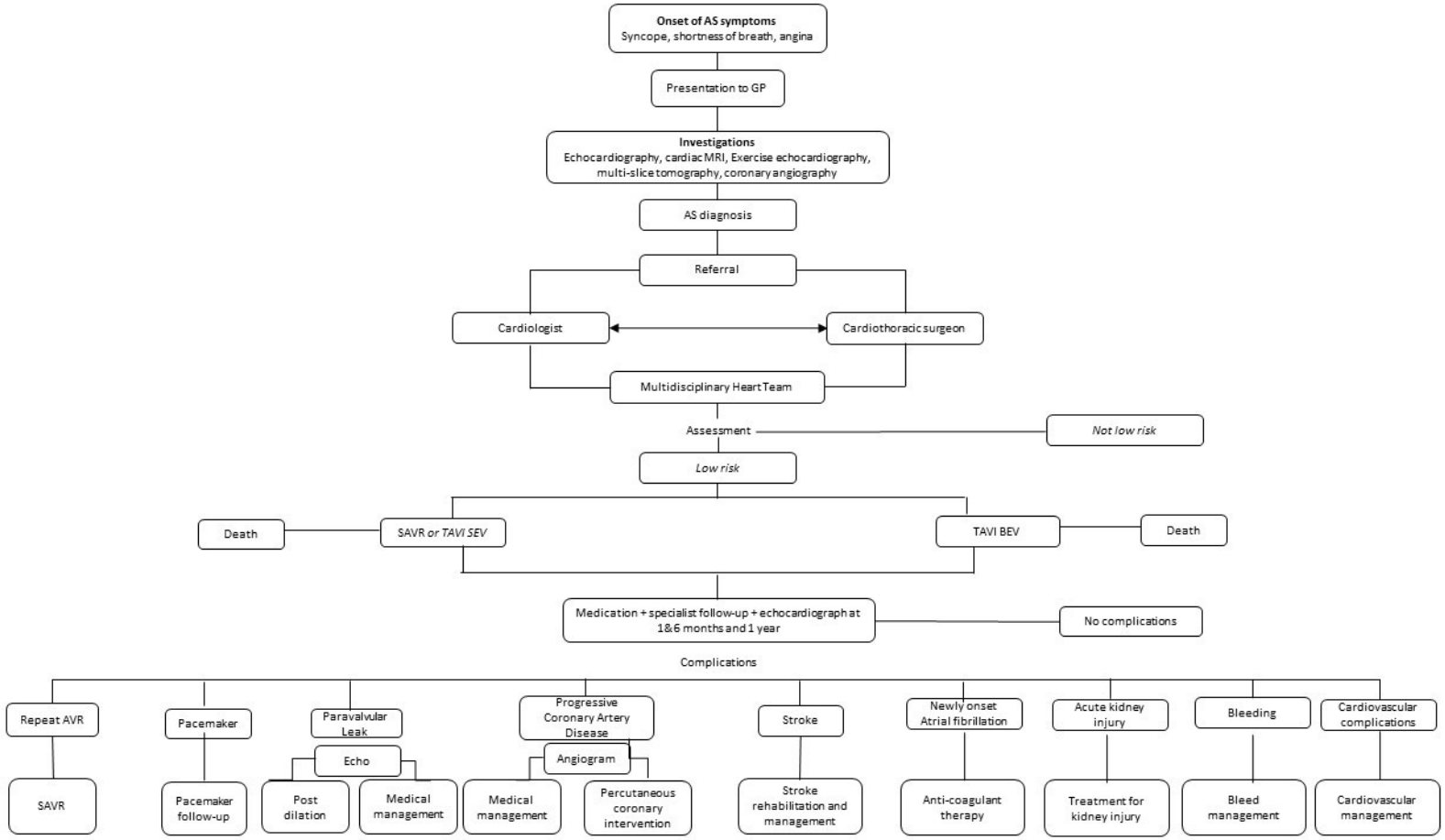

Figure 2 Proposed clinical management algorithm of patients with symptomatic severe AS categorised as low-risk for SAVR

Source: Compiled during preparation of PICO from Attachment 2 of 1635 Application Form

Abbreviations: AS = aortic stenosis; GP = general practitioner; MRI = magnetic resonance imaging; SAVR = surgical aortic valve repair; Echo = echocardiogram

Italicised represents added in during preparation of the PICO

TAVI is a new approach in Australia for treating patients who have symptomatic aortic stenosis and are at low surgical risk. The clinical pathway after TAVI is the same as after SAVR.

During preparation of the PICO, the assessment group queried whether repeat aortic valve repair (or re-intervention) with TAVI, would be with the same TAVI device as used in the index procedure (e.g. TAVI BEV if TAVI BEV performed as index procedure), or whether it would be with a different TAVI device (e.g. TAVI SEV if TAVI BEV performed as index procedure). The applicant indicated that aside from the choice of the valve made by the Heart Team, the time duration of the re-intervention with TAVI after the index procedure is an important consideration, noting that if re-intervention would occur within 30 days of the index surgery, and thus the re-intervention is a complication that might be attributed to the index procedure (e.g. intraprocedural complication), the Heart Team might choose the same TAVI device, in which case the second valve can be implanted over the top of the first valve.

Proposed economic evaluation

PASC confirmed that the economic evaluation should be a cost-effectiveness or cost-utility analysis. Similar to the assessment of clinical evidence, PASC considered that the superiority claim of TAVI BEV vs. SAVR from direct evidence and the superiority claim of TAVI BEV vs. SEV from indirect evidence would need rigorous assessment, and ongoing large-scale data gathering would be required.

PASC noted the applicant's advice which noted that out-of-pocket (OOP) costs for TAVI could vary across practitioners, but the patient has choice so could identify OOP gaps for TAVI. PASC agreed with the applicant that OOP costs for TAVI would be no different to OOP costs associated with other procedures on the MBS.

The clinical claim is that TAVI using the SAPIEN 3 BEV system is superior to SAVR in patients with symptomatic severe AS categorised as low risk. The appropriate economic evaluation is a cost-effectiveness or cost-utility analysis.

An abstract assessing the cost-effectiveness comparing TAVI with BEV or SEV with SAVR in patients with severe AS at low surgical risk (19) was provided in the 1635 Application Form. The cost-utility analysis (CUA) was assessed from the Australian healthcare system, using a Markov model over 10 years with monthly cycles, and using key data inputs from the PARTNER 3 trial for TAVI BEV, and from the Evolut Low Risk trial for TAVI SEV. The authors indicated that over ten years, TAVI BEV lowered costs by AUD$3,085 (USD$2,141) and increased quality-adjusted life years (QALYs) by 0.15 compared to SAVR, while TAVI SEV lowered costs by AUD$425 (USD$295) and increased QALYs by 0.07. Thus, from a health economic perspective, TAVR was dominant over SAVR. The authors considered that results were robust to sensitivity analyses, with TAVI BEV being dominant in 61% of 10,000 Monte Carlo iterations and cost-effective in 85% of iterations (at an incremental cost-effectiveness ratio threshold of AUD$50,000 per QALY saved). TAVI SEV was dominant in 51% of iterations and cost-effective in 67% of iterations (19).

Proposed MBS item descriptor and MBS fee

PASC confirmed the MBS item descriptor and fee, but considered that the brand name of the device (SAPIEN 3) should be removed from the proposed item descriptor.

The applicant agreed to the removal of the brand name (SAPIEN 3) from the item descriptor.

PASC discussed the appropriateness of an alternative item descriptor to broaden TAVI BEV to all levels of surgical risk (i.e. agnostic to surgical risk). PASC noted this was the applicant's preference, and feedback from one specialist organisation, but noted that this proposal would not align with that the current item descriptor for the high-risk TAVI population (MBS item 38495), which is agnostic to TAVI device.

The applicant considered that if the item descriptor for the proposed MBS item extends the 'coverage' of TAVI-BEV to patients at all levels of surgical risk, then it will supersede MBS item 38495 for TAVI-BEV among high-risk patients.

PASC noted that the appropriateness of a device specific item descriptor for TAVI BEV would be assessed by MSAC at the assessment phase, and would rely on a robust assessment of the applicant's superiority claim of TAVI BEV vs. SEV.

PASC recalled the applicant's previous advice from Application 1603 that the utilisation of case conference items for TAVI (Table 8-9) might not reflect current utilisation due to the modest MBS fee for these items and the complexity associated with claiming an item where multiple people are involved.

The applicant-proposed item descriptor, including proposed fee is summarised in Table 5. *The proposed fee appears to be based on the existing TAVI agnostic MBS item 38495 for high-risk population (see Table 7 in Appendix).* The application stated as access to TAVI is determined by the TAVI Heart Team, it is unlikely that there would be leakage to populations outside the eligible population.

The assessment group considered that the brand name should be removed from the proposed item descriptor (see Table 6). The assessment group also considered that for consistency, the brand name could also be removed from the title of this document, which as agreed upon by pPASC.

Table 5 Applicant-proposed MBS item descriptor

Category 3 – Therapeutic Procedures – Surgical Operations
XXXXX TAVI using the SAPIEN 3 balloon-expandable system, for the treatment of symptomatic severe aortic stenosis, performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible, in a TAVI Hospital on a TAVI Patient by a TAVI Practitioner – includes all intraoperative diagnostic imaging that the TAVI Practitioner performs upon the TAVI Patient (Not payable more than once per patient in a five year period.) MBS Fee: $1,476. 95 Benefit: 75% = $1,107.75 85% = $1,392.25

Source: p24 of 1635 Application Form

Note, updated for recent MBS indexation

The *Health Insurance (Section 3C General Medical Services - Transcatheter Aortic Valve Implantation) Determination 2017(Cth)* (Department of Health 2017) outlines the definitions of a TAVI Patient, TAVI Hospital and TAVI Practitioner.

TAVI Patient is a patient who, as a result of a TAVI Case Conference, has been assessed as having a low risk for surgical aortic valve replacement and is recommended as being suitable to receive the service described in item XXXXX.

TAVI Hospital means a hospital, as defined by subsection 121-5(5) of the *Private Health Insurance Act 2007*, that is clinically accepted as being a suitable hospital in which the service described in Item XXXXX may be performed.

TAVI Practitioner is either a cardiothoracic surgeon or interventional cardiologist who is accredited by the Cardiac Accreditation Services Limited.

TAVI Case Conference Items

There is an existing MBS item for coordination (item 6080) of the case conference and an existing MBS item for participation in the conference (6081). The present application seeks to have these same 'accompanying' MBS items for the proposed new MBS item.

6080	Coordination of a TAVI Case Conference by a TAVI Practitioner where the TAVI Case Conference has a duration of 10 minutes or more. (Not payable more than once per patient in a five-year period.) MBS Fee: $51.70

6081	Attendance at a TAVI Case Conference by a specialist or consultant physician who does not also perform the service described in item 6080 for the same case conference where the TAVI Case Conference has a duration of 10 minutes or more. (Not payable more than twice per patient in a five-year period.) MBS Fee: $38.55

It is not anticipated that this definition of a TAVI Case Conference will require amendment.

TAVI Case Conference means a process by which:

(a) there is a team of 3 or more participants, where:

(i) the first participant is a cardiothoracic surgeon; and

(ii) the second participant is an interventional cardiologist; and

(iii) the third participant is a specialist or consultant physician who does not perform a service described in Item XXXX for the patient being assessed; and

(iv) either the first or the second participant is also a TAVI Practitioner; and

(b) the team assesses a patient's risk and technical suitability to receive the service described in Item XXXXX, taking into account matters such as:

(i) the patient's risk and technical suitability for a surgical aortic valve replacement; 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 XXXXX; and

(d) the particulars of the assessment and recommendation are recorded in writing.

Table 6 Assessment group- proposed MBS item descriptor

Category 3 – Therapeutic Procedures – Surgical Operations
XXXXX TAVI using a ~~SAPIEN 3~~ balloon-expandable system, for the treatment of symptomatic severe aortic stenosis, performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible, in a TAVI Hospital on a TAVI Patient by a TAVI Practitioner – includes all intraoperative diagnostic imaging that the TAVI Practitioner performs upon the TAVI Patient Multiple Operation Rule (Not payable more than once per patient in a five year period.) (Anaes.) (Assist.) MBS Fee: $1,476. 95 Benefit: 75% = $1,107.75 85% = $1,392.25

Source: p24 of 1635 Application Form
Note, updated for recent MBS indexation

Consultation feedback

PASC noted the mixed support for the application from consultation feedback:

- *One specialist organisation was highly supportive of the application, noting that TAVI is the standard of care for the treatment of symptomatic severe AS and that the eligibility of TAVI-able patient is more pertinent than the categorisation of low-high surgical risk. This feedback also considered that the fee is undervalued for the procedure and should be higher*
- *One specialist organisation was concerned that patient populations in studies of low risk patients for TAVI were highly selected, and excluded patients with bicuspid disease, excluded younger patients; as a consequence the results are not representative of the wider population with severe symptomatic AS (i.e. applicability concerns). This feedback also noted that the descriptor did not match patient selection criteria in the quoted literature and considered that long term results of TAVI in this population are unknown. Thus, this specialist organisation appended their Society position statement on TAVI in low risk patients*
- *One specialist organisation suggested that the anaesthesia cost estimate for the proposed intervention needed amendment*
- *One industry association and individual specialist were highly supportive of the application*
- *Feedback was also received that it was inappropriate for MSAC applications to be limited to one device and that all TAVI valves should be included (balloon, self and mechanically expanding valves). This feedback also considered that comparing device performance is difficult and misleading as noted by Abdel-Waha & Thiele et al. (2020) (20). Further, it was noted that if hospitalisation was added to the primary endpoint of death or stroke in Evolut low risk trial, the results would have shown superiority to SAVR. This feedback also highlighted that, compared with SAVR, the use of TAVI enables efficiencies related to hospital resource use.*

Next steps

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.

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

Appendix

Table 7 MBS item 38495 for TAVI in patients assessed as having unacceptably high-risk for SAVR (population not included in this application)

Category 3 – Therapeutic Procedures – Surgical Operations
38495 TAVI, for the treatment of symptomatic severe aortic stenosis, performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible, in a TAVI Hospital on a TAVI Patient by a TAVI Practitioner – includes all intraoperative diagnostic imaging that the TAVI Practitioner performs upon the TAVI Patient. (Not payable more than once per patient in a five year period.) Multiple Operation Rule (Anaes.) (Assist.) MBS Fee: $1,476. 95 Benefit: 75% = $1,107.75 85% = $1,392.25 (See para AN.33.1, TN.8.135 of explanatory notes[a] to this Category

Source: *Compiled from* MBS online
SAVR = Surgical aortic valve repair
[a] *From explanatory notes: A TAVI Patient means a patient who, as a result of a TAVI Case Conference, has been assessed as having an unacceptably high risk for surgical aortic valve replacement and is recommended as being suitable to receive the service described in item 38495.*
Note, updated for recent MBS indexation

Table 8 MBS item 38488 for comparator, SAVR

Category 3 – Therapeutic Procedures – Surgical Operations
38488 VALVE REPLACEMENT with BIOPROSTHESIS OR MECHANICAL PROSTHESIS Multiple Operation Rule MBS Fee: $1,969.25 Benefit: 75% = $1,476.95

Source: *Compiled from* p16 of 1635 Application Form and MBS online
Note, updated for recent MBS indexation

Table 9 MBS item 38489 for comparator, SAVR

Category 3 – Therapeutic Procedures – Surgical Operations
38489 VALVE REPLACEMENT with BIOPROSTHESIS OR MECHANICAL PROSTHESIS Multiple Operation Rule MBS Fee: $2,342.00 Benefit: 75% = $1,756.50

Source: *Compiled from* p16 of 1635 Application Form and MBS online
Note, updated for recent MBS indexation

Table 10 Relevant MBS costing information for the proposed intervention

Cost Item	MBS Item Number	100% MBS Fee	75% Benefit
TAVI Case Conference Organiser	6080	$51.70	$38.80
TAVI Case Conference Attendance * 3	6081	$38.55	$28.95
TAVI Procedure including all intraoperative diagnostic imaging	XXXX	$1,455.10 (Same as MBS item 38495)	$1091.35
Assistant	51303	"one fifth of the established fee for the operation or combination of operations"	
Initiation of Anaesthesia	21941	$140.70	$105.55
ICU Attendance	13870	$367.90	$275.95
Transthoracic echocardiography	55113	$230.65	$173.00

Source: Table 8.1, p24 of Application Form
ICU = intensive care unit; TAVI = transcatheter aortic valve implanatation

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